Evelo Biosciences Announces Positive Interim Phase 1b Clinical Data and Provides Second Quarter 2019 Financial Results

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-EDP1815 and EDP1066 were Well Tolerated with No Overall Difference Reported from Placebo-
-Clinical Response Observed Consistent with Reductions in Cellular Histological and Blood Immune Cell Biomarkers in Psoriasis Patients at Low Dose of EDP1815-
- EDP1815 Phase 2 Initiation Planned for Early 2020-
-Positive EDP1066 Blood Immune Cell Biomarker Data in Psoriasis Patients at High Dose-
-First in Human Data Suggest that Oral Biologics that Act on Cells in the Small Intestine Modulate Systemic Inflammation-

CAMBRIDGE, Mass., Aug. 06, 2019 (GLOBE NEWSWIRE) -- Evelo Biosciences, Inc. (Nasdaq:EVLO), a biotechnology company developing oral biologics that act on cells in the small intestine with systemic therapeutic effects, today announced positive interim Phase 1b clinical data and provided second quarter 2019 financial results.

"Evelo is harnessing the therapeutic potential of cells in the small intestine which play a central role in governing the immune, metabolic, and nervous systems. Our platform has generated a diversified portfolio of oral biologic candidates that act on these cells to drive systemic effects relevant to the potential treatment of a broad range of diseases," said Simba Gill, Ph.D., chief executive officer of Evelo. "Today's positive interim data show, for the first time in patients, clinical and biomarker responses that support our core scientific hypothesis and our vision of developing effective, oral, safe, and affordable medicines for people with major chronic diseases and cancer. We look forward to advancing into later stage trials and continuing to expand our clinical portfolio."

Inflammation: Interim Clinical Data Highlights and Anticipated Milestones

About the EDP1815 and EDP1066 Phase 1b clinical trials
Each of EDP1815 and EDP1066 are in ongoing signal-finding Phase 1b clinical trials in mild to moderate psoriasis and atopic dermatitis. Patients in these trials are randomized 2:1 to receive daily, oral administration of active drug, or placebo, for 28 days. The primary endpoint of these trials is safety and tolerability. Prospectively defined secondary and exploratory endpoints include clinical measures of disease, cellular histological biomarkers and blood immune cell biomarkers taken from biopsies and blood samples, respectively, at the start and end of the 28-day dosing period.

EDP1815 - positive interim Phase 1b clinical data at low dose in mild to moderate psoriasis patients

- In a separate press release this morning Evelo reported positive EDP1815 clinical data from an initial 12-patient cohort in its ongoing trial in mild to moderate psoriasis.
- EDP1815 was well tolerated with no overall difference reported from placebo.
- Patients dosed once per day for 28 days with 550mg (1x dose) of the enteric capsule formulation of EDP1815 showed a statistically significant ($p<0.05$) reduction in mean lesion severity score (LSS) at 28 days of 2 points, compared to a mean increase of 0.25 points in patients who received placebo. LSS reductions over the dosing period of patients dosed with EDP1815 ranged from 0-67 percent. LSS, a secondary endpoint, is a component of the Psoriasis Area and Severity Index (PASI) score and measures redness, thickness, and scaling of an individual psoriatic lesion across the dosing period and is a sensitive clinical measure for patients with mild to moderate disease.
- Analysis of the basal epithelium mitotic count, a secondary endpoint and cellular driver of psoriasis pathology, showed a mean reduction over the dosing period of 2.25 cells/mm^2 in patients who received EDP1815 compared to no change in patients receiving placebo. Lower basal epithelium mitotic counts indicate a reduction of psoriasis pathology.
- In an analysis of the change over the dosing period of blood immune cell cytokine production following stimulation with lipopolysaccharide, an exploratory endpoint, the EDP1815 dosed patient group showed a reduction in cytokine production indicative of a systemic anti-inflammatory response, compared to no reduction in the placebo group.
- Based on these data, Evelo plans to advance EDP1815 into Phase 2 in early 2020. This placebo-controlled dose and formulation optimization trial will investigate daily dosing of EDP1815 in mild to moderate psoriasis patients over 24 weeks.
- Enrollment is underway in the ongoing Phase 1b clinical trial of an additional cohort of mild to moderate psoriasis patients to be dosed at a 2.76g (5x) dose of the enteric capsule formulation. Data from this cohort are expected in the fourth quarter of 2019.

EDP1066 - positive interim Phase 1b biomarker data at high dose in mild to moderate psoriasis patients

- Today, Evelo reports positive EDP1066 biomarker data at the high dose from its ongoing Phase 1b trial in patients with mild to moderate psoriasis.
- EDP1066 was well tolerated with no overall difference reported from placebo.
- In an analysis of the change over the dosing period of blood immune cell cytokine production following stimulation by lipopolysaccharide, an exploratory endpoint, patients who received a 3.3g (5x) dose of EDP1066 showed a reduction in cytokine production consistent with a pharmacodynamic effect. No reduction was observed in patients receiving a 660mg (1x) dose of EDP1066 or placebo.
- No effects were observed in the secondary endpoints of clinical measures of disease or cellular histological biomarkers at either the 660mg or 3.3g dose of EDP1066.

- Evelo is focusing the current EDP1066 Phase 1b trial on investigating the activity of a new formulation, which was up to 30-fold more potent in preclinical models, in a cohort of mild to moderate atopic dermatitis patients. Evelo expects to report data from this cohort in the first quarter of 2020.
- Given the EDP1815 data, Evelo will not develop EDP1066 any further in psoriasis.

Oncology: Clinical Studies and Anticipated Milestones

EDP1503 - Phase 1/2

- Evelo is conducting a Phase 1/2 clinical trial of EDP1503 in combination with KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 therapy, in microsatellite stable colorectal cancer, triple-negative breast cancer, and patients with other tumor types that have relapsed on prior PD-1/L1 inhibitor treatment. Initial clinical data is expected in the first half of 2020.

EDP1503 - Phase 2a

- The University of Chicago is conducting a Phase 2a investigator-sponsored clinical trial of EDP1503 in combination with KEYTRUDA in naive melanoma patients and melanoma patients who have relapsed on prior PD-1/L1 inhibitor treatment. Evelo will no longer be providing guidance as to timing related to this investigator-sponsored trial.

Business Highlights

- In June 2019, Evelo appointed Jose-Carlos Gutiérrez-Ramos, Ph.D. to its board of directors. Dr. Gutiérrez-Ramos brings to the board significant experience in research, clinical development and company building over a long career in senior leadership roles at major pharmaceutical and biotech companies. Dr. Gutiérrez-Ramos has served as chief executive officer and president of Cogen Immune Medicine, Inc., a biotechnology company, since August 2018. Dr. Gutiérrez-Ramos has also served as a venture partner at Flagship Pioneering since 2018. From 2015 to May 2018 he served as chief executive officer and president of Synlogic, Inc. Prior to joining Synlogic, Dr. Gutiérrez-Ramos was group senior vice president of Worldwide Research and Development and global head of Biotherapeutics Research and Development at Pfizer, Inc. Dr. Gutiérrez-Ramos received a B.S. from Universidad Complutense de Madrid and his Ph.D. in immunochemistry from the Universidad Autonoma de Madrid.
- In July 2019, Evelo entered into a loan and security agreement with K2 HealthVentures (K2HV). Under the terms of the agreement, Evelo can borrow up to $45 million subject to certain time conditions and clinical development milestones. On closing, Evelo borrowed $20 million; the funds were used to fully repay its $15 million loan facility with Pacific Western Bank and for general corporate purposes.
- In July 2019, Evelo entered into a collaboration agreement with Sacco S.r.l. (Sacco), an existing contract manufacturing partner. Under the terms of this 5-year agreement, Sacco will manufacture and supply single strain, non-genetically modified microbes for oral delivery or oral use in pharmaceutical products exclusively for Evelo, with the exception of pre-existing products for pre-existing customers. This collaboration is consistent with Evelo's manufacturing strategy of combining best-in-class manufacturing partners with internal manufacturing capacity and deep internal expertise in process development and formulation.

Second Quarter 2019 Financial Results

- **Cash Position:** As of June 30, 2019, cash, cash equivalents and investments were $113.5 million, as compared to $178.9 million as of June 30, 2018 and $129.4 million as of March 31, 2019. This decrease was due to cash used to fund operating activities and capital expenditures. Evelo expects that its cash, cash equivalents and investments will enable it to fund its planned operating expenses and capital expenditure requirements, including the planned EDP1815 Phase 2 clinical trial, into the fourth quarter of 2020.
- **Research and Development Expenses:** R&D expenses were $15.5 million for the three months ended June 30, 2019, compared to $10.2 million for the three months ended June 30, 2018. The increase of $5.3 million was due primarily to increases in costs related to Evelo's inflammation and oncology clinical development programs, and research platform expenses, as well as increased personnel costs.
- **General and Administrative Expenses:** G&A expenses were $5.9 million for the three months ended June 30, 2019, compared to $5.1 million for the three months ended June 30, 2018. The increase of $0.8 million was due primarily to increased personnel costs and professional and consulting fees necessary to support Evelo's growing organization and corporate operational activities.
- **Net Loss:** Net loss attributable to common stockholders was $20.9 million for the three months ended June 30, 2019, or $(0.65) per basic and diluted share, as compared to a net loss attributable to common stockholders of $16.7 million for the three months ended June 30, 2018, or $(0.85) per basic and diluted share.

Conference Call

Evelo will host a conference call and webcast to discuss these data and the second quarter financial results today at 8:30 a.m. ET. To access the call please dial 866-795-3242 (domestic) and 409-937-8909 (international) and provide the passcode 6380636. A live webcast of the call, including an accompanying slide presentation, will be available on the Investors sections of the Evelo website at www.evelobio.com. The archived webcast will be

available approximately two hours after the conference call and will be available for 30 days following the call.

About Evelo Biosciences
Evelo Biosciences, Inc. is a clinical stage biotechnology company developing oral biologics that act on cells in the small intestine with systemic therapeutic effects. These cells in the small intestine play a central role in governing the immune, metabolic and neurological systems. The company's first product candidates are monoclonal microbials, single strains of microbes selected for defined pharmacological properties. They have been observed in preclinical studies to have systemic dose-dependent effects, modulating multiple clinically validated pathways. Evelo's therapies have the potential to be effective, safe and affordable medicines to improve the lives of people with chronic disease and cancer.

Evelo currently has three product candidates, EDP1066 and EDP1815 for the treatment of inflammatory diseases and EDP1503 for the treatment of cancer. Evelo is also advancing additional oral biologics through preclinical development in other disease areas.

For more information, please visit www.evelobio.com.

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 our development plans and new formulations, the promise and potential impact of any of our monoclonal microbials or preclinical or clinical trial data, the timing of and plans to initiate clinical studies of EDP1815, the timing and results of any clinical studies or readouts, and the sufficiency of cash to fund operations.

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 Quarterly Report on Form 10-Q for the quarter ended March 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 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.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS (UNAUDITED)
(in thousands, except share and per share amounts)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	**2018**	**2019**	**2018**
Operating Expenses(1):				
Research and development	$ 15,464	$ 10,172	$ 31,141	$ 17,315
General and administrative	5,923	5,056	11,050	8,338
Total operating expenses	21,387	15,228	42,191	25,653
Loss from operations	(21,387)	(15,228)	(42,191)	(25,653)
Other income (expense), net	446	82	951	7
Net loss	$ (20,941)	$ (15,146)	$ (41,240)	$ (25,646)
Preferred stock dividends	—	(1,520)	—	(3,937)
Net loss attributable to common stockholders	$ (20,941)	$ (16,666)	$ (41,240)	$ (29,583)

Net loss per share - basic and diluted	$ (0.65)	$ (0.85)	$ (1.29)	$ (2.50)
Weighted-average common shares used in computing net loss per share - basic and diluted	32,041,401	19,626,985	31,983,558	11,818,302

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

Research and development	$ 973	$ 761	$ 1,864	$ 1,003
General and administrative	1,162	1,486	2,224	1,896

EVELO BIOSCIENCES, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS (UNAUDITED)
(in thousands)

	June 30, 2019	**December 31, 2018**
Assets:		
Cash, cash equivalents and investments	$ 113,473	$ 147,919
Property and equipment, net	7,488	6,925
Other assets	5,247	5,023
Total assets	$ 126,208	$ 159,867
Liabilities and stockholders' equity:		
Accounts payable and current liabilities	$ 9,889	$ 9,235
Long-term debt	14,856	12,305
Other liabilities	1,375	1,378
Total liabilities	26,120	22,918
Total stockholders' equity	100,088	136,949
Total liabilities and stockholders' equity	$ 126,208	$ 159,867

Source: Evelo Biosciences, Inc.