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Evelo Biosciences to enter Ph2/3 trials for EDP1815 to treat COVID-19

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EDP1815 therapy has been observed to have favourable tolerability and anti-inflammatory activity as part of TACTIC-E clinical trial for combating COVID-19

Evelo Biosciences, Inc. a clinical stage biotechnology company developing a new modality of orally delivered, systemically acting biologic therapies, announced on 24 June 2020 that EDP1815 will be included in the TACTIC-E clinical trial. The trial will evaluate the safety and efficacy of certain experimental therapies in the prevention and treatment of life-threatening complications associated with COVID-19 in hospitalized patients at early stages of the disease. The trial's lead investigator is Dr. Joseph Cheriyan, Consultant Clinical Pharmacologist at Addenbrooke's Hospital in Cambridge, and is sponsored by Cambridge University Hospitals NHS Foundation Trust.

Dr. Cheriyan said, " TACTIC-E will test the effectiveness of a number of experimental medicines in patients admitted to hospital, with a strong focus on identifying novel and clinically useful drugs early on. It will collect high-quality data that can be used by our partner pharmaceutical companies to potentially seek approvals for widespread international use. We have opted to investigate EDP1815 in this trial given the tolerability and the modulation of multiple inflammatory pathways observed in a Phase 1b clinical trial for psoriasis. We look forward to evaluating EDP1815 as part of TACTIC-E."

TACTIC-E is a Phase 2/3 randomised trial which will evaluate up to 469 patients per arm at Addenbrooke's Hospital and other leading UK clinical centres. The trial will enroll patients with COVID-19 who have identified risk factors for developing severe complications and are at risk of progression to the intensive care unit or death. Eligible patients will be randomised equally to either one of the active arms or treated with standard of care alone. Patients in arm 1 will be dosed with EDP1815 in addition to standard of care; patients in arm 2 will be dosed with a combination of ambrisentan and dapagliflozin in addition to standard of care; and patients in arm 3 will be treated with standard of care only. The primary outcome measure is a reduction in the number of patients who develop severe complications of organ failure, ventilation, or death. Secondary outcome measures include duration of stay in hospital, duration of oxygen therapy, changes in biomarkers associated with COVID-19 progression, and time to clinical improvement. Interim analyses will be performed over the course of the trial to evaluate results for signals of safety and efficacy.

Interim data from the trial are anticipated during the fourth quarter of 2020. If the Phase 2/3 data are positive, Evelo plans to engage in discussions with global regulatory agencies to determine if the data support registration.

“The recent results with dexamethasone suggest that an oral agent, such as EDP1815, with potentially broad antiinflammatory effects, could help prevent the severe complications of COVID-19, reducing the impact of the disease on individual patients and the demand on hospitals,” said Mark Bodmer, Ph.D., chief scientific officer of Evelo. “EDP1815 has the potential to address the complex inflammatory chaos associated with cytokine storm in COVID19 without immunosuppression. In a prior clinical trial in psoriasis, EDP1815 was well tolerated with no overall difference in safety findings from placebo. EDP1815’s mechanism of action may make it suitable for early intervention in COVID-19 patients who have not yet been shown to benefit from anti-inflammatory therapy. If EDP1815 is successfully developed and approved, it can be manufactured at scale and at an affordable cost, which could potentially address a large patient population. We want to thank Addenbrooke’s Hospital and the wider TACTIC team for their collaboration and interest in including EDP1815 in this trial.”

Scientific and Clinical Rationale for EDP1815 in COVID-19

The progression to severe COVID-19 is associated with cytokine storm and hyperinflammation. Based on data from a Phase 1b clinical trial in psoriasis, EDP1815 has the potential to modulate multiple immune pathways associated with cytokine storm and resolve the inflammation without the risks associated with immunosuppression.

In a Phase 1b clinical trial in psoriasis, EDP1815 limited the production of multiple inflammatory cytokines, including IL-6, IL-8, TNF, and IL-1b. It was well tolerated with no overall difference from placebo. In preclinical models, EDP1815 resolved inflammation across TH1, TH2, and TH17 pathways. This led to down-regulation of multiple cytokines including TNF, IL-4, IL-5, IL-6, IL-12p40, IL-13, and IL-17. Several of these cytokines have been implicated in the cytokine storm associated with severe complications of COVID-19. In these models, no activity was observed on type 1 interferons, which are important for anti-viral responses.

EDP1815 is designed to harness the connections between intestinal mucosal immunology and systemic inflammation for broad inflammation resolution without immunosuppression. It is potentially unique amongst therapies currently being tested in COVID-19 patients for this mechanism of action, which, if approved, could result in a safe, effective, oral, and affordable product.

If EDP1815 is approved for the treatment of COVID-19, Evelo could rapidly scale its manufacturing to supply the drug at a reasonable cost. Additionally, if the COVID-19 trial is successful, the Company plans to investigate EDP1815 as a potential therapy for other diseases, such as influenza, in which cytokine storm and hyperinflammation play a role.