# 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): September 27, 2021**

# 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, including 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 ☒

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 September 27, 2021, Evelo Biosciences, Inc. (Evelo) announced data from its Phase 2 clinical trial of EDP1815 in psoriasis and hosted a corporate update conference call with a live webcast. A copy of the slide presentation from the webcast is furnished as Exhibit 99.1 to this Current Report on Form 8-K and 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. The information contained in this Item 7.01 shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (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 8.01. Other Events.**

Phase 2 Clinical Data with EDP1815 in Psoriasis

On September 27, 2021, Evelo announced data from its Phase 2 clinical trial of EDP1815 in psoriasis. A statistically significant reduction in the Psoriasis Area and Severity Index (PASI) score, as measured by the proportion of patients achieving at least 50% improvement in PASI from baseline at the week 16 timepoint, was observed in the study. EDP1815 is an investigational oral biologic currently in development for the treatment of a broad range of inflammatory diseases, including clinical programs in psoriasis, atopic dermatitis, and COVID-19.

In the Phase 2 study, the PASI scores were assessed by both mean changes from baseline and responder rates. The primary endpoint was the mean percentage change in PASI between treatment and placebo and was prespecified as a Bayesian analysis. The Bayesian approach provides an estimate of the probability that EDP1815 is superior to placebo. The 16-week primary endpoint gave probabilities that EDP1815 is superior to placebo ranging from 80% to 90% across the prespecified analyses and cohorts.

The responder endpoint reports the proportion of patients who had a meaningful clinical response, which is defined as PASI-50 or greater. 25% to 32% of patients across the three cohorts who were treated with EDP1815 achieved a PASI-50 at week 16 compared to 12% on placebo. In cohorts 1 and 2 this difference in response rate was statistically significant ($p < 0.05$). Cohort 3 was directionally similar (25% vs. 12%). The pooled PASI-50 response across all three EDP1815 cohorts, an exploratory analysis, was 29% vs. 12% for placebo and was also statistically significant with a p-value of 0.027. An increase in the number of capsules of EDP1815 did not lead to a dose response.

Additionally, several patients on EDP1815 achieved a PASI-75 or better, which was sustained or improved post treatment. For individuals who had a PASI-50 response or better, consistent effects in secondary and exploratory endpoints, including improvements in patient reported outcomes such as Dermatology Life Quality Index (DLQI) and Psoriasis Symptom Inventory (PSI), were observed.

EDP1815 was observed to be well tolerated in the Phase 2 study. The safety data were comparable to placebo and consistent with what was previously reported in a Phase 1b study. Adverse events (AEs) classified as "gastrointestinal" were comparable between active and placebo groups, with no meaningful differences in rates of diarrhea, abdominal pain, nausea, or vomiting. There were no related serious adverse events.

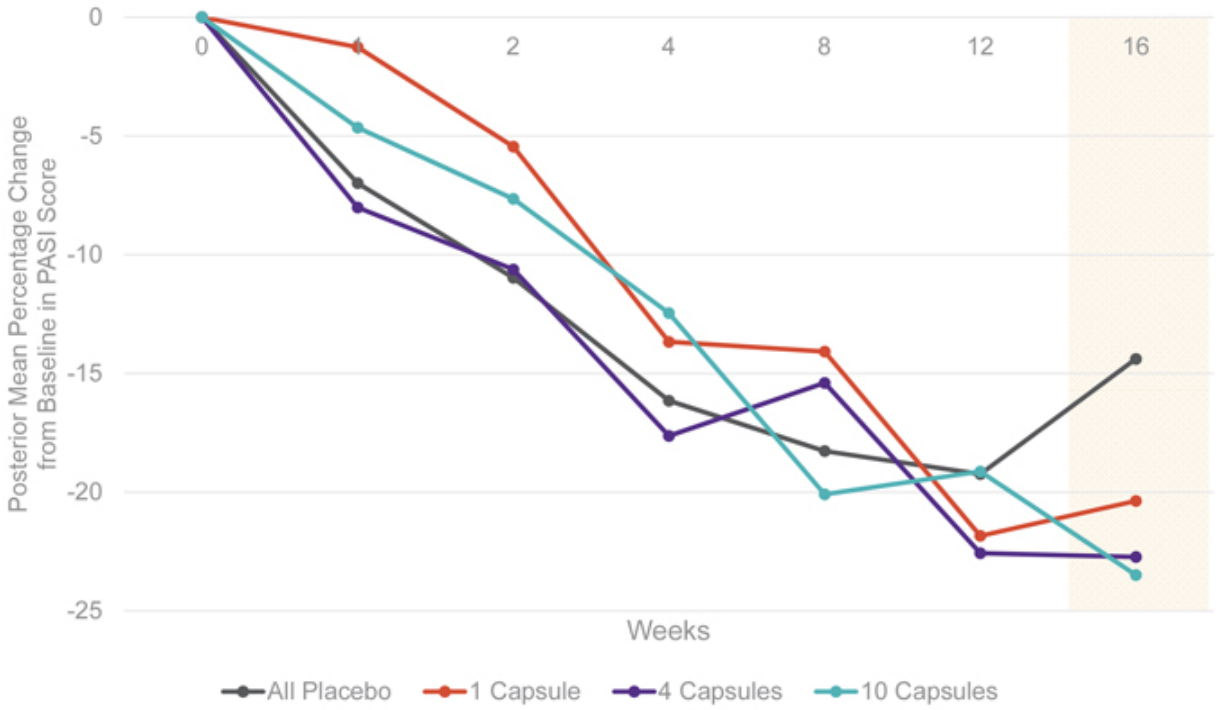
EDP1815-201 is a double-blind, placebo-controlled, dose-ranging Phase 2 study designed to evaluate three doses of an enteric capsule formulation of EDP1815 versus placebo in 249 patients with mild and moderate psoriasis over a 16-week treatment period. In the study, the PASI scores were assessed by both mean changes from baseline and responder rates. The primary endpoint is mean percentage reduction in PASI score at 16 weeks. Secondary endpoints include the proportion of study participants who achieve a PASI-50 response or greater and other clinical measures of disease such as Physicians Global Assessment (PGA), Body Surface Area (BSA), PGA x BSA, PSI, and DLQI.

The corporate update included the following information:

**Baseline characteristics are well-balanced across treatment groups**

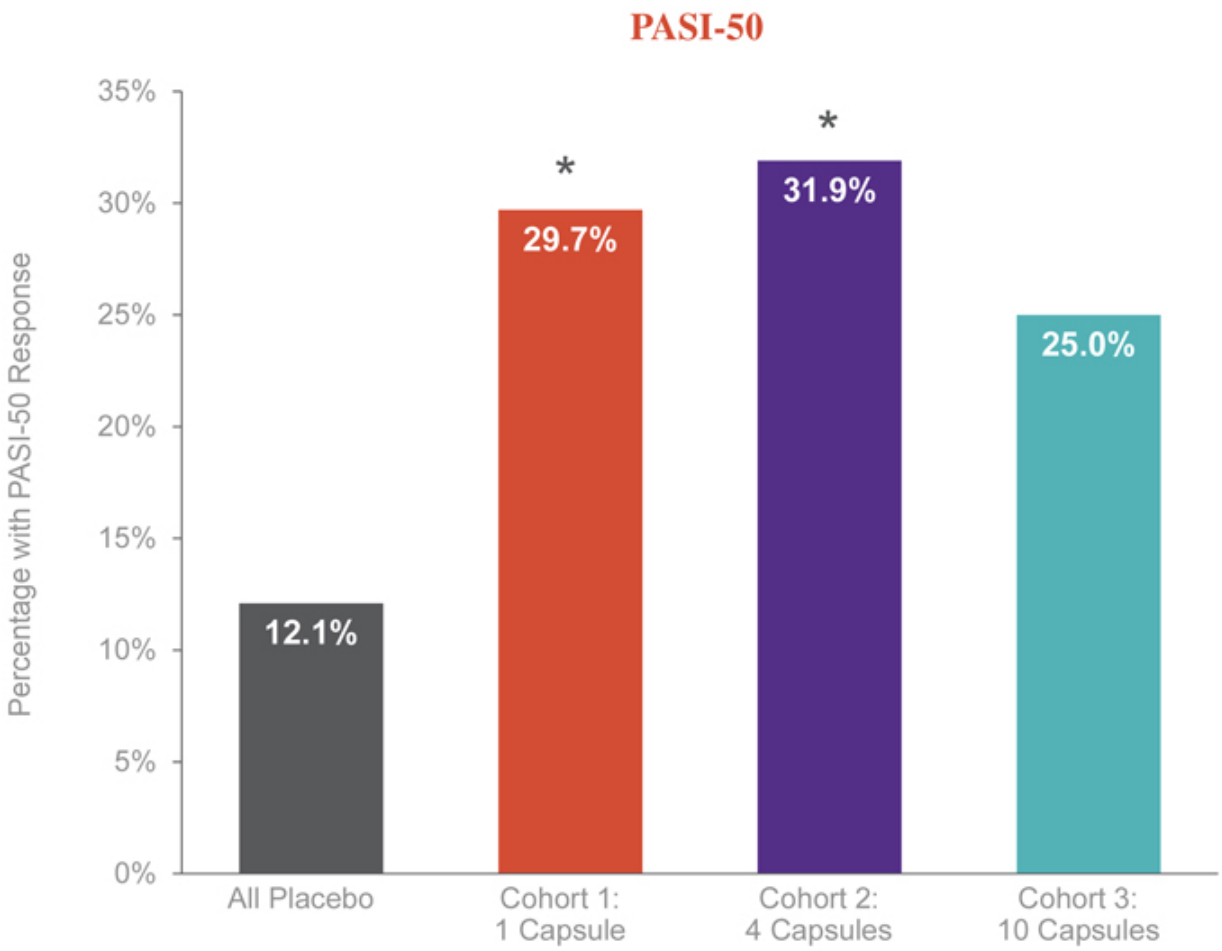
| Parameter | All | Placebo (pooled) | Cohort 1 (1 capsule) | Cohort 2 (4 capsules) | Cohort 3 (10 capsules) |
|---|---|---|---|---|---|
| Number | 249 | 83 | 56 | 55 | 55 |
| Age, mean years | 44 | 44.4 | 44.5 | 41.2 | 45.5 |
| Female (%) | 36.9 | 39.8 | 39.3 | 43.6 | 23.6 |
| BMI, mean kg/m$^2$ | 29.7 | 30.2 | 29.9 | 28.5 | 29.7 |
| PGA 3 (%) | 62.2 | 65.1 | 62.5 | 54.5 | 65.4 |
| PASI mean | 8.5 | 8.7 | 8.4 | 8.7 | 8.3 |
| BSA mean % | 7.3 | 7.3 | 7.4 | 7.3 | 7.1 |

**EDP1815 is superior to placebo after 16 weeks of treatment**




Bayesian Analysis, Modified intent to treat. 80-90% probability that EDP1815 is superior

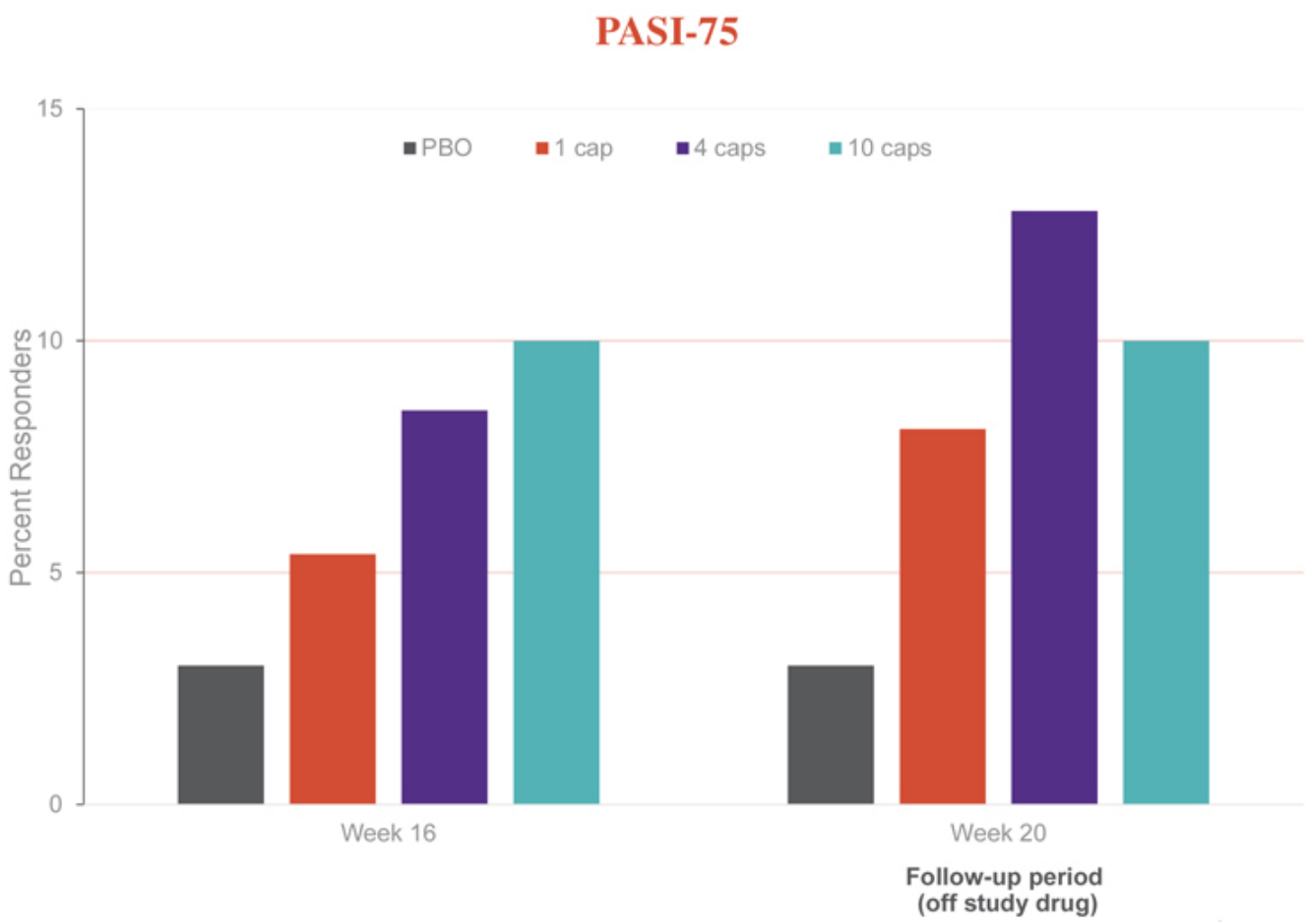
**Robust PASI-50 responses with EDP1815 at week 16**




*p<0.05

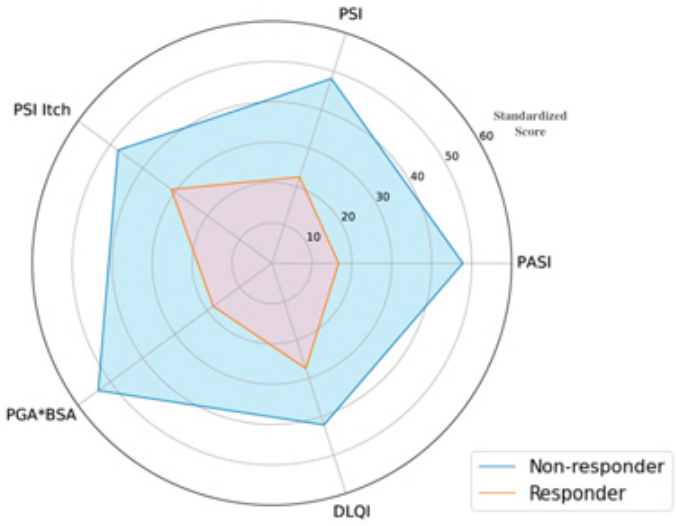
Statistically significant p-value (<0.05) for 2 of the 3 individual dose cohorts, and for all 3 cohorts when pooled

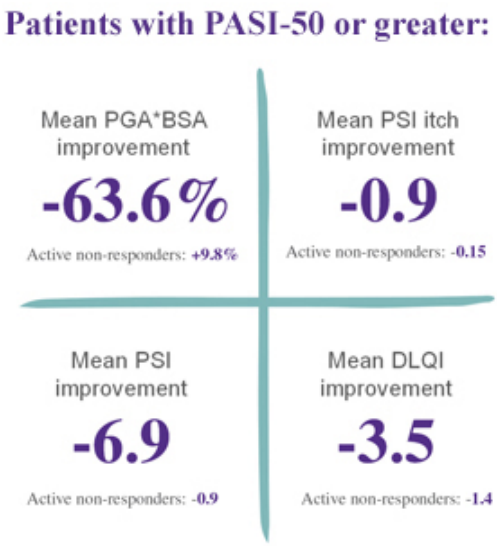
**PASI-75 responses increase with time**




Difference from placebo not statistically significant at week 16

**Consistent improvements across multiple endpoints at week 16 in active cohort: responder vs. non-responder***




*Responder = Active patients who achieved PASI-50 or greater

**EDP1815 demonstrates placebo-like tolerability**

- Oral drug candidate that should not require screening or laboratory monitoring
- Gastrointestinal related Adverse Events (AEs) comparable to placebo with no meaningful difference

| | All Placebo (N=83) % | All EDP1815 (N=166) % |
|---|---|---|
| Any Treatment Emergent Adverse Events (TEAE) | 54.2 | 58.4 |
| Any Related* TEAE | 16.9 | 19.3 |
| Any Related* TEAE of Common Terminology Criteria for Adverse Event (CTCAE) Grade 2 or above | 7.2 | 7.8 |
| Any Related* TEAE of CTCAE Grade 3 or above | 0 | 0.6 (n=1) |
| Any Related* TEAE of CTCAE Grade 4 or above | 0 | 0 |
| Any Related* Serious TEAE | 0 | 0 |
| AE: Related* Infections and Infestations | 0 | 0.6 (n=1) |
| AE: Related* Gastrointestinal | 10.8 | 12.7 |

* Related TEAEs are those with probable, possible or definitely relationship to study drug, or where relationship is missing.

Update on Phase 2 Clinical Trial with EDP1815 in Atopic Dermatitis

Based on the results from the EDP1815-201 trial in psoriasis and other external feedback, Evelo is extending the endpoint of its EDP1815-207 Phase 2 trial in atopic dermatitis from 12 to 16 weeks and modifying the primary endpoint to be the percent of patients achieving an EASI-50 (Eczema Area and Severity Index) score at week 16. As a consequence of this change, Evelo has increased the number of patients in the trial to 300, with a target of 225 on active and 75 on placebo. In addition to these changes, Evelo recently received and has responded to a clinical hold letter from the U.S. Food and Drug Administration (FDA) related to Evelo's recently submitted Investigational New Drug Application for this atopic dermatitis trial. The FDA requested that additional detail in Evelo's protocol be added around risks to patients that require their current atopic dermatitis medications be discontinued, the manner in which safety data is collected, and defined study halting criteria. Evelo now anticipates reporting results from this trial in the fourth quarter of 2022, which, if positive, will be used to support the dose selection for the Phase 3 atopic dermatitis program.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit No. | Description |
|---|---|
| 99.1 | Corporate Slide Presentation, dated September 27, 2021 |
| 99.2 | Press Release issued on September 27, 2021 |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) |

**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: September 27, 2021

By: /s/ Daniel S. Char
Daniel S. Char
General Counsel & Secretary

Exhibit 99.1

EVELO

# Topline Results for Phase 2 Study of EDP1815 in Mild and Moderate Psoriasis

September 27, 2021

# 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 statements concerning the development of EDP1815, the promise and potential impact of EDP1815, the timing of and plans for clinical studies, 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 cash runway; 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 three months ended June 30, 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 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.*

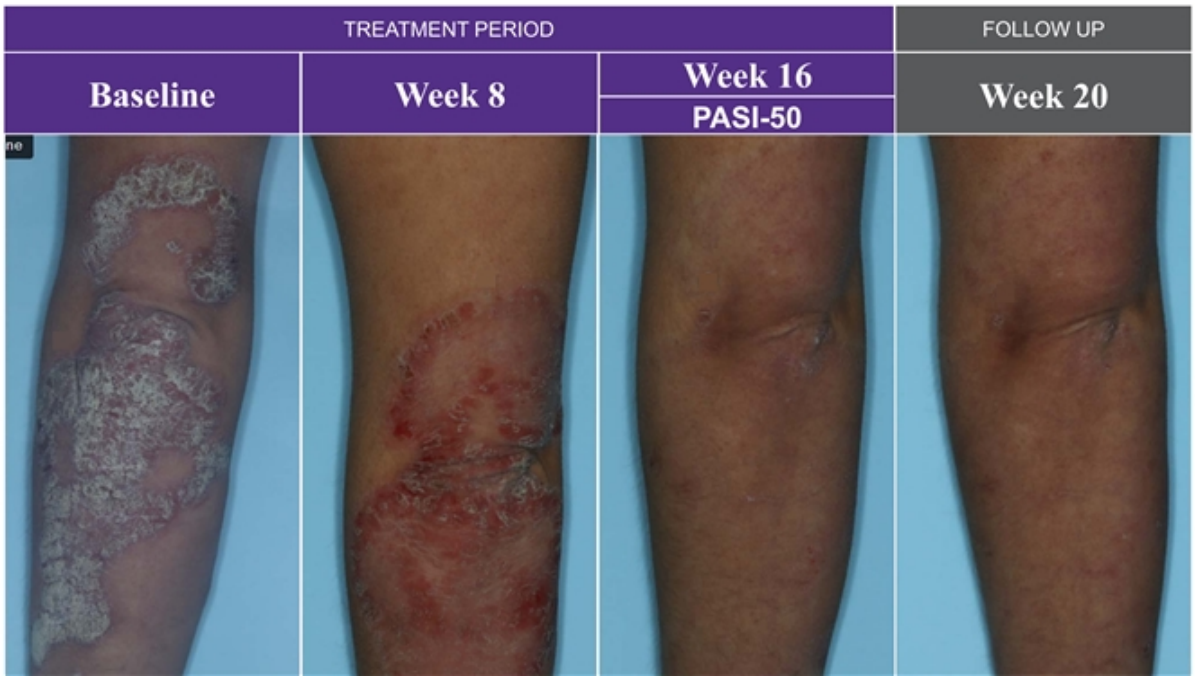
*Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and we make no representation as to the adequacy, fairness, accuracy or completeness of any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.*

# Positive Phase 2 data of EDP1815 confirms ability to harness the small intestinal axis, SINTAX™, to treat systemic inflammatory diseases

- Clinically and statistically significant improvement in PASI-50 score achieved
- Oral EDP1815 can drive potent effects with placebo-like safety and tolerability
- EDP1815 advancing towards registration studies in psoriasis

EVELO

# PASI-50 response at week 16



**Majority of psoriasis sufferers have mild or moderate disease**

**93%**

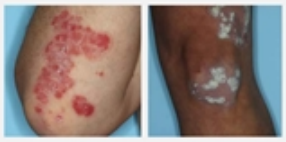
## Psoriasis

| 55M | 8.6M | 6.7M |
|---|---|---|
| Worldwide prevalence | U.S. prevalence | U.S. diagnosed |


Source: Datamonitor Healthcare, Vanderpuye-Orgle et al., J Am Acad Dermatol. 2015; 72:961–7

# Mild and moderate psoriasis is a serious condition that significantly impacts patients

## Burdensome Lesions



- **Painful, cracked skin**
- **Itchy and irritating**
- **Highly visible**

## Quality of Life Impact

**65%** of mild and **93%** of moderate psoriasis sufferers report moderate - extremely high impact on daily life[1]

## Psychosocial Impact

**34% - 40%** of mild and moderate psoriasis sufferers have depression; **27% - 57%** suffer sleep disturbance[2]

[1] Martin G., et al., J Clin Aesthet Dermatol. 2019;12(4):13-26. [2] Luca M, Musumeci ML, D'Agata E, Micali G. Int J Psychiatry Clin Pract. 2020 Mar;24(1):102-104.

# Current therapies for psoriasis have limitations related to safety, tolerability, convenience, and price

***>50%** of patients are dissatisfied with current treatment options[1]*

### Topicals

- Not convenient
- Low compliance
- No systemic impact

### Traditional Systemics

- Safety concerns
- Monitoring
- Immunosuppressant

### Oral Immunosuppressant

- Apremilast:
  - Safety and tolerability issues
  - High price

### Injectable Biologics

- Not convenient & needle fear
- Immunosuppressant
- High price

- **As many as 50%** of patients in the U.S. not on any Rx treatment[7]
- **<8%** of patients in the U.S. receive injectable antibody therapies or oral systemics[2-6]

[1] Florek, Aleksandra G., et al., Archives of dermatological research 310.4 (2018): 271-319. [2] IQVIA and Symphony Health Data [3]Armstrong A, et al., Dermatol Ther (Heidelb). 2017 Mar; 7(1) [4]IQVIA Prescription data from Analyst Report, Oct 2020 [5]DRG Epidemiology Database 2017 [6] Lebwohl MG, et al., J Am Acad Dermatol. 2014 May;70(5):871-81.e1-30. [7]Armstrong, April W., et al. JAMA dermatology 149.10 (2013): 1180-1185.

# Apremilast is limited by tolerability

## Significant Tolerability Issues

**>30%**

of patients with moderate PsO experienced one or more of:

diarrhea, nausea, vomiting, and headache[1]

## High Discontinuation

**>66%**

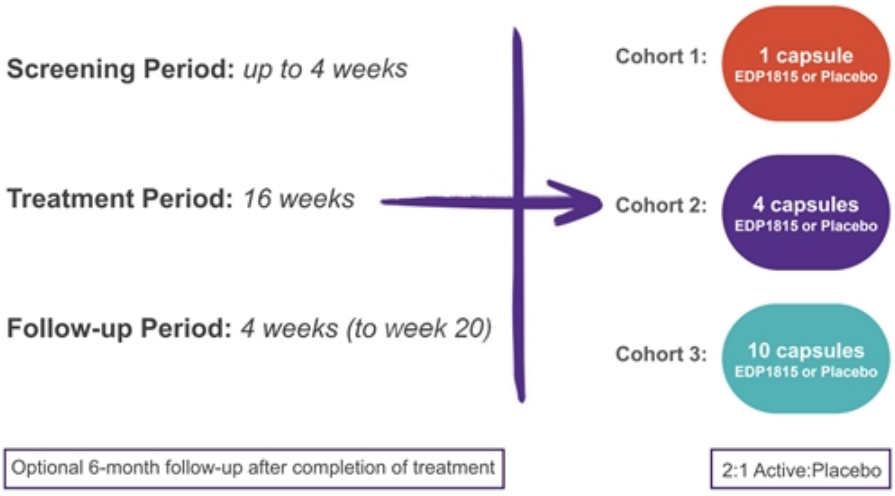
discontinued therapy in 1st year[2,3]; majority of discontinuation attributed to tolerability[2,3,4]

[1] UNVEIL trial results, clinicaltrials.gov [2] Sbidian, et al. Br J Dermatol. 2020: 182(3):690-697 [3] Wu, et al. J Dermatol Treatment. 2019. ISSN: 0954-6634. [4] Sponsored primary research

# EDP1815 Phase 2 study in mild and moderate psoriasis

**Key Inclusion Criteria:**

- BSA of ≥3% and ≤10%
- PASI score of ≥6 and ≤15
- PGA score of 2 or 3




Optional 6-month follow-up after completion of treatment

2:1 Active:Placebo

# PASI scores assessed by mean effect and response rate

**Primary Endpoint:**
***Mean treatment effect across all patients***

*Mean % change in PASI from baseline to week 16 vs. placebo*

**Result Measure:**
*Bayesian probability (%) that EDP1815 is superior to placebo; threshold to proceed ≥ 80%*

**Responder Endpoint:**
***Proportion of patients with a meaningful clinical response***

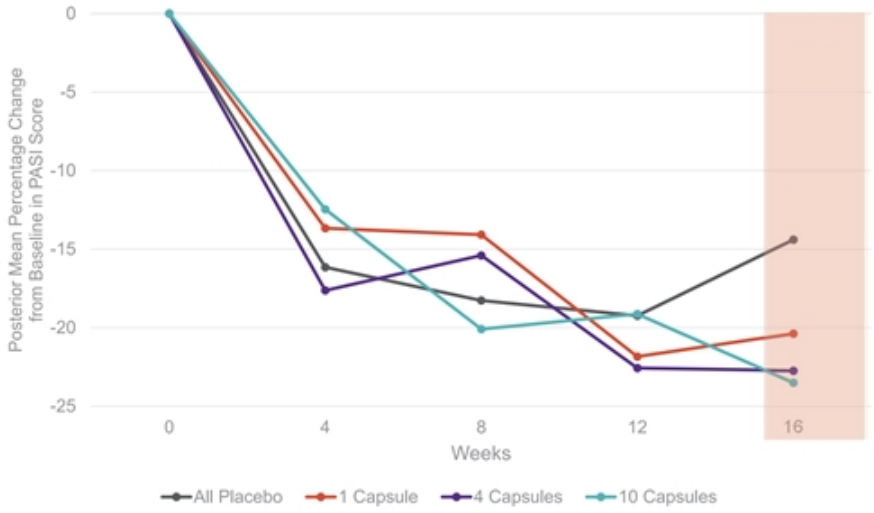
*% achieving at least PASI-50 by week 16*

**Result Measure:**
*Statistical significance represented by p<0.05*

# Baseline characteristics are well-balanced across treatment groups

| Parameter | All | Placebo (pooled) | Cohort 1 (1 capsule) | Cohort 2 (4 capsules) | Cohort 3 (10 capsules) |
|---|---|---|---|---|---|
| Number | 249 | 83 | 56 | 55 | 55 |
| Age, mean years | 44 | 44.4 | 44.5 | 41.2 | 45.5 |
| Female (%) | 36.9 | 39.8 | 39.3 | 43.6 | 23.6 |
| BMI, mean $kg/m^2$ | 29.7 | 30.2 | 29.9 | 28.5 | 29.7 |
| PGA 3 (%) | 62.2 | 65.1 | 62.5 | 54.5 | 65.4 |
| PASI mean | 8.5 | 8.7 | 8.4 | 8.7 | 8.3 |
| BSA mean % | 7.3 | 7.3 | 7.4 | 7.3 | 7.1 |

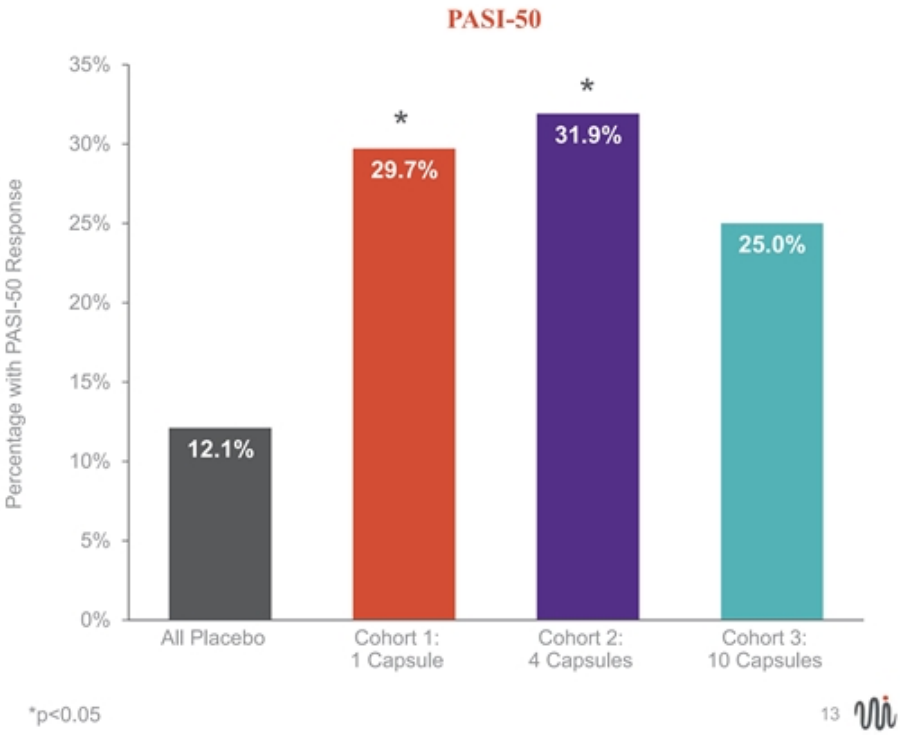
# EDP1815 is superior to placebo after 16 weeks of treatment




Bayesian Analysis, modified intent to treat. 80-90% probability that EDP1815 is superior.

# Robust PASI-50 responses with EDP1815 at week 16

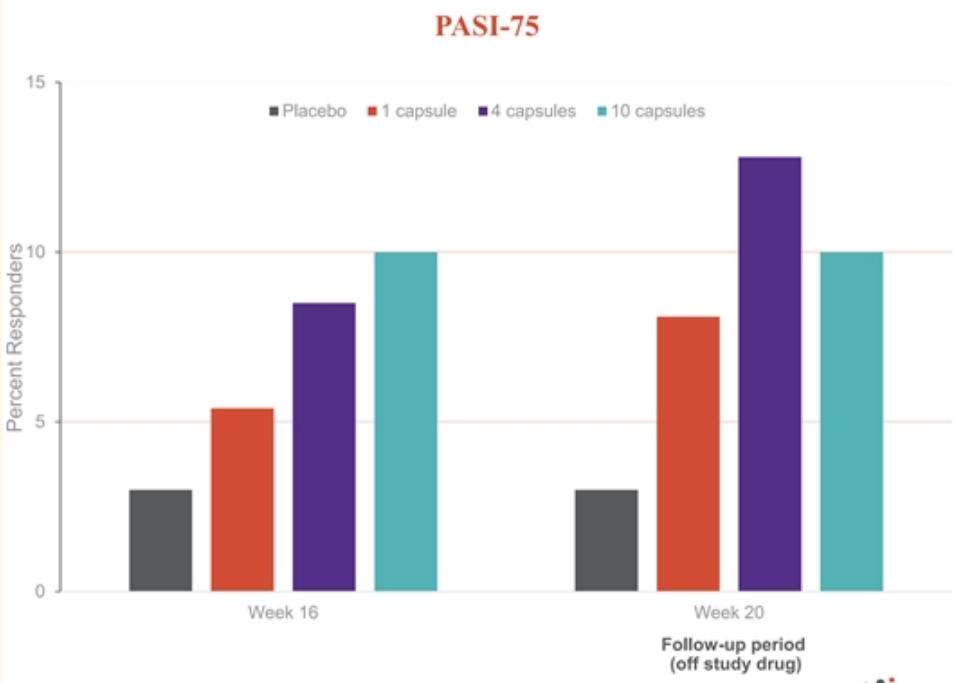
*Statistically significant p-value (<0.05) for 2 of the 3 individual dose cohorts, and for all 3 cohorts when pooled*




*p<0.05

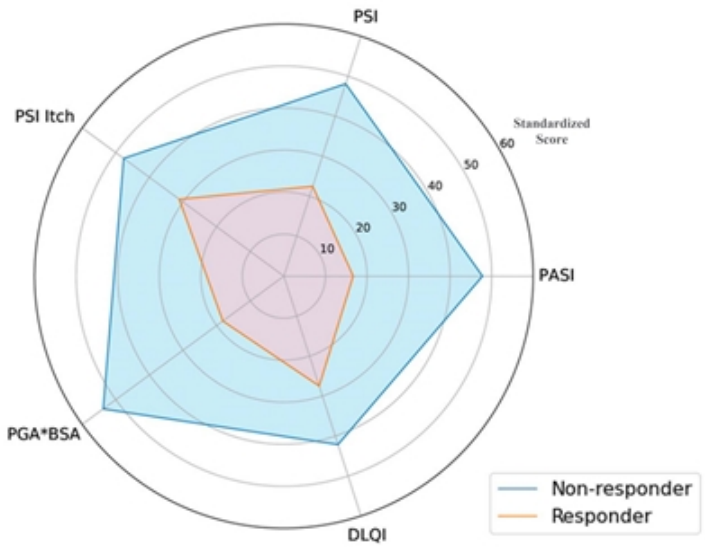
# PASI-75 responses increase with time

*Studies of longer treatment with EDP1815 may lead to deeper responses*




Difference from placebo not statistically significant at week 16

# Consistent improvements across multiple endpoints at week 16 in active cohort: responder vs. non-responder*




## Patients with PASI-50 or greater:

Mean PGA*BSA improvement

**-63.6%**

Active non-responders: **+9.8%**

Mean PSI itch improvement

**-0.9**

Active non-responders: **-0.15**

Mean PSI improvement

**-6.9**

Active non-responders: **-0.9**

Mean DLQI improvement

**-3.5**

Active non-responders: **-1.4**

*Responder = active patients who achieved PASI-50 or greater

# EDP1815 demonstrates placebo-like safety and tolerability

- Oral drug candidate that should not require screening or laboratory monitoring
- Gastrointestinal related Adverse Events (AEs) comparable to placebo with no meaningful difference

| | All Placebo (N=83) % | All EDP1815 (N=166) % |
|---|---|---|
| Any Treatment Emergent Adverse Events (TEAE) | 54.2 | 58.4 |
| Any Related* TEAE | 16.9 | 19.3 |
| Any Related* TEAE of Common Terminology Criteria for Adverse Event (CTCAE) Grade 2 or above | 7.2 | 7.8 |
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| AE: Related* Infections and Infestations | 0 | 0.6 (n=1) |
| AE: Related* Gastrointestinal | 10.8 | 12.7 |

**Related TEAEs are those with probable, possible or definitely relationship to study drug, or where relationship is missing.*

# Photographs of EDP1815 treatment responders

- Mild or moderate psoriasis
- Illustrating PASI-50 and greater responses at week 16 (on daily EDP1815)
- All maintained or improved response at week 20 (4 weeks after cessation of EDP1815)
- No use of topical steroids

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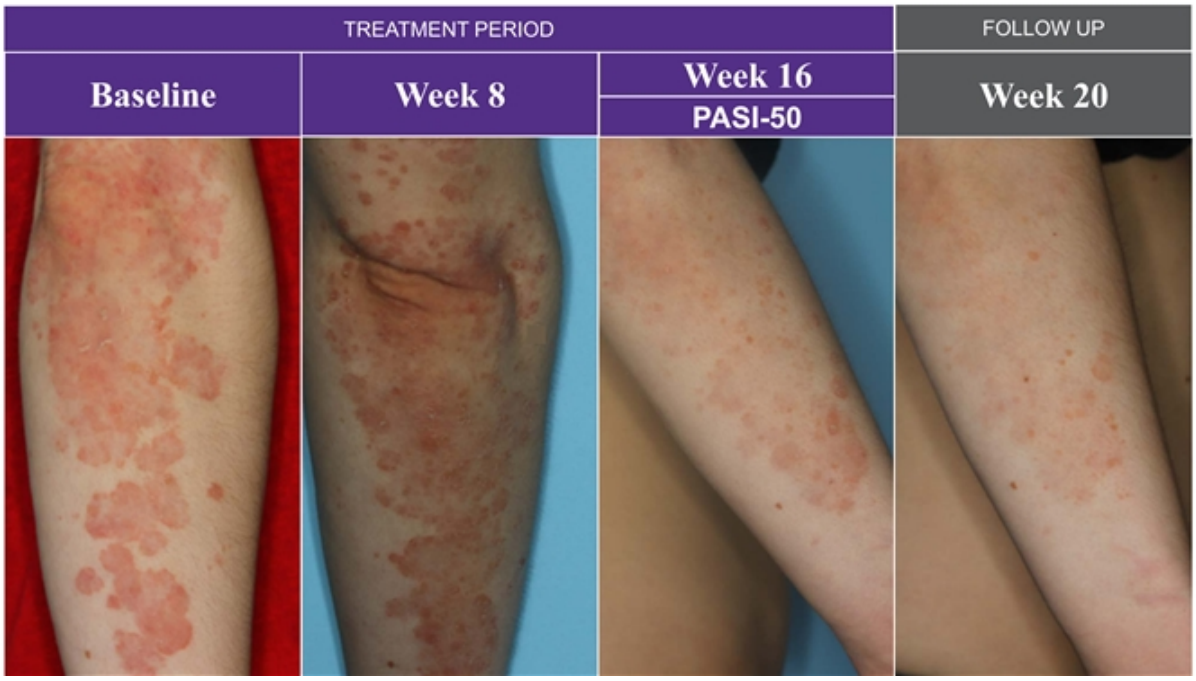
# MILD disease: PASI-50 responder

| | PASI | PGA | DLQI | PSI |
|---|---|---|---|---|
| **Baseline** | 7.2 | 2 | 3 | 4.1 |
| **Week 16** | 3.6 | 1 | 0 | 0.4 |

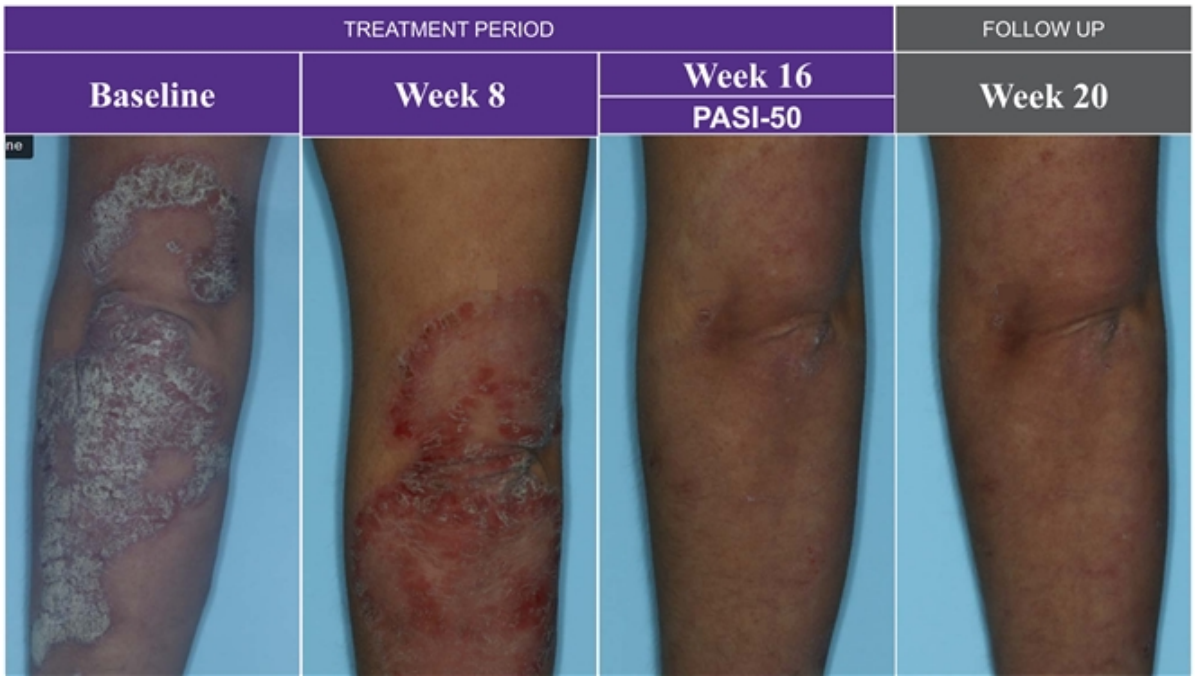
# PASI-50 response at week 16



# MODERATE disease: PASI-50 responder

| | PASI | PGA | DLQI | PSI |
|---|---|---|---|---|
| **Baseline** | 10.3 | 3 | 12 | 24.1 |
| **Week 16** | 3.1 | 1 | 1 | 1.6 |

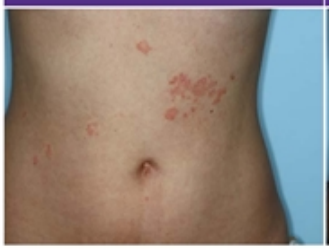
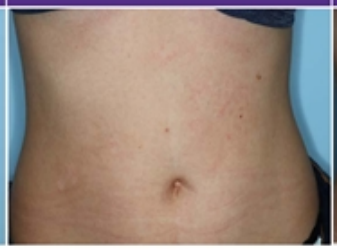
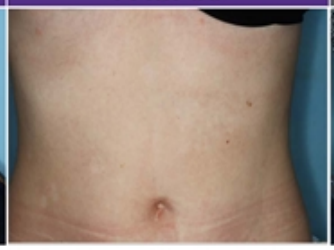
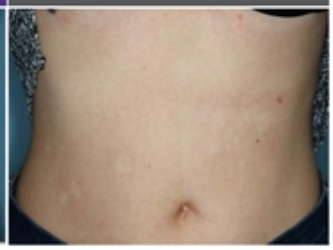
# PASI-50 response at week 16



# MILD disease: PASI-90 responder

| | PASI | PGA | DLQI | PSI |
|---|---|---|---|---|
| **Baseline** | 6.2 | 2 | 15 | 27.1 |
| **Week 16** | 0.6 | 1 | 1 | 3 |

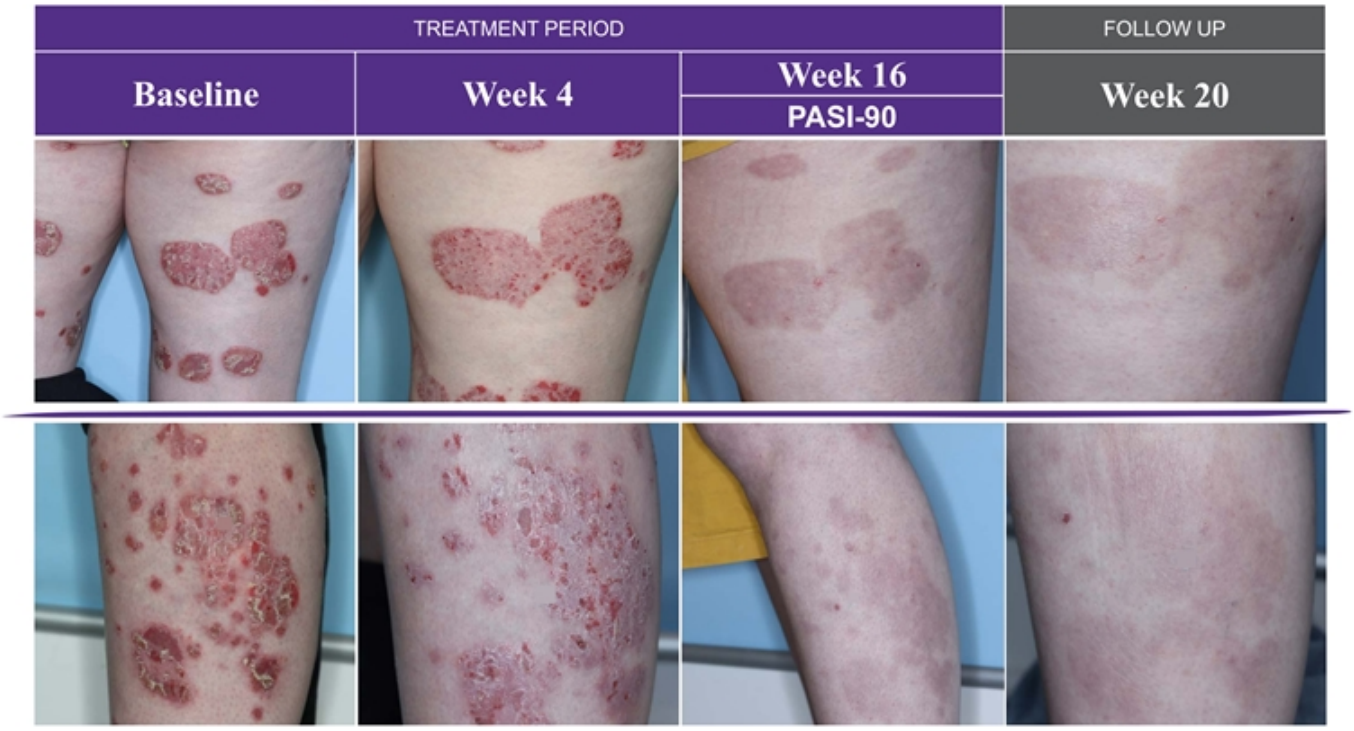
# PASI-90 response at week 16

| TREATMENT PERIOD | | | FOLLOW UP |
|---|---|---|---|
| Baseline | Week 8 | Week 16<br>PASI-90 | Week 20 |
|  |  |  |  |

# MODERATE disease: PASI-90 responder

| | PASI | PGA | DLQI | PSI |
|---|---|---|---|---|
| **Baseline** | 11.8 | 3 | 6 | 8.7 |
| **Week 16** | 1.1 | 0 | 2 | n/a |

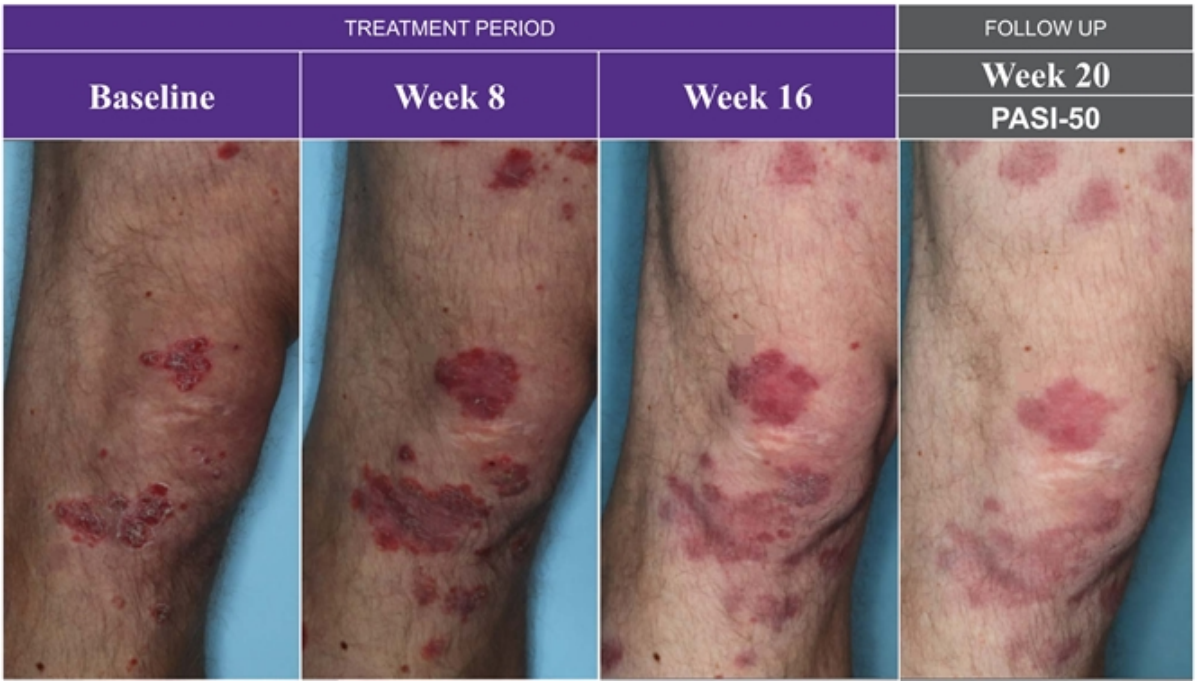
# PASI-90 response at week 16



# MODERATE disease: Week 20 PASI-50 response

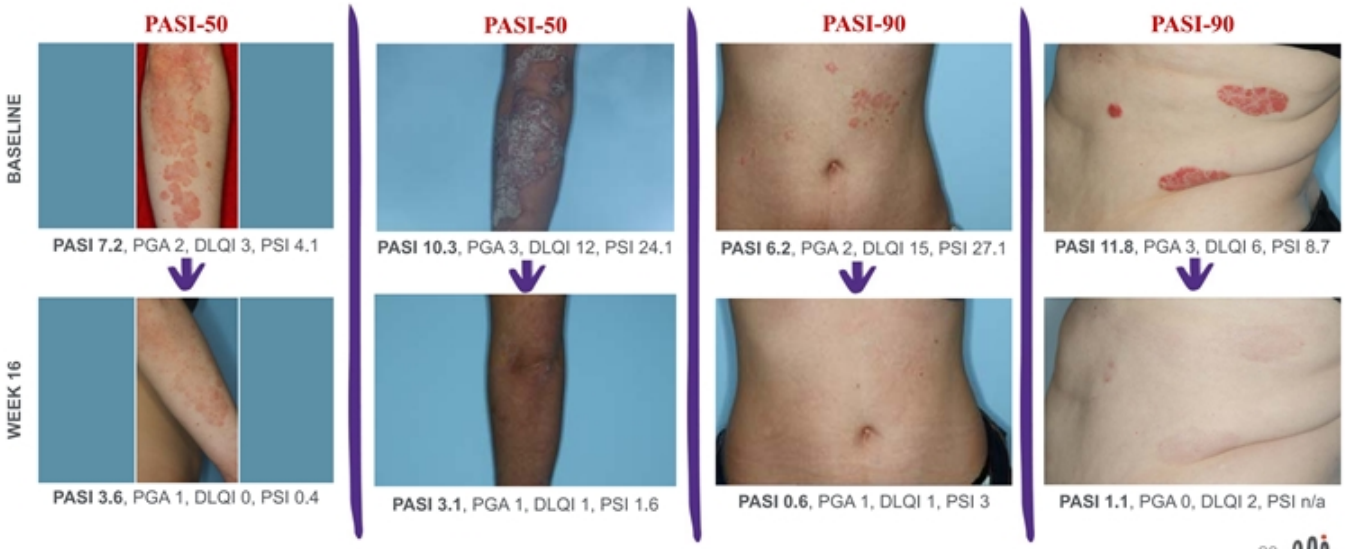
| | PASI | PGA | DLQI | PSI |
|---|---|---|---|---|
| **Baseline** | 10.5 | 3 | 3 | 4.9 |
| **Week 16** | 5.7* | 2 | 0 | 2.0 |

# PASI-50 response at week 20



# EDP1815 led to robust treatment responses → demonstrating potential of SINTAX platform

Deepening responses over time → Longer treatment may lead to greater activity



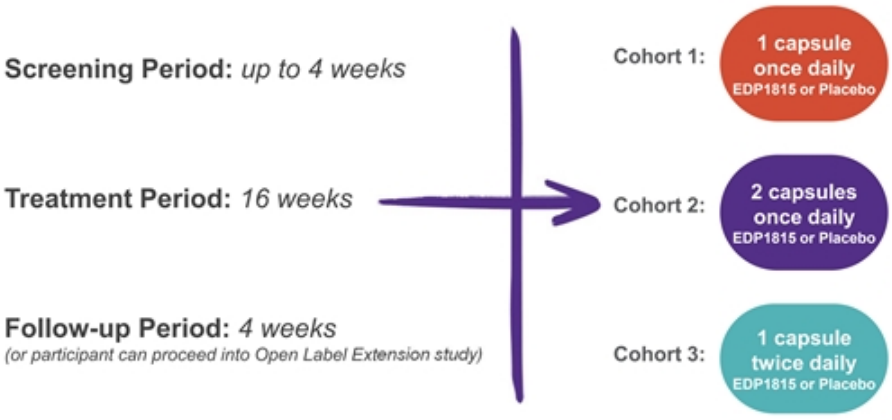
# Summary of additional Phase 1b studies

- Mild and moderate psoriasis using EDP1815 capsule dosage form
  - Results from this 8-week study were consistent with the 8-week time point in Phase 2
  - Successful bridge to future studies using the commercial manufacturing process
- Human scintigraphy of capsule and tablet dosage forms
  - Tablets take longer to release EDP1815 than capsules
  - Results underscore the importance of an optimized release profile
- Mild and moderate psoriasis using EDP1815 tablet dosage form
  - There was no clear evidence of a drug effect after 8 weeks of treatment
  - Likely explanation is the different release profile of tablets vs. capsules

# EDP1815 Phase 2 study in mild, moderate and severe atopic dermatitis

**Key Inclusion Criteria:**

- IGA of 2, 3 or 4
- BSA of ≥ 5%
- EASI of ≥ 6




N=300

**Primary Endpoint:** *Achievement of an EASI-50 response at week 16*

# Positive Phase 2 data of EDP1815 confirms ability to harness the small intestinal axis, SINTAX, to treat systemic inflammatory diseases

- Clinically and statistically significant improvement in PASI-50 score achieved
- Oral EDP1815 can drive potent effects with placebo-like safety and tolerability
- EDP1815 advancing towards registration studies in psoriasis

EVELO

# Multiple clinical catalysts

| Time | 3Q 2021 | 4Q 2021 | 4Q 2022 | 4Q 2022 | Ongoing |
|---|---|---|---|---|---|
| Readout | **EDP1815**<br>**Psoriasis**<br>• Phase 2 data<br>• Data from multiple Phase 1b cohorts aimed at defining formulation and concentration of drug | **EDP1867**<br>• Phase 1b data in Atopic Dermatitis | **EDP1815**<br>**Atopic Dermatitis**<br>• Phase 2 data | **EDP2939**<br>• Phase 1 data in inflammatory indication(s) | **EDP1815 –TACTIC-E**<br>• Phase 2/3 data in COVID-19 |

# Q&A

EVELO

**Evelo Biosciences Announces Positive Phase 2 Clinical Data with EDP1815 in Psoriasis;**
**Confirms Ability to Harness the Small Intestinal Axis, SINTAX™, to Treat Systemic Inflammatory Disease**

–Clinically and statistically significant improvement in PASI-50 score achieved–
–EDP1815 safety and tolerability data comparable to placebo in study–
–EDP1815 advancing towards registration studies in psoriasis–
–Management to host conference call at 8:00 a.m. ET–

**CAMBRIDGE, Mass., September 27, 2021 –** 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 announced positive data from its Phase 2 study evaluating EDP1815 versus placebo for the treatment of mild and moderate psoriasis. A statistically significant reduction in the Psoriasis Area and Severity Index (PASI) score, as measured by the proportion of patients achieving at least 50% improvement in PASI from baseline at the week 16 timepoint, was observed in the study. EDP1815 is an investigational oral biologic currently in development for the treatment of a broad range of inflammatory diseases, including clinical programs in psoriasis, atopic dermatitis, and COVID-19.

“These clinical results represent a significant advancement for those who live with inflammatory disease. This is the first Phase 2 study to demonstrate that we can harness the small intestinal axis to make a clinical impact on patients with an oral product candidate with safety and tolerability data comparable to placebo,” said Simba Gill, Chief Executive Officer of Evelo. “Based on these data, we intend to advance EDP1815 towards registration studies in psoriasis. We look forward to discussing our proposed next steps with health and regulatory authorities. This milestone brings us one step closer to realizing our vision of transforming healthcare by developing broadly acting oral, safe, effective, and affordable medicines to address the unmet needs of hundreds of millions of patients who live with inflammatory diseases.”

In the Phase 2 study, the PASI scores were assessed by both mean changes from baseline and responder rates. The primary endpoint was the mean percentage change in PASI between treatment and placebo and was prespecified as a Bayesian analysis. The Bayesian approach provides an estimate of the probability that EDP1815 is superior to placebo. The 16-week primary endpoint gave probabilities that EDP1815 is superior to placebo ranging from 80% to 90% across the prespecified analyses and cohorts.

The responder endpoint reports the proportion of patients who had a meaningful clinical response, which is defined as PASI-50 or greater. 25% to 32% of patients across the three cohorts who were treated with EDP1815 achieved a PASI-50 at week 16 compared to 12% on placebo. In cohorts 1 and 2 this difference in response rate was statistically significant ($p < 0.05$). Cohort 3 was directionally similar (25% vs. 12%). The pooled PASI-50 response across all three EDP1815 cohorts, an exploratory analysis, was 29% vs. 12% for placebo and was also statistically significant with a p-value of 0.027. An increase in the number of capsules of EDP1815 did not lead to a dose response.

Additionally, several patients on EDP1815 achieved a PASI-75 or better, which was sustained or improved post treatment. For individuals who had a PASI-50 response or better, consistent effects in secondary and exploratory endpoints, including improvements in patient reported outcomes such as Dermatology Life Quality Index (DLQI) and Psoriasis Symptom Inventory (PSI), were observed.

EDP1815 was observed to be well tolerated in the Phase 2 study. The safety data were comparable to placebo and consistent with what was previously reported in a Phase 1b study. Adverse events (AEs) classified as “gastrointestinal” were comparable between active and placebo groups, with no meaningful differences in rates of diarrhea, abdominal pain, nausea, or vomiting. There were no related serious adverse events.

“I am very encouraged to see this Phase 2 data of EDP1815 in psoriasis,” said Benjamin Ehst, M.D., Ph.D., Board-certified Dermatologist, Investigator and Clinical Associate Professor with the Oregon Medical Research Center, and Chief Investigator of EDP1815-201. “It advances our scientific understanding of how to treat systemic inflammatory diseases and offers the prospect of a truly novel modality of treatment for patients with psoriasis. A drug with the combination of efficacy and safety results as observed here will likely be well received by dermatologists and their patients with mild and moderate disease, who are often faced with limited treatment options.”

EDP1815-201 is a double-blind, placebo-controlled, dose-ranging Phase 2 study designed to evaluate three doses of an enteric capsule formulation of EDP1815 versus placebo in 249 patients with mild and moderate psoriasis over a 16-week treatment period. In the study, the PASI scores were assessed by both mean changes from baseline and responder rates. The primary endpoint is mean percentage reduction in PASI score at 16 weeks. Secondary endpoints include the proportion of study participants who achieve a PASI-50 response or greater and other clinical measures of disease such as Physicians Global Assessment (PGA), Body Surface Area (BSA), PGA x BSA, PSI, and DLQI. Today's results report out on the initial treatment phase of the study, which is now complete, and includes the 16-week treatment period with a 4- week follow-up. A six-month follow-up phase of the study is ongoing.

**Conference Call**

Evelo will host a conference call and webcast at 8:00 a.m. ET today. To access the call please dial (866) 795-3242 (domestic) or (409) 937-8909 (international) and refer to conference ID 5177247. 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 Psoriasis**

Psoriasis is a common chronic immune-mediated inflammatory skin disease, affecting up to 3% of the population worldwide. The disease is driven by Th17-inflammation, which results in the formation of thick red plaques with scaling. Psoriatic lesions can appear anywhere on the body but are most often seen on the knees, elbows, scalp, and lumbar area. In addition to the skin lesions, there are systemic manifestations of the disease including arthritis and fatigue, and a strong association with depression and metabolic syndrome.

Patients with mild and moderate psoriasis are underserved by current treatments. Topical therapies do not control systemic inflammation, have low rates of compliance, and in the case of topical steroids are not recommended for long- term use. The majority of novel therapies, including injectable high-cost biologics, are only approved for patients with moderate and severe disease. Even in the severe patient population, the majority of eligible patients do not receive biologics, instead opting for topical therapies or oral systemic therapies, which are associated with tolerability issues and/or with monitoring requirements tied to safety concerns.

**About Evelo Biosciences**

Evelo Biosciences is a clinical stage biotechnology company developing orally delivered medicines 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. Evelo's first product candidates are pharmaceutical preparations of single strains of microbes selected for their 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 and cancer.

Evelo currently has four product candidates in development: EDP1815, EDP1867, and EDP2939 for the treatment of inflammatory diseases and EDP1908 for the treatment of cancer. Evelo is advancing additional product candidates in other disease areas.

For more information, please visit www.evelobio.com and engage with Evelo on LinkedIn.

**Forward Looking Statements**

*This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including statements concerning the development of EDP1815, the promise and potential impact of EDP1815, the timing of and plans for clinical studies, and the timing and results of clinical study 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 studies, and the continuity of our business; that 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 studies, 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; issues with the 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's and principal stockholders 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 three months ended June 30, 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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