Evelo Biosciences Announces Fourth Quarter and Full Year 2021 Financial Results and Business Highlights

–Oral presentation on EDP1815 Phase 2 data in psoriasis accepted in late-breaking abstract session at AAD on Saturday, March 26, 2022 –
–Positive data reported on faster release capsule–
–Phase 2 data from EDP1815 in atopic dermatitis on-track for 1H 2023 readout–
–Management to host conference call at 8:30 a.m. ET–

CAMBRIDGE, Mass., March 24, 2022 – Evelo Biosciences, Inc. (Nasdaq: EVLO), a clinical stage biotechnology company developing SINTAX™ medicines as a new modality of orally delivered treatments for inflammatory disease, today reported financial results and business highlights for the fourth quarter and full year 2021.

"We heard from Dr. Bruce Strober and Dr. Daniel Roling at our recent KOL event, that Evelo's Phase 2 clinical data supports the potential use of EDP1815 in almost all patients, including the mild and moderate population which represents over 85% of the 55 million patients with psoriasis worldwide. These patients are generally not treated with biologics or oral small molecules. The primary unmet need in psoriasis is for this segment of patients," said Simba Gill, Ph.D., Chief Executive Officer of Evelo. "In the last quarter we have hit all three of our major clinical milestones with positive results: 1) the maintenance and deepening of clinical responses of psoriasis patients in the Part B follow-up of the Phase 2 trial of EDP1815; 2) the reduction in inflammatory cytokines produced by systemically circulating immune cells and inflammatory cytokine production at the site of disease; and 3) the faster release profile of EDP1815 capsules. The data from the Phase 2 trial have also been selected for a coveted late-breaking oral presentation on Saturday, March 26th, at the 2022 meeting of the American Association of Dermatology (AAD) - an important external recognition of the potential of SINTAX medicines. We believe this puts EDP1815 and SINTAX medicines in a strong position as we move closer to realizing our vision to improve health for the hundreds of millions of people living with inflammatory disease around the globe."

Highlights and Recent Progress

EDP1815 in Psoriasis

Summary of Data from Phase 2 Trial

- The Phase 2 trial evaluated EDP1815 versus placebo for the treatment of mild and moderate psoriasis, and was comprised of a Part A, where patients received either EDP1815 or placebo for 16 weeks, and a Part B, where patients were followed for up to 24 weeks after they had stopped receiving EDP1815 or placebo.
    - During the 16-week dosing period, statistically significant reductions in the Psoriasis Area and Severity Index (PASI) score were observed in two of the three cohorts treated with EDP1815, as measured by the proportion of patients achieving at least 50% improvement in PASI (PASI-50) from baseline at week 16. An ad hoc analysis comparing the combined EDP1815 group also showed a statistically significant improvement over placebo in rates of PASI-50 response.
    - For patients who achieved a PASI-50 response or better, consistent effects in secondary and exploratory endpoints were observed, including improvements in patient reported outcomes such as Dermatology Life Quality Index (DLQI) and Psoriasis Symptom Inventory (PSI).
    - Blood samples were taken from 96 patients at baseline and after 16 weeks of dosing with EDP1815 or placebo. Treatment with EDP1815 led to a statistically significant reduction in the release of pro-inflammatory cytokines compared to placebo: interleukin 6 (IL-6) (p=0.0003), interleukin 8 (IL-8) (p=0.0007), and tumor necrosis factor (TNF) (p=0.0037).
    - During the post-treatment period, durable and deepening clinical responses were observed, with no flare or rebound of psoriasis. There were 83 patients who had received EDP1815 in Part A who entered Part B. Thirty of these 83 patients achieved a PASI-50 or greater reduction at the end of the 16-week dosing period. Eighteen of the 30 patients remained at PASI-50 or greater at the end of Part B. Ten of these 30 patients achieved a PASI-75 or greater at the end of Part A and 5 of them remained at PASI-75 or greater at the end of Part B.
    - EDP1815 safety and tolerability data were comparable to placebo in the trial.

Human Volunteer Scintigraphy Study

- In March 2022, results from an ongoing Phase 1 single center clinical trial in healthy volunteers showed that a capsule with an improved release profile was able to deliver EDP1815 higher up in the small intestine. 88% (15 out of 17) of the human volunteers studied showed EDP1815 released in the jejunum, the upper part of the small intestine.
- Preclinical data have shown that the higher EDP1815 is released in the small intestine, the greater the observed effect.
- Evelo plans to evaluate this faster release capsule in an upcoming clinical trial.

Pediatric Investigation Plan (PIP)

- The European Medicines Agency (EMA) agreed to Evelo's pediatric investigation plan for EDP1815 in psoriasis, in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council.
- The PIP allows Evelo to:
  - include patients 12–17 years old in Phase 3 trials,
  - conduct a single clinical trial in patients 2–5 years old and 6-11 years old after the adult Marketing Authorization Application has been submitted, and
  - develop a pediatric formulation suitable for administration to patients 2 -11 years old.
- The EMA also confirmed juvenile toxicity studies are not required for EDP1815 and granted the Company a waiver from studying EDP1815 in patients <2 years old.

EDP1815 in Atopic Dermatitis

- Evelo announced dosing of the first patient in the Phase 2 trial of EDP1815 in atopic dermatitis in February 2022.

Business Highlights

- Evelo will have an oral presentation in the Late Breaking Abstract session of the 2022 AAD Annual Meeting on Saturday, March 26th, at 10:10 a.m. ET. The title of the presentation is "A phase 2 study investigating the effect of EDP1815, an orally-delivered, anti-inflammatory, gut-restricted commensal microbe in the treatment of mild and moderate plaque psoriasis."
- On March 8, 2022, the United States Patent and Trademark Office granted U.S. Patent No. 11,266,700 to Evelo. The claims of the patent relate to a method of treating psoriasis using a bacterial composition that comprises a proprietary *Lactococcus lactis* strain.

Upcoming Key Milestones

EDP1815 – Psoriasis

- Evelo intends to move towards registration trials in psoriasis following the completion of meetings with health authorities this year

EDP1815 – Atopic Dermatitis

- Topline data from 16-weeks of dosing in the Phase 2 trial anticipated in 1H 2023; recruitment on-track

EDP1867 – Atopic Dermatitis

- Interim data from Phase 1b trial expected in early 2Q 2022

EDP2939 – Inflammation

- Initiation of clinical development of first extracellular vesicle (EV) anticipated in 3Q 2022
- Phase 2 data from a cohort of patients with psoriasis expected in 2H 2023

Fourth Quarter and Full Year 2021 Financial Results (Unaudited)

- **Cash Position:** As of December 31, 2021, cash and cash equivalents were $68.4 million, as compared to cash and cash equivalents of $68.9 million as of December 31, 2020. The $0.5 million decrease was primarily due to $96.7 million of cash used in operating activities, principally offset by $97.5 million of net proceeds received from the issuance of common shares and an additional draw down of funds under our debt facility.

- **Research and Development Expenses:** R&D expenses were $18.9 million and $83.6 million for the three and twelve-month periods ended December 31, 2021, compared to $22.1 million and $69.6 million for the three and twelve-month periods ended

December 31, 2020, respectively. The year-over-year increase of $14.0 million was primarily driven by higher personnel costs related to Evelo's clinical development and technical operations headcount supporting clinical programs, higher inflammation program costs from the progression of clinical trials, and increased spending toward platform investment, partially offset by lower spending on oncology programs.

- **General and Administrative Expenses:** G&A expenses were $8.7 million and $31.8 million for the three and twelve-month periods ended December 31, 2021, compared to $6.1 million and $22.3 million for the three and twelve-month periods ended December 31, 2020, respectively. The increase of $9.5 million year-over-year was due to increases in our pre-commercial and other general and administrative headcount, higher consulting and other professional fees, and increased travel and other costs associated with a return to the office.

- **Net Loss:** Net loss was $28.7 million and $122.2 million for the three and twelve-month periods ended December 31, 2021, compared to $29.1 million and $93.7 million for the three and twelve-month periods ended December 31, 2020, respectively. Earnings per basic and diluted shares were $(0.54) and $(2.31) for the three and twelve-month periods ended December 31, 2021, compared to $(0.62) and $(2.37) for the three and twelve-month periods ended December 31, 2020, respectively.

Conference Call
Evelo will host a conference call and webcast at 8:30 a.m. ET today to review fourth quarter and full year 2021 highlights. To access the call, please dial (866) 795-3242 (domestic) or (409) 937-8909 (international) and refer to conference ID 6076311. 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 product candidates that are designed to act on the small intestinal axis, SINTAX™, 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 the potential to offer 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.

Evelo currently has three product candidates in development: EDP1815, EDP1867, and EDP2939 for the treatment of inflammatory diseases. 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 including 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 development of EDP1815, EDP1867, and EDP2939, the promise and potential impact of our product candidates, the timing of and plans for clinical trials, and the timing and results of clinical trial readouts.

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 Annual Report on Form 10-K for the fiscal year ended December 31, 2021, 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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Evelo Biosciences, Inc.

Consolidated Statements of Operations (Unaudited)

(In thousands, except share and per share data)

	Three Months Ended December 31,		Year Ended December 31,	
	2021	2020	2021	2020
Operating expenses:				
Research and development	$ 18,881	$ 22,113	$ 83,643	$ 69,616
General and administrative	8,678	6,085	31,753	22,270
Total operating expenses (1)	27,559	28,198	115,396	91,886
Loss from operations	(27,559)	(28,198)	(115,396)	(91,886)
Other (expense) income:				
Interest expense, net	(1,010)	(756)	(3,612)	(2,109)
Loss on extinguishment of debt	—	—	(3,226)	—
Other income, net	14	92	486	738
Other expense, net	(996)	(664)	(6,352)	(1,371)
Net loss before income taxes	(28,555)	(28,862)	(121,748)	(93,257)
Income tax expense	(97)	(188)	(428)	(409)
Net loss	$ (28,652)	$ (29,050)	$ (122,176)	$ (93,666)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.54)	$ (0.62)	$ (2.31)	$ (2.37)
Weighted-average number of common shares outstanding, basic and diluted	53,515,636	46,711,281	52,910,982	39,479,197

(1) Expenses include the following amount of non-cash stock-based compensation expense.

(Unaudited)	Three Months Ended December 31		Year Ended December 31,	
	2021	2020	2021	2020
Research and development	$ 2,079	$1,262	$ 8,004	$ 4,487
General and administrative	2,290	1,113	7,842	3,981
Total stock-based compensation expense	$ 4,369	$2,375	$ 15,846	$ 8,468

Evelo Biosciences, Inc.

Consolidated Balance Sheets (Unaudited)

(In thousands, except per share and share amounts)

	December 31,	
	2021	**2020**
Assets		
Current assets:		
Cash and cash equivalents	$ 68,441	$ 68,857
Prepaid expenses and other current assets	2,585	2,123
Total current assets	71,026	70,980
Property and equipment, net	6,622	7,478
Right of use asset - operating lease	8,910	10,757
Other assets	1,313	1,424
Total assets	$ 87,871	$ 90,639
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,601	$ 1,442
Accrued expenses	13,068	16,254
Operating lease liability, current portion	1,951	1,674
Other current liabilities	742	463
Total current liabilities	17,362	19,833
Noncurrent liabilities:		
Long-term debt	46,557	30,048
Operating lease liability, net of current portion	7,785	9,989
Deferred revenue	7,500	—
Other noncurrent liabilities	—	284
Total liabilities	79,204	60,154
Commitments and contingencies (Note 10)		
Stockholder's equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized; no shares issued and outstanding at December 31, 2021 and 2020, respectively	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized; 53,576,454 and 47,488,505 shares issued and 53,576,454 and 47,470,119 shares outstanding at December 31, 2021 and 2020, respectively	54	47
Additional paid-in capital	423,308	322,957
Accumulated deficit	(414,695)	(292,519)
Total stockholders' equity	8,667	30,485
Total liabilities and stockholders' equity	$ 87,871	$ 90,639