Evelo Biosciences Reports Positive Topline Clinical Data in Phase 1b Trial of EDP1815 in Atopic Dermatitis

–Treatment with EDP1815 demonstrates statistically and clinically significant improvement in mean EASI and IGA BSA scores–*

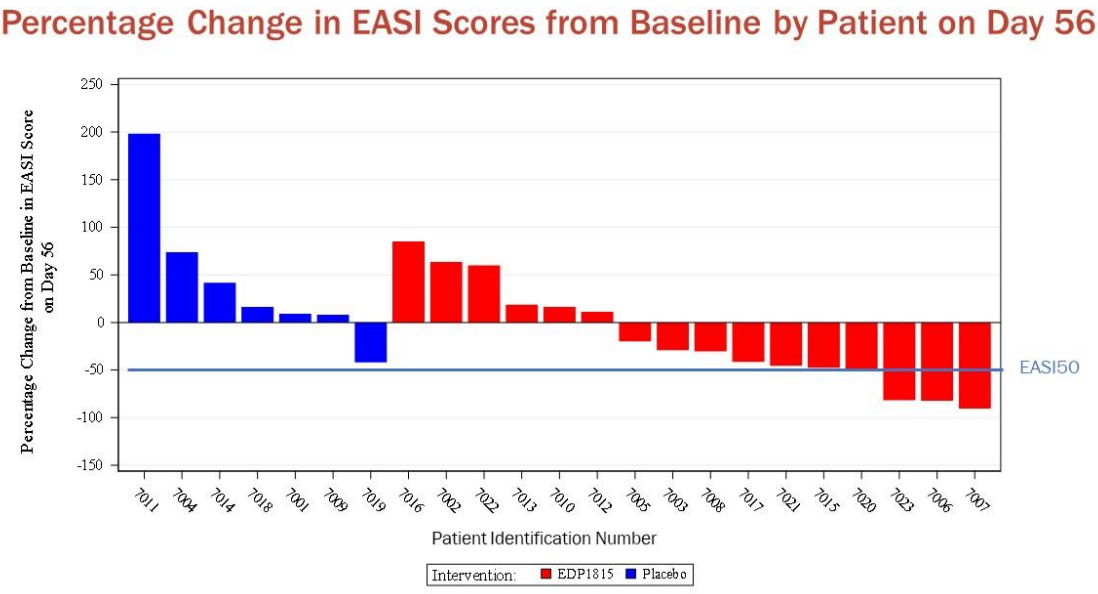
–EDP1815 first-ever candidate targeting SINTAX™ to show clinical activity in Th1, Th2, and Th17-mediated inflammation–

–Further validates platform and potential new modality of medicine –

– Management to host conference call at 9:00 a.m. ET today to discuss clinical results and company strategy –

CAMBRIDGE, Mass., December 9, 2020 – Evelo Biosciences, Inc. (Nasdaq:EVLO), a clinical stage biotechnology company developing a new modality of orally delivered product candidates which act in the small intestine with systemic effects, today announced positive topline clinical data from its Phase 1b clinical trial of EDP1815 in 23 evaluable subjects with mild to moderate atopic dermatitis. The primary endpoint of the Phase 1b trial was safety and tolerability. EDP1815 was observed to be well tolerated with no serious adverse events.

Secondary endpoints included a range of established markers of clinical efficacy in atopic dermatitis, such as the percentage change in Eczema Area and Severity Index (EASI) score, which is the most common tool used to measure extent and severity of atopic eczema, and the percentage change in Investigator's Global Assessment and Body Surface Area (IGA* BSA). Clinical differences between EDP1815 and placebo for evaluable subjects were statistically significant at day 56 in both the percentage change in EASI (62% difference, p=0.034) and the percentage change in IGA*BSA (71% difference, p=0.019). Improvements in these measures were observed as early as day 14. At day 56, 10/16 patients in the active group showed improvements in EASI score, with 4/16 patients having achieved an EASI50 clinical response, 3 of which achieved at least an EASI75, compared to 0/7 of patients in the placebo group. These results provide further evidence that modulating SINTAX can drive significant clinical benefit without the need for systemic exposure.



Waterfall plot above shows % change in EASI scores from baseline by patient on day 56; EDP1815 shown in red, placebo shown in blue

"These positive clinical results, together with those previously seen in psoriasis, support the significant potential of EDP1815 not only in atopic dermatitis, but also more broadly across a range of inflammatory diseases," said Dr. Benjamin Ehst, M.D., Ph.D., Board-certified Dermatologist, Investigator and Clinical Associate Professor with the Oregon Medical Research Center. "The observed clinical responses are exciting. The rapid onset of clinically important activity in atopic dermatitis patients, and the absence of the regular use of a moisturizer in either arm of the trial, suggests the results were driven by EDP1815 alone. A new oral drug which acts broadly across multiple inflammation types, while being safe and well tolerated, would be easy to prescribe for the vast number of patients with mild to moderate atopic dermatitis. This is a large population currently lacking any approved oral treatment options."

"Today's data provide a clear path forward for the development of EDP1815 for the tens of millions of people living with atopic dermatitis, in addition to the current psoriasis program," said Duncan McHale, M.B.B.S., Ph.D., Chief Medical Officer of Evelo. "For the fourth time in clinical trials we have observed that EDP1815 reduces systemic inflammation, showing positive results across Th1, Th2, and Th17-mediated inflammation. We look forward to sharing the complete dataset from this Phase 1b trial in early 2021 and advancing EDP1815 into later-stage trials in atopic dermatitis."

About the EDP1815 Phase 1b Clinical Trial

EDP1815-101 is a double-blind, placebo-controlled Phase 1b trial designed to evaluate the safety and tolerability of EDP1815 in healthy volunteers and patients with psoriasis or atopic dermatitis. The atopic dermatitis cohort enrolled 24 patients with mild to moderate atopic dermatitis, randomized 2:1 to receive oral administration of the enteric capsule formulation of EDP1815 or placebo once daily, for 56 days. As of December 1, 2020, 23 patients had reached the day 56 analysis, including all 16 patients in the treatment group and 7/8 patients in the placebo group. Patients were not allowed to use active topical treatments and were not required to use emollients. Efficacy data provided is for 23 of the 24 patients in the study; safety data provided is for all 24 patients. The primary endpoint was safety and tolerability. Secondary endpoints included a range of established markers of atopic dermatitis. The full clinical data set, including final subject visits, blood biomarkers, and the SCORAD, POEM and DLQI scores, will be analyzed and reported in early 2021.

About EDP1815

EDP1815 is an investigational oral medicine being developed for the treatment of inflammatory diseases. It is a non-live pharmaceutical preparation of a strain of *Prevotella histicola*, selected for its potential to provide systemic pharmacological effects after oral administration with gut-restricted distribution. Being non-live, it does not colonize the gut or modify the microbiome. Preclinically, EDP1815 had anti-inflammatory effects in models that cover multiple pathways of inflammation, including Th1, Th2, and Th17. Clinical results from four independent cohorts provide evidence supporting EDP1815's potential to address Th1, Th, and Th17-mediated inflammation.

In the psoriasis cohorts of the Phase 1b clinical trial, EPD1815 was also observed to limit the systemic production of multiple inflammatory cytokines, including IL-6, IL-8, TNF, and IL-1, which are well-established mediators of potentially harmful effects in patients with inflammatory diseases. Preclinical and clinical data showed that EDP1815 achieved this anti-inflammatory activity without inducing immunosuppression. EDP1815 has been observed to be well-tolerated in clinical studies to date.

EDP1815 is currently in a Phase 2 dose-ranging trial in mild to moderate psoriasis and in two studies in hospitalized COVID-19 patients. Additional experimental studies are continuing to investigate optimal formulation and dosage.

About Atopic Dermatitis

Atopic dermatitis, also known as eczema, is a common chronic inflammatory skin disease that affects both children and adults, with a prevalence of up to 10% in adults worldwide. It typically presents as a red, intensely itchy rash that may cause lifelong symptoms. Due to the chronic nature and frequency of relapses, atopic dermatitis is associated with a substantial physical and psychosocial burden on patients and their families. It can also occur alongside other atopic diseases including food allergy, asthma, and allergic rhinitis, as these conditions are all

associated with an imbalance towards a Th2 inflammatory response – an immune pathway on which EDP1815 has been shown to have potent preclinical, and now also clinical, activity.

Patients with atopic dermatitis are often treated with topical medications, which are inconvenient and burdensome in application, leading to poor adherence and reduced efficacy in a real-world setting. Beyond topicals, patients have limited treatment options, especially patients with mild to moderate disease, who represent 80-90% of atopic dermatitis patients worldwide. This group of patients typically do not have access to high-cost, injectable antibody therapies or may be uncomfortable with the toxicity concerns and monitoring requirements of systemic immunosuppressants. There is a large need across the spectrum of disease severity, and especially for these midline, pre-biologic patients, for a safe and well-tolerated oral medicine that resolves the systemic inflammation that drives atopic dermatitis.

Conference Call
Evelo will host a conference call and webcast today at 9:00 a.m. ET to discuss clinical results and corporate strategy. To access the call, please dial (866) 795-3242 (domestic) or (409) 937-8909 (international) and refer to conference ID 2881825. A live webcast of the event will also be available under "News and Events" in the Investors section of Evelo's website at http://ir.evelobio.com. The archived webcast will be available on Evelo's website approximately two hours after the completion of the event and will be available for 30 days following the call.

About Evelo Biosciences
Evelo Biosciences is a clinical stage biotechnology company developing orally delivered medicines 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 five product candidates in development: EDP1815, EDP1867, and EDP2939 for the treatment of inflammatory diseases and EDP1503 and EDP1908 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 statements concerning the timing and results of any clinical trials or readouts for EDP1815, our development plans, and the promise and potential impact of any of our therapies.

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 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" in our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2020, as may be updated in our other filings 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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