EVELO

Harnessing the Small Intestinal Axis to Create Big Change

Evelo Corporate Presentation

September 2021

Legal Disclaimer

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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: 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.

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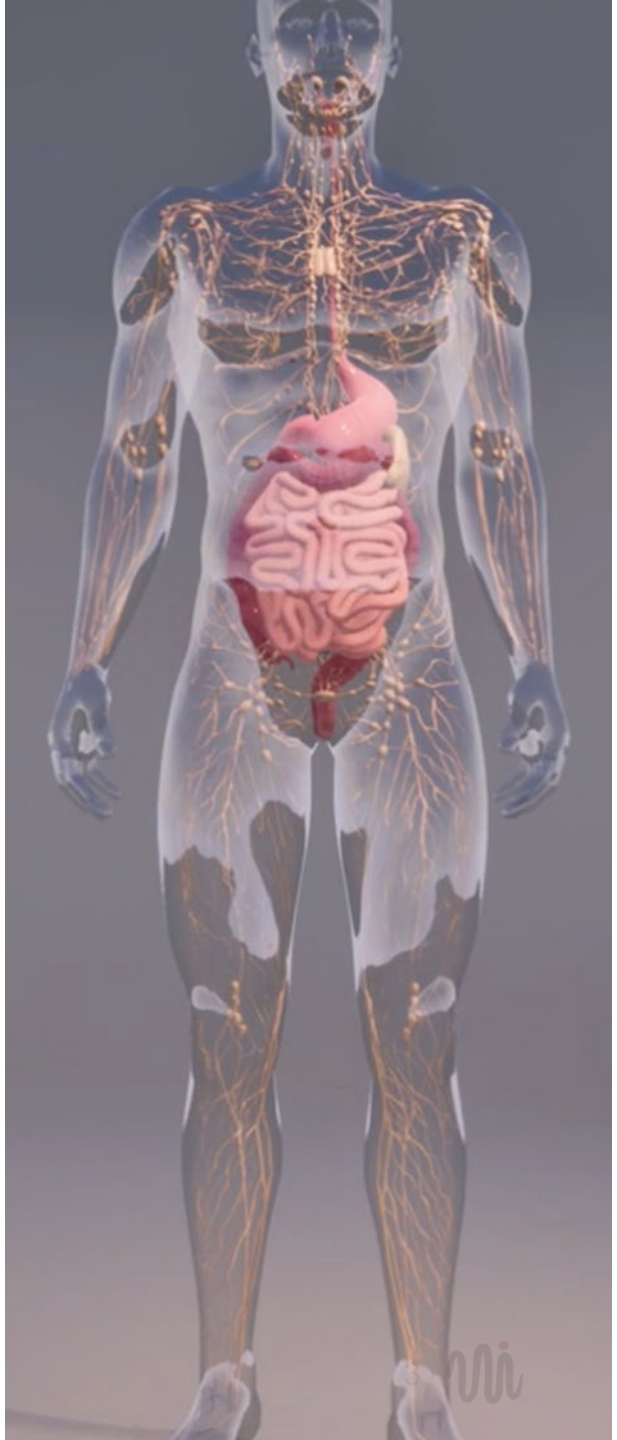
Harnessing the Small Intestinal Axis to Transform Medicine

- The small intestinal axis, SINTAX™ - a newly uncovered area of central biology
- SINTAX is the sensing system in the gut that governs inflammation and immunity throughout the body
- Evelo is harnessing SINTAX to develop a new type of medicine that has the potential to be:
  - Safe, effective, convenient, and affordable for billions of people, and
  - Used at all stages of disease



What are Evelo's Investigational Medicines?

Evelo's potential medicines target SINTAX with oral microbial therapies

- Sourced from the gut mucosa
- Selected for a particular immune profile

SINTAX medicines are non-living pharmaceutical preparations of either single strains of bacteria or their extracellular vesicles

- Effects systemic immunity through interactions with immune cells in the gut
- No modification of the microbiome

Evelo's Sector-Defining Platform Integrates Seven Discoveries

Oral, gut-restricted investigational medicines with systemic effects

Consortia	→	**Single strains**
Live	→	**Non-live**
Stool-derived	→	**Mucosa-derived**
Colon microbiota	→	**Small intestinal axis**
Indirect action	→	**Direct action**
Microbes	→	**Extracellular vesicles**
Systemic drugs	→	**SINTAX - remote control of systemic immunity**

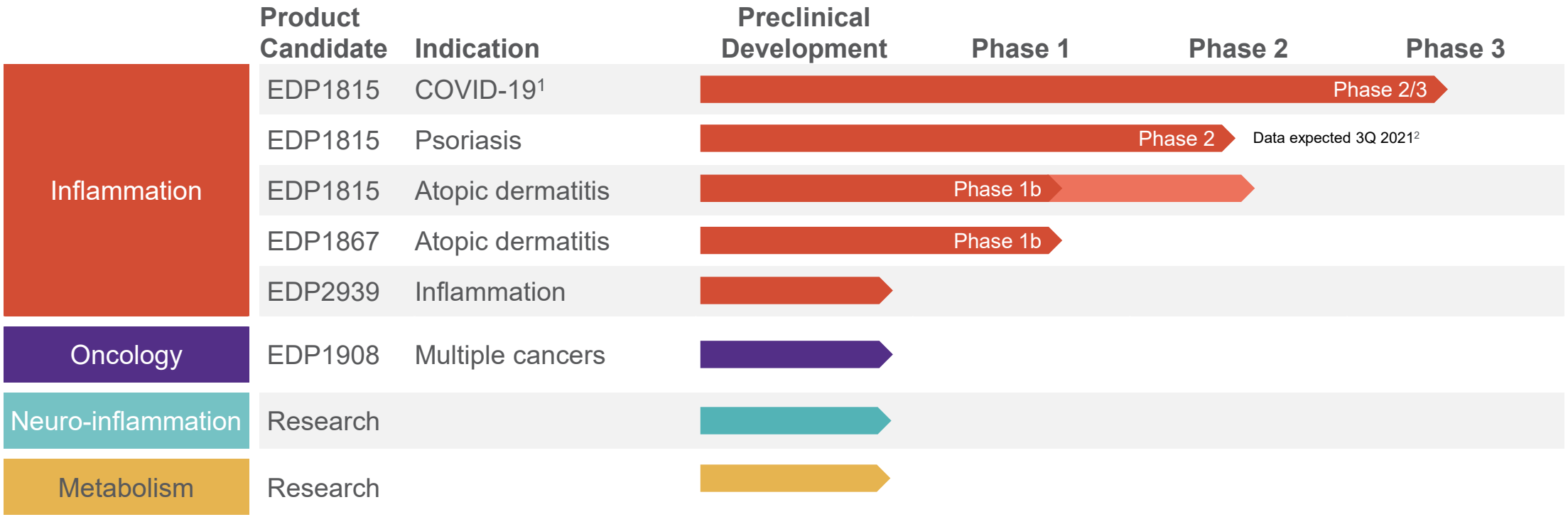
Five Positive Sets of Clinical Data with Lead Product, EDP1815

- Positive preclinical and Phase 1b clinical results across Th1, Th2, and Th17 inflammation pathways
- Generally well tolerated
- Potential utility across all stages of disease: mild and moderate to severe
- Profile has potential to be used across broad spectrum of inflammatory diseases

Pipeline is Rich in Anticipated Near-Term Clinical Catalysts

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

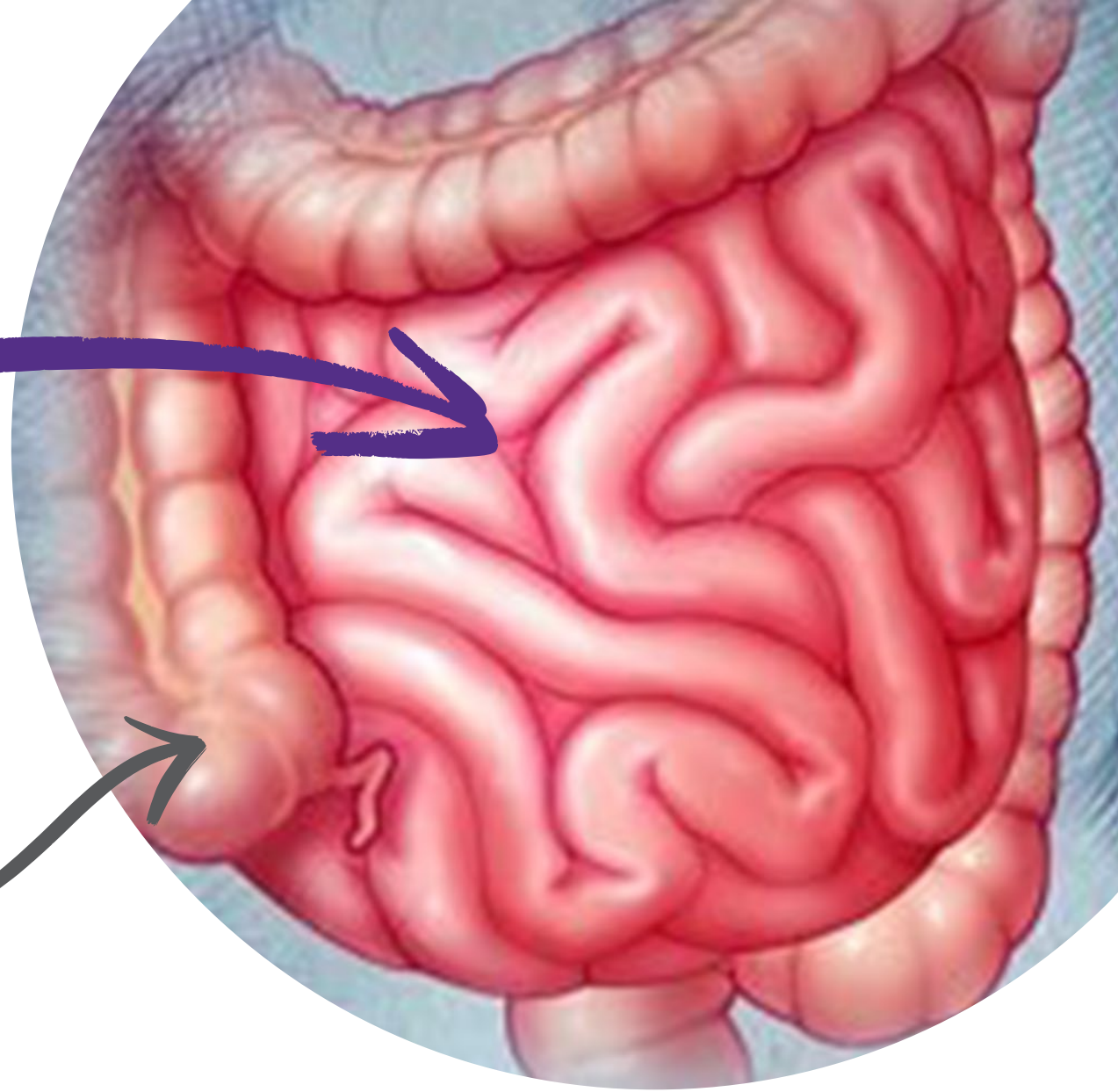
Broad Clinical and Preclinical Pipeline with Multiple Upcoming Readouts



[1] The Phase 2/3 TACTIC-E study is an investigator-sponsored study being conducted by Cambridge University Hospitals NHS Foundation Trust
[2] Phase 1b data on different formulations and concentrations also expected in 3Q 2021

How Does SINTAX Work?

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

Microbiome company's focus

Large Intestine

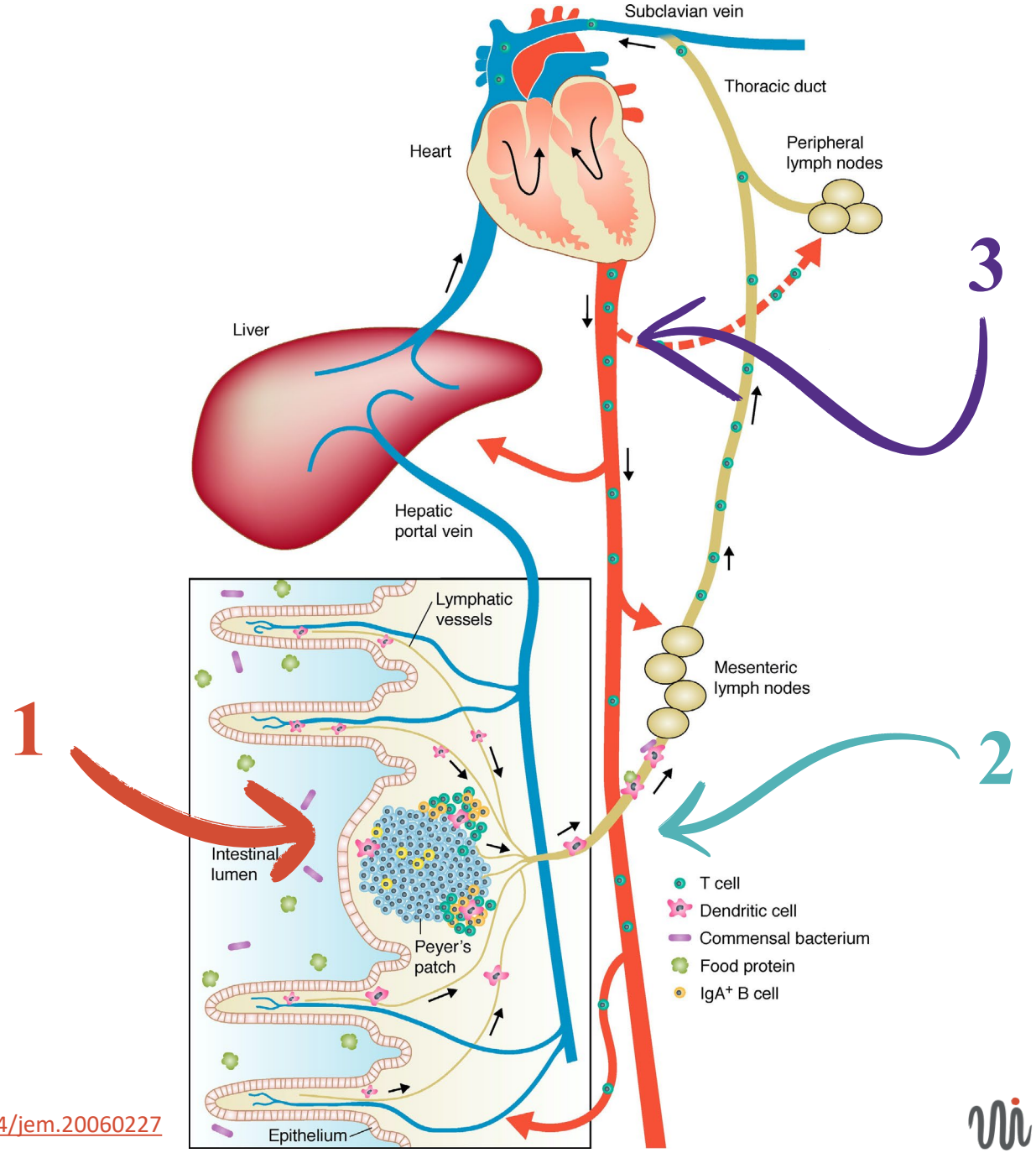
- 10-20% of the gut surface area
- Limited range of specialized cells
- Contains ~99.99% of the gut microbiome

Three-Step Process for Immunomodulation by SINTAX Medicines

1. **Sampling of SINTAX medicines by 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. **Conditioning of T cells by dendritic cells and macrophages in lymph nodes**

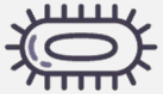
3. **Migration of effector T cells throughout the body via systemic lymphatic circulation**
   Depending on the structural motifs of the SINTAX medicine, effects can be inflammation resolving or anti-tumor



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

SINTAX Product Candidates: Microbes and Microbial Extracellular Vesicles (EVs)

- Product candidates are pharmaceutical preparations of single strains of microbes and EVs
- Effects are thought to be driven by recognition of structural motifs by immune cells in the small intestine

Whole, inactivated microbes 

- Non-replicating, non-colonizing, and gut restricted
- Biomarkers show inflammation resolution without immunosuppression

Microbial Extracellular Vesicles  (EVs)

- Lipoprotein nanoparticles naturally produced by some bacteria- macromolecular content is a subset of the parent; non-viable
- 1/1,000th volume of whole microbes, potentially enabling increased target engagement and potency
- Potent efficacy in oncology and inflammation pre-clinical models
- Initiation of clinical development in 2022

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The Opportunity

SINTAX Medicines:
Potential to Treat Inflammation and Beyond

Inflammation

- Atopic Dermatitis
- Psoriasis
- Rheumatoid Arthritis
- Inflammatory Bowel Disease

Oncology

- Immunologically active tumors
  - Melanoma
  - Lung
  - Renal
  - Bladder
- Solid tumors

Metabolism and CV

- Type 2 Diabetes
- NASH
- Obesity
- Atherosclerosis

Neuro-Inflammation/ Degeneration

- Multiple Sclerosis
- Alzheimer's Disease
- Parkinson's Disease

Autoimmune

- Type 1 Diabetes
- ITP
- Myasthenia Gravis

Neuro-psychiatric

- Autism
- Anxiety
- Depression

Vaccines

- Oral vaccines for:
  - Autoimmune disease
  - Infectious disease
  - Cancer
- Conditioning responses to current vaccines

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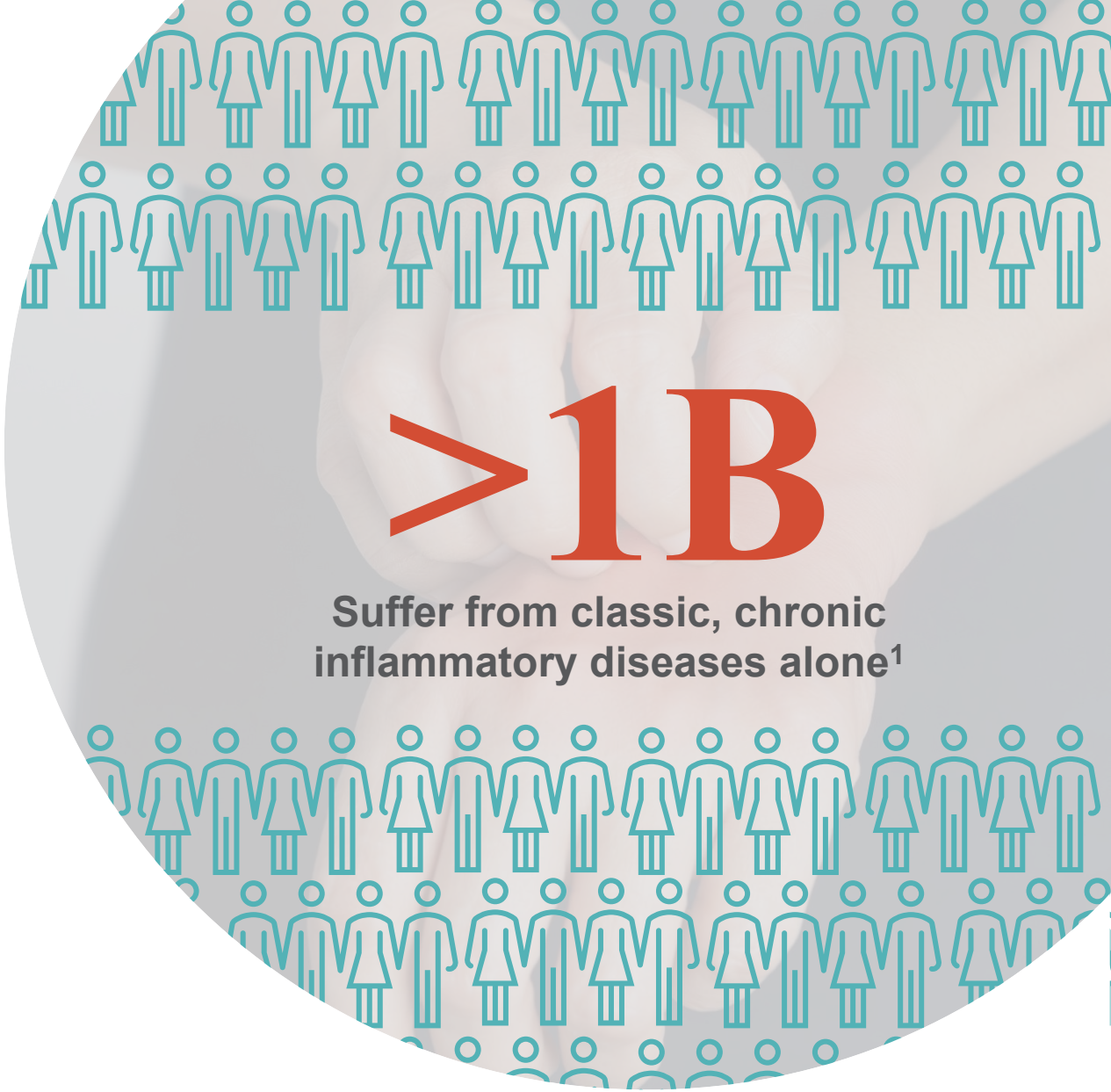
Chronic Inflammation Impacts Billions of People Worldwide

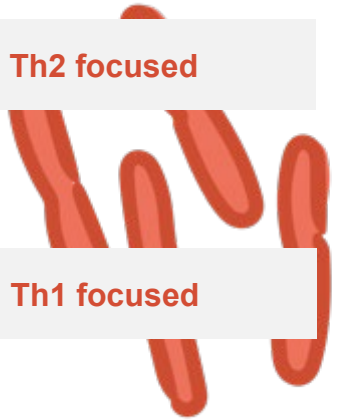
- Atopic dermatitis
- Psoriasis
- Psoriatic arthritis
- Rheumatoid arthritis
- Asthma
- Food allergy
- Axial spondylarthritis
- Inflammatory bowel disease



[1] Datamonitor Healthcare, accessed Feb 2020

SINTAX Medicines Have Potential Use Across Spectrum of Inflammatory Diseases

Evelo Plans to Capture Breadth of Platform in Stages



Th17 focused

PSORIASIS

- Reduction in skin lesions vs placebo in 2 Phase 1b cohorts
- Systemic Inhibition of multiple inflammatory cytokines
- Ongoing Phase 2b trial

- Psoriatic arthritis
- Axial spondylarthritis*
- Rheumatoid arthritis*

- Acne
- Alopecia areata
- Chronic obstructive pulmonary disease
- Crohn's disease
- Giant cell arteritis
- Hidradenitis suppurative
- Inflammatory myopathies
- Lichen planus
- Sarcoidosis
- Sjögren's syndrome
- Ulcerative colitis
- Vitiligo
- Scleroderma / Systemic sclerosis

Th2 focused

ATOPIC DERMATITIS

- Improvement in atopic dermatitis vs placebo in Phase 1b
- Positive results provide basis for Phase 2b

- Asthma
- Allergy

- Allergic bronchopulmonary aspergillosis
- Allergic rhinitis
- Bullous pemphigoid
- Chronic spontaneous urticaria
- Eosinophilic esophagitis
- Eosinophilic granulomatosis with polyangiitis
- Hypereosinophilic syndrome
- Prurigo nodularis
- Nasal polyps

Th1 focused

HUMAN KLH

- >90% reduction in inflammation vs placebo

- Axial spondylarthritis
- Rheumatoid arthritis
- Psoriasis*
- Psoriatic Arthritis*

- Crohn's disease
- Giant cell arthritis
- Hidradenitis suppurativa
- Inflammatory myopathies
- Sjögren's syndrome
- Systemic lupus erythematosus
- Lupus nephritis

Next Wave of SINTAX Medicines: EVs

EVs are a Fundamental Advance for SINTAX Medicines

- Pharmacologically active strains of gut mucosa-derived microbes naturally shed EVs
- Small size and diffusion properties enable target engagement in the gut
- Future EV product candidates potentially enable greater SINTAX activation for greater efficacy

Stokes-Einstein Equation

$$D = \frac{k_B T}{C \pi \eta a}$$

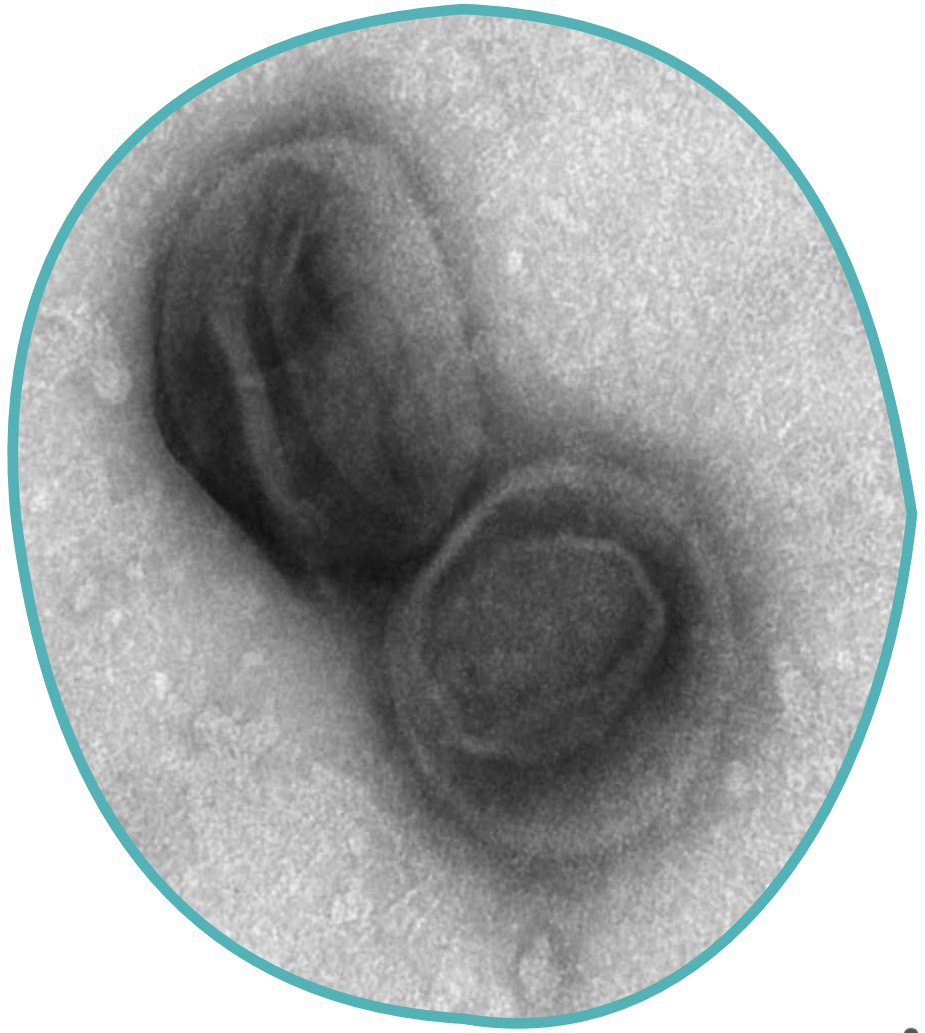
Fick's Laws of Diffusion

$$J \propto \frac{d\varphi}{dx} \quad \text{or} \quad J = -D \frac{d\varphi}{dx}$$

EVs are Recognized by SINTAX

Have the potential to drive dramatically improved efficacy vs. microbes

- EVs are lipoprotein nanoparticles naturally produced by most bacteria
- Their molecular content is a subset of the parent
- Compared to microbes, EVs are:
  - ~1/1000th volume of microbes - potential for higher dosing
  - Non-viable
- Evelo has scaled manufacturing of EVs



EDP2939: EV for Inflammation

Orally Delivered Microbial Extracellular Vesicles Modulate Systemic Inflammation Through the Small Intestinal Axis (SINTAX™)

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Evelo Biosciences, Cambridge MA

Introduction

Evelo Biosciences is developing a new class of oral medicines which engage the immune system in the small intestine with anti-inflammatory effects throughout the body.

EDP2939 is an orally-delivered and gut-restricted bacterial EV which potently attenuates inflammation in murine models of Th1 and Th17 inflammation.

The small intestinal axis (SINTAX™) is a network of anatomic and functional connections with the rest of the body. It acts as a sensory system, integrating environmental signals that link gut mucosal immunology with immunological processes throughout the body.

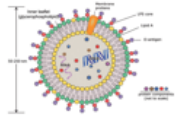
This suggests that SINTAX is a control mechanism for systemic immunity centred in the small intestine. This mechanism has novel features of considerable interest for the development of immunomodulatory therapies. It may be harnessed for orally delivered medicines that are systemically effective without systemic distribution.

We have previously shown clinical proof of the SINTAX mechanism with EDP1815, an orally delivered single strain of commensal bacteria. It has systemic anti-inflammatory effects with a safety profile comparable to placebo. EDP1815 comprises almost entirely non-living bacteria. It exerts its effects through direct action on host cells in the gut with no colonization, alteration of the microbiome, or exposure outside the gut.

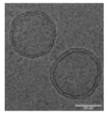
Some bacteria produce extracellular vesicles (EVs) that share molecular content with the parent bacterium in a particle that is roughly 1/1000th the volume in a non-replicating form.

We report here the preclinical pharmacological effects, mechanism of action, and biodistribution of EDP2939, an orally administered preparation of EVs derived from a single gram-negative bacterial strain of the family *Prevotellaceae* that was selected from screens of EVs for anti-inflammatory pharmacology.

Extracellular Vesicles (EVs)



Anand *et al* 2017



Cryo-EM image of EDP2939

- Extracellular vesicles (EV) are lipoprotein nanoparticles naturally produced by some species of bacteria
- Their macromolecular content is a subset of the parent
- EVs enable bacterial communication and survival during stress, host-immune modulation, material exchange, and cell-cell interactions
- Compared to whole microbes EVs are:
  - ~1/1000th volume of microbes enabling improved target engagement
  - Non-viable
  - Incapable of establishing infection or sepsis

EDP2939 is an effective anti-inflammatory drug requiring multiple pathways for efficacy

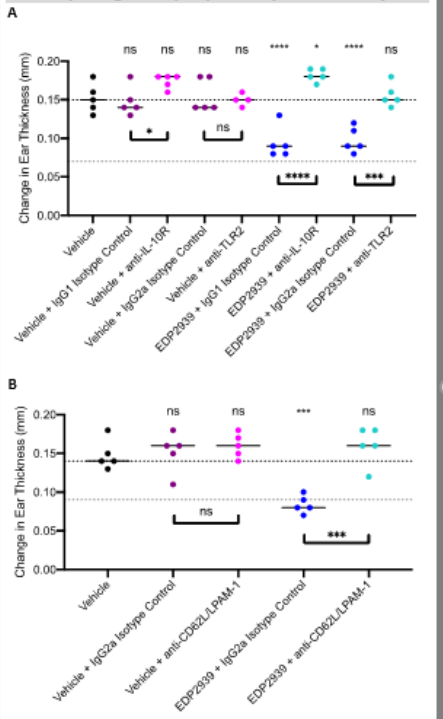


Figure 1: Orally-administered EDP2939 requires multiple pathways for anti-inflammatory effects. Mice undergoing a delayed type hypersensitivity (DTH) reaction against keyhole limpet hemagglutinin (KLH) were dosed with 2E10 particles/dose of EDP2939 by oral gavage on days 5–8. During the study, various mechanisms of action were interrogated by intraperitoneal injection of antibodies as indicated. **A)** Graph shows changes in ear thickness 24 hours after challenge with KLH protein and blockade of TLR2 or IL-10R signaling. **B)** Graph shows changes in ear thickness 24 hours after challenge with KLH protein and inhibition of lymphocyte gut homing. Points indicate individual mice and line shows median change in ear thickness. Data are representative of 2 independent studies. Statistical analyses were performed using a one-way ANOVA (vs. vehicle) or two-tailed unpaired t-test (isotype vs. treated). NS = not significant, *p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001.

Orally administered fluorescently-labelled EDP2939 is gut-restricted

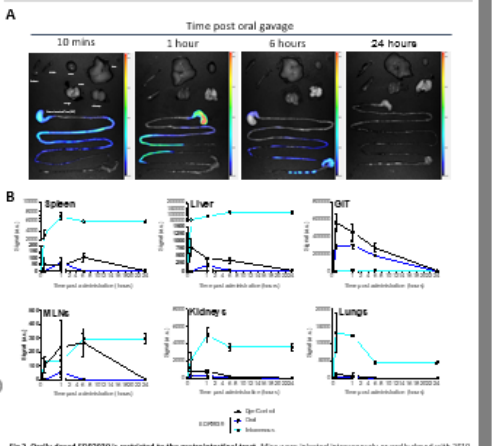


Fig 2. Orally dosed EDP2939 is restricted to the gastrointestinal tract. Mice were injected intravenously or orally dosed with 2E10 EDP2939 particles covalently labeled with IRDye800 or dye-only control. After 10 mins, 1 hour, 6 hours, or 24 hours, fluorescence was measured in the indicated organs using a small animal imaging system (Licor Pearl®). **A)** Representative images showing fluorescence from labelled EDP2939 in various organs at indicated time points post oral gavage. **B)** Graphs showing total signal measured in indicated organs and time points after oral gavage of dye control (*black*) or labelled EDP2939 (*dark blue*) or intravenous injection of labelled EDP2939 (*light blue*). Points show fluorescence intensity mean ± SD. Data are representative of 2 independent experiments.

Conclusions

- Orally-delivered microbial extracellular vesicles enact broad-based resolution of inflammation establishing homeostatic inflammatory status
- Efficacy of EDP2939 requires the stimulation of both the TLR2 receptor and the IL-10 receptor in addition to lymphocyte homing to the intestinal lymphoid tissue
- EDP2939 induces TLR2-dependent release of IL-10
- EVs are an orally-dosed, gut-restricted therapeutic with no apparent safety or tolerability issues in animal models, making for a desirable therapeutic profile

These data support the development of EVs as a new class of immunotherapeutic drugs. They are particularly effective at engaging the small intestinal axis, acting locally on host cells in the gut to activate distal immune responses. EDP2939 is in preclinical development for inflammatory disorders involving both aberrant Th1 and Th17 immune responses.

EDP2939 induces the release of IL-10 through TLR2 stimulation

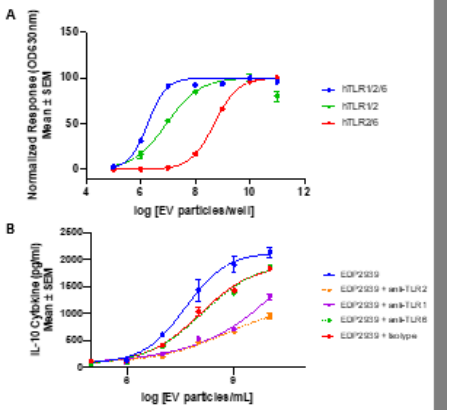


Fig 3. EDP2939 induces release of IL-10 following stimulation of TLR2. A) EDP2939 stimulates both TLR1/2 and TLR2/6 heterodimers, with greater potency towards the TLR1/2 heterodimer. HEK293-SEAP reporter cells (Invivogen) expressing human TLR1, TLR2, and TLR6 combinations were incubated for 24 hours with EDP2939 at the indicated concentrations. Supernatants were collected and analyzed for secreted embryonic alkaline phosphatase (SEAP) production to determine stimulation of TLR2 heterodimers. **B)** EDP2939 stimulated IL-10 release from U937 cells is impaired by antibody-mediated blockade of either TLR1 or TLR2, but not TLR6. PMA-differentiated human monocytic U937 cells were incubated with EDP2939 ± 2.5 µg/mL anti-TLR1, TLR2, TLR6 or isotype control antibody for 24 hours. Supernatants were collected and analyzed for IL-10 response by MSD. Data are representative of 2 independent experiments.

EDP2939 stimulates anti-inflammatory cytokine secretion from human PBMCs

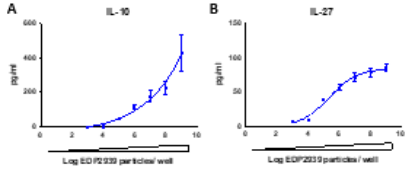


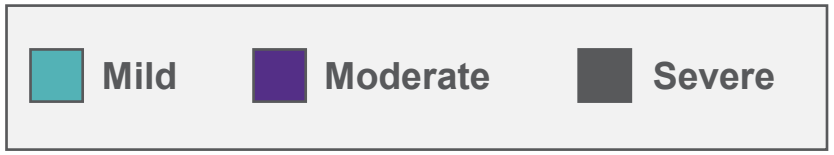
Fig 4. EDP2939 induces IL-10 and IL-27 concentration-dependent production from human PBMCs. PBMCs were isolated from whole blood of six human donors, plated at 100,000 cells per well, rested overnight, and then incubated with varying concentrations of EDP2939 for 24 hours. Supernatants were collected and **A)** IL-10 and **B)** IL-27 concentrations were determined via MSD. Data are representative of 6 independent donors.

EDP1815

- EDP1815 has shown positive preclinical and Phase 1b clinical results across Th1, Th2, and Th17 inflammation pathways
- Generally well tolerated
- Broad potential applicability across inflammatory diseases: dermatology, rheumatology, inflammatory bowel disease, and beyond
- Potential utility across all stages of disease: mild and moderate to severe

Majority of Psoriasis and Atopic Dermatitis Patients Have Mild or Moderate Disease

***93%** of PsO patients*
***85%** of AD patients*



Psoriasis

55M Worldwide prevalence
8.6M US prevalence
6.7M US diagnosed

Atopic Dermatitis

201M Worldwide prevalence
21.3M US prevalence
10M US diagnosed

Source: Datamonitor Healthcare

Psoriasis and Atopic Dermatitis Patients in the U.S.

Psoriasis

LESS THAN 8% in the US receive biologics or oral systemics[1-2, 6-9]

Atopic Dermatitis

LESS THAN 2% in the US receive dupilumab (no oral systemics approved)[5]

46% of psoriasis and atopic dermatitis patients in the US receive no treatment[2-4]; 47% use only topicals[1-2]

[1] IQVIA and Symphony Health Data [2] Arcutis Investor Presentation, Feb 2021 [3] Incyte Investor Presentation, Jan 2021 [4] Analyst Report, Feb 2020 [5] Regeneron 2020 4th quarter earnings call [6] Armstrong A, et al., Dermatol Ther (Heidelb). 2017 Mar; 7(1) [7] BMS Investor Presentation, Jun 2020 [8] IQVIA Prescription data from Analyst Report, Oct 2020 [9] Novartis Investor Presentation, Jan 2018

Therapies for Psoriasis and Atopic Dermatitis Have Limitations Related to Safety, Tolerability, Convenience, and Price

>60% of PsO and **>90%** of AD patients are dissatisfied with current treatment options[1,2]

Topicals

PsO/AD

- Steroids, calcineurin inhibitors. pipeline
- Mainstay treatment
- Not convenient
- Low compliance
- No impact on systemic inflammation

Old-school Systemics

PsO

- Safety concerns
- Monitoring requirement
- Immunosuppressant

Oral Immunosuppressant

PsO

- Apremilast:
  - Safety and tolerability issues
  - High price

Injectable Biologics

PsO/AD

- Not convenient & needle fear
- Immunosuppressant
- High price

[1] Florek, Aleksandra G., et al., Archives of dermatological research 310.4 (2018): 271-319. [2] National Eczema Association report, 2020

Despite Modest Efficacy, Apremilast Experienced Strong Launch Uptake by Focusing on Convenience and a Perceived Favorable Safety Profile

Modest Efficacy

~30%

Apremilast works in ~1/3 of patients with moderate – severe psoriasis[1]

Strong Uptake

~30%

of all new RXs in 2017-18 were for apremilast – higher share than any biologic and entirety of Janssen's biologics portfolio[2]

BUT

Significant Tolerability Issues

>30%

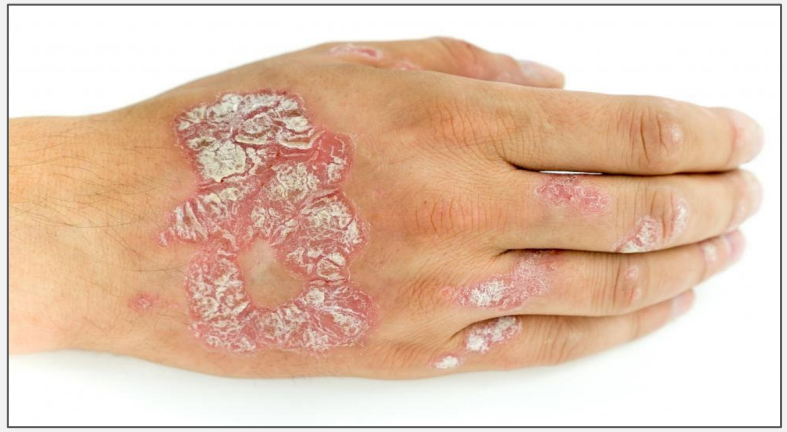
of patients with moderate PsO (UNVEIL trial) experienced one or more of:

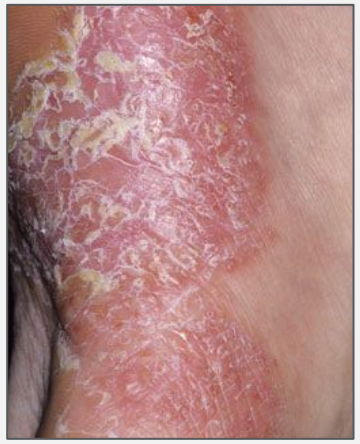
diarrhea, nausea, vomiting, and headache

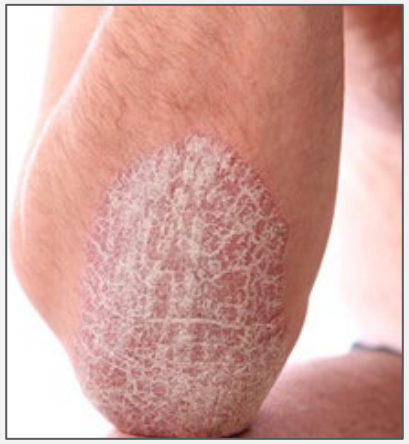
[1] Otezla website [2] Barclays Research, IQVIA BrandImpact

Psoriasis

Mild and Moderate Psoriasis is a Serious Condition with Few Existing Effective Treatments

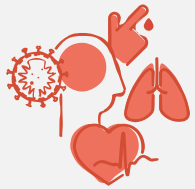






Mild and moderate disease

While characterized as mild and moderate in terms of body surface area, individual lesions can be severe



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

~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]

Evelo's initial commercial focus is on mild to moderate population with potential to address over 3.5 million[2] of these individuals in U.S. 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

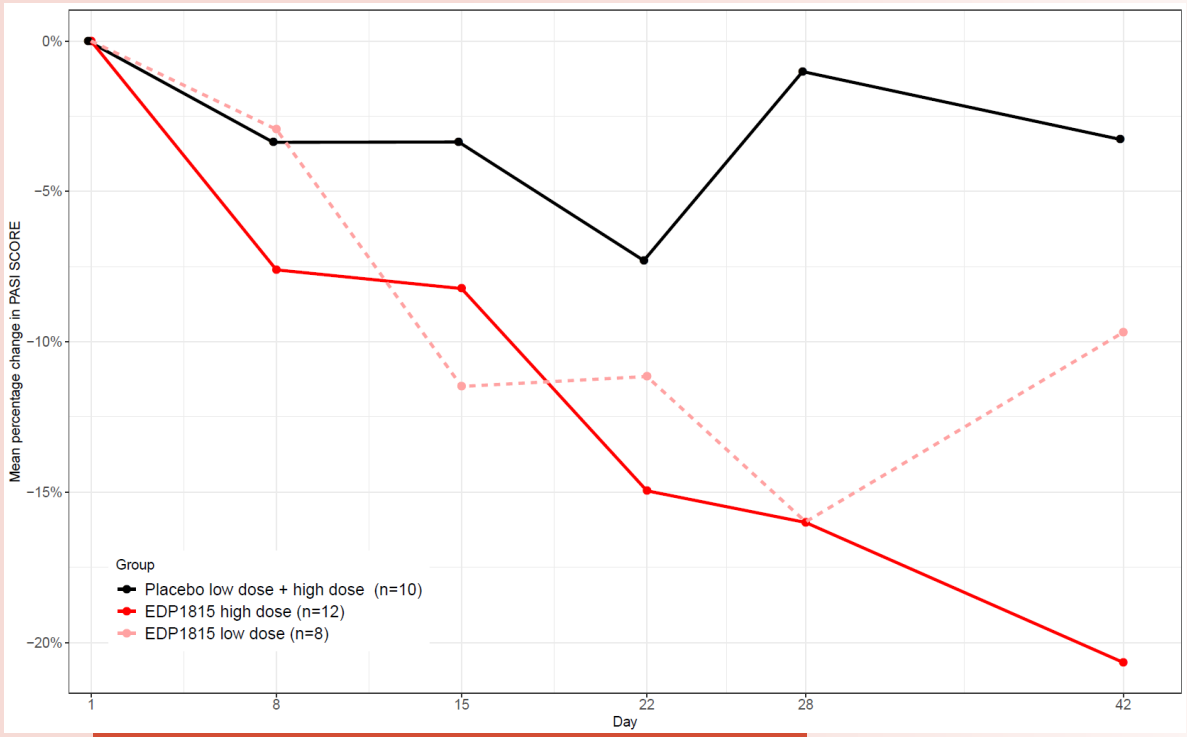
[2] 2018 company-sponsored market research; EU5 consisting of France, Germany, Italy, Spain and the UK

Positive Phase 1b Clinical Data with EDP1815 in Mild and Moderate Psoriasis

Double-blind, placebo-controlled Phase 1b trial with low (n=12) and high dose (n=18) cohorts, 28 days of oral administration of EDP1815 in a capsule, follow-up at day 42:

- 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

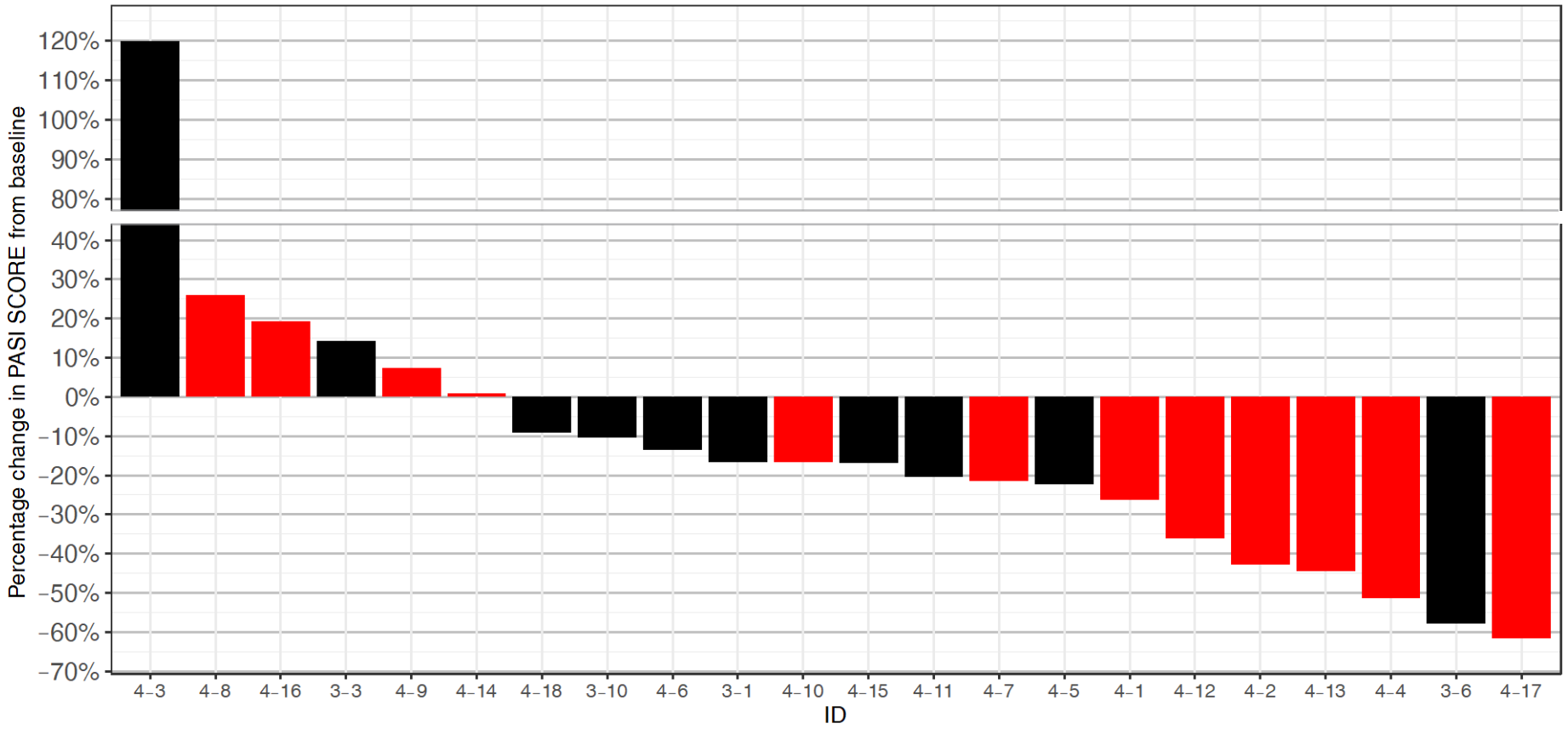
Clinically meaningful reduction in PASI at high dose
21% at day 42 versus placebo of 3%



Dosing period

After 4 Weeks, 6 of 12 Patients Have PASI Reduction of 25% or Greater

Potential ongoing effects and improvements post dosing period



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

6/12 treated patients have PASI reduction of **>25%**

1/10 placebo has **>25%** PASI reduction

The continuing downward trend in PASI suggests that the maximum effect has not yet been reached after 28 days' treatment

16 weeks treatment may increase the range of response, consistent with many psoriasis treatments

EDP1815 Phase 2 Dose-Ranging Trial in Mild and Moderate Psoriasis

Trial Summary

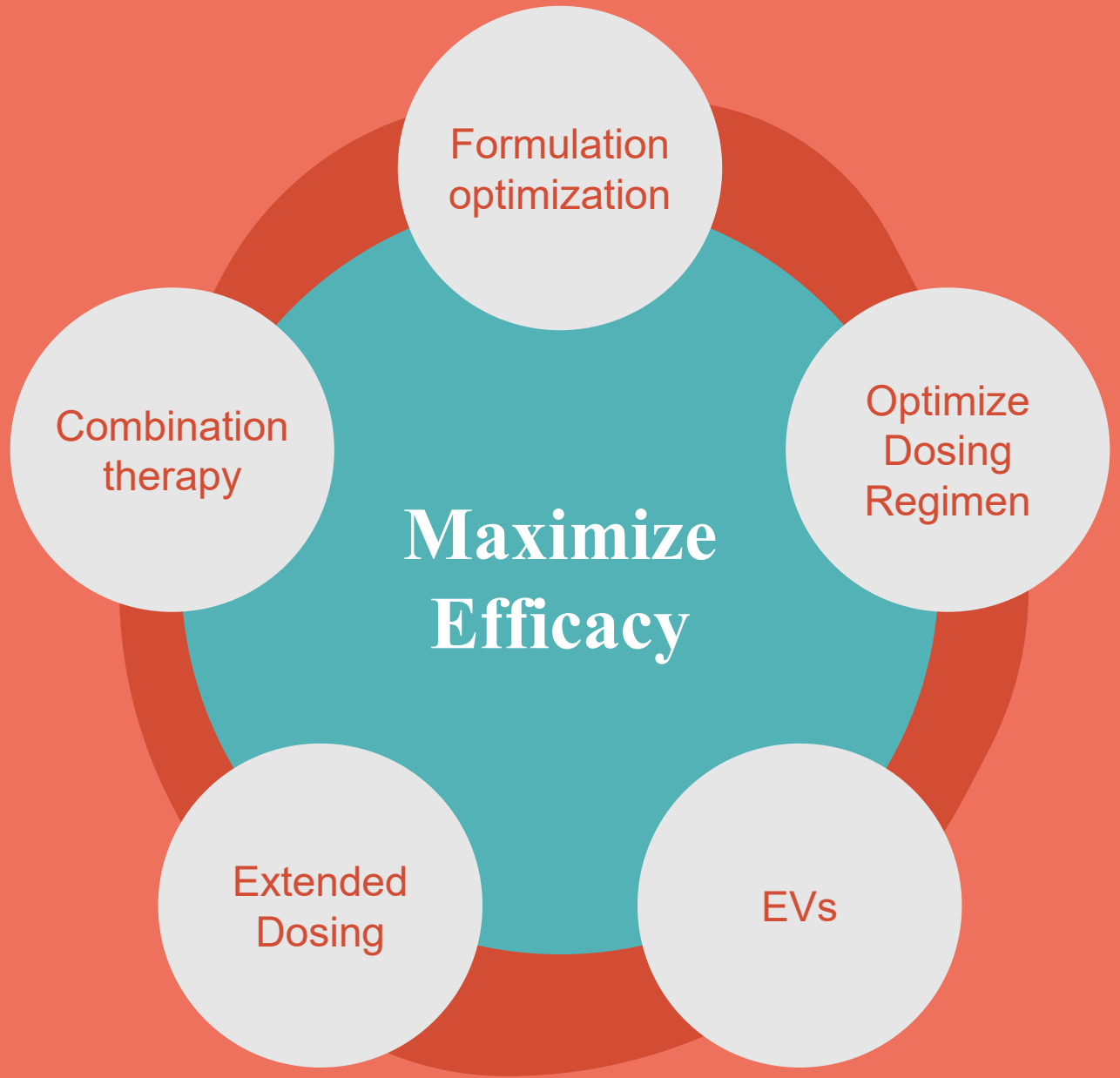
- 16 week, double-blind, placebo-controlled, dose-ranging trial of ~225 patients
- Individuals with mild and moderate disease
- Evaluate three doses of enteric capsule formulation of EDP1815 vs. placebo
  - Randomized 2:1 (active:placebo) in each arm
- Follow-up at week 20

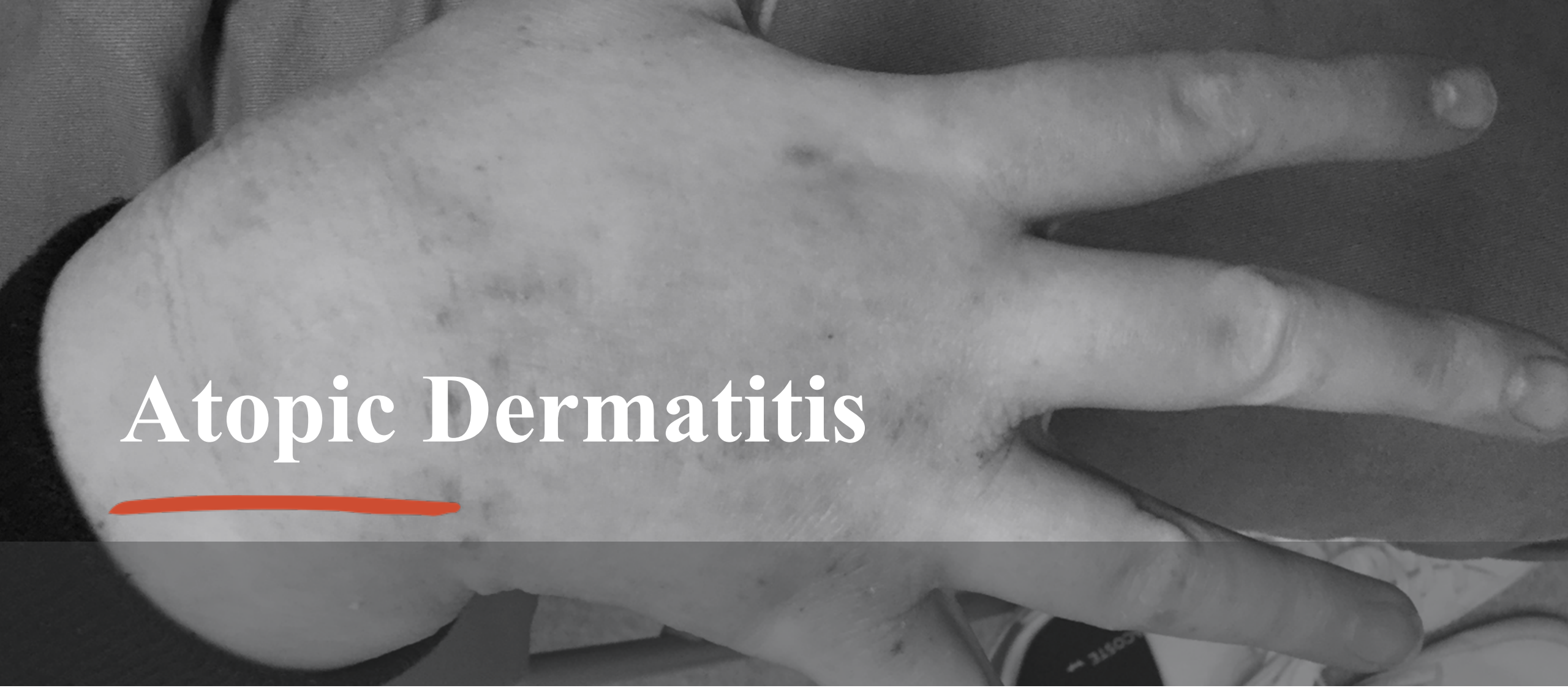
Data expected 3Q 2021

Summary of Endpoints

- Primary endpoint: mean reduction in PASI score at 16 weeks
- Key secondary endpoint: PASI-50
- Other secondary endpoints:
  - PASI-75
  - PGA (Physician's Global Assessment)
  - BSA (Body Surface Area)
  - PGA x BSA
- Key patient-reported secondary endpoints:
  - DLQI (Dermatology Life Quality Index)
    - Includes itch and sleep

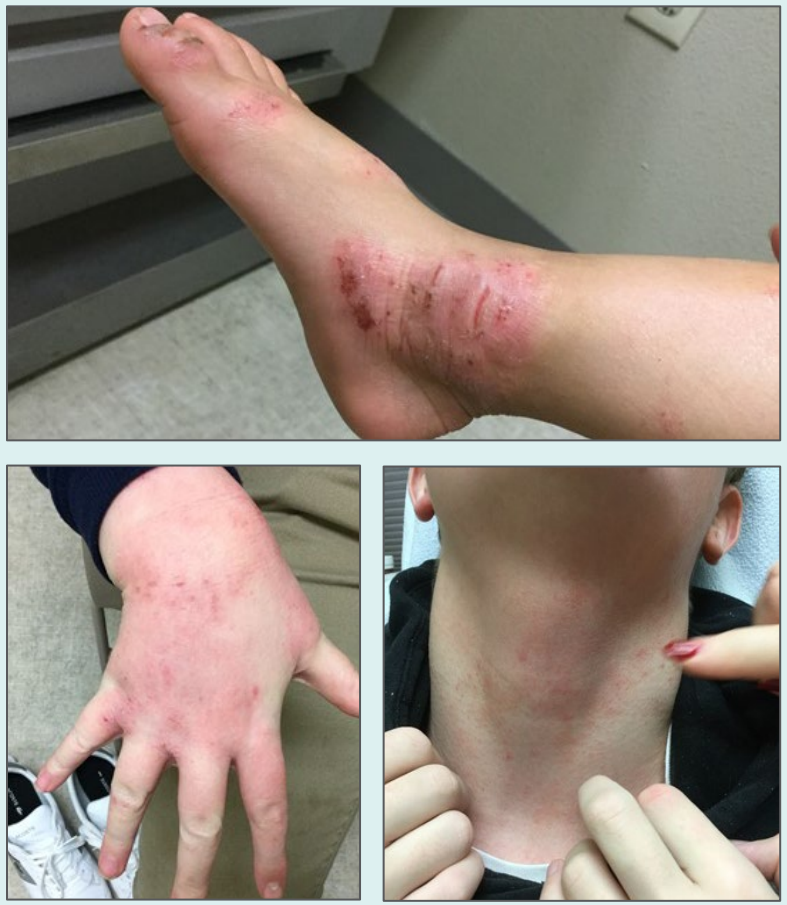
Levers to Enhance Efficacy





Atopic Dermatitis

Mild and Moderate Atopic Dermatitis: Significant Disease Burden



Patients in these pictures have mild and 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.

Hundreds of Millions of Cases of Atopic Dermatitis Worldwide with Few Acceptable Treatment Options

- 15-20% of children and 3-6% of adults worldwide[1] are estimated to suffer from atopic dermatitis
- Of all diagnosed atopic dermatitis patients in the U.S., 43% are not taking any medications for their disease[2]

Oral medications

Treatments include azathioprine, cyclosporine, methotrexate*, oral steroids
44% are dissatisfied with treatment
77% experience side effects
*Not approved for AD in US

Topical medications

Prescription topical steroids
52% are dissatisfied with treatment
60% experience side effects

Topical calcineurin inhibitors
63% are dissatisfied with treatment
40% experience side effects

Phototherapy

60% are dissatisfied with treatment
33% experience side effects

"Lack of safe and effective treatments"

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

[1] Datamonitor Healthcare; DaVeiga, 2012; GBD, 2018; Nutten, 2015, National Eczema Foundation
[2] Evaluate Pharma, accessed Jul 2018
Source: Atopic Dermatitis: Survey of 192 patients from the National Eczema Association, 2016 https://nationaleczema.org/in-your-words-survey-series

EDP1815 Phase 1b in Atopic Dermatitis

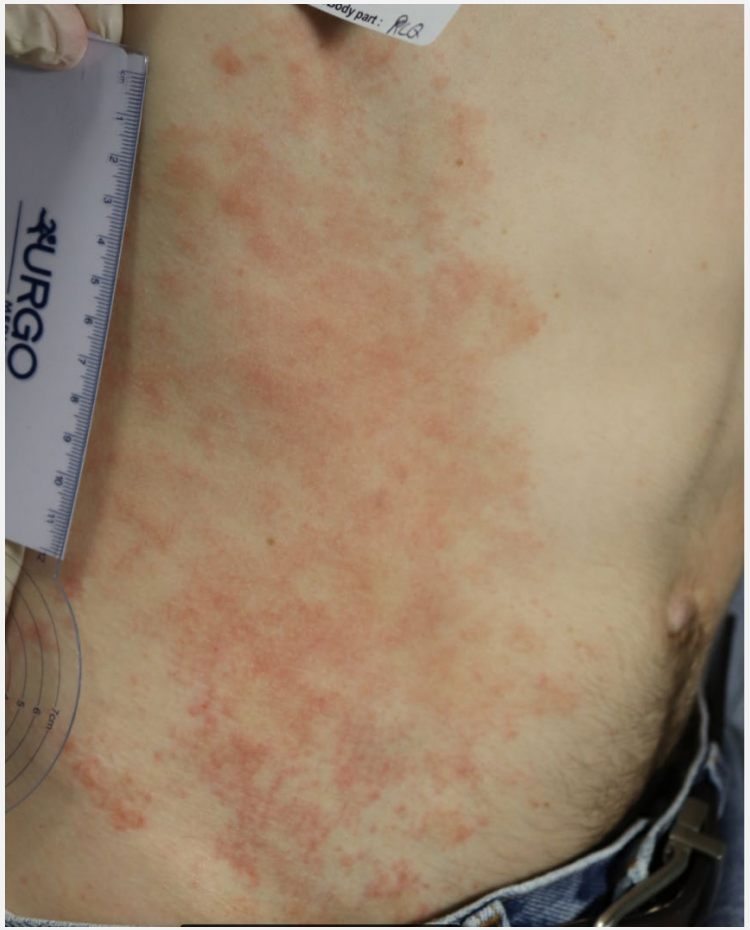
Trial Summary

- Double-blind, placebo-controlled trial of 24 patients
- Mild and moderate atopic dermatitis, randomized 2:1 (active:placebo)
- 56 days of oral administration of EDP1815 in a capsule, follow-up at day 70
- Once daily
- No active topical treatments, no requirement to use emollients

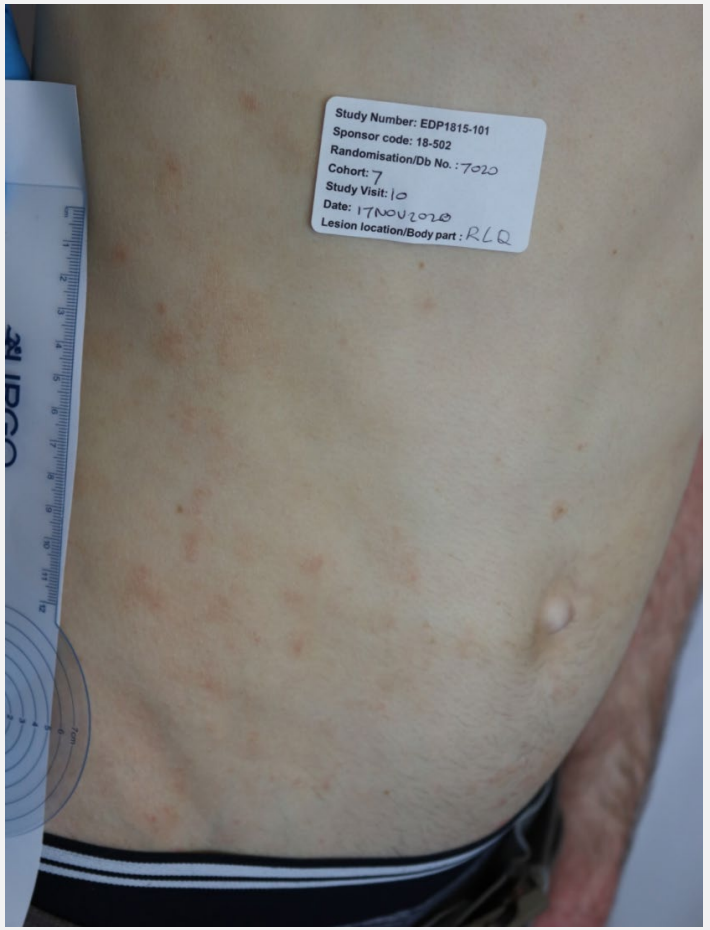
Summary of Endpoints

- Primary endpoint: Safety and tolerability
  - EDP1815 was well tolerated with no treatment related adverse events of moderate or severe intensity, and no serious adverse events
- Key physician-reported secondary endpoints:
  - EASI (Eczema Area and Severity Index)
  - IGA*BSA (Investigator Global Assessment x Body Surface Area)
  - SCORAD (SCORing Atopic Dermatitis)
- Key patient-reported secondary endpoints:
  - DLQI (Dermatology Life Quality Index)
  - POEM (Patient-Oriented Eczema Measure)
  - Pruritus-NRS (Numerical Rating Scale)

Efficacy of EDP1815 in Atopic Dermatitis



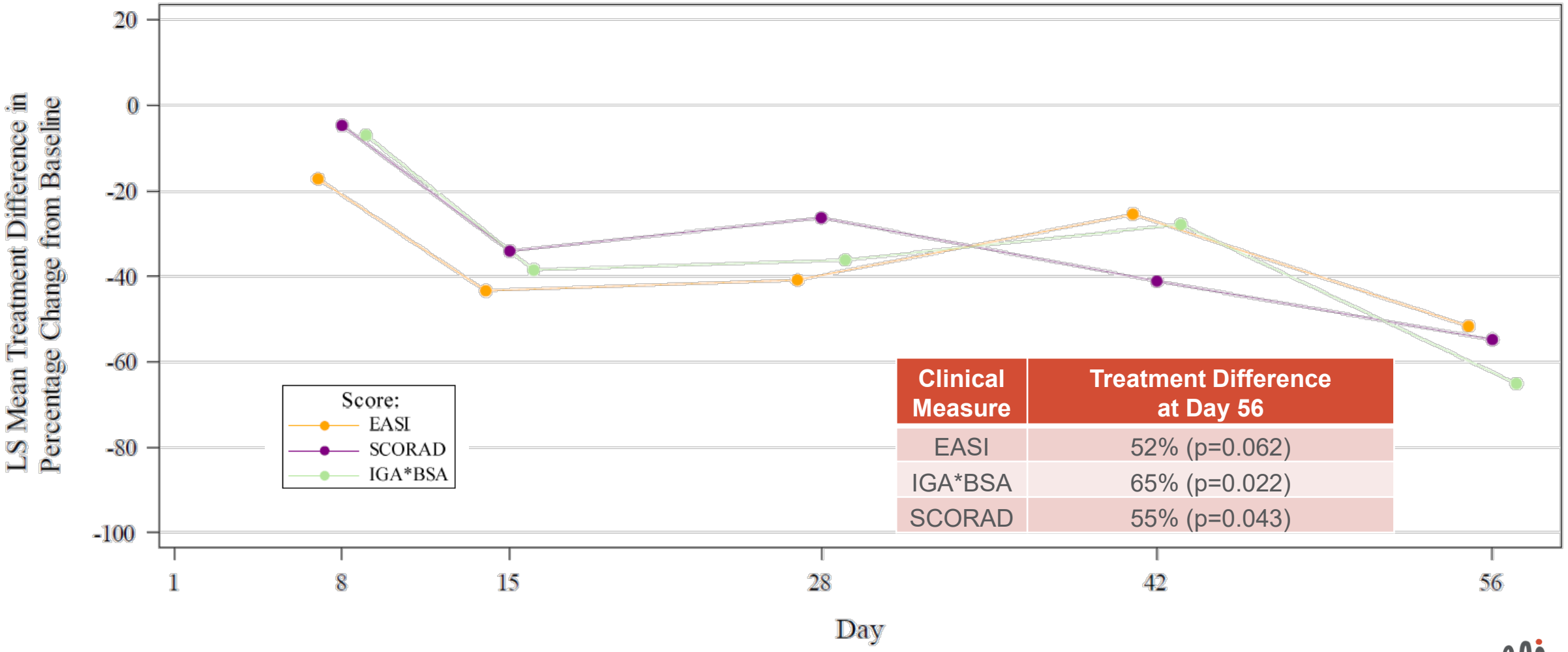
Patient on once daily EDP1815 and no topical treatments: before and after (patient achieved EASI50 score)



Before, day 0

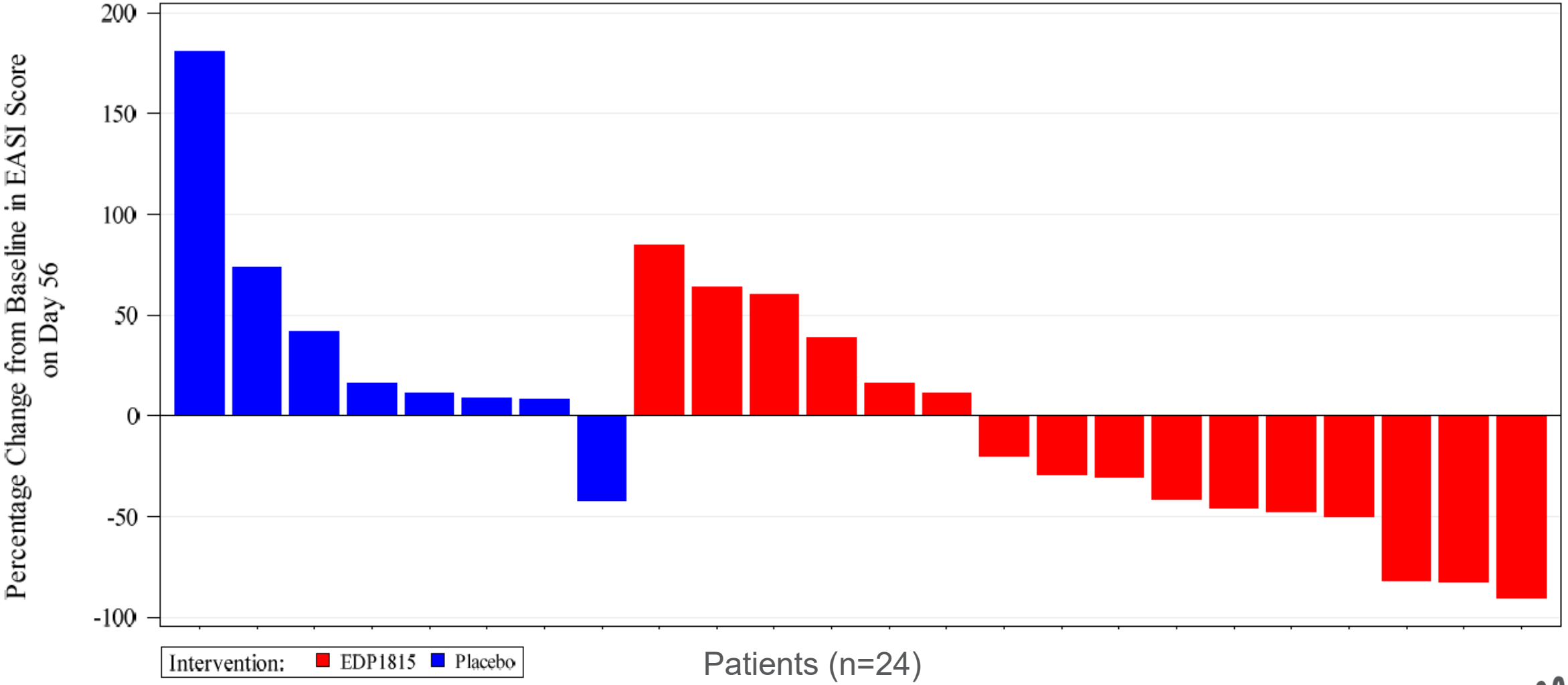
After, day 56

Improvements in EASI, IGA*BSA, and SCORAD with EDP1815 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



Clinically Meaningful Improvements in Patient-Reported Outcomes Including Itch and Sleep

For EDP1815-treated patients at day 56:

- DLQI (Dermatology Life Quality Index)
  mean improvement exceeded the clinically validated threshold[1]
- POEM (Patient-Oriented Eczema Measure)
  mean improvement exceeded the clinically validated threshold[2]
- Improvement in itch across all measured scores
  (including Pruritus-NRS and within SCORAD)
- Improvement in sleep across all measured scores
  (including POEM and within SCORAD)

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.

EDP1815 Phase 2 in Atopic Dermatitis

Trial Summary

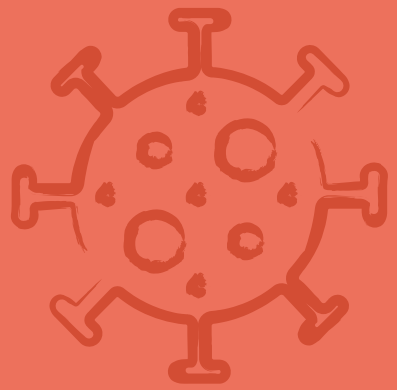
- 12 week, double-blind, placebo-controlled, multiple cohort trial in patients with mild, moderate, and severe atopic dermatitis
- ~198 patients randomized to EDP1815; ~66 patients randomized to placebo.
  - Patients receive either 1 capsule once daily, 2 capsules once daily, or 1 capsule twice daily

Summary of Endpoints

- Primary endpoint: Mean difference between EDP1815 and placebo in the percentage change from baseline in Eczema Area and Severity Index (EASI) score at week 12
- Key physician-reported secondary endpoints:
  - IGA (Investigator Global Assessment)
  - BSA (Body Surface Area)
  - SCORAD (SCORing Atopic Dermatitis)
- Key patient-reported secondary endpoints:
  - DLQI (Dermatology Life Quality Index)
  - POEM (Patient-Oriented Eczema Measure)
  - Pruritus-NRS (Numerical Rating Scale)

COVID-19

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
  - Generally well tolerated with no treatment-related adverse events of moderate or severe intensity and no serious adverse events
- **Orally administered**, allowing for easy and flexible administration
- **Scalable manufacturing** for 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 COVID-19 Trial 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

*The investigators of the study are-expanding the trial to countries where COVID-19 remains prevalent, including Mexico and Brazil

Pipeline

Pipeline Provides Multiple Diversified Non-Correlated Opportunities

EDP1815: Th17 Effects

*Multiple readouts expected in **3Q 2021**; potential to expand into other Th17-mediated diseases*

Psoriasis

- Phase 2 and series of Phase 1b readouts in **3Q 2021**

Other Potential Indications

- Psoriatic arthritis, axial spondyloarthritis, rheumatoid arthritis, and ulcerative colitis
- Numerous others

EDP1815: Th1/Th2 Effects

*Start of Phase 2 in **3Q 2021**; potential to expand in other Th2-mediated diseases*

Atopic Dermatitis

- Phase 2 data expected **3Q 2022**

Other Potential Indications

- Asthma and allergy
- Neuroinflammation
- Numerous others

EDP1815: Integrated Effects

Two COVID-19 trials underway; potential to expand into other viral diseases

COVID-19

- Phase 2/3 TACTIC-E trial ongoing

Other Potential Indications

- Influenza
- Future strains of COVID-19
- Future viral infections

EDP1867: Th2 Effects

Strong preclinical activity in Th2-mediated diseases; initial program in atopic dermatitis

Atopic Dermatitis

- Phase 1b data readout in **4Q 2021**

Other Potential Indications

- Asthma and allergy
- Neuroinflammation
- Numerous others

Pipeline Provides Multiple Diversified Non-Correlated Opportunities

EDP2939: EV

Preclinical data suggests broad use across inflammation

Inflammation

- Phase 1 data anticipated in inflammatory indication(s) in **4Q 2022**

Broad use across all inflammatory diseases

EDP1908: EV

Preclinical data suggests broad use across oncology

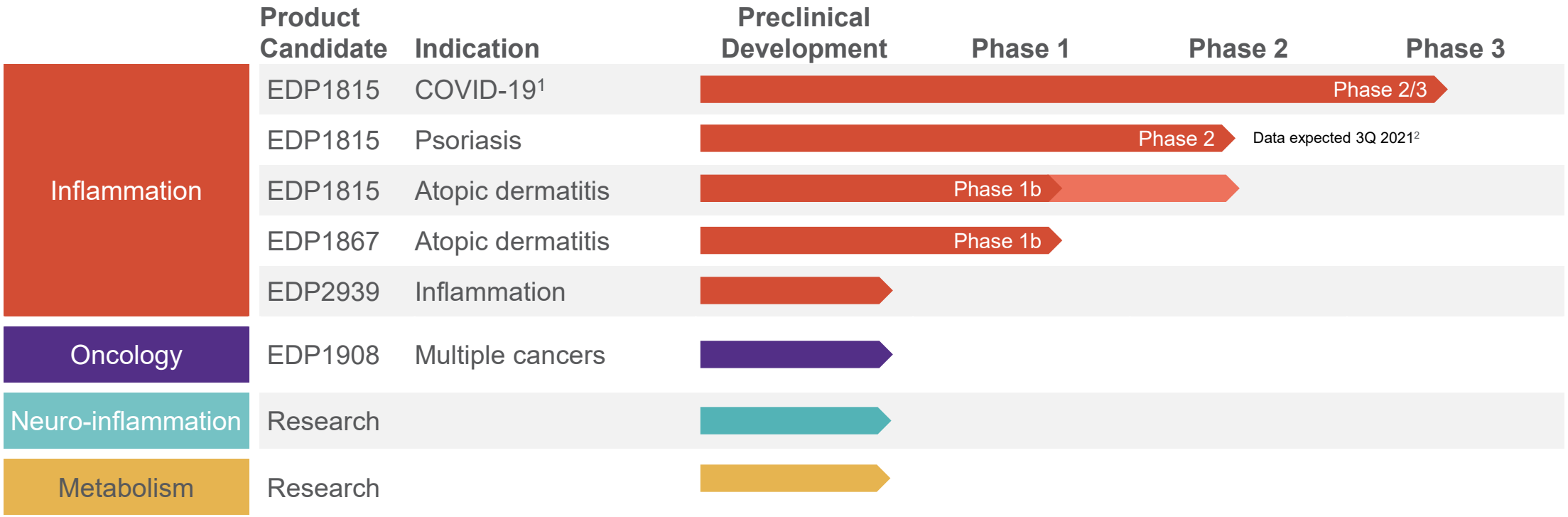
Oncology

- Initiation of clinical development in **2022**

Potential Indications

- Multiple indications in poorly treated solid tumors
- MSS colorectal carcinoma
- Triple-negative breast cancer
- Non-small cell lung cancer
- Numerous others

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] Phase 1b data on different formulations and concentrations also expected in 3Q 2021

Appendix

Corporate Information

~120 employees

Cash and cash equivalents of more than $120 million*

~$40 million ATM program with substantial capacity remaining

Long-term debt outstanding of $45 million

*As of June 30, 2021