Adagene Reports Full Year 2022 Financial Results and Provides Corporate Update

March 28, 2023

- Clinical data for wholly-owned anti-CTLA-4 franchise show best-in-class safety profiles for unmasked and masked candidates, unlocking the full therapeutic benefit of anti-CTLA-4 in combination with anti-PD-1 and beyond -

- Roche sponsoring randomized, multi-national phase 1b/2 trial of novel triple combination therapy in first-line liver cancer, leveraging safety profile of masked, anti-CTLA-4 SAFEbody® ADG126 -

- Sanofi and Exelixis collaborations present multi-billion dollar opportunity for non-dilutive funding via milestones and royalties -

- Cash balance of US$143.8 million supports streamlined operations into 2025 -

SAN DIEGO and SUZHOU, China, March 28, 2023 (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 2022 and provided corporate updates.

"We are investing in R&D activities to strengthen the differentiation and impact of our anti-CTLA-4 franchise, while generating non-dilutive funding through collaborations," said Peter Luo, Ph.D., Co-Founder, Chief Executive Officer and Chairman of the Board of Adagene. "Through CTLA-4-mediated intra-tumoral Treg depletion, we are addressing the dose-dependent toxicities of anti-CTLA-4 therapies, thereby unleashing their power as a cornerstone of cancer immunotherapy across a broad spectrum of tumors. We expect continued momentum with both existing and prospective partners to validate our SAFEbody technology and pipeline programs."

PIPELINE & BUSINESS HIGHLIGHTS

Anti-CTLA-4 Programs

- ***Phase 1b/2 data for ADG116, an unmasked anti-CTLA-4 NEObody™ targeting a unique epitope showed a differentiated safety profile and anti-tumor activity, both in monotherapy and in combination with anti-PD-1:***
  - In monotherapy studies of 50 patients with advanced/metastatic tumors, ADG116 was administered up to 15 mg/kg every three weeks with repeat dosing.
  - No Grade 3 or higher treatment-related adverse events (TRAEs) were reported at the 15 mg/kg dose level, while Grade 3 or higher TRAEs at 10 mg/kg (13%) were lower than the reported rate (36%) for a currently approved anti-CTLA-4 therapy, ipilimumab, at 10 mg/kg in first-line monotherapy in melanoma patients in a non-head-to-head comparison.
  - ADG116 monotherapy in heavily pre-treated patients with difficult-to-treat tumors resulted in two partial responses in Kaposi's sarcoma and renal cell carcinoma. In February 2023, a third partial response with monotherapy was reported in a patient with MSI-H endometrial cancer. The patient had received five cycles of ADG116 at 10 mg/kg with only Grade 1 TRAEs reported.
  - ADG116 in combination with anti-PD-1 therapies also demonstrated a differentiated safety profile and anti-tumor activity at 3 mg/kg with repeat dosing. Results were presented at the Society for Immunotherapy of Cancer's (SITC) annual meeting, including one confirmed, durable complete response observed after six cycles in a patient with platinum-refractory recurrent head and neck squamous cell carcinoma who remains on therapy (n=5; ORR = 20%; DCR = 100%). Additionally, a significant reduction in a tumor-related biomarker (carcinoembryonic antigen levels) was observed in two patients with metastatic microsatellite-stable (MSS) colorectal cancer (CRC); both patients had either liver or lung metastases.
  - Combination dose expansion of ADG116 in combination with anti-PD-1 is ongoing for dose optimization.

- ***Phase 1b/2 data for ADG126, a masked anti-CTLA-4 SAFEbody targeting a unique epitope, showed compelling safety and promising efficacy profiles at high dose levels with repeat dosing both in monotherapy and in combination with anti-PD-1:***
  - In dose escalation, ADG126 monotherapy was well tolerated with no dose-limiting toxicities or Grade 3 or higher TRAEs observed when administered up to 20 mg/kg every three weeks with repeat dosing in 26 patients with advanced/metastatic solid tumors.
  - Clinical evaluation with anti-PD-1 therapies is ongoing with interim data from dose escalation portions of phase 1b/2 trials in combination with toripalimab and pembrolizumab to be presented at the upcoming American Association for Cancer Research annual meeting April 14 – 18, 2023 in Orlando, Florida.
  - Interim results announced in January 2023 from ongoing phase 1b/2 trials of ADG126 in combination with anti-PD-1 therapy include:
    - No dose-limiting toxicities observed when ADG126 combined up to 10 mg/kg with repeat cycles, highlighting the potential of SAFEbody anti-CTLA-4 therapy. SAFEbody ADG126 provides systemic delivery of CTLA-4

treatment similar to intra-tumoral delivery to reach a higher concentration at the tumor site, enabling concentration-dependent, intra-tumoral Treg depletion for effective immunotherapy.
    - Multiple partial responses were confirmed in several tumor types during combination dose escalation.
    - Continuous tumor shrinkage in cold tumors and anti-PD-1 resistant patients.
    - Efficacy results consistent with data for parental antibody (ADG116) in warm and cold tumors due to its strong intra-tumoral depletion of regulatory T cells in the tumor microenvironment (TME).
  - Dose expansion for ADG126 in combination with anti-PD-1 is ongoing with multiple dosing regimens being evaluated, in alignment with the Food & Drug Administration's Project Optimus for dose optimization of cancer drugs.

Additional Clinical & Preclinical Programs

- ***Initiated dosing of the first patient in a phase 1 trial evaluating safety, efficacy and tolerability profiles for ADG206, a masked, IgG1 F_C-enhanced anti-CD137 POWERbody™ in patients with advanced/metastatic tumors.*** This next generation anti-CD137 candidate is the first POWERbody candidate to advance into clinic, combining precision masking, Fc-engineering and targeting of a unique epitope to solve the safety and efficacy challenges of anti-CD137 therapies.

- ***Continued investigator-initiated trials (IITs) for ADG106, an anti-CD137 agonist NEObody,*** in selected combination settings, including advanced non-small cell lung cancer (NSCLC) and early-stage, HER2-negative breast cancer.

- ***Presented best-in-class profiles for multiple preclinical product candidates in IND-enabling studies, including ADG153 (anti-CD47 IgG1 SAFEbody) and ADG138 (HER2xCD3 POWERbody), which apply SAFEbody precision masking technology***. The robust preclinical profiles for these and other product candidates are published here.

- ***Proprietary bispecific T-cell engager (TCE) capability with CD28 designed to mitigate the serious safety concerns of CD28 activation***. CD28 bispecific POWERbody TCEs in preclinical evaluation exhibit enormous potential to fulfill the promise of safe and durable T cell-mediated synergistic immunotherapies when combined with CD3 bispecific TCEs and/or checkpoint inhibitors. The full poster presentation may be viewed here.

Collaborations

- ***Roche:*** Established a clinical trial collaboration in December 2022 where Roche will sponsor and conduct a randomized phase 1b/2 multi-national trial to evaluate the efficacy, safety and pharmacokinetic profiles of ADG126 in a triple combination with bevacizumab and atezolizumab, versus the approved combination of atezolizumab and bevacizumab alone in first-line hepatocellular carcinoma (HCC). Each company is supplying its respective anti-cancer agent(s) to support the trial, which will be initially conducted in 60 patients. The trial reflects Roche's leadership and commitment to HCC, where they pioneered the established standard-of-care doublet combination, and validates Adagene's differentiated ADG126 anti-CTLA-4 clinical program. Adagene will retain global development and commercialization rights to ADG126.

- ***Sanofi***: Established a technology licensing agreement with Sanofi in March 2022 to generate masked versions of antibodies provided by Sanofi, including monoclonal and bispecific candidate antibodies, with a potential transaction value of US$2.5 billion. The collaboration included an upfront payment of US$17.5 million received in April 2022 for the initial two programs (US$8.75 million per program), an option fee for two additional programs, potential milestone payments of up to US$2.5 billion (US$625 million per program), and tiered royalties.

- ***Exelixis:*** Received a US$3.0 million milestone payment from Exelixis in January 2022 for the successful nomination of lead SAFEbody candidates for one of the collaboration programs and an additional $1.1 million upfront payment for an expanded collaboration in SAFEbody discovery in June 2022, based on a technology licensing agreement to develop novel masked antibody-drug conjugate candidates. Terms of the agreement, which was executed in February 2021, include an upfront payment of US$11 million for two programs, potential milestones and tiered royalties.

- ***China:*** Advanced global partnerships and collaboration with Sanjin and Dragon Boat Biopharmaceutical for two antibodies out-licensed in Greater China, including an anti-PD-L1 (ADG104) in phase 2 and a novel anti-CSF-1R (ADG125/BC006) in phase 1 development.

CORPORATE UPDATES

- In March 2023, appointed Professor Aurélien Marabelle, MD, PhD, to the company's Scientific and Strategic Advisory Board. Professor Marabelle is a physician-scientist with expertise in oncology and immunology working within the Drug Development Department (DITEP) of Gustave Roussy Cancer Center in France. Professor Marabelle brings deep insight in tumor-specific Treg depletion for anti-CTLA-4 therapies delivered intra-tumorally to overcome dose dependent toxicities

through systemic delivery of anti-CTLA-4 therapies.

- In November 2022, appointed Cuong Do, MBA, to the company's board of directors as an independent director. He also serves as an audit committee member and will be chairing a strategy committee of the board. Mr. Do is President and CEO of BioVie Inc., a clinical-stage company developing innovative drug therapies. He was previously the Chief Strategy Officer for Merck, a leading global pharmaceuticals company, where he played a key role in defining the company's strategy, including the focus on oncology and creating its leading position with the anti-PD-1 therapy, pembrolizumab.

UPDATED MILESTONES & OUTLOOK

Following initiatives to streamline its operations over the past year, Adagene expects its cash balance to sufficiently fund activities into 2025, with the following milestones during 2023:

- Establish registration path and strategy (e.g., recommended phase 2 dose, indication and design) for phase 2/3 pivotal trial of anti-CTLA-4 in combination with anti-PD-1 therapy in targeted tumors
  - ADG126 phase 2 proof-of-concept data from combination dose expansion cohorts
  - Advance ADG116 phase 2 combination dose expansion cohorts
- Providing the path to a potential registrational trial for triple combination with Roche's atezolizumab/bevacizumab, advance ADG126 randomized phase 1b/2 trial in first-line hepatocellular carcinoma (HCC) conducted by Roche; provide update on trial status.
- Advance ADG206 phase 1 trial (masked, FC enhanced, IgG1 anti-CD137) and advance IND-enabling programs as resources allow.
- Additional collaborations and/or technology licensing agreements.

FINANCIAL HIGHLIGHTS

Cash and Cash Equivalents:
Cash and cash equivalents were US$143.8 million as of December 31, 2022, compared to US$174.4 million as of December 31, 2021. The 2022 cash balance includes an upfront payment of US$17.5 million for the first two projects from Sanofi, and a milestone payment of US$3.0 million and an additional upfront payment of US$1.1 million from Exelixis.

Total non-dilutive funding received from business development collaborations increased to US$21.9 million for the year ended December 31, 2022 from US$11.9 million for the year ended December 31, 2021. Total borrowings (denominated in RMB) from commercial banks in China increased to US$27.8 million as of December 31, 2022 from US$7.5 million as of December 31, 2021. The associated loan proceeds were primarily used to pay for the company's R&D activities in China, including CMC costs of clinical and preclinical programs.

Net Revenue:
Net revenue was US$9.3 million for the year ended December 31, 2022, compared to US$10.2 million in 2021. Net revenue was recognized due to fulfillment of performance obligations over time associated with the collaboration and technology licensing agreement with Sanofi to develop antibody-based therapies. Revenue was also recognized from the material transfer and option agreement with ADC Therapeutics SA as performance obligation was satisfied at a point in time.

Research and Development (R&D) Expenses:
R&D expenses were US$81.3 million for the year ended December 31, 2022, compared to US$68.1 million in 2021. The rise in R&D expenses was primarily due to increased R&D activities for the company's clinical programs and preclinical testing for candidates in the IND-enabling phase.

Administrative Expenses:
Administrative expenses were US$11.9 million for the year ended December 31, 2022, compared to US$14.4 million in 2021. The decrease was primarily due to a reduction in share-based compensation expenses.

Net Loss:
The net loss attributable to Adagene Inc.'s shareholders was US$80.0 million for the year ended December 31, 2022, compared to US$73.2 million for the year ended December 31, 2021.

Non-GAAP Net Loss:
Non-GAAP net loss, which is defined as net loss attributable to ordinary shareholders for the period after excluding (i) share-based compensation expenses and (ii) accretion of convertible redeemable preferred shares to redemption value, as applicable, was US$69.5 million for the year ended December 31, 2022, compared to US$54.5 million for the year ended December 31, 2021. 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 (i) share-based compensation expenses, and (ii) accretion of convertible redeemable preferred shares to redemption value. 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 unmet patient needs. 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. Adagene has forged strategic collaborations with reputable global partners that leverage its technology in multiple approaches at the vanguard of science.

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

SAFEbody® is a registered trademark in the United States, China, Australia, Japan, Singapore, and the European Union.

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 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 annual report for the year of 2021 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.

FINANCIAL TABLES FOLLOW

Unaudited Consolidated Balance Sheets

	December 31, 2021 US$	December 31, 2022 US$
ASSETS		
Current assets:		
Cash and cash equivalents	174,391,243	143,758,678
Accounts receivable, net	3,000,000	—
Amounts due from related parties	4,506,670	619,432
Prepayments and other current assets	4,055,921	4,937,323
Total current assets	**185,953,834**	**149,315,433**
Property, equipment and software, net	3,487,617	2,782,963
Operating lease right-of-use assets	—	191,877
Other non-current assets	69,275	109,572
TOTAL ASSETS	**189,510,726**	**152,399,845**
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		

Accounts payable	3,321,615	3,666,124
Contract liabilities	5,500,000	15,107,276
Amounts due to related parties	10,466,061	19,323,337
Accruals and other current liabilities	4,379,243	3,212,809
Income tax payable	1,657,450	—
Short-term borrowings	3,121,226	10,768,745
Current portion of long-term borrowings	1,376,319	2,850,128
Current portion of operating lease liabilities	—	151,983
Total current liabilities	**29,821,914**	**55,080,402**
Long-term borrowings	2,991,829	14,146,541
Operating lease liabilities	—	53,834
Deferred tax liabilities	44,163	—
Other non-current liabilities	94,107	28,718
TOTAL LIABILITIES	**32,952,013**	**69,309,495**
Commitments and contingencies		
Shareholders' equity:		
Ordinary shares	5,627	5,497
Treasury shares	(619,605)	(4)
Additional paid-in capital	336,099,931	342,739,268
Accumulated other comprehensive income (loss)	(93,981)	(849,305)
Accumulated deficit	(178,833,259)	(258,805,106)
Total shareholders' equity	**156,558,713**	**83,090,350**
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	**189,510,726**	**152,399,845**

Unaudited Consolidated Statements of Comprehensive Loss

	For the Year Ended December 31, 2021 US$	For the Year Ended December 31, 2022 US$
Revenues		
Licensing and collaboration revenue	10,175,258	9,292,724
Expenses		
Research and development expenses	(68,099,385)	(81,339,540)
Third parties	(55,020,367)	(46,212,077)
Related parties	(13,079,018)	(35,127,463)
Administrative expenses	(14,439,962)	(11,873,867)
Loss from operations	**(72,364,089)**	**(83,920,683)**
Interest income	76,166	377,501
Interest expense	(363,762)	(693,323)
Other income, net	1,778,822	2,168,388
Foreign exchange gain (loss), net	(603,459)	2,555,325
Loss before income tax	**(71,476,322)**	**(79,512,792)**
Income tax expense	(1,701,613)	(459,055)
Net loss attributable to Adagene Inc.'s shareholders	**(73,177,935)**	**(79,971,847)**
Other comprehensive income (loss)		
Foreign currency translation adjustments, net of nil tax	257,000	(755,324)
Total comprehensive loss attributable to Adagene Inc.'s shareholders	**(72,920,935)**	**(80,727,171)**
Net loss attributable to Adagene Inc.'s shareholders	**(73,177,935)**	**(79,971,847)**
Accretion of convertible redeemable preferred shares to redemption value	(28,553)	—
Net loss attributable to ordinary shareholders	**(73,206,488)**	**(79,971,847)**
Weighted average number of ordinary shares used in per share calculation:		
—Basic	50,032,009	54,135,084
—Diluted	50,032,009	54,135,084
Net loss per ordinary share		
—Basic	(1.46)	(1.48)
—Diluted	(1.46)	(1.48)

Reconciliation of GAAP and Non-GAAP Results

	For the Year Ended December 31, 2021	For the Year Ended December 31, 2022
	US$	US$
GAAP net loss attributable to ordinary shareholders	**(73,206,488)**	**(79,971,847)**
Add back:		
Share-based compensation expenses	18,679,658	10,520,282
Accretion of convertible redeemable preferred shares to redemption value	28,553	—
Non-GAAP net loss	**(54,498,277)**	**(69,451,565)**
Weighted average number of ordinary shares used in per share calculation:		
—Basic	50,032,009	54,135,084
—Diluted	50,032,009	54,135,084
Non-GAAP net loss per ordinary share		
—Basic	(1.09)	(1.28)
—Diluted	(1.09)	(1.28)

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

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Source: Adagene Inc.