

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

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.

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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

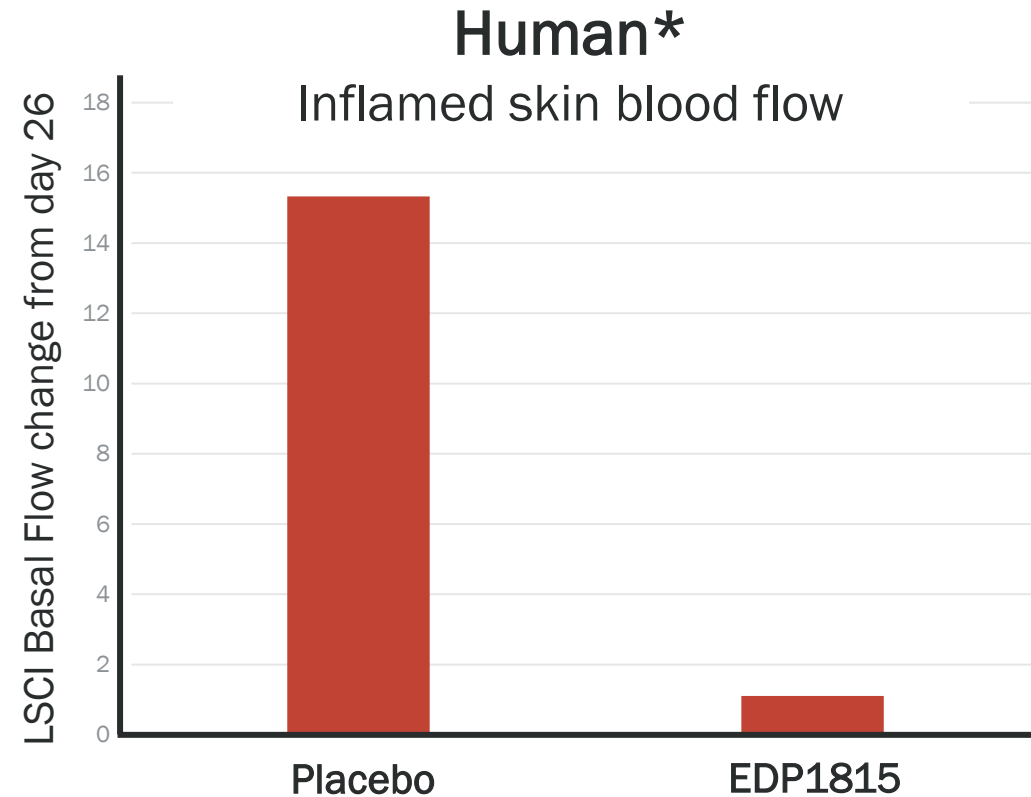
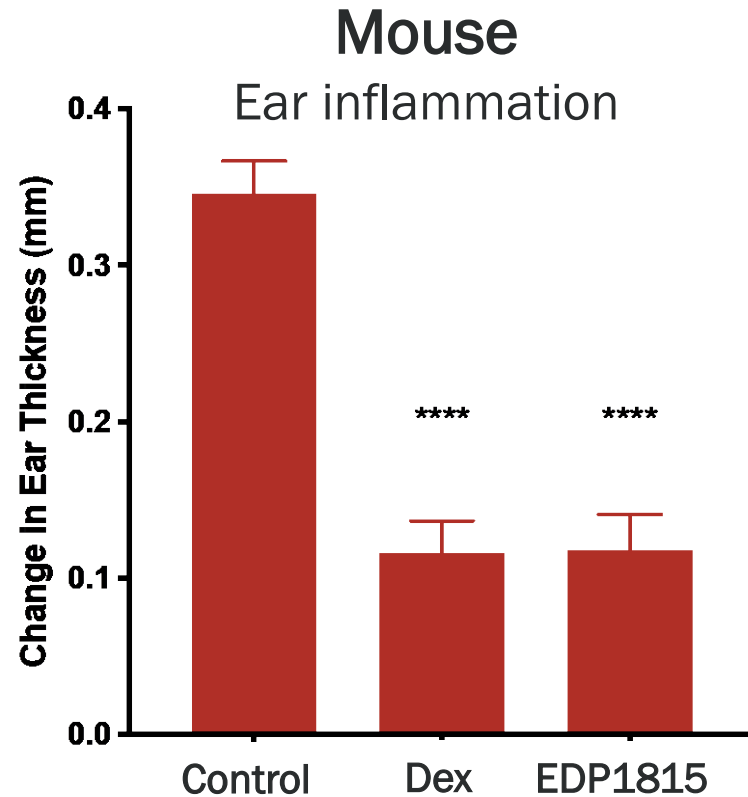
Phase 1b Psoriasis

- 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

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 patients³
- Standard of care is topical treatments with low adherence due to inconvenient/burdensome application

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

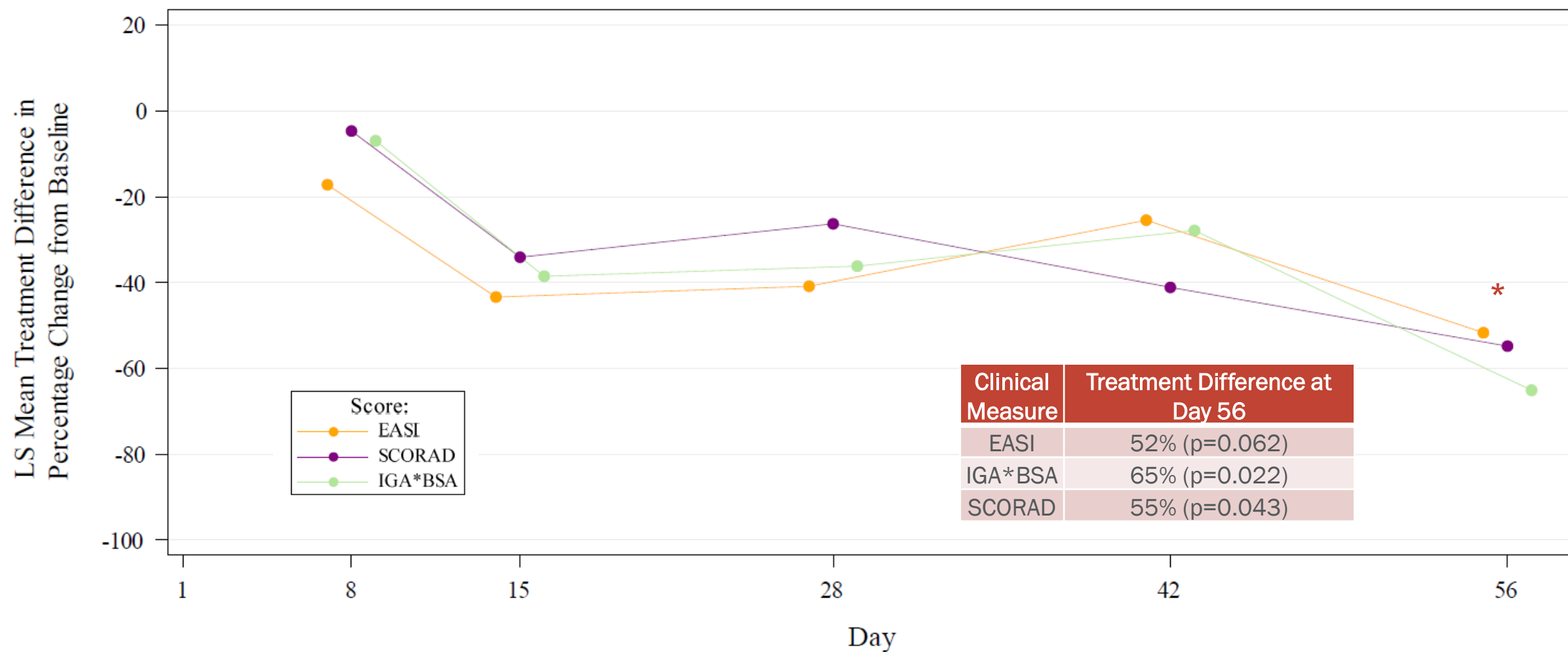
*Baseline Disease Severity

Inclusion criteria:

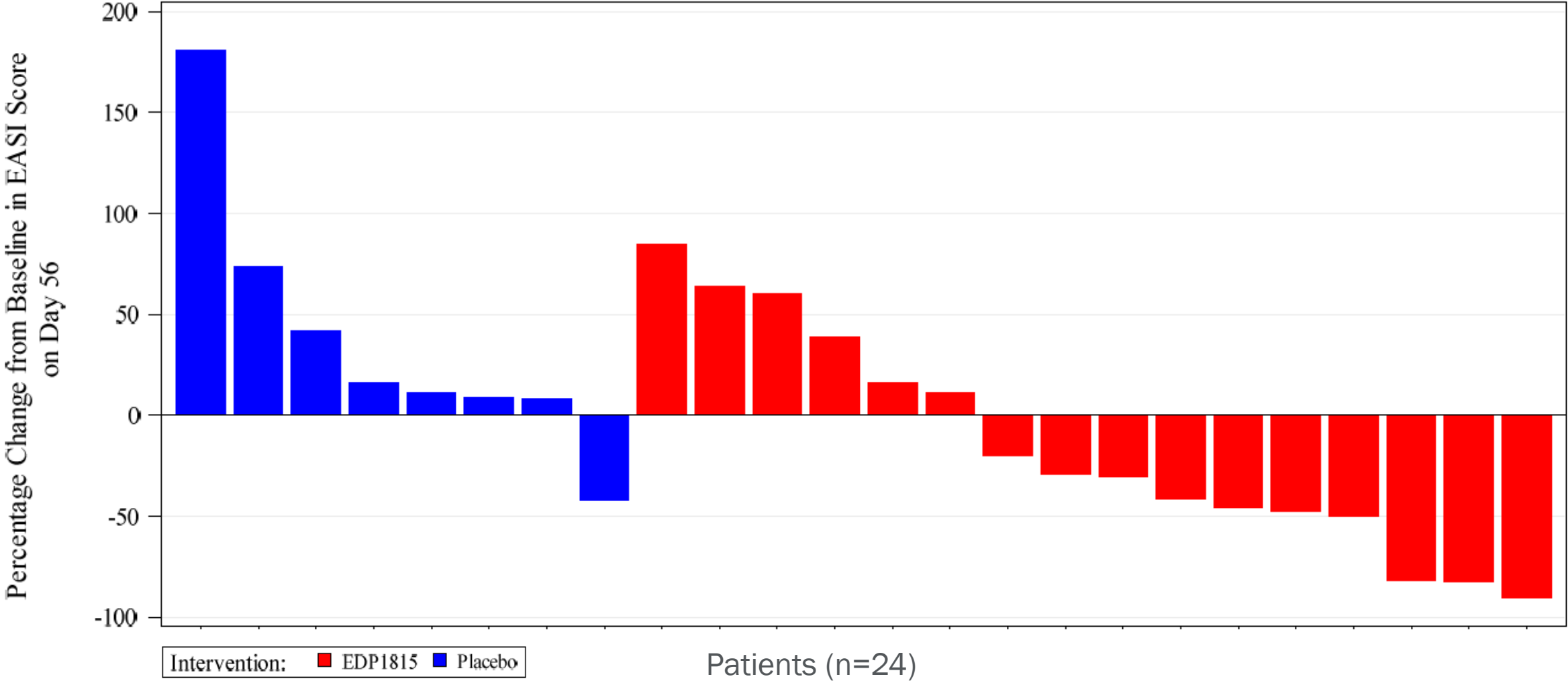
- IGA 2 or 3
- BSA 5-40%

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

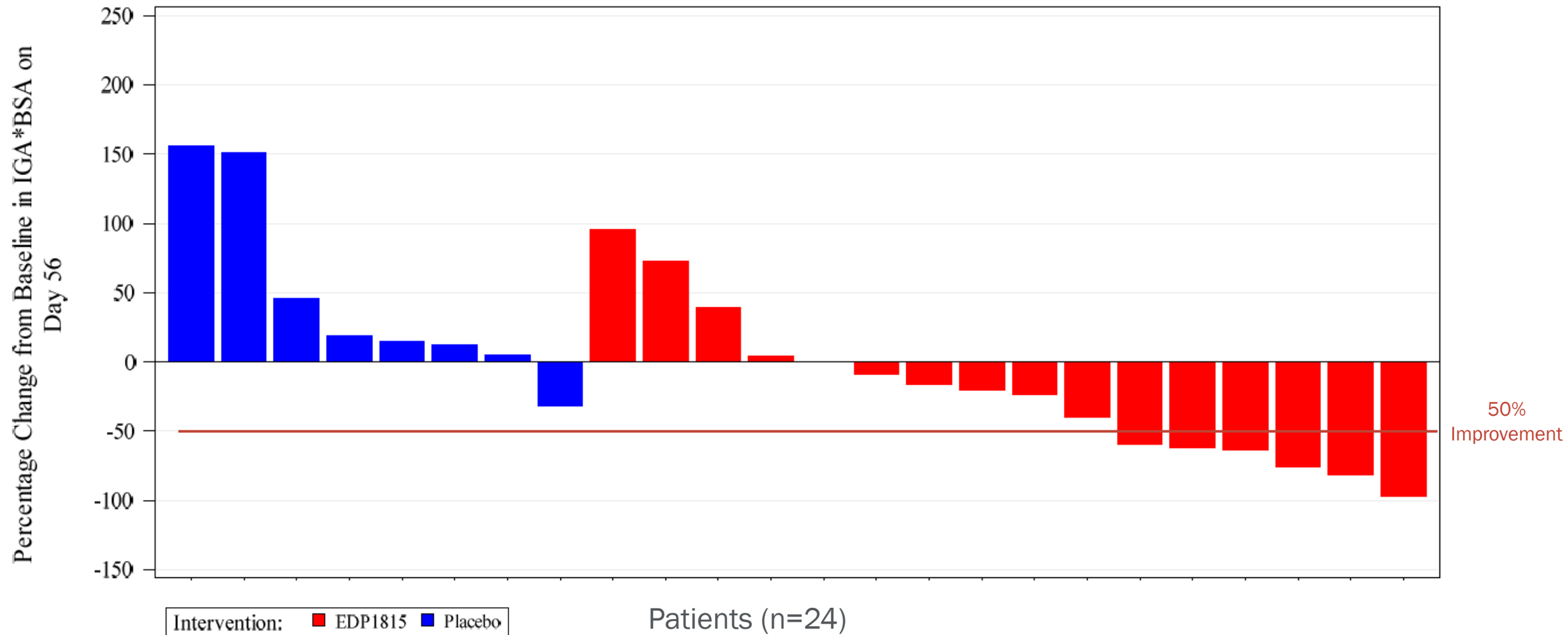
Improvements in EASI, IGA*BSA, and SCORAD at day 56



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	Placebo Mean change, day 56
DLQI (Dermatology Life Quality Index)	-3.6*	-0.3
POEM (Patient-Oriented Eczema Measure)	-4.1*	+1.6

*Results 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

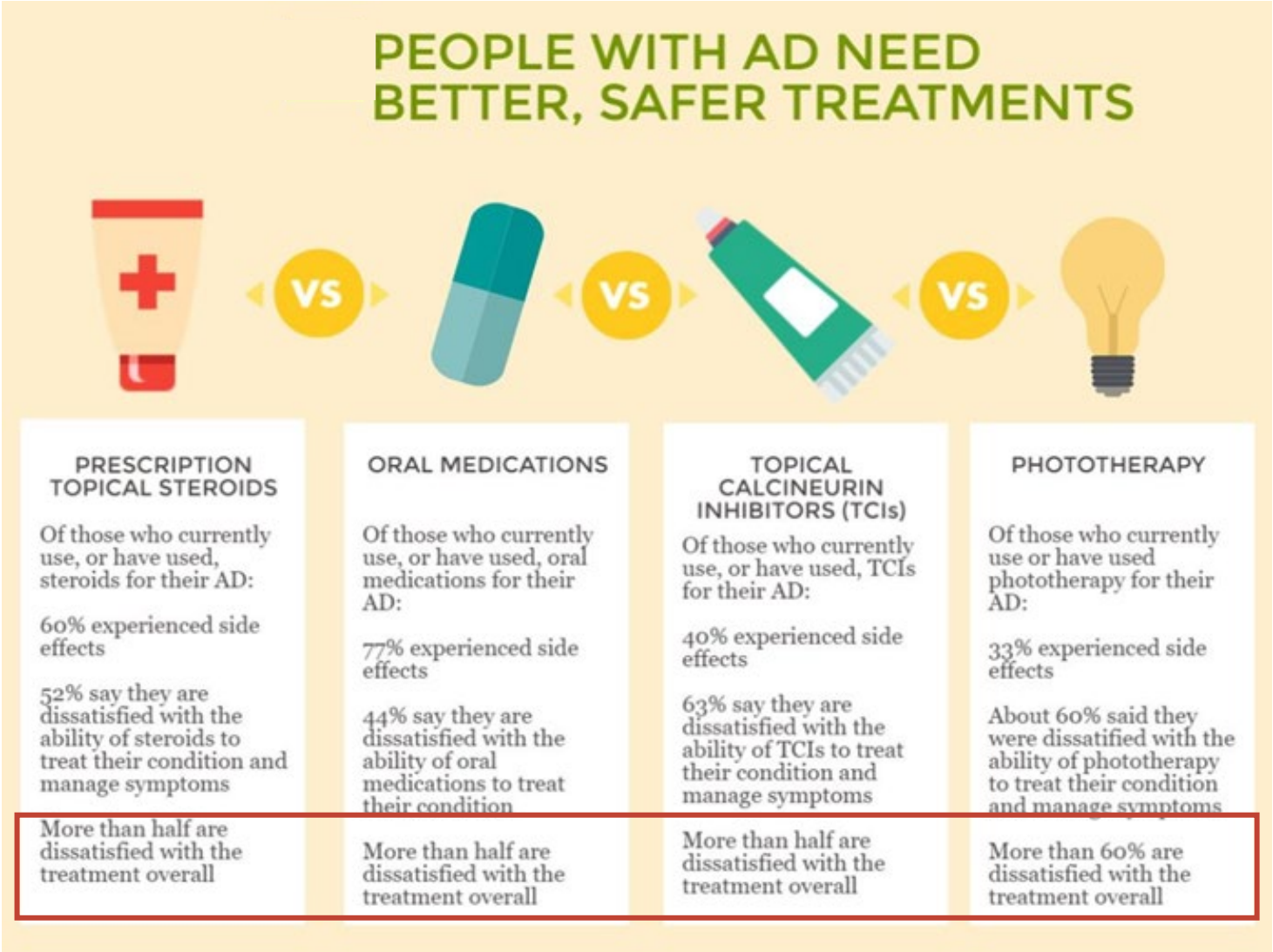
Patient on once daily oral EDP1815 and no topical treatments: before and after (patient achieved EASI50 score)



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”

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 therapies¹
- 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 million² of these individuals in US and EU5 and then expand globally

¹Armstrong 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

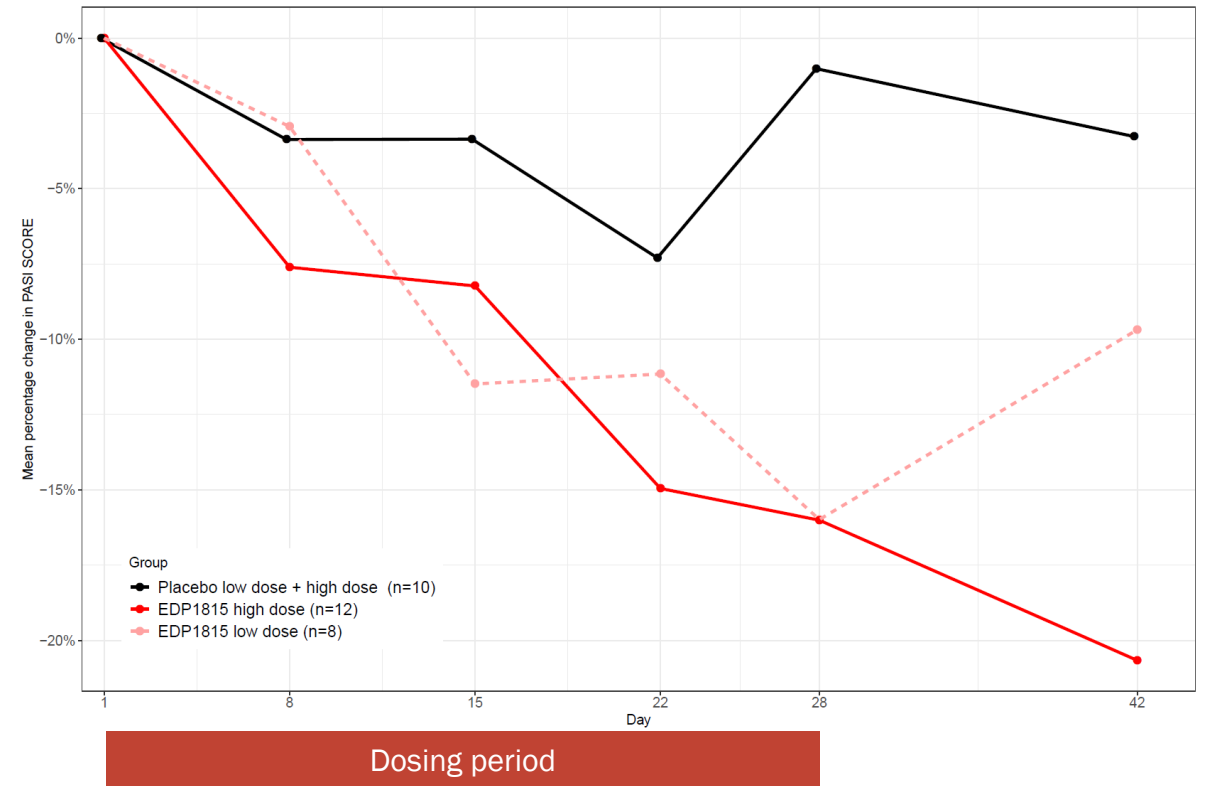
²2018 company-sponsored market research; EU5 consisting of France, Germany, Italy, Spain and the UK

Positive clinical data with EDP1815 in mild to moderate psoriasis

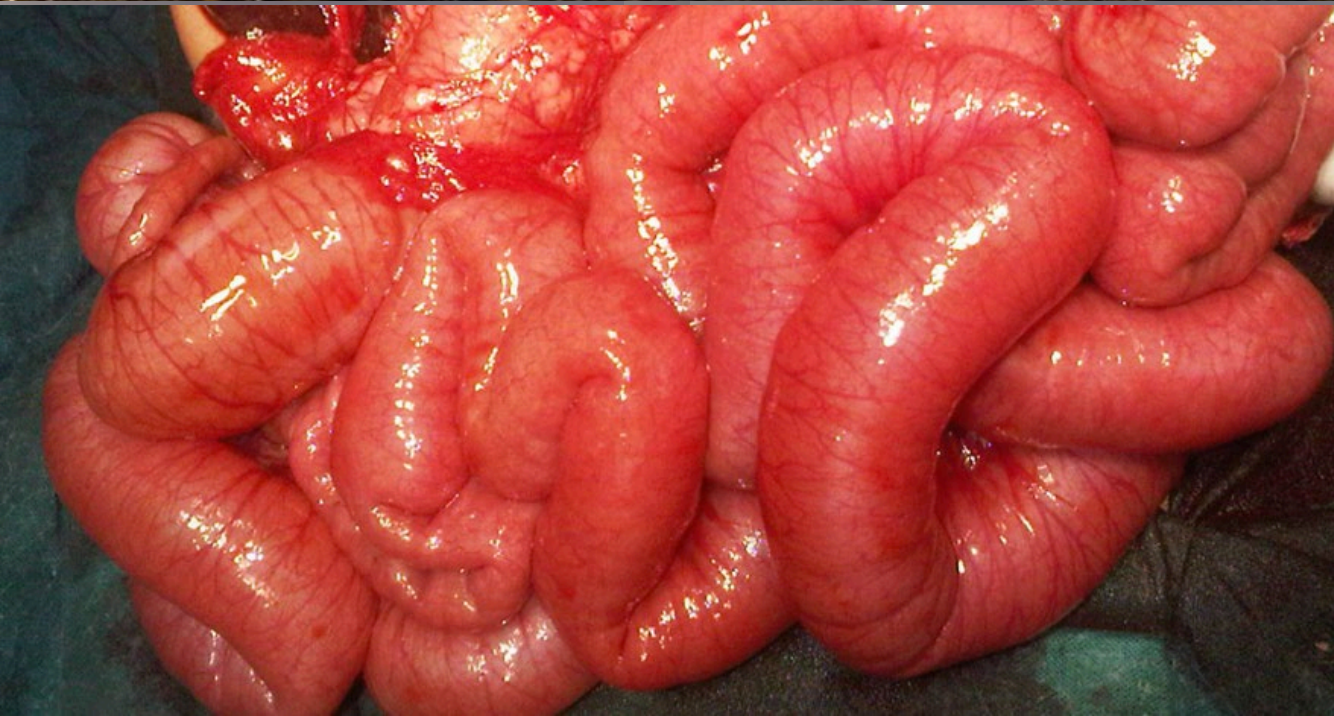
Phase 1b study with low (n=12) and high dose (n=18) cohorts:

- 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

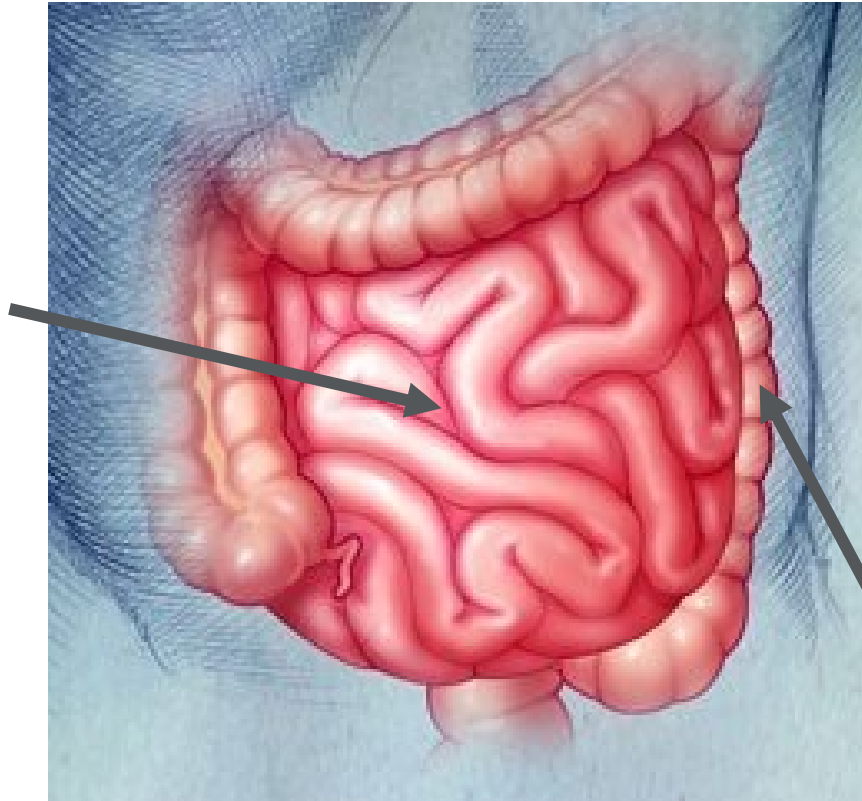


Cells in the small intestine are therapeutic targets for SINTAX medicines

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

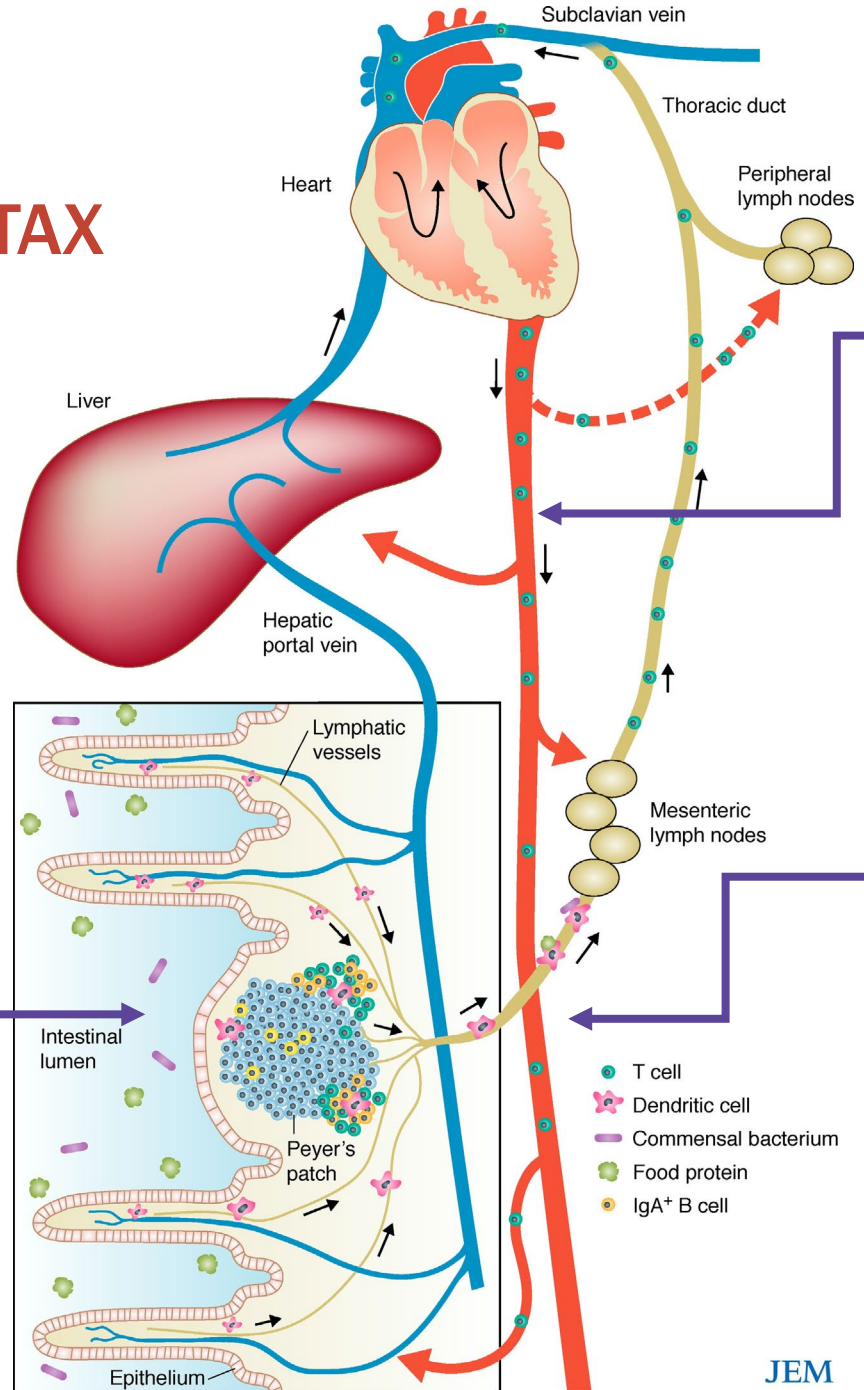
Three-step process for immunomodulation by SINTAX medicines

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

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



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

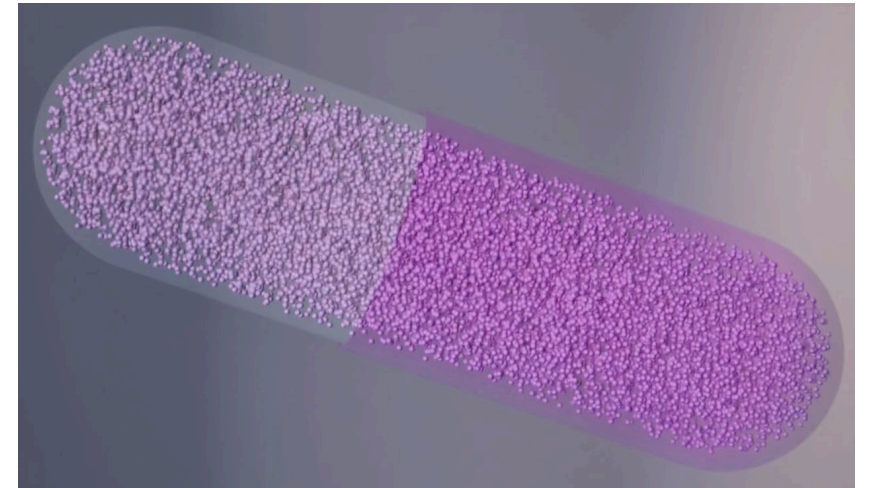
2

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

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

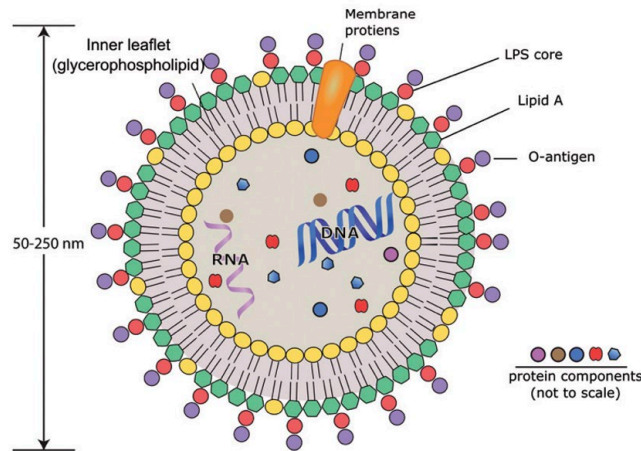


The next wave of SINTAX medicines: orally delivered bacterial extracellular vesicles (EVs)

- 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

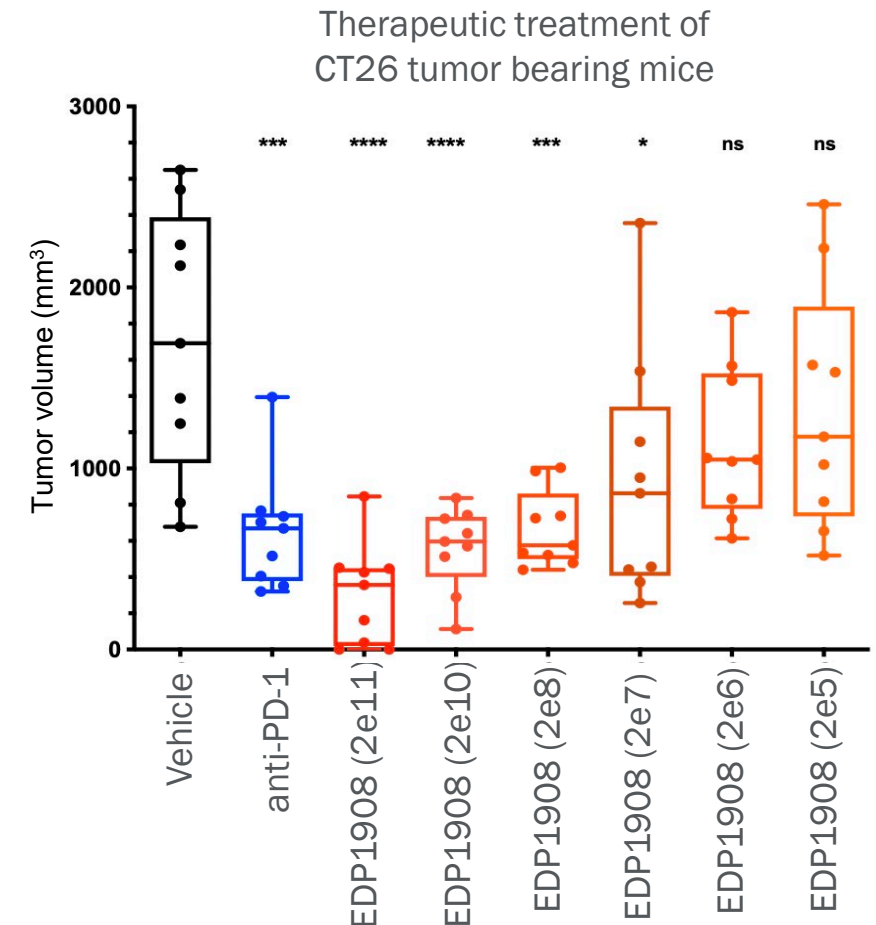
EVs represent a potential new class of broad immune activating, orally delivered, safe therapies

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



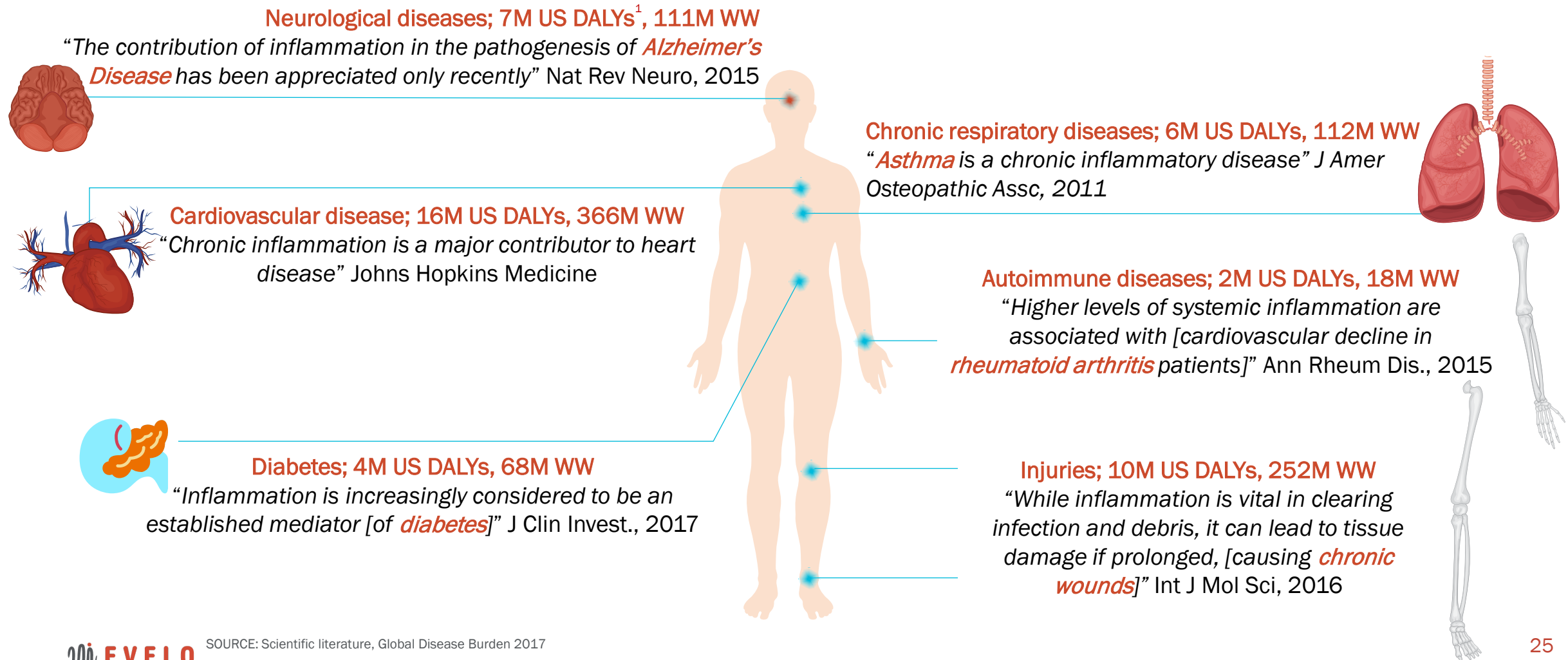
Anand et al 2017

- 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
 - ~1/1000th volume of microbes enabling improved target engagement
 - Non-viable

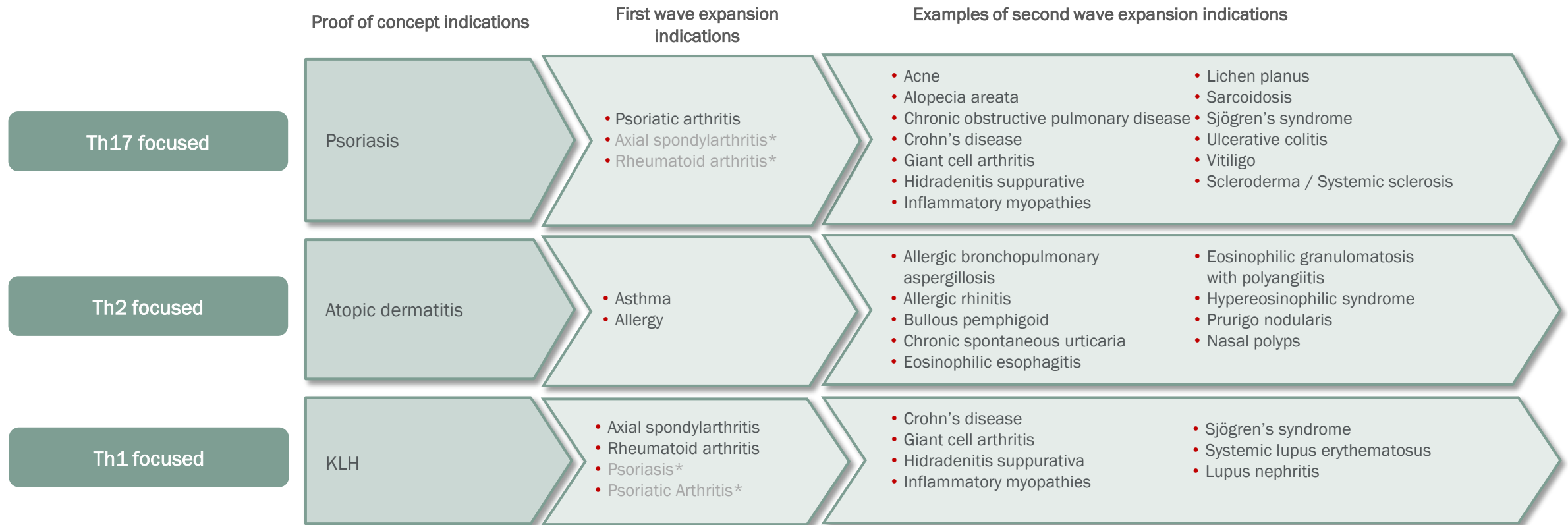


The Opportunity

Chronic inflammation is the driver of our most burdensome diseases



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

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 worldwide¹



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

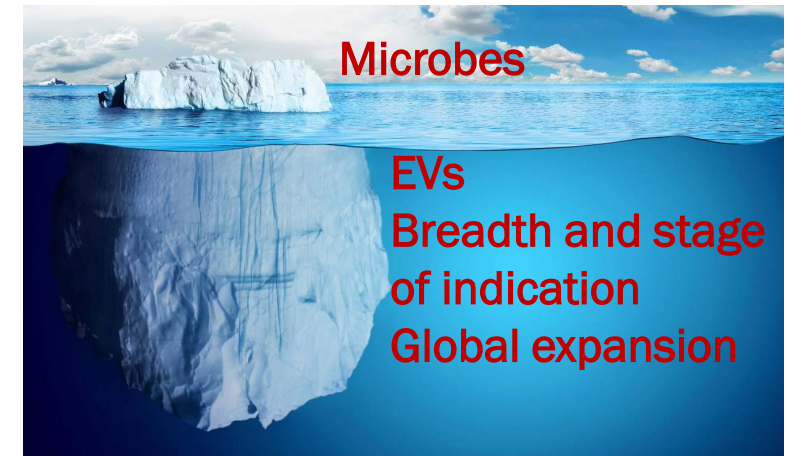
The strategy breaks down into 5 themes which work together to meet the overall goal:

Nature of the drugs

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

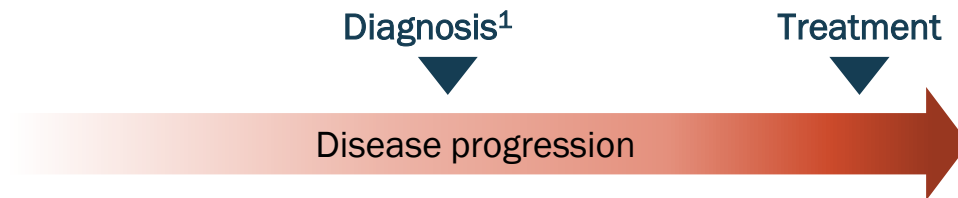
Uses of the drugs

- Disease application
- Combinations

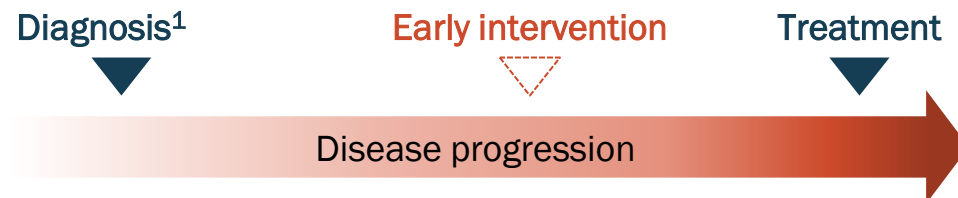


Future of medicine: treating early and enabling maintenance of health

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

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

Broad clinical and preclinical pipeline with multiple upcoming readouts

	Product Candidate	Indication	Preclinical Development	Phase 1	Phase 2	Phase 3
Inflammation	EDP1815	COVID-19 ¹	Phase 2/3			
	EDP1815	COVID-19	Phase 2			
	EDP1815	Psoriasis ³	Phase 2			Interim data expected 2Q 2021
	EDP1815	Atopic dermatitis ³	Phase 1b			Anticipate moving into Phase 2 in 3Q 2021
	EDP1815	Psoriasis formulation ²	Phase 1b			
	EDP1867	Atopic dermatitis				
	EDP2939	Inflammation				
Oncology	EDP1908	Multiple cancers				
Neuro-inflammation	EDP1632					
Metabolism	Research					

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.

Pipeline is rich in anticipated near-term clinical catalysts

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

*Progression to Phase 3 dependent on positive Phase 2 data

Corporate information

- ~100 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 10Q filing on 9/30/20; does not reflect net proceeds from subsequent equity offerings