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# SINTAX™

The network of connections between the small intestine and the rest of the body

Developing effective, safe, oral, affordable medicines for millions of patients

August 2020

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# 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 of EDP1815 for the treatment of patients with COVID-19, our development plans, 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, the scalability of manufacturing for EDP1815, and the sufficiency of cash to fund operations.*

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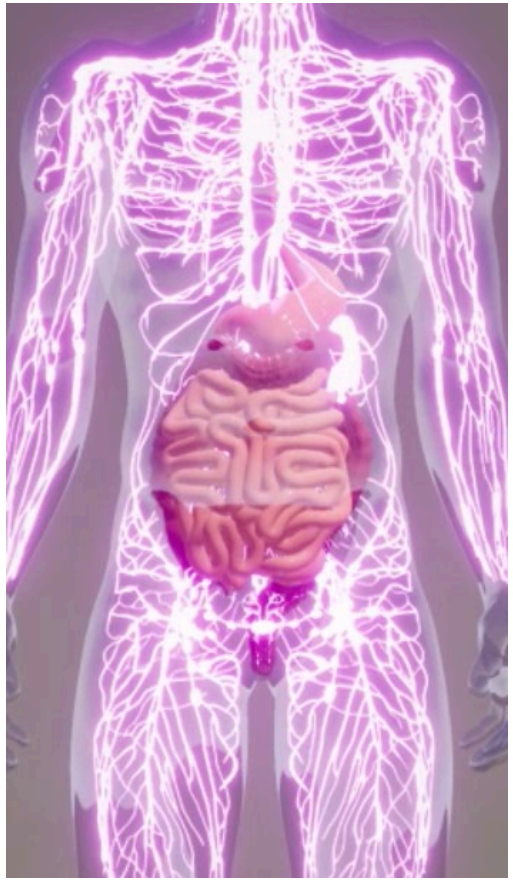
# The small intestine is the motherboard of the immune system



SINTAX – the Small Intestinal Axis

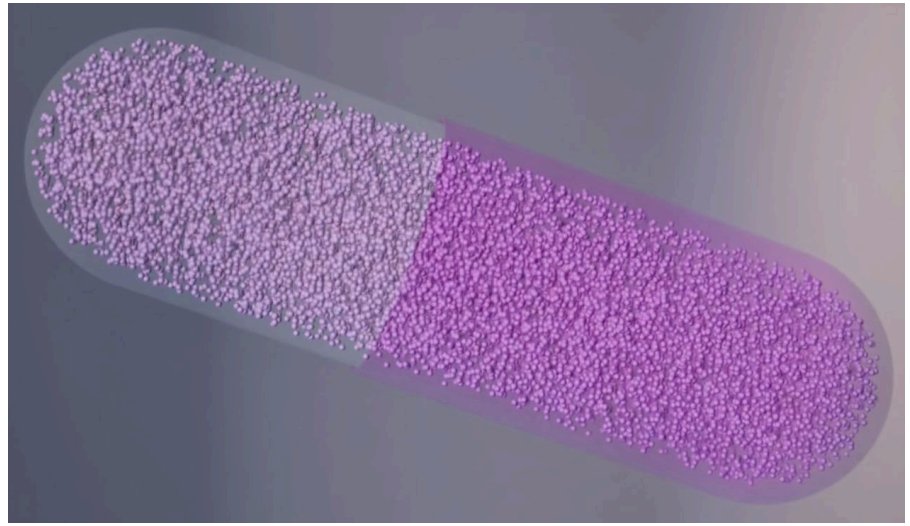
The small intestine is a sensory window to the external world

SINTAX relays messages from the external world throughout the body

These messages govern inflammation resolution or stimulation

# Product candidates are pharmaceutical preparations of single microbes

- Capsule intended to release in the small intestine for dose-dependent effects via host cells
- Microbes do not need to be alive to be active
- Microbes have not been detected outside of the gut
- Effects are believed to be driven by recognition of structural motifs by cells in the small intestine
- Microbes have not been observed to colonize the gut and are not intended to reconstitute the microbiome



# Candidates targeting SINTAX active in clinical and preclinical studies

## Preclinical activity with novel mechanism of action

Effects on inflammation on par with injectable biologics and existing oral medicines in preclinical models

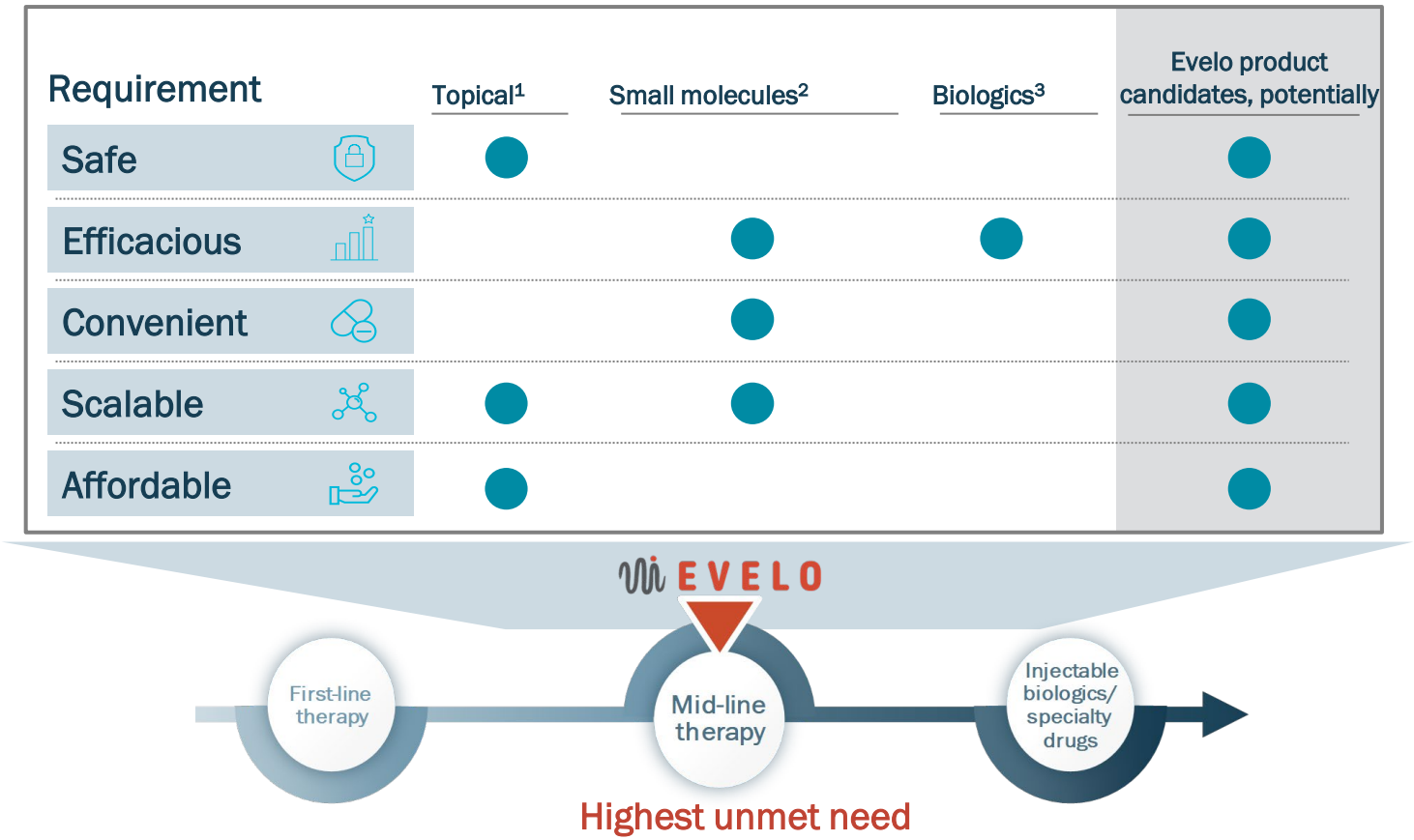
Active across multiple pathways simultaneously

Effects on inflammation achieved with no observed systemic exposure

## Proof of principle observed in clinical studies; well tolerated with no overall difference from placebo

| | |
|---|---|
| **Psoriasis Phase 1b** | Reductions in PASI and LSS vs. placebo |
| **Immune biomarkers Phase 1b** | Inhibition of multiple cytokines, including those associated with COVID-19 cytokine storm |
| **Immuno-pharmacology study** | 15-fold reduction in inflammatory reaction, compared to placebo |

# Candidates targeting SINTAX could open up treatment for more patients




Potential to create new market as mid-line therapy and defer use of injectable biologics / specialty drugs and expand to first-line treatment to become foundational therapy for patients globally



[1] e.g., topical gels, UV-B, PUVA, Excimer laser [2] e.g., apremilast, tofacitinib [3] e.g. etanercept, adalimumab

# Differentiated target profile may enable early intervention in COVID-19

- Inflammation resolution without complete immunosuppression
  - Modulation of multiple inflammatory pathways associated with cytokine storm
  - No suppression of type 1 interferons important for anti-viral response
  - Well tolerated
- Convenient, oral administration – potential for treatment in the community setting
- Scalable and affordable for the treatment of large populations

# Data from two parallel studies will drive potential accelerated path

## Phase 2/3 Platform Trial in U.K.

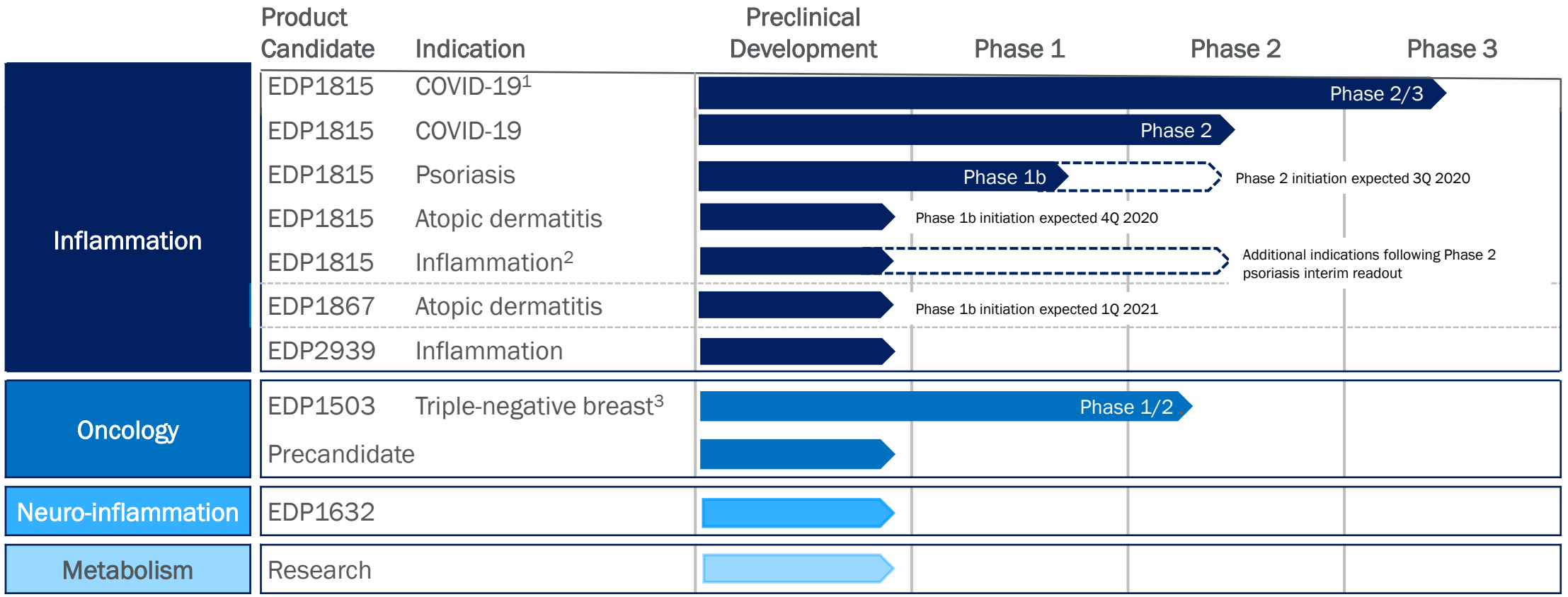
- Regulatory authorization in June 2020
- Sponsored by Cambridge University Hospitals NHS Foundation Trust
- Enrolling COVID-19 patients at high-risk of progressing to ICU and/or death
- Interim safety data and completion of futility analysis expected in 4Q 2020

## Phase 2 Trial in U.S.

- IND authorization in July 2020
- Collaboration with Rutgers University and Robert Wood Johnson University Hospital
- Enrolling newly diagnosed COVID-19 patients who present at ER
- Clinical data expected in 4Q 2020

**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




[1] The Phase 2/3 TACTIC-E study is an investigator-sponsored study being conducted by Cambridge University Hospitals NHS Foundation Trust.
[2] Evelo intends to advance EDP1815 into additional indications after the interim readout of the EDP1815 Phase 2 clinical trial anticipated during the middle of 2021. Potential indications include psoriatic arthritis, axial spondyloarthritis, and rheumatoid arthritis.
[3] The Phase 1/2 study of EDP1503 in combination with KEYTRUDA (pembrolizumab) is being conducted in a clinical collaboration with Merck & Co., Inc.

# Clinical readouts could drive significant value over next 6 - 12 months

- Interim safety data and futility analysis from Phase 2/3 trial of EDP1815 in COVID-19 in 4Q 2020*
- Data from Phase 2 trial of EDP1815 in COVID-19 in 4Q 2020*
- Data from Phase 1/2 trial of EDP1503 in triple-negative breast cancer in 4Q 2020
- Data from Phase 1b trial of EDP1815 in atopic dermatitis in 1Q 2021
- Interim data from Phase 2 trial of EDP1815 in moderate psoriasis by mid-2021
- Data from Phase 1b trial of EDP1867 in atopic dermatitis in mid-2021
- Continue disciplined investments in high-value pipeline programs and platform

* If final data in these trials are positive Evelo plans to engage in discussions with global regulatory agencies to determine if the data support registration

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# Inflammation

## EDP1815

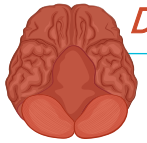
- Phase 2/3 trial in COVID-19 – interim safety data and futility analysis expected in 4Q 2020
- Phase 2 trial in COVID-19 – data expected in 4Q 2020
- Phase 2 trial in psoriasis – planned initiation in 3Q 2020; interim data expected by mid-2021
- Phase 1b trial in atopic dermatitis –planned initiation in 4Q 2020; data expected in 1Q 2021

## EDP1867

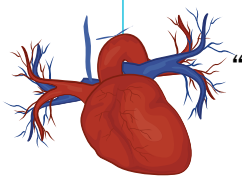
- Phase 1b trial in atopic dermatitis – planned initiation in 1Q 2021; data expected in mid-2021

# Chronic inflammation is the driver of our most burdensome diseases

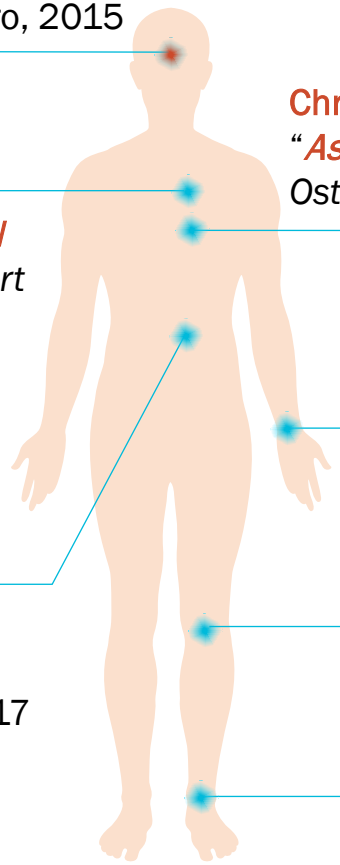
**Neurological diseases; 7M US DALYs[1], 111M WW**
*"The contribution of inflammation in the pathogenesis of Alzheimer's Disease has been appreciated only recently"* Nat Rev Neuro, 2015



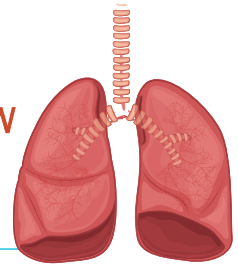
**Cardiovascular disease; 16M US DALYs, 366M WW**
*"Chronic inflammation is a major contributor to heart disease"* Johns Hopkins Medicine



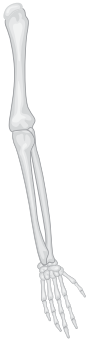
**Diabetes; 4M US DALYs, 68M WW**
*"Inflammation is increasingly considered to be an established mediator [of diabetes]"* J Clin Invest., 2017



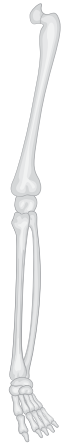
**Chronic respiratory diseases; 6M US DALYs, 112M WW**
*"Asthma is a chronic inflammatory disease" J Amer Osteopathic Assc, 2011*



**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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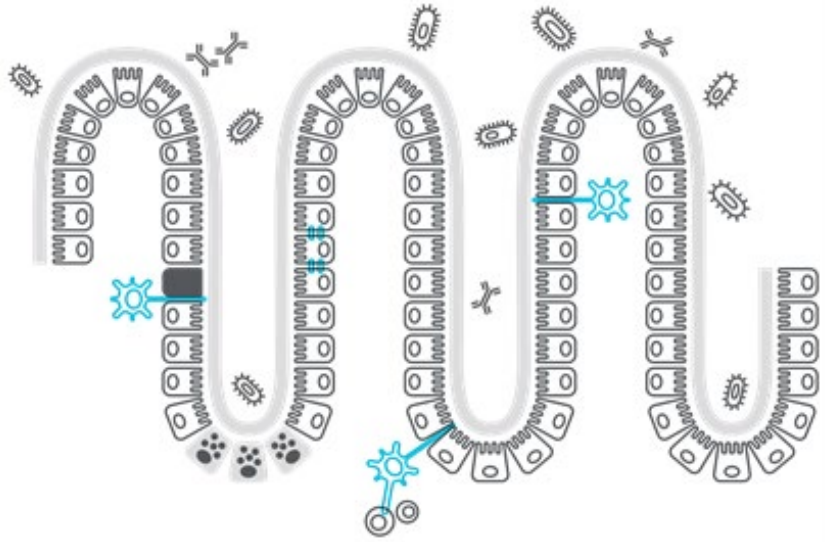
SOURCE: Scientific literature, Global Disease Burden 2017

[1] Disability-Adjusted Life Year (DALY)

# EDP1815 impacts clinically validated cytokines – potential to address multiple 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 |

Clinical and preclinical observations support broad potential use of EDP1815 across a broad spectrum of inflammatory diseases

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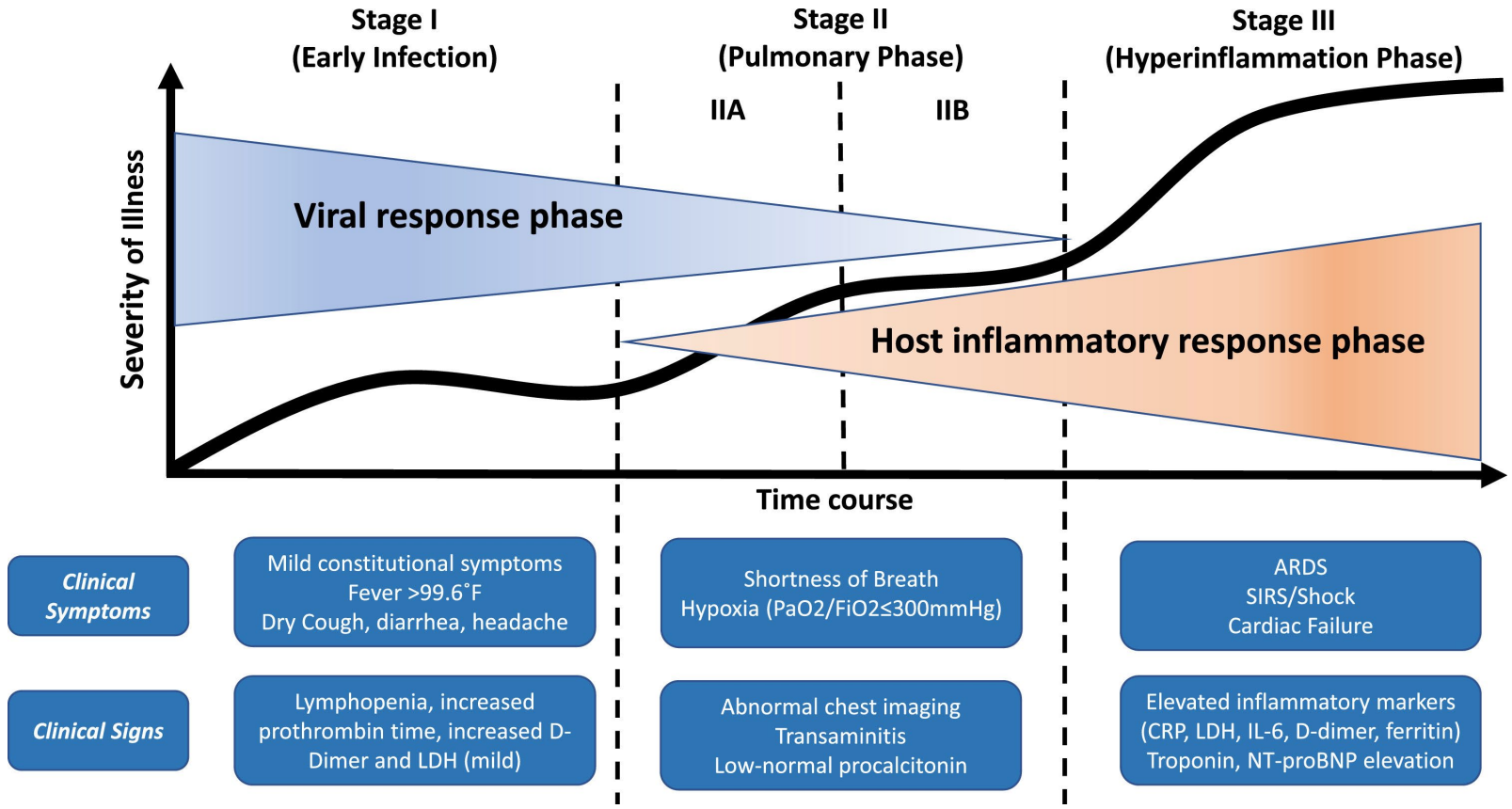
[1] Company-sponsored market research; [2]Arthritis Foundation, Rheumatol Int. 2019; 39(1): 121–130; Epidemiology Of Psoriasis And Psoriatic Arthritis M.A. Cimmino; [3] US only, JAMA Netw Open. 2019;2(1):e185630; [4] Clinical Rheumatology, March 2019, AJMC December 2018; [5]Datamonitor

# EDP1815 in COVID-19

# Early intervention is critical for COVID-19 patients




- Certain life-threatening effects of COVID-19 are driven by hyperinflammation and cytokine storm
- Preventing or reducing this hyperinflammation is crucial to reduce respiratory complications and hospital/ICU admissions

Goal: Intervene at earlier stages of infection to **modify the inflammatory impact of COVID-19**

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Siddiqi, Hassan K., and Mandeep R. Mehra. "COVID-19 Illness in Native and Immunosuppressed States: A Clinical-Therapeutic Staging Proposal." The Journal of Heart and Lung Transplantation, 20 Mar. 2020, Elsevier Inc., Figure 1, doi: https://www.jhltonline.org/article/S1053-2498(20)31473-X/pdf

# EDP1815 key potential advantages from other anti-inflammatories

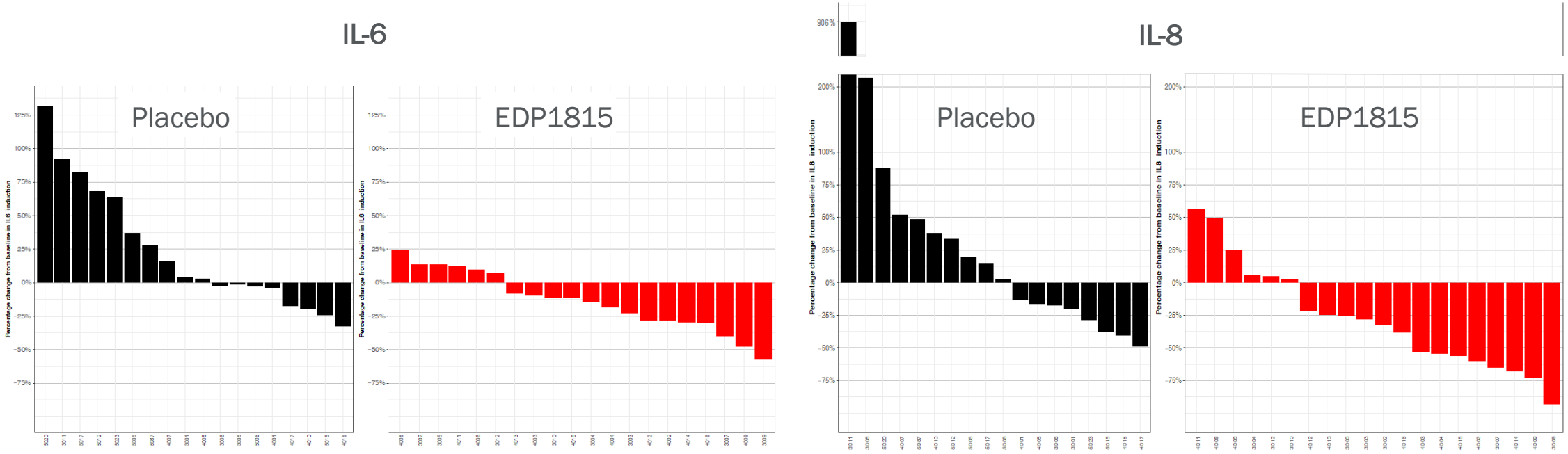
- **Unique mechanism of action:** designed to resolve inflammation without complete immunosuppression
  - Modulates multiple immune pathways associated with cytokine storm
  - Does not suppress type 1 interferons important for anti-viral immune response
- **Safety data:** neither immunosuppressive nor systemically absorbed, limiting risk of secondary infections or potential interaction with other medicines
- **Orally administered**, allowing for easy and flexible administration
- **Scalable and affordable** 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

# EDP1815 anti-inflammatory data provides strong scientific rationale

Inflammatory cytokines including IL-6, IL-8, TNF, and IL-1β are associated with hyperinflammation and cytokine storm in COVID-19

EDP1815 reduced production of these cytokines in human blood cells after 28 days treatment in Phase 1b psoriasis study




- Difference in cytokine production from LPS stimulation of whole blood at baseline and day 28
- High and low dose EDP1815 cohorts pooled

# TACTIC-E: Phase 2/3 platform trial investigating potential to prevent and treat life-threatening complications of COVID-19

## Trial Summary

- 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

## Summary of Endpoints

- Primary endpoint: Reduction in the progression of patients to organ failure or death
- Secondary endpoints:
  - Duration of hospitalization
  - Duration of oxygen therapy
  - Changes in biomarkers associated with COVID-19 progression
  - Time to clinical improvement

**Interim safety data and futility analysis expected in 4Q 2020**



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

# EDP1815-205: Phase 2 trial evaluating EDP1815 in hospitalized patients with newly diagnosed COVID-19

## Trial Summary

- 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

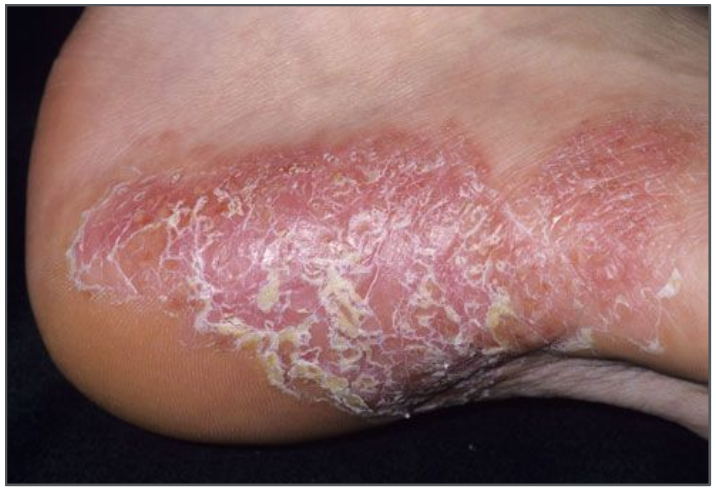
## Summary of Endpoints

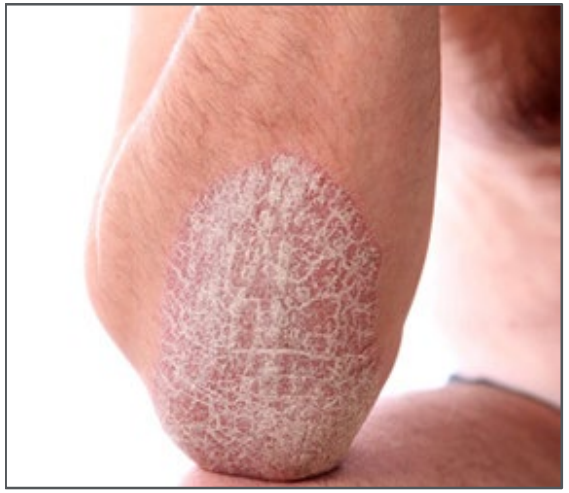
- Primary endpoint: Reduced requirements for oxygen therapy (as measured by SpO2/FiO2)
- Key secondary endpoints: Total symptom duration, progression along WHO scale of disease severity, and mortality

**Data expected in 4Q 2020**

# EDP1815 in Psoriasis

# 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 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

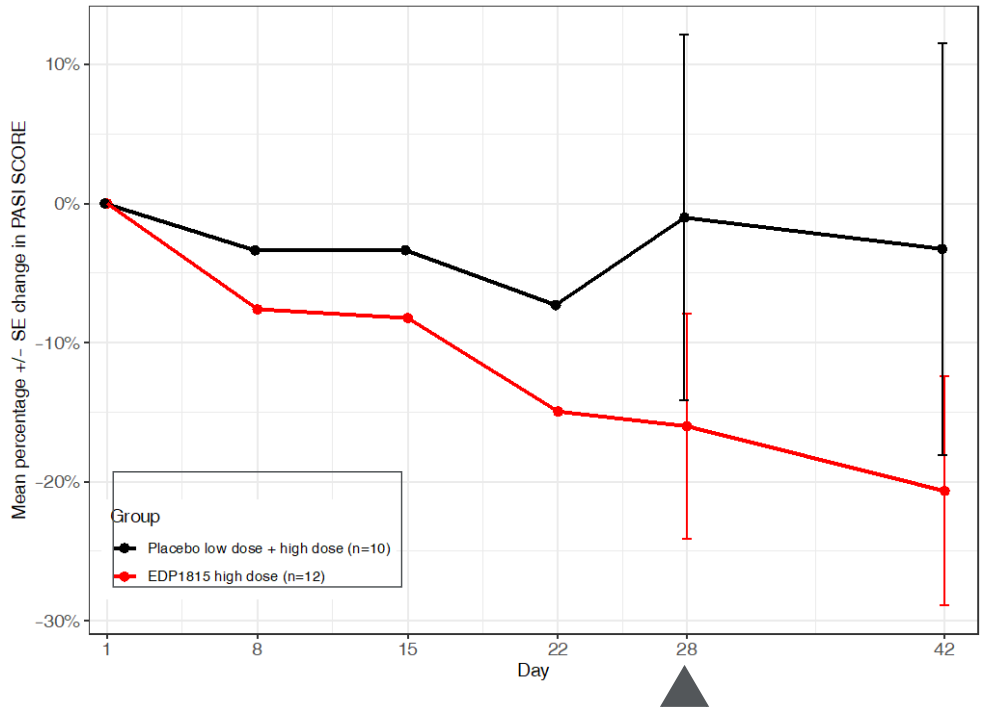
[2] 2018 company-sponsored market research; EU5 consisting of France, Germany, Italy, Spain and the UK

# EDP1815 POC in mild to moderate psoriasis in two separate cohorts

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

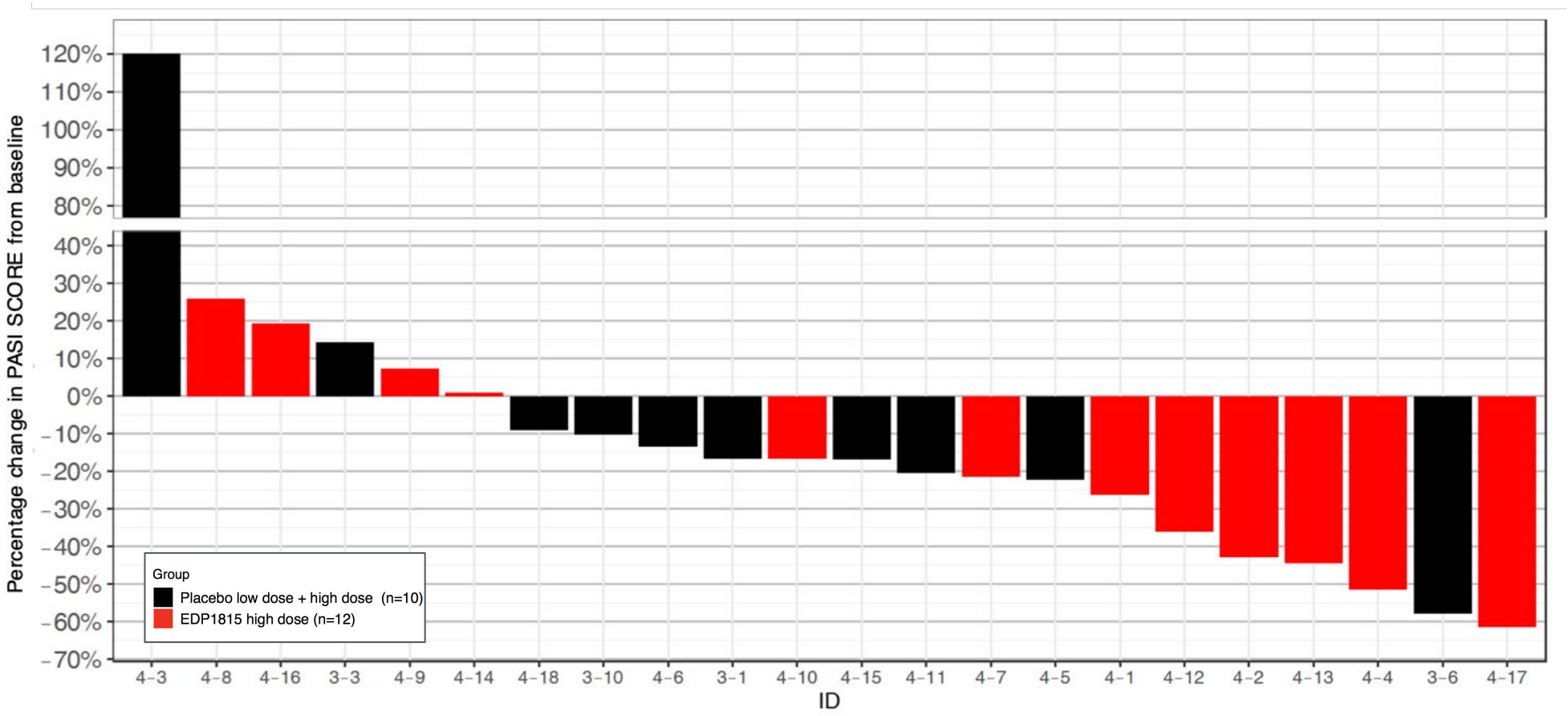
- Well tolerated with no overall difference vs. placebo
- Clinical activity observed, including:
  - Reduction in mean PASI scores vs. placebo
  - Reduction in Lesion Severity Score in-line with PASI
- Continued reduction observed in high dose cohort at day 42, two weeks after cessation of dosing, indicates maximum reduction may not have been reached

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




[1]Primary endpoint of safety and tolerability; secondary endpoints of clinical response (PASI and Lesion Severity Score) and biomarkers

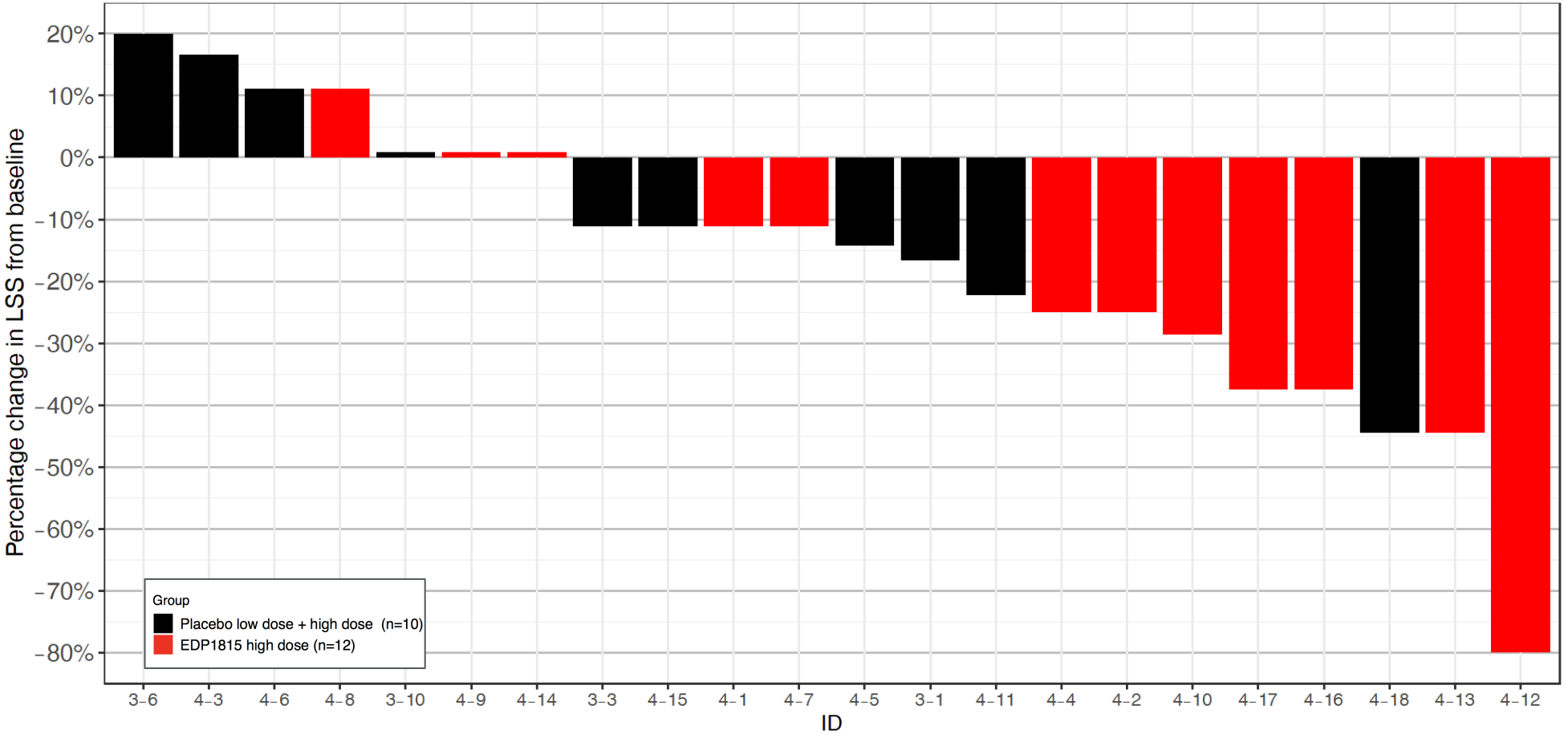
# Reduction in PASI of up to 61% at day 42




- 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 – reduction of up to 80% at day 42




| 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)

- 9/12 dosed with EDP1815 showed a reduction in LSS
- 7 of those 9 achieved >25% reduction
- Individual lesions were severe on 12-point scale

| 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) |

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# EDP1815 Phase 2 dose ranging trial in moderate psoriasis

## Trial Summary

- Randomized placebo-controlled dose ranging trial ~225 individuals
- Evaluate three doses of EDP1815 vs placebo
- 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 3Q 2020; interim data expected by mid-2021**

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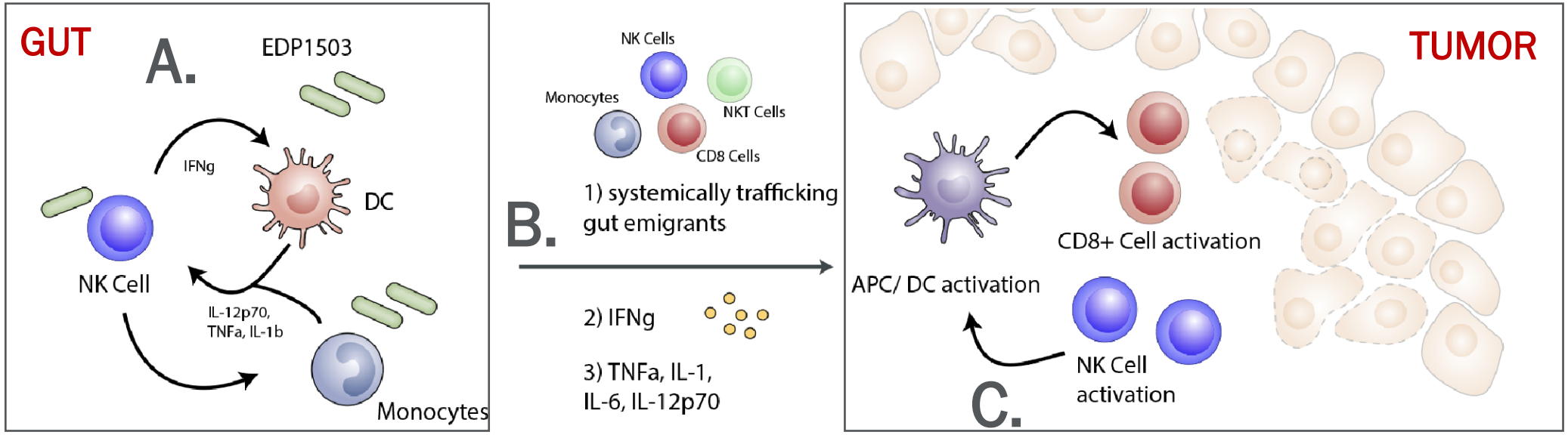
# Oncology

## EDP1503

- Phase 1/2 trial in triple-negative breast cancer in collaboration with Merck
- Data expected in 4Q 2020

# EDP1503 impacts multiple anti-tumor immune mechanisms

EDP1503 is an orally delivered, naturally occurring commensal microbe designed to stimulate immune responses via SINTAX to combat tumor growth. Preclinical R&D is ongoing to identify additional oncology candidates.




(**A**) EDP1503 treatment promotes the production of type-I effector molecules by cells of the innate immune system, including the transactivation of human NK cells
(**B**) This treatment promotes the immunogenic remodeling of the tumor microenvironment to favor the infiltration of protective effector cells
(**C**) This protection is dependent on both NK and $CD8^+$ T cells; however, NK cells require $CD8^+$ cytotoxic T lymphocytes (CTL) to mediate protection
EDP1503 stimulates NK cell transactivation, which potentiates cross-priming of tumor-specific CTL by $XCR1^+$ cDC1 to limit tumor growth

# Evelo is developing EDP1503 for TNBC in collaboration with Merck

Metastatic triple-negative breast cancer (TNBC) is an aggressive disease with few treatment options.

Most patients receive cytotoxic chemotherapy in the relapsed setting but only 10-20% have a clinical response.

Based on initial clinical response data, Evelo is focusing enrollment in the Phase 1/2 trial on TNBC patients at the high dose of EDP1503; further data expected in TNBC in 4Q 2020

**Open label Phase 1/2 study evaluating EDP1503 in combination with KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 therapy**

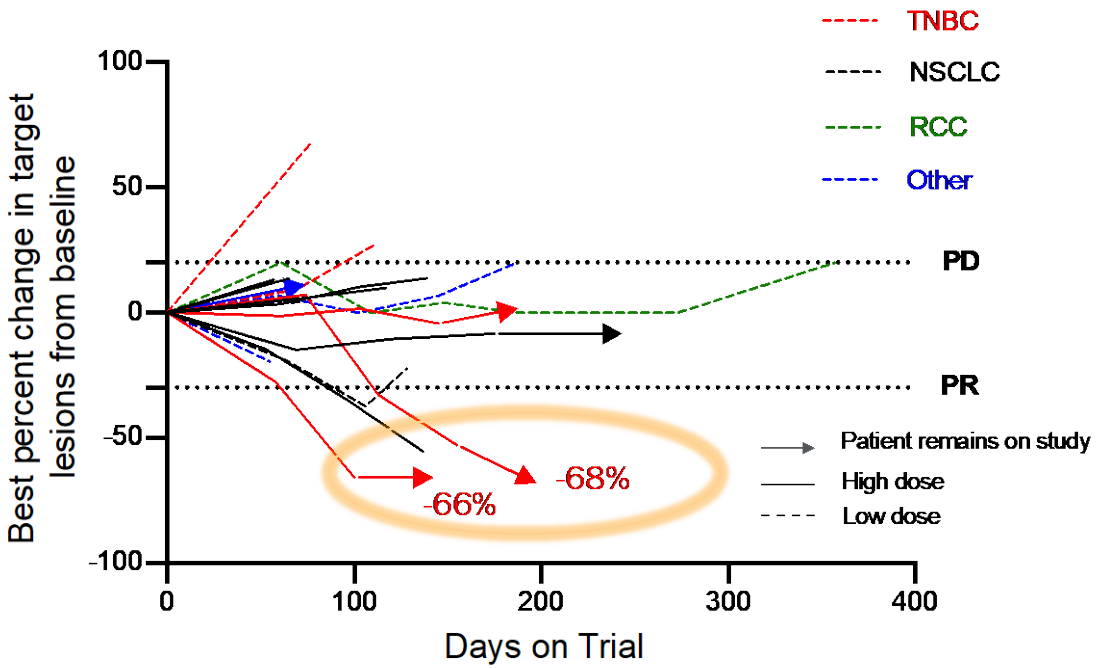
| | |
|---|---|
| **Endpoints:** | Safety and tolerability<br>Overall response rates<br>Biomarkers in paired tumor biopsies taken before and after 2-week EDP1503 monotherapy |
| **Dosing:** | 4 enteric capsules twice daily[2] |


[1]Given newly approved treatments for triple-negative breast cancer, Evelo is recruiting triple-negative breast cancer patients who have relapsed on a prior PD-1/L1 therapy as well as patients who have not received a prior PD-1/L1 therapy.
[2]High dose of 4 enteric capsules twice daily selected as dose level for further recruitment.

# Initial clinical data suggests potential benefit in TNBC at high dose

## The combination of EDP1503 and pembrolizumab was well-tolerated[1]

- Phase 1/2 open-label trial in patients with advanced metastatic colorectal carcinoma, TNBC, and checkpoint inhibitor-relapsed tumors (n=62)
- Treatment-related adverse events were mostly low-grade GI; there were no grade 4/5 AEs or SAEs




## Initial efficacy data in two patients with TNBC who received high dose showed tumor reduction of >65%[1]

- ORR of 25% (2/8) was observed across all high dose patients
- Clinical benefit was observed in TNBC patients with and without prior anti-PD-(L)1 therapy
- Historic studies of anti-PD-(L)1 monotherapy in heavily pretreated TNBC patients yielded ORR of 5-10%

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[1]Safety and initial response data presented at the World Congress for Gastrointestinal Cancers 2020

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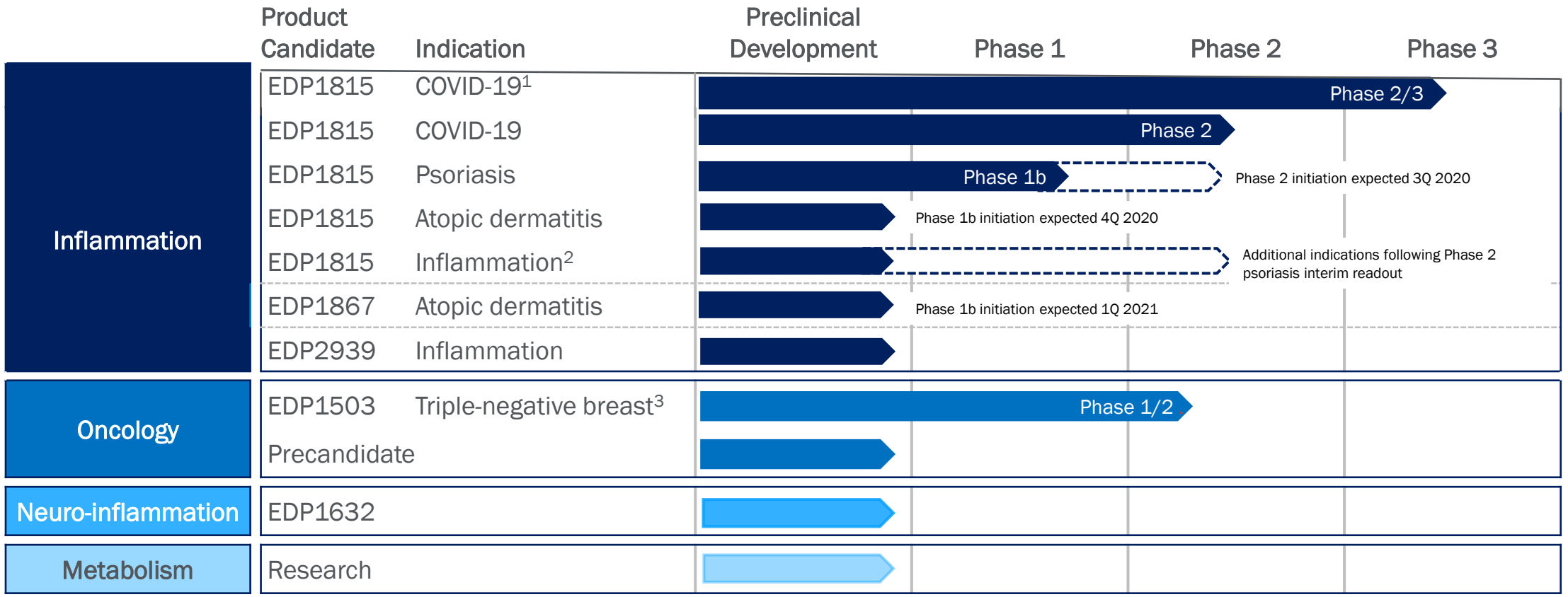
# The Evelo Opportunity

# 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 intends to advance EDP1815 into additional indications after the interim readout of the EDP1815 Phase 2 clinical trial anticipated during the middle of 2021. Potential indications include psoriatic arthritis, axial spondyloarthritis, and rheumatoid arthritis.
[3] The Phase 1/2 study of EDP1503 in combination with KEYTRUDA (pembrolizumab) is being conducted in a clinical collaboration with Merck & Co., Inc.

EVELO

# Pipeline is rich in anticipated near-term catalysts

| Candidate | Catalyst |
|---|---|
| **EDP1815 – TACTIC-E**<br>COVID-19 | **4Q 2020:** Phase 2/3 interim safety data and futility analysis |
| **EDP1815-205**<br>COVID-19 | **4Q 2020:** Phase 2 data |
| **EDP1815**<br>Psoriasis | **3Q 2020:** Phase 2 initiation<br>**Mid-2021:** Phase 2 interim data |
| **EDP1815**<br>Atopic dermatitis | **4Q 2020:** Phase 1b initiation<br>**1Q 2021:** Phase 1b data |
| **EDP1503**<br>Oncology | **4Q 2020:** Phase 1/2 data in triple-negative breast cancer |
| **EDP1867**<br>Atopic dermatitis | **1Q 2021:** Phase 1b initiation<br>**Mid-2021:** Phase 1b data |

# Clinical readouts could drive significant value over next 6 - 12 months

- Interim safety data and futility analysis from Phase 2/3 trial of EDP1815 in COVID-19 in 4Q 2020*
- Data from Phase 2 trial of EDP1815 in COVID-19 in 4Q 2020*
- Data from Phase 1/2 trial of EDP1503 in triple-negative breast cancer in 4Q 2020
- Data from Phase 1b trial of EDP1815 in atopic dermatitis in 1Q 2021
- Interim data from Phase 2 trial of EDP1815 in psoriasis by mid-2021
- Data from Phase 1b trial of EDP1867 in atopic dermatitis in mid-2021
- Continue disciplined investments in high-value pipeline programs and platform

* If final data in these trials are positive Evelo plans to engage in discussions with global regulatory agencies to determine if the data support registration

# Corporate information

- ~95 employees
- Cash and cash equivalents of $90.2 million*
- $50 million of availability under ATM program
- Long-term debt outstanding of $30 million, total facility of $45 million**
- Funded into 3Q 2021 with current cash and cash equivalents, including the $10 million additional debt

*As of 6/30/20
** As of 7/30/20