Adagene Announces Clinical Data at SITC 2022 on Anti-CTLA-4 NEObody™, ADG116, Showing Differentiated Safety and Anti-tumor Activity in Heavily Pre-treated Patients with Difficult-to-Treat Tumors

November 10, 2022

- Interim phase 1b/2 data report safety profile of ADG116 across dosing levels, with repeat dosing of more than four cycles both as monotherapy and in combination with anti-PD-1 therapy -

- Results include two partial responses as monotherapy in Kaposi's sarcoma and renal cell carcinoma, and a confirmed, durable complete response in combination with toripalimab in recurrent head and neck squamous cell carcinoma -

- Preliminary update on study evaluating ADG116 in combination with pembrolizumab shows potent activity in MSS-CRC, with no dose limiting toxicities -

SAN DIEGO and SUZHOU, China, Nov. 10, 2022 (GLOBE NEWSWIRE) -- Adagene Inc. ("Adagene") (Nasdaq: ADAG), a company transforming the discovery and development of novel antibody-based therapies, today announced clinical data from phase 1b/2 studies of its anti-CTLA-4 antibody candidate, ADG116, in two poster presentations at the Society for Immunotherapy of Cancer's (SITC) Annual Meeting taking place in Boston.

One poster titled "*A Phase 1b/2 Study of a Novel Anti-CTLA-4 NEObody™ ADG116 Monotherapy and in Combination with Toripalimab (Tori; Anti-PD-1 Antibody) in Patients with Advanced/Metastatic Solid Tumors*" reviewed data from an open label, phase 1b/2 dose escalation and dose expansion trial evaluating ADG116 as monotherapy and in combination with toripalimab in heavily pre-treated patients with advanced metastatic solid tumors.

Comprehensive monotherapy safety data were reported in 50 patients at escalating doses of ≤6mg/kg (n=24), 10 mg/kg (n=23) and 15 mg/kg (n=3) to build a solid understanding of ADG116 safety in context of the known dose-dependent toxicity of anti-CTLA-4 therapy, especially the late-onset toxicity with repeat dosing across different dose levels. The safety and preliminary efficacy readout included patients with over 20 different tumor types, the majority (64%) of whom received three or more lines of prior therapies and over one third (36%) of whom progressed from prior immuno-oncology (IO) therapy. Combination data from dose escalation of ADG116 plus the anti-PD-1 therapy, toripalimab, were also reported from nine heavily pre-treated patients, close to half (44%) of whom received three or more lines of prior therapy.

Key findings as of the data cutoff date on September 19, 2022 include:

- ***Compelling, differentiated safety profile demonstrated with ADG116 monotherapy up to 15 mg/kg***: ADG116 is well tolerated across dose levels with repeat dosing. Grade 1/2 and Grade 3/4 treatment-related adverse events (TRAEs) were reported in 28 (56%) and 3 (6%) patients, respectively. With repeat dosing and tracking for late-onset toxicities in the same 10mg/kg cohort, the overall rate of Grade 3 or higher TRAEs is 13%. For reference, the reported rate of TRAEs Grade 3 and higher for the currently approved anti-CTLA-4 therapy, ipilimumab, is approximately 36% at 10 mg/kg in first-line monotherapy in melanoma patients[1] . There were no Grade 3 or higher TRAEs reported at the 15 mg/kg dose level for ADG116 monotherapy.

- ***Monotherapy efficacy shown in heavily pre-treated patients***: Among 36 efficacy evaluable patients, an initial partial response was observed after two cycles of treatment in a Kaposi's sarcoma patient who was one of three treated with ADG116 monotherapy at 15 mg/kg. The overall disease control rate (DCR) was 33% across all monotherapy dose levels, with additional tumor reduction observed in patients with both warm and cold tumors.

  Of special note, an additional partial response was observed as of November 2, 2022 in a patient with renal cell carcinoma who progressed after two prior lines of therapy, including an anti-PD-L1 inhibitor. The patient received four cycles of ADG116 monotherapy at 10 mg/kg with no Grade 3 or higher TRAEs reported.

- ***Combination dosing optimization advances:*** ADG116 was dosed every three weeks at 3 mg/kg or 6 mg/kg in combination with 240 mg of toripalimab (N=9). Although ADG116 with toripalimab at 6 mg/kg did not meet the target toxicity level (TTL) (i.e., lower rate of Grade 3 or higher TRAEs than those approved for anti-CTLA-4 and anti-PD-1 combination therapies), 3 mg/kg of ADG116 every three weeks with toripalimab was both manageable within the TTL and demonstrated impressive efficacy in difficult-to-treat tumors. Further dose optimization is planned, including ongoing evaluation of an extended dosing interval of ADG116 every six weeks plus toripalimab to meet the desired TTL.

- ***Potential combination efficacy demonstrated in cold tumors, and an intriguing case study of a confirmed, durable complete response in head and neck cancer:*** Among seven efficacy evaluable combination therapy patients, one confirmed complete response was observed in a patient with platinum-refractory recurrent head and neck squamous cell carcinoma (HNSCC). The patient received 3 mg/kg of ADG116 in combination with toripalimab and was one of five efficacy evaluable patients at that dose at the cutoff date (Objective response rate = 20%; DCR = 100% for these difficult-to-treat

tumor types in heavily pretreated patient population). Lesions completely disappeared after two cycles of therapy, and the durable response has been maintained beyond six cycles.

Findings from a second poster, "*A Phase 1b/2, Open-Label, Dose Escalation and Expansion Study of an Anti-CTLA-4 NEObody™ADG116 in Combination with Pembrolizumab (Anti-PD-1 Antibody) in Patients with Advanced/Metastatic Solid Tumors: A Preliminary Update"*, established a safe and potentially active dose level for ADG116 in combination with pembrolizumab.

Data evaluating ADG116 in combination with pembrolizumab in six heavily pre-treated patients primarily with cold tumors further support the differentiated safety profile of ADG116 dosed at 3 mg/kg every three weeks, and its efficacy potential when combined with pembrolizumab at a flat dose of 200 mg. No TRAEs higher than Grade 3 were reported and no DLT was observed.

Additionally, significant changes were observed in a tumor-related biomarker in two patients with metastatic microsatellite-stable (MSS) colorectal cancer (CRC), who experienced a 43% and 27% reduction in carcinoembryonic antigen (CEA) levels, respectively. Both patients had either liver or lung metastases and remain on treatment. The data support continued evaluation of ADG116 plus pembrolizumab as a combination of anti-CTLA-4 and anti-PD-1 therapies that may improve outcomes in certain patients with difficult-to-treat tumor types such as MSS-CRC observed here.

"These data provide compelling clinical evidence for our unique approach to targeting a distinct and highly conserved epitope of CTLA-4 with NEObody ADG116 to achieve enhanced anti-CTLA-4 blockade for both improved efficacy and safety profiles in single agent and combination settings, when combined with two different anti-PD-1 therapies," said Peter Luo, Ph.D., Co-founder, Chief Executive Officer and Chairman of Adagene. "These data further support our effort to optimize the dosing regimens ofADG116 in combination with anti-PD-1 therapy, as well as the intensified clinical development of its masked version, ADG126, in tumor types where encouraging anti-tumor efficacy is observed but current anti-CTLA-4 therapy is not approved or ineffective due to safety and/or efficacy reasons."

Both posters presented at SITC are available on Adagene's website at www.adagene.com/pipeline/publications.

References

[1] Ascierto PA, et al. J Immunother Cancer 2020;8:e000391. doi:10.1136/jitc-2019-000391

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.

Safe Harbor Statement

This press release contains forward-looking statements, including statements regarding certain clinical results of ADG116, the potential implications of clinical results of the product candidate, and Adagene's advancement of, and anticipated clinical development, regulatory milestones and commercialization of Adagene pipeline 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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Source: Adagene Inc.