UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER
PURSUANT TO RULE 13a-16 OR 15d-16
UNDER THE SECURITIES EXCHANGE ACT OF 1934

For the Month of July 2023

Commission File Number: 001-39997

Adagene Inc.
(Exact Name of Registrant as Specified in Its Charter)

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

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F ☒ Form 40-F ☐

Explanatory Note

Senior management of Adagene Inc. (the "Company") plan to present the information in the presentation slides attached hereto as Exhibit 99.1 for meetings with potential partners and members of the investor community scheduled during the weekend of July 8, 2023 and from time to time.

The furnishing of the attached presentation is not an admission as to the materiality of any information therein. The information contained in the presentation is summary information that is intended to be considered in the context of more complete information included in the Company's filings with the Securities and Exchange Commission (the "SEC") and other public announcements that the Company has made and may make from time to time. The Company undertakes no duty or obligation to update or revise the information contained in this report, although it may do so from time to time as its management believes is appropriate. Any such updating may be made through the filing or furnishing of other reports or documents with the SEC or through other public disclosures, including publishing on the Company's website.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Adagene Inc.

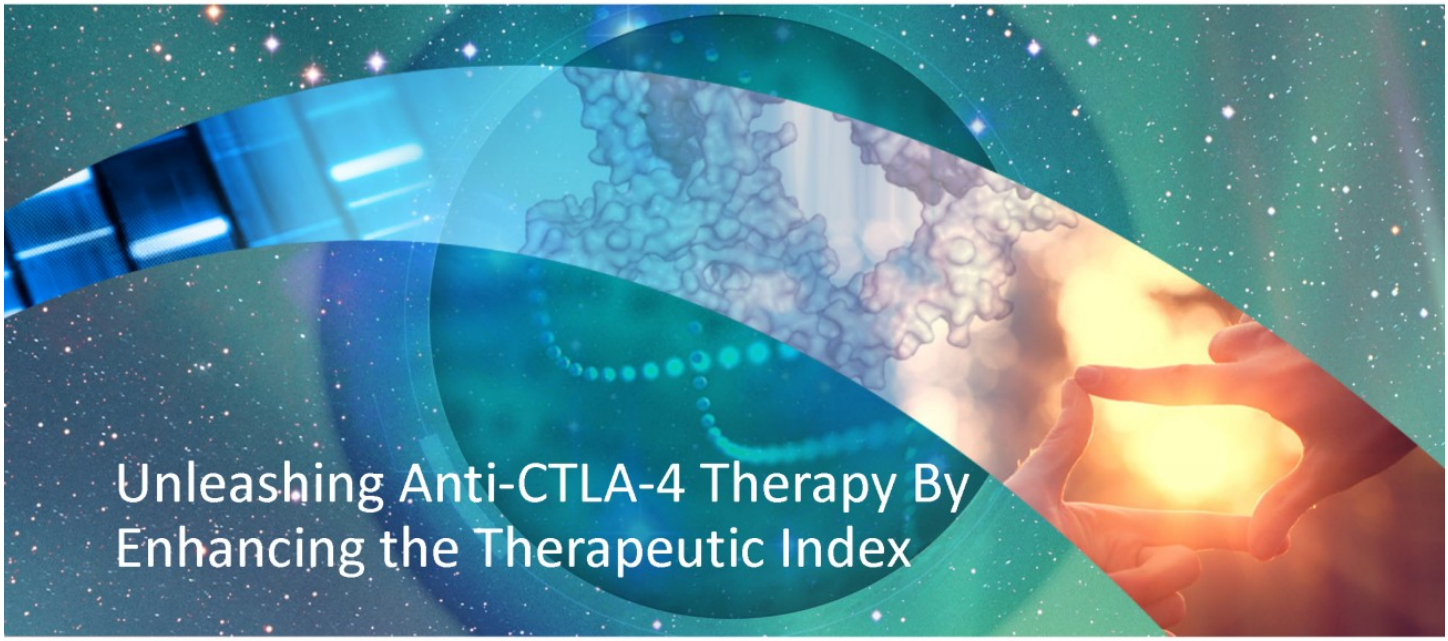
By: /s/ Peter (Peizhi) Luo
Name: Peter (Peizhi) Luo
Title: Chief Executive Officer

Date: July 7, 2023

EXHIBIT INDEX

Exhibit	Description
99.1	Company Presentation

Exhibit 99.1



July 2023

ADAGENE

Disclaimer and Cautionary Note on Forward-Looking Statements

The following presentation has been prepared by Adagene Inc. ("Adagene" or the "Company") solely for informational purposes and should not be construed to be, directly or indirectly, in whole or in part, an offer to buy or sell and/or an invitation and/or a recommendation and/or a solicitation of an offer to buy or sell any security or instrument or to participate in any investment or trading strategy, nor shall any part of it form the basis of, or be relied on in connection with, any contract or investment decision in relation to any securities or otherwise. This presentation does not contain all relevant information relating to the Company or its securities, particularly with respect to the risks and special considerations involved with an investment in the securities of the Company. Nothing contained in this document shall be relied upon as a promise or representation as to the past or future performance of the Company. Past performance does not guarantee or predict future performance. You acknowledge that any assessment of the Company that may be made by you will be independent of this document and that you will be solely responsible for your own assessment of the market and the market position of the Company and that you will conduct your own analysis and be solely responsible for forming your own view of the potential future performance of the business of the Company.

This document contains certain statements that constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1953, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, with respect to the Company's future financial or business performance, anticipated clinical activities and development, strategies or expectations. These statements typically contain words such as "believe," "may," "will," "could," "expects" and "anticipates" and words of similar import. Any statement in this document that is not a statement of historical fact is a forward-looking statement and involves known and unknown risks, uncertainties and other factors which may cause the Company's actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by such forward-looking statements. Such forward-looking statements including statements regarding the potential implications of clinical data for patients, and Adagene's advancement of, and anticipated clinical activities, clinical development, regulatory milestones, and commercialization of its product candidates. Actual results may differ materially from those indicated in the forward-looking statements as a result of various important 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 U.S. Securities and Exchange Commission. There can be no assurance that the results and events contemplated by the forward-looking statements contained herein will in fact occur. None of the future projections, expectations, estimates or prospects in this document should be taken as forecasts or promises nor should they be taken as implying any indication, assurance or guarantee that the assumptions on which such future projections, expectations, estimates or prospects have been prepared are correct or exhaustive or, in the case of assumptions, fully stated in the document. The Company also cautions that forward-looking statements are subject to numerous assumptions, risks and uncertainties, which change over time and which may be beyond the Company's control.

This presentation concerns product candidates that are or have been under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration, European Medicines Agency, The China National Medical Products Administration, or other foreign regulatory authorities. These product candidates are currently limited by U.S. Federal law to investigational use, and no representations are made as to their safety or effectiveness for the purposes for which they are being investigated.

The information that can be accessed through the hyperlinks included in this presentation is not incorporated by reference into this presentation, and you should not consider such information to be part of this presentation.

This document speaks as of July 7, 2023. Neither the delivery of this document nor any further discussions of the Company with any of the recipients shall, under any circumstances, create any implication that there has been no change in the affairs of the Company since that date. Adagene undertakes no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required by law.

Why Focus on Next Generation Anti-CTLA-4 Therapies?

- CTLA-4 is a proven target with a need to "troubleshoot" safety to maximize its therapeutic potential
  - Only approved checkpoint inhibitor for ***both*** single agent & combination use besides anti-PD-(L)1 therapies
- Treg depletion is crucial for overcoming immune suppression
  - CTLA-4 is over-expressed on Treg cells, especially in tumor microenvironment (TME) of "cold" tumors
  - Traditional CTLA-4 therapies struggle to achieve meaningful intra-tumoral Treg depletion
- To address these challenges, we target a unique epitope of CTLA-4 with enhanced Treg depletion and then add precision masking technology

Sharma et al. Clin Cancer Res. 2019 Feb 15;25(4):1233-1238. doi: 10.1158/1078-0432.CCR-18-0762.
Marabelle. Targets for Cancer Immunology: A deep dive into enhanced CTLA-4 targeted therapeutics. SITC webinar on Oct 5, 2022

A New Paradigm for Anti-CTLA-4 Therapy: Targeting CTLA-4 in the Tumor Microenvironment

Thesis for first generation anti-CTLA-4 therapies:
Efficacy is driven by T cell activation through CTLA-4 blockade.

By widening the therapeutic window, Adagene is taking anti-CTLA-4 therapy to the next level with an enhanced ratio of effector T cells (Teff) over regulatory T cells (Treg) within the TME.

"Anti-CTLA-4 Immunotherapy Does Not Deplete FOXP3+ Regulatory T Cells (Tregs) in Human Cancers"
Sharma et al. Clin Cancer Res. 2019 Feb 15;25(4):1233-1238. doi: 10.1158/1078-0432.CCR-18-0762.
Marabelle. Targets for Cancer Immunology: A deep dive into enhanced CTLA-4 targeted therapeutics. SITC webinar on Oct 5, 2022

Adagene Product Candidates are Focused on Unleashing the Potential of Anti-CTLA-4 Therapy by Enhancing the Therapeutic Index (TI)

- Two unique anti-CTLA-4 candidates in phase 1b/2 studies:
  - ADG116 NEObody™ targets a unique binding site
  - ADG126 SAFEbody® is masked version of ADG116
  - Dose escalation completed for both as monotherapy and in combination with anti-PD-1
  - Dose expansion ongoing with anti-PD-1 therapies in targeted tumors, including MSS CRC
  - Roche sponsoring & conducting randomized clinical trial in 1L HCC of ADG126 + atezolizumab + bevacizumab

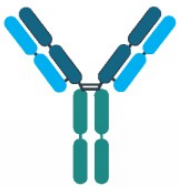
- Both ADG116 and ADG126 in combination with anti-PD-1 agents demonstrated fast & robust clinical responses while maintaining superior safety profiles
  - Efficacy shown in both PD-1 naïve and PD-1 resistant patients, as well as cold tumors (MSS CRC)

- Collaborations validate SAFEbody masking technology
  - Sanofi and Exelixis technology licensing agreements
  - Adagene eligible to receive ≥$2.5B in potential milestones

sanofi EXELIXIS

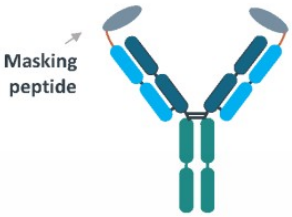
Dynamic Precision Library & Antibody Technologies Enable Wider Therapeutic Window for Anti-CTLA-4 & Other Immunotherapies

NEObody™



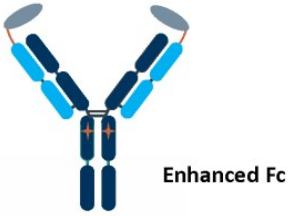
- Dynamic engagement with novel epitope of a given target
- Targets a unique epitope of CTLA-4 to widen therapeutic window

SAFEbody®



- Precision masking for antibody safety
- Further expands TI by preferential targeting of CTLA-4, which is highly expressed on Treg cells in TME

POWERbody™



- Empowered SAFEbody in different modalities with FC engineering for enhanced effector function

The Challenge: Uncouple Dose-dependent Efficacy from Toxicity of Anti-CTLA-4 as Monotherapy and in Combination with Anti-PD-1 Agents

Anti-CTLA-4 Ipilimumab	Dosage (mg/kg)	m-OS (years)	≥ Gr 3 TRAEs, %	Discontinuation Rate, %
Monotherapy 1L Melanoma	10	1.3	36%	34%
	3	1	20%	19%
Combined with PD-1 1L Melanoma	3	6	55%	29%
	1	>3	34%	24%

- ✓ **Greater efficacy for ipilimumab at higher doses in monotherapy and combination therapy was associated with more side effects and discontinuations**
  - ✓ **CTLA-4 and PD-1 combo is much more efficacious than monotherapy**
  - ✓ **Higher doses of anti-CTLA-4 are more efficacious, but also more toxic**

A reference list for this slide is at end of presentation.

Improving Safety of Anti-CTLA-4 Therapies Will Enable Improved Tolerability of Higher Effective Doses and Longer Administration

- **Safety** as monotherapy at higher effective dose
- **Safety** in combination with PD-1 at effective doses
- **Safety** that enables repeat dosing for continuous target engagement and improved duration of response

Safety is 'The Holy Grail'* for Anti-CTLA-4 Therapy to Unleash Efficacy

*Report by D. Graybosch, SVB Leerink, Nov 2022

Our Next Generation Anti-CTLA-4 Therapies Expand the Therapeutic Index

	Dosage	$AUC_{ss,\ tumor\ ISF}$ fold difference	$C_{max,ss,tumor\ ISF}$ fold difference
Masked	ADG126 (10 mg/kg Q3W) vs. Ipilimumab (1 mg/kg Q6W)	**~27x**	**~9x**
Unmasked	ADG116 (3 mg/kg Q3W) vs. Ipilimumab (1 mg/kg Q6W)	**~4x**	**~3x**

- ADG126 PK predicts significantly reduced active drug exposures to normal tissue with wider therapeutic index compared to ipilimumab, while ADG116 PK modelling predicts manageable drug exposures
- ADG126 enables continuous CTLA-4 target engagement in the tumor microenvironment
  - PK modelling predicts RO>90% throughout the steady state dosing cycle in TME

This slide contains information from various preclinical studies, which are not head-to-head comparisons. Data on file.


ADG116: Our NEObody Solution

ADG116: Single Agent and PD-1 Combination Efficacy with Repeat Dosing and Enhanced TI

- Favorable safety profile for ADG116 monotherapy at doses up to 15 mg/kg (N=59); manageable safety profile observed for ADG116 + anti-PD-1 therapy (N=22)

- ADG116 is clinically active and ready to advance into phase 2 tumor-specific cohorts:

  - Single agent activity observed with ADG116 in heavily pre-treated patients across tumors at ≥ 10 mg/kg Q3W; ORR = 13% (3/23 evaluable)
    - Confirmed PRs in RCC and MSI-H endometrial cancer
    - Initial PR in Kaposi's sarcoma

  - Encouraging efficacy profile for ADG116 + anti-PD-1 observed in dose escalation
    - ADG116 3 mg/kg Q3W + toripalimab: ORR = 20% (1/5 evaluable; sustained CR of >one year in HNSCC)
    - ADG116 3 mg/kg Q6W + toripalimab: ORR = 14% (1/7 evaluable; initial PR observed in MSS CRC)

ORR is reported in evaluable patients with at least one valid post-baseline tumor assessment. ADG116 data from ADG116-1003 and ADG116-1002 studies as of May 2023.

Design for ADG116 + PD-1 Combination Evaluation

- Prior monotherapy dose escalation conducted up to 15 mg/kg Q3W
- Prior combination dose escalation* conducted with either pembrolizumab (200 mg Q3W) or toripalimab (240 mg Q3W)
- Dose optimization/expansion ongoing in combination with toripalimab, including MSS CRC

* Data published in poster presentations at SITC 2022

ADG116 Monotherapy: Repeat Dosing (>7 cycles) Enabled by Safety Profile Demonstrates Continuing Clinical Benefit

		Baseline	6 weeks	12 weeks	21 weeks
Target Lesion	TL1 - Lymph Node	19 mm	17 mm	10 mm	10 mm
	TL2 - Lymph Node	31 mm	27 mm	19 mm	15 mm
	Sum	50 mm	44 mm (-12%)	29 mm (-42%)	25 mm (-50%)
Non-Target Lesions	Multiple	Present	Present	Present	Present
New Lesion		N/A	No	No	No
Overall		N/A	**SD**	**PR**	**PR**

Subject: Female, 44 years old

Tumor Type: Endometrial carcinoma, MSI-H

Site Location: China

Dose Regimen: 10 mg/kg ADG116 (7 cycles @ Q3W)

Prior Therapies: Docetaxel + cisplatin (1st line) followed by HH2853-G101 (EZH1/EZH2 inhibitor)

Safety Profile: Only G1 TRAEs in Cycle 4 (12 weeks); rash and hyperthyroidism

ADG116 Monotherapy: Additional PR Further Reinforces Safety & Efficacy Profiles with Repeat Dosing in IO-experienced RCC Patient

		Baseline	6 weeks	12 weeks	21 weeks	30 weeks	39 weeks
Target Lesion	TL1- Lung RLL	15 mm	11 mm	11 mm	9 mm	9 mm	9 mm
	TL2 - Lung RML	16 mm	14 mm	14 mm	13 mm	13 mm	13 mm
	TL3 – Lymph Node	22 mm	14 mm	14 mm	14 mm	14 mm	14 mm
	TL4 - Right kidney	47 mm	47 mm	30 mm	27 mm	27 mm	27 mm
	TL5 - Lymph Node	15 mm	10 mm	7 mm	5 mm	5 mm	5 mm
	Sum	115 mm	96 mm (-17%)	76 mm (-34%)	68 mm (-41%)	68 mm (-41%)	68 mm (-41%)
Non-Target Lesions	Multiple	Present	Present	Present	Present	Present	Present
New Lesion		N/A	No	No	No	No	No
Overall		N/A	SD	PR	PR	PR	PR

Subject: Male, 56 years old

Tumor Type: Clear cell renal cell carcinoma

Site Location: South Korea

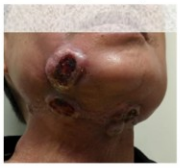
Dose Regimen: 10 mg/kg ADG116 (13 cycles @ Q3W)

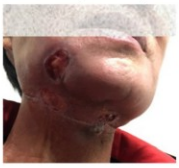
Prior Therapies: Sunitinib (1st line) followed by INCB86550 (Oral PD-L1 inhibitor in development)

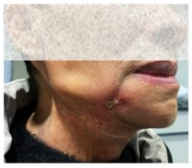
Safety Profile: No TRAEs up to 12 weeks (4 cycles); G2 adrenal insufficiency during Cycle 5

Lung RLL: lung right lower lobe; Lung RML: lung right middle lobe.

ADG116 + PD-1 Combination with Repeat Dosing: Rapid Complete Response in HNSCC Patient Sustained Beyond One Year







Photos of external lesions (right mandibular and right submandibular) at C1D1, C2D1 and C4D2

		Baseline	Week 6	Week 18	Week 50
Target Lesion	TL1 - Right mandibular	32 mm	Disappeared	Disappeared	Disappeared
	TL2 - Right submandibular	18 mm	Disappeared	Disappeared	Disappeared
	TL3 - Lymph node	15 mm	8 mm	5 mm	5 mm
	Sum	65 mm	8 mm	5 mm	5 mm
Non-target Lesions	3	Present	Disappeared	Disappeared	Disappeared
New Lesion			No	No	No
Overall			**CR**	**CR**	**CR**

Subject: Male, 64 years old, ECOG PS 1

Tumor Type: HPV negative recurrent head and neck squamous cell carcinoma (HNSCC)

Site Location: Singapore

Dose Level: 10 mg/kg ADG116 (initially Q3W; then Q6W) + Tori 240 mg

Prior Therapies: Right modified cervical lymph node dissection followed by adjuvant radiotherapy (local therapy); concurrent chemoradiotherapy, including weekly cisplatin

Safety Profile: TRAEs include G3 lipase increase, G2 amylase increase, G2 arthralgia and G1 pyrexia

Data from ADG116-1003 study as of May 2023.

ADG116 + PD-1 Combination with Repeat Dosing: Initial Partial Response in MSS CRC Observed Within Two Cycles

		Baseline	6 weeks
Target Lesion	TL1- LN (right paraaortic)	25 mm	15 mm
	TL2 -LN (common iliac)	20 mm	15 mm
	Sum (percent change)	45 mm	30 mm **(-33%)**
Non-Target Lesions	NTL1- LN (right lower paratracheal)	Present	Present
	NTL2- LN (right upper paratracheal)	Present	Present
New Lesion		N/A	No
Overall		N/A	**PR**

Subject: Female, 50 years old

Tumor type: MSS CRC with lung, kidneys and lymph node metastasis

Site Location: Singapore

Dose Regimen: ADG116 3 mg/kg Q6W + Tori 240 mg

Prior Therapies: Curative surgery followed by three lines of therapy (MFOLFOXIRI + bevacizumab; Encorafenib + Cetuximab; TAS102 + bevacizumab)

Safety Profile: TRAEs include G3 AST elevated, G2 ALT elevated, G1 (e.g., rash)

ADG116 data from ADG116-1003 as of May 2023.


ADG126: Our SAFEbody Solution

ADG126: Encouraging Efficacy Profile Observed with Anti-PD-1 at High Dose Levels with Repeat Dosing and Further Enhanced TI

- No DLT or ≥ G3 TRAEs observed for ADG126 monotherapy up to 20 mg/kg Q3W (N=30)
- Safety profile of ADG126 + PD-1 dose escalation demonstrates best-in-class potential (N=31)
  - Continuous dosing beyond 4 cycles may enable combination with agents beyond anti-PD-1
  - TI enables novel dosing regimens for double and triple combinations:
    - Roche sponsoring triple combination study of ADG126 + atezolizumab + bevacizumab (NCT04524871)
- Efficacy profile observed for ADG126 10 mg/kg Q3W + PD-1: ORR = 40% (4/10 evaluable)
  - Confirmed PR in a cervical cancer patient who previously progressed on pembrolizumab
  - Three confirmed PRs in previously treated patients with anal SCC, penile SCC and MSI-H endometrial cancer
  - Significant tumor shrinkage (≥20% reduction in target lesion) and prolonged stable disease observed in cold tumors, including MSS CRC

ORR is reported in evaluable patients with at least one valid post-baseline tumor assessment. ADG126 + PD-1 data was from dose escalation patients who received ADG126 10 mg/kg Q3W + toripalimab 240 mg in ADG126-1001 study (March 14, 2023 datacut) and ADG126 10 mg/kg Q3W + pembrolizumab 200 mg in ADG126-P001 study (March 9, 2023 datacut) as presented in AACR 2023 posters.

Design for ADG126 + Anti-PD-1 Combination Evaluation

- Prior monotherapy dose escalation conducted up to 20 mg/kg Q3W
- Prior combination dose escalation* with either pembrolizumab (200 mg Q3W) or toripalimab (240 mg Q3W)
- Dose expansion ongoing, primarily with pembrolizumab in ~20 patients with advanced/ metastatic MSS CRC

* Data published in poster presentations at AACR 2023

Uncoupling Efficacy from Safety: ADG126 + PD-1 Combination Unleashes Efficacy with Enhanced TI

ADG126 Dosing Regimen	Patients Dosed (N)	Safety	Efficacy
6 mg/kg Q3W	11 (10 evaluable for efficacy)	• No DLT or >G3 TRAEs reported • 27% G3 TRAEs	DCR = 30%
10 mg/kg Q6W	10 (9 evaluable for efficacy)	• No DLT or >G3 TRAEs reported • 30% G3 TRAEs	DCR = 56%
10 mg/kg Q3W*	10 (from 2 different studies)	• No DLT or >G3 TRAEs reported • 10% G3 TRAEs	**ORR = 40% (4 partial responses)** DCR= 60%

Emerging data show higher & more frequent doses of ADG126 in combination with anti-PD-1 therapy increase efficacy without increasing G3 TRAEs

* Early data cut from patients dosed by ADG126 + anti-PD-1 therapies in ADG126-1001 study (data cutoff: Mar 14, 2023) and ADG126-P001 study (data cutoff: Mar 9, 2023) as reported in poster presentations at AACR 2023.

ADG126 at 10 mg/kg Q3W Enables Repeat Dosing with Anti-PD-1 to Achieve Efficacy Profile

- 4 PRs (4/29) have been observed in the dose escalations of ADG126 in combination with anti-PD-1 therapy
  - ORR of 40% (4/10) in the ADG126 10 mg/kg Q3W cohort
  - One PR each for anal SCC, penile SCC, endometrial (MSI-H) and cervical cancer
    - 3 IO-naïve patients and **one patient w/ cervical cancer who progressed on 9 cycles of pembrolizumab monotherapy**
- Prolonged stable disease with reduced target lesions in patients with "cold" tumors (MSS CRC)

ADG126 with anti-PD-1 therapy correlates with observed response in PD-1 resistant patients and tumor reduction in MSS CRC, the primary tumor type selected for cohort expansion

ADG126 + PD-1 Combination: Confirmed PR with Continuous Tumor Shrinkage in a PD-1 Resistant Patient with Low PD-L1 Expression

	Lesion #	Location	Baseline	6 Weeks	12 Weeks	18 Weeks	24 Weeks	30 Weeks
Target lesion	TL#1	Lymph node (Subcarinal)	25 mm	25 mm	21mm	17 mm	13 mm	9 mm
	TL#2	Lymph node (Pre-carinal)	29 mm	29 mm	30 mm	30 mm	25 mm	17 mm
	Sum		54 mm	54 mm	51 mm	47 mm	38 mm	26 mm
Non target lesion		Lymph node (Right Supra-clavicular)	Present	Present	Present	Present	Present	Present
New lesion				No	No	No	No	No
Overall response				**SD (+0%)**	**SD (-5.6%)**	**SD (-13%)**	**PR (-30%)**	**PR (-52%)**

Tumor Type: Female, 70 years old, advanced cervical cancer (stage IV squamous carcinoma)
- PD-L1 CPS score = 1, TMB high: 24 Muts/Mb
- Concurrent clear cell renal cancer

Site Location: United States

Prior Therapies: Previously received 2 lines of therapies:
- Carboplatin/paclitaxel/bevacizumab x 6 cycles
- Pembrolizumab monotherapy × 9 cycles

Dose Regimen: ADG126 10 mg/kg Q3W + Pembro 200 mg Q3W (10 cycles)

Safety Profile: Only G2 TRAEs

ADG126 + PD-1 Combination: 58% Reduction in Target Lesions in a Mixed Response in MSS CRC

Tumor assessment on study		Baseline	Week 7	Week 13	Week 17
Target Lesion	TL1 – Lung	15 mm	14 mm	13 mm	16 mm
	TL2 – Lymph Node	22 mm	12 mm	12 mm	Disappeared
	TL3 – Lymph Node	18 mm	10 mm	6 mm	Disappeared
	TL4 – Lymph Node	19 mm	14 mm	15 mm	Disappeared
	TL5 – Liver	17 mm	20 mm	22 mm	22 mm
	Sum	91 mm	70 mm **(-23%)**	68 mm **(-25%)**	38 mm **(-58%)**
Non-Target Lesion	NTL1 – Lung	Present	Present	Present	Disappeared
	NTL2 – Bone	Present	Present	Present	Present
New Lesion		NA	No	No	Yes
Overall Response		NA	SD	SD	PD (iuPD)

Tumor Type: Male, 53 years old, ECOG PS 0, MSS rectosigmoid adenocarcinoma with liver metastasis at baseline

Site Location: Singapore

Prior Therapies: Previously received curative & palliative surgery for liver metastasis and 3 lines of therapies (Leucovorin + 5FU + irinotecan + oxaliplatin; bevacizumab + TAS102; regorafenib)

Dose Regimen: ADG126 10 mg/kg Q6W + Toripalimab 240 mg Q3W

Safety Profile: TRAEs include G3 lipase increase and G2 amylase increase

The Case for ADG126 in MSS CRC: Evidence of Activity in Cold & Difficult-to-Treat Tumors

- Objective responses and/or tumor shrinkage, and prolonged stable disease by ADG116 (unmasked parental antibody) and ADG126 in MSS CRC patients
- Correlation of clinical activities with the reduction in carcinoembryonic antigen (CEA) levels
- Efficacy correlated with dosing schedule of ADG126 10 mg/kg Q3W with anti-PD-1 (ORR = 40%; N=10) in heavily pre-treated patients across multiple tumors during dose escalation
- CTLA-4 is over-expressed in Treg cells, therefore enhancing Teff/Treg in TME of “cold” tumors

A Path Forward for ADG126 in MSS CRC

- **95%** of metastatic CRC patients are microsatellite stable (MSS)
- **$18.6B** growing CRC global market*
- **Limited clinical benefit** from SoC:
  - No immunotherapy approved
  - Approved therapies include regorafenib (TKI) or TAS-102 (trifluridine/tipiracil)
    - mPFS = ~2 months; ORR = <5%
  - Recent progress for trifluridine/tipiracil +/- bevacizumab (from Sunlight Trial)
    - mPFS = 2.4 – 5.6 months; ORR = <7%

- ADG126 SAFEbody is the **most advanced clinical stage anti-CTLA-4 candidate**+ that integrates masking technology and Treg depletion for superior safety & efficacy profiles
- Dose expansion cohort of ADG126 plus pembrolizumab enrolling ~20 MSS CRC patients, with **preliminary efficacy readout end of 2023**

* the insight partners 2022
+ Based on review of publicly available data as of May 2023 for anti-CTLA-4 candidates in clinical trials.


Next Steps & Takeaways

Status & Next Steps

	Status	Next Steps
ADG116	• Confirming dosing regimens for future trials	• Advance into Ph 2 tumor-specific cohorts
ADG126	• Ongoing dose expansion at 10 mg/kg Q3W & Q6W • Randomized trial with novel triple combination in HCC	• Ph 2 MSS CRC and HCC efficacy readouts

Establishing registration path and strategy (e.g., RP2D, indication and design) for pivotal trial of anti-CTLA-4 with anti-PD-1 therapy in targeted tumors

Key Takeaways

Adagene's next-generation CTLA-4 candidates are designed to widen the therapeutic window by targeting a unique epitope of CTLA-4 and then combining it with precision masking technology:

- Enhanced Treg depletion in TME
- Repeat dosing for sustained target engagement

ADG116 & ADG126 demonstrate ability to unleash the full potential of anti-CTLA-4 therapy in multiple patient populations:

- Efficacy profile in cold tumors
- Activity in PD-1 resistant/refractory patients
- Ability for novel dosing regimens and combinations across modalities


Additional Information

Both Masked and Unmasked Anti-CTLA-4 Candidates Show Favorable Safety Profiles Compared to Historical Controls

		Dose	TRAE ≥ Grade 3	Safety (HNSTD, mg/kg)
Masked	**ADG126* (SAFEbody)**	10 and 20 mg/kg Q3W (n=17) With repeat dosing	0%	200
Masked	**BMS 986249 (Ipi-Probody)**	20 mg/kg** Q4W (n=10)	60%	50#
Unmasked	**ADG116**	≤ 6 mg/kg Q3W (n=30)	0%	30
		10 & 15 mg/kg Q3W (n=29)	14%	
Unmasked	**Ipilimumab+**	3 mg/kg Q3W	20-27%	10#
		10 mg/kg Q3W	36%	

This slide contains information from various clinical trials which are not head-to-head comparisons. Data on file.
* ADG126 data from ADG126-1001 study (March 14, 2023 datacut). ADG116 data from ADG116-1002 and ADG116-1003 study (May 2023 datacut).
** Dosing of 10 & 20 mg/kg is calculated from 800 mg and 1600 mg, assuming 80kg body weight from ESMO 2022, 740P, NCT03369223
+ Clinical data for Ipilimumab from trials in melanoma. Reference on file.
# John Engelhardt, et al. Preclinical characterization of novel anti–CTLA-4 prodrug antibodies with an enhanced therapeutic index. AACR 2020. Poster 4551.
HNSTD = highest non-severely toxic dose. From preclinical GLP toxicology studies.

Reference List for Slide 7

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