

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM 20-F

(Mark One)

REGISTRATION STATEMENT PURSUANT TO SECTION 12(B) OR 12(G) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

**ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2020.**

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

**SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934
Date of event requiring this shell company report**

Commission file number: 001-39997

Adagene Inc.

(Exact name of Registrant as specified in its charter)

N/A

(Translation of Registrant's name into English)

Cayman Islands

(Jurisdiction of incorporation or organization)

**4F, Building C14, No. 218
Xinghu Street, Suzhou Industrial Park
Suzhou, Jiangsu Province, 215123
People's Republic of China**

(Address of principal executive offices)

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At the address of the Company set forth above

(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Securities registered or to be registered pursuant to Section 12(b) of the Act:

<u>Title of each class</u>	<u>Trading Symbol</u>	<u>Name of each exchange on which registered</u>
American depositary shares, each ADS representing one and one quarter ordinary shares, par value US\$0.0001 per share	ADAG	The Nasdaq Stock Market LLC (The Nasdaq Global Market)
Ordinary shares, par value US\$0.0001 per share*	N/A	The Nasdaq Stock Market LLC (The Nasdaq Global Market)

* Not for trading, but only in connection with the listing on the Nasdaq Global Market of American depositary shares.

Securities registered or to be registered pursuant to Section 12(g) of the Act:

None

(Title of Class)

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None

(Title of Class)

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report.

43,852,894 ordinary shares, par value US\$0.0001 per share, as of
December 31, 2020.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes o No x

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.

Yes o No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes x No o

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).

Yes x No o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or an emerging growth company. See definition of "large accelerated filer," "accelerated filer," and "emerging growth company" in Rule 12b-2 of the Exchange Act. Check one:

Large Accelerated Filer o

Accelerated Filer o

Non-accelerated Filer x

Emerging growth company x

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards † provided pursuant to Section 13(a) of the Exchange Act. o

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accountant firm that prepared or issued its audit report. Yes o No x

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP x

International Financial Reporting Standards as issued by the International
Accounting Standards Board o

Other o

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow.

o Item 17 o Item 18

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes o No x

APPLICABLE ONLY TO ISSUERS INVOLVED IN BANKRUPTCY PROCEEDINGS DURING THE PAST FIVE YEARS

Indicate by check mark whether the registrant has filed all documents and reports required to be filed by Sections 12, 13 or 15(d) of the Securities Exchange Act of 1934 subsequent to the distribution of securities under a plan confirmed by a court.

Yes o No o

† The term "new or revised financial accounting standard" refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

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INTRODUCTION

Except where the context otherwise indicates and for the purpose of this annual report only:

- “Adagene Suzhou” refers to Adagene (Suzhou) Limited.
- “ADSs” refers to the American depositary shares, each representing one and one quarter (1.25) of our ordinary shares;
- “Antibody binding interface” or “antibody binding sites” refers to the antibody binding surface spots in contact with its recognition antigen;
- “China” or “PRC” refers to the People’s Republic of China, excluding, for the purpose of this annual report only, Taiwan, Hong Kong and Macau;
- “conformational diversity” or “dynamic diversity” refers to the existence of more than one conformation or structure due to dynamic fluctuation of the structures for a given protein sequence, independent of any conformational changes caused by external binding;
- “epitopes” or “epitope of an antigen” refers to the specific binding spots of an antigen in contact with its antibody binding surface;
- “Greater China”, for the purpose of this annual report, refers to the People’s Republic of China, Hong Kong, Macau and Taiwan;
- “multi-specificity” refers to a protein exerting a similar function (such as binding) on distinctly different ligands, perhaps while using different active site residues;
- “NEObody” refers to antibody designed with dynamic binding sites that adapt kinetically to unique epitopes through novel MOA, using our NEObody technology;
- “POWERbody” refers to antibody that utilizes our SAFEbody technology to create new bispecific T-cell engagers, antibody-drug conjugates, or antibodies, which are designed to reach beyond the therapeutic potency of traditional monospecific antibodies;
- “RMB” or “Renminbi” refers to the legal currency of the People’s Republic of China;
- “SAFEbody” refers to antibody engineered with its binding sites masked, which are designed to be selectively activated in the TME, potentially limiting on-target off-tumor toxicity in normal tissues;
- “species cross-reactivity” refers to reactivity of the same protein that recognizes and binds to similar epitopes of a given class of targets in different species;
- “US\$,” “dollars” or “U.S. dollars” refers to the legal currency of the United States; and
- “we,” “us,” “our company,” and “our,” refer to Adagene Inc., a Cayman Islands exempted company and its subsidiaries.
- “NEObodies” refer to antibodies designed with dynamic binding sites that adapt kinetically to unique epitopes through novel MOAs, using our NEObody technology;
- “ordinary shares” or “shares” refers to our ordinary shares of par value US\$0.0001 per share;

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- “POWERbodies” refer to antibodies that utilize our SAFEbody technology to create new bispecific T-cell engagers, antibody-drug conjugates, or antibodies, which are designed to reach beyond the therapeutic potency of traditional monospecific antibodies; and
- “SAFEbodies” refer to antibodies engineered with their binding sites masked, which are designed to be selectively activated in the TME, potentially limiting on-target off-tumor toxicity in normal tissues.

FORWARD-LOOKING INFORMATION

This annual report contains forward-looking statements that reflect our current expectations and views of future events. All statements other than statements of historical facts are forward-looking statements. These forward-looking statements are made under the “safe harbor” provision under Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and as defined in the Private Securities Litigation Reform Act of 1995. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements. In some cases, you can identify these forward-looking statements by terminology such as “may,” “will,” “expect,” “anticipate,” “aim,” “estimate,” “intend,” “plan,” “believe,” “is/are likely to,” “potential,” “continue” or other similar expressions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements include, but are not limited to, statements about:

- our goals and growth strategies;
- our future business development, results of operations and financial condition;
- the timing of the initiation, progress and potential results of our preclinical studies, clinical trials and our discovery programs;
- our ability to utilize our proprietary Dynamic Precision Library platform, or DPL, to design, construct and develop next-generation antibodies;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the timing or likelihood of regulatory filings and approvals;
- our estimates of the number of patients who suffer from the diseases we are targeting and the number of patients that may enroll in our clinical trials;
- the commercializing of our product candidates, if approved;
- our ability and the potential to successfully manufacture and supply our product candidates for clinical trials and for commercial use, if approved;
- future strategic arrangements and/or collaborations and the potential benefits of such arrangements;
- our anticipated use of our existing resources and the proceeds from our initial public offering;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing and our ability to obtain additional capital;
- the sufficiency of our existing cash and cash equivalents to fund our future operating expenses and capital expenditure requirements;
- our ability to retain the continued service of our key personnel and to identify, hire and retain additional qualified professionals;
- the implementation of our business model, strategic plans for our business and product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights, such as our proprietary DPL, which includes NEObody platform, SAFEbody platform and POWERbody platform, product candidates and discovery programs;

- our potential to enter into new collaborations;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the pricing, coverage and reimbursement of our product candidates, if approved;
- developments relating to our competitors and our industry, including competing product candidates and therapies;
- the direct and indirect impact of the COVID-19 pandemic on our business and operations and on development of our clinical and preclinical programs, and the duration and impact of COVID-19 or any of its variants that may affect, precipitate or exacerbate one or more of any of the risks and uncertainties mentioned in this annual report;
- relevant government policies and regulations relating to our business and industry;
- general economic and business condition in the markets we have businesses; and
- assumptions underlying or related to any of the foregoing.

We would like to caution you not to place undue reliance on these forward-looking statements and you should read these statements in conjunction with the risk factors disclosed in “Item 3. Key Information—D. Risk Factors” of this annual report and other risks outlined in our other filings with the Securities and Exchange Commission, or the SEC. Those risks are not exhaustive. We operate in an evolving environment. New risks emerge from time to time and it is impossible for our management to predict all risk factors and uncertainties, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statement. We qualify all of our forward-looking statements by these cautionary statements.

You should not rely upon forward-looking statements as predictions of future events. We do not undertake any obligation to update or revise the forward-looking statements except as required under applicable law. You should read this annual report and the documents that we reference in this annual report completely and with the understanding that our actual future results may be materially different from what we expect.

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

3.A. Selected Financial Data

The following selected consolidated statements of comprehensive loss data for the years ended December 31, 2018, 2019 and 2020 and selected consolidated balance sheet data as of December 31, 2019 and 2020 have been derived from our audited consolidated financial statements included in this annual report beginning on page F-1.

The selected consolidated financial data should be read in conjunction, and are qualified in their entirety by reference to, our consolidated financial statements and related notes and “Item 5. Operating and Financial Review and Prospects” included elsewhere in this annual report. Our historical results are not necessarily indicative of results expected for future periods.

	For the Year Ended December 31,		
	2018 US\$	2019 US\$ (in thousands)	2020 US\$
Revenue:			
Licensing revenue	1,511	480	701
Expenses:			
Research and development expenses	(16,081)	(16,212)	(33,538)
Administrative expenses	(2,765)	(3,438)	(10,315)
Total operating expenses	(18,846)	(19,650)	(43,853)
Loss from operations	(17,335)	(19,170)	(43,152)
Interest income	711	923	629
Interest expense	(91)	(138)	(202)
Other income	902	723	972
Foreign exchange gain (loss), net	13	22	(645)
Change in fair value of warrant liabilities	534	1,207	—
Loss before income tax	(15,266)	(16,432)	(42,397)
Income tax expense	—	—	—
Net loss attributable to Adagene Inc.’s shareholders	(15,266)	(16,432)	(42,397)
Other comprehensive income (loss):			
Foreign currency translation adjustments, net of nil tax	(11)	66	(6)
Total comprehensive loss attributable to Adagene Inc.’s shareholders	(15,277)	(16,367)	(42,403)
Net loss attributable to Adagene Inc.’s shareholders	(15,266)	(16,432)	(42,397)
Deemed contribution from convertible redeemable preferred shareholders	1,186	—	—
Accretion of convertible redeemable preferred shares to redemption value	(223)	(246)	(248)
Net loss attributable to ordinary shareholders	(14,303)	(16,678)	(42,645)
Weighted average number of ordinary shares used in per share calculation:			
—Basic	15,159	15,178	15,951

	For the Year Ended December 31,		
	2018	2019	2020
	US\$	US\$	US\$
—Diluted	15,159	15,178	15,951
Net loss per ordinary share			
—Basic	(0.94)	(1.10)	(2.67)
—Diluted	(0.94)	(1.10)	(2.67)

Summary Consolidated Balance Sheet Data

The following table presents our summary consolidated balance sheet data as of December 31, 2019 and 2020.

	2019	2020
	US\$	US\$
	(in thousands)	
Current assets:		
Cash and cash equivalents	92,533	75,151
Short-term investments	8,000	—
Total current assets	103,923	79,097
Total assets	105,889	84,263
Current liabilities:		
Amounts due to related parties	1,896	2,535
Accruals and other current liabilities	2,540	6,059
Short-term borrowings	717	3,831
Total current liabilities	7,181	16,146
Long-term borrowings	1,516	2,966
Total liabilities	8,697	19,203
Total mezzanine equity	154,201	154,449
Ordinary shares (par value of US\$0.0001 per share; 500,000,000 and 500,000,000 shares authorized; 15,193,136 shares issued and outstanding as of December 31, 2019; 18,888,070 shares issued and 16,603,070 shares outstanding as of December 31, 2020)	2	2
Total shareholders' equity (deficit)	(57,009)	(89,390)

Summary Consolidated Cash Flow Data

The following table presents our summary consolidated cash flow data for the years ended December 31, 2018, 2019 and 2020.

	Year Ended December 31,		
	2018	2019	2020
	(in USD thousands)		
Net cash used in operating activities	(14,265)	(18,154)	(28,530)
Net cash generated (used in) from investing activities	(29,510)	24,856	7,073
Net cash generated from financing activities	51,058	69,694	4,439
Effect of exchange rate on cash and cash equivalents	39	78	(364)
Net increase (decrease) in cash and cash equivalents	7,322	76,474	(17,382)
Cash and cash equivalents at the beginning of year/period	8,736	16,058	92,533
Cash and cash equivalents at the end of year/period	16,058	92,533	75,151

Non-GAAP Financial Measures

We use non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period, which are non-GAAP financial measures, in evaluating our operating results and for financial and operational decision-making purposes. We believe that non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period help identify underlying trends in our business that could otherwise be distorted by the effect of certain expenses that we include in our loss for the year/period. We believe that non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period provide useful information about our results of operations, enhance the overall understanding of its past performance and future prospects and allow for greater visibility with respect to key metrics used by its management in our financial and operational decision-making.

Non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period should not be considered in isolation or construed as an alternative to operating profit, loss for the year/period or any other measure of performance or as an indicator of its operating performance. Investors are encouraged to review non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period and the reconciliation to their most directly comparable GAAP measures. Non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period here may not be comparable to similarly titled measures presented by other companies. Other companies may calculate similarly titled measures differently, limiting their usefulness as comparative measures to our data. We encourage investors and others to review our financial information in its entirety and not rely on a single financial measure.

Non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period represent net loss attributable to ordinary shareholders for the year/period excluding (i) share-based compensation expenses, and (ii) accretion of convertible redeemable preferred shares to redemption value.

Please see the “Reconciliation of GAAP and Non-GAAP Results” below for a full reconciliation of GAAP net loss attributable to ordinary shareholders for the year/period to non-GAAP net loss attributable to ordinary shareholders and non-GAAP net loss per ordinary share for the year/period.

Reconciliation of GAAP and Non-GAAP Results

	For the years ended December 31,	
	2019 US\$	2020 US\$
GAAP net loss attributable to ordinary shareholders	(16,678,492)	(42,645,392)
Add back:		
Share-based compensation expense	611,711	10,129,541
Accretion of convertible redeemable preferred shares to redemption value	246,184	248,113
Non-GAAP net loss attributable to ordinary shareholders	(15,820,597)	(32,267,738)
Weighted average number of ordinary shares used in per share calculation:		
—Basic	15,178,232	15,950,698
—Diluted	15,178,232	15,950,698
Non-GAAP net loss per ordinary share		
—Basic	(1.04)	(2.02)
—Diluted	(1.04)	(2.02)

3.B. Capitalization and Indebtedness

Not applicable.

3.C. Reason for the Offer and Use of Proceeds

Not applicable.

3.D. Risk Factors

Risks Related to Our Financial Prospects and Need for Additional Capital

We have a limited operating history, which may make it difficult to evaluate our current business and predict our future performance.

We are a clinical stage biopharmaceutical company with a limited operating history. Since our inception in 2011, we have focused substantially all of our efforts and financial resources on the discovery and development of antibody therapeutics for the treatment of cancer. We have no products approved for commercial sale and therefore we have not generated any revenue from product sales. We have not obtained regulatory approvals for any of our product candidates and there is no assurance that we will obtain approvals in the future. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and may continue to have an adverse effect on our working capital.

Our operations to date have focused on developing our product candidates, building our intellectual property portfolio, conducting preclinical testing and clinical trials, and raising capital. These operations provide a limited basis for you to assess our ability to successfully market and commercialize our product candidates. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history. We will encounter risks and difficulties frequently experienced by early-stage companies in rapidly evolving fields as we seek to shift our focus to late stage development and commercial activities. If we do not address these risks and difficulties successfully, we may not be successful in such a transition.

We have incurred net losses historically and we may continue to incur net losses in the near future.

Since our inception in 2011, we have devoted our resources to the development of innovative antibodies in the therapeutic area. While we have generated revenues from licensing and collaboration deals, we have not generated any revenue from commercial product sales to date, and we have had significant operating losses since our inception. For the years ended December 31, 2018, 2019 and 2020, we incurred net losses of US\$15.3 million, US\$16.4 million and US\$42.4 million, respectively. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs. To date, we have financed our operations principally through private placements and proceeds from our initial public offering. Our product candidates and programs are in preclinical development or early stage clinical development, and we have not received marketing approval for any of our product candidates. Our product candidates will require substantial investments and significant marketing efforts before we generate any revenues from product sales, if ever. We expect our net losses will increase as more product candidates enter into clinical trial stage. Our ability to generate product revenue and achieve profitability depends on, among other things:

- completing research and development of our product candidates;
- initiating, enrolling patients in and completing clinical trials of product candidates on a timely basis;
- obtaining regulatory approvals and marketing authorizations for any product candidates for which we complete clinical trials;
- developing and maintaining adequate manufacturing capabilities either by ourselves or in connection with third-party manufacturers;
- launching and commercializing any product candidates for which we obtain regulatory approvals and marketing authorizations;
- establishing a sales, marketing and commercialization team for any future products for which we may obtain regulatory approval;
- seeking to identify additional product candidates;
- addressing any competing technological and market developments; and

- maintaining, protecting and expanding our portfolio of intellectual property rights.

We may never succeed in these activities and, even if we do, may never generate revenue that is significant enough to achieve profitability. Because of the numerous risks and uncertainties associated with the development, delivery and commercialization of complex innovative antibody therapeutic, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability. If we are required by regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in the initiation and completion of our clinical trials or the development of any of our product candidates, our expenses could increase and profitability could be further delayed.

If we fail to become profitable or are unable to sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and be forced to reduce our operations. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become or remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business or continue our operations. Failure to become and remain profitable may adversely affect the market price of the ADSs and our ability to raise capital and continue operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We may need to obtain substantial additional financing to fund our growth and operations, which may not be available on acceptable terms, if at all.

The development of biopharmaceutical product candidates is capital-intensive. We have used substantial funds to advance our discovery programs and develop our technology and product candidates, and will require significant funds to conduct further research and development, preclinical testing and clinical trials of our product candidates, to seek regulatory approvals for our product candidates and to manufacture and market products, if any, that are approved for commercial sales. If our product candidates enter and advance through preclinical studies and clinical trials, we will need substantial additional funds to expand our development, regulatory and manufacturing capabilities. In addition, we expect to incur additional costs associated with operating as a public company.

- To date, we have funded our operations primarily through capital contributions from our shareholders via private placements and proceeds from our initial public offering. Our operations have consumed substantial amounts of cash since inception. As of December 31, 2020, we had US\$75.2 million in cash and cash equivalents. The net cash used in our operating activities was US\$14.3 million, US\$18.2 million and US\$28.5 million for the years ended December 31, 2018, 2019 and 2020, respectively. Our future funding requirements and the period for which we expect increasing capital need may be different than what we are planning. Our monthly spending levels vary based on new and ongoing research and development activities. Because of the numerous risks and uncertainties associated with our product development, we are unable to accurately predict the timing and amount of our operating expenditures, which will depend largely on:
 - the scope, timing, progress, costs and results of discovery, preclinical development, laboratory testing and clinical development activities of our current product candidates;
 - the number, scope, progress and results of preclinical and clinical programs we decide to pursue;
 - the progress of the development efforts of parties with whom we have entered or may in the future enter into collaborations and research and development agreements;
 - our ability to maintain our current licenses, research and development programs, and to establish new collaboration arrangements;
 - the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
 - the cost, timing and outcome of regulatory review of any of our product candidates;
 - the costs and timing of future commercialization activities, including manufacturing, marketing, sales, and distribution, for any of our product candidates for which we receive marketing approval;

- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval; and
- our efforts to enhance operational systems and hire additional personnel, including personnel to support development of our product candidates and satisfy our obligations as a public company.

We will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. Any additional capital-raising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our current and future product candidates, if approved. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or altogether cease our research and development programs or future commercialization efforts.

Raising additional capital may lead to dilution of shareholdings by our existing shareholders and restrict our operations or require us to relinquish rights to our technologies or product candidates.

We may seek additional funding through a combination of equity and debt financings and collaborations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the beneficial ownership interest of existing holders of our shares and/or ADSs will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of existing holders of our shares and/or ADSs.

The incurrence of additional indebtedness or the issuance of certain equity securities could result in increased fixed payment obligations and could also result in certain additional restrictive covenants, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise additional funds through partnerships, collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, product candidates, or future revenue streams, or grant licenses on terms that are not favorable to us.

We have certain shareholders who have board representation rights and their individual interests may differ from yours.

In 2014, we completed private placements of our Series A-1 and A-2 preferred shares, in which we raised gross proceeds of approximately US\$8.5 million. In 2016, we completed a private placement of our Series B preferred shares, in which we raised gross proceeds of approximately US\$28.0 million. In 2018, we completed a private placement of our Series C-1 preferred shares, in which we raised gross proceeds of approximately US\$50.0 million. In 2019, we completed private placements of our Series C-2 and C-3 preferred shares, in which we raised gross proceeds of approximately US\$69.0 million in aggregate. As a result of these private placements, a significant portion of our outstanding equity is currently held by multiple separate institutional investors through several separate funds and our founders.

These institutional investors will continue have a significant level of influence because of their level of ownership, including a greater ability than you and our other shareholders to influence the election of directors and the potential outcome of other matters submitted to a vote of our shareholders, such as mergers, the sale of substantially all of our assets and other extraordinary corporate matters. These investors and our founder, Peter Luo, also have certain rights, such as board representation right and registration right that our other shareholders do not have.

For instance, our current effective memorandum and articles of association provides that JSR Limited shall have the right to designate, appoint, remove and replace and reappoint one director so long it holds at least five percent of the shares outstanding on a fully-diluted basis and an as-converted basis, respectively; as long as Wuxi Pharmatech Healthcare Fund I L.P., which is controlled by the ultimate controlling party of our sole supplier, holds at least five percent of the shares outstanding on a fully-diluted basis, it shall have the right to nominate one independent non-executive director and such one director shall be appointed and agreed by the board; as long as Peter Luo holds or beneficially owns any shares or is employed by us or any of our subsidiaries, he will serve as one of our directors and the Chairman of the Board of Directors; in addition, during the period commencing upon February 2021 and ending on the earlier of (i) the date upon which Peter Luo beneficially owns less than five percent of the shares outstanding on a fully diluted basis, (ii) the death or legal determination of Peter Luo's incapacity or (iii) the termination of Peter Luo as an executive officer or principal scientific advisor to us or any of our subsidiaries or for cause (as determined under his related employment or consulting arrangements and subject to all related cure provisions), Peter Luo shall have the right to designate, appoint, remove and replace and reappoint one additional director; and as long as General Atlantic Singapore AI Pte. Ltd. and its affiliates hold at least five percent of the shares outstanding on a fully-diluted basis, they shall have the right to designate, appoint, remove and replace and reappoint one director.

The interests of these investors could conflict with the interests of our other shareholders, including you, and any future transfer by these investors of their shares of preferred or ordinary share to other investors who have different business objectives could have a material adverse effect on our business, results of operations, financial condition and the market value of our ordinary shares or ADSs.

Risks Related to Clinical Development of Our Product Candidates

We may not be able to identify or discover new product candidates, and may allocate our limited resources to pursue a particular product candidate and fail to capitalize on product candidates that may later prove to be more profitable, or for which there is a greater likelihood of success.

Although we will focus our efforts on continued preclinical and clinical developments, regulatory approval process and commercialization with respect to our existing product candidates, the success of our business depends in part upon our ability to identify, license, discover, develop, or commercialize additional product candidates. Research programs to identify new product candidates require substantial technical, financial, and human resources. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates;
- our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to obtain marketing approval; and
- potential product candidates may not be effective in treating their targeted diseases.

Because we have limited financial and managerial resources, we focus on research programs and product candidates for specific targets. As a result, we may forgo or delay pursuit of opportunities with other product candidates that later may be proved to have greater commercial potential or a greater likelihood of success. On the other hand, if we do not prioritize the allocation of our resources and conduct research programs that cover a broad range of targets or engage clinical programs that are overly expansive, we may be subject to significant risk of loss as a large part of the research and clinical programs fail. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

Accordingly, there can be no assurance that we will ever be able to develop suitable potential product candidates through internal research programs, which could materially adversely affect our future growth and prospects.

We may not be successful in our efforts to use and expand our proprietary platforms to build a pipeline of product candidates.

A key element of our strategy is to leverage our technology platform to expand our pipeline of antibody product candidates and in order to do so, we will continue to invest in our platform and development capabilities. Although our research and development efforts to date have resulted in a pipeline of product candidates, these product candidates may not be safe and effective. In addition, although we expect that our platform will allow us to develop a diverse pipeline of novel and differentiated product candidates, we may not prove to be successful at doing so. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval or achieve market acceptance. Even after approval, if we cannot successfully develop or commercialize our products, or if serious adverse events are discovered after commercialization, we will not be able to generate any product revenue, which would adversely affect business.

Any failures or setbacks in our platforms or our other proprietary technologies could negatively affect our business and financial condition.

Our product candidates are created with, and dependent upon, our proprietary antibody discovery platforms, such as our proprietary Dynamic Precision Library platform, which includes our NEObody platform, SAFEbody platform and POWERbody platform. These proprietary technology platforms are also the basis of our collaborations with certain other partners. To date, no products based on any of these technologies have been approved for commercial sale in any jurisdiction. Any failures or setbacks with respect to our proprietary technologies, including adverse effects resulting from the use of product candidates derived from these technologies in human clinical trials and/or the imposition of clinical holds on trials of any product candidates using our proprietary technologies, could have a detrimental impact on our clinical pipeline, as well as our ability to maintain and enter into new corporate collaborations regarding our technologies or otherwise, which would negatively affect our business and financial conditions.

Our product candidates, for which we intend to seek approval as biologics products, may face competition sooner than anticipated.

Even if we are successful in achieving a final regulatory approval to commercialize a product candidate ahead of our competitors, our product candidates may face competition from biosimilar products. In the United States, our product candidates are regulated by the FDA as biologic products and we intend to seek approval for these product candidates pursuant to the Biologics License Application (BLA) pathway. The Biologics Price Competition and Innovation Act of 2009 (BPCIA) created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as “interchangeable” based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our product candidates.

There is a risk that any of our product candidates approved as a biological product under a BLA would not qualify for the 12-year period of exclusivity or that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for interchangeable or generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

Jurisdictions in addition to the United States have established abbreviated pathways for regulatory approval of biological products that are biosimilar to earlier approved reference products. For example, the European Union has had an established regulatory pathway for biosimilars since 2005.

The increased likelihood of biosimilar competition has increased the risk of loss of innovators’ market exclusivity. Due to this risk, and uncertainties regarding patent protection, if our clinical candidates are approved for marketing, it is not possible to predict the length of market exclusivity for any particular product with certainty based solely on the expiration of the relevant patent(s) or the current forms of regulatory exclusivity. It is also not possible to predict changes in United States regulatory law that might reduce biological product regulatory exclusivity. The loss of market exclusivity for a product would likely materially and negatively affect revenues and we may not generate adequate or sufficient revenues from them or be able to reach or sustain profitability.

We depend substantially on the success of our product candidates, particularly ADG106, ADG126, ADG116 and ADG104, which are in clinical development, and our ability to identify additional product candidates. Clinical trials of our product candidates may not be successful. If we are unable to successfully identify new product candidates, complete clinical development, obtain regulatory approval and commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

Our business and the ability to generate revenue related to product sales, if ever, will depend on the successful development, regulatory approval and commercialization of our antibody product candidates for the treatment of patients with cancer, particularly ADG106, ADG126, ADG116 and ADG104, which are still in clinical stage. Other than ADG106, ADG126, ADG116 and ADG104 which are currently in Phase Ib and Phase II development, our current product candidates are in relatively early stages of development. We have invested a significant portion of our efforts and financial resources in the development of our existing product candidates and all of our product candidates will require significant further development, financial resources. The success of our product candidates, including ADG106, ADG126, ADG116 and ADG104, will depend on several factors, including:

- successful enrollment in, and completion of, preclinical studies and clinical trials;
- receipt of regulatory approvals from the FDA, NMPA and other comparable regulatory authorities for our product candidates;
- establishing commercial manufacturing capabilities, either by building facilities ourselves or making arrangements with third-party manufacturers;
- relying on third parties to conduct our clinical trials safely and efficiently;
- obtaining and maintaining patent, trade secret and other intellectual property protection and regulatory exclusivity;
- protecting our rights in our intellectual property;
- ensuring we do not infringe, misappropriate or otherwise violate the patent, trade secret or other intellectual property rights of third parties;
- launching commercial sales of our product candidates, if and when approved;
- competition with other product candidates and drugs; and
- continued acceptable safety profile for our product candidates following final regulatory approval, if and when received.

Due to the uncertain, time-consuming and costly clinical development and regulatory approval process, we may not successfully develop any of our product candidates, or we or our partners may choose to discontinue the development of product candidates for a variety of reasons. Our failure to effectively advance our development programs could have a material adverse effect on our business, financial condition, results of operations and future growth prospects, and cause the market price of our ADSs to decline.

Clinical trials are expensive, time consuming and difficult to design and implement and may fail to demonstrate adequate safety and efficacy of our product candidates. The results of our current and previous preclinical studies or clinical trials may not be predictive of future results, and the results of our current and planned clinical trials may not satisfy the requirements of the FDA or comparable foreign regulatory authorities or provide the basis for regulatory approval.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct preclinical studies and extensive clinical trials to demonstrate their safety and efficacy in humans. Clinical testing is expensive and difficult to design and implement. Clinical testing can take many years to complete, and its ultimate outcome is uncertain. A failure of one or more clinical trials can occur at any stage of the process. We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe, pure, and potent for use in a diverse patient population before we can seek final regulatory approvals for their commercial sale. Our clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional and expansive preclinical or clinical testings.

We cannot assure that the results of later clinical trials will replicate the results of prior clinical trials and preclinical testing. The results are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data becomes available. Product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA, the NMPA and comparable foreign regulatory authorities, despite having progressed through preclinical studies or initial clinical trials. Product candidates that have shown promising results in early clinical trials may still suffer significant setbacks in subsequent clinical trials or registration clinical trials. For example, a number of companies in the biopharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials.

A failure of a clinical trial to meet its predetermined endpoints may cause us to abandon a pipeline product or an indication and may delay development of any other pipeline products. Any delay in, or termination of, our clinical trials will delay the submission for regulatory approval and application, and, ultimately, our ability to commercialize any of our pipeline products and generate revenue.

Moreover, principal investigators for our clinical trials may serve and have served as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of our pipeline products.

We may experience delays in our ongoing clinical trials.

We may experience delays in our ongoing clinical trials, and we do not know whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time, or be completed on schedule, if at all. Clinical trials can be delayed, suspended, or terminated for a variety of reasons, including the following:

- delays in or failure to obtain regulatory authorization to commence a trial;
- delays in or failure to obtain institutional review board, or IRB, approval at each site;
- delays in or failure to reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- difficulty in recruiting clinical trial investigators of appropriate competencies and experience;
- delays in establishing the appropriate dosage levels in clinical trials;
- delays in or failure to recruit and enroll suitable patients to participate in a trial, particularly considering study inclusion and exclusion criteria and patients' prior lines of therapy and treatment;
- the difficulty in certain countries in identifying the sub-populations that we are trying to treat in a particular trial, which may delay enrollment and reduce the power of a clinical trial to detect statistically significant results;
- lower than anticipated retention rates of patients in clinical trials;
- failure to have patients complete a trial or return for post-treatment follow-up;

- clinical sites deviating from trial protocol or dropping out of a trial;
- delays adding new investigators or clinical trial sites;
- safety or tolerability concerns could cause us or our collaborators or governmental authorities, as applicable, to suspend or terminate a trial if it is found that the participants are being exposed to unacceptable health risks, undesirable side effects or other unfavorable characteristics of the product candidate, or if such undesirable effects or risks are found to be caused by a chemically or mechanistically similar therapeutic or therapeutic candidate;
- our third-party research contractors failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- changes in regulatory requirements, policies and guidelines;
- failure to comply with the applicable regulatory requirements through the clinical process;
- manufacturing sufficient quantities of a product candidate for use in clinical trials;
- the quality or stability of a product candidate falling below acceptable standards;
- changes in the treatment landscape for our target indications that may make our product candidates no longer relevant; and
- third-party actions claiming infringement by our product candidates in clinical trials outside the United States and obtaining injunctions interfering with our progress.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. Moreover, while we plan to submit additional investigational new drug applications, or INDs, for other product candidates, we may not be able to file such INDs on the timeline we expect. For example, we may experience manufacturing delays or other delays with IND-enabling preclinical studies. Moreover, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate clinical trials. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND, we cannot guarantee that such regulatory authorities will not change their requirements in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs.

If we are required to conduct additional clinical trials or other studies with respect to any of our product candidates beyond those that we initially contemplated, if we are unable to successfully complete our clinical trials or other studies or if the results of these studies are not positive or are only modestly positive, we may be delayed in obtaining regulatory approval for that product candidate, we may not be able to obtain regulatory approval at all or we may obtain approval for indications that are not as broad as intended. Our drug development costs will also increase if we experience delays in testing or approvals, and we may not have sufficient funding to complete the testing and approval process. Significant clinical trial delays could allow our competitors to bring drugs to market before we do and impair our ability to commercialize our drugs, if and when approved. If any of this occurs, our business will be materially harmed.

Clinical trials must be conducted in accordance with the FDA and other applicable regulatory authorities' legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and Ethics Committees or IRBs at the medical institutions where the clinical trials are conducted. We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs or Ethics Committees of the institutions in which such trials are being conducted, by the Data Review Committee or Data Safety Monitoring Board for such trial or by the FDA, or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial or to perform obligations in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Significant clinical trial delays could also allow our competitors to bring products to market before we do or shorten any periods during which we have the exclusive right to commercialize our product candidates and impair our ability to commercialize our product candidates and may harm our business and results of operations.

Further, clinical trials must be conducted with supplies of our product candidates produced under current good manufacturing practices, or cGMP, requirements and other regulations. Furthermore, we rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their committed activities, we have limited influence over their actual performance. We depend on our collaborators and on medical institutions and CROs to conduct our clinical trials in compliance with good clinical practice, or GCP, requirements. To the extent our collaborators or the CROs fail to enroll participants for our clinical trials, fail to conduct the study in accordance with GCP or are delayed for a significant time in the execution of trials, including achieving full enrollment, we may be affected by increased costs, program delays or both, which may harm our business. In addition, clinical trials that are conducted in countries outside the United States may subject us to further delays and expenses as a result of increased shipment costs, additional regulatory requirements and the engagement of non-U.S. CROs, as well as expose us to risks associated with clinical investigators who are unknown to the FDA, and different standards of diagnosis, screening and medical care.

If we encounter difficulties in enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients. Our clinical trials may be subject to delays for a variety of reasons, including as a result of enrollment taking longer than anticipated, subject withdrawal or adverse events. These types of developments could cause us to delay the trial or halt further development.

While we believe our differentiated product candidates address highly unmet medical needs that will facilitate our patient enrollment, clinical trials may compete with other clinical trials that are in the same therapeutic areas as our product candidates, and this competition reduces the number and types of patients available to us, as some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Moreover, enrolling patients in clinical trials for cancer therapies is challenging, as cancer patients will first receive the applicable standard of care. Many patients who respond positively to the standard of care antibody therapy (and thus do not enroll in clinical trials) are believed to have tumor types that would have responded well to our product candidates. Patients who fail to respond positively to the standard of care treatment will be eligible for clinical trials of unapproved product candidates. However, these patients may have either compromised immune function from prior administration of chemotherapy or an enhanced immune response from the prior administration of checkpoint inhibitors. Either of these prior treatment regimens may render our therapies less effective in clinical trials. Additionally, patients who have failed approved therapies will typically have more advanced cancer and a poorer long-term prognosis.

Because the number of qualified clinical investigators and clinical trial sites is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including:

- severity of the disease under investigation;
- the size and nature of the patient population;
- the patient eligibility criteria defined in the protocol;
- the size of the study population required for analysis of the trial's primary endpoints;
- perceived risks and benefits of our pipeline products;

- our resources to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain patients' consent; and
- the risk that patients enrolled in clinical trials will not complete a clinical trial.

These factors may make it difficult for us to enroll enough patients to complete our clinical trials in a timely and cost-effective manner. Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, some of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

Interim, topline or preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline or data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects, or financial condition.

Risks Related to Obtaining Regulatory Approval of Our Drug Candidates

The regulatory approval processes of the FDA, NMPA and other comparable regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approvals for our product candidates, our business will be substantially harmed.

In the United States, marketing approval of biologics requires the submission of a BLA to the FDA, and we are not permitted to market any product candidate in the United States until we obtain approval from the FDA of the BLA for that product candidate. A BLA must be supported by extensive clinical and preclinical data, as well as extensive information regarding pharmacology, chemistry, manufacturing and controls. Outside the United States, many comparable foreign regulatory authorities employ similar approval processes.

We have not previously submitted a BLA to the FDA or similar regulatory approval filings to the NMPA or other comparable foreign authorities, for any product candidate, and we cannot be certain that any of our product candidates will receive regulatory approval. Obtaining approval of a BLA can be a lengthy, expensive and uncertain process, and as a company we have no experience with the preparation of a BLA submission or any other application for marketing approval. In addition, the FDA has the authority to require a risk evaluation and mitigation strategies, or REMS, plan as part of a BLA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved biologic, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry.

FDA approval is not guaranteed, and the time required to obtain approval by the FDA, NMPA and other comparable regulatory authorities is unpredictable but typically takes many years following the commencement of preclinical trials and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, due to external issues such as pandemics or other public health emergencies, FDA, NMPA and other comparable regulatory authorities may be delayed in their review of product applications. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may discover, in-license or acquire and seek to develop in the future will ever obtain regulatory approval.

Our product candidates could fail to receive regulatory approval from the FDA, NMPA or a comparable regulatory authority for many reasons, including:

- disagreement with the design or implementation of our clinical trials;
- failure to demonstrate that a product candidate is safe and effective or safe, pure, and potent for its proposed indication;
- failure of clinical trial results to meet the level of statistical significance required for approval;
- failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- disagreement with our interpretation of data from preclinical trials or clinical trials;
- the insufficiency of data collected from clinical trials of our product candidates to support the submission and filing of a BLA or other submission or to obtain regulatory approval;
- the FDA, NMPA or comparable regulatory authority's finding of deficiencies related to the manufacturing processes;
- failure of our product candidates to pass current Good Manufacturing Practice, or cGMP, inspections during the regulatory review process or across the production cycle of our product; and
- changes in approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA and other regulatory authorities have substantial discretion in the approval process, and determining when or whether regulatory approval will be obtained for any of our product candidates. For example, regulatory authorities in various jurisdictions have in the past had, and may in the future have, differing requirements for, interpretations of and opinions on our preclinical and clinical data. As a result, we may be required to conduct additional preclinical studies, alter our proposed clinical trial designs or conduct additional clinical trials to satisfy the regulatory authorities in each of the jurisdictions in which we hope to conduct clinical trials and develop and market our products, if approved. Further, even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA or any other regulatory authority.

The FDA, NMPA or a comparable regulatory authority may require more information, including additional preclinical or clinical data, to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program. If we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post-marketing clinical trials, may approve a product candidate with a label that is not desirable for the successful commercialization of that product candidate, or may be difficult to meet manufacturing requirements. In addition, if our product candidate produces undesirable side effects or safety issues, the FDA may require the establishment of Risk Evaluation Mitigation Strategies, or REMS, or the NMPA or a comparable regulatory authority may require the establishment of a similar strategy, that may, for instance, restrict distribution of our drugs and impose burdensome implementation requirements on us. Any of the foregoing scenarios could materially harm the commercial prospects of our product candidates.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new biologics or modifications to licensed biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Even if we obtain FDA approval of any of our product candidates, we may never obtain approval or commercialize such products outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other countries. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking regulatory approvals in various jurisdictions could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed.

We are conducting clinical trials and may in the future conduct additional clinical trials for our product candidates outside the United States and/or China, and FDA, NMPA and similar foreign regulatory authorities may not accept data from such trials.

We are conducting clinical trials and may in the future conduct additional clinical trials for our product candidates outside the United States, including in Australia, Europe or other foreign jurisdictions. The acceptance of trial data from clinical trials conducted outside the United States by the FDA may be subject to certain conditions. In cases where data from clinical trials conducted outside the United States are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; (ii) the trials were performed by clinical investigators of recognized competence and (iii) the data may be considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Otherwise, for studies that are conducted at sites outside of the United States and not subject to an IND and which are intended to support a marketing application (but which are not intended to serve as the sole basis for marketing approval), the FDA requires the clinical trial to have been conducted in accordance with good clinical practice, or GCP, requirements and the FDA must be able to validate the data from the clinical trial through an on site inspection if it deems such inspection necessary. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies, such as NMPA, have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, NMPA or any similar foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, NMPA or any similar foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

Our product candidates may cause undesirable adverse events or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any regulatory approval.

Undesirable adverse events caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, NMPA or other comparable regulatory authority. Results of our trials could reveal a high and unacceptable severity or prevalence of adverse events. In such an event, our trials could be suspended or terminated and the FDA, NMPA or other comparable regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Drug-related adverse events could affect patient recruitment or the ability of enrolled subjects to complete the trial, and could result in potential product liability claims. Moreover, such events may require us to amend our trials, including reducing the dosage in our clinical trials.

For instance, in September 2019, in our Phase I trial of ADG116 in the United States, we reported to the FDA the death of the only patient dosed in the trial. The FDA subsequently placed the trial on clinical hold on September 30, 2019. The FDA noted that there was insufficient information to assess the risk of drug-induced liver toxicity in patients receiving ADG116 but requested us to revise the study protocol to mitigate the risk of drug-induced liver toxicity. We submitted to the FDA an amendment to the study protocol, which significantly lowered the starting dose of ADG116, tightened the inclusion and exclusion criteria to exclude, among others, patients with liver dysfunction, history of alcohol abuse, or poorly controlled diabetes, and stipulated additional post-dosing monitoring to closely follow treated patients for safety or toxicity signals. The FDA removed the clinical hold on December 5, 2019. We have obtained authorization from the Australian Therapeutic Goods Administration under a CTN to start a Phase I clinical trial of ADG116 and have completed five levels of dose escalation at 0.003, 0.01, 0.03, 0.1, 0.3 mg/kg without observing any \geq Grade 2 TEAEs or other drug related safety issues. We have completed dosing three patients in the cohort at 1 mg/kg. We have decided to focus on conducting the Australian clinical trial of ADG116 at a higher starting dose than currently permitted in the United States, and consequently, we have not re-commenced patient enrollment in the United States. Nevertheless, with favorable clinical data in Australia clinical trial as of April 19, 2021, we look forward to expanding the global Phase 1 trial, with the acceptance of revised study protocol by FDA, to expand the trial in the United States.

We cannot provide any assurance that there will not be treatment-related severe adverse events with our product candidates, that the trials for our product candidates will not be suspended in the future, or that patient recruitment for trials with our product candidates will not be adversely impacted by the ADG116 related adverse events, any of which could materially and adversely affect our business and prospects. Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. In the event that any of our product candidates receives marketing approval and we or others later identify undesirable or unacceptable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- we may suspend marketing of such products;
- regulatory authorities may withdraw or limit approvals of such products or require us to take an approved product off the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies, or issue other communications containing warnings or other safety information about the product;
- regulatory authorities may require a medication guide outlining the risks of such side effects for distribution to patients, or that we implement a REMS plan to ensure that the benefits of the product outweigh its risks or to develop a similar strategy as required by a comparable regulatory authority, that may, for instance, restrict distribution of our drugs and impose burdensome implementation requirements on us;
- we may be required to conduct post-market studies;
- we may be subject to limitations on how we may promote or manufacture the product;
- sales of the product may decrease significantly;
- we could be sued and held liable for harm caused to subjects or patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

Further, combination therapy involves unique adverse events that could be exacerbated compared to adverse events from monotherapies. These types of adverse events could be caused by our product candidates and could also cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, NMPA or other comparable regulatory authority. Results of our trials could reveal a high and unacceptable severity or prevalence of adverse events.

We may seek Orphan Drug Designation for some of our product candidates, and we may be unsuccessful.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a disease with a patient population of fewer than 200,000 individuals in the United States, or a patient population of greater than 200,000 individuals in the United States, but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States.

Generally, if a drug with an Orphan Drug Designation subsequently receives the first FDA approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug for the same indication during the period of exclusivity. The applicable period is seven years in the United States. Orphan Drug exclusivity may be lost if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain Orphan Drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition and the same drugs can be approved for a different condition but used off-label for any orphan indication we may obtain. Even after an orphan drug is approved, the FDA can subsequently approve a different drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We may attempt to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated approval pathways. If we are unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.

We may in the future seek an accelerated approval for our one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug.

Prior to seeking accelerated approval for any of our product candidates, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit a BLA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent FDA feedback we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or receive an expedited regulatory designation (e.g., breakthrough therapy designation) for our product candidates, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Even if we receive regulatory approvals for our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory reviews, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

If our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, import, export, adverse event reporting, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA, NMPA and comparable regulatory authority requirements, including, in the United States, ensuring that quality control and manufacturing procedures conform to current cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any BLA, other marketing application, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase IV clinical trials and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA, NMPA, or a comparable regulatory authority approves our product candidates, we will have to comply with requirements including, for example, submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and Good Clinical Practices, or cGCPs, for any clinical trials that we conduct post approval.

The FDA and NMPA may impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the drug reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-market studies or clinical trials to assess new safety risks, or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our drugs, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, untitled or warning letters, or holds on clinical trials;
- refusal by the FDA, NMPA or comparable regulatory authorities to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA, NMPA and other regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. The policies of the FDA, NMPA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any regulatory approval that we may have obtained and we may not achieve or sustain profitability.

All material aspects of the research, development and commercialization of pharmaceutical products are heavily regulated.

All jurisdictions in which we intend to conduct our pharmaceutical-industry activities regulate these activities in great depth and detail. We intend to focus our activities in the major markets such as the United States and China. These jurisdictions strictly regulate the pharmaceutical industry, and in doing so they employ broadly similar regulatory strategies, including regulation of product development and approval, manufacturing, and marketing, sales and distribution of products. However, there are differences in the regulatory regimes that make for a more complex and costly regulatory compliance burden for a company like ours that plans to operate in these regions.

The process of obtaining regulatory approvals and compliance with appropriate laws and regulations require substantial time and financial resources. Failure to comply with the applicable requirements at any time during the product development process and approval process, or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include: refusal to approve pending applications; withdrawal of an approval; license revocation; clinical hold; voluntary or mandatory product recalls; product seizures; total or partial suspension of production or distribution; injunctions; fines; refusals of government contracts; providing restitution; undergoing disgorgement; or other civil or criminal penalties. Failure to comply with these regulations could have a material adverse effect on our business.

Future strategic partnerships may be important to us. We will face significant competition in seeking new strategic partners.

We do not yet have any capability for manufacturing, sales, marketing or distribution. For some of our product candidates, we may in the future determine to collaborate with pharmaceutical and biotechnology companies for development and potential commercialization of therapeutic products. The competition for strategic partners is intense. Our ability to reach a definitive agreement for collaboration will depend, among other things, upon our assessment of the strategic partner's resources and expertise, the terms and conditions of the proposed collaboration and the proposed strategic partner's evaluation of a number of factors. These factors may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The strategic partner may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such collaboration could be more attractive than the one with us for our product candidate.

Strategic partnerships are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future strategic partners. Even if we are successful in entering into collaboration, the terms and conditions of that collaboration may restrict us from entering into future agreements with other potential collaborators.

If we are unable to reach agreements with suitable strategic partners on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into strategic partnerships and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our technology platform and our business may be materially and adversely affected. Any collaboration may be on terms that are not optimal for us, and we may not be able to maintain any new collaboration if, for example, development or approval of a product candidate is delayed, sales of an approved product candidate do not meet expectations or the partner terminates the collaboration. Any such collaboration, or other strategic transaction, may require us to incur non-recurring or other charges, and increase our near- and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business. Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and have a material and adverse effect on our business, financial condition, results of operations, and prospects. Conversely, any failure to enter any collaboration or other strategic transaction that would be beneficial to us could delay the development and potential commercialization of our product candidates and have a negative impact on the competitiveness of any product candidate that reaches the market.

We may not be able to enter into additional collaboration agreements beyond our existing strategic partnerships or collaborations with NIH, Exelixis, ADC Therapeutics and Guilin Sanjin. If we are unable to maintain existing and future strategic partnerships or collaborations, or if these strategic partnerships or collaborations are not successful, our business could be adversely affected.

Our existing strategic partnerships, collaborations and any future strategic partnerships we enter into may pose a number of risks, including the following:

- we may not be able to enter into critical strategic partnerships or enter into them on favorable terms;
- strategic partners or collaborators have significant discretion in determining the effort and resources that they will apply to such a partnership, and they may not perform their obligations as agreed, expected, or in compliance with applicable legal requirements;
- strategic partners or collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the partners' strategic focus or available funding, or external factors, such as an acquisition that diverts resources or creates competing priorities;
- strategic partners or collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- strategic partners or collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the strategic partners or collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than our product candidates;
- product candidates discovered in collaboration with us may be viewed by our strategic partners or collaborators as competitive with their own product candidates or products, which may cause strategic partners or collaborators to cease to devote resources to the commercialization of our product candidates;
- a strategic partner or collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product candidates;
- disagreements with strategic partners or collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- strategic partners or collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

- strategic partners or collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- strategic partners or collaborators may claim for a substantial compensation for our failure of development of the product candidates specified under the relevant out-licensing agreements that solely arose out of problems of our previous R&D basis; and
- strategic partnerships or collaborations may be terminated for the convenience of the partner or the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If any partnerships or collaboration we enter into do not result in the successful development of our product candidates or if one of our partners or collaborator terminates the agreement with us, our continued development of our product candidates could be delayed and our business may be materially and adversely affected.

We will need to grow our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As of December 31, 2020, we had 198 full-time employees. As our development and commercialization plans and strategies develop, and as we transition into operating as a public company, we expect to expand our employee base for managerial, operational, financial and other resources. As our product candidates enter and advance through preclinical studies and clinical trials, we will need to expand our development, regulatory and manufacturing capabilities or contract with other organizations to provide these capabilities for us. In the future, we expect to enter into additional relationships with collaborators or partners, suppliers and other organizations and establish a sales and marketing team in preparation for commercialization activities. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. Our inability to successfully manage our growth and expand our operations could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Disruptions in the financial markets and economic conditions could affect our ability to raise capital.

Global economies could suffer dramatic downturns as the result of a deterioration in the credit markets and related financial crisis as well as a variety of other factors including, extreme volatility in security prices, severely diminished liquidity and credit availability, ratings downgrades of certain investments and declining valuations of others. In the past, governments have taken unprecedented actions in an attempt to address and rectify these extreme market and economic conditions by providing liquidity and stability to the financial markets. If these actions are not successful, the return of adverse economic conditions may cause a significant impact on our ability to raise capital, if needed, on a timely basis and on acceptable terms or at all.

In addition, there is considerable uncertainty over the long-term effects of the expansionary monetary and fiscal policies adopted by the central banks and financial authorities of some of the world's leading economies, including the United States and China. There have been concerns over unrest and terrorist threats in the Middle East, Europe and Africa and over the conflicts involving Ukraine, Syria and North Korea. There have also been concerns on the relationship among China and other Asian countries, which may result in or intensify potential conflicts in relation to territorial disputes or the trade related disputes between the United States and China. In addition, the U.K. held a referendum on June 23, 2016 on its membership in the EU, in which voters approved an exit from the EU, commonly referred to as "Brexit"; the U.K. formally left the EU on January 31, 2020. The U.K. is currently in a transition period which is expected to continue through December 31, 2020, when agreements surrounding trade and other aspects of the U.K.'s future relationship with the EU will need to be finalized. Brexit could adversely affect European and worldwide economic and market conditions and could contribute to instability in global financial and foreign exchange markets. It is unclear whether these challenges and uncertainties will be contained or resolved, and what effects they may have on the global political and economic conditions in the long term.

If we face allegations of non-compliance with laws and encounter sanctions, our reputation, revenues and liquidity may suffer, and our product candidates and approved products, if any, could be subject to restrictions or withdrawal from the market.

Any government investigation of alleged violations of laws or regulations could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to obtain approvals commercialize and generate revenues from our drugs. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected. Additionally, if we are unable to generate revenues from our product sales, our potential for achieving profitability will be diminished and the capital necessary to fund our operations will be increased.

Our reputation is important to our success. Negative publicity may adversely affect our reputation and business prospects.

Any negative publicity concerning us, our affiliates or any entity that shares the “Adagene” name, even if untrue, could adversely affect our reputation and business prospects. There can be no assurance that negative publicity about us or any of our affiliates or any entity that shares the “Adagene” name would not damage our brand image or have a material adverse effect on our business, results of operations and financial condition.

Potential future acquisitions or strategic collaborations may increase our capital requirements, dilute our shareholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

We may evaluate various acquisitions and strategic collaborations, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic collaboration may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management’s attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and/or
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

Our business operations and current or future relationships with healthcare professionals, principal investigators, consultants, customers and third-party payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, physician payment transparency and other healthcare laws and regulations. If we or our employees, independent contractors, consultants, commercial partners, or vendors violate these laws, we could face substantial penalties.

Our business operations and current or future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include, without limitation:

- the U.S. federal civil and criminal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal false claims laws, including the False Claims Act, which can be enforced through whistleblower actions, and civil monetary penalties laws, which, among other things, impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the United States Physician Payments Sunshine Act and its implementing regulations, which require certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians, as defined by such law, and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members. Effective January 1, 2022, the U.S. federal physician transparency reporting requirements will extend to include transfers of value made during the previous year to certain non-physician providers such as physician assistants and nurse practitioners;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales;
- the U.S. Foreign Corrupt Practices Act of 1977, as amended, which prohibits, among other things, U.S. companies and their employees and agents from authorizing, promising, offering or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office and foreign political parties or officials thereof; and

- marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state and local laws that require the registration of pharmaceutical sales representatives; and state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities. For detailed discussion on material applicable PRC regulation, see “Item 4 Information on the Company—PRC Regulation” Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly and time-consuming and may require significant personnel resources. Even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

Recently enacted and future legislation in the United States and other countries may affect the prices we may obtain for our product candidates and increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates.

In the United States and many other countries, rising healthcare costs have been a concern for governments, patients and the health insurance sector, which resulted a number of changes to laws and regulations, and may result in further legislative and regulatory action regarding the healthcare and health insurance systems that could affect our ability to profitably sell any product candidates for which we obtain marketing approval.

For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, was enacted in the United States in March 2010 with the stated goals of containing healthcare costs, improving quality and expanding access to healthcare, and includes measures to change health care delivery, increase the number of individuals with insurance, ensure access to certain basic health care services, and contain the rising cost of care. Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, various portions of the ACA are currently facing legal and constitutional challenges in the Fifth Circuit Court of Appeals and the United States Supreme Court. Additionally, the current administration has issued various Executive Orders which eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices, and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. It is unclear whether the ACA will be overturned, repealed, replaced, or further amended.

In addition, other federal health reform measures have been proposed and adopted in the United States. For example, as a result of the Budget Control Act of 2011, providers are subject to Medicare payment reductions of 2% per fiscal year through 2030, with the exception of a temporary suspension from May 1, 2020 through December 31, 2020, unless additional Congressional action is taken. Further, the American Taxpayer Relief Act of 2012 reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments from providers from three to five years. The Medicare Access and CHIP Reauthorization Act of 2015 also introduced a quality payment program under which certain individual Medicare providers will be subject to certain incentives or penalties based on new program quality standards. Payment adjustments for the Medicare quality payment program began in 2019. At this time, it is unclear how the introduction of the quality payment program will impact overall physician reimbursement under the Medicare program. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics.

Since January 2017, there has been legislation considered in Congress to restrict the pricing of drug products to a governmental negotiated rate or to other similar rates that would reduce the costs to government, commercial payers and individuals. In July 2020, President Trump signed four Executive Orders directing the Department of Health and Human Services and other agencies to take specific actions to reduce prescription drug prices. The first order directs federally qualified health centers to pass along significant discounts on insulin and epinephrine from drug companies to low-income individuals. The second order would allow the importation of prescription drugs from Canada into the United States where the prices are deemed to be lower. The third order would eliminate safe harbor protections under the federal Anti-Kickback Statute that currently covers rebates paid by manufacturers to Medicare Part D plans and Medicaid managed care organizations, either directly or through pharmacy benefit managers under contract with such plans or organizations, so long as such actions are not projected to increase federal spending, Medicare beneficiary premiums or patients' total out-of-pocket cases. The fourth order will reduce the payment for Medicare part B drugs to be paid at the same rate as other developed nations, thereby reducing the reimbursement. All of these Executive Orders require rulemaking prior to implementation and could be stalled by Congress or the next election.

The combination of healthcare cost containment measures, increased health insurance costs, reduction of the number of people with health insurance coverage, as well as future legislation and regulations focused on reducing healthcare costs by reducing the cost of or reimbursement and access to pharmaceutical products, may limit or delay our ability to generate revenue, attain profitability, or commercialize our pipeline products, if approved.

We face intense competitions and rapid technological changes, as well as the possibility that our competitors may develop therapies that are similar, more advanced, or more effective than ours, which may adversely affect our ability to successfully commercialize our product candidates and our financial condition.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We are currently aware of various existing therapies and development candidates that may compete with ADG106, ADG126, ADG116 and ADG104 for the potential treatment of similar targets, such as urelumab and utomilumab targeting CD137 and ipilimumab targeting CTLA-4. While we are developing ADG126 and ADG116, both targeting CTLA-4, we intend to focus on and prioritize ADG126 as it is generated by our SAFEbody technology designed to enhance its safety profile. We have competitors in the United States, China and internationally, including major multinational pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies. Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development, marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products as well. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization and market penetration than we do. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

We have no experience in launching and marketing product candidates. We may not be able to effectively build and manage our sales network, or benefit from third-party collaborators' sales network.

We currently have no manufacturing, sales, marketing or commercial product distribution capabilities and have no experience in marketing drugs. We intend to develop an in-house marketing organization and sales force, which will require significant capital expenditures, management resources and time. We will have to compete with other biopharmaceutical companies to recruit, hire, train and retain marketing and sales personnel.

If we are unable or decide not to establish internal sales, marketing and commercial distribution capabilities for any or all of the drugs we develop, we will likely pursue collaborative arrangements regarding the sales and marketing of our product candidates, if approved. However, there can be no assurance that we will be able to establish or maintain such collaborative arrangements, or, if we are able to do so, that they will have effective sales forces. Any revenue we receive will depend on the efforts of such third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of such third parties, and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We will also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates, if approved.

There can be no assurance that we will be able to develop in-house sales and commercial distribution capabilities or establish or maintain relationships with third-party collaborators to successfully commercialize any product candidate, if approved, and as a result, we may not be able to generate product sales revenue.

Even if we are able to commercialize any approved product candidates, coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, and we may be subject to unfavorable pricing regulations, which could harm our business.

The regulations that govern regulatory approvals, pricing and reimbursement for new therapeutic products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or licensing approval is granted. In some non-U.S. markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a drug in a particular country, but then be subject to price regulations that delay our commercial launch of the drug and negatively impact our revenues.

A primary trend in the global healthcare industry is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Our ability to commercialize any drugs successfully also will depend in part on the extent to which coverage and reimbursement for these drugs and related treatments will be available on adequate terms, or at all, from government health administration authorities, private health insurers and other organizations.

In the United States, no uniform policy of coverage and reimbursement for biopharmaceutical products exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a drug from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our drugs on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given drug, the resulting reimbursement rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Increasingly, third-party payors are requiring that companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of our genetically modified drugs. Patients are unlikely to use our drugs and any approved product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of the drug. Because some of our product candidates have a higher cost of goods than conventional therapies, may require long-term follow up evaluations, and will likely be administered under the supervision of a physician, the risk that coverage and reimbursement rates may be inadequate for us to achieve profitability may be greater.

If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate that we successfully develop.

There may be significant delays in obtaining reimbursement for approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or other comparable regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on payments allowed for lower cost drugs that are already reimbursed, and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future weakening of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for our drugs and any new product candidates that we develop could have a material adverse effect on our business, our operating results, and our overall financial condition.

In China, the Ministry of Human Resources and Social Security of China or provincial or local human resources and social security authorities, together with other government authorities, review the inclusion or removal of drugs from China's National Drug Catalog for Basic Medical Insurance, Work-related Injury Insurance and Maternity Insurance, or the National Reimbursement Drug List, or the NRDL, or provincial or local medical insurance catalogues for the National Medical Insurance Program regularly, and the tier under which a drug will be classified, both of which affect the amounts reimbursable to program participants for their purchases of those drugs. There can be no assurance that our drugs and any approved product candidates will be included in the NRDL or provincial reimbursements lists. Products included in the NRDL have been typically generic and essential drugs. Innovative drugs similar to our product candidates have historically been more limited on their inclusion in the NRDL due to the affordability of the government's Basic Medical Insurance, although this has been changing in recent years. According to currently effective PRC laws and regulations, the prices of approved drugs are determined by market competition. The government regulate prices mainly by establishing a consolidated procurement mechanism, revising the NRDL and strengthening regulation of medical and pricing practices. We cannot predict the extent to which our business may be affected by potential future legislative or regulatory developments. Changes in pricing regulation could restrict the amount that we are able to charge for our future approved drugs, which would adversely affect our revenue, profitability and results of operations.

We intend to seek approval to market our product candidates in the United States, China and in other jurisdictions. In some non-U.S. countries, the pricing of drugs and biologics is subject to governmental control, which can take considerable time even after obtaining regulatory approval. Market acceptance and sales of our drugs will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for drugs and may be affected by existing and future health care reform measures.

As we engage in collaboration worldwide, we may be exposed to specific risks of conducting our business and operations in international markets.

We are a biopharmaceutical company with global footprints. We are currently building our clinical and technology infrastructures to support our future global operations and prepare to serve global markets. If we fail to obtain applicable licenses or fail to enter into strategic collaboration arrangements with third parties in these markets, or if these collaboration arrangements turn out unsuccessful, our revenue-generating growth potential will be adversely affected.

Moreover, international business relationships subject us to additional risks that may materially adversely affect our ability to attain or sustain profitable operations, including:

- efforts to enter into collaboration or licensing arrangements with third parties in connection with our international sales, marketing and distribution efforts may increase our expenses or divert our management's attention from the acquisition or development of product candidates;
- changes in a specific country's or region's political and cultural climate or economic condition;
- differing regulatory requirements for drug approvals and marketing internationally;
- difficulty of effective enforcement of contractual provisions in local jurisdictions;
- potentially reduced protection for intellectual property rights;
- potential third-party patent rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation or political instability;

- compliance with tax, employment, immigration and labor laws for employees traveling abroad;
- the effects of applicable tax structures and potentially adverse tax consequences;
- currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incidental to doing business in another country;
- workforce uncertainty and labor unrest and failure to comply with the applicable laws and regulations in relation to management of the employment of foreigners within the PRC;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from an international market with low or lower prices rather than buying them locally;
- failure of our employees and contracted third parties to comply with Office of Foreign Assets Control rules and regulations and the Foreign Corrupt Practices Act of the United States, and other applicable rules and regulations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes and fires.

These and other risks may materially adversely affect our ability to attain or sustain revenue from international markets.

Building our commercialization capabilities will require significant investment of time and money. There would be no assurance that we will successfully set up our commercialization capabilities in any of the proposed jurisdictions or at all, or that we will successfully commercialize any of our product candidates in the future.

We are currently in the early stages of building and expanding our commercial capabilities to allow us to market our own products, if approved, in the future. We will need to set up full commercialization capabilities in the jurisdictions, including China and the United States, which would require substantial investment of time and money and will divert significant management focus and resources. We also face competition with multinational and local pharmaceutical and biotechnology companies with established commercialization capabilities in terms of marketing and attracting talents.

Therefore, there can be no assurance that our efforts to set up commercialization capabilities will be successful in any of the proposed jurisdictions or at all.

Even if ADG106 or one of our other proprietary product candidates obtains regulatory approval, we may determine that commercializing such product candidate ourselves would not be the most effective way to create value for our shareholders or holders of ADSs. In addition, if we choose to commercialize any of our product candidates, our marketing efforts may be unsuccessful as a result of unfavorable pricing or reimbursement limitations, delays, competition or other factors. Failure to successfully market one or more of our approved products, or delays in our commercialization efforts, may diminish the commercial prospects for such products and may result in financial losses or damage to our reputation, each of which may have a negative impact on the market price of our ADSs and our financial condition, results of operations and future growth prospects.

We may continue to pursue collaborations or licensing arrangements, joint ventures, strategic alliances, partnerships or other strategic investment or arrangements, which may fail to produce anticipated benefits and adversely affect our operations.

We may continue to pursue opportunities for collaboration, out-license, joint ventures, acquisitions of products, assets or technology, strategic alliances, or partnerships that we believe would advance our development. We may consider pursuing growth through the acquisition of technology, assets or other businesses that may enable us to enhance our technologies and capabilities. Proposing, negotiating and implementing these opportunities may be a lengthy and complex process. Other companies, including those with substantially greater financial, marketing, technology, or other business resources, may compete with us for these opportunities or arrangements. We may not be able to identify, secure, or complete any such transactions or arrangements in a timely manner, on a cost-effective basis, on acceptable terms, or at all.

We have limited experience with respect to these business development activities. Management and integration of a licensing arrangement, collaboration, joint venture or other strategic arrangement may disrupt our current operations, decrease our profitability, result in significant expenses, or divert management resources that otherwise would be available for our existing business. We may not realize the anticipated benefits of any such transaction or arrangement.

Furthermore, partners, collaborators, or other parties to such transactions or arrangements may fail to fully perform their obligations or meet our expectations or cooperate with us satisfactorily for various reasons and subject us to potential risks, including the followings:

- partners, collaborators, or other parties have significant discretion in determining the efforts and resources that they will apply to a transaction or arrangement;
- partners, collaborators, or other parties could independently develop, or develop with third parties, services and products that compete directly or indirectly with our product candidates;
- partners, collaborators, or other parties may stop, delay or discontinue clinical trials as well as repeat clinical trials or conduct new clinical trials by using our intellectual property or proprietary information;
- partners, collaborators, or other parties may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liabilities;
- disputes may arise between us and partners, collaborators, or other parties that cause the delay or termination of the research, development or commercialization of our product candidates, or that result in costly litigation or arbitration that diverts management's attention and resources;
- partners, collaborators, or other parties may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable services and products; and
- partners, collaborators, or other parties may own or co-own intellectual properties covering our product candidates that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual properties.

Any such transactions or arrangements may also require actions, consents, approval, waiver, participation or involvement of various degrees from third parties, such as regulators, government authorities, creditors, licensors or licensees, related individuals, suppliers, distributors, shareholders or other stakeholders or interested parties. There is no assurance that such third parties will be cooperative as we desire, or at all, in which case we may be unable to carry out the relevant transactions or arrangements.

We rely on third parties to support, conduct and monitor our preclinical studies and clinical trials. Therefore, we may not be able to directly control the timing, process, expense and quality of our clinical trials and we cannot assure these third parties can duly perform their obligations as agreed and expected.

We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators and third-party CROs, to conduct our preclinical studies and clinical trials and to monitor and manage data for our ongoing preclinical and clinical programs. We rely on these parties for execution of our preclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors and CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our products candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat or suspend clinical trials, which would delay the regulatory approval process.

Further, these investigators and CROs are not our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. If independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if their performance is substandard, it may delay or compromise the prospects for approval and commercialization of any product candidates that we develop. In addition, the use of third-party service providers may require us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated.

Our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Additionally, CROs may lack the capacity to absorb higher workloads or take on additional capacity to support our needs. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We currently rely on a third-party manufacturer to produce our product candidates. Any failure by the third-party manufacturer to produce acceptable product candidates for us pursuant to our specifications and regulatory standards may delay or impair our ability to initiate or complete our clinical trials, obtain and maintain regulatory approvals or commercialize approved products, if any.

We currently rely on a third-party manufacturer and expect to continue to rely for some time on third parties to manufacture our product candidates for preclinical testing and clinical trials, in compliance with applicable regulatory and quality standards, and may do so for the commercial manufacture of some of our product candidates, if approved. To date, we have obtained bulk drug substance for ADG106, ADG126 and ADG116 from a single-source third-party contract manufacturer. Any reduction or halt in supply of the drug substance from such contract manufacturer could severely constrain our ability to develop our product candidates until a replacement contract manufacturer is found and qualified. If we are unable to arrange for and maintain such third-party manufacturing sources that are capable of meeting regulatory standards, or fail to do so on commercially reasonable terms, we may not be able to successfully produce sufficient supply of product candidate or we may be delayed in doing so. If we were to experience an unexpected loss of supply of our product candidates, for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials. Such failure or substantial delay or loss of supply could materially harm our business. We are continuously evaluating multiple vendors both in China and abroad to ensure that we have a continuous supply of products for global trials.

We may have little to no control regarding the occurrence of third-party manufacturer incidents. Any failure by our third-party manufacturer to comply with good manufacturing practices, or GMPs, or failure to scale up manufacturing processes, including any failure to deliver sufficient quantities of product candidates in a timely manner, would lead to a delay in, or failure to seek or obtain, regulatory approval of any of our product candidates. Furthermore, any change in manufacturer of our product candidates or approved products, if any, would require new regulatory approvals, which could delay completion of clinical trials or disrupt commercial supply of approved products.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer, we may have difficulty transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

If our current research collaborators or scientific advisors and employees terminate their relationships with us or develop relationships with our competitors, our ability to discover antibodies and to conduct research and development could be adversely affected.

The responsibility of overseeing research and development of our product candidates is concentrated among a number of key research collaborators and/or scientific advisors. There can be no assurance that there will not be a detrimental impact on us if one or more of these key research collaborators and/or scientific advisors were to cease relationship or employment with us, potentially as a result of lateral recruitment by existing or new competitors. As a result, this may adversely affect our ability to conduct research and development on antibody product candidates.

Furthermore, our ability to continue to conduct and expand operations depends on our ability to attract and retain a large and growing number of personnel. The ability to meet our expertise needs, including the ability to find qualified personnel to fill positions that become vacant at our research and development department or to collaborate with us in research and development efforts, while controlling our costs, is generally subject to numerous external factors, including the availability of a sufficient number of qualified persons in the biopharmaceutical industry, the unemployment levels within those markets, prevailing wage rates, changing demographics, health and other insurance costs and adoption of new or revised employment and labor laws and regulations. If we are unable to locate, to attract or to retain qualified personnel, the quality of services and products provided to customers may decrease and our financial performance may be adversely affected. In addition, if costs of labor or related costs to maintain relationships with research collaborators increase for other reasons or if new or revised labor laws, rules or regulations or healthcare laws are adopted or implemented that further increase labor costs, our business, financial condition and results of operations could be materially adversely affected.

We may not be able to attract and retain key senior management members or research and development personnel.

Our future success depends upon the continuing services of members of our senior management team and key research and development personnel and consultants. In particular, Peter Luo, our Chief Executive Officer, Fangyong (Felix) Du, our Chief Technology Officer, Hua Gong, our Chief Operating Officer and Head of Clinical Development and Precision Medicine, JC Xu, our Chief Scientific Officer, Qinghai Zhao, our Chief Manufacturing Officer and Yu (Albert) Ren, our Chief Strategy and Corporate Development Officer are crucial to our research and development and operations. Although we typically require our key personnel to enter into non-compete and confidentiality agreements with us, we cannot prevent them from joining our competitors after the non-compete period. The loss of their services could adversely impact our ability to achieve our business objectives. If one or more of our senior management or key clinical and scientific personnel are unable or unwilling to continue in their present positions or joins a competitor or forms a competing company, we may not be able to replace them in a timely manner or at all, which will have a material and adverse effect on our business, financial condition and results of operations. We do not maintain “key person” insurance for any of our executives or other employees.

In addition, the continued growth of our business depends on our ability to hire additional qualified personnel with expertise in molecular biology, chemistry, biological information processing, computational biology, software, engineering, sales, marketing, and technical support. We compete for qualified management and scientific personnel with other life science and technology companies, universities, and research institutions in China and overseas. Competition for these individuals is intense, and the turnover rate can be high. Failure to attract and retain management and scientific and engineering personnel could prevent us from pursuing collaborations or developing our product candidates or technologies.

We face risks related to health epidemics, severe weather conditions and other outbreaks.

China has in the past experienced significant natural disasters, including earthquakes, extreme weather conditions, as well as health scares related to epidemic diseases, and any similar event could materially impact our business in the future. If a disaster or other disruption were to occur in the future that affects the regions where we operate our business, our operations could be materially and adversely affected due to loss of personnel and damage to property. Even if we are not directly affected, such a disaster or disruption could affect the operations or financial conditions of our customers, which could harm our results of operations.

In addition, our business could be affected by public health epidemics and pandemics, such as the outbreak of avian influenza, severe acute respiratory syndrome, or SARS, Zika virus, Ebola virus or other diseases. In late December 2019, a strain of SARS-CoV-2, which causes the COVID-19 disease, was reported to have surfaced in Wuhan, China. On January 30, 2020, the World Health Organization reportedly declared this COVID-19 outbreak a health emergency of international concern. On February 28, 2020, the World Health Organization reportedly increased the assessment of the risk of spread and the risk of impact of COVID-19 to very high at global level. In March 2020, the World Health Organization declared the COVID-19 a pandemic. As COVID-19 has evolved into a worldwide health crisis, it has resulted in adverse effects in the global economy and financial markets, such as significant declines in the global stock markets. If the COVID-19 outbreak is not effectively controlled globally, our business and results of operations could be adversely affected to the extent the COVID-19 outbreak harms the Chinese or world economy generally. The extent to which the COVID-19 outbreak impacts our financial condition and results of operations for the full year of 2020 cannot be reasonably estimated at this time and will depend on future developments that currently cannot be predicted, including the development of a COVID-19 vaccine and the actions taken to contain the COVID-19 outbreak, among others. Any future outbreak of public health epidemics may restrict economic activities in affected regions, disrupt our business operations and adversely affect our results of operations.

The COVID-19 pandemic could adversely impact our business, including our clinical trials.

The spread of the COVID-19 coronavirus in many countries continues to adversely impact global economic activity and has contributed to significant volatility and negative pressure in financial markets and supply chains. The pandemic has had, and could have a significantly greater, material adverse effect on the global economy. The pandemic has resulted, and may continue to result for an extended period, in significant disruption of global financial markets, which may reduce our ability to access capital in the future, which could negatively affect our liquidity.

The COVID-19 pandemic has adversely affected the clinical development of our product candidates. Our clinical development program timelines could continue to be negatively affected by COVID-19, which could materially and adversely affect our business, financial condition, and results of operations. Further, due to “shelter in place” orders and other public health guidance measures, we may be required to implement a work-from-home policy for all staff members excluding those necessary to maintain minimum basic operations. In such an instance, our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay or otherwise adversely impact our business. For example, with our personnel working from home, some of our research activities that require our personnel to be in our laboratories may be delayed.

The COVID-19 pandemic may impact our workforce, supply chains or distribution networks or otherwise impact our ability to restock our medical device and supply inventories and depending upon the severity of the COVID-19 pandemic's continued spread in the United States and other countries, we may experience disruptions that could severely impact our business and clinical trials, including:

- limitation of company operations, including work from home policies and office closures;
- one or more key officers and/or employees could contract COVID-19 or otherwise be adversely affected by the virus;
- delays or difficulties in receiving deliveries of critical experimental materials;
- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation or expansion, including difficulties in recruiting clinical site investigators and clinical site staff;
- increased rates of patients withdrawing from our clinical trials following enrollment as a result of contracting COVID-19 or other health conditions or being forced to quarantine;
- delays or disruptions in preclinical experiments and IND-enabling studies due to restrictions of on-site staff and unforeseen circumstances at contract research organizations, or CROs, and vendors;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- changes in regulations as part of a response to the COVID-19 pandemic, which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- delays in necessary interactions with regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government or contractor personnel;
- refusal of the FDA or other regulatory authorities to accept data from clinical trials in affected geographies; and
- limitations in employee resources that would otherwise be focused on our business, including the conduct of our clinical trials, such as because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people.

The global outbreak of the COVID-19 coronavirus continues to rapidly evolve. The extent to which the COVID-19 coronavirus may impact our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions and social distancing in China, the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

We have limited insurance coverage, and any claims beyond our insurance coverage may result in us incurring substantial costs and a diversion of resources.

We maintain insurance policies that are required under PRC laws and regulations as well as insurance based on our assessment of our operational needs and industry practice. We also maintain liability insurance covering our clinical trials as well as maintain key-man insurance policy. In line with industry practice in the PRC, we have elected not to maintain certain types of insurances, such as business interruption insurance. Our insurance coverage may be insufficient to cover any claim for product liability, damage to our fixed assets or employee injuries. Any uninsured risks may result in substantial costs and the diversion of resources, which could adversely affect our results of operations and financial condition.

We have adopted a share incentive plan and will continue to grant share-based awards in the future, which may increase expenses associated with share-based compensation. Exercise of the awards granted will increase the number of our outstanding ordinary shares, which may adversely affect the market price of our ADSs.

We adopted the Second Amended and Restated Share Incentive Plan in December 2019 and the 2021 Performance Incentive Plan in January 2021, which we refer to as the 2019 Plan and the 2021 Plan, respectively, in this annual report, to enhance our ability to attract and retain exceptionally qualified individuals and to encourage them to acquire a proprietary interest in the growth and performance of us. We have terminated the authority to grant additional awards under the 2019 Plan and all future awards will be granted under the 2021 Plan. Therefore, the effective maximum number of shares issuable under the 2019 Plan will be 10,828,501. A total of 2,994,000 of our ordinary shares is authorized for issuance with respect to awards granted under the 2021 Plan. As of March 31, 2021, the aggregate number of our ordinary shares underlying our outstanding awards under the 2019 Plan is 3,681,522. As of March 31, 2021, we have granted 631,733 shares awards under the 2021 Plan. See “Item 6 Directors, Senior Management and Employees—Share Incentive Plan. “We believe the granting of share-based awards is of significant importance to our ability to attract and retain key personnel and employees, and we will continue to grant share-based compensation to employees in the future. As a result, our expenses associated with share-based compensation may increase, which may have an adverse effect on our results of operations.

Our employees, third-party suppliers, consultants and commercial partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, third-party suppliers, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of the NMPA and overseas regulators that have jurisdictions over us, comply with healthcare fraud and abuse laws and regulations in China and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We currently have a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and our code of conduct and the other precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses, or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could result in the imposition of significant civil, criminal and administrative penalties, including, without limitation, damages, monetary fines, individual imprisonment, disgorgement of profits, contractual damages, reputational harm, diminished profits and future earnings, additional reporting or oversight obligations if we become subject to a corporate integrity agreement or other agreement to resolve allegations of noncompliance with the law and curtailment or restructuring of our operations, which could have a significant impact on our business. Whether or not we are successful in defending against such actions or investigations, we could incur substantial costs, including legal fees and divert the attention of management in defending ourselves against any of these claims or investigations.

We may be subject to liability lawsuits arising from our clinical trials.

We currently carry liability insurance covering our clinical trials. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or which is in excess of the limits of our insurance coverage. Our insurance policies also contain various exclusions, and we may be subject to particular liability claims for which we have no coverage. We will have to pay any amount awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. In addition, if we cannot successfully defend ourselves against such claims, we may incur substantial liabilities and be required to suspend or delay our ongoing clinical trials. Even a successful defense would require significant financial and management resources.

Regardless of the merits or eventual outcome, liability claims may result in significant negative consequences to our business and prospects, including, but not limited to:

- decreased demand for our product candidates or any resulting products;
- damage to our reputation;
- withdrawal of other clinical trial participants;
- costs to defend the related litigation;
- a diversion of our management's time and resources;
- substantial monetary awards to trial participants or patients;
- inability to commercialize our product candidates; and
- a decline in the market price of our ADSs.

We are subject to changing law and regulations regarding regulatory matters, corporate governance and public disclosure that have increased both our costs and the risk of noncompliance.

We are subject to rules and regulations by various governing bodies, including, for example, the FDA, the NMPA, the SEC, which is charged with the protection of investors and the oversight of companies whose securities are publicly traded, and the various regulatory authorities in China, the United States, the EU, the Cayman Islands, and to new and evolving regulatory measures under applicable law. Our efforts to comply with new and changing laws and regulations have resulted in and are likely to continue to result in, increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities.

Moreover, because these laws, regulations and standards are subject to varying interpretations, their application in practice may evolve over time as new guidance becomes available. This evolution may result in continuing uncertainty regarding compliance matters and additional costs necessitated by ongoing revisions to our disclosure and governance practices. If we fail to address and comply with these regulations and any subsequent changes, we may be subject to penalties and our business may be harmed.

We may be exposed to liabilities under the U.S. Foreign Corrupt Practices Act and Chinese anti-corruption laws, and any determination that we have violated these laws could have a material adverse effect on our business or our reputation.

We are subject to anti-bribery laws in China that generally prohibit companies and their intermediaries from making payments to government officials for the purpose of obtaining or retaining business or securing any other improper advantage. In addition, although currently our primary operating business is in China, we are subject to the Foreign Corrupt Practices Act, or the FCPA. The FCPA generally prohibits us from making improper payments to non-U.S. officials for the purpose of obtaining or retaining business. We are also subject to the anti-bribery laws of other jurisdictions, particularly China. As our business expands, the applicability of the FCPA and other anti-bribery laws to our operations will increase. Our procedures and controls to monitor anti-bribery compliance may fail to protect us from reckless or criminal acts committed by our employees or agents. If we, due to either our own deliberate or inadvertent acts or those of others, fail to comply with applicable anti-bribery laws, our reputation could be harmed and we could incur criminal or civil penalties, other sanctions and/or significant expenses, which could have a material adverse effect on our business, including our financial condition, results of operations, cash flows and prospects.

Any failure to comply with applicable regulations and industry standards or obtain various licenses and permits could harm our reputation, business, results of operations and prospects.

A number of governmental agencies or industry regulatory bodies in China, the United States and other applicable jurisdictions impose strict rules, regulations and industry standards governing biopharmaceutical research and development activities, which apply to us. Our or our CROs' failure to comply with such regulations could result in the termination of ongoing research, administrative penalties imposed by regulatory bodies or the disqualification of data for submission to regulatory authorities. This could harm our business, reputation, prospects for future work and results of operations. For example, if we or our CROs were to treat research animals inhumanely or in violation of international standards set out by the Association for Assessment and Accreditation of Laboratory Animal Care, it could revoke any such accreditation and the accuracy of our animal research data could be questioned.

If we or our third-party research collaborators or other contractors or consultants fail to comply with environmental, fire protection, drainage or health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We and third parties, such as our CROs, are subject to numerous environmental, fire protection, drainage or health and safety laws and regulations, including but not limited to those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes discharge of stationary pollution sources. The cost of compliance with health and safety regulations is substantial. Our business activities involve the controlled use of hazardous materials. Our research and development activities involve the controlled storage, use and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials, which could cause an interruption of our commercialization efforts, research and development efforts and business operations. We cannot guarantee that the safety procedures utilized by our partners and by third-party manufacturers and suppliers with whom we may contract will comply with the standards prescribed by laws and regulations or will eliminate the risk of accidental contamination or injury from these materials. In such an event, we could be held liable for any resulting damages, and such liability could exceed our resources. In addition, we may be required to incur substantial costs to comply with current or future environmental, health and safety laws and regulations which are complex, change frequently and have tended to become more stringent. We do not currently carry biological or hazardous waste insurance coverage. In the event of an accident or environmental discharge, we may be held liable for any consequential damage and any resulting claims for damages, which may exceed our financial resources and may materially adversely affect our business, financial condition, results of operations and future growth prospects, and the value of our ADSs.

Security breaches, loss of data, and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability, which could adversely affect our business and our reputation.

In the ordinary course of our business, we collect and store preclinical trial data and clinical trial data which could be sensitive, including research and development information, health-related information, personally identifiable information, intellectual property, and proprietary business information owned or controlled by ourselves or other parties. We manage and maintain our applications and data utilizing a combination of on-site systems and cloud-based application systems. We utilize external security and infrastructure vendors to manage parts of our data centers. We also communicate sensitive data with third parties. We face a number of risks relative to protecting this critical information, including material system failure or security breach, loss of access risk, inappropriate use or disclosure, inappropriate modification, and the risk of our being unable to adequately monitor, audit, and modify our controls over our critical information. This risk extends to the third-party vendors and subcontractors we use to manage this sensitive data and third-party collaborators who share with us sensitive data.

Despite the implementation of security measures to protect sensitive data from unauthorized access, use or disclosure, our information technology and infrastructure may be vulnerable to attacks by hackers or viruses or breached due to employee error, malfeasance, or other malicious or inadvertent disruptions that could result in unauthorized access to, use or disclosure of, corruption of, or loss of sensitive, and/ or proprietary data, including health-related and other personal information, and could subject us to significant liabilities and regulatory and enforcement actions, and reputational damage. The COVID-19 pandemic is generally increasing the attack surface available to criminals, as more companies and individuals work online and work remotely, and as such, the risk of a cybersecurity incident potentially occurring, and our investment in risk mitigations against such an incident, is increasing. For example, there has been an increase in phishing and spam emails as well as social engineering attempts from “hackers” hoping to use the COVID-19 pandemic to their advantage. In addition, while we have implemented security measures to prevent unauthorized access to patient data, such data is currently accessible through multiple channels, and there is no guarantee we can protect our data from breach. Unauthorized access, loss, or dissemination could also result in delays of our product development and regulatory approval efforts as well as damage our reputation.

For example, the loss of clinical trial data from completed or ongoing clinical trials could result in delays in any regulatory approval or clearance efforts and significantly increase our costs to recover or reproduce the data, and subsequently commercialize the product. If we or our third-party collaborators, consultants, contractors, suppliers, or service providers were to suffer an attack or breach, for example, that resulted in the unauthorized access to or use or disclosure of health-related or other personal information, we may have to notify consumers, partners, collaborators, government authorities, and the media, and may be subject to investigations, civil penalties, administrative and enforcement actions, and litigation, any of which could harm our business and reputation. Likewise, we rely on our third-party research institution collaborators and other third parties to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business.

Our insurance policies may not be adequate to compensate us for the potential losses arising from such disruptions, failure, or security breach. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and defending a suit, regardless of its merit, could be costly, divert management attention, and harm our reputation.

Failure to comply with existing or future laws and regulations related to privacy or data security could lead to government enforcement actions, which could include civil or criminal fines or penalties, private litigation, other liabilities, and/or adverse publicity. Compliance or the failure to comply with such laws could increase the costs of our products and services, limit their use or adoption, and otherwise negatively affect our operating results and business.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of personal information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Regulatory authorities in virtually every jurisdiction in which we operate have implemented and are considering a number of legislative and regulatory proposals concerning personal data protection.

Regulatory authorities in China have implemented and are considering a number of legislative and regulatory proposals concerning data protection. For example, China’s Cyber Security Law, which became effective in June 2017, created China’s first national-level data protection for “network operators,” which may include all organizations in China that provide services over the internet or another information network. Numerous regulations, guidelines and other measures are expected to be adopted under the umbrella of the Cyber Security Law. Drafts of some of these measures have now been published, including (i) the draft rules on cross-border data transfers of personal information and important data published by the China Cyberspace Administration in 2017, and draft rules on measures for security assessment for cross-border transfer of personal information published by China Cyberspace Administration in 2019, which may, upon enactment, require security review before transferring human health-related data out of China, and (ii) the Draft Data Security Law promulgated by the Standing Committee of PRC National People’s Congress in 2020, which outlines the main system framework of data security protection. In addition, certain industry-specific laws and regulations affect the collection and transfer of personal data in China. For example, the PRC State Council promulgated Regulations on the Administration of Human Genetic Resources (effective in July 2019), which require approval from or filings with the Science and Technology Administration Department of the State Council where human genetic resources, or HGR, are involved in any international collaborative project and additional approval for any export or cross-border transfer of the HGR samples or human genetic resource information. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices, potentially resulting in confiscation of HGR samples and human genetic resource information and administrative fines or in worst cases, criminal penalties. In addition, the interpretation and application of data and personal information protection laws in China and elsewhere are often uncertain and in flux.

In the United States, we and our partners may be subject to state and federal laws and regulations that govern data privacy, protection and security. Numerous laws and regulations, including security breach notification laws, health information privacy laws, and consumer protection laws, govern the collection, use, disclosure and protection of health-related and other personal information. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, and regulations implemented thereunder (collectively, “HIPAA”). Depending on the facts and circumstances, we could be subject to criminal penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Even when HIPAA does not apply, according to the Federal Trade Commission, or the FTC, violating consumers’ privacy rights or failing to take appropriate steps to keep consumers’ personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act. The FTC expects a company’s data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

In addition, certain state and non-U.S. laws, such as the European Union General Data Protection Regulation, or the GDPR, govern the privacy and security of health information and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. For example, California recently enacted legislation, the California Consumer Privacy Act, or CCPA, which went into effect January 1, 2020. The CCPA, among other things, creates new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. In Europe, the GDPR went into effect in May 2018 and introduces strict requirements for processing the personal data of individuals within the EU, and the European Economic Area, or the EEA. In addition, the GDPR increases the scrutiny of transfers of personal data from clinical trial sites located in the EEA to the United States and other jurisdictions that the European Commission does not recognize as having “adequate” data protection laws, and recent legal developments in Europe have created complexity and compliance uncertainty regarding certain transfers of personal data from the EEA. For example, on July 16, 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-US Privacy Shield Framework, or Privacy Shield, under which personal data could be transferred from the EU and the EEA to United States entities who had self-certified under the Privacy Shield scheme. Moreover, it is uncertain whether the standard contractual clauses will also be invalidated by the European courts or legislature. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to A20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Additionally, following Brexit, companies will have to comply with the GDPR and the GDPR as incorporated into United Kingdom national law, the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. The relationship between the U.K. and the EU in relation to certain aspects of data protection law remains unclear, for example around how data can lawfully be transferred between each jurisdiction, which exposes us to further compliance risk.

Given the variability and evolving state of these laws, we face uncertainty as to the exact interpretation of the new requirements, and we may be unsuccessful in implementing all measures required by regulators or courts in their interpretation.

We expect that we will continue to face uncertainty as to whether our efforts to comply with evolving obligations under global data protection, privacy and security laws will be sufficient. Any failure or perceived failure by us to comply with applicable laws and regulations could result in reputational damage or proceedings or actions against us by governmental entities, individuals or others. These proceedings or actions could subject us to significant civil or criminal penalties and negative publicity, result in the delayed or halted transfer or confiscation of certain personal information, require us to change our business practices, increase our costs and materially harm our business, prospects, financial condition and results of operations. In addition, our current and future relationships with customers, vendors, pharmaceutical partners and other third parties could be negatively affected by any proceedings or actions against us or current or future data protection obligations imposed on them under applicable law, including the GDPR. In addition, a data breach affecting personal information, including health information, could result in significant legal and financial exposure and reputational damage that could potentially have an adverse effect on our business.

Business disruptions could seriously harm our future revenue, increase our costs and expenses, and have adverse effect on our financial condition.

Our operations and third parties with which we have collaborations could be subjected to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. In addition, we partially rely on our CROs for conducting research and development, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Although we maintain incident management and disaster response plans, in the event of a major disruption caused by a natural disaster or man-made problem, such as power disruptions, computer viruses, data security breaches or terrorism, we may be unable to continue our operations and may endure system interruptions, reputational harm, delays in our development activities, lengthy interruptions in service, breaches of data security and loss of critical data, any of which could adversely affect our business, results of operations and financial condition.

If we fail to implement and maintain an effective system of internal controls, we may be unable to accurately or timely report our results of operations or prevent fraud, and investors' confidence and the market price of our ADSs may be materially and adversely affected.

Prior to our initial public offering, we were a private company with limited accounting personnel and other resources with which to address our internal controls and procedures. Our management has not completed an assessment of the effectiveness of our internal control over financial reporting, and our independent registered public accounting firm has not conducted an audit of our internal control over financial reporting. In the course of auditing our consolidated financial statements as of December 31, 2019 and 2020 and for each of the three years in the period ended December 31, 2020, we and our independent registered public accounting firm identified two material weaknesses in our internal control over financial reporting and other control deficiencies as of December 31, 2019 and 2020. A “material weakness” is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company’s annual or interim financial statements will not be prevented or detected on a timely basis. The material weaknesses identified relate to:

- Our lack of sufficient and competent financial reporting and accounting personnel with appropriate knowledge of U.S. GAAP and SEC reporting and compliance requirements; and
- Our lack of sufficient documented financial closing policies and procedures, specifically those related to period end expenses cut-off and accruals.

We have taken measures and plan to continue to take measures to remedy the material weaknesses. For details, please refer to “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Internal Control over Financial Reporting.” The implementation of these measures may not fully address the material weaknesses in our internal control over financial reporting, and we cannot conclude that they have been fully remedied. Our failure to correct these material weaknesses or our failure to discover and address any other material weaknesses could result in inaccuracies in our financial statements and could also impair our ability to comply with applicable financial reporting requirements and related regulatory filings on a timely basis.

We are a public company in the United States subject to the Sarbanes-Oxley Act of 2002. Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, will require that we include a report from management on our internal control over financial reporting in our annual report on Form 20-F beginning with our annual report for the fiscal year ending December 31, 2021. In addition, once we cease to be an “emerging growth company” as such term is defined in the JOBS Act, our independent registered public accounting firm must attest to and report on the effectiveness of our internal control over financial reporting. Our management may conclude that our internal control over financial reporting is not effective. Moreover, even if our management concludes that our internal control over financial reporting is effective, our independent registered public accounting firm, after conducting its own independent testing, may issue a report that is qualified if it is not satisfied with our internal controls or the level at which our controls are documented, designed, operated or reviewed, or if it interprets the relevant requirements differently from us. In addition, after we become a public company, our reporting obligations may place a significant strain on our management, operational and financial resources and systems for the foreseeable future. We may be unable to timely complete our evaluation testing and any required remediation.

During the course of documenting and testing our internal control procedures, in order to satisfy the requirements of Section 404, we may identify weaknesses and deficiencies in our internal control over financial reporting. In addition, if we fail to maintain the adequacy of our internal control over financial reporting, as these standards are modified, supplemented or amended from time to time, we may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting in accordance with Section 404. Generally speaking, if we fail to achieve and maintain an effective internal control environment, we could suffer material misstatements in our financial statements and fail to meet our reporting obligations, which would likely cause investors to lose confidence in our reported financial information. This could, in turn, limit our access to capital markets, harm our results of operations and lead to a decline in the trading price of our ADSs. Additionally, ineffective internal control over financial reporting could expose us to increased risk of fraud or misuse of corporate assets and subject us to potential delisting from the stock exchange on which we list, regulatory investigations and civil or criminal sanctions.

Risks Related to Our Intellectual Property

It is difficult and costly to protect our proprietary rights and technology, and we may not be able to protect our intellectual property rights throughout the world.

Our commercial success will depend, in part, on our ability to obtain, maintain and defend patent and other intellectual property protection (including trademarks and trade secrets) with respect to our product candidates. We cannot be certain that patents will be issued or granted with respect to our patent applications that are currently pending, or that issued or granted patents will not later be found to be invalid and/or unenforceable, be interpreted in a manner that does not adequately protect our product candidates, or otherwise provide us with any competitive advantage. Additionally, the patent applications in respect of patents licensed under our in-license arrangements may not be issued or granted, and as a result, we may not be able to have adequate protection with respect to such patents.

The patent position of biotechnology and pharmaceutical companies is generally uncertain because it involves complex legal and factual considerations. Patent applications we have filed may not be granted or issued as valid enforceable patents. Moreover, some of our patents and patent applications may in the future be, co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owned interest in such patents or patent applications, such co-owners may be able to license or transfer their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects. As such, we do not know the degree of future protection that we will have on our product candidates and technology, if any, and a failure to obtain adequate intellectual property protection with respect to our product candidates could have a material adverse impact on our business.

Composition-of-matter patents on the active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. Method-of-use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our products for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products “off-label.” Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute. We endeavor to seek composition-of-matter patent protection for all of our product candidates. Where appropriate, we also seek method-of-use patents and patents protecting other aspects of our product candidates, including processes for discovery and manufacturing.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. The issuance of a patent is not conclusive as to its scope, validity or enforceability, and our owned and in-licensed patents may be challenged in the courts or patent offices in the PRC and abroad. For example, we may become involved in opposition, interference, derivation, inter partes review or other similar proceedings challenging our patent rights, and the outcome of any proceedings are highly uncertain. Such challenges may result in the patent claims of our owned or in-licensed patents being narrowed, invalidated or held unenforceable, which could limit our ability to stop or prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or otherwise provide us with a competitive advantage.

Despite the measures we can take to increase our likelihood of obtaining patent and other intellectual property protections with respect to our product candidates, there can be no assurance that the existence, validity, enforceability, or scope of our intellectual property rights will not be challenged by a third party, or that we can obtain sufficient scope of claim in those patents to prevent a third party from competing against our product candidates. For example, in an infringement proceeding, a court may hold that patent rights or other intellectual property rights owned by us are invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the ground that our patent rights or other intellectual property rights do not cover the technology in question. An adverse result in any litigation proceedings could put our patent, as well as any patents that may issue in the future from our pending patent applications, at risk of being invalidated, held unenforceable or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

In addition, if we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the National Intellectual Property Administration of China, or NIPA, or the applicable foreign counterpart, or made a misleading statement, during prosecution. Although we believe that we have conducted our patent prosecution in accordance with all applicable duty of candor and in good faith, the outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Even if a defendant does not prevail on a legal assertion of invalidity and/or unenforceability, our patent claims may be construed in a manner that would limit our ability to enforce such claims against the defendant and others.

Third parties may also raise similar claims before administrative bodies in the PRC or abroad, even outside the context of litigation. Such mechanisms include ex parte re-examination, inter partes review, post-grant review, derivation and equivalent proceedings, such as opposition proceedings. Such legal proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our product candidates. The outcome following legal assertions of invalidity and unenforceability can be unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we may lose part or all of the patent protection on our product candidates. Any loss of patent protection could have a material adverse impact on one or more of our product candidates and our business.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. We may also rely on trade secret protection as temporary protection for concepts that may be included in a future patent filing. However, trade secret protection will not protect us from innovations that a competitor develops independently of our proprietary know-how. If a competitor independently develops a technology that we protect as a trade secret and files a patent application on that technology, then we may not be able to patent that technology in the future, may require a license from the competitor to use our own know-how, and if the license is not available on commercially viable terms, then we may not be able to launch our product. Although we require our employees to assign their inventions to us, and require our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of different countries do not protect proprietary rights to the same extent or in the same manner as the laws of the PRC. We may encounter significant problems in protecting and defending our intellectual property both in the PRC and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, and this scenario could materially adversely affect our business, financial condition and results of operations.

Moreover, trade secrets are difficult to protect, and we have limited control over the protection of trade secrets used by our collaborators and suppliers. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors or use such information to compete with us. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. If our confidential or proprietary information is divulged to or acquired by third parties, including our competitors, our competitive position in the marketplace will be adversely affected and this would have a material adverse effect on our business.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries do not favor the enforcement or protection of patents, trade secrets and other intellectual property, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in certain countries could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. We and our contractors and partners operate in certain countries that are at heightened risk of theft of technology, data and intellectual property through direct or indirect intrusion by private parties or international actors, including those affiliated with or controlled by state actors. Accordingly, our efforts to protect or enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the pharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in various countries could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. For example, patent reform legislation in the United States includes provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents via post-grant proceedings. The Leahy-Smith Act and any continuing changes in patent laws and regulations in various patent jurisdictions could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our or our collaboration partners' patent applications and the enforcement or defense of our or our collaboration partners' issued patents, all of which could harm our business, results of operations, financial condition and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain due to changes in law and courts' interpretation of the law. For example, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Other courts in the United States, for example, have heightened the bar for broadly claiming antibodies. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Additionally, there are periodic proposals for changes to the patent laws of China, United States and other countries that, if adopted, could impact our ability to enforce our proprietary technology. Depending on future actions by the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Similarly in China, intellectual property laws are constantly evolving, with efforts being made to improve intellectual property protection in China. For example, a Draft Amendment to the PRC Patent Law was released in January 2019 and updated in July 2020, which proposes introduction of patent term extensions to eligible innovative drug patents. If adopted, the terms of our Chinese patents may be eligible for extension and allow us to extend patent protection of our products, and the terms of the patents owned by third parties may also be extended, which may in turn affect our ability to commercialize our products candidates, if and when approved, without facing infringement risks. The length of any such patent term extension is uncertain. If we are required to delay commercialization for an extended period of time, technological advances may develop and new competitor products may be launched, which may render our product non-competitive. We also cannot guarantee that other changes to Chinese intellectual property laws would not have a negative impact on our intellectual property protection.

We may not be successful in obtaining or maintaining necessary rights for our development pipeline through acquisitions and licensing deals.

Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire and maintain licenses or other rights to use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, or other intellectual property rights from third parties that we identify. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects for growth.

Additionally, we may sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. These institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

Licensing of intellectual property involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;

- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patents and other rights to third parties;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- our right to transfer or assign the license; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we license in the future prevent or impair our ability to maintain our licensing arrangements on acceptable terms, we may not be able to successfully develop and commercialize the affected product candidates, which would have a material adverse effect on our business.

In addition, certain of our future agreements with third parties may limit or delay our ability to consummate certain transactions, may impact the value of those transactions, or may limit our ability to pursue certain activities. For example, we may in the future enter into license agreements that are not assignable or transferable, or that require the licensor's express consent in order for an assignment or transfer to take place.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful, and any unfavorable outcome from such litigation could limit our research and development activities and/or our ability to commercialize our product candidates.

Competitors may infringe our patent rights or misappropriate or otherwise violate our intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us, alleging that we infringed their patents. In addition, in a patent infringement proceeding, there is a risk that a court will decide that our asserted patents are invalid or unenforceable, in whole or in part, and that we do not have the right to stop the others from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the others from using the invention at issue on the grounds that our patents do not cover the alleged infringing activity or product. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties and other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects, and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that our asserted marks are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of our trademarks.

In any litigation involving our intellectual property, the award of monetary damages we receive may not be commercially valuable or even sufficient to cover our cost of bringing such action. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a material adverse effect on the price of our ADSs. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Our commercial success depends significantly on our ability to operate without infringing upon, misappropriating or otherwise violating the intellectual property rights of third parties.

The life sciences industry is subject to rapid technological change and substantial litigation regarding patent and other intellectual property rights. Our potential competitors in both the PRC and abroad, may have substantially greater resources than us and are likely to make substantial investments in patent portfolios and competing technologies, and may apply for or obtain patents that could prevent, limit or otherwise interfere with our ability to make, use and sell our products. Numerous third-party patents exist in fields relating to our products and technologies, and it is difficult for industry participants, including us, to identify all third-party patent rights relevant to our products and technologies. Moreover, because some patent applications are maintained as confidential for a certain period of time, we cannot be certain that third parties have not filed patent applications that will cover our products and technologies if they issue as patents.

Patents could be issued to third parties that we may ultimately be found to infringe. Third parties may have or obtain valid and enforceable patents or proprietary rights that could block us from using our technology. Our failure to obtain or maintain a license from third parties to any technology that we require may materially harm our business, financial condition and results of operations. Furthermore, we would be exposed to a threat of litigation.

Third-party intellectual property right holders may also actively bring infringement or other intellectual property-related claims against us, even if we have received patent protection for our technologies, products, and services. Regardless of the merit of third parties claims against us for infringement, misappropriation or violations of their intellectual property rights, such third parties may seek and obtain injunctive or other equitable relief, which could effectively block our ability to perform clinical trials or develop, manufacture or sell our products. Further, if a patent infringement suit were brought against us, we could be forced to temporarily or permanently stop or delay our development or regulatory approval process or other activities that are the subject of such suit. Defense of these claims, even if such claims are resolved in our favor, could cause us to incur substantial expenses and be a substantial diversion of our employee resources even if we are ultimately successful. Any adverse ruling or perception of an adverse ruling in defending ourselves could have a material adverse impact on our cash position and stock price. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a material adverse effect on the price of our ADSs. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. The occurrence of any of these events may have a material adverse effect on our business, results of operation, financial condition or cash flows.

Obtaining and maintaining patent protection depend on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent authorities, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The NIPA, and various foreign governmental patent agencies including the USPTO, JPO, and EPO require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application and prosecution process. Periodic maintenance fees, renewal fees, annuity fees, and various other governmental fees on patents and/or applications will be due to be paid to the NIPA and various other governmental patent agencies outside of China in several stages over the lifetime of the patents and/or applications. We employ reputable professionals and rely on such third parties to help us comply with these requirements and effect payment of these fees with respect to the patents and patent applications that we own. Noncompliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official communications within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case, which could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

We may not enter into invention assignment and confidentiality agreements with all of our employees and third parties and such agreements may not prevent ownership disputes or unauthorized disclosure of trade secrets and other proprietary information.

We rely in part upon unpatented or unpatentable trade secrets, know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by entering into agreements, including confidentiality agreements and non-disclosure agreements, with parties that have a need for access to them, such as certain of our employees, consultants, academic institutions, corporate partners and, other third-party service providers. Nevertheless, there can be no guarantee that an employee or a third party will not make an unauthorized use or disclosure of our proprietary confidential information. This might happen intentionally or inadvertently. It is possible that a competitor will gain access to such information and make use of such information, and that our competitive position will be compromised, in spite of any legal action we might take against persons making such unauthorized disclosures. In addition, to the extent that our employees, consultants or contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors or business partners might intentionally or inadvertently disclose our trade secret information to competitors or our trade secrets may otherwise be misappropriated. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable.

We sometimes engage individuals or research institutions to conduct research relevant to our business. The ability of these individuals or research institutions to publish or otherwise publicly disclose data and other information generated during the course of their research is subject to certain contractual limitations. These contractual provisions may be insufficient or inadequate to protect our confidential information. If we do not apply for patent protection prior to such publication, or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized, which could adversely affect our business, financial condition and results of operations.

We also seek to enter agreements with our employees and consultants that obligate them to assign any inventions created during their work for us to us. However, we may not obtain these agreements in all circumstances and the assignment of intellectual property under such agreements may not be self-executing. And it is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants who are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets and inventions through such breaches or violations. Any of the foregoing could have a material and adverse effect on our business, financial condition and results of operations.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Some of our employees and consultants were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and our specific personnel.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Also, former employees may become employed by competitors who develop similar technology, and could assist the competitor in designing around our patents. While it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and litigation may be necessary to defend against these and other claims challenging inventorship or our ownership of our patents, trade secrets or other intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Intellectual property rights do not necessarily protect us from all potential threats to our competitive advantages.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to independently develop similar or alternative technologies or designs that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or may in the future exclusively license, which could result in the patent applications not issuing or being invalidated after issuing;
- we might not have been the first to file patent applications covering certain of our inventions, which could result in the patent applications not issuing or being invalidated after issuing;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive services and products for commercialization in our major markets;
- we may fail to develop additional proprietary technologies that are patentable;
- we may fail to apply for or obtain adequate intellectual property protection in all the jurisdictions in which we operate; and
- the patents of others may have an adverse effect on our business, for example by preventing us from commercializing one or more of our product candidates for one or more indications.

Any of the aforementioned threats to our competitive advantage could have a material adverse effect on our business.

Patent terms may not be sufficient to effectively protect our product candidates.

In most countries in which we plan to file applications for patents, the term of an issued patent is generally 20 years from the earliest claimed filing date of the priority application to which a non-provisional patent application in the applicable country claims priority. Although various extensions may be available in various countries, the life of a patent and the protection it affords are limited. Even if patents covering our product candidates are obtained, we may be open to competition from other companies once our patent rights expire. Accordingly, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Excluding any patent term adjustment and patent term extension, our currently issued patents are expected to expire from 2033 to 2034. As a result, our patent portfolio may not provide us with sufficient rights over a sufficient length of time to exclude others from commercializing products similar or identical to ours.

Uncertainty of the length of patent term extensions and data and market exclusivities for our pharmaceutical products could increase the risk of generic competition.

In the United States, the Federal Food, Drug, and Cosmetic Act, as amended by the law generally referred to as the “Hatch-Waxman Amendments,” provides the opportunity for patent-term restoration of up to five years to reflect patent term lost during certain portions of product development and the FDA regulatory review process. The Hatch-Waxman Amendments also have a process for patent linkage, pursuant to which FDA will stay approval of certain follow-on applications during the pendency of litigation between the follow-on applicant and the patent holder or licensee, generally for a period of 30 months. Finally, the Hatch-Waxman Amendments provide for statutory exclusivities that can prevent submission or approval of certain follow-on marketing applications. For example, federal law provides a five-year period of exclusivity within the United States to the first applicant to obtain approval of a new chemical entity (as defined) and three years of exclusivity protecting certain innovations to previously approved active ingredients where the applicant was required to conduct new clinical investigations to obtain approval for the modification. Similarly, the Orphan Drug Act provides seven years of market exclusivity for certain drugs to treat rare diseases, where FDA designates the product candidate as an orphan drug and the drug is approved for the designated orphan indication.

These provisions, designed to promote innovation, can prevent competing products from entering the market for a certain period of time after FDA grants marketing approval for the innovative product.

In China, however, there is no currently effective law or regulation providing patent term extension, patent linkage, or data exclusivity (referred to as regulatory data protection). Therefore, a lower-cost generic drug can emerge onto the market much more quickly. Chinese regulators have set forth a framework for integrating patent linkage and data exclusivity into the Chinese regulatory regime, as well as for establishing a pilot program for patent term extension. To be implemented, this framework will require adoption of regulations. To date, the NMPA has issued several draft implementing regulations in this regard for public comment but no regulations have been formally issued. These factors result in weaker protection for us against generic competition in China than could be available to us in the United States until the relevant implementing regulations for extension, patent linkage, or data exclusivity are put into effect officially in China.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our products in all countries throughout the world would be prohibitively expensive. We may also encounter difficulties in protecting and defending such rights in foreign jurisdictions. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the jurisdictions of the registration of our intellectual properties. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products. Our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain jurisdictions. The legal systems of many other countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents in such countries.

Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

We may not be able to protect and enforce our trademarks.

We currently hold issued trademark registrations and have trademark applications pending, any of which may be the subject of a governmental or third-party objection, which could prevent the registration or maintenance of the same. If we are unsuccessful in obtaining trademark protection for our primary brands, we may be required to change our brand names, which could materially adversely affect our business. Moreover, as our products mature, our reliance on our trademarks to differentiate us from our competitors will increase, and as a result, if we are unable to prevent third parties from adopting, registering or using trademarks and trade dress that infringe, dilute or otherwise violate our trademark rights, or engaging in conduct that constitutes unfair competition, defamation or other violation of our rights, our business could be materially adversely affected. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

Risks Related to Doing Business in the PRC

Uncertainties with respect to the PRC legal system and changes in laws and regulations in China could adversely affect us.

Our operations in China are governed by the PRC laws and regulations. The PRC legal system is a civil law system based on written statutes. Unlike the common law system, prior court decisions under the civil law system may be cited for reference but have limited precedential value. In addition, any new PRC laws or changes in PRC laws and regulations related to, among other things, foreign investment and manufacturing in China could have a material adverse effect on our business and our ability to operate our business in China.

From time to time, we may have to resort to administrative and court proceedings to enforce our legal rights. Any administrative and court proceedings in China may be protracted, resulting in substantial costs and diversion of resources and management attention. Since PRC administrative and court authorities have significant discretion in interpreting and implementing statutory provisions and contractual terms, it may be more difficult to evaluate the outcome of administrative and court proceedings and the level of legal protection we enjoy, than in more developed legal systems. These uncertainties may impede our ability to enforce contracts in China and could materially and adversely affect our business and results of operations.

Furthermore, the PRC legal system is based in part on government policies and internal rules, some of which are not published on a timely basis, or at all, and may have retroactive effect. As a result, we may not be aware of our violation of any of these policies and rules until sometime after the violation. Such unpredictability towards our contractual, property and procedural rights could adversely affect our business, and impede our ability to continue our operations and proceed with our future business plans.

We may be restricted from transferring our scientific data abroad.

On March 17, 2018, the General Office of the PRC State Council promulgated the Measures for the Management of Scientific Data, or the Scientific Data Measures, which provide a broad definition of scientific data and relevant rules for the management of scientific data. According to the Scientific Data Measures, enterprises in China must seek governmental approval before any scientific data involving a state secret may be transferred abroad or to foreign parties. Further, any researcher conducting research funded, at least in part, by the PRC government is required to submit relevant scientific data for management by the entity to which such researcher is affiliated before such data may be published in any foreign academic journal. Currently, as the term “state secret” is not clearly defined, there is no assurance that we can always obtain relevant approvals for sending scientific data (such as the results of our preclinical studies or clinical trials conducted within China) abroad, or to our foreign partners in China.

If we are unable to obtain the necessary approvals in a timely manner, or at all, our research and development of product candidates may be hindered, which may materially and adversely affect our business, results of operations, financial conditions and prospects. If relevant government authorities consider the transmission of our scientific data to be in violation of the requirements under the Scientific Data Measures, we may be subject to specific administrative penalties imposed by those government authorities

Recent litigation and negative publicity surrounding China-based companies listed in the United States may result in increased regulatory scrutiny of us and negatively impact the trading price of the ADSs and could have a material adverse effect upon our business, including our results of operations, financial condition, cash flows and prospects.

We believe that litigation and negative publicity surrounding companies with operations in China that are listed in the United States have negatively impacted stock prices for these companies. Various equity-based research organizations have published reports on China-based companies after examining their corporate governance practices, related party transactions, sales practices and financial statements, and these reports have led to special investigations and listing suspensions on U.S. national exchanges. Any similar scrutiny of us, regardless of its lack of merit, could result in a diversion of management resources and energy, potential costs to defend ourselves against rumors, decreases and volatility in the ADS trading price, and increased directors and officers insurance premiums and could have an adverse effect upon our business, including our results of operations, financial condition, cash flows and prospects.

Changes in U.S. and international trade policies, particularly with regard to China, may adversely impact our business and operating results.

The U.S. government has recently made statements and taken certain actions that may lead to potential changes to U.S. and international trade policies, including imposing several rounds of tariffs affecting certain products manufactured in China. In March 2018, U.S. President Donald J. Trump announced the imposition of tariffs on steel and aluminum entering the United States and in June 2018 announced further tariffs targeting goods imported from China. Recently both China and the United States have each imposed tariffs indicating the potential for further trade barriers. It is unknown whether and to what extent new tariffs (or other new laws or regulations) will be adopted, or the effect that any such actions would have on us or our industry. While we have not started commercialization of product candidates, any unfavorable government policies on international trade, such as capital controls or tariffs, may affect the demand for our drug products, the competitive position of our drug products, the hiring of scientists and other research and development personnel, and import or export of raw materials in relation to drug development, or prevent us from selling our drug products in certain countries. If any new tariffs, legislation and/or regulations are implemented, or if existing trade agreements are renegotiated or, in particular, if the U.S. government takes retaliatory trade actions due to the recent U.S.-China trade tension, such changes could have an adverse effect on our business, financial condition and results of operations.

You may be subject to PRC income tax on dividends from us or on any gain realized on the transfer of our ADSs.

Under the Enterprise Income Tax Law of the PRC, or the EIT Law, and its implementation rules, PRC withholding tax at the rate of 10% is generally applicable to dividends from PRC sources paid to investors that are resident enterprises outside of China and that do not have an establishment or place of business in China, or that have an establishment or place of business in China but the relevant income is not effectively connected with the establishment or place of business. Any gain realized on the transfer of shares by such investors is subject to 10% PRC income tax if this gain is regarded as income derived from sources within China. Under the PRC Individual Income Tax Law and its implementation rules, dividends from sources within China paid to foreign individual investors who are not PRC residents are generally subject to a PRC withholding tax at a rate of 20% and gains from PRC sources realized by these investors on the transfer of shares are generally subject to 20% PRC income tax. Any such PRC tax liability may be reduced by the provisions of an applicable tax treaty.

Although substantially all of our business operations are in China, it is unclear whether the dividends we pay with respect to our shares or ADSs, or the gains realized from the transfer of our shares or ADSs, would be treated as income derived from sources within China and as a result be subject to PRC income tax if we are considered a PRC resident enterprise. If PRC income tax is imposed on gains realized through the transfer of our ADSs or on dividends paid to our non-resident investors, the value of your investment in our ADSs may be adversely affected. Furthermore, our shareholders whose jurisdictions of residence have tax treaties or arrangements with China may not qualify for benefits under these tax treaties or arrangements.

In addition, pursuant to the Double Tax Avoidance Arrangement between Hong Kong and China, or the Double Tax Avoidance Treaty, and the Notice on Certain Issues with Respect to the Enforcement of Dividend Provisions in Tax Treaties, or the Notice on Tax Treaties, issued on

February 20, 2009 by the State Administration of Taxation, or the SAT, if a Hong Kong resident enterprise owns more than 25% of the equity interest of a PRC company at all times during the twelvemonth period immediately prior to obtaining a dividend from such company, the 10% withholding tax on such dividend is reduced to 5%, provided that certain other conditions and requirements under the Double Tax Avoidance Treaty and other applicable PRC laws are satisfied at the discretion of the relevant PRC tax authority. However, based on the Notice on Tax Treaties, if the relevant PRC tax authorities determine, in their discretion, that a company benefits from such reduced income tax rate due to a structure or arrangement that is primarily tax-driven, the PRC tax authorities may adjust the preferential tax treatment. Based on the Notice on Issues concerning Beneficial Owner in Tax Treaties, or Circular 9, issued on February 3, 2018 by the SAT and effective on April 1, 2018, when determining the applicant's status as a "beneficial owner" for purpose of tax treatments in connection with dividends, interests or royalties in the tax treaties, several factors will be taken into account, and it will be analyzed according to the actual circumstances of the specific cases. If our Hong Kong subsidiary is determined by PRC government authorities as receiving benefits from reduced income tax rates due to a structure or arrangement that is primarily tax-driven, the dividends paid by our PRC subsidiary to our Hong Kong subsidiary will be taxed at a higher rate, which will have an adverse effect on our financial and operational conditions.

The biopharmaceutical industry in China is highly regulated and such regulations are subject to changes which may affect approval and commercialization of our product candidates.

Part of our research and development operations are in China, which we believe confers clinical, commercial and regulatory advantages. The biopharmaceutical industry in China is subject to comprehensive government regulation and supervision, encompassing the approval, registration, manufacturing, packaging, licensing and marketing of new product candidates. See "Item 4 Information on the Company—Regulation" for a discussion of the regulatory requirements that are applicable to our current and planned business activities in China. In recent years, the regulatory framework in China regarding the biopharmaceutical industry has undergone significant changes, and we expect that it will continue to undergo significant changes. Any such changes or amendments may result in increased compliance costs on our business or cause delays in or prevent the successful development or commercialization of our product candidates in China and reduce the current benefits we believe are available to us from developing and manufacturing drugs in China. PRC authorities have become increasingly vigilant in enforcing laws in the biopharmaceutical industry and any failure by us or our partners to maintain compliance with applicable laws and regulations or obtain and maintain required licenses and permits may result in the suspension or termination of our business activities fines, warnings, administrative or criminal penalties in China. We believe our strategy and approach are aligned with the PRC government's regulatory policies, but we cannot ensure that our strategy and approach will continue to be aligned.

Substantial uncertainties exist with respect to the interpretation and implementation of the newly enacted Foreign Investment Law and how it may impact the viability of our current corporate structure, corporate governance and business operations.

On March 15, 2019, the PRC National People's Congress approved the Foreign Investment Law, which came into effect on January 1, 2020 and replaces the trio of existing laws regulating foreign investment in the PRC, namely, the Sino-Foreign Equity Joint Venture Enterprise Law, the Sino-Foreign Cooperative Joint Venture Enterprise Law and the Wholly Foreign-Invested Enterprise Law, together with their implementation rules and ancillary regulations and become the legal foundation for foreign investment in the PRC. Meanwhile, the *Implementation Regulation of the Foreign Investment Law and the Measures for Reporting of Information on Foreign Investment* came into effect as of January 1, 2020, which clarified and elaborated the relevant provisions of the *Foreign Investment Law*.

The Foreign Investment Law sets out the basic regulatory framework for foreign investments and proposes to implement a system of pre-entry national treatment with a negative list for foreign investments, pursuant to which (i) foreign entities and individuals are prohibited from investing in the areas that are not open to foreign investments, (ii) foreign investments in the restricted industries must satisfy certain requirements under the law, and (iii) foreign investments in business sectors outside of the negative list will be treated equally with domestic investments. The Foreign Investment Law also sets forth necessary mechanisms to facilitate, protect and manage foreign investments and proposes to establish a foreign investment information reporting system, through which foreign investors or foreign-invested enterprises are required to submit initial report, report of changes, report of deregistration and annual report relating to their investments to the Ministry of Commerce, or MOFCOM, or its local branches.

You may experience difficulties in effecting service of legal process, enforcing foreign judgments or bringing actions in China against us or our management named in the annual report based on foreign laws.

We are an exempted company incorporated under the laws of the Cayman Islands, we conduct most of our operations in China, and substantially all of our assets are located in China. As a result, it may be difficult for our shareholders to effect service of process upon us or those persons inside China. In addition, China does not have treaties providing for the reciprocal recognition and enforcement of judgments of courts with the Cayman Islands and many other countries and regions. Therefore, recognition and enforcement in China of judgments of a court in any of these non-PRC jurisdictions in relation to any matter not subject to a binding arbitration provision may be difficult or impossible.

Shareholder claims that are common in the United States, including securities law class actions and fraud claims, generally are difficult to pursue as a matter of law or practicality in China. For example, in China, there are significant legal and other obstacles to obtaining information needed for shareholder investigations or litigation outside China or otherwise with respect to foreign entities. Although the local authorities in China may establish a regulatory cooperation mechanism with the securities regulatory authorities of another country or region to implement cross-border supervision and administration, such regulatory cooperation with the securities regulatory authorities in the United States have not been efficient in the absence of mutual and practical cooperation mechanism. According to Article 177 of the PRC Securities Law which became effective in March 2020, no overseas securities regulator is allowed to directly conduct investigation or evidence collection activities within the territory of the PRC. Accordingly, without the consent of the competent PRC securities regulators and relevant authorities, no organization or individual may provide the documents and materials relating to securities business activities to overseas parties. See also “Item 3 Key Information—Risk Factors—Risks Related to the ADSs—You may face difficulties in protecting your interests, and your ability to protect your rights through U.S. courts may be limited, because we are incorporated under Cayman Islands law” for risks associated with investing in us as a Cayman Islands exempted company.

Our business may be negatively affected by the potential obligations to make additional social insurance and housing fund contributions.

We are required by PRC labor laws and regulations, such as the Social Insurance Law, Administrative Regulations on the Housing Provident Fund and other related rules, to pay various statutory employee benefits, including pensions insurance, medical insurance, work-related injury insurance, unemployment insurance, maternity insurance and housing fund, to designated government agencies for the benefit of our employees. The relevant government agencies may examine whether an employer has made adequate and timely payments of the requisite statutory employee benefits, and employers who fail to make adequate and timely payments may be subject to supplemental contributions, late payment fees, fines compulsory enforcement and/or other penalties. If the relevant PRC authorities determine that we shall make supplemental social insurance and housing fund contributions or that we are subject to fines and legal sanctions in relation to our failure to make social insurance and housing fund contributions in full for our employees, our business, financial condition and results of operations may be adversely affected.

The lease agreements of our leased properties have not been registered with the relevant PRC government authorities as required by PRC law, which may expose us to potential fines.

Under PRC law, lease agreements of commodity housing tenancy are required to be registered with the local construction (real estate) departments. Although failure to do so does not in itself invalidate the leases, the parties of the lease agreements may be exposed to potential fines if they fail to rectify such non-compliance within the prescribed time frame after receiving notice from the relevant PRC government authorities. The penalty ranges from RMB1,000 to RMB10,000 for each unregistered lease, at the discretion of the relevant authority. As of the date of this annual report, the lease agreements for our leased properties in China have not been registered with the relevant PRC government authorities. As of the date of this annual report, we are not aware of any regulatory or governmental actions, claims or investigations being contemplated or any challenges by third parties to our use of our leased properties that the lease agreements of which have not been registered with the government authorities. However, we cannot assure you that the government authorities will not impose fines on us due to our failure to register any of our lease agreements, which may negatively impact our financial condition.

Any failure to comply with PRC regulations regarding the registration requirements for employee stock incentive plans may subject the PRC plan participants or us to fines and other legal or administrative sanctions.

In February 2012, SAFE promulgated the Notices on Issues Concerning the Foreign Exchange Administration for Domestic Individuals Participating in Stock Incentive Plan of Overseas Publicly Listed Company, replacing earlier rules promulgated in 2007. Pursuant to these rules, PRC citizens and non-PRC citizens who reside in China for a continuous period of not less than one year who participate in any stock incentive plan of an overseas publicly listed company, subject to a few exceptions, are required to register with SAFE through a domestic qualified agent, which could be the PRC subsidiary of such overseas-listed company, and complete certain other procedures. In addition, an overseas-entrusted institution must be retained to handle matters in connection with the exercise or sale of stock options and the purchase or sale of shares and interests. We and our executive officers and other employees who are PRC citizens or who reside in the PRC for a continuous period of not less than one year and who have been granted options will be subject to these regulations. Failure to complete the SAFE registrations may subject them to fines and legal sanctions, there may be additional restrictions on the ability of them to exercise their stock options or remit proceeds gained from the sale of their stock into the PRC. We also face regulatory uncertainties that could restrict our ability to adopt incentive plans for our directors, executive officers and employees under PRC law.

If we are classified as a PRC resident enterprise for PRC income tax purposes, such classification could result in unfavorable tax consequences to us and our non-PRC shareholders or ADS holders.

Under the PRC Enterprise Income Tax Law and its implementation rules, an enterprise established outside of the PRC with a “de facto management body” within the PRC is considered a “resident enterprise” and will be subject to the enterprise income tax on its global income at the rate of 25%. The implementation rules define the term “de facto management body” as the body that exercises full and substantial control over and overall management of the business, productions, personnel, accounts and properties of an enterprise. In 2009, SAT issued a circular, known as SAT Circular 82, which provides certain specific criteria for determining whether the “de facto management body” of a PRC-controlled enterprise that is incorporated offshore is located in China. Although this circular only applies to offshore enterprises controlled by PRC enterprises or PRC enterprise groups, not those controlled by PRC individuals or foreigners, the criteria set forth in the circular may reflect the SAT’s general position on how the “de facto management body” test should be applied in determining the tax resident status of all offshore enterprises. According to SAT Circular 82, an offshore incorporated enterprise controlled by a PRC enterprise or a PRC enterprise group will be regarded as a PRC tax resident by virtue of having its “de facto management body” in China and will be subject to PRC enterprise income tax on its global income only if all of the following conditions are met: (i) the primary location of the day-to-day operational management and the places where they perform their duties are in the PRC; (ii) decisions relating to the enterprise’s financial and human resource matters are made or are subject to approval by organizations or personnel in the PRC; (iii) the enterprise’s primary assets, accounting books and records, company seals, and board and shareholder resolutions, are located or maintained in the PRC; and (iv) at least 50% of voting board members or senior executives habitually reside in the PRC.

We believe that we are not a PRC resident enterprise for PRC tax purposes. See “Item 10 Additional Information—People’s Republic of China Taxation.” However, the tax resident status of an enterprise is subject to determination by the PRC tax authorities and uncertainties remain with respect to the interpretation of the term “de facto management body.” If the PRC tax authorities determine that we or any of our non-PRC subsidiaries are a PRC resident enterprise for enterprise income tax purposes, we may be required to withhold a 10% withholding tax from dividends we pay to our shareholders that are non-resident enterprises, including the holders of the ADSs. In addition, non-resident enterprise shareholders (including ADS holders) may be subject to PRC tax on gains realized on the sale or other disposition of ADSs or ordinary shares, if such income is treated as sourced from within the PRC. Furthermore, if we are deemed a PRC resident enterprise, dividends payable to our non-PRC individual shareholders (including ADS holders) and any gain realized on the transfer of ADSs or ordinary shares by such shareholders may be subject to PRC tax at a rate of 20% (which, in the case of dividends, may be withheld at source by us). Any PRC tax liability may be reduced under applicable tax treaties. However, it is unclear whether in practice our non-PRC shareholders would be able to obtain the benefits of any tax treaties between their countries of tax residence and the PRC in the event that we are treated as a PRC resident enterprise. Any such tax may reduce the returns on your investment in the ADSs or our ordinary shares.

We face uncertainty with respect to indirect transfers of equity interests in PRC resident enterprises by their non-PRC holding companies.

Pursuant to the Notice on Strengthening Administration of Enterprise Income Tax for Share Transfers by Non-PRC Resident Enterprises, or SAT Circular 698, issued by the SAT in 2009 with retroactive effect from January 1, 2008, where a non-resident enterprise transfers the equity interests of a PRC resident enterprise indirectly by disposition of the equity interests of an overseas holding company, or an Indirect Transfer, and such overseas holding company is located in a tax jurisdiction that: (i) has an effective tax rate less than 12.5% or (ii) does not tax foreign income of its residents, the non-resident enterprise, being the transferor, shall report to the competent tax authority of the PRC resident enterprise this Indirect Transfer.

On February 3, 2015, the SAT issued the Announcement of the State Administration of Taxation on Several Issues Concerning the Enterprise Income Tax on Indirect Property Transfer by Non-Resident Enterprises, or SAT Bulletin 7. SAT Bulletin 7 supersedes the rules with respect to the Indirect Transfer under SAT Circular 698. SAT Bulletin 7 has introduced a new tax regime that is significantly different from the previous one under SAT Circular 698. SAT Bulletin 7 extends the PRC’s tax jurisdiction to not only Indirect Transfers set forth under SAT Circular 698 but also transactions involving a transfer of other taxable assets through an offshore transfer of a foreign intermediate holding company. In addition, SAT Bulletin 7 provides clearer criteria than SAT Circular 698 for assessment of reasonable commercial purposes and has introduced safe harbors for internal group restructurings and the purchase and sale of equity through a public securities market. SAT Bulletin 7 also brings challenges to both foreign transferor and transferee (or another person who is obligated to pay for the transfer) of taxable assets. Where a non-resident enterprise transfers taxable assets indirectly by disposing of the equity interests of an overseas holding company, which is an Indirect Transfer, the non-resident enterprise, being the transferor, or the transferee, or the PRC entity that directly owns the taxable assets, may report such Indirect Transfer to the relevant tax authority. Using a “substance over form” principle, the PRC tax authority may disregard the existence of the overseas holding company if it lacks a reasonable commercial purpose and was established for the purpose of reducing, avoiding or deferring PRC tax. As a result, gains derived from such Indirect Transfer may be subject to PRC enterprise income tax, and the transferee or another person who is obligated to pay for the transfer is obligated to withhold the applicable taxes, currently at a rate of 10% for the transfer of equity interests in a PRC resident enterprise. Both the transferor and the transferee may be subject to penalties under PRC tax laws if the transferee fails to withhold the taxes and the transferor fails to pay the taxes.

On October 17, 2017, the SAT issued the Announcement of the State Administration of Taxation on Matters Concerning Withholding of Income Tax of Non-resident Enterprises at Source, or SAT Bulletin 37, which, among others, repealed the SAT Circular 698 on December 1, 2017. SAT Bulletin 37 further details and clarifies the tax withholding methods in respect of income of non-resident enterprises under SAT Circular 698. And certain rules stipulated in SAT Bulletin 7 are replaced by SAT Bulletin 37. Where the non-resident enterprise fails to declare the tax payable pursuant to Article 39 of the PRC Enterprise Income Tax Law, the tax authority may order it to pay the tax due within required time limits, and the non-resident enterprise shall declare and pay the tax payable within such time limits specified by the tax authority; however, if the non-resident enterprise voluntarily declares and pays the tax payable before the tax authority orders it to do so within required time limits, it shall be deemed that such enterprise has paid the tax in time.

We face uncertainties as to the reporting and other implications of certain past and future transactions where PRC taxable assets are involved, such as offshore restructuring, sale of the shares in our offshore subsidiaries and investments. Our company may be subject to filing obligations or taxed if our company is a transferor in such transactions, and may be subject to withholding obligations if our company is a transferee in such transactions, under SAT Bulletin 7 and SAT Bulletin 37. For transfer of shares in our company by investors who are non-PRC resident enterprises, our PRC subsidiary may be requested to assist in the filing under SAT Bulletin 7 and SAT Bulletin 37. As a result, we may be required to expend valuable resources to comply with SAT Bulletin 7 and SAT Bulletin 37 or to request the relevant transferors from whom we purchase taxable assets to comply with these circulars, or to establish that our company should not be taxed under these circulars, which may have a material adverse effect on our financial condition and results of operations.

If our preferential tax treatments are revoked, become unavailable or if the calculation of our tax liability is challenged by the PRC tax authorities, we may be required to pay tax, interest and penalties in excess of our tax provisions, and our results of operations could be materially and adversely affected.

The Chinese government has provided various tax incentives to our subsidiaries in China. These incentives include reduced enterprise income tax rates. For example, under the Enterprise Income Tax Law and its implementation rules, the statutory enterprise income tax rate is 25%. However, the income tax of an enterprise that has been determined to be a technologically advanced service enterprise can be reduced to a preferential rate of 15%. Any increase in the enterprise income tax rate applicable to our PRC subsidiary, or any discontinuation or retroactive or future reduction of any of the preferential tax treatments currently enjoyed by our PRC subsidiary, could adversely affect our business, financial condition and results of operations. In addition, in the ordinary course of our business, we are subject to complex income tax and other tax regulations and significant judgment is required in the determination of a provision for income taxes. Although we believe our tax provisions are reasonable, if the PRC tax authorities successfully challenge our position and we are required to pay tax, interest and penalties in excess of our tax provisions, our financial condition and results of operations would be materially and adversely affected.

Certain PRC regulations may make it more difficult for us to pursue growth through acquisitions.

Among other things, the Regulations on Mergers and Acquisitions of Domestic Enterprises by Foreign Investors, or the M&A Rules, adopted by six PRC regulatory agencies in 2006 and amended in 2009, established additional procedures and requirements that could make merger and acquisition activities by foreign investors more time-consuming and complex. Such regulation requires, among other things, the MOFCOM be notified in advance or its approval be obtained in certain situations, such as any change-of-control transaction in which a foreign investor acquires control of a PRC domestic enterprise of Undertakings, issued by the State Council in 2008 and amended in 2018, were triggered. Moreover, the Anti-Monopoly Law promulgated by the Standing Committee of the PRC National People's Congress, or NPC, which became effective in 2008 requires that transactions which are deemed concentrations and involve parties with specified turnover thresholds must be cleared by the MOFCOM before they can be completed. In addition, PRC national security review rules which became effective in September 2011 require acquisitions by foreign investors of PRC companies engaged in military-related or certain other industries that are crucial to national security be subject to security review before consummation of any such acquisition. We may pursue potential strategic acquisitions that are complementary to our business and operations. Complying with the requirements of these regulations to complete such transactions could be time-consuming, and any required approval processes, including obtaining approval or clearance from the MOFCOM, may delay or inhibit our ability to complete such transactions, which could affect our ability to expand our business or maintain our market share.

PRC regulations relating to offshore investment activities by PRC residents may limit our PRC subsidiaries' ability to change their registered capital or distribute profits to us or otherwise expose us or our PRC resident beneficial owners to liability and penalties under PRC laws.

In July 2014, SAFE promulgated the Circular on Relevant Issues Concerning Foreign Exchange Control on Domestic Residents' Offshore Investment and Financing and Roundtrip Investment Through Special Purpose Vehicles, or SAFE Circular 37. SAFE Circular 37 requires PRC residents (including PRC individuals and PRC corporate entities as well as foreign individuals that are deemed as PRC residents for foreign exchange administration purpose) to register with SAFE or its local branches in connection with their direct or indirect offshore investment activities. SAFE Circular 37 is applicable to our shareholders who are PRC residents and may be applicable to any offshore acquisitions that we make in the future.

Under SAFE Circular 37, PRC residents who make, or have prior to the implementation of SAFE Circular 37 made, direct or indirect investments in offshore special purpose vehicles, or SPVs, will be required to register such investments with SAFE or its local branches. In addition, any PRC resident who is a direct or indirect shareholder of an SPV, is required to update its filed registration with the local branch of SAFE with respect to that SPV, to reflect any material change, including, among other things, any major change of a PRC resident shareholder, name or term of operation of the SPVs, or any increase or reduction of the SPVs' registered capital, share transfer or swap, merger or division. Moreover, any subsidiary of such SPV in China is required to urge the PRC resident shareholders to update their registration with the local branch of SAFE. If any PRC shareholder of such SPV fails to make the required registration or to update the previously filed registration, the subsidiary of such SPV in China may be prohibited from distributing its profits or the proceeds from any capital reduction, share transfer or liquidation to the SPV, and the SPV may also be prohibited from making additional capital contributions into its subsidiary in China. On February 13, 2015, SAFE promulgated a Notice on Further Simplifying and Improving Foreign Exchange Administration Policy on Direct Investment, or SAFE Notice 13, which became effective on June 1, 2015. Under SAFE Notice 13, applications for foreign exchange registration of inbound foreign direct investments and outbound overseas direct investments, including those required under SAFE Circular 37, will be filed with qualified banks instead of SAFE or its branches. The qualified banks will directly examine the applications and accept registrations under the supervision of SAFE.

Some of our existing shareholders, each of whom owns our ordinary shares, including but not limited to as a result of exercising share options, are PRC residents under SAFE Circular 37. However, we cannot provide any assurance that these PRC residents comply with our request to make or obtain any applicable registrations or change registration or comply with all of the requirements under SAFE Circular 37 or other related rules. Furthermore, we may not be informed of the identities of all the PRC residents holding direct or indirect interest in our company. The failure or inability of our PRC resident shareholders to comply with the registration procedures set forth in these regulations may subject us to fines and legal sanctions, restrict our cross-border investment activities, limit the ability of our wholly foreign-owned subsidiary in China to distribute dividends and the proceeds from any reduction in capital, share transfer or liquidation to us, and we may also be prohibited from injecting additional capital into the subsidiary. Moreover, failure to comply with the various foreign exchange registration requirements described above could result in liability under PRC law for circumventing applicable foreign exchange restrictions. As a result, our business operations and our ability to distribute profits to you could be materially and adversely affected.

Furthermore, as these foreign exchange regulations are still relatively new and their interpretation and implementation has been constantly evolving, it is unclear how these regulations, and any future regulation concerning offshore or cross-border transactions, will be interpreted, amended and implemented by the relevant government authorities. For example, we may be subject to a more stringent review and approval process with respect to our foreign exchange activities, such as remittance of dividends and foreign-currency-denominated borrowings, which may adversely affect our financial condition and results of operations. In addition, if we decide to acquire a PRC domestic company, we cannot assure you that we or the owners of such company, as the case may be, will be able to obtain the necessary approvals or complete the necessary filings and registrations required by the foreign exchange regulations. This may restrict our ability to implement our acquisition strategy and could adversely affect our business and prospects.

We may be materially adversely affected if our shareholders and beneficial owners who are PRC entities fail to comply with the relevant PRC overseas investment regulations.

On December 26, 2017, the NDRC promulgated the Administrative Measures on Overseas Investments, or NDRC Order No. 11, which took effect as of March 1, 2018. According to NDRC Order No. 11, non-sensitive overseas investment projects are subject to record-filing requirements with the local branch of the NDRC. On September 6, 2014, MOFCOM promulgated the *Administrative Measures on Overseas Investments*, which took effect as of October 6, 2014. According to this regulation, overseas investments of PRC enterprises that involve non-sensitive countries and regions and non-sensitive industries are subject to record-filing requirements with a local MOFCOM branch. According to the *Circular of the State Administration of Foreign Exchange on Issuing the Regulations on Foreign Exchange Administration of the Overseas Direct Investment of Domestic Institutions*, which was promulgated by SAFE on July 13, 2009 and took effect on August 1, 2009, PRC enterprises must register for overseas direct investment with a local SAFE branch.

We may not be fully informed of the identities of all our shareholders or beneficial owners who are PRC entities, and we cannot provide any assurance that all of our shareholders and beneficial owners who are PRC entities has or will comply with our request to complete the overseas direct investment procedures under the aforementioned regulations or other related rules in a timely manner, or at all. If they fail to complete the filings or registrations required by the overseas direct investment regulations, the relevant authorities may order them to suspend or cease the implementation of such investment impose warnings and sanctions and make corrections within a specified time, or limit our ability to distribute dividends and proceeds to our PRC subsidiary, which may adversely affect our business, financial condition and results of operations.

PRC regulation of loans to and direct investment in PRC entities by offshore holding companies and governmental control of currency conversion may delay or prevent us from using the proceeds of our initial public offering to make loans or additional capital contributions to our PRC subsidiary, which could materially and adversely affect our liquidity and our ability to fund and expand our business.

We are an offshore holding company conducting our operations in China through our PRC subsidiary. We also hold certain intellectual properties and outsource certain research and development activities related to these intellectual properties to our subsidiaries. We may in the future make loans or provide guarantee to our PRC subsidiary subject to the approval or registration from governmental authorities and limitation of amount, or we may make additional capital contributions to our wholly foreign-owned subsidiary in China. Any loans to our wholly foreign-owned subsidiary in China, which are treated as foreign-invested enterprises under PRC law, are subject to foreign exchange loan registrations. In addition, a foreign-invested enterprise, or FIE, shall use its capital pursuant to the principle of authenticity and self-use within its business scope. The capital of an FIE shall not be used for the following purposes: (i) directly or indirectly used for payment beyond the business scope of the enterprises or the payment prohibited by relevant laws and regulations; (ii) directly or indirectly used for investment in securities or investments other than banks' principal-secured products unless otherwise provided by relevant laws and regulations; (iii) the granting of loans to non-affiliated enterprises, except where it is expressly permitted in the business license; and (iv) paying the expenses related to the purchase of real estate that is not for self-use (except for the foreign-invested real estate enterprises).

In light of the various requirements imposed by PRC regulations on loans to and direct investment in PRC entities by offshore holding companies, we cannot assure you that we will be able to complete the necessary government registrations or obtain the necessary government approvals on a timely basis, if at all, with respect to future loans by us to our PRC subsidiary or with respect to future capital contributions by us to our PRC subsidiary. If we fail to complete such registrations or obtain such approvals, our ability to use the proceeds from our initial public offering and to capitalize or otherwise fund our PRC operations may be negatively affected, which could materially and adversely affect our liquidity and our ability to fund and expand our business.

We may rely on dividends and other distributions on equity paid by our PRC subsidiary to fund any cash and financing requirements we may have, and any limitation on the ability of our PRC subsidiary to make payments to us could have a material and adverse effect on our ability to conduct our business.

We are a Cayman Islands holding company and we rely principally on dividends and other distributions on equity from our PRC subsidiary for our cash requirements, including the funds necessary to pay dividends and other cash distributions to our shareholders for services of any debt we may incur. If our PRC subsidiary incurs debt on its own behalf in the future, the instruments governing the debt may restrict its ability to pay dividends or make other distributions to us. Under PRC laws and regulations, our PRC subsidiary, which is a wholly foreign-owned enterprise, may pay dividends only out of its respective accumulated profits as determined in accordance with PRC accounting standards and regulations. In addition, a wholly foreign-owned enterprise is required to set aside at least 10% of its accumulated after-tax profits each year, if any, to fund a certain statutory reserve fund, until the aggregate amount of such fund reaches 50% of its registered capital. Such reserve funds cannot be distributed to us as dividends. At its discretion, a wholly foreign-owned enterprise may allocate a portion of its after-tax profits based on PRC accounting standards to an enterprise expansion fund, or a staff welfare and bonus fund.

A portion of our revenue was generated by our PRC subsidiary in Renminbi, which is not freely convertible into other currencies. As a result, any restriction on currency exchange may limit the ability of our PRC subsidiary to use its Renminbi revenues to pay dividends to us.

The PRC government may continue to strengthen its capital controls, and more restrictions and substantial vetting process may be put forward by SAFE for cross-border transactions falling under both the current account and the capital account. Any limitation on the ability of our PRC subsidiary to pay dividends or make other kinds of payments to us could materially and adversely limit our ability to grow, make investments or acquisitions that could be beneficial to our business, pay dividends, or otherwise fund and conduct our business.

In addition, the Enterprise Income Tax Law and its implementation rules provide that a withholding tax rate of up to 10% will be applicable to dividends payable by Chinese companies to non-PRC-resident enterprises unless otherwise exempted or reduced according to treaties or arrangements between the PRC central government and governments of other countries or regions where the non-PRC-resident enterprises are incorporated.

Fluctuations in exchange rates could have a material adverse effect on our results of operations and the value of your investment.

The value of the Renminbi against the U.S. dollar and other currencies may fluctuate and is affected by, among other things, changes in political and economic conditions in China and by China's foreign exchange policies. On July 21, 2005, the PRC government changed its policy of pegging the value of the Renminbi to the U.S. dollar, and the Renminbi appreciated more than 20% against the U.S. dollar over the following three years. Between July 2008 and June 2010, this appreciation halted and the exchange rate between the Renminbi and the U.S. dollar remained within a narrow band. Since June 2010, the Renminbi has fluctuated against the U.S. dollar, at times significantly and unpredictably. Since October 1, 2016, Renminbi has joined the International Monetary Fund's basket of currencies that make up the Special Drawing Right, or SDR, along with the U.S. dollar, the Euro, the Japanese yen and the British pound. In the fourth quarter of 2016, the Renminbi has depreciated significantly in the backdrop of a surging U.S. dollar and persistent capital outflows of China. With the development of the foreign exchange market and progress towards interest rate liberalization and Renminbi internationalization, the PRC government may in the future announce further changes to the exchange rate system, and we cannot assure you that the Renminbi will not appreciate or depreciate significantly in value against the U.S. dollar in the future. It is difficult to predict how market forces or PRC or U.S. government policy may impact the exchange rate between the Renminbi and the U.S. dollar in the future.

Significant revaluation of the Renminbi may have a material and adverse effect on your investment. For example, to the extent that we need to convert U.S. dollars we receive from our initial public offering into Renminbi for our operations, appreciation of the Renminbi against the U.S. dollar would have an adverse effect on the Renminbi amount we would receive from the conversion. Conversely, if we decide to convert our Renminbi into U.S. dollars for the purpose of making payments for dividends on our ordinary shares or the ADSs or for other business purposes, appreciation of the U.S. dollar against the Renminbi would have a negative effect on the U.S. dollar amount available to us.

Very limited hedging options are available in China to reduce our exposure to exchange rate fluctuations. To date, we have not entered into any hedging transactions in an effort to reduce our exposure to foreign currency exchange risk. While we may decide to enter into hedging transactions in the future, the availability and effectiveness of these hedges may be limited and we may not be able to adequately hedge our exposure or at all. In addition, our currency exchange losses may be magnified by PRC exchange control regulations that restrict our ability to convert Renminbi into foreign currency.

Governmental control of currency conversion may limit our ability to utilize our cash balance effectively and affect the value of your investment.

The PRC government imposes controls on the convertibility of the Renminbi into foreign currencies and, in certain cases, the remittance of currency out of China. In the years ended December 31, 2020, we did not receive any of our revenues in Renminbi in cash. Under our current corporate structure, our Cayman Islands holding company primarily relies on previous rounds of private financing to fund any cash and financing requirements we may have. Under existing PRC foreign exchange regulations, payments of current account items, including profit distributions, interest payments and trade and service-related foreign exchange transactions, can be made in foreign currencies without prior approval of SAFE by complying with applicable laws and regulations, as well as certain procedural requirements. Specifically, under the existing exchange restrictions, without prior approval of SAFE, cash generated from the operations of our PRC subsidiary may be used to pay dividends to our company. However, approval from or registration with appropriate government authorities is required where Renminbi is to be converted into foreign currency and remitted out of China to pay capital expenses such as the repayment of loans denominated in foreign currencies. As a result, we need to obtain SAFE approval to use the cash generated from the operations of our PRC subsidiary to pay off their respective debt in a currency other than Renminbi owed to entities outside China, or to make other capital expenditure payments outside China in a currency other than Renminbi. The PRC government may at its discretion restrict access to foreign currencies for current account transactions in the future. If the foreign exchange control system prevents us from obtaining sufficient foreign currencies to satisfy our foreign currency demands, we may not be able to pay dividends in foreign currencies to our shareholders, including holders of the ADSs.

The audit report included in this annual report was prepared by an auditor that is not inspected by the Public Company Accounting Oversight Board and, as such, our investors are deprived of the benefits of such inspection. In addition, various legislative and regulatory developments related to U.S.-listed China based companies due to lack of PCAOB inspection and other developments due to political tensions between the United States and China may have a material adverse impact on our listing and trading in the U.S. and the trading prices of our ADSs..

Our auditor, the independent registered public accounting firm that issued the audit reports included in our annual report filed with the U.S. Securities and Exchange Commission, or the SEC, as an auditor of companies that are traded publicly in the United States and a firm registered with the Public Company Accounting Oversight Board (United States), or the PCAOB, is subject to laws in the United States pursuant to which the PCAOB conducts regular inspections to assess its compliance with applicable professional standards. Our auditor is located in, and organized under the laws of, the PRC, which is a jurisdiction where the PCAOB has been unable to conduct inspections without the approval of the Chinese authorities. Accordingly, our auditor is not currently inspected by the PCAOB.

This lack of PCAOB inspections in China prevents the PCAOB from fully evaluating audits and quality control procedures of our independent registered public accounting firm. As a result, we and investors in our ADSs are deprived of the benefits of such PCAOB inspections. The inability of the PCAOB to conduct inspections of auditors in China makes it more difficult to evaluate the effectiveness of our independent registered public accounting firm's audit procedures or quality control procedures as compared to auditors outside of China that are subject to PCAOB inspections, which could cause investors and potential investors in our ADSs to lose confidence in our audit procedures and reported financial information and the quality of our financial statements.

In addition, as part of a continued regulatory focus in the United States on access to audit and other information currently protected by national law, in particular China's, former U.S. President Trump signed into law on December 18, 2020 the Holding Foreign Companies Accountable Act (HFCA Act), which requires the SEC to propose rules within 90 days after its enactment to prohibit securities of any registrant from being listed on any of the U.S. securities exchanges or traded "over the counter" if the auditor of the registrant's financial statements is not subject to PCAOB inspection for three consecutive years after the law becomes effective. On March 24, 2021, the SEC has adopted interim final amendments to implement congressionally mandated submission and disclosure requirements of the HFCA Act. The interim final amendments will apply to registrants that the SEC identifies as having filed an annual report on Forms 10-K, 20-F, 40-F or N-CSR with an audit report issued by a registered public accounting firm that is located in a foreign jurisdiction and that the PCAOB has determined it is unable to inspect or investigate completely because of a position taken by an authority in that jurisdiction. Before any registrant will have to comply with the interim final amendments, however, the SEC must implement a process for identifying such a registrant. Thus, the SEC is currently seeking public comment on this identification process.

Consistent with the HFCA Act, the amendments will require any such identified registrant to submit documentation to the SEC establishing that the registrant is not owned or controlled by a governmental entity in that foreign jurisdiction, and will also require disclosure in a foreign issuer's annual report regarding the audit arrangements of, and governmental influence on, such a registrant. As of the date of this annual report, the SEC staff is also currently assessing how best to implement other requirements of the HFCA Act, including the identification process and the trading prohibition requirements.

Enactment of this legislation or other efforts to increase U.S. regulatory access to audit information could cause investor uncertainty for affected issuers, including us, and the market price of the ADSs could be adversely affected, and we could be delisted if we are unable to cure the situation to meet the PCAOB inspection requirement in time. It is unclear if and when any of such proposed legislations will be enacted. See "Item 3 Key Information—3.D. Risk Factors — We could be delisted if we are unable to meet the PCAOB inspection requirements in time." The delisting of our ADSs and inability to trade, or the threat thereof, may materially and adversely affect the value of your investment."

We could be delisted if we are unable to meet the PCAOB inspection requirements in time.

On December 18, 2020, the Holding Foreign Companies Accountable Act was enacted. In essence, the act requires the SEC to prohibit securities of any foreign companies from being listed on U.S. securities exchanges or traded “over-the-counter” if a company retains a foreign accounting firm that cannot be inspected by the PCAOB for three consecutive years, beginning in 2021. Our independent registered public accounting firm is located in and organized under the laws of the PRC, a jurisdiction where the PCAOB is currently unable to conduct inspections without the approval of the Chinese authorities, and therefore our auditors are not currently inspected by the PCAOB.

The enactment of the Holding Foreign Companies Accountable Act and any additional rulemaking efforts to increase U.S. regulatory access to audit information in China could cause investor uncertainty for affected SEC registrants, including us, and the market price of our ADSs could be materially adversely affected. Additionally, whether the PCAOB will be able to conduct inspections of our auditors in the next three years, or at all, is subject to substantial uncertainty and depends on a number of factors out of our control. If we are unable to meet the PCAOB inspection requirement in time, we could be delisted from the Nasdaq Global Market and our ADSs will not be permitted for trading “over-the-counter” either. Such a delisting would substantially impair your ability to sell or purchase our ADSs when you wish to do so, and the risk and uncertainty associated with delisting would have a negative impact on the price of our ADSs. Also, such a delisting would significantly affect our ability to raise capital on terms acceptable to us, or at all, which would have a material adverse impact on our business, financial condition and prospects.

Proceedings instituted by the SEC against certain PRC-based accounting firms, including the affiliate of our independent registered public accounting firm, or any related adverse regulatory development in the PRC, could result in our financial statements being determined to not be in compliance with the requirements of the Exchange Act.

In December 2012, the SEC instituted administrative proceedings against the Big Four PRC-based accounting firms, including our independent registered public accounting firm, alleging that these firms had violated U.S. securities laws and the SEC’s rules and regulations thereunder by failing to provide to the SEC the firms’ audit work papers with respect to certain PRC-based companies that are publicly traded in the United States.

On January 22, 2014, the administrative law judge presiding over the matter rendered an initial decision that each of the firms had violated the SEC’s rules of practice by failing to produce audit papers and other documents to the SEC. The initial decision censured each of the firms and barred them from practicing before the SEC for a period of six months.

On February 6, 2015, the four China-based accounting firms each agreed to a censure and to pay a fine to the SEC to settle the dispute and avoid suspension of their ability to practice before the SEC and audit U.S.-listed companies. The settlement required the firms to follow detailed procedures and to seek to provide the SEC with access to Chinese firms’ audit documents via the CSRC. Under the terms of the settlement, the underlying proceeding against the four China-based accounting firms was deemed dismissed with prejudice four years after entry of the settlement. The four-year mark occurred on February 6, 2019.

While we cannot predict if the SEC will further challenge the four China-based accounting firms’ compliance with U.S. law in connection with U.S. regulatory requests for audit work papers or if the results of such a challenge would result in the SEC imposing penalties such as suspensions, if the accounting firms are subject to additional remedial measures, our ability to file our financial statements in compliance with SEC requirements could be impacted. A determination that we have not timely filed financial statements in compliance with SEC requirements could ultimately lead to the delisting of our ordinary shares or ADSs or the termination of the registration of our ordinary shares or ADSs under the Exchange Act, or both, which would substantially reduce or effectively terminate the trading of our ordinary shares or ADSs in the United States.

Risks Related to the ADSs

You may be subject to limitations on transfer of your ADSs.

Your ADSs are transferable on the books of the depository. However, the depository may close its transfer books at any time or from time to time when it deems expedient in connection with the performance of its duties. In addition, the depository may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depository are closed, or at any time if we or the depository deems it advisable to do so because of any requirement of law or of any government or governmental body, or under any provision of the deposit agreement, or for any other reason in accordance with the terms of the deposit agreement.

The trading price of the ADSs is likely to be volatile, which could result in substantial losses to investors.

The trading price of our ADSs ranged from US\$12.67 to US\$31.83 per ADS since the listing of ADSs on Nasdaq. The trading price of the ADSs is likely to be volatile and could fluctuate widely due to factors beyond our control. This may happen because of broad market and industry factors, including the performance and fluctuation of the market prices of other companies with business operations located mainly in China that have listed their securities in the United States. In addition to market and industry factors, the price and trading volume for the ADSs may be highly volatile for factors specific to our own operations, including the following:

- variations in our net revenues, earnings and cash flow;
- announcements of new investments, acquisitions, strategic partnerships, or joint ventures by us or our competitors;
- announcements of new products and services and expansions by us or our competitors;
- changes in financial estimates by securities analysts;
- fluctuations in operating metrics;
- failure on our part to realize monetization opportunities as expected;
- changes in revenues generated from our significant business partners;
- additions or departures of key personnel;
- release of lock-up or other transfer restrictions on our outstanding equity securities or sales of additional equity securities;
- detrimental negative publicity about us, our management, our competitors or our industry;
- regulatory developments affecting us or our industry; and
- potential litigation or regulatory investigations.

Any of these factors may result in large and sudden changes in the trading volume and price of the ADSs.

In the past, shareholders of public companies have often brought securities class action suits against those companies following periods of instability in the market price of their securities. If we were involved in a class action suit, it could divert a significant amount of our management's attention and other resources from our business and operations and require us to incur significant expenses to defend the suit, which could harm our results of operations. Any such class action suit, whether or not successful, could harm our reputation and restrict our ability to raise capital in the future. In addition, if a claim is successfully made against us, we may be required to pay significant damages, which could have a material adverse effect on our financial condition and results of operations.

We are an emerging growth company within the meaning of the Securities Act and may take advantage of certain reduced reporting requirements.

We are an “emerging growth company,” as defined in the JOBS Act, and we may take advantage of certain exemptions from requirements applicable to other public companies that are not emerging growth companies including, most significantly, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 for so long as we remain an emerging growth company. As a result, if we elect not to comply with such auditor attestation requirements, our investors may not have access to certain information they may deem important.

If securities or industry analysts cease to publish research or reports about our business, or if they adversely change their recommendations regarding the ADSs, the market price for the ADSs and trading volume could decline.

The trading market for the ADSs will be influenced by research or reports that industry or securities analysts publish about our business. If one or more analysts who cover us downgrade the ADSs, the market price for the ADSs would likely decline. If one or more of these analysts cease to cover us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which, in turn, could cause the market price or trading volume for the ADSs to decline.

The sale or availability for sale, or perceived sale or availability for sale, of substantial amounts of the ADSs could adversely affect their market price.

Sales of substantial amounts of the ADSs in the public market, or the perception that these sales could occur, could adversely affect the market price of the ADSs and could materially impair our ability to raise capital through equity offerings in the future. The ADSs sold in our initial public offering are freely tradable by persons other than our “affiliates” without restriction or further registration under the Securities Act, and shares held by our existing shareholders may also be sold in the public market in the future subject to the restrictions in Rule 144 and Rule 701 under the Securities Act and the applicable lock-up agreements.

Our memorandum and articles of association contain anti-takeover provisions that could have a material adverse effect on the rights of holders of our ordinary shares and the ADSs.

We have adopted amended and restated memorandum and articles of association. Our new memorandum and articles of association contain provisions to limit the ability of others to acquire control of our company or cause us to engage in change-of-control transactions. These provisions could have the effect of depriving our shareholders of an opportunity to sell their shares at a premium over prevailing market prices by discouraging third parties from seeking to obtain control of our company in a tender offer or similar transaction. Our board of directors has the authority, without further action by our shareholders, to issue preferred shares in one or more series and to fix their designations, powers, preferences, privileges, and relative participating, optional or special rights and the qualifications, limitations or restrictions, including dividend rights, conversion rights, voting rights, terms of redemption and liquidation preferences, any or all of which may be greater than the rights associated with our ordinary shares, including ordinary shares represented by ADSs. Preferred shares could be issued quickly with terms calculated to delay or prevent a change in control of our company or make removal of management more difficult. If our board of directors decides to issue preferred shares, the price of the ADSs may fall and the voting and other rights of the holders of our ordinary shares and the ADSs may be materially and adversely affected.

We have not determined a specific use for a portion of the net proceeds from our initial public offering, and we may use these proceeds in ways with which you may not agree, and such use may not produce income or increase the ADS price.

We have not determined a specific use for a portion of the net proceeds of our initial public offering, and our management will have considerable discretion in deciding how to apply these proceeds. You will not have the opportunity to assess whether the proceeds are being used appropriately before you make your investment decision. You must rely on the judgment of our management regarding the application of the net proceeds of our initial public offering. We cannot assure you that the net proceeds will be used in a manner that would improve our results of operations or increase the ADS price, nor that these net proceeds will be placed only in investments that generate income or appreciate in value. Currently, we do not have any plans, commitments or understandings to acquire complementary business, assets and technologies.

We are entitled to amend the deposit agreement and to change the rights of ADS holders under the terms of such agreement, or to terminate the deposit agreement, without the prior consent of the ADS holders.

We are entitled to amend the deposit agreement and to change the rights of the ADS holders under the terms of such agreement, without the prior consent of the ADS holders. We and the depositary may agree to amend the deposit agreement in any way we decide is necessary or advantageous to us. Amendments may reflect, among other things, operational changes in the ADS program, legal developments affecting ADSs or changes in the terms of our business relationship with the depositary. In the event that the terms of an amendment are disadvantageous to ADS holders, ADS holders will only receive 30 days' advance notice of the amendment, and no prior consent of the ADS holders is required under the deposit agreement. Furthermore, we may decide to terminate the ADS facility at any time for any reason. For example, terminations may occur when we decide to list our shares on a non-U.S. securities exchange and determine not to continue to sponsor an ADS facility or when we become the subject of a takeover or a going-private transaction. If the ADS facility will terminate, ADS holders will receive at least 90 days' prior notice, but no prior consent is required from them. Under the circumstances that we decide to make an amendment to the deposit agreement that is disadvantageous to ADS holders or terminate the deposit agreement, the ADS holders may choose to sell their ADSs or surrender their ADSs and become direct holders of the underlying ordinary shares, but will have no right to any compensation whatsoever.

ADSs holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could result in less favorable outcomes to the plaintiff(s) in any such action.

The deposit agreement governing the ADSs representing our ordinary shares provides that, to the fullest extent permitted by law, ADS holders waive the right to a jury trial of any claim they may have against us or the depositary arising out of or relating to our shares, the ADSs or the deposit agreement, including any claim under the U.S. federal securities laws.

If we or the depositary opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable based on the facts and circumstances of that case in accordance with the applicable state and federal law. To our knowledge, the enforceability of a contractual pre-dispute jury trial waiver in connection with claims arising under the federal securities laws has not been finally adjudicated by the United States Supreme Court. However, we believe that a contractual pre-dispute jury trial waiver provision is generally enforceable, including under the laws of the State of New York, which govern the deposit agreement, by a federal or state court in the City of New York, which has non-exclusive jurisdiction over matters arising under the deposit agreement. In determining whether to enforce a contractual pre-dispute jury trial waiver provision, courts will generally consider whether a party knowingly, intelligently and voluntarily waived the right to a jury trial. We believe that this is the case with respect to the deposit agreement and the ADSs. It is advisable that you consult legal counsel regarding the jury waiver provision before entering into the deposit agreement.

If you or any other holders or beneficial owners of ADSs bring a claim against us or the depositary in connection with matters arising under the deposit agreement or the ADSs, including claims under federal securities laws, you or such other holder or beneficial owner may not be entitled to a jury trial with respect to such claims, which may have the effect of limiting and discouraging lawsuits against us or the depositary. If a lawsuit is brought against us or the depositary under the deposit agreement, it may be heard only by a judge or justice of the applicable trial court, which would be conducted according to different civil procedures and may result in different outcomes than a trial by jury would have had, including results that could be less favorable to the plaintiff(s) in any such action.

Nevertheless, if this jury trial waiver provision is not permitted by applicable law, an action could proceed under the terms of the deposit agreement with a jury trial.

No condition, stipulation or provision of the deposit agreement or ADSs serves as a waiver by any holder or beneficial owner of ADSs or by us or the depositary of compliance with any substantive provision of the U.S. federal securities laws and the rules and regulations promulgated thereunder.

The voting rights of holders of ADSs are limited by the terms of the deposit agreement, and you may not be able to exercise your right to direct the voting of the underlying ordinary shares represented by your ADSs.

Holders of ADSs do not have the same rights as our registered shareholders. As a holder of ADSs, you will not have any direct right to attend general meetings of our shareholders or to cast any votes at such meetings. You will only be able to exercise the voting rights attached to the ordinary shares underlying your ADSs indirectly by giving voting instructions to the depositary in accordance with the provisions of the deposit agreement. Where any matter is to be put to a vote at a general meeting, then upon receipt of your voting instructions, the depositary will try, as far as is practicable, to vote the underlying ordinary shares represented by your ADSs in accordance with your instructions. You will not be able to directly exercise your right to vote with respect to the underlying ordinary shares unless you cancel and withdraw the shares and become the registered holder of such shares prior to the record date for the general meeting.

When a general meeting is convened, you may not receive sufficient advance notice of the meeting to withdraw the ordinary shares represented by your ADSs and become the registered holder of such shares to allow you to attend the general meeting and to vote directly with respect to any specific matter or resolution to be considered and voted upon at the general meeting. In addition, under our post-offering memorandum and articles of association, for the purposes of determining those shareholders who are entitled to attend and vote at any general meeting, our directors may close our register of members and/or fix in advance a record date for such meeting, and such closure of our register of members or the setting of such a record date may prevent you from withdrawing the underlying ordinary shares represented by your ADSs and from becoming the registered holder of such shares prior to the record date, so that you would not be able to attend the general meeting or to vote directly. Where any matter is to be put to a vote at a general meeting, upon our instruction the depositary will notify you of the upcoming vote and will arrange to deliver our voting materials to you. We cannot assure you that you will receive the voting materials in time to ensure that you can instruct the depositary to vote the underlying ordinary shares represented by your ADSs.

In addition, the depositary and its agents are not responsible for failing to carry out voting instructions or for their manner of carrying out your voting instructions. This means that you may not be able to exercise your right to direct how the underlying ordinary shares represented by your ADSs are voted and you may have no legal remedy if the underlying ordinary shares represented by your ADSs are not voted as you requested. In addition, in your capacity as an ADS holder, you will not be able to call a shareholders' meeting.

Under the deposit agreement, if you do not vote, the depositary may give us a discretionary proxy to vote the ordinary shares underlying the ADSs at shareholders' meetings if we have timely provided the depositary with notice of meeting and related voting materials and (i) we have instructed the depositary that we wish a discretionary proxy to be given, (ii) we have informed the depositary that there is no substantial opposition as to a matter to be voted on at the meeting, and (iii) a matter to be voted on at the meeting would not have a material adverse impact on shareholders.

The effect of this discretionary proxy is that you cannot prevent the underlying ordinary shares represented by the ADSs from being voted, except under the circumstances described above. This may make it more difficult for ADS holders to influence the management of the company. Holders of ordinary shares are not subject to this discretionary proxy.

Because we do not expect to pay dividends in the foreseeable future, you must rely on price appreciation of the ADSs for return on your investment.

We currently intend to retain most, if not all, of our available funds and any future earnings to fund the development and growth of our business. As a result, we do not expect to pay any cash dividends in the foreseeable future. Therefore, you should not rely on an investment in the ADSs as a source for any future dividend income.

Our board of directors has complete discretion as to whether to distribute dividends, subject to certain requirements of Cayman Islands law. In addition, our shareholders may, subject to the provisions of our articles of association, by ordinary resolution declare a dividend, but no dividend may exceed the amount recommended by our directors. Under Cayman Islands law, a Cayman Islands company may pay a dividend out of either profit, retained earnings, or share premium account, provided that in no circumstances may a dividend be paid if this would result in the company being unable to pay its debts as they fall due in the ordinary course of business. Even if our board of directors decides to declare and pay dividends, the timing, amount and form of future dividends, if any, will depend on our future results of operations and cash flow, our capital requirements and surplus, the amount of distributions, if any, received by us from our subsidiary, our financial condition, contractual restrictions and other factors deemed relevant by our board of directors. Accordingly, the return on your investment in the ADSs will likely depend entirely upon any future price appreciation of the ADSs. There is no guarantee that the ADSs will appreciate in value or even maintain the price at which you purchased the ADSs. You may not realize a return on your investment in the ADSs and you may even lose your entire investment in the ADSs.

You may not receive dividends or other distributions on our ordinary shares and you may not receive any value for them, if it is illegal or impractical to make them available to you.

The depositary has agreed to pay to you the cash dividends or other distributions it or the custodian receives on ordinary shares or other deposited securities underlying the ADSs, after deducting its fees and expenses. You will receive these distributions in proportion to the number of ordinary shares your ADSs represent. However, the depositary is not responsible if it decides that it is unlawful or impractical to make a distribution available to any holders of ADSs. For example, it would be unlawful to make a distribution to a holder of ADSs if it consists of securities that require registration under the Securities Act of 1933 but that are not properly registered or distributed under an applicable exemption from registration. The depositary may also determine that it is not feasible to distribute certain property through the mail. Additionally, the value of certain distributions may be less than the cost of mailing them. In these cases, the depositary may determine not to distribute such property. We have no obligation to register under U.S. securities laws any ADSs, ordinary shares, rights or other securities received through such distributions. We also have no obligation to take any other action to permit the distribution of ADSs, ordinary shares, rights or anything else to holders of ADSs. This means that you may not receive distributions we make on our ordinary shares or any value for them if it is illegal or impractical for us to make them available to you. These restrictions may cause a material decline in the value of the ADSs.

You may experience dilution of your holdings due to the inability to participate in rights offerings.

We may, from time to time, distribute rights to our shareholders, including rights to acquire securities. Under the deposit agreement, the depositary will not distribute rights to holders of ADSs unless the distribution and sale of rights and the securities to which these rights relate are either exempt from registration under the Securities Act with respect to all holders of ADSs, or are registered under the provisions of the Securities Act. The depositary may, but is not required to, attempt to sell these undistributed rights to third parties, and may allow the rights to lapse. We may be unable to establish an exemption from registration under the Securities Act, and we are under no obligation to file a registration statement with respect to these rights or underlying securities or to endeavor to have a registration statement declared effective. Accordingly, holders of ADSs may be unable to participate in our rights offerings and may experience dilution of their holdings as a result.

We will incur increased costs as a result of being a public company, particularly after we cease to qualify as an “emerging growth company.”

We are a public company and expect to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, as well as rules subsequently implemented by the Securities and Exchange Commission, or the SEC, and the Nasdaq Global Market, impose various requirements on the corporate governance practices of public companies. As a company with less than US\$1.07 billion in revenues for our last fiscal year, we qualify as an “emerging growth company” pursuant to the JOBS Act. An emerging growth company may take advantage of specified reduced reporting and other requirements that are otherwise applicable generally to public companies. These provisions include exemption from the auditor attestation requirement under Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, in the assessment of the emerging growth company’s internal control over financial reporting and permission to delay adopting new or revised accounting standards until such time as those standards apply to private companies.

We expect these rules and regulations to increase our legal and financial compliance costs and to make some corporate activities more time-consuming and costly. After we are no longer an “emerging growth company,” we expect to incur significant expenses and devote substantial management effort toward ensuring compliance with the requirements of Section 404 of the Sarbanes-Oxley Act of 2002 and the other rules and regulations of the SEC. For example, as a result of becoming a public company, we will need to increase the number of independent directors and adopt policies regarding internal controls and disclosure controls and procedures. We also expect that operating as a public company will make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. In addition, we will incur additional costs associated with our public company reporting requirements. It may also be more difficult for us to find qualified persons to serve on our board of directors or as executive officers. We are currently evaluating and monitoring developments with respect to these rules and regulations, and we cannot predict or estimate with any degree of certainty the number of additional costs we may incur or the timing of such costs.

You may face difficulties in protecting your interests, and your ability to protect your rights through U.S. courts may be limited, because we are incorporated under Cayman Islands law.

We are an exempted company incorporated under the laws of the Cayman Islands with limited liability. Our corporate affairs are governed by our memorandum and articles of association, the Companies Act (as amended) of the Cayman Islands and the common law of the Cayman Islands. The rights of shareholders to take action against our directors, actions by our minority shareholders and the fiduciary duties of our directors to us under Cayman Islands law are to a large extent governed by the common law of the Cayman Islands. The common law of the Cayman Islands is derived in part from comparatively limited judicial precedent in the Cayman Islands as well as from the common law of England, the decisions of whose courts are of persuasive authority, but are not binding, on a court in the Cayman Islands. The rights of our shareholders and the fiduciary duties of our directors under Cayman Islands law are not as clearly established as they would be under statutes or judicial precedent in some jurisdictions in the United States. In particular, the Cayman Islands has a less developed body of securities laws than the United States. Some U.S. states, such as Delaware, have more fully developed and judicially interpreted bodies of corporate law than the Cayman Islands. In addition, Cayman Islands companies may not have the standing to initiate a shareholder derivative action in a federal court of the United States.

Shareholders of Cayman Islands exempted companies like us have no general rights under Cayman Islands law to inspect corporate records or to obtain copies of lists of shareholders of these companies. Our directors have discretion under our articles of association to determine whether or not, and under what conditions, our corporate records may be inspected by our shareholders, but are not obliged to make them available to our shareholders. This may make it more difficult for you to obtain the information needed to establish any facts necessary for a shareholder motion or to solicit proxies from other shareholders in connection with a proxy contest.

As a result of all of the above, our public shareholders may have more difficulties in protecting their interests in the face of actions taken by management, members of our board of directors or controlling shareholders than they would as public shareholders of a company incorporated in the United States.

Certain judgments obtained against us by our shareholders may not be enforceable.

We are a Cayman Islands exempted company and substantially all of our assets are located outside of the United States. Our current operations are primarily conducted in China. In addition, some of our current directors and officers are nationals and residents of countries other than the United States. Substantially all of the assets of these persons are located outside the United States. As a result, it may be difficult or impossible for you to bring an action against us or against these individuals in the United States in the event that you believe that your rights have been infringed under the U.S. federal securities laws or otherwise. Even if you are successful in bringing an action of this kind, the laws of the Cayman Islands and of China may render you unable to enforce a judgment against our assets or the assets of our directors and officers.

As an exempted company incorporated in the Cayman Islands, we are permitted to adopt certain home country practices in relation to corporate governance matters that differ significantly from the Nasdaq listing standards; these practices may afford less protection to shareholders than they would enjoy if we complied fully with the Nasdaq listing standards.

As a Cayman Islands exempted company listed on the Nasdaq Global Market, we are subject to the Nasdaq listing standards. However, Nasdaq rules permit a foreign private issuer like us to follow the corporate governance practices of its home country. Certain corporate governance practices in the Cayman Islands, which is our home country, may differ significantly from the Nasdaq listing standards. We may elect to rely on home country practice to be exempted from the corporate governance requirements. As a result, our shareholders may be afforded less protection than they would otherwise enjoy under the Nasdaq listing standards applicable to U.S. domestic issuers.

We are a foreign private issuer within the meaning of the rules under the Exchange Act, and as such we are exempt from certain provisions applicable to U.S. domestic public companies.

Because we qualify as a foreign private issuer under the Exchange Act, we are exempt from certain provisions of the securities rules and regulations in the United States that are applicable to U.S. domestic issuers, including:

- the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q or current reports on Form 8-K;
- the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act;
- the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and
- the selective disclosure rules by issuers of material nonpublic information under Regulation FD.

We will be required to file an annual report on Form 20-F within four months of the end of each fiscal year. In addition, we intend to publish our results on a semi-annually basis as press releases, distributed pursuant to the rules and regulations of the Nasdaq Global Market. Press releases relating to financial results and material events will also be furnished to the SEC on Form 6-K. However, the information we are required to file with or furnish to the SEC will be less extensive and less timely compared to that required to be filed with the SEC by U.S. domestic issuers. As a result, you may not be afforded the same protections or information that would be made available to you were you investing in a U.S. domestic issuer.

There can be no assurance that we will not be a passive foreign investment company, or PFIC, for U.S. federal income tax purposes for any taxable year, which could subject U.S. investors in our ADSs or ordinary shares to significant adverse U.S. federal income tax consequences.

In general, a non-U.S. corporation will be a PFIC for any taxable year in which (i) 75% or more of its gross income consists of passive income, or the income test, or (ii) 50% or more of the average value of its assets (generally determined on a quarterly basis) consists of assets that produce, or are held for the production of, passive income, or the asset test. For purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the ordinary shares of another corporation is treated as if it held its proportionate share of the assets of the other corporation and received directly its proportionate share of the income of the other corporation. Passive income generally includes interest, dividends, gains from certain property transactions, rents and royalties (other than certain rents or royalties derived in the active conduct of a trade or business). Cash is a passive asset for PFIC purposes. Goodwill is an active asset under the PFIC rules to the extent attributable to activities that produce active income.

The assets shown on our balance sheet are expected to consist primarily of cash and cash equivalents for the foreseeable future. Therefore, whether we will satisfy the asset test for the current or any future taxable year will depend largely on the value of our goodwill and on how quickly we utilize the cash in our business. We cannot give any assurance as to whether we will be a PFIC for the current or any future taxable year because (i) the value of our goodwill may be determined by reference to the market price of our ADSs, which may be volatile given the nature and early stage of our business, (ii) we expect to hold a significant amount of cash, and (iii) a company's PFIC status is an annual determination that can be made only after the end of each taxable year. In addition, prior to commercialization of our product candidates, we could be a PFIC for any taxable year in which our interest and other investment income constitutes 75% or more of our total gross income.

If we were a PFIC for any taxable year during which a U.S. investor owns our ADSs or ordinary shares, certain adverse U.S. federal income tax consequences could apply to such U.S. investor. See "Item 10 Additional Information—Material U.S. Federal Income Tax Consequences—Passive Foreign Investment Company Rules."

ITEM 4. INFORMATION ON THE COMPANY

4.A. History and Development of the Company

In February 2011, Adagene Inc. was incorporated under the laws of the Cayman Islands as our offshore holding company.

In December 2011, we established Adagene (Hong Kong) Limited, or Adagene Hong Kong, a wholly-owned subsidiary incorporated under the laws of Hong Kong, as our intermediary holding company. In February 2012, Adagene Hong Kong incorporated Adagene (Suzhou) Limited, or Adagene Suzhou, in China, through which we commenced our research and development activities in China.

In September 2017, we established a wholly-owned subsidiary in the state of Delaware, the United States, Adagene Incorporated, to conduct our research and development activities in the United States to facilitate the discovery and development of product candidates and expand our global presence, we have further incorporated several subsidiaries overseas, such as Australia, Singapore and Switzerland.

We are a holding company and do not directly own any substantive business operations in the PRC. We currently focus our business operations within the PRC through Adagene Suzhou. We (Adagene Inc.), however, hold certain intellectual properties and outsource certain research and development activities related to these intellectual properties to our subsidiaries. See “Items 3 Key Information—D. Risk Factors—Risks Related to Doing Business in the PRC.”

In February 2021, we completed an initial public offering in which we offered and sold an aggregate of 10,571,375 ordinary shares in the form of ADSs. Upon the initial public offering, all of our then issued and outstanding preferred shares were automatically converted into ordinary shares on a one-for-one basis. On February 5, 2021, the ADSs began trading on the Nasdaq under the symbol “ADAG.”

Our corporate headquarters is located at 4F, Building C14, No. 218, Xinghu Street, Suzhou Industrial Park Suzhou, Jiangsu Province, 215123, People’s Republic of China. Our registered office is located at Vistra (Cayman) Limited, P. O. Box 31119 Grand Pavilion, Hibiscus Way, 802 West Bay Road, Grand Cayman, KY1 - 1205 Cayman Islands. Our telephone number is +86-512-8777-3632. Our agent for service of process in the United States is Cogency Global Inc., located at 10E 40th Street, 10th Floor, New York, NY 10016. Our corporate website is www.adagene.com. The information contained on or that can be accessed through our website is not incorporated by reference into this annual report, and you should not consider information on our website to be part of this annual report.

The SEC maintains an internet site at www.sec.gov that contains reports, information statements, and other information regarding issuers that file electronically with the SEC.

4.B. Business Overview

OVERVIEW

We are a platform-driven, clinical-stage biopharmaceutical company committed to transforming the discovery and development of novel antibody-based cancer immunotherapies. Our platform is designed to generate therapeutic antibody candidates with unique functional epitopes and species cross-reactivity as highlighted by our immunotherapy pipeline. These features enable our novel drug discovery strategy to advance from lead identification through vigorous preclinical modeling to biomarker-guided mono-and combination immunotherapy development in clinical settings. We have pioneered a dynamic interface design to harness the conformational diversity of antibodies, which enlarges epitope sampling of a given drug target for differentiated therapeutic antibody development. We aim to push the boundaries of antibody discovery and engineering through the precise design, construction, and selection of antibody product candidates intractable to traditional antibody technology.

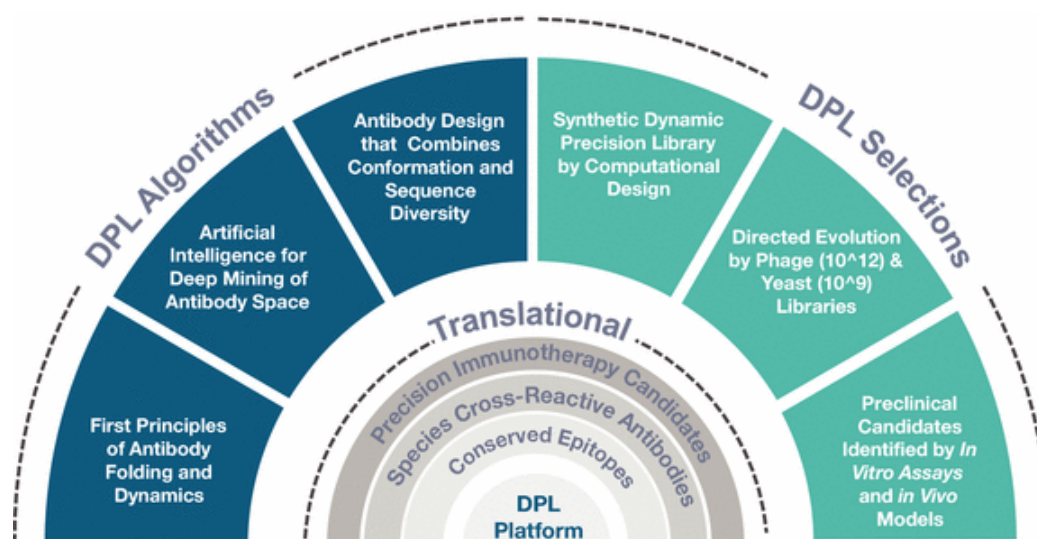
Life is motion. The motion of proteins and their dynamic interactions trigger a cascade of complex biological and pharmacological effects. Our core technology is built upon our fundamental understanding of the role that protein folding and the motion of molecules play in giving rise to dynamic conformational diversity, where an amino acid sequence can adopt multiple structures and functions. Our approach recognizes that a protein’s native state is not accurately represented by a single static structure but rather by a variety of structures in dynamic equilibrium, resulting in a high level of functional diversity, in contrast to the conventional static antibody drug discovery paradigm of “one sequence, one structure and one function.” We have developed our proprietary AI-Powered DPL platform to explore the dynamic conformational diversity of protein sequences, and the flexible binding sites of antibody sequences in particular, as a new paradigm for antibody drug discovery. Our DPL platform combines artificial intelligence, or AI, algorithms and ever-increasing big data in antibody sequence, structure, binding epitope and affinity from public and our own proprietary databases to design, construct and screen high-quality proprietary antibody libraries with well-defined sequence, scaffold and biophysical attributes for antibody drug discovery. Powered by computational physics in combination with AI and big data, our DPL platform samples a potentially infinite number of dynamic binding interface structures arising from the conformational diversity of a finite number of antibody amino acid sequences, allowing us to exponentially expand the universe of candidate antibody binding sites far beyond conventional natural or synthetic antibody repertoires. By exploiting conformational diversity, we have designed and precisely constructed approximately one trillion (10^{12}) antibody sequences in our DPL. These antibodies feature broad epitope (the portion of an antigen that are recognized by an antibody) coverage and robust chemistry, manufacturing, and control, or CMC, attributes.

We believe our AI-powered antibody discovery and engineering DPL platform significantly increase R&D productivity for antibody drug discovery, as illustrated by our clinical anti-CD137 and anti-CTLA-4 programs. DPL library screening against CD137 or CTLA-4 antigens has yielded a large number of high affinity primary hits. The abundant discovery hits with diversified binding epitopes show the power of our AI-powered DPL platform not only in creating novel antibodies in targeting different epitopes of a given antigen, but also in targeting the conserved epitope across different species of a given antigen with broad species cross-reactivity from human, monkey to mouse, which enables us to study their efficacy and safety in extensive immunocompetent or syngeneic animal models, to explore their pharmacodynamics and predictive biomarkers in responding vs nonresponding tumor models *in vivo*, and to understand their deep target biology and novel MOA before testing them in human clinical trials to look for their clinical signals consistent with their MOA. Our DPL platform empowers us to engage the dynamic epitope of the conformationally dynamic target which might be challenging using conventional antibody discovery approaches. We believe that the high-affinity and cross-reactive primary hits from our AI-Powered DPL library screening save time and cost from discovery to early clinical proof of concept. The broad species cross-reactivity of the primary hits also streamlines lead identification and potentially enables high fidelity translation from preclinical to clinical studies. Furthermore, we believe our AI-powered dynamic precision library expands the diversity at the start of discovery to maximize the chance that suitable leads are found on the first pass.

Translational fidelity from preclinical modeling to informed clinical development is one of the top challenges to developing cancer immunotherapies. Most traditionally developed antibodies do not cross react between their human and murine targets due to their limited species cross-reactivity, making it very difficult to reliably evaluate the same antibody in both the preclinical and clinical settings. Some of the most contentious issues related to preclinical and clinical studies of CD137 and CTLA-4, the targets of our lead product candidates, immunotherapies are traceable to the differences between the antibodies used for preclinical and clinical studies. For example, according to Frost & Sullivan, two of the leading clinical anti-CD137 agonist antibodies bind to different epitopes and exhibit dramatic differences in their respective clinical safety and efficacy results, underscoring the importance of finding suitable species cross-reactive antibodies like those we have utilized for comprehensive preclinical evaluation before entering clinical trials.

We believe that it is essential to model the interactions between tumors and an intact host immune system *in vivo* to evaluate the therapeutic potential of antibodies in preclinical studies. The flexibility of antibody binding interface is fundamental to the NEObody technology of our DPL Platform and allows us to generate species cross-reactive antibodies to assess the safety and efficacy potential of mono- and combination therapy candidates in syngeneic animal models before launching clinical trials. We use syngeneic animal models which are known for their intact *in vivo* immune systems to provide the original proof of concept for cancer immunotherapies by blocking immune check points with monoclonal antibodies, or mAbs. We believe that the use of species cross-reactive antibodies, rather than surrogate antibodies used in traditional syngeneic mouse models, should facilitate the translational relevance and clinical utility of these well-established preclinical models for determining optimal dose, schedule, sequencing, combination synergy, risk and benefit features. The results from the assessment of new species cross-reactive antibodies in rigorous preclinical models may allow us to control the scope and cost of clinical trials, enable the identification of potential clinical biomarkers useful to monitor clinical pharmacological and safety signals, and help preselect patients for precision mono- and combination therapies.

The figure below illustrates how our DPL platform integrates our computational algorithm-enabled high-throughput screening and functional antibody evaluation for preclinical candidates suitable for clinical development as explained above.

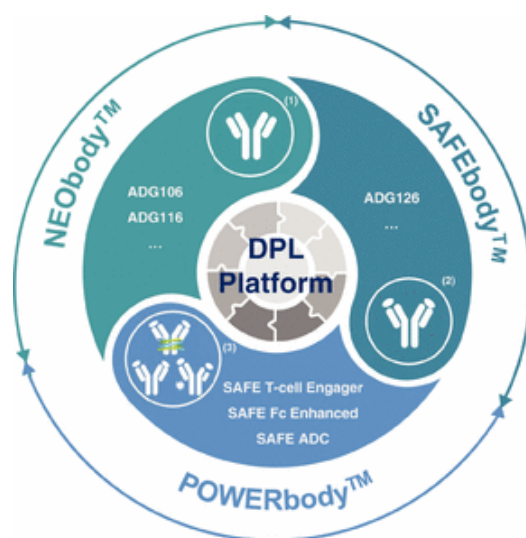


Our DPL platform is further composed of three proprietary enabling technologies tailored to three key attributes of antibody-based therapeutic modalities:

- NEObody technology is a fully synthetic phage display and yeast display-based antibody discovery technology, which we believe is differentiated from other synthetic antibody technologies through its innovative designs and precise constructions. NEObody technology enables the generation of antibodies designed with dynamic binding sites that adapt kinetically to unique epitopes, triggering a novel MOA. The species cross-reactive antibodies generated by NEObody technology not only have the potential to reveal new biological functions of the targets, but also facilitate preclinical studies using various immune system intact animal models, resulting in high fidelity translation from preclinical to clinical studies. We refer to antibodies generated by our NEObody technology as NEObodies.
- SAFEbody technology is designed to mask an antibody binding interface with a masking motif, which then prevents an antibody from binding to its target in healthy tissues. The masking motif is designed to activate, or unmask, the antibody to allow binding in the tumor microenvironment, or TME, where certain activation conditions such as a protease is upregulated as compared to healthy tissues, allowing the antibody to bind to its target for tumor killing. Our SAFEbody enabled therapeutic candidates are therefore designed to be activated predominantly in the TME while remaining largely in an inactive state in healthy tissues. Our SAFEbody technology can be applied to mask the binding sites of any antibodies including but not limited to NEObodies. We refer to such masked antibodies including NEObodies as SAFEbodies.
- POWERbody technology, which enables the creation of new versions of bispecific T-cell engagers, or TCEs, with enhanced safety profiles, antibody-drug conjugates, or ADCs, or antibodies that are designed to reach beyond the therapeutic potency of traditional monospecific antibodies.
- SAFEbody technology can be applied to our NEObodies, such as what we did with ADG116 to convert into ADG126. POWERbody is created by applying the SAFEbody technology to a bispecific TCE in either CD3 or both in CD3 and antigen binding arms to enhance the safety profile. Our POWERbody technology is designed to improve antitumor activity while maintaining the enhanced safety profile.

We believe that comprehensive *in vivo* preclinical evaluations are the key to assess the efficacy and safety potential of tailor-made antibody candidates before progressing them into lengthy and costly clinical trials. NEObody, SAFEbody and POWERbody technologies are all designed to facilitate favorable druggability, manageable CMC attributes, and reduced immunogenicity. As highlighted by our lead product candidates, such as ADG106, ADG126 and ADG116, our NEObody technology allows us to engineer and select species cross-reactive NEObodies designed to dynamically adapt to unique and evolutionally conserved epitopes. ADG126 has been further engineered using our SAFEbody technology to address the safety concerns associated with existing CTLA-4 therapeutics.

The figure below shows how our NEObody, SAFEbody, and POWERbody technologies on the one hand and DPL platform on the other hand are interconnected and utilized for the building of our product pipeline of mono- and combination immunotherapies.



Notes:

- (1) Antibodies generated by NEObody technology, which are designed with dynamic binding sites that adapt kinetically to unique epitopes, triggering a novel MOA.
- (2) NEObodies or traditional antibodies are masked in their binding sites by SAFEbody technology as shown by the blocking bar in the antibody binding sites in the figure, which are designed to be selectively activated in the TME, potentially limiting on-target off-tumor toxicity in normal tissues.
- (3) Multiple potent modalities, including bispecific T-cell engagers, ADC, and Fc engineering for enhanced ADCC, etc., are masked in their binding sites by SAFEbody to create a POWERbody.

Our most advanced NEObody product candidate, ADG106, is a fully human ligand-blocking agonistic anti-CD137 mAb currently being evaluated in Phase Ib clinical trials in the United States and China. ADG106 is designed to target a unique epitope of CD137 that is different from other anti-CD137 antibodies currently under clinical development. Epitope mapping and X-ray structural analysis of ADG106 with CD137 have shown in preclinical studies that ADG106 is capable of binding to CD137 in a fashion similar to its natural ligand, CD137L. Our first SAFEbody product candidate, ADG126, is a fully human anti-CTLA-4 masked antibody designed to address the safety concerns associated with existing CTLA-4 therapeutics. It is designed to enhance the safety features by masking the antibody binding site of ADG126, which would be unmasked in the TME, where the activated ADG126 would block CTLA-4 and deplete regulatory T-cells by means of enhanced antibody-dependent cellular cytotoxicity, or ADCC. In preclinical studies, ADG126 was tolerated at doses of up to 200 mg/kg in nonhuman primate models. As ADG126 is also species cross-reactive in humans, cynomolgus monkeys and mice, we believe that preclinical studies of ADG126 will support the rational design of clinical trials to expedite its development. Our third product candidate, ADG116, is a fully human anti-CTLA-4 NEObody. Epitope mapping and X-ray structural analysis have shown that in preclinical studies, ADG116 is capable of binding to a novel epitope of CTLA-4 different from ipilimumab, the only CTLA-4 mAb approved globally. The dynamic interface of ADG116 enabled not only its species cross-reactivity with human, cynomolgus monkey, and mouse CTLA-4 for preclinical studies, but also its dynamic engagement on a unique epitope of CTLA-4 to trigger a novel MOA distinct from ipilimumab by softer ligand blocking and stronger regulatory T-cell depletion via strong ADCC.

Our species cross-reactive ADG106, ADG126 and ADG116 have enabled a deep understanding of the interaction between tumor and host immune system *in vivo* in syngeneic animal models. This understanding has been utilized to design and guide the clinical development of rational, mechanism-based mono- and combination therapies using ADG106, ADG126 and ADG116. Because there is limited clinical safety and efficacy data available for anti-CD137 agonists, we have followed our preclinical and mechanistic study for the clinical development of ADG106. We observed three patients with \geq Grade 3 liver enzyme increase; among them, one patient with abnormal liver enzyme baseline showed a Grade 3 AST increase. ADG106 showed preliminary clinical antitumor activity in patients who have progressed after several lines of treatment in our completed Phase Ia dose escalation and ongoing Phase Ib dose expansion trials in the United States and China. It is very encouraging to observe the clinical response in connection with the changes in PD biomarkers due to target engagement in a dose dependent manner. We have also observed a correlation with a potential predictive biomarker for patient selection in three patients with more than 30% tumor shrinkage across different indications in retrospective analysis in our ongoing Phase I trials. This predictive biomarker is related to the CD137 pathway. We intend to further explore this predictive biomarker in order to guide our development of precision mono- and combination immunotherapies based on our preclinical and preliminary clinical data.

Our Clinical Pipeline

By leveraging our proprietary DPL platform, we have developed a robust pipeline of innovative product candidates in various stages of development, ranging from research and discovery to preclinical and clinical development. Our highly differentiated clinical-stage pipeline consists of ADG106, ADG126 and ADG116. We also have a robust preclinical pipeline in various stages of development. In addition, we have out-licensed the Greater China rights of ADG104, a PD-L1 mAb under clinical development, to our partner, Sanjin. We have the right to apply for the patents derived from our core and key technologies pertaining to ADG104 in the rest of the world and we retain a majority of the economic benefits derived from ADG104 in the rest of the world.

The following chart provides an overview of the status of each of our clinical-stage programs for which we have global rights.

Drug Target	Trial	Design	Preclinical	IND Enabling	Phase I	Phase II	Phase III	Anticipated Milestones in 2021
ADG106 Anti-CD137 NEObody	1001 (US)	Mono	Solid tumors and NHL					Study completion
	1002 (China)	Mono	Solid tumors and NHL					Study completion
	1003 (Australia)	Combo	All tumor types					Phase Ib read out
	1008 (China)	Combo	All tumor types					Phase Ib read out
	2001 (Global)	Mono/Combo (Biomarker*)	All tumor types					Phase Ib/II read out
ADG116 Anti-CTLA-4 Neobody	1001 (US)	Mono/Combo	Solid tumors					Study has been converted to the global ADG116-1003 trial
	1002 (China)	Mono/Combo	Solid tumors					Expansion in selected indications following ADG116-1003 trial
	1003 (Global)	Mono/Combo	Solid tumors					Safety and efficacy read out in selected indications. Expand patient enrollments in US as a global trial
ADG126 Anti-CTLA-4 SAFEbody	1001 (Global)	Mono/Combo	Solid tumors					Safety and efficacy read out in selected indications, lead SAFEbody
	1002 (China)	Mono/Combo	Solid tumors					Expansion in selected indications following ADG126-1001 trial

Notes:

* denotes biomarker driven patient enrollment

NHL = non-Hodgkin's lymphoma

ADG106: Novel agonistic anti-CD137 NEObody candidate

ADG106, is a fully human ligand-blocking, agonistic anti-CD137 immunoglobulin G4, or IgG4, mAb generated using our NEObody technology. ADG106 is being developed for the treatment of advanced solid tumors and non-Hodgkin's lymphoma, or NHL. CD137 stimulates the immune system to attack cancer cells and is a key driver for T-cell and natural killer cell, or NK cell, proliferation. ADG106 is designed to target a unique conserved epitope of CD137 with a novel MOA for CD137 agonism by its natural ligand-like binding and cross-linking by Fcγ receptors. The broad species cross-reactivity of ADG106 observed in preclinical studies has enabled us to explore robust translational studies concerning the biology of CD137 in mouse, rat, nonhuman primate, and human, especially for anti-CD137 as a single agent and in combination therapies in immuno-competent syngeneic tumor models. In preclinical studies to date, we observed that ADG106 had encouraging antitumor activity and was well tolerated as a monotherapy and in combination with the existing standard-of-care, or SOC, and other immuno-oncology therapies, which was confirmed in the Phase I clinical trials in cancer patients as a monotherapy. These data indicate that ADG106 has the potential to address the limitations of other existing anti-CD137 therapies.

As of March 31, 2021, we have completed patient enrollments in each of our Phase I studies of ADG106 in both the United States and China as a monotherapy in patients with advanced or metastatic solid tumors and/or NHL. We held a successful End of Phase I meeting with the FDA on March 2, 2021 and received productive feedback for biomarker-stratified single agent and combination Phase Ib/II study design from the FDA. ADG106 was dose escalated up to 10 mg/kg and is well tolerated at dose expansion at 3 mg/kg, 5 mg/kg and at 300mg and 400 mg flat doses. A total number of 98 patients have been dosed. Both clinical trials, namely ADG106-1001 and ADG106-1002, have limited Treatment Emergent Adverse Effects, or TEAEs, liver toxicity or hematologic abnormalities. We observed three patients with >_Grade 3 liver enzyme increase; among them, one patient with abnormal liver enzyme baseline showed a Grade 3 AST increase. Two patients developed hemolytic anemia in ADG106-1002 which were controlled; one of the two patients received prior therapies which were known to cause autoimmune hemolytic anemia. One patient with a solid tumor who previously failed chemotherapies, radiotherapy, and an anti-PD-L1 related antibody treatment showed a partial response to ADG106 treatment with a 40% tumor size reduction after two treatment cycles. In addition, two NHL patients showed more than a 30% tumor size reduction after one and two ADG106 treatment cycles, respectively. Furthermore, biomarker studies showed target engagement with specific PD biomarkers indicative of immune system activation, and clinical response correlated with changes in CD137 target engagement. These data are encouraging given that the enrolled population was not preselected and was heavily pretreated. We have identified a potential predictive biomarker which correlates with patient response to ADG106 treatment from a retrospective analysis of the ongoing Phase I clinical trial. Based on this finding, we are in the process of preparing an additional Phase Ib/II trial which we expect to initiate in 2021 and for which we intend to stratify and preselect patients using this predictive biomarker to potentially enhance clinical response of patients to ADG106 treatment.

We have also evaluated ADG106 in combination with other therapies including chemotherapies, immune modulators, and immuno-oncology therapies in preclinical studies. Data from combination studies in tumor bearing mice showed that the combination of ADG106 with immune checkpoint inhibitors, including an anti-PD-1/L1 mAb or anti-CTLA-4 mAb, enhanced *in vivo* antitumor activity. We plan to explore the combination of ADG106 with other targeted antibody therapies for the treatment of hematologic malignancies and solid tumors. We also have identified tumor-specific biomarkers that we believe may correlate with ADG106 antitumor activity in multiple mouse tumor models. These preclinical study findings are consistent with the interim results from our ongoing Phase Ib clinical trials.

Currently, we focus on evaluating combinations of ADG106 with various therapies in clinical trials. We have received NMPA approval for the ADG106-1008 trial in China, which is a Phase Ib/II combination trial of ADG106 with anti-PD-1 in advanced solid tumors and hematological malignancies. In March 2021, we initiated patients enrollment in China for ADG106-1008 study to evaluate clinical safety and efficacy of ADG106 in combination with anti-PD-1 therapy. We are also in the process of submitting a Clinical Trial Notification, or CTN, for our ADG106-1003 clinical trial in Australia, which will combine ADG106 with anti-PD-1, and other therapies in advanced solid tumors and hematological malignancies.

ADG126: Novel anti-CTLA-4 SAFEbody candidate

Our most advanced SAFEbody program, ADG126, is a masked fully-human anti-CTLA-4 mAb engineered to address the safety concerns associated with existing CTLA-4 therapeutics, while maintaining potency when locally activated in the TME. The FDA approval of ipilimumab validated anti-CTLA-4 for cancer treatment. However, due to its on-target off-tumor toxicity, the approved indications for ipilimumab are limited, which we believe has caused sales of ipilimumab to trail other immuno-oncology therapies such as anti-PD-1/L1 antibodies.

ADG126 is designed to address the toxicity and efficacy issues related to the MOA of existing approved CTLA-4 immuno-oncology therapies and to expand the potential of CTLA-4 as a target for the treatment of cancer. In preclinical studies, ADG126 was tolerated at doses of up to 200 mg/kg in nonhuman primate models. We believe the encouraging preclinical tolerability of ADG126 suggests its potential in combination with other immunotherapies such as an anti-PD-1/PD-L1 antibody or an anti-CD137 antibody, including ADG106. We have presented updated preclinical data at the American Association for Cancer Research (AACR) Annual Meeting 2021. The data shows that ADG126 demonstrated an impressive safety margin while maintaining its potent antitumor efficacy.

We have started the Phase I dose escalation in March 2021 and have successfully finished DLT evaluation of three patients at 0.1 mg/kg in Australia for the treatment of various advanced solid tumors without observing any dosing limiting toxicity and other treatment related safety issues. We currently plan to do dose escalation for up to 10mg/kg. We have also received approval from the FDA for enrolling patients in the Phase I clinical trial of ADG126 in the United States. We are on track for safety and efficacy data readout in selected indications in 2021. Meanwhile, the NMPA has accepted our pre-IND request to start ADG126 Phase I trial in China with revised protocol at higher starting dose than that in the original submission.

ADG116: Novel anti-CTLA-4 NEObody candidate

ADG116 is a fully-human ligand-blocking anti-CTLA-4 mAb generated using our NEObody technology. ADG116 is designed to target a unique conserved epitope of CTLA-4. In preclinical studies, ADG116 was observed to have softer CTLA-4 ligand blocking and stronger ADCC for depleting regulatory T-cells than ipilimumab. In a head-to-head *in vivo* efficacy study, ADG116 was observed to have a five-fold greater anti-tumor activities in comparison with ipilimumab. In addition, ADG116 was observed to induce antitumor responses concomitant with reduced immunosuppressive regulatory T-cell and enhanced cytotoxic T lymphocyte (CD8⁺ T-cells) activities in the TME. We believe that these preclinical results support the further clinical evaluation of ADG116 both as monotherapy and combination therapy for a wide range of tumor types.

Summary of clinical data

Status: As of April 19, 2021, we have enrolled more than 10 patients in ADG116-1003. We have completed five levels of dose escalation at 0.003, 0.01, 0.03, 0.1, 0.3 mg/kg without observing any \geq Grade 2 TEAEs or other drug related safety issues and have dosed all three patients in the cohort at 1 mg/kg. We currently plan to do dose escalation for up to 10mg/kg.

Safety Assessment: Analysis of all safety data generated to date demonstrates that ADG116 has been well-tolerated in more than 10 patients with no dose-limiting toxicities or unexpected safety signals. No drug related Grade 2, Grade 3 or Grade 4 toxicities have been observed.

Pharmacodynamics Assessment: A dose-dependent change in CD8⁺ and CD4⁺ TEM / Treg ratios, important pharmacodynamic (PD) biomarkers indicating immune activation, was observed for patients dosed by ADG116. In particular, a patient, refractory to prior pembrolizumab therapy (> 25 cycles), demonstrated striking increases in T and NK cells, and CD8⁺ and CD4⁺ TEM / Treg. The Grade 1 treatment-related pruritus of this patient is a clinical symptom consistent with immune-mediated action of ADG116 treatment.

Pharmacokinetics Assessment: The terminal half-life of ADG116 was within the normal range of IgG1 based antibodies.

The Phase 1 dose escalation data demonstrates the clinical proof of mechanism for ADG116 in targeting CTLA-4, consistent with preclinical observations for the potency of ADG116 starting from 0.03 to 0.3 mg/kg.

The ADG116-1001 Phase I trial in the United States was placed on clinical hold on September 30, 2019 by the FDA, after we reported to the FDA the death of the only patient dosed in the trial. The FDA removed the clinical hold on December 5, 2019 after we submitted an amendment to the study protocol. With favorable clinical data in Australia as of April 19, 2021, we look forward to expanding the ongoing global Phase I trial, with the acceptance of revised study protocol by the FDA, to expand the trial in the United States. Separately, the NMPA has accepted our application to proceed with revised protocol at higher starting dose than that in the original submission.

Our Global Partnerships and Collaborations

We have a successful track record of collaborations and partnerships with global biopharmaceutical companies and academic institutions. So far, we have established multiple collaboration programs and will continue to seek partnership opportunities where we can leverage our proprietary technology platform to develop novel antibodies to address unmet medical needs. Over the past two years, we have established partnerships and collaborations with multiple biopharmaceutical companies.

- We entered into a material transfer and collaboration and license agreement with ADC Therapeutics SA, or ADC Therapeutics, under which ADC Therapeutics intends to use our SAFEbody technology to generate a masked antibody that could be combined with the pyrrolobenzodiazepine cytotoxic payload technology used in ADC Therapeutics' ADCs for the development of a novel ADC against a solid tumor target. Under the agreement, we could be eligible to receive royalty payments and could have an exclusive option to negotiate a license to develop and commercialize co-developed assets in certain territories; and

- We are also collaborating with Guilin Sanjin Pharmaceutical Co., Ltd., or Sanjin, and its affiliates to develop two different monoclonal antibodies with the first being ADG104, a monospecific antibody that targets PD-L1 and is in Phase Ib and Phase II clinical trials concurrently in China, and the second being an undisclosed monoclonal antibody, which Sanjin and its affiliates have received IND approval from the NMPA in March 2021 to initiate clinical trials. This will mark the fifth antibody into the clinical trial stage generated by our platform;
- We have recently extended the term of our research collaboration agreement, or the NIH RCA, with the National Heart Lung and Blood Institute, part of the National Institutes of Health, or NIH, to 2023. We first entered into the NIH RCA in March 2018 to collaborate with Dr. Richard Childs, Chief of the Laboratory of Transplantation Immunotherapy at NHLBI, who has used antibodies discovered by us to develop a CAR-T cell therapy candidate targeting a human endogenous retrovirus expressed in the majority of clear cell kidney tumors. The extension of the NIH RCA will allow us to use our proprietary antibody technology to further collaborate with Dr. Richard Childs and his team to develop other antibodies; and
- We entered into a collaboration and license agreement with Exelixis, Inc., or Exelixis, under which Exelixis will utilize our SAFEbody technology platform to generate masked versions of mAbs from Exelixis' growing preclinical pipeline for the development of ADCs or other innovative biologics against Exelixis-nominated targets. Under the agreement, we could be eligible to receive upfront payment as well as milestone and royalty payments on net sales of any potential products developed around each of these targets. In March 2021, we received an upfront payment of US\$11 million from Exelixis.

We are also working with global biopharmaceutical companies to potentially develop additional strategic partnerships.

- We had worked with Celgene (now Bristol-Myers Squibb) to discover antibodies targeting novel antigens using our proprietary DPL platform;
- Under a material transfer agreement, we are developing SAFEbody drug conjugates against a tumor target selected by Tanabe Research Laboratories, Inc., or TRL, with potential for negotiating a future license agreement with TRL if our pilot work proves successful;
- We entered into an evaluation agreement with a global biotechnology company, or the Evaluation Agreement, under which we are developing bispecific antibodies leveraging our SAFEbody and bispecific technologies against tumor targets provided by the counterparty. The Evaluation Agreement could facilitate the parties' interest in a further collaboration concerning the development of a new antibody therapeutic; and
- We had previously collaborated with GlaxoSmithKline (China), or GSK China, where we were engaged to generate high affinity antibodies against multiple epitopes of multi-transmembrane targets; and we previously worked with Jiangsu Hengrui Medicine Company Limited, or Jiangsu Hengrui, where we were able to discover cross-reactive agonistic antibody for immuno-oncology.

OUR CLINICAL PIPELINE

By leveraging our proprietary DPL platform, we have developed a robust pipeline of innovative product candidates in various stages of development, ranging from research and discovery to preclinical and clinical development. Our highly differentiated pipeline consists of our lead clinical-stage candidates, ADG106, ADG126 and ADG116. We also have a robust preclinical pipeline in various stages of development. In addition, we have out-licensed the Greater China rights of ADG104, a PD-L1 mAb in Phase Ib and Phase II trials concurrently in China to our partner Sanjin. We have the right to apply for the patents derived from our core and key technologies pertaining to ADG104 in the rest of the world and we retain a majority of the economic benefits derived from ADG104 in the rest of the world.

ADG106: Novel Agonistic Anti-CD137 NEObody Candidate

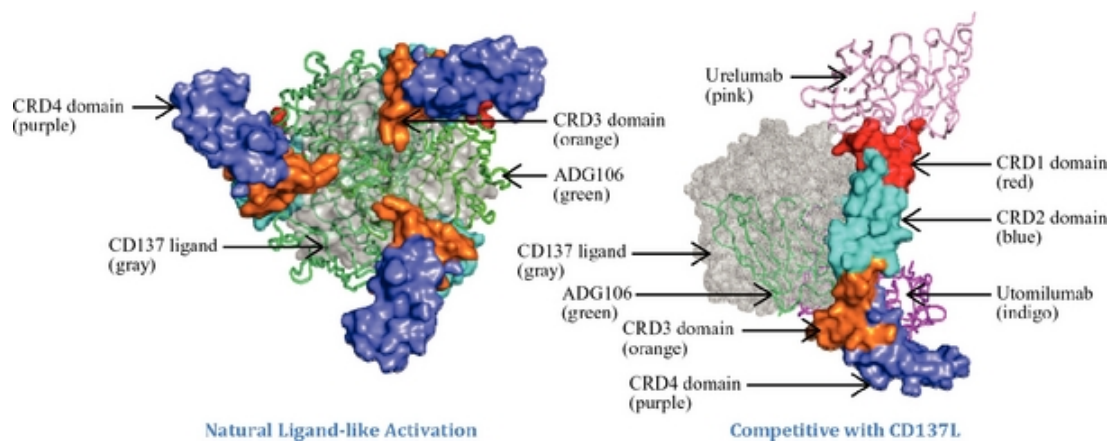
Summary

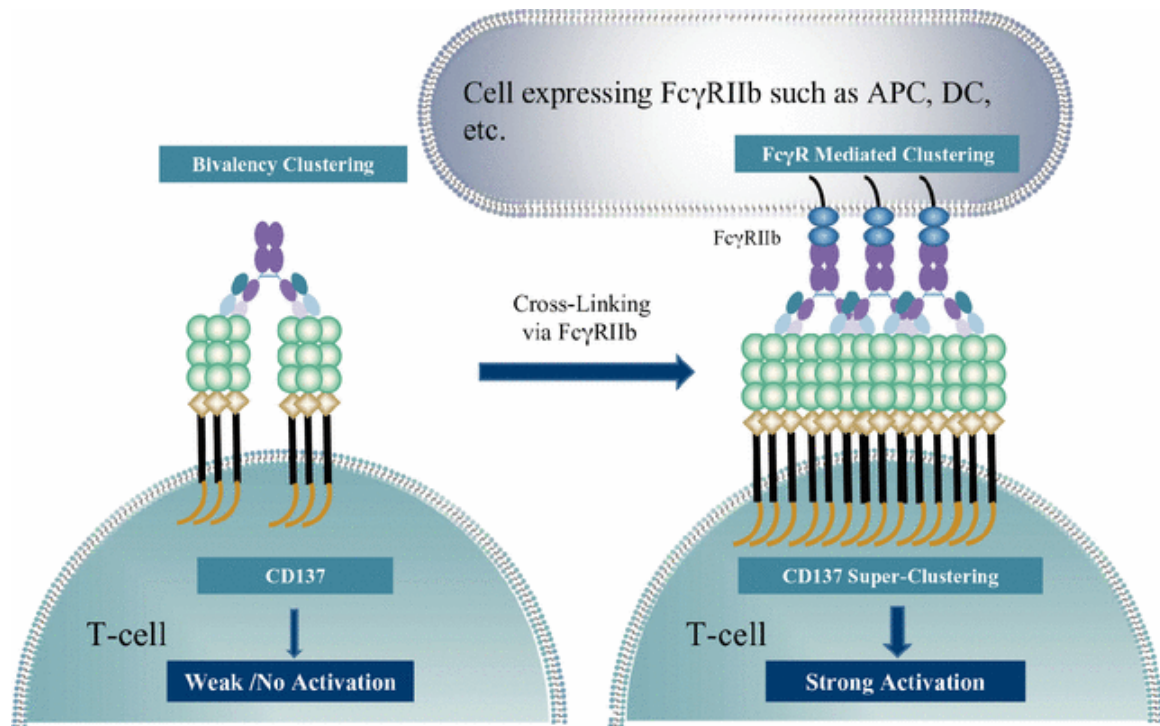
Our lead product candidate, ADG106, is a fully human ligand-blocking, agonistic anti-CD137 IgG4 mAb designed to target a unique conserved epitope of CD137. As of March 31, 2021, we have completed patient enrollment in each of our two Phase I trials of ADG106 as a monotherapy in patients with advanced or metastatic solid tumors and/or NHL in the United States, or the ADG106-1001 clinical trial, and in China, or the ADG106-1002 clinical trial. ADG106 was well-tolerated in the completed Phase Ia dose escalation of the Phase I clinical trials. Early efficacy signals were also observed with tumor size reduction, significant target modulations and increased T-cell and NK proliferation, consistent with MOA.

Mechanism of Action

CD137 is a member of the tumor necrosis factor, or TNF, receptor superfamily. As illustrated in the figure below, the binding of an antibody to this receptor induces a co-stimulatory signal on activated enhanced cytotoxic T lymphocyte, or CD8⁺ T-cells, and natural killer, or NK cells, resulting in proliferation, and increased pro-inflammatory cytokine secretion and cytolytic function. CD137 co-stimulation is a clinically validated pathway for T-cell activation and its antitumor response is highlighted by the approval of a CD137-targeting CAR-T therapy by the FDA. Because most tumors are killed by cytotoxic T-cells in an antigen specific manner, we believe agents that mediate CD8⁺ T-cell activation can impart strong cytolytic activity. Therefore, we believe that CD137 agonists are promising candidates with potential to enhance and mediate long lasting antitumor immunity.

ADG106 is designed to bind to activated human CD4⁺ and CD8⁺ T-cells with low nanomolar affinity and block CD137 ligand binding in a concentration-dependent manner to disable its reverse signaling. As shown in the figure below, ADG106 is designed to target a unique conserved epitope of CD137 with a novel MOA for CD137 agonism by its natural ligand-like binding and cross-linking by Fcγ receptors. ADG106 has not been observed to bind to unstimulated naïve T-cells, which have no detectable level of CD137 expression. ADG106 is also designed to bind to activated NK cells to boost their cytotoxic and ADCC functions.



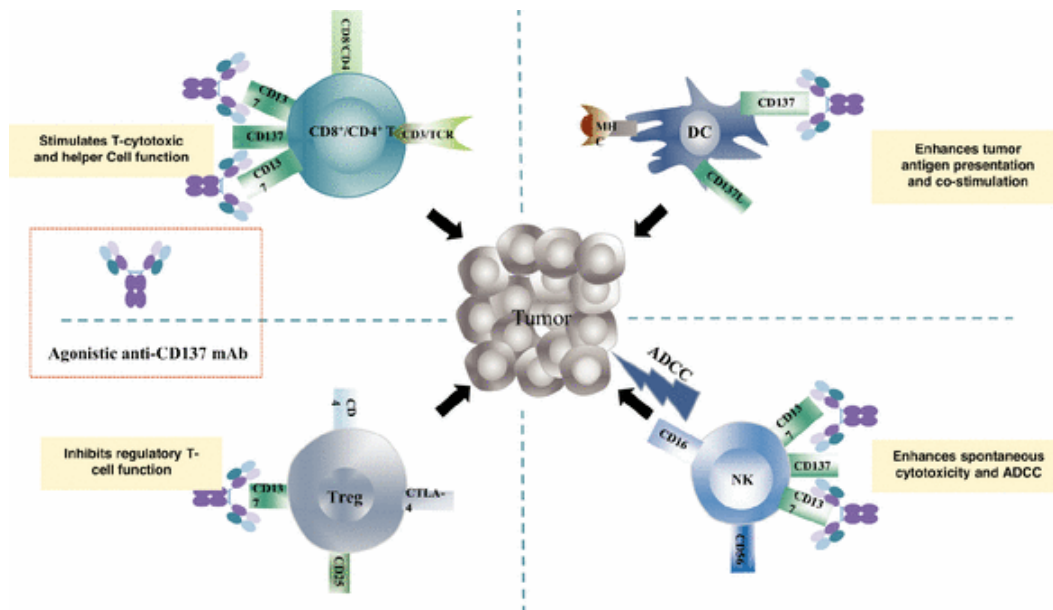


Notes:

“APC” refers to antigen-presenting cells;

“DC” refers to dendritic cells.

The MOA of ADG106 in tumor TME is illustrated below.



Notes:

“DC” refers to dendritic cells;

“Treg” refers to regulatory T-cell.

Summary of Clinical Trial Data

Overview: As of March 31, 2021, ADG106 was dose escalated up to 10 mg/kg and had been observed to be well-tolerated at dose expansion at 3 mg/kg, 5 mg/kg and at 300 mg and 400 mg flat doses for a total number of 98 patients dosed. Liver enzyme elevation of \geq Grade 3 was reported in three patients, with one determined to be not treatment related. We also observed tumor shrinkage in some patients.

Trial Design: Our Phase I clinical trials were designed to evaluate the safety and tolerability of ADG106, as well as its pharmacokinetics, or PK, immunogenicity, and preliminary clinical response. There were two parts to the dose escalation study: for the ADG106-1001 trial, the accelerated titration phase at 0.03, 0.1, and 0.3 mg/kg and a conventional “3+3” dose escalation phase at 1, 3, 5 and 10 mg/kg. For ADG106-1002 trial, the accelerated titration phase at 0.1 mg/kg and a conventional “3+3” dose escalation phase at 0.5, 1.5, 3, 5 and 10 mg/kg. ADG106 was administered once every three weeks by intravenous infusion.

Dose-expansion cohorts started at dose levels that were observed to be well-tolerated in the dose escalation phase and showed evidence of clinical and biological activities. Patients with advanced or metastatic solid tumors or NHL, who were refractory or relapsed after exhausting almost all available therapies, were enrolled for a maximum of 24 months unless they withdrew earlier due to disease progression, intolerable toxicity, or withdrawal of consent. The protocol allowed for up to 52 patients in ADG106-1001 and 124 patients in ADG106-1002 to be enrolled in the accelerated titration, dose escalation, and dose expansion phases.

The primary objective of the Phase I clinical trials, including both the dose escalation phase and dose expansion phase, is to assess safety and tolerability at increasing dose levels of ADG106 as a monotherapy in patients with advanced or metastatic solid tumors and/or NHL. The secondary objectives of the Phase I clinical trial are to characterize the PK profile of ADG106 and to evaluate the immunogenicity of ADG106 and potential antitumor activity of ADG106. An exploratory objective of such Phase I clinical trial is to identify potential biomarkers of patients who respond to treatment with ADG106.

Status: As of March 31, 2021, we have completed patient enrollments in each of our Phase I studies of ADG106 in both the United States and China as a monotherapy in patients with advanced or metastatic solid tumors and/or NHL. 98 patients were enrolled, among whom 36 patients were enrolled and treated in the ADG106-1001 clinical trial and 62 patients were enrolled and treated in the ADG106-1002 clinical trial. Thirty-eight patients were enrolled in the dose escalation phase and 60 patients were enrolled in the dose expansion phase. Patients in the expansion cohort of both trials were still on the study treatment.

Safety Assessment: As of March 31, 2021, 36 patients and 62 patients were enrolled in the two Phase I trials in the United States and China, respectively. ADG106 is generally well tolerated at 3mg/kg and 5mg/kg with dose escalation up to 10mg/kg. We observed limited TEAEs, liver toxicity or hematologic abnormalities in both trials.

As of March 31, 2021, 36 patients enrolled in the ADG106-1001 clinical trial in United States had safety assessments. 35 of 36 (97%) patients discontinued ADG106 treatment (26 patients discontinued due to progression disease, 6 patients discontinued due to adverse events, 2 patients due to un-related death, and 1 patient due to non-compliance). Two DLTs were observed, including a Grade 2 hypoglossal nerve disorder at 5 mg/kg and a Grade 3 adrenal insufficiency at 10mg/kg cohorts. Across all dose cohorts, liver function tests showed two patients with \geq Grade 3 AST increase, including one patient who had abnormal baseline liver enzyme exhibited Grade 3 AST increase. Hematologic tests showed two patients with Grade 3 hemoglobin decreases, and five patients had Grade 3 lymphocyte decreases.

As of March 31, 2021, 62 patients enrolled in the ADG106-1002 clinical trial in China had safety assessments. 48 of 62 (77.4%) patients discontinued ADG106 treatment (34 patients discontinued due to progression disease, 7 patients discontinued due to adverse events, 5 due to withdrawal of consent, 1 due to death of disease progression and 1 due to clinical deterioration). One DLT (Grade 4 neutrophil count decreased, 10mg/kg) was observed in one patient with mantle cell lymphoma. Across all dose cohorts of 62 patients, only one patient showed Grade 3 AST and ALT liver enzyme increases. Two patients dosed at 5mg/kg or 10mg/kg experienced Grade 3 and 4 hemolytic anemia, respectively. Both patients were treated and subsequently recovered.

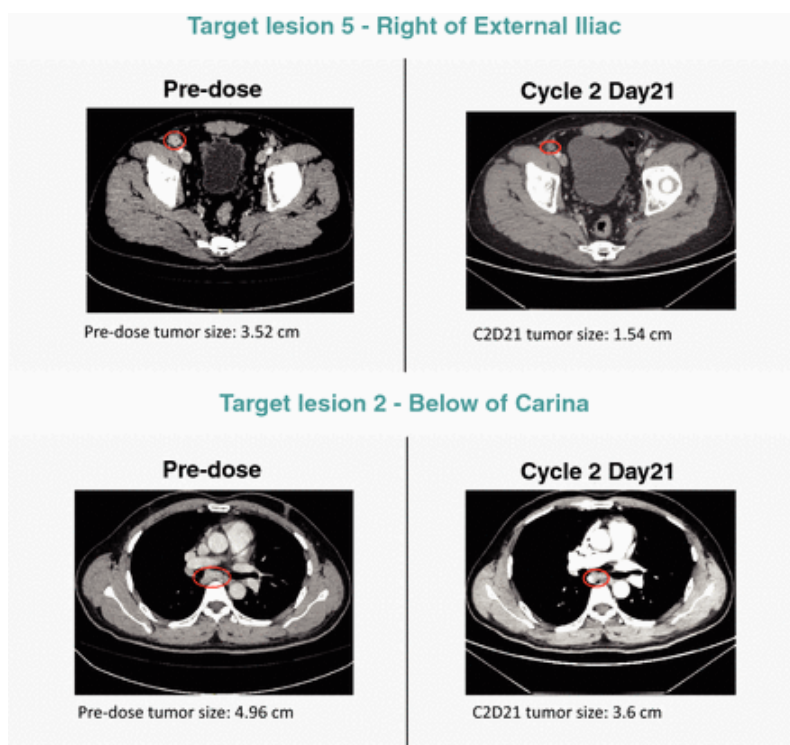
Clinical Efficacy Assessment: As of March 31, 2021, 81 of 98 patients enrolled in both trials received post-treatment scans and were evaluated for preliminary efficacy assessment. The responses observed in these patients included one partial response, 44 stable disease, and 36 progressive diseases. The disease control rate was 56% (45 of 81 patients). Three patients enrolled in ADG106-1002 clinical trial achieved greater than 30% tumor shrinkage. One patient with solid tumor had a partial response with an approximately 40% tumor size reduction in the target lesions and two NHL patients showed tumor shrinkage of 32% and 33% at the end of the Cycle two. A third ADG106-1002 NHL patient showed tumor size reduction of 17% and a patient with esophageal carcinoma enrolled in ADG106-1001 achieved 18% tumor shrinkage.

As of March 31, 2021, of the 81 patients who received post-treatment scans, 30 were enrolled in ADG106-1001 clinical trial. The observed responses were 15 stable disease and 15 progressive diseases and a disease control rate of 50% (15 of 30 patients). Tumor shrinkage and a decrease in standard uptake value scores on PET CT images were observed in three patients, including one patient with stage IV follicular lymphoma who was refractory to multiple prior therapies including rituximab, another patient with endometrial carcinoma, and a third patient with esophageal carcinoma.

As of March 31, 2021, of the 81 patients who received post-treatment scans, 51 were enrolled in ADG106-1002 clinical trial. The observed responses were one partial response, 29 stable disease, and 21 progressive disease with a disease control rate of 59% (30 of 51 patients). One patient with nasopharyngeal carcinoma demonstrated partial response with an approximately 40% tumor size reduction in the target lesion.

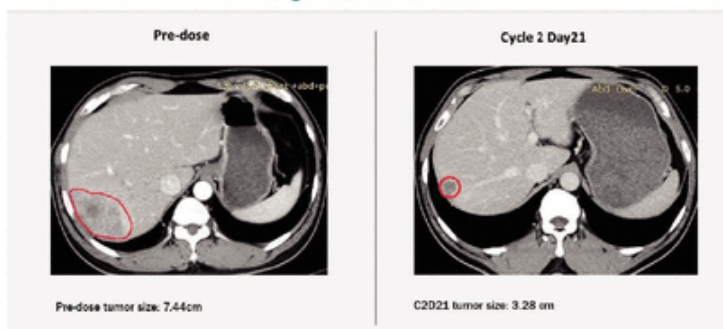
In conclusion, we observed a disease control rate of 56% among 81 patients including one patient with refractory nasopharyngeal carcinoma who had failed four prior therapies including anti-PD-L1 and four other patients with deep responses that exhibited 33%, 32%, 18%, and 17% tumor size reductions. Six patients remained on ADG106 treatment for over six months including one patient who received 3 mg/kg ADG106 treatment for over one year.

Case 1: Patient A with NHL, who relapsed after multiple chemotherapies and stem cell transplantation achieved 33% tumor size reduction after one dose of ADG106 at 3 mg/kg.

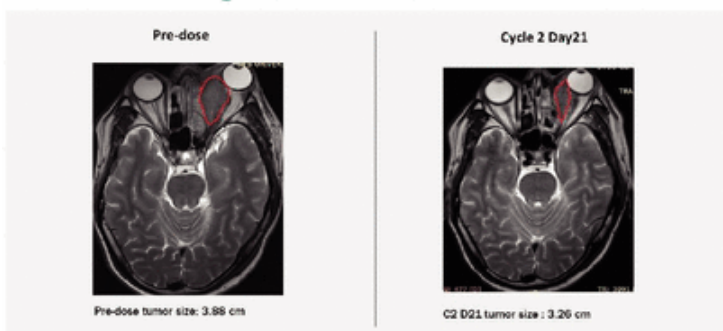


Case 2: Patient B with solid tumor (stage IV), who relapsed after multiple lines of treatment (chemotherapies, radiotherapy, target therapy, and immune checkpoint inhibition therapy), showed 40% tumor size reduction after two doses of ADG106 at 5 mg/kg.

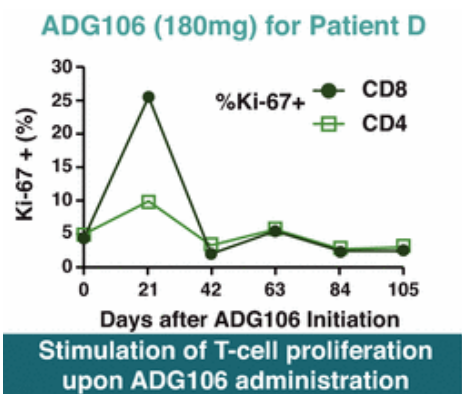
Target Lesion 1 – Liver



Target Lesion 3 – Left Ethmoid Sinus



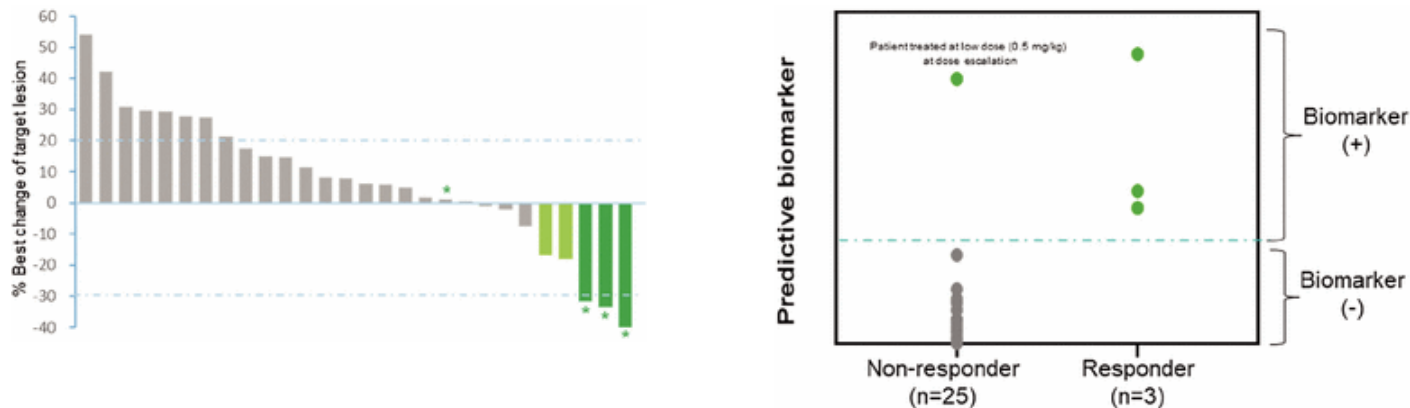
Pharmacodynamic Biomarker Measure of CD137 Target Modulation: As shown below, we have observed stimulation of T-cell proliferation and expansion in one patient treated with ADG106, evidenced by an increase in percentage of Ki-67 protein (an indicator of proliferative activity).



As illustrated below, we have also observed increased proliferation of NK cells in patients treated with ADG106 after the first cycle of treatment. Dose dependent stimulations of the identified immune cell subpopulation following ADG106 treatment at doses of 0.1, 0.5, and 1.5 mg/kg (see figure below on the right) were observed. No significant difference was observed from <_1.5 to 10 mg/kg, suggesting that the drug may have saturated CD137 receptors on the target cells at the doses >_1.5 mg/kg. This is the first report of an anti-CD137 antibody drug showing stimulation of NK cell proliferation in human. This finding also clarifies the MOA of ADG106, suggesting involvement of diverse immune cells in ADG106 mediated anti-tumor activities in human.

Our ADG106 Phase I clinical trials enrolled cancer patients without regard to cancer types. As shown in the figure below on the left, the effect of ADG106 on soluble CD137 was not tumor type specific, but rather a universal event observed for most of the patients. As seen in the figures below, we observed dose-dependent increases in the biomarker level in patient serum after ADG106 treatment and correlation of the change of the soluble CD137 with patient response.

Identification of a Potential Predictive Biomarker for ADG106 Treatment Response: We have identified a potential predictive biomarker that correlated with patient treatment responses based on a retrospective analysis of pretreatment biopsy specimens from 28 patients with clinical outcome data as shown in the diagram below on the right panel. As of March 31, 2021, three patients who achieved greater than 30% tumor shrinkage after ADG106 treatment were found to be biomarker positive. One Phase Ia patient who was treated with a low dose of ADG106 was biomarker positive and showed stable disease, as shown in the waterfall plot below on the left panel. Twenty-four biomarker negative patients did not show significant response as measured by tumor size reduction in CT images.



We have developed a high sensitivity multiplex IHC assay to measure the expression of the predictive biomarker. We measured expression of the predictive biomarker in 746 tumor microarray, or TMA, samples from patients with 14 different tumor types and identified biomarker positive expression of up to 42% in various types of solid tumors and hematological malignancies.

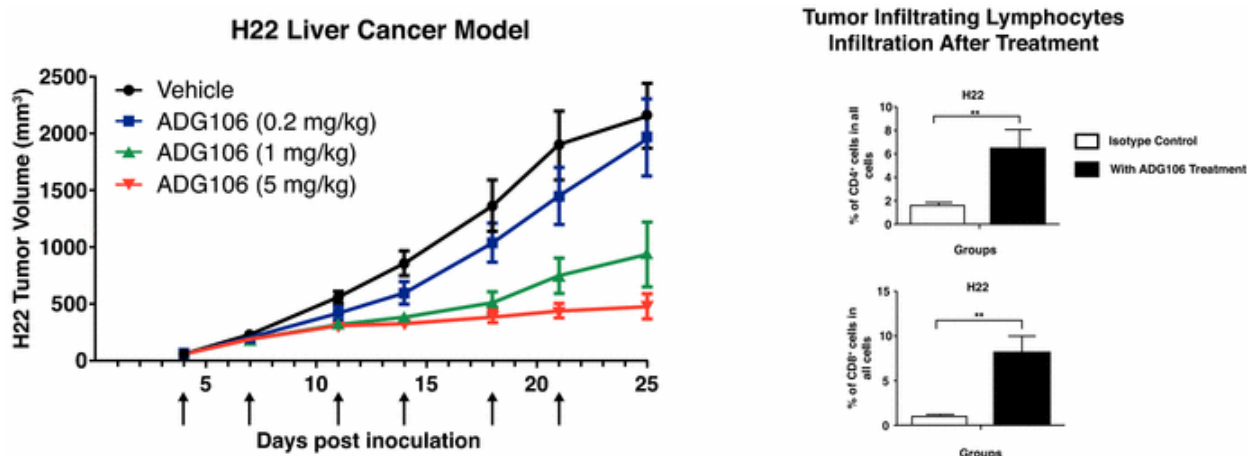
We will stratify and preselect patients using this biomarker in the upcoming Phase Ib/II clinical trials in 2021. In the early stage of the Phase Ib/II clinical trials, biomarker positive and negative patients will be identified using our multiplex IHC clinical trial assay in order to prospectively validate the predictive biomarker. This tumor biomarker test may be developed as companion diagnostic to facilitate ADG106 registration according to FDA requirements.

Summary of Preclinical Studies and Results

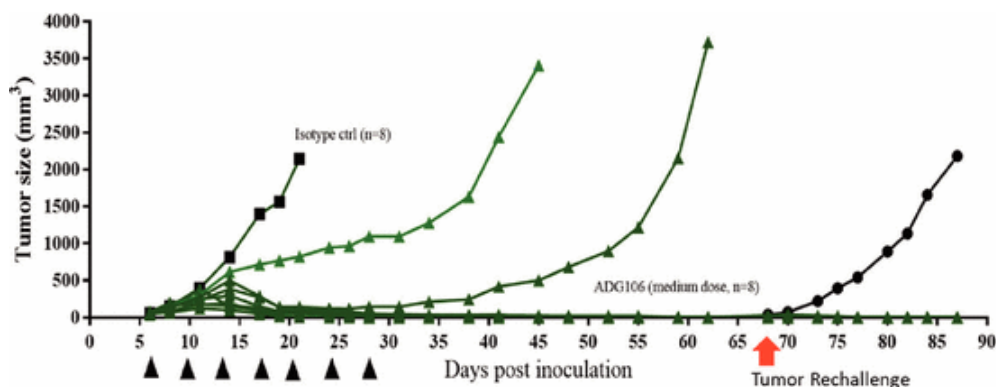
Overview: ADG106 was evaluated extensively in both *in vitro* and *in vivo* preclinical studies. ADG106 was observed in *in vitro* studies to enhance activation of, and cytokine release by, primed T-cells alone or in combination with other immunomodulatory agents. ADG106 was also observed to have antitumor activities *in vivo* as a monotherapy in a dose dependent manner in multiple tumor models. When combined with a variety of cancer therapeutics, ADG106 exhibited antitumor activity *in vivo* in animal models, including in immunotherapy resistant models. Our mechanistic analyses suggest that ADG106 promotes an antitumor response by stimulating infiltration and expansion of CD4⁺ and CD8⁺ T-cells in tumors. ADG106 was well tolerated in animals, with a no-observed-adverse-effect-level, or NOAEL, ≥ 100 mg/kg/dose and ≥ 200 mg/kg/dose in rats and cynomolgus monkeys, respectively. These findings support our belief that the ADG106-boosted immune response could offer an effective alternative solution for cancer immunotherapy as a monotherapy and in combination with other therapies, especially for PD-1/PD-L1 resistant patient populations.

Preclinical Pharmacology: Our *in vitro* studies showed that ADG106 bound with high affinity and specificity to a unique epitope of CD137 that blocks the CD137L ligand binding with subsequent enhancement and proliferation of T-cells and pro-inflammatory interferon- γ responses. Interferon- γ is a master checkpoint regulator for many cytokines that targets a common component of many heterodimeric cytokine receptors.

ADG106 was species cross-reactive against human, mouse, and cynomolgus monkey CD137 and was active as a monotherapy in multiple preclinical tumor models. As shown below (left figure), in an H22 liver cancer syngeneic mouse model, ADG106 was observed to have *in vivo* antitumor activities as a monotherapy in a dose dependent manner. As shown below (right figure), tumors treated with ADG106 showed increased CD4⁺ and CD8⁺ infiltration compared to an isotype control.

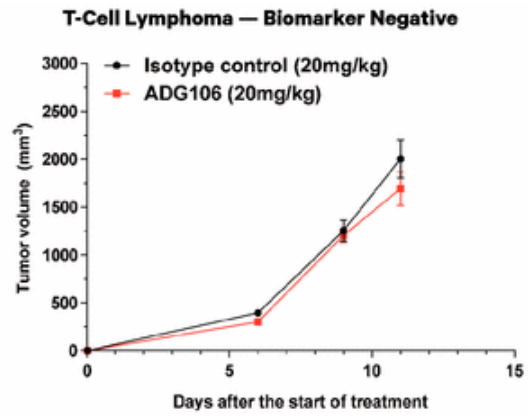
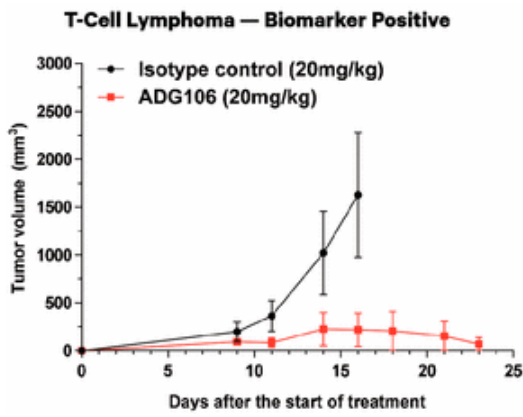


As illustrated in the figure below, ADG106 also showed a durable antitumor response in a CT26 colon cancer syngeneic mouse model. ADG106 treatment induced a complete response, or CR, in six out of eight mice. These CR mice received reinoculation of CT26 tumor cells, or rechallenge, and remained tumor-free without additional ADG106 treatment, indicating development of antitumor memory response elicited by ADG106. Tumors treated with ADG106 showed increased CD4⁺ and CD8⁺ infiltration compared to an isotype control, similar to the H22 liver cancer model (data not shown). These data are consistent with the mechanism of ADG106 as a CD137 agonist in stimulating T-cell proliferation, activation, and infiltration into the TME to induce an antitumor effect.

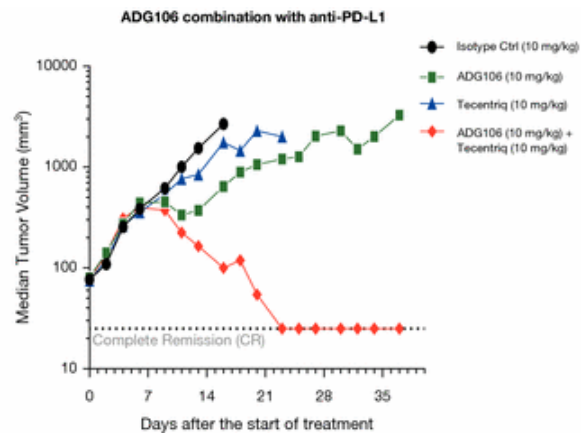
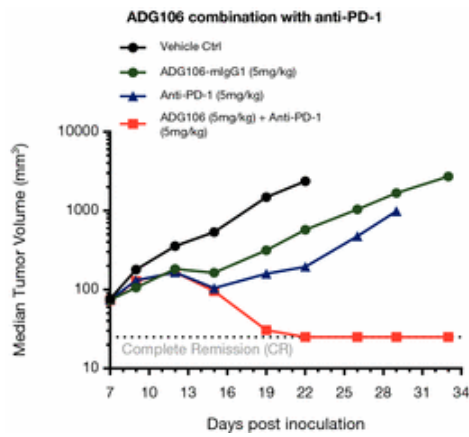


- durable response in syngeneic mouse colon cancer model
- CR previously dosed with ADG106 showed no tumor growth upon tumor re-challenge

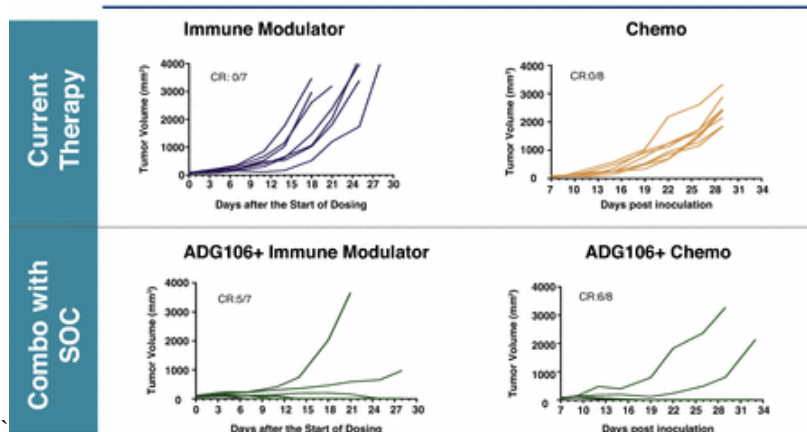
Patient stratification: Understanding which patient populations may preferentially benefit from ADG106 treatment is important in designing clinical trials. Our preclinical studies have identified a biomarker that is associated with *in vivo* sensitivity of tumor models to ADG106 treatment. We determined biomarker level in ten syngeneic mouse tumor models and tested ADG106 *in vivo* in these ten models. In the seven models that were biomarker positive, four models were sensitive to ADG106 treatment while three were resistant or less sensitive to ADG106. The three biomarker negative models were resistant to ADG106 treatment. Additionally, the three resistant or less sensitive biomarker positive models showed synergistic effect to ADG106 treatments in combination with anti-CTLA-4 or anti-PD-L1. As illustrated in the figures below, among two T-cell lymphoma models, the biomarker positive model was observed to be sensitive to ADG106 treatment (see figure below on the left) and the biomarker negative model was observed to be resistant to ADG106 treatment (see figure below on the right). This biomarker provides a potential mechanism for stratifying patients that may benefit from ADG106 treatment in future clinical trials.



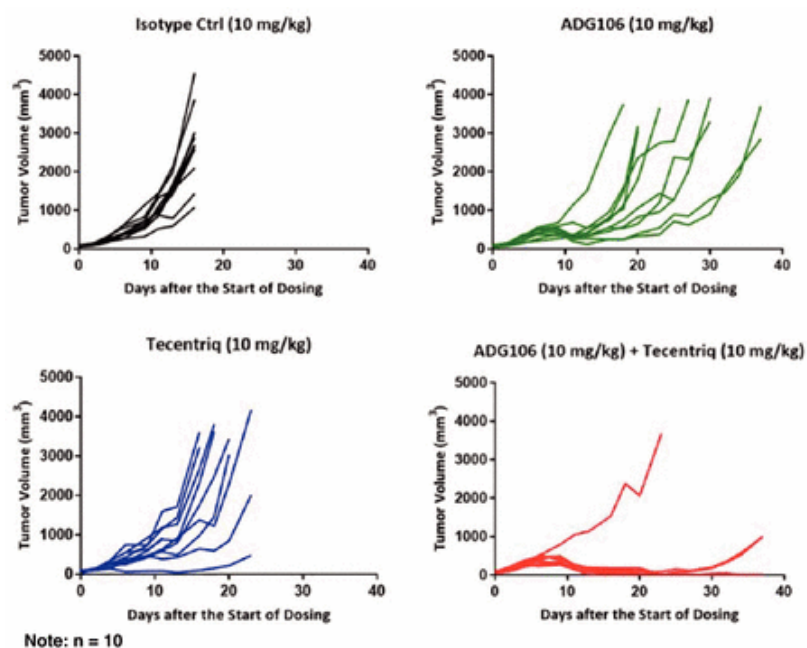
In addition to monotherapy antitumor activities, we observed that ADG106 had antitumor activities in combination with other therapies in preclinical studies. As shown below, ADG106 produced a synergistic effect with an anti-PD-1/L1 therapy, and SOC, in *in vivo* tumor models, including models that are resistant to current PD-1/PD-L1 and SOC therapies.



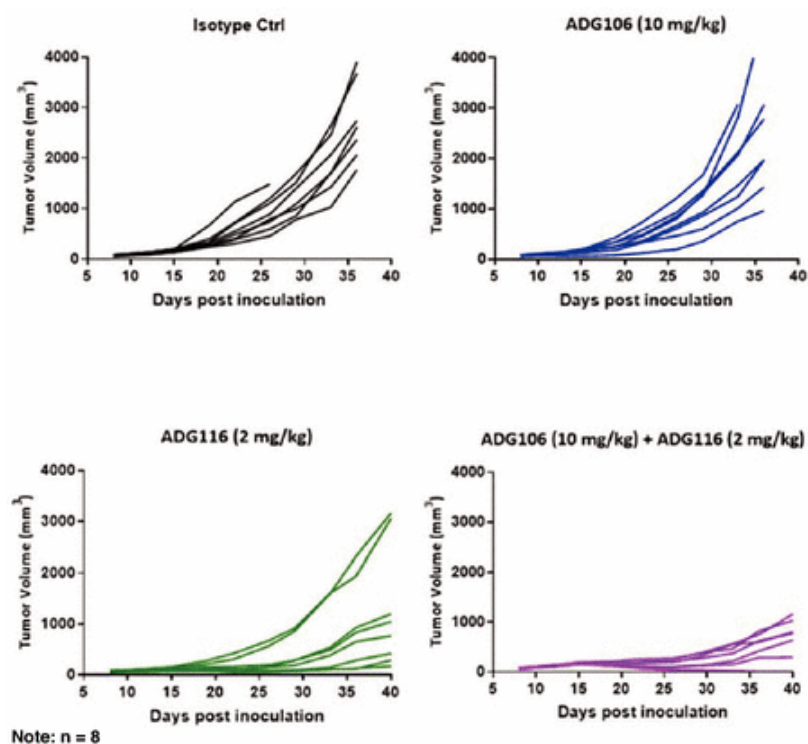
Combination with Standard of Care



In a syngeneic tumor that is biomarker (mentioned above) positive, although ADG106 did not show anti-tumor activity in this model, combination of ADG106 with atezolizumab (Tecentriq), an approved anti-PD-L1 antibody that blocks PD-1/PD-L1 interaction, showed enhanced antitumor response compared to the corresponding monotherapies.



As demonstrated below, ADG106 was also observed to show antitumor activities when combined with our CTLA-4 antibody ADG116 in a mouse tumor model that is biomarker (mentioned above) positive, while ADG106 alone did not show antitumor activities. We believe that this data provides a strong rationale for combining our pipeline programs including ADG106 with ADG116.



Clinical Development Plan

We have completed patient enrollment in each of our two Phase I trials of ADG106 as a monotherapy in patients with advanced or metastatic solid tumors and/or NHL in the United States, or the ADG106-1001 clinical trial, and in China, or the ADG106-1002 clinical trial. We completed evaluation of the safety and tolerability, PK and PD and clinical efficacy of ADG106 in advanced or metastatic solid tumors and NHL. We identified a potential predictive biomarker to enhance patient selection. In retrospective analysis, the majority of patients selected with the biomarker demonstrated more than 30% tumor shrinkage across different indications. We developed a high sensitivity biomarker assay and obtained a CLIA certification for the upcoming biomarker driven clinical trial of ADG106-2001.

Our population PK modeling determined a recommended starting dose used for ADG106 in combination with other immunotherapies. In March 2021, we initiated patient enrollment in China for ADG106-1008 study to evaluate clinical safety and efficacy of ADG106 in combination with anti-PD-1 therapy. We are also preparing for ADG106-1003 trial in Australia to evaluate ADG106 in combination with other therapies in advanced solid tumors and hematological malignancies.

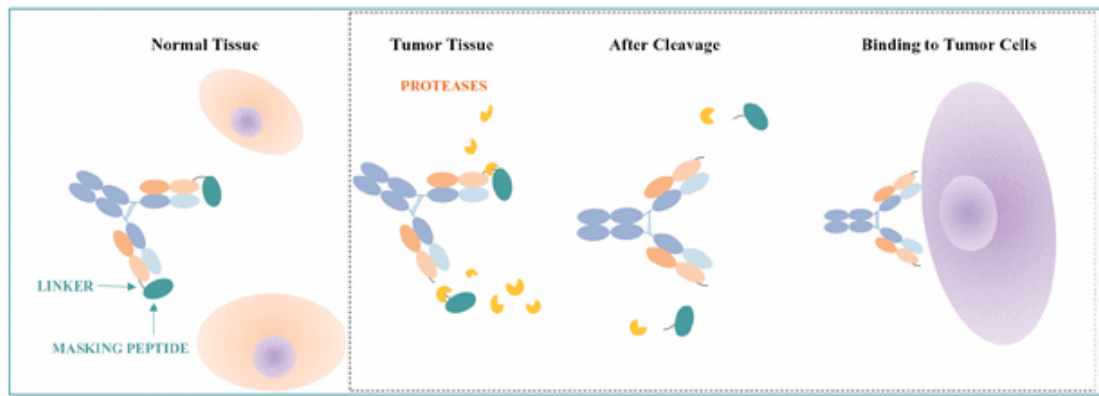
ADG126: Novel Anti-CTLA-4 SAFEbody Candidate

Summary

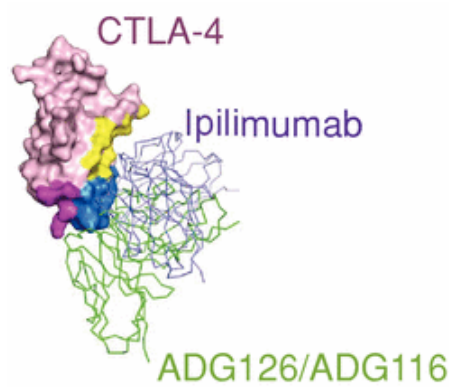
Our most advanced SAFEbody program, ADG126, is a fully human anti-CTLA-4 mAb generated using our SAFEbody technology designed to address the safety concerns with associated existing CTLA-4 therapeutics, while maintaining efficacy in the TME. Our proprietary SAFEbody technology is designed to enable ADG126 to be activated only in tumor tissues rather than healthy tissues. In preclinical studies, we observed that ADG126 had an enhanced therapeutic window and improved safety features. Furthermore, in PD studies of ADG126, it was observed that while the CTLA-4 binding affinity was masked in an intact ADG126 antibody, once the masking peptide was cleaved off of ADG126, its high binding affinity to CTLA-4 was restored. We have presented updated preclinical data at the American Association for Cancer Research (AACR) Annual Meeting 2021. The data shows that ADG126 demonstrated an impressive safety margin while maintaining its potent antitumor efficacy.

Mechanism of Action

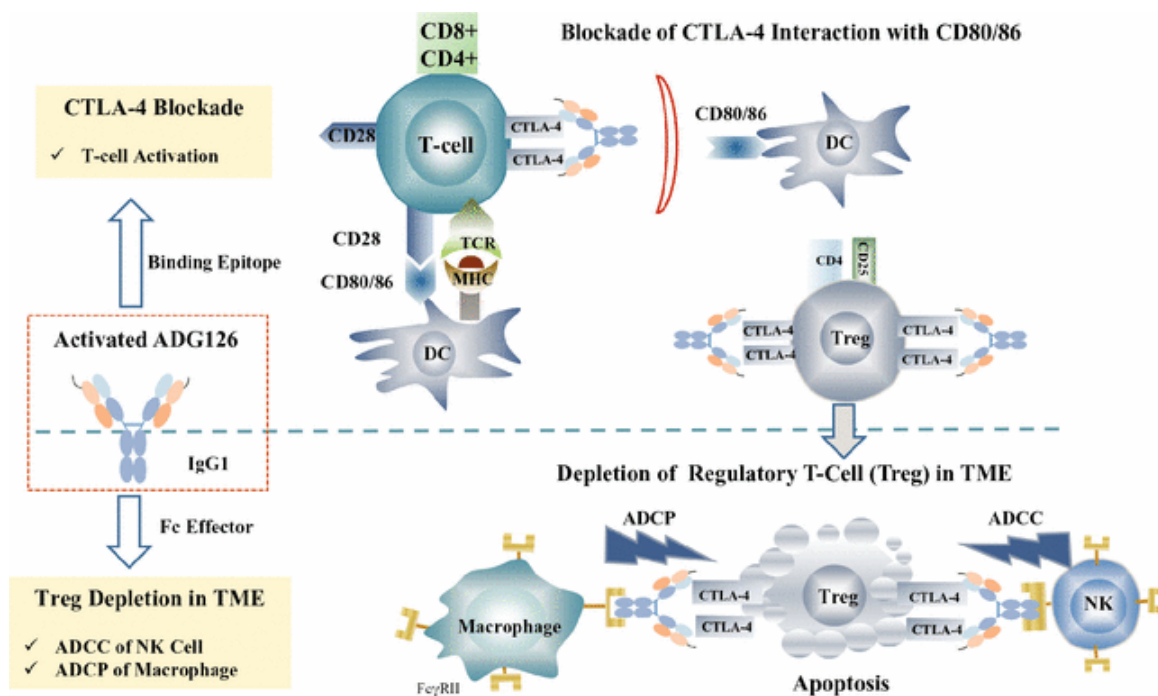
ADG126 is a fully human anti-CTLA-4 mAb. The masking moiety in ADG126 functions to block the interaction between ADG126 and its target CTLA-4 protein. Once ADG126 enters the TME, proteases overexpressed in the TME cleave off the masking moiety, and the antibody is then activated, binding to CTLA-4 and inhibiting its function. ADG126 is locally activated specifically in the TME, rather than systemically, to stimulate antitumor immune response. The following diagram illustrates the activation process of ADG126 in tumor tissue.



We believe that activated ADG126 potentiates T-cell immune response by blocking the inhibitory effect of CTLA-4. ADG126/ADG116 is designed to target CTLA-4 conserved epitope with species cross-reactivity for translational fidelity.



Moreover, ADG126 has been observed in preclinical animal studies to mediate effector functions to eliminate CTLA-4 expressing cells, particularly regulatory T-cells, primarily through ADCC. These actions of ADG126 could lead to enhanced activation and proliferation of tumor infiltrating T-effector cells and reduced T-regulatory cell function, which may contribute to a general increase in T-cell responsiveness, including an enhanced antitumor immune response. The below diagram illustrates the MOA of activated ADG126.



Notes:

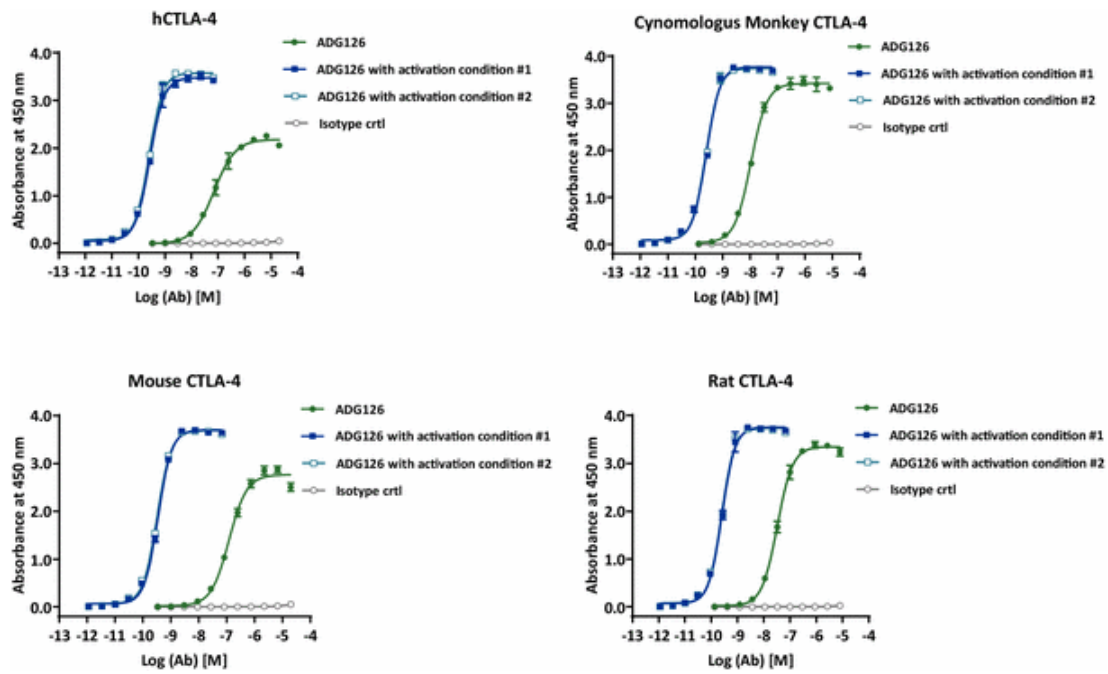
“ADCP” refers to antibody-dependent cell-mediated phagocytosis;

“MHC” refers to major histocompatibility complex;

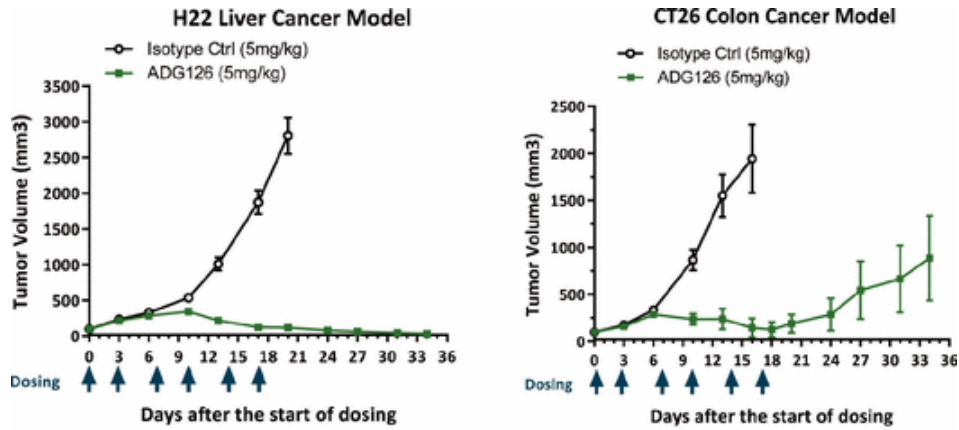
“TCR” refers to T-cell receptor;

Summary of Preclinical Studies

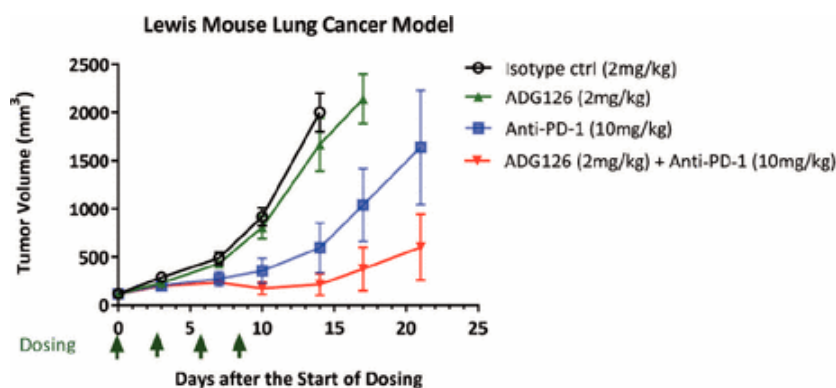
Preclinical Pharmacology: We observed in PD studies that ADG126, in its intact SAFEbody form, bound weakly to CTLA-4. However, once the proteases cleaved off the masking peptide, ADG126 was activated and bound at a high affinity to human, cynomolgus monkey and mouse CTLA-4, as shown in the figures below. Activated ADG126 was observed to lead to the release of CD80/CD86 ligands from CTLA-4 sequestration, and stimulation of CD28 signaling to boost T-cell activity. It also targets regulatory T-cells for depletion within the by means of ADCC, to mediate antitumor T-cell immunity.



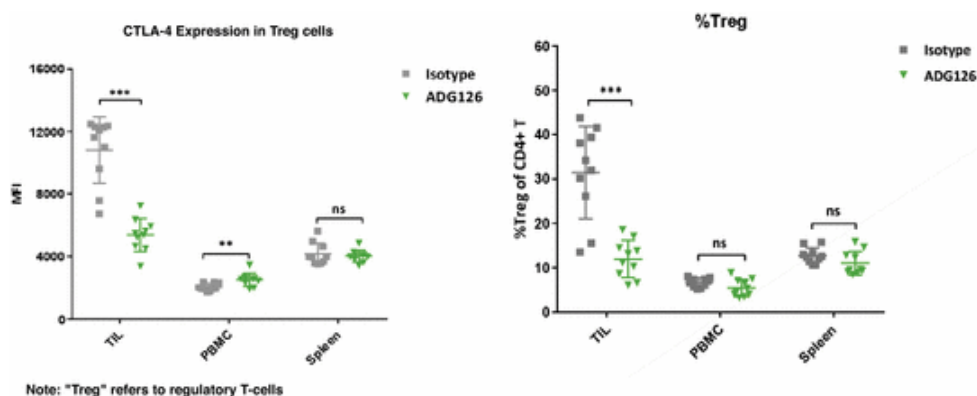
We evaluated the *in vivo* antitumor efficacy of ADG126 in syngeneic mouse tumor models. As shown in the figures below, in these studies, ADG126 was observed to inhibit tumor growth in different mouse tumor models as a monotherapy.



As shown in the figure below, ADG126 synergized with an anti-PD-1 antibody to elicit a stronger anti-tumor response than ADG126 or the anti-PD-1 antibody alone in a Lewis lung cancer syngeneic



ADG126 treatment was observed to specifically deplete regulatory T-cells in the tumor, but not in peripheral tissues. The following figures illustrate the reduction of CTLA-4 expression in infiltrating lymphocytes, or TILs (see figure below on the left) and regulatory T-cell depletion (see figure below on the right) by ADG126 in CT26 tumor model.



Preclinical Toxicology: We performed preclinical toxicology studies designed to assess the toxicity features of ADG126. We selected cynomolgus monkeys and mice as toxicology species for animal toxicity evaluation. No abnormal findings attributable to ADG126 were observed. We utilized a nonobese diabetic mouse model to determine percentage of survival with ADG126 treatment. All mice survived after six treatments of ADG126 at 50 mg/kg.

In a four-week GLP repeat-dose toxicology studies, intravenous infusion of ADG126 to cynomolgus monkeys at 5, 30, or 200 mg/kg/dose once weekly for five doses followed by a 28-day recovery period was well-tolerated. Adverse, but reversible, microscopic findings of minimal to moderate mixed perivascular infiltrates were observed at 200 mg/kg in both sexes in the kidney, liver, pancreas, epididymis, skin, and were observed in the ovaries in females, and the connective tissue associated with the mesenteric lymph node and thyroid gland. The NOAEL was considered to be 30 mg/kg/dose and the highest non-severely toxic dose was considered to be 200 mg/kg/dose.

Clinical Development Plan

We have started the Phase I dose escalation in March 2021 and have successfully finished DLT evaluation of three patients at 0.1 mg/kg in Australia for the treatment of various advanced solid tumors without observing any dose limiting toxicity and other safety issues. We currently plan to do dose escalation for up to 10mg/kg. We have also received approval from the FDA for enrolling patients in the Phase I clinical trial of ADG126 in the United States. We are on track for safety and efficacy data readout in selected indications in 2021. Meanwhile, the NMPA has accepted our pre-IND request to start ADG126 Phase I trial in China with revised protocol at higher starting dose than that in the original submission.

ADG116: Novel Anti-CTLA-4 NEObody Candidate

Summary

ADG116 is a fully human anti-CTLA-4 antibody generated using our NEObody technology, designed to enhance the efficacy and to address toxicity concerns associated with existing CTLA-4 therapeutics. In our preclinical studies, ADG116 was observed to potentiate CD28 signaling and T-cell immune responses (cytokine production) in the presence of primary stimulatory signaling. Furthermore, ADG116 reduced immunosuppressive regulatory T-cell activity and enhanced CD8⁺ T-cells activity in the TME to induce antitumor responses. We believe these preclinical results support the further clinical evaluation of ADG116 both as a monotherapy and in combination with other therapies for a wide range of tumor types. In July 2020, we obtained authorization from the Australian Therapeutic Goods Administration under a CTN to start a Phase I clinical trial of ADG116.

Summary of clinical data

Status: As of April 19, 2021, we have enrolled more than 10 patients in ADG116-1003. We have completed five levels of dose escalation at 0.003, 0.01, 0.03, 0.1, 0.3 mg/kg without observing any \geq Grade 2 TEAEs or other drug related safety issues and have dosed all three patients in the cohort at 1 mg/kg.

Safety Assessment: Analysis of all safety data generated to date demonstrates that ADG116 has been well-tolerated in more than 10 patients with no dose-limiting toxicities or unexpected safety signals. No drug related Grade 2, Grade 3 or Grade 4 toxicities have been observed.

Pharmacodynamics Assessment: A dose-dependent change in CD8⁺ and CD4⁺ TEM / Treg ratios, important pharmacodynamic (PD) biomarkers indicating immune activation, was observed for patients dosed by ADG116. In particular, a patient, refractory to prior pembrolizumab therapy (> 25 cycles), demonstrated striking increases in T and NK cells, and CD8⁺ and CD4⁺ TEM / Treg. The Grade 1 treatment-related pruritus of this patient is a clinical symptom consistent with immune-mediated action of ADG116 treatment.

Pharmacokinetics Assessment: The terminal half-life of ADG116 was within the normal range of IgG1 based antibodies.

The Phase 1 dose escalation data demonstrates the clinical proof of mechanism for ADG116 in targeting CTLA-4, consistent with preclinical observations for the potency of ADG116 starting from 0.03 to 0.3 mg/kg.

The ADG116-1001 Phase I trial in the United States was placed on clinical hold on September 30, 2019 by the FDA, after we reported to the FDA the death of the only patient dosed in the trial. The FDA removed the clinical hold on December 5, 2019 after we submitted an amendment to the study protocol. With favorable clinical data in Australia as of April 19, 2021, we look forward to expanding the ongoing global Phase I trial, with the acceptance of revised study protocol by the FDA, to expand the trial in the United States. Separately, the NMPA has accepted our application to proceed with revised protocol at higher starting dose than that in the original submission.

Mechanism of Action

ADG116 is designed to target a unique conserved epitope of CTLA-4. In preclinical studies, ADG116 was observed to have softer CTLA-4 ligand blocking and stronger ADCC for regulatory T-cell depletion than ipilimumab. Based on the PD results observed in our preclinical studies, we believe that ADG116 has the potential to specifically bind to human CTLA-4, or hCTLA-4, without binding to other CD28 family receptors, which could potentially block the CTLA-4/CD80 and CTLA-4/CD86 ligand interactions. We believe that ADG116 potentiates CD28 signaling and T-cell immune response in the presence of a primary stimulatory signaling. Moreover, ADG116 has been observed in preclinical animal studies to mediate effector functions to eliminate CTLA-4 expressing cells, particularly regulatory T-cells, primarily through ADCC by NK cells. These actions of ADG116 could lead to enhanced activation and proliferation of tumor infiltrating T-effector cells and reduced T-regulatory cell function, which may contribute to a general increase in T-cell responsiveness, including an enhanced antitumor immune response.

Clinical Trial Design

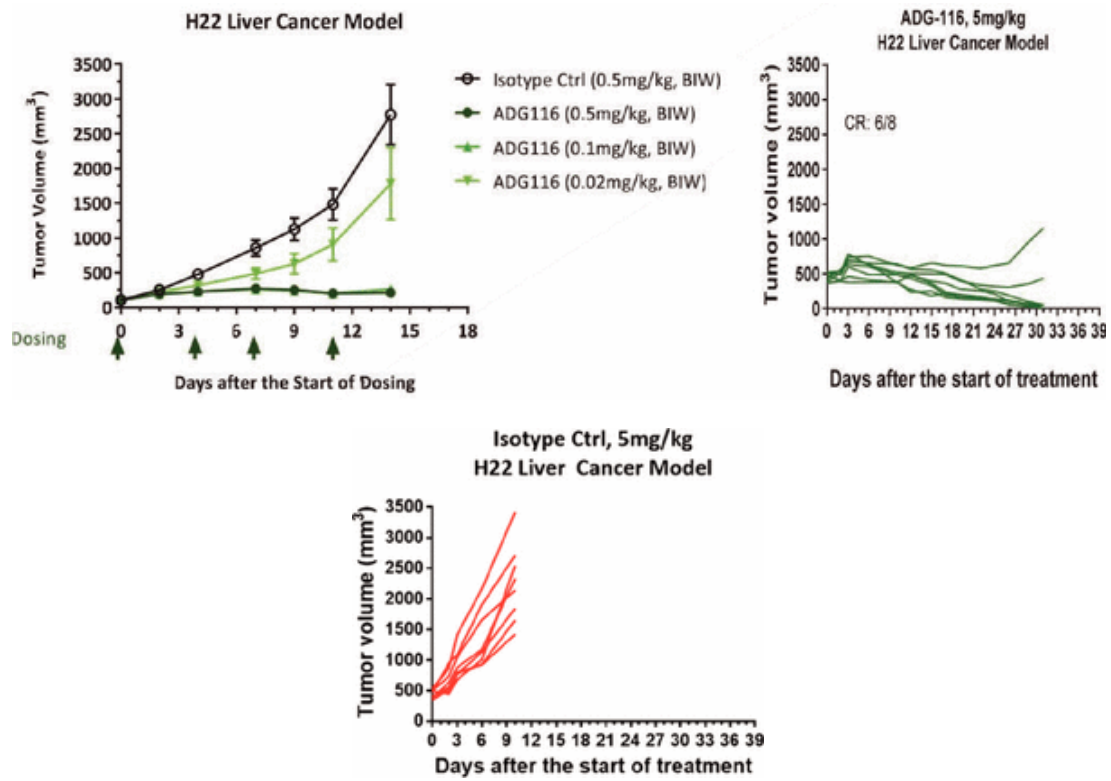
The following summarizes the Australia clinical trial design of ADG116. During the accelerated titration phase, one patient per dose level will be treated. If the patient experiences a DLT or two Grade 2 or above drug-related toxicity, as agreed upon by the investigator and sponsor, the dose level will be expanded according to a "3+3" dose escalation design. During the traditional "3+3" dose escalation phase, from the dosage level at 0.03mg/kg onwards, dose escalation will follow a traditional "3+3" design with three or six patients treated at each dosage level, depending on the incidence of DLTs. Initially, three patients will be enrolled into the dosage level with the sentinel patient treated at least 24 hours before the subsequent patients. Duration of treatment is expected to continue up to two years, if the investigator considers that continued treatment could benefit the patient, or until disease progression and/or unacceptable toxicity, or withdrawal of informed consent.

The primary objectives of the dose escalation stage of the planned clinical trial will be to assess DLT and recommended Phase II dose, or RP2D. The safety profile of ADG116 will also be assessed in terms of severity, seriousness, and frequency of AEs, laboratory results, vital signs, physical examinations, and ECGs of patients enrolled in the study. The secondary objectives of the planned clinical trial are to (i) assess plasma PK parameters; (ii) evaluate anti-drug antibodies, or ADAs, in patients' blood before, during and after treatment with ADG116; (iii) evaluate objective response in accordance with RECIST v1.1 and/or iRECIST; and (iv) evaluate preliminary evidence of antitumor activity of ADG116, as characterized by ORR, DCR, duration of response, or DOR, duration of stable disease, PFS, and OS. The exploratory objective is to identify PD biomarkers for ADG116, including but not limited to cytokines, plasma proteins, immune cells, and tissue biomarkers.

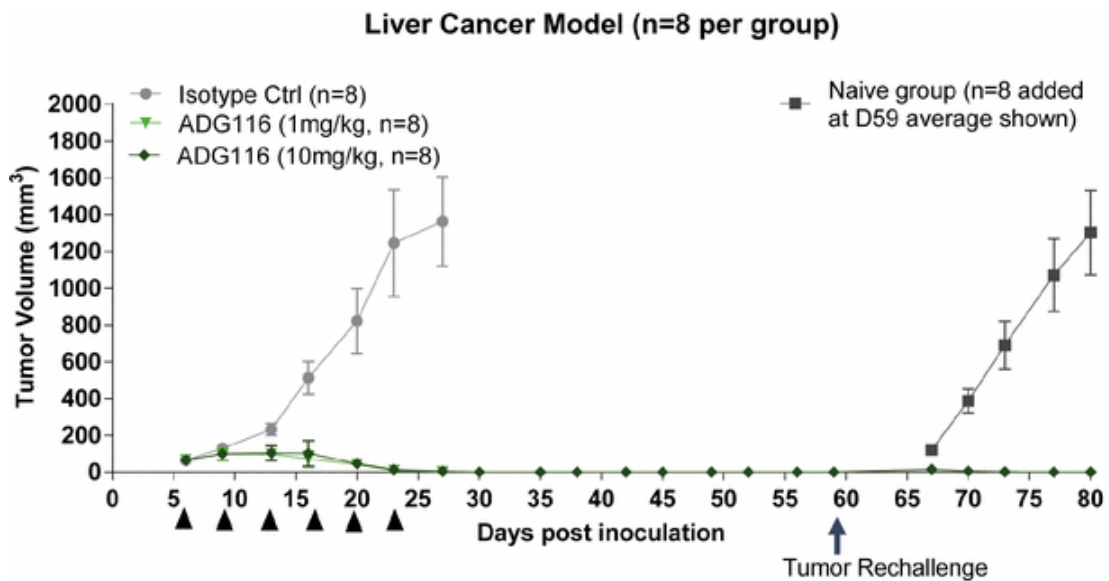
Summary of Preclinical Studies and Results

We extensively evaluated ADG116 in both *in vitro* and *in vivo* preclinical studies. Our *in vivo* efficacy studies were conducted in mice, and safety evaluations were conducted in both cynomolgus monkeys and rats. ADG116 was observed to show robust *in vivo* anti-tumor activity in multiple syngeneic mouse tumor models. Ipilimumab was included as a benchmark and was compared with ADG116 in a series of our preclinical studies. In these preclinical studies, we observed that ADG116 had a potential advantage over ipilimumab in potentiating T-cell activation. While ADG116 has softer CTLA-4 ligand blocking, it was observed to have superior ability in eliminating CTLA-4 positive regulatory T-cells via ADCC in tumors resulting in enhanced antitumor responses. ADG116 was well tolerated in rats and cynomolgus monkeys at doses up to 30 mg/kg in GLP-compliant four-week repeat-dose toxicology studies.

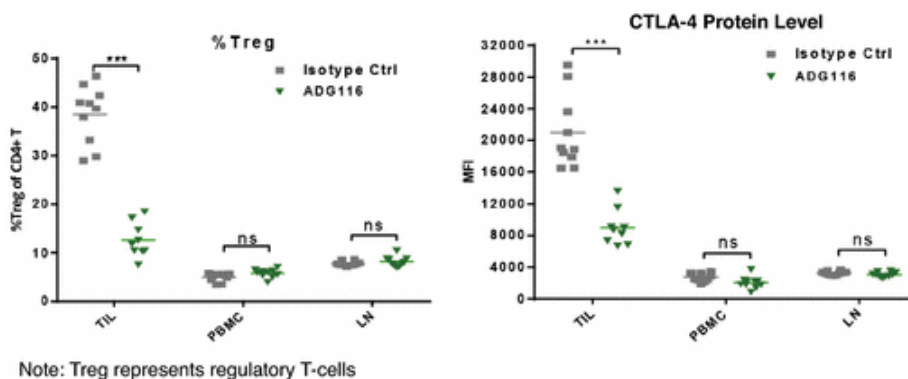
Preclinical Pharmacology: We evaluated ADG116 as a monotherapy *in vivo* in an H22 liver cancer syngeneic mouse model. As shown in the figure below, ADG116 was observed to induce an encouraging antitumor response at low doses in a dose-dependent manner (see figure below on the left). Additionally, ADG116 was observed to inhibit tumor growth of large tumors in the same model (see figure below on the right).



As illustrated in the below figure, in a liver cancer tumor rechallenge study, ADG116 was observed to induce significant antitumor response. Fifty-nine days after the initial tumor inoculation and more than 30 days after the last ADG116 treatment, mice were then rechallenged with the same tumor. We observed that mice that responded to the initial ADG116 treatment remained tumor-free even without additional ADG116 treatment while naive mice developed tumors, indicating the development of antitumor memory response elicited by ADG116.



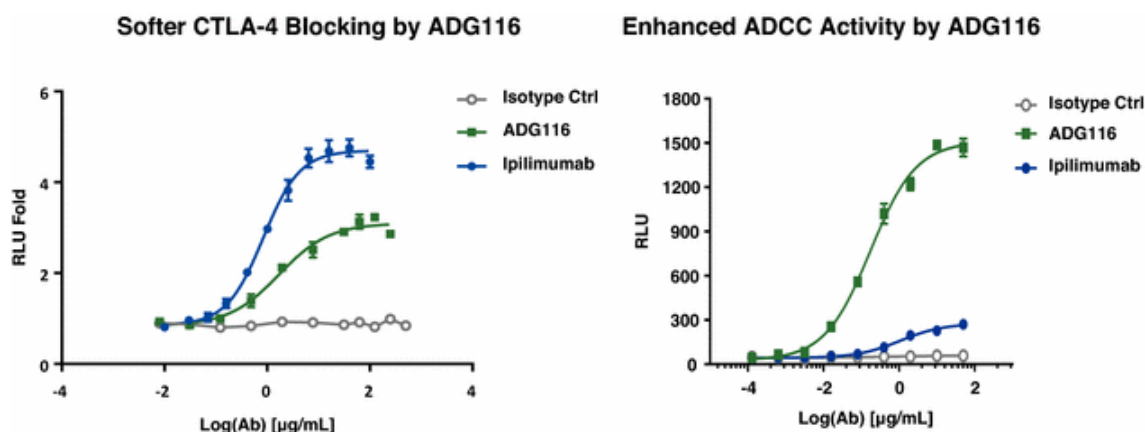
Since ADG116 was observed to exhibit strong ADCC activity *in vitro*, we evaluated the ability of ADG116 to deplete regulatory T-cells *in vivo* in a CT26 mouse colon cancer syngeneic model. ADG116 treatment was observed to specifically deplete regulatory T-cells in the tumor, but not in peripheral blood mononuclear cells, or PBMCs, or lymph nodes. The following figure shows significant regulatory T-cell depletion (left figure) and inhibition of CTLA-4 expression (right figure) in tumors by ADG116.



Note: Treg represents regulatory T-cells

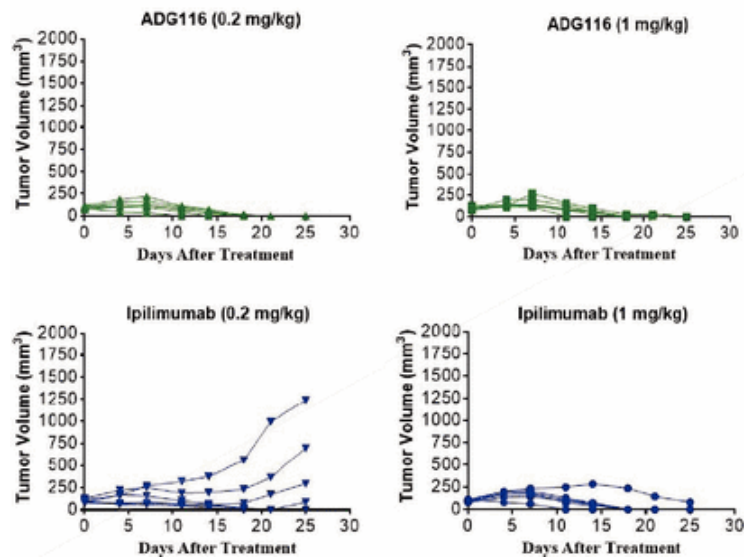
In a series of preclinical studies, we compared the effect of ADG116 to ipilimumab. We believe that these studies suggest that ADG116 has a unique MOA compared to ipilimumab and has a potential advantage over ipilimumab in eliciting antitumor responses. These preclinical trial results support the further clinical evaluation of ADG116 as a monotherapy and in combination with other therapies for a wide range of tumor types.

In the CTLA-4 blockade bioassay illustrated in the figure below on the left, ADG116 was observed to exhibit weaker blocking than ipilimumab of CTLA-4's ability to inhibit CD80- and CD86-induced IL-2 production. This result supports our belief that ADG116 can function as a CTLA-4 checkpoint inhibitor with weaker activity than ipilimumab, which may result in less systemic autoimmune side effects on normal tissues. On the other hand, ADG116 was observed to exhibit notably stronger ADCC activity than ipilimumab in the *in vitro* assay shown in the figure below on the right. Since CTLA-4 is expressed on regulatory T-cells, we believe that ADG116 offers a potential advantage over ipilimumab in depleting regulatory T-cells by means of ADCC. We subsequently investigated this *in vivo* in a syngeneic mouse tumor model.



To compare ADG116's *in vivo* antitumor activity to ipilimumab, we utilized a subcutaneous MC38 mouse syngeneic colon cancer model in hCTLA-4, knock-in, or KI, C57BL/6 mice. We selected the hCTLA-4 KI mice as ipilimumab does not cross-react with mouse CTLA-4. As shown in the figure below, ADG116 was observed in this study to exhibit stronger antitumor activity than ipilimumab (ADG116 at 0.2 mg/kg induced equivalent antitumor response as 1 mg/kg of ipilimumab).

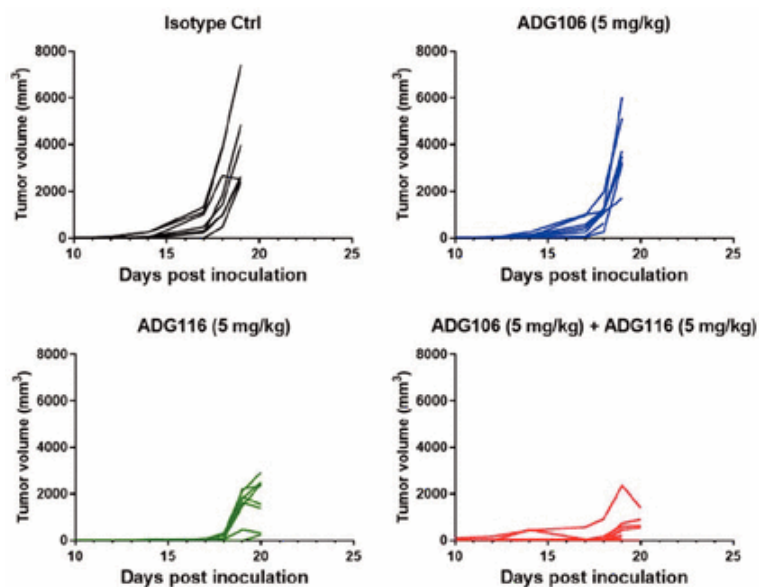
Antitumor Activity of ADG116 vs Ipilimumab in MC38 Colon Cancer Model in hCTLA-4 KI Mice



As shown in the figure below, we measured tumor infiltrating regulatory T-cells in the subcutaneous hCTLA-4 KI MC38 mouse colon cancer model after ADG116 or ipilimumab treatment. Among the TILs, the percentage of regulatory T-cells was observed to be significantly reduced after ADG116 treatment while the regulatory T-cell reduction after ipilimumab treatment was not significant. Notably, we observed that regulatory T-cell depletion by ADG116 occurred only in the TME, and not in PBMCs or the spleen. We believe that these results provide a mechanistic rationale for the enhanced *in vivo* antitumor activity of ADG116 compared to ipilimumab. ADG116 may reduce the immunosuppressive regulatory T-cell activity specifically in the TME to enhance antitumor immune responses.

As illustrated below, in addition to evaluating the efficacy of ADG116 as a monotherapy, we also evaluated ADG116 in combination therapies. ADG116 was observed to have an antitumor effect with an anti-PD-1 treatment in a Lewis lung cancer syngeneic mouse model.

We also examined the effects of ADG116 in combination with our CD137 agonistic antibody, ADG106, in a B16F10 melanoma syngeneic mouse model. As shown below, we observed that the combination of ADG116 with ADG106 enhanced the antitumor activity compared with ADG116 or ADG106 alone.



Preclinical Toxicology: We performed preclinical toxicology studies in cynomolgus monkeys and rats to evaluate the toxicity of ADG116. There were no abnormal findings in the single-dose toxicology studies. We observed that ADG116 was well tolerated in both cynomolgus monkeys and rats at up to 200 mg/kg. In a GLP-compliant, four-week repeat-dose toxicology study, ADG116 was tolerated at doses up to 30 mg/kg/dose (five doses per week). In this study, ADG116 related hematology parameter changes, serum chemistry changes, mononuclear infiltration of predominantly lymphocytes with fewer macrophages into the parenchyma of numerous organs were the primary test article-related effects evaluated. These changes were reversible at ≤ 30 mg/kg/dose, and consistent with the biological role of CTLA-4 in regulating and maintaining peripheral immune tolerance. The NOAEL was considered to be 30 mg/kg/dose in both rats and cynomolgus monkeys.

Clinical Development Plan

As of April 19, 2021, we have completed five levels of dose escalation at 0.003, 0.01, 0.03, 0.1, 0.3 mg/kg without observing any \geq Grade 2 TEAEs or other drug related safety issues. We currently plan to do dose escalation for up to 10mg/kg. In the Phase I clinical trial of ADG116 in Australia, we have completed dosing three patients in the cohort at 1 mg/kg, much higher than 0.03mg/kg, which was the dose that we had initiated a Phase I trial of ADG116 in the United States. We submitted the safety data collected from the Australia trial to the FDA and NMPA. With favorable clinical data in Australia as of April 19, 2021, we look forward to expanding the ongoing global Phase I trial, with the acceptance of revised study protocol by the FDA, to expand the trial in the United States. Separately, the NMPA has accepted our application to proceed with revised protocol at higher starting dose than that in the original submission.

DEEP, BROAD, DIFFERENTIATED PRECLINICAL DISCOVERY PIPELINE

In addition to our three clinical-stage product candidates, ADG106, ADG126 and ADG116, we are building a deep, broad and differentiated preclinical pipeline with programs at various stages of the drug discovery and development process, utilizing our three DPL platform technologies NEObody, SAFEbody, and POWERbody.

We have over ten programs in discovery and five highly differentiated programs undergoing IND-enabling studies, namely three POWERbody programs and two SAFEbody programs. All five programs have robust CMC profile with encouraging preclinical safety and efficacy data. Our POWERbody programs include SAFE bispecific T-cell engager programs, such as CD20xCD3 SAFE bispecific antibody, or bsAb. Our SAFEbody programs include multiple SAFE NEObodies, such as SAFE CD47 NEObody. The class of anti-CD47 therapies has attracted significant interests from leading biopharmaceutical companies given its significant potential.

Below is an example of our POWERbody preclinical discovery program, which is tumor-associated antigen, or TAA, and CD3 bispecific T-cell engager program.

POWERbody TAAxCD3 BsAb T-cell Engager Program

Summary

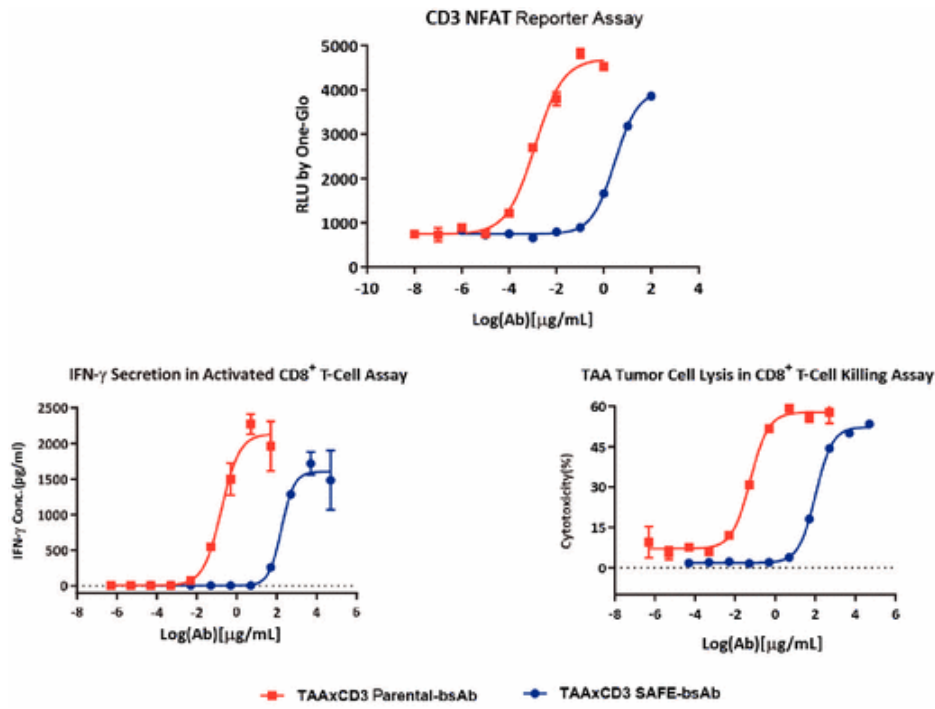
Bispecific T-cell engager antibodies have been explored as a means to recruit cytolytic T-cells to kill tumor cells. This is based on the simultaneous recognition of an antigen on tumor cells and binding to the CD3 epsilon chain, or CD3e, within the T-cell receptor complex on T-cells that bridges malignant tumor cells directly to CD3⁺ T-cells. Blinatumomab, or Blincyto, the first bispecific T-cell engager reactive with the B-cell antigen CD19, was approved by the FDA in 2014 for the treatment of neoplasms. While early studies showed promising clinical efficacy, bispecific T-cell engagers were also hampered by severe dose-limiting toxicities primarily manifesting as cytokine release syndrome which resulted in a prohibitively narrow therapeutic window.

Through our DPL platform, we have developed a deep pipeline of bispecific T-cell engager antibodies for both liquid and solid tumors. To address the safety issues of current CD3 T-cell engager antibodies, we leveraged our proprietary POWERbody technology to develop differentiated bispecific T-cell engagers.

Our TAAxCD3 SAFE-bsAbs comprise anti-human TAA and CD3 SAFEbodies and are intended for the treatment of TAA⁺ malignancies. Our TAAxCD3 SAFE-bsAb in their activated forms have been observed to stimulate T-cell activation and TAA⁺ tumor cell killing. We did not observe our TAAxCD3 SAFE-bsAbs to have visible cytokine release syndrome and other adverse events in exploratory toxicity studies in cynomolgus monkeys. Our TAAxCD3 SAFE-bsAbs highlight a potential new approach in tumor immunotherapy and provide a rationale for safe and effective treatment of TAA⁺ tumors. Based on our preclinical studies, we are moving forward with generating stable cell lines and CMC development of our two TAAxCD3 SAFE-bsAb programs.

Preclinical Studies

To evaluate the functional activity of parental and SAFE-bsAbs, we tested our bsAbs in multiple cell-based assays. As shown below, the TAAxCD3 parental-bsAb significantly stimulated CD3 signaling in a Jurkat cell-based NFAT reporter assay. Furthermore, the TAAxCD3 parental-bsAb was observed to significantly increase IFN γ secretion from CD8⁺ T-cells and induce TAA overexpressing tumor cell death by activating CD8⁺ T-cells in the T-cell-dependent cellular cytotoxicity assay. These results suggest that our CD3 bsAb potentially stimulated T-cells to kill tumor cells. Consistent with our expectation, the masked SAFE-bsAb was observed to have lower activity in these functional assays.

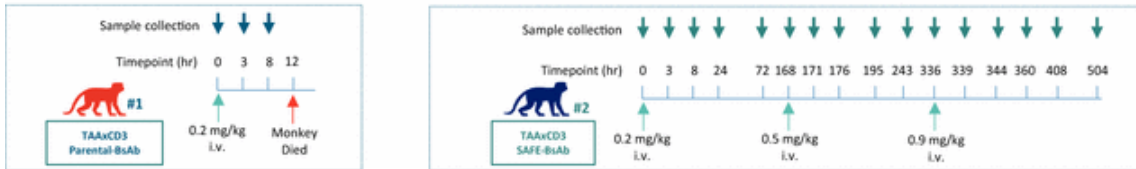


Exploratory Toxicity Study in Cynomolgus Monkeys

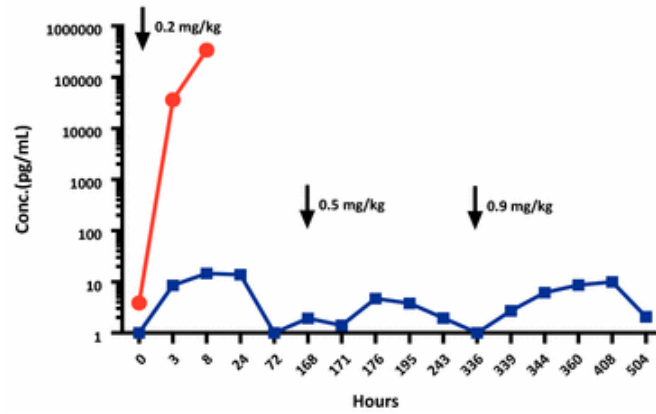
As current efforts in developing therapeutic CD3-based T-cell engagers are impeded by severe dose-limiting toxicities, primarily manifesting as non-specific cytokine release syndrome, we evaluated the safety results while developing CD3 bsAbs with our POWERbody technology. Particularly, we evaluated the cytokine and immune-associated events, for TAAxCD3 bsAbs in cynomolgus monkeys.

Cynomolgus monkeys were dosed intravenously with our TAAxCD3 parental- or SAFE-bsAbs. We observed significant IL-6 release with the parental-bsAb; while we did not observe SAFE-bsAb induced IL-6 release at any of the three-dose levels during the testing period, which indicates a noticeable improvement in safety results by SAFEbody masking.

Exploratory Safety Study: Single Monkey Dose Escalation Study

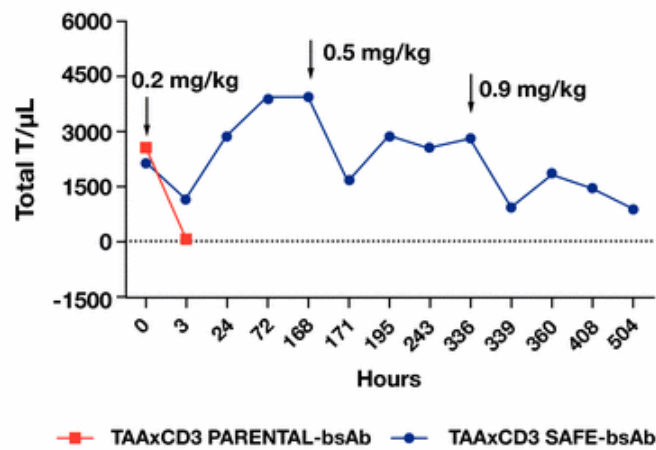


IL-6 release in cynomolgus monkeys treated with BsAbs



The cynomolgus monkey treated with the parental-bsAb died approximately 12 hours after first dosing at 0.2 mg/kg, likely due to acute cytokine release syndrome, which is consistent with severe dose-limiting toxicities observed in other bispecific T-cell engager antibodies. Moreover, total T-cells were nearly undetectable at three hours following the initial parental-bsAb treatment at 0.2 mg/kg. The SAFE-bsAb treated cynomolgus monkey also exhibited reduction of total T-cell counts, but to a lesser degree, and absolute lymphocyte counts rebounded at 24 hours after each dosing of SAFE-bsAb.

Absolute Lymphocyte Count After Treatment with bsAbs



OUR PLATFORM

Overview

Our proprietary DPL platform is built upon our insights into precise and dynamic antibody-antigen interaction. As such, our DPL platform has been designed to enable the discovery of antibodies with better developability properties. By addressing the challenges in traditional antibody design and engineering, we believe that our DPL platform will enable us to improve the efficacy and safety profile of antibody therapeutics. Our DPL platform is empowered by our computational platform, artificial intelligence and three innovative technologies: NEObody, SAFEbody, and POWERbody.

AI-Powered Antibody Discovery

We believe that efficient drug discovery requires significant commitment to resolve three key challenges: 1) the selection of targets with preclinical and/or clinical validation; 2) the availability of abundant hits at discovery stage for the identification of Pre-Clinical Candidates, or PCC, that usually takes a highly iterative process from target-to-hits, lead identification and lead optimization; and 3) deep understanding of target biology and MOA from detailed molecular, cellular, *in vivo* preclinical and human disease models. To address these challenges and to improve antibody R&D productivity, we have designed and built our AI-powered DPL platform to provide sufficient discovery capacity, capable of generating abundant high quality hits against targets, and then selecting the right leads for extensive preclinical testing in order to understand their MOAs, their efficacy and safety potential before going for clinical proof of concept testing. Our current focus on oncology portfolio is to establish early clinical proof of concept, preferably in Phase I trials.

We believe that it is critical to pair the right PCC with the specific epitope of a chosen target. The affinity and precise orientation by which the specific epitope of a given target is engaged by the PCC can have a profound impact on the pharmacology and toxicity of drug candidate. Therefore, we believe precision design and engineering of antibody-based drugs make a fundamental difference on the success of a drug discovery program. As demonstrated by extensive preclinical data of our ADG106, ADG126 and ADG116 programs and early clinical data of our ADG106 program, targeting the conserved epitope of CD137 by ADG106 and that of CTLA-4 by ADG126/ADG116, respectively, across humans, monkeys and mice can give rise to novel biological and pharmacological activities. The broad species cross-reactivity of these NEObody drug candidates above can facilitate seamless translational studies from different immune-competent syngeneic tumor models to monkeys, and then subsequent clinical trials in humans. The novel MOA and biology concerning CD137 and CTLA-4 targets include their regulation in peripheral and tumor microenvironments, the involvement of different immune cells upon target engagement such as NK cells by anti-CD137 ADG106 agonist and T-regulatory cells by anti-CTLA-4 specific antibodies ADG116 and ADG126. We believe these examples provide strong support for our proposal to search for “The Right PCC” that is paired with the specific epitope of a given target in order to unlock the biology of such target and its pathway and to facilitate a deep understanding of its MOA in triggering a cascade of biological and pharmacological events leading to disease control.

In order to search for “The Right PCC”, our proprietary DPL platform uses a deep learning approach to explore the conformational diversity of antibody binding sites. Our DPL platform combines AI algorithms and ever-increasing big data in antibody sequence, structure, and binding epitope and affinity from public and our own proprietary databases to design, construct and screen high-quality proprietary antibody libraries with well-defined sequence, scaffold and biophysical attributes for antibody drug discovery. Our computational engine combines software, AI and visualization tools to mine, organize, compute, and interactively explore these immense multidimensional big data sets. We iteratively inform wetlab experimentation with *in silico* computation, and vice versa. By exploiting conformational diversity through the combination of our proprietary computational algorithms with AI, we have designed and precisely constructed approximately one trillion (10^{12}) antibody sequences in our DPL. These antibodies feature broad epitope (the portion of an antigen that are recognized by an antibody) coverage and robust CMC attributes. The antibodies discovered can be further engineered into NEObody, SAFEbody and POWERbody antibodies depending on the targeted product profile of a given therapeutic target.

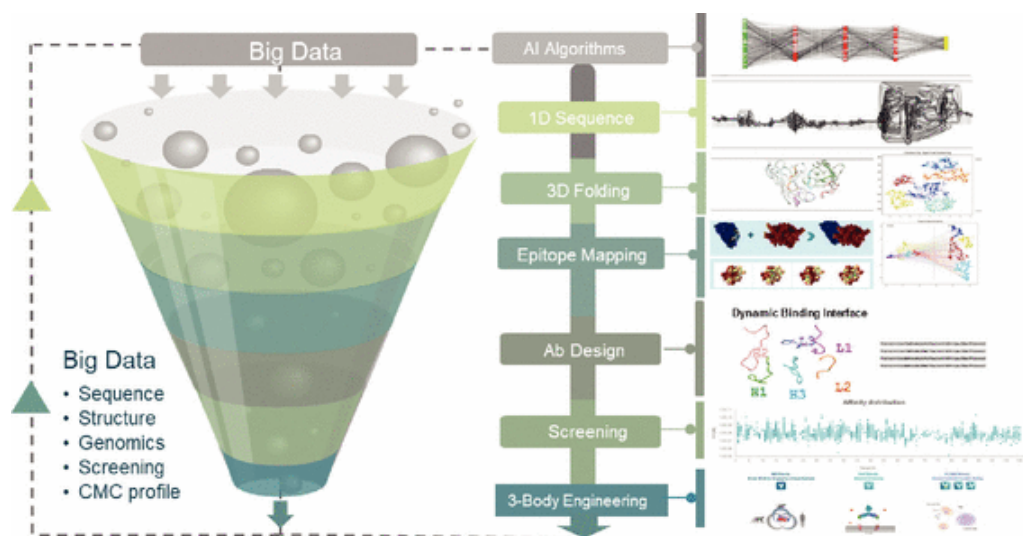
Our ADG106, ADG126 and ADG116 clinical programs illustrate how our AI-powered DPL platform has improved our R&D productivity. Our DPL library is a large physical phage library ($\sim 10^{12}$) that contain our AI-powered synthetic designer antibodies with flexible antibody binding interface. The combination of binding interface flexibility with the variation of amino acid sequences in the antigen binding interface exponentially increases the conformational diversity of our AI-powered DPL libraries, far beyond conventional natural or synthetic antibody libraries. Our AI-Powered DPL library screening against CD137 or CTLA4 antigens have yielded a large number of high affinity primary hits. For example, our anti-CD137 agonist antibody ADG106 was identified from 60 high affinity primary hits with a wide range of epitope diversity in terms of their species cross-reactivity, which compared favorably with the number and epitope diversity of high affinity anti-CD137 antibody hits reported by our global peers on their publicly filed documents. Our anti-CTLA-4 antibody ADG116 was identified from 74 high affinity primary hits with a wide range of epitope diversity in terms of their species cross-reactivities: 19 clones are human, monkey, canine and mouse cross-reactive; 12 clones are human and monkey cross reactive but weak mouse cross-reactive; 32 clones are human and monkey cross-reactive; 11 clones only recognize human CTLA-4. The abundant discovery hits with diversified binding epitopes for varying degree of species cross-reactivity show the power of our AI-powered DPL platform not only in creating novel ADG106 and ADG116 NEObodies in targeting different epitopes of a given antigen, but also in targeting the conserved epitope across different species of a given antigen for both CD137 and CTLA-4 to enable translational studies from immune-competent animal tumor models to human patients due to their broad species cross-reactivities.

We believe that the high affinity and species cross-reactive primary hits from our DPL library screening saves time and cost from primary hits to straight PCC. The broad species cross-reactivity of the primary hits also streamlines lead identification through simple syngeneic tumor models for safety and efficacy testing. The robust CMC attributes of our DPL library are designed to also eliminate the requirement to optimize antibody sequences before starting CMC process for IND enabling and formulation studies. Furthermore, we believe our AI-powered dynamic precision library of approximately one trillion (10^{12}) antibody sequences expands the diversity at the start of discovery to maximize the chance that suitable leads are found on the first pass. In conclusion, we believe our AI-powered antibody discovery and engineering DPL platform significantly increases R&D productivity for antibody drug discovery. It has enabled us to generate highly differentiated PCC molecules that we believe can target the conserved epitope across different species for novel MOAs and also facilitate seamless translational studies from animals to human via their broad species cross-reactivity.

Briefly, our AI-powered antibody discovery engine includes six steps:

1. First principle of antibody folding and dynamics. We fold the antibody primary amino acid sequence into three-dimensional structures based on machine learning or homology modeling in combination with the Molecular Dynamic Simulation in the presence and absence of dynamic interaction with their antigen targets.
2. AI-powered deep learning of antibody sequence and structure and binding epitopes. AI algorithm and machine learning have been widely used to map protein sequence and structure variation and connectivity. Deep learning has been used to map the antibody and antigen epitope in order to learn the landscape of the epitope space and their correlation with antibody binding interface.
3. Antibody design that combines the conformational diversity with primary amino acid sequence variation. We have designed antibody libraries that contain dynamic binding units and their combination in the context of different CDRs and framework scaffold to capture their conformational diversity of antibody binding interface in combination with variation in primary amino acid sequences far beyond conventional natural or synthetic antibody libraries.
4. Synthetic dynamic precision library by AI-powered computational design. The amino acid sequence library is converted into synthetic DNAs that can be assembled and constructed for phage and yeast library screening.
5. Directed evolution by phage and yeast libraries. The synthetic phage and yeast libraries can be screened semi-automatically for more than 100 antigens to yield high affinity primary hits.
6. PCC identification by targeting conserved epitope with broad species cross-reactivity to unlock the deep biology of target and its MOA upon target engagement by the PCC. PCC is designed and selected to target the conserved epitope of a given target across different species. Traditionally, affinity of primary hits from synthetic antibody libraries have to be improved before subjecting them to extensive in vitro and in vivo assays for lead identification and optimization through an iterative process between functional assays and antibody engineering. Our DPL platform can yield high affinity primary hits, which can then become product candidate leads subject to functional characterization without intensive iterative lead optimization process.

The following diagram illustrates how AI algorithms and big data empower rapid antibody discovery with improved productivity:



NEObody™

NEObody technology is a fully synthetic phage display and yeast display-based antibody discovery technology, which we believe is differentiated from other synthetic antibody technologies through its innovative designs and precise constructions. Our designs are based on critical insights gained from extensive studies of antibody structural variability made possible by our proprietary in-house developed computational tools.

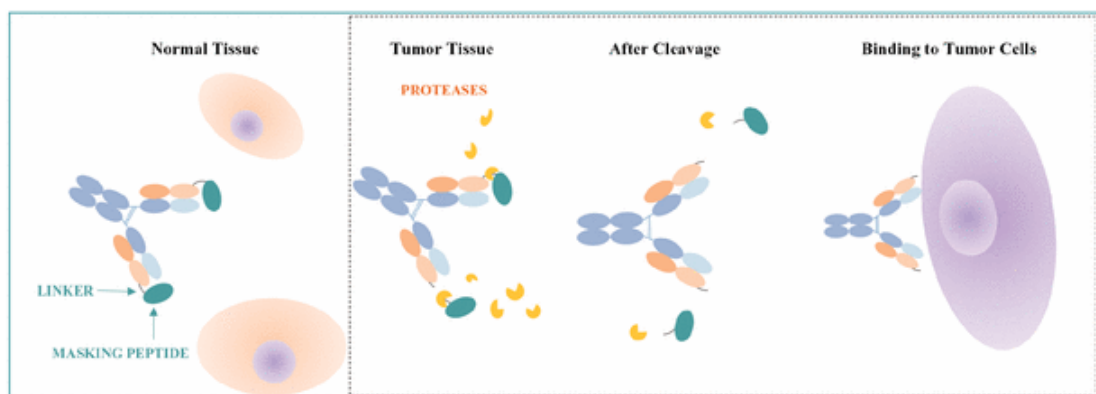
Innovative antibody library design: We believe that diversity of an antibody library should be defined at the quaternary structural level, instead of the traditional primary amino acid sequence level. Comparison of structural and sequence diversity revealed that variability as assessed by structural alignments was generally lower than the variability observed with sequence alignments. Based on our deep understanding of chemical principles governing antibody folding and extensive analysis of a vast number of antibody structural variability, through novel statistical tools developed in-house, we have redefined the antibody hyper-variable regions, or HVRs, that are critical for antigen recognition. These HVRs, as defined based on structural variability, are distinct from but complementary with complementarity-determining regions that are traditionally defined based on amino acid sequence variability. In addition, we have defined and designed dynamic motifs which adopt multiple conformations and incorporated them into our DPL antibody library design to enable the coverage of a wide range of structural diversity with a limited number of amino acid sequences.

Broad epitope coverage, particularly of evolutionarily conserved epitopes: NEObody technology enables us to discover antibodies targeting numerous epitopes against a broad range of antigens. In particular, we focus on the antibodies targeting the conserved epitopes of divergent antigens. These species cross-reactive antibodies not only have the potential to reveal new biological functions of the targets, but also facilitate preclinical studies using various immune intact animal models, resulting in high fidelity translation from preclinical to clinical studies. Our NEObody technology has been evaluated in preclinical studies with numerous antigens, including some difficult antigens such as membrane or oligomeric proteins. The success criteria in our preclinical assays include high affinity of primary hits with diverse antibody sequences, broad epitope coverage, as well as favorable CMC development properties. For example, ADG106 was discovered using our NEObody technology to target a conserved epitope of CD137 that mostly overlaps with its ligand binding site, which we believe enables ADG106 to activate CD137 in its natural ligand-like fashion, with complete blocking of CD137L, which may differentiate it from two other investigational leading CD137 agonistic antibodies.

Enhanced developability profiles: NEObody technology is designed to preemptively eliminate the chemically unstable sites, or combinations of “problematic” sites that may pose risk for downstream manufacturing processes. This precision design strategy coupled with precision oligonucleotides and library construction have resulted in our high-quality antibody discovery libraries. The primary hits from these libraries generally lack severe “problematic” and spurious amino acid sites, and therefore, may offer promising characteristics for further development.

SAFEbody™

SAFEbody is our proprietary differentiated precision antibody masking technology designed to enable an antibody to bind its target specifically only after conditional activation of the antibody in target tissues. By engineering our antibody therapeutic candidates to selectively activate in the TME, our SAFEbody technology is designed to improve safety and tolerability of antibody therapeutics while simultaneously maintaining clinical activity. Through this technology, we believe we can provide a solution to on-target off-tumor toxicity, one of the long-lasting challenges with many approved antibody therapeutics.



Activation in the TME: SAFEbody technology is designed to mask an antibody binding interface with a masking motif, which then prevents an antibody from binding to its target in healthy tissues. The masking motif is designed to activate or unmask the antibody binding in the TME where certain activation conditions such as a protease is upregulated as compared to healthy tissues, allowing the antibody to bind to and attack the tumor. Our SAFEbody enabled therapeutic candidates are therefore designed to be activated predominantly in the TME while remaining largely in an inactive state in healthy tissues.

Innovative masking moiety library design: Leveraging computational biology, we have designed multiple masking libraries with structured scaffolds and balanced chemistry of amino acids with favorable attributes for masking, easier manufacturing processes, and lower immunogenicity.

Precision masking without self-inhibition: To differentiate from other masking technologies, our antibody masking moieties have been designed and discovered in the right context in an effort to provide greater expression and specificity with no self-inhibition upon activation. We employ sophisticated screening processes for rapid discovery of highly masked SAFEbody product candidates subject to systematic tuning of the masking efficiency to match the target biology.

Improved pharmacology and safety features: We believe our SAFEbody technology has the potential to also reduce the dose-limiting toxicities observed in combination therapies and thus potentially enable new combinations with other cancer therapies that were previously difficult to use. Our SAFEbody technology may also provide favorable for PK and PD profiles for antibodies and ADCs to reduce the drug clearance from circulation in healthy tissues.

Our SAFEbody technology has been applied to multiple target antibodies that have been either discovered with NEObody technology or supplied by our partners. Our ADG126 was discovered by combining SAFEbody technology with its parental antibody discovered through our NEObody technology.

POWERbody™

In recent years, multiple modalities have been developed to enhance the potency of traditional antibody drugs. These include Fc engineering for enhanced ADCC or cross-linking efficiency, ADCs and TCEs. Some of them, such as TCEs, can be so potent that only micrograms of the active ingredient are needed for a single dose, in contrast to regular antibody where hundreds of milligrams or even grams are required for a single dose. NEObodies can be converted into SAFEbodies which can be further reformatted into SAFEbody ADCs, bispecific TCEs, and Fc engineered antibodies. We refer to these as POWERbodies to indicate their potentially enhanced potency and safety profile.

We believe SAFEbodies can be applied to these modalities. Since an unmasked ADC, TCE, or Fc engineered antibody can be so potent, there is the risk that it will cause severe toxicity due to damage to healthy tissues or fast lysis of tumor cells, resulting in a narrow therapeutic window, as is frequently observed with some ADC drugs or TCEs that have been FDA approved or are in clinical development. We believe our POWERbodies enabled by our SAFEbody technology with ADC, TCE, etc., due to their inactivity in circulation and specific local activation in TME, could significantly reduce toxicity and at the same time retain efficacy.

POWERbody technology aims to boost the efficacy of antibody candidates with safety profiles enhanced by our SAFEbody technology. We believe our POWERbody technology will unleash the full power of antibody-based therapeutics to kill cancer cells with enhanced safety, achieving full potential in antibody based therapies such as bispecific TCEs and ADCs.

COLLABORATIONS WITH BIOPHARMACEUTICAL COMPANIES

We enter into collaborations with biotechnology and pharmaceutical companies to advance the development and commercialization of our technology platforms and product candidates. We seek collaborations that will allow us to retain significant future participation in product sales through royalties paid on net sales. For example, we have entered into agreements with ADC Therapeutics to develop antibody drug conjugates against tumor targets using our SAFEbody technology. In addition, we have also out-licensed the Greater China rights to an anti-PD-L1 antibody and second antibody candidate to Dragon Boat Pharmaceuticals and its affiliates. Our collaborations empower our growth in many ways, including generating cash flow and revenues that partially offset expenditures on our internal research and development programs, expanding our knowledge base regarding antibody technology across multiple targets and antibodies provided by our partners, and providing us with future pipeline opportunities through opt-in licensing rights to new product candidates created using our technology. Below are the highlights of collaborations we formed with our business partners:

Exelixis Collaboration and License Agreement

In February 2021, we entered into a collaboration and license agreement (the “Exelixis Agreement”) with Exelixis, Inc., pursuant to which we agreed to generate masked antibodies with our SAFEbody technology against an initial target and a second target to be selected by Exelixis. Pursuant to the Exelixis Agreement, we granted Exelixis an exclusive, worldwide, sublicensable license to research, develop, make, have made, sell, offer for sale, import and commercialize products containing the masked antibodies to be generated by us with respect to both targets.

We are subject to certain exclusivity provisions limiting our right to research, develop, make, and commercialize any other antibodies directed to the selected targets during the term of the Exelixis Agreement, subject to exceptions for antibodies with sequence identities that differ by a specified amount. Exelixis is subject to certain exclusivity provisions limiting its rights to research, develop, make, and commercialize any other masked antibodies directed to the selected targets during the term of the Exelixis Agreement, subject to exceptions for antibodies with sequence identities that differ by a specified amount or use different masking technology.

We are required to use commercially reasonable efforts to generate masked antibodies in accordance the program plan for each target at our cost. Exelixis is required to use commercially reasonable efforts to further develop, obtain regulatory approval and commercialize a product for each target.

Under the Exelixis Agreement, we are entitled to receive an \$11,000,000 upfront payment. In addition, we could be eligible to receive, on a target-by-target basis, up to \$27,500,000 in development milestone payments and up to \$100,000,000 in regulatory milestone payments upon the achievement of specified development and regulatory milestones, respectively, and up to \$262,500,000 in sales milestone payments upon the achievement of specified commercial milestones. In the aggregate, we could be eligible to receive up to \$55,000,000 in development milestone payments, \$200,000,000 in regulatory milestone payments, and up to \$525,000,000 in sales milestone payments for both targets under the Exelixis Agreement. In addition, we are entitled to receive mid-single-digit percentage net sales-based royalties on products developed under the Exelixis Agreement, subject to certain reductions. Royalties, if any, will be payable on a country-by-country and product-by-product basis, until the latest of (i) the tenth anniversary of the first commercial sale of such product in such country, (ii) the expiration of the last-to-expire of certain specified patents that cover such product’s composition of matter or method of use as sold in such country or (iii) the expiration of regulatory or data exclusivity for such product in such country. As of the date of this annual report, we have received US\$11,000,000 in aggregate payments under the Exelixis Agreement.

The Exelixis Agreement will expire upon the termination of all royalty obligations. Exelixis will own the inventions relating to the compounds arising in connection with the Exelixis Agreement and we will own the inventions relating to our platform. Exelixis may terminate the Exelixis Agreement without cause, in its entirety or on a target-by-target basis, upon a specified notice period, and may terminate for safety reasons on a target-by-target basis immediately upon notice. Either party has the right to terminate the Exelixis Agreement for cause upon the other party's uncured material breach or insolvency, provided that, upon our material uncured breach, Exelixis may elect to instead continue the Exelixis Agreement, and any subsequent milestones or royalty amounts payable to us after such time will be reduced by a specified percentage. Upon termination of the Exelixis Agreement for any reason, the license granted to Exelixis will terminate.

ADC Therapeutics Agreements

In April 2019, we entered into a material transfer and collaboration agreement (the "ADCT Collaboration Agreement") and a license agreement (the "ADCT License Agreement") with ADC Therapeutics, a late clinical-stage oncology-focused biotechnology company pioneering the development and commercialization of targeted ADCs.

ADCT Collaboration Agreement

Pursuant to the ADCT Collaboration Agreement, we agreed to generate masked antibodies with our SAFEbody technology that could be combined with the pyrrolbenzodiazepine-based cytotoxic payload used in ADC Therapeutics' ADCs to create novel ADCs. ADC Therapeutics entered into the ADCT Collaboration Agreement with us to evaluate the use of our SAFEbody technology with respect to up to two exclusive targets selected by ADC Therapeutics. Upon our delivery of certain initial results, ADC Therapeutics has the option to license our SAFEbody technology with respect to one or both targets as further detailed below. ADC Therapeutics has not yet exercised such options as of the date of this annual report.

Both parties are required to use commercially reasonable efforts to perform certain development obligations under the ADCT Collaboration Agreement. Additionally, we are subject to exclusivity obligations to ADC Therapeutics under the ADCT Collaboration Agreement with respect to (i) the targets for which ADC Therapeutics has a license or an option to license and (ii) the use or licensing of our intellectual property that is necessary or useful to the development plan under the ADCT Collaboration Agreement or that would preclude us from granting to ADC Therapeutics the licenses under the ADCT License Agreement. ADC Therapeutics owns intellectual property that are specific to the SAFEbodies that we develop under the ADCT Collaboration Agreement with respect to the two elected targets, and we will own all intellectual property developed under the ADCT Collaboration Agreement that relates generally to our SAFEbody platform.

Under the ADCT Collaboration Agreement, we are eligible to receive up to US\$1,600,000 in consideration for our exclusivity obligations, upon achievement of certain development milestones and upon ADC Therapeutics' election to proceed with development for the two elected targets. As of the date of this annual report, we have received US\$437,500 in aggregate payments under the ADCT Collaboration Agreement. ADC Therapeutics has the right to terminate the ADCT Collaboration Agreement at any time and for any reason in its entirety or on a target-by-target basis upon thirty days' prior written notice to us. Either party may terminate the ADCT Collaboration Agreement, in its entirety or on a target-by-target basis, upon the other party's uncured material breach of the agreement or the other party's insolvency-related events.

ADCT License Agreement

Subject to the exercise of the options contained in the ADCT Collaboration Agreement, we have granted ADC Therapeutics, with respect to each elected target, an exclusive, worldwide, perpetual and irrevocable (subject only to the termination provisions) license (with the right to grant sublicenses) to develop, make, use, commercialize and import the antibody drug conjugates that comprise masked antibodies generated by us under these programs. Subject to certain conditions, including the exercise by ADC Therapeutics of its first option to license our SAFEbody" technology, ADC Therapeutics will grant us the option to negotiate a license to develop, manufacture and commercialize ADCs containing our SAFEbodyT" technology in Greater China.

Under the ADCT License Agreement, if ADC Therapeutics exercises both of its options granted thereunder, we could be eligible to receive up to US\$166,090,000 in aggregate milestone payments, in addition to mid-single-digit percentage net sales-based tiered royalties on products licensed under the ADCT License Agreement, subject to certain reductions. Royalties, if any, will be payable on a country-by-country and product-by-product basis, until the earlier of (i) the tenth anniversary of the first commercial sale of such product or (ii) the expiration of the last-to-expire patent licensed under the agreement in such country, unless earlier terminated by the parties, following which any licenses granted to ADC Therapeutics under the ADCT License Agreement shall become fully paid up, perpetual and irrevocable. In addition to the contingent milestone and royalty payments, if ADC Therapeutics exercises both of its options granted under the ADCT Collaboration Agreement, we are also entitled to a mid-six-figure dollar amount annual maintenance fee. ADC Therapeutics has not yet exercised the options contained in the ADCT Collaboration Agreement as of the date of this annual report. Therefore, we have not received any payment under the ADCT License Agreement.

ADC Therapeutics has the right to terminate the ADCT License Agreement before the expiration of the royalty term on a product-by-product basis or in its entirety (i) for any reason or no reason upon thirty days' written notice to us, or (ii) if ADC Therapeutics chooses to discontinue the development or sale of the applicable licensed product worldwide. Each party has certain rights to terminate the ADCT License Agreement with prior written notice upon the other party's uncured material breach or insolvency.

Sanjin Collaboration/ Out-Licensing Agreements

2018 Collaboration Agreements

In December 2018, we entered into (i) a collaboration agreement (the "Sanjin Greater China Agreement") that covers Greater China with Guilin Sanjin Pharmaceutical Co., Ltd. ("Sanjin") and certain of its subsidiaries (collectively, "Sanjin Parties") and (ii) a collaboration agreement (the "Sanjin ROW Agreement", together with the Sanjin Greater China Agreement, the "2018 Sanjin Agreements") that covers the regions other than Greater China with Sanjin. Pursuant to the Sanjin Greater China Agreement, we transferred the Chinese intellectual property directly related to a monoclonal antibody molecule that binds to the PD-L1 target (the "PD-L1 Project"), including patent rights, patent application rights and technologies based on the core sequence of the molecule, to Sanjin Parties. Sanjin Parties will own all the Chinese intellectual property developed in the exercise of Sanjin Parties' rights under the agreement, including but not limited to improvements (including combination products), clinical trials, regulatory filings, and commercialization rights relating thereto. We also granted Sanjin Parties a royalty-free license to use our other existing intellectual property and improvements thereto which are related to the PD-L1 Project for the purposes of exploiting its rights and performing its obligations under the agreement. Sanjin Parties will enjoy all the economic benefits deriving from the PD-L1 Project in Greater China, including but not limited to patent transfer fee, licensing fee, sales revenue and sales commission, etc. Sanjin Parties will pay us (i) within the validity period of the patent of PD-L1 molecule, single-digit percentage of net sales of the products that use the licensed antibody after such products enter the market and (ii) a low to mid-low double-digit percentage of the profits resulting from any transfer of the license to any third parties depending on the timing of the transfer relative to the development stage of the product. We also received a low-seven figure dollar upfront fee upon the effectiveness of the agreement from Sanjin Parties.

Pursuant to the Sanjin ROW Agreement, we granted Sanjin a royalty-free license to use all intellectual property relating to (i) the collaboration under the agreement that we controlled before we entered into the agreement or acquired independently of the agreement and (ii) improvements thereto for the purposes of exploiting its rights and performing its obligations under the agreement. Any intellectual property generated independently by a party under the agreement will be solely owned by that party who generated such intellectual property, and any intellectual property generated from cooperation between us and Sanjin's affiliates in connection with the collaboration will be jointly owned. We have the right to apply for the patents derived from our core and key technologies pertaining to the PD-L1 molecule in the rest of the world and we retain a majority of the economic benefits derived from the Sanjin ROW Agreement, including but not limited to any patent transfer fee, licensing fee and gains realized under such transfer. In case we intend to transfer to a third party our share of economic interests in any country outside of Greater China, we must notify Sanjin and Sanjin will receive a right of first refusal if it pays us a deposit equal to a low double-digit percentage of the consideration that we expect to receive from such third party. If Sanjin waives the right of first refusal, we can proceed with the transfer, provided that the final transaction price with the third party is not lower than the amount of the offering price that was included in our notice to Sanjin.

Under the 2018 Sanjin Agreements, we agreed not to (i) independently develop any monospecific antibodies that bind to the PD-L1 target or (ii) grant any rights associated with such antibodies to any third parties during the three-year period from the effective date of the agreements. The exclusivity obligation does not prevent us from (i) developing or granting any licenses to third parties for intellectual property that covers bispecific antibodies, ADCs, diagnostic antibodies, nano-particles and probody against PD-L1 target and (ii) continuing to provide antibody screening service that were commenced before the execution of the Sanjin Greater China Agreement and either party has the independent right to conduct combination therapy studies outside of the Greater China. Either non-breaching party may terminate the 2018 Sanjin Agreements if the other party's ability to comply with its respective obligations under the agreements is negatively affected by contingencies such as failure to maintain operation or changes in core project management and the other party fails to take effective remedial measures. Each agreement automatically terminates upon the termination of the other agreement. Upon the rescission or termination, Sanjin Parties will return to us all the intellectual property transferred by us to the Sanjin Parties as well as documents and data provided by us under the 2018 Sanjin Agreements. The 2018 Sanjin Agreements are governed by PRC law.

2019 Collaboration Agreements

In May 2019, we entered into (i) a collaboration agreement that covers Greater China (the "Dragon Boat Greater China Agreement") and (ii) a collaboration agreement that covers the regions other than Greater China (the "Dragon Boat ROW Agreement," together with the Dragon Boat Greater China Agreement, the "2019 Dragon Boat Agreements"), with Dragon Boat Biopharmaceutical (Shanghai) Limited. ("Dragon Boat"), a subsidiary of Sanjin. Pursuant to the Dragon Boat Greater China Agreement, we will transfer the Chinese intellectual property directly related to a certain monoclonal antibody molecule (the "Specified Molecule") that binds to a specified target (the "Specified Project"), including the patent rights, patent application rights and technologies based on the core sequence of the molecule, to Dragon Boat. Dragon Boat will own all the Chinese intellectual property developed in the exercise of Dragon Boat's rights under the agreement, including but not limited to improvements (including combination products), clinical trials, regulatory filings, and commercialization rights relating thereto. The target is not disclosed as of the date of this annual report. We also granted Dragon Boat a royalty-free license to use our other existing intellectual property and improvements thereto which are related to the Specified Project for the purposes of exploiting its rights and performing its obligations under the agreement. Dragon Boat will enjoy all the economic benefits deriving from the Specified Project in Greater China, including but not limited to patent transfer fee, licensing fee, sales revenue and sales commission, etc. and will pay us (i) RMB6,000,000 (equivalent to approximately US\$0.9 million) milestone payments and (ii) a single-digit percentage of net sales of the products that within the validity period of the patent of the Specified Molecule use the licensed antibody after such products enter the market. Dragon Boat also paid us a mid-six figure dollar upfront fee upon the signing of the agreement.

Pursuant to the Dragon Boat ROW Agreement, we granted Dragon Boat a royalty-free license to use all intellectual property relating to (i) the collaboration under the agreement that we controlled before we entered into the agreement or acquired independently of the agreement and (ii) improvements thereto for the purposes of exploiting its rights and performing its obligations under the agreement. Any intellectual property generated independently by a party under the agreement will be solely owned by that party who generated such intellectual property, and any intellectual property generated from cooperation between us and Dragon Boat in connection with the collaboration will be jointly owned. We have the right to apply for the patents derived from our core and key technologies pertaining to the Specified Molecule in the rest of the world and we retain a majority of the economic benefits derived from the Dragon Boat ROW Agreement, including but not limited to any patent transfer fee, licensing fee and gains realized under such transfer. In case we intend to transfer to a third party our share of economic interests in any country outside of Greater China, we must notify Dragon Boat and Dragon Boat will receive a right of first refusal if it pays us a deposit equal to a low double-digit percentage of the consideration that we expect to receive from such third party. If Dragon Boat waives the right of first refusal, we can proceed with the transfer, provided that the final transaction price with the third party is not lower than the amount of the offering price that was included in our notice to Dragon Boat.

Under the 2019 Dragon Boat Agreements, we agreed not to (i) independently develop any monospecific antibodies that bind to the specified target or (ii) grant any rights associated with such antibodies to any third parties during the three-year period from the effective date of the agreements. The exclusivity obligation does not prevent us from (i) developing or granting any licenses to third parties for intellectual property that covers bispecific antibodies, ADCs, diagnostic antibodies, nano-particles and probody against the specific target and (ii) continuing to provide antibody screening service that were commenced before the execution of the Dragon Boat Greater China Agreement and either party has the independent right to conduct combination therapy studies outside of the Greater China. Either nonbreaching party may terminate the 2019 Dragon Boat Agreements if the other party's ability to comply with its obligations under the agreements is negatively affected by contingencies such as failure to maintain operation or changes in core project management and the other party fails to take effective remedial measures. Each agreement automatically terminates upon the termination of the other agreement. Upon the rescission or termination, Dragon Boat will return to us all the intellectual property transferred by us to Dragon Boat as well as documents and data provided by us under the 2019 Dragon Boat Agreements. The 2019 Dragon Boat Agreements are governed by PRC law.

As of the date of this annual report, we have received approximately US\$1.5 million and US\$0.6 million in aggregate payments under the 2018 Sanjin Agreements and the 2019 Dragon Boat Agreements, respectively.

INTELLECTUAL PROPERTY

Protection of our intellectual property is fundamental to the long-term success of our business. Specifically, our success is dependent on our ability to obtain and maintain protection for our technology and the know-how related to our business, defend and enforce our intellectual property rights, and operate our business without infringing, misappropriating, or otherwise violating valid and enforceable intellectual property rights of others. Our patent strategy is focused on seeking coverage for our core technologies and products, such as the DPL platform, ADG106, ADG126, and ADG116. We also rely on trade secret protection of our confidential information and know-how relating to our proprietary technology, platforms and product candidates, and continuing innovation to develop, strengthen, and maintain our proprietary position in our technology, platforms and product candidates. We expect to rely on data exclusivity, market exclusivity, patent term adjustment and patent term extensions when available.

As of March 31, 2021, we own two issued patents and nine pending patent applications in China and we also own two issued patents and seven pending applications in Europe filed with the European Patent Office, twelve pending patent applications and two pending provisional applications in the United States, as well as nine pending international PCT applications and 69 pending patent applications in other jurisdictions. Our patents and patent applications cover our key technologies and products, including the DPL platform, ADG106, ADG126, and ADG116. Excluding any patent term adjustment and patent term extension, our currently issued patents are expected to expire from 2033 to 2034. If any patents issue from our pending patent applications, excluding any patent term adjustments and patent term extension, such patents will be expected to expire from 2033 to 2041. The following table summarizes material pending patent applications in the United States, China, Europe and under Patent Cooperation Treaty, or PCT, covering our product candidates, including ADG106, ADG126, ADG116 and ADG104.

Product Candidates	Title of Patent Application	Type of Patent Applications(1)	Jurisdiction
ADG106	Anti-CD137 molecules and uses thereof Combination therapy comprising anti-CD137 antibodies	Composition of matter/ method of use/ method of making method of treatment/ method of use	United States of America China and European Patent Office United States of America
ADG126	Anti-CTLA4 antibodies and methods of making and using the same	Composition of matter/ method of use/ method of making	United States of America, China and European Patent Office
ADG116	Anti-CTLA4 antibodies and methods of making and using the same	Composition of matter/ method of use/ method of making	United States of America, China and European Patent Office
ADG104	Anti-PD-L1 antibodies and use thereof	Composition of matter/ method of use/ method of making	United States of America and European Patent Office

(1) You should read the Risk Factors included elsewhere in this annual report for important information about risks posed by the loss of patent protection, in particular the risks described under “Item 3 Key Information—3.D.Risk Factors—Risks Related to Our Intellectual Property”.

The following table summarizes material issued patents in Europe and China covering our proprietary technologies.

Application No.	Title of Patent	Type of Patent(1)	Jurisdiction
13877452.6	An Integrated System for Library Construction, Affinity Binder Screening and Expression Thereof	Method	European Patent Office
201380074656.1	An Integrated System for Library Construction, Affinity Binder Screening and Expression Thereof	Method	China
14908246.3	Methods and Systems for Autoinduction of Protein Expression	Method	European Patent Office
201410789857.6	Filter Vector System And Its Applications	Method	China

(1) You should read the Risk Factors included elsewhere in this annual report for important information about risks posed by the loss of patent protection, in particular the risks described under “Item 3 Key Information—3.D.Risk Factors—Risks Related to Our Intellectual Property”.

We continually assess and refine our intellectual property strategy as we develop new platform technologies and product candidates. To that end, we are prepared to file additional patent applications relating to the new technologies that we develop if our intellectual property strategy requires such filings, or where we seek to adapt to competition or seize business opportunities. In addition to filing and prosecuting patent applications in China and the United States, we may elect to file counterpart patent applications in additional countries and regions where we believe such foreign filing is likely to be beneficial.

As with other biopharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our platform technologies and product candidates will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our owned pending patent applications, and any patent applications that we may in the future file or license from third parties may not result in the issuance of patents. In addition, the term of individual issued patents depends upon the legal term for patents in the countries in which they are obtained. In most countries in which we have filed or intend to file in the future, including the United States, the patent term is 20 years from the earliest filing date of a nonprovisional patent application. We intend to seek patent term extensions to any of our issued patents in any jurisdiction where these are available; however, there is no guarantee that the applicable authorities will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. The life of a patent, and the protection it affords, is therefore limited and once the patent life of our issued patents has expired, we may face competition, including from other competing technologies. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

We seek to ensure that investments made into the development of our technology are protected by relying on a combination of patents, trademarks, copyrights, trade secrets and contractual rights, including license agreements. In addition to our patent portfolio described above, as of March 31, 2021, our PRC subsidiary owns 33 registered trademarks relating to various aspects of our operations, and two registered domain names in China. To protect our rights, we seek to enter into confidentiality agreements, nondisclosure agreements and employee disclosure and invention assignment agreements with our employees, contractors and other third parties who may have or need access to our confidential information. We have also employed internal policies, encryptions and data security measures to protect our proprietary rights. However, there can be no assurance that our efforts will be successful. If our employees, contractors or other third parties violate these agreements or otherwise infringe upon, misappropriate or otherwise violate our intellectual property rights, we may seek to enforce our rights against such parties. In addition, from time to time, third parties may initiate litigation against us alleging infringement, misappropriation or other violation of their proprietary rights or declaring their noninfringement of our intellectual property rights. An adverse result in any such proceeding could enjoin the commercialization of our technology platform and product candidates, result in significant damages, and have a material adverse effect on our business. Even if we are successful in any such litigation, we may be required to incur significant costs and dedicate significant personnel time in defending such litigation. For more information on these and other risks related to intellectual property, see “Item 3 Key Information—3.D. Risk Factors—Risks Related to Our Intellectual Property”.

MANUFACTURING AND SUPPLY

We do not currently operate a cGMP-compliant manufacturing facility. We currently outsource the GMP manufacturing and quality control testing and cGMP quality assurance release of clinical trial material to WuXi Biologics. We have entered into a framework agreement with Wuxi Biologics, under which it provides services to us on a project-by-project basis. We are also working with other qualified manufacturers to provide diversified manufacturing and supply services. We also monitor the manufacturing activities of clinical trial material to ensure the compliance with local and international cGMP and applicable regulations. We have assembled a seasoned internal team with rich experience to drive and monitor the manufacturing process. Currently, Wuxi Biologics obtains raw materials and supplies for manufacturing activities from multiple suppliers who we believe have sufficient capacity to meet our demands. We expect to continue our relationships with WuXi Biologics but are continuously evaluating multiple vendors globally to ensure continuous supply of products for global clinical trials.

COMPETITION

The biotechnology and pharmaceutical industries are highly competitive and characterized by continuing technological advancement, significant competition and an emphasis on intellectual property. While we believe that our management's research, development and commercialization experience provide us with competitive advantages, we face potential competition from many different sources, including global biopharmaceutical companies, major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, universities, academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for the research, development, manufacturing and commercialization of cancer immunotherapies. Any product candidates that we successfully develop and commercialize will compete with new immunotherapies and other drug products that may become available in the future. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer and more effective, have fewer or less severe side effects or are more convenient than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we do.

We compete in the segments of the pharmaceutical, biotechnology and other related markets that develop cancer treatments. There are many other companies that have commercialized and/or are developing immuno-oncology treatments for cancer, including large pharmaceutical and biotechnology companies. Many of our competitors have significantly greater financial, technical and human resources than we have, and mergers and acquisitions in the biopharmaceutical industry may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our commercial opportunities could be reduced or eliminated if our competitors develop or market products or other novel therapies that are more effective, safer or less costly than our current or future product candidates, or obtain regulatory approval for their products more rapidly than we may obtain approval for our product candidates.

Our lead product candidate, ADG106, is an investigational fully human ligand-blocking, agonistic anti- CD137 IgG4 mAb that is designed to target a unique conserved epitope of CD137. While potentially unique for this type of product candidate, we expect our primary competition to be with other clinical-stage CD137 agonist product candidates. As of the date of this annual report, there are no marketed CD137 agonist drugs. The two leading molecules in clinical trials are utomilumab (PF-05082566) from Pfizer and urelumab (BMS-663513) from BMS. The following chart reflects CD137 agonist mAb programs in the global pipeline:

Global Pipelines of CD137 Agonist Mab Programs		
Drug	Company	Phase
		I/II
		I
		I
PF-05082566	Pfizer	II
		I/II
		I
		I/II
BMS-663513	BMS	II
		I/II
ATOR-1017	Alligator	I
AGEN2373	Agenus/Gilead	I
CTX-471	Compass	I
LVGN6051	Lyvgen	I

ADG126 and ADG116 are investigational, fully human anti-CTLA-4 mAbs generated through our NEObody and SAFEbody technologies, respectively. We expect our primary competition to be within the CTLA-4 antibody market, especially with ipilimumab. According to Frost & Sullivan, as of July 31, 2020, Yervoy (ipilimumab) from BMS is the only market CTLA-4 drug targeting cancer with six indications including monotherapy and combination therapies approved by FDA.

In January 2020, BMS submitted a biologics license application, or BLA, with the FDA for Opdivo in combination with Yervoy for the first-line treatment of patients with metastatic or recurrent NSCLC with no EGFR or ALK genomic tumor aberrations. In April 2020, the FDA approved Opdivo plus Yervoy, administered concomitantly with a limited course of chemotherapy, for the first-line treatment of patients with metastatic or recurrent NSCLC with no EGFR or ALK genomic tumor aberrations.

While Yervoy is the only marketed CTLA-4 antibody drug, there are over ten CTLA-4 antibody monotherapies and combination therapies in clinical development globally, according to Frost & Sullivan.

There are no marketed CTLA-4 antibody drugs in China, but at least seven CTLA-4 antibodies pipelines are in clinical development, according to the Frost & Sullivan Report. Major limitations of CTLA-4 mAbs include toxicity. According to the Frost & Sullivan Report, nivolumab and ipilimumab combination therapy has shown relatively higher toxicity in clinical studies even at lower dosages, which was observed from the published clinical data. We believe that the continued expansion of indications, and the launch of innovative novel CTLA-4 antibodies with potential for higher safety and better efficacy may increase the market for CTLA-4 antibodies significantly.

INSURANCE

We provide social security insurance including pension insurance, unemployment insurance, work-related injury insurance and medical insurance for our employees. We maintain property insurance, general liability insurance, products/completed operations insurance, auto and international auto liability insurance, workers compensation insurance, key-men insurance, international workers compensation insurance, accident and health insurance and director and officer liabilities insurance. We consider our insurance coverage sufficient and in line with market practice for our business operations in the industry.

LEGAL PROCEEDINGS

From time to time, we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. As of the date of this annual report, we are not presently a party to any legal proceedings that, if determined adversely to us, would individually or taken together have a material adverse effect on our business, results of operations, financial condition or cash flows. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

REGULATION

United States Regulation

The FDA and other regulatory authorities at federal, state, and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of biologics such as those we are developing. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates.

In the United States, the FDA regulates biologic products under the Federal Food, Drug and Cosmetic Act, its implementing regulations and other laws, including, in the case of biologics, the Public Health Service Act. Our product candidates are subject to regulation by the FDA as biologics. Biologics require the submission of a BLA and licensure, which constitutes approval, by the FDA before being marketed in the United States. None of our product candidates has been approved by the FDA for marketing in the United States, and we currently have no BLAs pending. Failure to comply with applicable FDA or other requirements at any time during product development, clinical testing, the approval process or after approval may result in administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, suspension or revocation of approved applications, warning letters, product recalls, product seizures, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution.

The process required by the FDA before biologic product candidates may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's GLP regulations;
- submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent Institutional Review Board, or IRB, or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials to establish the safety and effectiveness of the proposed biologic product candidate for its intended indications;
- preparation of and submission to the FDA of a BLA when adequate data are obtained from pivotal clinical trials;
- a determination by the FDA within 60 days of its receipt of a BLA to accept the application for review;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with Good Clinical Practices, or GCP regulations; and

- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical and Clinical Development

Prior to beginning the first clinical trial with a product candidate in the United States, we must submit an IND application to the FDA. An IND application is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND application is on the general investigational plan and the protocol(s) for clinical trials. The IND application also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. If the IND sponsor is not able to address FDA's concerns satisfactorily within the 30-day time frame, the IND may be placed on clinical hold. The IND sponsor and the FDA must resolve any outstanding concerns or questions before the IND is cleared by the FDA and the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Generally, a separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board, or DSMB, which provides recommendation on whether or not a study should move forward at designated check points based on access to certain data from the study. The DSMB may recommend halting of the clinical trial if it determines that there is an unacceptable safety risk for subjects or on other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase I—The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. For investigational products developed for oncology indications, the Phase I trials are normally conducted in patients with serious or life-threatening diseases without other treatment alternatives.
- Phase II—The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase II clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase III clinical trials. For certain indications in patients with serious or life-threatening diseases and with no available therapies, it may be possible to obtain BLA approval based on data from Phase II trials if a positive benefit risk profile is demonstrated.
- Phase III—The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

BLA Submission and Review

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. The submission of a BLA requires payment of a substantial application user fee to the FDA unless a waiver or exemption applies.

Once an original BLA has been submitted, FDA has 60 days to determine whether the application can be filed. If FDA determines that an application to be deficient, on its face, in a way that precludes a complete review, FDA may not accept the application for review and may issue a refuse-to-file letter to the sponsor. If FDA determines the application is filable, the FDA's goal is to review standard applications within ten months after it accepts the application for filing, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facilities in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may convene an advisory committee to provide clinical insight on application review questions. Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the commercial product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response letter will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the Complete Response letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. The fast track program is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, new products are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a fast track product has opportunities for frequent interactions with the review team during product development and, once a BLA is submitted, the product may be eligible for priority review. A fast track product may also be eligible for rolling review, in which case the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

A product intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase I and an organizational commitment to expedite the development and review of the product, including involvement of senior managers.

Any marketing application for a biologic submitted to the FDA for approval, including a product with a fast track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition compared to marketed products. For products containing new molecular entities, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (compared with ten months under standard review).

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical trials to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

In 2017, FDA established a new regenerative medicine advanced therapy, or RMAT, designation as part of its implementation of the 21st Century Cures Act, which was signed into law in December 2016. The RMAT designation program is intended to fulfill the 21st Century Cures Act requirement that FDA facilitate an efficient development program for, and expedite review of, any drug that meets the following criteria: (1) it qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (2) it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition. Like fast track and breakthrough therapy designation, RMAT designation provides potential benefits that include more frequent meetings with the FDA to discuss the development plan for the product candidate and eligibility for rolling review and priority review. Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites. Once approved, when appropriate, the FDA can permit fulfillment of post-approval requirements under accelerated approval through the submission of clinical evidence, clinical trials, patient registries, or other sources of real-world evidence such as electronic health records; through the collection of larger confirmatory datasets; or through post-approval monitoring of all patients treated with the therapy prior to approval.

Fast track designation, breakthrough therapy designation, priority review, accelerated approval, and RMAT designation do not change the standards for approval but may expedite the development or approval process.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making available a drug or biologic for this type of disease or condition will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusive approval (or exclusivity), which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing user fee requirements, under which FDA assesses an annual program fee for each product identified in an approved BLA. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of a product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal of the FDA to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Biosimilars and Reference Product Exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-approved reference biological product.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or studies. Interchangeability requires that a product be biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered to a patient more than once, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. Complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the FDA may not approve a biosimilar product until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of the competing product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate implementation and impact of the BPCIA is subject to significant uncertainty.

Other Healthcare Laws and Compliance Requirements

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under any federal healthcare program;
- federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment to the federal government, including federal healthcare programs, that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes which prohibit, among other things, executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters, and which, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, also imposes certain requirements on HIPAA covered entities and their business associates relating to the privacy, security and transmission of individually identifiable health information;
- the U.S. federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to the federal government, information related to payments or other transfers of value made to physicians, as defined by such law, certain other health care providers beginning in 2022, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- United States state and foreign law equivalents of each of the above federal laws, which, in some cases, differ from each other in significant ways, and may not have the same effect, thus complicating compliance efforts, including laws governing the privacy and security of personal data, such as the GDPR, which imposes obligations and restrictions on the collection and use of personal data relating to individuals located in the EU and EEA (including with regard to health data).

If their operations are found to be in violation of any of such laws or any other governmental regulations that apply, they may be subject to significant penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological product for which we obtain regulatory approval. Sales of any product depend, in part, on the extent to which such product will be covered by third-party payers, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payers. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. As there is no uniform policy of coverage and reimbursement for drug products among third-party payers in the United States, coverage and reimbursement policies for drug products can differ significantly from payer to payer. There may be significant delays in obtaining coverage and reimbursement as the process of determining coverage and reimbursement is often time-consuming and costly which will require us to provide scientific and clinical support for the use of our products to each payer separately, with no assurance that coverage or adequate reimbursement will be obtained. It is difficult to predict at this time what government authorities and third-party payers will decide with respect to coverage and reimbursement for our drug products. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third-party payers are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical or biological products, medical devices and medical services, in addition to questioning safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payer not to cover a product could reduce physician usage and patient demand for the product.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of reform proposals to change the healthcare system. There is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by federal and state legislative initiatives, including those designed to limit the pricing, coverage, and reimbursement of pharmaceutical and biopharmaceutical products, especially under government-funded healthcare programs, and increased governmental control of drug pricing.

In March 2010, the ACA was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States, and significantly affected the pharmaceutical industry. The ACA contains a number of provisions of particular import to the pharmaceutical and biotechnology industries, including, but not limited to, those governing enrollment in federal healthcare programs, a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and annual fees based on pharmaceutical companies' share of sales to federal healthcare programs.

Since its enactment, there have been judicial, Congressional, and executive branch challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, the 2020 federal spending package permanently eliminates, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. In addition, the Tax Act was enacted, which, among other things, removes penalties for not complying with ACA's individual mandate to carry health insurance. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseparable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review this case, although it is unclear when or how the Supreme Court will rule. It is also unclear how other efforts to challenge, repeal or replace the ACA will impact the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year and reduced payments to several types of Medicare providers, which will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through December 31, 2020, unless additional Congressional action is taken. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

At the federal level, the Trump administration’s budget proposal for fiscal year 2021 includes a US\$135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. Further, the Trump administration released a “Blueprint,” or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out- of-pocket costs of drug products paid by consumers. The Department of Health and Human Services, or HHS, has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, the Centers for Medicare & Medicaid Services, or CMS, issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS’s policy change that was effective January 1, 2019. Most recently, in July 2020, President Trump also signed a number of executive orders that attempt to implement several of the Administration’s proposals. While some of measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product.

PRC Regulation

We are subject to a variety of PRC laws, rules and regulations affecting many aspects of our business. This section sets out a summary of the major relevant laws, regulations, rules and policies which may have material impact on our business and operations.

Regulations on Company Establishment and Foreign Investment

The establishment, operation and management of corporate entities in China are governed by the Company Law of PRC, or the PRC Company Law, which was promulgated by the Standing Committee of the National People’s Congress, or the NPC, in December 1993 and further amended in December 1999, August 2004, October 2005, December 2013 and October 2018, respectively. According to the PRC Company Law, companies are generally classified into two categories: limited liability companies and companies limited by shares. The PRC Company Law also applies to foreign-invested limited liability companies. According to the PRC Company Law, where laws on foreign investment have other stipulations, such stipulations shall prevail.

Investment activities in the PRC by foreign investors are governed by the Guiding Foreign Investment Direction, which was promulgated by the State Council in February 2002 and came into effect in April 2002, and the Special Administrative Measures for the Access of Foreign Investment (Negative List), or the Negative List, which was promulgated by the Ministry of Commerce of the PRC, or the MOFCOM, and the National Development and Reform Commission, or the NDRC, in June 2020 and came into effect in July 2020. The Negative List sets out the restrictive measures in a unified manner, such as the requirements on shareholding percentages and management, for the access of foreign investments, and the industries that are prohibited from receiving foreign investment. The Negative List covers 12 industries, and any field not falling under the Negative List shall be administered under the principle of equal treatment to domestic and foreign investment.

Foreign Investment Law of the PRC, or the Foreign Investment Law, was promulgated by the NPC in March 2019 and came into effect in January 2020. When the Foreign Investment Law came into effect, the Law on Wholly Foreign-owned Enterprises of the PRC, the Law on Sino-foreign Equity Joint Ventures of the PRC and the Law on Sino-foreign Cooperative Joint Ventures of the PRC were repealed simultaneously. The investment activities of foreign natural persons, enterprises or other organizations (collectively, the “foreign investors”) directly or indirectly within the territory of China shall comply with and be governed by the Foreign Investment Law. Such activities include: 1) establishing by foreign investors of foreign-invested enterprises in China alone or jointly with other investors; 2) acquiring by foreign investors of shares, equity, property shares, or other similar interests of Chinese domestic enterprises; 3) investing by foreign investors in new projects in China alone or jointly with other investors; and 4) other forms of investment prescribed by laws, administrative regulations or the State Council.

In December 2019, the State Council promulgated the Regulations on Implementing the Foreign Investment Law of the PRC, which came into effect in January 2020. When the Regulations on Implementing the Foreign Investment Law of the PRC came into effect, the Regulation on Implementing the Sino-Foreign Equity Joint Venture Enterprise Law of the PRC, Provisional Regulations on the Duration of Sino-Foreign Equity Joint Venture Enterprise, the Regulations on Implementing the Wholly Foreign-Invested Enterprise Law of the PRC and the Regulations on Implementing the Sino-Foreign Cooperative Joint Venture Enterprise Law of the PRC were repealed simultaneously.

In December 2019, the MOFCOM and the State Administration for Market Regulation, or the SAMR promulgated the Measures on Reporting of Foreign Investment Information, which came into effect in January 2020. When the Measures on Reporting of Foreign Investment Information came into effect, the Interim Measures for the Administration of Filing for Establishment and Changes in Foreign Investment Enterprises were repealed simultaneously. Since January 1, 2020, for foreign investors carrying out investment activities directly or indirectly in China, the foreign investors or foreign-invested enterprises shall submit investment information to the relevant commerce administrative authorities according to the Measure on Reporting of Foreign Investment Information.

Regulation on Pharmaceutical Product Development, Approval and Registration

Drug Regulatory Regime

The Drug Administration Law of the PRC, or the Drug Administration Law, was promulgated by the Standing Committee of the NPC, in September 1984. The two latest amendments to the Drug Administration Law were the amendment promulgated in April 2015 and in August 2019. The Regulations for the Implementation of the Drug Administration Law was promulgated by the State Council in August 2002, and was last amended in March 2019. The Drug Administration Law and the Regulations for the Implementation of the Drug Administration Law have jointly established the legal framework for the administration of pharmaceutical products in China, including the research, development and manufacturing of new drugs. The Drug Administration Law applies to entities and individuals engaged in the development, production, trade, application, supervision and administration of pharmaceutical products. It regulates and provides for a framework for the administration of pharmaceutical manufacturers, pharmaceutical trading companies and medicinal preparations of medical institutions, and the development, research, manufacturing, distribution, packaging, pricing and advertisements of pharmaceutical products. The Regulations for the Implementation of the Drug Administration Law, at the same time, provide the detailed implementation regulations for the Drug Administration Law.

In 2017, the drug regulatory system entered a new and significant period of reform. The General Office of the State Council and the General Committee of China Communist Party jointly issued Opinions on Deepening the Reform of the Evaluation and Approval Systems and Encouraging Innovation on Drugs and Medical Devices, or the Innovation Opinions. The expedited programs, the record-filing system, the prioritized review mechanism, the acceptance of foreign clinical data under the Innovation Opinions and other recent reforms encourage drug manufacturers to seek marketing approval in China first for the development of drugs in highly prioritized therapeutic areas, such as oncology or rare diseases.

To implement the regulatory reform introduced by Innovation Opinions, the Standing Committee of the NPC, the National Medical Products Administration, or the NMPA, a newly formed government authority as well as other authorities, are currently responsible for revising the laws, regulations and rules governing the pharmaceutical products and the industry.

In August 2019, the Standing Committee of the NPC promulgated the new Drug Administration Law, or the 2019 Amendment, which came into effect in December 2019. The 2019 Amendment contains many of the major reform initiatives implemented by the Chinese government since 2015, including but not limited to the Marketing Authorization Holder, or the MAH, system, conditional approvals of drugs, traceability system of drugs, and the cancellation of relevant certification according to the Good Manufacturing Practice, or the GMP, and the Good Supply Practice, or the GSP.

Regulatory Authorities

Pharmaceutical products in China are monitored and supervised on a national scale by the NMPA. The local provincial medical products administrative authorities are responsible for supervision and administration of drugs within their respective administrative regions. The NMPA was newly formed under the SAMR. The NMPA's predecessor, the State Drug Administration, or the SDA, was replaced by the State Food and Drug Administration, or the SFDA, which was later reorganized into the China Food and Drug Administration, or the CFDA, as part of the institutional reforms implemented by the State Council.

The primary responsibilities of the NMPA include:

- monitoring and supervising the administration of pharmaceutical products, medical appliances and equipment as well as cosmetics in the PRC;
- formulating administrative rules and policies concerning the supervision and administration of pharmaceutical, medical devices, and cosmetics industry;
- evaluating, registering and approving new drugs, generic drugs, imported drugs and traditional Chinese medicine;
- approving and issuing permits for the manufacture and export/import of pharmaceutical products, medical appliances and equipment;
- approving the establishment of enterprises to be engaged in the manufacture and distribution of pharmaceutical products;
- examining and evaluating the safety of pharmaceutical products, medical devices, and cosmetics; and
- managing significant accidents involving pharmaceutical products, medical devices and cosmetics.

In 2013, the Ministry of Health, or the MOH, and the National Population and Family Planning Commission were integrated into the National Health and Family Planning Commission of the PRC, or the NHFPC. In March 2018, the First Session of the Thirteenth NPC approved the State Council Institutional Reform Proposal, according to which, NHFPC and certain other governmental authorities were consolidated into the National Health Commission, or the NHC. The responsibilities of the NHC include coordinating the formulation of national drug policies, the national essential medicine system and the National Essential Medicines List and drafting the administrative rules for the procurement, distribution and use of national essential medicines.

According to the Decision of the CFDA on Adjusting the Approval Procedures under the Administrative Approval Items for Certain Drugs, which was promulgated by the CFDA in March 2017 and came into effect in May 2017, the Investigational New Drug Application, or the IND, approval should be issued by the Center for Drug Evaluation, or the CDE, on behalf of the CFDA.

Regulations on Clinical Trials and Registration of Drugs

Administrative Measures for Drug Registration

In July 2007, the SFDA promulgated the amended version of the Administrative Measures for Drug Registration, or the Registration Measures, which became effective in October 2007. The Registration Measures mainly cover: (1) definitions of drug registration applications and regulatory responsibilities of drug administration; (2) general requirements for drug registration, including application for registration of new drugs, generic drugs, imported drugs and supplemental application, as well as application for re-registration; (3) clinical trials; (4) application, examination and approval of new drugs, generic drugs and imported drugs; (5) supplemental applications and re-registrations of drugs; (6) inspections; (7) registration standards and specifications; (8) time limit; (9) re-examination; and (10) liabilities and other supplementary provisions.

According to the Registration Measures, drug registration applications are divided into three different types, namely Domestic New Drug Application, Domestic Generic Drug Application and Imported Drug Application. Drugs which fall into one of three general types are divided according to the drug's working mechanism, namely whether the drug is classified as a chemical medicine, a biological product, a traditional Chinese medicine or a natural medicine. New Drug Application, or NDA, refers to an application for registration of a drug that has not yet been marketed for sale in China. In addition, the registration of drugs that change the dosage form of the marketed drugs, change the route of administration and increase the new indications shall be reported in accordance with the application procedures for new drugs. Under the Registration Measures, a Category 1 drug refers to a new drug that has never been marketed in any country, and such drug is eligible for special review or fast track approval by the NMPA.

In January 2020, the SAMR released the amended Administrative Measures for Drug Registration, or the Amended Registration Measures, which came into effect in July 2020. The Amended Registration Measures provide detailed procedural and substantive requirements for the key regulatory concepts established by the Drug Administration Law, and confirms a number of reform actions that have been taken in the past years, including but not limited to: (i) the full implementation of the MAH system and implied approval of the commencement of clinical trial; (ii) the implementation of associated review of drugs, excipients and packaging materials; and (iii) the introduction of four procedures for expedited registration of drugs, which are procedures for ground-breaking therapeutic drugs, procedures for conditional approval, procedures for prioritized reviews and approval, and procedures for special examination and approval. Detailed implementation rules for drug classification and requirements for corresponding application materials will be promulgated by the NMPA.

In March 2016, the CFDA issued the Reform Plan for Registration Category of Chemical Medicine, which outlined the reclassifications of drug applications under the Registration Measures. According to the Reform Plan for Registration Category of Chemical Medicine, Category 1 drugs refer to innovative new drugs that have not been marketed anywhere in the world. Improved new drugs that are not marketed anywhere in the world fall into Category 2 drugs. Generic drugs, that have equivalent quality and efficacy to the originator's drugs and have been marketed abroad but not yet in China, can be classified as Category 3 drugs. Generic drugs, that have equivalent quality and efficacy to the originator's drugs and have been marketed in China, fall into Category 4 drugs. Category 5 drugs are drugs which have already been marketed abroad, but are not yet approved in China. Category 1 drugs and Category 5 drugs can be registered through the Domestic New Drug Application and the Imported Drug Application Procedures under the Registration Measures, respectively.

The SFDA promulgated the Administrative Provisions on Special Examination and Approval of Registration of New Drugs in January 2009, according to which, the SFDA conducts special examination and approval for new drug registration applications when: (1) the effective constituent of drug extracted from plants, animals, minerals, etc., as well as the preparations thereof have never been marketed in China, and the material medicines and the preparations thereof are newly discovered; (2) the chemical raw material medicines as well as the preparations thereof and the biological product have not been approved for marketing at home and abroad; (3) the new drugs have obvious clinical treatment advantages for such diseases as AIDS, malignant tumors and orphan diseases, etc. or (4) the new drugs treat diseases currently with no effective methods of treatment.

The Special Examination and Approval of Registration of New Drugs provides that the applicant may file for special examination and approval at the clinical trial application stage if the product candidate falls within items (1) or (2). The provisions provide that for product candidates that fall within items (3) or (4), the application for special examination and approval cannot be made until filing for production.

Accelerated Approval for Clinical Trial and Registration

The Innovation Opinions established a framework for reforming the evaluation and approval system for drugs, medical devices and equipment. The Innovation Opinions enhanced the standard of approval for drug registration and accelerated the evaluation and approval process for innovative drugs as well as drug clinical trials.

The CFDA released the Circular Concerning Several Policies on Drug Registration Review and Approval in November 2015, which further clarified the measures and policies for simplifying and accelerating the approval process of clinical trials, including:

- a one-time umbrella approval procedure allowing the overall approval of all phases of a new drug's clinical trials, replacing the current phase-by-phase application and approval procedure; and
- a fast track drug registration or clinical trial approval pathway for the following applications: (1) registration of innovative new drugs for treating HIV, cancer, serious infectious diseases and orphan diseases, etc.; (2) registration of pediatric drugs; (3) registration of geriatric drugs and drugs treating PRC-prevalent diseases in elders; (4) registration of drugs listed in national major science and technology projects or national key research and development plan; (5) registration of clinical urgently needed drugs using advanced technology, using innovative treatment methods, or having distinctive clinical benefits; (6) registration of foreign innovative drugs to be manufactured locally in China; (7) concurrent applications for new drug clinical trials which are already approved in the United States or EU or concurrent drug registration applications for drugs which have applied to the competent drug approval authorities for marketing authorization and passed such authorities' onsite inspections in the United States or EU and are manufactured using the same production line in China; and (8) clinical trial applications for drugs with urgent clinical need and patent expiry within three years, and manufacturing authorization applications for drugs with urgent clinical need and patent expiry within one year.

The NMPA released the Circular on Adjusting Evaluation and Approval procedures for Clinical Trials for Drugs in July 2018, according to which, within 60 days after the acceptance of and the fees paid for the IND application, the applicant may conduct the clinical trials for the drug in accordance with the clinical trial protocol submitted, if the applicant has not received any negative or questioning opinion from the CDE. Such approval process has been further enacted into the 2019 Amendment.

Trial Exemptions and Acceptance of Foreign Data

The NMPA issued the Technical Guidance Principles on Accepting Foreign Drug Clinical Trial Data in July 2018, as one of the implementing rules for the Innovation Opinions, which provides that overseas clinical data can be submitted for the drug registration applications in China. Such applications can be in the form of waivers to China-based clinical trials, bridging trials and direct NDAs. According to the Technical Guidance Principles on Accepting Foreign Drug Clinical Trial Data, sponsors may use the data of foreign clinical trials to support drug registration in China, provided that sponsors must ensure the authenticity, completeness, accuracy and traceability of foreign clinical trial data and such data must be obtained consistent with the relevant requirements under the Good Clinical Trial Practice of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, or the ICH. Sponsors must also comply with other relevant sections of the Registration Measures when applying for drug registrations in China using foreign clinical trial data.

The NMPA now officially permits, and its predecessor agencies have permitted on a case-by-case basis in the past, drugs approved outside of China to be approved in China on a conditional basis without pre-approval clinical trials being conducted in China. Specifically, the NMPA and the NHC released the Procedures for Reviewing and Approval of Clinical Urgently Needed Overseas New Drugs in October 2018, permitting drugs that have been approved within the last ten years in the United States, the EU or Japan and that prevent or treat orphan diseases, or prevent or treat serious life-threatening illnesses for which there is either no effective therapy in China, or for which the foreign-approved drug would have clear clinical advantages. Applicants will be required to establish a risk mitigation plan and may be required to complete trials in China after the drug has been marketed. The CDE has developed a list of qualifying drugs that meet the foregoing criteria.

Clinical Trial Process and Good Clinical Practices

According to the Registration Measures, a clinical trial consists of Phases I, II, III and IV. Phase I refers to the initial clinical pharmacology and safety evaluation studies in humans. Phase II refers to the preliminary evaluation of a product candidate's therapeutic effectiveness and safety for particular indications in patients, to provide evidence and support for the design of Phase III clinical trials and to settle the administrative dose regimen. Phase III refers clinical trials undertaken to confirm the therapeutic effectiveness and safety on patients with target indications, to evaluate the overall benefit-risk relationships of the drug, and ultimately to provide sufficient evidence for the review of drug registration application. Phase IV refers to a new drug's post-marketing study to assess therapeutic effectiveness and adverse reactions when the drug is widely used, to evaluate the overall benefit-risk relationships of the drug when used among the general population or specific groups and to adjust the administration dose.

To improve the quality of clinical trials, the SFDA promulgated the Good Clinical Trial Practice for Drugs in August 2003, or the GCP Rules, which was replaced by the revised Good Clinical Trial Practice for Drugs, the Revised GCP Rules, promulgated by the NMPA and the NHC in April 2020 and coming into effect in July 2020. According to the Administration of Quality of Drug Clinical Practice, clinical trial means systematical investigation of drugs conducted on human subjects (patients or healthy volunteers) to prove or reveal the function, adverse reactions and/or absorption, distribution, metabolism and excretion of the drug being investigated. The purpose of a clinical trial is to determine the therapeutic efficacy and safety of the drug. The Revised GCP Rules provide comprehensive and substantive requirements on the design and conduct of clinical trials in China. In particular, the Revised GCP Rules enhance the protection for study subjects and tighten the control over bio-samples collected under clinical trials.

The Revised GCP Rules also set out the qualifications and requirements for the investigators and centers participating in clinical trial, who must: (i) have professional certification at a clinical trial center, professional knowledge, training experience and capability of clinical trial, and be able to provide the latest resume and relevant qualification documents per request; (ii) be familiar with the trial protocol, investigator's brochure and relevant information of the trial drug provided by the applicant; (iii) be familiar with and comply with the Revised GCP Rules and relevant laws and regulations relating to clinical trials; (iv) keep a copy of the authorization form on work allocation signed by investigators; (v) accept supervision and inspection organized by the applicant and inspection by the drug regulatory authorities; and (vi) in the case of investigators and clinical trial centers authorizing other individual or institution to undertake certain responsibilities and functions relating to clinical trial, they shall ensure such individual or institution are qualified and establish complete procedures to ensure the responsibilities and functions are fully performed and generate reliable data.

Communication with the CDE

According to the Circular on Adjusting Evaluation and Approval Procedures for Clinical Trials for Drugs, where the application for clinical trial of new investigational drug has been approved, upon the completion of Phases I and II clinical trials and prior to Phase III clinical trial, the applicant shall submit the application for Communication Session to the CDE to discuss the key technical questions including the design of Phase III clinical trial protocol. Within 60 days after the acceptance of and the fees paid for the IND application, the applicant may conduct the clinical trials for the drug in accordance with the clinical trial protocol submitted, if the applicant has not received any negative or questioning opinion from the CDE.

The NMPA promulgated the Administrative Measures for Communication on the Research, Development and Technical Evaluation of Drugs in September 2018, according to which, during the research and development periods and in the registration applications of, among others, the innovative new drugs, the applicants may propose to conduct communication meetings with the CDE. The communication meetings can be classified into three types. Type I meetings are convened to address key safety issues in clinical trials of drugs and key technical issues in the research and development of breakthrough therapeutic drugs. Type II meetings are held during the key research and development periods of drugs, mainly including meetings before the IND application, meetings upon the completion of Phase II trials and before the commencement of Phase III trials, meetings before submitting a marketing application for a new drug, and meetings for risk evaluation and control. Type III meetings refer to meetings not classified as Type I or Type II.

Drug Clinical Trial Registration

According to the Registration Measures, upon obtaining the approval of its IND applications and before conducting a clinical trial, an applicant shall file a registration form with the SFDA containing various details, including the clinical trial protocol, the name of the principal researcher of the leading institution, the names of participating institutions and researchers, an approval letter from the ethics committee, and a sample of the informed consent form, with a copy sent to the competent provincial administration departments where the trial institutions will be located. The CFDA released the Announcement on Drug Clinical Trial Information Platform in September 2013, according to which, instead of the aforementioned registration field with the CFDA, all clinical trials approved by the CFDA and conducted in China shall complete a clinical trial registration and publish trial information through the Drug Clinical Trial Information Platform. The applicant shall complete the trial pre-registration within one month after obtaining the approval of the clinical trial approval in order to obtain the trial's unique registration number and complete registration of certain follow-up information before the first subject's enrollment in the trial. If the registration is not completed within one year after the approval of the IND applications, the applicant shall submit an explanation, and if the first submission is not completed within three years, the approval of the IND applications shall automatically expire.

New Drug Application

According to the Registration Measures, drug registration applications include domestic NDA, domestic generic drug application and imported drug application. Drugs are classified into chemical drugs, biological products and traditional Chinese medicine or natural drugs. When Phases I, II and III clinical trials have been completed, the applicant may apply to the SFDA for approval of the NDA. The SFDA then determines whether to approve the application according to the comprehensive evaluation opinion provided by the CDE.

Pilot Plan for the MAH System

The Innovation Opinions provide a pilot plan for the MAH system.

Under the authorization of the Standing Committee of the NPC, the General Office of the State Council issued the Pilot Plan for the Drug Marketing Authorization Holder Mechanism in May 2016, which provides a detailed pilot plan for the MAH system in 10 Chinese provinces. Under the MAH system, domestic drug research and development institutions and individuals in the pilot regions are eligible to be holders of drug registrations without having to become drug manufacturers. The marketing authorization holders may engage contract manufacturers for manufacturing, provided that the contract manufacturers are licensed and located within the pilot regions. Drugs that qualify for the MAH system are: (1) new drugs (including but not limited to drugs under category I to category IV of chemical drugs, and targeted preparation, sustained release preparation, controlled release preparation under category V of chemical drugs, biological products approved as category I and VII drugs and biosimilars under the Registration Measures) approved after the implementation of the MAH system; (2) generic drugs approved as category III or IV drugs under the Reform Plan for Registration Category of Chemical Medicine; (3) previously approved generics that have passed equivalence assessments against original drugs; and (4) previously approved drugs whose licenses were held by drug manufacturers originally located within the pilot regions, but which have moved out of the pilot regions due to corporate mergers or other reasons.

The CFDA promulgated the Circular on the Matters Relating to Promotion of the Pilot Program for the Drug Marketing Authorization Holder System in August 2017. It clarified the legal liability of the MAH, who is responsible for managing the whole manufacturing and marketing chain and the whole life cycle of drugs and legally liable for preclinical drug study, clinical trials, manufacturing, marketing, distribution and adverse drug reaction monitoring. According to the Circular on the Matters Relating to Promotion of the Pilot Program for the Drug Marketing Authorization Holder System, the MAH shall submit a report of drug manufacturing, marketing, prescription, techniques, pharmacovigilance, quality control measures and other situations to the CFDA within 20 working days after the end of each year.

According to the Pilot Plan for the Drug Marketing Authorization Holder Mechanism, the pilot plan was originally set for a three-year period and was scheduled to expire in November 2018. The Standing Committee of the NPC promulgated the Decision of Extending the Pilot Period of Authorizing the State Council to Carry Out the Pilot Plan for the Drug Marketing Authorization Holder Mechanism in Certain Places in October 2018, which extended the term of the MAH system to November 4, 2019.

According to the 2019 Amendment, which came into effect on December 1, 2019, the MAH system will be applicable throughout the country and the legal representative and the key person-in-charge of a drug MAH shall be fully responsible for the quality of drugs.

International Multi-Center Clinical Trials

The International Multi-Center Clinical Trial Guidelines (Trial), or the Multi-Center Clinical Trial Guidelines, which was promulgated by the CFDA in January 2015 and came into effect in March 2015, provided guidance on the implementation of Multi-Regional Clinical Trials, or the MRCT, in China. According to the Multi-Center Clinical Trial Guidelines, international multi-center clinical trial applicants may simultaneously perform clinical trials in different centers using the same clinical trial protocol. Where the applicants plan to implement the international multi-center clinical trials in the PRC, the applicants shall comply with relevant laws and regulations, such as the Drug Administration Law, the Implementing Regulations of the Drug Administration Law and the Registration Measures, execute the GCP Rules, make reference to universal international principles such as the ICH-GCP and comply with the laws and regulations of the countries involved in the international multi-center clinical trials. Where the applicants plan to use the data derived from the international multi-center clinical trials for approval of a drug registration in the PRC, it shall involve at least two countries, including China, and shall satisfy the requirements for clinical trials set forth in the Multi-Center Clinical Trial Guidelines, Registration Measures and other related laws and regulations.

In April 2020, the NMPA and the NHC promulgated the Revised GCP Rules, which came into effect in July 2020. The Revised GCP Rules summarize the requirements for initiating an MRCT, that is, before initiating an MRCT: (i) the applicant shall ensure that all the centers participating in the clinical trial comply with the trial protocol; (ii) the applicant shall provide each center with the same trial protocol, and each center shall comply with the same unified evaluation criterion for clinical trial and laboratory data and the same guidance for case report form; (iii) each center shall use the same case report form to record the data of each human subject obtained during the trial; (iv) before initiating a clinical trial, a written document is required to specify the responsibilities of the investigators of each center; and (v) the applicant shall ensure the communication among the investigators of each center.

Data derived from international multi-center clinical trials can be used for the new drug applications with the NMPA. When using international multi-center clinical trial data to support new drug applications in China, applicants shall submit the completed global clinical trial report, statistical analysis report and database, along with relevant supporting data in accordance with the content and format requirements under the International Conference on Harmonization-Common Technical Document; subgroup research results summary and comparative analysis shall also be conducted concurrently. Leveraging the clinical trial data derived from international multi-center clinical trials conducted by our partners, we may avoid unnecessarily repetitive clinical trials and thus further accelerate the NDA process in China.

The CFDA released the Decision on Adjusting Items concerning the Administration of Imported Drug Registration in October 2017, which includes the following key points:

- If the International Multicenter Clinical Trial, or the IMCCT, of a drug is conducted in China, Phase I clinical trial of the drug is allowed simultaneously. The IMCCT drug does not need to be approved or to enter into either a Phase II or III clinical trial in a foreign country, except for preventive biological products;
- If the IMCCT is conducted in China, the application for drug marketing authorization can be submitted directly after the completion of the IMCCT. The Registration Measures and relevant laws and regulations shall be complied with for registration application;
- With respect to applications for clinical trial and marketing of the imported innovative chemical drugs and therapeutic biological products, the marketing authorization in the country or region where the foreign drug manufacturer is located will not be required; and
- With respect to drug applications that have been accepted before the release of this Decision, if relevant requirements are met, importation permission can be granted if such applications request exemption of clinical trials for the imported drugs based on the data generated from the IMCCT.

Approval of Human Genetic Resources

The Interim Administrative Measures on Human Genetic Resources, promulgated by the Ministry of Science and Technology and the MOH in June 1998, aimed at protecting and fairly utilizing human genetic resources in the PRC. The Ministry of Science and Technology promulgated the Service Guide for Administrative Licensing Items concerning Examination and Approval of Sampling, Collecting, Trading or Exporting Human Genetic Resources, or Taking Such Resources out of the PRC in July 2015, according to which, the sampling, collection or research activities of human genetic resources by a foreign-invested sponsor fall within the scope of international cooperation, and the cooperating Chinese organization shall apply for approval of the China Human Genetic Resources Management Office through an online system. The Ministry of Science and Technology further promulgated the Circular on Optimizing the Administrative Examination and Approval of Human Genetic Resources in October 2017 and October 2020, which became effective in December 2017 and October 2020, respectively and simplified the approval of sampling and collecting human genetic resources for listing a drug in the PRC.

The Regulations of the PRC on the Administration of Human Genetic Resources, which was promulgated by the State Council in May 2019 and came into effect in July 2019, further stipulates that, in order to obtain marketing authorization for relevant drugs and medical devices in China, no approval is required in international clinical trial cooperation using China's human genetic resources at clinical institutions without export of human genetic resource materials. However, the type, quantity and usage of the human genetic resource to be used shall be filed with the administrative department of science and technology under the State Council before clinical trials.

Regulations on Drug Manufacturing and Distribution

Drug Manufacturing

According to the Drug Administration Law and the Implementing Regulations of the Drug Administration Law, a drug manufacturing enterprise is required to obtain a drug manufacturing license from the relevant provincial drug administration authority of the PRC. The grant of such license is subject to an inspection of the manufacturing facilities, and an inspection to determine whether the sanitary condition, quality assurance systems, management structure and equipment meet the required standards. According to the Implementing Regulations of the Drug Administration Law and the Measures on the Supervision and Administration of the Manufacture of Drugs, which was promulgated in August 2004, amended in November 2017 and January 2020 and came into effect in July 2020, the drug manufacturing license is valid for five years and shall be renewed at least six months prior to its expiration date upon a re-examination by the relevant authority. In addition, the name, legal representative, registered address and type of the enterprise specified in the drug manufacturing certificate shall be identical to that set forth in the business license as approved and issued by the industrial and commercial administrative department. To the extent the MAH does not manufacture the drug internally but through a contract manufacturing organization, the MAH shall apply for drug manufacturing license with the provincial counterpart of the NMPA, subject itself to inspections and other regulatory oversight by the agency.

The Good Manufacturing Practice for Drugs was promulgated in March 1988 and was amended in December 1992 and June 1999 and January 2011. The latest amendment was in June 2020 and will come into effect in October 2020. The Good Manufacturing Practice for Drugs comprises a set of detailed standard guidelines governing the manufacture of drugs, which include institution and staff qualifications, production premises and facilities, equipment, hygiene conditions, production management, quality controls, product operation, raw material management, maintenance of sales records, management of customer complaints and adverse event reports.

Drug Distribution

According to the Drug Administration Law, its implementing regulations and the Measures for the Supervision and Administration of Circulation of Pharmaceuticals, which was promulgated by the SFDA in December 2006 and came into effect in May 2007, pharmaceutical enterprises shall be responsible for the quality of the pharmaceuticals that they manufacture, operate, use, purchase, sell, transport, or store.

According to the Measures for the Administration of Pharmaceutical Operation Certificate, which was promulgated in February 2004 and amended in November 2017 by the CFDA, a Medicine Operation Certificate is valid for five years. Each holder of the Medicine Operation Certificate must apply for an extension of its permit six months prior to expiration. The establishment of a wholesale pharmaceutical distribution company requires the approval of provincial medicine administrative authorities. Upon approval, the authority will grant a Medicine Operation Certificate in respect of the wholesale pharmaceutical product distribution company. The establishment of a retail pharmacy store requires the approval of the local medicine administrative authorities at or above the county level. Upon approval, the authority will grant a Medicine Operation Certificate in respect of the retail pharmacy store.

Other PRC Government Regulations

Regulations on Intellectual Property Rights

In terms of international conventions, China has entered into (including but not limited to) the Agreement on Trade-Related Aspects of Intellectual Property Rights, the Paris Convention for the Protection of Industrial Property, the Madrid Agreement Concerning the International Registration of Marks and the Patent Cooperation Treaty.

Patents

According to the Patent Law of the PRC, which was promulgated by the Standing Committee of the NPC in March 1984, amended in September 1992, August 2000 and December 2008, and came into effect in October 2009, and the Implementation Rules of the Patent Law of the PRC, which was promulgated by the State Council in June 2001 and amended in December 2002 and January 2010, there are three types of patents in the PRC: invention patents, utility model patents and design patents. The protection period is 20 years for an invention patent and 10 years for a utility model patent and a design patent, commencing from their respective application dates. Any individual or entity that utilizes a patent or conducts any other activities that infringe a patent without prior authorization of the patent holder shall pay compensation to the patent holder and is subject to a fine imposed by relevant administrative authorities and, if constituting a crime, shall be held criminally liable in accordance with the law. According to the Patent Law of the PRC, any organization or individual that applies for a patent in a foreign country for an invention or utility model patent established in China is required to report to the NIPA for confidentiality examination.

Trade Secrets

According to the PRC Anti-Unfair Competition Law, which was promulgated by the Standing Committee of the NPC in September 1993 and amended in November 2017 and April 2019, respectively, the term “trade secrets” refers to technical and business information that is unknown to the public, has utility, may create business interests or profits for its legal owners or holders, and is maintained as a secret by its legal owners or holders. Under the PRC Anti-Unfair Competition Law, business persons are prohibited from infringing others’ trade secrets by: (1) obtaining the trade secrets from the legal owners or holders by any unfair methods such as theft, bribery, fraud, coercion, electronic intrusion, or any other illicit means; (2) disclosing, using or permitting others to use the trade secrets obtained illegally under item (1) above; (3) disclosing, using or permitting others to use the trade secrets, in violation of any contractual agreements or any requirements of the legal owners or holders to keep such trade secrets in confidence; or (4) instigating, inducing or assisting others to violate a confidentiality obligation or to violate a rights holder’s requirements on keeping confidentiality of trade secrets, disclosing, using or permitting others to use the trade secrets of the rights holder. If a third party knows or should have known of the above-mentioned illegal conduct but nevertheless obtains, uses or discloses trade secrets of others, the third party may be deemed to have committed a misappropriation of the others’ trade secrets. The parties whose trade secrets are being misappropriated may petition for administrative corrections, and regulatory authorities may stop any illegal activities and fine infringing parties.

Trademarks

According to the Trademark Law of the PRC promulgated by the Standing Committee of the NPC in August 1982, and amended in February 1993, October 2001, August 2013 and April 2019, respectively, the period of validity for a registered trademark is ten years, commencing on the date of registration. The registrant shall go through the formalities for renewal within twelve months prior to the expiry date of the trademark if continued use is intended. Where the registrant fails to do so, a grace period of six months may be granted. The validity period for each renewal of registration is ten years, commencing on the day immediately after the expiry of the preceding period of validity for the trademark. In the absence of a renewal upon expiry, the registered trademark shall be cancelled. Industrial and commercial administrative authorities have the authority to investigate any behavior that infringes the exclusive right under a registered trademark in accordance with the law. In case of a suspected criminal offense, the case shall be timely referred to a judicial authority and decided according to the law.

Domain Names

Domain names are protected under the Administrative Measures on the Internet Domain Names, which was promulgated by the Ministry of Industry and Information Technology in August 2017, and the Implementing Rules on Registration of National Top-level Domain Names, which was promulgated by China Internet Network Information Center in and came into effect in June 2019. The Ministry of Industry and Information Technology is the main regulatory body responsible for the administration of PRC internet domain names. Domain name registrations are handled through domain name service agencies established under the relevant regulations, and the applicants become domain name holders upon successful registration.

Regulations on Product Liability

In addition to the strict new drug approval process, certain PRC laws have been promulgated to protect the rights of consumers and to strengthen the control of medical products in the PRC. Under current PRC laws, manufacturers and vendors of defective products in the PRC may incur liability for loss and injury caused by such products. According to the General Principles of the Civil Law of the PRC promulgated in April 1986 and amended in August 2009 and General Rules of the Civil Law of the People's Republic of China promulgated in March 2017 and took effect in October 2017 (collectively, the "PRC Civil Law"), the manufacturer or vendor of a defective product which causes property damage or physical injury to any person may be subject to civil liability for such damage or injury.

In February 1993, the Product Quality Law of the PRC, or the Product Quality Law, was promulgated to supplement the PRC Civil Law, aiming to protect the legitimate rights and interests of the end-users and consumers and to strengthen the supervision and control of the quality of products. The Product Quality Law was last revised in December 2018. According to the revised Product Quality Law, manufacturers who produce defective products may be subject to civil or criminal liability and have their business licenses revoked.

The Law of the PRC on the Protection of the Rights and Interests of Consumers was promulgated in October 1993 and amended in October 2013 to protect consumer rights when they purchase or use goods and services. According to which, all business operators must comply with this law when they manufacture or sell goods and/or provide services to customers. Under the latest amendment, all business operators shall protect the customers' privacy and keep any consumer information they obtain during the business operation strictly confidential. In addition, in extreme situations, pharmaceutical product manufacturers and operators may be subject to criminal liability if their goods or services lead to the death or injuries of customers or other third parties.

Regulations on Tort

According to the Tort Law of the PRC promulgated by the Standing Committee of the NPC in December 2009, if damages to other persons are caused by defective products due to the fault of third parties, such as the parties providing transportation or warehousing, the producers and the sellers of the products have the right to recover their respective losses from such third parties. If defective products are identified after they have been put into circulation, the producers or the sellers shall take remedial measures such as issuance of a warning, recall of products, etc., in a timely manner. The producers or the sellers shall be liable under tort if they fail to take remedial measures in a timely manner or have not made efforts to take remedial measures, thus causing damages. If the products are produced or sold with known defects, causing deaths or severe adverse health issues, the infringed party has the right to claim punitive damages in addition to compensatory damages.

Regulations on Environment Protection

Pursuant to the Environmental Protection Law of the PRC promulgated by the Standing Committee of the NPC, in December 1989, amended in April 2014 and effective in January 2015, any entity which discharges or will discharge pollutants during its course of operations or other activities must implement effective environmental protection safeguards and procedures to control and properly treat waste gas, waste water, waste residue, dust, malodorous gases, radioactive substances, noise vibrations, electromagnetic radiation and other hazards produced during such activities. According to the provisions of the Environmental Protection Law, in addition to other relevant laws and regulations of the PRC, the Ministry of Environmental Protection and its local counterparts take charge of administering and supervising said environmental protection matters.

Pursuant to the Environmental Protection Law, the environmental impact statement on any construction project must assess the pollution that the project is likely to produce and its impact on the environment, and stipulate preventive and curative measures; the statement shall be submitted to competent administrative department of environmental protection for approval. Installations for the prevention and control of pollution in construction projects must be designed, built and commissioned together with the principal part of the project.

Pursuant to the Law of the People's Republic of China on Environment Impact Assessment, which was promulgated in October 2002 and most recently amended in December 2018, the State implements a classification-based management on the environmental impact assessment of construction projects according to the impact of the construction projects on the environment. Construction units shall prepare an Environmental Impact Report or an Environmental Impact Statement, or fill out the Environmental Impact Registration Form.

Pursuant to the Regulations on Urban Drainage and Sewage Disposal, which was promulgated in October 2013 and came into effect in January 2014, and the Measures for the Administration of Permits for the Discharge of Urban Sewage into the Drainage Network, which was promulgated in January 2015 and came into effect in March 2015, drainage entities covered by urban drainage facilities shall discharge sewage into urban drainage facilities in accordance with the relevant provisions of the state. Where a drainage entity needs to discharge sewage into urban drainage facilities, it shall apply for a drainage license in accordance with the provisions of these Measures. The drainage entity that has not obtained the drainage license shall not discharge sewage into urban drainage facilities.

Regulations on Fire Protection

The Fire Prevention Law of the PRC, or the Fire Prevention Law, was adopted in April 1998 and last amended in April 2019. The Fire Prevention Law provides that fire control design and construction of a construction project shall comply with the State's fire control technical standards. Developers, designers, builders and project supervisors shall be responsible for the quality of the fire control design and construction of the construction project pursuant to the law. Development project fire safety design examinations and acceptance systems shall be implemented for development projects which are required to have fire safety design in accordance with the national fire protection technical standards.

According to the Eight Measures for the Public Security Fire Department to Deepen Reform and Serve Economic and Social Development promulgated by the Ministry of Public Security of the PRC in

August 2015, the fire protection design and completion acceptance fire protection record of construction projects with an investment of less than RMB300,000 or a building area of less than 300 square meters (or below the limit set by the housing and urban construction department of the provincial people's government) was no longer required.

Regulations on Foreign Exchange and Dividend Distribution

Foreign Exchange Control

According to the PRC Regulation for the Foreign Exchange promulgated by the State Council in January 1996, which was amended in January 1997 and August 2008, and the Regulation on the Administration of the Foreign Exchange Settlement, Sales and Payment promulgated by the People's Bank of China in June 1996, foreign exchanges required for distribution of profits and payment of dividends may be purchased from designated foreign exchange banks in the PRC upon presentation of a board resolution authorizing distribution of profits or payment of dividends.

According to the Circular of the State Administration of Foreign Exchange, or the SAFE, on Further Improving and Adjusting the Foreign Exchange Policies on Direct Investment and its appendix promulgated in November 2012 and amended in May 2015, October 2018 and December 2019 by the SAFE, (1) the opening of and payment into foreign exchange accounts under direct investment accounts are no longer subject to approval by the SAFE; (2) reinvestment with legal income of foreign investors in China is no longer subject to approval by SAFE; (3) the procedures for capital verification and confirmation that foreign-funded enterprises need to go through are simplified; (4) purchase and external payment of foreign exchange under direct investment accounts are no longer subject to approval by SAFE; (5) domestic transfer of foreign exchange under direct investment account is no longer subject to approval by SAFE; and (6) the administration over the conversion of foreign exchange capital of foreign-invested enterprises is improved. Later, the SAFE promulgated the Circular on Further Simplifying and Improving Foreign Exchange Administration Policies in Respect of Direct Investment in February 2015, which was further amended in December 2019 and prescribed that the bank instead of the SAFE can directly handle the foreign exchange registration and approval under foreign direct investment while the SAFE and its branches indirectly supervise the foreign exchange registration and approval under foreign direct investment through the bank.

The Provisions on the Administration of Foreign Exchange in Foreign Direct Investments by Foreign Investors, which were promulgated by the SAFE in May 2013 and amended in October 2018 and December 2019, regulate and clarify the administration over foreign exchange administration in foreign direct investments.

According to the Circular on the Reform of the Management Method for the Settlement of Foreign Exchange Capital of Foreign-invested Enterprises promulgated by the SAFE in March 2015 and amended in December 2019, and the Circular on the Reform and Standardization of the Management Policy of the Settlement of Capital Projects promulgated by the SAFE in June 2016, the settlement of foreign exchange by foreign invested enterprises shall be governed by the policy of foreign exchange settlement on a discretionary basis. However, the settlement of foreign exchange shall only be used for their own operational purposes within the business scope of the foreign invested enterprises and follow the principles of authenticity.

Dividend Distribution

The SAFE promulgated the Notice on Improving the Check of Authenticity and Compliance to Further Promote Foreign Exchange Control in January 2017, which stipulates several capital control measures with respect to outbound remittance of profits from domestic entities to offshore entities, including the following: (1) under the principle of genuine transaction, banks shall check board resolutions regarding profit distribution, the original version of tax filing records and audited financial statements; and (2) domestic entities shall hold income to account for previous years' losses before remitting the profits. Moreover, domestic entities shall make detailed explanations of sources of capital and utilization arrangements, and provide board resolutions, contracts and other proof when completing the registration procedures in connection with an outbound investment.

Foreign Exchange Registration of Offshore Investment by PRC Residents

The SAFE promulgated the SAFE Circular 37 in July 2014. The SAFE Circular 37 requires PRC residents (including PRC institutions and individuals) to register with local branches of SAFE in connection with their direct or indirect offshore investment in an overseas special purpose vehicle, or the SPV, directly established or indirectly controlled by PRC residents for offshore investment and financing with their legally owned assets or interests in domestic enterprises, or their legally owned offshore assets or interests. Such PRC residents are also required to amend their registrations with the SAFE when there is a change to the basic information of the SPV, such as changes of a PRC resident individual shareholder, the name or operating period of the SPV, or when there is a significant change to the SPV, such as changes of the PRC individual resident's increase or decrease of its capital contribution in the SPV, or any share transfer or exchange, merger, division of the SPV.

The Circular on Further Simplifying and Improving Foreign Exchange Administration Policies in Respect of Direct Investment, which was promulgated in February 2015 and effective in June 2015 and further amended in December 2019, provides that PRC residents may register with qualified banks instead of the SAFE in connection with their establishment or control of an offshore entity established for the purpose of overseas direct investment. The SAFE and its branches shall implement indirect supervision over foreign exchange registration of direct investment via the banks.

Failure to comply with the registration procedures set forth in the SAFE Circular 37 may result in restrictions on the foreign exchange activities of the relevant onshore company, including the payment of dividends and other distributions to its offshore parent or affiliate, the capital inflow from the offshore entities and settlement of foreign exchange capital, and may also subject relevant onshore company or PRC residents to penalties under PRC foreign exchange administration regulations.

Regulations on Labor

Labor Law and Labor Contract Law

According to the PRC Labor Law, which was promulgated by the Standing Committee of the NPC in July 1994 and amended in August 2009 and December 2018, respectively, the PRC Labor Contract Law, which was promulgated by the Standing Committee of the NPC in June 2007 and amended in December 2012 and came into effect July 2013, and the Implementing Regulations of the Employment Contracts Law of the PRC, which was promulgated by the State Council in September 2008, labor contracts in written form shall be executed to establish labor relationships between employers and employees. In addition, wages cannot be lower than the local minimum wage. The employers must establish a system for labor safety and sanitation, strictly abide by State rules and standards, provide education regarding labor safety and sanitation to its employees, provide employees with labor safety and sanitation conditions and necessary protection materials in compliance with State rules, and carry out regular health examinations for employees engaged in work involving occupational hazards.

Social Insurance and Housing Provident Funds

According to the Social Insurance Law of PRC, which was promulgated by the Standing Committee of the NPC in October 2010 and came into effect in July 2011, and further amended in December 2018, and the Interim Regulations on the Collection and Payment of Social Security Funds, which was promulgated by the State Council in January 1999 and amended in March 2019, and the Regulations on the Administration of Housing Provident Funds, which was promulgated by the State

Council in April 1999 and amended in March 2002 and March 2019, employers are required to contribute, on behalf of their employees, to a number of social security funds, including funds for basic pension insurance, unemployment insurance, basic medical insurance, occupational injury insurance, maternity insurance and to housing provident funds. Any employer who fails to contribute may be fined and ordered to make good the deficit within a stipulated time limit.

Regulations on Taxation

Enterprise Income Tax

According to the Enterprise Income Tax Law promulgated by the NPC in March 2007 and amended in February 2017 and December 2018, and the Implementation Rules of the Enterprise Income Tax Law of the PRC promulgated by the State Council in December 2007 and amended in April 2019, other than a few exceptions, the income tax rate for both domestic enterprises and foreign-invested enterprises is 25%. Enterprises are classified as either “resident enterprises” or “non-resident enterprises”. Besides enterprises established within the PRC, enterprises established outside China whose “de facto management bodies” are located in China are considered “resident enterprises” and subject to the uniform 25% enterprise income tax rate for their global income. A non-resident enterprise refers to an entity established under foreign law whose “de facto management bodies” are not within the PRC but which have an establishment or place of business in the PRC, or which do not have an establishment or place of business in the PRC but have income sourced within the PRC. An income tax rate of 10% will normally be applicable to dividends declared to non-PRC resident enterprise investors that do not have an establishment or place of business in the PRC, or that have such establishment or place of business but the relevant income is not effectively connected with the establishment or place of business, to the extent such dividends are derived from sources within the PRC.

According to the Notice on Promoting the Implementation of Corporate Income Tax Policies for Advanced Technology Service Enterprises Nationwide, or the Notice, since January 2017, an enterprise which is recognized as an “Advanced Technology Service Enterprises” under the Notice enjoys a reduced enterprise income tax rate of 15%.

According to the Arrangement Between the Mainland of China and the Hong Kong Special Administrative Region for the Avoidance of Double Taxation and Prevention of Fiscal Evasion with Respect to Taxes on Income, or the Double Tax Avoidance Arrangement, which was promulgated and came into effect in August 2006, and other applicable PRC laws, if a Hong Kong resident enterprise is determined by the competent PRC tax authority to have satisfied the relevant conditions and requirements under such Double Tax Avoidance Arrangement and other applicable laws, the 10% withholding tax on the dividends the Hong Kong resident enterprise receives from a PRC resident enterprise may be reduced to 5%. However, based on the Circular on Certain Issues with Respect to the Enforcement of Dividend Provisions in Tax Treaties which was promulgated by the State Administration of Taxation, the STA, in February 2009, if the relevant PRC tax authorities determine, in their discretion, that a company benefits from such reduced income tax rate due to a structure or arrangement that is primarily tax-driven, such PRC tax authorities may adjust the preferential tax treatment. Based on the Announcement on Certain Issues with Respect to the “Beneficial Owner” in Tax Treaties, which was promulgated by the STA in February 2018 and came into effect in April 2018, if an applicant’s business activities do not constitute substantive business activities, it could result in the negative determination of the applicant’s status as a “beneficial owner”, and consequently, the applicant could be precluded from enjoying the above-mentioned reduced income tax rate of 5% under the Double Tax Avoidance Arrangement.

Value Added Tax

According to the Provisional Regulations of the PRC on Value-Added Tax, effective in January 1994 and further amended in November 2008, February 2016, and November 2017, and its implementation rules effected in January 1994 and amended in December 2008 and October 2011, except stipulated otherwise, taxpayers who sell goods, labor services or tangible personal property leasing services or import goods shall be subject to a 17% tax rate; taxpayers who sell transport services, postal services, basic telecommunications services, construction services, or real property leasing services, sell real property, transfer the land use right shall be subject to an 11% tax rate, and taxpayers who sell services or intangible assets shall be subject to a 6% tax rate.

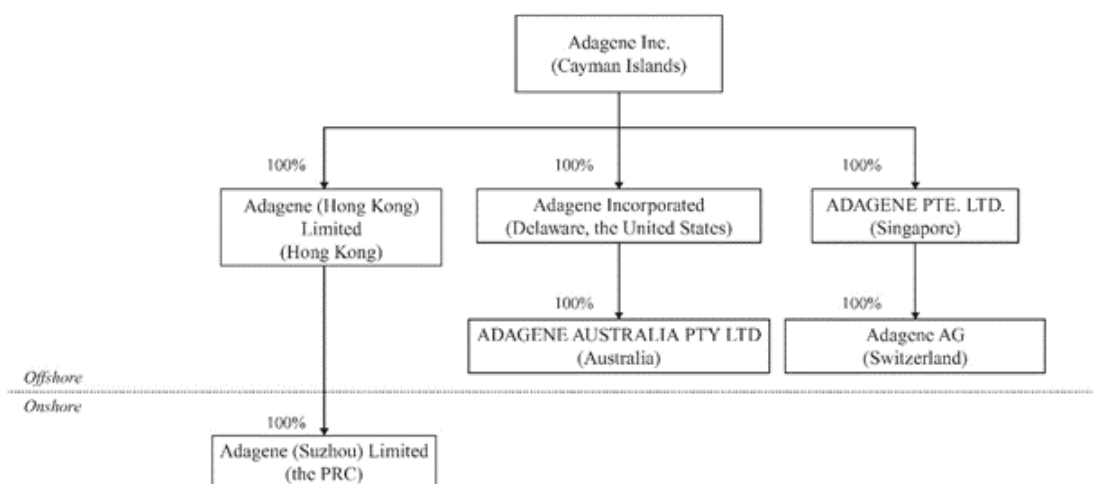
According to the Circular of the Ministry of Finance and the State Administration of Taxation on Adjusting Value-added Tax Rates adopted in April 2018, as of May 2018, where a taxpayer engages in a taxable sales activity for the value-added tax purpose or imports goods, the previous applicable 17% and 11% rates are adjusted to 16% and 10%.

According to the Announcement on Relevant Policies for Deepening Value-Added Tax Reform, effective in April 2019, the 16% VAT tax rate, which applies to the sales or imported goods of a VAT general taxpayer, will be lowered to 13%; and the 10% VAT tax rate will be lowered to 9%.

According to the Measures for the Exemption of Value-Added Tax from Cross-Border Taxable Activities in the Collection of Value-Added Tax in Lieu of Business Tax (for Trial Implementation) revised in June 2018, if domestic enterprises provide cross-border taxable activities such as professional technical services, technology transfer, software services, the above-mentioned cross-border taxable activities are exempt from VAT.

4.C. Organizational Structure

The following diagram illustrates our corporate structure as of the date of this annual report, including our material subsidiaries:



4.D. Property, Plants and Equipment

Our headquarter is based in Suzhou, China, where we have our main administrative and laboratory offices, which are approximately 2,946 square meters in size. The expiration dates of the lease agreements for this facility range from September 15, 2021 to October 7, 2023. We also have a 2,673 square feet facility in San Diego, California for laboratory, research and development functions, the lease for which expires on August 31, 2023. We believe our current facilities are sufficient to meet our near-term needs and we do not expect difficulties in renewing lease agreements for our facilities.

ITEM 4A. UNRESOLVED STAFF COMMENTS

None.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with the section entitled “Selected Consolidated Financial Data” and our consolidated financial statements and the related notes included elsewhere in this annual report. This discussion contains forward-looking statements that involve risks and uncertainties. Our actual results and the timing of events could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those we describe under “Item 3.D. Risk Factors” and elsewhere in this annual report.

5.A. Operating Results

We are a platform-driven, clinical-stage biopharmaceutical company committed to transforming the discovery and development of novel antibody-based cancer immunotherapies. Our platform is designed to generate therapeutic antibody candidates with unique functional epitopes and species cross-reactivity. These features enable our novel drug discovery strategy to advance from lead identification through vigorous preclinical modeling to biomarker-guided mono- and combination immunotherapy development in clinical settings. We have pioneered a dynamic interface design to harness the conformational diversity of antibodies, which enlarges epitope sampling of a given drug target for differentiated therapeutic antibody development. Our platform is designed to enable the rapid development of precision immunotherapy candidates, through the identification of predictive biomarkers for patient stratification and preselection. We aim to push the boundaries of antibody discovery and engineering through the precise design, construction, and selection of antibody product candidates intractable to traditional antibody technology.

We have developed our proprietary Dynamic Precision Library, or DPL, platform to explore the dynamic conformational diversity of protein sequences, and the flexible binding sites of antibody sequences in particular, as a new paradigm for antibody drug discovery. Our DPL platform samples a potentially infinite number of dynamic binding interface structures arising from the conformational diversity of a finite number of antibody amino acid sequences, allowing us to exponentially expand the universe of candidate antibody binding sites far beyond conventional natural or synthetic antibody repertoires. By exploiting conformational diversity through the combination of our proprietary computational algorithms and artificial intelligence, we have designed and precisely constructed approximately one trillion (10^{12}) antibody sequences in our DPL. These antibodies feature broad epitope (the portion of an antigen that are recognized by an antibody) coverage and robust chemistry, manufacturing, and control, or CMC, attributes. Our DPL platform is designed to enable high fidelity translation from preclinical to clinical studies by identifying antibodies well suited for broad species cross-reactivity against the transiently accessible epitopes of challenging targets.

By leveraging our proprietary DPL platform, we have developed a robust pipeline of innovative product candidates in various stages of development, ranging from research and discovery to preclinical and clinical development. Our highly differentiated clinical-stage pipeline consists of ADG106, ADG126 and ADG116. We also have a robust preclinical pipeline in various stages of development.

Since our inception in 2011, our operations have focused on organizing and staffing our company, conducting preclinical studies and clinical trials, business planning, establishing our intellectual property portfolio and raising capital. We do not have any product candidates approved for sale and have not generated any revenue from product sales. We have financed operations mainly through the private placements of our preferred shares.

Since inception, we have incurred significant operating losses. Our net losses were US\$15.3 million, US\$16.4 million and US\$42.4 for the years ended December 31, 2018, 2019 and 2020, respectively. As of December 31, 2020, we had accumulated deficit of US\$105.7 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- continue advancement of and investment in our proprietary DPL platform;
- advance the development of ADG106, ADG126, ADG116 and other preclinical drug candidates;
- continue our ongoing and planned research and development of other lead product candidates;
- discover and develop additional antibody product candidates and further expand our preclinical and clinical product pipeline;
- maintain, expand and protect our intellectual property portfolio;
- expand our collaborations with contract manufacturing organizations and contract research organizations;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- establish sales and marketing teams and distribution network to commercialize any product candidate for which we may obtain regulatory approval;
- attract, hire and retain additional clinical, scientific, management and administrative personnel;
- expand our operations globally; and
- incur additional costs associated with operating as a public company.

Beginning in January 2020, the emergence and wide spread of COVID-19 has resulted in quarantines, travel restrictions, and the temporary closure of stores and facilities in the United States and China and elsewhere. Substantially all of our operating and workforce are based in the United States and China. Consequently, the COVID-19 outbreak could potentially delay a patient's access to hospital and the progress of our clinical trials, including patient enrollment, which may adversely affect our business operations, financial condition and operating results for 2021. The extent of the impact of the COVID-19 pandemic on our business, operations and regulatory and commercialization timelines will depend on certain developments, including the duration and spread of the outbreak and its impact on clinical trials, regulatory authorities and our key scientific and management personnel as well as its impact on our partners, laboratory sites, and other third parties with whom we collaborate, and the extent of future resurgences of the disease and its variants, vaccine distribution and other actions in response to the virus or to contain its impact, and we are closely monitoring its impact on us. See "Item 3 Key Information—Risk Factors—Risks relating to obtaining regulatory approval of our drug candidates—The COVID-19 pandemic could adversely impact our business, including our clinical trials." We will continue to actively monitor the rapidly evolving situation related to COVID-19 and may take further actions that alter our business operations, including those that may be required by government authorities, or that we determine are in the best interests of our employees, partners and shareholders. At this point, the extent to which the COVID-19 pandemic may impact our business, operations and regulatory and commercialization timelines remains uncertain.

Key Components of Results of Operations

Revenue

Licensing revenue. Our licensing revenue is currently comprised of royalties, milestone payments, license fees and reimbursement income. Our licensing and collaboration revenue for the years ended December 31, 2018, 2019 and 2020 was primarily derived from granting licenses to use and otherwise exploit certain of our intellectual properties. To date, we have not generated any revenue from the sale of products and do not expect to generate any revenue from product sales in the near future.

Expenses

Research and Development Expenses. Our research and development expenses consist principally of (1) payroll and other related costs of personnel engaged in research and development activities, (2) costs related to pre-clinical testing of our technologies under development and clinical trials such as payments to contract research organizations, or CRO, and contract manufacturing organization, or CMO, investigators and clinical trial sites that conduct the clinical studies; (3) costs to develop the product candidates, including raw materials and supplies, product testing, depreciation and amortization, and facility related expenses, (4) other research and development expenses.

For the years ended December 31, 2018, 2019 and 2020, our research and development expenses were US\$16.1 million, US\$16.2 million and US\$33.5 million, respectively. The increase is primarily due to (1) an increase in payroll and other related costs of personnel due to headcount growth in research and development and increased share-based compensation expenses and (2) an increase in costs related to preclinical testing and clinical trials due to progression of the programs and increased contract manufacturing costs.

Our research and development expenses may vary substantially from period to period according to the status of our research and development activities. The timing of expenses is impacted by the commencement of clinical trials and enrollment of patients in clinical trials. Research and development expenses are expected to increase as we advance the clinical development of ADG106, ADG126 and ADG116, and further advance the research and development of our other product candidates. The successful development of our product candidates is uncertain.

The following table summarizes our research and development expenses for our clinical-stage product candidates, preclinical product candidates and research pipeline for the years ended December 31, 2018 and 2019 and the nine months ended September 30, 2019 and 2020, respectively.

	For the Year Ended December 31,		
	2018	2019	2020
	US\$	US\$	US\$
	(in thousands)		
ADG106	5,145	5,742	12,504
ADG126	1,210	2,326	12,091
ADG116	6,812	5,329	3,156
Preclinical product candidates, research pipeline and others	2,914	2,814	5,787
Total	16,081	16,212	33,538

At this time, we cannot reasonably estimate the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, or the period, if any, in which material net cash inflows may commence from, any of our product candidates. This is due to numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress, results and cost of our clinical trials, preclinical studies and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of any product candidates;
- the number and characteristics of product candidates that we pursue;
- the cost, timing and outcomes of regulatory approvals;
- the cost and timing of establishing sales, marketing and distribution capabilities; and

- the terms and timing of any collaboration, licensing or other arrangements that we may establish, including any required milestone and royalty payments thereunder.

A change in the outcome of any of these variables with respect to the development of our product candidates or any other current or future product candidates could mean a significant change in the costs and timing associated with the development of such product candidate. For example, if we are required to conduct additional clinical trials or other testing of any of our product candidates beyond those that are contemplated or if we experience significant delays in enrollment in any clinical trials, we could incur significant additional costs and the clinical development timeline for our product candidates may be delayed.

Administrative expenses. Our administrative expenses consist primarily of wages, salaries and benefits for personnel other than research and development staff. We expect our administrative expenses to increase in absolute amount in the foreseeable future as we incur additional costs as a result of operating as a public company and as we increase the number of employees and advance our product candidates through clinical development, which will also increase our general and administrative expenses.

Interest income

Interest income consists primarily of interest income derived from our term deposit.

Other income

Other income primarily includes government subsidies that Adagene Suzhou received from local government in the PRC. The receipt of such government subsidies is not dependent on our performance of any obligations.

Taxation

Cayman Islands

We were incorporated in the Cayman Islands. Under the current laws of the Cayman Islands, we are not subject to income, corporation or capital gains tax in the Cayman Islands. In addition, our payment of dividends, if any, is not subject to withholding tax in the Cayman Islands.

Hong Kong

Our subsidiaries in Hong Kong, including Adagene (Hong Kong) Limited, our wholly-owned subsidiary, are subject to Hong Kong profits tax on their activities conducted in Hong Kong at a uniform tax rate of 16.5%. Under Hong Kong tax law, our subsidiary in Hong Kong is exempted from income tax on their foreign-derived income and there is no withholding tax in Hong Kong on remittance of dividends. No provision for Hong Kong profits tax was made as we had no estimated assessable profit that was subject to Hong Kong profits tax during fiscal years 2019 or 2020.

PRC

Our subsidiaries in China are companies incorporated under PRC law and, as such, are subject to PRC enterprise income tax on their taxable income in accordance with the relevant PRC income tax laws. Pursuant to the PRC Enterprise Income Tax Law, or EIT Law, which became effective on January 1, 2008, a uniform 25% enterprise income tax rate is generally applicable to both foreign-invested enterprises and domestic enterprises, except where a special preferential rate applies. In accordance with the implementation rules of EIT Law, a qualified Technology Advanced Service Enterprises, or TASE, is eligible for a preferential tax rate of 15%. The TASE certificate is effective for three years. An entity must file required supporting documents with the tax authority and ensure fulfillment of the relevant TASE criteria before using the preferential rate. An entity could apply for the TASE certificate every year. Adagene Suzhou was first recognized as a qualified TASE in March 2015 and renewed in December 2018. Adagene Suzhou can enjoy the preferential tax rate of 15% from 2015 to 2021. In addition, the research and development expenses of Adagene Suzhou are subject to a 75% super-deduction for the income tax. The enterprise income tax is calculated based on the entity's global income as determined under PRC tax laws and accounting standards.

We are subject to VAT at a rate of 3%, 6%, or 13% on the services we provide and related surcharges. We are also subject to surcharges on VAT payments in accordance with PRC law.

As a Cayman Islands holding company, we may receive dividends from Adagene Suzhou. The PRC EIT Law and its implementing rules provide that dividends paid by a PRC entity to a nonresident enterprise for income tax purposes is subject to PRC withholding tax at a rate of 10%, subject to reduction by an applicable tax treaty with China. Pursuant to the Arrangement between Mainland China and the Hong Kong Special Administrative Region for the Avoidance of Double Taxation and Tax Evasion on Income, the withholding tax rate in respect to the payment of dividends by a PRC enterprise to a Hong Kong enterprise may be reduced to 5% from a standard rate of 10% if the Hong Kong enterprise directly holds at least 25% of the PRC enterprise. Pursuant to the Notice of the State Administration of Taxation on the Issues concerning the Application of the Dividend Clauses of Tax Agreements, or SAT Circular 81, a Hong Kong resident enterprise must meet the following conditions, among others, in order to apply the reduced withholding tax rate: (i) it must be a company; (ii) it must directly own the required percentage of equity interests and voting rights in the PRC resident enterprise; and (iii) it must have directly owned such required percentage in the PRC resident enterprise throughout the 12 months prior to receiving the dividends. In August 2015, the State Administration of Taxation promulgated the Administrative Measures for Nonresident Taxpayers to Enjoy Treatment under Tax Treaties, or SAT Circular 35, which became effective on January 1, 2020, 2015. SAT Circular 35 provides that nonresident enterprises are not required to obtain pre-approval from the relevant tax authority in order to enjoy the reduced withholding tax. Instead, nonresident enterprises and their withholding agents may, by self-assessment and on confirmation that the prescribed criteria to enjoy the tax treaty benefits are met, directly apply the reduced withholding tax rate, and file necessary forms and supporting documents when performing tax filings, which will be subject to post-tax filing examinations by the relevant tax authorities. Accordingly, Adagene (Hong Kong) Limited may be able to benefit from the 5% withholding tax rate for the dividends it receives from its PRC subsidiaries, if it satisfies the conditions prescribed under SAT Circular 81 and other relevant tax rules and regulations. However, according to SAT Circular 81 and SAT Circular 35, if the relevant tax authorities consider the transactions or arrangements we have are for the primary purpose of enjoying a favorable tax treatment, the relevant tax authorities may adjust the favorable withholding tax in the future.

If our holding company in the Cayman Islands or any of our subsidiaries outside of China were deemed to be a “resident enterprise” under the PRC EIT Law, it would be subject to enterprise income tax on its worldwide income at a rate of 25%. See “Item 3 Key Information— Risk Factors—Risks Related to Doing Business in China—If we are classified as a PRC resident enterprise for PRC income tax purposes, such classification could result in unfavorable tax consequences to us and our non-PRC shareholders or ADS holders.”

Critical Accounting Policies, Judgments and Estimates

Basis of presentation

Our consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP.

Principles of Consolidation

Our consolidated financial statements include the financial statements of Adagene Inc. and its subsidiaries. All significant intercompany balances and transactions have been eliminated upon consolidation.

Use of estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosures of contingent assets and liabilities at the balance sheet dates and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in our consolidated financial statements include, but are not limited to, the useful lives and impairment of long-lived assets, tax valuation allowance, share-based compensation expenses and the fair value of warrant liabilities. Management bases the estimates on historical experience and various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results could materially differ from those estimates.

Foreign currency translation

The functional currency of Adagene Inc., Adagene (Hong Kong) Limited and Adagene Incorporated is the U.S. dollar, or US\$. The functional currency of our PRC subsidiary is Renminbi, or RMB. The functional currency of our Australia subsidiary is Australian dollar, or AU\$. The determination of the respective functional currency is based on the criteria stated in Accounting Standard Codification, or ASC, 830, Foreign Currency Matters. We use US\$ as our reporting currency. The financial statements of our PRC subsidiary and Australia subsidiaries are translated from the functional currency to the reporting currency.

Transactions denominated in foreign currencies are re-measured into the functional currency at the exchange rates quoted by the People's Bank of China, or the PBOC, prevailing on the transaction dates. Monetary assets and liabilities denominated in foreign currencies are re-measured at the exchange rates prevailing at the balance sheet date. Non-monetary items that are measured in terms of historical costs in foreign currency are re-measured using the exchange rates at the dates of the initial transactions. Exchange gains and losses are included in the consolidated statements of comprehensive loss.

Assets and liabilities are translated at the exchange rates at the balance sheet date, equity accounts are translated at historical exchange rates and revenues, expenses, gains and losses are translated using the average rate for the year. Translation adjustments are reported as accumulated comprehensive loss and are shown as a separate component of other comprehensive loss in the consolidated statements of comprehensive loss.

Revenue recognition

At contract inception of collaboration and out-licensing arrangement, we analyze the arrangements to assess whether they are within the scope of ASC 808, *Collaborative Arrangements* or ASC 808, to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, we first determine which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are reflective of a vendor-customer relationship and therefore within the scope of ASC 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently.

Under the criteria of *Accounting Standard Codification*, or ASC, 606, *Revenue from Contracts with Customers* (Topic 606), or ASC 606, we recognize revenue to depict the transfer of control of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to receive in exchange for those goods or services. We adopted ASC 606 for all periods presented. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step model to contracts when it is probable that the entity will collect substantially all the consideration to which it is entitled in exchange for the goods or services it transfers to the customer. We review the contract to determine which performance are distinct and represent a promise to provide distinct goods or services or a series of distinct goods or services as defined by the standard. We recognize as revenue the amount of the transaction price that is allocated to each performance obligation as and when that performance obligation is satisfied.

Licenses of Intellectual Property: Upfront non-refundable payments for licensing our intellectual property are evaluated to determine if the license is distinct from the other performance obligations identified in the arrangement. For licenses determined to be distinct, we recognize revenues from non-refundable, up-front fees allocated to the license at a point in time, when the transfer of control of the license to the licensee occurs and the licensee is able to use and benefit from the license.

Milestone Payments: At the inception of each arrangement that includes development, commercialization, and regulatory milestone payments, we evaluate whether the milestones are considered probable of being reached and to the extent that a significant reversal of cumulative revenue would not occur in future periods, estimates the amount to be included in the transaction price using the most likely amount method. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achieving such development milestones and any related constraint, and if necessary, adjust the estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

To date, no milestone payments or royalty payments were received. Substantially all of our revenue has been derived from its out-licensing agreements with respect to licensed products such as DNA sequences, cell lines, etc., and such revenues are recognized when the customer obtains control of the licensed product, which occurs at a point in time, upon delivery to the customer.

Contract assets and contract liabilities: When a customer pays consideration before we transfer products or services, we record our obligation as a contract liability; when we satisfy our performance obligations by providing products or services to a customer before the customer pays consideration and before payment is due, we recognize our rights to consideration as a contract asset.

Fair value measurements

We apply ASC 820, *Fair Value Measurements and Disclosures*. ASC 820 defines fair value, establishes a framework for measuring fair value and expands disclosures about fair value measurements. ASC 820 requires disclosures to be provided for fair value measurements. ASC 820 establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1—Observable inputs that reflect quoted prices (unadjusted) for identical assets or liabilities in active markets.

Level 2—Includes other inputs that are directly or indirectly observable in the marketplace.

Level 3—Unobservable inputs which are supported by little or no market activity.

ASC 820 describes three main approaches to measuring the fair value of assets and liabilities: (1) market approach; (2) income approach; and (3) cost approach. The market approach uses prices and other relevant information generated from market transactions involving identical or comparable assets or liabilities. The income approach uses valuation techniques to convert future amounts to a single present value amount. The measurement is based on the value indicated by current market expectations about those future amounts. The cost approach is based on the amount that would currently be required to replace an asset.

The carrying amounts of cash and cash equivalent, short-term investments, accounts receivable, amounts due to related parties and other current assets, accounts payable, amounts due to related parties, accrued liabilities and other current liabilities and short-term borrowings approximate their fair values because of their generally short maturities. The carrying amount of long-term borrowings approximate their fair values since they bear interest rates which approximate market interest rates.

We measured our warrant liabilities at fair value on a recurring basis. As our warrants are not traded in an active market with readily observable prices, we use significant unobservable inputs to measure the fair value of warrant liabilities. These instruments are categorized in the Level 3 valuation hierarchy based on the significance of unobservable factors in the overall fair value measurement.

The following table presents a reconciliation of all financial instruments measured at fair value on a recurring basis using Level 3 unobservable inputs:

	Warrant liabilities
	US\$
Initial recognition during the year ended December 31, 2018	1,741,720
Fair value change	(534,305)
Balance as of December 31, 2018	1,207,415
Fair value change	(1,207,415)
Balance as of December 31, 2019	—

We did not transfer any assets or liabilities in or out of Level 3 during the year ended December 31, 2018, 2019 and 2020.

We had no financial assets and liabilities measured and recorded at fair value on a nonrecurring basis as of December 31, 2018, 2019 and 2020.

Research and development expenses

Elements of research and development expenses primarily include (1) payroll and other related costs of personnel engaged in research and development activities, (2) costs related to pre-clinical testing of our technologies under development and clinical trials such as payments to contract research organizations, or CRO, and contract manufacturing organizations, or CMO, investigators and clinical trial sites that conduct the clinical studies; (3) costs to develop the product candidates, including raw materials and supplies, product testing, depreciation and amortization, and facility related expenses, (4) other research and development expenses. Research and development expenses are charged to expense as incurred when these expenditures relate to our research and development services and have no alternative future uses. As of December 31, 2020, we have several ongoing clinical studies in various clinical trial stages. The contracts with CRO and CMO are generally cancellable, with notice, at our option. We did not record any accrued expenses related to cancellation of CRO or CMO contracts as of December 31, 2020 as we did not have any plan to cancel the existing CRO or CMO contracts.

Income taxes

We follow the liability method of accounting for income taxes in accordance with ASC 740, *Income Taxes*, or ASC 740. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and tax bases of assets and liabilities using enacted tax rates that will be in effect in the period in which the differences are expected to reverse. We record a valuation allowance to offset deferred tax assets if based on the weight of available evidence, it is more likely than not that some portion, or all, of the deferred tax assets will not be realized. The effect on deferred taxes of a change in tax rate is recognized in tax expense in the period that includes the enactment date of the change in tax rate.

We evaluate our uncertain tax positions using the provisions of ASC 740, which prescribes a recognition threshold that a tax position is required to meet before being recognized in the consolidated financial statements.

We recognize in the consolidated financial statements the benefit of a tax position which is “more likely than not” to be sustained under examination based solely on the technical merits of the position assuming a review by tax authorities having all relevant information. Tax positions that meet the recognition threshold are measured using a cumulative probability approach, at the largest amount of tax benefit that has a greater than fifty percent likelihood of being realized upon settlement. It is our policy to recognize interest and penalties related to unrecognized tax benefits, if any, as a component of income tax expense.

We have incurred net accumulated operating losses for income tax purposes since our inception. We believe that it is more likely than not that these net accumulated operating losses will not be utilized in the future. Therefore, we have provided full valuation allowances for the deferred tax assets as of December 31, 2018, 2019 and 2020. There was no income tax expense for the years ended December 31, 2018, 2019 and 2020, as our subsidiaries did not have any taxable profits.

Share-based compensation

We grant restricted shares and stock options to eligible employees and nonemployees and accounts for share-based compensation in accordance with ASC 718, Compensation—Stock Compensation.

Share-based compensation awards are measured at the grant date fair value of the awards and recognized as expenses a) immediately at the grant date if no vesting conditions are required; or b) for share-based awards granted with only service conditions, using the straight-line method over the vesting period; or c) for share-based awards granted with service conditions and performance conditions, using the graded vesting method over the vesting period if and when the company concludes that it is probable that the performance conditions will be achieved.

A change in any of the terms or conditions of share-based awards is accounted for as a modification of the awards. We calculate incremental compensation expense of a modification as the excess of the fair value of the modified awards over the fair value of the original awards immediately before its terms are modified at the modification date. For vested awards, we recognize incremental compensation cost in the period when the modification occurs. For awards not being fully vested, we recognize the sum of the incremental compensation expense and the remaining unrecognized compensation expense for the original awards over the remaining requisite service period after modification.

The fair value of share options was determined using the binomial option valuation model, with the assistance from an independent third-party appraiser. The binomial model requires the input of highly subjective assumptions, including the expected volatility, the exercise multiple, the risk-free rate and the dividend yield. For expected volatility, we have made reference to historical volatility of several comparable companies in the same industry. The exercise multiple was estimated as the average ratio of the stock price to the exercise price of when employees would decide to voluntarily exercise their vested share options. The risk-free rate for periods within the contractual life of the share options is based on the market yield of U.S. Treasury Bonds in effect at the time of grant. The dividend yield is based on the expected dividend policy over the contractual life of the share options. The estimated fair value of the ordinary shares, at the share option grant dates, was determined with the assistance from an independent third-party appraiser. Our management is ultimately responsible for the determination of the estimated fair value of its ordinary shares.

The assumptions used to estimate the fair value of the share options granted are as follows:

	<u>For the year ended December 31,</u>	
	<u>2019</u>	<u>2020</u>
Risk-free interest rate	1.78%-2.73%	0.68% - 0.83%
Dividend yield	0%	0%
Expected volatility range	67.5%-71.0%	72.3%- 73.4%
Exercise multiple	2.2-2.8	2.2 - 2.8
Contractual life	10 years	10 years

Borrowings

Borrowings are recognized initially at fair value, net of transaction costs incurred. Borrowings are subsequently stated at amortized cost; any difference between the proceeds (net of transaction costs) and the redemption value is recognized in the consolidated statements of comprehensive loss over the period of the borrowings using the effective interest method.

Recent accounting pronouncements

A list of recent relevant accounting pronouncements is included in Note 2 “Summary of Significant Accounting Policies” to our consolidated financial statements included elsewhere in this annual report.

Results of Operations

The following table summarizes our consolidated results of operations for the periods presented. This information should be read together with our consolidated financial statements and related notes included elsewhere in this annual report. The operating results in any period are not necessarily indicative of the results that may be expected for any future period.

	For the Year Ended December 31,		
	2018	2019	2020
	US\$	US\$	US\$
	(in thousands)		
Revenue:			
Licensing revenue	1,511	480	701
Expenses:			
Research and development expenses	(16,081)	(16,212)	(33,538)
Administrative expenses	(2,765)	(3,438)	(10,315)
Total operating expenses	(18,846)	(19,650)	(43,853)
Loss from operations	(17,335)	(19,170)	(43,152)
Interest income	711	923	629
Interest expense	(91)	(138)	(202)
Other income	902	723	972
Foreign exchange gain (loss), net	13	22	(645)
Change in fair value of warrant liabilities	534	1,207	—
Loss before income tax	(15,266)	(16,432)	(42,397)
Income tax expense	—	—	—
Net loss attributable to Adagene Inc.'s shareholders	(15,266)	(16,432)	(42,397)
Other comprehensive income (loss):			
Foreign currency translation adjustments, net of nil tax	(11)	66	(6)
Total comprehensive loss attributable to Adagene Inc.'s shareholders	(15,277)	(16,367)	(42,403)
Net loss attributable to Adagene Inc.'s shareholders	(15,266)	(16,432)	(42,397)
Deemed contribution from convertible redeemable preferred shareholders	1,186	—	—
Accretion of convertible redeemable preferred shares to redemption value	(223)	(246)	(248)
Net loss attributable to ordinary shareholders	(14,303)	(16,678)	(42,645)
Weighted average number of ordinary shares used in per share calculation:			
—Basic	15,159	15,178	15,951
—Diluted	15,159	15,178	15,951
Net loss per ordinary share			
—Basic	(0.94)	(1.10)	(2.67)
—Diluted	(0.94)	(1.10)	(2.67)

Year Ended December 31, 2020 Compared to Year Ended December 31, 2019

Licensing revenue

Our licensing revenue increased by 46.0% from US\$0.5 million for the year ended December 31, 2019 to US\$0.7 million for the year ended December 31, 2020. For the year ended December 31, 2019, we recognized revenue of US\$0.5 million from Signal Pharmaceuticals LLC, a subsidiary of Celgene Corporation (now Bristol Myers Squibb). For the year ended December 31, 2020, we recognized revenue of US\$0.3 million, US\$0.23 million and US\$0.15 million from Signal Pharmaceuticals LLC, ADC Therapeutics SA and Tanabe Research Laboratories, Inc. respectively.

Research and development expenses

The following table sets forth a breakdown of the major components of our research and development expenses in absolute amounts and as a percentage of our total research and development expenses for the periods indicated:

	For the Year Ended			
	December 31		December 31	
	2019		2020	
	US\$	%	US\$	%
(in thousands, except percentages)				
Research and development expenses				
Payroll and other related costs of personnel	4,880	30.1%	14,003	41.8%
Costs related to clinical trials	3,361	20.7%	4,702	14.0%
Costs related to preclinical testing	4,726	29.2%	9,982	29.8%
Costs to develop the product candidates	1,599	9.9%	2,114	6.3%
Other research and development expenses	1,645	10.1%	2,736	8.2%
Total	16,212	100%	33,538	100%

Our research and development expenses increased by 106.9% from US\$16.2 million for the year ended December 31, 2019 to US\$33.5 million for the year ended December 31, 2020, primarily attributable to (i) an increase of US\$9.1 million in payroll and other related costs of personnel due to headcount growth in research and development and increased share-based compensation expenses and (ii) an increase of US\$5.3 million in costs related to preclinical testing and clinical trials due to progression of the programs and increased contract manufacturing costs.

Administrative expenses

Our administrative expenses increased by 200.0% from US\$3.4 million for the year ended December 31, 2019 to US\$10.3 million for the year ended December 31, 2020, primarily attributable to (i) an increase of US\$1.5 million in employee compensations due to a rise in average payroll and an increase in the number of employees and (ii) an increase of US\$3.5 million in share-based compensation expenses.

Loss from operations

As a result of the foregoing, our loss from operations increased by 125.1% from approximately US\$19.2 million in the year ended December 31, 2019 to approximately US\$43.2 million in 2020.

Interest income

Our interest income was US\$0.6 million for the year ended December 31, 2020, as compared to US\$0.9 million for the year ended December 31, 2019, representing a decrease of US\$0.3 million. This decrease was primarily attributable to a decrease of cash balance and amount of short-term investments.

Other income

Our other income increased from US\$0.7 million for the year ended December 31, 2019 to US\$1.0 million for the year ended December 31, 2020, primarily attributable to (i) an increase in government subsidies received by Adagene Suzhou to support our ongoing operations in Jiangsu Province during the year ended December 31, 2020 and (ii) an exclusivity payment from ADC Therapeutics pursuant to our collaboration arrangement with ADC Therapeutics, which is not related to our major operation activities.

Foreign exchange loss, net

We recorded foreign exchange gain of US\$21.9 thousand for the year ended December 31, 2019 and foreign exchange loss of US\$0.6 million for the year ended December 31, 2020. This loss of foreign exchange was primarily attributable to the weakening of U.S. dollars against Renminbi which negatively impacted our U.S. dollars denominated accounts receivable of Adagene Suzhou.

Change in fair value of warrant liabilities

We recorded a gain from change in the fair value of warrant liabilities of US\$1.2 million for the year ended December 31, 2019. The corresponding amount was nil for the year ended December 31, 2020 because the warrants to subscribe for Series C-2 Preferred Shares had expired on April 1, 2019.

Net loss attributable to Adagene Inc.'s shareholders

A As a result of the foregoing, our net loss for the period increased by 158.0% from US\$16.4 million for the year ended December 31, 2019 to US\$42.4 million for the year ended December 31, 2020.

Year Ended December 31, 2019 Compared to Year Ended December 31, 2018

See “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Year Ended December 31, 2019 Compared to Year Ended December 31, 2018” beginning on page 121 of our prospectus filed with the Securities and Exchange Commission on [February 10, 2021 pursuant to Rule 424\(b\)\(4\) under the Securities Act \(Securities Act File No. 333-252210\)](#) incorporated by reference into this annual report.

Non-GAAP Financial Measures

We use non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period, which are non-GAAP financial measures, in evaluating our operating results and for financial and operational decision-making purposes. We believe that non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period help identify underlying trends in our business that could otherwise be distorted by the effect of certain expenses that we include in our loss for the year/period. We believe that non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period provide useful information about our results of operations, enhance the overall understanding of its past performance and future prospects and allow for greater visibility with respect to key metrics used by its management in our financial and operational decision-making.

Non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period should not be considered in isolation or construed as an alternative to operating profit, loss for the year/period or any other measure of performance or as an indicator of its operating performance. Investors are encouraged to review non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period and the reconciliation to their most directly comparable GAAP measures. Non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period here may not be comparable to similarly titled measures presented by other companies. Other companies may calculate similarly titled measures differently, limiting their usefulness as comparative measures to our data. We encourage investors and others to review our financial information in its entirety and not rely on a single financial measure.

Non-GAAP net loss and non-GAAP net loss per ordinary share for the year/period represent net loss attributable to ordinary shareholders for the year/period excluding (i) share-based compensation expenses, and (ii) accretion of convertible redeemable preferred shares to redemption value.

Please see the “Reconciliation of GAAP and Non-GAAP Results” below for a full reconciliation of GAAP net loss attributable to ordinary shareholders for the year/period to non-GAAP net loss attributable to ordinary shareholders and non-GAAP net loss per ordinary share for the year/period.

Reconciliation of GAAP and Non-GAAP Results

	For the years ended December 31,	
	2019 US\$	2020 US\$
GAAP net loss attributable to ordinary shareholders	(16,678,492)	(42,645,392)
Add back:		
Share-based compensation expense	611,711	10,129,541
Accretion of convertible redeemable preferred shares to redemption value	246,184	248,113
Non-GAAP net loss attributable to ordinary shareholders	(15,820,597)	(32,267,738)
Weighted average number of ordinary shares used in per share calculation:		
—Basic	15,178,232	15,950,698
—Diluted	15,178,232	15,950,698
Non-GAAP net loss per ordinary share		
—Basic	(1.04)	(2.02)
—Diluted	(1.04)	(2.02)

5.B. Liquidity and Capital Resources

Since the inception, we have incurred net losses and negative cash flow from our operations. We do not expect to generate any revenue from product sales unless and until we obtain regulatory approval and subsequently commercialize one of our current or future drug candidates. We expect to incur additional operating losses in the near future and our operating expenses will increase as we continue to expand our research and development capabilities, invest in preclinical tests and clinical trials and increase our efforts in obtaining regulatory approvals. In addition, subject to obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing and manufacturing. Moreover, we expect to incur additional costs associated with operating as a public company, including expenses related to legal, accounting, regulatory, maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums, and investor relations.

Our principal source of liquidity has been cash generated from the proceeds received from the issuance and sale of our shares. As of December 31, 2020, we had US\$75.2 million in cash and cash equivalents. In February 2021, we completed our initial public offering in which we issued and sold an aggregate of 8,457,100 ADSs, representing 10,571,375 ordinary shares, resulting in net proceeds to us of approximately US\$145.9 million, net of the underwriting discounts and commissions and other fees paid or payable by us in connection with the offering.

We intend to finance our future working capital requirements and capital expenditures primarily from funds raised from financing activities, including the net proceeds we received from our initial public offering.

Based on our current operating plan, we believe that our current cash and cash equivalents and proceeds from our initial public offering will be sufficient to meet our current and anticipated working capital requirements and capital expenditures for at least the next 12 months. In that time, we expect that our expenses will increase substantially as we fund new and ongoing research and development activities and working capital needs. The assumptions on which our estimates are based may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development and commercialization of our product candidates.

In utilizing the proceeds that we received from our initial public offering, we may make capital contributions to our subsidiaries in PRC, the United States, Australia, Hong Kong, Singapore and Switzerland, acquire or establish new subsidiaries, or give loans to our subsidiaries. However, uses of the proceeds by our PRC subsidiary are subject to PRC regulations. See “Item 3 Key Information—Risk Factors—Risks Relating to Doing Business in China—PRC regulation of loans to and direct investment in PRC entities by offshore holding companies and governmental control of currency conversion may delay or prevent us from using the proceeds of our initial public offering to make loans or additional capital contributions to our PRC subsidiary, which could materially and adversely affect our liquidity and our ability to fund and expand our business.” Our operations are primarily based in China. A significant portion of our transactions are settled in Renminbi and our financial statements are presented in U.S. dollars. Under existing PRC foreign exchange regulations, Renminbi may be converted into foreign currencies for current account items, including profit distributions, interest payments and trade- and service-related foreign exchange transactions, without prior SAFE approval as long as certain routine procedural requirements are fulfilled. Our PRC subsidiary is allowed to pay dividends in foreign currencies to us without prior SAFE approval by following certain routine procedural requirements. However, approval from or registration with competent government authorities is required where the Renminbi is to be converted into foreign currency and remitted out of China to pay capital expenses such as the repayment of loans denominated in foreign currencies. The PRC government may at its discretion restrict access to foreign currencies for current account transactions in the future.

The following table presents our selected consolidated cash flow data for the years ended December 31, 2018, 2019 and 2020.

	For the Year Ended		
	December 31,		
	2018	2019	2020
	US\$	US\$	US\$
	(in thousands)		
Net cash used in operating activities	(14,265)	(18,154)	(28,530)
Net cash (used in) generated from investing activities	(29,510)	24,856	7,073
Net cash generated from financing activities	51,058	69,694	4,439
Effect of exchange rate on cash and cash equivalents	39	78	(364)
Net increase (decrease) in cash and cash equivalents	7,322	76,474	(17,382)
Cash and cash equivalents at the beginning of year/period	8,736	16,058	92,533
Cash and cash equivalents at the end of year/period	16,058	92,533	75,151

Operating activities

Net cash used in operating activities was US\$28.5 million in 2020. The difference between our net loss of US\$42.4 million and the net cash used in operating activities was mainly due to (i) an increase in prepayments and other current assets of US\$2.3 million due to our prepaid service fees to our vendor, (ii) a decrease in contract liabilities of US\$0.3 million, offset by (i) an increase in share-based compensation expenses of US\$10.1 million, (ii) an increase in accounts payable of US\$1.1 million (iii) a decrease in accounts receivable of US\$0.5 million, (iv) a decrease in amount due from related parties of US\$1.3 million, (v) an increase in accruals and other current liabilities of US\$1.2 million, and (vi) depreciation and amortization of US\$0.9 million.

Net cash used in operating activities was US\$18.2 million in 2019. The difference between our net loss of US\$16.4 million and the net cash used in operating activities was mainly due to (i) a decrease in amount due to related parties of US\$1.8 million due to our payment of services fees to Wuxi Biologics, (ii) an increase in amount due from related parties of US\$0.7 million, and (iii) change in fair value of warrant liabilities of US\$1.2 million, partially offset by depreciation and amortization of US\$0.8 million.

Net cash used in operating activities was US\$14.3 million in 2018. The difference between our net loss of US\$15.3 million and the net cash used in operating activities was mainly due to (i) an increase in prepayments and other current assets of US\$1.3 million, (ii) a decrease in accruals and other current liabilities of US\$0.9 million, and (iii) a decrease in fair value of warrant liabilities of US\$0.5 million, partially offset by (i) an increase in amount due to related parties of US\$2.1 million, (ii) an increase in accounts payable of US\$0.4 million, and (ii) depreciation and amortization of US\$0.9 million.

Investing activities

Net cash generated from investing activities was US\$7.1 million in 2020, which was primarily attributable to withdrawal of short-term investments of US\$8.0 million, partially offset by purchase of property, equipment and software of US\$0.9 million.

Net cash generated from investing activities was US\$24.9 million in 2019, which was primarily attributable to withdrawal of short-term investments of US\$44.0 million, partially offset by placement of short-term investments of US\$19.0 million.

Net cash used in investing activities was US\$29.5 million in 2018, which was primarily attributable to placement of short-term investments of US\$58.0 million, partially offset by withdrawal of short-term investments of US\$29.0 million.

Financing activities

Net cash generated from financing activities was US\$4.4 million in 2020, which was mainly attributable to proceeds from borrowings of US\$6.1 million, partially offset by repayment of borrowings of US\$1.1 million.

Net cash generated from financing activities was US\$69.7 million in 2019, which was mainly attributable to proceeds from issuance of convertible redeemable preferred shares and warrants of US\$69.0 million, partially offset by repayment of borrowings of US\$2.4 million.

Net cash generated from financing activities was US\$51.1 million in 2018, which was mainly attributable to proceeds from issuance of convertible redeemable preferred shares and warrants of US\$50.0 million, partially offset by repayment of borrowings of US\$1.4 million.

Capital Expenditures

Our capital expenditures are incurred primarily in connection with research and development equipment. Our capital expenditures were US\$0.5 million, US\$0.2 million and US\$0.9 million, respectively, in 2018, 2019 and 2020. We intend to fund our future capital expenditures with our existing cash balance and proceeds from our initial public offering. We will continue to incur capital expenditures to meet the expected growth of our business.

Holding Company Structure

Adagene Inc. is a holding company with no material operations of its own. Adagene Inc. holds certain intellectual properties and outsources certain research and development activities related to these intellectual properties to its subsidiaries. We conduct our operations primarily through our subsidiaries. As a result, our ability to pay dividends depends upon dividends paid by our subsidiaries. If our subsidiaries or any newly formed subsidiaries incur debt on their own behalf in the future, the instruments governing their debt may restrict their ability to pay dividends to us.

In addition, our subsidiary in China is permitted to pay dividends to us only out of their retained earnings, if any, as determined in accordance with the Accounting Standards for Business Enterprise as promulgated by the Ministry of Finance of the PRC, or PRC GAAP. Pursuant to the law applicable to China's foreign investment enterprise, our subsidiaries that are foreign investment enterprises in the PRC have to make appropriation from their after-tax profit, as determined under PRC GAAP, to reserve funds including (i) general reserve fund, (ii) enterprise expansion fund and (iii) staff bonus and welfare fund. The appropriation to the general reserve fund must be at least 10% of the after-tax profits calculated in accordance with PRC GAAP. Appropriation is not required if the reserve fund has reached 50% of the registered capital of our subsidiary. Appropriation to the other two reserve funds are at our subsidiary's discretion.

As an offshore holding company, we are permitted under PRC laws and regulations to provide funding from the proceeds of our offshore fund raising activities to our PRC subsidiaries only through loans or capital contributions, and to our consolidated affiliated entity only through loans, in each case subject to the satisfaction of the applicable government registration and approval requirements. See "Item 3 Key Information— Risk Factors—Risks Related to Doing Business in China—PRC regulation of loans to and direct investment in PRC entities by offshore holding companies and governmental control of currency conversion may delay or prevent us from using the proceeds of our initial public offering to make loans or additional capital contributions to our PRC subsidiary, which could materially and adversely affect our liquidity and our ability to fund and expand our business." As a result, there is uncertainty with respect to our ability to provide prompt financial support to our PRC subsidiaries when needed.

5.C. Research and Development, Patents and Licenses, Etc.

See "Item 4 Information on the Company—4.B. Business Overview — Our Platform" and "—Intellectual Property."

5.D. Trend Information

Other than as disclosed elsewhere in this annual report, we are not aware of any trends, uncertainties, demands, commitments or events for the year ended December 31, 2020 that are reasonably likely to have a material and adverse effect on our net revenues, income, profitability, liquidity or capital resources, or that would cause the disclosed financial information to be not necessarily indicative of future results of operations or financial condition.

5.E. Off-Balance Sheet Commitments and Arrangements

We have not entered into any financial guarantees or other commitments to guarantee the payment obligations of any third parties. We have not entered into any derivative contracts that are indexed to our shares and classified as shareholder's equity or that are not reflected in our consolidated financial statements. Furthermore, we do not have any retained or contingent interest in assets transferred to an unconsolidated entity that serves as credit, liquidity or market risk support to such entity. We do not have any variable interest in any unconsolidated entity that provides financing, liquidity, market risk or credit support to us or engages in leasing, hedging or product development services with us.

5.F. Tabular Disclosure of Contractual Obligations.

The following table sets forth our commitments as of December 31, 2020.

	Payments Due by Years Ending				
	Total	Less than 1 year	1 - 3 years (in thousands)	3 - 5 years	More than 5 years
Short-term and long-term borrowings	7,981	5,015	2,966	—	—
Operating Leases(1)	676	306	370	—	—
Total commitments	8,657	5,321	3,336	—	—

(1) Operating leases relate to certain office buildings under non-cancellable operating lease agreements.

Other than those shown above, we did not have any significant capital and other commitments, long-term obligations or guarantees as of December 31, 2020.

5.G. Safe harbor

See "Forward-Looking Information."

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES**6.A. Directors and Senior Management**

The following table sets forth information regarding our executive officers, key employees and directors as of the date of this annual report.

<u>Executive Officers</u>	<u>Age</u>	<u>Position/Title</u>
Peter (Peizhi) Luo, Ph.D	55	Co-Founder, Chief Executive Officer and Chairman of the Board
Fangyong (Felix) Du, Ph.D	51	Chief Technology Officer
Hua Gong, M.D., Ph.D	53	Chief Operating Officer & Head of Clinical Development and Precision Medicine
JC Xu, M.D., Ph.D	56	Chief Scientific Officer
Qinghai Zhao, Ph.D	60	Chief Manufacturing Officer
Man Kin (Raymond) Tam, M.B.A., B. Eng.	43	Chief Financial Officer and Director
Yu (Albert) Ren, Ph.D.	46	Chief Strategy and Corporate Development Officer

Key Employees	Age	Position/Title
Yan Li, M.B.A.	46	Senior Vice President, Bioinformatics and Information Technology
Xiaohong (Kristine) She	54	Senior Vice President, Head of Clinical Operations
Guizhong Liu, Ph.D.	50	Head of Biology and Pharmacology
Alexander Goergen	34	Head of Business Development
Yuren (Ron) Wang, Ph.D.	59	Head of Portfolio Management
Wei Shi, M.D., Ph.D.	50	Senior Vice President of Clinical Development
Jin Shang, Ph.D.	53	Senior Vice President of Global Regulatory Affairs
Songmao Zheng, Ph.D.	37	Associate Vice President of Research and Development

Non-Employee Directors	Age	Position/Title
Yu Miao	32	Director
Lefei Sun	41	Director
Andy (Yiu Leung) Cheung	61	Independent Director
Min Li	58	Independent Director

Executive Officers

Peter (Peizhi) Luo, Ph.D. is our Co-Founder and has served as our Chief Executive Officer since November 2011 and Chairman of the Board of the Directors since February 2018. Dr. Luo served as the first lead scientist in computational protein design and protein laboratory at Xencor (Nasdaq: XNCR) from July 1998 to August 2000. In September 2000, Dr. Luo founded Abmaxis Inc. and served as its Co-Founder, Chief Technology Officer, president, and director. In May 2006, Dr. Luo led the acquisition of Abmaxis Inc. by Merck & Co. (NYSE: MRK), after which Dr. Luo served as a director of Biologics Technology at Merck, and Chief Technology Officer of Abmaxis, the subsidiary of Merck & Co. Throughout his career, Dr. Luo also led the business development efforts in connection with collaborations and strategic partnerships with multiple global partners. Dr. Luo received his bachelor's degree in applied chemistry in technical physics from Peking University in 1986, master's degree in applied physics from The Institute of High Energy Physics of the Chinese Academy of Sciences in 1989, and Ph.D. degree in chemistry from The University of Chicago in 1995. Dr. Luo also completed his postdoctoral research in protein folding at Stanford University in 1998. Dr. Luo's spouse is Xiaohong (Kristine) She who is our Senior Vice President, Head of Clinical Operations.

Fangyong (Felix) Du, Ph.D. joined us as Vice President of Technology Development in January 2012 and has served as our Chief Technology Officer since May 2019. Dr. Du has over 20 years of experience in biological research and discovery industry, and has published numerous peer-reviewed articles in world-renowned scientific journals such as Nature and Science. Dr. Du worked at Affomix from October 2009 to July 2010 and Illumina (Nasdaq: ILMN) from July 2010 to January 2012, and then joined the Company in January 2012 as the Vice President of Technology Development. Dr. Du received his bachelor's degree and master's degree in physiology and biophysics in 1991 and 1994, respectively, from Peking University, and his Ph.D. degree in biology from the California Institute of Technology in 2001. Dr. Du also completed his postdoctoral research from Yale University in 2007.

Hua Gong, M.D., Ph.D. has served as our Chief Operating Officer and Head of Clinical Development and Precision Medicine since July 2020. Dr. Gong served as the principal scientist of Pfizer (NYSE: PFE) from January 1999 to March 2009. From April 2009 to October 2011, she served as the associate director of Prometheus Diagnostics & Therapeutics. From November 2011 to January 2013, Dr. Gong served as an executive director of Premier Research. From January 2013 to June 2020, she served as the senior director and head of genomics biomarker of Novartis. Dr. Gong received her M.D. degree from An Hui Medical University in 1989, master's degree in biostatistics from Sun Yat-Sen University of Medical Sciences in 1992 and Ph.D. degree in cancer biology from Wayne State University in 1999.

JC Xu, M.D., Ph.D. has served as our Chief Scientific Officer since August 2020. Dr. Xu has more than 20 years of experience in oncology drug discovery and development, and more than four years of experience in business development, strategy, and operations in the biopharmaceutical industry in the United States. Prior to joining Adagene, Dr. Xu was head of R&ED China Strategy at Celgene now BMS from 2017 to 2020. Prior to that, Dr. Xu was Director of Strategy & Operations at Celgene Quantical Research and Director of Biology at Quantical Pharmaceuticals from 2012 to 2017. Prior to Quantical, Dr. Xu worked in leadership roles at a number of biopharmaceutical companies, including Pfizer, Amgen, and Corixa.

Dr. Xu received her M.D. degree from Beijing Medical University (now Peking University Health Science Center) in 1987 and her Ph.D. degree in Immunology from University of Alabama at Birmingham in 1993. She completed her post-doctoral training at DNAX Research Institute (now Merck Palo Alto) in 1996. She is an inventor of more than 120 issued and pending patents and has published more than 50 articles in peer-reviewed journals.

Qinghai Zhao, Ph.D. has served as our Chief Manufacturing Officer since October 2020. Dr. Zhao has more than 25 years of experience in protein therapeutics development and defining product development strategy from early stage IND through commercial filing. Prior to joining Adagene, Dr. Zhao was Vice President of Technical Development and Manufacturing at Forty Seven Inc. (NASDAQ:FTSV) from 2017 to October 2020. Prior to that, Dr. Zhao was vice president of CMC/ Manufacturing at AnaptysBio (NASDAQ:ANAB) from 2016 to 2017. Prior to AnaptysBio, Dr. Zhao worked as an Executive Director and the Head of CMC at NGM Biopharmaceuticals from 2014 to 2016. Dr. Zhao also held various positions at Human Genome Sciences, Inc., Cogenesys and Teva Biopharmaceuticals USA from 2001 to 2014. Dr. Zhao received his bachelor's degree from Shanghai Chemical Engineering Institute (now East China University of Sciences and Technology) in 1982, master's degree from Shanghai Medical University (now merged with Fudan University) in 1986 and Ph.D. degree from University of Uppsala in 1998.

Man Kin (Raymond) Tam has served as our Chief Financial Officer since September 2019 and our director since February 2021. Mr. Tam has over 20 years of management experience in finance and banking across the Asia-Pacific region. Mr. Tam worked in HSBC and J.P. Morgan Chase Bank, N.A. from 1999 to 2010. Mr. Tam served as project director of Mineralogy Pty Limited and Chief Financial Officer of Resourcehouse Limited from April 2010 to October 2015. From October 2015 to August 2019, Mr. Tam consecutively served as the Chief Financial Officer of China Regenerative Medicine International Limited (HKEx: 8158), Beijing Gas Blue Sky Holdings Limited (HKEx: 6828), and AgenTus Therapeutics, Inc. Mr. Tam is a fellow of CPA Australia, a member of the American Institute of Certified Public Accountants and the Hong Kong Institute of Certified Public Accountants. He is also a CFA and FRM charter-holder. He received his bachelor's degree in civil & resources engineering from the University of Auckland in 1997, master's degree in practising accounting from Monash University in 2001 and an Executive Master of Business Administration degree from the University of Western Ontario in 2005.

Yu (Albert) Ren, Ph.D. has served as our Chief Strategy and Corporate Development Officer since January 2021. Prior to joining us, Dr. Ren held various positions at Merck & Co., Inc. (NYSE: MRK). He had previously worked at Portfolio Management & Global Clinical Development Finance responsible for financial / strategic planning on KEYTRUDA® development and facilitation of KEYTRUDA® clinical trials prioritization. He also worked at Merck Corporate Strategy Office on enterprise strategy and at Merck Corporate Business Development on a variety of business development transactions. Before returning to Merck, Dr. Ren served as a principal consultant at Quintiles/IQVIA Consulting from 2009 to 2010. Dr. Ren gained extensive consulting experience at McKinsey & Company from 2007 to 2009. Dr. Ren started his professional career at Merck Research Lab working on Pharmaceutical Research & Development from discovery to early clinical development from 2001 to 2006. Dr. Ren received his Ph.D. in Chemistry from University of Minnesota in 2001, and bachelor's degree in Chemistry from Peking University in 1996.

Key Employees

Yan Li, M.B.A. has served as our Senior Vice President of Bioinformatics and Information Technology since November 2011. Ms. Li has over 25 years of experience in software development, with about 20 years focusing on the development of informatics software tools for antibody library design and analysis. Ms. Li served as the senior software engineer and applications scientist at Abmaxis from November 2001 to May 2006. Following the acquisition of Abmaxis by Merck & Co, Ms. Li worked at Merck & Co from May 2006 to December 2010. She received the Merck Award for Excellence in "Innovative Technologies" with the team and a Special Award for her contribution. Ms. Li received her bachelor's degree in information science from East China University of Science and Technology in 1995 and a Master of Business Administration degree in 2010 from Santa Clara University.

Xiaohong (Kristine) She has served as our Senior Vice President, Head of Clinical Operations since November 2011. Ms. She has over 20 years of laboratory and laboratory management experience in the renowned laboratories in the United States and has completed multiple projects in molecular biology and immunology at the labs of University of Chicago, the Genome Center at Stanford University, neurological animal studies at Stanford Palo Alto Veteran's Hospital, and cloning and functional screening of cDNA libraries at Caltech. Her work has been published in Nature, Science, Biotechnology, among many other notable publications. Ms. She received her bachelor's degree in microbiology from Wuhan University in 1986 and master's degree in biochemistry and microbiology from the Institute of Microbiology of the Chinese Academy of Sciences in 1989. Ms. She's spouse is Peter (Peizhi) Luo, Ph.D., our Co-Founder, Chief Executive Officer and Chairman of the Board.

Guizhong Liu, Ph.D. has served as our Head of Biology and Pharmacology since October 2015. Dr. Liu has over 15 years of experience in drug discovery and development, both in small molecule kinase inhibitors and large molecule antibodies in oncology and immunology field. He has published over 40 peer-reviewed papers in high-profile journals involving key signalling pathways and targets in cancer biology. From July 2007 to August 2011, Dr. Liu served as an assistant professor of the department of oncological science at Mount Sinai School of Medicine. Prior to joining us, Dr. Liu served as head of molecular cancer biology in CrownBio from October 2011 to September 2015. Dr. Liu received his bachelor's degree in biology in 1992 and master's degree in cell biology in 1995 from Beijing Normal University and Ph.D. degree in cell biology from Peking Union Medical College in 1998. He also completed his postdoctoral training in cancer biology at Mount Sinai School of Medicine in 2004.

Alexander Goergen has served as our Head of Business Development since October 2017 when he joined the Company. Mr. Goergen has worked in various roles at the Covance, TRC and International AIDS Vaccine Initiative from October 2008 to October 2012. Prior to joining us, Alexander worked in business development for Catalent Pharma Solutions Biologics Division since October 2012. Mr. Goergen completed many licensing, manufacturing, and cell line development programs both domestically and internationally during his previous employment. Mr. Goergen received his bachelor's degree in Chemistry from Lafayette College in 2008 and master's degree in Biotechnology from the University of Wisconsin-Madison in 2011.

Yuren (Ron) Wang, Ph.D. has served as our Head of Portfolio Management since September 2019. Dr. Wang served as the senior director of business development in Reaction Biology Corporation from March 2013 to December 2018. Prior to joining us, he served as the vice president of R&D research for Jemincare Therapeutics (USA), responsible for the scientific evaluation of projects, in-licensing and portfolio management from December 2018 to August 2019. Dr. Wang received his bachelor's degree in plant science from Shandong Agricultural University in 1982, master's degree in biochemistry from the Graduate School of Chinese Academy of Agricultural Sciences in 1986 and Ph.D. degree in cell and molecular biology from the University of Pennsylvania in 1996. He also completed his postdoctoral training in molecular pharmacology at the University of Pennsylvania in 1999.

Wei Shi, M.D., Ph.D., has served as our Senior Vice President of Clinical Development since March 2021. Prior to joining us, Dr. Shi served as Head of China Oncology Clinical Development; Early Oncology Pipeline at Amgen with a focus on solid tumors as well as hematologic malignancies. Dr. Shi also held leadership positions at Antengene, Covance, BioMarin Pharmaceuticals and Novartis. Dr. Shi received M.D. degree from Tongji Medical University in 1993, master's degree in gynecology oncology from Tongji Medical University in 1996 and Ph.D. degree in biology from Uppsala University in 2005.

Jin Shang, Ph.D., has served as our Senior Vice President of Global Regulatory Affairs since April 2021. Prior to joining us, Dr. Shang served as global and US regulatory lead in AstraZeneca for multiple oncology development programs, including KOSELUGO. Dr. Shang led the submission and regulatory defense to gain FDA approval of Elepsia XR. Dr. Shang also served as Principal Scientist/Program Team Lead at Merck Research Laboratories, and served as Therapeutic Area Lead on the non-human primate study execution committee. Dr. Shang received her bachelor's degree in cell biology and genetics from Peking University in 1990 and Ph.D. degree in development biology from Stanford University in 1997.

Songmao Zheng, Ph.D., has served as our Associate Vice President of Research and Development since March 2021, leading quantitative model-informed drug discovery and development in both preclinical and clinical space. Prior to joining us, Dr. Zheng had served as Scientific Director/Group Leader, leading numerous biologics programs at Janssen BioTherapeutics, Janssen R&D since 2013. Dr. Zheng received his bachelor's degree in biological sciences from Sichuan University in 2007 and Ph.D. degree in pharmaceutical sciences from University of Washington in 2012.

Non-Employee Directors

Yu Miao has served as our director since May 2020 designated by JSR Limited pursuant to our current effective shareholders agreement. He also serves as the executive director of GP Healthcare Capital Co., Ltd, mainly responsible for equity investment focusing on healthcare industry. Prior to joining GP Healthcare Capital in April 2015, Mr. Yu worked at Eli Lilly & Co. focusing on quality assurance from July 2011 to June 2012 and Oriza Seed Fund Management Co., Ltd., focusing on equity investment from July 2014 to April 2015. Mr. Miao received his bachelor's degree in pharmacy from China Pharmaceutical University in 2011, and master's degree in pharmaceutical science from Northeastern University in 2014.

Lefei Sun has served as our director since December 2019 designated by General Atlantic Singapore AI Pte. Ltd. pursuant to our current effective shareholders agreement. Mr Sun has been a non-executive director of Hong Kong Asia Medical Holding Limited, a leading hospital management group in Asia with hospital assets such as Wuhan Asia Heart Hospital, from November 2018. He is also a non-executive director of various biotech companies such as Ocumension Therapeutics (HKEx: 1477) and CANbridge Pharmaceuticals Inc. Mr. Sun has served as head of China healthcare at General Atlantic since May 2018, and has been a managing director since January 2020, in charge of private equity investment and portfolio management in healthcare and life sciences sectors. From December 2014 to April 2018, Mr. Sun was a founding partner and a member of investment committee of Beijing HuaTai Ruihe Investment Fund Management Company (LLP), also known as Huatai Healthcare Investment Fund. Prior to joining General Atlantic, Mr. Sun served as various investment roles at Hony Capital, Credit Suisse, OrbiMed, Orchid Asia, and as a management consultant at McKinsey & Company, all in the healthcare sector. Mr. Sun obtained his master’s degree in neurosciences from Johns Hopkins University School of Medicine in 2006, and his bachelor’s degree in mathematics and physics from Tsinghua University in 2002.

Andy (Yiu Leung) Cheung has served as our independent director since February 2021. Mr. Cheung has many years of auditing and accounting professional experience. Mr. Cheung was deputy area managing partner of Ernst & Young (“EY”) in Asia Pacific overseeing the business operations, finance, information technology and risk management functions from July 2018 to June 2020. Mr. Cheung was the assurance leader for EY in Greater China from July 2013 to June 2018. Mr. Cheung has served as an independent non-executive director of JW (Cayman) Therapeutics Co. Ltd (HKEX:2126) since October 2020. Mr. Cheung received his bachelor’s degree in accounting and finance from the University of Lancaster in the United Kingdom in June 1982. He obtained a master’s degree in accounting and finance from London School of Economics in the United Kingdom in August 1983. Mr. Cheung is a member of Hong Kong Institute of Certified Public Accountants.

Min Li, Ph.D. has served as our independent director since February 2021. Dr. Min Li is the founder, CEO and director of SciNeuro Pharmaceuticals, a biotechnology company headquartered in Shanghai focused on developing innovative therapeutics for CNS diseases. Dr. Li was formerly Senior Vice President, Global Head of Neuroscience R&D at GSK from 2013 to 2019. During his employment with GSK, he also served as General Manager of GSK R&D China, the highest-ranking officer at the country level. Before moving into industry, Dr. Li had served as a tenured Professor of Neuroscience at Johns Hopkins University School of Medicine for over 20 years. Dr. Li served on scientific advisory boards, non-profit and corporate boards that include multinational corporations (Corning, Pfizer and Merck), disease foundations (RYR-foundation, AHA) and biotech companies (Xencor, Affymax, Datavant, Icagen, and Coda Biotechnologies). He is also an Adjunct Professor of Neuroscience at Johns Hopkins School of Medicine. Dr. Li received his B.S. degree in biochemistry from Wuhan University in 1984 and his Ph.D. in molecular immunology from Johns Hopkins University in 1990. As a Helen Hay Whitney Fellow, he performed postdoctoral research at University of California San Francisco. With a Sloan Award, in 1994 he returned to Johns Hopkins to join the faculty as an Esther A & Joseph Klingenstein Neuroscience Fellow. Dr. Li has published more than 120 scientific articles and holds patents in biotechnologies. His research and scholarship were recognized internationally with awards including being a fellow of American Association for Advancement of Science and an established fellow of American Heart Association.

6.B. Compensation

Compensation

For the fiscal year ended December 31, 2020, we paid an aggregate of US\$2.6 million in cash to our executive officers, and we paid US\$54,000 cash compensation to our then non-executive director, Mr. Tom Beck, for the fiscal year ended December 31, 2020. We did not pay any cash compensation to other non-executive directors. For the fiscal year ended December 31, 2020, we did not set aside or accrue expenses related to pension, retirement or other similar benefits to our executive officers and directors. Our PRC subsidiary is required by law to make contributions equal to certain percentages of each employee’s salary for his or her pension insurance, medical insurance, unemployment insurance and other statutory benefits and a housing provident fund. For share incentive grants to our directors and executive officers, see “Item 6 Directors, Senior Management and Employees—Share Incentive Plan.”

Employment Agreements and Indemnification Agreements

We have entered into employment agreements with each of our executive officers. Each of our executive officers is employed for a period of twelve months, which will be renewed automatically and extended automatically for a period of twelve months unless the executive or us gives prior written notice. We may terminate an executive officer's employment for cause at any time without advance notice in certain events. We may terminate an executive officer's employment by giving a prior written notice or by paying certain compensation. In such case of termination by us, we will provide severance payments to the executive officer as expressly required by applicable law of the jurisdiction where the executive officer is based. An executive officer may terminate his or her employment at any time by giving a prior written notice.

Each executive officer has agreed to hold, unless expressly consented to by us, at all times during and after the termination of his or her employment agreement, in strict confidence and not to use, any of our confidential information or the confidential information of our customers and suppliers. In addition, each executive officer has agreed to be bound by certain non-competition and non-solicitation restrictions during the term of his or her employment and for a maximum of two years following the last date of employment.

We have entered into indemnification agreements with each of our directors and executive officers. Under these agreements, we agree to indemnify our directors and executive officers against certain liabilities and expenses incurred by such persons in connection with claims made by reason of their being a director or officer of our company.

Share Incentive Plan

Adagene Inc. Second Amended and Restated Share Incentive Plan

In November 2015, we adopted Adagene Inc. Share Incentive Plan, or the 2015 Plan, which was later superseded and replaced by Adagene Inc. Amended and Restated Share Incentive Plan, or the 2017 Plan, in September 2017. In December 2019, we adopted the Second Amended and Restated Share Incentive Plan, or the 2019 Plan, to supersede and replace the 2017 Plan. The terms of the 2015 Plan, the 2017 Plan and the 2019 Plan are substantially the same other than the maximum aggregate number of shares we may issue under the respective plan.

The purpose of the 2019 Plan is to attract, motivate, retain and reward certain officers, employees, directors and other eligible persons and to further link the interests of award recipients with those of our shareholders generally. The 2019 Plan provides for the issuance of up to an aggregate of 11,391,131 of our ordinary shares. We have terminated the authority to grant additional awards under the 2019 Plan and all future awards will be granted under the 2021 Plan. Therefore, the effective maximum number of shares issuable under the 2019 Plan will be 10,828,501. As of March 31, 2021, the aggregate number of our ordinary shares underlying our outstanding awards under the 2019 Plan is 3,681,522, excluding awards that were forfeited, cancelled or exercised after the relevant grant dates. The term of the awards will expire not more than ten years after the date of grant.

The following paragraphs summarize the principal terms of the 2019 Plan.

Types of Awards. The 2019 Plan permits the awards of options, share appreciation rights, ordinary shares or restricted shares.

Plan Administration. The 2019 Plan shall be administrated by our board of directors or one or more committees appointed by the board of directors or another committee (within its delegated authority), the Plan Administrator.

Promissory Notes. The promissory notes with respect to the 2019 Plan, or the 2019 Promissory Notes are full recourse, repayable within a period of time determined by the Plan Administrator, which should not exceed five years (subject to certain early repayment events), and bear interest at the interest rate determined by the Plan Administrator but not less than the interest rate necessary to avoid the imputation of interest under United States Internal Revenue Code of 1986, as amended or other applicable tax law. Certain plan participants previously purchased our shares with such promissory notes. The largest aggregate amount outstanding since the first issuance of the promissory notes was US\$7.0 million. All amounts outstanding under the promissory notes have been settled.

Repayment of the Promissory Notes. The terms, repayment provisions, and collateral release provisions of the note and the pledge securing the note shall conform with all applicable rules and regulations, including those of the Federal Reserve Board of the United States and any applicable law, as then in effect.

Eligibility. The plan administrators may decide that an award under the 2019 Plan be granted to any employee, officer or director of the Company or its affiliates, or that it be granted to any consultant or adviser who provides services to the Company or its affiliates.

Award Agreements. Each award under the 2019 Plan shall be evidenced by an award agreement in the form approved by the plan administrators. The terms of the award agreements will be determined by the plan administrators and consistent with the terms of the 2019 Plan.

Conditions of Award. The plan administrators shall determine the participants, types of awards, numbers of shares to be covered by awards, terms and conditions of each award, including, but not limited to, the price and number of securities to be offered or awarded, the installments (if applicable) in which such awards will become exercisable or will vest, performance targets (if applicable), the events of termination or reversion of such awards.

Transfer Restrictions. With a few exceptions, no right of interest of a participant in any award may be subject in any manner to sale, transfer, anticipation, alienation, assignment, pledge, encumbrance or charge. This restriction does not apply to (i) transfers to our company, (ii) transfers by gift or domestic relations order to one or more family members, (iii) the designation of a beneficiary to receive benefits if a participant dies or transfers by will, (iv) permitted transfers or exercises on behalf of a participant by the participant's duly authorized legal representative if the participant has suffered a disability.

Reduction or Clawback of Awards. The awards granted under the 2019 Plan are subject to the terms of our recoupment, clawback or similar policy as it may be in effect from time to time, as well as any similar provisions of applicable law, any of which could in certain circumstances require repayment or forfeiture of awards or any ordinary shares or other cash or property received with respect to the awards (including any value received from a disposition of the shares acquired upon payment of the Awards).

Amendment and Termination of the 2019 Plan. The board of directors may, at any time, terminate or, from time to time, amend, modify or suspend the 2019 Plan, in whole or in part. No awards may be granted during any period that the board of directors suspends the 2019 Plan. To the extent then required by applicable law or listing agency, any amendment to the 2019 Plan may be subject to shareholder approval. Unless earlier terminated by the board of directors, the 2019 Plan will terminate at the close of business on the day before the 10th anniversary of the date the board of directors approved the 2019 Plan.

Adagene Inc. 2021 Performance Incentive Plan

In January 2021, our board of directors adopted, and our shareholders approved, the 2021 Performance Incentive Plan, or the 2021 Plan, to provide an additional means through the grant of awards to attract, motivate, retain and reward selected employees and other eligible persons. The terms of the 2021 Plan are summarized below. Employees, officers, directors and consultants that provide services to us or one of our subsidiaries may be selected to receive awards under the 2021 Plan.

Our board of directors or a committee appointed by the board administers the 2021 Plan. The plan administrator has broad authority to:

- select participants and determine the types of awards that they are to receive;
- determine the number of shares that are to be subject to awards and the terms and conditions of awards, including the price (if any) to be paid for the shares or the award and establish the vesting conditions (if applicable) of such shares or awards;
- cancel, modify or waive our rights with respect to, or modify, discontinue, suspend or terminate any or all outstanding awards, subject to any required consents;
- construe and interpret the terms of the 2021 Plan and any agreements relating to the plan;

- accelerate or extend the vesting or exercisability or extend the term of any or all outstanding awards subject to any required consent;
- subject to the other provisions of the 2021 Plan, make certain adjustments to one or more outstanding awards (including a repricing of the exercise or base price of any outstanding option or share appreciation right without shareholder approval) and authorize the termination, conversion, substitution or succession of awards; and
- allow the purchase price of an award or our ordinary shares to be paid in the form of cash, check or electronic funds transfer, by the delivery of previously-owned ordinary shares or by a reduction of the number of shares deliverable pursuant to the award, by services rendered by the recipient of the award, by notice and third party payment or cashless exercise on such terms as the plan administrator may authorize or any other form permitted by law.

A total of 2,994,000 of our ordinary shares is authorized for issuance with respect to awards granted under the 2021 Plan. The share limit will automatically increase on the first trading day in January of each year (commencing with 2022) by an amount equal to (1) 5% of the total number of our outstanding ordinary shares on December 31 of the prior year, or (2) such lesser number as determined by our board of directors. Any shares subject to awards granted under the 2021 Plan or our Second Amended and Restated Share Incentive Plan that are not paid, delivered or exercised before they expire or are canceled or terminated, or otherwise fail to vest, as well as shares used to pay the purchase or exercise price of such awards or related tax withholding obligations, will become available for new award grants under the 2021 Plan. As of March 31, 2021, we had granted equity awards representing 631,733 ordinary shares under the 2021 Plan, and 2,362,267 ordinary shares authorized under the 2021 Plan is available for award purposes.

Awards under the 2021 Plan may be in the form of incentive or nonqualified stock options, share appreciation rights, share bonuses, restricted shares, share units, restricted share units and other forms of awards including cash awards. Awards under the plan generally will not be transferable other than by will or the laws of descent and distribution, except that the plan administrator may authorize certain transfers.

Options and share appreciation rights may not be granted under the 2021 Plan at exercise prices below the fair market value of the underlying ordinary shares on the date of grant, except that the plan administrator may grant such awards with exercise prices below the fair market value of the underlying shares to service-providers who are not subject to U.S. taxes. The maximum term of options and share appreciation rights granted under the plan is ten years. Incentive stock options granted to any 10% owner of our ordinary shares must have an exercise price that is at least 110% of the fair market value of our ordinary shares on the grant date and a maximum term of five years. These and other awards may also be issued solely or in part for services. Awards are generally paid in cash or our ordinary shares. The plan administrator may provide for the deferred payment of awards and may determine the terms applicable to deferrals.

As is customary in incentive plans of this nature, the number and type of shares available under the 2021 Plan and any outstanding awards, as well as the exercise or purchase prices of awards, will be subject to adjustment in the event of certain reorganizations, mergers, combinations, recapitalizations, share splits, share dividends or other similar events that change the number or kind of shares outstanding, and extraordinary dividends or distributions of property to the shareholders.

Generally, and subject to limited exceptions set forth in the 2021 Plan, if we dissolve or undergo certain corporate transactions such as a merger, business combination or other reorganization, or a sale of all or substantially all of our assets, all awards then-outstanding under the 2021 Plan will become fully vested or paid, as applicable, and will terminate or be terminated in such circumstances, unless the plan administrator provides for the assumption, substitution or other continuation of the award. The plan administrator also has the discretion to establish other change in control provisions with respect to awards granted under the 2021 Plan. For example, the administrator could provide for the acceleration of vesting or payment of an award in connection with a corporate event that is not described above and provide that any such acceleration shall be automatic upon the occurrence of any such event.

Our board of directors may amend or terminate the 2021 Plan at any time, but no such action will affect any outstanding award in any manner materially adverse to a participant without the consent of the participant. Plan amendments will be submitted to shareholders for their approval as required by applicable law or deemed necessary or advisable by the board. The 2021 Plan is not exclusive; our board of directors and compensation committee may grant shares and performance incentives or other compensation, in shares or cash, under other plans or authority.

The plan will terminate on January 16, 2031. However, the plan administrator will retain its authority until all outstanding awards are exercised or terminated.

The following table summarizes, as of March 31, 2021, the number of ordinary shares under outstanding awards that we granted to our directors and executive officers under the 2019 Plan, which replaced the 2015 Plan, and under the 2021 Plan, excluding awards that were exercised, forfeited or canceled after the relevant grant dates.

Name	Ordinary Shares Underlying Equity Awards Granted	Exercise Price (US\$/Share)	Date of Grant	Date of Expiration
Executive Officers				
Peter (Peizhi) Luo, Ph. D.	287,415	\$ 13.85	January 2021	January 2031
Fangyong (Felix) Du, Ph. D.	111,744	\$ 13.85	January 2021	January 2031
Hua Gong, M.D., Ph. D.	*	\$ 2.26	August 2020	August 2030
JC Xu, M.D., Ph. D.	*	\$ 2.26	August 2020	August 2030
Qinghai Zhao, Ph. D.	*	\$ 2.26	October 2020	October 2030
Man Kin (Raymond) Tam, M.B.A., B. Eng.	*	\$ 1.83	August 2020	August 2030
	*	\$ 1.48	March 2020	March 2030
Yu (Albert) Ren, Ph. D.	*	\$ 17.10	March 2021	March 2031
Non-Employee Directors				
Yu Miao	—	—	—	—
Lefei Sun	—	—	—	—
Andy (Yiu Leung) Cheung	—	—	—	—
Min Li	—	—	—	—
All directors and executive officers as a group	2,312,986		Various dates from March 2020 to March 2021	Various dates from March 2030 to March 2031

Note:

* The shares held by each of these directors and executive officers represent less than 1% of our total outstanding shares.

As of March 31, 2021, our award holders other than our directors and executive officers as a group held outstanding awards to purchase 1,976,536 ordinary shares. For discussions of our accounting policies and estimates for awards granted pursuant to the 2019 Plan and 2021 Plan, see “Item 5 Operating and Financial Review and Prospects—Share-based compensation.”

6.C. Board Practices

Board of Directors

Our board of directors consists of six directors, including two independent directors, namely Andy (Yiu Leung) Cheung and Min Li. A director is not required to hold any shares in our company to qualify to serve as a director. The Corporate Governance Rules of the Nasdaq generally require that a majority of an issuer’s board of directors must consist of independent directors. However, the Corporate Governance Rules of the Nasdaq permit foreign private issuers like us to follow “home country practice” in certain corporate governance matters. We rely on this “home country practice” exception and do not have a majority of independent directors serving on our board of directors.

A director who is in any way, whether directly or indirectly, interested in a contract or proposed contract with our company is required to declare the nature of his or her interest at a meeting of our directors. A general notice given to the directors by any director to the effect that he or she is a member, shareholder, director, partner, officer or employee of any specified company or firm and is to be regarded as interested in any contract or transaction with that company or firm shall be deemed a sufficient declaration of interest for the purposes of voting on a resolution in respect to a contract or transaction in which he/she has an interest, and after such general notice it shall not be necessary to give special notice relating to any particular transaction. A director may vote in respect of any contract or proposed contract or arrangement notwithstanding that he/she may be interested therein and if he/ she does so, his/her vote shall be counted and he/she may be counted in the quorum at any meeting of the directors at which any such contract or proposed contract or arrangement is considered, subject to any separate requirement for Audit Committee approval under applicable law or the Listing Rules of the Nasdaq. Our board of directors may exercise all of the powers of our company to borrow money, to mortgage or charge its undertaking, property and uncalled capital, or any part thereof, and to issue debentures, debenture stock or other securities whenever money is borrowed or as security for any debt, liability or obligation of our company or of any third party. None of our directors has a service contract with us that provides for benefits upon termination of service as a director.

Committees of the Board of Directors

We have established an audit committee, a compensation committee and a nominating and corporate governance committee under our board of directors. We have also adopted a charter for each of the three committees. Each committee's members and functions are described below.

Audit Committee. Our audit committee consists of Andy (Yiu Leung) Cheung and Min Li, and is chaired by Andy (Yiu Leung) Cheung. We have determined that Andy (Yiu Leung) Cheung and Min Li satisfy the requirements of Rule 5605(a)(2) of the Listing Rules of the Nasdaq and meet the independence standards under Rule 10A-3 under the Securities Exchange Act of 1934, as amended. We have determined that Andy (Yiu Leung) Cheung qualifies as an "audit committee financial expert." The audit committee oversees our accounting and financial reporting processes and the audits of the financial statements of our company. The audit committee is responsible for, among other things:

- reviewing and recommending to our board for approval, the appointment, re-appointment or removal of the independent auditor, after considering its annual performance evaluation of the independent auditor;
- approving the remuneration and terms of engagement of the independent auditor and pre-approving all auditing and non-auditing services permitted to be performed by our independent auditors at least annually;
- obtaining a written report from our independent auditor describing matters relating to its independence and quality control procedures;
- reviewing with the independent registered public accounting firm any audit problems or difficulties and management's response;
- discussing with our independent auditor, among other things, the audits of the financial statements, including whether any material information should be disclosed, issues regarding accounting and auditing principles and practices;
- reviewing and approving all proposed related party transactions, as defined in Item 404 of Regulation S-K under the Securities Act;
- reviewing and recommending the financial statements for inclusion within our quarterly earnings releases and to our board for inclusion in our annual reports;
- discussing the annual audited financial statements with management and the independent registered public accounting firm;
- reviewing the adequacy and effectiveness of our accounting and internal control policies and procedures and any special steps taken to monitor and control major financial risk exposures;
- at least annually, reviewing and reassessing the adequacy of the committee charter;

- approving annual audit plans, and undertaking an annual performance evaluation of the internal audit function;
- establishing and overseeing procedures for the handling of complaints and whistleblowing;
- meeting separately and periodically with management and the independent registered public accounting firm;
- monitoring compliance with our code of business conduct and ethics, including reviewing the adequacy and effectiveness of our procedures to ensure proper compliance; and
- reporting regularly to the board.

Compensation Committee. Our compensation committee consists of Peter Luo, Andy (Yiu Leung) Cheung and Min Li and is chaired by Peter Luo. We have determined that Andy (Yiu Leung) Cheung and Min Li satisfy the “independence” requirements of Rule 5605(a)(2) of the Listing Rules of the Nasdaq. The compensation committee assists the board in reviewing and approving the compensation structure, including all forms of compensation, relating to our directors and executive officers. Our Chief Executive Officer may not be present at any committee meeting during which their compensation is deliberated upon. The compensation committee is responsible for, among other things:

- overseeing the development and implementation of compensation programs in consultation with our management;
- at least annually, reviewing and approving, or recommending to the board for its approval, the compensation for our executive officers;
- at least annually, reviewing and recommending to the board for determination with respect to the compensation of our non-executive directors;
- at least annually, reviewing periodically and approving any incentive compensation or equity plans, programs or other similar arrangements;
- reviewing executive officer and director indemnification and insurance matters;
- overseeing our regulatory compliance with respect to compensation matters, including our policies on restrictions on compensation plans and loans to directors and executive officers;
- at least annually, reviewing and reassessing the adequacy of the committee charter;
- selecting compensation consultant, legal counsel or other adviser only after taking into consideration all factors relevant to that person’s independence from management; and
- reporting regularly to the board.

Nominating and Corporate Governance Committee. Our nominating and corporate governance committee consists of Peter Luo, Andy (Yiu Leung) Cheung and Min Li, and is chaired by Peter Luo. We have determined that Andy (Yiu Leung) Cheung and Min Li satisfy the “independence” requirements of Rule 5605(a)(2) of the Listing Rules of the Nasdaq. The nominating and corporate governance committee assists the board in selecting individuals qualified to become our directors and in determining the composition of the board and its committees. The nominating and corporate governance committee is responsible for, among other things:

- recommending nominees to the board for election or re-election to the board, or for appointment to fill any vacancy on the board;
- reviewing annually with the board the current composition of the board with regards to characteristics such as independence, knowledge, skills, experience, expertise, diversity and availability of service to us;

- developing and recommending to our board such policies and procedures with respect to nomination or appointment of members of our board and chairs and members of its committees or other corporate governance matters as may be required pursuant to any SEC or Nasdaq rules, or otherwise considered desirable and appropriate;
- selecting and recommending to the board the names of directors to serve as members of the audit committee and the compensation committee, as well as of the nominating and corporate governance committee itself;
- at least annually, reviewing and reassessing the adequacy of the committee charter;
- developing and reviewing at least annually the corporate governance principles adopted by the board and advising the board with respect to significant developments in the law and practice of corporate governance and our compliance with such laws and practices; and
- evaluating the performance and effectiveness of the board as a whole.

Duties and Functions of Directors

Under Cayman Islands law, our directors owe fiduciary duties to our company, including a duty of loyalty, a duty to act honestly and a duty to act in what they consider in good faith to be in our best interests. Our directors must also exercise their powers only for a proper purpose. Our directors also owe to our company a duty to exercise the skill they actually possess and such care and diligence that a reasonable prudent person would exercise in comparable circumstances. It was previously considered that a director need not exhibit in the performance of his duties a greater degree of skill than may reasonably be expected from a person of his knowledge and experience. However, English and Commonwealth courts have moved towards an objective standard with regard to the required skill and care and these authorities are likely to be followed in the Cayman Islands. In fulfilling their duty of care to us, our directors must ensure compliance with our memorandum and articles of association, as amended and restated from time to time. Our company has the right to seek damages if a duty owed by our directors is breached. In limited exceptional circumstances, a shareholder may have the right to seek damages in our name if a duty owed by our directors is breached. The functions and powers of our board of directors include, among others, (i) convening shareholders' annual general meetings and reporting its work to shareholders at such meetings, (ii) declaring dividends, (iii) appointing officers and determining their terms of offices and responsibilities, (iv) exercising the borrowing powers of our company, and (v) approving the transfer of shares of our company, including the registering of such shares in our share register.

Terms of Directors and Officers

Our officers are elected by and serve at the discretion of the board of directors. Other than Andy (Yiu Leung) Cheung, Min Li and Man Kin (Raymond) Tam, each director is not subject to a term of office and holds office until such time as his successor takes office or until the earlier of his death, resignation or removal from office pursuant to the applicable provisions of our memorandum and articles of association. The initial term of our independent director nominees, namely Andy (Yiu Leung) Cheung and Min Li, is two-year from the effectiveness of the appointment. The initial term of our non-independent director nominee, Man Kin (Raymond) Tam, is one-year from the effectiveness of the appointment. The initial term for each of Andy (Yiu Leung) Cheung, Min Li and Man Kin (Raymond) Tam is subject to re-appointment by the board of directors and affirmative vote of Chairman of the board of directors. A director will be removed from office automatically if, among other things, the director (i) becomes bankrupt or makes any arrangement or composition with his creditors; (ii) dies or is found by our company to be of unsound mind; (iii) resigns by notice in writing to our company; (iv) without special leave of absence from our board of directors, is absent from three consecutive meetings of the board and the board resolves that his office be vacated; (v) is prohibited by law from being a director; or (vi) is removed from office pursuant to any other provisions of our post-offering amended and restated memorandum and articles of association.

Interested Transactions

A director may, subject to any separate requirement for audit and risk committee approval under applicable law or applicable Nasdaq listing rules, vote in respect of any contract or transaction in which he or she is interested, provided that the nature of the interest of any directors in such contract or transaction is disclosed by him or her at or prior to its consideration and any vote in that matter.

6.D. Employees

We had a total of 198 employees as of December 31, 2020. The following table sets forth the numbers of our employees categorized by function as of December 31, 2020. We also engage consultants and part-time staff as and when appropriate.

Function	Number of Employees
Research and Development	159
Computational Biology and Informatics	25
Technology Development	71
Drug Discovery	40
Clinical Development	23
General Administration	36
HR	6
Finance	9
IT	5
Administration	16
Business Development and Marketing	3
Total	198

Our success depends on our ability to attract, motivate, train and retain qualified personnel. We believe we offer our employees competitive compensation packages and an environment that encourages self-development. We regularly recruit new talents through campus events and colleague referral to build and develop our own talent pool. Through employee succession planning, we help employees understand their career path within Adagene, motivate them to remain in the organization and to achieve their personal career goals. Other initiatives for talent retention include executive coaching, employee surveys or engagement, training and development, compensation and rewards. As a result of these efforts, we have generally been able to attract and retain qualified personnel and maintain a stable core management team.

As required by regulations in China, we participate in various employee social security plans that are organized by municipal and provincial governments, including pension insurance, unemployment insurance, maternity insurance, work-related injury insurance, medical insurance and housing funds. We are required under PRC law to make contributions to employee benefit plans at specified percentages of the salaries, bonuses and certain allowances of our employees, up to a maximum amount specified by the local government from time to time. We have granted, and plan to continue to grant, share-based incentive awards to our employees in the future to incentivize their contributions to our growth and development.

We believe that we maintain a good working relationship with our employees, and we have not experienced any material labor disputes. None of our employees is requested by labor unions.

6.E. Share Ownership

The following table sets forth information concerning the beneficial ownership of our ordinary shares, as of March 31, 2021, by:

- each of our directors and executive officers; and
- each person known to us to beneficially own more than 5% of our ordinary shares.

The calculations in the table below are based on 54,397,383 ordinary shares issued and outstanding as of March 31, 2021, excluding the 2,012,500 ordinary shares, issued but deemed to be not outstanding as of March 31, 2021, held by Great Han Fortune LP.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC. In computing the number of shares beneficially owned by a person and the percentage ownership of that person, we have included shares that the person has the right to acquire within 60 days, including through the exercise of any option, warrant, or other right or the conversion of any other security.

These shares, however, are not included in the computation of the percentage ownership of any other person.

	Ordinary Shares Beneficially Owned as of March 31, 2021	
	Number	%*
Directors and Executive Officers:†		
Peter (Peizhi) Luo(1)	10,518,217	19.1%
Fangyong (Felix) Du(2)	1,057,188	1.9%
Hua Gong	**	**%
JC Xu	**	**%
Qinghai Zhao	**	**%
Man Kin (Raymond) Tam	**	**%
Yu (Albert) Ren	**	**%
Non-employee Directors		
Yu Miao	**	**%
Lefei Sun	**	**%
Andy (Yiu Leung) Cheung (independent director)	—	—
Min Li (independent director)	—	—
All directors and executive officers as a group	10,518,217	19.1%
Principal Shareholders:		
Peter Luo act-in-concert group(3)	10,518,217	19.1%
JSR Limited(4)	5,353,242	9.8%
Asia Ventures II L.P.(5)	4,826,037	8.9%
F-Prime Capital Partners Healthcare Fund III LP(6)	4,826,037	8.9%
Wuxi Pharmatech Healthcare Fund I L.P.(7)	5,356,946	9.8%
General Atlantic Singapore AI Pte. Ltd.(8)	4,782,441	8.8%

Notes:

- * For each person and group included in this table, percentage ownership is calculated by dividing the number of shares beneficially owned by such person or group by the sum of (i) 54,397,383 being the number of ordinary shares as of March 31, 2021 and (ii) the number of ordinary shares underlying share options held by such person or group that are exercisable within 60 days after March 31, 2021.
- ** Represents beneficial ownership of less than one percent.
- † The business address of our directors and executive officers, except for Fangyong (Felix) Du, Man Kin (Raymond) Tam, Daniel Auerbach, Chong Xu, Yunxia Yang, Yu Miao and Lefei Sun, is Center 2150, 315 Montgomery Street, 9th Floor, San Francisco CA 94104, United States of America. The business address of Fangyong (Felix) Du and Man Kin (Raymond) Tam is 4F, Building C14, No. 218, Xinghu Street, Suzhou Industrial Park, China 215123; the business address of Daniel Auerbach is Suite 2201, Level 22, Pacific Place Two, 88 Queensway, Admiralty, Hong Kong, the business address of Chong Xu is One Main Street, 13th Floor, Cambridge, MA 02142; the business address of Yunxia Yang is Room 3606, China Central Place Tower 3, 77 Jianguo Road, Beijing 100025, PRC, the business address of Yu Miao is Unit 4901, One Lujiazui, No.68, Yin Cheng(C) Rd., Shanghai 200120, PRC; and the business address of Lefei Sun is Suite 5704-5706, 57F, Two IFC, 8 Finance Street, Central, Hong Kong; the business address of Andy (Yiu Leung) Cheung is Queen's Terrace, Tower 1 51/F Unit D, 1 Queen Street, Sheungwan, Hong Kong.
- (1) Represents 10,518,217 ordinary shares held by Peter Luo act-in-concert group, as set forth in note (3) below.
- (2) Represents (i) 810,944 ordinary shares held by Ping Ren, who is the spouse of Fangyong (Felix) Du, (ii) 117,500 ordinary shares held by Great Han Fortune LP for the benefit of Ping Ren, (iii) 17,000 ordinary shares held by Great Han Fortune LP for the benefit of Ping Ren that are vested or will be vested within 60 days, (iv) 111,744 ordinary shares underlying 111,744 share options granted to Ping Ren that that are vested or will be vested within 60 days of March 31, 2021. Great Han Fortune LP is controlled by Peter Luo and is formed to hold ordinary shares in connection with the share awards issued under the 2019 Plan.
- (3) Represents (i) 7,783,488 ordinary shares held by HAN 2020 GRAT, for which Peter Luo is a Trustee, (ii) 287,415 ordinary shares underlying 287,415 share options granted to Peter Luo that that are vested or will be vested within 60 days of March 31, 2021, (iii) 116,667 ordinary shares held by Great Han Fortune LP for the benefit of Peter Luo and (iv) 83,333 ordinary shares held by Great Han Fortune LP for the benefit of Peter Luo that are vested or will be vested within 60 days; (v) 13,667 ordinary shares held by Peter Luo; (vi) 45,980 ordinary shares underlying 45,980 share options granted to Xiaohong She that are vested or will be vested within 60 days of March 31, 2021, (vii) 67,083 ordinary shares held by Great Han Fortune LP for the benefit of Xiaohong She, and (viii) 7,167 ordinary shares held by Great Han Fortune LP for the benefit of Xiaohong She that are vested or will be vested within 60 days; (ix) 2,278 ordinary shares held by Xiaohong She; (x) 1,057,188 ordinary shares and share options beneficially owned by Fangyong (Felix) Du, as set forth in note (2) above; (xi) total of 890,195 ordinary shares held by Raymond Tam and several key employees of the Company, and (xii) total of 163,756 share options granted to Raymond Tam, Hua Gong, JC Xu, Yu (Albert) Ren and several key employees that are vested or will be vested within 60 days of March 31, 2021. On December 14, 2020, Peter Luo, Fangyong (Felix) Du, Ping Ren, Hua Gong, JC Xu, Qinghai Zhao, Man Kin (Raymond) Tam, Xiaohong (Kristine) She, Yu (Albert) Ren, Yan Li, Guizhong Liu and Alexander Goergen entered into a concert party agreement, pursuant to which the parties agree to (i) always be acting in concert in respect of their respective direct or indirect voting rights at our shareholders' general meetings, (ii) recognize the controlling position of Peter Luo; and (iii) act in concert in accordance with Peter Luo's opinions in respect of the daily operations and management and the major decision-making of us.

- (4) Represents 5,353,242 ordinary shares held by JSR Limited, a British Virgin Islands company. JSR Limited is controlled by GP Healthcare Capital Co., Ltd. The registered address of JSR Limited is Vistra Corporate Services Centre, Wickhams Cay II, Road Town, Tortola, VG1110, British Virgin Islands.
- (5) Represents 4,826,037 ordinary shares held by Asia Ventures II L.P., a limited partnership incorporated in the Bermuda. The general partner of Asia Ventures II L.P. is Asia Partners II L.P. a Bermuda exempt limited partnership. The general partner of Asia Partners II L.P. is Eight Roads GP, who is ultimately controlled by Eight Roads Holdings Limited. The registered address of Asia Ventures II L.P. is Pembroke Hall, 42 Crow Lane, Pembroke, Bermuda HM 19.
- (6) Represents 4,826,037 ordinary shares held by F-Prime Capital Partners Healthcare Fund III LP. F-Prime Capital Partners Healthcare Advisors Fund III LP is the general partner of F-Prime Capital Partners Healthcare Fund III LP. F-Prime Capital Partners Healthcare Advisors Fund III LP is solely managed by Impresa Management LLC, its general partner and investment manager. Each of the entities listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The address of these entities is 245 Summer Street, Boston, MA 02210.
- (7) Represents (i) 4,706,946 ordinary shares and (ii) 650,000 ordinary shares in the form of ADSs held by Wuxi Pharmatech Healthcare Fund I L.P., a limited partnership incorporated in the Cayman Islands. WuXi Pharmatech Healthcare Fund I L.P. is an indirect wholly owned subsidiary of WuXi AppTec Co., Ltd (SSE: 603259; SEHK: 2359). WuXi AppTec Co., Ltd. is a listed company on the Shanghai Stock Exchange and the Main Board of the Hong Kong Stock Exchange. The registered address of WuXi Pharmatech Healthcare Fund I L.P. is P.O. Box 309, Uglan House, Grand Cayman, KY1-1104, Cayman Islands.
- (8) Represents 4,782,441 ordinary shares beneficially owned by General Atlantic Singapore AI Pte. Ltd., a company incorporated under the laws of Singapore. General Atlantic Singapore AI Pte. Ltd. is wholly-owned by General Atlantic Singapore Fund Pte. Ltd., which is controlled by General Atlantic Singapore Interholdco Ltd. The registered address of General Atlantic Singapore AI Pte. Ltd. is 80 Robinson Road, #02-00 Singapore 068898.

As of March 31, 2021, a total of 10,571,375 ordinary shares, representing 19.4% of our outstanding ordinary shares, are held by one record holder in the United States. The holder is the depository of our ADS program. In addition, 29.5% of our outstanding ordinary shares were held by record holders in the United States.

Our principal shareholders do not have different voting rights. We are not aware of any arrangement that may, at a subsequent date, result in a change of control of our company.

Item 7. Major Shareholders and Related Party Transactions

7.A. MAJOR SHAREHOLDERS

Please refer to “Item 6. Directors, Senior Management and Employees — E. Share Ownership.”

7.B. RELATED PARTY TRANSACTIONS

The following is a summary of transactions since January 1, 2018 to which we have been a participant in which any of our then directors, executive officers or holders of more than 5% of any class of our voting securities at the time of such transaction, or any members of their immediate family, had or will have a direct or indirect material interest.

Employment Agreements and Indemnification Agreements

See “Item 6 Directors, Senior Management and Employees—6.B. Compensation—Employment Agreements and Indemnification Agreements.”

Share Incentives

See “Item 6 Directors, Senior Management and Employees—6.B. Compensation—Share Incentive Plan.”

Other Related Party Transactions

Transactions with Peter Luo

Since November 2016, we had received subsidies from the local government for attracting highly skilled personnel on behalf of Peter Luo, our Chairman, CEO and shareholder. We settled this transaction by paying Peter Luo a total amount of US\$84.6 thousand, which corresponds to the total amount of subsidies, after deducting individual income tax, in January 2020.

Transactions with WuXi AppTec Group

We received research and development services from WuXi AppTec Group, the parent company of one of our principal shareholders. The amounts for the purchase of the services were US\$1.0 million, US\$2.1 million, and US\$2.7 million in 2018, 2019 and 2020, respectively. As of December 31, 2018, 2019 and 2020, the amounts due to WuXi AppTec Group were US\$0.2 million, US\$0.4 million and US\$0.2 million, respectively.

As of December 31, 2020, the amount due to WuXi AppTec Group was US\$174 thousand.

Transactions with WuXi Biologics (Shanghai) Co., Ltd. or WuXi Biologics

We received research and development services, including provision of manufacturing and quality control testing services, from WuXi Biologics, an entity controlled by the ultimate controlling party of one of our principal shareholders. The amounts for the purchase of the services were US\$6.5 million, US\$3.6 million and US\$7.2 million in 2018, 2019 and 2020, respectively. As of December 31, 2018, 2019 and 2020, the amounts due to WuXi Biologics were US\$3.4 million, US\$1.4 million and US\$2.4 million, respectively.

As of December 31, 2020, the amount due to WuXi Biologics was US\$2.4 million.

Director and Executive Officers

Exercise of Share Options

In October and November 2017, Dr. Peter (Peizhi) Luo, Xiaohong (Kristine) She and Dr. Fangyong (Felix) Du exercised their respective vested share options under the 2015 Plan. The payment for exercise of such share options is repaid in installments with nil interest. The aggregate exercise price for Dr. Luo, Ms. She and Dr. Du was US\$365.0 thousand, US\$67.4 thousand and US\$173.4 thousand, respectively. Each of Dr. Luo, Ms. She and Dr. Du has settled the payments for their respective exercise of such share options.

Promissory Notes

The following table sets forth the material terms of the promissory notes issued in connection with the share purchase plans between us and our directors and executive officers:

Name of Director or Executive Officer	Latest Amount Previously Outstanding
Peter (Peizhi) Luo	US\$4.2 million
Xiaohong (Kristine) She*	US\$0.6 million
Fangyong (Felix) Du	US\$1.5 million

Note:

Xiaohong (Kristine) She is the spouse of Dr. Peter (Peizhi) Luo

All promissory notes were made pursuant to our 2019 Plan. All amounts outstanding under the promissory notes have been settled. For further information, see “Item 6 Directors, Senior Management and Employees—Share Incentive Plan—Adagene Inc. Second Amended and Restated Share Incentive Plans—Repayment of the Promissory Notes.”

7.C. Interests of Experts and Counsel

Not applicable.

Item 8. Financial Information

8.A. Consolidated Statements and Other Financial Information

We have appended consolidated financial statements filed as part of this annual report.

Legal and Administrative Proceedings

As of the date of this annual report, we are not a party to any material legal or administrative proceedings. We may from time to time be subject to various legal or administrative claims and proceedings arising in the ordinary course of business. Litigation or any other legal or administrative proceeding, regardless of the outcome, is likely to result in a substantial cost and diversion to our resources, including our management’s time and attention. For risks relating to legal and administrative proceedings against us, please see “Item 3 Key Information—D. Risk Factors—Risks Relating to Our Operations—Allegations or lawsuits against us or our management may harm our reputation and business.”

Dividend Policy

We have not previously declared or paid cash dividends and we have no plan to declare or pay any dividends in the near future on our shares or the ADSs representing our ordinary shares. We currently intend to retain most, if not all, of our available funds and any future earnings to operate and expand our business.

We are a holding company incorporated in the Cayman Islands. In the future, we may rely on dividends from our subsidiaries, including our PRC subsidiary, for our cash requirements, including any payment of dividends to our shareholders. PRC regulations may restrict the ability of our PRC subsidiary to pay dividends to us. See “Item 4 Information of the Company—B. Business Overview—Regulation—Regulations relating to Dividend Distribution.”

Our board of directors has discretion as to whether to distribute dividends, subject to certain requirements of Cayman Islands law. In addition, our shareholders may, subject to the provisions of our post-offering articles of association, by ordinary resolution declare a dividend, but no dividend may exceed the amount recommended by our board of directors. Under Cayman Islands law, a Cayman Islands company may pay a dividend out of either profit or share premium account, provided that in no circumstances may a dividend be paid if this would result in the company being unable to pay its debts as they fall due in the ordinary course of business. Even if our board of directors decides to pay dividends, the form, frequency and amount will depend upon our future operations and earnings, capital requirements and surplus, general financial condition, contractual restrictions and other factors that the board of directors may deem relevant. If we pay any dividends on our ordinary shares, we will pay those dividends which are payable in respect of the ordinary shares underlying the ADSs to the depositary, as the registered holder of such ordinary shares, and the depositary then will pay such amounts to the ADS holders in proportion to the ordinary shares underlying the ADSs held by such ADS holders, subject to the terms of the deposit agreement, including the fees and expenses payable thereunder. See “Item 12 Description of Securities Other Than Equity Securities—D. American Depositary Shares.”

8.B. Significant Changes

Except as otherwise disclosed in this report, we have not experienced any significant changes since the date of the annual financial statements included herein.

Item 9. The Offer and Listing

9.A. Offering and Listing Details

Our ADSs have been listed on the Nasdaq Global Market since February 9, 2021 under the symbol “ADAG.” Each ADS represents one and one quarter ordinary shares, par value US\$0.0001 per share.

9.B. Plan of Distribution

Not applicable.

9.C. Markets

Our ADSs have been listed on the Nasdaq Global Market since February 9, 2021 under the symbol “ADAG.”

9.D. Selling Shareholders

Not applicable.

9.E. Dilution

Not applicable.

9.F. Expenses of the Issue

Not applicable.

Item 10. Additional Information

10.A. Share Capital

Not applicable.

10.B. Memorandum and Articles of Association

We are a Cayman Islands exempted company and our affairs are governed by our memorandum and articles of association, as amended and restated from time to time, and Companies Act of the Cayman Islands, and the common law of the Cayman Islands.

We incorporate by reference into this annual report our amended and restated memorandum and articles of association, the form of which was filed as [Exhibit 3.2 to our registration statement on Form F-1 \(File Number 333-252210\)](#), as amended, filed with the Securities and Exchange Commission on February 1, 2021. Our members adopted our amended and restated memorandum and articles of association by a special resolution on January 19, 2021, which became effective immediately prior to completion of our initial public offering of ADSs representing our ordinary shares.

The following are summaries of material provisions of our Seventh Amended and Restated Memorandum and Articles of Association and the Companies Act insofar as they relate to the material terms of our ordinary shares.

Registered Office and Objects

Our registered office in the Cayman Islands is at the offices of Vistra (Cayman) Limited, P. O. Box 31119 Grand Pavilion, Hibiscus Way, 802 West Bay Road, Grand Cayman, KY1 - 1205 Cayman Islands or at such other location as the Directors may from time to time determine.

According to Clause 3 of our Seventh Amended and Restated Memorandum of Association, the objects for which the Company is established are unrestricted and the Company shall have full power and authority to carry out any object not prohibited by any law as provided by Section 7(4) of the Companies Act (as amended) of the Cayman Islands.

Board of Directors

See "Item 6 Directors, Senior Management and Employees."

Ordinary shares

General. Our authorized share capital is US\$80,000 divided into 800,000,000 shares comprising (i) 640,000,000 ordinary shares of a par value of US\$0.0001 each, and (ii) 160,000,000 shares of a par value of US\$0.0001 each of such class or classes (however designated) as our board of directors may determine in accordance with our amended and restated memorandum and articles of association. Holders of ordinary shares will have the same rights. All of our issued and outstanding ordinary shares are fully paid and non-assessable. Certificates representing the ordinary shares are issued in registered form. We may not issue share to bearer. Our shareholders who are nonresidents of the Cayman Islands may freely hold, transfer and vote their ordinary shares.

Dividends. The holders of our ordinary shares are entitled to such dividends as may be declared by our board of directors subject to our post-offering memorandum and articles of association and the Companies Act. In addition, our shareholders may, subject to the provisions of our articles of association, by ordinary resolution declare a dividend, but no dividend may exceed the amount recommended by our directors. Our post-offering memorandum and articles of association provide that dividends may be declared and paid out of our profits, realized or unrealized, or from any reserve set aside from profits which our board of directors determine is no longer needed. Dividends may also be declared and paid out of the share premium account or any other fund or account which can be authorized for this purpose in accordance with the Companies Act. No dividend may be declared and paid unless our directors determine that, immediately after the payment, we will be able to pay our debts as they become due in the ordinary course of business and we have funds lawfully available for such purpose.

Voting Rights. In respect of all matters subject to a shareholders' vote, holder of an Ordinary Share is entitled to one vote for each Ordinary Share registered in his or her name on our register of members. Voting at any meeting of shareholders is by way of a poll unless a show of hands is permitted. A poll may be demanded by the chairman of such meeting or any one shareholder.

A quorum required for a meeting of shareholders consists of two or more shareholders holding not less than one-half of the votes attaching to the issued and outstanding shares entitled to vote at general meetings present in person or by proxy or, if a corporation or other non-natural person, by its duly authorized representative. As a Cayman Islands exempted company, we are not obliged by the Companies Act to call shareholders' annual general meetings. Our post-offering memorandum and articles of association provide that we may (but are not obliged to) in each year hold a general meeting as our annual general meeting in which case we will specify the meeting as such in the notices calling it, and the annual general meeting will be held at such time and place as may be determined by our board of directors. We, however, will hold an annual shareholders' meeting during each fiscal year, as required by the Listing Rules of the Nasdaq Global Market. Each general meeting, other than an annual general meeting, shall be an extraordinary general meeting. Shareholders' annual general meetings and any other general meetings of our shareholders may be called by a majority of our board of directors or our chairman or upon a requisition of shareholders holding at the date of deposit of the requisition not less than one-third of the votes attaching to the issued and outstanding shares entitled to vote at general meetings, in which case the directors are obliged to call such meeting and to put the resolutions so requisitioned to a vote at such meeting; however, our post-offering memorandum and articles of association do not provide our shareholders with any right to put any proposals before annual general meetings or extraordinary general meetings not called by such shareholders. Advance notice of at least seven (7) days is required for the convening of our annual general meeting and other general meetings in accordance with our post-offering memorandum and articles of association.

An ordinary resolution to be passed at a meeting by the shareholders requires the affirmative vote of a simple majority of the votes attaching to the ordinary shares cast by those shareholders entitled to vote who are present in person or by proxy at a general meeting, while a special resolution also requires the affirmative vote of no less than two-thirds of the votes attaching to the ordinary shares cast by those shareholders entitled to vote who are present in person or by proxy at a general meeting. A special resolution will be required for important matters such as a change of name or making changes to our post-offering memorandum and articles of association.

Transfer of Ordinary Shares. Subject to the restrictions in our post-offering memorandum and articles of association as set out below, any of our shareholders may transfer all or any of his or her ordinary shares by an instrument of transfer in the usual or common form or any other form approved by our board of directors.

Our board of directors may, in its absolute discretion, decline to register any transfer of any Ordinary Share. Our board of directors may also decline to register any transfer of any Ordinary Share unless:

- the instrument of transfer is lodged with us, accompanied by the certificate for the ordinary shares to which it relates and such other evidence as our board of directors may reasonably require to show the right of the transferor to make the transfer;
- the instrument of transfer is in respect of only one class of shares;
- the instrument of transfer is properly stamped, if required;
- in the case of a transfer to joint holders, the number of joint holders to whom the Ordinary Share is to be transferred does not exceed four;
- the shares are free from any lien in favor of us; and
- a fee of such maximum sum as the Nasdaq may determine to be payable or such lesser sum as our directors may from time to time require is paid to us in respect thereof.

If our directors refuse to register a transfer, they shall, within three months after the date on which the instrument of transfer was lodged, send to each of the transferor and the transferee notice of such refusal.

The registration of transfers may, after compliance with any notice requirement of the Nasdaq, be suspended and the register closed at such times and for such periods as our board of directors may from time to time determine, *provided, however*, that the registration of transfers shall not be suspended nor the register closed for more than 30 days in any year as our board may determine.

Liquidation. On a return of capital on winding up or otherwise (other than on conversion, redemption or purchase of ordinary shares), if the assets available for distribution amongst our shareholders shall be more than sufficient to repay the whole of the share capital at the commencement of the winding up, the surplus shall be distributed amongst our shareholders in proportion to the par value of the shares held by them at the commencement of the winding up, subject to a deduction from those shares in respect of which there are monies due, of all monies payable to our company for unpaid calls or otherwise. If our assets available for distribution are insufficient to repay all of the paid-up capital, the assets will be distributed so that the losses are borne by our shareholders in proportion to the par value of the shares held by them. Any distribution of assets or capital to a holder of ordinary shares will be the same in any liquidation event.

Calls on Ordinary Shares and Forfeiture of Ordinary Shares. Our board of directors may from time to time make calls upon shareholders for any amounts unpaid on their ordinary shares in a notice served to such shareholders at least 14 clear days prior to the specified time of payment. The ordinary shares that have been called upon and remain unpaid are subject to forfeiture.

Redemption, Repurchase and Surrender of Ordinary Shares. We may issue shares on terms that such shares are subject to redemption, at our option or at the option of the holders thereof, on such terms and in such manner as may be determined, before the issue of such shares, by our board of directors or by an ordinary resolution of our shareholders. Our company may also repurchase any of our shares provided that the manner and terms of such purchase have been approved by our board of directors or by an ordinary resolution of our shareholders, or are otherwise authorized by our post-offering memorandum and articles of association. Under the Companies Act, the redemption or repurchase of any share may be paid out of our company's profits or out of the proceeds of a fresh issue of shares made for the purpose of such redemption or repurchase, or out of capital (including share premium account and capital redemption reserve) if the Company can, immediately following such payment, pay its debts as they fall due in the ordinary course of business. In addition, under the Companies Act no such share may be redeemed or repurchased (a) unless it is fully paid up, (b) if such redemption or repurchase would result in there being no shares outstanding, or (c) if the company has commenced liquidation. In addition, our company may accept the surrender of any fully paid share for no consideration.

Variations of Rights of Shares. If at any time our share capital is divided into different classes or series of shares, the rights attached to any class or series of shares (unless otherwise provided by the terms of issue of the shares of that class or series), whether or not our company is being wound-up, may be varied with the consent in writing of holders of not less than a majority of the issued shares of that class or series or with the sanction of a special resolution at a separate meeting of the holders of the shares of the class or series. The rights conferred upon the holders of the shares of any class issued shall not, unless otherwise expressly provided by the terms of issue of the shares of that class, be deemed to be varied by the creation or issue of further shares ranking *pari passu* with such existing class of shares.

Inspection of Books and Records. Holders of our ordinary shares have no general right under Cayman Islands law to inspect or obtain copies of our list of shareholders or our corporate records. However, we will provide our shareholders with annual audited financial statements.

Issuance of Additional Shares. Our post-offering memorandum and articles of association authorizes our board of directors to issue additional ordinary shares from time to time as our board of directors shall determine, to the extent of available authorized but unissued shares.

Our post-offering memorandum and articles of association also authorizes our board of directors to establish from time to time one or more series of preferred shares and to determine, with respect to any series of preferred shares, the terms and rights of that series, including:

- the designation of the series;
- the number of shares of the series;
- the dividend rights, dividend rates, conversion rights, voting rights; and
- the rights and terms of redemption and liquidation preferences.

Our board of directors may issue preferred shares without action by our shareholders to the extent authorized but unissued. Issuance of these shares may dilute the voting power of holders of ordinary shares.

Anti-Takeover Provisions. Some provisions of our post-offering memorandum and articles of association may discourage, delay or prevent a change of control of our company or management that shareholders may consider favorable, including provisions that authorize our board of directors to issue preferred shares in one or more series and to designate the price, rights, preferences, privileges and restrictions of such preferred shares without any further vote or action by our shareholders.

Changes in Capital.

We may from time to time by ordinary resolution:

- increase the share capital by such sum, to be divided into shares of such classes and amount, as the resolution shall prescribe;

- consolidate and divide all or any of our share capital into shares of a larger amount than our existing shares;
- sub-divide our existing shares, or any of them into shares of a smaller amount; or
- cancel any shares which, at the date of the passing of the resolution, have not been taken or agreed to be taken by any person and diminish the amount of our share capital by the amount of the shares so canceled.

We may by special resolution, subject to any confirmation or consent required by the Companies Act, reduce our share capital or any capital redemption reserve in any manner permitted by law.

Exempted Company. We are an exempted company with limited liability under the Companies Act. The Companies Act distinguishes between ordinary resident companies and exempted companies. Any company that is registered in the Cayman Islands but conducts business mainly outside of the Cayman Islands may apply to be registered as an exempted company. The requirements for an exempted company are essentially the same as for an ordinary company except that an exempted company:

- does not have to file an annual return of its shareholders with the Registrar of Companies;
- is not required to open its register of members for inspection;
- does not have to hold an annual general meeting;
- may issue shares with no par value;
- may obtain an undertaking against the imposition of any future taxation (such undertakings are usually given for 30 years in the first instance);
- may register by way of continuation in another jurisdiction and be deregistered in the Cayman Islands;
- may register as a limited duration company; and
- may register as a segregated portfolio company.

“Limited liability” means that the liability of each shareholder is limited to the amount unpaid by the shareholder on that shareholder’s shares of the company.

10.C. Material Contracts

We have not entered into any material contracts other than in the ordinary course of business and other than those described in this annual report.

10.D. Exchange Controls

The Cayman Islands currently has no exchange control regulations or currency restrictions. For exchange control regulations or currency restrictions in China, see “Item 4 Information of the Company—B. Business Overview—Regulation—Regulations Relating to Foreign Exchange.”

10.E. Taxation

The following discussion of Cayman Islands, PRC and U.S. federal income tax consequences of the ownership and disposition of the ADSs or ordinary shares is based upon laws and relevant interpretations thereof in effect as of the date of this annual report, all of which are subject to change. This discussion does not deal with all possible tax consequences relating to the ownership and disposition of the ADSs or ordinary shares, such as the tax consequences under state, local and other tax laws. To the extent that the discussion relates to matters of Cayman Islands tax law, it represents the opinion of Walkers (Hong Kong), our Cayman Islands counsel. To the extent that the discussion relates to matters of PRC tax law, it represents the opinion of Tian Yuan Law Firm, our PRC legal counsel.

Cayman Islands Taxation

The Cayman Islands currently levies no taxes on individuals or corporations based upon profits, income, gains or appreciation, and there is no taxation in the nature of inheritance tax or estate duty. There are no other taxes likely to be material to us or holders of our ADSs or ordinary shares levied by the government of the Cayman Islands, except for stamp duties which may be applicable on instruments executed in, or after execution brought within the jurisdiction of the Cayman Islands. The Cayman Islands is not party to any double tax treaties that are applicable to any payments made to or by our company. There are no exchange control regulations or currency restrictions in the Cayman Islands.

Payments of dividends and capital in respect of the ADSs or ordinary shares will not be subject to taxation in the Cayman Islands and no withholding will be required on the payment of a dividend or capital to any holder of the ADSs or ordinary shares, nor will gains derived from the disposal of the ADSs or ordinary shares be subject to Cayman Islands income or corporation tax.

Material PRC Income Tax Considerations

Under the PRC EIT Law, which became effective on January 1, 2008 and was lastly amended on December 29, 2018, an enterprise established outside the PRC with “de facto management bodies” within the PRC is considered a “resident enterprise” for PRC enterprise income tax purposes and is generally subject to a uniform 25% enterprise income tax rate on its worldwide income. Under the implementation rules to the PRC EIT Law, a “de facto management body” is defined as a body that has material and overall management and control over the manufacturing and business operations, personnel and human resources, finances and properties of an enterprise.

In addition, the SAT Circular 82 issued by the SAT in April 2009 specifies that certain offshore incorporated enterprises controlled by PRC enterprises or PRC enterprise groups will be classified as PRC resident enterprises if the following are located or resident in the PRC: (a) senior management personnel and departments that are responsible for daily production, operation and management; (b) financial and personnel decision-making bodies; (c) key properties, accounting books, company seal, minutes of board meetings and shareholders’ meetings; and (d) half or more of the senior management or directors having voting rights. Further to SAT Circular 82, the SAT issued the SAT Bulletin 45, which took effect in September 2011, to provide more guidance on the implementation of SAT Circular 82. SAT Bulletin 45 provides for procedures and administration details of determination on resident status and administration on post-determination matters. Our company is a company incorporated outside the PRC. As a holding company, its key assets are its ownership interests in its subsidiaries, and its key assets are located, and its records (including the resolutions of its board of directors and the resolutions of its shareholders) are maintained, outside the PRC. As such, we do not believe that our company meets all of the conditions above or is a PRC resident enterprise for PRC tax purposes. For the similar reasons, we believe our other entities outside China are not PRC resident enterprises either. However, the tax resident status of an enterprise is subject to determination by the PRC tax authorities and uncertainties remain with respect to the interpretation of the term “de facto management body.” There can be no assurance that the PRC government will ultimately take a view that is consistent with us. If the PRC tax authorities determine that our Cayman Islands holding company is a PRC resident enterprise for PRC enterprise income tax purposes, a number of unfavorable PRC tax consequences could follow. For example, a 10% withholding tax would be imposed on dividends we pay to our non-PRC enterprise shareholders (including our ADS holders). In addition, nonresident enterprise shareholders (including our ADS holders) may be subject to PRC tax on gains realized on the sale or other disposition of ADSs or ordinary shares, if such income is treated as sourced from within the PRC. Furthermore, if we are deemed a PRC resident enterprise, dividends paid to our non-PRC individual shareholders (including our ADS holders) and any gain realized on the transfer of ADSs or ordinary shares by such shareholders may be subject to PRC tax at a rate of 20% (which, in the case of dividends, may be withheld at source by us). These rates may be reduced by an applicable tax treaty, but it is unclear whether in practice non-PRC shareholders of our company would be able to obtain the benefits of any tax treaties between their country of tax residence and the PRC in the event that we are treated as a PRC resident enterprise. See “Item 3 Key Information—D. Risk Factors—Risks Relating to Doing Business in the PRC—If we are classified as a PRC resident enterprise for PRC income tax purposes, such classification could result in unfavorable tax consequences to us and our non-PRC shareholders or ADS holders.”

Material U.S. Federal Income Tax Considerations

The following are material U.S. federal income tax consequences to the U.S. Holders described below of the ownership and disposition of the ADSs or ordinary shares. This discussion is not a comprehensive description of all of the tax considerations that may be relevant to your decision to acquire the ADSs or ordinary shares. This discussion applies to you only if you are a U.S. Holder and hold the ADSs or underlying ordinary shares as capital assets for U.S. federal income tax purposes. In addition, it does not describe all of the tax consequences that may be relevant in light of your particular circumstances, including the alternative minimum tax, the Medicare contribution tax on net investment income, and tax consequences applicable to you if you are subject to special rules, such as:

- one of certain financial institutions;
- a dealer or trader in securities that uses a mark-to-market method of tax accounting;
- a person holding ADSs or ordinary shares as part of a straddle, conversion transaction, integrated transaction or similar transaction;
- a person whose functional currency for U.S. federal income tax purposes is not the U.S. dollar;
- an entity classified as partnerships for U.S. federal income tax purposes (and investors therein);
- a tax-exempt entity, “individual retirement account” or “Roth IRA”;
- a person who acquired our ADSs or ordinary shares pursuant to the exercise of an employee stock option or otherwise as compensation;
- a person that owns or is deemed to own 10% or more of our stock by vote or value; or
- a person holding ADSs or ordinary shares in connection with a trade or business conducted outside the United States.

If you are a partnership for U.S. federal income tax purposes, the U.S. federal income tax consequences to your partners will generally depend on their status and your activities. Partnerships holding ADSs or ordinary shares and their partners should consult their tax advisers as to the particular U.S. federal income tax consequences of acquiring, owning or disposing of the ADSs or ordinary shares.

This discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, administrative pronouncements, judicial decisions and final, temporary and proposed Treasury regulations, and the income tax treaty between the United States and the PRC, or the Treaty, all as of the date hereof, any of which is subject to change, possibly with retroactive effect.

For purposes of this discussion, you are a “U.S. Holder” if for U.S. federal income tax purposes you are a beneficial owner of ADSs or ordinary shares and:

- a citizen or individual resident of the United States;
- a corporation or other entity taxable as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state therein or the District of Columbia; or
- an estate or trust the income of which is subject to U.S. federal income taxation regardless of its source.

In general, if you own ADSs you will be treated as the owner of the underlying ordinary shares represented by those ADSs for U.S. federal income tax purposes. Accordingly, no gain or loss will be recognized if you exchange ADSs for the underlying ordinary shares represented by those ADSs.

Taxation of Distributions

Except as described under “—*Passive Foreign Investment Company Rules*” below, distributions paid on ADSs or ordinary shares, other than certain pro rata distributions of ordinary shares, will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we do not maintain calculations of our earnings and profits under U.S. federal income tax principles, we expect that any distributions will be reported to you as dividends. Dividends will not be eligible for the dividends-received deduction generally available to United States corporations under the Code. Subject to applicable limitations, dividends paid on our ADSs to certain non-corporate U.S. Holders may be taxable at a favorable rate. Dividends will be included in your income on the date of your, or in the case of ADSs, the depository’s, receipt of the dividend. The amount of any dividend income paid in non-U.S. currency will be its U.S. dollar value calculated by reference to the spot rate in effect on the date of receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, you generally should not be required to recognize foreign currency gain or loss in respect of the dividend income. You may have foreign currency gain or loss, which will be United States source, if the dividend is converted into U.S. dollars after the date of receipt.

Dividends will be treated as foreign-source income for foreign tax credit purposes. As described in “—Material PRC Income Tax Considerations”, dividends paid by us may be subject to PRC withholding tax. For U.S. federal income tax purposes, the amount of the dividend income will include any amounts withheld in respect of PRC withholding tax. Subject to applicable limitations, which vary depending upon your circumstances, PRC taxes withheld from dividend payments (at a rate not exceeding the applicable rate provided in the Treaty) generally will be creditable against your U.S. federal income tax liability. The rules governing foreign tax credits are complex and you should consult your tax advisers regarding the creditability of foreign tax credits in your particular circumstances. In lieu of claiming a credit, you may elect to deduct PRC taxes in computing its taxable income, subject to applicable limitations. An election to deduct foreign taxes instead of claiming foreign tax credits must apply to all foreign taxes paid or accrued in the taxable year.

Sale or Other Disposition of ADSs or Ordinary Shares

Except as described under “—*Passive Foreign Investment Company Rules*” below, gain or loss realized on the sale or other taxable disposition of ADSs or ordinary shares will be capital gain or loss, and will be long-term capital gain or loss if you held the ADSs or ordinary shares for more than one year. The amount of the gain or loss will equal the difference between your tax basis in the ADSs or ordinary shares disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations.

As described in “—Material PRC Income Tax Considerations” gains on the sale of ADSs or ordinary shares may be subject to PRC taxes. You are entitled to use foreign tax credits to offset only the portion of your U.S. federal income tax liability that is attributable to foreign-source income. Because under the Code capital gains of U.S. persons are generally treated as U.S.-source income, this limitation may preclude you from claiming a credit for all or a portion of any PRC taxes imposed on any such gains. However, if you are eligible for the benefits of the Treaty, you may elect to treat the gain as PRC-source and therefore claim foreign tax credits in respect of PRC taxes on such disposition gains. You should consult your tax advisor regarding their eligibility for the benefits of the Treaty and the creditability of any PRC tax on disposition gains in your particular circumstances.

Passive Foreign Investment Company Rules

In general, a non-U.S. corporation will be a passive foreign investment company, or a PFIC, for any taxable year in which (i) 75% or more of its gross income consists of passive income, or the income test, or (ii) 50% or more of the average value of its assets (generally determined on a quarterly basis) consists of assets that produce, or are held for the production of, passive income, or the asset test. For purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the ordinary shares of another corporation is treated as if it held its proportionate share of the assets of the other corporation and received directly its proportionate share of the income of the other corporation. Passive income generally includes interest, dividends, gains from certain property transactions, rents and royalties (other than certain rents or royalties derived in the active conduct of a trade or business). Cash is a passive asset for PFIC purposes. Goodwill is an active asset under the PFIC rules to the extent attributable to activities that produce active income.

The assets shown on our balance sheet are expected to consist primarily of cash and cash equivalents for the foreseeable future. Therefore, whether we will satisfy the asset test for the current or any future taxable year will depend largely on the value of our goodwill and on how quickly we utilize the cash in our business. We cannot give any assurance as to whether we will be a PFIC for the current or any future taxable year because (i) the value of our goodwill may be determined by reference to the market price of our ADSs, which may be volatile given the nature and early stage of our business, (ii) we expect to hold a significant amount of cash, and (iii) a company’s PFIC status is an annual determination that can be made only after the end of each taxable year. In addition, prior to commercialization of our product candidates, we could be a PFIC for any taxable year in which our interest and other investment income constitutes 75% or more of our total gross income.

If we were a PFIC for any taxable year and any of our subsidiaries were also a PFIC (any such entity, a “Lower-tier PFIC “), you would be deemed to own a proportionate amount (by value) of the ordinary shares of each Lower-tier PFIC and would be subject to U.S. federal income tax according to the rules described in the subsequent paragraph on (i) certain distributions by a Lower-tier PFIC and (ii) dispositions of shares of Lower-tier PFICs, in each case as if you held your proportionate share of these shares directly, even though you will not receive the proceeds of those distributions or dispositions.

Generally, if we are a PFIC for any taxable year during which you own ADSs or ordinary shares, gain recognized upon a disposition (including, under certain circumstances, a pledge) of ADSs or ordinary shares will be allocated ratably over your holding period for the ADSs or ordinary shares. The amounts allocated to the taxable year of disposition and to years before we became a PFIC will be taxed as ordinary income. The amount allocated to each other taxable year will be subject to tax at the highest rate in effect for that taxable year for individuals or corporations, as appropriate, and an interest charge will be imposed on the resulting tax liability for each relevant taxable year. Further, to the extent that any distribution received by you on your ADSs or ordinary shares exceeds 125% of the average of the annual distributions on the ADSs or ordinary shares received during the preceding three years or your holding period, whichever is shorter, that distribution will be subject to taxation in the same manner.

If we are a PFIC for any taxable year during which you own ADSs or ordinary shares, we will generally continue to be treated as a PFIC with respect to you for all succeeding years during which you own ADSs or ordinary shares, even if we cease to meet the threshold requirements for PFIC status. If we are a PFIC for any taxable year but cease to be PFIC for subsequent years, you should consult your tax advisor regarding the availability of a “deemed sale” election that would allow you to eliminate the continuing PFIC status under certain circumstances.

Alternatively, if we are a PFIC and if our ADSs or ordinary shares are “regularly traded” on a “qualified exchange,” you may be able to make a mark-to-market election that would result in tax treatment different from the general tax treatment described in the preceding paragraphs. Our ADSs will be treated as “regularly traded” in any calendar year in which more than a *de minimis* quantity of the ADSs, as the case may be, are traded on a qualified exchange on at least 15 days during each calendar quarter. The Nasdaq Global Market, on which the ADSs expected to be listed, is a qualified exchange for this purpose. If you make the mark-to-market election, you generally will recognize as ordinary income any excess of the fair market value of the ADSs at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the ADSs over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If you make the election, your tax basis in the ADSs will be adjusted to reflect these income or loss amounts. Any gain recognized on the sale or other disposition of ADSs in a year in which we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election) and any remaining loss will be capital loss. There is no provision under U.S. federal income tax law that provides for a right to make a mark-to-market election with respect to any lower-tier PFICs that are not publicly traded.

We do not intend to provide the information that would otherwise enable you to make a “qualified electing fund election,” which would result in alternate treatment if we were a PFIC for any taxable year.

If you own ADSs or ordinary shares during any year in which we are a PFIC, you generally will be required to file annual reports on Internal Revenue Service Form 8621 (or any successor form) with respect to us. Additionally, if we are a PFIC for the taxable year in which we paid a dividend or the prior taxable year, the favorable rate discussed above with respect to dividends paid to certain non-corporate U.S. Holders would not apply. You should consult your tax adviser regarding our PFIC status for any taxable year and the potential application of the PFIC rules.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds from the sale or exchange of our ADSs or ordinary shares that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (i) you are a corporation or other exempt recipient or (ii) in the case of backup withholding, you provide a correct taxpayer identification number and certify that you are not subject to backup withholding. Backup withholding is not an additional tax. The amount of any backup withholding from a payment to you will be allowed as a credit against your U.S. federal income tax liability and may entitle you to a refund, provided that the required information is timely furnished to the Internal Revenue Service.

Certain U.S. Holders who are individuals (and certain specified entities) may be required to report information relating to their ownership of ordinary shares, or non-U.S. accounts through which ADSs or ordinary shares are held. You should consult your tax adviser regarding your reporting obligations with respect to the ADSs or ordinary shares.

10.F. Dividends and Paying Agents

Not applicable.

10.G. Statement by Experts

Not applicable.

10.H. Documents on Display

We previously filed with the SEC registration statement on Form F-1 (File Number 333-252210), as amended, including annual report contained therein, to register our ordinary shares in relation to our initial public offering. We also filed with the SEC related registration statement on Form F-6 (File Number 333-252543) to register the ADSs.

We are subject to the periodic reporting and other informational requirements of the Exchange Act as applicable to foreign private issuers. Under the Exchange Act, we are required to file reports and other information with the SEC. Specifically, we are required to file annually a Form 20-F within four months after the end of each fiscal year. Copies of reports and other information, when so filed with the SEC, can be inspected and copied at the public reference facilities maintained by the SEC at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents, upon payment of a duplicating fee, by writing to the SEC. The public may obtain information regarding the Washington, D.C. Public Reference Room by calling the Commission at 1-800-SEC-0330. The SEC also maintains a web site at www.sec.gov that contains reports, proxy and information statements, and other information regarding registrants that make electronic filings with the SEC using its EDGAR system. As a foreign private issuer, we are exempt from the rules of the Exchange Act prescribing the furnishing and content of quarterly reports and proxy statements, and our executive officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act.

We will furnish JPMorgan Chase Bank, N.A., the depository of our ADSs, with our annual reports, which will include a review of operations and annual audited consolidated financial statements, and all notices of shareholders' meetings and other reports and communications that are made generally available to our shareholders. The depository will make such notices, reports and communications available to holders of ADSs and, upon our request, will mail to all record holders of ADSs the information contained in any notice of a shareholders' meeting received by the depository from us.

10.I. Subsidiary Information

Not applicable.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest rate risk

Our exposure to interest rate risk primarily relates to the interest income generated by excess cash, which is mostly held in interest-bearing bank deposits. We have not used any derivative financial instruments to manage our interest risk exposure. Interest-earning instruments carry a degree of interest rate risk. We have not been exposed, nor do we anticipate being exposed, to material risks due to changes in interest rates. However, our future interest income may be lower than expected due to changes in market interest rates.

Foreign exchange risk

We are a global business enterprise with part of our operations based in the PRC. A part of our transactions were settled in Renminbi, and our financial statements are presented in U.S. dollars. We do not believe that we currently have any significant direct foreign exchange risk and have not used any derivative financial instruments to hedge our exposure to such risk. Although, in general, our exposure to foreign exchange risks should be limited, the value of your investment in the ADSs will be affected by the exchange rate between U.S. dollar and Renminbi because a portion of value of our business is effectively denominated in Renminbi, while the ADSs representing our ordinary shares will be traded in U.S. dollars.

The value of the Renminbi against the U.S. dollar and other currencies is affected by changes in China's political and economic conditions and by China's foreign exchange policies, among other things. In July 2005, the PRC government changed its decades-old policy of pegging the value of the Renminbi to the U.S. dollar, and the Renminbi appreciated more than 20% against the U.S. dollar over the following three years. Between July 2008 and June 2010, this appreciation subsided and the exchange rate between the Renminbi and the U.S. dollar remained within a narrow band. Since June 2010, the Renminbi has fluctuated against the U.S. dollar, at times significantly and unpredictably. While appreciating approximately by 7% against the U.S. dollar in 2017, the Renminbi in 2018 depreciated approximately by 5% against the U.S. dollar. Since October 1, 2016, the Renminbi has joined the International Monetary Fund (IMF)'s basket of currencies that make up the Special Drawing Right (SDR), along with the U.S. dollar, the Euro, the Japanese yen and the British pound. With the development of the foreign exchange market and progress towards interest rate liberalization and Renminbi internationalization, the PRC government may in the future announce further changes to the exchange rate system and there is no guarantee that the RMB will not appreciate or depreciate significantly in value against the U.S. dollar in the future. It is difficult to predict how market forces or PRC or U.S. government policy may impact the exchange rate between the Renminbi and the U.S. dollar in the future.

To the extent that we need to convert U.S. dollars into Renminbi for our operations, appreciation of Renminbi against the U.S. dollar would reduce the Renminbi amount we receive from the conversion. Conversely, if we decide to convert Renminbi into U.S. dollars for the purpose of making payments for dividends on our ordinary shares or ADSs, servicing our outstanding debt, or for other business purposes, appreciation of the U.S. dollar against the Renminbi would reduce the U.S. dollar amounts available to us.

Inflation risk

Since our inception, inflation in China has not materially impacted our results of operations. According to the National Bureau of Statistics of China, the year-over-year percent changes in the consumer price index for December 2019 and 2020 were increases of 2.9% and 2.5%, respectively. Although we have not in the past been materially affected by inflation since our inception, we can provide no assurance that we will not be affected in the future by higher rates of inflation in China.

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

12.A. Debt Securities

Not applicable.

12.B. Warrants and Rights

Not applicable.

12.C. Other Securities

Not applicable.

12.D. American Depositary Shares

Fees and Expense

The depositary may charge each person to whom ADSs are issued, including, without limitation, issuances against deposits of shares, issuances in respect of share distributions, rights and other distributions, issuances pursuant to a stock dividend or stock split declared by us or issuances pursuant to a merger, exchange of securities or any other transaction or event affecting the ADSs or deposited securities, and each person surrendering ADSs for withdrawal of deposited securities or whose ADRs are cancelled or reduced for any other reason, \$5.00 for each 100 ADSs (or any portion thereof) issued, delivered, reduced, cancelled or surrendered, or upon which a share distribution or elective distribution is made or offered, as the case may be. The depositary may sell (by public or private sale) sufficient securities and property received in respect of a share distribution, rights and/or other distribution prior to such deposit to pay such charge.

The following additional charges shall also be incurred by the ADR holders, the beneficial owners, by any party depositing or withdrawing shares or by any party surrendering ADSs and/or to whom ADSs are issued (including, without limitation, issuance pursuant to a stock dividend or stock split declared by us or an exchange of stock regarding the ADSs or the deposited securities or a distribution of ADSs), whichever is applicable:

- a fee of U.S.\$1.50 per ADR or ADRs for transfers of certificated or direct registration ADRs;
- a fee of U.S.\$0.05 or less per ADS held for any cash distribution made, or for any elective cash/ stock dividend offered, pursuant to the deposit agreement;
- an aggregate fee of U.S.\$0.05 or less per ADS per calendar year (or portion thereof) for services performed by the depositary in administering the ADRs (which fee may be charged on a periodic basis during each calendar year and shall be assessed against holders of ADRs as of the record date or record dates set by the depositary during each calendar year and shall be payable in the manner described in the next succeeding provision);
- a fee for the reimbursement of such fees, charges and expenses as are incurred by the depositary and/or any of its agents (including, without limitation, the custodian and expenses incurred on behalf of ADR holders in connection with compliance with foreign exchange control regulations or any law or regulation relating to foreign investment) in connection with the servicing of the shares or other deposited securities, the sale of securities (including, without limitation, deposited securities), the delivery of deposited securities or otherwise in connection with the depositary's or its custodian's compliance with applicable law, rule or regulation (which fees and charges shall be assessed on a proportionate basis against ADR holders as of the record date or dates set by the depositary and shall be payable at the sole discretion of the depositary by billing such ADR holders or by deducting such charge from one or more cash dividends or other cash distributions);
- a fee for the distribution of securities (or the sale of securities in connection with a distribution), such fee being in an amount equal to the \$0.05 per ADS issuance fee for the execution and delivery of ADSs which would have been charged as a result of the deposit of such securities (treating all such securities as if they were shares) but which securities or the net cash proceeds from the sale thereof are instead distributed by the depositary to those ADR holders entitled thereto;
- stock transfer or other taxes and other governmental charges;
- cable, telex and facsimile transmission and delivery charges incurred at your request in connection with the deposit or delivery of shares, ADRs or deposited securities;
- transfer or registration fees for the registration of transfer of deposited securities on any applicable register in connection with the deposit or withdrawal of deposited securities; and

- fees of any division, branch or affiliate of the depositary utilized by the depositary to direct, manage and/or execute any public and/or private sale of securities under the deposit agreement.

To facilitate the administration of various depositary receipt transactions, including disbursement of dividends or other cash distributions and other corporate actions, the depositary may engage the foreign exchange desk within JPMorgan Chase Bank, N.A. (the “Bank”) and/or its affiliates in order to enter into spot foreign exchange transactions to convert foreign currency into U.S. dollars. For certain currencies, foreign exchange transactions are entered into with the Bank or an affiliate, as the case may be, acting in a principal capacity. For other currencies, foreign exchange transactions are routed directly to and managed by an unaffiliated local custodian (or other third party local liquidity provider), and neither the Bank nor any of its affiliates is a party to such foreign exchange transactions.

The foreign exchange rate applied to a foreign exchange transaction will be either (a) a published benchmark rate, or (b) a rate determined by a third party local liquidity provider, in each case plus or minus a spread, as applicable. The depositary will disclose which foreign exchange rate and spread, if any, apply to such currency on the “Disclosures” page (or successor page) of ADR.com. Such applicable foreign exchange rate and spread may (and neither the depositary, the Bank nor any of their affiliates is under any obligation to ensure that such rate does not) differ from rates and spreads at which comparable transactions are entered into with other customers or the range of foreign exchange rates and spreads at which the Bank or any of its affiliates enters into foreign exchange transactions in the relevant currency pair on the date of the foreign exchange transaction. Additionally, the timing of execution of a foreign exchange transaction varies according to local market dynamics, which may include regulatory requirements, market hours and liquidity in the foreign exchange market or other factors. Furthermore, the Bank and its affiliates may manage the associated risks of their position in the market in a manner they deem appropriate without regard to the impact of such activities on the depositary, us, holders or beneficial owners. *The spread applied does not reflect any gains or losses that may be earned or incurred by the Bank and its affiliates as a result of risk management or other hedging related activity.*

Notwithstanding the foregoing, to the extent we provide U.S. dollars to the depositary, neither the Bank nor any of its affiliates will execute a foreign exchange transaction as set forth herein. In such case, the depositary will distribute the U.S. dollars received from us.

Further details relating to the applicable foreign exchange rate, the applicable spread and the execution of foreign exchange transactions will be provided by the depositary on ADR.com. Each holder and beneficial owner by holding or owning an ADR or ADS or an interest therein, and we, each acknowledge and agree that the terms applicable to foreign exchange transactions disclosed from time to time on ADR.com will apply to any foreign exchange transaction executed pursuant to the deposit agreement.

We will pay all other charges and expenses of the depositary and any agent of the depositary (except the custodian) pursuant to agreements from time to time between us and the depositary.

The right of the depositary to receive payment of fees, charges and expenses survives the termination of the deposit agreement, and shall extend for those fees, charges and expenses incurred prior to the effectiveness of any resignation or removal of the depositary.

The fees and charges described above may be amended from time to time by agreement between us and the depositary.

The depositary may make available to us a set amount or a portion of the depositary fees charged in respect of the ADR program or otherwise upon such terms and conditions as we and the depositary may agree from time to time. The depositary collects its fees for issuance and cancellation of ADSs directly from investors depositing shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions, or by directly billing investors, or by charging the book-entry system accounts of participants acting for them. The depositary will generally set off the amounts owing from distributions made to holders of ADSs. If, however, no distribution exists and payment owing is not timely received by the depositary, the depositary may refuse to provide any further services to ADR holders that have not paid those fees and expenses owing until such fees and expenses have been paid. At the discretion of the depositary, all fees and charges owing under the deposit agreement are due in advance and/or when declared owing by the depositary.

Payments by Depositary

Our depositary anticipates to reimburse us for certain expenses we incur in respect of the ADR program established pursuant to the Deposit Agreement, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as the Depositary agrees with us from time to time. As of the date of this annual report, we have not received such reimbursement from the depositary.

PART II

ITEM 13. ITEM DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

None.

ITEM 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

14.A. — 14.D. Material Modifications to the Rights of Security Holders

See “Item 10 Additional Information” for a description of the rights of shareholders, which remain unchanged.

14.E. Use of Proceeds

The following “Use of Proceeds” information relates to the registration statement on Form F-1, as amended (File No. 333- 252210) in relation to our initial public offering, which was declared effective by the SEC on February 8, 2021. In February 2021, we completed our initial public offering in which we issued and sold an aggregate of 8,457,100 ADSs, representing 10,571,375 ordinary shares, resulting in net proceeds to us of approximately US\$145.9 million, net of the underwriting discounts and commissions and other fees paid or payable by us in connection with the offering.

The F-1 Registration Statement was declared effective by the SEC on February 8, 2021. The total expenses incurred for our company’s account in connection with our initial public offering was approximately US\$14.8 million, which included US\$11.2 million in underwriting discounts and commissions for the initial public offering and approximately US\$3.6 million in other costs and expenses for our initial public offering. We received net proceeds of approximately US\$145.9 million from our initial public offering. None of the transaction expenses included payments to directors or officers of our company or their associates, persons owning more than 10% or more of our equity securities or our affiliates. None of the net proceeds from the initial public offering were paid, directly or indirectly, to any of our directors or officers or their associates, persons owning 10% or more of our equity securities or our affiliates.

We still intend to use the remainder of the proceeds from our initial public offering as disclosed in our registration statements on Form F-1.

ITEM 15. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has performed an evaluation of the effectiveness of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act) as of the end of the period covered by this report, as required by Rule 13a-15(b) under the Exchange Act.

Based upon that evaluation, our management has concluded that, due to the material weaknesses identified below, as of December 31, 2020, our disclosure controls and procedures were not effective in ensuring that the information required to be disclosed by us in the reports that we file or submit under the Exchange Act was recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms, and that the information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, to allow timely decisions regarding required disclosure.

Management’s Annual Report on Internal Control Over Financial Reporting

This annual report on Form 20-F does not include a report of management’s assessment regarding internal control over financial reporting due to a transition period established by rules of the SEC for newly public companies.

Attestation Report of the Registered Public Accounting Firm

This annual report on Form 20-F does not include an attestation report of our registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Internal Control Over Financial Reporting

In the course of preparing the audit of our consolidated financial statements as of December 31, 2019 and 2020 and for each of the three years in the period ended December 31, 2020, our independent registered public accounting firm identified two material weaknesses in our internal control over financial reporting as of December 31, 2019 and 2020. As defined in standards established by the PCAOB, a “material weakness” is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis.

The two material weaknesses that have been identified related to:

- Our lack of sufficient and competent financial reporting and accounting personnel with appropriate knowledge of U.S. GAAP and SEC reporting and compliance requirements; and
- Our lack of sufficient documented financial closing policies and procedures, specifically those related to period end expenses cut-off and accruals.

Such material weaknesses, if not timely remedied, may lead to significant misstatements in our consolidated financial statements in the future.

To remediate our identified material weakness, we are in the process of adopting several measures to improve our internal control over financial reporting, including (i) hiring more qualified accounting personnel, with relevant U.S. GAAP and SEC reporting experience and qualifications to strengthen the financial reporting function and setting up a financial and system control framework; (ii) implementing regular and continuous U.S. GAAP accounting and financial reporting training programs for our accounting and financial reporting personnel; and (iii) preparing comprehensive accounting policies, manuals and closing procedures to improve the quality and accuracy of our period-end financial closing process.

We expect that we will incur significant costs in the implementation of such measures. However, we cannot assure you that all these measures will be sufficient to remediate our material weakness in time, or at all. See “Item 3 Key Information—D. Risk factors—Risks Relating to Our Operations—If we fail to implement and maintain an effective system of internal controls, we may be unable to accurately or timely report our results of operations or prevent fraud, and investor confidence and the market price of our ADSs may be materially and adversely affected.”

Changes in Internal Control over Financial Reporting

Except as described above, there were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the period covered by this annual report on Form 20-F that have materially affected, or that are reasonably likely to materially affect, our internal control over financial reporting.

Item 16.A. Audit Committee Financial Expert

Our Board of Directors has determined that Mr. Andy (Yiu Leung) Cheung, an independent director and the chairperson of our audit committee, qualifies as an “audit committee financial expert” within the meaning of the SEC rules and in accordance with applicable Nasdaq Global Market standards. Mr. Andy (Yiu Leung) Cheung satisfies the “independence” requirements of Rule 10A-3 under the Securities Exchange Act of 1934, as amended, and the applicable Nasdaq Global Market standards.

Item 16.B. Code of Ethics

Our Board of Directors has adopted a code of business conduct and ethics that applies to all of our directors, officers, employees, including certain provisions that specifically apply to our principal executive officer, principal financial officer, principal accounting officer or controller and any other persons who perform similar functions for us. We have filed our code of business conduct and ethics as Exhibit 99.1 of our registration statement on Form F-1 (File No. 333- 252210), as amended, filed with the SEC on January 19, 2021 and posted a copy of our code of business conduct and ethics on our website at <http://investor.adagene.com>. We hereby undertake to provide to any person without charge, a copy of our code of business conduct and ethics within ten working days after we receive such person’s written request.

Item 16.C. Principal Accountant Fees and Services**Auditor Fees**

The following table sets forth the aggregate fees by categories specified below in connection with certain professional services rendered by PricewaterhouseCoopers Zhong Tian LLP, our independent registered public accounting firm, for the periods indicated.

	Year Ended December 31,	
	2019	2020
	RMB	RMB
	(in thousands)	
Services		
Audit Fees(1)	0	7,300
Audit-Related Fees(2)	0	0
Tax Fees(3)	0	0
Other Fees(4)	0	0
Total	0	7,300

- (1) *Audit Fees.* Audit fees mean the aggregate fees billed in each of the fiscal periods listed for professional services rendered by our principal auditors for the audit of our annual consolidated financial statements and assistance with and review of documents filed with the SEC.
- (2) *Audit-related Fees.* Audit-related fees mean the aggregate fees billed for professional services rendered by our principal auditors for the assurance and related services, which were not included under Audit Fees above.
- (3) *Tax Fees.* Tax fees mean fees incurred from professional services related to tax compliance.
- (4) *Other Fees.* Other fees mean fees incurred from professional services related to training, advisory and assurance for corporate and social responsibility reporting and professional services related to tax advice.

The policy of our audit committee is to pre-approve all audit and non-audit services provided by PricewaterhouseCoopers Zhong Tian LLP, our independent registered public accounting firm, including audit services and audit-related services as described above, other than those for de minimis services which are approved by the audit committee prior to the completion of the audit.

16.D. Exemptions from the Listing Standards for Audit Committees

Not applicable.

16.E. Purchases of Equity Securities by the Issuer and Affiliated Purchasers

Neither we nor any “affiliated purchaser,” as defined in Rule 10b-18(a)(3) of the Exchange Act, purchased any of our equity securities during the period covered by this annual report.

16.F. Change in Registrant’s Certifying Accountant

Not applicable.

16.G. Corporate Governance

Rule 5635(c) of the Nasdaq Rules requires a Nasdaq-listed company to obtain its shareholders' approval of all equity compensation plans, including stock plans, and any material amendments to such plans. Rule 5615 of the Nasdaq Rules permits a foreign private issuer like our company to follow home country practice in certain corporate governance matters. Currently, we currently intend to follow Cayman Islands corporate governance practices in lieu of the corporate governance requirements of the Nasdaq Rules that listed companies must have a majority of independent directors and establish a nominating committee and a compensation committee composed entirely of independent directors. To the extent that we choose to follow home country practice in the future, our shareholders may be afforded less protection than they otherwise would under the Nasdaq Global Market corporate governance listing standards applicable to U.S. domestic issuers. See "Item 3 Key Information—D. Risk Factors—Risks Relating to the ADSs—As a company incorporated in the Cayman Islands, we are permitted to adopt certain home country practices in relation to corporate governance matters that differ significantly from the Nasdaq Stock Market corporate governance listing standards; these practices may afford less protection to shareholders than they would enjoy if we complied fully with the Nasdaq Stock Market corporate governance listing standards."

16.H. Mine Safety Disclosure

Not applicable.

PART III**ITEM 17. FINANCIAL STATEMENTS**

We have elected to provide financial statements pursuant to Item 18.

ITEM 18. FINANCIAL STATEMENTS

Our consolidated financial statements are included at the end of this annual report.

ITEM 19. EXHIBITS

<u>Exhibit Number</u>	<u>Description of Document</u>
1.1	Seventh Amended and Restated Memorandum and Articles of Association of the Registrant, as currently effective (incorporated by reference to Exhibit 3.2 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
2.1	Form of Registrant's Specimen American Depositary Receipt ((incorporated by reference to Exhibit 4.3 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021))
2.2	Registrant's Specimen Certificate for Ordinary Shares (incorporated by reference to Exhibit 4.2 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
2.3	Form of Deposit Agreement between the Registrant, the depository and holders of the American Depositary Shares (incorporated by reference to Exhibit 4.3 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
2.4	Fifth Amended and Restated Shareholders Agreement by and among Adagene Inc. and shareholders of Adagene Inc. named therein dated December 19, 2019 (incorporated by reference to Exhibit 4.4 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
2.5*	Description of Registrant's Securities
4.1	Fourth Amended and Restated Right of First Refusal and Co-Sale Agreement by and between Adagene Inc., non-investor shareholders and investors named therein dated December 19, 2019 (incorporated by reference to Exhibit 4.5 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.2	Adagene Inc. Second Amended and Restated Share Incentive Plan (incorporated by reference to Exhibit 10.1 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.3	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers (incorporated by reference to Exhibit 10.2 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.4	Form of Employment Agreement between the Registrant and an executive officer of the Registrant (incorporated by reference to Exhibit 10.3 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.5	Shares Purchase Agreement by and among Adagene Inc., its subsidiaries and General Atlantic Singapore AI Pte. Ltd. dated October 15, 2019 (incorporated by reference to Exhibit 10.4 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.6	Shares Purchase Agreement by and among Adagene Inc., its subsidiaries and certain investors of Adagene Inc. named therein dated June 9, 2019 (incorporated by reference to Exhibit 10.5 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)

<u>Exhibit Number</u>	<u>Description of Document</u>
4.7	Shares Purchase Agreement by and among Adagene Inc., its subsidiaries and certain investors of Adagene Inc. named therein dated February 2, 2018 (incorporated by reference to Exhibit 10.6 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.8	English translation of Cooperation Agreement on the PD-L1 Project by and among Guilin Sanjin Pharmaceutical Co., Ltd. and its affiliates and Adagene (Suzhou) Limited dated December 2018 (incorporated by reference to Exhibit 10.7 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.9	English translation of Cooperation Agreement on International Interests of PD-L1 Project between Guilin Sanjin Pharmaceutical Co., Ltd. and Adagene Inc. dated December 2018 (incorporated by reference to Exhibit 10.8 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.10	English translation of Cooperation Agreement on the Undisclosed Project between Dragon Boat Biopharmaceutical (Shanghai) Limited and Adagene (Suzhou) Limited dated May 2019 (incorporated by reference to Exhibit 10.9 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.11	English translation of Cooperation Agreement on International Interests of Undisclosed Project between Dragon Boat Biopharmaceutical (Shanghai) Limited and Adagene Inc. dated May 2019 (incorporated by reference to Exhibit 10.10 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.12	Material Transfer and Collaboration Agreement between ADC Therapeutics SA and Adagene Inc. dated April 11, 2019 (incorporated by reference to Exhibit 10.11 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.13	License Agreement Among ADC Therapeutics SA and Adagene Inc. dated April 11, 2019 (incorporated by reference to Exhibit 10.12 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.14	Adagene Inc. 2021 Performance Incentive Plan (incorporated by reference to Exhibit 10.13 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
4.15	Collaboration and License Agreement between Exelixis, Inc. and Adagene Incorporated dated February 1, 2021 (incorporated by reference to Exhibit 10.14 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
8.1	List of subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
11.1	Code of Business Conduct and Ethics of the Registrant (incorporated by reference to Exhibit 99.1 from our registration statement on Form F-1 (File No. 333-252210), as amended, initially filed publicly with the SEC on January 19, 2021)
12.1*	Certification by Principal Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
12.2*	Certification by Principal Accounting Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
13.1**	Certification by Principal Executive Officer Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
13.2**	Certification by Principal Accounting Officer Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

<u>Exhibit Number</u>	<u>Description of Document</u>
15.1*	Consent of Tian Yuan Law Firm
15.2*	Consent of Walkers (Hong Kong)
15.3*	Consent of PricewaterhouseCoopers Zhong Tian LLP, Independent Registered Public Accounting Firm
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith

** Furnished herewith

SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing its annual report on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

Date: April 28, 2021

Adagene Inc.

By: /s/ PETER (PEIZHI) LUO

Name: Peter (Peizhi) Luo

Title: *Chief Executive Officer*

ADAGENE INC.

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Adagene Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Adagene Inc. and its subsidiaries (the “Company”) as of December 31, 2020 and 2019, and the related consolidated statements of comprehensive loss, of changes in shareholders’ deficit and of cash flows for each of the three years in the period ended December 31, 2020, including the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers Zhong Tian LLP

Shanghai, the People’s Republic of China
April 28, 2021

We have served as the Company’s auditor since 2020.

ADAGENE INC.
CONSOLIDATED BALANCE SHEETS
AS OF DECEMBER 31, 2019 AND 2020

	Notes	As of December 31	
		2019 US\$	2020 US\$
ASSETS			
Current assets:			
Cash and cash equivalents		92,532,788	75,150,998
Short-term investments		8,000,000	—
Accounts receivable, net	3	480,000	—
Amounts due from related parties	13	1,433,186	132,396
Prepayments and other current assets	4	1,476,973	3,813,984
Total current assets		103,922,947	79,097,378
Property, equipment and software, net	5	1,879,325	2,067,125
Other non-current assets		87,227	3,098,234
TOTAL ASSETS		105,889,499	84,262,737
LIABILITIES, MEZZANINE EQUITY AND SHAREHOLDERS' DEFICIT			
Current liabilities:			
Accounts payable		712,714	1,809,975
Contract liabilities		993,378	725,536
Amounts due to related parties	13	1,895,779	2,535,358
Accruals and other current liabilities	6	2,540,164	6,059,497
Warrant liabilities	8	—	—
Short-term borrowings	7	716,723	3,831,476
Current portion of long-term borrowings	7	322,525	1,183,926
Total current liabilities		7,181,283	16,145,768
Long-term borrowings	7	1,515,868	2,965,563
Other non-current liabilities		—	91,955
TOTAL LIABILITIES		8,697,151	19,203,286
Commitments and contingencies	14		
LIABILITIES, MEZZANINE EQUITY AND SHAREHOLDERS' DEFICIT (CONTINUED)			
Mezzanine equity:	8		
Series A-1 convertible redeemable preferred shares (par value of US\$0.0001 per share; 5,473,957 and 5,473,957 shares authorized, issued and outstanding as of December 31, 2019 and 2020, respectively)		5,473,957	5,473,957
Series A-2 convertible redeemable preferred shares (par value of US\$0.0001 per share; 2,370,414 and 2,370,414 shares authorized, issued and outstanding as of December 31, 2019 and 2020, respectively)		3,000,000	3,000,000
Series B convertible redeemable preferred shares (par value of US\$0.0001 per share; 7,494,537 and 7,494,537 shares authorized, issued and outstanding as of December 31, 2019 and 2020, respectively)		27,999,995	27,999,995
Series C-1 convertible redeemable preferred shares (par value of US\$0.0001 per share; 5,597,354 and 5,597,354 shares authorized, issued and outstanding as of December 31, 2019 and 2020, respectively)		48,727,343	48,975,456
Series C-2 convertible redeemable preferred shares (par value of US\$0.0001 per share; 1,861,121 and 1,861,121 shares authorized, issued and outstanding as of December 31, 2019 and 2020, respectively)		18,999,999	18,999,999
Series C-3 convertible redeemable preferred shares (par value of US\$0.0001 per share; 4,452,441 and 4,452,441 shares authorized, issued and outstanding as of December 31, 2019 and 2020, respectively)		50,000,000	50,000,000
Total mezzanine equity		154,201,294	154,449,407
Shareholders' deficit:			
Ordinary shares (par value of US\$0.0001 per share; 500,000,000 and 500,000,000 shares authorized; 15,193,136 shares issued and outstanding as of December 31, 2019; 18,888,070 shares issued and 16,603,070 shares outstanding as of December 31, 2020)		1,519	1,889
Subscriptions receivable from shareholders		(197,068)	(7,172,192)
Additional paid-in capital		6,789,542	23,786,652
Accumulated other comprehensive loss		(344,894)	(350,981)
Accumulated deficit		(63,258,045)	(105,655,324)
Total shareholders' deficit		(57,008,946)	(89,389,956)
TOTAL LIABILITIES, MEZZANINE EQUITY AND SHAREHOLDERS' DEFICIT		105,889,499	84,262,737

The accompanying notes are an integral part of these consolidated financial statements.

ADAGENE INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
FOR THE YEARS ENDED DECEMBER 31, 2018, 2019 AND 2020

	Notes	For the years ended December 31,		
		2018 US\$	2019 US\$	2020 US\$
Revenues				
Licensing revenue	10	1,511,168	480,000	700,913
Expenses				
Research and development expenses		(16,080,560)	(16,211,750)	(33,538,035)
Third parties		(8,575,969)	(10,507,444)	(23,645,740)
Related parties		(7,504,591)	(5,704,306)	(9,892,295)
Administrative expenses		(2,765,134)	(3,437,900)	(10,314,536)
Loss from operations		(17,334,526)	(19,169,650)	(43,151,658)
Interest income		710,711	922,680	629,288
Interest expense		(91,085)	(138,096)	(202,165)
Other income		901,713	723,476	971,949
Foreign exchange gain, net		12,698	21,867	(644,693)
Change in fair value of warrant liabilities		534,305	1,207,415	—
Loss before income tax		(15,266,184)	(16,432,308)	(42,397,279)
Income tax expense	11	—	—	—
Net loss attributable to Adagene Inc.'s shareholders		(15,266,184)	(16,432,308)	(42,397,279)
Other comprehensive income (loss)				
Foreign currency translation adjustments, net of nil tax		(11,288)	65,799	(6,087)
Total comprehensive loss attributable to Adagene Inc.'s shareholders		(15,277,472)	(16,366,509)	(42,403,366)
Net loss attributable to Adagene Inc.'s shareholders		(15,266,184)	(16,432,308)	(42,397,279)
Deemed contribution from convertible redeemable preferred shareholders	8	1,186,187	—	—
Accretion of convertible redeemable preferred shares to redemption value	8	(222,846)	(246,184)	(248,113)
Net loss attributable to ordinary shareholders		(14,302,843)	(16,678,492)	(42,645,392)
Weighted average number of ordinary shares used in per share calculation:				
—Basic	12	15,159,136	15,178,232	15,950,698
—Diluted	12	15,159,136	15,178,232	15,950,698
Net loss per ordinary share				
—Basic	12	(0.94)	(1.10)	(2.67)
—Diluted	12	(0.94)	(1.10)	(2.67)

The accompanying notes are an integral part of these consolidated financial statements.

ADAGENE INC.
CONSOLIDATED STATEMENTS OF CHANGES IN SHAREHOLDERS' DEFICIT
FOR THE YEARS ENDED DECEMBER 31, 2018, 2019 AND 2020

	Ordinary shares		Subscriptions receivable from shareholders US\$	Additional paid-in capital US\$	Accumulated other comprehensive loss US\$	Accumulated deficit US\$	Total shareholders' deficit US\$
	Number of shares	Amount US\$					
Balance as of January 1, 2018	15,159,136	1,516	(197,068)	7,687,811	(399,405)	(32,745,740)	(25,652,886)
Net loss	—	—	—	—	—	(15,266,184)	(15,266,184)
Other comprehensive loss	—	—	—	—	(11,288)	—	(11,288)
Share-based compensation	—	—	—	126,540	—	—	126,540
Modification of convertible redeemable preferred shares	—	—	—	(1,186,187)	—	1,186,187	—
Accretion of convertible redeemable preferred shares to redemption value	—	—	—	(222,846)	—	—	(222,846)
Balance as of December 31, 2018	15,159,136	1,516	(197,068)	6,405,318	(410,693)	(46,825,737)	(41,026,664)
Net loss	—	—	—	—	—	(16,432,308)	(16,432,308)
Other comprehensive income	—	—	—	—	65,799	—	65,799
Exercise of share options (Note 9)	34,000	3	—	18,697	—	—	18,700
Share-based compensation	—	—	—	611,711	—	—	611,711
Accretion of convertible redeemable preferred shares to redemption value	—	—	—	(246,184)	—	—	(246,184)
Balance as of December 31, 2019	15,193,136	1,519	(197,068)	6,789,542	(344,894)	(63,258,045)	(57,008,946)
Net loss	—	—	—	—	—	(42,397,279)	(42,397,279)
Other comprehensive income	—	—	—	—	(6,087)	—	(6,087)
Exercise of share options (Note 9)	3,694,934	370	(6,975,124)	7,115,682	—	—	140,928
Share-based compensation	—	—	—	10,129,541	—	—	10,129,541
Accretion of convertible redeemable preferred shares to redemption value	—	—	—	(248,113)	—	—	(248,113)
Balance as of December 31, 2020	18,888,070	1,889	(7,172,192)	23,786,652	(350,981)	(105,655,324)	(89,389,956)

The accompanying notes are an integral part of these consolidated financial statements.

ADAGENE INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
FOR THE YEARS ENDED DECEMBER 31, 2018, 2019 AND 2020

	For the years ended		
	2018	2019	2020
	US\$	US\$	US\$
Cash flows from operating activities:			
Net loss	(15,266,184)	(16,432,308)	(42,397,279)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	909,002	816,686	858,408
Gain on disposal of property, equipment and software	(846)	(1,841)	327
Share-based compensation	126,540	611,711	10,129,541
Change in fair value of warrant liabilities	(534,305)	(1,207,415)	—
Foreign exchange gain, net	(12,698)	(21,867)	644,693
Changes in operating assets and liabilities:			
Accounts receivable, net	—	(480,000)	480,000
Prepayments and other current assets	(1,337,063)	111,516	(2,337,011)
Amount due from related parties	268,671	(704,253)	1,300,790
Other non-current assets	(28,808)	(38,040)	(13,292)
Accounts payable	389,124	153,737	1,097,261
Contract liabilities	—	993,378	(267,842)
Amount due to related parties	2,135,397	(1,778,469)	639,579
Accruals and other current liabilities	(913,495)	(34,277)	1,243,150
Other non-current liabilities	—	(142,114)	91,955
Net cash used in operating activities	(14,264,665)	(18,153,556)	(28,529,720)
Cash flows from investing activities:			
Placement of short-term investments	(58,000,000)	(19,000,000)	—
Withdrawal of short-term investments	29,000,000	44,000,000	8,000,000
Proceeds from disposal of property, equipment and software	5,166	7,697	7,930
Purchase of property, equipment and software	(514,703)	(151,829)	(935,199)
Net cash (used in) generated from investing activities	(29,509,537)	24,855,868	7,072,731
Cash flows from financing activities:			
Proceeds from borrowings	2,417,868	2,651,874	6,083,650
Proceeds from issuance of convertible redeemable preferred shares and warrants	50,000,033	68,999,999	—
Proceeds from exercise of share options	—	459,796	140,928
Repayment of borrowings	(1,360,051)	(2,417,192)	(1,063,670)
Payment of initial public offering costs	—	—	(721,532)
Net cash generated from financing activities	51,057,850	69,694,477	4,439,376
Effect of exchange rate on cash and cash equivalents	38,703	77,544	(364,177)
Net increase (decrease) in cash and cash equivalents	7,322,351	76,474,333	(17,381,790)
Cash and cash equivalents at the beginning of year	8,736,104	16,058,455	92,532,788
Cash and cash equivalents at the end of year	16,058,455	92,532,788	75,150,998
Supplemental cashflow disclosures:			
Interest paid	91,085	142,058	202,165
Non-cash activities:			
Accretion of convertible redeemable preferred shares to redemption value	222,846	246,184	248,113
Deemed contribution from convertible redeemable preferred shareholders	1,186,187	—	—
Payables for deferred initial public offering cost	—	—	2,276,183

The accompanying notes are an integral part of these consolidated financial statements.

ADAGENE INC.
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS
FOR THE YEARS ENDED DECEMBER 31, 2018, 2019 AND 2020

1. ORGANIZATION AND BASIS OF PRESENTATION

Adagene Inc. (the “Company”) is a limited liability company incorporated in the Cayman Islands on February 25, 2011. The Company, together with its subsidiaries (collectively, the “Group”) are principally engaged in research, development and production of monoclonal antibody drugs for cancers.

As of December 31, 2020, the Company’s principal subsidiaries are as follows:

Entity	Date of incorporation	Place of incorporation	Percentage of legal ownership by the Company	Principal activities
Adagene (Hong Kong) Limited	December 12, 2011	Hong Kong	100%	Investment holding
Adagene Incorporated	September 20, 2017	The United States of America	100%	Research and development of innovative medicines
Adagene (Suzhou) Limited	February 28, 2012	The People’s Republic of China (“PRC” or “China”)	100%	Research and development of innovative medicines
Adagene Australia PTY Ltd.	May 30, 2018	Australia	100%	Research and development of innovative medicines
Adagene PTE. Ltd.	March 27, 2020	Singapore	100%	Research and development of innovative medicines
Adagene AG	August 31, 2020	Switzerland	100%	Research and development of innovative medicines

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of presentation

The accompany consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles (“U.S. GAAP”).

Principles of Consolidation

The consolidated financial statements of the Group include the financial statements of the Company and its subsidiaries. All significant intercompany balances and transactions have been eliminated upon consolidation.

Use of estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosures of contingent assets and liabilities at the balance sheet dates and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in the Group’s consolidated financial statements include, but are not limited to, the useful lives and impairment of long-lived assets, tax valuation allowance, share-based compensation expenses and the fair value of warrant liabilities. Management bases the estimates on historical experience and various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results could materially differ from those estimates.

Foreign currency translation

The functional currency of the Company, Adagene (Hong Kong) Limited, Adagene Incorporated and Adagene PTE. Ltd. is the United States dollar (“US\$”). The functional currency of the Company’s PRC subsidiary is Renminbi (“RMB”). The functional currency of the Company’s Australia subsidiary is Australian dollar (“AUS\$”). The functional currency of the Company’s Switzerland subsidiary is Swiss Franc (“CHF”). The determination of the respective functional currency is based on the criteria stated in Accounting Standard Codification (“ASC”) 830, *Foreign Currency Matters*. The Company uses US\$ as its reporting currency. The financial statements of the Company’s PRC, Australia and Switzerland subsidiaries are translated from the functional currency to the reporting currency.

Transactions denominated in foreign currencies are remeasured into the functional currency at the exchange rates quoted by the People's Bank of China (the "PBOC") prevailing on the transaction dates. Monetary assets and liabilities denominated in foreign currencies are re-measured at the exchange rates prevailing at the balance sheet date. Non-monetary items that are measured in terms of historical costs in foreign currency are re-measured using the exchange rates at the dates of the initial transactions. Exchange gains and losses are included in the consolidated statements of comprehensive loss.

Assets and liabilities are translated at the exchange rates at the balance sheet date, equity accounts are translated at historical exchange rates and revenues, expenses, gains and losses are translated using the average rate for the year. Translation adjustments are reported as accumulated comprehensive loss and are shown as a separate component of other comprehensive loss in the consolidated statements of comprehensive loss.

Cash and cash equivalents

Cash and cash equivalents primarily consist of cash and demand deposits which are highly liquid. The Group considers highly liquid investments that are readily convertible to known amounts of cash and with original maturities from the date of purchase of three months or less to be cash equivalents. All cash and cash equivalents are unrestricted as to withdrawal and use.

Short-term investments

Short-term investments are deposits at bank with maturities of greater than three months, but less than twelve months. Short-term investments are stated at cost, which approximates fair value. Interest earned is included in interest income.

Accounts receivable and allowance for doubtful accounts

Account receivable is recorded when the Group has an unconditional right to consideration. A right to consideration is unconditional if only the passage of time is required before payment of that consideration is due. Accounts receivable are carried at net realizable value. An allowance for doubtful accounts is recorded in the period when collection of the amount is no longer probable. In evaluating the collectability of receivable balances, the Group considers specific evidence including the aging of the receivable, the customer's payment history, its current credit-worthiness and other factors. Accounts receivable are written off when management determines a balance is uncollectable after all collection efforts have ceased.

Fair value measurements

The Group applies ASC 820, *Fair Value Measurements and Disclosures*. ASC 820 defines fair value, establishes a framework for measuring fair value and expands disclosures about fair value measurements. ASC 820 requires disclosures to be provided for fair value measurements. ASC 820 establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1—Observable inputs that reflect quoted prices (unadjusted) for identical assets or liabilities in active markets.

Level 2—Includes other inputs that are directly or indirectly observable in the marketplace.

Level 3—Unobservable inputs which are supported by little or no market activity.

ASC 820 describes three main approaches to measuring the fair value of assets and liabilities: (1) market approach; (2) income approach; and (3) cost approach. The market approach uses prices and other relevant information generated from market transactions involving identical or comparable assets or liabilities. The income approach uses valuation techniques to convert future amounts to a single present value amount. The measurement is based on the value indicated by current market expectations about those future amounts. The cost approach is based on the amount that would currently be required to replace an asset.

The carrying amounts of cash and cash equivalent, short-term investments, accounts receivable, amounts due to related parties and other current assets, accounts payable, amounts due to related parties, accrued liabilities and other current liabilities and short-term borrowings approximate their fair values because of their generally short maturities. The carrying amount of long-term borrowings approximate their fair values since they bear interest rates which approximate market interest rates.

As more fully described in Note 8, the Group issued warrants to two Series C-1 preferred shareholders to purchase its preferred shares. The warrants have expired on April 1, 2019. The Group measured its warrant liabilities at fair value on a recurring basis. As the Group's warrants are not traded in an active market with readily observable prices, the Group uses significant unobservable inputs to measure the fair value of warrant liabilities. These instruments are categorized in the Level 3 valuation hierarchy based on the significance of unobservable factors in the overall fair value measurement.

The following table presents a reconciliation of all financial instruments measured at fair value on a recurring basis using Level 3 unobservable inputs:

	<u>Warrant liabilities</u> US\$
Initial recognition during the year ended December 31, 2018	1,741,720
Fair value change	(534,305)
Balance as of December 31, 2018	1,207,415
Fair value change	(1,207,415)
Balance as of December 31, 2019	—

The Group did not transfer any assets or liabilities in or out of Level 3 during the years ended December 31, 2018, 2019 and 2020.

The Group had no financial assets and liabilities measured and recorded at fair value on a nonrecurring basis as of December 31, 2019 and 2020.

Property, equipment and software

Property and equipment and software are stated at cost less accumulated depreciation and amortization. Depreciation and amortization is computed using the straight-line method over the estimated useful lives of the assets as follows:

<u>Category</u>	<u>Estimated Useful Life</u>
Machinery and laboratory equipment	5 years
Vehicles	4 years
Furniture and tools	3 - 5 years
Electronic equipment	3 years
Computer software	3 - 5 years
Leasehold improvements	Lesser of lease terms or estimated useful lives of the assets

Repair and maintenance costs are charged to expense as incurred, whereas the cost of renewals and betterments that extend the useful lives of property, equipment and software are capitalized as additions to the related assets. Retirements, sales and disposals of assets are recorded by removing the cost and accumulated depreciation and amortization from the asset and accumulated depreciation and amortization accounts with any resulting gain or loss reflected in the consolidated statements of comprehensive loss.

Impairment of long-lived assets

The Group evaluates the recoverability of its long-lived assets, including fixed assets and intangible assets with finite lives, for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be fully recoverable. When these events occur, the Group measures impairment by comparing the carrying amount of the assets to the estimated undiscounted future cash flows expected to result from the use of the assets and their eventual disposition. If the sum of the expected undiscounted cash flows is less than the carrying amount of the assets, the Group recognizes an impairment loss based on the excess of the carrying amount of the assets over their fair value. Fair value is generally determined by discounting the cash flows expected to be generated by the assets, when the market prices are not readily available. The adjusted carrying amount of the assets is the new cost basis and is depreciated over the assets' remaining useful lives. Long-lived assets are grouped with other assets and liabilities at the lowest level for which identifiable cash flows are largely independent of the cash flows of other assets and liabilities.

No impairment loss was recorded for the years ended December 31, 2019 and 2020.

Segment reporting

In accordance with ASC 280, *Segment Reporting*, the Group's chief operating decision maker ("CODM") has been identified as the Chief Executive Officer. The Group's CODM reviews the consolidated results of operations when making decisions about allocating resources and assessing performance of the Group. The Group operates and manages its business as a single segment. No geographical segments are presented as substantially all of the Group's long-lived assets are located in the PRC.

Revenue recognition

At contract inception of collaboration and out-licensing arrangements, the Group analyzes its arrangements to assess whether they are within the scope of ASC 808, *Collaborative Arrangements* ("ASC 808") to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, the Group first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are reflective of a vendor-customer relationship and therefore within the scope of ASC 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently. Under the criteria of Accounting Standard Codification ("ASC") 606, *Revenue from Contracts with Customers* (Topic 606) ("ASC 606"), the Group recognizes revenue to depict the transfer of control of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to receive in exchange for those goods or services.

The Group adopted ASC 606 for all periods presented. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Group only applies the five-step model to contracts when it is probable that the entity will collect substantially all the consideration to which it is entitled in exchange for the goods or services it transfers to the customer. The Group reviews the contract to determine which performance obligations are distinct and represent a promise to provide distinct goods or services or a series of distinct goods or services as defined by the standard. The Group recognizes as revenue the amount of the transaction price that is allocated to each performance obligation as and when that performance obligation is satisfied.

Licenses of Intellectual Property: Upfront non-refundable payments for licensing the Group's intellectual property are evaluated to determine if the license is distinct from the other performance obligations identified in the arrangement. For licenses determined to be distinct, the Group recognizes revenues from non-refundable, up-front fees allocated to the license at a point in time, when the transfer of control of the license to the licensee occurs and the licensee is able to use and benefit from the license.

Milestone Payments: At the inception of each arrangement that includes development, commercialization, and regulatory milestone payments, the Group evaluates whether the milestones are considered probable of being reached and to the extent that a significant reversal of cumulative revenue would not occur in future periods, estimates the amount to be included in the transaction price using the most likely amount method. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Group recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Group re-evaluates the probability of achieving such development milestones and any related constraint, and if necessary, adjust the estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Group recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

To date, no milestone payments or royalty payments were received. Substantially all of the Group's revenue has been derived from its out-licensing agreements with respect to licensed products such as DNA sequences, cell lines, etc., and such revenues are recognized when the customer obtains control of the licensed product, which occurs at a point in time, upon delivery to the customer.

Contract assets and contract liabilities

When a customer pays consideration before the Group transfers products or services, the Group records its obligation as a contract liability; When the Group satisfies its performance obligations by providing products or services to a customer before the customer pays consideration and before payment is due, the Group recognizes its rights to consideration as a contract asset.

Research and development expenses

Elements of research and development expenses primarily include (1) payroll and other related costs of personnel engaged in research and development activities, (2) costs related to pre-clinical testing of the Group's technologies under development and clinical trials such as payments to contract research organizations ("CRO") and contract manufacturing organizations ("CMO"), investigators and clinical trial sites that conduct the clinical studies; (3) costs to develop the product candidates, including raw materials and supplies, product testing, depreciation and amortization, and facility related expenses, (4) other research and development expenses. Research and development expenses are charged to expense as incurred when these expenditures relate to the Group's research and development services and have no alternative future uses. As of December 31, 2020, the Group has several ongoing clinical studies in various clinical trial stages. The contracts with CRO and CMO are generally cancellable, with notice, at the Group's option. The Group did not record any accrued expenses related to cancellation of CRO or CMO contracts as of December 31, 2020 as the Group did not have any plan to cancel the existing CRO or CMO contracts.

Government subsidies

Government subsidies primarily consist of financial subsidies received from provincial and local governments for operating a business in their jurisdictions and compliance with specific policies promoted by the governments. The Group's PRC based subsidiary received government subsidies from certain local government. The Group's government subsidies consist of specific subsidies and other subsidies. Specific subsidies are subsidies that the local government has set certain conditions for the subsidies. Other subsidies are the subsidies that the local government has not set any conditions and are not tied to future trends or performance of the Group, receipt of such subsidy income is not contingent upon any further actions or performance of the Group and the amounts do not have to be refunded under any circumstances. The Group recorded specific subsidies as other non-current liabilities when received and recognized as other income when the conditions are met. Other subsidies are recognized as other income upon receipt as further performance by the Group is not required.

Leases

Leases are classified at the inception date as either a capital lease or an operating lease. The Group assesses a lease to be a capital lease if any of the following conditions exists: a) ownership is transferred to the lessee by the end of the lease term, b) there is a bargain purchase option, c) the lease term is at least 75% of the property's estimated remaining economic life or d) the present value of the minimum lease payments at the beginning of the lease term is 90% or more of the fair value of the leased property to the lessor at the inception date. A capital lease is accounted for as if there was an acquisition of an asset and an incurrence of an obligation at the inception of the lease.

All other leases are accounted for as operating leases wherein rental payments are expensed on a straight-line basis over their respective lease terms. The Group leases certain office space under non-cancelable operating lease agreements. Certain lease agreements contain rent holidays. Rent holidays are considered in determining the straight-line rent expense to be recorded over the lease term. The lease term begins on the date of initial possession of the leased property for purpose of recognizing lease expense on straight-line basis over the term of the lease.

Comprehensive loss

Comprehensive loss is defined as the changes in equity of the Group during a period from transactions and other events and circumstances excluding transactions resulting from investments by shareholders and distributions to shareholders. Accumulated other comprehensive loss of the Group includes foreign currency translation adjustments related to the Group and its subsidiaries whose functional currency is not US\$.

Income taxes

The Group follows the liability method of accounting for income taxes in accordance with ASC 740, *Income Taxes* (“ASC 740”). Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and tax bases of assets and liabilities using enacted tax rates that will be in effect in the period in which the differences are expected to reverse. The Group records a valuation allowance to offset deferred tax assets if based on the weight of available evidence, it is more likely than not that some portion, or all, of the deferred tax assets will not be realized. The effect on deferred taxes of a change in tax rate is recognized in tax expense in the period that includes the enactment date of the change in tax rate.

The Group evaluates its uncertain tax positions using the provisions of ASC 740, which prescribes a recognition threshold that a tax position is required to meet before being recognized in the consolidated financial statements.

The Group recognizes in the consolidated financial statements the benefit of a tax position which is “more likely than not” to be sustained under examination based solely on the technical merits of the position assuming a review by tax authorities having all relevant information. Tax positions that meet the recognition threshold are measured using a cumulative probability approach, at the largest amount of tax benefit that has a greater than fifty percent likelihood of being realized upon settlement. It is the Group’s policy to recognize interest and penalties related to unrecognized tax benefits, if any, as a component of income tax expense.

Borrowings

Borrowings are recognized initially at fair value, net of transaction costs incurred. Borrowings are subsequently stated at amortized cost; any difference between the proceeds (net of transaction costs) and the redemption value is recognized in the consolidated statements of comprehensive loss over the period of the borrowings using the effective interest method.

Share-based compensation

The Company grants restricted shares and stock options to eligible employees and nonemployees and accounts for share-based compensation in accordance with ASC 718, *Compensation—Stock Compensation*.

Share-based compensation awards are measured at the grant date fair value of the awards and recognized as expenses a) immediately at the grant date if no vesting conditions are required; or b) for share-based awards granted with only service conditions, using the straight-line method over the vesting period; or c) for share-based awards granted with service conditions and performance conditions, using the graded vesting method over the vesting period if and when the company concludes that it is probable that the performance conditions will be achieved.

A change in any of the terms or conditions of share-based awards is accounted for as a modification of the awards. The Group calculates incremental compensation expense of a modification as the excess of the fair value of the modified awards over the fair value of the original awards immediately before its terms are modified at the modification date. For vested awards, the Group recognizes incremental compensation cost in the period when the modification occurs. For awards not being fully vested, the Group recognizes the sum of the incremental compensation expense and the remaining unrecognized compensation expense for the original awards over the remaining requisite service period after modification.

Net loss per share

In accordance with ASC 260, *Earnings Per Share*, basic net loss per share is computed by dividing net loss attributable to ordinary shareholders by the weighted average number of unrestricted ordinary shares outstanding during the year using the two-class method. Under the two-class method, net loss is allocated between ordinary shares and other participating securities based on dividends declared (or accumulated) and participating rights in undistributed earnings as if all the earnings for the reporting period had been distributed. The Company’s convertible redeemable preferred shares are participating securities because they are entitled to receive dividends or distributions on an as converted basis. Diluted net loss per share is calculated by dividing net loss attributable to ordinary shareholders, as adjusted for the effect of dilutive ordinary equivalent shares, if any, by the weighted average number of ordinary and dilutive ordinary equivalent shares outstanding during the period. Ordinary equivalent shares include ordinary shares issuable upon the conversion of the convertible redeemable preferred shares using the if-converted method, and ordinary shares issuable upon the exercise of share options, using the treasury stock method. Ordinary share equivalents are excluded from the computation of diluted earnings per share if their effects are anti-dilutive. For the periods presented herein, the computation of basic net loss per share using the two-class method is not applicable as the Group is in a net loss position and the participating securities do not have contractual rights and obligations to share in the losses of the Group.

Employee defined contribution plan

As stipulated by the regulations of the PRC, full-time employees of the Group are entitled to staff welfare benefits including medical care, welfare subsidies, unemployment insurance and pension benefits through a PRC government-mandated multi-employer defined contribution plan. The Group is required to accrue for these benefits based on certain percentages of the qualified employees' salaries. The Group is required to make contributions to the plans out of the amounts accrued. The PRC government is responsible for the medical benefits and the pension liability to be paid to these employees and the Group's obligations are limited to the amounts contributed. The Group has no further payment obligations once the contributions have been paid. The Group recorded employee benefit expenses of US\$1,145,165 and US\$622,377 for the years ended December 31, 2019 and 2020, respectively.

Concentration of risks

Concentration of credit risk

As of December 31, 2019 and 2020, the aggregate amount of cash and cash equivalents and short-term investments of US\$801,923 and US\$3,424,456 respectively, were held at major financial institutions located in the mainland of China, and US\$99,730,865 and US\$71,726,542, respectively, were deposited with major financial institutions located outside the mainland of China. Management believes that these financial institutions are of high credit quality and continually monitors the credit worthiness of these financial institutions.

Accounts receivable are typically unsecured and denominated in US\$ and are derived from revenues earned from customers. The Group manages credit risk of accounts receivable through ongoing monitoring of the outstanding balances.

Concentration of suppliers

A significant portion of the Group's research and development services were purchased from its one supplier, who collectively accounted for 23.13% and 21.51% of the Group's total research and development services purchases for the years ended December 31, 2019 and 2020, respectively.

Business and economic risk

The Group believes that changes in any of the following areas could have a material adverse effect on the Group's future consolidated financial position, results of operations or cash flows: changes in the overall demand for services; competitive pressures due to new entrants; advances and new trends in new technologies and industry standards; changes in certain strategic relationships; regulatory considerations and risks associated with the Group's ability to attract employees necessary to support its growth. The Group's operations could also be adversely affected by significant political, regulatory, economic and social uncertainties in the PRC.

Foreign currency exchange rate risk

A significant portion of the Group's businesses are transacted in RMB, which is not a freely convertible currency. On January 1, 1994, the PRC government abolished the dual rate system and introduced a single rate of exchange as quoted daily by the People's Bank of China (the "PBOC"). However, the unification of the exchange rates does not imply that the RMB may be readily convertible into US\$ or other foreign currencies. All foreign exchange transactions continue to take place either through the PBOC or other banks authorized to buy and sell foreign currencies at the exchange rates quoted by the PBOC. Approval of foreign currency payments by the PBOC or other institutions requires submitting a payment application form together with suppliers' invoices, shipping documents and signed contracts.

From July 21, 2005, the RMB is permitted to fluctuate within a narrow and managed band against a basket of certain foreign currencies. For U.S. dollar against RMB, there was appreciation and depreciation of approximately 1.3% and 6.5% in the years ended December 31, 2019 and 2020, respectively. It is difficult to predict how market forces or PRC or U.S. government policy may impact the exchange rate between the RMB and the U.S. dollar in the future.

The functional currency and the reporting currency of the Company are the US\$. However, large portion of the expenses of the Group are denominated in RMB. Any significant fluctuation of the valuation of RMB may materially affect the Group's cash flows, expenses, losses and financial position, and the value of any dividends payable on the American Depositary Shares in US\$.

Recently issued accounting pronouncements

The Group is an emerging growth company ("EGC") as defined by the Jumpstart Our Business Startups Act ("JOBS Act"). The JOBS Act provides that an EGC can take advantage of extended transition periods for complying with new or revised accounting standards. This allows an EGC to delay adoption of certain accounting standards until those standards would otherwise apply to private companies. The Group elected to take advantage of the extended transition periods. However, this election will not apply should the Group cease to be classified as an EGC.

In February 2016, the FASB issued ASU No. 2016-02 ("ASU 2016-02"), Leases (Topic 842), which modifies lease accounting for lessees to increase transparency and comparability by recording lease assets and liabilities for operating leases and disclosing key information about leasing arrangements. In July 2018, the FASB issued ASU No. 2018-10 ("ASU 2018-10"), Codification Improvements to Topic 842, Leases, which clarifies certain aspects of the guidance issued in ASU 2016-02; and ASU No. 2018-11 ("ASU 2018-11"), Leases (Topic 842): Targeted Improvements, which provides entities with an additional (and optional) transition method to adopt the new leases standard. Under this new transition method, an entity initially applies the new leases standard at the adoption date and recognizes a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption. Consequently, an entity's reporting for the comparative periods presented in the financial statements in which it adopts the new leases standard will continue to be in accordance with current GAAP (Topic 840, Leases). Further, the FASB issued ASU No. 2020-05 ("ASU 2020-05"), Revenue from Contracts with Customers (Topic 606) and Leases (Topic 842): Effective Dates for Certain Entities, which extends the adoption date for certain entities. For the Group, the updated guidance is effective for fiscal years beginning after December 15, 2021 and interim periods within fiscal years beginning after December 15, 2022. Early adoption is permitted. The Group does not plan to early adopt the new lease standards and the Group expects that applying the ASU 2016-02 would materially increase the assets and liabilities due to the recognition of right-of-use assets and lease liabilities on its consolidated balance sheets, with an immaterial impact on its consolidated statements of comprehensive loss and consolidated statements of cash flows.

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments ("ASU 2016-13"). ASU 2016-13 is intended to improve financial reporting by requiring timelier recording of credit losses on loans and other financial instruments held by financial institutions and other organizations. This ASU requires the measurement of all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions, and reasonable and supportable forecasts. This ASU requires enhanced disclosures to help investors and other financial statement users better understand significant estimates and judgments used in estimating credit losses, as well as the credit quality and underwriting standards of the Group's portfolio. These disclosures include qualitative and quantitative requirements that provide additional information about the amounts recorded in the financial statements. In November 2019, the FASB issued ASU 2019-10, which extends the adoption date for certain registrants. The amendments in ASU 2016-13 are effective for fiscal years beginning after December 15, 2022, including interim periods within fiscal years beginning after December 15, 2023. The Group does not plan to early adopt ASU 2016-13 and is currently in the process of evaluating the impact of adoption of this guidance on its consolidated financial statements.

In June 2018, the FASB issued ASU No. 2018-07, Compensation—Stock Compensation (Topic 718): Improvements to nonemployee share-based payment accounting ("ASU 2018-07"). The amendments in this update expand the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. The amendments are effective for fiscal years beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020. Early adoption is permitted, but no earlier than an entity's adoption date of Topic 606. The Group adopted on January 1, 2018 this guidance which do not have a significant impact on the consolidated financial statements.

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement ("ASU 2018-13"). ASU 2018-13 modifies the disclosure requirements for fair value measurements by removing, modifying, or adding certain disclosures. The amendments in ASU 2018-13 are effective for all entities for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. The amendments on changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments should be applied retrospectively to all periods presented upon their effective date. Early adoption is permitted upon issuance of ASU 2018-13. An entity is permitted to early adopt any removed or modified disclosures upon issuance of ASU 2018-13 and delay adoption of the additional disclosures until their effective date. The Group elected to early adopt this ASU and applied this guidance retrospectively to all periods presented. The impact of this ASU to the consolidated financial statements is immaterial.

In November 2018, the FASB issued ASU 2018-18, Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606. This update clarifies that certain transactions between participants in a collaborative arrangement should be accounted for under ASC 606 when the counterparty is a customer and precludes an entity from presenting consideration from a transaction in a collaborative arrangement as revenue from contracts with customers if the counterparty is not a customer for that transaction. The update is effective in fiscal years beginning after December 15, 2021, and interim periods therein, and early adoption is permitted for entities that have adopted ASC 606. This guidance should be applied retrospectively to the date of initial application of Topic 606. The Group elected to early adopt this ASU and applied this guidance retrospectively to all periods presented. The impact of this ASU to the consolidated financial statements is immaterial.

In December 2019, the FASB issued ASU 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes. This update simplifies the accounting for income taxes as part of the FASB's overall initiative to reduce complexity in accounting standards. The amendments include removal of certain exceptions to the general principles of ASC 740, *Income taxes*, and simplification in several other areas such as accounting for a franchise tax (or similar tax) that is partially based on income. The update is effective in fiscal years beginning after December 15, 2022, and interim periods therein, and early adoption is permitted. Certain amendments in this update should be applied retrospectively or modified retrospectively, all other amendments should be applied prospectively. The Group does not plan to early adopt ASU 2019-12 and is currently evaluating the impact on its financial statements of adopting this guidance.

In August 2020, the FASB issued ASU 2020-06, Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity, which simplifies the accounting for convertible instruments by removing certain separation models in Subtopic 470-20, Debt—Debt with Conversion and Other Options, for convertible instruments and also increases information transparency by making disclosure amendments. The standard is effective for private companies for fiscal years beginning after December 15, 2023, including interim periods within those fiscal years. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. The Company is currently evaluating the impact of this accounting standard update on its condensed consolidated financial statements.

3. ACCOUNTS RECEIVABLE, NET

	As of December 31,	
	2019	2020
	US\$	US\$
Accounts receivable	480,000	—
Allowance for doubtful accounts	—	—
	<u>480,000</u>	<u>—</u>

4. PREPAYMENTS AND OTHER CURRENT ASSETS

Prepayments and other current assets consist of the following:

	As of December 31,	
	2019	2020
	US\$	US\$
Prepayments	211,435	1,907,781
Deposits(a)	970,394	1,646,446
Interest receivables	227,278	—
Others	67,866	259,757
	<u>1,476,973</u>	<u>3,813,984</u>

Note (a): The deposits represented the amounts that the Group paid to its CRO vendors for various outsourced research and development programs according to the terms of respective CRO agreement. The Group expects to recover the deposits if the program fails or the contract is cancelled.

5. PROPERTY, EQUIPMENT AND SOFTWARE

Property, equipment and software consist of the following:

	As of December 31,	
	2019 US\$	2020 US\$
Machinery and laboratory equipment	3,462,343	4,150,822
Leasehold improvements	767,205	915,208
Electronic equipment	605,882	962,684
Furniture and tools	98,396	106,492
Vehicles	80,133	126,764
Software	71,056	95,586
Total property, equipment and software	5,085,015	6,357,556
Less: accumulated depreciation and amortization	(3,205,690)	(4,290,431)
Net book value	1,879,325	2,067,125

Depreciation and amortization expenses recognized for the years ended December 31, 2019 and 2020 were US\$816,686 and US\$858,408, respectively.

6. ACCRUALS AND OTHER CURRENT LIABILITIES

Accrued liabilities and other current liabilities consist of the following:

	As of December 31,	
	2019 US\$	2020 US\$
Professional service fees	145,157	3,459,430
Payroll and related liabilities	2,370,523	2,390,025
Utility and maintenance	4,595	459
Other taxes and surcharge	—	63,919
Others	19,889	145,664
	2,540,164	6,059,497

7. BORROWINGS

	As of December 31,	
	2019 US\$	2020 US\$
Current		
Short-term borrowings:		
Bank loans	716,723	3,831,476
Current portion of long-term borrowings	322,525	1,183,926
Total current borrowings	1,039,248	5,015,402
Non-Current		
Long-term borrowings:		
Bank loans	1,515,868	2,965,563
Total non-current borrowings	1,515,868	2,965,563
Total borrowings	2,555,116	7,980,965

Short-term borrowings

In March 2018, the Group borrowed a loan with the amount of RMB3,000,000 (equivalent to approximately US\$437,114) from Bank of Jiangsu Co., Ltd. for a term of one year and at the interest rate of 5.22% per annum. The borrowing was repaid in March 2019. In June 2018, the Group borrowed a loan with the amount of RMB2,000,000 (equivalent to approximately US\$291,409) from Bank of Jiangsu Co., Ltd. for a term of one year and at the interest rate of 5.22% per annum. The borrowing was repaid in June 2019. These borrowings with Bank of Jiangsu Co., Ltd were guaranteed by Peter Luo and Kristine She. Peter Luo is the Chairman, Chief Executive Officer and a principal shareholder of the Company. Kristine She is one of the senior management personnel of the Company.

In May 2018, the Group borrowed a loan with the amount of RMB3,000,000 (equivalent to approximately US\$437,114) from Bank of Ningbo Co., Ltd. for a term of one year and at the interest rate of 5.00% per annum. The borrowing was repaid in May 2019. In June 2018, the Group borrowed a loan with the amount of RMB2,000,000 (equivalent to approximately US\$291,409) from Bank of Ningbo Co., Ltd. for a term of one year and at the interest rate of 5.00% per annum. The borrowing was repaid in June 2019.

In July 2018, the Group borrowed a loan with amount of RMB6,000,000 (equivalent to approximately US\$874,228) from Agricultural Bank of China Limited for a term of one year and at the interest rate of 5.22% per annum. The borrowing was guaranteed by Peter Luo, who is the Chairman, Chief Executive Officer and a principal shareholder of the Company. The borrowing was repaid in July 2019.

In September 2019, the Group borrowed a loan with amount of RMB5,000,000 (equivalent to approximately US\$766,295.27) from Bank of Ningbo Co., Ltd. for a term of one year and at the interest rate of 4.35% per annum and the borrowing was repaid in September 2020.

In June 2020, the Group borrowed a loan with the amount of RMB10,000,000 (equivalent to approximately US\$1,532,590.54) from Agricultural Bank of China Limited for a term of one year and at the interest rate of 4.2% per annum.

In September 2020, the Group borrowed a loan with the amount of RMB5,000,000 (equivalent to approximately US\$766,295.27) from Bank of Ningbo Co., Ltd. for a term of one year and at the interest rate of 4.2% per annum.

In November 2020, the Group borrowed a loan with the amount of RMB5,000,000 (equivalent to approximately US\$766,295.27) from China Merchants Bank Co., Ltd. for a term of one year and at the interest rate of 4.1% per annum.

In November 2020, the Group borrowed another loan with the amount of RMB5,000,000 (equivalent to approximately US\$766,295.27) from China Merchants Bank Co., Ltd. for a term of one year and at the interest rate of 4.1% per annum.

Long-term borrowings

In February 2019, the Group borrowed a loan with amount of RMB7,500,000 (equivalent to approximately US\$1,149,442.90) from Shanghai Pudong Development Bank Co., Ltd. for a term of three years and at the interest rate of 5.46% per annum. The Group repaid RMB375,000 (equivalent to approximately US\$57,472.15) in August 2019 and RMB1,250,000 (equivalent to approximately US\$191,573.82) in 2020. As of December 31, 2020, RMB3,375,000 (equivalent to approximately US\$517,249.31) repayable within twelve months for this agreement was classified as “Current portion of long-term borrowing”.

In June 2019, the Group borrowed a loan with amount of RMB6,000,000 (equivalent to approximately US\$919,554.32) from Shanghai Pudong Development Bank Co., Ltd. for a term of three years and at the interest rate of 5.23% per annum. The Group repaid RMB300,000 (equivalent to approximately US\$45,977.72) in December 2019 and RMB1,000,000 (equivalent to approximately US\$153,259.05) in December 2020. As of December 31, 2020, RMB2,700,000 (equivalent to approximately US\$413,799.45) repayable within twelve months for this agreement was classified as “Current portion of long-term borrowing”.

In September 2020, the Group borrowed a loan with amount of RMB16,500,000 (equivalent to approximately US\$2,528,774.39) from Shanghai Pudong Development Bank Co., Ltd. for a term of three years and at the interest rate of 4.27% per annum. As of December 31, 2020, RMB1,650,000 (equivalent to approximately US\$252,877.44) repayable within twelve months for this agreement was classified as “Current portion of long-term borrowing”.

Future maturities of short-term borrowings and long-term borrowings

Future principal maturities of short-term borrowings and long-term borrowings as of December 31, 2020 are as followings:

	US\$
2021	5,015,402
2022	1,279,713
2023	1,685,850
	<u>7,980,965</u>

8. CONVERTIBLE REDEEMABLE PREFERRED SHARES AND WARRANTS

In November 2011, the Company issued convertible notes (“Series Pre-A Convertible Notes”) to certain investors in the amount of 4,590,908. The notes carried a simple interest (non-compounding) of 6% per annum as set out in the note purchase agreement. All outstanding principal balance and accrued but unpaid interest of the notes should be automatically converted into the convertible redeemable preferred shares of the Company at a price no more than US\$1 per share.

In November 2014, the Company issued 5,473,957 Series A-1 convertible redeemable preferred shares (“Series A-1 Preferred Shares”) to certain investors upon conversion of the Company’s Series Pre-A convertible notes at a conversion price of US\$1 per share. Concurrently, the Company issued 2,370,414 Series A-2 convertible redeemable preferred shares (“Series A-2 Preferred Shares”) to certain investors at US\$1.27 per share for a total consideration of US\$3,000,000. Series A-1 Preferred Shares and Series A-2 Preferred Shares are collectively referred to as the Series A Preferred Shares.

From January through June 2016, the Company issued 7,494,537 Series B convertible redeemable preferred shares (“Series B Preferred Shares”) to certain investors at US\$3.74 per share for a total consideration of US\$27,999,995.

From February through May 2018, the Company issued 5,597,354 Series C-1 convertible redeemable preferred shares (“Series C-1 Preferred Shares”) to certain investors at US\$8.93 per share for a total consideration of US\$50,000,033. Concurrently, in February 2018, the Company also issued warrants to two Series C-1 investors at nil consideration (“Series C-1 Warrants”). The Series C-1 Warrants allowed the holders to purchase Series C-2 Preferred Shares (defined below) at the exercise price of US\$10.21 per share for a total consideration of up to US\$7,500,000. Series C-1 Warrants were exercisable, in whole or in part, at any time from the warrant issuance date to the earlier of i) April 1, 2019, ii) a deemed liquidation event or iii) the closing of the Qualified IPO. Series C-1 Warrants expired on April 1, 2019.

From June through November 2019, the Company issued 1,861,121 Series C-2 convertible redeemable preferred shares (“Series C-2 Preferred Shares”) to certain investors at US\$10.21 per share for a total consideration of US\$18,999,999.

In December 2019, the Company issued 4,452,441 Series C-3 convertible redeemable preferred shares (“Series C-3 Preferred Shares”) to a certain investor at US\$11.23 per share for a total consideration of US\$50,000,000.

Series C-1 Preferred Shares, Series C-2 Preferred Shares and Series C-3 Preferred Shares are collectively referred to as the Series C Preferred Shares.

The key features of the Series A Preferred Shares, Series B Preferred Shares and Series C Preferred Shares (collectively the “Preferred Shares”) are as follows:

Dividends

Each holder of the Preferred Shares will be entitled to receive non-cumulative dividends when declared by the Board of Directors prior and in preference to ordinary shareholders. The dividend should be paid at the rate of 6% of the original issue price per share per annum on each Preferred Shares in the sequence of Series C Preferred Shares and Preferred Shares other than the Series C Preferred Shares. After the preferential dividends relating to the Preferred Shares have been paid in full or declared and set apart in any fiscal year of the Company, any additional dividends out of funds or assets legally available therefore may be declared in that fiscal year for the Shares and, if such additional dividends are declared, the preferred shareholders shall be entitled to participate on an as converted-basis pro-rata in any dividends or distributions paid to the ordinary shareholders.

Voting

Each Preferred Share has voting rights equivalent to the number of ordinary shares to which it is convertible at the record date. The Preferred Shares shall vote separately as a class with respect to certain specified matters. Otherwise, the preferred shareholders and ordinary shareholders shall vote together as a single class.

Liquidation preference

In the event of any liquidation, dissolution or winding up of the Company, or the cessation of the business of the Company or of a substantial portion of the business of the Company, whether voluntary or involuntary, or any deemed liquidation event (unless waived by the preferred shareholders), the preferred shareholders shall be entitled to receive a per share amount equal to 100% of the original issue price of the respective series of the Preferred Shares, in the sequence of Series C Preferred Shares, Series B Preferred Shares and Series A Preferred Shares. After such liquidation amounts have been paid in full, the preferred shareholders are entitled to receive a simple interest accruing on each Preferred Share at 6% of its original issue price per annum from the date of issuance of such Preferred Share to the date of distribution of such amount, in the sequence of Series C Preferred Shares, Series B Preferred Shares and Series A Preferred Shares. After such interest amounts have been paid in full, any remaining funds or assets of the Company legally available for distribution to shareholders shall be distributed on a pro rata basis among the preferred shareholders, on an as-converted basis, together with the ordinary shareholders.

Conversion

Each Preferred Share may be converted at any time into ordinary shares at the option of the preferred shareholders based on the then-effective conversion price. The initial conversion ratio is 1:1, subject to adjustment in the event of share splits, share combinations, ordinary share dividends or distributions, other dividends, reorganizations, mergers, consolidations, reclassifications, exchanges, substitutions, or dilutive issuance.

All Preferred Shares are converted automatically into ordinary shares at the then effective applicable conversion price upon the earlier of a Qualified Public Offering (public offering of the Company's shares with an offering price (exclusive of underwriting commissions and expenses) that reflects a market capitalization (immediately prior to the public offering) of not less than US\$650,000,000 and with an aggregate proceeds of no less than US\$75 million) or a date specified by written consent or agreement of the holders of at least 80% of the voting power of the then outstanding Preferred Shares.

Redemption

The Preferred Shares are redeemable upon request by the holders of the majority outstanding Preferred Shares if the Company fails to consummate a Qualified Public Offering or complete a deemed liquidation event on or before March 31, 2025 at the redemption price equal to the original issue price plus any declared but unpaid dividends.

Accounting for Preferred Shares

The Preferred Shares are classified as mezzanine equity in the consolidated balance sheets because they are contingently redeemable upon the occurrence of an event outside of the Company's control (e.g. the Company not achieving a Qualified Public Offering or a deemed liquidation event before March 31, 2025 ("Target QIPO Date")). The Preferred Shares were determined to be mezzanine equity with no embedded feature to be bifurcated and no beneficial conversion features to be recognized. The Preferred Shares are initially recorded at their respective issuance date fair value, net of issuance cost and fair value allocated to the detachable warrants. The Company did not incur material issuance cost for any Preferred Shares issued.

The Company concluded that the Preferred Shares are not currently redeemable, but are probable to become redeemable. The Company accreted changes in the redemption value over the period from the date of issuance to the earliest redemption date using the interest method. No accretion charge was recorded as the redemption value is fixed to original issue price for the years presented, except for Series C-1 Preferred Shares issued with detachable warrants.

Modification of Preferred Shares

The Company made several amendments to the Preferred Shares, mainly including: 1) added redemption rights for Series A Preferred Shares upon the issuance of the Series B Preferred Shares; 2) extended the Target QIPO Date upon the issuance of the Series C-1 Preferred Shares and the Series C-3 Preferred Shares. These amendments are accounted for as modifications rather than extinguishments as the fair values of these Preferred Shares immediately after the amendments were not significantly different from their respective fair values immediately before the amendment. When Preferred Shares are modified and such modification results in value transfer between preferred shareholders and ordinary shareholders, the value transferred is treated as a deemed dividend to or deemed contribution from the preferred shareholders.

On February 2, 2018, the Target QIPO Date was extended from January 19, 2023 to February 2, 2025 (7th anniversary of Series C-1 closing) upon issuance of Series C-1 Preferred Shares. On the date of the modifications, the Company assessed the total fair value of preferred shares immediately before and after the change of the terms with the assistance from an independent third-party appraiser. The combined change in fair value of Preferred Shares immediately before and after the modification was US\$1,186,187. The increase in fair value of the ordinary shares of is US\$1,186,187, in substance, a transfer of wealth mostly from the preferred shareholders to the ordinary shareholder, and therefore are recorded as deemed contribution from the Preferred Shareholders.

The Company's Preferred Shares activities for the periods presented are summarized below:

<u>Mezzanine equity</u>	<u>Series A-1</u> US\$	<u>Series A-2</u> US\$	<u>Series B</u> US\$	<u>Series C-1</u> US\$	<u>Series C-2</u> US\$	<u>Series C-3</u> US\$	<u>Total</u> US\$
Balance as of December 31, 2017	5,473,957	3,000,000	27,999,995	—	—	—	36,473,952
Issuance of Series C-1 Preferred Shares	—	—	—	48,258,313	—	—	48,258,313
Accretion of Series C-1 Preferred Shares to redemption value	—	—	—	222,846	—	—	222,846
Balance as of December 31, 2018	5,473,957	3,000,000	27,999,995	48,481,159	—	—	84,955,111
Issuance of Series C-2 Preferred Shares	—	—	—	—	18,999,999	—	18,999,999
Issuance of Series C-3 Preferred Shares	—	—	—	—	—	50,000,000	50,000,000
Accretion of Series C-1 Preferred Shares to redemption value	—	—	—	246,184	—	—	246,184
Balance as of December 31, 2019	5,473,957	3,000,000	27,999,995	48,727,343	18,999,999	50,000,000	154,201,294
Accretion of Series C-1 Preferred Shares to redemption value	—	—	—	248,113	—	—	248,113
Balance as of December 31, 2020	<u>5,473,957</u>	<u>3,000,000</u>	<u>27,999,995</u>	<u>48,975,456</u>	<u>18,999,999</u>	<u>50,000,000</u>	<u>154,449,407</u>

The warrants are freestanding instruments and classified as liabilities in accordance with ASC 480. The warrants are initially recognized at fair value, with subsequent changes in fair value recorded currently in earnings. The Company recognized gains from the decrease in fair value of the warrants of US\$534,305, US\$1,207,415 and nil for the years ended December 31, 2018, 2019 and 2020, respectively.

The Company has measured the warrant liabilities at fair values on a recurring basis using significant unobservable inputs (Level 3) for the years ended December 31, 2018. The Group used the Black-Scholes option pricing model to estimate the fair value of warrant liabilities using the following assumptions:

	<u>For the year ended December 31, 2018</u>
Risk-free interest rate	1.92%, 2.37%
Exercise price	US\$10.2089
Maturity date	01/04/2019
Estimated volatility rate	63.78%, 71.00%

The model requires the input of highly subjective assumptions including the risk-free rate interest rate, maturity date, estimated volatility rate and fair value of underlying preferred shares. The risk-free rate for periods within the contractual life is based on the US treasury strip bond with maturity similar to the maturity of the warrants as of valuation dates. For expected volatilities, the Company has made reference to the historical daily stock prices volatilities of ordinary shares of several comparable companies in the same industry as the Company. The estimated fair value of the preferred shares was determined with assistance from an independent third-party valuation firm.

The significant unobservable inputs used in the fair value measurement of the warrant liabilities include risk-free interest rate, interval between valuation date and maturity date, estimated volatility rate and fair value of underlying preferred shares. Significant decreases in interval between valuation date and maturity date, estimated volatility rate and fair value of underlying preferred shares would result in a significantly lower fair value measurement. Significant increases in risk-free interest rate would result in a significantly lower fair value measurement.

9. SHARE-BASED COMPENSATION

On November 7, 2015, the Company adopted a share incentive plan (“2015 Plan”). Under the 2015 Plan, the Company’s Board of Directors has approved that a maximum aggregate number of shares that may be issued pursuant to all awards granted shall be 4,336,126. In September 2017, the Company replaced 2015 Plan with the amended and restated share incentive plan (“2017 Plan”) and increased the maximum number of shares issuable to 6,336,126. In December 2019, the Company replaced 2017 Plan with the second amended and restated share incentive plan (“2019 Plan”) and further increased the maximum number of shares issuable to 11,391,131. The terms of the 2015 Plan, 2017 Plan and 2019 Plan are substantially the same other than the maximum aggregate number of shares the Company may issue under the respective plan.

Share options containing only service conditions granted to each grantee under the share incentive plan will generally be exercisable upon the grantee renders service to the Company in accordance with a stipulated vesting schedule. Grantees are generally subject to a vesting schedule of no longer than five years, under which the grantee earns an entitlement to vest a certain percentage of his option grants at the end of each month or year of completed service. The share option awards shall expire no more than 10 years from their grant dates.

Share options containing both service conditions and performance conditions granted to each grantee under the share incentive plan shall become eligible for vesting upon the occurrence of their applicable performance conditions (including but not limited to the occurrence of an initial public offering (“IPO”), the completion of business and operational goals, etc.). Upon being eligible for vesting, each such performance-based option shall vest in a series of four equal and continuous annual installments for each full year of services completed following the award date of such option.

On August 15, 2020, pursuant to board resolution, 184,692 share options that granted to a senior management was modified and the vesting period of the 184,692 share options has been shortened from 5 years to 4 years. Since the fair value of the modified award is lower than the fair value of the original award immediately before the modification, there is no incremental compensation cost to be recognized.

On November 9, 2020, the Company passed a board resolution to waive the vesting schedules and conditions of 2,375,000 share options granted to certain management members. Pursuant to this board resolution, these management members exercised all these share options at the original exercise price per share ranging from US\$1.83 to US\$2.26 and as a result, 2,375,000 ordinary shares were issued to them. These management members paid the exercise price by issuing recourse promissory notes in the total amount of US\$5,197,650. However, the Company still has the repurchase right to buy back such shares at the original exercise price if the grantees do not meet the original vesting conditions. The Company assessed and considered that in accordance with guidance set out in ASC 718-10-55-31, given such arrangement allows the shares received on exercise be returned to the Company if the original vesting conditions are not satisfied, there has been no substantial change to the vesting conditions and the Company shall continue to account for the share awards in accordance with their original terms. As of December 31, 2020, there were 2,285,000 shares unvested according to the original vesting conditions.

As of December 31, 2020, the Company has granted 2,178,808 share options containing both service conditions and performance conditions. All other share options granted contain only service conditions.

	Number of Options	Weighted- Average Exercise Price US\$ per option	Weighted- Average Grant Date Fair Value US\$ per option	Weighted Average Remaining Contractual Term Years	Aggregate Intrinsic Value US\$
Outstanding at January 1, 2018	848,828	0.38	3.75	8.56	4,907,569
Forfeited	(274,500)	0.55	5.71	—	—
Outstanding at January 1, 2019	574,328	0.30	2.80	7.14	3,734,644
Granted	372,500	1.26	5.46	—	—
Exercised	(34,000)	0.55	5.71	—	—
Forfeited	(46,800)	1.22	5.75	—	—
Outstanding at December 31, 2019	866,028	0.65	3.67	7.27	6,328,171
Granted	6,313,373	2.00	7.01	—	—
Exercised	(3,694,934)	1.93	6.55	—	—
Forfeited	(190,000)	1.70	6.91	—	—
Outstanding at December 31, 2020	3,294,467	1.75	6.65	8.78	33,410,968
Vested and expected to vest at December 31, 2020	3,294,467	1.75	6.65	8.78	33,410,968
Exercisable at December 31, 2020	393,424	0.75	4.46	6.68	4,859,836

The aggregate intrinsic value in the table above represents the difference between the exercise price of the awards and the fair value of the underlying ordinary shares at each reporting date, for those awards that had exercise price below the estimated fair value of the relevant ordinary shares.

The aggregate fair value of the equity awards vested during the years ended December 31, 2018, 2019 and 2020 was US\$165,609, US\$366,113 and US\$8,430,085, respectively. As of December 31, 2020, there was US\$34,096,227 of total unrecognized employee share-based compensation expense, may be adjusted for actual forfeitures occurring in the future. Total unrecognized compensation cost will be recognized over a weighted-average period of 3.39 years.

Fair value of share options

The fair value of share options was determined using the binomial option valuation model, with the assistance from an independent third-party appraiser. The binomial model requires the input of highly subjective assumptions, including the expected volatility, the exercise multiple, the risk-free rate and the dividend yield. For expected volatility, the Group has made reference to historical volatility of several comparable companies in the same industry. The exercise multiple was estimated as the average ratio of the stock price to the exercise price of when employees would decide to voluntarily exercise their vested share options. The risk-free rate for periods within the contractual life of the share options is based on the market yield of U.S. Treasury Bonds in effect at the time of grant. The dividend yield is based on the expected dividend policy over the contractual life of the share options. The estimated fair value of the ordinary shares, at the share option grant dates, was determined with the assistance from an independent third-party appraiser.

The assumptions used to estimate the fair value of the share options granted are as follows:

	For the year ended December 31, 2019	For the year ended December 31, 2020
Risk-free interest rate	1.78% - 2.73%	0.68% - 0.83%
Dividend yield	0%	0%
Expected volatility range	67.5% - 71.0%	72.3% - 73.4%
Exercise multiple	2.2 - 2.8	2.2 - 2.8
Contractual life	10 years	10 years

Total share-based compensation expenses recognized for the years ended December 31, 2018, 2019 and 2020 were as follows:

	For the years ended December 31,		
	2018	2019	2020
	US\$	US\$	US\$
Research and development expenses	126,540	404,620	6,472,083
Administrative expenses	—	207,091	3,657,458
Total share-based compensation expenses	126,540	611,711	10,129,541

Up to the date of the issuance of these consolidated financial statements, some proceeds of the subscription capital arising from the exercise of vested share options by certain employees remained outstanding and such amount was presented as subscriptions receivable, a contra-equity balance on the consolidated balance sheets as of December 31, 2019 and 2020, respectively.

10. COLLABORATION ARRANGEMENTS

Guilin Sanjin Pharmaceutical Co., Ltd. License Agreement

In December 2018, the Group entered into (i) a collaboration agreement (the “Sanjin Greater China Agreement”) that covers Greater China with Guilin Sanjin Pharmaceutical Co., Ltd. (“Sanjin”) and certain of its subsidiaries (collectively, “Sanjin Parties”) and (ii) a collaboration agreement (the “Sanjin ROW Agreement”, together with the Sanjin Greater China Agreement, the “2018 Sanjin Agreements”) that covers the regions other than Greater China with Sanjin. Pursuant to the Sanjin Greater China Agreement, the Group licensed the Chinese intellectual property directly related to a monospecific antibody molecule that binds to the PD-L1 target (the “PD-L1 Project”), including patent rights, patent application rights and technologies based on the core sequence of the molecule, to Sanjin Parties. Sanjin Parties will own all the Chinese intellectual property developed in the exercise of Sanjin Parties’ rights under the agreement, including but not limited to improvements (including combination products), clinical trials, regulatory filings, and commercialization rights relating thereto. The Group also granted Sanjin Parties a royalty-free license to use our other existing intellectual property and improvements thereto which are related to the PD-L1 Project for the purposes of exploiting its rights and performing its obligations under the agreement. Sanjin Parties will enjoy all the economic benefits deriving from the PD-L1 Project in Greater China, including but not limited to patent transfer fee, licensing fee, sales revenue and sales commission, etc. Sanjin Parties will pay the Group (i) single-digit percentage of net sales of the products that use the licensed antibody after such products enter the market and (ii) a low to mid-low double-digit percentage of the profits resulting from any transfer of the license to any third parties depending on the timing of the transfer relative to the development stage of the product. The Group also received RMB10,000,000 (equivalent to approximately US\$1,511,168) upfront fee upon the effectiveness of the agreement from Sanjin Parties.

Pursuant to the Sanjin ROW Agreement, the Group granted Sanjin a royalty-free license to use all intellectual property relating to (i) the collaboration under the agreement that the Group controlled before the Group entered into the agreement or acquired independently of the agreement and (ii) improvements thereto for the purposes of exploiting its rights and performing its obligations under the agreement. Any intellectual property generated independently by a party under the agreement will be solely owned by that party who generated such intellectual property, and any intellectual property generated from cooperation between the Group and Sanjin’s affiliates in connection with the collaboration will be jointly owned. The Group retain the ownership of patent rights of key intellectual property pertaining to PD-L1 outside of the Greater China. In addition, all the results obtained by Sanjin relating to the research and development of any new antibody developed under the agreement will be owned by Sanjin. The Group retain a majority of the economic benefits derived from the Sanjin ROW Agreement, including but not limited to any patent transfer fee, licensing fee and gains realized under such transfer. In case the Group intend to transfer to a third party our share of economic interests in any country outside of Greater China, the Group must notify Sanjin and Sanjin will receive a right of first refusal if it pays the Group a deposit equal to a low double-digit percentage of the consideration that the Group expect to receive from such third party. If Sanjin waives the right of first refusal, the Group can proceed with the transfer, provided that the final transaction price with the third party is not lower than the amount of the offering price that was included in our notice to Sanjin.

The Group agreed not to (i) independently develop any monospecific antibodies that bind to the PD-L1 target or (ii) grant any rights associated with such antibodies to any third parties during the three-year period from the effective date of the agreement. The exclusivity obligation does not prevent the Group from (i) developing or granting any licenses to third parties for intellectual property that covers bispecific antibodies, ADCs, diagnostic antibodies, nano-particles and masked antibody against PD-L1 target and (ii) continuing to provide antibody screening service that were commenced before the execution of the Sanjin Greater China Agreement and either party has the independent right to conduct combination therapy studies outside of the Greater China. Either non-breaching party may terminate the 2018 Sanjin Agreements if the other party’s ability to comply with its respective obligations under the agreements is negatively affected by contingencies such as failure to maintain operation or changes in core project management and the other party fails to take effective remedial measures. Each agreement automatically terminates upon the termination of the other agreement. Upon the rescission or termination, Sanjin Parties will return to the Group all the intellectual property, documents and data provided by the Group under the 2018 Sanjin Agreements.

In the event that the failure of the development of the product candidate solely arises from the Group’s research and development basis specified under this agreement, Sanjin has the right to claim back all the payment made to the Group. The Group considers the possibility of occurrence of such event is very remote.

For the year ended December 31, 2018, the Group recognized revenue of RMB10,000,000 (equivalent to approximately US\$1,511,168) for this agreement.

Dragon Boat Biopharmaceutical (Shanghai) Limited License Agreement

In May 2019, the Group entered into (i) a collaboration agreement that covers Greater China (the “Dragon Boat Greater China Agreement”) and (ii) a collaboration agreement that covers the regions other than Greater China (the “Dragon Boat ROW Agreement,” together with the Dragon Boat Greater China Agreement, the “2019 Dragon Boat Agreements”), with Dragon Boat Biopharmaceutical (Shanghai) Limited (“Dragon Boat”), a subsidiary of Sanjin. Pursuant to the Dragon Boat Greater China Agreement, the Group will license the Chinese intellectual property directly related to a certain monospecific antibody molecule that binds to a specified target (the “Specified Project”), including the patent rights, patent application rights and technologies based on the core sequence of the molecule, to Dragon Boat. Dragon Boat will own all the Chinese intellectual property developed in the exercise of Dragon Boat’s rights under the agreement, including but not limited to improvements (including combination products), clinical trials, regulatory filings, and commercialization rights relating thereto. The Group also granted Dragon Boat a royalty-free license to use our other existing intellectual property and improvements thereto which are related to the Specified Project for the purposes of exploiting its rights and performing its obligations under the agreement. Dragon Boat will enjoy all the economic benefits deriving from the Specified Project in Greater China, including but not limited to patent transfer fee, licensing fee, sales revenue and sales commission, etc. and will pay the Group (i) certain high-six figure dollar milestone payments upon the achievement of certain milestones (including milestones of launch of pre-clinical safety evaluation animal test, obtaining Investigational New Drug (“IND”) approval in PRC and completion of clinical phase I test in PRC) and (ii) a single-digit percentage of net sales of the products that use the licensed antibody after such products enter the market.

Pursuant to the Dragon Boat ROW Agreement, the Group granted Dragon Boat a royalty-free license to use all intellectual property relating to (i) the collaboration under the agreement that the Group controlled before the Group entered into the agreement or acquired independently of the agreement and (ii) improvements thereto for the purposes of exploiting its rights and performing its obligations under the agreement. Any intellectual property generated independently by a party under the agreement will be solely owned by that party who generated such intellectual property, and any intellectual property generated from cooperation between the Group and Dragon Boat in connection with the collaboration will be jointly owned. The Group retain the ownership of patent rights of key intellectual property pertaining to the specified target outside of the Greater China. In addition, all the results obtained by Dragon Boat relating to the research and development of any new antibody developed under the agreement will be owned by Dragon Boat. The Group retains a majority of the economic benefits derived from the Dragon Boat ROW Agreement, including but not limited to any patent transfer fee, licensing fee and gains realized under such transfer. In case the Group intend to transfer to a third party our share of economic interests in any country outside of Greater China, the Group must notify Dragon Boat and Dragon Boat will receive a right of first refusal if it pays the Group a deposit equal to a low double-digit percentage of the consideration that the Group expects to receive from such third party. If Dragon Boat waives the right of first refusal, the Group can proceed with the transfer, provided that the final transaction price with the third party is not lower than the amount of the offering price that was included in our notice to Dragon Boat.

Under the 2019 Dragon Boat Agreements, the Group agreed not to (i) independently develop any monospecific antibodies that bind to the specified target or (ii) grant any rights associated with such antibodies to any third parties during the three-year period from the effective date of the agreements. The exclusivity obligation does not prevent the Group from (i) developing or granting any licenses to third parties for intellectual property that covers bispecific antibodies, ADCs, diagnostic antibodies, nano-particles and masked antibody against the specific target and (ii) continuing to provide antibody screening service that were commenced before the execution of the Dragon Boat Greater China Agreement and either party has the independent right to conduct combination therapy studies outside of the Greater China. Either nonbreaching party may terminate the 2019 Dragon Boat Agreements if the other party’s ability to comply with its obligations under the agreements is negatively affected by contingencies such as failure to maintain operation or changes in core project management and the other party fails to take effective remedial measures. Each agreement automatically terminates upon the termination of the other agreement. Upon the rescission or termination, Dragon Boat will return to the Group all the intellectual property, documents and data provided by the Group under the 2019 Dragon Boat Agreements.

In the event that the failure of the development of the product candidate solely arises from the Group’s research and development basis specified under this agreement, Dragon Boat has the right to claim back all the payment made to the Group.

For the year ended December 31, 2019, no revenue was recognized for this agreement since the licensed product has not been transferred to Dragon Boat.

As of December 31, 2020, upfront fee of RMB4,000,000 (equivalent to approximately US\$573,378) that was received by the Group was recorded as contract liabilities in the consolidated balance sheets, as the performance obligation had not been satisfied by the Group.

Signal Pharmaceuticals LLC Agreements

In January 2019, the Group entered into an agreement with Signal Pharmaceuticals LLC, a subsidiary of Celgene Corporation, for a purchase order of delivery of certain sequences with total consideration of US\$480,000. For the year ended December 31, 2019, the Group recognized revenue of US\$480,000 upon delivery of such sequences.

In October 2018 and May 2019, the Group entered into agreements with Signal Pharmaceuticals LLC, for purchase orders of for a purchase order of delivery of certain sequences with total consideration of US\$237,500 and US\$72,000, respectively. For the year ended December 31, 2020, the Group recognized revenue of US\$309,500 upon delivery of such sequences.

ADC Therapeutics SA License and Collaboration Agreements

In April 2019, the Group entered into a material transfer and collaboration agreement (the “ADCT Collaboration Agreement”) and a license agreement (the “ADCT License Agreement”) with ADC Therapeutics SA (“ADC Therapeutics”). These two agreements are combined as a single contract as the agreements were negotiated as a package with a single commercial objective.

ADCT Collaboration Agreement

Pursuant to the ADCT Collaboration Agreement, the Group agreed to generate masked antibodies with respect to up to two exclusive targets selected by ADC Therapeutics. Upon our delivery of certain initial results, ADC Therapeutics has the option to license the Group’s technology with respect to one or both targets as further detailed below. ADC Therapeutics has not yet exercised such options as of December 31, 2020.

Under the ADCT Collaboration Agreement, the Group is eligible to receive up to a low-seven-figure dollar amount in consideration for the Group’s exclusivity obligations, upon achievement of certain development milestones (including milestones of delivery of certain amino acid sequences and successful outcome of the first in-vivo study) and upon ADC Therapeutics’ election to proceed with development for the two elected targets. Apart from performance obligation to deliver the amino acid sequences of the corresponding masking peptides, the Group is not required to perform any additional research and development services. ADC Therapeutics has the right to terminate the ADCT Collaboration Agreement at any time and for any reason in its entirety or on a target-by-target basis upon thirty days’ prior written notice to the Group. Either party may terminate the ADCT Collaboration Agreement, in its entirety or on a target-by-target basis, upon the other party’s uncured material breach of the agreement or the other party’s insolvency-related events.

The Group also granted ADC Therapeutics an exclusive target reservation right for one year from the commencement of the agreement and an option to renewal for another year with a consideration of low-six-figure dollar amount.

ADCT License Agreement

Subject to the exercise of the options contained in the ADCT Collaboration Agreement, the Group has granted ADC Therapeutics, with respect to each elected target, an exclusive, worldwide, perpetual and irrevocable (subject only to the termination provisions) license (with the right to grant sublicenses) to develop, make, use, commercialize and import the antibody drug conjugates that comprise masked antibodies generated by the Group under these programs.

Under the ADCT License Agreement, if ADC Therapeutics exercises both of its options granted thereunder, the Group could be eligible to receive up to a low-nine-figure dollar amount in development and regulatory milestone payments upon the achievement of certain milestones (including milestones of successful completion of Good Laboratory Practice Toxicology studies, launch of clinical trials and start of commercial sales in difference countries and etc.) and up to a mid-eight-figure dollar amount in sales milestone payments, in addition to mid-single-digit percentage net sales-based tiered royalties on products licensed under the ADCT License Agreement, subject to certain reductions. Royalties, if any, will be payable on a country-by-country and product-by-product basis, until the earlier of (i) the tenth anniversary of the first commercial sale of such product or (ii) the expiration of the last-to-expire patent licensed under the agreement in such country, unless earlier terminated by the parties, following which any licenses granted to ADC Therapeutics under the ADCT License Agreement shall become fully paid up, perpetual and irrevocable.

ADC Therapeutics has the right to terminate the ADCT License Agreement before the expiration of the royalty term on a product-by-product basis or in its entirety (i) for any reason or no reason upon thirty days’ written notice to the Group, or (ii) if ADC Therapeutics chooses to discontinue the development or sale of the applicable licensed product worldwide. Each party has certain rights to terminate the ADCT License Agreement with prior written notice upon the other party’s uncured material breach or insolvency.

For the year ended December 31, 2020, the Group recognized US\$225,000 upon delivery of such results. For the year ended December 31, 2020, the Group recognized US\$100,000 as other income due to the expiration of exclusive target reservation right, which is not related to the Group’s major operation activity.

11. INCOME TAX EXPENSE

PRC

Effective from January 1, 2008, the PRC's statutory, Enterprise Income Tax ("EIT") rate is 25%. In accordance with the implementation rules of EIT Law, a qualified "Technology Advanced Service Enterprises" ("TASE") is eligible for a preferential tax rate of 15%. The TASE certificate is effective for three years. An entity must file required supporting documents with the tax authority and ensure fulfillment of the relevant TASE criteria before using the preferential rate. An entity could apply for the TASE certificate every year.

Adagene (Suzhou) Limited was first recognized as a qualified TASE in March 2015 and renewed in December 2018. Adagene (Suzhou) Limited was authorized to enjoy the preferential tax rate of 15% from 2015 to 2021.

Cayman Islands

Adagene Inc. is incorporated in the Cayman Islands. Under the current laws of the Cayman Islands Adagene Inc. is not subject to tax on income or capital gain. Additionally, the Cayman Islands does not impose a withholding tax on payments of dividends to shareholders.

Hong Kong

Adagene (Hong Kong) Limited is incorporated in Hong Kong. Companies registered in Hong Kong are subject to Hong Kong profits tax on the taxable income as reported in their respective statutory financial statements adjusted in accordance with the relevant Hong Kong tax laws. The applicable tax rate in Hong Kong is 16.5%. For the years ended December 31, 2018 and 2019, Adagene (Hong Kong) Limited did not make any provisions for Hong Kong profit tax as there were no assessable profits derived from or earnings in Hong Kong for any of the periods presented. Under the Hong Kong tax law, Adagene (Hong Kong) Limited is exempted from income tax on its foreign-derived income and there are no withholding taxes in Hong Kong on remittance of dividends.

Australia

Adagene Australia Pty Ltd. is incorporated in Australia. Companies registered in Australia are subject to Australia profits tax on the taxable income as reported in their respective statutory financial statements adjusted in accordance with the relevant Australia tax laws. The applicable tax rate in Australia is 30%. Adagene Australia Pty Ltd. has no taxable income for all periods presented, therefore, no provision for income taxes is required.

United States

Adagene Incorporated is incorporated in U.S. and is subject to U.S. federal corporate income tax at a rate of 21%. Adagene Incorporated is also subject to state income tax in California of 8.84%. Adagene Incorporated has no taxable income for all periods presented, therefore, no provision for income taxes is required. Reconciliation between the income tax expense computed by applying the statutory tax rate to loss before income tax and the actual provision for income tax is as follows:

	For the years ended December 31,		
	2018 US\$	2019 US\$	2020 US\$
Loss before income tax	(15,266,184)	(16,432,308)	(42,397,279)
Income tax computed at respective applicable tax rate	(30,560)	27,875	(1,073,105)
Research and development super-deduction ^(a)	(579,090)	(230,126)	(718,979)
Non-deductible expenses	4,010	3,306	1,238
Changes in valuation allowance	605,640	198,945	1,790,846
Income tax expense	—	—	—

Note (a): Due to the impacts of research and development super-deduction, the Group's subsidiary, Adagene (Suzhou) Limited did not have any taxable profit for the years ended December 31, 2018, 2019 and 2020.

Deferred tax assets and liabilities

Deferred taxes were measured using the enacted tax rates for the periods in which the temporary differences are expected to be reversed. The tax effects of temporary differences that give rise to the deferred tax balances as of December 31, 2018, 2019 and 2020 are as follows:

	For the years ended December 31,		
	2018 US\$	2019 US\$	2020 US\$
Deferred tax assets:			
Net operating loss carry forward	735,717	928,989	1,504,966
Depreciation and amortization of property, equipment and software	4,213	9,886	7,428
Gross deferred tax assets	739,930	938,875	1,512,394
Less: valuation allowance	(739,930)	(938,875)	(1,512,394)
Total deferred tax assets, net	—	—	—

Movement of the valuation allowance is as follows:

	For the years ended December 31,		
	2018 US\$	2019 US\$	2020 US\$
Balance as of January 1	134,290	739,930	938,875
Addition	605,640	198,945	573,519
Balance as of December 31	739,930	938,875	1,512,394

A valuation allowance is provided to reduce the amount of deferred tax assets if it is considered more likely than not that some portion or all of the deferred tax assets will not be realized in the foreseeable future. In making such determination, the Group evaluates a variety of positive and negative factors including the Group's operating history, accumulated deficit, the existence of taxable temporary differences and reversal periods.

The Group has incurred net accumulated operating losses for income tax purposes since its inception. The Group believes that it is more likely than not that these net accumulated operating losses will not be utilized in the future. Therefore, the Group has provided full valuation allowances for the deferred tax assets as of December 31, 2019 and 2020.

The Group evaluates each uncertain tax position (including the potential application of interest and penalties) based on the technical merits, and measure the unrecognized benefits associated with the tax positions. As of December 31, 2019 and 2020, the Group did not have any significant unrecognized uncertain tax positions.

12. NET LOSS PER SHARE

Basic and diluted net loss per share for the years ended December 31, 2018, 2019 and 2020 are calculated as follows:

	For the years ended December 31,		
	2018	2019	2020
	US\$	US\$	US\$
Numerator:			
Net loss attributable to Adagene Inc.'s shareholders	(15,266,184)	(16,432,308)	(42,397,279)
Deemed contribution from convertible redeemable preferred shareholders	1,186,187	—	—
Accretion of convertible redeemable preferred shares to redemption value	(222,846)	(246,184)	(248,113)
Net loss attributable to ordinary shareholders	<u>(14,302,843)</u>	<u>(16,678,492)</u>	<u>(42,645,392)</u>
Denominator:			
Weighted-average number of ordinary shares outstanding—basic and diluted	15,159,136	15,178,232	15,950,698
Net Loss per share—basic and diluted	(0.94)	(1.10)	(2.67)

The effects of all outstanding convertible redeemable preferred shares and share options have been excluded from the computation of diluted loss per share for the years ended December 31, 2018, 2019 and 2020 as their effects would be anti-dilutive.

The potentially dilutive securities that have not been included in the calculation of diluted net loss per share as their inclusion would be anti-dilutive are as follows:

	For the years ended December 31,		
	2018	2019	2020
Convertible redeemable preferred shares	20,430,200	21,977,914	27,249,824
Share options	293,133	582,526	1,795,932

13. RELATED PARTY TRANSACTIONS*a) Related Parties*

Name of related parties	Relationship
Peter Luo	Chairman, Chief Executive Officer and a principal shareholder of the Company
Four senior management personnel	Management and ordinary shareholders of the Company
WuXi AppTec Co., Ltd. (“WuXi AppTec Group”)	A principal shareholder of the Group
WuXi Biologics (Shanghai) Co., Ltd.	Controlled by the ultimate controlling party of a principal shareholder of the Group

b) The Group had the following related party balances at the end of the year:

	As of December 31,	
	2019 US\$	2020 US\$
WuXi AppTec Group	739,051	124,704
Four senior management personnel(i)	350,865	—
Peter Luo(i)	338,818	—
WuXi Biologics (Shanghai) Co., Ltd.	4,452	7,692
Total amounts due from related parties	1,433,186	132,396

	As of December 31,	
	2019 US\$	2020 US\$
WuXi Biologics (Shanghai) Co., Ltd.	1,379,741	2,361,503
WuXi AppTec Group	432,784	173,855
Peter Luo(ii)	83,254	—
Total amounts due to related parties	1,895,779	2,535,358

c) The Group had the following related party transactions:

	For the years ended December 31,		
	2018 US\$	2019 US\$	2020 US\$
Receipt of CRO and CMO services:			
WuXi Biologics (Shanghai) Co., Ltd.	6,535,512	3,567,962	7,217,709
WuXi AppTec Group	969,079	2,136,344	2,674,586
	7,504,591	5,704,306	9,892,295

- (i) In October and November 2017, Peter Luo and other four senior management personnel elected to exercise the vested share options that granted under 2015 Plan. As of December 31, 2018, the balance of amounts due from Peter Luo and other four senior management personnel represented the receivables arising from the exercise of share options and related withholding individual income tax amounts. The receivables arising from the exercise of share options were subsequently received in the year ended December 31, 2019. As of December 31, 2019, the balance of amounts due from Peter Luo and other four senior management personnel represented withholding individual income tax amounts.
- (ii) As of December 31, 2019, the balance of amounts due to Peter Luo represented the Group's receipt of personal subsidy on behalf of Peter Luo, which was subsequently remitted to Peter Luo in May 2020.

14. COMMITMENTS AND CONTINGENCIES

Operating lease commitments

Future minimum payments under non-cancelable operating leases with initial terms in excess of one year consist of the following as of December 31, 2020:

	US\$
For the years ending:	
2021	306,311
2022	240,530
2023	129,555
Total	<u>676,396</u>

Payments under operating leases are expensed on a straight-line basis over the periods of their respective leases. The Group's lease arrangements have no renewal options, rent escalation clauses, restrictions or contingent rents and are all executed with third parties. For the years ended December 31, 2019 and 2020, total rental related expenses for all operating leases amounted to US\$175,812 and US\$177,453, respectively.

Contingencies

The Group is currently not involved in any legal or administrative proceedings that may have a material adverse impact on the Group's business, financial position or results of operations.

15. RESTRICTED NET ASSETS

The Group's ability to pay dividends may depend on the Group receiving distributions of funds from its PRC subsidiary. Relevant PRC statutory laws and regulations permit payments of dividends by the Group's PRC subsidiary only out of its retained earnings, if any, as determined in accordance with PRC accounting standards and regulations. The results of operations reflected in the consolidated financial statements prepared in accordance with U.S. GAAP differ from those reflected in the statutory financial statements of the Group's PRC subsidiary.

In accordance with the Company law of the PRC, a domestic enterprise is required to provide statutory reserves of at least 10% of its annual after-tax profit until such reserve has reached 50% of its respective registered capital based on the enterprise's PRC statutory accounts. A domestic enterprise is also required to provide discretionary surplus reserve, at the discretion of the Board of Directors, from the profits determined in accordance with the enterprise's PRC statutory accounts. The aforementioned reserves can only be used for specific purposes and are not distributable as cash dividends. The Group's PRC subsidiary was established as domestic invested enterprise and therefore is subject to the above mentioned restrictions on distributable profits.

As of December 31, 2019 and 2020, the total restricted net assets of the Company's subsidiary incorporated in PRC and subjected to restriction amounted to approximately US\$1,267,900 and US\$1,267,900, respectively. Other subsidiaries are not subjected to such restriction.

As a result of these PRC laws and regulations subject to the limit discussed above that require annual appropriations of 10% of after-tax income to be set aside, prior to payment of dividends, as general reserve fund, the Group's PRC subsidiary is restricted in their ability to transfer a portion of their net assets to the Group.

Foreign exchange and other regulations in the PRC further restrict the Company's PRC subsidiaries from transferring funds to the Company in the form of dividends, loans and advances.

Since the Group has a consolidated shareholders' deficit, its net asset base for purposes of calculating the proportionate share of restricted net assets of consolidated subsidiaries should be zero. Therefore, the restrictions placed on the net assets of the Company's PRC subsidiaries with positive equity would result in the 25 percent threshold being exceeded and a corresponding requirement to provide parent company financial information (Note 18).

16. SUBSEQUENT EVENTS

On January 16, 2021, the Company passed a board resolution whereby certain management members surrendered a total of 491,119 ordinary shares as repayment for their respective promissory notes issued in connection with the exercising of options granted to them. In the meantime, the Company further granted these management members the right to repurchase the surrendered shares by way of new option grants with an exercise price of US\$13.85 per share. The fair values of these share options were US\$7.85 per option, determined by using the binomial option valuation model. The share-based compensation expense related to these share options is expected to be recognized immediately upon grants.

Pursuant to the same board resolution, the 2021 Performance Incentive Plan (the “2021 Plan”) was also adopted, under which an aggregate of 2,994,000 ordinary shares shall be reserved for issuance, and the share limit will automatically increase on the first trading day in January of each year (commencing with 2022) by an amount equal to (1) 5% of the total number of the Company’s outstanding ordinary shares on December 31 of the prior year, or (2) such lesser number as determined by the board of directors. On March 12, 2021, pursuant to the 2021 Plan, the Compensation Committee of Board of Directors of the Company passed resolutions and granted 200,000 share options to a certain employee with an exercise price of US\$17.10 per share. On March 16, 2021, pursuant to the 2021 Plan, the Chair of the Compensation Committee of the Company passed resolutions and (1) granted 408,000 share options to certain employees with an exercise price of US\$17.56 per share, (2) issued 23,733 ordinary shares to management personnel.

On January 18, 2021, the subscriptions receivable from shareholders of US\$197,068 was settled.

On February 1, 2021, the Company entered into a collaboration and license agreement (the “Exelixis Agreement”) with Exelixis, Inc., pursuant to which the Company agreed to generate masked antibodies with the Company’s SAFEbody technology against an initial target and a second target to be selected by Exelixis. Under the Exelixis Agreement, the Company has received an US\$11,000,000 upfront payment. In addition, the Company could be eligible to receive, on a target-by-target basis, up to US\$127,500,000 in development and regulatory milestone payments upon the achievement of specified development and regulatory milestones and up to US\$262,500,000 in sales milestone payments upon the achievement of specified commercial milestones. In the aggregate, the Company could be eligible to receive up to US\$255,000,000 in development and regulatory milestone payments and up to US\$525,000,000 in sales milestone payments for both targets under the Exelixis Agreement. In addition, the Company are entitled to receive mid-single-digit percentage net sales-based royalties on products developed under the Exelixis Agreement, subject to certain reductions.

On February 11, 2021, the Company completed its IPO. At the closing of its IPO, the Company issued 8,457,100 American depository shares (“ADSs”) at public offering price of US\$19.00 per ADS. The number of ADSs issued at closing included the exercise in full of the underwriters’ option to purchase 1,103,100 additional ADSs from the Company. The aggregate gross proceeds from the IPO were approximately US\$161 million, before deducting underwriting discounts and commissions and estimated offering expenses payable by the Company. Each ADS represents one and one quarter (1.25) ordinary shares of the Company.

Upon the completion of the IPO, the Company’s then outstanding 5,473,957 Series A-1 Preferred Shares, 2,370,414 Series A-2 Preferred Shares, 7,494,537 Series B Preferred Shares, 5,597,354 Series C-1 Preferred Shares, 1,861,121 Series C-2 Preferred Shares and 4,452,441 Series C-3 Preferred Shares were converted into 5,473,957, 2,370,414, 7,494,537, 5,597,354, 1,861,121 and 4,452,441 ordinary shares, respectively.

17. CONDENSED FINANCIAL INFORMATION OF THE PARENT COMPANY

The Company performed a test on the restricted net assets of consolidated subsidiaries in accordance with Securities and Exchange Commission Regulation S-X Rule 4-08 I(3), “General Notes to Financial Statements” and concluded that it was applicable for the Company to disclose the financial statements for the parent company.

The subsidiaries did not pay any dividends to the Company for the years presented. For the purpose of presenting parent company only financial information, the Company records its investments in its subsidiaries under the equity method of accounting. Such investments are presented on the separate condensed balance sheets of the Company as “Investments (deficit) in subsidiaries” and the loss of the subsidiaries is presented as “share of losses of subsidiaries”. Certain information and footnote disclosures generally included in financial statements prepared in accordance with U.S. GAAP have been condensed and omitted. The footnote disclosures contain supplemental information relating to the operations of the Company, as such, these statements should be read in conjunction with the notes to the consolidated financial statements of the Company.

The Company did not have significant capital and other commitments, long-term obligations, other long-term debt, or guarantees as of December 31, 2019 and 2020.

Balance sheets

	As of December 31,	
	2019	2020
	US\$	US\$
ASSETS		
Current assets:		
Cash and cash equivalents	91,168,159	52,973,889
Short-term investments	8,000,000	—
Amounts due from related parties ^(a)	6,362,724	27,308,613
Prepayments and other current assets	1,211,891	1,625,197
Total current assets	106,742,774	81,907,699
Investments in subsidiaries	2,507,052	—
Other non-current assets	4,299	3,056,931
TOTAL ASSETS	109,254,125	84,964,630
LIABILITIES, MEZZANINE EQUITY AND SHAREHOLDERS' DEFICIT		
Current liabilities:		
Accounts payable	326,762	443,604
Contract liabilities	325,000	112,500
Amounts due to related parties ^(a)	11,247,674	12,787,321
Accruals and other current liabilities	162,341	3,165,097
Warrant liabilities	—	—
Total current liabilities	12,061,777	16,508,522
Deficit in subsidiaries	—	3,396,657
TOTAL LIABILITIES	12,061,777	19,905,179

	As of December 31,	
	2019	2020
	US\$	US\$
LIABILITIES, MEZZANINE EQUITY AND SHAREHOLDERS' DEFICIT (CONTINUED)		
Mezzanine equity:		
Series A-1 convertible redeemable preferred shares (par value of US\$0.0001 per share; 5,473,957 and 5,473,957 shares authorized, issued and outstanding as of December 31, 2019 and 2020, respectively)	5,473,957	5,473,957
Series A-2 convertible redeemable preferred shares (par value of US\$0.0001 per share; 2,370,414 and 2,370,414 shares authorized, issued and outstanding as of December 31, 2019 and 2020, respectively)	3,000,000	3,000,000
Series B convertible redeemable preferred shares (par value of US\$0.0001 per share; 7,494,537 and 7,494,537 shares authorized, issued and outstanding as of December 31, 2019 and 2020, respectively)	27,999,995	27,999,995
Series C-1 convertible redeemable preferred shares (par value of US\$0.0001 per share; 5,597,354 and 5,597,354 shares authorized, issued and outstanding as of December 31, 2019 and 2020, respectively)	48,727,343	48,975,456
Series C-2 convertible redeemable preferred shares (par value of US\$0.0001 per share; 1,861,121 and 1,861,121 shares authorized, issued and outstanding as of December 31, 2019 and 2020, respectively)	18,999,999	18,999,999
Series C-3 convertible redeemable preferred shares (par value of US\$0.0001 per share; 4,452,441 and 4,452,441 shares authorized, issued and outstanding as of December 31, 2019 and 2020, respectively)	50,000,000	50,000,000
Total mezzanine equity	154,201,294	154,449,407
Shareholders' deficit:		
Ordinary shares (par value of US\$0.0001 per share; 500,000,000 and 500,000,000 shares authorized; 15,193,136 shares issued and outstanding as of December 31, 2019; 18,888,070 shares issued and 16,603,070 shares outstanding as of December 31, 2020)	1,519	1,889
Subscriptions receivable from shareholders	(197,068)	(7,172,192)
Additional paid-in capital	6,789,542	23,786,652
Accumulated other comprehensive loss	(344,894)	(350,981)
Accumulated deficit	(63,258,045)	(105,655,324)
Total shareholders' deficit	(57,008,946)	(89,389,956)
TOTAL LIABILITIES, MEZZANINE EQUITY AND SHAREHOLDERS' DEFICIT	109,254,125	84,964,630

Statements of comprehensive loss

	For the years ended December 31,		
	2018	2019	2020
	US\$	US\$	US\$
Revenues			
Service revenue from a related party ^(b)	—	288,983	398,883
Licensing revenue	—	—	225,000
Expenses			
Research and development expenses	(15,803,341)	(18,318,724)	(31,745,136)
Third parties	(1,810,899)	(2,844,722)	(9,582,687)
Related parties	(13,992,442)	(15,474,002)	(22,162,449)
Administrative expenses	(556,382)	(787,568)	(6,092,443)
Loss from operations	(16,359,723)	(18,817,309)	(37,213,696)
Interest income	691,448	908,981	616,933
Other income, net	—	—	103,896
Foreign exchange loss, net	—	(47)	1,616
Change in fair value of warrant liabilities	534,305	1,207,415	—
Equity in income (share of losses) of subsidiaries	(132,214)	268,652	(5,906,028)
Loss before income tax	(15,266,184)	(16,432,308)	(42,397,279)
Income tax expense	—	—	—
Net loss attributable to Adagene Inc.'s shareholders	(15,266,184)	(16,432,308)	(42,397,279)
Other comprehensive income (loss)			
Foreign currency translation adjustments, net of nil tax	(11,288)	65,799	(6,087)
Total comprehensive loss attributable to Adagene Inc.'s shareholders	(15,277,472)	(16,366,509)	(42,403,366)
Net loss attributable to Adagene Inc.'s shareholders	(15,266,184)	(16,432,308)	(42,397,279)
Deemed contribution from convertible redeemable preferred shareholders	1,186,187	—	—
Accretion of convertible redeemable preferred shares to redemption value	(222,846)	(246,184)	(248,113)
Net loss attributable to ordinary shareholders	(14,302,843)	(16,678,492)	(42,645,392)

Statements of cash flows

	For the years ended		
	2018	2019	2020
	US\$	US\$	US\$
Net cash used in operating activities	(16,346,700)	(14,521,997)	(45,755,914)
Third parties	(2,919,363)	(2,660,397)	(26,135,688)
Related parties	(13,427,337)	(11,861,600)	(19,620,226)
Net cash generated from (used in) investing activities	(28,535,658)	25,941,876	7,991,594
Net cash generated from (used in) financing activities	50,018,733	68,999,999	(429,950)
Net increase (decrease) in cash and cash equivalents	5,136,375	80,419,878	(38,194,270)
Cash and cash equivalents at the beginning of year	5,611,906	10,748,281	91,168,159
Cash and cash equivalents at the end of year	10,748,281	91,168,159	52,973,889

(a) The Company had the following related party balances at the end of the year:

	As of December 31,	
	2019	2020
	US\$	US\$
Adagene (Hong Kong) Limited ⁽ⁱ⁾	3,032,766	4,331,082
Adagene Incorporated ⁽ⁱ⁾	2,790,233	7,123,583
Adagene PTE. Ltd ⁽ⁱ⁾	—	15,192,454
Adagene AG ⁽ⁱ⁾	—	630,719
Adagene Australia PTY Ltd. ⁽ⁱ⁾	22,557	—
WuXi AppTec Group	517,168	30,775
Total amounts due from related parties	6,362,724	27,308,613

	As of December 31,	
	2019	2020
	US\$	US\$
Adagene (Suzhou) Limited ⁽ⁱⁱ⁾	9,126,474	12,743,614
Adagene Incorporated ⁽ⁱⁱ⁾	1,743,435	—
Adagene (Hong Kong) Limited ⁽ⁱⁱ⁾	13	—
WuXi AppTec Group	377,752	43,707
Total amounts due to related parties	11,247,674	12,787,321

(i) As of December 31, 2019 and 2020, the amounts due from Adagene (Hong Kong) Limited, Adagene Incorporated and Adagene Australia PTY Ltd. represented the receivables arising from the expenses paid by the Company on behalf of these subsidiaries.

(ii) As of December 31, 2019 and 2020, the amounts due to Adagene (Suzhou) Limited and Adagene Incorporated mainly represented the payables arising from the research and development services provided by these two subsidiaries.

(b) For the years ended December 31, 2020, the service revenue from a related party was for Adagene Incorporated, with zero gross margin rate charged.

Description of Rights of Each Class of Securities Registered under Section 12 of the Securities Exchange Act of 1934 (the “Exchange Act”)

American Depositary Shares (“ADSs”), each representing one and one quarter ordinary shares of Adagene Inc. (“our company” or “us”) are listed on the Nasdaq Global Market and the shares are registered under Section 12(b) of the Exchange Act. This exhibit contains a description of the rights of (i) the holders of ordinary shares and (ii) ADS holders. Shares underlying the ADSs are held by JPMorgan Chase Bank, N.A., as depositary, and holders of ADSs will not be treated as holders of the ordinary shares.

Description of Ordinary Shares

The following is a summary of material provisions of our currently effective seventh amended and restated memorandum and articles of association (the “seventh amended and restated memorandum and articles of association”), as well as the Companies Act (as amended) of the Cayman Islands (the “Companies Act”) insofar as they relate to the material terms of our ordinary shares. Notwithstanding this, because it is a summary, it may not contain all the information that you may otherwise deem important. For more complete information, you should read the entire seventh amended and restated memorandum and articles of association, which has been filed with the Securities and Exchange Commission (the “SEC”) as an exhibit to our Registration Statement on Form F-1 (File Number 333-252210), as amended, initially filed with the SEC on January 19, 2021.

Type and Class of Securities (Item 9.A.5 of Form 20-F)

Each ordinary share has US\$0.0001 par value. The number of ordinary shares that have been issued as of the last day of the financial year ended December 31, 2020 is provided on the cover of the annual report on Form 20-F filed on April 28, 2021 (the “2020 Form 20-F”). Our ordinary shares may be held in either certificated or uncertificated form. Certificates representing the ordinary shares are issued in registered form. We may not issue share to bearer. Our shareholders who are non-residents of the Cayman Islands may freely hold and transfer their ordinary shares.

Preemptive Rights (Item 9.A.3 of Form 20-F)

Our shareholders do not have preemptive rights.

Limitations or Qualifications (Item 9.A.6 of Form 20-F)

Not applicable.

Rights of Other Types of Securities (Item 9.A.7 of Form 20-F)

Not applicable.

Rights of Ordinary Shares (Item 10.B.3 of Form 20-F)

General. Immediately prior to the completion of this offering, our authorized share capital is US\$80,000 divided into 800,000,000 shares comprising (i) 640,000,000 ordinary shares of a par value of US\$0.0001 each, and (ii) 160,000,000 shares of a par value of US\$0.0001 each of such class or classes (however designated) as our board of directors may determine in accordance with our seventh amended and restated memorandum and articles of association. Holders of ordinary shares will have the same rights. All of our issued and outstanding ordinary shares are fully paid and non-assessable. Certificates representing the ordinary shares are issued in registered form. We may not issue share to bearer. Our shareholders who are nonresidents of the Cayman Islands may freely hold, transfer and vote their ordinary shares.

Dividends. The holders of our ordinary shares are entitled to such dividends as may be declared by our board of directors subject to our seventh amended and restated memorandum and articles of association and the Companies Act. In addition, our shareholders may, subject to the provisions of our articles of association, by ordinary resolution declare a dividend, but no dividend may exceed the amount recommended by our directors. Our seventh amended and restated memorandum and articles of association provide that dividends may be declared and paid out of our profits, realized or unrealized, or from any reserve set aside from profits which our board of directors determine is no longer needed. Dividends may also be declared and paid out of the share premium account or any other fund or account which can be authorized for this purpose in accordance with the Companies Act. No dividend may be declared and paid unless our directors determine that, immediately after the payment, we will be able to pay our debts as they become due in the ordinary course of business and we have funds lawfully available for such purpose.

Voting Rights. In respect of all matters subject to a shareholders' vote, holder of an each Ordinary Share is entitled to one vote for each Ordinary Share registered in his or her name on our register of members. Voting at any meeting of shareholders is by way of a poll unless a show of hands is permitted. A poll may be demanded by the chairman of such meeting or any one shareholder.

A quorum required for a meeting of shareholders consists of two or more shareholders holding not less than one-half of the votes attaching to the issued and outstanding shares entitled to vote at general meetings present in person or by proxy or, if a corporation or other non-natural person, by its duly authorized representative. As a Cayman Islands exempted company, we are not obliged by the Companies Act to call shareholders' annual general meetings. Our seventh amended and restated memorandum and articles of association provide that we may (but are not obliged to) in each year hold a general meeting as our annual general meeting in which case we will specify the meeting as such in the notices calling it, and the annual general meeting will be held at such time and place as may be determined by our board of directors. We, however, will hold an annual shareholders' meeting during each fiscal year, as required by the Listing Rules of the Nasdaq Global Market. Each general meeting, other than an annual general meeting, shall be an extraordinary general meeting. Shareholders' annual general meetings and any other general meetings of our shareholders may be called by a majority of our board of directors or our chairman or upon a requisition of shareholders holding at the date of deposit of the requisition not less than one-third of the votes attaching to the issued and outstanding shares entitled to vote at general meetings, in which case the directors are obliged to call such meeting and to put the resolutions so requisitioned to a vote at such meeting; however, our seventh amended and restated memorandum and articles of association do not provide our shareholders with any right to put any proposals before annual general meetings or extraordinary general meetings not called by such shareholders. Advance notice of at least seven (7) days is required for the convening of our annual general meeting and other general meetings in accordance with our seventh amended and restated memorandum and articles of association.

An ordinary resolution to be passed at a meeting by the shareholders requires the affirmative vote of a simple majority of the votes attaching to the ordinary shares cast by those shareholders entitled to vote who are present in person or by proxy at a general meeting, while a special resolution also requires the affirmative vote of no less than two-thirds of the votes attaching to the ordinary shares cast by those shareholders entitled to vote who are present in person or by proxy at a general meeting. A special resolution will be required for important matters such as a change of name or making changes to our seventh amended and restated memorandum and articles of association.

Transfer of Ordinary Shares. Subject to the restrictions in our seventh amended and restated memorandum and articles of association as set out below, any of our shareholders may transfer all or any of his or her ordinary shares by an instrument of transfer in the usual or common form or any other form approved by our board of directors.

Our board of directors may, in its absolute discretion, decline to register any transfer of any Ordinary Share. Our board of directors may also decline to register any transfer of any Ordinary Share unless:

- the instrument of transfer is lodged with us, accompanied by the certificate for the ordinary shares to which it relates and such other evidence as our board of directors may reasonably require to show the right of the transferor to make the transfer;
- the instrument of transfer is in respect of only one class of shares;
- the instrument of transfer is properly stamped, if required;
- in the case of a transfer to joint holders, the number of joint holders to whom the Ordinary Share is to be transferred does not exceed four;
- the shares are free from any lien in favor of us; and
- a fee of such maximum sum as the Nasdaq may determine to be payable or such lesser sum as our directors may from time to time require is paid to us in respect thereof.

If our directors refuse to register a transfer, they shall, within three months after the date on which the instrument of transfer was lodged, send to each of the transferor and the transferee notice of such refusal.

The registration of transfers may, after compliance with any notice requirement of the Nasdaq, be suspended and the register closed at such times and for such periods as our board of directors may from time to time determine, *provided, however*, that the registration of transfers shall not be suspended nor the register closed for more than 30 days in any year as our board may determine.

Liquidation. On a return of capital on winding up or otherwise (other than on conversion, redemption or purchase of ordinary shares), if the assets available for distribution amongst our shareholders shall be more than sufficient to repay the whole of the share capital at the commencement of the winding up, the surplus shall be distributed amongst our shareholders in proportion to the par value of the shares held by them at the commencement of the winding up, subject to a deduction from those shares in respect of which there are monies due, of all monies payable to our company for unpaid calls or otherwise. If our assets available for distribution are insufficient to repay all of the paid-up capital, the assets will be distributed so that the losses are borne by our shareholders in proportion to the par value of the shares held by them. Any distribution of assets or capital to a holder of ordinary shares will be the same in any liquidation event.

Calls on Ordinary Shares and Forfeiture of Ordinary Shares. Our board of directors may from time to time make calls upon shareholders for any amounts unpaid on their ordinary shares in a notice served to such shareholders at least 14 clear days prior to the specified time of payment. The ordinary shares that have been called upon and remain unpaid are subject to forfeiture.

Redemption, Repurchase and Surrender of Ordinary Shares. We may issue shares on terms that such shares are subject to redemption, at our option or at the option of the holders thereof, on such terms and in such manner as may be determined, before the issue of such shares, by our board of directors or by an ordinary resolution of our shareholders. Our company may also repurchase any of our shares provided that the manner and terms of such purchase have been approved by our board of directors or by an ordinary resolution of our shareholders, or are otherwise authorized by our seventh amended and restated memorandum and articles of association. Under the Companies Act, the redemption or repurchase of any share may be paid out of our company's profits or out of the proceeds of a fresh issue of shares made for the purpose of such redemption or repurchase, or out of capital (including share premium account and capital redemption reserve) if the Company can, immediately following such payment, pay its debts as they fall due in the ordinary course of business. In addition, under the Companies Act no such share may be redeemed or repurchased (a) unless it is fully paid up, (b) if such redemption or repurchase would result in there being no shares outstanding, or (c) if the company has commenced liquidation. In addition, our company may accept the surrender of any fully paid share for no consideration.

Requirements to Change the Rights of Holders of Ordinary Shares (Item 10.B.4 of Form 20-F)

Variations of Rights of Shares. If at any time our share capital is divided into different classes or series of shares, the rights attached to any class or series of shares (unless otherwise provided by the terms of issue of the shares of that class or series), whether or not our company is being wound-up, may be varied with the consent in writing of holders of not less than a majority of the issued shares of that class or series or with the sanction of a special resolution at a separate meeting of the holders of the shares of the class or series. The rights conferred upon the holders of the shares of any class issued shall not, unless otherwise expressly provided by the terms of issue of the shares of that class, be deemed to be varied by the creation or issue of further shares ranking *pari passu* with such existing class of shares.

Limitations on the Rights to Own Ordinary Shares (Item 10.B.6 of Form 20-F)

There are no limitations under the laws of the Cayman Islands or under the seventh amended and restated memorandum and articles of association that limit the right of non-resident or foreign owners to hold or vote ordinary shares, other than anti-takeover provisions contained in the seventh amended and restated memorandum and articles of association to limit the ability of others to acquire control of our company or cause our company to engage in change-of-control transactions.

Provisions Affecting Any Change of Control (Item 10.B.7 of Form 20-F)

Anti-Takeover Provisions. Some provisions of our seventh amended and restated memorandum and articles of association may discourage, delay or prevent a change of control of our company or management that shareholders may consider favorable, including provisions that authorize our board of directors to issue preferred shares in one or more series and to designate the price, rights, preferences, privileges and restrictions of such preferred shares without any further vote or action by our shareholders.

Ownership Threshold (Item 10.B.8 of Form 20-F)

There are no provisions under the laws of the Cayman Islands or under the seventh amended and restated memorandum and articles of association that govern the ownership threshold above which shareholder ownership must be disclosed.

Differences Between the Law of Different Jurisdictions (Item 10.B.9 of Form 20-F)

We are incorporated under, and are governed by, the laws of the Cayman Islands. The Companies Act is derived, to a large extent, from the older Companies Acts of England, but does not follow many recent English law statutory enactments. In addition, the Companies Act differs from laws applicable to United States corporations and their shareholders. Set forth below is a summary of the significant differences between the provisions of the Companies Act applicable to us and the laws applicable to companies incorporated in the State of Delaware.

Mergers and Similar Arrangements. The Companies Act permits mergers and consolidations between Cayman Islands companies and between Cayman Islands companies and non-Cayman Islands companies. For these purposes, (a) “merger” means the merging of two or more constituent companies and the vesting of their undertaking, property and liabilities in one of such companies as the surviving company, and (b) a “consolidation” means the combination of two or more constituent companies into a consolidated company and the vesting of the undertaking, property and liabilities of such companies to the consolidated company. In order to effect such a merger or consolidation, the directors of each constituent company must approve a written plan of merger or consolidation, which must then be authorized by (a) a special resolution of the shareholders of each constituent company, and (b) such other authorization, if any, as may be specified in such constituent company’s articles of association. The written plan of merger or consolidation must be filed with the Registrar of Companies of the Cayman Islands together with a declaration as to the solvency of the consolidated or surviving company, a declaration as to the assets and liabilities of each constituent company and an undertaking that a copy of the certificate of merger or consolidation will be given to the members and creditors of each constituent company and that notification of the merger or consolidation will be published in the Cayman Islands Gazette. Court approval is not required for a merger or consolidation which is effected in compliance with these statutory procedures.

A merger between a Cayman parent company and its Cayman subsidiary or subsidiaries does not require authorization by a resolution of shareholders of that Cayman subsidiary if a copy of the plan of merger is given to every member of that Cayman subsidiary to be merged unless that member agrees otherwise. For this purpose, a company is a “parent” of a subsidiary if it holds issued shares that together represent at least ninety percent (90%) of the votes at a general meeting of the subsidiary.

The consent of each holder of a fixed or floating security interest over a constituent company is required unless this requirement is waived by a court in the Cayman Islands.

Save in certain limited circumstances, a shareholder of a Cayman constituent company who dissents from the merger or consolidation is entitled to payment of the fair value of his shares (which, if not agreed between the parties, will be determined by the Cayman Islands court) upon dissenting to the merger or consolidation, *provided* that the dissenting shareholder complies strictly with the procedures set out in the Companies Act. The exercise of dissenter rights will preclude the exercise by the dissenting shareholder of any other rights to which he or she might otherwise be entitled by virtue of holding shares, save for the right to seek relief on the grounds that the merger or consolidation is void or unlawful.

Separate from the statutory provisions relating to mergers and consolidations, the Companies Act also contains statutory provisions that facilitate the reconstruction and amalgamation of companies by way of schemes of arrangement, *provided* that the arrangement is approved by a majority in number of each class of shareholders and creditors with whom the arrangement is to be made, and who must in addition represent three-fourths in value of each such class of shareholders or creditors, as the case may be, that are present and voting either in person or by proxy at a meeting, or meetings, convened for that purpose. The convening of the meetings and subsequently the arrangement must be sanctioned by the Grand Court of the Cayman Islands. While a dissenting shareholder has the right to express to the court the view that the transaction ought not to be approved, the court can be expected to approve the arrangement if it determines that:

- the statutory provisions as to the required majority vote have been met;
- the shareholders have been fairly represented at the meeting in question and the statutory majority are acting bona fide without coercion of the minority to promote interests adverse to those of the class;
- the arrangement is such that may be reasonably approved by an intelligent and honest man of that class acting in respect of his interest; and
- the arrangement is not one that would more properly be sanctioned under some other provision of the Companies Act.

The Companies Act also contains a statutory power of compulsory acquisition which may facilitate the “squeeze out” of a dissenting minority shareholder upon a tender offer. When a tender offer is made and accepted by holders of 90.0% of the shares affected within four months, the offeror may, within a two-month period commencing on the expiration of such four-month period, require the holders of the remaining shares to transfer such shares to the offeror on the terms of the offer. An objection can be made to the Grand Court of the Cayman Islands but this is unlikely to succeed in the case of an offer which has been so approved unless there is evidence of fraud, bad faith or collusion.

If an arrangement and reconstruction is thus approved, or if a tender offer is made and accepted, a dissenting shareholder would have no rights comparable to appraisal rights, which would otherwise ordinarily be available to dissenting shareholders of Delaware corporations, providing rights to receive payment in cash for the judicially determined value of the shares.

Shareholders' Suits. In principle, we will normally be the proper plaintiff to sue for a wrong done to us as a company, and as a general rule a derivative action may not be brought by a minority shareholder. However, based on English authorities, which would in all likelihood be of persuasive authority in the Cayman Islands, the Cayman Islands court can be expected to follow and apply the common law principles (namely the rule in *Foss v. Harbottle* and the exceptions thereto) which permit a minority shareholder to commence a class action against or derivative actions in the name of the company to challenge actions where:

- a company acts or proposes to act illegally or ultra vires;
- the act complained of, although not ultra vires, could only be effected duly if authorized by more than a simple majority vote that has not been obtained; and
- those who control the company are perpetrating a “fraud on the minority.”

Indemnification of Directors and Executive Officers and Limitation of Liability.

Cayman Islands law does not limit the extent to which a company’s memorandum and articles of association may provide for indemnification of officers and directors, except to the extent any such provision may be held by the Cayman Islands courts to be contrary to public policy, such as to provide indemnification against civil fraud or the consequences of committing a crime. Our post-offering memorandum and articles of association provide that that we shall indemnify our officers and directors against all actions, proceedings, costs, charges, expenses, losses, damages or liabilities incurred or sustained by such directors or officer, other than by reason of such person’s dishonesty, willful default or fraud, in or about the conduct of our company’s business or affairs (including as a result of any mistake of judgment) or in the execution or discharge of his duties, powers, authorities or discretions, including without prejudice to the generality of the foregoing, any costs, expenses, losses or liabilities incurred by such director or officer in defending (whether successfully or otherwise) any civil proceedings concerning our company or its affairs in any court whether in the Cayman Islands or elsewhere. This standard of conduct is generally the same as permitted under the Delaware General Corporation Law for a Delaware corporation.

In addition, we have entered into indemnification agreements with our directors and executive officers that provide such persons with additional indemnification beyond that provided in our post-offering memorandum and articles of association.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers or persons controlling us under the foregoing provisions, we have been informed that in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Directors’ Fiduciary Duties. Under Delaware corporate law, a director of a Delaware corporation has a fiduciary duty to the corporation and its shareholders. This duty has two components: the duty of care and the duty of loyalty. The duty of care requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of, and disclose to shareholders, all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director acts in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. This duty prohibits self-dealing by a director and mandates that the best interest of the corporation and its shareholders take precedence over any interest possessed by a director, officer or controlling shareholder and not shared by the shareholders generally. In general, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Should such evidence be presented concerning a transaction by a director, the director must prove the procedural fairness of the transaction, and that the transaction was of fair value to the corporation.

As a matter of Cayman Islands law, a director of a Cayman Islands company is in the position of a fiduciary with respect to the company and therefore it is considered that he owes the following duties to the company—a duty to act bona fide in the best interests of the company, a duty not to make a profit based on his position as director (unless the company permits him to do so), a duty not to put himself in a position where the interests of the company conflict with his personal interest or his duty to a third party, and a duty to exercise powers for the purpose for which such powers were intended. A director of a Cayman Islands company owes to the company a duty to act with skill and care. It was previously considered that a director need not exhibit in the performance of his duties a greater degree of skill than may reasonably be expected from a person of his knowledge and experience. However, English and Commonwealth courts have moved towards an objective standard with regard to the required skill and care and these authorities are likely to be followed in the Cayman Islands.

Under our post-offering memorandum and articles of association, directors who are in any way, whether directly or indirectly, interested in a contract or proposed contract with our company must declare the nature of their interest at a meeting of the board of directors.

Shareholder Action by Written Consent. Under the Delaware General Corporation Law, a corporation may eliminate the right of shareholders to act by written consent by amendment to its certificate of incorporation. The Companies Act and our post-offering memorandum and articles of association provide that our shareholders may approve corporate matters by way of a unanimous written resolution signed by or on behalf of each shareholder who would have been entitled to vote on such matter at a general meeting without a meeting being held.

Shareholder Proposals. Under the Delaware General Corporation Law, a shareholder has the right to put any proposal before the annual meeting of shareholders, provided it complies with the notice provisions in the governing documents. A special meeting may be called by the board of directors or any other person authorized to do so in the governing documents, but shareholders may be precluded from calling special meetings.

The Companies Act provides shareholders with only limited rights to requisition a general meeting, and does not provide shareholders with any right to put any proposal before a general meeting. However, these rights may be provided in a company's articles of association. Our post-offering memorandum and articles of association allow our shareholders holding in aggregate not less than twenty percent of all votes attaching to the issued and outstanding shares of our company entitled to vote at general meetings to requisition an extraordinary general meeting of our shareholders, in which case our board is obliged to convene an extraordinary general meeting and to put the resolutions so requisitioned to a vote at such meeting. Other than this right to requisition a shareholders' meeting, our post-offering memorandum and articles of association do not provide our shareholders with any other right to put proposals before annual general meetings or extraordinary general meetings not called by such shareholders. As an exempted Cayman Islands company, we are not obliged by law to call shareholders' annual general meetings.

Cumulative Voting. Under the Delaware General Corporation Law, cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation specifically provides for it. Cumulative voting potentially facilitates the representation of minority shareholders on a board of directors since it permits the minority shareholder to cast all the votes to which the shareholder is entitled on a single director, which increases the shareholder's voting power with respect to electing such director. There are no prohibitions in relation to cumulative voting under the laws of the Cayman Islands but our post-offering memorandum and articles of association do not provide for cumulative voting. As a result, our shareholders are not afforded any less protections or rights on this issue than shareholders of a Delaware corporation.

Removal of Directors. Under the Delaware General Corporation Law, a director of a corporation with a classified board may be removed only for cause with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise. Under our post-offering memorandum and articles of association, directors not appointed by Peter Peizhi Luo, JSR Limited, and General Atlantic Singapore AI Pte. Ltd. may be removed with or without cause, by an ordinary resolution of our shareholders. A director shall hold office until the expiration of his or her term or his or her successor shall have been elected and qualified, or until his or her office is otherwise vacated. In addition, a director's office shall be vacated if the director (i) becomes bankrupt or makes any arrangement or composition with his creditors; (ii) is found to be or becomes of unsound mind or dies; (iii) resigns his office by notice in writing to the company; (iv) without special leave of absence from our board of directors, is absent from three consecutive meetings of the board and the board resolves that his office be vacated; (v) is prohibited by law from being a director; or (vi) is removed from office pursuant to any other provisions of our post-offering memorandum and articles of association.

Transactions with Interested Shareholders. The Delaware General Corporation Law contains a business combination statute applicable to Delaware corporations whereby, unless the corporation has specifically elected not to be governed by such statute by amendment to its certificate of incorporation, it is prohibited from engaging in certain business combinations with an “interested shareholder” for three years following the date that such person becomes an interested shareholder. An interested shareholder generally is a person or a group who or which owns or owned 15% or more of the target’s outstanding voting share within the past three years. This has the effect of limiting the ability of a potential acquirer to make a two-tiered bid for the target in which all shareholders would not be treated equally. The statute does not apply if, among other things, prior to the date on which such shareholder becomes an interested shareholder, the board of directors approves either the business combination or the transaction which resulted in the person becoming an interested shareholder. This encourages any potential acquirer of a Delaware corporation to negotiate the terms of any acquisition transaction with the target’s board of directors.

Cayman Islands law has no comparable statute. As a result, we cannot avail ourselves of the types of protections afforded by the Delaware business combination statute. However, although Cayman Islands law does not regulate transactions between a company and its significant shareholders, the directors of the Company are required to comply with fiduciary duties which they owe to the Company under Cayman Islands laws, including the duty to ensure that, in their opinion, any such transactions must be entered into bona fide in the best interests of the company, and are entered into for a proper corporate purpose and not with the effect of constituting a fraud on the minority shareholders.

Dissolution; Winding up. Under the Delaware General Corporation Law, unless the board of directors approves the proposal to dissolve, dissolution must be approved by shareholders holding 100% of the total voting power of the corporation. Only if the dissolution is initiated by the board of directors may it be approved by a simple majority of the corporation’s outstanding shares. Delaware law allows a Delaware corporation to include in its certificate of incorporation a supermajority voting requirement in connection with dissolutions initiated by the board.

Under Cayman Islands law, a company may be wound up by either an order of the courts of the Cayman Islands or by a special resolution of its members or, if the company is unable to pay its debts as they fall due, by an ordinary resolution of its members. The court has authority to order winding up in a number of specified circumstances including where it is, in the opinion of the court, just and equitable to do so.

Variation of Rights of Shares. Under the Delaware General Corporation Law, a corporation may vary the rights of a class of shares with the approval of a majority of the outstanding shares of such class, unless the certificate of incorporation provides otherwise. Under Cayman Islands law and our post-offering memorandum and articles of association, if our share capital is divided into more than one class of shares, we may vary the rights attached to any class with the written consent of the holders of not less than a majority of the issued shares of that class or with the sanction of a special resolution passed at a general meeting of the holders of the shares of that class.

Amendment of Governing Documents. Under the Delaware General Corporation Law, a corporation’s governing documents may be amended with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise. Under the Companies Act and our post-offering memorandum and articles of association, our memorandum and articles of association may only be amended by a special resolution of our shareholders.

Rights of Nonresident or Foreign Shareholders. There are no limitations imposed by our post-offering memorandum and articles of association on the rights of nonresident or foreign shareholders to hold or exercise voting rights on our shares. In addition, there are no provisions in our post-offering seventh amended and restated memorandum and articles of association governing the ownership threshold above which shareholder ownership must be disclosed.

Changes in Capital (Item 10.B.10)

We may from time to time by ordinary resolution:

- increase the share capital by such sum, to be divided into shares of such classes and amount, as the resolution shall prescribe;
- consolidate and divide all or any of our share capital into shares of a larger amount than our existing shares;
- sub-divide our existing shares, or any of them into shares of a smaller amount; or
- cancel any shares which, at the date of the passing of the resolution, have not been taken or agreed to be taken by any person and diminish the amount of our share capital by the amount of the shares so canceled.

We may by special resolution, subject to any confirmation or consent required by the Companies Act, reduce our share capital or any capital redemption reserve in any manner permitted by law.

Debt Securities (Item 12.A of Form 20-F)

Not applicable.

Warrants and Rights (Item 12.B of Form 20-F)

Not applicable.

Other Securities (Item 12.C of Form 20-F)

Not applicable.

Description of American Depositary Shares (Items 12.D.1 and 12.D.2 of Form 20-F)

JPMorgan Chase Bank, N.A. (“JPMorgan”), as depositary registers and delivers the ADSs. Each ADS represents one and one quarter ordinary shares, deposited with the custodian, as agent of the depositary, under the deposit agreement among ourselves, the depositary and yourself as an ADR holder. Each ADS also represents any securities, cash or other property deposited with the depositary but which they have not distributed directly to you.

The depositary’s office is located at 383 Madison Avenue, Floor 11, New York, NY 10179.

As an ADR holder or beneficial owner, we will not treat you as a shareholder of ours and you will not have any shareholder rights. Cayman Island law governs shareholder rights. Because the depositary or its nominee will be the shareholder of record for the shares represented by all outstanding ADSs, shareholder rights rest with such record holder. Your rights are those of an ADR holder or of a beneficial owner. Such rights derive from the terms of the deposit agreement to be entered into among us, the depositary and all holders and beneficial owners from time to time of ADRs issued under the deposit agreement and, in the case of a beneficial owner, from the arrangements between the beneficial owner and the holder of the corresponding ADRs. The obligations of the depositary and its agents are also set out in the deposit agreement. Because the depositary or its nominee will actually be the registered owner of the shares, you must rely on it to exercise the rights of a shareholder on your behalf.

The following is a summary of what we believe to be the material terms of the deposit agreement. Notwithstanding this, because it is a summary, it may not contain all the information that you may otherwise deem important. For more complete information, you should read the entire deposit agreement and the form of ADR which contains the terms of your ADSs. You can read a copy of the deposit agreement which has been filed as an exhibit to a Registration Statement on Form F-6 (File Number 333-252543). The form of ADR has been filed with the SEC as an exhibit to our Registration Statement on Form F-1 (File Number 333-252210), as amended, initially filed with the SEC on January 19, 2021.

Share Dividends and Other Distributions

How will I receive dividends and other distributions on the shares underlying my ADSs?

We may make various types of distributions with respect to our securities. The depositary has agreed that, to the extent practicable, it will pay to you the cash dividends or other distributions it or the custodian receives on shares or other deposited securities, after converting any cash received into U.S. dollars (if it determines such conversion may be made on a reasonable basis) and, in all cases, making any necessary deductions provided for in the deposit agreement. The depositary may utilize a division, branch or affiliate of JPMorgan to direct, manage and/or execute any public and/or private sale of securities under the deposit agreement. Such division, branch and/or affiliate may charge the depositary a fee in connection with such sales, which fee is considered an expense of the depositary. You will receive these distributions in proportion to the number of underlying securities that your ADSs represent.

Except as stated below, the depositary will deliver such distributions to ADR holders in proportion to their interests in the following manner:

- *Cash.* The depositary will distribute any U.S. dollars available to it resulting from a cash dividend or other cash distribution or the net proceeds of sales of any other distribution or portion thereof (to the extent applicable), on an averaged or other practicable basis, subject to (i) appropriate adjustments for taxes withheld, (ii) such distribution being impermissible or impracticable with respect to certain registered ADR holders, and (iii) deduction of the depositary's and/or its agents' expenses in (1) converting any foreign currency to U.S. dollars to the extent that it determines that such conversion may be made on a reasonable basis, (2) transferring foreign currency or U.S. dollars to the United States by such means as the depositary may determine to the extent that it determines that such transfer may be made on a reasonable basis, (3) obtaining any approval or license of any governmental authority required for such conversion or transfer, which is obtainable at a reasonable cost and within a reasonable time and (4) making any sale by public or private means in any commercially reasonable manner. *If exchange rates fluctuate during a time when the depositary cannot convert a foreign currency, you may lose some or all of the value of the distribution.*
- *Shares.* In the case of a distribution in shares, the depositary will issue additional ADRs to evidence the number of ADSs representing such shares. Only whole ADSs will be issued. Any shares which would result in fractional ADSs will be sold and the net proceeds will be distributed in the same manner as cash to the ADR holders entitled thereto.
- *Rights to receive additional shares.* In the case of a distribution of rights to subscribe for additional shares or other rights, if we timely provide evidence satisfactory to the depositary that it may lawfully distribute such rights, the depositary will distribute warrants or other instruments in the discretion of the depositary representing such rights. However, if we do not timely furnish such evidence, the depositary may:
 - (i) sell such rights if practicable and distribute the net proceeds in the same manner as cash to the ADR holders entitled thereto; or
 - (ii) if it is not practicable to sell such rights by reason of the non-transferability of the rights, limited markets therefor, their short duration or otherwise, do nothing and allow such rights to lapse, in which case ADR holders will receive nothing and the rights may lapse.

- *Other Distributions.* In the case of a distribution of securities or property other than those described above, the depositary may either (i) distribute such securities or property in any manner it deems equitable and practicable or (ii) to the extent the depositary deems distribution of such securities or property not to be equitable and practicable, sell such securities or property and distribute any net proceeds in the same way it distributes cash.

If the depositary determines in its discretion that any distribution described above is not practicable with respect to any specific registered ADR holder, the depositary may choose any method of distribution that it deems practicable for such ADR holder, including the distribution of foreign currency, securities or property, or it may retain such items, without paying interest on or investing them, on behalf of the ADR holder as deposited securities, in which case the ADSs will also represent the retained items.

Any U.S. dollars will be distributed by checks drawn on a bank in the United States for whole dollars and cents. Fractional cents will be withheld without liability and dealt with by the depositary in accordance with its then current practices.

The depositary is not responsible if it fails to determine that any distribution or action is lawful or reasonably practicable.

There can be no assurance that the depositary will be able to convert any currency at a specified exchange rate or sell any property, rights, shares or other securities at a specified price, nor that any of such transactions can be completed within a specified time period. All purchases and sales of securities will be handled by the depositary in accordance with its then current policies, which are currently set forth on the "Disclosures" page (or successor page) of www.adr.com (as updated by the depositary from time to time, "ADR.com").

Deposit, Withdrawal and Cancellation

How does the depositary issue ADSs?

The depositary will issue ADSs if you or your broker deposit shares or evidence of rights to receive shares with the custodian and pay the fees and expenses owing to the depositary in connection with such issuance. In the case of the ADSs to be issued under this prospectus, we will arrange with the underwriters named herein to deposit such shares.

Shares deposited in the future with the custodian must be accompanied by certain delivery documentation and shall, at the time of such deposit, be registered in the name of JPMorgan Chase Bank, N.A., as depositary for the benefit of holders of ADRs or in such other name as the depositary shall direct.

The custodian will hold all deposited shares (including those being deposited by or on our behalf in connection with the offering to which this prospectus relates) for the account and to the order of the depositary, in each case for the benefit of ADR holders. ADR holders and beneficial owners thus have no direct ownership interest in the shares and only have such rights as are contained in the deposit agreement. The custodian will also hold any additional securities, property and cash received on or in substitution for the deposited shares. The deposited shares and any such additional items are referred to as "deposited securities".

Deposited securities are not intended to, and shall not, constitute proprietary assets of the depositary, the custodian or their nominees. Beneficial ownership in deposited securities is intended to be, and shall at all times during the term of the deposit agreement continue to be, vested in the beneficial owners of the ADSs representing such deposited securities. Notwithstanding anything else contained herein, in the deposit agreement, in the form of ADR and/or in any outstanding ADSs, the depositary, the custodian and their respective nominees are intended to be, and shall at all times during the term of the deposit agreement be, the record holder(s) only of the deposited securities represented by the ADSs for the benefit of the ADR holders. The depositary, on its own behalf and on behalf of the custodian and their respective nominees, disclaims any beneficial ownership interest in the deposited securities held on behalf of the ADR holders.

Upon each deposit of shares, receipt of related delivery documentation and compliance with the other provisions of the deposit agreement, including the payment of the fees and charges of the depositary and any taxes or other fees or charges owing, the depositary will issue an ADR or ADRs in the name or upon the order of the person entitled thereto evidencing the number of ADSs to which such person is entitled. All of the ADSs issued will, unless specifically requested to the contrary, be part of the depositary's direct registration system, and a registered holder will receive periodic statements from the depositary which will show the number of ADSs registered in such holder's name. An ADR holder can request that the ADSs not be held through the depositary's direct registration system and that a certificated ADR be issued.

How do ADR holders cancel an ADS and obtain deposited securities?

When you turn in your ADR certificate at the depositary's office, or when you provide proper instructions and documentation in the case of direct registration ADSs, the depositary will, upon payment of certain applicable fees, charges and taxes, deliver the underlying shares to you or upon your written order. Delivery of deposited securities in certificated form will be made at the custodian's office. At your risk, expense and request, the depositary may deliver deposited securities at such other place as you may request.

The depositary may only restrict the withdrawal of deposited securities in connection with:

- temporary delays caused by closing our transfer books or those of the depositary or the deposit of shares in connection with voting at a shareholders' meeting, or the payment of dividends;
- the payment of fees, taxes and similar charges; or
- compliance with any U.S. or foreign laws or governmental regulations relating to the ADRs or to the withdrawal of deposited securities.

This right of withdrawal may not be limited by any other provision of the deposit agreement.

Record Dates

The depositary may, after consultation with us if practicable, fix record dates (which, to the extent applicable, shall be as near as practicable to any corresponding record dates set by us) for the determination of the registered ADR holders who will be entitled (or obligated, as the case may be):

- to receive any distribution on or in respect of deposited securities,
- to give instructions for the exercise of voting rights at a meeting of holders of shares, or
- to pay the fee assessed by the depositary for administration of the ADR program and for any expenses as provided for in the ADR,
- to receive any notice or to act in respect of other matters,

all subject to the provisions of the deposit agreement.

Voting Rights

How do I vote?

If you are an ADR holder and the depositary asks you to provide it with voting instructions, you may instruct the depositary how to exercise the voting rights for the shares which underlie your ADSs. As soon as practicable after receipt from us of notice of any meeting at which the holders of shares are entitled to vote, or of our solicitation of consents or proxies from holders of shares, the depositary shall fix the ADS record date in accordance with the provisions of the deposit agreement, provided that if the depositary receives a written request from us in a timely manner and at least 30 days prior to the date of such vote or meeting, the depositary shall, at our expense, distribute to the registered ADR holders a "voting notice" stating (i) final information particular to such vote and meeting and any solicitation materials, (ii) that each ADR holder on the record date set by the depositary will, subject to any applicable provisions of Cayman Islands law, be entitled to instruct the depositary as to the exercise of the voting rights, if any, pertaining to the deposited securities represented by the ADSs evidenced by such ADR holder's ADRs and (iii) the manner in which such instructions may be given or deemed given in accordance with the deposit agreement, including instructions for giving a discretionary proxy to a person designated by us. Each ADR holder shall be solely responsible for the forwarding of voting notices to the beneficial owners of ADSs registered in such ADR holder's name. There is no guarantee that ADR holders and beneficial owners generally or any holder or beneficial owner in particular will receive the notice described above with sufficient time to enable such ADR holder or beneficial owner to return any voting instructions to the depositary in a timely manner.

Following actual receipt by the ADR department responsible for proxies and voting of ADR holders' instructions (including, without limitation, instructions of any entity or entities acting on behalf of the nominee for DTC), the depositary shall, in the manner and on or before the time established by the depositary for such purpose, endeavor to vote or cause to be voted the deposited securities represented by the ADSs evidenced by such ADR holders' ADRs in accordance with such instructions insofar as practicable and permitted under the provisions of or governing deposited securities.

To the extent that (A) we have provided the depositary with at least 35 days' notice of the proposed meeting, (B) the voting notice will be received by all ADR holders and beneficial owners no less than 10 days prior to the date of the meeting and/or the cut-off date for the solicitation of consents, and (C) the depositary does not receive instructions on a particular agenda item from an ADR holder (including, without limitation, any entity or entities acting on behalf of the nominee for DTC) in a timely manner, such ADR holder shall be deemed, and in the deposit agreement the depositary is instructed to deem such ADR holder, to have instructed the depositary to give a discretionary proxy for such agenda item(s) to a person designated by us to vote the deposited securities represented by the ADSs for which actual instructions were not so given by all such ADR holders on such agenda item(s), provided that no such instruction shall be deemed given and no discretionary proxy shall be given unless (1) we inform the depositary in writing (and we agree to provide the depositary with such instruction promptly in writing) that (a) we wish such proxy to be given with respect to such agenda item(s), (b) there is no substantial opposition existing with respect to such agenda item(s) and (c) such agenda item(s), if approved, would not materially or adversely affect the rights of holders of shares, and (2) the depositary has obtained an opinion of counsel, in form and substance satisfactory to the depositary, confirming that (i) the granting of such discretionary proxy does not subject the depositary to any reporting obligations in the Cayman Islands, (ii) the granting of such proxy will not result in a violation of the laws, rules, regulations or permits of the Cayman Islands, (iii) the voting arrangement and deemed instruction as contemplated herein will be given effect under the laws, rules and regulations of the Cayman Islands, and (iv) the granting of such discretionary proxy will not under any circumstances result in the shares represented by the ADSs being treated as assets of the depositary under the laws, rules or regulations of the Cayman Islands.

The depositary may from time to time access information available to it to consider whether any of the circumstances described above exist, or request additional information from us in respect thereto. By taking any such action, the depositary shall not in any way be deemed or inferred to have been required, or have had any duty or responsibility (contractual or otherwise), to monitor or inquire whether any of the circumstances described above existed. In addition to the limitations provided for in the deposit agreement, ADR holders and beneficial owners are advised and agree that (a) the depositary will rely fully and exclusively on us to inform it of any of the circumstances set forth above, and (b) neither the depositary, the custodian nor any of their respective agents shall be obliged to inquire or investigate whether any of the circumstances described above exist and/or whether we complied with our obligation to timely inform the depositary of such circumstances. Neither the depositary, the custodian nor any of their respective agents shall incur any liability to ADR holders or beneficial owners (i) as a result of our failure to determine that any of the circumstances described above exist or our failure to timely notify the depositary of any such circumstances or (ii) if any agenda item which is approved at a meeting has, or is claimed to have, a material or adverse effect on the rights of holders of shares. Because there is no guarantee that ADR holders and beneficial owners will receive the notices described above with sufficient time to enable such ADR holders or beneficial owners to return any voting instructions to the depositary in a timely manner, ADR holders and beneficial owners may be deemed to have instructed the depositary to give a discretionary proxy to a person designated by us in such circumstances, and neither the depositary, the custodian nor any of their respective agents shall incur any liability to ADR holders or beneficial owners in such circumstances.

ADR holders are strongly encouraged to forward their voting instructions to the depositary as soon as possible. For instructions to be valid, the ADR department of the depositary that is responsible for proxies and voting must receive them in the manner and on or before the time specified, notwithstanding that such instructions may have been physically received by the depositary prior to such time. The depositary will not itself exercise any voting discretion in respect of deposited securities. The depositary and its agents will not be responsible for any failure to carry out any instructions to vote any of the deposited securities, for the manner in which any voting instructions are given or deemed to be given in accordance with the deposit agreement, including instructions to give a discretionary proxy to a person designated by us, for the manner in which any vote is cast, including, without limitation, any vote cast by a person to whom the depositary is instructed to grant a discretionary proxy (or deemed to have been instructed to grant a discretionary proxy in accordance with the deposit agreement), or for the effect of any such vote. Notwithstanding anything contained in the deposit agreement or any ADR, the depositary may, to the extent not prohibited by any law, regulation, or requirement of the stock exchange on which the ADSs are listed, in lieu of distribution of the materials provided to the depositary in connection with any meeting of or solicitation of consents or proxies from holders of deposited securities, distribute to the registered holders of ADRs a notice that provides such ADR holders with or otherwise publicizes to such ADR holders instructions on how to retrieve such materials or receive such materials upon request (*i.e.*, by reference to a website containing the materials for retrieval or a contact for requesting copies of the materials).

We have advised the depositary that under Cayman Islands law and our constituent documents, each as in effect as of the date of the deposit agreement, voting at any meeting of shareholders is by show of hands unless a poll is (before or on the declaration of the results of the show of hands) demanded. In the event that voting on any resolution or matter is conducted on a show of hands basis in accordance with our constituent documents, the depositary will refrain from voting and the voting instructions received by the depositary from ADR holders shall lapse. The depositary will not demand a poll or join in demanding a poll, whether or not requested to do so by ADR holders or beneficial owners.

There is no guarantee that you will receive voting materials in time to instruct the depositary to vote and it is possible that you, or persons who hold their ADSs through brokers, dealers or other third parties, will not have the opportunity to exercise a right to vote.

Reports and Other Communications

Will ADR holders be able to view our reports?

The depositary will make available for inspection by ADR holders at the offices of the depositary and the custodian the deposit agreement, the provisions of or governing deposited securities, and any written communications from us which are both received by the custodian or its nominee as a holder of deposited securities and made generally available to the holders of deposited securities.

Additionally, if we make any written communications generally available to holders of our shares, and we furnish copies thereof (or English translations or summaries) to the depositary, it will distribute the same to registered ADR holders.

Amendment and Termination

How may the deposit agreement be amended?

We may agree with the depository to amend the deposit agreement and the ADSs without your consent for any reason. ADR holders must be given at least 30 days' notice of any amendment that imposes or increases any fees or charges (other than stock transfer or other taxes and other governmental charges, transfer or registration fees, SWIFT, cable, telex or facsimile transmission costs, delivery costs or other such expenses), or otherwise prejudices any substantial existing right of ADR holders or beneficial owners. Such notice need not describe in detail the specific amendments effectuated thereby, but must identify to ADR holders and beneficial owners a means to access the text of such amendment. If an ADR holder continues to hold an ADR or ADRs after being so notified, such ADR holder and any beneficial owner are deemed to agree to such amendment and to be bound by the deposit agreement as so amended. No amendment, however, will impair your right to surrender your ADSs and receive the underlying securities, except in order to comply with mandatory provisions of applicable law.

Any amendments or supplements which (i) are reasonably necessary (as agreed by us and the depository) in order for (a) the ADSs to be registered on Form F-6 under the Securities Act of 1933 or (b) the ADSs or shares to be traded solely in electronic book-entry form and (ii) do not in either such case impose or increase any fees or charges to be borne by ADR holders, shall be deemed not to prejudice any substantial rights of ADR holders or beneficial owners. Notwithstanding the foregoing, if any governmental body or regulatory body should adopt new laws, rules or regulations which would require amendment or supplement of the deposit agreement or the form of ADR to ensure compliance therewith, we and the depository may amend or supplement the deposit agreement and the ADR at any time in accordance with such changed laws, rules or regulations. Such amendment or supplement to the deposit agreement in such circumstances may become effective before a notice of such amendment or supplement is given to ADR holders or within any other period of time as required for compliance.

Notice of any amendment to the deposit agreement or form of ADRs shall not need to describe in detail the specific amendments effectuated thereby, and failure to describe the specific amendments in any such notice shall not render such notice invalid, provided, however, that, in each such case, the notice given to the ADR holders identifies a means for ADR holders and beneficial owners to retrieve or receive the text of such amendment (*i.e.*, upon retrieval from the SEC's, the depository's or our website or upon request from the depository).

How may the deposit agreement be terminated?

The depository may, and shall at our written direction, terminate the deposit agreement and the ADRs by mailing notice of such termination to the registered holders of ADRs at least 30 days prior to the date fixed in such notice for such termination; provided, however, if the depository shall have (i) resigned as depository under the deposit agreement, notice of such termination by the depository shall not be provided to registered ADR holders unless a successor depository shall not be operating under the deposit agreement within 60 days of the date of such resignation, and (ii) been removed as depository under the deposit agreement, notice of such termination by the depository shall not be provided to registered holders of ADRs unless a successor depository shall not be operating under the deposit agreement on the 60th day after our notice of removal was first provided to the depository.

If the shares are not listed or quoted for trading on a stock exchange or in a securities market as of the date so fixed for termination, then after such date fixed for termination (a) all direct registration ADRs shall cease to be eligible for the direct registration system and shall be considered ADRs issued on the ADR register maintained by the depository and (b) the depository shall use its reasonable efforts to ensure that the ADSs cease to be DTC eligible so that neither DTC nor any of its nominees shall thereafter be a holder of ADRs. At such time as the ADSs cease to be DTC eligible and/or neither DTC nor any of its nominees is a holder of ADRs, the depository shall (a) instruct its custodian to deliver all shares and/or deposited securities to us along with a general stock power that refers to the names set forth on the ADR register maintained by the depository and (b) provide us with a copy of the ADR register maintained by the depository. Upon receipt of such shares and/or deposited securities and the ADR register maintained by the depository, we have agreed to use our best efforts to issue to each register ADR holder a share certificate representing the shares represented by the ADSs reflected on the ADR register maintained by the depository in such registered ADR holder's name and to deliver such share certificate to the registered ADR holder at the address set forth on the ADR register maintained by the depository. After providing such instruction to the custodian and delivering a copy of the ADR register to us, the depository and its agents will perform no further acts under the deposit agreement or the ADRs and shall cease to have any obligations under the deposit agreement and/or the ADRs. After we receive the copy of the ADR register and the shares and/or deposited securities from the depository, we shall be discharged from all obligations under the deposit agreement except (i) to distribute the shares to the registered ADR holders entitled thereto and (ii) for its obligations to the depository and its agents.

If the shares are listed or quoted for trading on a stock exchange or in a securities market as of the date so fixed for termination, then instead of the provisions in the prior paragraph, after the date so fixed for termination, the depositary and its agents will perform no further acts under the deposit agreement or the ADRs, except to receive and hold (or sell) distributions on shares and/or deposited securities and deliver shares and/or deposited securities being withdrawn. As soon as practicable after the date so fixed for termination, the depositary has agreed to use its reasonable efforts to sell the shares and/or deposited securities and shall thereafter (as long as it may lawfully do so) hold in an account (which may be a segregated or unsegregated account) the net proceeds of such sales, together with any other cash then held by it under the deposit agreement, without liability for interest, in trust for the pro rata benefit of the registered ADR holders not theretofore surrendered. After making such sale, the depositary shall be discharged from all obligations in respect of the deposit agreement and the ADRs, except to account for such net proceeds and other cash. After the date so fixed for termination, we shall be discharged from all obligations under the deposit agreement except for our obligations to the depositary and its agents.

Notwithstanding anything to the contrary, in connection with any such termination, the depositary may, in its sole discretion and without notice to us, establish an unsponsored American depositary share program (on such terms as the depositary may determine) for our shares and make available to ADR holders a means to withdraw the shares represented by the ADSs issued under the deposit agreement and to direct the deposit of such shares into such unsponsored American depositary share program, subject, in each case, to receipt by the depositary, at its discretion, of the fees, charges and expenses provided for under the deposit agreement and the fees, charges and expenses applicable to the unsponsored American depositary share program.

Limitations on Obligations and Liability to ADR holders

Limits on our obligations and the obligations of the depositary; limits on liability to ADR holders and holders of ADSs

Prior to the issue, registration, registration of transfer, split-up, combination, or cancellation of any ADRs, or the delivery of any distribution in respect thereof, and from time to time in the case of the production of proofs as described below, we or the depositary or its custodian may require:

- payment with respect thereto of (i) any stock transfer or other tax or other governmental charge, (ii) any stock transfer or registration fees in effect for the registration of transfers of shares or other deposited securities upon any applicable register and (iii) any applicable fees and expenses described in the deposit agreement;
- the production of proof satisfactory to it of (i) the identity of any signatory and genuineness of any signature and (ii) such other information, including without limitation, information as to citizenship, residence, exchange control approval, beneficial or other ownership of, or interest in, any securities, compliance with applicable law, regulations, provisions of or governing deposited securities and terms of the deposit agreement and the ADRs, as it may deem necessary or proper; and
- compliance with such regulations as the depositary may establish consistent with the deposit agreement.

The issuance of ADRs, the acceptance of deposits of shares, the registration, registration of transfer, split-up or combination of ADRs or the withdrawal of shares, may be suspended, generally or in particular instances, when the ADR register or any register for deposited securities is closed or when any such action is deemed advisable by the depositary; provided that the ability to withdraw shares may only be limited under the following circumstances: (i) temporary delays caused by closing transfer books of the depositary or our transfer books or the deposit of shares in connection with voting at a shareholders' meeting, or the payment of dividends, (ii) the payment of fees, taxes, and similar charges, and (iii) compliance with any laws or governmental regulations relating to ADRs or to the withdrawal of deposited securities.

The deposit agreement expressly limits the obligations and liability of the depository, ourselves and our respective agents, provided, however, that no disclaimer of liability under the Securities Act of 1933 is intended by any of the limitations of liabilities provisions of the deposit agreement. The deposit agreement provides that each of us, the depository and our respective agents will:

- incur or assume no liability (including, without limitation, to holders or beneficial owners) if any present or future law, rule, regulation, fiat, order or decree of the Cayman Islands, Hong Kong, the People's Republic of China, the United States or any other country or jurisdiction, or of any governmental or regulatory authority or securities exchange or market or automated quotation system, the provisions of or governing any deposited securities, any present or future provision of our charter, any act of God, war, terrorism, epidemic, pandemic, nationalization, expropriation, currency restrictions, work stoppage, strike, civil unrest, revolutions, rebellions, explosions, computer failure or circumstance beyond our, the depository's or our respective agents' direct and immediate control shall prevent or delay, or shall cause any of them to be subject to any civil or criminal penalty in connection with, any act which the deposit agreement or the ADRs provide shall be done or performed by us, the depository or our respective agents (including, without limitation, voting);
- incur or assume no liability (including, without limitation, to holders or beneficial owners) by reason of any non-performance or delay, caused as aforesaid, in the performance of any act or things which by the terms of the deposit agreement it is provided shall or may be done or performed or any exercise or failure to exercise discretion under the deposit agreement or the ADRs including, without limitation, any failure to determine that any distribution or action may be lawful or reasonably practicable;
- incur or assume no liability (including, without limitation, to holders or beneficial owners) if it performs its obligations under the deposit agreement and ADRs without gross negligence or willful misconduct;
- in the case of the depository and its agents, be under no obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any deposited securities the ADSs or the ADRs;
- in the case of us and our agents, be under no obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any deposited securities the ADSs or the ADRs, which in our or our agents' opinion, as the case may be, may involve it in expense or liability, unless indemnity satisfactory to us or our agent, as the case may be against all expense (including fees and disbursements of counsel) and liability be furnished as often as may be requested;
- not be liable (including, without limitation, to holders or beneficial owners) for any action or inaction by it in reliance upon the advice of or information from any legal counsel, any accountant, any person presenting shares for deposit, any registered holder of ADRs, or any other person believed by it to be competent to give such advice or information and/or, in the case of the depository, us; or
- may rely and shall be protected in acting upon any written notice, request, direction, instruction or document believed by it to be genuine and to have been signed, presented or given by the proper party or parties.

Neither the depositary nor its agents have any obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any deposited securities, the ADSs or the ADRs. We and our agents shall only be obligated to appear in, prosecute or defend any action, suit or other proceeding in respect of any deposited securities, the ADSs or the ADRs, which in our opinion may involve us in expense or liability, if indemnity satisfactory to us against all expense (including fees and disbursements of counsel) and liability is furnished as often as may be required. The depositary and its agents may fully respond to any and all demands or requests for information maintained by or on its behalf in connection with the deposit agreement, any registered holder or holders of ADRs, any ADRs or otherwise related to the deposit agreement or ADRs to the extent such information is requested or required by or pursuant to any lawful authority, including without limitation laws, rules, regulations, administrative or judicial process, banking, securities or other regulators. The depositary shall not be liable for the acts or omissions made by, or the insolvency of, any securities depositary, clearing agency or settlement system. Furthermore, the depositary shall not be responsible for, and shall incur no liability in connection with or arising from, the insolvency of any custodian that is not a branch or affiliate of JPMorgan. Notwithstanding anything to the contrary contained in the deposit agreement or any ADRs, the depositary shall not be responsible for, and shall incur no liability in connection with or arising from, any act or omission to act on the part of the custodian except to the extent that any registered ADR holder has incurred liability directly as a result of the custodian having (i) committed fraud or willful misconduct in the provision of custodial services to the depositary or (ii) failed to use reasonable care in the provision of custodial services to the depositary as determined in accordance with the standards prevailing in the jurisdiction in which the custodian is located. The depositary and the custodian(s) may use third party delivery services and providers of information regarding matters such as, but not limited to, pricing, proxy voting, corporate actions, class action litigation and other services in connection with the ADRs and the deposit agreement, and use local agents to provide services such as, but not limited to, attendance at any meetings of security holders of issuers. Although the depositary and the custodian will use reasonable care (and cause their agents to use reasonable care) in the selection and retention of such third party providers and local agents, they will not be responsible for any errors or omissions made by them in providing the relevant information or services. The depositary shall not have any liability for the price received in connection with any sale of securities, the timing thereof or any delay in action or omission to act nor shall it be responsible for any error or delay in action, omission to act, default or negligence on the part of the party so retained in connection with any such sale or proposed sale.

The depositary has no obligation to inform ADR holders or beneficial owners about the requirements of the laws, rules or regulations or any changes therein or thereto of the Cayman Islands, Hong Kong, the People's Republic of China, the United States or any other country or jurisdiction or of any governmental or regulatory authority or any securities exchange or market or automated quotation system.

Additionally, none of the depositary, the custodian or us, or any of their or our respective directors, officers, employees, agents or affiliates shall be liable for the failure by any registered holder of ADRs or beneficial owner therein to obtain the benefits of credits or refunds of non-U.S. tax paid against such ADR holder's or beneficial owner's income tax liability. The depositary is under no obligation to provide the ADR holders and beneficial owners, or any of them, with any information about our tax status. None of the depositary, custodian, us or any of their or our respective directors, officers, employees, agents or affiliates shall incur any liability for any tax or tax consequences that may be incurred by registered ADR holders or beneficial owners on account of their ownership or disposition of ADRs or ADSs.

Neither the depositary nor its agents will be responsible for any failure to carry out any instructions to vote any of the deposited securities, for the manner in which any voting instructions are given or deemed to be given pursuant to the terms of the deposit agreement, including instructions to give a discretionary proxy to a person designated by us, for the manner in which any vote is cast, including, without limitation, any vote cast by a person to whom the depositary is instructed (or deemed to have been instructed to grant a discretionary proxy in accordance with the deposit agreement), or for the effect of any such vote. The depositary may rely upon instructions from us or our counsel in respect of any approval or license required for any currency conversion, transfer or distribution. The depositary shall not incur any liability for the content of any information submitted to it by us or on our behalf for distribution to ADR holders or for any inaccuracy of any translation thereof, for any investment risk associated with acquiring an interest in the deposited securities, for the validity or worth of the deposited securities, for the credit-worthiness of any third party, for allowing any rights to lapse upon the terms of the deposit agreement or for the failure or timeliness of any notice from us. The depositary shall not be liable for any acts or omissions made by a successor depositary whether in connection with a previous act or omission of the depositary or in connection with any matter arising wholly after the removal or resignation of the depositary. Subject to certain customary exceptions, neither the depositary nor us, nor any of its or our agents shall be liable to the other for any indirect, special, punitive or consequential damages (excluding reasonable fees and expenses of counsel) or lost profits, in each case of any form incurred by any of them, or liable to any other person or entity (including, without limitation holders or beneficial owners of ADRs and ADSs) for any indirect, special, punitive or consequential damages (including fees and expenses of counsel) or lost profits, whether or not foreseeable and regardless of the type of action in which such a claim may be brought.

In the deposit agreement each party thereto (including, for avoidance of doubt, each ADR holder and beneficial owner) irrevocably waives, to the fullest extent permitted by applicable law, any right it may have to a trial by jury in any suit, action or proceeding against the depository and/or us directly or indirectly arising out of or relating to the shares or other deposited securities, the ADSs or the ADRs, the deposit agreement or any transaction contemplated therein, or the breach thereof (whether based on contract, tort, common law or any other theory). No provision of the deposit agreement or the ADRs is intended to constitute a waiver or limitation of any rights which an ADR holder or any beneficial owner may have under the Securities Act of 1933 or the Securities Exchange Act of 1934, to the extent applicable.

The depository and its agents may own and deal in any class of securities of our company and our affiliates and in ADRs.

Disclosure of Interest in ADSs

To the extent that the provisions of or governing any deposited securities may require disclosure of or impose limits on beneficial or other ownership of, or interest in, deposited securities, other shares and other securities and may provide for blocking transfer, voting or other rights to enforce such disclosure or limits, you as ADR holders or beneficial owners agree to comply with all such disclosure requirements and ownership limitations and to comply with any reasonable instructions we may provide in respect thereof. We reserve the right to instruct you as ADS holders to deliver your ADSs for cancellation and withdrawal of the deposited securities so as to permit us to deal directly with the holder thereof as a holder of shares and, by holding an ADS or an interest therein, you and beneficial owners will be agreeing to comply with such instructions.

Books of Depository

The depository or its agent will maintain a register for the registration, registration of transfer, combination and split-up of ADRs, which register shall include the depository's direct registration system. Registered holders of ADRs may inspect such records at the depository's office at all reasonable times, but solely for the purpose of communicating with other ADR holders in the interest of the business of our company or a matter relating to the deposit agreement. Such register may be closed at any time or from time to time, when deemed expedient by the depository or, in the case of the issuance book portion of the ADR Register, when reasonably requested by the Company solely in order to enable the Company to comply with applicable law.

The depository will maintain facilities for the delivery and receipt of ADRs.

Appointment

In the deposit agreement, each registered holder of ADRs and each beneficial owner, upon acceptance of any ADSs or ADRs (or any interest in any of them) issued in accordance with the terms and conditions of the deposit agreement will be deemed for all purposes to:

- be a party to and bound by the terms of the deposit agreement and the applicable ADR or ADRs,
- appoint the depository its attorney-in-fact, with full power to delegate, to act on its behalf and to take any and all actions contemplated in the deposit agreement and the applicable ADR or ADRs, to adopt any and all procedures necessary to comply with applicable laws and to take such action as the depository in its sole discretion may deem necessary or appropriate to carry out the purposes of the deposit agreement and the applicable ADR and ADRs, the taking of such actions to be the conclusive determinant of the necessity and appropriateness thereof; and

acknowledge and agree that (i) nothing in the deposit agreement or any ADR shall give rise to a partnership or joint venture among the parties thereto, nor establish a fiduciary or similar relationship among such parties, (ii) the depository, its divisions, branches and affiliates, and their respective agents, may from time to time be in the possession of non-public information about us, ADR holders, beneficial owners and/or their respective affiliates, (iii) the depository and its divisions, branches and affiliates may at any time have multiple banking relationships with us, ADR holders, beneficial owners and/or the affiliates of any of them, (iv) the depository and its divisions, branches and affiliates may, from time to time, be engaged in transactions in which parties adverse to us, ADR holders, beneficial owners and/or their respective affiliates may have interests, (v) nothing contained in the deposit agreement or any ADR(s) shall (A) preclude the depository or any of its divisions, branches or affiliates from engaging in any such transactions or establishing or maintaining any such relationships, or (B) obligate the depository or any of its divisions, branches or affiliates to disclose any such transactions or relationships or to account for any profit made or payment received in any such transactions or relationships, (vi) the depository shall not be deemed to have knowledge of any information held by any branch, division or affiliate of the depository and (vii) notice to an ADR holder shall be deemed, for all purposes of the deposit agreement and the ADRs, to constitute notice to any and all beneficial owners of the ADSs evidenced by such ADR holder's ADRs. For all purposes under the deposit agreement and the ADRs, the ADR holders thereof shall be deemed to have all requisite authority to act on behalf of any and all beneficial owners of the ADSs evidenced by such ADRs.

Governing Law

The deposit agreement, the ADSs and the ADRs are governed by and construed in accordance with the internal laws of the State of New York. In the deposit agreement, we have submitted to the non-exclusive jurisdiction of the courts of the State of New York and appointed an agent for service of process on our behalf. Any action based on the deposit agreement, the ADSs, the ADRs or the transactions contemplated therein or thereby may also be instituted by the depository against us in any competent court in the Cayman Islands, Hong Kong, the People's Republic of China and the United States.

Under the deposit agreement, by holding or owning an ADR or ADS or an interest therein, ADR holders and beneficial owners each irrevocably agree that any legal suit, action or proceeding against or involving ADR holders or beneficial owners brought by us or the depository, arising out of or based upon the deposit agreement, the ADSs, the ADRs or the transactions contemplated thereby, may be instituted in a state or federal court in New York, New York, irrevocably waive any objection which you may have to the laying of venue of any such proceeding, and irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. By holding or owning an ADR or ADS or an interest therein, ADR holders and beneficial owners each also irrevocably agree that any legal suit, action or proceeding against or involving the depository brought by ADR holders or beneficial owners, arising out of or based upon the deposit agreement, the ADSs, the ADRs or the transactions contemplated thereby, may only be instituted in a state or federal court in New York, New York.

Notwithstanding the foregoing, (i) the depository may, in its sole discretion, elect to institute any dispute, suit, action, controversy, claim or proceeding directly or indirectly based on, arising out of or relating to the deposit agreement, the ADSs, the ADRs or the transactions contemplated therein or thereby, including without limitation any question regarding its or their existence, validity, interpretation, performance or termination, against any other party or parties to the deposit agreement (including, without limitation, against ADR holders and beneficial owners of interests in ADSs), by having the matter referred to and finally resolved by an arbitration conducted under the terms described below, and (ii) the depository may in its sole discretion require, by written notice to the relevant party or parties, that any dispute, suit, action, controversy, claim or proceeding against the depository by any party or parties to the deposit agreement (including, without limitation, by ADR holders and beneficial owners of interests in ADSs) shall be referred to and finally settled by an arbitration conducted under the terms described below. Any such arbitration shall be conducted in the English language either in New York, New York in accordance with the Commercial Arbitration Rules of the American Arbitration Association or in Hong Kong following the arbitration rules of the United Nations Commission on International Trade Law (UNCITRAL).

Jury Trial Waiver

In the deposit agreement, each party thereto (including, for the avoidance of doubt, each holder and beneficial owner of, and/or holder of interests in, ADSs or ADRs) irrevocably waives, to the fullest extent permitted by applicable law, any right it may have to a trial by jury in any suit, action or proceeding against the depository and/or us directly or indirectly arising out of or relating to the shares or other deposited securities, the ADSs or the ADRs, the deposit agreement or any transaction contemplated therein, or the breach thereof (whether based on contract, tort, common law or any other theory), including any claim under the U.S. federal securities laws.

If we or the depository were to oppose a jury trial demand based on such waiver, the court would determine whether the waiver was enforceable in the facts and circumstances of that case in accordance with applicable state and federal law, including whether a party knowingly, intelligently and voluntarily waived the right to a jury trial. The waiver to right to a jury trial in the deposit agreement is not intended to be deemed a waiver by any holder or beneficial owner of ADSs of our or the depository's compliance with the U.S. federal securities laws and the rules and regulations promulgated thereunder.

**CERTIFICATION BY THE PRINCIPAL EXECUTIVE OFFICER PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Peter (Peizhi) Luo, certify that:

1. I have reviewed this annual report on Form 20-F of Adagene Inc. (the “Company”);
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;
4. The Company’s other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the company and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) [Omitted];
 - (c) Evaluated the effectiveness of the Company’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the Company’s internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company’s internal control over financial reporting; and
5. The Company’s other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company’s auditors and the audit committee of the Company’s board of directors:
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company’s ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company’s internal control over financial reporting.

Date: April 28, 2021

By: /s/ Peter (Peizhi) Luo
Peter (Peizhi) Luo
Chief Executive Officer (principal executive officer)

**CERTIFICATION BY PRINCIPAL FINANCIAL OFFICER PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Man Kin (Raymond) Tam, certify that:

1. I have reviewed this annual report on Form 20-F of Adagene Inc. (the "Company");
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;
4. The Company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the company and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) [Omitted];
 - (c) Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and
5. The Company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's board of directors:
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: April 28, 2021

By: /s/ Man Kin (Raymond) Tam
Man Kin (Raymond) Tam
Chief Financial Officer (principal financial and accounting officer)

**CERTIFICATION PURSUANT TO
18 U.S.C. 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Adagene Inc. (the "Company") on Form 20-F for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Peter (Peizhi) Luo, Chief Executive Officer, certify, pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: April 28, 2021

By: /s/ Peter (Peizhi) Luo
Peter (Peizhi) Luo
Chief Executive Officer (principal executive officer)

**CERTIFICATION PURSUANT TO
18 U.S.C. 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Adagene Inc. (the "Company") on Form 20-F for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Man Kin (Raymond) Tam, Chief Financial Officer, certify, pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: April 28, 2021

By: /s/ Man Kin (Raymond) Tam
Man Kin (Raymond) Tam
Chief Financial Officer (principal financial and accounting officer)

天元律师事务所
TIAN YUAN LAW FIRM

10/F, Tower B, CPIC Plaza, No. 28 Fengsheng Lane, Xicheng District, Beijing 100032, China
Tel: 86 10 5776 3888 Fax: 86 10 5776 3777

April 28, 2021

To:

Adagene Inc.

4F, Building C14, No. 218
Xinghu Street, Suzhou Industrial Park
Suzhou, Jiangsu Province, People's Republic of China

(as the "Company")

Dear Sirs,

We consent to the references to our firm under the headings "Item 10. Additional Information—E. Taxation" in Adagene Inc.'s Annual Report on Form 20-F for the year ended December 31, 2020 (the "**Annual Report**"), which will be filed with the Securities and Exchange Commission (the "**SEC**") on April 28, 2021 and further consent to the incorporation by reference of the summaries of our opinions that appear in the Annual Report into the registration statements (No. 333-255250) on Form S-8. We also consent to the filing with the SEC of this consent letter as an exhibit to the Annual Report.

In giving such consent, we do not thereby admit that we come within the category of persons whose consent is required under Section 7 of the Securities Act of 1933, or under the Securities Exchange Act of 1934, in each case, as amended, or the regulations promulgated thereunder.

Yours faithfully,

/s/ Tian Yuan Law Firm

Tian Yuan Law Firm

Partners:

Paul Aherne **
 Joanne Collett *
 Mark Cummings *****
 Stuart D'Addona *****
 Nicholas Davies ***
 Shamar Ennis ***
 James Gaden *****
 Kristen Kwok **
 Jo Lit *
 Callum McNeil **
 Alice Molan *****
 Andrew Randall **
 Rupen Shah *****
 Denise Wong **

28 April 2021

Adagene Inc.

4F, Building C14, No.218
 Xinghu Street, Suzhou Industrial Park
 Suzhou, Jiangsu Province, 215123
 People's Republic of China

Dear Sirs,

Form 20-F

We consent to the reference to our firm under the heading “Item 10.E. Additional Information—Taxation—Cayman Islands Taxation” in the Annual Report on Form 20-F of Adagene Inc. for the fiscal year ended 31 December 2020 (the “**Annual Report**”), which will be filed with the U.S. Securities and Exchange Commission (the “**Commission**”) under the U.S. Securities Exchange Act of 1934, as amended (the “**Exchange Act**”) in the month of April 2021.

We further consent to the incorporation by reference into the Registration Statement (Form S-8 No. 333-255250) pertaining to Adagene Inc. Second Amended and Restated Share Incentive Plan and Adagene Inc. 2021 Performance Incentive Plan of the summary of our opinion under the heading “Item 10.E. Additional Information—Taxation—Cayman Islands Taxation” in the Annual Report.

We also consent to the filing with the Commission of this consent letter as an exhibit to the Annual Report.

In giving such consent, we do not thereby admit that we come within the category of persons whose consent is required under the Exchange Act, or the Rules and Regulations of the Commission thereunder.

Yours faithfully

/s/ WALKERS (HONG KONG)

WALKERS (HONG KONG)

Walkers (Hong Kong)
滙嘉律師事務所 (香港)

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Bermuda | British Virgin Islands | Cayman Islands | Dubai | Guernsey | Hong Kong | Ireland | Jersey | London | Singapore

*England and Wales; **BVI; ***Cayman Islands; ****New South Wales (Australia); *****Ireland; *****Victoria (Australia); *****Bermuda

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (File No. 333-255250) of Adagene Inc. of our report dated April 28, 2021 relating to the financial statements, which appears in this Form 20-F.

/s/PricewaterhouseCoopers Zhong Tian LLP

Shanghai, the People's Republic of China
April 28, 2021
