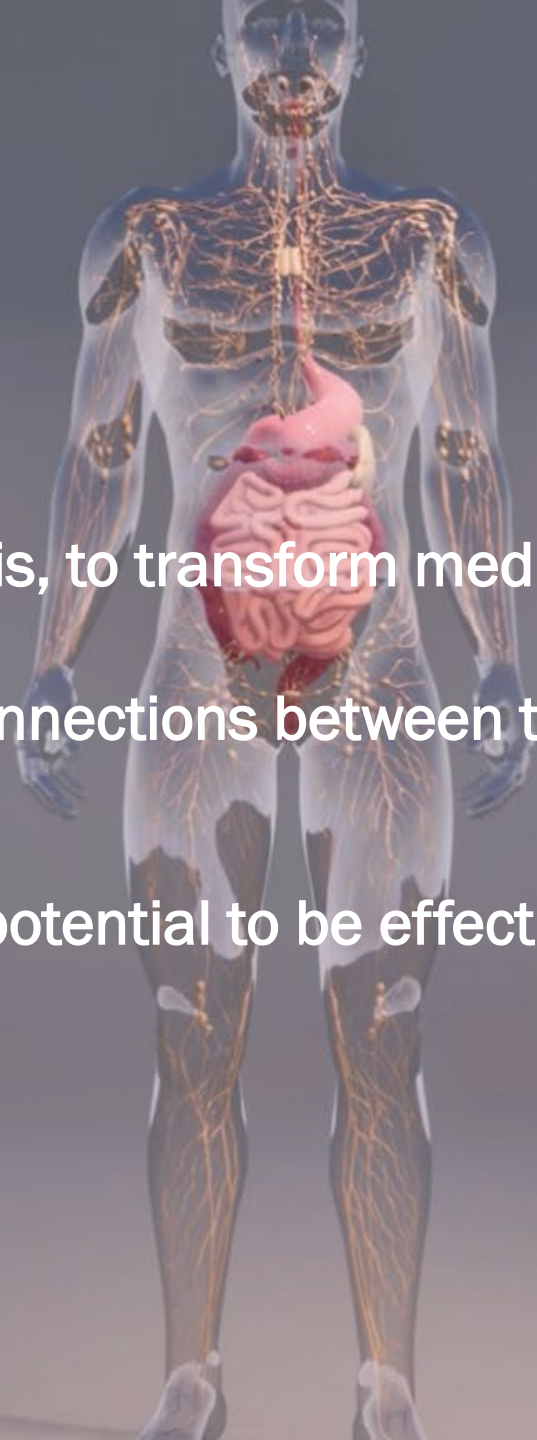
# EVELO BIOSCIENCES



Harnessing SINTAX™, the small intestinal axis, to transform medicine

The small intestinal axis is the network of connections between the small intestine and the rest of the body

Evelo is developing therapies that have the potential to be effective, safe, oral, affordable medicines for billions of people

January 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, EDP1867, EDP2939, and EDP1908, the promise and potential impact of any of our product candidates, the timing of and plans to initiate clinical studies of EDP1815, EDP1867, EDP2939, and EDP1908, the timing and results of any clinical studies or readouts, and the scalability of manufacturing for EDP1815.*

*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 quarter ended September 30, 2020 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.*

# 2020 accomplishments: Positive clinical data in potential blockbuster product, scaled manufacturing, advanced platform, expanded pipeline

## EDP1815 – Positive clinical data suggests potential blockbuster product across inflammatory diseases

- Phase 1b clinical data showed favorable efficacy and tolerability profile in atopic dermatitis
- Positive results observed in a human experimental model of inflammation
- Translation of results across Th1, Th2, and Th17 inflammation; data suggest broad potential in multiple inflammatory diseases
- Advanced into Phase 2 dose-ranging trial in mild to moderate psoriasis, as well as formulation and manufacturing optimization; working towards Phase 3 trials in mild to moderate psoriasis and atopic dermatitis

## Scaled manufacturing

- Investments in manufacturing and supply chain to advance ability to deliver products at commercial scale globally

## Advanced platform

- Disclosed preclinical data for extracellular vesicle (EV) candidate; plan to advance EV candidates EDP2939 for inflammatory diseases and EDP1908 for oncology into clinic in 2022

## Continued to advance clinical and preclinical pipeline

- Several clinical and preclinical candidates evaluated across multiple therapeutic areas
- Multiple forms and formulations under evaluation

# Positive Data in EDP1815

- Evelo products have shown positive clinical and preclinical results across Th1, Th2, and Th17 inflammation
- Broad potential applicability across inflammatory disease: dermatology, rheumatology, inflammatory bowel disease, and beyond
- Potential utility across all stages of disease: mild to moderate to severe as well as maintenance therapy

# SINTAX medicines are active preclinically and clinically

## Preclinical mechanism of action

### Efficacy

- Comparable with biologics and orals

### Pharmacology

- Modulation of multiple pathways
- Inflammation resolution without suppression

### Non-GLP Toxicology

- No clinical or histological adverse effects
- No observed systemic exposure

## Clinical proof of principle and safety results

### Clinical Immunopharmacology

- Observed >90% reduction in inflammation vs placebo

### Phase 1b Atopic Dermatitis

- Improved atopic dermatitis measures vs placebo

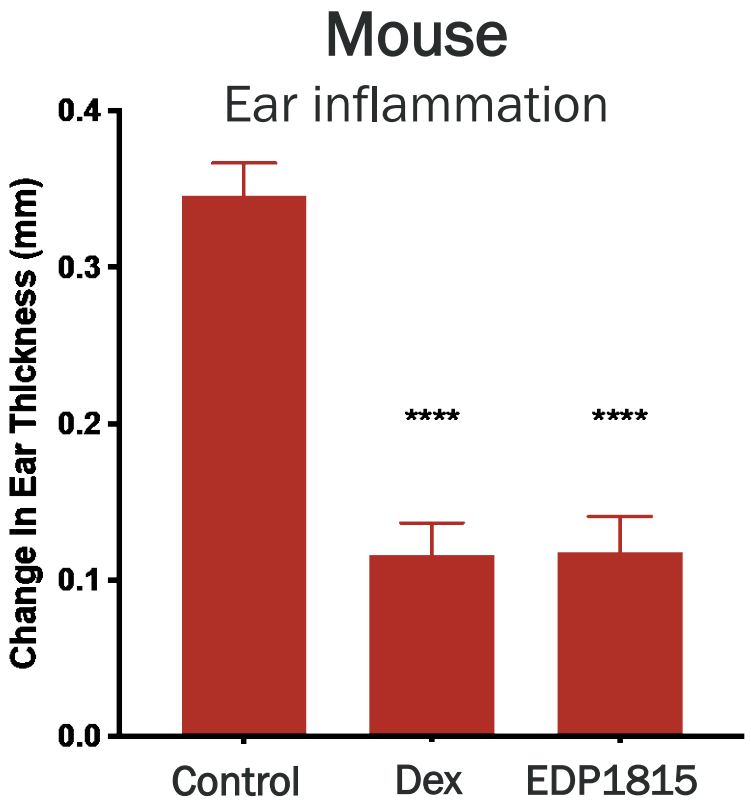
### Phase 1b Psoriasis

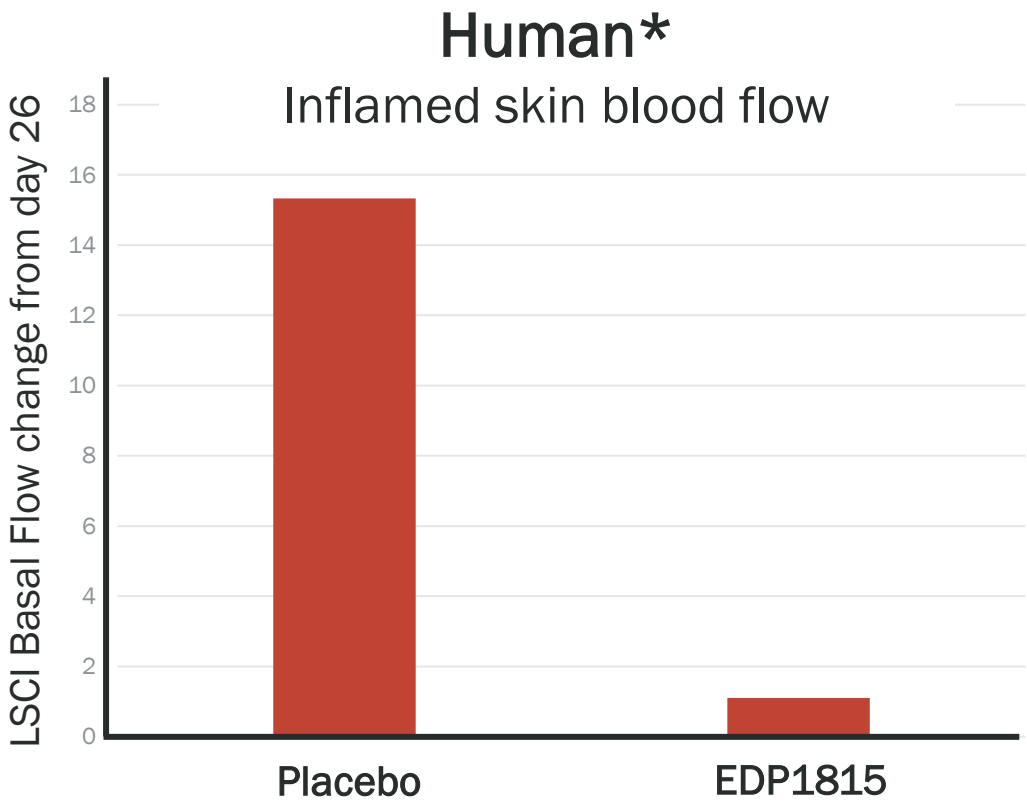
- Reduced skin lesions vs placebo in 2 cohorts
- Inhibited multiple systemic inflammatory cytokines

### Safety and tolerability

- Well tolerated with no overall difference reported from placebo in all three studies
- No observed systemic exposure

# EDP1815 inflammation resolution translated from mouse to human



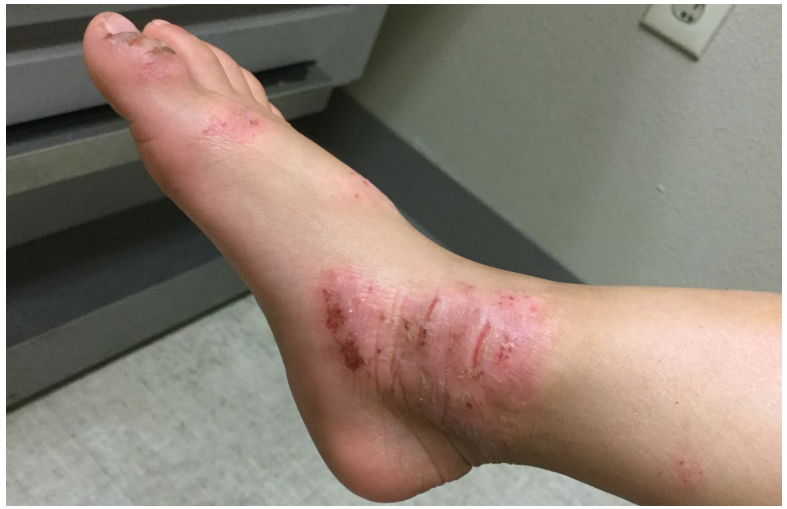



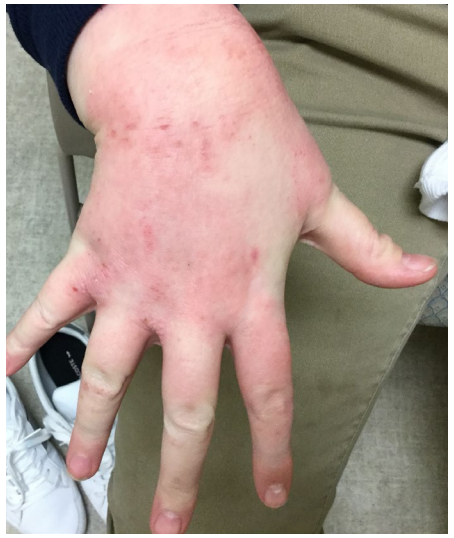

Mice and human volunteers were immunized with KLH, treated daily for 4 weeks, and then challenged with KLH

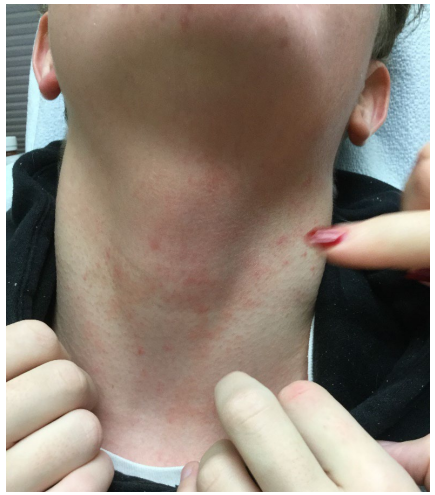


* Results from immunopharmacology study in healthy volunteers

# Mild and moderate atopic dermatitis: significant disease burden







Patients in these pictures have mild to moderate disease

- Atopic dermatitis is the most common chronic inflammatory disease affecting an estimated 10% of adults and 25% of children worldwide [1]
- Characterized by a cycle of intense itching and scratching that leads to red, cracked, scaly, and oozing skin [2]
- Range of symptoms creates significant physical and psychosocial burden on patients[3]
- Standard of care is topical treatments with low adherence due to inconvenient/burdensome application



[1] Eichenfield LF, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. J Am Acad Dermatol. 2014;70(2):338-351. doi:10.1016/j.jaad.2013.10.010
[2] Nutten S. Atopic Dermatitis: Global Epidemiology and Risk Factors. Ann Nutr Metab 2015;66(suppl 1):8–16.
[3] EFA. Atopic Eczema: Itching for Life Report. 2018. Available at: https://www.efanet.org/images/2018/EN_-_Itching_for_life_Quality_of_Life_and_costs_for_people_with_severe_atopic_eczema_in_Europe_.pdf.

# Phase 1b clinical trial design

## Trial Summary

- Double-blind, placebo-controlled trial of 24 patients
- Mild and moderate atopic dermatitis*, randomized 2:1 (active : placebo)
- 56 days of oral administration of enteric capsule formulation, follow-up at day 70
- Once daily
- No active topical treatments, no requirement to use emollients

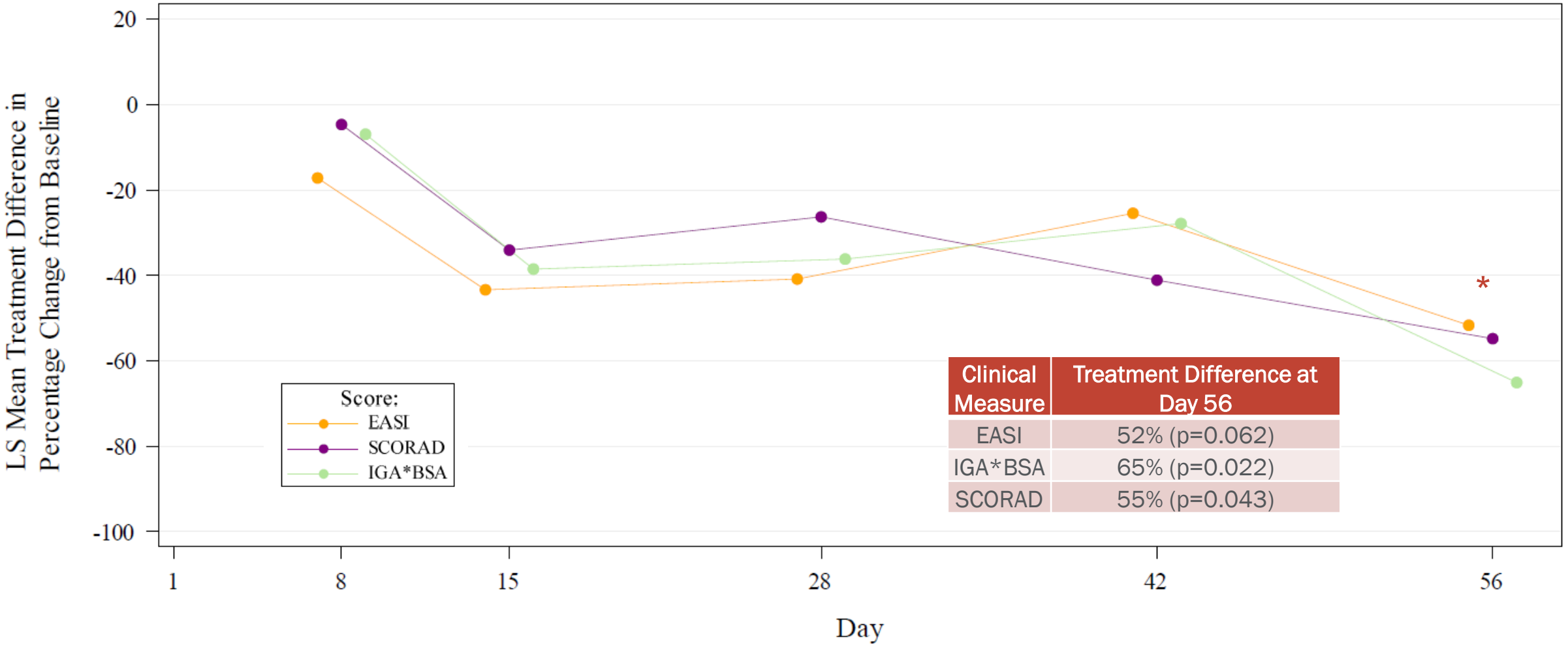
## *Baseline Disease Severity

*Inclusion criteria:*

- IGA 2 or 3
- BSA 5-40%

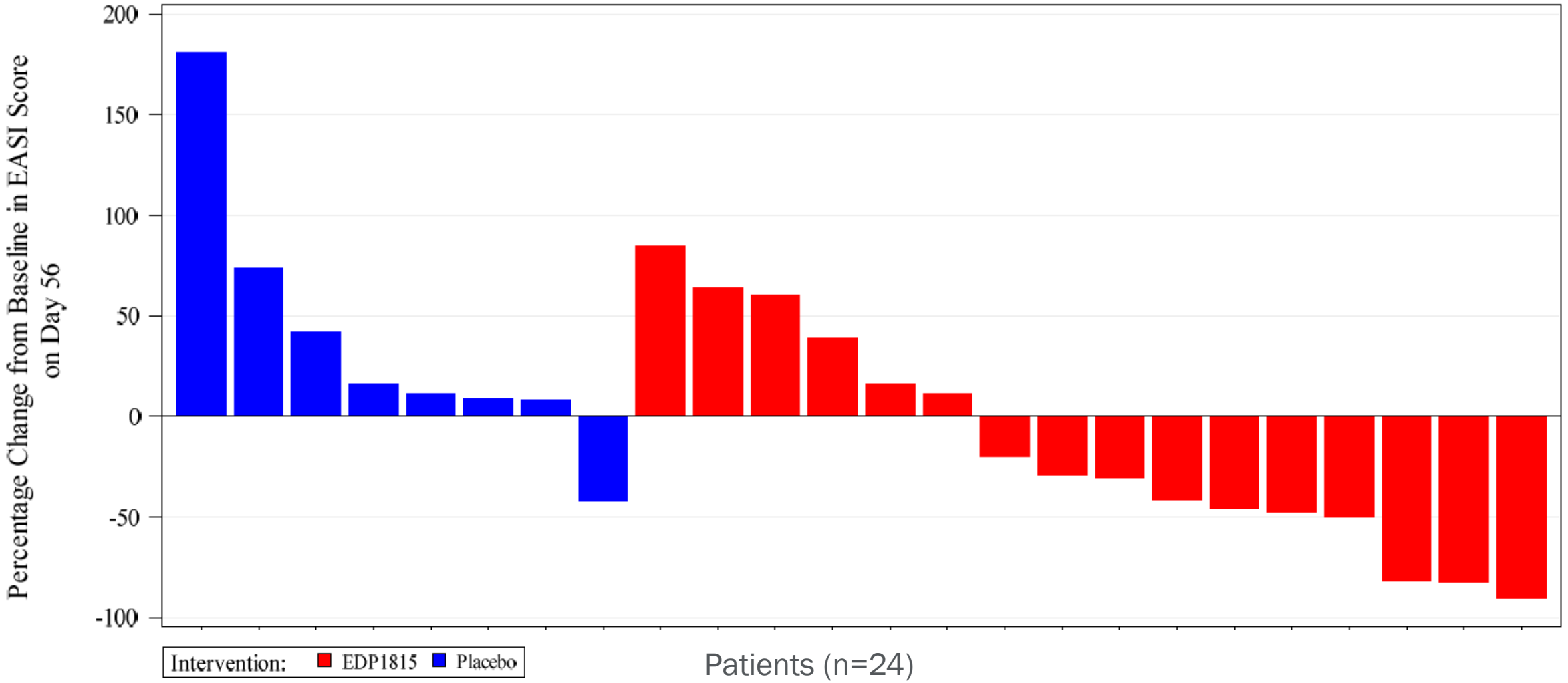
| Mean baseline characteristics | EDP1815 (n=16) | Placebo (n=8) |
|---|---|---|
| EASI | 8.31 | 9.31 |
| IGA | 2.63 | 2.75 |

# Improvements in EASI, IGA*BSA, and SCORAD at day 56

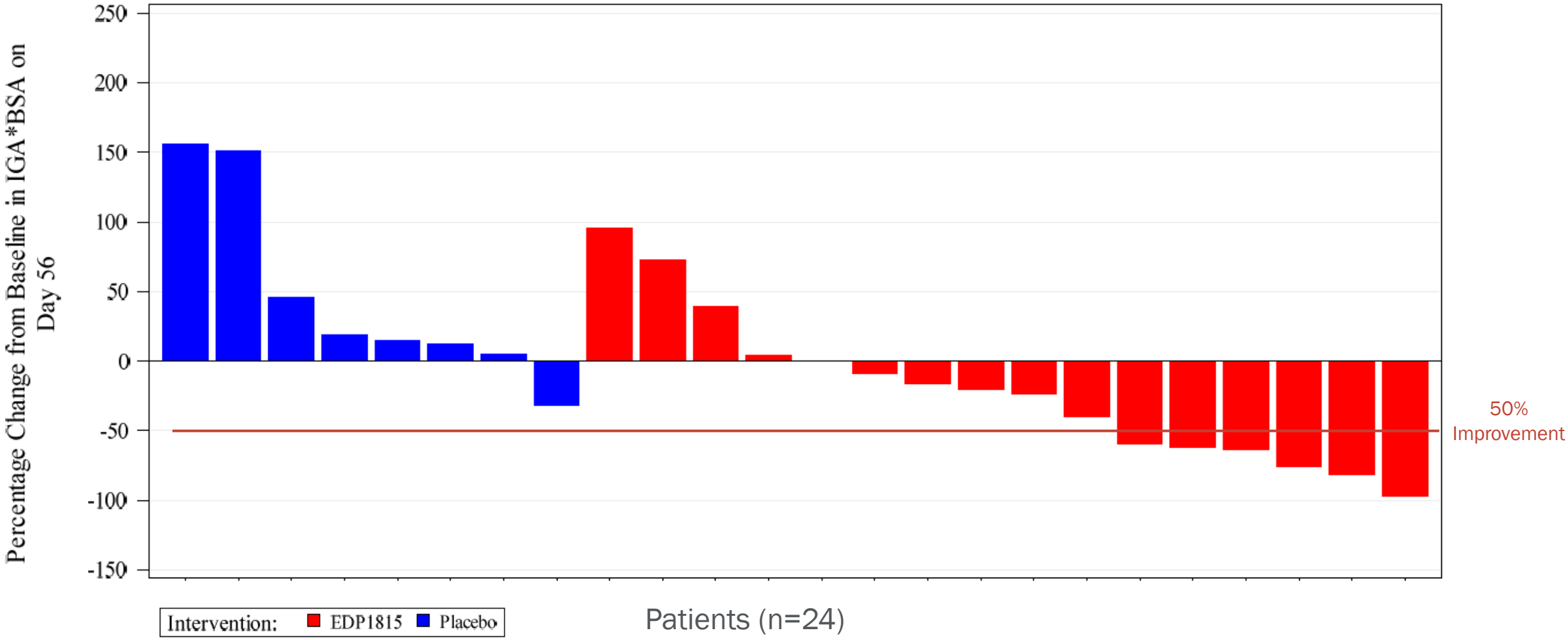



| Clinical Measure | Treatment Difference at Day 56 |
|---|---|
| EASI | 52% (p=0.062) |
| IGA*BSA | 65% (p=0.022) |
| SCORAD | 55% (p=0.043) |

# EASI: 10/16 patients on EDP1815 improved at day 56



# IGA*BSA: 6 patients achieved a >50% improvement at day 56 with EDP1815



# Clinically meaningful improvements in Patient-Reported Outcomes at day 56, including itch and sleep

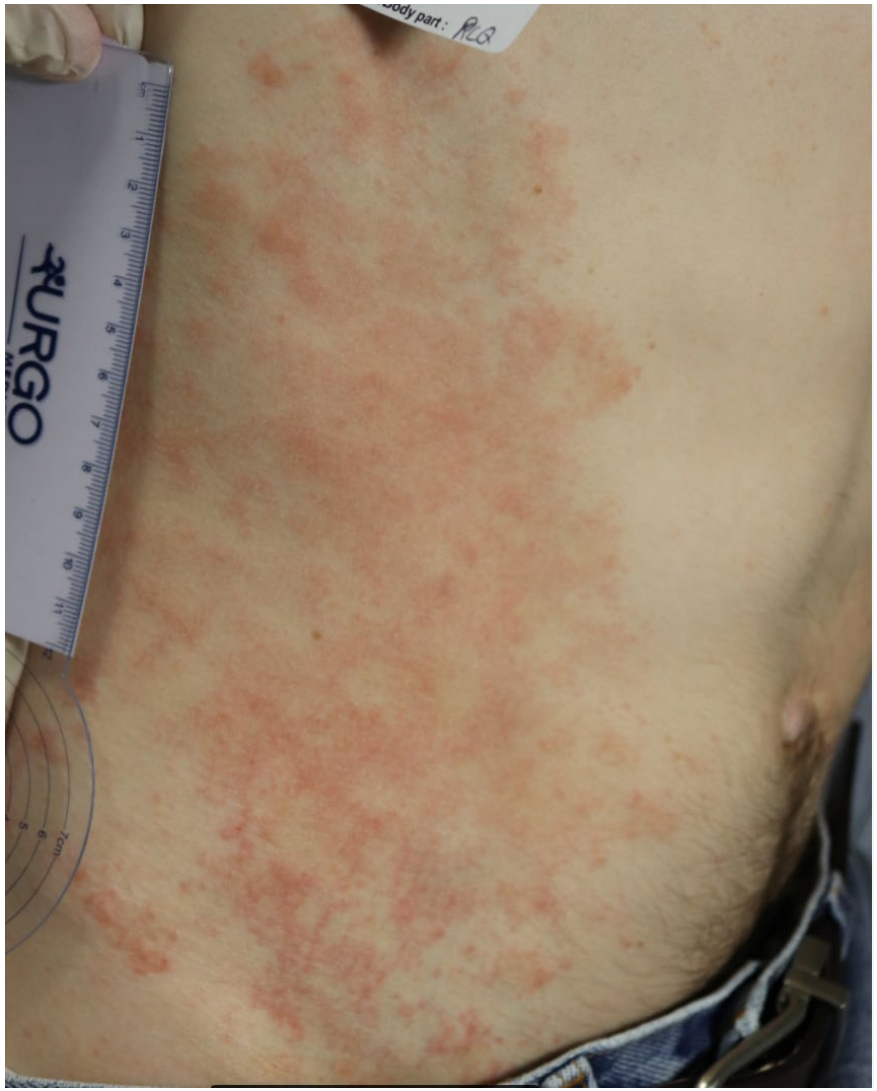
| Patient-Reported Outcome | **EDP1815** Mean change, day 56 (mean % change per patient) | **Placebo** Mean change, day 56 (mean % change per patient) |
|---|---|---|
| DLQI (Dermatology Life Quality Index) | –3.6* (-35%) | –0.3 (+46%) |
| POEM (Patient-Oriented Eczema Measure) | –4.1* (-21%) | +1.6 (+22%) |

*Mean improvement exceeded the minimally clinically important difference[1,2]

- EDP1815 led to improvement in itch across all measured scores at day 56
- EDP1815 led to improvement in sleep across all measured scores at day 56

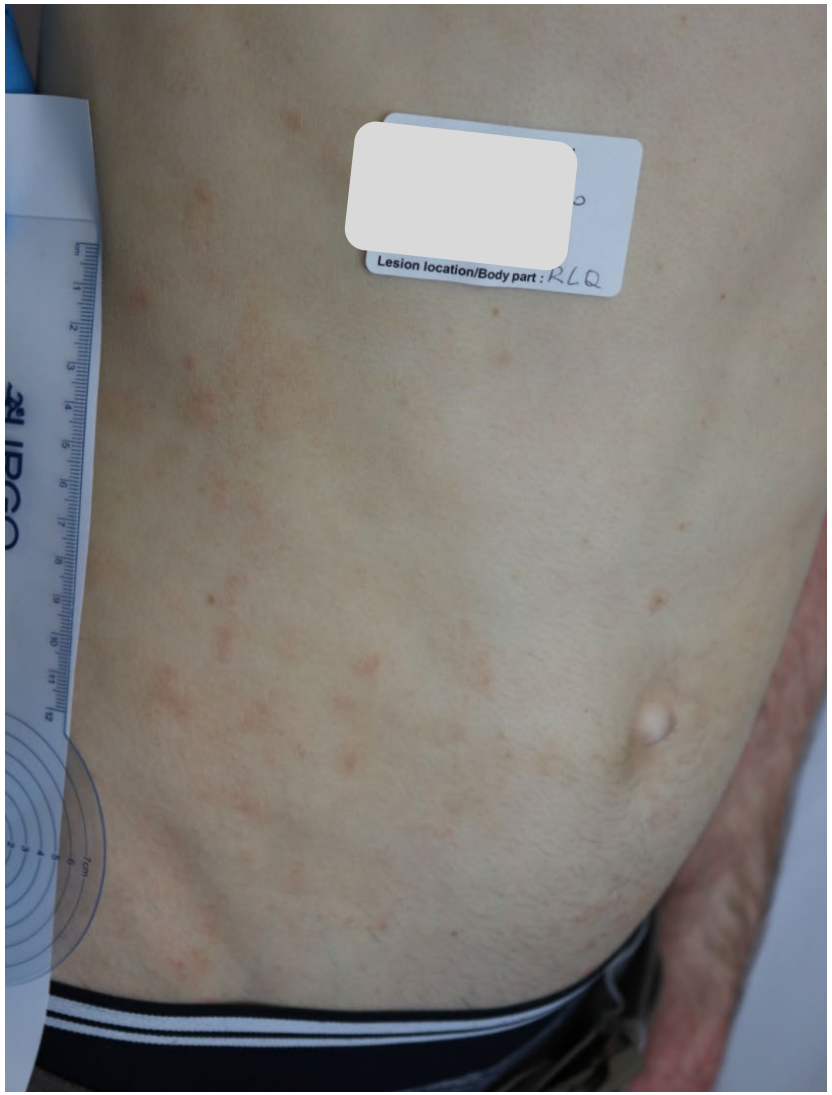

1. Basra MK, Salek MS, Camilleri L, Sturkey R, Finlay AY. Determining the minimal clinically important difference and responsiveness of the Dermatology Life Quality Index (DLQI): further data. Dermatology. 2015;230(1):27-33. doi: 10.1159/000365390. Epub 2015 Jan 20. PMID: 25613671.
2. Schram ME, Spuls PI, Leeflang MM, Lindeboom R, Bos JD, Schmitt J. EASI, (objective) SCORAD and POEM for atopic eczema: responsiveness and minimal clinically important difference. Allergy. 2012 Jan;67(1):99-106. doi: 10.1111/j.1398-9995.2011.02719.x. Epub 2011 Sep 27. PMID: 21951293.

# Efficacy of oral EDP1815 in atopic dermatitis



Before, day 0

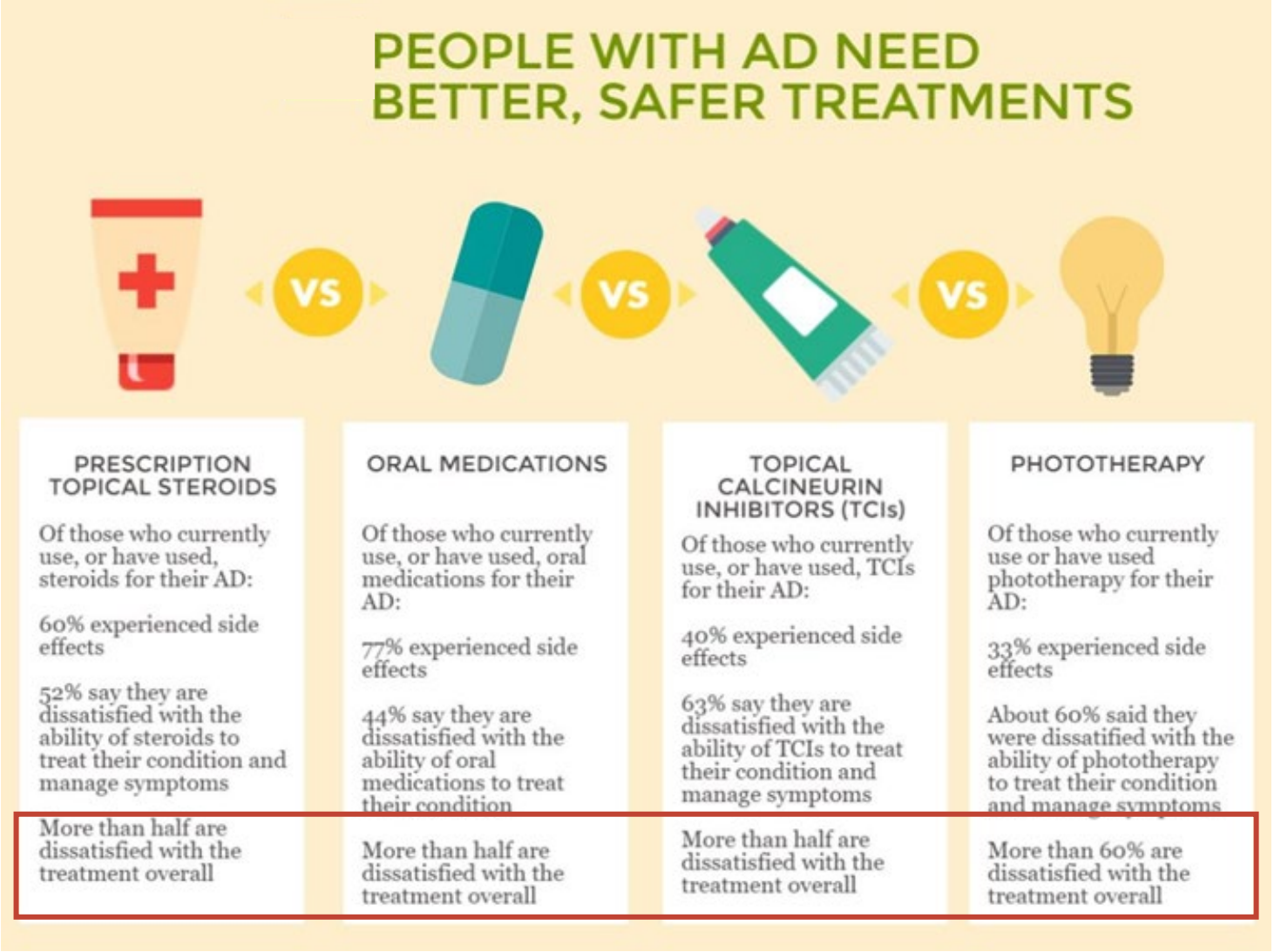
Patient on once daily oral EDP1815 and no topical treatments: before and after (patient achieved EASI50 score)




After, day 56

# Safety and convenience of therapies are key for atopic dermatitis patients

*"1 in 3 takes one or more hours per day to treat their AD"*

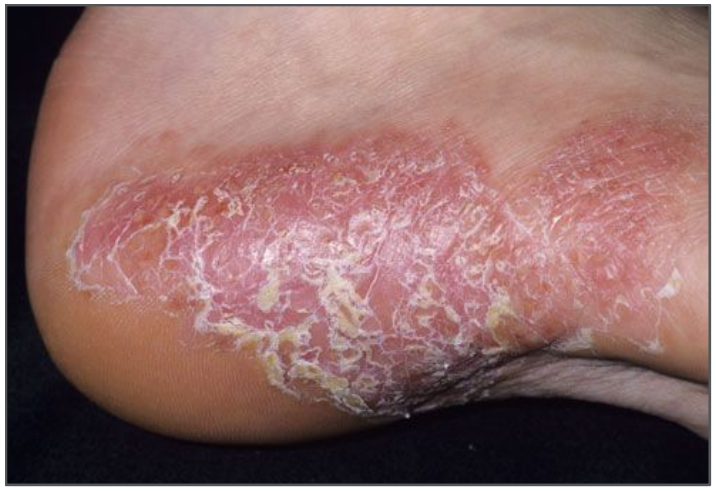


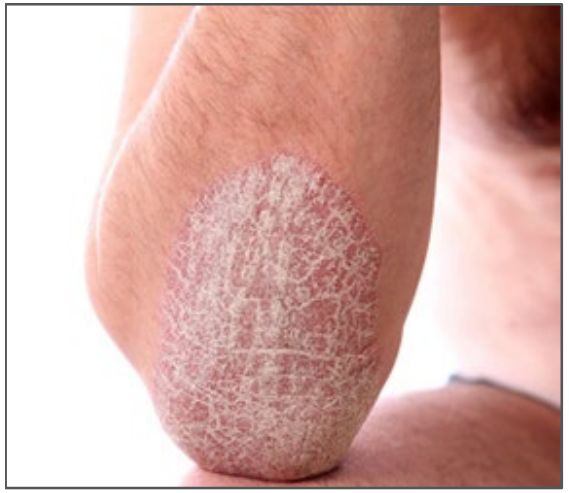

*"Lack of safe and effective treatments"*



Atopic Dermatitis: Survey of 192 patients from the National Eczema Association, 2016
https://nationaleczema.org/in-your-words-survey-series

# Mild to moderate psoriasis is a serious condition with few existing effective treatments





- While characterized as mild to moderate in terms of body surface area, individual lesions can be severe
- ~49% of mild and ~24% of moderate patients do not initiate or maintain treatment due to concerns about long-term safety, tolerability, or efficacy of currently available therapies[1]
- Along with the cosmetic, emotional, and functional disease burden of psoriasis are comorbidities such as psoriatic arthritis, increased risk of depression, inflammatory bowel disease, and ischaemic heart disease

Evelo's initial commercial focus is on mild to moderate population with potential to address over 3.5 million[2] of these individuals in US and EU5 and then expand globally

[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

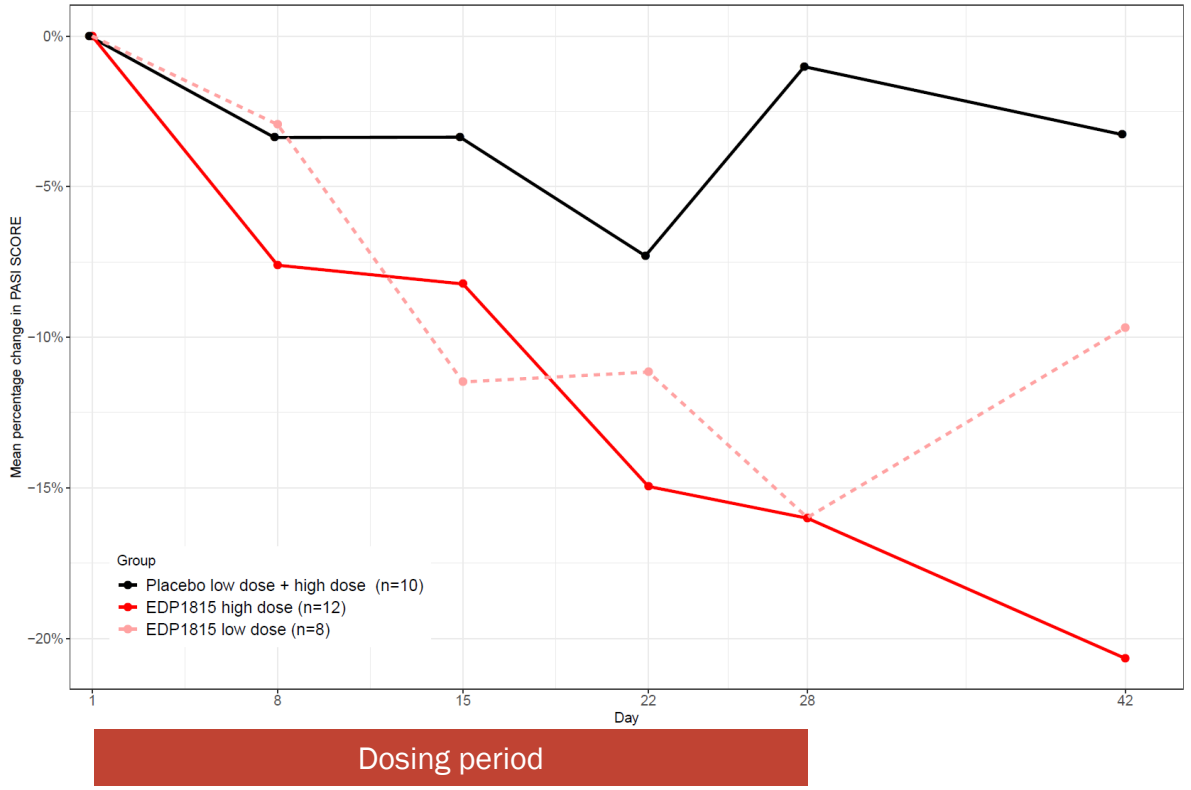
[2] 2018 company-sponsored market research; EU5 consisting of France, Germany, Italy, Spain and the UK

# Positive clinical data with EDP1815 in mild to moderate psoriasis

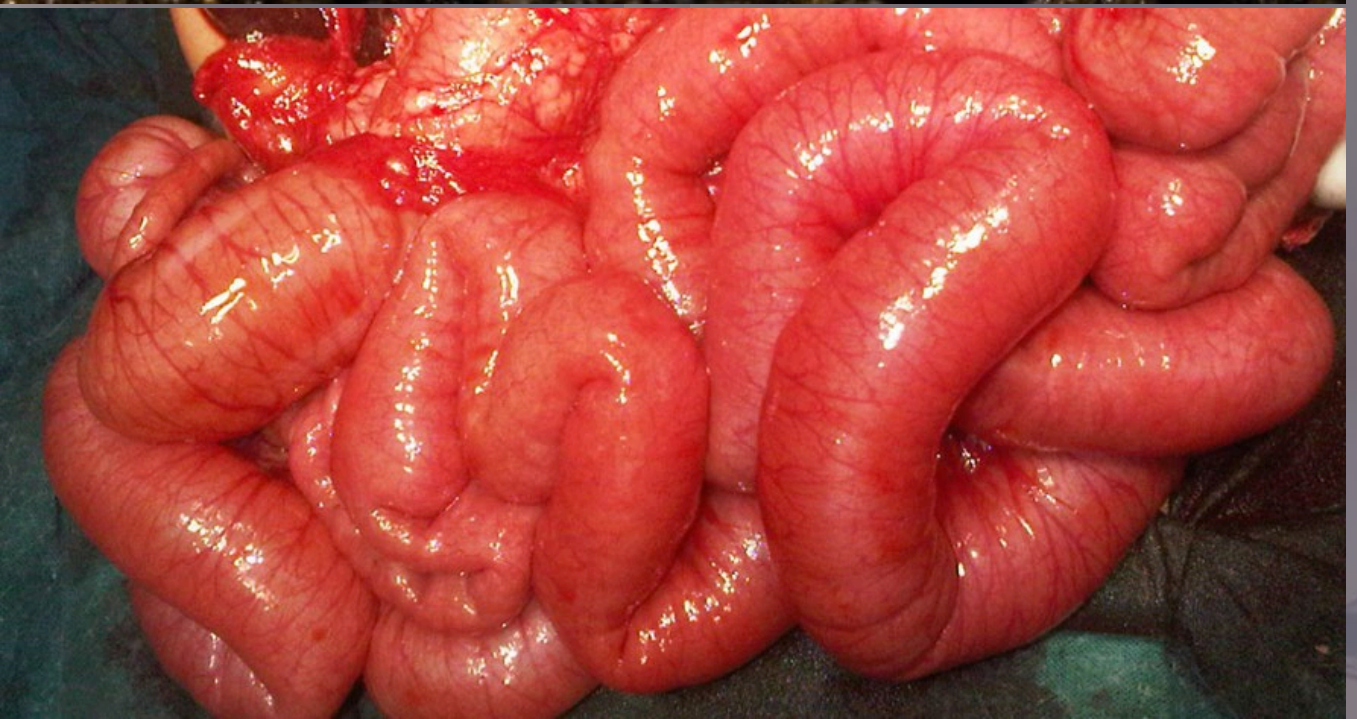
Phase 1b study with low (n=12) and high dose (n=18) cohorts:

- Well tolerated with no overall difference vs. placebo
- Clinical activity observed, including:
  - Reduction in mean PASI scores vs. placebo
  - Reduction in Lesion Severity Score in-line with PASI
- Continued reduction observed in high dose cohort at day 42, two weeks after cessation of dosing, may be indicative of a sustained clinical effect and dose response

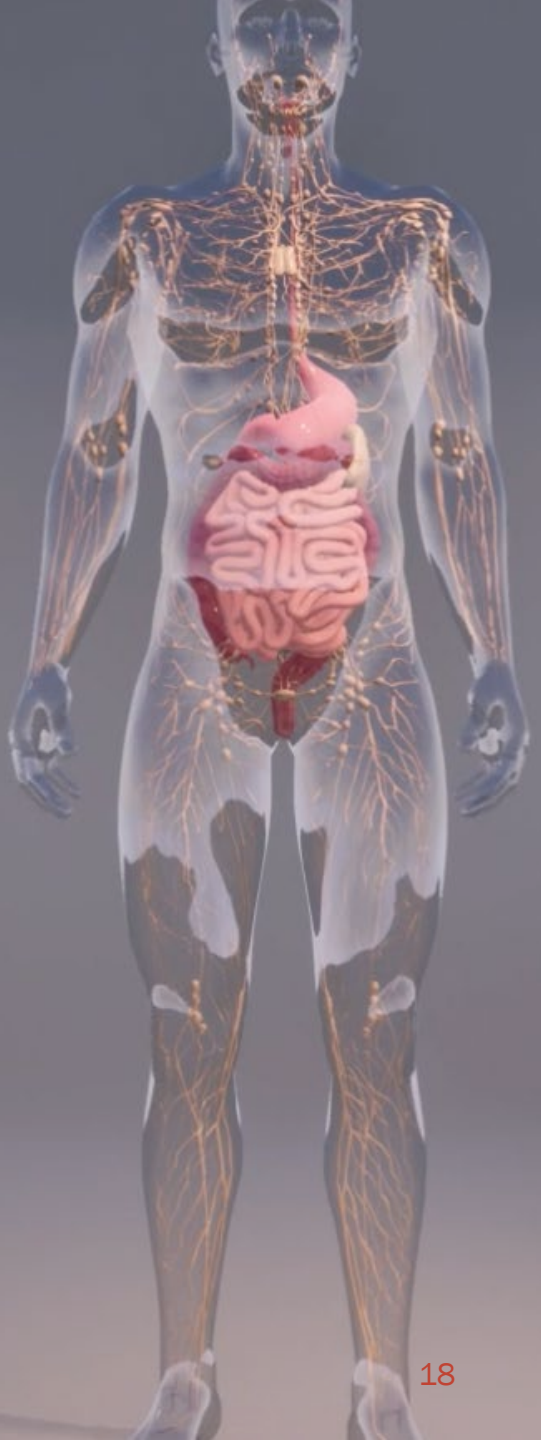
**Clinically meaningful reduction in PASI at high dose**
21% at day 42 versus placebo of 3%



# Evelo product candidates & how they work



600 million years

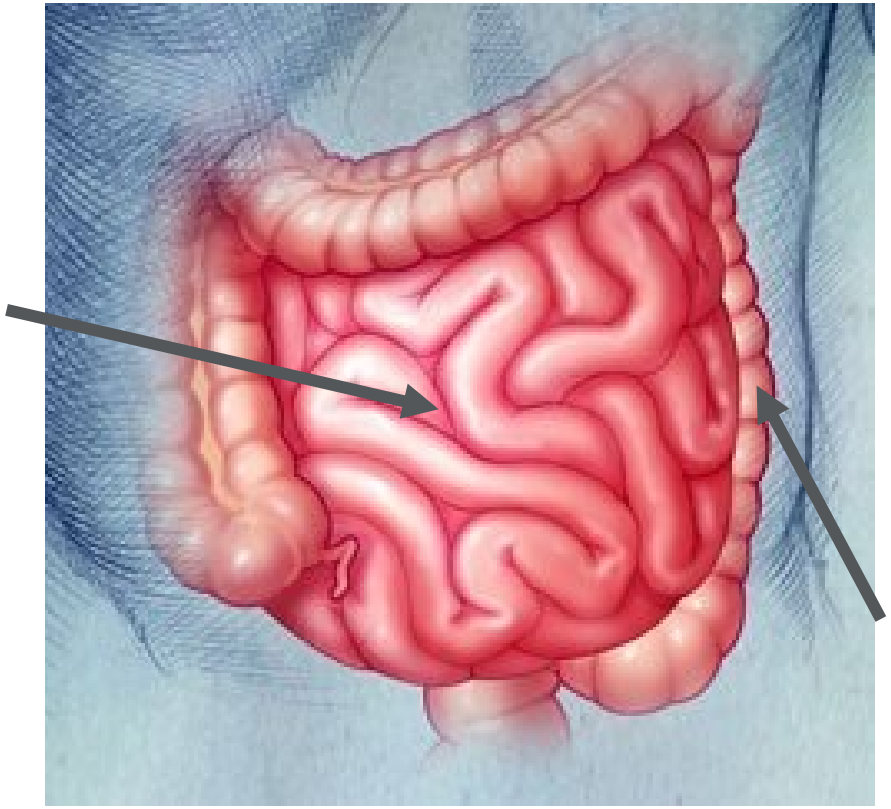


# Cells in the small intestine are therapeutic targets for SINTAX medicines

## Evelo's focus

### Small Intestine

- 80-90% of the gut surface area
- Epithelium includes specialized cells
  - *Immune, endocrine, neural*
- Sensing of signals and govern physiology throughout the body
- Very low level of resident gut microbes



## The field's focus

### Large Intestine

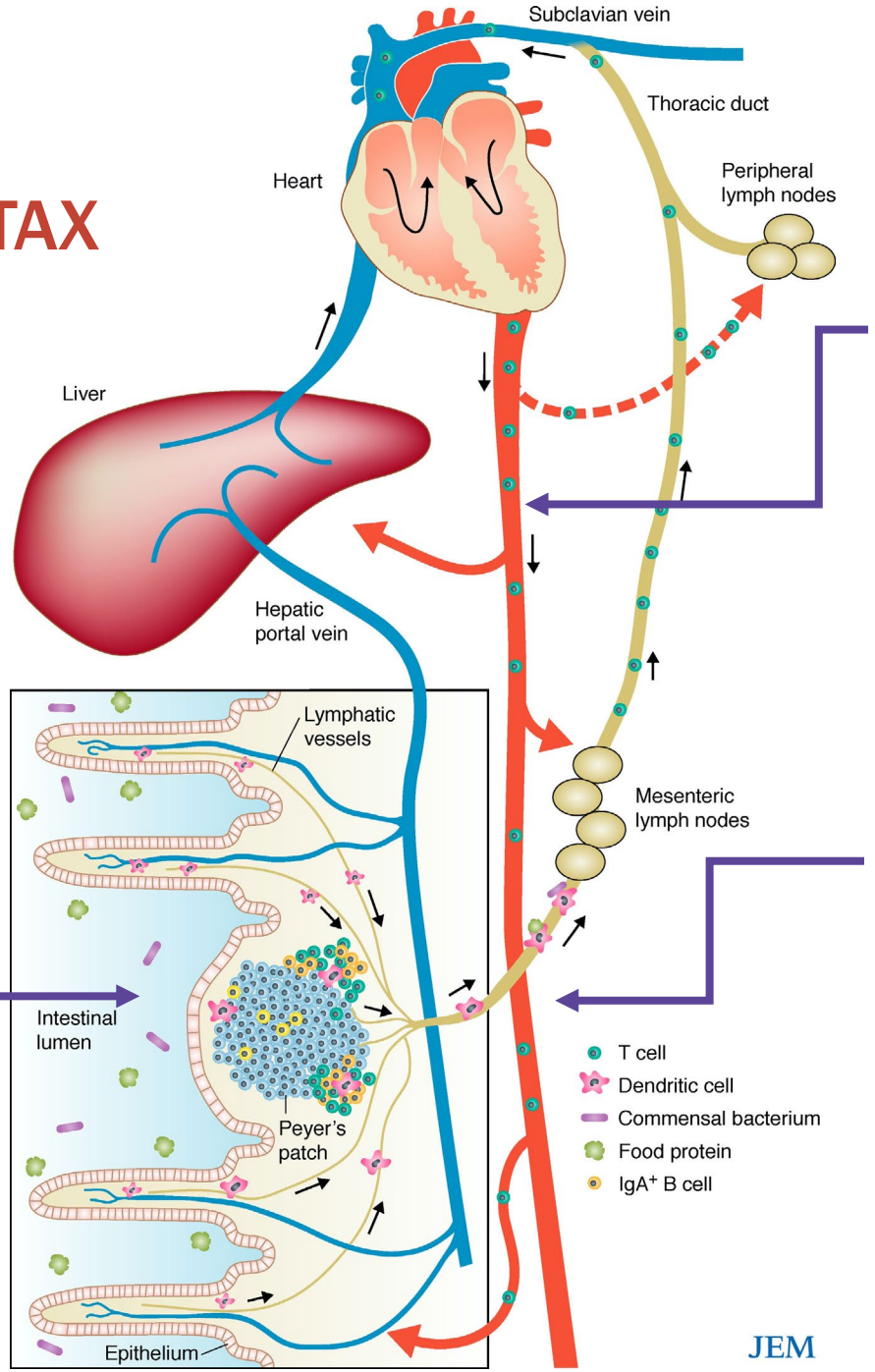
- 10-20% of the gut surface area
- Limited range of specialized cells
- Contains ~99.99% of the gut microbiome

# Three-step process for immunomodulation by SINTAX medicines

## 1

### Interaction between the SINTAX medicine and cells in the small intestine

*Effects are believed to be driven by recognition of structural motifs by host intestinal immune cells in the small intestine*




## 2

### Activated T cells trafficking through the mesenteric lymph node encounter gut-migrating dendritic cells, which instruct effector T cells

## 3

### T cells leave the mesenteric lymph node, enter the systemic circulation to migrate to peripheral tissue and exert their effects

*Depending on the structural motifs of the SINTAX medicine, effects can be inflammation resolving or anti-tumor*

*J Exp Med* (2006) 203 (3): 497–500.
https://doi.org/10.1084/jem.20060227

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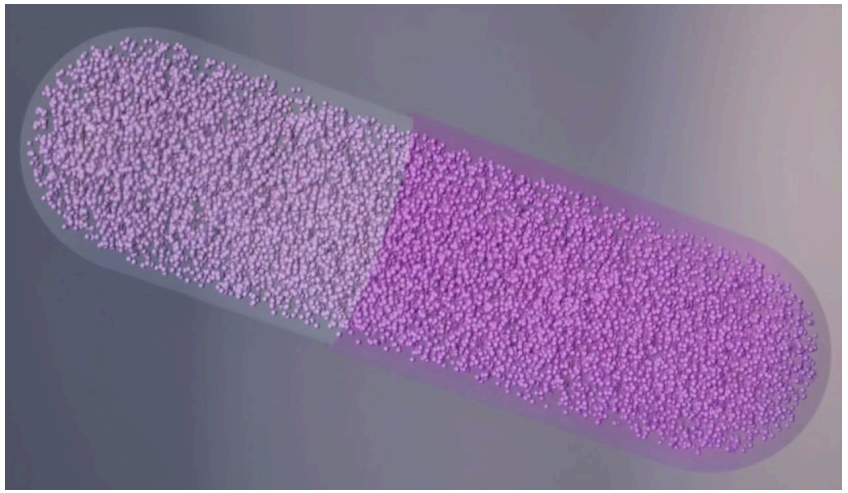
JEM

# SINTAX medicines: potential to be effective, safe, and affordable

Evelo product candidates are composed of orally delivered, gut-restricted single strains of non-replicating and non-colonizing microbes & microbial extracellular vesicles

Effects are believed to be driven by recognition of structural motifs by host intestinal immune cells in the small intestine

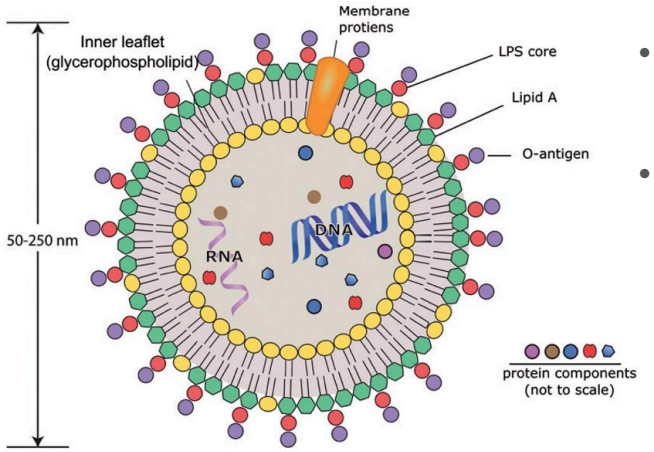


# The next wave of SINTAX medicines: orally delivered bacterial extracellular vesicles (EVs)

- Oral EVs have potential to be more potent than microbes
- MOA potentially applicable in both inflammation resolution and immune activation
- Advancing oncology EVs into clinical development
  - Effects on multiple aspects of immune activation observed preclinically
  - Potentially synergistic with other immuno-oncology (I/O) therapies
  - Potential tolerability, as well as oral delivery, opens up possibility to use at all stages of cancer treatment, from first to last line
- Also advancing anti-inflammatory EVs into clinical development
- Potential broad, long-term applications

# EVs represent a potential new class of broad immune activating, orally delivered, safe therapies

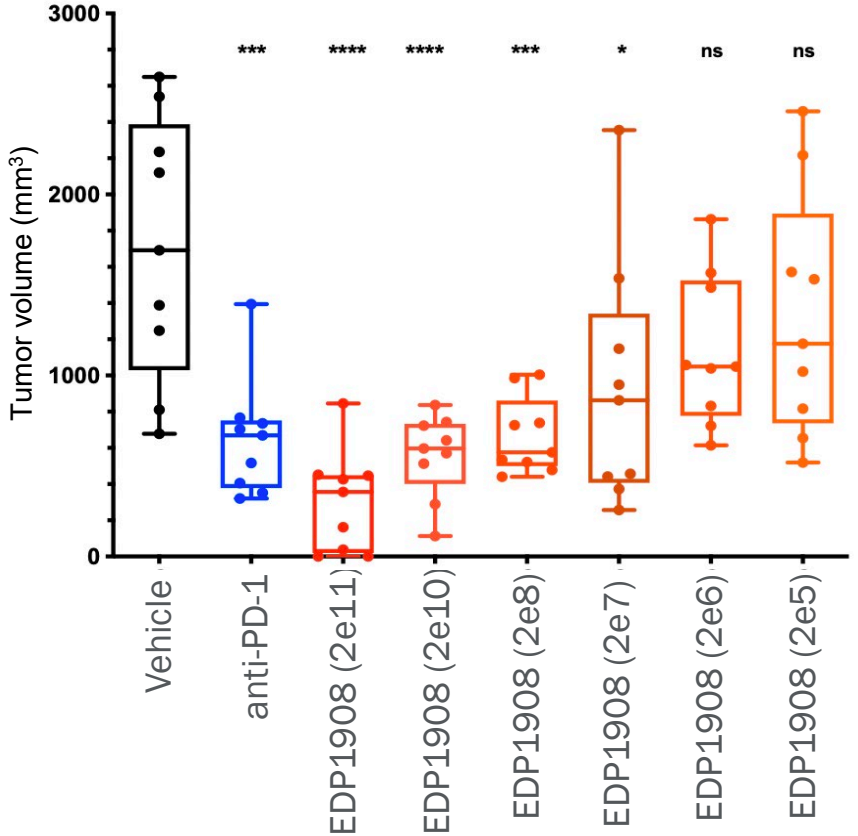
EVs have potential in oncology across all stages of disease and may be well suited for synergistic combinations with checkpoints and therapies which augment neoantigen exposure




Anand et al 2017

- Extracellular vesicles (EVs) are lipoprotein nanoparticles naturally produced by some species of bacteria.
- EVs enable communication with other bacteria and with host cells.
- Compared to microbes, EVs are:
  - More efficacious in preclinical models
  - ~1/1000$^{th}$ volume of microbes enabling improved target engagement
  - Non-viable

Therapeutic treatment of CT26 tumor bearing mice

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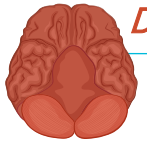
# The Opportunity

# Chronic inflammation is the driver of our most burdensome diseases

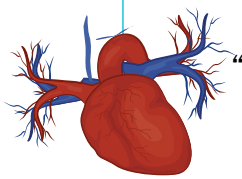
**Neurological diseases; 7M US DALYs[1], 111M WW**

*"The contribution of inflammation in the pathogenesis of Alzheimer's Disease has been appreciated only recently"* Nat Rev Neuro, 2015



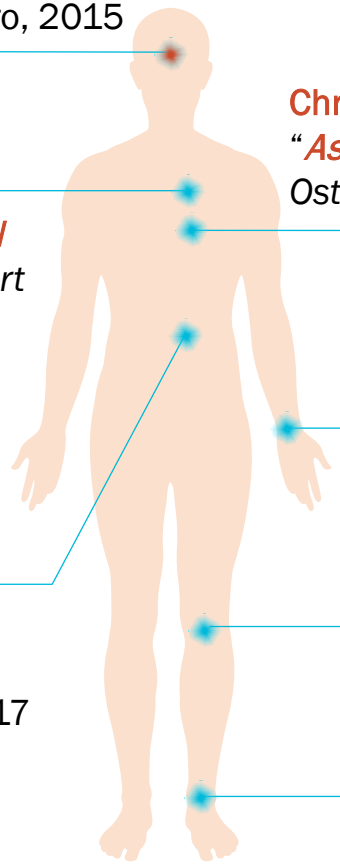
**Cardiovascular disease; 16M US DALYs, 366M WW**

*"Chronic inflammation is a major contributor to heart disease"* Johns Hopkins Medicine



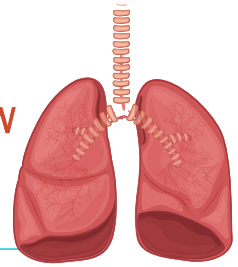
**Diabetes; 4M US DALYs, 68M WW**

*"Inflammation is increasingly considered to be an established mediator [of diabetes]"* J Clin Invest., 2017



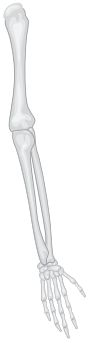
**Chronic respiratory diseases; 6M US DALYs, 112M WW**

*"Asthma is a chronic inflammatory disease" J Amer Osteopathic Assc, 2011*



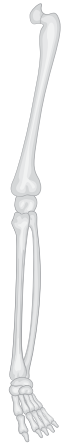
**Autoimmune diseases; 2M US DALYs, 18M WW**

*"Higher levels of systemic inflammation are associated with [cardiovascular decline in rheumatoid arthritis patients]"* Ann Rheum Dis., 2015



**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



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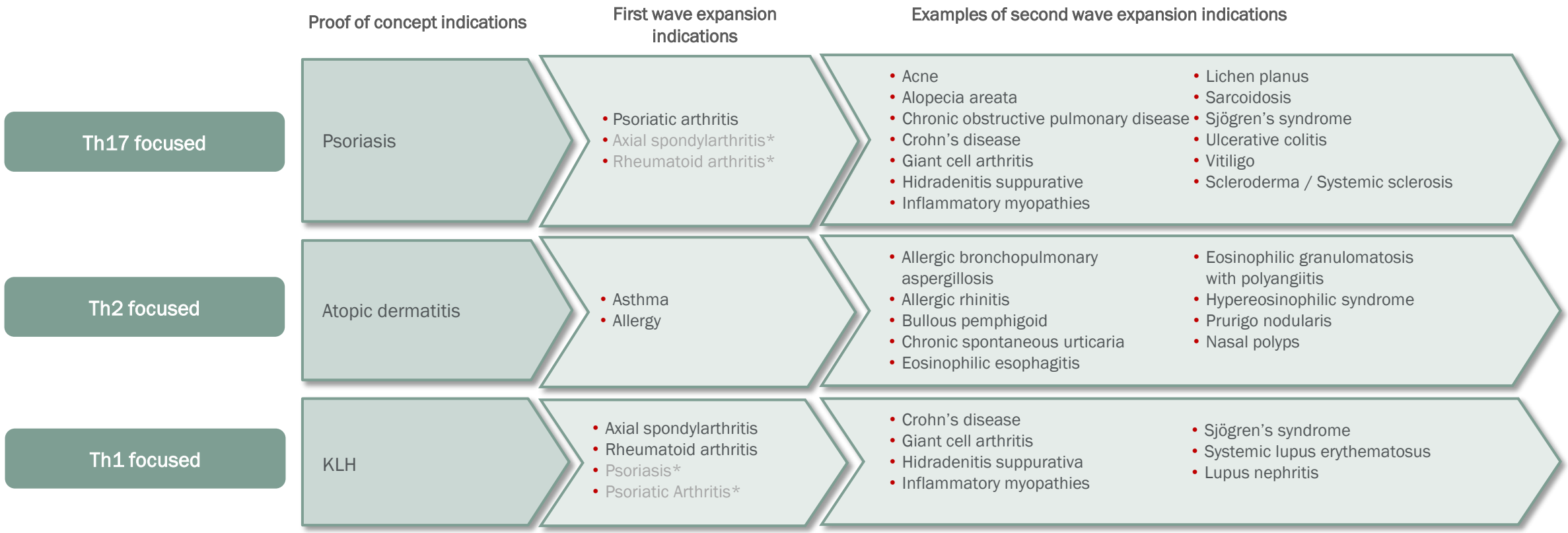
SOURCE: Scientific literature, Global Disease Burden 2017

[1] Disability-Adjusted Life Year (DALY)

# SINTAX medicines show potential application across spectrum of inflammatory diseases - plan to capture full breadth in staged manner




Evelo has generated compelling clinical and preclinical data across inflammatory diseases



*Simplified view of inflammation and in reality, there is overlap

# Evelo's initial focus with SINTAX medicines is to become a foundational treatment for over 600 million people with classic inflammatory diseases

Potential to create new market as mid-line therapy and defer use of injectable biologics / specialty drugs


Highest unmet need

## Potential of SINTAX medicines

- Safe
- Efficacious
- Convenient
- Scalable
- Affordable

Global prevalence for select immune disorders of 641M people worldwide[1]



[1] Includes psoriasis, psoriatic arthritis, axial spondyloarthropathy, rheumatoid arthritis, atopic dermatitis, asthma, IBD, MS, Parkinson's, and Alzheimer's- SOURCE: Websearch, DRG reports, IQVIA reports, Global Health Data Exchange

# The breadth of opportunity for SINTAX medicines is enormous and Evelo has just begun to scratch the surface

Central to this is developing a drug platform to ensure that orally-delivered drugs effectively target the small intestine for maximal efficacy

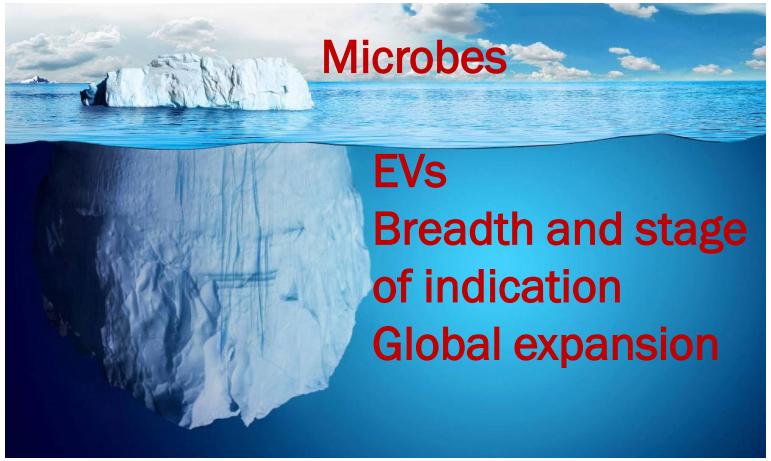
The strategy breaks down into 5 themes which work together to meet the overall goal:

**Nature of the drugs**

- Source and selection of microbes
- Formulation and dose
- Form of product

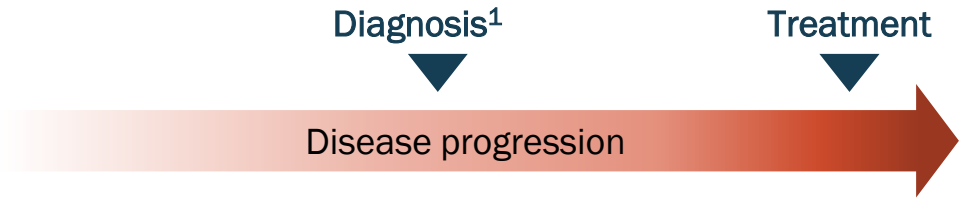
**Uses of the drugs**

- Disease application
- Combinations

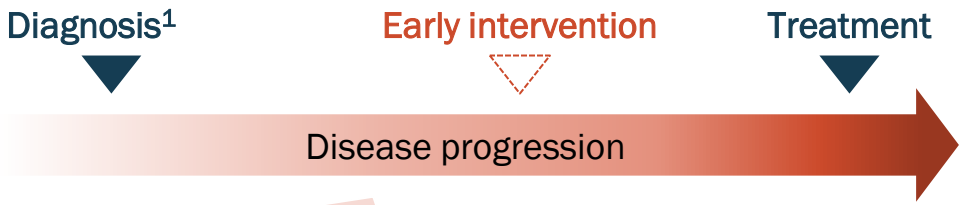


# Future of medicine: treating early and enabling maintenance of health

Diagnostic players are intentionally moving to diagnose disease earlier. Previously…




As diagnosis improves…




People may soon know they have elevated risks for disease that they cannot proactively treat. Lack of early intervention treatment creates massive unmet need for broad patient groups.

Early intervention requires:

- Safe and well tolerated medicines
  - Return to homeostasis, not immune suppression
- Convenient administration
- Affordable medicines

[1] Based on genetic and/or environmental pre-dispositions

# Pipeline & Catalysts

# EDP1815 is a potentially differentiated treatment for COVID-19

- **Inflammation resolution without immunosuppression observed in Phase 1b clinical trial in psoriasis; "Goldilocks effect"**
  - Modulating multiple pathways associated with cytokine storm
  - Did not suppress type 1 interferons which are important for anti-viral immune response
- **Favorable safety and tolerability results in Phase 1b clinical trial in psoriasis and atopic dermatitis**
  - No systemic exposure observed, limiting risk of secondary infections or potential interaction with other medicines
- **Orally administered**, allowing for easy and flexible administration
- **Scalable** for the treatment of large populations

Potential to explore EDP1815 as treatment in other diseases in which hyperinflammation and cytokine storm may play a key role, such as influenza

# Data from two parallel studies has potential to drive accelerated path

## TACTIC-E: Phase 2/3 Platform Trial

- Phase 2/3 randomized platform trial across multiple UK centers, sponsored by Cambridge University Hospitals NHS Foundation Trust*
- Patients with identified risk factors who are at high risk of progression to ICU and/or death
- N=up to 469 per arm, 1:1:1 randomization
  - Arm 1: EDP1815 + standard of care
  - Arm 2: Ambrisentan and dapagliflozin + standard of care
  - Arm 3: Standard of care
- Interim safety data and completion of futility analysis expected in 2Q 2021

## Rutgers Phase 2 Trial

- Double-blind, placebo-controlled trial in collaboration with Rutgers University and Robert Wood Johnson University Hospital (N=60)
- Patients 15 or older who present at ER within the last 36 hours and test positive for COVID-19
- Evaluate EDP1815 vs. placebo, on top of standard of care, in preventing progression of COVID-19 symptoms and development of COVID-related complications
- Clinical data expected in 2Q 2021

Manufacturing plans expedited; potential to rapidly scale production to supply drug at reasonable cost in 2021

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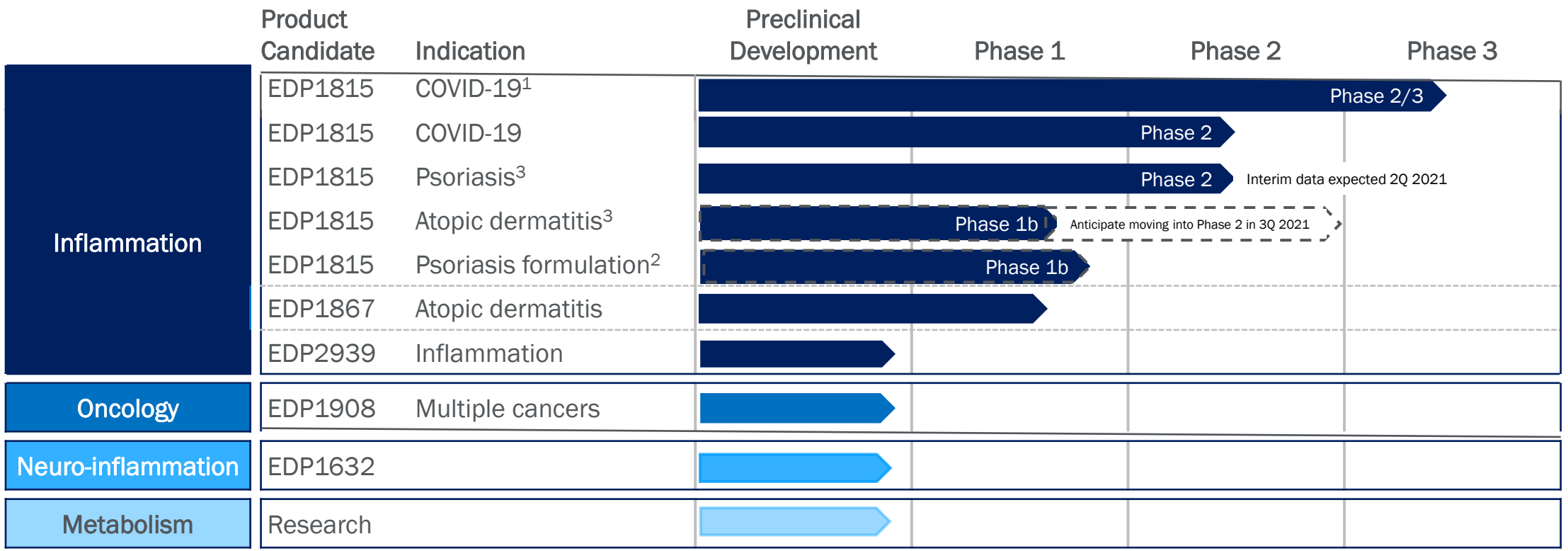
*The investigators of the study plan to expand the trial to countries where COVID-19 remains prevalent

# Broad clinical and preclinical pipeline with multiple upcoming readouts




[1] The Phase 2/3 TACTIC-E study is an investigator-sponsored study being conducted by Cambridge University Hospitals NHS Foundation Trust.
[2] Evelo is initiating a Phase 1b tablet formulation trial in psoriasis in 1Q 2021.
[3] Evelo intends to advance EDP1815 in both psoriasis and atopic dermatitis into Phase 3 trials in 2022 dependent on positive Phase 2 data.

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# Pipeline is rich in anticipated near-term clinical catalysts

| Candidate | Catalyst |
|---|---|
| **EDP1815**<br>Psoriasis | **1Q 2021:** Phase 1b tablet formulation trial initiation<br>**2Q 2021:** Phase 2 interim data<br>**3Q 2021:** Phase 1b tablet formulation data<br>**2H 2021:** Full Phase 2 dataset<br>**1H 2022:** Phase 3 initiation* |
| **EDP1815**<br>Atopic dermatitis | **3Q 2021:** Phase 2 initiation<br>**1Q 2022:** Phase 2 interim data<br>**2022:** Phase 3 initiation* |
| **EDP1815–TACTIC-E**<br>COVID-19 | **2Q 2021:** Phase 2/3 interim safety data and futility analysis |
| **EDP1815–Rutgers University**<br>COVID-19 | **2Q 2021:** Phase 2 data |
| **EDP1867**<br>Atopic dermatitis | **1Q 2021:** Phase 1b initiation<br>**4Q 2021:** Phase 1b data |
| **EDP2939**<br>Inflammation | **2022:** Phase 1b initiation |
| **EDP1908**<br>Oncology | **2022:** Phase 1 initiation |

*Progression to Phase 3 dependent on positive Phase 2 data

# Corporate information

- ~95 employees
- Cash and cash equivalents of $81.6 million*
- $50 million ATM program with meaningful capacity remaining
- Long-term debt outstanding of $30 million

*As of 9/30/20