Adagene Presents Data Demonstrating the Best-in-Class Therapeutic Index for Masked Anti-CTLA-4 SAFEbody® ADG126 at SITC 2023

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- MSS CRC case examples reinforce optimal dosing regimen in ongoing phase 2 dose expansion, with a confirmed partial response at ADG126 10 mg/kg every three weeks plus pembrolizumab –

- Integrated pharmacokinetic and clinical data analyses support the mechanism of action for ADG126 and its profile as a potential best-in-class CTLA-4 therapy across tumor types -

SAN DIEGO and SUZHOU, China, Nov. 03, 2023 (GLOBE NEWSWIRE) -- Adagene Inc. ("Adagene") (Nasdaq: ADAG), a company transforming the discovery and development of novel antibody-based therapies, today presented new data on its masked, anti-CTLA-4 SAFEbody ADG126 at the Society for Immunotherapy of Cancer (SITC) 38th Annual Meeting taking place in San Diego. The poster presentation, *Optimal Dose Selection of ADG126 (Masked Anti-CTLA-4 SAFEbody®) with Significantly Widened Therapeutic Index Compared to Ipilimumab in Combination with anti-PD-1 Antibodies Informed by QSP Modeling*, is available on the company's website.

The data, which integrate clinical results with physiologically based pharmacokinetic and quantitative systems pharmacology modeling, demonstrated that Adagene's lead SAFEbody candidate, ADG126, is effective at targeting CTLA-4 within the tumor microenvironment (TME). This resulted in an approximately 30-fold projected pharmacokinetic difference at 10 mg/kg every three weeks (Q3W) in the TME indicating a wider therapeutic index (TI) compared to ipilimumab at 1 mg/kg Q6W, when either is combined with anti-PD-1 therapies.

The enhanced TI of ADG126 enables higher, more frequent and repeat dosing of ADG126 in combination with anti-PD-1, resulting in significantly increased CTLA-4 engagement by activated ADG126 at steady state in tumors versus circulating blood. Analyses also demonstrated that the optimal dose of ADG126 at 10 mg/kg Q3W plus pembrolizumab results in a dose-dependent efficacy profile, without a significant increase in treatment related adverse events (TRAEs).

Importantly, a clinical case example presented for the first time from an ongoing dose expansion cohort in advanced/metastatic MSS CRC* patients free of liver metastases showed that ADG126 10 mg/kg Q3W plus pembrolizumab resulted in a confirmed PR after four cycles (i.e., 12 weeks). The patient was previously treated with two lines of therapy (bevacizumab plus FOLFOX; aflibercept plus FOLFIRI) and experienced manageable Grade 3 TRAEs consistent with known adverse events from immunotherapy.

The poster concluded that initial clinical data from the SAFEbody ADG126 program support that ADG126 may provide greater clinical benefit than ipilimumab in combination with anti-PD-1 in both 'hot' and 'cold' tumors, including MSS CRC, driven by better target engagement in the TME and a favorable safety profile that enables higher, more frequent and repeat dosing.

ADG126 SAFEbody is the most advanced clinical stage anti-CTLA-4 candidate integrating masking technology and Treg depletion for superior safety and efficacy profiles. A phase 2 dose expansion cohort is ongoing to evaluate ADG126 plus pembrolizumab in patients with MSS CRC without liver metastases.

About ADG126 & SAFEbody Technology

SAFEbody technology is designed to address safety and tolerability challenges of antibody therapeutics by minimizing on-target off-tumor toxicity in healthy tissues. ADG126 is a masked anti-CTLA-4 therapy that applies the SAFEbody precision-masking technology to its parental antibody, ADG116, for conditional activation in the TME to expand the therapeutic index by addressing dose dependent toxicity issues that severely limit the dosage and dosing cycles for effective anti-CTLA-4 therapies.

Binding to the same distinct and highly conserved epitope as ADG116, the masked ADG126 is designed to provide enhanced safety and efficacy profiles due to the combination of the potent Treg depletion in the TME and partial ligand blocking by the activated ADG126, which is accumulated steadily for the prolonged tumor killing effect.

Clinical results together with detailed pharmacokinetic analyses support the unique mechanism of action for ADG126 and its profile as a potential best-in-class anti-CTLA-4 therapy.

* *Microsatellite stable colorectal cancer (MSS CRC) accounts for approximately 95% of metastatic colorectal cancer patients. MSS tumors are referred to as 'cold' tumors, which means they don't typically trigger a strong response from the body's immune system. There is no currently approved immune-oncology treatment for MSS CRC.*

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.

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Safe Harbor Statement

This press release contains forward-looking statements, including statements regarding certain clinical results of ADG126, 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 filings 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.

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