MEI Pharma Reports Initial Data from Clinical Study Evaluating ME-344 in Combination with Bevacizumab (Avastin®) in Relapsed Metastatic Colorectal Cancer Patients

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– Cohort 1 Exceeds Predetermined Non-Progression Threshold in the Ongoing Phase 1b Study –

– ME-344 in Combination with Bevacizumab was Generally Well-tolerated with no Evidence of Overlapping Toxicity –

– MEI to Continue Advancing ME-344 via Development of a New Formulation with the Potential to Increase Biological Activity, Patient Convenience and Commercial Opportunity –

SAN DIEGO--(BUSINESS WIRE)--Apr. 11, 2024-- MEI Pharma, Inc. (Nasdaq: MEIP), a clinical-stage pharmaceutical company evaluating novel drug candidates to address known resistance mechanisms to standard-of-care cancer therapies, today reported that 25% of evaluable patients with relapsed metastatic colorectal cancer (“mCRC”) in Cohort 1 of the ongoing Phase 1b study evaluating ME-344, an investigational inhibitor of mitochondrial oxidative phosphorylation (“OXPHOS”), in combination with bevacizumab (Avastin®) had no disease progression at Week 16. This landmark analysis exceeded the 20% threshold set in the Clinical Study Protocol to add an additional 20 patients to the study via the initiation of Cohort 2. The combination was also observed to be generally well-tolerated to date. While the threshold was met to proceed to Cohort 2, it was separately reported today that following a strategic review, the Company decided to continue to advance ME-344 development via its ongoing development of a new formulation rather than through the addition of a new cohort. The Company believes this represents the optimal approach to leveraging the potential of the program. The Company has already initiated research and development activity of the new formulation with encouraging results, with the goal of increasing biological activity, improving convenience of administration and increasing commercial opportunity.

"The data reported today, including progression-free survival, overall survival, and safety results of the combination, represent an important development supporting the potential of ME-344 in combination with Avastin to induce synthetic lethality in tumors using a completely novel therapeutic strategy,” said Richard Ghalie, chief medical officer of MEI Pharma. “The development of a new formulation with enhanced biologic activity is aimed at further improving patient outcomes and treatment convenience in a well-tolerated manner.”

“At MEI we are committed to our mission of developing novel drug candidates to address known resistance mechanisms to standard-of-care cancer therapies, and ME-344 holds significant potential as a novel therapeutic strategy to advance this mission,” said David Urso, president and chief executive officer of MEI Pharma. “We believe that the best approach to optimize the potential of ME-344 for patients, prioritize resource utilization, and build value for shareholders, is to continue advancing the program via development of a new formulation of ME-344. In the short term, this plan will reduce expenditures on the ME-344 program and ultimately, if successful, create an improved formulation for continued clinical development.”

Phase 1 Study Details

The ongoing Phase 1b study is evaluating ME-344 in combination with bevacizumab in patients with relapsed metastatic colorectal cancer (“mCRC”) after failure of standard therapies. The combination of ME-344 and bevacizumab is intended to create metabolic synthetic lethality by leveraging the ability of antiangiogenics like bevacizumab to reduce glycolysis, forcing tumors to switch to mitochondrial respiration via OXPHOS, which is

inhibited by ME-344.

The study was designed to evaluate ME-344 plus bevacizumab in up to two cohorts of approximately 20 patients each. The option to enroll the second cohort was conditioned upon Cohort 1 reaching a predetermined non-progression threshold of at least 20% at four months. Patients in the study are treated until disease progression or intolerability. The primary endpoint of the study is 16-week progression free survival (“PFS”), and secondary endpoints include overall PFS, duration of response, overall survival and safety.

ME-344 is administered at 10 mg/kg once weekly for 3 weeks in combination with bevacizumab every two weeks in 28-day cycles. Cohort 1 enrolled a total of 23 patients with relapsed mCRC, with a median age 58 years (range 42-83). Patients were generally heavily pretreated; the median number of prior lines of therapy was 4 (range 1-8), 18 (78%) patients had ≥3 prior lines, and all patients had previously received bevacizumab and standard chemotherapy.

In the first cohort, 5 of 20 (25%) evaluable patients completed 16 weeks of therapy without evidence of disease progression, exceeding the 20% predetermined threshold as set forth in the Clinical Study Protocol to proceed to Cohort 2. Although Cohort 1 exceeded the predetermined PFS threshold, the Company decided not to initiate enrollment in a second cohort in favor of continuing to advance ME-344 development via a new formulation. Two patients are currently enrolled in Cohort 1.

The Phase 1b study is being conducted at member centers of the Academic GI Cancer Consortium (AGICC), an oncology consortium dedicated to identifying new drugs to treat gastrointestinal cancers.

ME-344 Plus Bevacizumab Combination: Initial Safety and Tolerability Data

ME-344 in combination with bevacizumab at the dose and schedule evaluated was generally well tolerated with no overlapping toxicities observed. Two patients (9%) discontinued therapy due to an adverse event: fatigue considered related to study drugs and sepsis considered unrelated. The most common (≥10% of patients) drug-related adverse events (all grades/grade ≥3) were fatigue in 8 (35%) / 3 (13%) patients and abdominal pain in 3 (13%) / 2 (9%) patients.

ME-344 Plus Bevacizumab Combination: Initial Efficacy Data

Of the 23 patients enrolled in Cohort 1, three patients were not evaluable for 16-weeks disease progression analysis due to early discontinuation prior to first disease assessment on therapy. Of the 20 patients that were evaluable, 5 (25%) completed at least 16 weeks of therapy without disease progression, exceeding the predetermined threshold of 4 (20%) patients defined by the protocol as the condition to initiate enrollment in a second cohort. The median PFS was 1.9 months, the 4-month PFS rate was 31.2%, and the median overall survival was 6.7 months with 15 patients censored at the time of analysis. Nine (45%) of the 20 evaluable patients had stable disease.

About ME-344

ME-344, an investigational drug candidate, is a novel inhibitor of mitochondrial oxidative phosphorylation (OXPHOS), a fundamental metabolic pathway involved in the production of adenosine triphosphate (ATP) in the mitochondria. ATP provides energy to drive many metabolic cell processes, including division, proliferation, and growth. By disrupting the production of ATP, ME-344 has been shown to induce cancer cell death in nonclinical models and was associated with antitumor activity in clinical studies.

The two main sources of ATP production in cells are OXPHOS and glycolysis; the latter is highly active in most tumors. Anti-angiogenics, like the vascular endothelial growth factor (“VEGF”) inhibitor bevacizumab (Avastin®), have the potential to normalize vasculature and decrease reliance on glycolysis. The resulting reduction in glycolysis may trigger an increased dependence on mitochondrial ATP production for energy to support continued tumor proliferation. In such cases of tumor plasticity, the combination of ME-344 and bevacizumab may induce metabolic synthetic lethality, providing a novel therapeutic strategy. Specifically, leveraging the ability of antiangiogenics like bevacizumab to reduce glycolysis and force tumor cells to switch to mitochondrial respiration via OXPHOS, which is inhibited by ME-344, may reduce access to ATP needed for cell division and growth in tumors.

This approach was first clinically evaluated in a multicenter, investigator-initiated, randomized, open-label, window of opportunity clinical study, evaluating ME-344 (3 doses) plus bevacizumab (1 dose) in 42 women with early

HER2-negative breast cancer. Study results demonstrated significant biological antitumor activity as measured by a reduction in the proliferative biomarker Ki-67 compared to placebo. The combination appeared to be generally well tolerated. The data from this study were consistent with preclinical data suggesting that combining ME-344 can augment anti-angiogenic therapy and provided support for continued evaluation of the combination of ME-344 with bevacizumab and other VEGF inhibitors. An earlier Phase 1 clinical study evaluating ME-344 as a single-agent in patients with refractory solid tumors also demonstrated anti-tumor activity, further supporting the potential of inhibition of OXHPOS by ME-344 as a promising therapeutic modality.

About MEI Pharma

MEI Pharma, Inc. (Nasdaq: MEIP) is a clinical-stage pharmaceutical company committed to developing novel and differentiated cancer therapies. We build our pipeline by acquiring promising cancer agents and creating value in programs through development, strategic partnerships, out-licensing and commercialization, as appropriate. Our approach to oncology drug development is to evaluate our drug candidates in combinations with standard-of-care therapies to overcome known resistance mechanisms and address clear medical needs to provide improved patient benefit. The drug candidate pipeline includes voruciclib, an oral cyclin-dependent kinase 9 ("CDK9") inhibitor, and ME-344, a novel small molecule inhibitor of mitochondrial oxidative phosphorylation (OXPHOS). For more information, please visit www.meipharma.com. Follow us on X (formerly Twitter) @MEI_Pharma and on LinkedIn.

Forward-Looking Statements

Certain information contained in this press release that are not historical in nature are "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995 including, without limitation, statements regarding: the potential, safety, efficacy, and regulatory and clinical progress of our product candidates, including the anticipated timing for initiation of clinical trials and release of clinical trial data and our expectations surrounding potential regulatory submissions, approvals and timing thereof, our business strategy and plans; the sufficiency of our cash, cash equivalents and short-term investments to fund our operations; and our ability to fund future capital returns. You should be aware that our actual results could differ materially from those contained in the forward-looking statements, which are based on management's current expectations and are subject to a number of risks and uncertainties, including, but not limited to our failure to successfully commercialize our product candidates; the availability or appropriateness of utilizing the FDA's accelerated approval pathway for our product candidates; final data from our pre-clinical studies and completed clinical trials may differ materially from reported interim data from ongoing studies and trials; costs and delays in the development and/or FDA approval, or the failure to obtain such approval, of our product candidates; uncertainties or differences in interpretation in clinical trial results; uncertainty regarding the impact of rising inflation and the increase in interest rates as a result; potential economic downturn; geopolitical conflicts; activist investors; our inability to maintain or enter into, and the risks resulting from, our dependence upon collaboration or contractual arrangements necessary for the development, manufacture, commercialization, marketing, sales and distribution of any products; competitive factors; our inability to protect our patents or proprietary rights and obtain necessary rights to third party patents and intellectual property to operate our business; our inability to operate our business without infringing the patents and proprietary rights of others; general economic conditions; the failure of any products to gain market acceptance; our inability to obtain any additional required financing; technological changes; government regulation; changes in industry practice; and one-time events. We do not intend to update any of these factors or to publicly announce the results of any revisions to these forward-looking statements. Under U.S. law, a new drug cannot be marketed until it has been investigated in clinical studies and approved by the FDA as being safe and effective for the intended use.

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David A. Walsey
MEI Pharma
Tel: 858-369-7104
investor@meipharma.com

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