Adagene Reports Full Year 2023 Financial Results and Provides Corporate Update

March 29, 2024

- Data for masked anti-CTLA-4 SAFEbody® ADG126 (muzastotug) highlight best-in-class therapeutic index and demonstrate clinical benefits in metastatic microsatellite-stable (MSS) colorectal cancer (CRC) with higher, more frequent and repeat dosing of anti-CTLA-4 therapy in combination with anti-PD-1 -

- Ongoing combination phase 2 dose expansion in MSS CRC increased to over 50 patients, including initiation of a new, unprecedented 20 mg/kg loading dose regimen, with data anticipated during 2024 -

- Validation of SAFEbody masking technology by Exelixis and Sanofi showcases versatility of platform across modalities including antibody-drug conjugates, bi-specific and monoclonal antibodies -

- Cash balance of approximately US$110 million funds streamlined operations into 2026 -

SAN DIEGO and SUZHOU, China, March 29, 2024 (GLOBE NEWSWIRE) -- Adagene Inc. (“Adagene”) (Nasdaq: ADAG), a platform-driven, clinical-stage biotechnology company transforming the discovery and development of novel antibody-based therapies, today reported financial results for the full year 2023 and provided corporate updates.

“The SAFEbody precision masking technology platform remains at the core of our value proposition given its ability to enhance next generation antibody-based therapies that span modalities, including bispecific T-cell engagers and antibody-drug conjugates, both areas where a wider therapeutic index is needed to fully address solid tumors,” said Peter Luo, Ph.D., Chairman, CEO and President of R&D at Adagene.

He continued, “Turning to our clinical pipeline, we remain steadfast in our belief that anti-CTLA-4 therapy can be reimagined as a cornerstone of cancer care by enabling higher, more frequent and repeated doses in combination with anti-PD-1 and other therapies. With our SAFEbody platform, we have a 30-fold improved therapeutic index for ADG126 and a mechanism enabling CTLA-4 mediated intratumoral Treg depletion. We are taking anti-CTLA-4 therapy to a new level unleashing this proven immunotherapy where safety has limited its therapeutic potential.”

“In particular, our new loading dose regimen in late-stage MSS CRC patients enables our masked anti-CTLA-4 therapy to reach a high initial concentration, close to the steady state of activated species within the tumor tissue to immediately engage the CTLA-4 pathway and stop the tumor from aggressive growth. This loading dose strategy, together with repeated maintenance doses at 10 mg/kg showing limited treatment-related grade 3 and no higher toxicities with minimal late-onset toxicities for ADG126, is expected to engage the CTLA-4 target consistently, thereby maintaining and sustaining clinical benefit, via both the initial response rate and prolonged survival benefit. We look forward to reporting more clinical results for the ADG126 combination dose expansion in MSS CRC later this year.”

PIPELINE HIGHLIGHTS

- ***Phase 1b/2 data for ADG126, a masked anti-CTLA-4 SAFEbody targeting a unique epitope of CTLA-4 on regulatory T cells (Tregs) in tumor tissue as driven by the fundamental biology of CTLA-4, showed a potential best-in-class profile in combination with Merck’s anti-PD-1 therapy, KEYTRUDA ® (pembrolizumab)*, in MSS CRC, PD-1 experienced and PD-L1 low tumors:***
  - Results presented at the 2024 American Society of Clinical Oncology (ASCO) Gastrointestinal (GI) Symposium from dose escalation and dose expansion cohorts of ADG126 in combination with pembrolizumab (200 mg/Q3W) demonstrated a differentiated safety profile for ADG126 at doses from 6 mg/kg to 10 mg/kg in heavily pre-treated advanced/metastatic patients (N=46):
    - Limited dose-dependent toxicities were observed.
    - Grade 3 TRAEs occurred in 5/46 patients (10.8%), with no Grade 4 or 5 TRAEs and a discontinuation rate of 6.5% (3/46).
  - In dose escalation across tumor types, two partial confirmed responses (PRs) were observed among the three patients treated with ADG126 10 mg/kg Q3W, which triggered expansion cohorts at this dosing regimen. One of the patients had PD-1 refractory cervical cancer and the other had endometrial cancer. Both confirmed PRs are sustained after more than one year with repeat dosing while maintaining robust safety profiles.
  - In dose expansion of patients with MSS CRC, 12 evaluable patients without liver metastases were treated at the active, potent dose of 10 mg/kg Q3W:
    - Two confirmed PRs were observed in nine of these patients without peritoneal and liver metastases, resulting in an overall response rate of 22% in this subset.
    - An additional seven of these nine patients experienced stable disease (SD) for an overall disease control rate of 100% (2 PRs and 7 SD).
    - Observation of these clinical activities triggered further expansion into the second stage of the Simon’s 2-stage design for this dose level.
  - In a preliminary progression-free survival (PFS) analysis of those MSS CRC patients free of liver and peritoneal metastasis, a median PFS of seven months was observed in those treated with ADG126 10 mg/kg at two dosing

frequencies pooled together [every three weeks (n=9) and every six weeks (n=6)]. The durable clinical activity of ADG126 in combination with pembrolizumab will continue to be evaluated as a larger cohort of subjects becomes evaluable at the 10 mg/kg Q3W dose level.
    - Following the ASCO GI Symposium, Adagene announced progress and expansion of the ADG126 clinical program, which increases the ongoing phase 2 dose expansion in MSS CRC to over 50 patients. Updates included:
        - Enrollment of 12 additional patients in the second stage of the Simon's 2-stage design was completed in the fourth quarter of 2023 for the ongoing phase 2 dose expansion cohort evaluating ADG126 10 mg/kg Q3W in combination with pembrolizumab in MSS CRC. These Part 2 results will supplement data from Part 1 of the dose expansion in MSS CRC as recently presented at the 2024 ASCO GI Symposium.
        - Given the ADG126 safety profile, evaluation of the 20 mg/kg loading dose regimen has been initiated in combination with pembrolizumab in patients with advanced/metastatic cancer. Pending outcome of the ongoing safety evaluation, the company plans to evaluate the efficacy profile of the loading dose regimen in expansion cohorts, followed by maintenance with ADG126 10 mg/kg Q3W in combination with pembrolizumab at sites in the US and Asia Pacific.
        - Clearance received from China's Center for Drug Evaluation to initiate clinical evaluation of ADG126 in combination with pembrolizumab. This enables the company to broaden its dose expansion cohorts for MSS CRC at selected dosing regimens, and potentially in other tumor types, in its clinical trial collaboration and supply agreement with Merck.
    - Additionally, the company recently initiated dosing of a small number of patients with advanced/metastatic cancers at 30 mg/kg ADG126 monotherapy Q3W in China to define the potential maximum tolerated dose of ADG126 monotherapy.

- ***Phase 1b/2 data for ADG116, an unmasked anti-CTLA-4 NEObody™ targeting a unique epitope, showed a favorable safety profile and clinical responses, both in monotherapy and in combination with anti-PD-1:***
    - ADG116 monotherapy has demonstrated a favorable safety profile at doses up to 15 mg/kg (N=59) and an overall response rate (ORR) of 13% (3/23 evaluable), including confirmed and durable PRs in multiple tumor types.
    - In combination with anti-PD-1 therapy, ADG116 (3 mg/kg Q6W) (N=22) showed a manageable safety profile and an encouraging efficacy profile in dose escalation. Clinical responses from the combination cohorts include a complete response (CR) sustained for nearly two years in a head and neck squamous cell carcinoma (HNSCC) patient dosed with repeat cycles of ADG116 3 mg/kg (initially every three weeks, then every six weeks) plus toripalimab (ORR = 20%; 1/5 evaluable). An initial PR was also observed in a patient with MSS CRC dosed with repeat cycles of ADG116 3 mg/kg every six weeks plus toripalimab, further demonstrating the potential clinical benefit associated with targeting a unique epitope of CTLA-4 and the essential effects of Treg depletion.
    - ADG116 is clinically active and ready to advance into further clinical development as resources allow.
- ***Phase 1 evaluation is ongoing for ADG206, a masked, IgG1 F_C-enhanced anti-CD137 POWERbody™ in patients with advanced/metastatic tumors:***
    - Adagene has enrolled 10 patients in an ongoing phase 1 trial of ADG206 to evaluate safety, efficacy and tolerability profiles for this next generation anti-CD137 candidate. Dose escalation continues with a cohort ongoing at 3 mg/kg Q3W. No maximum tolerated dose (MTD) has yet been reached.
    - Preclinical data demonstrated that ADG206 was well tolerated and had robust anti-tumor activity as a single agent in multiple tumor models, with 4-fold stronger anti-CD137 agonistic activity of its activated form than a benchmark antibody (urelumab analog) that displayed dose-dependent liver toxicity with an MTD of 0.1 mg/kg Q3W.
    - ADG206 is the company's first SAFEbody with Fc enhancement, called a POWERbody, to advance into clinic. ADG206 combines SAFEbody precision masking, Fc enhancement and targeting of a unique epitope to solve the safety and efficacy challenges of anti-CD137 therapies, reflecting versatility of Adagene's dynamic antibody discovery and masking platform.

COLLABORATIONS

- ***Exelixis:*** In June 2023, Adagene received a US$3.0 million milestone payment from Exelixis for the successful nomination of lead SAFEbody candidates for the second collaboration program under a technology licensing agreement to develop novel masked antibody-drug conjugate candidates.

- ***Sanofi***: Adagene and Sanofi are collaborating to develop both bispecific and monoclonal SAFEbody antibody candidates, preparing preclinical candidates using Adagene's SAFEbody precision masking technology for future development and commercialization by Sanofi. The collaboration announced in March 2022 included an upfront payment of US$17.5 million for the initial two programs, an option fee for two additional programs, potential milestone payments of up to US$2.5 billion, and tiered royalties.

- ***Roche:*** Roche is sponsoring and conducting a phase 1b/2 multi-national trial to evaluate ADG126 in a triple combination with atezolizumab and bevacizumab in first-line hepatocellular carcinoma (HCC). Adagene retains global development and

commercialization rights to ADG126.

CHANGE OF BOARD OF DIRECTORS

The following changes to Adagene's Board of Directors will be effective upon the filing of its 2023 annual report on Form 20-F ("2023 Annual Report"), unless otherwise noted:

- Dr. Ulf Grawunder will join the Board of Directors (the "Board") as an independent director and serves as a member of Audit Committee and Strategy Committee of the Board. Dr. Grawunder is an experienced Swiss/German life-science entrepreneur with over 20 years of experience in the therapeutic antibody development industry.
- Dr. Zhu Li, currently an independent director, will serve as a member of Compensation Committee of the Board.
- Term of Mr. Andy (Yiu Leung) Cheung, Dr. Mervyn Turner and Mr. Man Kin (Raymond) Tam will be extended.
- Dr. Min Li, currently an independent director and a member of Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee, and Ms. Yan Li, Senior Vice President of Bioinformatics and Information Technology and currently a member of the Board, will resign as directors of the Board and membership of the various committees, as applicable, due to person reasons. Ms. Yan Li's resignation from the board will be effective on June 15, 2024, after which she will continue to serve as an observer to the Board. Each of Dr. Min Li and Ms. Yan Li confirmed that he or she has no disagreement with the Board, and there is no other matter relating to his or her resignation that needs to be brought to the attention of the shareholders of the company.

The Board would like to take this opportunity to express their sincere gratitude to Dr. Min Li and Ms. Yan Li for their valuable contributions to the Board during their tenure. Background of the newly appointed directors and their terms are detailed in the 2023 Annual Report.

2024 MILESTONES & CASH RUNWAY INTO 2026

Consistent with ongoing initiatives to prudently manage its cash balance, Adagene expects its current cash balance to fund activities into 2026, with the following milestones:

- Data from the ongoing phase 1b/2 clinical trial of ADG126 in combination with pembrolizumab, including dose expansion cohorts in MSS CRC, are anticipated throughout 2024:
  - Follow up of Part 1 evaluable patients at 10 mg/kg Q3W (n=12) and 10 mg/kg Q6W (n=10)
  - Data from Part 2 patients at 10 mg/kg Q3W (n=12)
  - Evaluation of 20 mg/kg loading doses for Project Optimus requirements:
    - Safety data with repeat doses
    - Dose expansion in MSS CRC (n~10)
  - Additional patients in China (n≥10)
- Additional technology licensing agreement(s) and/or milestone(s).

FINANCIAL HIGHLIGHTS

Cash and Cash Equivalents
Cash and cash equivalents were US$109.9 million as of December 31, 2023, compared to US$143.8 million as of December 31, 2022. Total borrowings from commercial banks in China (denominated in RMB) decreased to US$21.9 million as of December 31, 2023 from US$27.8 million as of December 31, 2022. The associated loan proceeds were primarily used to pay for the company's R&D activities in China.

Net Revenue:
Net revenue was US$18.1 million for the year ended December 31, 2023, compared to US$9.3 million in 2022. The increase of approximately 95% reflects net revenue recognized upon fulfillment of certain performance obligations associated with the collaboration and technology licensing agreements with Exelixis and Sanofi, respectively. Net revenue also included a milestone payment of US$3.0 million from Exelixis received in June 2023.

Research and Development (R&D) Expenses:
R&D expenses were US$36.6 million for the year ended December 31, 2023, compared to US$81.3 million in 2022. The decrease of approximately 55% in R&D expenses reflects clinical focus on and prioritization of the company's masked, anti-CTLA-4 SAFEbody ADG126.

Administrative Expenses:
Administrative expenses were US$8.7 million for the year ended December 31, 2023, compared to US$11.9 million in 2022. The decrease was due to both a reduction in personnel and in office-related expenses as a result of cost-control measures.

Other Operating Income, Net:
Other operating income, net was US$3.5 million for the year ended December 31, 2023. Other operating income, net included a one-time compensation payment from a contract manufacturer for a preclinical-related outsourcing arrangement.

Net Loss:
Net loss attributable to Adagene Inc.'s shareholders was US$18.9 million for the year ended December 31, 2023, compared to US$80.0 million in 2022.

Ordinary Shares Outstanding:
As of December 31, 2023, there were 55,145,839 ordinary shares issued and outstanding. Each American depository share, or ADS, represents one and one quarter (1.25) ordinary shares of the company.

Non-GAAP Net Loss:
Non-GAAP net loss, which is defined as net loss attributable to ordinary shareholders for the period after excluding share-based compensation expenses, was US$11.7 million for the year ended December 31, 2023, compared to US$69.5 million in 2022. Please refer to the section in this press release titled “Reconciliation of GAAP and Non-GAAP Results” for details.

Non-GAAP Financial Measures
The company uses non-GAAP net loss and non-GAAP net loss per ordinary shares for the year, which are non-GAAP financial measures, in evaluating its operating results and for financial and operational decision-making purposes. The company believes that non-GAAP net loss and non-GAAP net loss per ordinary shares for the year help identify underlying trends in the company’s business that could otherwise be distorted by the effect of certain expenses that the company includes in its loss for the year. The company believes that non-GAAP net loss and non-GAAP net loss per ordinary shares for the year provide useful information about its results of operations, enhances the overall understanding of its past performance and future prospects and allows for greater visibility with respect to key metrics used by its management in its financial and operational decision-making.

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

Non-GAAP net loss and non-GAAP net loss per ordinary shares for the year represent net loss attributable to ordinary shareholders for the year excluding share-based compensation expenses. Share-based compensation expense is a non-cash expense arising from the grant of stock-based awards to employees. The company believes that the exclusion of share-based compensation expenses from the net loss in the Reconciliation of GAAP and Non-GAAP Results assists management and investors in making meaningful period-to-period comparisons in the company's operating performance or peer group comparisons because (i) the amount of share-based compensation expenses in any specific period may not directly correlate to the company’s underlying performance, (ii) such expenses can vary significantly between periods as a result of the timing of grants of new stock-based awards, and (iii) other companies may use different forms of employee compensation or different valuation methodologies for their share-based compensation.

Please see the “Reconciliation of GAAP and Non-GAAP Results” included in this press release for a full reconciliation of non-GAAP net loss and non-GAAP net loss per ordinary shares for the year to net loss attributable to ordinary shareholders for the year/period.

About Adagene
Adagene Inc. (Nasdaq: ADAG) is a platform-driven, clinical-stage biotechnology company committed to transforming the discovery and development of novel antibody-based cancer immunotherapies. Adagene combines computational biology and artificial intelligence to design novel antibodies that address globally unmet patient needs. The company has forged strategic collaborations with reputable global partners that leverage its SAFEbody® precision masking technology in multiple approaches at the vanguard of science.

Powered by its proprietary Dynamic Precision Library (DPL) platform, composed of NEObody™, SAFEbody, and POWERbody™ technologies, Adagene’s highly differentiated pipeline features novel immunotherapy programs. The company’s 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 tumor microenvironment, this allows for tumor-specific targeting of antibodies in tumor microenvironment, while minimizing on-target off-tumor toxicity in healthy tissues.

Adagene’s lead clinical program, ADG126 (muzastotug), is a masked, anti-CTLA-4 SAFEbody that targets a unique epitope of CTLA-4 in regulatory T cells (Tregs) in the tumor microenvironment. ADG126 is currently in phase 1b/2 clinical studies in combination with anti-PD-1 therapy, particularly focused on Metastatic Microsatellite-stable (MSS) Colorectal Cancer (CRC). Validated by ongoing clinical research, the SAFEbody platform can be applied to a wide variety of antibody-based therapeutic modalities, including Fc enhanced antibodies, antibody-drug conjugates, and bi/multispecific T-cell engagers.

For more information, please visit: https://investor.adagene.com. Follow Adagene on WeChat, LinkedIn and Twitter.

Safe Harbor Statement

This press release contains forward-looking statements, including statements regarding the potential implications of clinical data for patients, and Adagene’s advancement of, and anticipated preclinical 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 outbreak of a widespread health epidemic 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 annual report for the year of 2023 on Form 20-F filed with the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Adagene, and 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.

Investor & Media Contact:
Ami Knoefler
650-739-9952
ir@adagene.com

FINANCIAL TABLES FOLLOW

Unaudited Consolidated Balance Sheets

	December 31, 2022 US$	December 31, 2023 US$
ASSETS		
Current assets:		
Cash and cash equivalents	143,758,678	109,934,257
Amounts due from related parties	619,432	222,027
Prepayments and other current assets	4,937,323	3,287,445
Total current assets	**149,315,433**	**113,443,729**
Property, equipment and software, net	2,782,963	1,835,121
Operating lease right-of-use assets	191,877	365,103
Other non-current assets	109,572	84,885
TOTAL ASSETS	**152,399,845**	**115,728,838**
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	3,666,124	3,093,752
Contract liabilities	15,107,276	—
Amounts due to related parties	19,323,337	16,714,326
Accruals and other current liabilities	3,212,809	3,001,508
Income tax payable	—	52,884
Short-term borrowings	10,768,745	4,235,673
Current portion of long-term borrowings	2,850,128	4,161,549
Current portion of operating lease liabilities	151,983	195,955
Total current liabilities	**55,080,402**	**31,455,647**
Long-term borrowings	14,146,541	13,540,034
Operating lease liabilities	53,834	173,660
Other non-current liabilities	28,718	—
TOTAL LIABILITIES	**69,309,495**	**45,169,341**
Commitments and contingencies		
Shareholders' equity:		
Ordinary shares (par value of US$0.0001 per share; 640,000,000 shares authorized, and 54,065,709 shares issued and outstanding as of December 31, 2022; and 640,000,000 shares authorized, and 55,145,839 shares issued and outstanding as of December 31, 2023)	5,497	5,547
Treasury shares, at cost (1 share as of December 31, 2022 and December 31, 2023)	(4)	(4)
Additional paid-in capital	342,739,268	350,105,518
Accumulated other comprehensive loss	(849,305)	(1,800,088)
Accumulated deficit	(258,805,106)	(277,751,476)
Total shareholders' equity	**83,090,350**	**70,559,497**
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	**152,399,845**	**115,728,838**

Unaudited Consolidated Statements of Comprehensive Loss

	For the Year Ended December 31, 2022 US$	For the Year Ended December 31, 2023 US$
Revenues		
Licensing and collaboration revenue	9,292,724	18,111,491
Operating expenses and income		
Research and development expenses	(81,339,540)	(36,639,146)
Third parties	(46,212,077)	(33,978,642)
Related parties	(35,127,463)	(2,660,504)
Administrative expenses	(11,873,867)	(8,672,843)
Other operating income, net	—	3,480,632

Loss from operations	**(83,920,683)**	**(23,719,866)**
Interest income	377,501	4,283,085
Interest expense	(693,323)	(1,107,820)
Other income, net	2,168,388	1,843,437
Foreign exchange gain, net	2,555,325	1,446,202
Loss before income tax	**(79,512,792)**	**(17,254,962)**
Income tax expense	(459,055)	(1,691,408)
Net loss attributable to Adagene Inc.'s shareholders	**(79,971,847)**	**(18,946,370)**
Other comprehensive loss		
Foreign currency translation adjustments, net of nil tax	(755,324)	(950,783)
Total comprehensive loss attributable to Adagene Inc.'s shareholders	**(80,727,171)**	**(19,897,153)**
Net loss attributable to Adagene Inc.'s shareholders	**(79,971,847)**	**(18,946,370)**
Net loss attributable to ordinary shareholders	**(79,971,847)**	**(18,946,370)**
Weighted average number of ordinary shares used in per share calculation:		
—Basic	54,135,084	54,737,530
—Diluted	54,135,084	54,737,530
Net loss per ordinary share		
—Basic	(1.48)	(0.35)
—Diluted	(1.48)	(0.35)

Reconciliation of GAAP and Non-GAAP Results

	For the Year Ended December 31, 2022	For the Year Ended December 31, 2023
	US$	US$
GAAP net loss attributable to ordinary shareholders	**(79,971,847)**	**(18,946,370)**
Add back:		
Share-based compensation expenses	10,520,282	7,271,700
Non-GAAP net loss	**(69,451,565)**	**(11,674,670)**
Weighted average number of ordinary shares used in per share calculation:		
—Basic	54,135,084	54,737,530
—Diluted	54,135,084	54,737,530
Non-GAAP net loss per ordinary share		
—Basic	(1.28)	(0.21)
—Diluted	(1.28)	(0.21)

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Source: Adagene Inc.