Evelo Biosciences Announces EDP1815 to Advance into Phase 2/3 TACTIC-E COVID-19 Trial

June 22, 2020

—Phase 2/3 platform trial sponsored by Cambridge University Hospitals NHS Foundation Trust—
—Experimental therapies with potential to prevent and treat complications of COVID-19—
—EDP1815 selected as one of two experimental therapies in the trial—
—EDP1815 has been observed to have favorable tolerability and anti-inflammatory activity in a prior clinical trial—
—Interim data expected in fourth quarter of 2020—

CAMBRIDGE, Mass. and LONDON, June 22, 2020 (GLOBE NEWSWIRE) -- Evelo Biosciences, Inc. (Nasdaq:EVLO) a clinical stage biotechnology company developing a new modality of orally delivered, systemically acting biologic therapies, announced today 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, "This is a critical time in the fight against COVID-19, and I am delighted that Cambridge is playing a key role in this. 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 anti-inflammatory 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 COVID-19 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.

About TACTIC-E
TACTIC-E is a platform Phase 2/3 trial in the UK that targets patients hospitalised with COVID-19 who are at high-risk of progression to the intensive care unit (ICU) and/or death. TACTIC-E will evaluate unlicensed drugs and novel combinations of licensed drugs with sufficient pre-clinical and clinical data to suggest a positive benefit-risk ratio in the treatment of COVID-19.

Update on EDP1815-205
In addition to the TACTIC-E trial, an Investigational New Drug (IND) application has been submitted for an Evelo-sponsored Phase 2 clinical trial, EDP1815-205, evaluating the safety and efficacy of EDP1815 for the treatment of hospitalised patients with newly diagnosed COVID-19 at Robert Wood Johnson University Hospital in New Brunswick, NJ. On June 17, the US Food and Drug Administration (FDA) issued a clinical hold letter directing Evelo to make certain revisions to the protocol for the trial, including alterations to the inclusion criteria for enrollment. The Company intends

to amend the protocol to address the FDA's comments and, provided the FDA agrees that the issues are adequately addressed, anticipates initiating the trial in July 2020, with data in 4Q 2020.

About Evelo Biosciences
Evelo Biosciences is a clinical stage biotechnology company developing oral biologics that act on SINTAX™, the small intestinal axis, with systemic therapeutic effects. SINTAX plays a central role in governing the immune, metabolic and neurological systems. The company's first product candidates are pharmaceutical preparations of single strains of microbes selected for defined pharmacological properties. Evelo's therapies have the potential to be effective, safe, and affordable medicines to improve the lives of people with inflammatory diseases and cancer.

Evelo currently has four product candidates in development: EDP1815, EDP1867, and EDP2939 for the treatment of inflammatory diseases, and EDP1503 for the treatment of cancer. Evelo is advancing additional product candidates in other disease areas.

For more information, please visit www.evelobio.com and engage with Evelo on LinkedIn.

Forward Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements concerning the development of EDP1815 for the treatment of patients with COVID-19, our development plans, the promise and potential impact of any of our monoclonal microbials or preclinical or clinical trial data, the timing of and plans for clinical studies of EDP1815, and the timing and results of any clinical studies or readouts, and the scalability of manufacturing for EDP1815.

These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: the impact of the COVID-19 pandemic on our operations, including our preclinical studies and clinical trials, and the continuity of our business; we have incurred significant losses, are not currently profitable and may never become profitable; our need for additional funding; our limited operating history; our unproven approach to therapeutic intervention; the lengthy, expensive, and uncertain process of clinical drug development, including potential delays in completing clinical trials or in seeking or obtaining regulatory approval; our reliance on third parties and collaborators to expand our microbial library, conduct our clinical trials, manufacture our product candidates, and develop and commercialize our product candidates, if approved; our lack of experience in manufacturing, selling, marketing, and distributing our product candidates; failure to compete successfully against other drug companies; protection of our proprietary technology and the confidentiality of our trade secrets; potential lawsuits for, or claims of, infringement of third-party intellectual property or challenges to the ownership of our intellectual property; our patents being found invalid or unenforceable; risks associated with international operations; our ability to retain key personnel and to manage our growth; the potential volatility of our common stock; our management and principal stockholders have the ability to control or significantly influence our business; costs and resources of operating as a public company; unfavorable or no analyst research or reports; and securities class action litigation against us.

These and other important factors discussed under the caption "Risk Factors" Report on Form 10-Q for the quarter ended March 31, 2020, and our other reports filed with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, except as required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

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