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Mustang Bio Announces a Phase 1 Clinical Trial Combining MB-101 (IL13Rα2-targeted CAR T cell therapy) and MB-108 (C134 oncolytic virus) for the Treatment of Glioblastoma

MB-101 (IL13Rα2-targeted CAR T cell therapy) and MB-108 (C134 oncolytic virus) are well tolerated in patients with recurrent GBM in ongoing Phase 1 clinical trials

Data support potential of MB-109, the combination of MB-101 + MB-108, to optimize treatment

Research presented by City of Hope's Dr. Christine Brown at the American Association for Cancer Research (AACR) Annual Meeting 2022

WORCESTER, Mass., April 13, 2022 (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 hematologic cancers, solid tumors and rare genetic diseases, today announced its plan to initiate a Phase I clinical trial combining CAR T cells and oncolytic virus for the treatment of recurrent glioblastoma (rGBM), supported by interim data from two ongoing investigator-sponsored Phase 1 clinical trials evaluating two clinical candidates, MB-108 (C134 oncolytic virus) and MB-101 (City of Hope's IL13Rα2-targeted CAR T cell therapy). Preclinical data also presented support the safety of administering these two therapies sequentially in a regimen designated as MB-109. The data are from a late-breaking poster at the American Association for Cancer Research ("AACR") Annual Meeting 2022.

"The data presented at the AACR Annual Meeting support the initiation of a Phase I clinical trial to evaluate combining locoregional delivery of MB-108 and MB-101 as an attractive strategy for improving outcomes for patients with rGBM. We are excited to build on the interim clinical safety and feasibility data for administering either single agent MB-101 or MB-108, as well as to take advantage of the potential of oncolytic viral therapy to make the tumor immunologically 'hot' since clinical data suggest that CAR T cells may be more effective in an inflamed tumor microenvironment," said Christine Brown, Ph.D., Deputy Director, T Cell Therapeutics Research Laboratory, Professor, Departments of Hematology & Hematopoietic Cell Transplantation and Immuno-Oncology, and The Heritage Provider

Network Professor in Immunotherapy at City of Hope, one of the largest cancer research and treatment organizations in the United States.

Outcomes presented by Dr. Brown from each of the clinical candidates are as follows:

MB-101 (IL13Rα2-targeted CAR T cell therapy)
City of Hope's Phase 1 clinical trial (NCT02208362) evaluated the feasibility and safety of repetitive administration of locoregionally delivered MB-101 in 65 heavily pretreated patients with recurrent or refractory malignant glioma, the majority of which were rGBM. Following maximal surgical resection / biopsy, dose escalating schedules of MB-101 were administered weekly either intratumorally ("ICT"), intraventricularly ("ICV") to the cerebrospinal fluid, or to both sites (dual ICT/ICV). Infusions appeared to be well tolerated with clinically manageable flu-like symptoms and two grade 3 events (transient encephalopathy and ataxia) possibly related to the CAR T cells. Optimization of manufacturing and administration in the final cohort of 19 evaluable patients suggest MB-101 provides a possible survival benefit versus historical controls. Two patients with high levels of intratumoral CD3+ T cells pre-therapy achieved complete responses lasting 7.5 and 31+ months, respectively.

MB-108 (C134 oncolytic virus)
University of Alabama at Birmingham ("UAB") researchers are conducting a Phase 1 clinical trial (NCT03657576) evaluating MB-108 for rGBM that will enroll up to 24 patients. Today's poster highlights one clinical trial participant who received a single infusion of MB-108 that was well-tolerated. MRI changes at approximately 7 weeks post-treatment could not discriminate between tumor progression and pseudoprogression. Therefore, the patient underwent tumor biopsy 7 weeks post treatment that showed necrotic areas in tumor after treatment with MB-108. Immune infiltrates, both treated and untreated, evaluated by flow cytometry at that time point suggested that MB-108-treated tumor regions exhibited T cell immune recruitment differences when compared to an untreated region, with increased numbers of CD3+ CD8+ effector T cells that express granzyme B and lower numbers of naïve T cells.

MB-109 (MB-101 (IL-13Rα2) + MB-108 oncolytic virus)
Preclinical data from orthotopic GBM models in nude mice show that pre-treatment with MB-108 re-shaped the tumor microenvironment by increasing immune cell infiltrates, and the overall treatment with MB-109 gave no adverse reactions. These data also show that MB-109 combination therapy could be safely administered at low doses and leads to tumor shrinkage. An upcoming Mustang-sponsored Phase 1 clinical trial will evaluate the safety, tolerability, feasibility and preliminary efficacy of MB-109 in patients with IL13Rα2-positive relapsed or refractory GBM and anaplastic astrocytoma. Correlative studies will evaluate whether the combination approach can modify the tumor microenvironment, facilitate CAR T cell trafficking, and mitigate tumor immune escape by antigen loss.

Manuel Litchman, M.D., President and Chief Executive Officer of Mustang, said, "Recurrent GBM remains a major challenge to treat with a median overall survival rate of 6 months. We thank Dr. Christine Brown for presenting the potential of our three clinical candidates at today's AACR Annual Meeting on behalf of the academic institutions researching these prospective treatment options. The MB-101 and MB-108 programs continue to enroll patients in Phase 1 clinical trials at City of Hope and UAB, respectively. Given the preclinical study outcomes, future efforts will include the combination therapy MB-109, for which we

plan to file an Investigational New Drug application later this year."

About MB-101 (IL13Rα2-targeted CAR T cells)
MB-101 is an IL13Rα2-targeted CAR T cell therapy developed by Dr. Brown and her City of Hope colleagues for treating GBM. It is the first CAR T cell therapy to demonstrate complete responses in GBM based on City of Hope's Phase 1 trial (NCT02208362), with Dr. Behnam Badie, Professor and Chief, Division of Neurosurgery, as the Principal Investigator. IL13Rα2 is a GBM-restricted receptor expressed abundantly on the majority of GBM tumors. Mustang is developing MB-101 as an optimized CAR T product incorporating City of Hope's enhancements in CAR design and T cell engineering to improve antitumor potency and T cell persistence. MB-101 includes a second-generation hinge-optimized CAR containing mutations in the IgG4 linker to reduce off-target Fc interactions, the 4-1BB (CD137) co-stimulatory signaling domain for improved persistence of CAR T cells and the extracellular domain of CD19 as a selection/safety marker. To further improve persistence, naïve and memory T cells are enriched and genetically engineered using a manufacturing process that limits *ex vivo* expansion to reduce T cell exhaustion and maintain a memory T cell phenotype. Ongoing MB-101 malignant glioma clinical trials under City of Hope's IND include a study in patients with leptomeningeal disease (NCT04661384) and a combination study with checkpoint inhibitors (NCT04003649).

About MB-108 (C134 oncolytic virus)
Developed by Dr. Kevin Cassady, Professor of Pediatrics at Nationwide Children's Hospital, and his colleagues for the treatment of malignant brain cancers, MB-108 (C134 oncolytic virus) is a second-generation attenuated herpes simplex virus type 1 (HSV-1) oncolytic virus that has improved replication in tumors in murine models, but with a similar toxicity profile as its first-generation predecessors. MB-108 preferentially replicates in tumor cells over non-malignant cells, thereby killing the infected tumor cells and causing the tumor cell to act as a factory to produce new virus. MB-108 can also induce pro-inflammatory signals and chemotaxis, thereby theoretically improving CAR T infiltration into the tumor mass. In February 2019, Mustang entered into a licensing agreement with Nationwide Children's Hospital for worldwide development rights to C134 oncolytic virus, including but not limited to developing MB-108 for the treatment of GBM, and a Phase 1 clinical trial is currently ongoing at the University of Alabama at Birmingham in patients with recurrent disease (NCT03657576), with Dr. James Markert, Professor and Chair, Department of Neurosurgery, as the Principal Investigator.

About MB-109 (MB-101 (IL-13Rα2) + MB-108 oncolytic virus)
MB-109 is Mustang's designation for the treatment regimen combining MB-101 (IL13Rα2-targeted CAR T cells) CAR T cell therapy with MB-108 (C134 oncolytic virus). The combination is designed to leverage MB-108 to make cold tumors "hot," as described above, and thereby improve the efficacy of MB-101 CAR T cell therapy. MB-108 oncolytic virus is first injected to infect tumor cells which, in turn, leads to reshaping of the tumor microenvironment (TME) through recruitment of endogenous CD8-positive effector T cells. This inflamed TME permits MB-101 CAR T cells injected into and around the tumor to better infiltrate into and throughout the tumor mass, undergo activation and effect tumor cell kill. Mustang intends to file a Phase 1 Investigational New Drug application for MB-109 combination therapy in the second half of 2022 for the treatment of IL13Rα2-positive relapsed or refractory GBM and anaplastic astrocytoma.

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 hematologic cancers, solid tumors 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 is registered under the Securities Exchange Act of 1934, as amended, and 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 may contain "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 include, but are not limited to, any statements relating to our growth strategy and product development programs and any other statements that are not historical facts. Forward-looking statements are based on management's current expectations and are subject to risks and uncertainties that could negatively affect our business, operating results, financial condition and stock value. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to our growth strategy; 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 our SEC filings. 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 Bill Begien
Mustang Bio, Inc.
(781) 652-4500
ir@mustangbio.com

Investor Relations Contact:
Daniel Ferry
LifeSci Advisors, LLC
(617) 430-7576
daniel@lifesciadvisors.com

Media Relations Contact:
Tony Plohoros

6 Degrees
(908) 591-2839
tplohoros@6degreespr.com

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