MEI Pharma Reports Update from Clinical Study Evaluating Oral CDK9 Inhibitor Voruciclib in Combination with Venetoclax in Patients with Relapsed and Refractory Acute Myeloid Leukemia

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– Enrollment Initiated in 12-Patient Expansion Cohort Evaluating Voruciclib Plus Venetoclax in Ongoing Phase 1 Study –

– Anti-leukemic Activity Across Multiple Heavily Pretreated Patients Demonstrated Along with Anticipated Decreases in Mcl-1 –

– No Evidence of Overlapping Toxicity, and No Dose Limiting Toxicities Observed to Date in Dose Escalation Cohorts –

SAN DIEGO--(BUSINESS WIRE)--Mar. 26, 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 initiation of enrollment in a 12-patient expansion cohort in the ongoing Phase 1 study evaluating voruciclib, an investigational selective oral cyclin-dependent kinase 9 ("CDK9") inhibitor, in combination with venetoclax (Venclexta®), a B-cell lymphoma 2 ("BCL2") inhibitor, in relapsed and refractory ("R/R") acute myeloid leukemia ("AML") patients. The Safety Review Committee recommended initiating the expansion cohort after observing anti-leukemic activity in multiple heavily pretreated patients in the dose escalation cohorts, including responses, anticipated decreases in myeloid leukemia cell differentiation protein ("Mcl-1") in available patient samples, no overlapping toxicity or dose limiting toxicities, and favorable safety results to date.

"MCL-1 overexpression has been associated with a poor prognosis and development of resistance to BCL-2 inhibition by venetoclax in patients with AML and CLL. Voruciclib is a potent, oral CDK9 inhibitor that indirectly also suppresses MCL-1. We are participating in the ongoing multicenter phase 1 study, where preliminary results are demonstrating good treatment tolerance and safety to date," said Yesid Alvarado-Valero, M.D., Associate Professor, Department of Leukemia, University of Texas MD Anderson Cancer Center and study chair of the combination therapy stage of the Phase 1 study. "When Voruciclib is used in combination with venetoclax, the combination appears to have no added toxicity, in addition there is evidence of synergistic, early clinical activity, with disease responses, in a group of heavily pretreated acute myeloid leukemia patients."

"Increasingly, venetoclax is being used as a standard treatment in patients with AML, but resistance to salvage therapy after venetoclax use is common and yields limited benefit upon relapse; only about 10% of patients respond to salvage therapy after venetoclax failure, representing a significant need for patients with AML," said Richard Ghalie, M.D., chief medical officer of MEI Pharma. "We see the voruciclib data to date demonstrating anti-leukemic activity as promising, particularly alongside the consistent reductions of Mcl-1 that provide evidence we are eliciting the anticipated biological response in patients, and we are excited to share additional updates as appropriate in the second half of 2024."

Dr. Ghalie continued: "As we enroll the expansion cohort evaluating the potential of voruciclib in combination with venetoclax among a larger group of patients, I would like to thank and recognize the continued engagement of our investigators, and the participation of the patients enrolling in this study."

Phase 1 Study Details

The Phase 1 study is a multiple stage, open-label, 3+3 dose escalation and expansion study evaluating voruciclib, an oral CDK9 inhibitor, as a monotherapy and in combination with venetoclax, a BCL2 inhibitor. The first stage of the study evaluated the dose and schedule of voruciclib as a single-agent in patients with AML or B-cell malignances after failure of standard therapies. This stage is complete.

The second stage of the study, evaluating voruciclib in combination with standard dose venetoclax in patients with R/R AML, has completed enrollment in the dose escalation cohorts evaluating seven voruciclib dose levels from 50 mg every other day to 300 mg daily for two weeks in a four-week cycle. The study is currently enrolling a 12-patient expansion cohort evaluating voruciclib administered at 300 mg daily for two weeks in a four-week cycle in combination with venetoclax. Considering the tolerability results for the combination to date, another arm of the study will evaluate escalating doses of voruciclib administered over three weeks in a four-week cycle in combination with venetoclax to increase dose intensity and potentially optimize patient response.

A total of 29 patients with R/R AML, median age 67 years (range 34-89), enrolled in the dose escalation stage of the study evaluating voruciclib in combination with venetoclax. These patients were generally heavily pretreated; the median number of prior therapies was 3 (range 1-7), and 15 (52%) patients had ≥3 prior lines. Almost all patients (28/29) were treated with venetoclax in an earlier line of therapy. Additionally, 21 (72%) patients were noted as being in an adverse 2017 ELN Risk Category due to adverse cytogenetics and molecular mutations.

The primary objectives of the study are to determine the safety and biologic effective dose of voruciclib monotherapy or voruciclib in combination with venetoclax. Secondary objectives of the study include assessing the preliminary efficacy, pharmacokinetics, pharmacodynamics, and biomarkers of voruciclib monotherapy or voruciclib in combination with venetoclax.

Voruciclib Plus Venetoclax Combination: Initial Safety and Tolerability Data

Voruciclib at doses up to 300 mg administered on 14 consecutive days in a 28-day cycle in combination with standard dose venetoclax was well tolerated with no dose limiting toxicities observed. The maximum tolerated dose of voruciclib administered on this schedule with venetoclax has not been established. There were no discontinuations due to drug-related adverse events. No evidence of overlapping toxicity has been observed to date. The most common (≥5% of patients) grade 3 adverse events were myelosuppression associated with AML. Only 1 patient was observed as having a non-hematologic grade 3 drug-related adverse event (diarrhea).

Voruciclib Plus Venetoclax Combination: Initial Efficacy Data

In the 20 patients administered voruciclib at a dose of 100 mg or more, three patients achieved a response, including two patients that achieved a complete response with incomplete hematologic recovery (CRi) and one patient that achieved a morphologic leukemia-free state (MLFS), in each case having received venetoclax in an earlier line of treatment. Responses lasted 7 months in one patient, 5 months and ongoing in the second patient, and the third patient was referred to stem cell transplant. Further, an additional 14 patients had stable disease which lasted more than 90 days in 5 patients.

In the patients administered voruciclib at a dose of 100 mg or more, initial results from correlative biomarker assay studies of available samples from patients treated with the combination demonstrate the anticipated decrease of Mcl-1. Further, the available assays from the dose escalation cohorts demonstrated dose proportional decreases in Mcl-1. Reductions in Mcl-1 are consistent with the known mechanism of action of CDK9, which regulates Mcl-1.

About Voruciclib

Voruciclib is an investigational orally administered cyclin-dependent kinase 9 (“CDK9”) inhibitor with potential to treat both hematological malignancies and solid tumors. It is in clinical development for acute myeloid leukemia and B-cell malignancies. Applications in solid tumors are also being considered.

The CDK family of proteins are important cell cycle regulators responsible for the control of cell proliferation, differentiation, apoptosis, and DNA repair. CDK9, one of several members of the CDK family of proteins, functions as a gene transcription controller and is also involved in regulating protein degradation. Specifically, CDK9 is a promising target to treat a range of cancers because of its role in controlling two other proteins often dysregulated in cancerous cells: myeloid leukemia cell differentiation protein (“Mcl-1”) and the MYC proto-oncogene protein ("MYC").

Mcl-1 is a member of the family of anti-apoptotic proteins which, when elevated, may prevent the cell from undergoing cell death. Inhibition of CDK9 blocks the production of Mcl-1, which is an established resistance mechanism to the B-cell lymphoma 2 ("BCL2") inhibitor venetoclax (marketed as Venclexta®).

MYC regulates cell proliferation and growth. Upregulation of MYC is implicated in many human cancers and is frequently associated with poor prognosis and unfavorable patient survival. CDK9, in addition to being a transcription factor for MYC, also decreases phosphorylation of MYC protein that is implicated in stabilizing MYC in KRAS mutant cancers. Targeting MYC directly has historically been difficult, but CDK9 is a promising approach to target this oncogene.

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, an intravenous small molecule mitochondrial inhibitor targeting the oxidative phosphorylation pathway. 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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