

As filed with the Securities and Exchange Commission on May 20, 2022

Registration No. 333 -264486

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

AMENDMENT No. 2

to

FORM F-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

Adagene Inc.

(Exact Name of Registrant as specified in its charter)

Cayman Islands(State or other jurisdiction of
Incorporation or Organization)**Not Applicable**(I.R.S. Employer
Identification Number)

**4F, Building C14, No. 218
Xinghu Street, Suzhou Industrial Park
Suzhou, Jiangsu Province, 215123
People's Republic of China
+86-512-8777-3632**

(Address and telephone number of Registrant's principal executive offices)

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(Name, address, and telephone number of Agent for Service)

Copy to:

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Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.C. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.C. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933.

Emerging growth company

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 7(a)(2)(B) of the Securities Act.

[†] 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.

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until this registration statement shall become effective on such date as the Securities and Exchange Commission acting pursuant to said Section 8(a) may determine.

Subject to completion, dated May 20, 2022

PROSPECTUS

US\$200,000,000
ADAGENE
Adagene Inc.
Ordinary Shares
Warrants
Units

Adagene Inc. (“Adagene” or “the Company”) or selling shareholders may offer from time to time up to a total amount of US\$200,000,000, consisting of (i) ordinary shares of the Company, par value US\$0.0001 per share (“Ordinary Shares”), including ordinary shares represented by American depository shares, or ADSs, (ii) warrants to purchase ordinary shares or other securities of the Company (“Warrants”), (iii) units (“Units” and, collectively with the Ordinary Shares and Warrants, the “Securities”), or any combination thereof, in one or more offerings under this prospectus. Each ADS represents one and one quarter (1.25) ordinary shares. When we or selling shareholders decide to sell Securities, we or the selling shareholders will provide specific terms of the offered Securities in a prospectus supplement.

This prospectus describes some of the general terms that may apply to these Securities and the general manner in which they may be offered. The specific terms of any Securities to be offered, and the specific manner in which they may be offered, will be described in one or more supplements to this prospectus. A prospectus supplement may also add, update or change information contained in this prospectus.

The Securities covered by this prospectus may be offered and sold from time to time in the same offering or in separate offerings; to or through underwriters, dealers, and agents; or directly to purchasers. The names of any underwriters, dealers, or agents, if any, involved in the sale of our Securities, their compensation and any over-allotment options held by them will be described in the applicable prospectus supplement. For a more complete description of the plan of distribution of these Securities, see the section entitled “Plan of Distribution” beginning on page 74 of this prospectus.

The ADSs are traded on the Nasdaq Global Market, or the Nasdaq, under the symbol “ADAG.” As of May 19, 2022, the last reported sale price for the ADSs was US\$2.86 per ADS. Pursuant to General Instruction I.B.5 of Form F-3, in no event will we sell the Securities covered hereby in a public primary offering with a value exceeding more than one-third of the aggregate market value of our voting and non-voting common equity held by non-affiliates in any 12-month period so long as the aggregate market value of our outstanding voting and non-voting common equity held by non-affiliates remains below US\$75,000,000. During the 12 calendar months prior to and including the date of this prospectus, we have not offered or sold any securities pursuant to General Instruction I.B.5 of Form F-3. This limitation does not apply to offerings of ordinary shares on a secondary basis that may be sold by selling shareholders pursuant to this prospectus (as described in “Selling Shareholders”) in accordance with General Instruction I.B.3 of Form F-3. For the avoidance of doubt, any potential offerings of ordinary shares on a secondary basis by selling shareholders made pursuant to this registration statement on Form F-3 are limited to the then currently outstanding ordinary shares.

Investors are purchasing securities of a Cayman Islands holding company rather than securities of our subsidiaries that have substantive business operations in China or in the United States. Adagene Inc. is a Cayman Islands holding company that conducts its operations and operate its business in China through its PRC subsidiary, Adagene (Suzhou) Limited (“Adagene Suzhou”). In addition, Adagene Inc. conducts a substantial portion of its operations in the U.S. through its U.S. subsidiary, Adagene Incorporated. Such structure involves unique risks to investors in the ADSs and ordinary shares. In particular, as we are a holding company with substantive business operations in China, you should pay special attention to disclosures included in our most recent annual report on Form 20-F incorporated by reference in this prospectus and risk factors included herein, including but not limited to risk factor such as “uncertainties with respect to the PRC legal system, including uncertainties regarding the enforcement of laws, and sudden or unexpected changes in policies, laws and regulations in China could adversely affect us.” The PRC government has significant authority to exert influence on the ability of a company with substantive operations in China, such as us, to conduct its business, accept foreign investments or list on a U.S. or other foreign exchanges. For example, we face risks associated with regulatory approvals of offshore offerings, anti-monopoly regulatory actions, oversight on cybersecurity and data privacy, as well as the lack of The Public Company Accounting Oversight Board (“PCAOB”) inspection on our auditor. Trading in our ADSs on the Nasdaq or over-the-counter will be prohibited, and as a result, our ADSs will be delisted under the Holding Foreign Companies Accountable Act (“HFCA Act”), if the PCAOB has determined that it has been unable to inspect our auditor located in China for three consecutive years, starting from 2022. The potential enactment

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

of the Accelerating Holding Foreign Companies Accountable Act would decrease the number of non-inspection years from three years to two, thus reducing the time period before our ADSs will be prohibited from trading on the Nasdaq Stock Market or OTC or delisted. On December 16, 2021, PCAOB issued the HFCA Act Determination Report, according to which our auditor is subject to the determinations that the PCAOB is unable to inspect or investigate completely. In March 2022, the SEC issued its first “Conclusive list of issuers identified under the HFCAA” indicating that those companies are now formally subject to the delisting provisions if they remain on the list for three consecutive years. We were provisionally identified by the SEC on May 4, 2022 under the HFCA Act and anticipate being conclusively identified 15 business days after May 4, 2022. See [https:// www.sec.gov/hfcaa](https://www.sec.gov/hfcaa). Such risks could result in a material change in our operations and/or the value of our ADSs or could significantly limit or completely hinder our ability to offer or continue to offer ADSs and/or other securities to investors and cause the value of such securities to significantly decline or be worthless. The PRC government also has significant oversight and discretion over the conduct of our business and as such may influence our operations at any time, which could result in a material adverse effect on our operations. The PRC government has recently published new policies that significantly affected certain industries, and we cannot rule out the possibility that it will in the future release regulations or policies regarding the industry where we operate, which could adversely affect our business, financial condition and results of operations. Furthermore, the PRC government has recently indicated an intent to exert more oversight and control over overseas securities offerings and other capital markets activities and foreign investment in China-based companies like us. These risks could result in a material change in our operations and the value of our ordinary shares or the ADSs, or could significantly limit or completely hinder our ability to offer or continue to offer securities to investors and cause the value of such securities to significantly decline or become worthless. For a detailed description of risks related to doing business in China, see “Risk Factors — Risks Related to Doing Business in the PRC.” As used in this prospectus, “Adagene” refers to Adagene Inc., a Cayman Islands exempted company with limited liability, “Adagene Suzhou” refers to Adagene (Suzhou) Limited, a PRC incorporated company with limited liability, “Adagene Hong Kong” refers to Adagene (Hong Kong) Limited, our Hong Kong intermediary holding company, “Adagene Incorporated” refers to Adagene Incorporated, our U.S. subsidiary, and “we,” “us,” “our company,” or “our” refers to Adagene Inc. and its subsidiaries.

With a holding company structure, we currently rely principally on equity financing for our cash requirements, including the funds necessary to pay cash considerations for services we may incur. In the future, when and after we become profitable and generate cash flows from operating activities, we may rely principally on dividends and other distributions on equity from our PRC and U.S. subsidiaries for our cash requirements, including the funds necessary to pay dividends and other cash distributions to our shareholders or for services of any debt we may incur. If any of 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 or make other distributions to us. In 2019, 2020 and 2021, Adagene Inc. made payments of US\$13.1 million, US\$15.5 million and US\$30.0 million, respectively, in cash to Adagene Suzhou as consideration for providing services associated with research and development activities related to those intellectual properties owned by Adagene Inc. There were no intercompany loans provided by Adagene Inc. to Adagene Suzhou during the years ended and as of December 31, 2019, 2020 and 2021. As advised by our PRC legal counsel, Tian Yuan Law Firm, Adagene Suzhou is able to mark up and charge to Adagene Inc., its ultimate parent, for providing services associated with research and development activities related to those intellectual properties owned by Adagene Inc. and Adagene Inc. is able to make cash payments to Adagene Suzhou for considerations of such services. In the future, cash proceeds raised from overseas financing activities, including this offering, may be transferred by Adagene Inc., the Cayman holding company, (i) through Adagene (Hong Kong) Limited, our Hong Kong subsidiary, to Adagene Suzhou, our PRC subsidiary, and (ii) to Adagene Incorporated, our U.S. subsidiary, via capital contribution, shareholder loans or consideration for the services rendered, as the case may be. Other than the above disclosed transfer of funds, we did not transfer any type of assets between Adagene Suzhou and other Adagene subsidiaries in 2019, 2020 and 2021. For risks associated with this structure, see “Risk Factors — We may rely on dividends and other distributions on equity paid by our PRC subsidiary to fund any cash and financing requirements that we may have, and any limitation on the ability of our PRC subsidiary to make payments to us could have material and adverse effect on our ability to conduct our business” and “— 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 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.”

Investing in these Securities involves certain risks. Please carefully consider the “Risk Factors” in Item 3.D of our most recent annual report on Form 20-F incorporated by reference in this prospectus, the “Risk Factors” beginning on page 17 of this prospectus, and in any applicable prospectus supplement, for a discussion of the factors you should consider carefully before deciding to purchase these Securities.

This prospectus may not be used to offer or sell any Securities unless accompanied by a prospectus supplement.

Neither the Securities and Exchange Commission nor any state or other securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is _____, 2022.

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You should rely only on the information contained or incorporated by reference into this prospectus, in the applicable prospectus supplement or in any free writing prospectus filed by us with the SEC. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. You should not assume that the information contained or incorporated by reference into this prospectus and any prospectus supplement or in any free writing prospectus is accurate as of any date other than the respective dates thereof. Our business, financial condition, results of operations and prospects may have changed since those dates.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, using a “shelf” registration process. Under this shelf registration process, we and the selling shareholders may, from time to time, sell up to US\$200,000,000 of any combination of the Securities described in this prospectus. This prospectus provides you with a general description of the Securities we may offer. Each time we or any selling shareholders use this prospectus to offer Securities, we will provide one or more prospectus supplements that will contain specific information about the offering and the terms of those Securities. We may also add, update or change other information contained in this prospectus by means of a prospectus supplement or by incorporating by reference information we file with the SEC. The registration statement on file with the SEC includes exhibits that provide more detail on the matters discussed in this prospectus. If there is any inconsistency between the information in this prospectus and any related prospectus supplement, you should rely on the information in the applicable prospectus supplement.

Before buying any of the Securities that we are offering, you should carefully read both this prospectus and any prospectus supplement with all of the information incorporated by reference in this prospectus, as well as the additional information described under the heading “Where You Can Find More Information” and “Incorporation of Certain Documents by Reference.” These documents contain important information that you should consider when making your investment decision. We have filed or incorporated by reference exhibits to the registration statement of which this prospectus forms a part. You should read the exhibits carefully for provisions that may be important to you.

The information contained in this prospectus, any applicable prospectus supplement or any document incorporated by reference in this prospectus is accurate only as of their respective dates, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or the documents incorporated by reference in this prospectus or the sale of any Securities. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Neither we nor any underwriters, dealers or agents have authorized anyone to provide you with information that is different from that contained in this prospectus, any amendment or supplement to this prospectus, or any free writing prospectus we may authorize to be delivered or made available to you. Neither we nor any underwriters, dealers or agents take responsibility for, or provide assurance as to the reliability of, any other information that others may give you. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any securities other than the Securities described in this prospectus or an offer to sell or the solicitation of an offer to buy such Securities in any circumstances in which such offer or solicitation is unlawful.

Neither we nor any underwriters, dealers or agents have taken any action that would permit the offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the Securities described herein and the distribution of this prospectus outside the United States.

In this prospectus, unless otherwise indicated or unless the context otherwise requires,

- “Adagene Suzhou” refers to Adagene (Suzhou) Limited, our subsidiary in the PRC;
- “Adagene Incorporated” refers to Adagene Incorporated, our subsidiary in the U.S.;
- “ADSs” refers to the American depository 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;
- “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;
- “Exchange Act” refers to the Exchange Act of 1934, as amended;
- “Greater China”, for the purpose of this prospectus/registration statement, 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(ies)” refers to antibody(ies) designed with dynamic binding sites that adapt kinetically to unique epitopes through novel MOA(s), using our NEObody technology;
- “ordinary shares” or “shares” refers to our ordinary shares of par value US\$0.0001 per share;
- “POWERbody(ies)” refers to antibody(ies) that utilize(s) our SAFEbody technology to create new bispecific T-cell engagers, antibody-drug conjugates, or antibody(ies), which is(are) designed to reach beyond the therapeutic potency of traditional monospecific antibody(ies);
- “RMB” or “Renminbi” refers to the legal currency of the People’s Republic of China;
- “SAFEbody(ies)” refers to antibody(ies) engineered with its(their) binding sites masked, which is(are) designed to be selectively activated in the tumor microenvironment (TME), potentially limiting on-target off-tumor toxicity in normal tissues; SAFEbody® is a registered trademark in the United States, China, Australia, Japan, Singapore, and the European Union;
- “Securities Act” refers to the Securities Act of 1933, as amended;
- “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.

References in any prospectus supplement to “the accompanying prospectus” are to this prospectus and to “the prospectus” are to this prospectus and the applicable prospectus supplement taken together.

OUR COMPANY

Overview

We are a platform-driven, clinical-stage biopharmaceutical company transforming the discovery and development of novel antibody-based cancer immunotherapies. We are combining computational biology and artificial intelligence to design novel antibodies that address unmet patient needs. Powered by our proprietary Dynamic Precision Library (DPL) platform, which fuels our NEObody™, SAFEbody®, and POWERbody™ technologies, we are developing a highly differentiated pipeline of novel immunotherapies. We have forged strategic collaborations with reputable global partners that leverage our technology in multiple approaches at the vanguard of science.

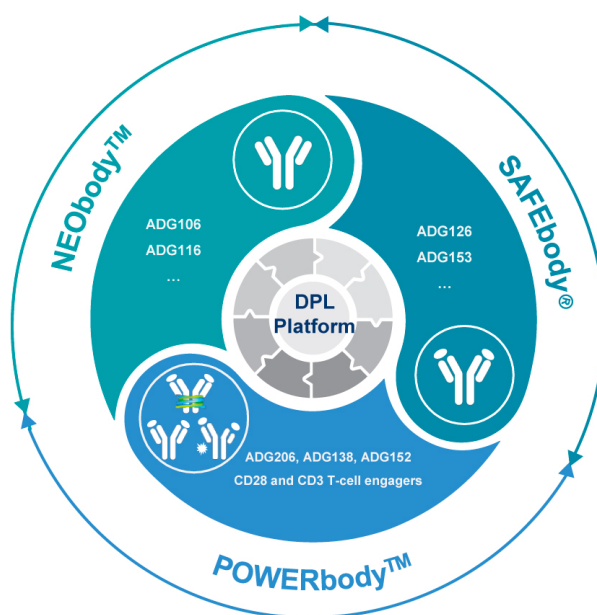
We aim to push the boundaries of antibody discovery and engineering through the precise design, construction, and selection of antibody product candidates intractable to traditional antibody technology. We have pioneered a dynamic antibody technology interface to harness the conformational diversity of antibodies, which enlarges epitope sampling of a given drug target for differentiated therapeutic antibody development. Additionally, we have a proprietary precision masking technology and specialized antibody engineering capabilities which enable us to design therapeutics with unique features.

Our Dynamic Precision Library (DPL) fuels our three antibody technology platforms, which can be used alone or together to create novel, differentiated antibody-based therapeutic candidates:

- The NEObody technology platform 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.
- The SAFEbody technology platform 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, minimizing on target, off tumor toxicities. 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 as SAFEbodies. Notably, SAFEbody technology can be applied to our NEObodies, such as what we did with ADG116 to potentially achieve an increased therapeutic index with ADG126.
- The POWERbody technology platform enables the creation of new versions of antibodies, which may be bispecific T-cell engagers, or TCEs, or Fc-engineered antibodies, antibody-drug conjugates, or ADCs, or antibodies that are designed to reach beyond the therapeutic potency of traditional monospecific antibodies. Our POWERbody candidates incorporate SAFEbody precision masking technology and are designed to improve antitumor activity while maintaining the enhanced safety profile. As an example, we have developed bispecific TCEs with either a CD3 or a CD28 arm and demonstrated the ability to combine them together for potentially safe and durable immunotherapies.

Our AI-powered technology allows us to engineer and select species cross-reactive antibodies designed to dynamically adapt to unique and evolutionally conserved epitopes. We believe that comprehensive *in vivo* preclinical evaluations using these species cross-reactive antibodies are the key to assess the efficacy and safety potential of tailor-made antibody candidates before progressing them into lengthy and costly clinical trials. Our NEObody, SAFEbody and POWERbody technology platforms are all designed to facilitate favorable druggability, manageable CMC attributes, and reduced immunogenicity.

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



Our DPL Platform fuels three antibody technology platforms, which can be used alone or together to create novel, differentiated antibody-based therapeutic candidates. Antibodies generated by NEObody technology are designed with dynamic binding sites that adapt kinetically to unique epitopes, thereby triggering a novel MOA. SAFEbody technology is designed to address safety and tolerability challenges associated with many antibody therapeutics by using precision masking technology to shield the binding domain of the biologic therapy. Through activation in the TME, this allows for tumor-specific targeting of antibodies, while minimizing on-target off-tumor toxicity in healthy tissues. POWERbody candidates are designed to unleash the efficacy of a therapeutic through Fc-engineering, drug conjugation, or T-cell engagement, while securing safety by precision masking with SAFEbody technology. Thus, POWERbody candidates also incorporate SAFEbody precision masking technology.

Our Robust, Transformative Pipeline

By leveraging our proprietary DPL platform and three platform technologies, 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 and wholly-owned clinical-stage pipeline consists of two anti-CTLA-4 antibodies ADG116 (NEObody) and ADG126 (SAFEbody), and an anti-CD137 antibody, ADG106 (NEObody). All three candidates are in Phase 1b/2 clinical evaluation in single agent and/or combination clinical trials designed to evaluate safety and preliminary efficacy. We also have a robust preclinical pipeline of five programs in IND-enabling studies, including a masked, Fc engineered anti-CD137 POWERbody and a masked anti-CD47 SAFEbody, which are both on track for clinical development, as well as over 50 programs in various stages of discovery.

In addition, we have out-licensed the Greater China rights of ADG104, an anti-PD-L1 mAb currently in Phase 2 clinical development, to Sanjin, and the Greater China rights of ADG125, a novel anti-CSF-1R mAb in Phase 1 development to Dragon Boat Biopharmaceuticals. We have the right to apply for the patents derived from our core and key technologies pertaining to ADG104 and ADG125 in the rest of the world, where we retain a majority of the economic benefits.

The following chart provides an overview of the status of each of our wholly-owned clinical and pre-clinical programs for which we have global rights:

Program & Technology	Target	Development stage					Rights
		Discovery	IND Enabling	Ph 1	Ph 2	Pivotal	
ADG116 NEO	CTLA-4						Global
ADG126 SAFE	CTLA-4						Global
ADG106 NEO	CD137						Global
ADG206 POWER	CD137						Global
ADG153 SAFE	CD47						Global
ADG138 POWER	HER2xCD3						Global
ADG152 POWER	CD20xCD3						Global
Undisclosed POWER	Undisclosed						Global
>50 Undisclosed	Various (e.g., CD28)						Global

We have deployed our NEObody and SAFEbody technology platforms to develop our three wholly-owned clinical candidates, ADG116, ADG126, ADG106, which are in ongoing Phase 1b/2 clinical evaluation as monotherapy and in combination with other targeted therapies:

- ADG116 is a fully human anti-CTLA-4 NEObody, which binds to a novel epitope of CTLA-4 different from ipilimumab, the only CTLA-4 mAb approved globally. The dynamic interface of ADG116 enables 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 antibody-dependent cellular cytotoxicity (ADCC). ADG116 is designed to overcome the safety challenges of existing CTLA-4 therapeutics, and it has shown in robust preclinical studies and clinical evaluation to have an improved safety profile and early efficacy activity, including dose-dependent T-cell activation and tumor suppression in treatment-resistant “cold” and “warm” tumors such as pancreatic, ovarian and renal cell cancers.
- ADG126 is a fully human anti-CTLA-4 SAFEbody, which applies SAFEbody precision masking technology to ADG116 to further enhance safety and efficacy profiles by masking the antibody binding site which is then conditionally activated in the TME to limit on target, off tumor toxicity. With the SAFEbody precision masking technology, ADG126 is designed to overcome the safety challenges of existing CTLA-4 therapeutics, and optimize efficacy by achieving doses that may unlock the full potential of CTLA-4 as a proven target for strong ADCC-mediated Treg depletion in the TME. ADG126 has consistently shown a potential best-in-class profile, which is supported by preclinical evaluation, including GLP toxicology data, and enabled by the broad species cross-reactivity of ADG126. In clinic, no dose-limiting toxicities have been observed as of March 31, 2022. Patients have received multiple cycles with continuous dosing, and favorable pharmacokinetic and pharmacodynamic activity compared to ADG116 has been observed.
- ADG106 is a fully human ligand-blocking agonistic anti-CD137 NEObody, which targets a unique epitope of CD137 that is different from other anti-CD137 antibodies currently under clinical development. Preclinical and clinical studies show that ADG106 is capable of binding to CD137 in a fashion similar to its natural ligand, CD137L. ADG106 is designed to balance safety and efficacy to overcome the known safety challenges of anti-CD137 targeted therapy, particularly when used in combination with anti-PD-1 or anti-CTLA-4 therapies. In clinic, ADG106 has shown a well-tolerated safety profile and evidence of single-agent efficacy, while combination therapy development is supported by the combined findings of our phase 1 monotherapy trials, data from extensive preclinical studies, as well as PD marker-based modelling from prior and ongoing trials.

Additionally, we have identified two of our five preclinical programs that are currently in IND-enabling studies, as candidates for the company's next two IND or equivalent submissions and for subsequent advancement into clinical trials:

- ADG206 is a masked, Fc engineered anti-CD137 agonistic POWERbody. ADG206 incorporates SAFEbody[®] precision masking technology and is designed to achieve improved safety and efficacy. We have conducted preclinical studies demonstrating that the FcγR-mediated crosslinking of ADG206 enhances T cell responses and antitumor activity, while the SAFEbody masking technology secures its activation only in the TME to limit on-target off-tumor toxicities.
- ADG153 is a masked anti-CD47 IgG1 SAFEbody. ADG153 is differentiated by its strong ADCC and antibody-dependent cellular phagocytosis (ADCP) activity designed to realize the full potential of anti-CD47 therapy for both hematologic and solid tumor indications. ADG153 incorporates SAFEbody masking technology to limit on-target off-tumor toxicities and overcome the known safety liabilities of anti-CD47 therapies. We have conducted preclinical studies showing that ADG153 has potent anti-tumor activity, without inducing human hemagglutination, while minimizing anemia-related and antigen sink liabilities.

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 collaborations and we continue to seek partnership opportunities where we can leverage our proprietary technology platform to develop novel antibodies to address unmet medical needs.

We enter into collaborations with biotechnology and pharmaceutical companies to leverage the power of our technology platforms, creating a network of potential future revenue streams that complement future long-term value from our wholly-owned pipeline. These collaborations include both technology licensing agreements and outlicensing of product candidates, both of which allow us to retain significant future participation in product sales through royalties paid on net sales. In the future, we may also enter into strategic collaborations which may involve joint development for our preclinical and/or clinical assets to both accelerate the path to clinic and drive global commercialization.

We have entered into technology licensing agreements with Sanofi, Exelixis and ADC Therapeutics to develop antibody-based therapeutics against tumor targets using our SAFEbody technology. We have also out-licensed the Greater China rights for two antibody candidates to Sanjin and its affiliates. Additionally, we have leveraged our DPL technology platform and antibody discovery and engineering capabilities in discovery collaborations with the U.S. National Institutes of Health (NIH), Mitsubishi Tanabe, Celgene (now BMS), GSK and Hengrui. To further advance our pipeline, we have also put in place various clinical collaborations, including clinical collaborations and supply agreements with Merck who will provide pembrolizumab for certain of our combination clinical trials, and an agreement with research organizations in Singapore for an investigator-initiated trial of our ADG106 clinical candidate in connection with nivolumab.

Our collaborations empower our growth by generating cash flow and revenues that partially offset expenditures on our internal research and development programs, expand our knowledge base regarding antibody technology across multiple targets and antibodies provided by our partners, and provide us with future joint development opportunities.

Corporate History and Structure

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.

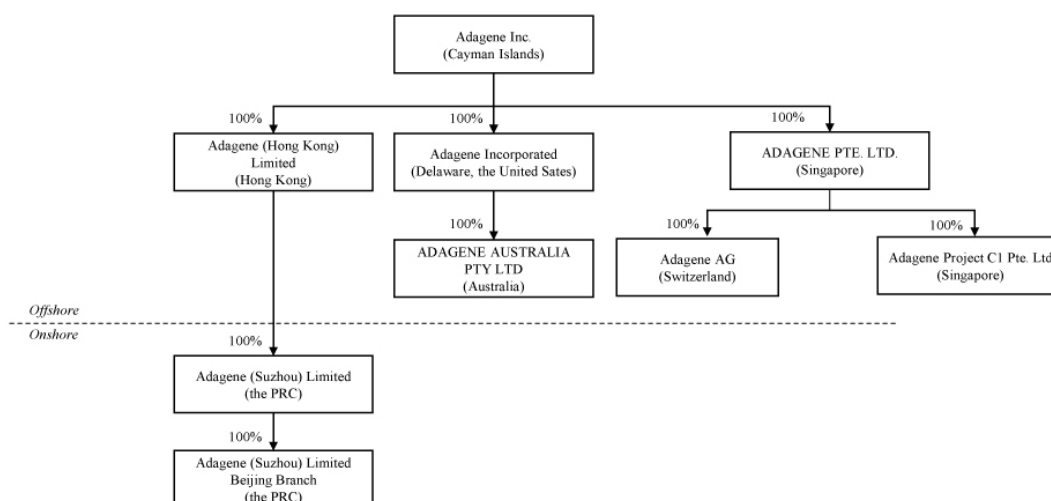
In September 2017, we established a wholly-owned subsidiary in the state of Delaware, the United States, Adagene Incorporated, to conduct our research and development activities in the United States to facilitate the discovery and development of product candidates and expand our global presence, we have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

We are a holding company and do not directly conduct any substantive business operations in the PRC. In addition to our R&D activities in the United States, Australia and Singapore, 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 “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.”

We were provisionally identified by the SEC on May 4, 2022 under the Holding Foreign Companies Accountable Act and anticipate being conclusively identified 15 business days after May 4, 2022. See <https://www.sec.gov/hfcaa>. See “Risk Factors — Risks Related to Doing Business in the PRC — Trading in our ADSs on the Nasdaq Stock Market or OTC will be prohibited, and as a result, our ADSs will be delisted under the HFCA Act, if the PCAOB is unable to inspect or fully investigate auditors located in China. On December 16, 2021, the PCAOB issued the HFCA Act Determination Report, according to which our auditor is subject to the determinations that the PCAOB is unable to inspect or investigate completely. The delisting of our ADSs, or the threat of their being delisted, may materially and adversely affect the value of your investment. If this happens there is no certainty that we will be able to list our ordinary shares on a non-U.S. exchange or that a market for our ordinary shares will develop outside of the United States.”

The following diagram illustrates our corporate structure as of the date of this prospectus, including our material subsidiaries directly or indirectly owned by us through equity ownership (our group structure does not include any variable interest entities):



Summary of Risk Factors

Investors are purchasing Securities of a Cayman Islands holding company rather than securities of our subsidiary that have substantive business operations in China or United States. Adagene Inc. is a Cayman Islands holding company that conducts its operations and operate its business in China through its PRC subsidiary, Adagene (Suzhou) Limited. In addition, Adagene Inc. conducts a substantial portion of its operations in the U.S. through its U.S. subsidiary, Adagene Incorporated. Our corporate group does not include any variable interest entities. Such structure involves unique risks to investors in the ADSs and

ordinary shares. You should carefully consider all of the information in this prospectus, including disclosures included in our most recent annual report on Form 20-F incorporated by reference in this prospectus, before making an investment in our ADSs. In particular, as we are a holding company with substantial business operations in China, you should pay special attention to subsections headed “Recent Regulatory Developments,” “Holding Company Structure”, and “Risks Related to Doing Business in the PRC,” including but not limited to risk factor such as “uncertainties with respect to the PRC legal system, including uncertainties regarding the enforcement of laws, and sudden or unexpected changes in policies, laws and regulations in China could adversely affect us.”

The PRC government has significant authority to exert influence on the ability of a company with substantive operations in China, such as us, to conduct its business, accept foreign investments or list on a U.S. or other foreign exchanges. For example, we face risks associated with regulatory approvals of offshore offerings, anti-monopoly regulatory actions, oversight on cybersecurity and data privacy, as well as the lack of PCAOB inspection on our auditor. Such risks could result in a material change in our operations and/or the value of our ADSs or could significantly limit or completely hinder our ability to offer or continue to offer ADSs and/or other securities to investors and cause the value of such securities to significantly decline or be worthless. The PRC government also has significant oversight and discretion over the conduct of our business and as such may influence our operations at any time, which could result in a material adverse effect on our operations. The PRC government has recently published new policies that significantly affected certain industries, and we cannot rule out the possibility that it will in the future release regulations or policies regarding the industry where we operate, which could adversely affect our business, financial condition and results of operations. Furthermore, the PRC government has recently indicated an intent to exert more oversight and control over overseas securities offerings and other capital markets activities and foreign investment in China-based companies like us. These risks could result in a material change in our operations and the value of our ordinary shares or the ADSs, or could significantly limit or completely hinder our ability to offer or continue to offer securities to investors and cause the value of such securities to significantly decline or become worthless. Below please find a summary of the principal risks we face, organized under relevant headings. These risks are discussed more fully in the section titled “Risk Factors.”

Risks Related to Doing Business in the PRC

Risks and uncertainties related to doing business in China include, but are not limited to, the following:

- uncertainties with respect to the PRC legal system, including uncertainties regarding the enforcement of laws, and sudden or unexpected changes in policies, laws and regulations in China could adversely affect us;
- PRC government has significant oversight over the conduct of our business and as such may influence our operations at any time, which may potentially result in a material adverse effect on our operations;
- the PCAOB is currently unable to inspect our auditor in relation to their audit work performed for our financial statements and the inability of the PCAOB to conduct inspections over our auditor deprives our investors with the benefits of such inspections;
- trading in our ADSs on the Nasdaq Stock Market or OTC will be prohibited, and as a result, our ADSs will be delisted under the HFCA Act, if the PCAOB is unable to inspect or fully investigate auditors located in China. On December 16, 2021, the PCAOB issued the HFCA Act Determination Report, according to which our auditor is subject to the determinations that the PCAOB is unable to inspect or investigate completely. The delisting of our ADSs, or the threat of their being delisted, may materially and adversely affect the value of your investment. If this happens there is no certainty that we will be able to list our ordinary shares on a non-U.S. exchange or that a market for our ordinary shares will develop outside of the United States;
- the potential enactment of the Accelerating Holding Foreign Companies Accountable Act would decrease the number of non-inspection years from three years to two, thus reducing the time period before our ADSs will be prohibited from trading on the Nasdaq Stock Market or OTC or delisted;
- 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; and

- the approval of or report and filing with the China Securities Regulatory Commission or other governmental authorities may be required in connection with our future offerings, and, if required, we cannot predict if we will be able to obtain such approval or complete such report and filing process.

Risks Related to Our Financial Prospects and Need for Additional Capital

Risks and uncertainties related to our financial prospectus and need for additional capital include, but are not limited to, the following:

- we have a limited operating history, which may make it difficult to evaluate our current business and predict our future performance;
- we have incurred net losses historically and we may continue to incur net losses in the near future;
- 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;
- 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; and
- we have certain shareholders who have board representation rights and their individual interests may differ from yours.

Risks Related to Clinical Development of Our Product Candidates

Risks and uncertainties related to clinical development of our product candidates include, but are not limited to, the following:

- 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;
- we may not be successful in our efforts to use and expand our proprietary platforms to build a pipeline of product candidates;
- any failures or setbacks in our platforms or our other proprietary technologies could negatively affect our business and financial condition;
- our product candidates, for which we intend to seek approval as biologics products, may face competition sooner than anticipated; and
- 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.

Risks Related to Obtaining Regulatory Approval of Our Drug Candidates

Risks and uncertainties related to obtaining regulatory approval of our drug candidates include, but are not limited to, the following:

- 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;
- 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;

- 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;
- 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; and
- our product candidates may cause undesirable adverse events, side effects 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.

Risks Related to Our Intellectual Property

Risks and uncertainties related to our intellectual property include, but are not limited to, the following:

- 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;
- changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates;
- we may not be successful in obtaining or maintaining necessary rights for our development pipeline through acquisitions and licensing deals;
- 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; and
- our commercial success depends significantly on our ability to operate without infringing upon, misappropriating or otherwise violating the intellectual property rights of third parties.

Risks Related to the ADSs

Risks and uncertainties related to the ADSs include, but are not limited to, the following:

- our business and financial results, including our ability to raise capital or raise capital on favorable terms and the market price of our ADSs, may be adversely affected by the geopolitical factors arising in connection with Russia's invasion of Ukraine, including particularly how countries like the United States and China choose to respond to this war. As a result, the value of our ADSs may significantly decline;
- you may be subject to limitations on transfer of your ADSs;
- the trading price of the ADSs is likely to be volatile, which could result in substantial losses to investors;
- we are an emerging growth company within the meaning of the Securities Act and may take advantage of certain reduced reporting requirements;
- 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 sale or availability for sale, or perceived sale or availability for sale, of substantial amounts of the ADSs could adversely affect their market price;
- due to our ADSs' price fluctuations there is a significant risk that we will be a passive foreign investment company for 2022 or any future taxable year, which could subject U.S. investors in our ADSs or ordinary shares to significant adverse U.S. federal income tax consequences; and
- if a person is treated as owning 10% or more of our stock by vote or value, such person may be subject to adverse U.S. federal income tax consequences.

Recent Regulatory Developments

Cybersecurity Review Measures

On December 28, 2021, the Cyberspace Administration of China, or the CAC, and 12 other relevant PRC government authorities published the amended Cybersecurity Review Measures, or the Cybersecurity Review Measures, which went on February 15, 2022 and supersede and replace the current Cybersecurity Review Measures previously promulgated on April 13, 2020. The Cybersecurity Review Measures provide that the purchase of network products and services by a “critical information infrastructure operator” and the data processing activities of a “network platform operator” that affect or may affect national security shall be subject to the cybersecurity review. Furthermore, if a “network platform operator” that possesses personal information of more than one million users intends to go public in a foreign country, it must apply for a cybersecurity review with the Cybersecurity Review Office. In addition, the relevant PRC governmental authorities may initiate cybersecurity review if they determine certain network products, services, or data processing activities affect or may affect national security.

In addition, on November 14, 2021, the CAC released the Regulations for the Administration of Network Data Security (Draft for Comment), or the Draft Data Security Regulations, for public comments. The Draft Data Security Regulations provide that (i) a data processor who processes personal information of more than one million individuals must complete a cybersecurity review if it intends to be listed in a foreign country, and (ii) a data processor who carries out other data processing activities which affect or may affect national security should also complete the cybersecurity review. The Draft Data Security Regulations provide a broad definition of “data processing activities”, including collection, storage, usage, processing, transfer, provision, publication, deletion and other activities, which covers the entire life cycle of data processing. The Draft Data Security Regulations also provide a broad definition of “data processors” as individuals and entities that may autonomously determine the purpose and method of data processing activities. In addition, the Draft Data Security Regulations require data processors who process important data or whose securities are listed outside of China to carry out annual data security assessment either by itself or through a third party data security service provider and submit the assessment report to a local agency of the CAC. See “Item 4. Information of the Company — 4.B. Business Overview — Regulation — Other PRC Government Regulations — Regulations on Information Security and Data Protection” in our annual report on Form 20-F for the year ended December 31, 2021, which is incorporated in this prospectus by reference, for detailed discussion. As advised by our PRC legal counsel, the Draft Data Security Regulations were released for public comment only with the deadline of submitting public comments or opinions by December 13, 2021, and its provisions and anticipated adoption or effective date are subject to changes and thus its interpretation and implementation remain substantially uncertain. We cannot predict the impact of the Draft Data Security Regulations, if any, at this stage, and we will closely monitor and assess any development in the rule-making process.

As advised by our PRC legal counsel, Tian Yuan Law Firm, given the nature of our business, since we do not possess or process personal information of more than one million users/individuals, and we do not believe we are a “critical information infrastructure operator”, “network platform operator” or a data processor whose purchase of network products and services or data processing activities affect or may affect national security, the offering of our ADSs will not be subject to the cybersecurity review process under the Cybersecurity Review Measures, although we cannot guarantee that the relevant PRC regulatory authority will agree with our interpretation. In addition, we believe, to the best of our knowledge, our business operations do not violate the regulations or policies that have been issued by the CAC to the date of this prospectus in all material aspects. As of the date of this prospectus, the Cybersecurity Review Measures and the Draft Data Security Regulations have not materially affected our business and operations, but in anticipation of the strengthened implementation of cybersecurity laws and regulations and the continued expansion of our business, we face potential risks if we are deemed as a critical information infrastructure operator, a network platform operator or data processing operator under the PRC cybersecurity laws and regulations. In such case, we must fulfill certain obligations as required under the PRC cybersecurity laws and regulations, including, among others, storing personal information and other important data collected and produced within the PRC territory as we advance our drug discovery pipelines as part of our future operations in China, and we may be subject to lengthy cybersecurity review, annual data security assessment and other enhanced regulatory requirements when purchasing network products and services or conducting

other data processing activities. We may face challenges in addressing such enhanced regulatory requirements and be required to make necessary changes to our internal policies and practices in data privacy and cybersecurity matters. As advised by our PRC legal counsel, Tian Yuan Law Firm, as of the date of this prospectus, no detailed rules or implementation of the Cybersecurity Review Measures have been issued by the CAC and the Draft Data Security Regulations were only released for public comments, and the PRC governmental authorities have broad discretion in the interpretation and enforcement of these laws and regulations. It also remains uncertain whether the future regulatory changes will impose additional restrictions on companies like us. We cannot predict the impact of the Cybersecurity Review Measures and/or the Draft Data Security Regulations, if any, at this stage, and we will closely monitor and assess any development in the rule-making process. If the future enacted laws and regulations, including the enacted version of the data security regulations mandate clearance of cybersecurity review and other specific actions to be completed by companies like us before we are able to complete this offering, we will face uncertainties as to whether such clearance and/or other specific actions can be timely obtained or completed, or at all. If we are not able to comply with the cybersecurity and data privacy requirements in a timely manner, or at all, we may be subject to government enforcement actions and investigations, fines, penalties, or suspension of our non-compliant operations, among other sanctions, which could materially and adversely affect our business and results of operations. As of the date of this prospectus, we have not been involved in any investigation on cybersecurity review made by the CAC on such basis, and we have not received any inquiry, notice, warning, or sanction in such respect. We have been making continuous efforts to comply with the relevant cybersecurity and data protection laws and regulations of the PRC, and will endeavor to comply with any updated applicable laws, regulations or guidelines as issued by any relevant regulatory authority in the PRC. See “Risk Factors — Risks Related to Doing Business in the PRC — 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, investigation or sanction by regulatory authorities, private litigation, other liabilities, and/or adverse publicity.”

Potential CSRC Approval Required for the Offering and Listing of Our ADSs

On December 24, 2021, the CSRC published the Provisions of the State Council on the Administration of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments), and Administrative Measures for the Filing of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments), or collectively, the Draft Overseas Listing Regulations, which set out the new regulatory requirements and filing procedures for Chinese companies seeking direct or indirect listing in overseas markets. The Draft Overseas Listing Regulations, among others, stipulate that (i) Chinese companies that seek to offer and list securities in overseas markets directly or indirectly shall fulfill the filing procedures with and report relevant information to the CSRC, (ii) in the context of an initial public offering, an initial filing shall be submitted within three (3) working days after the application for an initial public offering is submitted, and a second filing shall be submitted after the listing is completed, (iii) in the context of follow-on offering after the completion of the initial public offering, a filing shall be submitted within three (3) working days after the completion of the offering or within three (3) working days from the date of the first announcement of the transaction depending on the purpose for which the follow-on offering are conducted, and (iv) if an issuer issuing securities in batches after listing abroad (such as “shelf takedowns” or at-the-marketing offerings), it shall, after the completion of the initial batch offering, submit the fillings to the CSRC within three (3) working days, stating the total number of securities to be issued in connection with such batch issuance. Upon completion of each of the remaining batches, the issuer shall file a record of the issuance with CSRC within three (3) working days. Moreover, an overseas offering and listing is prohibited under circumstances if (i) it is prohibited by PRC laws, (ii) it may constitute a threat to or endanger national security as reviewed and determined by competent PRC authorities, (iii) it has material ownership disputes over equity, major assets, and core technology, (iv) in recent three years, the Chinese operating entities, and their controlling shareholders and actual controllers have committed relevant prescribed criminal offenses or are currently under investigations for suspicion of criminal offenses or major violations, (v) the directors, supervisors, or senior executives have been subject to administrative punishment for severe violations, or are currently under investigations for suspicion of criminal offenses or major violations, or (vi) it has other circumstances as prescribed by the State Council.

The Draft Overseas Listing Regulations, among others, stipulate that if the issuer meets the following conditions, its offering and listing shall be determined as an “indirect overseas offering and listing by a

Chinese company” and is therefore subject to the filing requirement: (1) the revenues, profits, total assets or net assets of the Chinese operating entities in the most recent financial year accounts for more than 50% of the corresponding data in the issuer’s audited consolidated financial statements for the same period; (2) the majority of senior management in charge of business operation are Chinese citizens or have domicile in PRC, and its principal place of business is located in PRC or main business activities are conducted in PRC.

According to the Draft Overseas Listing Regulations, if we failed to complete the filing procedures with the CSRC for our future offering as contemplated in applicable prospectus supplement or fell within any of the circumstances where any of our future follow-on offerings is prohibited by the State Council, we may be subject to penalties, sanctions and fines imposed by the CSRC and relevant departments of the State Council. In severe circumstances, the business of our PRC subsidiary may be ordered to suspend and their business qualifications and licenses may be revoked.

As advised by our PRC legal counsel, Tian Yuan Law Firm, the Draft Overseas Listing Regulations were released only for soliciting public comment as of the date of this prospectus and their provisions and anticipated adoption or effective date are subject to changes and thus their interpretation and implementation remain substantially uncertain, we cannot predict the impact of the Draft Overseas Listing Regulations on this Offering, if any, at this stage, or guarantee that we will be able to satisfy the scrutinized and new regulatory requirements in case they were adopted in the current form.

In addition, On July 6, 2021, certain PRC regulatory authorities issued Opinions on Strictly Cracking Down on Illegal Securities Activities, which emphasized the need to strengthen regulation over illegal securities activities and supervision on overseas listings by China-based companies and propose to take effective measures, such as promoting the development of relevant regulatory systems to deal with the risks and incidents faced by China-based overseas-listed companies. There are still uncertainties regarding the interpretation and implementation of these opinions, Draft Overseas Listing Regulations and further explanations or detailed rules and regulations with respect to these opinions may be issued in the future, which may impose additional requirements on us.

As of the date of this prospectus, no official guidance and related implementation rules have been issued in relation to these recently issued opinions and the interpretation and implementation of these opinions remain unclear at this stage. We cannot assure you that we will not be required to obtain the approval of the CSRC or of potentially other regulatory authorities to maintain the listing status of our ADSs on the Nasdaq or to conduct follow-on offerings of securities in the future. We intend to comply with applicable effective PRC laws and regulations governing our future potential follow-on offerings and complete relevant applicable filings with CSRC, if required. We have been closely monitoring regulatory developments in China regarding any necessary approvals from the CSRC, the CAC, or other PRC regulatory authorities required for overseas Listings.

As of the date of this prospectus, we have not received any inquiry, notice, warning, sanctions or regulatory objection from the CSRC.

Material Licenses and Approvals

Our PRC subsidiary’s operations in China are covered by permissions requirements from the State Administration for Market Regulation, or the SAMR, and the National Medical Products Administration, or the NMPA. Our PRC subsidiary has obtained all material licenses and approvals required for our operations in China. We believe, to the best of our knowledge, as of the date of this prospectus, our PRC subsidiary’s operations in China are not subject to the approvals or filing requirements from the CSRC or cyber security review process from the CAC. However, in connection with the potential offering of securities under this registration statement on Form F-3, filings or permissions from the CSRC or CAC may be required. See detailed discussions “Our Company — Recent Regulatory Developments.” If we or our PRC subsidiary (i) do not receive or maintain such permissions or approvals, (ii) inadvertently conclude that such permissions or approvals are not required or (iii) applicable laws, regulations, or interpretations change and we are required to obtain such permissions or approvals in the future, we may be subject to government enforcement actions, investigations, penalties, sanctions and fines imposed by the CSRC, the CAC and relevant departments of the State Council. In severe circumstances, the business of our PRC subsidiary may be ordered to suspend and its business qualifications and licenses may be revoked. For details of our material

licenses and approvals, see “Item 4. Information of the Company — 4.B. Business Overview — Material Licenses and Approvals.” For risks relating to licenses and approvals required for our operations in China, see “Item 3. Key Information — 3.D. Risk Factors — Risks Related to Doing Business in the PRC,” “— Risks Related to Clinical Development of Our Product Candidates,” and “— Risks Related to Obtaining Regulatory Approval of Our Drug Candidates.” in our annual report on Form 20-F for the year ended December 31, 2021, which is incorporated in this prospectus by reference.

Transfer of Funds and Other Assets

As of the date of this prospectus, we do not have cash management policies and procedures in place that dictate how funds are transferred through our organization. Rather, the funds can be transferred in accordance with the applicable PRC laws and regulations discussed in this section. See also “Item 8. — Financial Information — 8.A. Consolidated Statements and Other Financial Information — Dividend Policy” in our annual report on Form 20-F for the year ended December 31, 2021, which is incorporated in this prospectus by reference. Under relevant PRC laws and regulations, we are permitted to remit funds to Adagene Suzhou through loans, capital contributions or as payment of considerations for the services rendered. In 2019, 2020 and 2021, Adagene Inc. made payments of US\$13.1 million, US\$15.5 million and US\$30.0 million, respectively, in cash to Adagene Suzhou as consideration for providing services associated with research and development activities related to those intellectual properties owned by Adagene Inc. There were no intercompany loans provided by Adagene Inc. to Adagene Suzhou during the years ended and as of December 31, 2019, 2020 and 2021. In addition, as advised by our PRC legal counsel, Tian Yuan Law Firm, Adagene Suzhou is able to mark up and charge to Adagene Inc., its ultimate parent, for providing services associated with research and development activities related to those intellectual properties owned by Adagene Inc. and Adagene Inc. is able to make cash payments to Adagene Suzhou for considerations of such services.

Other than the above disclosed transfer of funds, we did not transfer any type of assets between Adagene Suzhou and other Adagene subsidiaries in 2019, 2020 and 2021.

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 subsidiary that is foreign investment enterprise in the PRC has to make appropriation from its 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 subsidiary through loans or capital contributions, subject to the satisfaction of the applicable government registration and approval requirements. See “Risk Factors — Risks Related to Doing Business in the PRC — 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 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 subsidiary when needed.

Corporate Information

Adagene was incorporated in the Cayman Islands in February 2011. We conduct our operations in China primarily through our subsidiary in China, Adagene Suzhou, which was incorporated in February 2012. 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. The ADSs, each representing one and one quarter (1.25) of our ordinary shares, par value US\$0.0001 per share, are currently traded on the Nasdaq under the symbol “ADAG”.

Our principal executive office of our main operations 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 business address of our San Diego office is 10179 Huennekens Street Suite 103, San Diego, CA 92121. We have appointed Cogency Global Inc., which is located at 122 East 42nd Street, 18th Floor, New York, NY 10168, as our agent upon whom process may be served in any action brought against us under the securities laws of the United States with an offering of Securities registered by the registration statement of which this prospectus is a part. Our corporate website is www.adagene.com. The reference to our website is an inactive textual reference only, and information contained therein or connected thereto is not incorporated into this prospectus or the registration statement of which it forms a part.

Implications of Being an Emerging Growth Company

We qualify as an “emerging growth company” as defined in the Jumpstart our Business Startups Act of 2012 (the “JOBS Act”). As an emerging growth company, we may take advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public companies. These provisions include:

- a requirement to have only two years of audited financial statements in addition to any required interim financial statements and correspondingly reduced Management’s Discussion and Analysis of Financial Condition and Results of Operations disclosure;
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 (the “Sarbanes-Oxley Act”); and
- to the extent that we no longer qualify as a foreign private issuer, (i) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (ii) exemptions from the requirements of holding a non-binding advisory vote on executive compensation, including golden parachute compensation.

We may take advantage of these provisions for up to five years or such earlier time that we are no longer an emerging growth company. We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of at least US\$1.07 billion; (ii) the last day of our fiscal year following the fifth anniversary of the completion of this offering; (iii) the date on which we have issued more than US\$1.0 billion in non-convertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC, which means the market value of our ordinary shares that are held by non-affiliates equals or exceeds US\$700.0 million as of the last business day of our most recently completed second fiscal quarter. We may choose to take advantage of some but not all of these reduced burdens. For example, Section 107 of the JOBS Act also provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards applicable to public companies. This provision allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We do not plan to “opt out” of such exemptions afforded to an emerging growth company.

Implications of Being a Foreign Private Issuer

We are also considered as a “foreign private issuer.” Accordingly, we report under the Exchange Act of 1934, as amended (the “Exchange Act”), as a non-U.S. company with foreign private issuer status. This means that, even after we no longer qualify as an emerging growth company, as long as we qualify as a foreign private issuer under the Exchange Act, we will be exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including:

- 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 rules under the Exchange Act requiring the filing with the Securities and Exchange Commission, or SEC, of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K, upon the occurrence of specified significant events.

We may take advantage of these exemptions until such time as we are no longer a foreign private issuer. We would cease to be a foreign private issuer at such time as more than 50% of our outstanding voting securities are held by U.S. residents and any of the following three circumstances applies: (i) the majority of our executive officers or directors are U.S. citizens or residents, (ii) more than 50% of our assets are located in the United States or (iii) our business is administered principally in the United States.

In this prospectus and in the documents incorporated by reference in this prospectus, we have taken advantage of certain of the reduced reporting requirements as a result of being an emerging growth company and a foreign private issuer. Accordingly, the information contained in this prospectus and in the documents incorporated by reference in this prospectus may be different than the information you receive from other public companies in which you hold equity securities.

RISK FACTORS

Investors in the Securities are purchasing securities of a Cayman Islands holding company rather than securities of its subsidiaries that have substantive business operations in China or in the U.S. Adagene is a Cayman Islands holding company that conducts its operations and operates its business in China through its PRC subsidiary, Adagene Suzhou. In addition, Adagene Inc. conducts a substantial portion of its operations in the U.S. through its U.S. subsidiary, Adagene Incorporated. Such structure involves unique risks to investors in the Securities. You should carefully consider all of the information in this prospectus before making an investment in the Securities.

Accordingly, you should carefully consider:

- the information contained in or incorporated by reference into this prospectus;
- the information contained in or incorporated by reference into any prospectus supplement relating to specific offerings of Securities;
- the risks described in our annual report on Form 20-F for our fiscal year ended December 31, 2021, on file with the SEC, which is incorporated by reference into this prospectus; and any updates to those risk factors in our reports on Form 6-K incorporated by reference in this prospectus; and
- other risks and other information that may be contained in, or incorporated by reference from, other filings we make with the SEC, including in any prospectus supplement relating to specific offerings of Securities.

The discussion of risks contained in or incorporated by reference into this prospectus or into any prospectus supplement comprises material risks of which we are aware. You should pay special attention to subsections headed “Recent Regulatory Developments,” “Holding Company Structure,” and “Risks Related to Doing Business in the PRC.” Our actual results could differ materially and adversely from those anticipated in this prospectus. If any of the events or developments described actually occurs, our business, financial condition or results of operations would likely suffer, and you may lose all or part of your investment. Although we discuss key risks in our discussion of risk factors, new risks may emerge in the future, which may prove to be significant. We cannot predict future risks or estimate the extent to which they may affect our business, results of operations, financial condition and prospects.

Please see “Where You Can Find More Information” and “Incorporation of Certain Documents by Reference” for information on where you can find the documents we have filed with or furnished to the SEC and which are incorporated into this prospectus by reference.

Risks Related to Doing Business in the PRC

Uncertainties with respect to the PRC legal system, including uncertainties regarding the enforcement of laws, and sudden or unexpected changes in policies, 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.

For example, two draft regulations relating to overseas offerings by domestic companies of equity shares, depository receipts, convertible corporate bonds, or other equity-like securities, and overseas listing of the securities for trading — namely the Provisions of the State Council on the Administration of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments) and the Administrative Measures for the Filing of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments) — were recently released in December 2021 for public comments. Pursuant to such draft regulations, a filing-based regulatory system would be implemented covering both direct and indirect overseas offering and listing, among which, (i) if an issuer listed in other overseas markets after overseas offerings, the issuer shall submit to the CSRC filing documents within three working days after such application is submitted; (ii) if an issuer issues overseas listed securities after listing abroad and issues such securities aiming

at purchasing assets, the issuer shall submit to the CSRC filing documents within three working days after the issue is completed, however, if the assets purchased are domestic assets, the filing procedure shall be performed within three working days from the date of the first announcement of the transaction; and (iii) if the significant events, such as change of control and termination of the listing, occur after the issuer's overseas listing, it should report the details to CSRC within three working days from the date of occurrence. Uncertainties exist regarding the final form of these regulations as well as the interpretation and implementation thereof after promulgation. If those two rules were adopted in the current form, we may be required to file documents regarding the events listed in the regulations with the CRSC before or after the events occurred.

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.

PRC government has significant oversight over the conduct of our business and as such may influence our operations at any time, which may potentially result in a material adverse effect on our operations.

PRC government has significant oversight over the conduct of our business and may intervene or influence our operations at any time, which may potentially result in a material adverse effect on our operations. PRC government has also recently indicated an intent to exert more oversight over offerings that are conducted overseas and foreign investment in China-based issuers, which could impact our ability to raise additional capital in international capital markets. In addition, the PRC government has recently published new policies that significantly affected certain industries, and we cannot rule out the possibility that it will in the future release regulations or policies regarding our industry that could adversely affect our business, financial condition and results of operations. Any such action could significantly limit or completely hinder our ability to offer or continue to offer Securities to investors and cause the value of such Securities to significantly decline or be worthless.

However, as there are still regulatory uncertainties in this regard, we cannot assure you that we will be able to comply with new laws and regulations in all respects, and we may be ordered to rectify, suspend or terminate any actions or services that are deemed illegal by the regulatory authorities and become subject to material penalties, which may materially harm our business, financial condition, results of operations and prospects.

The PCAOB is currently unable to inspect our auditor in relation to their audit work performed for our financial statements and the inability of the PCAOB to conduct inspections over our auditor deprives our investors with the benefits of such inspections.

Our auditor, the independent registered public accounting firm that issues the audit report included elsewhere in our most recent annual report on Form 20-F incorporated by reference in this prospectus, 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 the applicable professional standards. Since our auditor is located in China, a jurisdiction where the PCAOB has been unable to conduct inspections without the approval of the Chinese authorities, our auditor is not currently inspected by the PCAOB.

This lack of the 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 ordinary shares and/or ADS 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 the PCAOB inspections, which could cause investors and potential investors in our ordinary shares and/or ADSs to lose confidence in our audit procedures and reported financial information and the quality of our financial statements.

Trading in our ADSs on the Nasdaq Stock Market or OTC will be prohibited, and as a result, our ADSs will be delisted under the HFCA Act, if the PCAOB is unable to inspect or fully investigate auditors located in China. On December 16, 2021, the PCAOB issued the HFCA Act Determination Report, according to which our auditor is subject to the determinations that the PCAOB is unable to inspect or investigate completely. The delisting of our ADSs, or the threat of their being delisted, may materially and adversely affect the value of your investment. If this happens there is no certainty that we will be able to list our ordinary shares on a non-U.S. exchange or that a market for our ordinary shares will develop outside of the United States.

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, the Holding Foreign Companies Accountable Act, or the HFCA Act, has been signed into law on December 18, 2020. The HFCA Act requires the SEC to prohibit the trading of securities of a Chinese or a non-U.S. company on U.S. securities exchanges or the over-the-counter market if the PCAOB has determined that it has been unable to inspect the company's accounting firm for three consecutive years because of a position taken by an authority in the company's jurisdiction. The HFCA Act also requires such companies to make certain disclosures about their ownership by governmental entities and their relationships with the Chinese Communist Party.

On December 2, 2021, the SEC adopted final amendments to its rules implementing the HFCA Act (the "Final Amendments"). The Final Amendments finalize the interim final rules adopted in March with two major modifications. First, the Final Amendments clarify how the requirements apply to variable interest entities. Second, the Final Amendments include requirements to disclose information, including the auditor name and location, the percentage of shares of the issuer owned by governmental entities, whether governmental entities in the applicable foreign jurisdiction with respect to the auditor has a controlling financial interest with respect to the issuer, the name of each official of the Chinese Communist Party who is a member of the board of the issuer, and whether the articles of incorporation of the issuer contains any charter of the Chinese Communist Party. The Final Amendments also establish procedures the SEC will follow in identifying issuers and prohibiting trading by certain issuers under the HFCA Act.

On December 16, 2021, PCAOB issued the HFCA Act Determination Report, according to which our auditor is subject to the determinations that the PCAOB is unable to inspect or investigate completely. In March 2022, the SEC issued its first "Conclusive list of issuers identified under the HFCAA" indicating that those companies are now formally subject to the delisting provisions if they remain on the list for three consecutive years. We were provisionally identified by the SEC on May 4, 2022 under the HFCA Act and anticipate being conclusively identified 15 business days after May 4, 2022. See <https://www.sec.gov/hfcaa>.

The HFCA Act 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. Additionally, whether the PCAOB will be able to conduct inspections of our auditor in the three consecutive years or at all, is subject to substantial uncertainty and depends on factors out of our or our auditor's control. If our auditor is unable to meet the PCAOB inspection requirement in time, we will be delisted from the Nasdaq 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.

If our ADS are delisted from the U.S. securities exchange and are prohibited from trading in the over-the-counter market in the United States, there is no certainty that we will be able to list our ordinary shares on a non U.S. securities exchange or that a market for our ordinary shares will develop outside of the United States. 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.

The potential enactment of the Accelerating Holding Foreign Companies Accountable Act would decrease the number of non-inspection years from three years to two, thus reducing the time period before our ADSs will be prohibited from trading on the Nasdaq Stock Market or OTC or delisted.

On June 22, 2021, the U.S. Senate passed a bill, also known as the Accelerating Holding Foreign Companies Accountable Act, to amend Section 104(i) of the Sarbanes-Oxley Act of 2002 (15 U.S.C. 7214(i)) 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 two consecutive years, instead of three consecutive years as currently required under the HFCA Act, after the law becomes effective. On February 4, 2022, the U.S. House of Representatives passed the America COMPETES Act of 2022, which includes the exact same amendments as the bill passed by the Senate. The America COMPETES Act of 2022 however includes a broader range of legislation not related to the HFCA Act in response to the U.S. Innovation and Competition Act passed by the Senate in 2021. The U.S. House of Representatives and U.S. Senate will need to agree on amendments to these respective bills to align the legislation and pass their amended bills before the President can sign into law. It is unclear when the U.S. Senate and U.S. House of Representatives will resolve the differences in the U.S. Innovation and Competition Act and the America COMPETES Act of 2022 bills currently passed, or when the U.S. President will sign on the bill to make the amendment into law, or at all. In the case that the bill becomes the law, it will reduce the time period before our ADSs will be prohibited from trading on the Nasdaq or over-the-counter or be delisted.

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.

In the event that the SEC restarts the administrative proceedings, depending upon the final outcome, listed companies in the United States with major PRC operations, such as us, may find it difficult or impossible to retain auditor in respect of their operations in the PRC, which could result in financial statements being determined to not be in compliance with the requirements of the Exchange Act, including

possible delisting. Moreover, any negative news about any such future proceedings against these audit firms may cause investor uncertainty regarding China-based, U.S.-listed companies and the market price of our ADSs may be adversely affected.

If our independent registered public accounting firm was denied, even temporarily, the ability to practice before the SEC and we were unable to timely find another registered public accounting firm to audit and issue an opinion on our financial statements, our financial statements could be determined not to be in compliance with the requirements of the Exchange Act. Such a determination could ultimately lead to the delisting of our ADSs from the Nasdaq Stock Market or deregistration from the SEC, or both, which would substantially reduce or effectively terminate the trading of our ADSs in the United States.

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.

Moreover, the Cyberspace Administration of China, or the CAC, issued the Measures on Security Assessment of the Cross-border Transfer of Personal Information (Draft for Comment) in June 2019, pursuant to which, any cross-border transfer of information that may endanger national security, damage public interest, or fail to offer effective protection of personal information security, as assessed by relevant regulatory bodies, will be prohibited. In October 2021, CAC issued the Measures on Security Assessment of the Cross-border Data Transfer (Draft for Comment), which adjusts the thresholds for triggering mandatory security assessments not only in the cross-border transfers of personal information, but also in the cross-border transfers of “important data” collected and generated in China under certain circumstance. Given that the government body will have full discretion in the assessment, it is unclear if and the extent to which our clinical data will be considered as an endangerment to national or personal information security, if the regulation becomes effective.

Cross-border data transfer from other jurisdictions may also be limited if we fail to comply with relevant requirements, such as obtaining authorization from patients regarding the use, transfer and retrieval of their personal information or data and adopting measures to ensure the safety of personal information or data in the transfer. Also, cross-border transfer of personal data by its nature is subject to general data privacy regulations in various jurisdictions, and thus any failure to comply with data privacy protection may lead to a restriction of transferring our data across different jurisdictions.

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

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 and important data 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 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 Cybersecurity Law, which became effective in June 2017, established China's first national-level data protection for "network operators," which may include all organizations in China that connect to or provide services over the internet or other information network. The Cybersecurity Law requires network operators to perform certain functions related to cybersecurity protection. In addition, the Cybersecurity Law imposes certain requirements on network operators of critical information infrastructure, or the CIIOs. For example, the CIIOs generally shall, during their operations in the PRC, store the personal information and important data collected and produced within the territory of PRC, and shall perform certain security obligations as required under the Cybersecurity Law, including that the CIIOs shall pass the national security review when purchasing network product or service which may affect national security. In addition, China's Data Security Law, which was promulgated by the Standing Committee of PRC National People's Congress, or the SCNPC, on June 10, 2021 and came into effect on September 1, 2021, outlines the main system framework of data security protection. For example, the Data Security Law introduces a data classification and hierarchical protection system based on the importance of data in economic and social development, as well as the degree of harm it will cause to national security, public interests, or legitimate rights and interests of individuals or organizations when such data is tampered with, destroyed, leaked, or illegally acquired or used. Processors of "important data" are further required to conduct periodic risk assessment and submit assessment report to relevant regulatory authorities. In addition, the Data Security Law provides a national security review procedure for those data activities which may affect national security. Furthermore, Regulations on the Security Protection of Critical Information Infrastructure, which was promulgated by the State Council of PRC on July 30, 2021 and came into effect on September 1, 2021, or the CII Protection Regulations, stipulates the obligations and liabilities of the regulators, society and CIIOs in protecting the security of critical information infrastructure, or the CII. According to the CII Protection Regulations, regulators supervising specific industries shall formulate detailed guidance to recognize the CII in the respective sectors, and CIIOs shall take the responsibility to protect the CII's security by performing certain prescribed obligations. For example, CIIOs are required to conduct network security test and risk assessment, report the assessment results to relevant regulatory authorities, and timely rectify the issues identified at least once a year.

The Opinions on Strictly Cracking Down Illegal Securities Activities in Accordance with the Law, which were issued by the General Committee and State Council on July 6, 2021, require the speed-up of the revision of the provisions on strengthening the confidentiality and archives coordination between regulators related to overseas issuance and listing of securities, and improvement to the laws and regulations related to data security, cross-border data flow, and management of confidential information. Numerous regulations, guidelines and other measures have been or are expected to be adopted under the umbrella of, or in addition to the Cybersecurity Law and Data Security Law, including the Cybersecurity Review Measures published by Cyberspace Administration of China, or the CAC, and other 12 relevant PRC government authorities in December 2021, which provides that, among others, if a "network platform operator" that possesses personal information of more than one million users intends to go public in a foreign country, it must apply for a cybersecurity review with the Cybersecurity Review Office, and that the relevant PRC governmental authorities may initiate cybersecurity review if they determine certain network products, services, or data processing activities affect or may affect national security.

On October 29, 2021, the CAC published the Measures on Security Assessment of Cross-border Transfer of Data (Draft for Comments), or the draft security assessment measures, which provide that data processors shall make self-assessment of the risks before transferring data cross-border, and shall apply for security assessment for cross-border data transfer in any of the following circumstances: (i) transferring personal information and important data collected and produced by CIIO operators; (ii) important data is included in the data transferred cross-border; (iii) transferring personal information cross-border by personal information processors which process more than one million individuals' personal information; (iv) transferring more than one hundred thousand individuals' personal information or more than ten thousand individuals' sensitive personal information cumulatively; or (v) other circumstances which require the application for cross-border data transfer security assessment as determined by the CAC.

In addition, the CAC published the Regulations for the Administration of Cyber Data Security (Draft for Comment), or the Draft Data Security Regulations, for public comments in November 2021, which reiterate that a data processor who processes personal information of more than one million individuals must complete the cybersecurity review if it intends to be listed in a foreign country, and if a data processor conducts any data processing activities that affect or may affect national security, an application for cybersecurity review shall also be made by such a processor. The Draft Data Security Regulations also require that data processors who process important data or whose securities are listed outside of China shall carry out annual data security assessment by itself or through a third party data security service provider and submit the assessment report to local agency of the CAC. Also see “Item 4. Information on the Company — 4.B. Business Overview — Regulation — Other PRC Government Regulations — Regulations on Information Security and Data Protection” for detailed discussion.

As of the date of this prospectus, the exact scope of CIIOs and important data under the current laws, regulations and regulatory regime remains unclear, and the authorities may have wide discretion in the interpretation and enforcement of the related laws and regulations. If we are deemed as a CIIO, or as an operator who collects, uses and processes important data according to the Cybersecurity Law, Data Security Law and other relevant laws and regulations, we may need to perform or be subject to certain prescribed obligations, and if we were found to be in violation of these applicable laws and regulations, we may be subject to administrative penalties, including fines and service suspension. We also cannot rule out the possibility that certain of our customers may be deemed as CIIOs, or as operators processing important data, in which case our products or services or data processing activities, if being deemed as related to national security, will need to be submitted for cybersecurity review before we can enter into agreements with such customers, and before the conclusion of such procedure, the customers will not be allowed to use our products or services. If the reviewing authority considers that the use of our services by certain of our customers involves risk of disruption, is vulnerable to external attacks, or may negatively affect, compromise, or weaken the protection of national security, we may not be able to provide our products or services to such customers, which could have a material adverse effect on our results of operations and business prospects.

As of the date of this prospectus, we have not been involved in any investigations on cybersecurity review initiated by the Cyberspace Administration of China, and we have not received any inquiry, notice, warning, sanctions in such respect or any regulatory objections to our listing status on the Nasdaq. In addition, as advised by our PRC legal counsel, Tian Yuan Law Firm, given the nature of our business, the facts that we do not possess or process personal information of more than one million users/individuals, and our self-assessments that we are not a “critical information infrastructure operator”, “network platform operator” or a data processor whose purchase of network products and services or data processing activities affect or may affect national security, we believe, to the best of our knowledge, our business operations do not violate the regulations or policies that have been issued by the CAC to the date of this prospectus in all material aspects. As there are still uncertainties regarding the further enactment of new laws and regulations as well as the revision, interpretation and implementation of those existing laws and regulations, however, we cannot assure you that we will be able to comply with such regulations in all respects, and we may be ordered to rectify, suspend or terminate any actions or services that are deemed illegal or in compliance by the regulatory authorities and become subject to fines and/or other penalties. If we are unable to address such issue in a timely manner or at all, we may be required to suspend or terminate our related businesses or face other penalties, our business, financial condition, results of operations, and prospects could be materially harmed.

Furthermore, certain PRC regulatory authorities recently issued the Opinions on Strictly Cracking Down on Illegal Securities Activities. These opinions call for strengthened regulation over illegal securities activities and supervision of overseas listings by China-based companies and propose to take effective measures. As of the date of this prospectus, no official guidance or related implementation rules have been issued and taken into effect in relation to such opinions and as a result, the interpretation and implementation of these opinions remain unclear at this stage. We cannot assure you that we will not be required to obtain the pre-approval of the CSRC and potentially other regulatory authorities to pursue an offering of securities overseas or to maintain the listing status of our ADSs on the Nasdaq. See also “— The approval of or report and filing with the China Securities Regulatory Commission or other governmental authorities may be required in connection with this offering, and, if required, we cannot predict if we will be able to obtain such approval or complete such report and filing process.”

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.

Dividends we receive from our subsidiary located in the PRC may be taxed at a higher rate, which could materially and adversely affect the amount of dividends, if any, we may pay our shareholders.

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 of the PRC, 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 twelve-month 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.

Your investments in our ADSs, Ordinary Shares and/or other Securities are investments in securities of a Cayman Islands holding company rather than securities of our subsidiaries that have substantive business operations in China. As a result, you may experience difficulties in effecting service of legal process, enforcing foreign judgments or bringing actions in China against us or our management based on foreign laws.

Adagene Inc. is a holding company incorporated under the laws of the Cayman Islands with no operations of its own. It conducts a substantial portion of its operations in China primarily through its subsidiary in China, in particular Adagene (Suzhou) Limited. In addition, Adagene Inc. conducts its substantial portion of operations in the U.S. through its U.S. subsidiary, Adagene Incorporated. As such, investors in the ADSs, Ordinary Shares or other Securities are not purchasing equity securities or other securities of our subsidiaries that have substantive business operations in China or in the U.S. but instead are purchasing equity securities or other securities of a Cayman Islands holding company. In addition, some of our senior executive officers and directors reside within China for a significant portion of the time and some are PRC nationals. As a result, it may be difficult for our shareholders or investors 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” in our annual report on Form 20-F for the year ended December 31, 2021, which is incorporated in this prospectus by reference.

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.

Although cross-border business may not be an area of our focus, if we plan to expand our business internationally in the future, any unfavorable government policies on international trade, such as capital controls or tariffs, may affect the demand for our products and services, impact our competitive position, or prevent us from being able to conduct business in certain countries. If any new tariffs, legislation, or regulations are implemented, or if existing trade agreements are renegotiated, such changes could adversely affect our business, financial condition, and results of operations. Recently, there have been heightened tensions in international economic relations, such as the one between the United States and China. The U.S. government has recently imposed, and has recently proposed to impose additional, new, or higher tariffs on certain products imported from China to penalize China for what it characterizes as unfair trade practices. China has responded by imposing, and proposing to impose additional, new, or higher tariffs on certain products imported from the United States. Following mutual retaliatory actions for months, on January 15, 2020, the United States and China entered into the Economic and Trade Agreement between the United States of America and the People’s Republic of China as a phase one trade deal, effective on February 14, 2020. It remains unclear what additional actions, if any, will be taken by the U.S. or other governments with respect to international trade, tax policy related to international commerce, or other trade matters. The situation is further complicated by the political tensions between the United States and China that escalated during the COVID-19 pandemic and in the wake of the PRC National People’s Congress’ decision on Hong Kong national security legislation, sanctions imposed by the U.S. Department of Treasury on certain officials of the Hong Kong Special Administrative Region and the central government of the PRC and the executive orders issued by U.S. President in August 2020 that prohibit certain transactions with certain China-based companies and their respective subsidiaries. Rising trade and political tensions could reduce levels of trade, investments, technological exchanges and other economic activities between China and other countries, which would have an adverse effect on global economic conditions, the stability of global financial markets, and international trade policies.

Although the direct impact of the current international trade and political tension, and any escalation of such tension, on the biopharmaceutical companies in China is uncertain, the negative impact on general, economic, political and social conditions may adversely impact our business, financial condition and results of operations.

The approval of or report and filing with the China Securities Regulatory Commission or other governmental authorities may be required in connection with this offering, and, if required, we cannot predict if we will be able to obtain such approval or complete such report and filing process.

The Regulations on Mergers and Acquisitions of Domestic Enterprises by Foreign Investors, or the M&A Rules, requires an overseas special purpose vehicle formed for listing purposes through acquisitions of PRC domestic companies and controlled by PRC companies or individuals to obtain the approval of the CSRC prior to the listing and trading of such special purpose vehicle's securities on an overseas stock exchange. However, the application of the M&A Rules remains unclear. If CSRC approval is required, it is uncertain whether it would be possible for us to obtain the approval, and any failure to obtain or delay in obtaining CSRC approval for this offering would subject us to sanctions imposed by the CSRC and other PRC regulatory agencies.

Our PRC legal counsel has advised us based on their understanding of the current PRC laws, rules and regulations that no permission is required from CSRC for us to maintain our listing of the ADSs on the Nasdaq, given that (i) the CSRC currently has not issued any definitive rule or interpretation concerning whether offering such as this offering contemplated by our Company are subject to the M&A Rules; and (ii) our PRC subsidiary was incorporated as wholly foreign-owned enterprises by means of direct investment not subject to the M&A Rules. There can be no assurance that the relevant PRC government agencies, including the CSRC, would reach the same conclusion as our PRC legal counsel.

In addition, the recently issued Opinions on Strictly Cracking Down on Illegal Securities Activities emphasized the need to strengthen regulation over illegal securities activities and supervision on overseas listings by China-based companies and propose to take effective measures, such as promoting the development of relevant regulatory systems to deal with the risks and incidents faced by China-based overseas-listed companies. There are still uncertainties regarding the interpretation and implementation of these opinions, Draft Overseas Listing Regulations and further explanations or detailed rules and regulations with respect to these opinions may be issued in the future, which may impose additional requirements on us.

Furthermore, on December 24, 2021, the CSRC published the Provisions of the State Council on the Administration of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments), and Administrative Measures for the Filing of Overseas Securities Offering and Listing by Domestic Companies (Draft for Comments), or collectively, the Draft Overseas Listing Regulations, which set out the new regulatory requirements and filing procedures for Chinese companies seeking direct or indirect listing in overseas markets. The Draft Overseas Listing Regulations, among others, stipulate that (i) Chinese companies that seek to offer and list securities in overseas markets directly or indirectly shall fulfill the filing procedures with and report relevant information to the CSRC, (ii) in the context of an initial public offering, an initial filing shall be submitted within three (3) working days after the application for an initial public offering is submitted, and (iii) in the context of follow-on offering after the completion of the initial public offering, a filing shall be submitted within three (3) working days after the completion of the offering or within three (3) working days from the date of the first announcement of the transaction depending on the purpose for which the follow-on offering are conducted. Moreover, an overseas offering and listing is prohibited under circumstances if (i) it is prohibited by PRC laws, (ii) it may constitute a threat to or endanger national security as reviewed and determined by competent PRC authorities, (iii) it has material ownership disputes over equity, major assets, and core technology, (iv) in recent three years, the Chinese operating entities, and their controlling shareholders and actual controllers have committed relevant prescribed criminal offenses or are currently under investigations for suspicion of criminal offenses or major violations, (v) the directors, supervisors, or senior executives have been subject to administrative punishment for severe violations, or are currently under investigations for suspicion of criminal offenses or major violations, or (vi) it has other circumstances as prescribed by the State Council.

The Draft Overseas Listing Regulations, among others, stipulate that if the issuer meets the following conditions, its offering and listing shall be determined as an "indirect overseas offering and listing by a

Chinese company” and is therefore subject to the filing requirement: (1) the revenues, profits, total assets or net assets of the Chinese operating entities in the most recent financial year accounts for more than 50% of the corresponding data in the issuer’s audited consolidated financial statements for the same period; (2) the majority of senior management in charge of business operation are Chinese citizens or have domicile in PRC, and its principal place of business is located in PRC or main business activities are conducted in PRC.

According to the Draft Overseas Listing Regulations, if we failed to complete the filing procedures with the CSRC for our future offering or fell within any of the circumstances where our proposed listing overseas is prohibited by the State Council, we may be subject to penalties, sanctions and fines imposed by the CSRC and relevant departments of the State Council. In severe circumstances, the business of our PRC subsidiary may be ordered to suspend and their business qualifications and licenses may be revoked.

As advised by our PRC legal counsel, the Draft Overseas Listing Regulations were released only for soliciting public comment as of the date of this prospectus and their provisions and anticipated adoption or effective date are subject to changes and thus their interpretation and implementation remain substantially uncertain, we cannot predict the impact of the Draft Overseas Listing Regulations on this Offering, if any, at this stage, or guarantee that we will be able to satisfy the scrutinized and new regulatory requirements in case they were adopted in the current form.

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. 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 or the subsidiary will be subject to PRC tax at a rate of 25%. In addition, we may be required to withhold taxes from dividends, and non-PRC 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, as described below under “Risk Factors — Risks Related to the ADS — You may be subject to PRC income tax on dividends from us or any gain realized on the transfer of our ADSs.”

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, or able to obtain in practice, the benefits under these tax treaties or arrangements.

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” in our annual report on Form 20-F for the year ended December 31, 2021, which is incorporated in this prospectus by reference, 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.

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 prospectus, 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 prospectus, 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.

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. In addition, 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 subsidiary 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 subsidiary's 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 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 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 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, 2021, 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.

Risks Related to the ADSs

Although we believe we were not a passive foreign investment company, or PFIC, for 2021, due to our ADSs' price fluctuations there is a significant risk that we will be a PFIC for 2022 or any future 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 generally 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 any 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 any taxable year because (i) the value of our goodwill may be determined by reference to our market capitalization, which has been, and may continue to be, volatile, (ii) we expect to hold a significant amount of cash, and (iii) a company's PFIC status is an annual factual determination that can be made only after the end of each taxable year and depends on the composition of its income and assets and the value of its assets from time to time.

Based on the average price of our ADSs during 2021, we believe that we were not a PFIC for our taxable year ended December 31, 2021. However, while we hold a substantial amount of cash and cash equivalents our PFIC status for any taxable year will depend primarily on the average value of our goodwill. Because our market capitalization has declined substantially since our initial public offering (including in recent months), if the value of our goodwill is determined by reference to our market capitalization there is a significant risk that we will be a PFIC for our taxable year 2022, and possibly future taxable years. In addition, prior to the 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 are a PFIC for any taxable year during which a U.S. investor owns our ADSs or ordinary shares, the U.S. taxpayer generally will be subject to adverse U.S. federal income tax consequences, including increased tax liability on disposition gains and "excess distributions," and additional reporting requirements. This will generally continue to be the case even if we ceased to be a PFIC in a later taxable year, unless certain elections are made. For further discussion of the PFIC rules, see "Item 10 Additional Information — Taxation — Material U.S. Federal Income Tax Consequences — Passive Foreign Investment Company Rules" in our annual report on Form 20-F for the year ended December 31, 2021, incorporated here by reference.

Whether or not we will be treated as a PFIC with respect to a particular U.S. investor will depend on whether the U.S. investors owns our ADSs or ordinary share years during a taxable year in which we are a

PFIC. The applicable prospectus supplement will describe any changes in fact relevant to the determination of our PFIC status between the date of this registration statement and the date of such prospectus supplement.

If a U.S. person is treated as owning 10% or more of our stock by vote or value, such person may be subject to adverse U.S. federal income tax consequences.

If a U.S. person is treated as owning (directly, indirectly or constructively) 10% or more of our stock (including our ADSs and ordinary shares) by value or voting power, such person generally will be treated as a “United States shareholder” with respect to each “controlled foreign corporation”, or CFC, in our group. A CFC is a non-U.S. corporation more than 50% of the stock (by voting power or value) of which is owned (directly, indirectly or constructively) by “United States shareholders.” We have not determined whether we are a CFC. However, even if we are not a CFC, under certain ownership attribution rules our non-U.S. subsidiaries could be treated as owned by our U.S. subsidiary and thus may be treated as CFCs. A United States shareholder of a CFC may be subject to additional U.S. federal income tax liabilities and reporting requirements. We do not intend to furnish to any information that may be necessary for United States shareholders, if any, to comply with the CFC rules. Prospective U.S. investors that may be treated for purposes of the CFC rules as owning 10% of our stock by voting power or value should consult their tax advisers regarding the potential application of these rules in their particular circumstances.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus 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, including but not limited to Adagene’s ability to demonstrate the safety and efficacy of its drug candidates; the clinical results for its drug candidates, which may not support further development or regulatory approval; the content and timing of decisions made by the relevant regulatory authorities regarding regulatory approval of Adagene’s drug candidates; Adagene’s ability to achieve commercial success for its drug candidates, if approved; Adagene’s ability to obtain and maintain protection of intellectual property for its technology and drugs; Adagene’s reliance on third parties to conduct drug development, manufacturing and other services; Adagene’s limited operating history and Adagene’s ability to obtain additional funding for operations and to complete the development and commercialization of its drug candidates; Adagene’s ability to enter into additional collaboration agreements beyond its existing strategic partnerships or collaborations, and the impact of the COVID-19 pandemic on Adagene’s clinical development, commercial and other operations, as well as those risks more fully discussed in the “Risk Factors” section in Adagene’s filings with the SEC. Such known and unknown risks, uncertainties and other factors 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” in our annual report on Form 20-F for the year ended December 31, 2021, which is incorporated in this prospectus by reference, 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. The forward-looking statements contained in or incorporated into this prospectus and any applicable prospectus supplement speak only as of the date of hereof or thereof or of such documents incorporated by reference or, if obtained from third-party studies or reports, the date of the corresponding study or report, and are expressly qualified in their entirety by the cautionary statements in this prospectus, any applicable prospectus supplement and the documents incorporated by reference herein and therein. We do not undertake any obligation to update or revise the forward-looking statements except as required under applicable law. You should read this prospectus and the documents that we reference in this prospectus completely and with the understanding that our actual future results may be materially different from what we expect.

USE OF PROCEEDS

Unless the applicable prospectus supplement states otherwise, the net proceeds from the sale of Securities offered by our company will be used to fund research and development activities and for general corporate purposes, which may include additions to working capital, capital expenditures, financing of acquisitions and other business combinations, investments in or extensions of credit to our subsidiaries and the repayment of indebtedness.

CAPITALIZATION AND INDEBTEDNESS

Our capitalization and indebtedness will be set forth in a prospectus supplement to this prospectus or in a report subsequently furnished to the SEC and specifically incorporated herein by reference.

DESCRIPTION OF SHARE CAPITAL AND MEMORANDUM AND ARTICLES OF ASSOCIATION

The following is a summary of our share capital and certain provisions of our amended and restated memorandum and articles of association. This summary does not purport to be complete and is qualified in its entirety by the provisions of our amended and restated memorandum and articles of association and applicable provisions of the laws of the Cayman Islands.

See “Where You Can Find More Information” elsewhere in this prospectus for information on where you can obtain copies of our articles of incorporation and our bylaws, which have been filed with and are publicly available from the SEC.

As of the date of this prospectus, 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.

Our Memorandum and Articles of Association

General. Holders of ordinary shares 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 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 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 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 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 20% 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 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 amended and restated memorandum and articles of association.

Transfer of Ordinary Shares. Subject to the restrictions in our 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 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. See "Where You Can Find More Information."

Issuance of Additional Shares. Our amended and restated 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 amended and restated 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 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.

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.

Register of Members

Under the Companies Act, we must keep a register of members and there should be entered therein:

- the names and addresses of our members, and a statement of the shares held by each member, which shall include: (i) the amount paid or agreed to be considered as paid on the shares of each member, (ii) the number and category of shares held by each member, and (iii) whether each relevant category of shares held by a member carries voting rights under the post-offering memorandum and articles of association, and if so, whether such voting rights are conditional;
- the date on which the name of any person was entered on the register as a member; and
- the date on which any person ceased to be a member.

Under the Companies Act, the register of members of our company is prima facie evidence of the matters set out therein (that is, the register of members will raise a presumption of fact on the matters referred to above unless rebutted) and a member registered in the register of members is deemed as a matter of the Companies Act to have legal title to the shares as set against its name in the register of members. Upon completion of this offering, we will perform the procedure necessary to immediately update the register of members to record and give effect to the issuance of shares by us to the Depositary (or its nominee) as the depositary. Once our register of members has been updated, the shareholders recorded in the register of members will be deemed to have legal title to the shares set against their name.

If the name of any person is incorrectly entered in or omitted from our register of members, or if there is any default or unnecessary delay in entering on the register the fact of any person having ceased to be a member of our company, the person or member aggrieved (or any member of our company or our company itself) may apply to the Grand Court of the Cayman Islands for an order that the register be rectified, and the Court may either refuse such application or it may, if satisfied of the justice of the case, make an order for the rectification of the register.

Differences in Corporate Law

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 Law 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, Wuxi Pharmatech Healthcare Fund I L.P., 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 or the Listing Rules of the Nasdaq Global Market 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 amended and restated memorandum and articles of association governing the ownership threshold above which shareholder ownership must be disclosed.

History of Securities Issuances

The following is a summary of securities issuances by Adagene Inc. in the years ended December 31, 2019, 2020 and 2021.

Ordinary Shares

In the years ended December 31, 2019, 2020 and 2021, we issued a total of 4,709,313 ordinary shares to employees for an aggregate consideration of US\$8.0 million upon the exercise of certain share incentive awards. For the purpose of this paragraph only, such number of shares includes the 1,585,000 ordinary shares, issued but deemed to be not then outstanding to Great Han Fortune LP.

In March 2021, we issued a total of 23,734 ordinary shares to certain senior management for nominal consideration under the 2021 Plan as part of their compensation.

In February 2021, at the closing of our initial public offering, we offered and sold an aggregate of 10,571,375 ordinary shares in the form of ADSs at a public offering price of US\$19.00 per ADS.

Upon the completion of our initial public offering in February 2021, all of our then issued and outstanding preferred shares were automatically converted into ordinary shares on a one-for-one basis.

Preferred Shares

On June 13, 2019, we issued a total of 1,567,260 Series C-2 Preferred Shares to Mega Prime Development Limited, Poly Platinum Enterprises Limited and Chief Strategic International Limited for an aggregate consideration of US\$16.0 million.

On November 21, 2019, we issued 293,861 Series C-2 Preferred Shares to MODEST CHAMPION LIMITED for a consideration of US\$3.0 million.

On December 19, 2019, we issued 4,452,441 Series C-3 Preferred Shares to General Atlantic Singapore AI Pte. Ltd. for a consideration of US\$50.0 million.

Award Grants

We have granted awards to purchase our ordinary shares to certain of our directors, executive officers and employees pursuant to the Second Amended and Restated Share Incentive Plan in December 2019, or the 2019 Plan, and the 2021 Performance Incentive Plan, or the 2021 Plan. As of March 31, 2022, the aggregate number of our ordinary shares underlying our outstanding awards under the 2019 Plan is 2,872,514, 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. As of March 31, 2022, we have granted 2,746,732 shares awards under the 2021 Plan.

Share Cancellation

On January 16, 2021, certain management members surrendered a total of 491,119 ordinary shares for cancellation to settle the balance due under their respective promissory notes issued in connection with the share purchase plans.

Share Repurchase

On July 7, 2021, the Board of Directors approved a share repurchase program to repurchase up to US\$20 million of outstanding ADSs of the Company, from time to time over a 12-month period from the date on which a formal stock repurchase plan engagement agreement was signed with a qualified broker-dealer. As of December 31, 2021, 236,139 outstanding ADSs representing 295,174 ordinary shares were repurchased with a total consideration of US\$2.4 million, among which, 160,880 ADSs representing 201,100 ordinary shares repurchased shares were cancelled.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase ordinary shares or other securities. We may issue warrants independently or together with other securities. Warrants sold with other securities may be attached to or separate from the other securities. We will issue warrants under one or more warrant agreements between our company and a warrant agent that we will name in the applicable prospectus supplement.

The prospectus supplement relating to any warrants we offer will include specific terms relating to the offering. These terms will include some or all of the following:

- the title of the warrants;
- the aggregate number of warrants offered;
- the designation, number and terms of the ordinary shares or other securities purchasable upon exercise of the warrants and procedures by which those numbers may be adjusted;
- the exercise price of the warrants;
- the dates or periods during which the warrants are exercisable;
- the designation and terms of any securities with which the warrants are issued;
- if the warrants are issued as a unit with another security, the date on and after which the warrants and the other security will be separately transferable;
- if the exercise price is not payable in U.S. dollars, the foreign currency, currency unit or composite currency in which the exercise price is denominated;
- any minimum or maximum amount of warrants that may be exercised at any one time;
- any terms relating to the modification of the warrants;
- any terms, procedures and limitations relating to the transferability, exchange or exercise of the warrants; and
- any other specific terms of the warrants.

The terms of any warrants to be issued and a description of the material provisions of the applicable warrant agreement will be set forth in the applicable prospectus supplement.

DESCRIPTION OF UNITS

As specified in the applicable prospectus supplement, we may issue units consisting of one or more ordinary shares, warrants, or any combination of such securities. The applicable prospectus supplement will describe:

- the terms of the units and of the ordinary shares, and/or warrants comprising the units, including whether and under what circumstances the securities comprising the units may be traded separately;
- a description of the terms of any unit agreement governing the units; and
- a description of the provisions for the payment, settlement, transfer or exchange of the units.

FORMS OF SECURITIES

Each warrant and unit will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Certificated securities in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depository or its nominee as the owner of the warrants or units represented by these global securities. The depository maintains a computerized system that will reflect each investor's beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Registered Global Securities

We may issue the registered warrants and units in the form of one or more fully registered global securities that will be deposited with a depository or its nominee identified in the applicable prospectus supplement and registered in the name of that depository or nominee. In those cases, one or more registered global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by registered global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a registered global security may not be transferred except as a whole by and among the depository for the registered global security, the nominees of the depository or any successors of the depository or those nominees.

If not described below, any specific terms of the depository arrangement with respect to any securities to be represented by a registered global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depository arrangements.

Ownership of beneficial interests in a registered global security will be limited to persons, called participants, that have accounts with the depository or persons that may hold interests through participants. Upon the issuance of a registered global security, the depository will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a registered global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depository, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in registered global securities.

So long as the depository, or its nominee, is the registered owner of a registered global security, that depository or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the registered global security for all purposes under the applicable warrant agreement or unit agreement. Except as described below, owners of beneficial interests in a registered global security will not be entitled to have the securities represented by the registered global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be considered the owners or holders of the securities under the applicable warrant agreement or unit agreement. Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depository for that registered global security and, if that person is not a participant, on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the applicable warrant agreement or unit agreement. We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a registered global security desires to give or take any action that a holder is entitled to give or take under the applicable warrant agreement or unit agreement, the depository for the registered global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Any payments to holders with respect to warrants or units, represented by a registered global security registered in the name of a depository or its nominee will be made to the depository or its nominee, as the case may be, as the registered owner of the registered global security. None of Adagene, its affiliates, the trustees, the warrant agents, the unit agents or any other agent of Adagene, agent of the trustees or agent of the warrant agents or unit agents will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the registered global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depository for any of the securities represented by a registered global security, upon receipt of any payment of principal, premium, interest or other distribution of underlying securities or other property to holders on that registered global security, will immediately credit participants' accounts in amounts proportionate to their respective beneficial interests in that registered global security as shown on the records of the depository. We also expect that payments by participants to owners of beneficial interests in a registered global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers in bearer form or registered in "street name," and will be the responsibility of those participants.

If the depository for any of these securities represented by a registered global security is at any time unwilling or unable to continue as depository or ceases to be a clearing agency registered under the Exchange Act, and a successor depository registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the registered global security that had been held by the depository. Any securities issued in definitive form in exchange for a registered global security will be registered in the name or names that the depository gives to the relevant trustee, warrant agent, unit agent or other relevant agent of ours or theirs. It is expected that the depository's instructions will be based upon directions received by the depository from participants with respect to ownership of beneficial interests in the registered global security that had been held by the depository.

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

American Depositary Receipts

JPMorgan Chase Bank, N.A. (“JPMorgan”), as depositary, will issue the ADSs which you will be entitled to receive in this offering. Each ADS will represent an ownership interest in a designated number of shares which we will deposit with the custodian, as agent of the depositary, under the deposit agreement among ourselves, the depositary, yourself as an ADR holder and all other ADR holders, and all beneficial owners of an interest in the ADSs evidenced by ADRs from time to time.

The depositary’s office is located at 383 Madison Avenue, Floor 11, New York, NY 10179.

The ADS to share ratio is subject to amendment as provided in the form of ADR (which may give rise to fees contemplated by the form of ADR). In the future, each ADS will also represent any securities, cash or other property deposited with the depositary but which they have not distributed directly to you.

A beneficial owner is any person or entity having a beneficial ownership interest ADSs. A beneficial owner need not be the holder of the ADR evidencing such ADS. If a beneficial owner of ADSs is not an ADR holder, it must rely on the holder of the ADR(s) evidencing such ADSs in order to assert any rights or receive any benefits under the deposit agreement. A beneficial owner shall only be able to exercise any right or receive any benefit under the deposit agreement solely through the holder of the ADR(s) evidencing the ADSs owned by such beneficial owner. The arrangements between a beneficial owner of ADSs and the holder of the corresponding ADRs may affect the beneficial owner’s ability to exercise any rights it may have.

An ADR holder shall be deemed to have all requisite authority to act on behalf of any and all beneficial owners of the ADSs evidenced by the ADRs registered in such ADR holder’s name for all purposes under the deposit agreement and ADRs. The depositary’s only notification obligations under the deposit agreement and the ADRs is to registered ADR holders. 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.

Unless certificated ADRs are specifically requested, all ADSs will be issued on the books of our depositary in book-entry form and periodic statements will be mailed to you which reflect your ownership interest in such ADSs. In our description, references to American depositary receipts or ADRs shall include the statements you will receive which reflect your ownership of ADSs.

You may hold ADSs either directly or indirectly through your broker or other financial institution. If you hold ADSs directly, by having an ADS registered in your name on the books of the depositary, you are an ADR holder. This description assumes you hold your ADSs directly. If you hold the ADSs through your broker or financial institution nominee, you must rely on the procedures of such broker or financial institution to assert the rights of an ADR holder described in this section. You should consult with your broker or financial institution to find out what those procedures are.

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 is filed as an exhibit to the registration statement of which this prospectus forms a part. You may

also obtain a copy of the deposit agreement at the SEC's Public Reference Room which is located at 100 F Street, NE, Washington, DC 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-732-0330. You may also find the registration statement and the attached deposit agreement on the SEC's website at <http://www.sec.gov>.

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.

Fees and Expenses

What fees and expenses will I be responsible for paying?

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, US\$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 US\$1.50 per ADR or ADRs for transfers of certificated or direct registration ADRs;
- a fee of US\$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 US\$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 US\$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 an 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 an 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 depository, neither the Bank nor any of its affiliates will execute a foreign exchange transaction as set forth herein. In such case, the depository 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 depository 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 depository and any agent of the depository (except the custodian) pursuant to agreements from time to time between us and the depository.

The right of the depository 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 depository.

The fees and charges described above may be amended from time to time by agreement between us and the depository.

The depository may make available to us a set amount or a portion of the depository fees charged in respect of the ADR program or otherwise upon such terms and conditions as we and the depository may agree from time to time. The depository 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 depository 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 depository may collect its annual fee for depository 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 depository 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 depository, the depository 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 depository, all fees and charges owing under the deposit agreement are due in advance and/or when declared owing by the depository.

Payment of Taxes

ADR holders or beneficial owners must pay any tax or other governmental charge payable by the custodian or the depository on any ADS or ADR, deposited security or distribution. If any taxes or other governmental charges (including any penalties and/or interest) shall become payable by or on behalf of the custodian or the depository with respect to any ADR, any deposited securities represented by the ADSs evidenced thereby or any distribution thereon, including, without limitation, any Chinese Enterprise Income Tax owing if the Circular Guoshuifa [2009] No. 82 issued by the Chinese State Administration of Taxation (SAT) or any other circular, edict, order or ruling, as issued and as from time to time amended, is applied or otherwise, such tax or other governmental charge shall be paid by the ADR holder thereof to the depository and by holding or owning, or having held or owned, an ADR or any ADSs evidenced thereby, the ADR holder and all beneficial owners thereof, and all prior ADR holders and beneficial owners thereof, jointly and severally, agree to indemnify, defend and save harmless each of the depository, us and its and our agents in respect of such tax or other governmental charge. Notwithstanding the depository's right to seek payment from current and former beneficial owners, by holding or owning, or having held or owned, an ADR, the ADR holder thereof (and prior ADR holder thereof) acknowledges and agrees that the depository has no obligation to seek payment of amounts owing from any current or former beneficial owner. If an ADR holder owes any tax or other governmental charge, the depository may (i) deduct the amount thereof from any cash distributions, or (ii) sell deposited securities (by public or private sale) and deduct the amount owing from the net proceeds of such sale. In either case the ADR holder remains liable for any shortfall. If any tax or governmental charge is unpaid, the depository may also refuse to effect any registration, registration of transfer, split-up or combination of deposited securities or withdrawal of deposited securities until such payment is made. If any tax or governmental charge is required to be withheld on any cash distribution, the depository may deduct the amount required to be withheld from any cash distribution or, in the case of a

non-cash distribution, sell the distributed property or securities (by public or private sale) in such amounts and in such manner as the depository deems necessary and practicable to pay such taxes and distribute any remaining net proceeds or the balance of any such property after deduction of such taxes to the ADR holders entitled thereto.

As an ADR holder or beneficial owner, you will be agreeing to indemnify us, the depository, its custodian and any of our or their respective officers, directors, employees, agents and affiliates against, and hold each of them harmless from, any claims by any governmental authority with respect to taxes, additions to tax, penalties or interest arising out of any refund of taxes, reduced rate of withholding at source or other tax benefit obtained.

Reclassifications, Recapitalizations and Mergers

If we take certain actions that affect the deposited securities, including (i) any change in par value, split-up, consolidation, cancellation or other reclassification of deposited securities or (ii) any distributions of shares or other property not made to holders of ADRs or (iii) any recapitalization, reorganization, merger, consolidation, liquidation, receivership, bankruptcy or sale of all or substantially all of our assets, then the depository may choose to, and shall if reasonably requested by us:

- amend the form of ADR;
- distribute additional or amended ADRs;
- distribute cash, securities or other property it has received in connection with such actions;
- sell any securities or property received and distribute the proceeds as cash; or
- none of the above.

If the depository does not choose any of the above options, any of the cash, securities or other property it receives will constitute part of the deposited securities and each ADS will then represent a proportionate interest in such property.

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 depositary's or our website or upon request from the depositary).

How may the deposit agreement be terminated?

The depositary 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 depositary shall have (i) resigned as depositary under the deposit agreement, notice of such termination by the depositary shall not be provided to registered ADR holders unless a successor depositary shall not be operating under the deposit agreement within 60 days of the date of such resignation, and (ii) been removed as depositary under the deposit agreement, notice of such termination by the depositary shall not be provided to registered holders of ADRs unless a successor depositary shall not be operating under the deposit agreement on the 60th day after our notice of removal was first provided to the depositary.

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 depositary and (b) the depositary 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 depositary 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 depositary and (b) provide us with a copy of the ADR register maintained by the depositary. Upon receipt of such shares and/or deposited securities and the ADR register maintained by the depositary, 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 depositary 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 depositary. After providing such instruction to the custodian and delivering a copy of the ADR register to us, the depositary 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 depositary, 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 depositary 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 depositary, 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 depositary 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 depositary'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 depositary 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 depositary 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 depositary, 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 depository, 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 depositary 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 depositary 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 Depositary

The depositary or its agent will maintain a register for the registration, registration of transfer, combination and split-up of ADRs, which register shall include the depositary's direct registration system. Registered holders of ADRs may inspect such records at the depositary'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 depositary 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 depositary 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 depositary 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 depositary 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 depositary, 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 depositary 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 depositary 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 depositary 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 depositary 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 depositary shall not be deemed to have knowledge of any information held by any branch, division or affiliate of the depositary 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 depositary 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.

ENFORCEABILITY OF CIVIL LIABILITIES

Adagene Inc. is incorporated in the Cayman Islands in order to enjoy the following benefits:

- political and economic stability;
- an effective judicial system;
- a favorable tax system;
- the absence of exchange control or currency restrictions; and
- the availability of professional and support services.

However, certain disadvantages accompany incorporation in the Cayman Islands. These disadvantages include, but are not limited to, the following:

- the Cayman Islands has a less developed body of securities laws as compared to the United States and these securities laws provide significantly less protection to investors; and
- Cayman Islands companies may not have standing to sue before the federal courts of the United States.

Our constitutional documents do not contain provisions requiring that disputes, including those arising under the securities laws of the United States, between us, our officers, directors and shareholders, be arbitrated.

We have substantive business operations conducted in China, and a significant portion of our assets are located in China. A number of our directors and executive officers are nationals or residents of jurisdictions other than the United States and a substantial portion of their assets are located outside the United States. As a result, it may be difficult for a shareholder to effect service of process within the United States upon these persons, or to enforce against us or them judgments obtained in United States courts, including judgments predicated upon the civil liability provisions of the securities laws of the United States or any state in the United States.

We have appointed Cogency Global Inc., located at 122 East 42nd Street, 18th Floor, New York, NY 10168, as our agent upon whom process may be served in any action brought against us under the securities laws of the United States.

Walkers (Hong Kong), our counsel as to Cayman Islands law, and Tian Yuan Law Firm, our counsel as to PRC law, have advised us, respectively, that there is uncertainty as to whether the courts of the Cayman Islands and China, respectively, would:

- recognize or enforce judgments of United States courts obtained against us or our directors or officers predicated upon the civil liability provisions of the securities laws of the United States or any state in the United States; or
- entertain original actions brought in each respective jurisdiction against us or our directors or officers predicated upon the securities laws of the United States or any state in the United States.

We have been advised by our Cayman Islands legal counsel, Walkers (Hong Kong), that the courts of the Cayman Islands are unlikely (i) to recognize or enforce against us judgments of courts of the United States predicated upon the civil liability provisions of the securities laws of the United States or any State; and (ii) in original actions brought in the Cayman Islands, to impose liabilities against us predicated upon the civil liability provisions of the securities laws of the United States or any State, so far as the liabilities imposed by those provisions are penal in nature. In those circumstances, although there is no statutory enforcement in the Cayman Islands of judgments obtained in the United States, the courts of the Cayman Islands, will, at common law, recognize and enforce a foreign money judgment of a foreign court of competent jurisdiction without retrial on the merits of the underlying dispute, based on the principle that a judgment of a competent foreign court imposes upon the judgment debtor an obligation to pay the sum for which judgment has been given provided certain conditions are met. For such a foreign judgment to be enforced in the Cayman Islands, such judgment must be final and conclusive and for a liquidated sum, and must not be in respect of taxes or a fine or penalty nor inconsistent with a Cayman Islands judgment in respect of the

same matter, impeachable on the grounds of fraud or obtained in a manner, and be of a kind the enforcement of which is, contrary to natural justice or the public policy of the Cayman Islands (awards of punitive or multiple damages may well be held to be contrary to public policy). A Cayman Islands court may stay enforcement proceedings if concurrent proceedings are being brought elsewhere.

PRC

We have been advised by Tian Yuan Law Firm, our PRC legal counsel, that there is uncertainty as to whether the courts of the PRC would enforce judgments of United States courts or Cayman courts obtained against us or these persons predicated upon the civil liability provisions of the U.S. federal and state securities laws. Tian Yuan Law Firm has further advised us that the recognition and enforcement of foreign judgments are provided for under the PRC Civil Procedures Law. PRC courts may recognize and enforce foreign judgments in accordance with the requirements of the PRC Civil Procedures Law and other applicable laws and regulations based either on treaties between China and the country where the judgment is made or on principles of reciprocity between jurisdictions. China does not have any treaties or other form of reciprocity with the United States or the Cayman Islands that provide for the reciprocal recognition and enforcement of foreign judgments. In addition, some of our executive officers and directors reside within China for a significant portion of the time and some are PRC nationals. Further, according to the PRC Civil Procedures Law, courts in the PRC will not enforce a foreign judgment against us or our directors and officers if they decide that the judgment violates the basic principles of PRC law or national sovereignty, security or public interest. As a result, it may be difficult for our shareholders or investors to effect service of process upon us or such individuals inside China, and it is uncertain whether and on what basis a PRC court would enforce a judgment rendered by a court in the United States or in the Cayman Islands. Under the PRC Civil Procedures Law, foreign shareholders may originate actions based on PRC law against a company in the PRC, if they can establish sufficient nexus to the PRC for a PRC court to have jurisdiction, and meet other procedural requirements. However, it would be difficult for foreign shareholders to establish sufficient nexus to the PRC by virtue only of holding the ADSs or ordinary shares. See “Risk Factors — Risks Related to Doing Business in the PRC — Your investments in our ADSs, Ordinary Shares and/or other Securities are investments in securities of a Cayman Islands holding company rather than securities of our subsidiaries that have substantive business operations in China. As a result, you may experience difficulties in effecting service of legal process, enforcing foreign judgments or bringing actions in China against us or our management based on foreign laws.” and “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” in our annual report on Form 20-F for the year ended December 31, 2021, which is incorporated in this prospectus by reference.

TAXATION

Material income tax consequences relating to the purchase, ownership and disposition of any of the Securities offered by this prospectus will be set forth in the applicable prospectus supplement(s) relating to the offering of those Securities.

SELLING SHAREHOLDERS

Selling shareholders and their pledgees, donees, transferees or other successors-in-interest (collectively, the “Selling Shareholders”) to be named in a prospectus supplement may, from time to time, offer and sell some or all of the shares of our ordinary shares held by them pursuant to this prospectus and the applicable prospectus supplement.

Such Selling Shareholders may sell shares of our ordinary shares or ADSs held by them to or through underwriters, dealers or agents or directly to purchasers or as otherwise set forth in the applicable prospectus supplement. See “Plan of Distribution.” Such Selling Shareholders may also sell, transfer or otherwise dispose of some or all of our ordinary shares held by them in transactions exempt from the registration requirements of the Securities Act.

We will provide you with a prospectus supplement, which will set forth the name of each Selling Shareholder, the number of shares of our ordinary shares beneficially owned by such Selling Shareholders and the number of our ordinary shares or ADSs they are offering.

PLAN OF DISTRIBUTION

We and/or the Selling Shareholders may collectively offer and sell, from time to time, some or all of the Securities covered by this prospectus up to US\$200,000,000. We have registered the Securities covered by this prospectus for offer and sale by us and/or the Selling Shareholders so that those Securities may be freely sold to the public by us and/or Selling Shareholders. Registration of the Securities covered by this prospectus does not mean, however, that those Securities necessarily will be offered or sold.

Securities covered by this prospectus may be sold from time to time, in one or more transactions, at market prices prevailing at the time of sale, at prices related to market prices, at a fixed price or prices subject to change, at varying prices determined at the time of sale or at negotiated prices. The Securities being offered by this prospectus may be sold:

- through agents;
- to or through one or more underwriters on a firm commitment or agency basis;
- through put or call option transactions relating to the Securities;
- through broker-dealers (acting as agent or principal);
- directly to purchasers, through a specific bidding or auction process, on a negotiated basis or otherwise;
- through any other method permitted pursuant to applicable law; or
- through a combination of any such methods of sale.

At any time a particular offer of the Securities covered by this prospectus is made, a revised prospectus or prospectus supplement, if required, will be distributed which will set forth the aggregate amount of Securities covered by this prospectus being offered and the terms of the offering, including the name or names of any underwriters, dealers, brokers or agents, any discounts, commissions, concessions and other items constituting compensation from us and any discounts, commissions or concessions allowed or reallocated or paid to dealers. Such prospectus supplement, and, if necessary, a post-effective amendment to the registration statement of which this prospectus is a part, will be filed with the SEC to reflect the disclosure of additional information with respect to the distribution of the Securities covered by this prospectus. In order to comply with the securities laws of certain states, if applicable, the Securities sold under this prospectus may only be sold through registered or licensed broker-dealers. In addition, in some states the Securities may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from registration or qualification requirements is available and is complied with.

Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

The distribution of Securities may be effected from time to time in one or more transactions, including:

- block transactions (which may involve crosses) and transactions on Nasdaq or any other organized market where the Securities may be traded;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its own account pursuant to a prospectus supplement;
- ordinary brokerage transactions and transactions in which a broker-dealer solicits purchasers;
- sales “at the market” to or through a market maker or into an existing trading market, on an exchange or otherwise; and
- sales in other ways not involving market makers or established trading markets, including direct sales to purchasers.

The Securities may be sold at a fixed price or prices, which may be changed, or at market prices prevailing at the time of sale, at prices relating to the prevailing market prices or at negotiated prices. The consideration may be cash or another form negotiated by the parties. Agents, underwriters or broker-dealers may be paid compensation for offering and selling the Securities. That compensation may be in the form of

discounts, concessions or commissions to be received from us or from the purchasers of the Securities. Any dealers and agents participating in the distribution of the Securities may be deemed to be underwriters, and compensation received by them on resale of the Securities may be deemed to be underwriting discounts. If any such dealers or agents were deemed to be underwriters, they may be subject to statutory liabilities under the Securities Act.

Agents may from time to time solicit offers to purchase the Securities. If required, we will name in the applicable prospectus supplement any agent involved in the offer or sale of the Securities and set forth any compensation payable to the agent. Unless otherwise indicated in the prospectus supplement, any agent will be acting on a best efforts basis for the period of its appointment. Any agent selling the Securities covered by this prospectus may be deemed to be an underwriter, as that term is defined in the Securities Act, of the Securities.

If underwriters are used in a sale, Securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale, or under delayed delivery contracts or other contractual commitments. Securities may be offered to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. If an underwriter or underwriters are used in the sale of Securities, an underwriting agreement will be executed with the underwriter or underwriters, as well as any other underwriter or underwriters, with respect to a particular underwritten offering of Securities, and will set forth the terms of the transactions, including compensation of the underwriters and dealers and the public offering price, if applicable. The prospectus and prospectus supplement will be used by the underwriters to resell the Securities.

If a dealer is used in the sale of the Securities, we or an underwriter will sell the Securities to the dealer, as principal. The dealer may then resell the Securities to the public at varying prices to be determined by the dealer at the time of resale. To the extent required, we will set forth in the prospectus supplement the name of the dealer and the terms of the transactions.

We may directly solicit offers to purchase the Securities and may make sales of Securities directly to institutional investors or others. These persons may be deemed to be underwriters within the meaning of the Securities Act with respect to any resale of the Securities. To the extent required, the prospectus supplement will describe the terms of any such sales, including the terms of any bidding or auction process, if used.

Agents, underwriters and dealers may be entitled under agreements which may be entered into with us to indemnification by us against specified liabilities, including liabilities incurred under the Securities Act, or to contribution by us to payments they may be required to make in respect of such liabilities. If required, the prospectus supplement will describe the terms and conditions of the indemnification or contribution. Some of the agents, underwriters or dealers, or their affiliates may be customers of, engage in transactions with or perform services for us, our subsidiaries, the Selling Shareholders or their affiliates.

Under the Securities laws of some jurisdictions, the Securities offered by this prospectus may be sold in those jurisdictions only through registered or licensed brokers or dealers.

Any person participating in the distribution of Securities registered under the registration statement that includes this prospectus will be subject to applicable provisions of the Exchange Act, and the applicable SEC rules and regulations, including, among others, Regulation M, which may limit the timing of purchases and sales of any of our Securities by that person. Furthermore, Regulation M may restrict the ability of any person engaged in the distribution of our Securities to engage in market-making activities with respect to our Securities. These restrictions may affect the marketability of our Securities and the ability of any person or entity to engage in market-making activities with respect to our Securities.

Certain persons participating in an offering may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids that stabilize, maintain or otherwise affect the price of the offered Securities. These activities may maintain the price of the offered Securities at levels above those that might otherwise prevail in the open market, including by entering stabilizing bids, effecting syndicate covering transactions or imposing penalty bids, each of which is described below.

- A stabilizing bid means the placing of any bid, or the effecting of any purchase, for the purpose of pegging, fixing or maintaining the price of a security.
- A syndicate covering transaction means the placing of any bid on behalf of the underwriting syndicate or the effecting of any purchase to reduce a short position created in connection with the offering.
- A penalty bid means an arrangement that permits the managing underwriter to reclaim a selling concession from a syndicate member in connection with the offering when offered Securities originally sold by the syndicate member are purchased in syndicate covering transactions.

These transactions may be effected on an exchange or automated quotation system, if the Securities are listed on that exchange or admitted for trading on that automated quotation system, or in the over-the-counter market or otherwise.

If so indicated in the applicable prospectus supplement, we will authorize agents, underwriters or dealers to solicit offers from certain types of institutions to purchase offered Securities from us at the public offering price set forth in such prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. Such contracts will be subject only to those conditions set forth in the prospectus supplement and the prospectus supplement will set forth the commission payable for solicitation of such contracts.

Each series of offered Securities, other than the ordinary shares, will be a new issue of Securities and will have no established trading market. Any underwriters to whom offered Securities are sold for public offering and sale may make a market in such offered Securities, but such underwriters will not be obligated to do so and may discontinue any market making at any time without notice. The offered Securities may or may not be listed on a national Securities exchange. No assurance can be given that there will be a market for the offered Securities.

Any Securities that qualify for sale pursuant to Rule 144 or Regulation S under the Securities Act may be sold under Rule 144 or Regulation S rather than pursuant to this prospectus.

To the extent that we make sales to or through one or more underwriters or agents in at-the-market offerings, we will do so pursuant to the terms of a distribution agreement between us, the Selling Shareholders, if any, and the underwriters or agents. If we engage in at-the-market sales pursuant to a distribution agreement, we and/or the Selling Shareholders, if any, will offer and sell our ordinary shares to or through one or more underwriters or agents, which may act on an agency basis or on a principal basis. During the term of any such agreement, we and/or the Selling Shareholders, if any, may sell ordinary shares on a daily basis in exchange transactions or otherwise as and/or the Selling Shareholders, if any, agree with the underwriters or agents. The distribution agreement will provide that any ordinary shares sold will be sold at prices related to the then prevailing market prices for our ordinary shares. Therefore, exact figures regarding proceeds that will be raised or commissions to be paid cannot be determined at this time and will be described in a prospectus supplement. Pursuant to the terms of the distribution agreement, we and/or the Selling Shareholders, if any, also may agree to sell, and the relevant underwriters or agents may agree to solicit offers to purchase, blocks of our ordinary shares or other Securities. The terms of each such distribution agreement will be set forth in more detail in a prospectus supplement to this prospectus.

In connection with offerings made through underwriters or agents, we and/or the Selling Shareholders, if any, may enter into agreements with such underwriters or agents pursuant to which we and/or the Selling Shareholders, as applicable, receive our outstanding Securities in consideration for the Securities being offered to the public for cash. In connection with these arrangements, the underwriters or agents may also sell Securities covered by this prospectus to hedge their positions in these outstanding Securities, including in short sale transactions. If so, the underwriters or agents may use the Securities received from us under these arrangements to close out any related open borrowings of Securities.

One or more firms, referred to as “remarketing firms,” may also offer or sell the Securities, if the prospectus supplement so indicates, in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own accounts or as agents for us. These remarketing firms will offer or sell the Securities in accordance with a redemption or repayment pursuant to the terms of the

Securities. The prospectus supplement will identify any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm's compensation. Remarketing firms may be deemed to be underwriters in connection with the Securities they remarket. Remarketing firms may be entitled under agreements that may be entered into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

We may enter into derivative transactions with third parties or sell Securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, such third parties (or affiliates of such third parties) may sell Securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, such third parties (or affiliates of such third parties) may use Securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of shares, and may use Securities received from us in settlement of those derivatives to close out any related open borrowings of shares. The third parties (or affiliates of such third parties) in such sale transactions will be underwriters and, if not identified in this prospectus, will be identified in the applicable prospectus supplement (or a post-effective amendment).

We and/or the Selling Shareholders may loan or pledge Securities to a financial institution or other third party that in turn may sell the Securities using this prospectus. Such financial institution or third party may transfer its short position to investors in our Securities or in connection with a simultaneous offering of other Securities offered by this prospectus or in connection with a simultaneous offering of other Securities offered by this prospectus.

EXPENSES

The following table sets forth an estimate of the fees and expenses relating to the issuance and distribution of the Securities being registered hereby, all of which shall be borne by our company. All of such fees and expenses, except for the SEC registration fee, are estimated.

SEC registration fee	\$18,540
FINRA fees	\$30,500
Legal fees and expenses	\$ *
Printing fees and expenses	\$ *
Accounting fees and expenses	\$ *
Miscellaneous fees and expenses	\$ *
Total	\$ *

* To be provided by a prospectus supplement or as an exhibit to a report on Form 6-K that is incorporated by reference into this prospectus.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

We incorporate by reference the filed documents listed below, except as superseded, supplemented or modified by this prospectus:

- [our annual report on Form 20-F for the fiscal year ended December 31, 2021, filed with the SEC on April 26, 2022 \(File No. 001-39997\)](#);
- [the description of our ordinary shares contained in the registration statement on Form 8-A filed with the SEC on February 3, 2021, and any other amendment or report filed for the purpose of updating such description](#);
- any future annual reports on Form 20-F filed with the SEC after the date of this prospectus and prior to the termination of the offering of the Securities offered by this prospectus; and
- any future reports on Form 6-K that we furnished to the SEC after the date of this prospectus that are identified in such reports as being incorporated by reference in this prospectus.

Potential investors, including any beneficial owner, may obtain a copy of any of the documents summarized herein (subject to certain restrictions because of the confidential nature of the subject matter) or any of our SEC filings incorporated by reference herein without charge by written request directed to 4F, Building C14, No. 218, Xinghu Street, Suzhou Industrial Park Suzhou, Jiangsu Province, 215123, People's Republic of China.

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone else to provide you with different information. We are not making an offer of these Securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of those documents.

Any statement contained in a document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained herein, or in a subsequently filed document incorporated by reference herein, modifies or supersedes that statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute part of this prospectus.

LEGAL MATTERS

We are being represented by Davis Polk & Wardwell LLP with respect to certain legal matters as to United States federal securities and New York State law. Certain legal matters in connection with any offering made pursuant to this prospectus will be passed upon for the underwriters by a law firm named in the applicable prospectus supplement. The validity of the ordinary shares represented by the ADSs will be passed upon for us by Walkers (Hong Kong). Certain legal matters as to PRC law (excluding the laws of Taiwan, Hong Kong and Macau) will be passed upon for us by Tian Yuan Law Firm and for the underwriters by a law firm named in the applicable prospectus supplement. Davis Polk & Wardwell LLP may rely upon Walkers (Hong Kong) with respect to matters governed by Cayman Islands law and Tian Yuan Law Firm with respect to matters governed by PRC law (excluding the laws of Taiwan, Hong Kong and Macau).

EXPERTS

The financial statements incorporated in this Prospectus by reference to the Annual Report on Form 20-F for the year ended December 31, 2021 have been so incorporated in reliance on the report of PricewaterhouseCoopers Zhong Tian LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

The offices of PricewaterhouseCoopers Zhong Tian LLP are located at 42/F New Bund Center, 588 Dongyu Road, Pudong New Area, Shanghai 200126, the People's Republic of China.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form F-3 under the Securities Act with respect to the offer and sale of Securities pursuant to this prospectus. This prospectus, filed as a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules thereto in accordance with the rules and regulations of the SEC and no reference is hereby made to such omitted information. Statements made in this prospectus concerning the contents of any contract, agreement or other document filed as an exhibit to the registration statement are summaries of all of the material terms of such contract, agreement or document, but do not repeat all of their terms. Reference is made to each such exhibit for a more complete description of the matters involved and such statements shall be deemed qualified in their entirety by such reference. The registration statement and the exhibits and schedules thereto filed with the SEC may be obtained from the SEC's website that contains reports, proxy and information statements and other information regarding registrants that file electronically through the SEC's Electronic Data Gathering, Analysis and Retrieval ("EDGAR") system, including the Company, which can be accessed at <http://www.sec.gov>. For further information pertaining to the Securities offered by this prospectus and Adagene Inc., reference is made to the registration statement.

We furnish reports and other information to the SEC. You may read and copy any document we furnish at the SEC's public reference facilities and the website of the SEC referred to above. Our file number with the SEC is 001-39997.

\$200,000,000

ADAGENE

Adagene Inc.

**Ordinary Shares
Warrants
Units**

PROSPECTUS

, 2022

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 8. Indemnification of Directors and Officers.

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 the consequences of committing a crime, or against the indemnified person's own fraud or dishonesty. Our amended and restated memorandum and articles of association provides for indemnification of our officers and directors, to the fullest extent permitted by applicable law, against all actions, proceedings, costs, charges, expenses, losses, damages, or liabilities (collectively "Losses") incurred or sustained by him otherwise than by reason of his own dishonesty, willful default or fraud as determined by a court of competent jurisdiction, 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 him 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. Such Losses incurred in defending any such proceeding shall be paid by our company as they are incurred upon receipt, in each case, of an undertaking by or on behalf of the indemnified person to repay such amounts if it is ultimately determined by a non-appealable order of a court of competent jurisdiction that such indemnified person is not entitled to indemnification hereunder with respect thereto. However, our company will not indemnify our directors, officers, or persons controlling us for liabilities arising under the Securities Act, because it is the SEC's opinion that such indemnification is against public policy as expressed in such act and is, therefore, unenforceable.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to 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 theretofore unenforceable.

Item 9. Exhibits

The exhibit index attached hereto is incorporated herein by reference.

Item 10. Undertakings.

- (a) The undersigned Registrant hereby undertakes:
- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) to include any prospectus required by Section 10(a)(3) of the Securities Act;
 - (ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of Securities offered (if the total dollar value of Securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;
 - (iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the Registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the Securities offered therein, and the offering of such Securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the Securities being registered which remain unsold at the termination of the offering.
- (4) To file a post-effective amendment to the registration statement to include any financial statements required by Item 8.A of Form 20-F at the start of any delayed offering or throughout a continuous offering. Financial statements and information otherwise required by Section 10(a)(3) of the Securities Act need not be furnished, *provided* that the Registrant includes in the prospectus, by means of a post-effective amendment, financial statements required pursuant to this paragraph (a) (4) and other information necessary to ensure that all other information in the prospectus is at least as current as the date of those financial statements. Notwithstanding the foregoing, with respect to registration statements on Form F-3, a post-effective amendment need not be filed to include financial statements and information required by Section 10(a)(3) of the Securities Act or Item 8.A of Form 20-F if such financial statements and information are contained in periodic reports filed with or furnished to the SEC by the Registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the Form F-3.
- (5) That, for the purpose of determining liability under the Securities Act to any purchaser:
 - (i) Each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of Securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the Securities in the registration statement to which that prospectus relates, and the offering of such Securities at that time shall be deemed to be the initial bona fide offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date; or
- (6) That, for the purpose of determining liability of the Registrant under the Securities Act to any purchaser in the initial distribution of the Securities, the undersigned Registrant undertakes that in a primary offering of Securities of the undersigned Registrant pursuant to this registration statement, regardless of the underwriting method used to sell the Securities to the purchaser, if the Securities are offered or sold to such purchaser by means of any of the following communications,

the undersigned Registrant will be a seller to the purchaser and will be considered to offer or sell such Securities to such purchaser:

- (i) Any preliminary prospectus or prospectus of the undersigned Registrant relating to the offering required to be filed pursuant to Rule 424;
 - (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned Registrant or used or referred to by the undersigned Registrant;
 - (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned Registrant or its Securities provided by or on behalf of the undersigned Registrant; and
 - (iv) Any other communication that is an offer in the offering made by the undersigned Registrant to the purchaser.
- (b) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the Securities offered therein, and the offering of such Securities at that time shall be deemed to be the initial bona fide offering thereof.
- (c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the Securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

EXHIBIT INDEX

The following documents are filed as part of this registration statement:

Exhibit No.	Description
1.1*	Form of Underwriting Agreement
3.1	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)
4.1	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)
4.2	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)
4.3	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))
4.4*	Form of Warrant Agreement
4.5*	Form of Unit Agreement
5.1#	Opinion of Walkers (Hong Kong) regarding the validity of the ordinary shares
5.2#	Opinion of Davis Polk & Wardwell LLP
8.1#	Opinion of Walkers (Hong Kong) regarding certain Cayman Islands tax matters (included in Exhibit 5.1)
8.2#	Opinion of Tian Yuan Law Firm regarding certain PRC tax matters
23.1†	Consent of PricewaterhouseCoopers, Independent Registered Public Accounting Firm
23.2#	Consent of Walkers (Hong Kong) (included in Exhibit 5.1)
23.3#	Consent of Tian Yuan Law Firm (included in Exhibit 8.2)
24.1#	Power of Attorney (included in signature page of this registration statement)
107#	Calculation of Filing Fee Tables

* To be filed as an exhibit to a post-effective amendment to this registration statement or as an exhibit to a report filed or furnished pursuant to the Exchange Act of the Registrant and incorporated herein by reference.

† Filed with this registration statement on Form F-3.

Previously filed.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form F-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Francisco, State of California, on May 20, 2022.

Adagene Inc.

By: /s/ PETER (PEIZHI) LUO

Name: Peter (Peizhi) Luo

Title: *Chief Executive Officer*

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Peter (Peizhi) Luo</u> Peter (Peizhi) Luo	Chief Executive Officer and Director (principal executive officer)	May 20, 2022
<u>*</u> Man Kin (Raymond) Tam	Chief Financial Officer and Director (principal financial officer and principal accounting officer)	May 20, 2022
<u>*</u> Lefei Sun	Director	May 20, 2022
<u>*</u> Andy (Yiu Leung) Cheung	Director	May 20, 2022
<u>*</u> Min Li	Director	May 20, 2022
<u>*</u> Yuwen Liu	Director	May 20, 2022

*By: /s/ Peter (Peizhi) Luo

Name: Peter (Peizhi) Luo

Attorney-in-fact

SIGNATURE OF AUTHORIZED REPRESENTATIVE IN THE UNITED STATES

Pursuant to the Securities Act of 1933, as amended, the undersigned, the duly authorized representative in the United States of Adagene Inc., has signed this registration statement or amendment thereto in New York on May 20, 2022.

Authorized U.S. Representative

Cogency Global Inc.

By: /s/ Colleen A. De Vries

Name: Colleen A. De Vries

Title: Senior Vice President

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form F-3 of Adagene Inc. of our report dated April 26, 2022 relating to the financial statements, which appears in Adagene Inc.'s Annual Report on Form 20-F for the year ended December 31, 2021. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers Zhong Tian LLP
Shanghai, the People's Republic of China
May 20, 2022
