EVELO BIOSCIENCES

March 2020

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 relating to our development plans and new formulations, the promise and potential impact of any of our monoclonal microbials or preclinical or clinical trial data, the timing of and plans to initiate clinical studies of EDP1815, EDP1867, and EDP1503, the timing and results of any clinical studies or readouts, and the sufficiency of cash to fund operations.

These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: we have incurred significant losses, are not currently profitable and may never become profitable; our need for additional funding; our 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 Annual Report on Form 10-K for the year ended December 31, 2019 and our other reports filed with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management's estimates as of the date of this presentation. While we may elect to update such forward-looking statements at some point in the future, except as required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.

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Evelo is targeting SINTAX™, the small intestinal axis, to develop oral biologics with favorable safety and efficacy profiles

Broad potential for treating millions of people at all stages of disease

2019 accomplishments: Validated platform, advanced potential blockbuster lead candidate, continued pipeline progression

- Validated Platform
  - Oral biologics acting on SINTAX can drive therapeutic activity throughout the body without systemic exposure
  - Clinical and preclinical data support broad platform potential
- EDP1815 - Potential blockbuster lead candidate
  - Positioned ahead of antibody-based biologics and later stage therapies; potential to serve millions of patients
  - Interim Phase 1b clinical data shows attractive profile in psoriasis and broad potential in treating inflammatory disease
  - Regulatory feedback supports rapid and efficient Phase 2 trial potentially resulting in shorter development timeline to registration
- Clinical and preclinical pipeline continues to advance
  - Multiple clinical candidates
  - Multiple therapeutic areas
  - Multiple forms
  - Multiple formulations

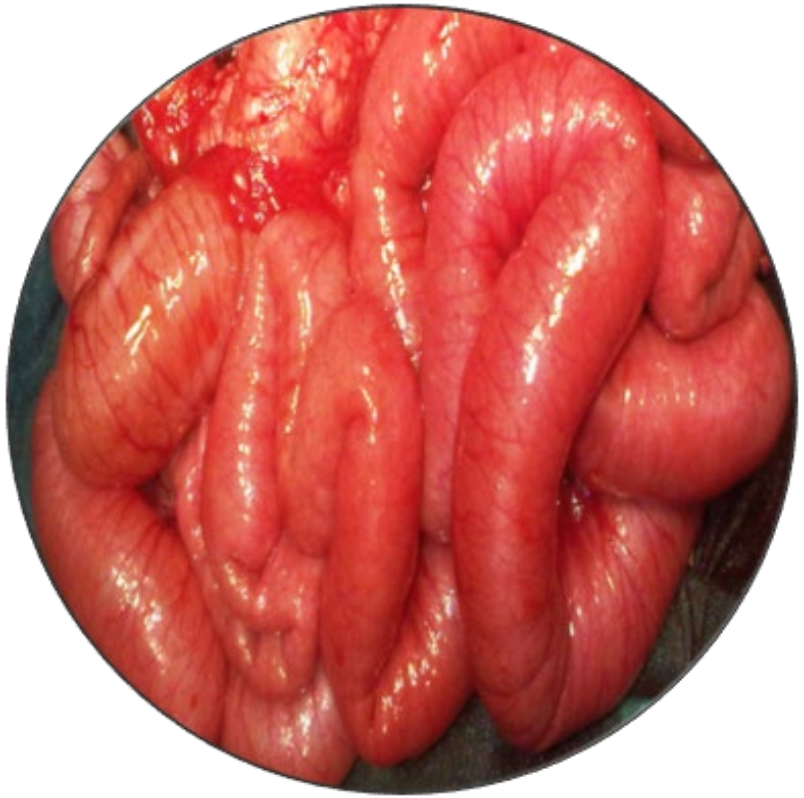
2020 clinical priorities and expected milestones

EDP1815 *Psoriasis*	• Data from Phase 1b trial with new formulation • Initiate Phase 2 trial • Interim data from Phase 2 trial	2Q 2020 2Q 2020 Late 2020
EDP1815 *Atopic Dermatitis*	• Data from Phase 1b trial with new formulation	2Q 2020
EDP1867 *Asthma*	• Initiate Phase 1b trial	2H 2020
EDP1503 *Oncology*	• Additional clinical data from Phase 1/2 trial in MSS-CRC, TNBC, anti-PD-1 relapsed responders	1H 2020

Continue to explore platform breadth, advancing preclinical programs and exploring form and formulation

The Small Intestinal Axis – SINTAX

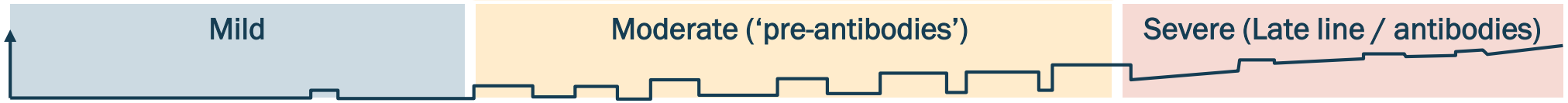
Druggable connections between cells in the small intestine and the rest of the body



- Cells in the small intestine are therapeutic targets; they play a central role in governing physiology throughout the body
- Specialized cells sense signals in the lumen to modulate physiology throughout the body
- Gut surgical procedures provide clinical evidence for the systemic impact of the small intestine
- Therapeutic potential to address immune, metabolic, and neurological disorders

Therapies targeting SINTAX open up mid-line therapy and treatment across all stages of disease

Requirement	Potential profile of therapies targeting SINTAX
Safe	Safe and well tolerated
Efficacious	Efficacious
Convenient	Encapsulated for oral delivery
Affordable	Broad patient access



Evelo's strategy

- Create new market as mid-line therapy and defer use of biologics / specialty drugs
- Serve individuals across all stages of diseases globally in the long term

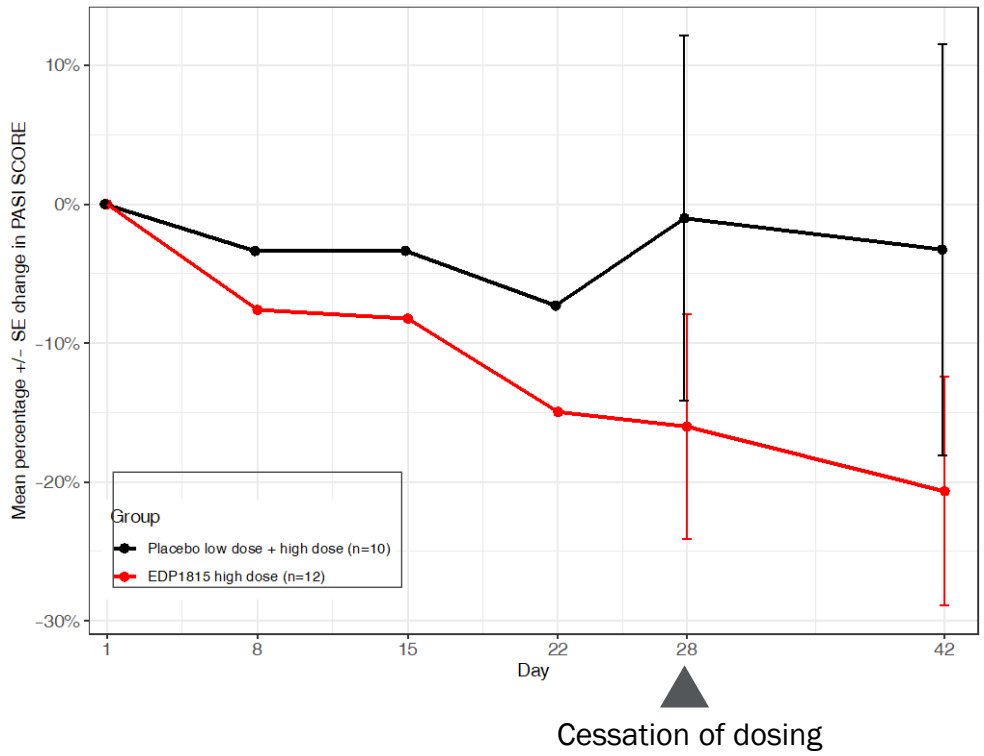
Lead immunology candidate, EDP1815, has achieved POC in mild to moderate psoriasis in two separate cohorts

- Well tolerated with no overall difference in tolerability reported from placebo over 28 days of daily oral administration and at day 42

- Positive clinical responses:
  - Reduction in mean PASI scores vs. placebo
  - Reduction in Lesion Severity Score in-line with PASI

- Durable response observed in high dose at day 42 - two weeks after cessation of dosing

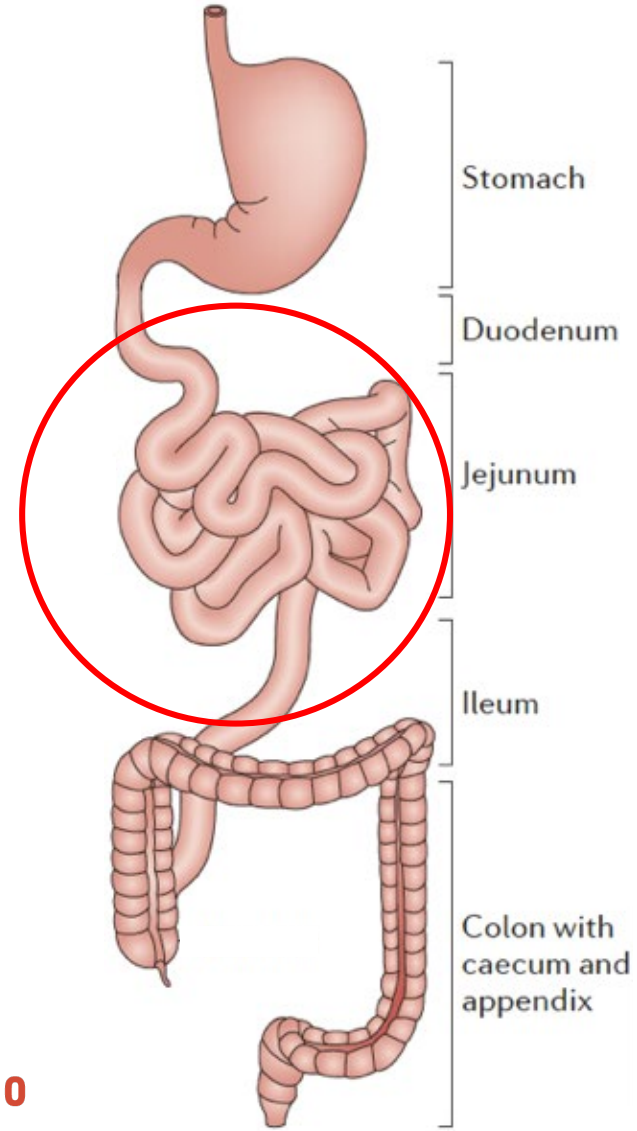
Clinically meaningful reduction in PASI at high dose



Evelo's platform discovers and develops oral biologics targeting SINTAX which modulate clinically validated cytokines

Product Discovery	Product Form	Formulation	Manufacturing
Identifying microbial strains with compelling pharmacology	**A single strain is the starting point for multiple possibilities**	**Target engagement of the right dose in the right place**	**The process affects the product pharmacology and quality**
Microbiology *In vitro* human assays Animal models	Monoclonal microbial Non-viable monoclonal microbial Derivative forms	Release profile Capsules Tablets	In-house process development Network of cGMP partners for DS &DP

Requirements for effective engagement of SINTAX



- Avoid low pH in the stomach
- Maximize upper intestinal exposure
- Deliver sufficient dose for modulation of target cells in the small intestine
- Engagement of target cells triggers systemic effects on SINTAX

Mowat and Agace.
Nat Rev. Imm. 2014

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Monoclonal Microbials: A new class of oral biologics acting on SINTAX for systemic effects without systemic exposure

Monoclonal Microbials are oral biologics which are dosed and formulated to engage SINTAX

They are single clonal microbial strains with defined, dose-dependent pharmacology

Efficacy

- Positive interim Phase 1b clinical data in psoriasis
- Supports core scientific hypothesis and translation of preclinical effects into humans

Safety & Tolerability

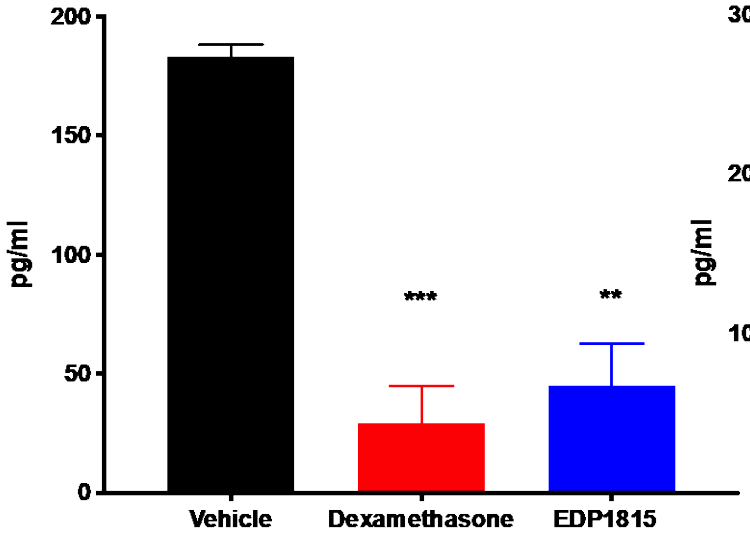
- Clinical data across 3 programs supports attractive tolerability profile
- No systemic exposure observed
- No gut colonization observed

Convenience and Affordability

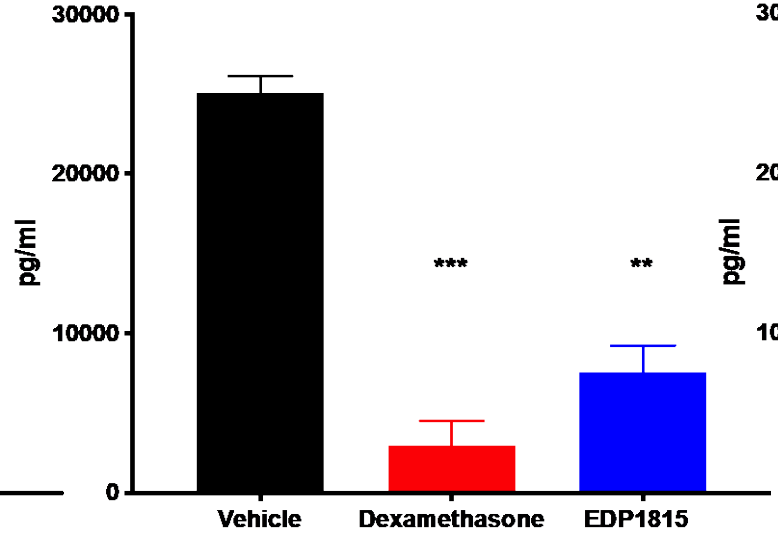
- Oral delivery
- Cost effective, scalable manufacturing to treat large patient populations

EDP1815 acts on SINTAX to drive effects on multiple clinically validated cytokines

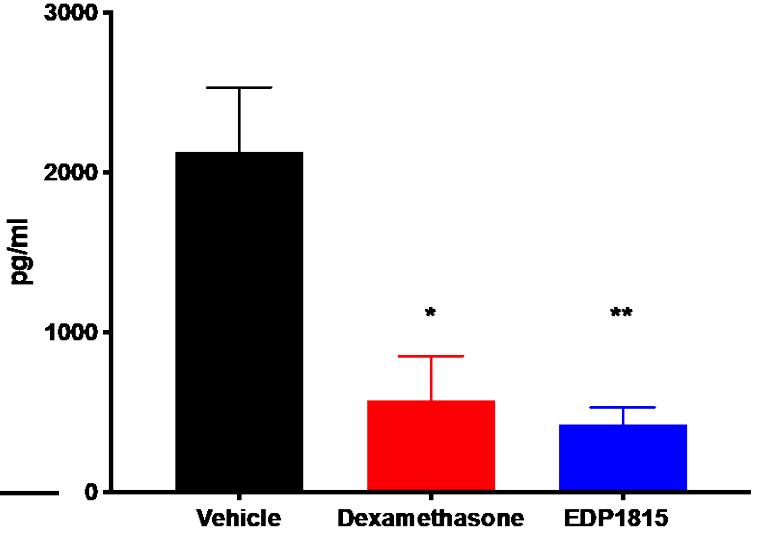
IL-12 – e.g. Ustekinumab/psoriasis



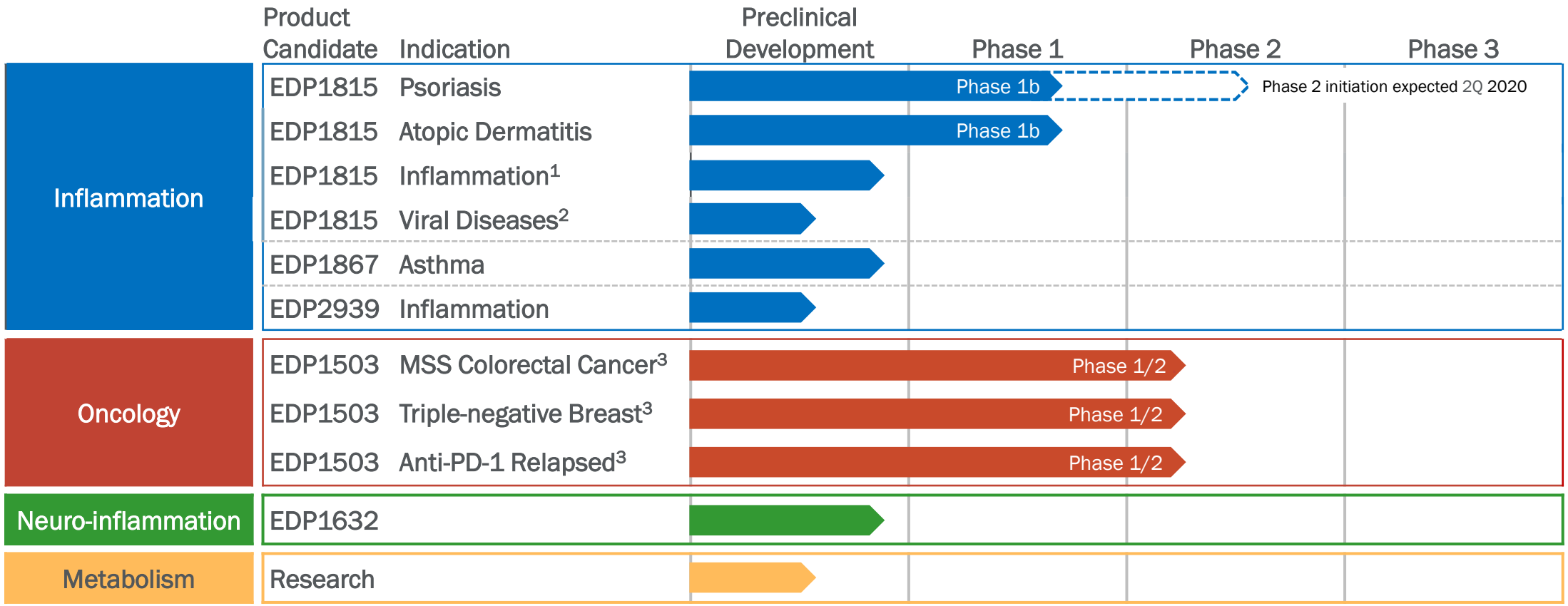
IL-6 – e.g. Tocilizumab/RA



IL-13 – e.g. Dupilumab/Atopy



Broad clinical and preclinical pipeline across therapeutic areas



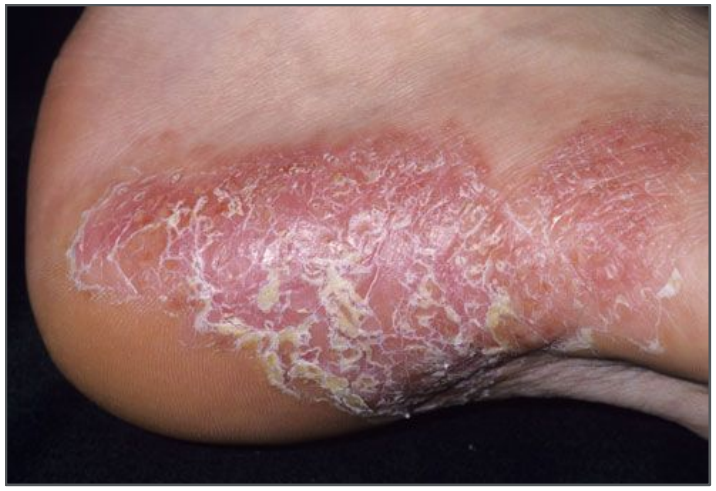
[1] *We intend to advance EDP1815 into additional indications after the interim readout of the EDP1815 Phase 2 clinical trial at the end of 2020. Potential indications include psoriatic arthritis, axial spondyloarthritis, rheumatoid arthritis, atopic dermatitis, and asthma.*

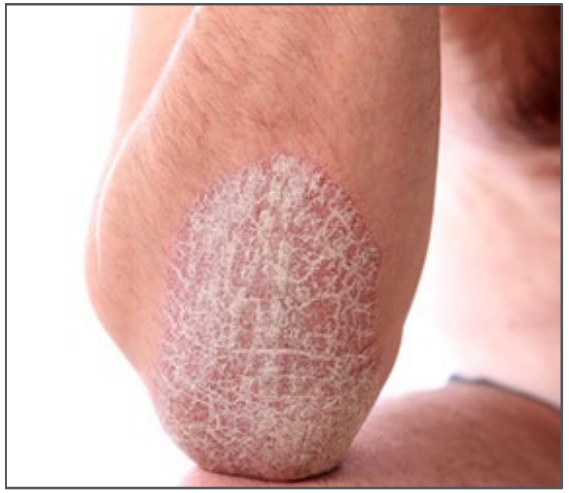
[2] *We are evaluating opportunities to develop EDP1815 for the treatment of diseases caused by viral infection, including influenza and coronaviruses (SARS-CoV-2).*

[3] *The Phase 1/2 study of EDP1503 in combination with KEYTRUDA is being conducted in a clinical collaboration with Merck.*

EDP1815 interim Phase 1b data and planned Phase 2 clinical trial

‘Mild to moderate’ psoriasis is a serious condition





- While characterized as mild to moderate in terms of body surface area, individual lesions can be severe
- Significant number of mild to moderate patients are not treated at all due to physician concern about long-term safety or tolerability, as well as 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 populations with potential to address over 3.5 million[2] of these individuals in US and EU5 and then expand globally

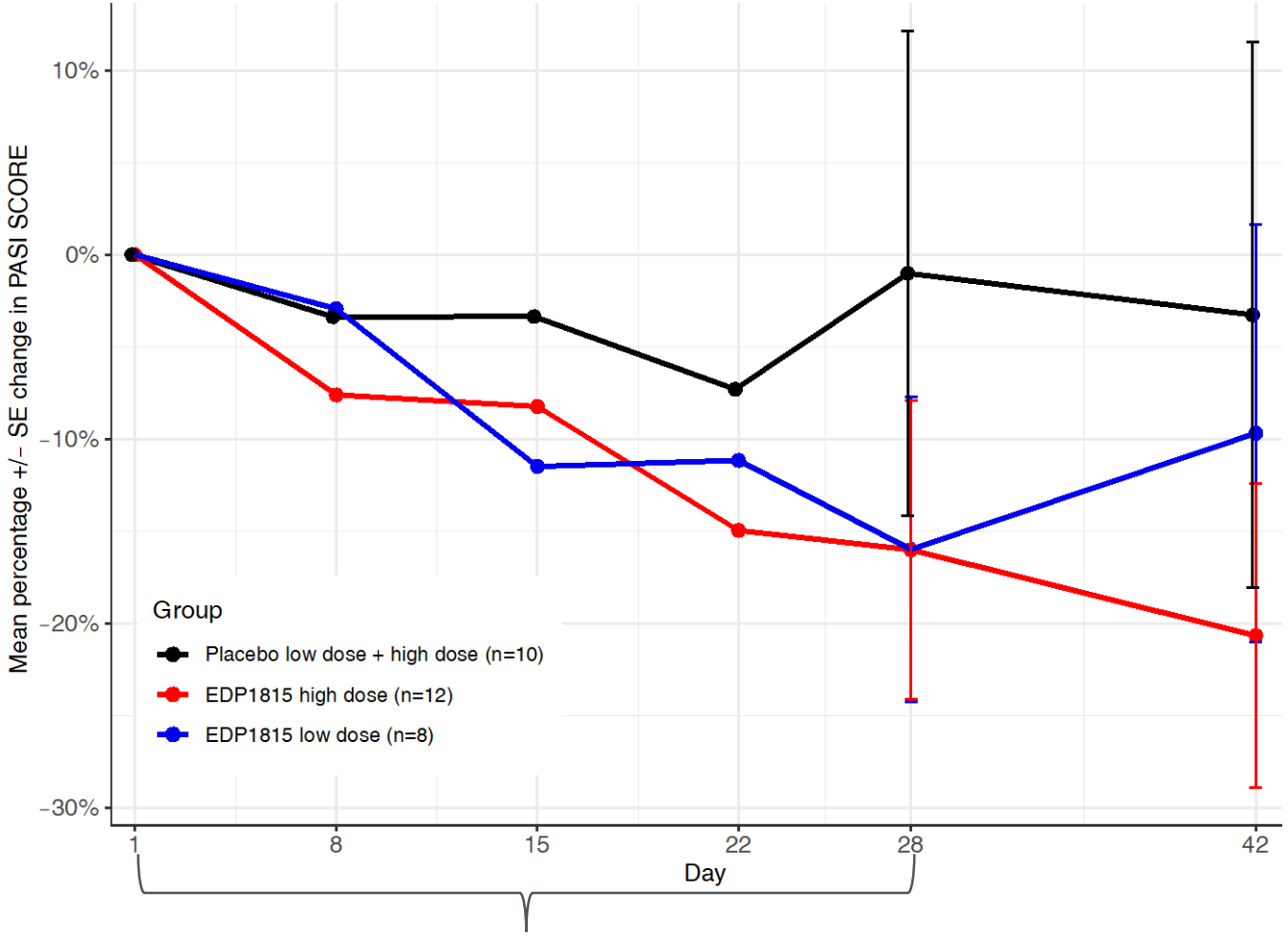
[1] Armstrong AW, Robertson AD, Wu J, Schupp C, Lebwohl MG. Undertreatment, Treatment Trends, and Treatment Dissatisfaction Among Patients With Psoriasis and Psoriatic Arthritis in the United States: Findings From the National Psoriasis Foundation Surveys, 2003-2011. JAMA Dermatol. 2013;149(10):1180–1185.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

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

EDP1815 Phase 1b trial in mild to moderate psoriasis

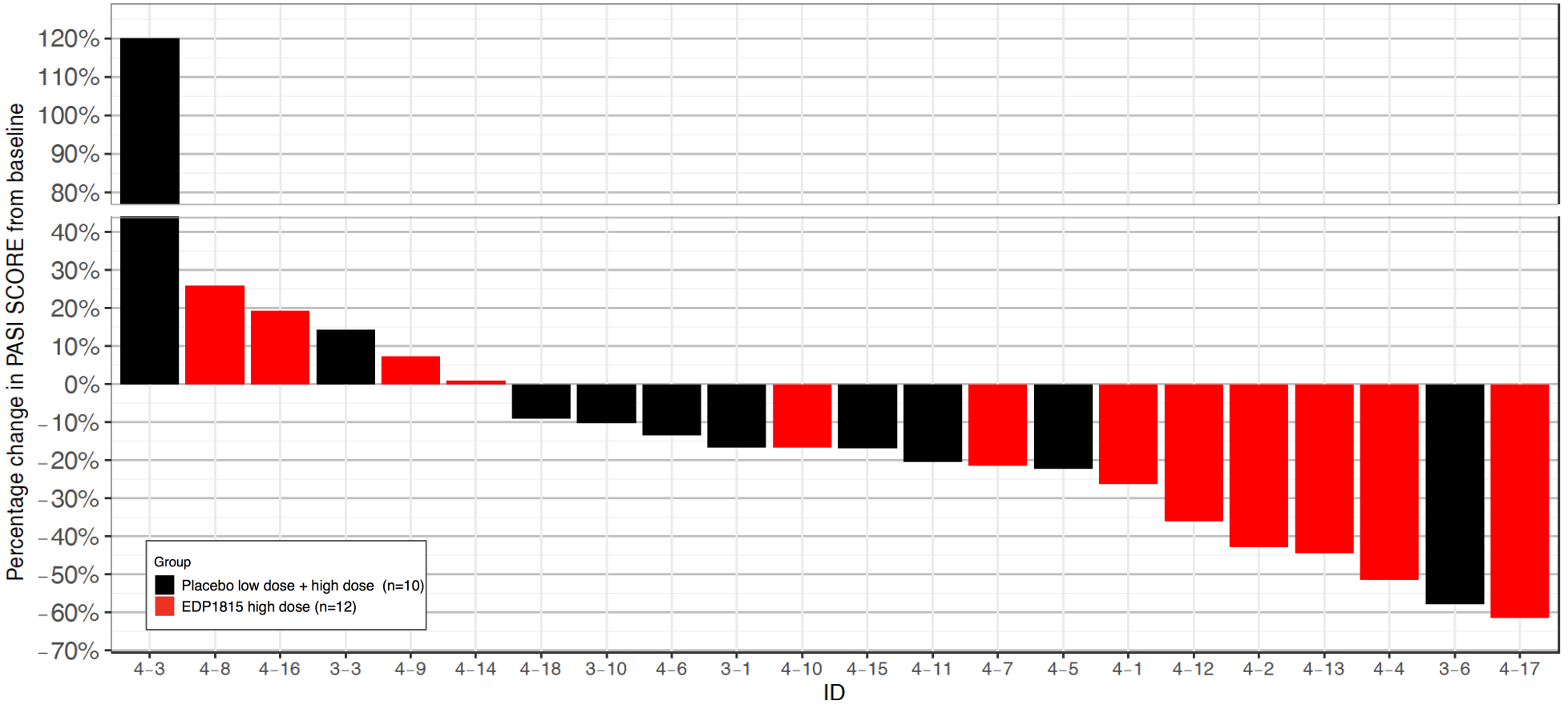
- 2 cohorts randomized 2:1 (active:placebo) for 28 days; daily oral administration of enteric capsule formulation; follow-up at 42 days
  - Low dose (550mg) - 12 individuals
  - High dose (2.76g) – 18 individuals
- Primary endpoint of safety and tolerability
  - EDP1815 was well tolerated with no overall difference reported from placebo
- Secondary and exploratory endpoints reported including PASI and Lesion Severity Score
  - Consistent baseline severity of disease across placebo and active arms
- Biomarker analysis of cytokine production after LPS stimulation of whole blood from baseline and day 28

Mean PASI reduction of 21% at day 42 at high dose - continued improvement after end of dosing suggests dose response



- PASI reduction at high dose
  - 16% at day 28 versus placebo of 1%
  - 21% at day 42 versus placebo of 3%
- Continued downward trend indicates that the maximum reduction may not yet have been reached

Reduction in PASI of up to 61% at day 42 at high dose



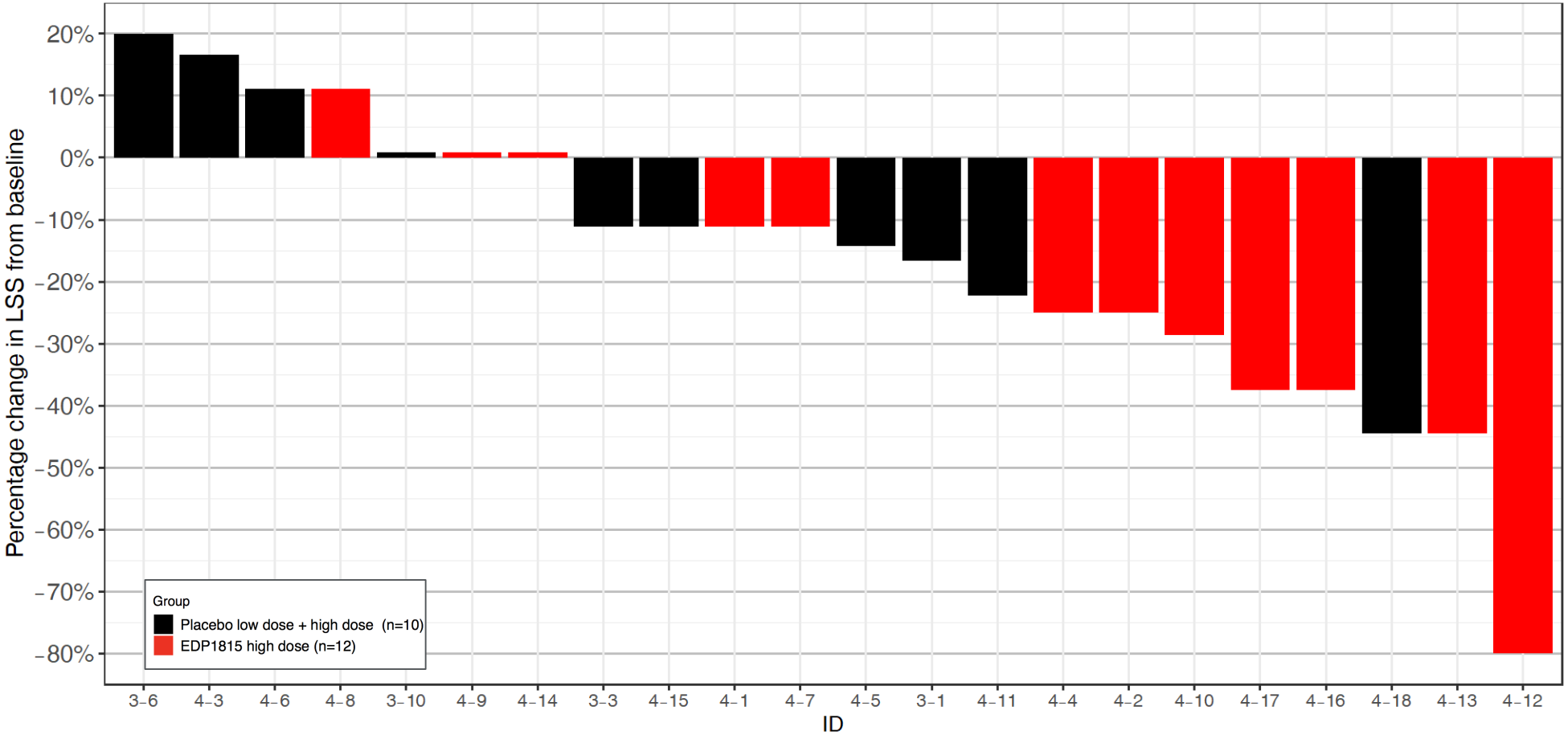
3.0	5.0	6.7	4.2	5.4	1.6	4.4	10.6	18.6	1.2	4.8	5.9	8.8	7.9	5.4	9.5	10.0	2.8	1.8	10.5	4.5	7.8

Baseline PASI score (72-point scale)

- 50% of those dosed with EDP1815 achieved at least PASI 25 at Day 42 vs. 10% with placebo

Group	Baseline PASI score median (IQR)
Placebo low dose + high dose (n=10)	4.95 (1.12-8.78)
EDP1815 high dose (n=12)	6.05 (2.05-10.05)

Individual lesions assessed for LSS were severe on 12-point scale; reduction of up to 80% at day 42



- 9/12 dosed with EDP1815 showed a reduction in LSS
- 7 of those 9 achieved >25% reduction

Group	Baseline LSS median (IQR)
Placebo low dose + high dose (n=10)	9 (6.25-11.75)
EDP1815 high dose (n=12)	8.5 (7.25-9.75)

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

Baseline LSS (12-point scale)

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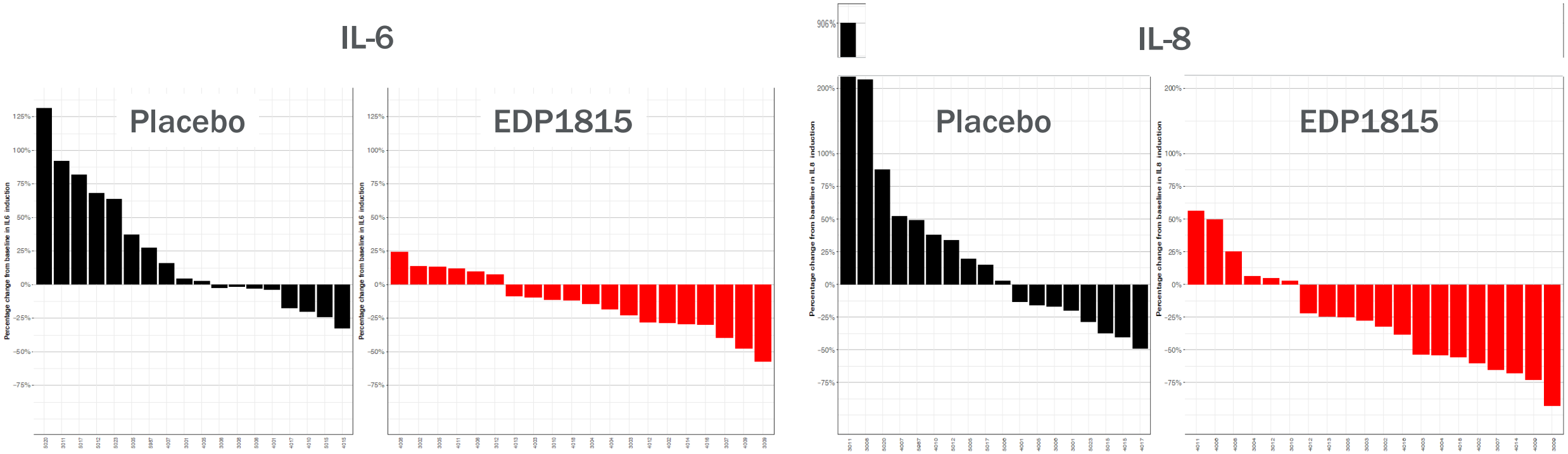
EDP1815 reduced production of IL-6 and IL-8 from human blood cells after 28 days treatment



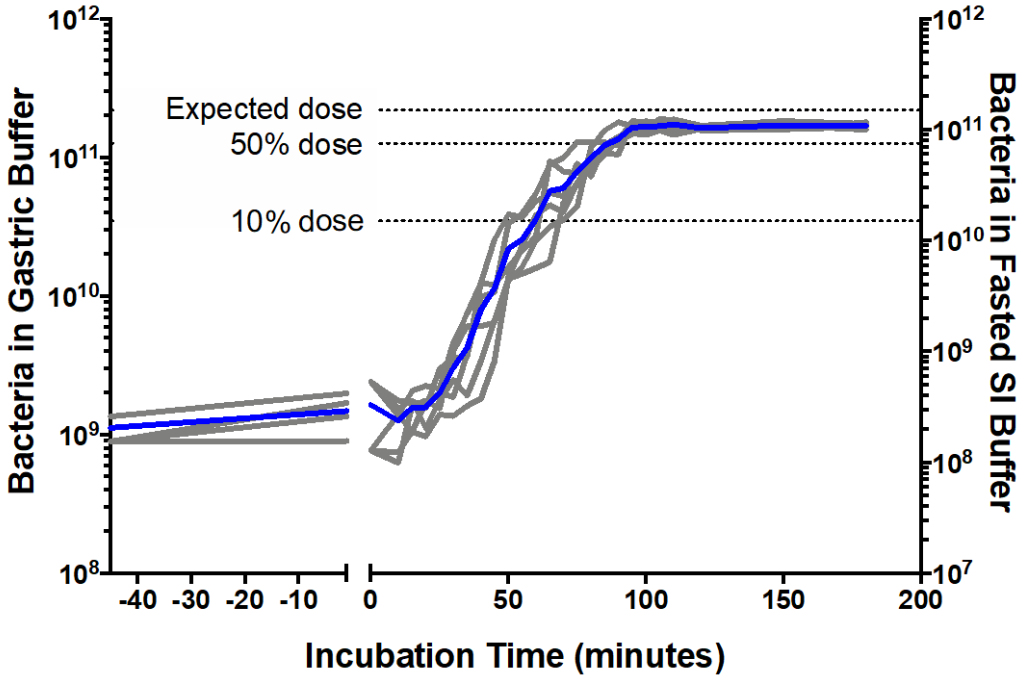
- Difference in cytokine production from LPS stimulation of whole blood at baseline and day 28
- High and low dose EDP1815 cohorts pooled
- Evelo is evaluating opportunities to develop EDP1815 for the treatment of diseases caused by viral infection, including influenza and coronaviruses (SARS-CoV-2)

Monoclonal microbials released faster from new formulation than enteric capsules enabling potentially superior targeting of SINTAX

Enteric capsule formulation

~90 minutes

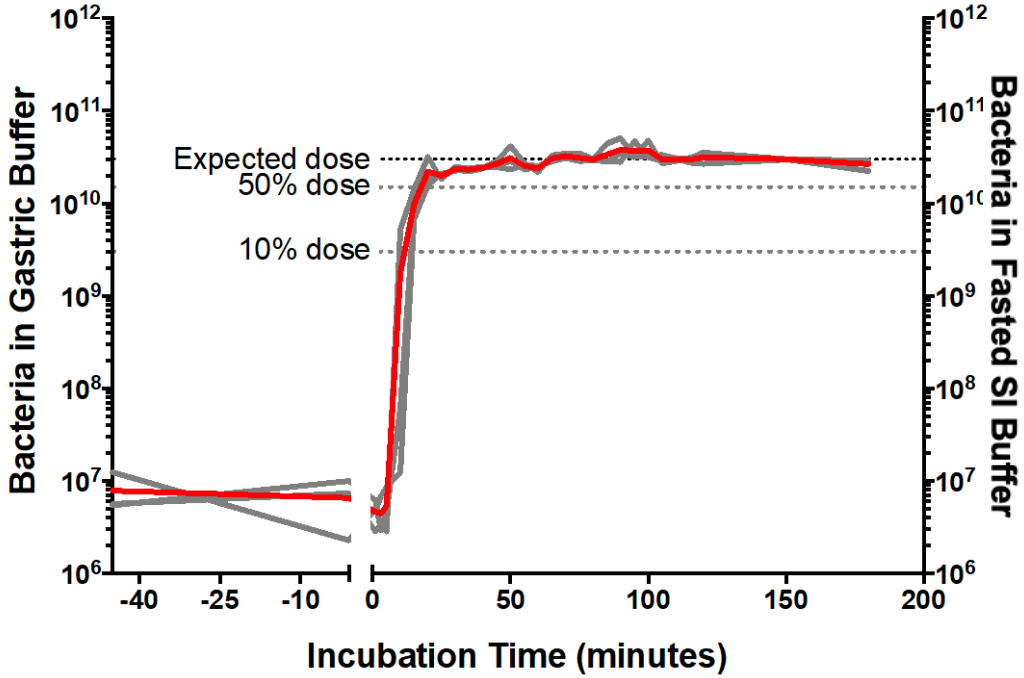
to 50% release



New, improved formulation

~5 minutes

to 50% release



Preclinical small intestinal *in vitro* conditions

EDP1815 Phase 2 in mild to moderate psoriasis: dose ranging study with new improved formulation

Trial Summary

- Randomized placebo-controlled dose ranging study ~180 individuals
- Evaluate three doses of new formulation of EDP1815 vs placebo
- New formulation uses same API, but has improved release profile to target SINTAX
- Will include individuals with higher baseline PASI scores than Phase 1b

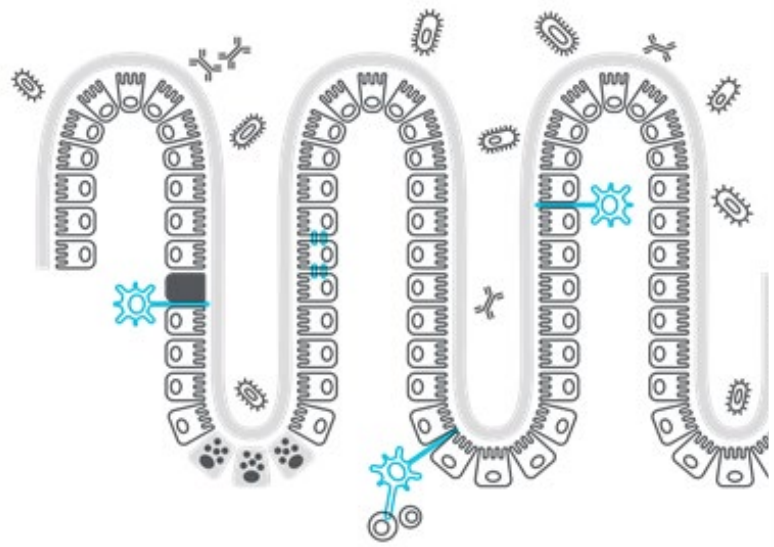
Summary of Endpoints

- Primary endpoint: Mean reduction in PASI score at 16 weeks
- Secondary endpoints: Safety and tolerability, other clinical measures of disease

Planned initiation in 2Q 2020 with interim data by late 2020

EDP1815 impacts clinically validated cytokines – potential to address multiple inflammatory diseases

Preclinical observations support broad potential across inflammatory diseases



Indication	Associated cytokine pathways	US/EU5 treated patients (estimate, millions)
Psoriasis[1]	IL17, TNFa, IL12p40	6.2
Psoriatic arthritis[2]		2.7
Atopic dermatitis[1]	IL4, IL5, IL13	10
Asthma[1]		28
Food allergy[3]		7.8
Rheumatoid arthritis[5]	TNFa, IL6	3.7
Axial spondyloarthritis[4]		1.7
Ulcerative colitis[5]	TNFa, IL12p40	2.3
Crohn's disease[5]		2.1

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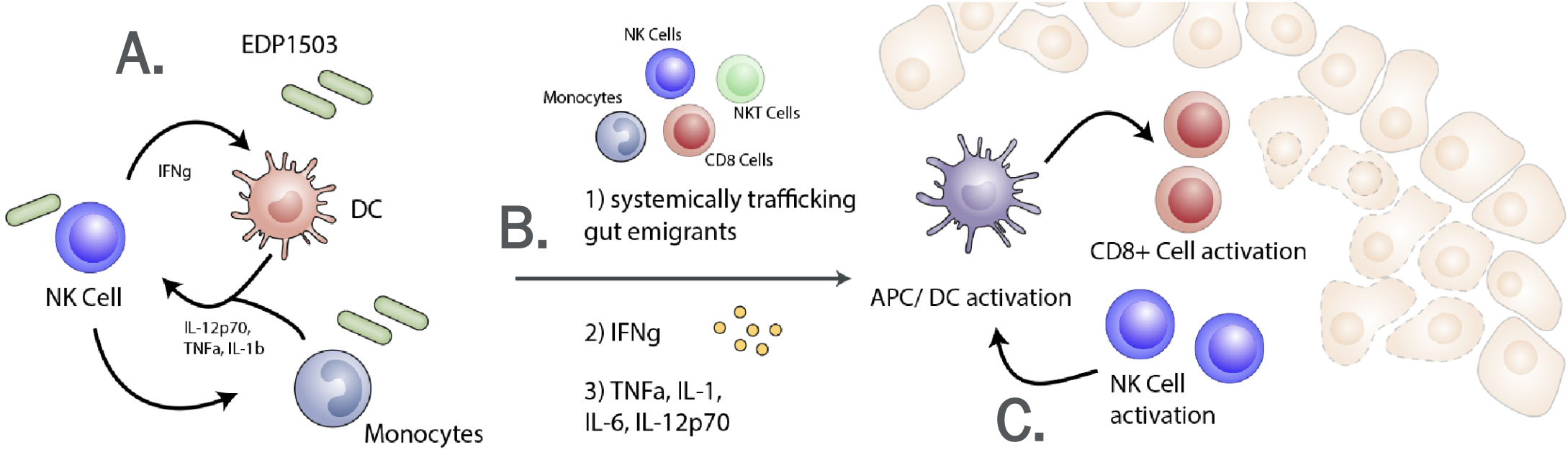
(1) Company-sponsored market research; (2) Arthritis Foundation, Rheumatol Int. 2019; 39(1): 121–130; Epidemiology Of Psoriasis And Psoriatic Arthritis M.A. Cimmino; (3) US only, JAMA Netw Open. 2019;2(1):e185630; (4) Clinical Rheumatology, March 2019, AJMC December 2018; (5) Datamonitor

EDP1503 designed to harness SINTAX to drive multiple anti-tumor immune mechanisms to treat cancer

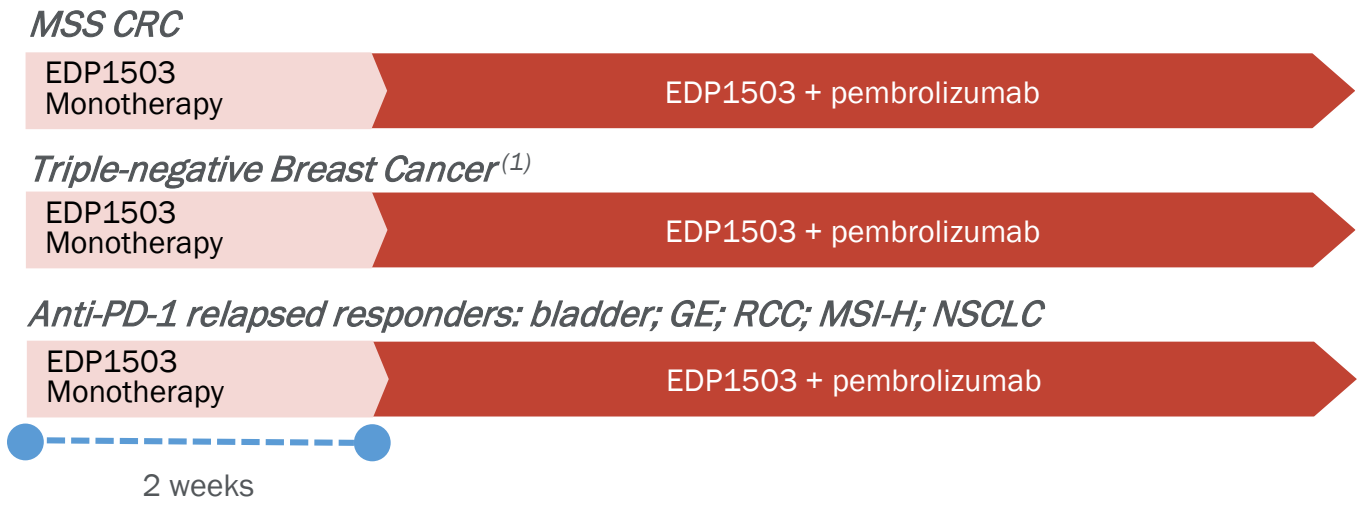
EDP1503 impacts multiple anti-tumor immune mechanisms



(A). Oral delivery of EDP1503 monotherapy leads to tumor control comparable to checkpoint inhibition in multiple subcutaneous syngeneic tumor models. This treatment promotes the immunogenic remodeling of the tumor microenvironment to favor the infiltration of protective effector cells (B). In the CT-26 colon carcinoma model, this protection is dependent on both NK and $CD8^+$ T cells, however, NK cells are insufficient to mediate protection in the absence of $CD8^+$ cytotoxic T lymphocytes (CTL). Our data suggests a model where EDP1503 stimulates NK cell transactivation which potentiates cross-priming of tumor-specific CTL by $XCR1^+$ cDC1 to limit tumor growth (C).

Clinical collaboration with Merck across multiple cancer types

Overview:	Open label safety, tolerability, and efficacy studies of EDP1503 in combination with a checkpoint inhibitor. n=~120
Endpoints:	Safety and tolerability Overall response rates Biomarkers of immune response in paired tumor biopsies taken before and after 2-week EDP1503 monotherapy
Dosing:	Daily oral administration; single dose



(1) Given newly approved treatments for triple-negative breast cancer, Evelo anticipates that the majority of triple negative breast cancer patients to be recruited will have relapsed following prior PD-1/L1 therapy, similarly to those in the PD-1 relapsed cohort.

Microsatellite stable colorectal cancer cohort fully enrolled*

- 32 individuals with MSS CRC who had previously failed all therapies for metastatic disease
- No clinical responses have been observed
- Several individuals with stable disease
- Cellular infiltration biomarker changes observed from biopsies taken during EDP1503 monotherapy for individuals with stable disease
  - Consistent with preclinical observations
- Continue to follow subjects that remain on the study

* *Based on a cutoff date of February 12, 2020*

Multiple near-term clinical milestones from current clinical portfolio and rich discovery pipeline

Multiple Phase 2 and other clinical readouts expected in 2020

Candidate	2020	
EDP1815 Psoriasis	**Phase 1b** New formulation **2Q 2020**	**Phase 2** Interim data **Late 2020**
EDP1815 Atopic dermatitis	**Phase 1b** New formulation **2Q 2020**	
EDP1503	**Phase 1/2** MSS colorectal carcinoma Triple negative breast cancer PD-1 relapsed **1H 2020**	

Evelo has a rich discovery pipeline

Monoclonal microbials

Single microbial strains with potent pharmacology

- Immunology follow-on pre-candidates
- Neuroinflammation pre-candidate
- Leads in metabolism

Product forms

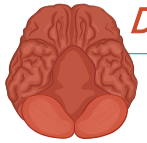
A single strain is the starting point for multiple possibilities

Opportunity for new generation of products

- Multiple non-viable monoclonal microbials
- Derivative forms of microbes

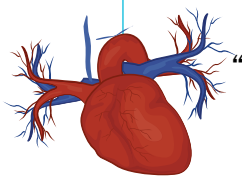
Inflammation | Oncology | Metabolism and CV | Neuro-inflammation/ Degeneration | Autoimmune | Neuro-psychiatric | Vaccines

Evelo's platform has broad potential in chronic inflammation, a central driver of society's most burdensome diseases



Neurological diseases; 7M US DALYs, 111M WW

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

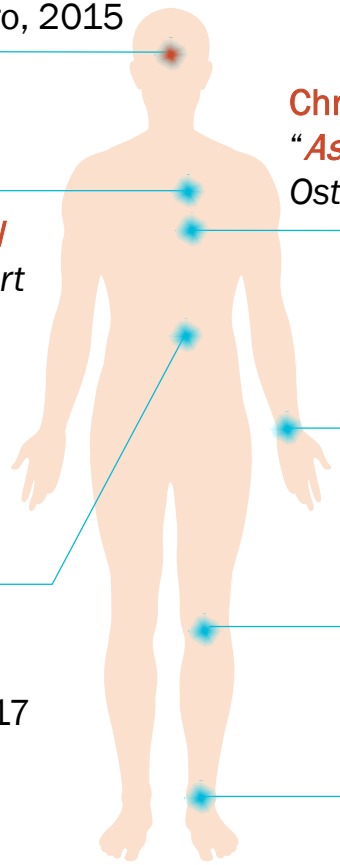


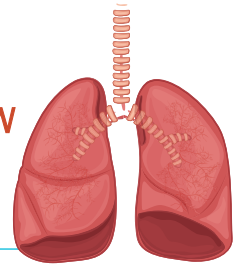
Cardiovascular disease; 16M US DALYs, 366M WW

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

Diabetes; 4M US DALYs, 68M WW

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



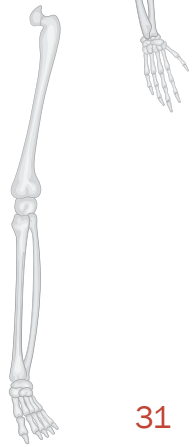


Chronic respiratory diseases; 6M US DALYs, 112M WW

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

Autoimmune diseases; 2M US DALYs, 18M WW

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

SOURCE: Scientific literature, Global Disease Burden 2017

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Appendix

Corporate information

- ~100 employees
- Cash and cash equivalents of $77.8 million*
- $50 million ATM filed
- Debt outstanding of $20 million, total facility of $45 million*
- Funded to the end of 2020 with current cash and cash equivalents

*As of 12/31/19