UAB and Mereo Announce Positive Top-line Results from "COSTA" a Phase 1b/2 Trial of Alvelestat (MPH966) in Hospitalized Patients with COVID-19 Respiratory Disease

Alvelestat reported safe and well-tolerated in patients with COVID-19

Alvelestat, on top of standard of care resulted in a more rapid time to improvement in WHO Disease Severity score of >=2 in the first 5-7 days compared to placebo plus standard of care

London and Redwood City, Calif., December 22, 2021 – The University of Alabama at Birmingham (UAB) and Mereo BioPharma Group plc (NASDAQ: MREO), today announced top-line data from a Phase 1b/2 clinical trial evaluating alvelestat, a novel, orally active Neutrophil Elastase (NE) inhibitor in hospitalized COVID-19 Respiratory Disease patients.

The COSTA Phase 1b/2 trial (NCT04539795) is an investigator-led, single-centre study (Principal Investigator Dr. James M Wells, Associate Professor in Pulmonary, Allergy and Critical Care Medicine, UAB). The trial is a double-blind, randomized, placebo-controlled study in adult patients (≥18 years) with COVID-19 Respiratory Disease, evaluating the safety and tolerability of alvelestat on top of Standard of Care in patients hospitalised with proven COVID-19 lung disease. Patients requiring mechanical ventilation were excluded. Enrolled subjects received alvelestat or matched placebo, twice daily, for 5 days, with optional extension to 10 days per investigator judgement. Initial subjects underwent dose escalation to evaluate safety and tolerability for the population. The Primary Endpoint was Safety and Tolerability to Day 60, with mortality assessment at Day 90. Secondary Endpoints were clinical outcomes to Day 60. Biomarkers of inflammation, coagulopathy, were measured; biomarkers of neutrophil extracellular traps (NETs) were explored and desmosine was measured to the end of study drug treatment. The study was signal seeking and not powered for the secondary measures.

Fifteen patients were randomized (10 male, 5 female), and all completed the Primary Endpoint Safety assessment to Day 60 and the Day 90 final study assessment. The original design involved a 2:1 active to placebo ratio, however patients were enrolled 1:1 resulting in 8 patients on alvelestat and 7 patients on placebo. The mean age was 47.8 years; the most common co-morbidities were hypertension, sleep apnea, hypercholesterolemia, and Type 2 diabetes. At entry to the study, all patients were requiring supplemental oxygen, all had initiated dexamethasone and 14 were on antiviral treatment with remdesivir at baseline or initiated after randomization (7/7 on placebo and 7/8 on alvelestat). The majority of patients were WHO COVID-19 Ordinal Severity Scale Score 4 (hospitalized mild disease requiring supplemental oxygen) or 5 (hospitalized severe disease, requiring non-invasive ventilation or high flow oxygen) at entry to the study.

TRIAL RESULTS HIGHLIGHTS

Primary Endpoint: Safety and Tolerability to Day 60

- Consistent with the known safety profile of alvelestat, no safety signals were observed in lab safety monitoring, including none in liver, renal and vital sign parameters.
- Treatment emergent headaches were more frequent in the alvelestat arm (4/8 - all of moderate severity) compared to placebo (1/8 of mild severity). Three patients in the alvelestat arm were noted to also have headache in the screening period. None were considered study-drug related by the investigator. There was no difference in frequency of other adverse events between alvelestat and placebo arms to Day 60.

- A single SAE of hospital readmission for acute hypoxemic respiratory failure COVID-19 was reported in the alvelestat arm and was not considered drug related by the investigator.
- There were no deaths on study (to end of study assessment at Day 90).

Secondary Efficacy Endpoints:

Clinical Outcome Measures

- In the alvelestat arm 62.5% (5/8) patients had a 2-point decrease in the WHO Disease Severity score by Day 5, compared to 28.5% (2/7) patients in the placebo arm. At Day 7 this improvement in WHO Severity score increased to 87.5% (7/8) in the alvelestat arm and 57% (4/7) in the placebo arm.

Inflammatory Biomarkers

- The pro-inflammatory blood biomarker, Interleukin-6 was elevated in this population and decreased in the alvelestat arm from baseline at end of treatment compared to an increase from baseline for placebo (p=0.193). Consistent with this response, a greater reduction in C-reactive Protein was observed in alvelestat compared to placebo (p=0.143) In addition, there was a reduction in D-Dimer in the alvelestat arm in comparison to the placebo arm which increased over the treatment period (p=0.199). These biomarkers support an early-onset of effect of alvelestat on the inflammatory and pro-coagulopathy pathways. The majority of the other inflammatory biomarkers were not elevated at baseline, as expected for patients treated with dexamethasone and consequently no clear changes with treatment could be observed. TNF-alpha which was elevated at baseline, showed a reduction in both alvelestat and placebo arms (p value NS).

Other Biomarkers

- Desmosine was not elevated in the majority of patients at baseline in the alvelestat arm and consequently no treatment effect could be detected.
- Detailed analysis of blood biomarkers of NETosis, generally within the normal range at baseline, is ongoing.

“There remains a significant unmet need to improve the outcomes of hospitalized patients with COVID-19. The early results with alvelestat suggest a potential for clinical benefit over and above standard of care including dexamethasone and remdesivir. This is exciting given the ease of administration of a well-tolerated oral therapy in this acutely ill population,” said Dr. Mike Wells, Associate Professor in Pulmonary, Allergy and Critical Care Medicine, UAB. “These findings provide strong data and set the stage for future studies with relevant clinical end-points.”

“These data whilst early and in a small study, are highly encouraging as the first evidence that alvelestat could offer clinical outcome benefit over and above standard of care in patients hospitalized with COVID-19,” said Dr. Denise Scots-Knight, Chief Executive Officer at Mereo. “This clearly warrants further evaluation in a larger study. We are grateful to the patients who participated in this study and to Dr Mike Wells and his team at UAB for leading this important work,”

About Alvelestat

Alvelestat is currently being investigated in two Phase 2 studies (ASTRAEUS and ATALANTa) for patients with alpha-1 antitrypsin deficiency (AATD) and a Phase 1b/2 for patients with bronchiolitis obliterans syndrome (BOS) following hematopoietic stem cell transplant. Mereo noted that both high and low doses of alvelestat in the ASTRAEUS Phase 2 study have shown good safety to-date and the study has now recruited 99 patients and per protocol, enrollment has been biased towards the high dose. Top-line data for ASTRAEUS continue to be expected in early Q2 2022.

About Mereo BioPharma

Mereo BioPharma is a biopharmaceutical company focused on the development and commercialization of innovative therapeutics that aim to improve outcomes for oncology and rare diseases. The Company has developed a portfolio of six clinical stage product candidates. Mereo's lead oncology product candidate, etigilimab (anti-TIGIT), has advanced into an open label Phase 1b/2 basket study evaluating anti-TIGIT in combination with an anti-PD-1 in a range of tumor types including three rare tumors and three gynecological carcinomas, cervical, ovarian, and endometrial carcinomas. The Company's second oncology product, navicixizumab, for the treatment of late line ovarian cancer, has completed a Phase 1 study and has been partnered with OncXerna Therapeutics, Inc., formerly Oncologie, Inc. The Company has two rare disease product candidates, alvelestat for the treatment of severe Alpha-1 antitrypsin deficiency (AATD) and setrusumab for the treatment of osteogenesis imperfecta (OI). Alvelestat has recently received U.S. Orphan Drug Designation for the treatment of AATD and is being investigated in an ongoing Phase 2 proof-of-concept study in the U.S. and Europe, with top-line data now expected in early Q2 2022. The Company's partner, Ultragenyx Pharmaceutical, Inc., is expected to initiate a pivotal pediatric study for setrusumab in OI before the end of 2021.

Forward-Looking Statements

This press release contains "forward-looking statements." All statements other than statements of historical fact contained in this press release are forward-looking statements within the meaning of Section 27A of the United States Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the United States Securities Exchange Act of 1934, as amended (the "Exchange Act"). Forward-looking statements relate to future events, including, but not limited to, statements regarding future clinical development, efficacy, safety, and therapeutic potential of clinical product candidates, including expectations as to reporting of data, conduct and timing and potential future clinical activity and milestones and expectations regarding the initiation, design and reporting of data from clinical trials. Forward-looking statements are often identified by the words "believe," "expect," "anticipate," "plan," "intend," "foresee," "should," "would," "could," "may," "estimate," "outlook" and similar expressions, including the negative thereof. The absence of these words, however, does not mean that the statements are not forward-looking. These forward-looking statements are based on the Company's current expectations, beliefs and assumptions concerning future developments and involve risks and uncertainties that could cause actual results, performance, or events to differ materially from those expressed or implied in such statements. You should carefully consider the foregoing factors and the other risks and uncertainties that affect the Company's business, including those described in the "Risk Factors" section of its latest Annual Report on Form 20-F, reports on Form 6-K and other documents furnished or filed from time to time by the Company with the Securities and Exchange Commission. You should not place undue reliance on any forward-looking statements, which speak only as of the date hereof. The Company undertakes no obligation to publicly update or revise any forward-looking statements after the date they are made, whether as a result of new information, future events or otherwise, except to the extent required by law.

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