UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of
the Securities Exchange Act of 1934

Date of report (Date of earliest event reported): April 27, 2020

EVELO BIOSCIENCES, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-38473**	**46-5594527**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

620 Memorial Drive
Cambridge, Massachusetts 02139
(Address of principal executive offices) (Zip Code)

(617) 577-0300
(Registrant's telephone number, include area code)

N/A
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	EVLO	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (ß230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (ß240.12b-2 of this chapter).

Emerging growth company x

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On April 27, 2020, in connection with the distribution of proxy materials for the Evelo Biosciences, Inc. (the "Company") annual meeting of stockholders, the Company included in its 2019 Annual Report a letter to stockholders from its Chief Executive Officer and President and its Chief Scientific Officer and President of Research and Development. A copy of the letter to stockholders is furnished as Exhibit 99.1 to this Current Report on Form 8-K and the 2019 Annual Report is available on the Investors section of the Company's website at *http://ir.evelobio.com*.

The information contained in Item 7.01 of this Current Report on Form 8-K (including Exhibit 99.1) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly provided by specific reference in such filing.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	Description
99.1	Letter to Stockholders dated April 27, 2020

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

EVELO BIOSCIENCES, INC.

Date: April 27, 2020

By: /s/ Daniel S. Char

Daniel S. Char

General Counsel & Secretary

Exhibit 99.1

April 27, 2020

Dear Stockholders,

Our vision and strategy. Our vision has consistently been to develop a new profile of medicines that are broadly applicable, effective, safe, convenient to take and affordable. This profile is enabled by the newly uncovered biology of the small intestinal axis, SINTAX™. SINTAX is the network of connections between the small intestine and the rest of the body. Quite remarkably, it allows orally delivered substances to work systemically - throughout the body - by their local action on cells in the small intestine. This biology opens up two important areas of medicine: early intervention and global treatment. Our aim is to create biotech drugs that can be used to treat hundreds of millions of patients globally at all stages of disease. The COVID-19 pandemic highlights more than ever the global need we have for a new and improved profile of medicines.

The validity of our platform and our lead product are supported by a growing body of clinical and preclinical data. We are on track for potential launch of our first anti-inflammatory product in the next few years. And behind this first product we have a broad pipeline and opportunity that comes from this platform.

Given our continued fast progress we thought it helpful to summarize our overall status and plans as we move into later stage clinical development and the next phase of our growth.

Evelo platform: validated preclinical. Our clinical and preclinical results tell us that SINTAX is real and functional in humans, and that it can be harnessed as a potent modulator of systemic inflammation.

The last 100 years have seen a handful of turning points in the treatment of diseases involving immunity and inflammation: corticosteroids, tissue necrosis factor and immune checkpoint inhibitors. Medicines targeting SINTAX may be another of those turning points.

Evelo's product candidates are monoclonal microbials, pharmaceutical preparations of single strains of gut mucosa-associated bacteria that are selected for their ability to modulate SINTAX. The therapeutic effects of these orally delivered medicines come from their action on a range of receptors on immune and epithelial cells in the lining of the small intestine. These cells, in turn, modulate immune cells circulating throughout the body. Monoclonal microbials are microbes, but do not target the microbiome. They do not colonize or persist in the gut and do not modify the colonic microbiome. They are locally acting in the gut (the outside of the body) with observed systemic activity inside of the body.

It turns out that the small intestine is a motherboard of the immune system. Preclinical models have shown striking activity of monoclonal microbials, matching or even exceeding that of injectable biologics and the best of existing oral medicines. This can be done with both anti-inflammatory and pro-inflammatory monoclonal microbials. It is astonishing that all of this is achieved with no observed systemic exposure via a previously unknown mechanism of inflammation resolution.

EDP1815: our lead anti-inflammatory clinical program. What we showed preclinically is now emerging as a clinical reality. This is best illustrated by EDP1815, Evelo's lead anti-inflammatory candidate product. It has recently been investigated in several cohorts in an on-going phase 1b study in patients with psoriasis. The striking effects of targeting SINTAX seen in preclinical models has been observed in humans.

The primary endpoints of the EDP1815 phase 1b study are safety and tolerability. EDP1815 has a placebo-like profile, consistent with the lack of systemic absorption. There has been no persistence of EDP1815 beyond the 28-day daily dosing period and no modification of the colonic microbiome by 16S RNA sequencing of patient stool samples.

Two cohorts of patients with mild-to-moderate psoriasis were treated with a low and high dose of EDP1815 daily for 28 days. The lower dose was estimated by allometric scaling of the just-maximally effective dose in mouse inflammation models. The high dose was 5X higher. There were 12 and 18 patients respectively in these cohorts. The cohorts were recruited independently and sequentially with internal placebo control with 2:1 randomization of active:placebo.

Clinical symptoms and biomarkers of systemic inflammation were the pharmacodynamic secondary and tertiary endpoints.

At both doses there was a clear clinical response measured by PASI and lesional severity score. Even with a short duration of treatment and small numbers of subjects, a clear and reproducible treatment effect was seen.

Biomarkers of systemic inflammation were determined by stimulation *ex vivo* with lipopolysaccharide (LPS) of whole blood samples taken at baseline and after 28 days of dosing. LPS is a potent activator of the myeloid compartment of innate immunity and inflammation, especially on human cells. Reduction of the production of inflammatory cytokine and chemokines in these cultures is a measure of the state of systemic inflammatory activation.

In both cohorts of psoriasis patients there was a reduction in inflammatory biomarkers. This mirrors the *ex vivo* analysis of preclinical models where a pronounced effect is the coordinated down-regulation of multiple inflammatory pathways. In patients there was a down-regulation of the production of interleukin-8 (IL-8) and interleukin-6 (IL-6) and tissue necrosis factor-alpha (TNFa) in the LPS stimulation assay.

The next stage in the development of EDP1815 is a phase 2 study in psoriasis patients. This study will aim to optimize the clinical and biomarkers signals seen in phase 1b with an extended duration of dosing and dose optimization.

EDP1815 as a potential therapy for COVID-19. The clinical data that we have generated with EDP1815 support the potential of EDP1815 in the treatment of COVID-19. We are actively exploring the possibility of one or more phase 2/3 clinical studies investigating the potential of EDP1815 to intervene early in the disease to shut down cytokine storms and prevent progression of serious COVID-19.

Tissue damage following infection with COVID19 appears to be due to an emergent, excess, host immune response. Approximately 7 days after SARS-CoV-2 infection the host immune system starts to become a driver of disease symptoms and in some individuals there is an exaggerated inflammatory response. This leads to lung and sometimes multi-organ damage. The development of these severe complications e.g. Diffuse Alveolar Damage (DAD) can be independent of high-titre viral replication. The immune and inflammatory response in affected lungs includes production of high levels of IL-6, TNFα, interleukin-1beta, influx of neutrophils and cytotoxic T cells.

A component of the treatment of COVID-19 should be the prevention of the exaggerated host inflammatory response responsible for COVID-19 related complications without immunosuppressing individuals, so as to retain the host anti-viral response. Early intervention in the disease process should prevent and/or reduce COVID-Related Complications (CRC) leading to lower morbidity and mortality and reduced demands on healthcare systems.

The tolerability profile of EDP1815 makes it potentially well-suited for early intervention in this host-mediated disease process. Emerging data suggests that early interruption of the exaggerated host inflammatory response may prevent progression to serious complications. EDP1815 potentially is one of very few therapeutic options which could meet this profile.

Importantly, EDP1815 manufacturing can be effectively scaled to allow for an affordable global treatment.

EDP1503: our lead oncology clinical program. EDP1503 continues to move forward in a clinical study in combination with KEYTRUDA® (pembrolizumab), in a clinical collaboration with Merck & Co. The aim of the studies is to find improved therapies for otherwise poorly treated forms of cancer such as microsatellite stable colorectal carcinoma and relapsed triple negative breast cancer and several other tumor types in which patients relapse after prior response to other therapy. We expect to report data from this set of clinical studies in 2020.

The next phase of our growth. Since founding Evelo we had a clear long-range plan. The first phase is complete: using our platform to advance rapidly a diversified portfolio of products into phase 1b/2a clinical development and to demonstrate safety and clinical signals.

Based on the findings of our first wave clinical studies we are moving into the next phase of our plan: advancing our products into later stage clinical development and expanding into additional clinical indications. As we look beyond 2020, we continue to invest in research on a next generation of product candidates and in our platform, including manufacturing and formulation development. We expect this will allow us to optimize for later stage drug development and commercialization. We also see future opportunities in metabolic and neurologic diseases and beyond.

COVID-19 is unexpected and places all of us in a particularly challenging macroenvironment. However, the big picture has not changed. We continue to focus on transforming medicine through harnessing SINTAX to develop better and earlier treatments for hundreds of millions of people worldwide. In additional to treatments for inflammatory diseases, cancers, neuroinflammation and metabolism, we also now hope to help treat COVID-19 and certain other viral infections. Our team at Evelo gives us the confidence that we will weather the storm and continue to make progress towards launching our first medicines in the next few years. We thank them for being who they are.

As always, we wanted to conclude by thanking the patients who work with us and thanking you, our stockholders, for your support and your belief in our vision, in us and in our science and our potential products.

Simba Gill
Chief Executive Officer and
President

Mark Bodmer
Chief Scientific Officer and
President of Research and Development

This letter contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this letter that do not relate to matters of historical fact should be considered forward-looking statements, including statements regarding our objectives and anticipated clinical milestones for 2020 and 2021, the promise and potential impact of any of our monoclonal microbials or preclinical or clinical trial data.

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: 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 annual report on Form 10-K for the year ended December 31, 2019 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 letter. Any such forward-looking statements represent management's estimates as of the date of this letter. 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 letter.