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): November 5, 2019

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 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-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 2.02. Results of Operations and Financial Condition.

On November 5, 2019, Evelo Biosciences, Inc. (the "Company") announced its financial results for the quarter ended September 30, 2019 and provided recent business highlights. A copy of the press release issued in connection with the announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

Item 7.01. Regulation FD Disclosure.

On November 5, 2019, the Company announced interim data from an ongoing Phase 1b clinical trial. A copy of the press release issued in connection with the announcement is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

On November 5, 2019, the Company hosted a quarterly corporate update conference call and live webcast that included a discussion of, among other things, the interim clinical data. A copy of the slide presentation from the webcast is furnished as Exhibit 99.3 to this Current Report on Form 8-K.

The information contained in Items 2.02 and 7.01 of this Current Report on Form 8-K (including Exhibits 99.1, 99.2 and 99.3) 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	First Press Release issued on November 5, 2019
99.2	Second Press Release issued on November 5, 2019
99.3	Corporate Slide Presentation, dated November 5, 2019

SIGNATURES

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: November 5, 2019

By: /s/ Jonathan Poole

Jonathan Poole

Chief Financial Officer

Exhibit 99.1

Evelo Biosciences Announces Further Positive Interim Phase 1b Clinical Data in Psoriasis and Reports Third Quarter 2019 Financial Results

--EDP1815 was Well Tolerated with No Overall Difference Reported from Placebo--
--Reduction in Mean Lesion Severity Score (LSS) at 28 Days Consistent between High and Low Dose Cohort--
-- Dose Response Trends Observed in LSS and PASI at Day 42--
--EDP1815 Phase 2 Study Initiation Expected in Early 2020--
--Further Clinical Support for Validation of Evelo Platform--
--Management to Host Conference Call at 8:30 a.m. EST--

CAMBRIDGE, Mass., November 5, 2019 - Evelo Biosciences, Inc. (Nasdaq:EVLO), a clinical stage biotechnology company developing a new modality of orally delivered, systemically acting biologics, today announced third quarter 2019 financial results. Additionally, in a separate press release, the Company announced positive interim clinical data in a Phase 1b trial in individuals with mild to moderate psoriasis being treated with a high dose of EDP1815, its clinical candidate for the treatment of a range of inflammatory diseases.

“We now have further clinical data that support our potential ability to treat systemic inflammatory disease through oral delivery of pharmaceuticals to the small intestinal axis,” said Simba Gill, Ph.D., chief executive officer of Evelo. “The clinical activity demonstrated by EDP1815 in psoriasis further validates our platform and highlights Evelo’s potential to bring new medicines with the potential to be effective, safe, convenient and affordable to millions of people living with chronic diseases.”

Inflammation

Interim Clinical Data Highlights

About the EDP1815 Phase 1b clinical trial in mild to moderate psoriasis, high dose cohort
Eighteen individuals with mild to moderate psoriasis were randomized 2:1 to receive a daily oral administration of 2.76g (5x or high dose) of EDP1815 or placebo for 28 days. The primary endpoint is safety and tolerability. Secondary and exploratory endpoints include lesion severity score (LSS) and Psoriasis Area and Severity Index (PASI), both measures of clinical activity, as well as cellular histological biomarkers and blood immune cell biomarkers taken from biopsies and blood samples at the start and end of the dosing period, respectively. Safety and tolerability and secondary clinical endpoints are also measured at day 42, 2 weeks after completion of dosing.

EDP1815 – positive interim Phase 1b clinical data at high dose
- In a separate press release, Evelo reported positive interim clinical data from the high dose cohort in its Phase 1b trial of EDP1815 in mild to moderate psoriasis.
- EDP1815 continued to be well tolerated in this cohort, with no overall difference reported from placebo.
- At the end of the 28-day dosing period, the high dose cohort showed a mean reduction in LSS consistent with previously reported data for a low dose cohort.
- Two weeks following the completion of the dosing period, at day 42, the high dose cohort showed continued reductions from baseline in both mean LSS and PASI, which may be indicative of a sustained clinical effect and dose response.
- A range of histological and molecular biomarkers were measured in the high dose cohort, with trends in line with the clinical effects of EDP1815 at the cohort level.
- Evelo plans to advance EDP1815 into Phase 2 in early 2020. This placebo-controlled dose and formulation selection trial will investigate daily dosing of EDP1815 in mild to moderate psoriasis patients over 16 weeks. Evelo expects to report initial data from the trial in late 2020.

Anticipated Milestones

EDP1815 – Phase 1b new formulation in psoriasis and atopic dermatitis
- Given the newly released positive EDP1815 data and the planned Phase 2 trial, Evelo will not enroll any further cohorts of individuals with psoriasis in the ongoing Phase 1b clinical trial.
- The Company expects to report initial clinical data from a cohort of individuals with mild to moderate atopic dermatitis to be dosed with a new formulation in the second quarter of 2020.

EDP1066 – Phase 1b new formulation in atopic dermatitis

- Evelo expects to report initial clinical data from a cohort of individuals with mild to moderate atopic dermatitis, dosed with a new formulation, in the first quarter of 2020.

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.
- The cohort of patients with microsatellite stable colorectal cancer who had previously failed all therapies for metastatic disease is fully recruited. No clinical responses have been evident, however, several patients in this cohort have experienced extended stable disease. Cellular infiltration biomarker changes were also observed in tumor biopsies taken from those patients during the EDP1503 monotherapy period, which are consistent with preclinical observations for EDP1503. Evelo continues to monitor patients in this cohort.
- Given newly approved treatments for triple-negative breast cancer, Evelo anticipates that the majority of triple negative breast cancer patients to be recruited will have relapsed following prior PD-1/L1 therapy, similarly to those in the PD-1 relapsed cohort.
- Evelo expects to report further clinical data from this trial in the first half of 2020.

Business Highlights

- In September 2019, Evelo appointed David Epstein as chairman of its Board of Directors. Mr. Epstein, who has been a director of Evelo since March 2017, brings extensive experience and relationships in the biotech and pharmaceutical industries to his role as chairman. He currently serves as chairman of the Board of Directors of Rubius Therapeutics and Axcella Health and as a director at International Flavors and Fragrances. From January 2010 - July 2016, Mr. Epstein served as chief executive officer of Novartis Pharmaceuticals, a division of Novartis AG. In conjunction with Mr. Epstein's appointment, Noubar Afeyan, Ph.D., co-founder of Evelo and chief executive officer of Flagship Pioneering, stepped down from his role on Evelo's Board.

Third Quarter 2019 Financial Results

- **Cash Position:** As of September 30, 2019, cash and cash equivalents were $97.1 million, as compared to cash, cash equivalents and investments of $147.9 million as of December 31, 2018 and $113.5 million as of June 30, 2019. This decrease was due to cash used to fund operating activities and capital expenditures for the third quarter of 2019. Evelo expects that its cash and cash equivalents, together with funds available under tranche 2 of its debt facility, will enable it to fund its planned operating expenses and capital expenditure requirements to the end of 2020.
- **Research and Development Expenses:** R&D expenses were $15.6 million for the three months ended September 30, 2019, compared to $11.2 million for the three months ended September 30, 2018. The increase of $4.4 million was due primarily to increases in costs related to Evelo's inflammation clinical 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 September 30, 2019, compared to $5.2 million for the three months ended September 30, 2018. The increase of $0.7 million was due primarily to increased personnel costs to support Evelo's growth.
- **Net Loss:** Net loss attributable to common stockholders was $21.6 million for the three months ended September 30, 2019, or $0.67 per basic and diluted share, as compared to a net loss of $15.9 million for the three months ended September 30, 2018, or $0.50 per basic and diluted share.

Conference Call

Evelo will host a conference call and webcast at 8:30 a.m. EST today to review the new clinical data for EDP1815. To access the call please dial 866-795-3242 (domestic) or 409-937-8909 (international) and refer to conference ID 7788384. 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, 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 pre-clinical models 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 diseases 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, 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, EDP1066 and EDP1503, 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 June 30, 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.

Contact
Evelo Biosciences
Jessica Cotrone, 978-760-5622
jcotrone@evelobio.com

EVELO BIOSCIENCES, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS (UNAUDITED)
(in thousands, except share and per share amounts)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	**2018**	**2019**	**2018**
Operating Expenses(1):				
Research and development	$ 15,610	$ 11,227	$ 46,751	$ 28,542
General and administrative	5,886	5,230	16,936	13,568
Total operating expenses	21,496	16,457	63,687	42,110
Loss from operations	(21,496)	(16,457)	(63,687)	(42,110)
Other income (expense), net	(137)	600	814	607
Net loss	$ (21,633)	$ (15,857)	$ (62,873)	$ (41,503)
Preferred stock dividends	—	—	—	(3,937)
Net loss attributable to common stockholders	$ (21,633)	$ (15,857)	$ (62,873)	$ (45,440)
Net loss per share - basic and diluted	$ (0.67)	$ (0.50)	$ (1.96)	$ (2.45)
Weighted-average common shares used in computing net loss per share - basic and diluted	32,060,747	31,741,683	32,009,571	18,532,408

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

Research and development	$ 980	$ 764	$ 2,844	$ 1,767
General and administrative	1,082	831	3,306	2,727

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

	September 30, 2019	December 31, 2018
Assets:		
Cash, cash equivalents and investments	$ 97,061	$ 147,919
Property and equipment, net	8,339	6,925
Other assets	5,740	5,023
Total assets	$ 111,140	$ 159,867
Liabilities and stockholders' equity:		
Accounts payable and current liabilities	$ 9,675	$ 9,235
Long-term debt	19,549	12,305
Other liabilities	1,370	1,378
Total liabilities	30,594	22,918
Total stockholders' equity	80,546	136,949
Total liabilities and stockholders' equity	$ 111,140	$ 159,867

Exhibit 99.2

Evelo Biosciences Reports Further Positive EDP1815 Interim Clinical Data in Patients with Psoriasis at High Dose in Phase 1b Trial

--EDP1815 was Well Tolerated with No Overall Difference Reported from Placebo--
--Reduction in Mean Lesion Severity Score (LSS) at 28 Days Consistent with Low Dose Cohort--
-- Dose Response Trends Observed in LSS and PASI at Day 42--
--Phase 2 Study Initiation Expected in Early 2020--
--Further Clinical Support for Validation of Evelo Platform--
--Management to Host Conference Call at 8:30 a.m. EST--

CAMBRIDGE, Mass., November 5, 2019 - Evelo Biosciences (Nasdaq:EVLO), a clinical stage biotechnology company developing a new modality of orally delivered, systemically acting biologics, today announced positive interim clinical data in an ongoing Phase 1b trial in individuals with mild to moderate psoriasis treated with a high dose of EDP1815, its clinical candidate for the treatment of a range of inflammatory diseases.

Eighteen individuals with mild to moderate psoriasis were randomized 2:1 to receive a daily oral administration of 2.76g (5x or high dose) of EDP1815 or placebo for 28 days. The primary endpoint is safety and tolerability. Secondary and exploratory endpoints include lesion severity score (LSS), Psoriasis Area and Severity Index (PASI), both measures of clinical activity, as well as cellular histological biomarkers and blood immune cell biomarkers taken from biopsies and blood samples at the start and end of the dosing period, respectively. Safety and tolerability and secondary clinical endpoints are also measured at day 42, 2 weeks after completion of dosing.

EDP1815 continued to be well tolerated in this cohort, with no overall difference reported from placebo. At the end of the 28-day dosing period, the high dose cohort showed a mean reduction in LSS consistent with previously reported data from a low dose cohort.

Two weeks following the completion of the dosing period, at day 42, the high dose cohort showed continued reductions from baseline in both mean LSS and PASI, which may be indicative of a sustained clinical effect and dose response.

A summary of the LSS and PASI results are shown in the tables below.

Mean (+/-SE) Percentage Change in LSS vs. Start of Dosing Period [(1)]

	n	At end of 28-day dosing period	At day 42
Placebo [(2)]	10	0.6% (9.0%)	-7.2% (6.2%)
EDP1815 (high dose)	12	-15.1% (6.4%)	-24.1% (7.1%)
EDP1815 (low dose)	8	-22.8% (9.9%)	-9.0% (12.7%)

Mean (+/-SE) Percentage Change in PASI vs. Start of Dosing Period [(1)]

	n	At end of 28-day dosing period	At day 42
Placebo [(2)]	10	-1.0% (13.2%)	-3.3% (14.8%)
EDP1815 (high dose)	12	-16.0% (8.1%)	-20.7% (8.2%)

Note:
[(1)] This study was not sufficiently powered to detect statistically significant differences in clinical effect between treatment groups.
[(2)] Represents the combination of placebo arms for the low dose (n=4) and high dose (n=6) cohorts.

A range of histological and molecular biomarkers were measured in the high dose cohort, with trends in line with the clinical effects of EDP1815 at the cohort level.

“We are extremely encouraged by the interim clinical data from our high dose cohort of EDP1815. In a small number of individuals and short treatment duration we have seen consistent results in this Phase 1 study and sustained and continued reductions in LSS and PASI at the high dose two weeks post treatment. This reinforces our belief in EDP1815’s potential for

patients with mild to moderate psoriasis and potentially for a wider range of inflammatory diseases," said Duncan McHale, M.B.B.S., Ph.D., chief medical officer of Evelo. "These interim results underpin the biology of the small intestinal axis, its importance on systemic physiology, and the potential of our platform to develop medicines which harness this effect."

"There are multiple efficacious options for severe psoriasis, but there is a significant need for new therapies for patients living with mild to moderate disease. Many patients suffer from limited but severe lesions that have a profound impact on quality of life," said Dr. Mark Lebwohl, M.D., Professor and Chairman of the Kimberly and Eric J. Waldman Department of Dermatology at the Icahn School of Medicine. "The interim data for EDP1815, which show continuing reductions in clinical measures of disease over a short duration and that EDP1815 has been well tolerated, are encouraging. I look forward to the Phase 2 data and understanding how these results translate to a larger patient population over a prolonged treatment period."

Evelo plans to advance EDP1815 into Phase 2 in early 2020. This placebo-controlled trial will investigate daily dosing of EDP1815 in individuals with mild to moderate psoriasis over 16 weeks, and the primary endpoint will be a reduction in PASI score. Part A of the trial is designed to select an optimal formulation and will test the high dose of the enteric capsule formulation versus the high dose of a new formulation of EDP1815 versus placebo in approximately 180 individuals. Evelo expects to perform an interim analysis, and to report initial data from Part A of the trial, in late 2020, which will enable the selection of the optimal formulation and potential initiation of Part B. Part B is designed to test three doses of the optimal formulation determined in Part A against placebo in approximately 250 individuals.

Lesion Severity Score (LSS)
LSS, a secondary endpoint, is a component of the Psoriasis Area and Severity Index (PASI) score. It is a 12-pont scale which measures redness, thickness, and scaling of an individual psoriatic lesion and is a sensitive clinical measure for patients with mild to moderate disease.

Psoriasis Area and Severity Index (PASI)
PASI, a secondary endpoint, is a quantitative rating score for measuring the severity of psoriatic lesions based on area coverage and plaque appearance. PASI combines this assessment into a single score in the range of 0 (no disease) to 72 (maximal disease). The body is divided into four sections (head, arms, trunk, and legs). The average lesion severity score and area affected by lesions is assessed for each of these areas individually, and then the four scores are weighted and combined into a final PASI score.

About the EDP1815-101 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 individuals with mild or moderate psoriasis or atopic dermatitis. Prospectively defined secondary and exploratory endpoints include the effect of EDP1815 on clinical measures of disease and a range of biomarkers. Evelo expects to report additional data from this study in a cohort of individuals with atopic dermatitis to be dosed with a new formulation of EDP1815 in Q2 2020. Based on the results today and the planned Phase 2 psoriasis study, Evelo will not enroll any further cohorts of individuals with psoriasis in this ongoing Phase 1b trial.

Evelo expects to present data from this trial at a future scientific conference or medical meeting.

About EDP1815
EDP1815 is an investigational orally delivered monoclonal microbial being developed for the treatment of inflammatory diseases. EDP1815 is a strain of *Prevotella histicola*, selected for its specific pharmacology. In preclinical studies EDP1815 has shown potent immunomodulatory effects on human immune cells *in vitro* and *in vivo* anti-inflammatory activity on a range of tissues, including skin, joints, gut, and the CNS.

Conference Call
Evelo will host a conference call and webcast at 8:30 a.m. EST today to review these clinical data. To access the call please dial 866-795-3242 (domestic) or 409-937-8909 (international) and refer to conference ID 7788384. 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.

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dose-dependent effects, modulating multiple clinically validated pathways. Evelo's product candidates have the potential to be effective, safe and affordable medicines to improve the lives of people with chronic diseases 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

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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 June 30, 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.

Contact

Evelo Biosciences
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jcotrone@evelobio.com

EVELO BIOSCIENCES

New Therapeutic Modality Supported by Positive Interim Clinical Data

EDP1815 Advancing into Phase 2

November 5, 2019

Legal Disclaimer

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including 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, and the timing and results of any clinical studies or 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: 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.

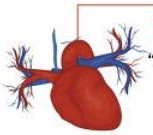
These and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, and our other reports filed with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management's estimates as of the date of this presentation. 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 presentation.

Positive Interim Clinical Data Support Evelo's Platform Opportunity

- EDP1815 could address significant unmet need for mild to moderate psoriasis patien
  - EDP1815 continued to be well tolerated
  - Mean reduction in LSS at 28 days at high dose was consistent with low dose
  - High dose showed continued mean reductions in both LSS and PASI at day 42
- Advancing into Phase 2 in early 2020

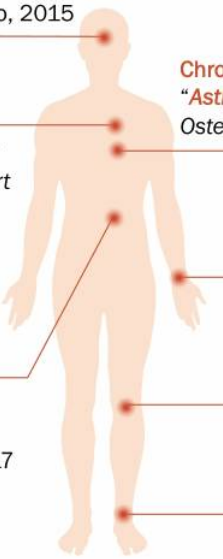
Chronic Inflammation is a Central Driver of Society's Most Burdenson Diseases

Neurological diseases; 7M US DALYs, 111M WW
"The contribution of inflammation in the pathogenesis of Alzheimer's Disease has been appreciated only recently" Nat Rev Neuro, 2015



Cardiovascular disease; 16M US DALYs, 366M WW
"Chronic inflammation is a major contributor to heart disease" Johns Hopkins Medicine

Diabetes; 4M US DALYs, 68M WW
"Inflammation is increasingly considered to be an established mediator [of diabetes]" J Clin Invest., 2017



Chronic respiratory diseases; 6M US DALYs, 112M WW
"Asthma is a chronic inflammatory disease" J Amer Osteopathic Assc, 2011

Autoimmune diseases; 2M US DALYs, 18M WW
"Higher levels of systemic inflammation are associated with [cardiovascular decline in rheumatoid arthritis patients]" Ann Rheum Dis., 201

Injuries; 10M US DALYs, 252M WW
"While inflammation is vital in clearing infection and debris, it can lead to tissue damage if prolonged, [causing chronic wounds]" Int J Mol Sci, 2016

SOURCE: Scientific literature, Global Disease Burden 2017

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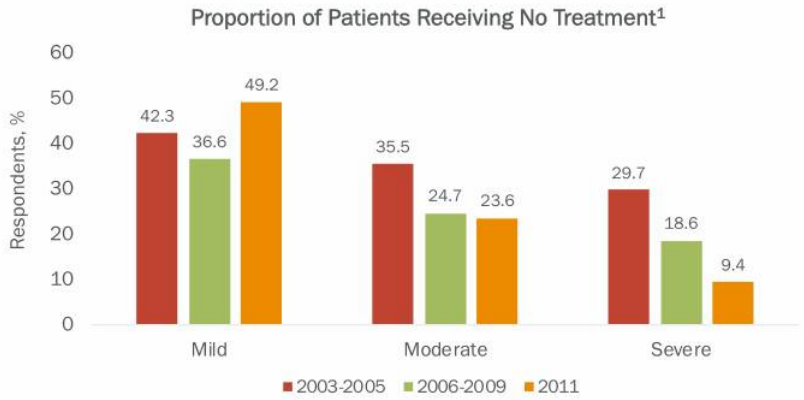
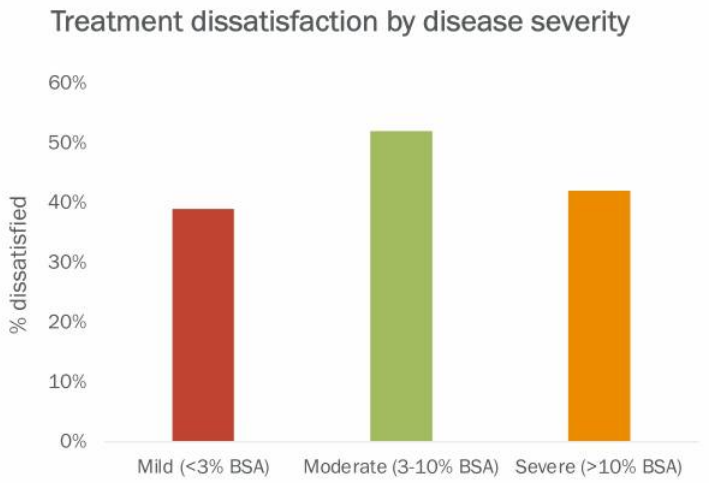
Significant Number of Patients with Psoriasis Go Untreated



The primary reasons physicians do not initiate or maintain treatments are due to concerns about long-term safety or tolerability and efficacy of currently available therapies.

[1]Armstrong AW, Robertson AD, Wu J, Schupp C, Lebwohl MG. Undertreatment, Treatment Trends, and Treatment Dissatisfaction Among Patients With Psoriasis and Psoriatic Arthritis in the United States: Findings From the National Psoriasis Foundation Surveys, 2003-2011. JAMA Dermatol. 2013;149(10):1180–1185. doi:10.1001/jamadermatol.2013.5264

Majority of Moderate Patients are Dissatisfied with Treatment Optio



In annual surveys conducted from 2003-2011 by the National Psoriasis Foundation, ~5,000 patients were asked...

"How satisfied have you been with the treatment you have received for your psoriasis?"[1]

52% of moderate patients were dissatisfied

[1]Armstrong AW, Robertson AD, Wu J, Schupp C, Lebwohl MG. Undertreatment, Treatment Trends, and Treatment Dissatisfaction Among Patients With Psoriasis and Psoriatic Arthritis in the United States: Findings From the National Psoriasis Foundation Surveys, 2003-2011. JAMA Dermatol. 2013;149(10):1180–1185. doi:10.1001/jamadermatol.2013.5264

EDP1815 High Dose Psoriasis Cohort

- 18 individuals with mild to moderate psoriasis
- Randomized 2:1 (active:placebo) with 2.76g dose (enteric capsule formulation), daily oral administration
- 28-day dosing period with follow up at day 42
- Primary endpoint of safety and tolerability

Secondary and Exploratory Endpoints Reported

- LSS
- PASI
- Cellular biomarkers from skin biopsies
- Blood immune cell biomarkers of cytokine production

Lesion Severity Score and PASI

Lesion Severity Score

12-point severity score for a single lesion
More sensitive in mild disease and
short treatment periods

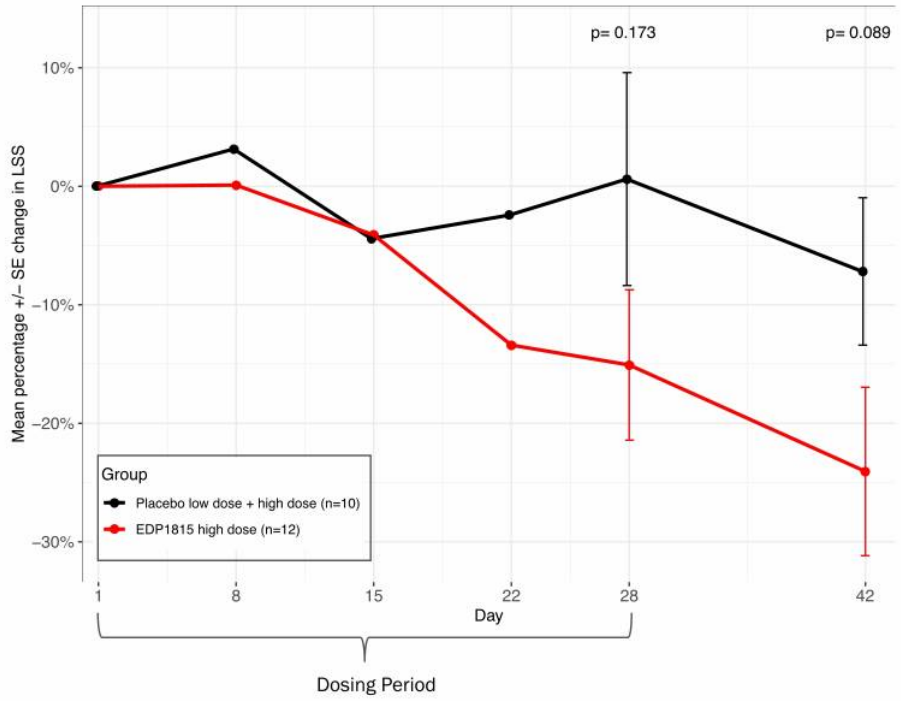
- 4 points – redness
- 4 points – thickness
- 4 points – scaling

PASI

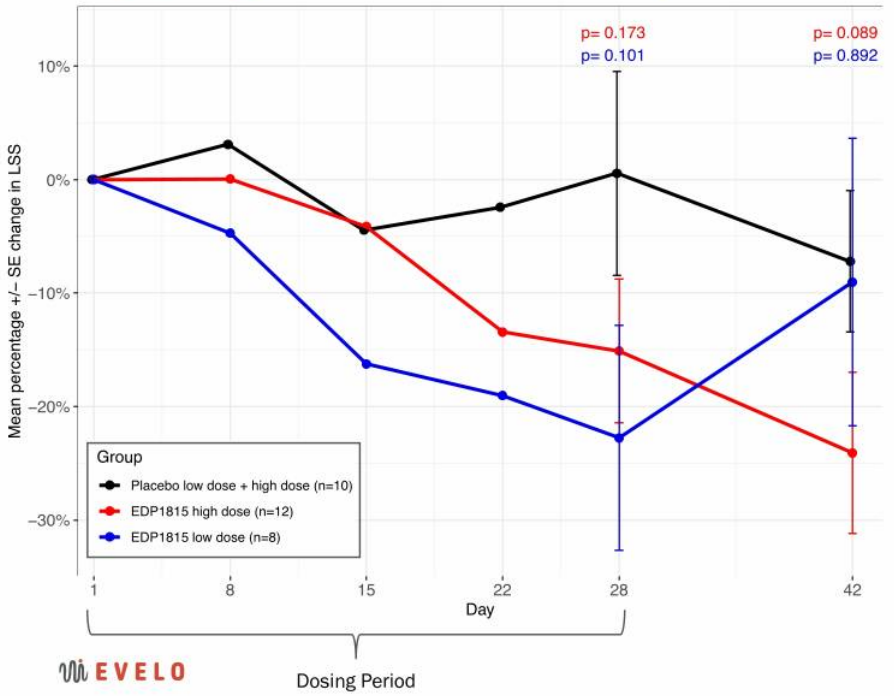
Severity score weighted for all lesions
Most appropriate for moderate to severe disease and
longer treatment periods

- Lesion Severity Score averaged across body region
- Weighted by affected surface area in region
- Weighted by proportion of region to total body area

Mean LSS Reduction of 15% at Day 28; 24% at Day 42

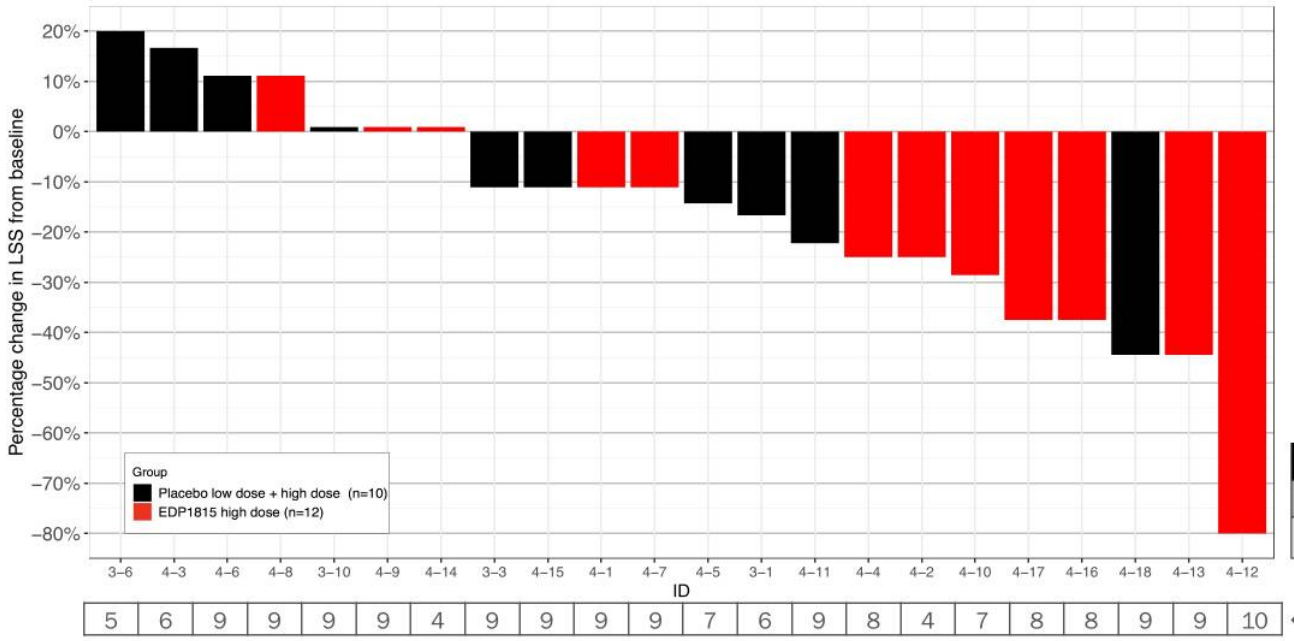


LSS Reduction Consistent Between High and Low Dose Over 28 Days; High Dose Better at Day 42



- Continued reduction in LSS to day 42 at high dose may be indicative of potential sustained effect and dose response

Reduction in LSS of up to 80% at Day 42 at High Dose



5	6	9	9	9	9	4	9	9	9	9	7	6	9	8	4	7	8	8	9	9	10

← Baseline LSS

Group	Baseline LSS
Placebo low dose + high dose (n=10)	9 (6.2
EDP1815 high dose (n=12)	8.5 (7.

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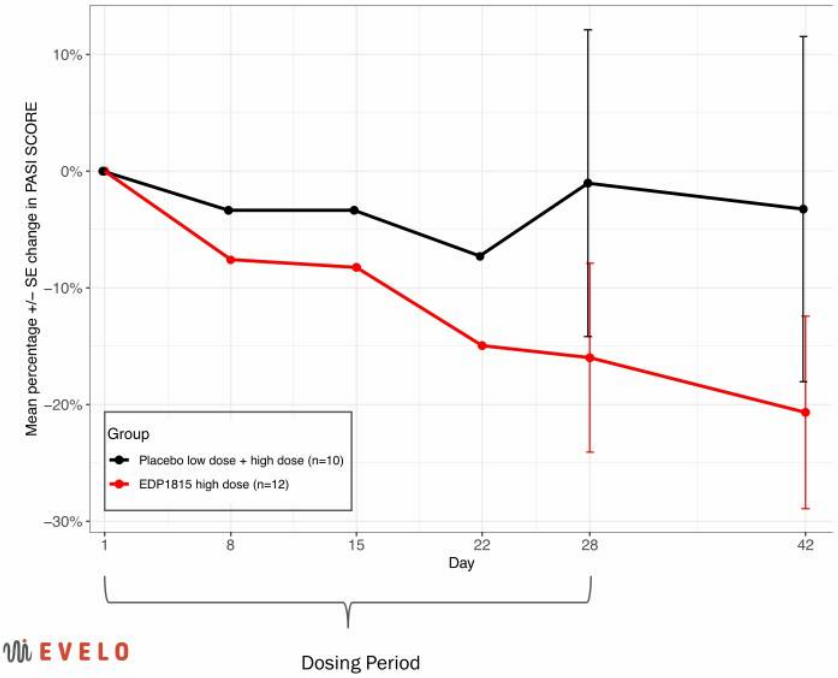
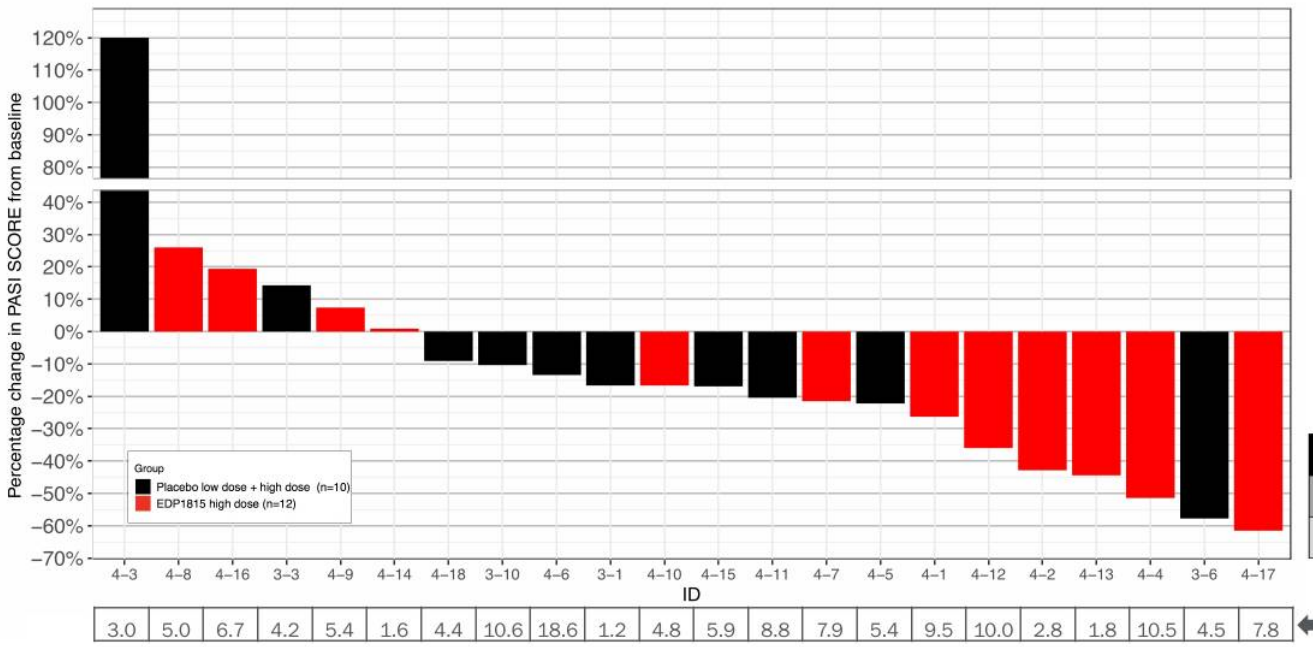
High Dose Mean PASI Reduction Consistent with LSS and Continued to Improve After End of Dosing



Dosing Period

- PASI reduction at high dose
  - 16% at day 28 versus placebo of 1%
  - 21% at day 42 versus placebo of 3%

Reduction in PASI of up to 61% at Day 42 at High Dose



Group	Baselin mec
Placebo low dose + high dose (n=10)	4.95
EDP1815 high dose (n=12)	6.05 (

3.0	5.0	6.7	4.2	5.4	1.6	4.4	10.6	18.6	1.2	4.8	5.9	8.8	7.9	5.4	9.5	10.0	2.8	1.8	10.5	4.5	7.8

← Baseline PASI s

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Interim Clinical Data Summary

- Potential for EDP1815 to address significant needs of mild to moderate psoriasis patients
- Encouraging early clinical activity
  - Mean LSS Reduction of 24% at Day 42 at high dose
  - Mean PASI Reduction of 21% at Day 42 at high dose

Planning for EDP1815 Phase 2 and Additional Indications

Placebo-controlled dose and formulation optimization study in mild to moderate psoriasis planned for early 2020 initiation

- Primary endpoint: change in PASI score at 16 weeks
- Interim analysis for Part A expected in late 2020

Part A	Part B
Goal: Formulation selection	Goal: Dose selection
n~180, 3 arms, original formulation vs. new formulation vs. placebo	n~250, 4 arms, 3 different doses of optimal formulation vs. placebo

Opportunity to evaluation EDP1815 in additional indications following Part A interim analysis

Evelo Platform Opportunity

Summary

Evelo Strategy: Develop New Medicines for Millions of People

Create new market as mid-line therapy and defer use of injectable biologics / specialty drugs
Expand to front line treatment to become foundational therapy

Inflammation	Oncology	Metabolism and CV	Neuro-inflammation/ Degeneration	Autoimmune	Neuro-psychiatric	Vaccines

EDP1815 Phase 2a 16-week Interim Data Expected in Late 2020

Candidate	2020	
EDP1815	**Phase 1b** Atopic Dermatitis New formulation **2Q 2020**	**Phase 2a 16-week interim** Psoriasis Enteric capsule and new formulation **Late 2020**
EDP1066	**Phase 1b** Atopic Dermatitis New formulation **1Q 2020**	
EDP1503	**Phase 1/2** MSS Colorectal Carcinoma PD-1 Relapsed **1H 2020**	

Today's Highlights and Next Steps

- Positive interim clinical data supports validation of Evelo's platform opportunity and vision
  - Oral biologics acting on cells in the small intestine have the potential to modulate systemic immunology
  - Potential to develop effective, safe, convenient, and affordable medicines for major chronic disease
- EDP1815 - Consistent clinical responses signal potential in psoriasis
  - Advancing into Phase 2 in psoriasis in early 2020
  - Expect to evaluate additional indications after interim 16-week Phase 2 data

EVELO BIOSCIENCES

New Therapeutic Modality Supported by Positive Interim Clinical Data

EDP1815 Advancing into Phase 2

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Q&A