March 7, 2024

Mustang Bio Announces Publication in Nature Medicine of Data from Phase 1 Trial Evaluating MB-101 IL13Rα2-targeted CAR T-Cells in High-Grade Glioma

MB-101 was well-tolerated and 50% of patients achieved stable disease or better with two partial responses and two complete responses lasting 7.5 and 66+ months, respectively

~70% improvement in median overall survival compared to expected survival rate in cohort with dual intratumoral (ICT)/ intraventricular (ICV) delivery and an optimized manufacturing process

This is the largest reported trial to date of CAR-T therapy for solid tumors

WORCESTER, Mass., March 07, 2024 (GLOBE NEWSWIRE) -- Mustang Bio, Inc. ("Mustang") (Nasdaq: MBIO), a clinical-stage biopharmaceutical company focused on translating today's medical breakthroughs in cell and gene therapies into potential cures for difficult-to-treat cancers and rare genetic diseases, today announced Phase 1 clinical data were published in *Nature Medicine* that demonstrated the promising safety and clinical activity of Mustang's MB-101 (IL13Ra2-targeted CAR T-cells) for the treatment of patients with recurrent and refractory malignant glioma, including glioblastoma.

MB-101 was developed by City of Hope, one of the largest cancer research and treatment organizations in the United States, and exclusively licensed to Mustang.

Highlights from the data include:

- Stable disease or better was achieved in 50% (29/58) of heavily pretreated patients for at least two months, with two partial responses, one complete response (CR), and a second CR after additional CAR-T cycles under compassionate use.
- Patients with recurrent GBM treated in the final cohort with dual intratumoral (ICT)/ intraventricular (ICV) delivery and an optimized manufacturing process exhibited superior median overall survival of 10.2 months, compared to the expected survival rate of six months in patients with recurrent GBM. The median overall survival for all patients was eight months.
- Intermediate/high pre-treatment tumor T-cell levels that are indicative of a "hot" tumor microenvironment (TME) correlated with a significant survival benefit over negative/low

pre-treatment tumor T-cell levels that are indicative of a “cold” TME.
- Overall, all routes of delivery (ICT, ICV and dual ICT + ICV) were well-tolerated at doses up to 200×10^6 CAR T-cells.
- Central nervous system (CNS) increases in inflammatory cytokines, including IFNγ, CXCL9, and CXCL10, were associated with CAR T-cell administration and bioactivity.

Dr. Christine Brown, Heritage Provider Network Professor in Immunotherapy, deputy director of the T-Cell Therapeutics Research Laboratories at City of Hope, and lead author on the publication, said, “These Phase 1 clinical trial results represent a significant step forward in our understanding of the potential of MB-101 CAR T-cell therapy to treat recurrent GBM, an extremely aggressive tumor with very limited treatment options. One of the main challenges for treating brain cancer is that medications have difficulty crossing the blood-brain barrier. To overcome that barrier, the trial delivered CAR T-cells directly into the brain tumor and the cerebrospinal fluid, the fluid that protects and surrounds the brain and spinal cord. Repetitive locoregional administration of IL13Rα2-CAR T-cells was feasible and well-tolerated with no dose limiting toxicities, even at the highest dose level of 200×10^6 CAR T-cells per infusion. The safety and promising therapy-related bioactivity data pave the way for future studies of MB-101 and offer hope for a transformative treatment approach. We look forward to continuing our work with Mustang on this promising therapy.”

Manuel Litchman, M.D., President and Chief Executive Officer of Mustang, said, “MB-101 has demonstrated compelling therapeutic potential, including delivering unprecedented complete responses in two high-grade glioma patients; the first patient who achieved a complete response was published in *The New England Journal of Medicine*. These two patients treated solely with MB-101 both had high levels of intratumoral CD3+ T-cells pre-therapy (i.e., “hot” tumors) and achieved complete responses lasting 7.5 and 66+ months, respectively. This trial has led to several other studies using MB-101, including supporting our upcoming novel combination clinical trial of MB-109 [MB-101 (IL-13Rα2 targeted CAR T-cell therapy) + MB-108 (HSV-1 oncolytic virus)] to improve treatment of recurrent GBM and high-grade astrocytoma. The combination leverages initial treatment with MB-108 to reshape the tumor microenvironment and make immunologically “cold” tumors “hot,” thereby potentially enabling the MB-101 CAR T-cell therapy to achieve efficacy equivalent to that seen in intrinsically “hot” tumors in this City of Hope Phase 1 trial.”

The data reported on 65 patients with recurrent high-grade glioma, the majority being glioblastoma (GBM; 2 + recurrences); 58 patients were evaluable for disease response. Primary endpoints were safety and feasibility, with secondary endpoints measuring therapy-related cytokine dynamics, CAR T-cell persistence and clinical outcomes. Patients were treated at one of three dose schedules with three weekly infusions administered without prior lymphodepleting chemotherapy and were evaluated one week after the third cycle for dose limiting toxicities. Additional infusions were allowed, and patients were followed for toxicities, response, and survival until they progressed or required subsequent therapy. This study evaluated five treatment arms: Arm 1, intratumoral following biopsy (ICT Biopsy); Arm 2, intratumoral following maximal surgical resection (ICT Resection); Arm 3, intraventricular (ICV); and Arms 4 and 5, combined ICT and ICV delivery (Dual ICT + ICV). ICV delivery (Arm 3) was added after trial initiation based on clinical experience, in which IL13Rα2-CAR T-cells that were administered ICV mediated a complete response in a patient with multifocal recurrent GBM, and preclinical data suggested ICV was more effective against multifocal tumors. Subsequently, City of Hope transitioned to dual delivery combining both ICV and

ICT (Arms 4–5) – rather than continuing with ICV alone – as preclinical data also suggested that intratumoral delivery was more effective for defined unifocal tumors in comparison to ICV-only delivery.

Weekly ICT and/or ICV administration of IL13Rα2-CAR T-cells was well-tolerated, with clinically manageable adverse events. No high-grade cytokine release syndrome or immune effector cell-mediated neurotoxicity adverse events were observed, and no dose limiting toxicities (DLTs) were noted during the 28-day dose limiting toxicity period. The most common toxicities with possible or higher attribution to CAR T-cells were fatigue, headache, and hypertension. Grade 3 and above toxicities with possible or higher attribution to CAR T-cells were seen in 35% of patients, including two incidences of transient grade 4 cerebral edema with possible attribution to CAR T-cells and one grade 3 encephalopathy and one grade 3 ataxia with probable attribution to CAR T-cells.

A link to the *Nature Medicine* publication can be found here.

Dr. Brown has a financial interest in Mustang and has previously been a paid consultant for the company.

Additional information on the Phase 1 study can be found on **www.ClinicalTrials.gov** using identifier **NCT02208362**.

About Mustang Bio

Mustang Bio, Inc. is a clinical-stage biopharmaceutical company focused on translating today's medical breakthroughs in cell and gene therapies into potential cures for difficult-to-treat cancers and rare genetic diseases. Mustang aims to acquire rights to these technologies by licensing or otherwise acquiring an ownership interest, to fund research and development, and to outlicense or bring the technologies to market. Mustang has partnered with top medical institutions to advance the development of CAR-T therapies across multiple cancers, as well as lentiviral gene therapies for severe combined immunodeficiency. Mustang's common stock is registered under the Securities Exchange Act of 1934, as amended, and Mustang files periodic reports with the U.S. Securities and Exchange Commission ("SEC"). Mustang was founded by Fortress Biotech, Inc. (Nasdaq: FBIO). For more information, visit www.mustangbio.com.

Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. Such statements, which are often indicated by terms such as "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "look forward to," "may," "plan," "potential," "predict," "project," "should," "will," "would" and similar expressions. The Company's forward-looking statements, include, but are not limited to, any statements relating to our growth strategy and product development programs, including the timing of and our ability to make regulatory filings such as INDs and other applications and to obtain regulatory approvals for our product candidates, statements concerning the potential of therapies and product candidates and any other statements that are not historical facts. Actual events or results may differ materially from those described in this press release due to a number of risks and uncertainties. Risks and uncertainties include, among other things, risks related to the satisfaction of the conditions necessary to transfer the lease of the Company's manufacturing facility and receive the contingent payment in connection with the

Company's sale of its manufacturing facility in the anticipated timeframe or at all; whether the purchaser of the Company's manufacturing facility is able to successfully perform its obligation to produce the Company's products under the manufacturing services agreement on a timely basis and to acceptable standards; disruption from the sale of the Company's manufacturing facility making it more difficult to maintain business and operational relationships; negative effects of the announcement or the consummation of the transaction on the market price of the Company's common stock; significant transaction costs; the development stage of the Company's primary product candidates, our ability to obtain, perform under, and maintain financing and strategic agreements and relationships; risks relating to the results of research and development activities; risks relating to the timing of starting and completing clinical trials; uncertainties relating to preclinical and clinical testing; our dependence on third-party suppliers; our ability to attract, integrate and retain key personnel; the early stage of products under development; our need for substantial additional funds; government regulation; patent and intellectual property matters; competition; as well as other risks described in Part I, Item 1A, "Risk Factors," in our Annual Report on Form 10-K filed on March 30, 2023, subsequent Reports on Form 10-Q, and our other filings we make with the SEC. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law, and we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

Company Contacts:
Jaclyn Jaffe and Nicole McCloskey
Mustang Bio, Inc.
(781) 652-4500
ir@mustangbio.com

Source: Mustang Bio, Inc.