Adagene Announces Clinical Advancement for ADG116

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-NEObody™ product candidate ADG116 has been well tolerated in ongoing Phase 1 clinical trial-
-Promising pharmacodynamic biomarker signals demonstrate clinical proof of mechanism-
-Poised for global expansion-

SAN FRANCISCO and SUZHOU, China, March 29, 2021 (GLOBE NEWSWIRE) -- Adagene Inc. (Nasdaq: ADAG), a platform-driven, clinical-stage biopharmaceutical company committed to transforming the discovery and development of novel antibody-based immunotherapies, today announced the interim dose-escalation data up to 0.3 mg/kg in its ongoing Phase 1 clinical trial in Australia evaluating the safety and tolerability of ADG116 in patients with advanced/metastatic solid tumors. ADG116 is a fully human, anti-CTLA-4 monoclonal antibody (mAb), designed to target a unique conserved epitope of CTLA-4 and utilizes Adagene's proprietary NEObody platform technology. ADG116 is designed to balance safety and efficacy through a novel mechanism of action; ADG116 maintains its original physiological function via partial blocking of CTLA-4 ligand binding, and in conjunction, depletes T_{reg} in the tumor microenvironment via strong antibody-dependent cellular cytotoxicity (ADCC).

Interim data for the ongoing Phase 1 clinical trial:

- **Safety:** Analysis of all safety data generated to date demonstrates that ADG116 has been well-tolerated in more than 10 patients with no dose-limiting toxicities or unexpected safety signals. No drug related Grade 3 and Grade 4 toxicities have been observed.
- **Notable findings in pharmacodynamics:** A dose-dependent change in $CD8^+$ and $CD4^+$ T_{EM} / T_{reg} ratios, important pharmacodynamic (PD) biomarkers indicating immune activation, was observed for patients dosed by ADG116. In particular, a patient, refractory to prior pembrolizumab therapy (> 25 cycles), demonstrated striking increases in T and NK cells, and $CD8^+$ and $CD4^+$ T_{EM} / T_{reg} ratios. The Grade 1 treatment-related pruritus of this patient is a clinical symptom consistent with immune-mediated action of ADG116 treatment.
- **Pharmacokinetics:** The terminal half-life of ADG116 was within the normal range of IgG1 based antibodies.
- **Clinical proof of mechanism:** The Phase 1 dose escalation data demonstrates the clinical proof of mechanism for ADG116 in targeting CTLA-4, consistent with preclinical observations for the potency of ADG116 starting from 0.03 to 0.3 mg/kg.

"We are encouraged by the positive PD marker signals and safety data," said Peter Luo, Ph.D., Co-founder, Chief Executive Officer and Chairman of Adagene. "It is particularly striking to observe immune activation biomarkers at 0.03 mg/kg, especially in the patient refractory to prior pembrolizumab therapies. We believe ADG116 has the potential to overcome the limitations of anti-CTLA-4 checkpoint inhibitors, extending the market potential beyond current anti-CTLA-4 inhibitors in both monotherapy and combination settings. Our highly differentiated anti-CTLA-4 therapeutics hold the potential to improve the clinical benefits by expanding clonal diversity, infiltrating into cold tumors, and treating patients resistant/refractory to current immuno-therapies."

"We look forward to developing a comprehensive clinical program to evaluate each of our anti-CTLA-4 assets," continued Dr. Luo. "We will leverage the modality-specific features demonstrated in the preclinical setting, that enable high-fidelity translation into the clinic by targeting unique, highly conserved epitope of CTLA-4 with broad species cross-reactivity. We remain committed to maximizing the full potential of our unique anti-CTLA-4 approach."

The progression of the Phase 1 dose-escalation trial to the 5^{th} dose, a 0.3mg/kg dose level, builds on encouraging signs of PD markers, normal PK data, strong early clinical data, extensive preclinical and safety tolerability data and a successful Safety Review Committee meeting. Multiple clinical sites are currently open in Australia. In this ongoing Phase 1 clinical trial of ADG116 in patients with advanced/metastatic solid tumors, no dose-limiting toxicity (DLT), treatment-related serious adverse events (SAEs), colitis or hepatitis have been observed. With favorable clinical data to date, Adagene looks forward to expanding the ongoing global Phase 1 trial, with the acceptance of revised study protocol by FDA to expand the trial in the U.S. Adagene has also obtained confirmation from China NMPA to proceed with revised protocol submission at higher starting dose than that in the original submission. Additional information about this clinical trial is available at ClinicalTrials.gov using the identifier: NCT04501276.

About ADG116
ADG116 is a fully human ligand-blocking anti-CTLA-4 mAb generated using NEObody technology. ADG116 is a differentiated anti-CTLA-4 approach, which leverages Adagene's Dynamic Precision technology to target a conserved epitope with broad species cross-reactivity for translational fidelity and a unique CTLA-4 mechanism of action. In preclinical studies, ADG116 was observed to have softer CTLA-4 ligand blocking and stronger ADCC for depleting regulatory T-cells than ipilimumab. In a head-to-head *in vivo* efficacy study, ADG116 was observed to have at least a five-fold greater preclinical antitumor activity in comparison with ipilimumab. In preclinical studies, ADG116 was well tolerated in rats and cynomolgus monkeys in four-week repeat-dose GLP toxicology studies at doses up to 30 mg/kg, and demonstrated an encouraging antitumor response in multiple immune-competent mouse tumor models in a dose-dependent manner both as a single agent (showing initial response at 0.02mg/kg, and complete response at 0.1 mg/kg for tumor size of ~100mm^3 in sensitive tumor models) and in combination with other therapies.

About Adagene
Adagene Inc. 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 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 data from the ADG116 preclinical studies and Phase 1 clinical trial, the potential implications of clinical data for patients, and Adagene's advancement of, and anticipated clinical development, regulatory milestones, and commercialization of ADG116. 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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