Adagene Announces First Patient Dosed in Randomized Dose Optimization Cohort of the Phase 2 Study of Muzastotug (ADG126) in Combination with KEYTRUDA® (pembrolizumab) in Microsatellite Stable Colorectal Cancer

October 31, 2025

Phase 2 clinical trial underway with first patient dosed in October to support a clear path to Phase 3 based on previous alignment with FDA

Patients randomized to either 10 or 20 mg/kg of muzastotug, in combination with KEYTRUDA with up to 30 patients per arm

Company anticipates trial completion in early 2027, and potential updates in 2026

Additional updates from the ongoing Phase 1b/2 trial with muzastotug, previously reported at ASCO 2025, are anticipated in the coming months

SAN DIEGO and SUZHOU, China, Oct. 31, 2025 (GLOBE NEWSWIRE) -- Adagene Inc. ("Adagene") (Nasdaq: ADAG), a company transforming the discovery and development of novel antibody-based therapies, today announced that the first patient has been dosed in its randomized, open label Phase 2 study of muzastotug in combination with Merck's (known as MSD outside of the United States and Canada) anti-PD-1 therapy, KEYTRUDA® (pembrolizumab) in patients with microsatellite stable colorectal cancer (MSS CRC) with no liver metastases. The Phase 2 primary endpoint is overall response rate (ORR).

"We are pleased that the randomized Phase 2 trial is now underway in order to confirm the preferred dose for Phase 3 in compliance with Project Optimus," stated Peter Luo, Ph.D., CEO and President of R&D at Adagene. "To date, muzastotug has been safely dosed at 20 mg/kg Q6W, with less than 20% Grade 3 adverse events and no discontinuations, supporting its position as the potential best in class Treg depleting anti-CTLA-4 agent with improved therapeutic window. Our approach was further highlighted by the recent 2025 Nobel Prize in physiology awarded for the seminal discovery of regulatory T cells function, consistent with the MOA of muzastotug, leveraging CTLA-4 mediated intratumoral regulatory T cell depletion strategy to treat cancer. We look forward to sharing additional data from the ongoing Phase 1b/2 to provide further evidence that muzastotug's improved safety profile allows for higher dosing and potentially better efficacy, which has precluded the use of first-generation anti-CTLA-4 therapies in this setting."

As previously announced in July 2025, both the Phase 2 and Phase 3 trial designs and endpoints were confirmed following a meeting with the US Food and Drug Administration (FDA):

- ***Patient Population:*** Future trials will enroll late-line patients with MSS CRC without liver metastases, including those with peritoneal metastasis/involvement.
- ***Dose and Regimen:*** Phase 2 dose optimization cohort will randomize patients to either 10 mg/kg or 20 mg/kg of muzastotug in combination with pembrolizumab, using an induction-maintenance regimen, without cycle limitations of muzastotug.
- ***Phase 2 Trial Design:*** Up to 30 patients will be enrolled in each arm of the Phase 2 study, without a requirement for a muzastotug monotherapy arm.
- ***Phase 3 Trial Design:*** The FDA agreed with Adagene's proposed standard-of-care (SOC) control arm for the Phase 3 clinical trial and confirmed that a muzastotug monotherapy arm was also not required.
- ***Phase 2 Endpoints:*** The primary endpoint of the Phase 2 trial will be overall response rate (ORR). Secondary endpoints include duration of response (DOR), progression-free survival (PFS), and overall survival (OS).
- ***Phase 3 Endpoints:*** The primary endpoint of the Phase 3 trial will be OS. Secondary endpoints will include PFS, DOR and ORR.

Phase 1b/2 Trial

As reported at ASCO in June 2025, in the Phase 1b/2 trial (NCT05405595), a total of 67 MSS CRC patients with no liver metastases including those with peritoneal involvement were treated with muzastotug at a dose of either 10 mg/kg or 20 mg/kg, in combination with pembrolizumab: 200 mg, Q3W. The 10 mg/kg dose was administered once every three weeks or once every six weeks. The 20 mg/kg dose was administered once as a loading dose, followed by 10 mg/kg every three weeks, or 20 mg/kg as a consistent dose every six weeks.

In the dose expansion phase of the study, patients in the 10 mg/kg Q3W cohort demonstrated an overall response rate (ORR) of 17% and patients in the 20 mg/kg cohorts demonstrated a confirmed ORR of 29%. Median duration of response (DoR) in the 10 mg/kg cohorts was 6.2 months, while the mDoR was not yet reached in the 20 mg/kg cohorts and all the responses were ongoing. Median overall survival (OS) for the 10 mg/kg cohorts was 19.4 months, comparing favorably with current treatments and historical benchmarks. Median OS for the 20 mg/kg cohorts has not yet been reached.

Both 20 mg/kg cohorts, with either a 20 mg/kg loading dose followed by 10 mg/kg Q3W, or 20 mg/kg as a consistent dose Q6W, achieved equivalent ORRs at 29%, while adverse events were less severe and seen less frequently with Q6W dosing compared to a 20mg/kg loading dose followed by 10mg/kg Q3W.

The ASCO 2025 poster and presentation can be found on the company's website. The company anticipates providing additional updates on the Phase 1b/2 study in the coming months.

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 globally unmet patient needs. The company has forged strategic collaborations with reputable global partners that leverage its SAFEbody precision masking technology in multiple approaches at the vanguard of science.

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. The company's SAFEbody technology is designed to address safety and tolerability challenges associated with many antibody therapeutics by using precision masking technology to shield the binding domain of the biologic therapy. Through activation in the tumor microenvironment, this allows for tumor-specific targeting of antibodies, while minimizing on-target off-tumor toxicity in healthy tissues.

Adagene's lead clinical program, ADG126 (muzastotug), is a masked, anti-CTLA-4 SAFEbody that targets a unique epitope of CTLA-4 in regulatory T cells (Tregs) in the tumor microenvironment. ADG126 is currently in phase 1b/2 clinical studies in combination with anti-PD-1 therapy, particularly focused on Metastatic Microsatellite-stable (MSS) Colorectal Cancer (CRC). Validated by ongoing clinical research, the SAFEbody platform can be applied to a wide variety of antibody-based therapeutic modalities, including Fc empowered antibodies, antibody-drug conjugates, and bi/multispecific T-cell engagers.

For more information, please visit: https://investor.adagene.com.
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