Adagene Presents Clinical Data Demonstrating Strong Safety and Early Signals of Efficacy in Cold Tumors Including Pancreatic and Ovarian Cancers for Anti-CTLA-4 Monoclonal Antibody, ADG116, at ESMO-IO 2021

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- Additional highlights include pharmacodynamic biomarker analyses from ongoing trial of anti-CD137 antibody, ADG106, in combination with anti-PD-1 toripalimab -

SAN DIEGO and SUZHOU, China, Dec. 06, 2021 (GLOBE NEWSWIRE) -- Adagene Inc. ("Adagene") (Nasdaq: ADAG), a platform-driven, clinical-stage biopharmaceutical company committed to transforming the discovery and development of novel antibody-based immunotherapies, today announced clinical data on its anti-CTLA-4 monoclonal antibody, ADG116, and anti-CD137 agonist, ADG106, in two poster presentations at the European Society for Medical Oncology Immuno-Oncology (ESMO-IO) Congress 2021, to be held virtually and in Geneva, Switzerland from December 8 to 11, 2021. Both posters are available in the Publications section of the company's website at www.adagene.com.

In the first presentation of results from an ongoing dose-escalation trial of monotherapy in patients with advanced metastatic tumors, ADG116 demonstrated a strong safety profile and early signals of efficacy, including dose-dependent T-cell activation and tumor suppression in treatment-resistant "cold" and "warm" tumors such as pancreatic, ovarian and renal cell cancers.

Commenting on the findings, Dr. Gary Richardson, OAM, MBBS, FRACP, Group Director at Cabrini Health Research, Director at Szalmuk Family Department of Medical Oncology and Professor of Medicine at Monash University, Australia, "These encouraging clinical data demonstrate the promising safety profile of ADG116 monotherapy in patients with advanced solid tumors across 15 different tumor types, the majority of which are resistant to standard therapy. The most exciting thing about these results is that we have also seen the early signals of efficacy in 'cold' tumors such as pancreatic and certain gynecological cancers, which do not respond to current immunotherapies. We want to see this type of unique activity, which suggests that this treatment may look different and potentially better than the options we have available today."

Additionally, a separate poster presentation describing results of pharmacodynamic (PD) biomarker analyses reinforced the synergy and strong T-cell activation of ADG106 in combination with the anti-PD-1 antibody toripalimab.

A summary of data from both posters is included below.

ADG116

Key findings from the poster (#137P) titled "Phase 1 dose-finding study of a novel anti–CTLA-4 antibody ADG116 as monotherapy in patients with advanced solid tumors" include:

- Clinical results from a global dose escalation and cohort expansion trial with sites in the U.S. and Australia (ADG116-1003) evaluated ADG116 monotherapy in 25 heavily pre-treated patients with advanced metastatic solid tumors, the majority of which are insensitive to immunotherapy:
    - Patients across 15 different tumor types were evaluated.
    - The majority (68 percent) received three or more lines of prior systemic therapy.
    - Nearly one quarter (24 percent) received prior immunotherapy treatment.
- ADG116 monotherapy was well-tolerated up to 6 mg/kg with only Grade 1 or 2 treatment-related adverse events (TRAEs) observed; rash (20 percent) and pruritus (20 percent) were the most common.
- In the ongoing 10 mg/kg cohort, a rash (Grade 3) and dose limiting toxicity event (Grade 4 hyperglycemia) occurred in a patient with renal cell carcinoma who relapsed on nivolumab. A significant increase in the patient's CD8 T cells after one cycle of treatment showed that ADG116 is highly active for triggering T cell activation.
- ADG116 treatment resulted in dose-dependent increases in peripheral CD8 and CD4 T cells, indicating immune activation by targeting the CTLA-4 pathway, starting at a dose as low as 0.03 mg/kg and becoming more striking at the 6 mg/kg and 10 mg/kg dose levels. In one example, a patient refractory to multiple cycles of pembrolizumab treated at 0.03 mg/kg showed increased CD8 and CD4 T cells.
- In the dose escalation portion of the trial, four prolonged stable diseases were observed amongst these heavily pre-treated patients.
- Of special note is a 22 percent tumor reduction observed in target lesions (after the data cut-off on October 15, 2021) following two cycles of ADG116 for a pancreatic cancer patient treated at 10 mg/kg. Only Grade 1 TRAEs were observed and the patient's non-target lesion (23 x 12mm) disappeared. The patient continues on treatment.

- Additionally, an ovarian cancer patient treated at 6mg/kg showed stable disease for more than 116 days with increased CD8 and CD4 T cells. The patient continues on treatment.
- ADG116 demonstrated dose-proportional increases in drug exposure with a half-life supporting convenient dosing every three weeks.

The findings support that ADG116 has achieved the recommended dosing range as a single agent and for evaluation in combination therapy. The ADG116-1003 trial continues with dose escalation at 10 mg/kg, while cohort expansion has been initiated at 6 mg/kg.

Adagene is also advancing ADG116 in combination with anti-PD-1 therapy (pembrolizumab or toripalimab) and with its proprietary anti-CD137 agonist (ADG106). Further, the company is evaluating a second anti-CTLA-4 antibody, ADG126, using its SAFEbody® precision masking technology in an ongoing phase 1 dose escalation as monotherapy. This reflects the company's commitment to unlock the value of CTLA-4 as a proven target and the backbone of future immunotherapies.

ADG106

Key findings from the poster (#43P) titled "Assessment of Biomarker Kinetics for ADG106 (anti-CD137 agonist) as monotherapy or combined with toripalimab" include:

- Results of PD biomarker analyses which demonstrated the synergistic effect of ADG106 in combination with an anti-PD-1 antibody, toripalimab, compared to ADG106 monotherapy at doses up to 3 mg/kg.
- The combination of ADG106 with toripalimab resulted in a 2-fold greater immune activation versus ADG106 alone. These results were observed even amongst patients who failed prior anti-PD-1 and CTLA-4 therapies.
- Soluble CD137 levels (sCD137) levels increased with immune activation suggesting this as a dose-dependent PD biomarker of T cell target engagement, which could be used to monitor potential clinical response.
- ADG106 treatment alone and in combination with anti-PD-1 therapy also increased serum IFN-γ, IL-6, natural killer cells, and T-cell subsets.
- Additional analyses demonstrate that the pharmacokinetic profile of ADG106 was not altered by the addition of toripalimab.

These findings highlight the synergistic activity of ADG106 in combination with the anti-PD-1 toripalimab for patients who failed anti-PD-1 and anti-CTLA-4 immunotherapies. This combination is being evaluated in the ongoing ADG106-1008 clinical trial, currently in a cohort dosing ADG106 at 3 mg/kg. The data support further exploration of combination therapy regimens with ADG106 at informed dose ranges for targeting biomarker enriched tumor types.

"The data presented today from two of our NEObody™ clinical programs show how we are creating transformative antibody-based immunotherapies that push the limits of antibody discovery and development, overcoming liabilities with some of the most promising yet challenging immuno-oncology targets today," said Peter Luo, Ph.D., Co-founder, Chief Executive Officer and Chairman of Adagene. "These findings strengthen confidence in our clinical pipeline and in the ability of our platform technologies to achieve unprecedented results that will ultimately benefit patient care."

About ADG116

This NEObody program, targeting a unique epitope of CTLA-4, is being evaluated in patients with advanced/metastatic solid tumors. ADG116 is designed to enhance efficacy by potent Treg depletion in the tumor microenvironment (TME) and maintain its physiological function by soft ligand blocking to address safety concerns associated with existing CTLA-4 therapeutics.

About ADG106

This NEObody program is a fully human ligand-blocking, agonistic anti-CD137 IgG4 monoclonal antibody (mAb) that is being evaluated in patients with advanced solid tumors and/or non-Hodgkin's lymphoma.

About Adagene

Adagene Inc. (Nasdaq: ADAG) is a platform-driven, clinical-stage biopharmaceutical 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.

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 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. 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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