

# Improvements in Histopathological Features of Eosinophilic Esophagitis Following a Single Administration of EP-104GI During Dose Escalation in the Phase 1b/2 RESOLVE Study

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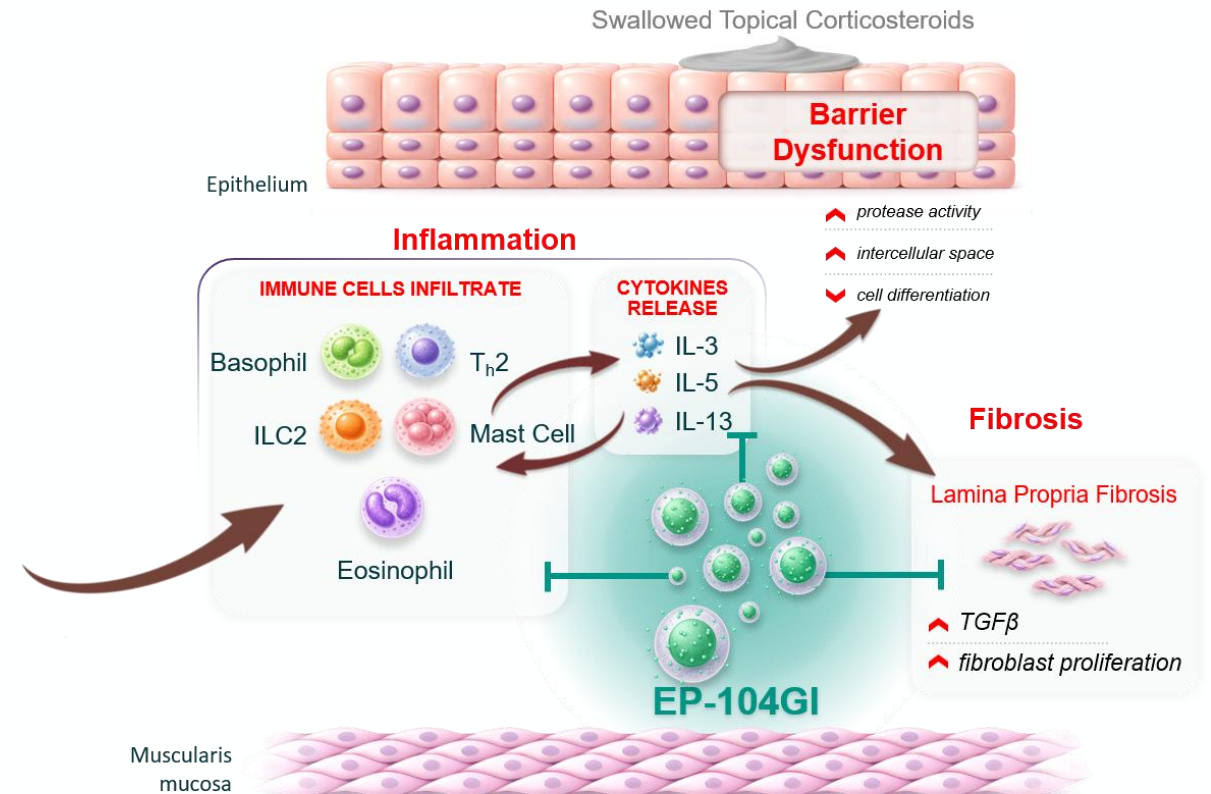
# The Eosinophilic Esophagitis (EoE) Inflammatory Cascade

- Esophageal inflammation and progressive structural remodeling in EoE can lead to dysphagia and food impaction.<sup>1</sup>
- Currently systemic and topical treatment options recommended in EoE can be limited by <sup>1</sup>
  - poor treatment adherence <sup>2</sup>
  - class-related or off-target adverse effects <sup>1</sup>

## EP-104GI - investigated for the treatment of EoE

- Local, long-acting, injectable fluticasone propionate with novel proprietary formulation <sup>3</sup>
- Drug core is coated in a polymer layer designed to release drug at a near-constant rate up to one year <sup>3</sup>

## Potential Mode of Action of EP-104GI In Eosinophilic Esophagitis

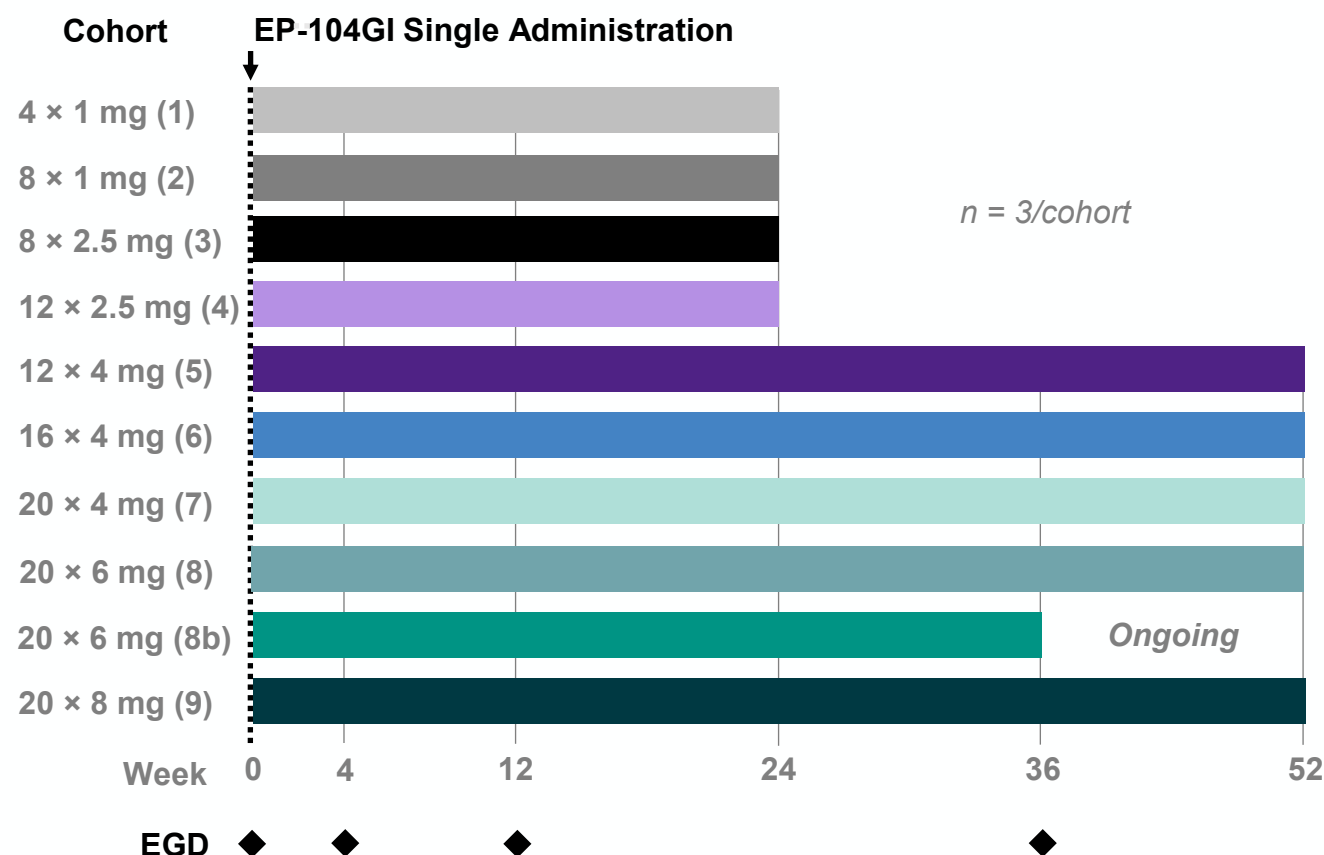


# RESOLVE (NCT05608681): Phase 1b/2 Multicenter, Open-Label, Dose-Escalation and Optimization Trial of EP-104GI In EoE

## Phase 1b - Dose Escalation Portion

*Aims to determine the safety, tolerability, PK and dose/pattern of administration of EP-104GI*

- EP-104GI was administered in dose cohorts of 3 participants in escalating number of injections or dose/injection
  - Administration for 2 dose cohorts (8b & 9) was performed using updated needle / catheter / concentration combinations
- EGDs were performed at Day 0 and weeks 4, 12 & 36
  - Improvements from baseline in EoE histopathology assessed using **EoE Histology Scoring System (EoEHSS)** (exploratory analysis)
- Ongoing EoEHSS data were included in this provisional analysis<sup>§</sup>



# Baseline Demographics & Characteristics

- Baseline demographics, histology, and symptom scores were overall balanced between dose cohorts

## RESOLVE Phase 1b – Baseline Demographics And Characteristics (full analysis set) \*

|                                            | 4 x 1 mg<br>(cohort 1) | 8 x 1 mg<br>(cohort 2) | 8 x 2.5 mg<br>(cohort 3) | 12 x 2.5 mg<br>(cohort 4) | 12 x 4 mg<br>(cohort 5) | 16 x 4 mg<br>(cohort 6) | 20 x 4 mg<br>(cohort 7) | 20 x 6 mg<br>(cohort 8) | 20 x 6 mg<br>(cohort 8b) ** | 20 x 8 mg<br>(cohort 9)** | Total              |
|--------------------------------------------|------------------------|------------------------|--------------------------|---------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-----------------------------|---------------------------|--------------------|
| <b>n</b>                                   | 3                      | 3                      | 3                        | 3                         | 3                       | 3                       | 3                       | 3                       | 3                           | 3                         | <b>30</b>          |
| <b>Age, years, mean ±std</b>               | 31 ±11                 | 51 ±16                 | 52 ±22                   | 45 ±12                    | 40 ±12                  | 41 ±9                   | 42 ±11                  | 37 ±13                  | 31 ±9                       | 41 ±16                    | <b>41 ±13</b>      |
| <b>Sex, Male n</b>                         | 1/3                    | 0/3                    | 1/3                      | 0/3                       | 2/3                     | 3/3                     | 1/3                     | 0/3                     | 2/3                         | 2/3                       | <b>12/30 (40%)</b> |
| <b>BMI, mean (kg/m<sup>2</sup>) ±std</b>   | 21.6 ±4.1              | 23.8 ±3.3              | 20.8 ±0.5                | 29.3 ±6.8                 | 28.1 ±4.0               | 28.5 ±5.5               | 33.0 ±12.5              | 28.8 ±8.0               | 26.5 ±4.0                   | 22.2 ±2.9                 | <b>26.3 ±6.3</b>   |
| <b>Disease Characteristics</b>             |                        |                        |                          |                           |                         |                         |                         |                         |                             |                           |                    |
| <b>Disease Duration, mean (years) ±std</b> | 4.6 ±3.0               | 4.2 ±3.8               | 6.7 ±2.5                 | 3.1 ±2.2                  | 3.5 ±3.9                | 9.5 ±9.4                | 4.1 ±3.2                | 5.0 ±6.0                | 2.0 ±1.7                    | 3.4 ±3.0                  | <b>4.6 ±4.2</b>    |
| <b>EoEHSS***<br/>mean ±std</b>             | Grade                  | 0.55 ±0.04             | 0.60 ±0.08               | 0.32 ±0.24                | 0.65 ±0.06              | 0.51 ±0.07              | 0.50 ±0.15              | 0.54 ±0.06              | 0.42 ±0.25                  | 0.64 ±0.18                | <b>0.53 ±0.15</b>  |
|                                            | Stage                  | 0.54 ±0.03             | 0.66 ±0.12               | 0.45 ±0.35                | 0.73 ±0.13              | 0.62 ±0.14              | 0.61 ±0.20              | 0.56 ±0.11              | 0.46 ±0.26                  | 0.59 ±0.16                | <b>0.59 ±0.18</b>  |
| <b>SDI mean ±std</b>                       | 5.3 ±0.6               | 6.7 ±0.6               | 6.0 ±1.0                 | 7.3 ±1.2                  | 5.7 ±0.6                | 6.3 ±0.6                | 5.0 ±0                  | 5.1 ±0                  | 6.0 ±0                      | 5.7 ±1.2                  | <b>5.9 ±1.0</b>    |

\* The full analysis set included only participants treated per protocol, without participant replacement

\*\* Administration for 2 dose cohorts (8b & 9) was performed using updated needle/catheter/concentration combinations

\*\*\* Assessed at the 4 worst affected biopsy locations, from the area of the esophagus receiving treatment based on Peak Eosinophil Count, as a composite score normalized on a 0-1 scale

# No Dose-Limiting Toxicities Observed During Dose Escalation

- Injections were escalated between cohorts from 4 to 20 injections with no observed dose-limiting toxicities.
- EP-104GI was safe and well tolerated to date for all dose cohorts, with no drug-related serious adverse events.

## RESOLVE Phase 1b - Treatment-Emergent Adverse Events (TEAEs) Reported (safety analysis set\*) §

|                                       | 4 x 1 mg<br>(cohort 1) | 8 x 1 mg<br>(cohort 2) | 8 x 2.5 mg<br>(cohort 3) | 12 x 2.5 mg<br>(cohort 4) | 12 x 4 mg<br>(cohort 5) | 16 x 4 mg<br>(cohort 6) | 20 x 4 mg<br>(cohort 7) | 20 x 6 mg<br>(cohort 8) | 20 x 6 mg<br>(cohort 8b) | 20 x 8 mg<br>(cohort 9) | Total     |
|---------------------------------------|------------------------|------------------------|--------------------------|---------------------------|-------------------------|-------------------------|-------------------------|-------------------------|--------------------------|-------------------------|-----------|
| n                                     | 3                      | 3                      | 3                        | 3                         | 3                       | 3                       | 4*                      | 3                       | 4*                       | 3                       | 32        |
| Any TEAE                              | 3 (100)                | 1 (33.3)               | 2 (66.7)                 | 2 (66.7)                  | 2 (66.7)                | 2 (66.7)                | 4 (100)                 | 3 (100)                 | 4 (100)                  | 3 (100)                 | 26 (81.2) |
| Serious TEAEs                         | 0 (0)                  | 0 (0)                  | 0 (0)                    | 0 (0)                     | 0 (0)                   | 0 (0)                   | 0 (0)                   | 0 (0)                   | 0 (0)                    | 0 (0)                   | 0 (0)     |
| <b>Most Common TEAE (≥3/32, n(%))</b> |                        |                        |                          |                           |                         |                         |                         |                         |                          |                         |           |
| Nausea                                | 1 (33.3)               | 0 (0)                  | 0 (0)                    | 1 (33.3)                  | 0 (0)                   | 0 (0)                   | 1 (25)                  | 1 (33.3)                | 1 (25)                   | 0 (0)                   | 5 (15.6)  |
| Chest pain                            | 0 (0)                  | 0 (0)                  | 1 (33.3)                 | 0 (0)                     | 0 (0)                   | 0 (0)                   | 0 (0)                   | 1 (33.3)                | 1 (25)                   | 1 (33.3)                | 4 (12.5)  |
| Dyspepsia                             | 0 (0)                  | 0 (0)                  | 0 (0)                    | 0 (0)                     | 0 (0)                   | 0 (0)                   | 0 (0)                   | 1 (33.3)                | 3 (75)                   | 0 (0)                   | 4 (12.5)  |
| Nasopharyngitis                       | 0 (0)                  | 0 (0)                  | 0 (0)                    | 0 (0)                     | 1 (33.3)                | 0 (0)                   | 1 (25)                  | 0 (0)                   | 2 (50)                   | 0 (0)                   | 4 (12.5)  |
| Dizziness                             | 0 (0)                  | 0 (0)                  | 0 (0)                    | 0 (0)                     | 0 (0)                   | 0 (0)                   | 1 (25)                  | 1 (33.3)                | 1 (25)                   | 0 (0)                   | 3 (9.4)   |
| Fatigue                               | 0 (0)                  | 0 (0)                  | 0 (0)                    | 0 (0)                     | 0 (0)                   | 0 (0)                   | 1 (25)                  | 0 (0)                   | 2 (50)                   | 0 (0)                   | 3 (9.4)   |

\* The safety analysis set included two participants (in cohort 7 & 8b) with injection protocol deviations not included in efficacy analyses

§ Cut-off: September 15, 2026

TEAE, Treatment-Emergent Adverse Event.

# EoE Histological Score System (EoEHSS) Assesses Disease Histopathology

## EoEHSS

- Assesses histopathological features of EoE:<sup>1</sup>
  - Grade (severity)
  - Stage (extent)
- Based on 8 features (each scored 0-3) of inflammation and structural remodelling

## Sub scores <sup>1</sup>

- EoEHSS **inflammatory** (EoEHSS-i)
  - *Based on features of inflammation*
- EoEHSS **architectural** (EoEHSS-a)
  - *Based on features of structural remodeling*

## Features of EoE Histological Score System

### Inflammatory Features

Eosinophilic Surface Layering (ESL)

Eosinophilic Abscess (EA)

Surface Epithelial Alteration (SEA)

Eosinophilic Inflammation (EI)

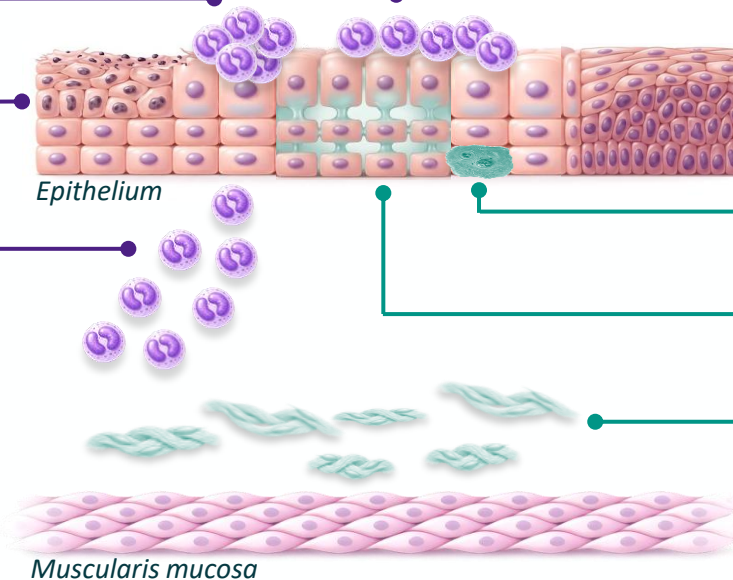
### Structural Features

Basal Zone Hyperplasia (BZH)

Dyskeratotic Epithelial Cell (DEC)

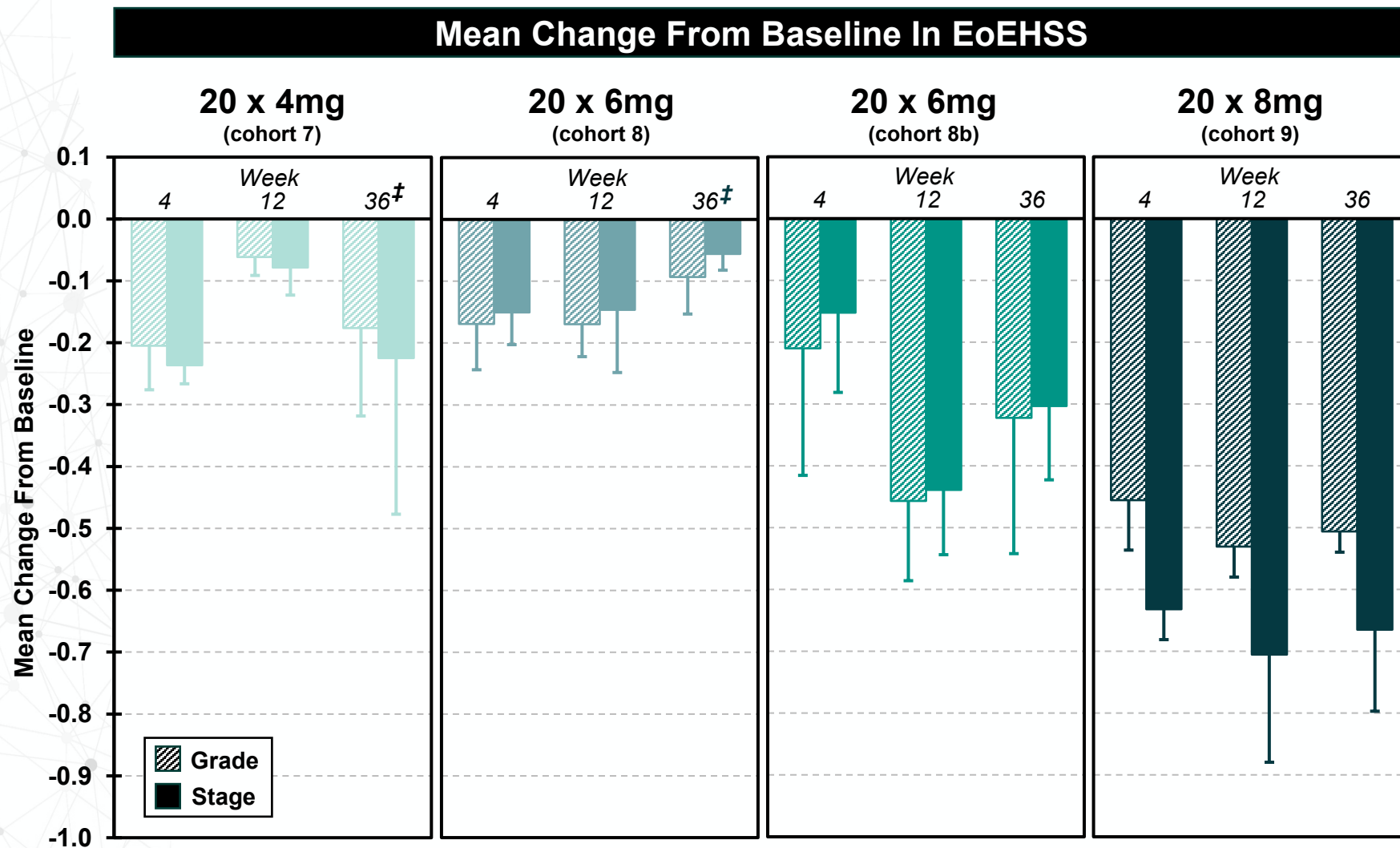
Dilated Interstitial Spaces (DIS)

Lamina Propria Fibrosis (LPF)



# EoE Histology Scoring System (EoEHSS) After EP-104GI Administration

- EoEHSS was assessed at the 4 worst affected biopsy locations, based on Peak Eosinophil Count and normalized as 0-1 composite scores
- All cohorts receiving 20 injections demonstrated numerical improvements in grade and stage from baseline in EoEHSS
  - From week 4
  - Persisting to week 36
- Largest, sustained improvements for 20x6mg (8b) and 20X8mg (9)



Error bars represent standard deviation

Provisional descriptive analysis of full analysis set; results subject to change

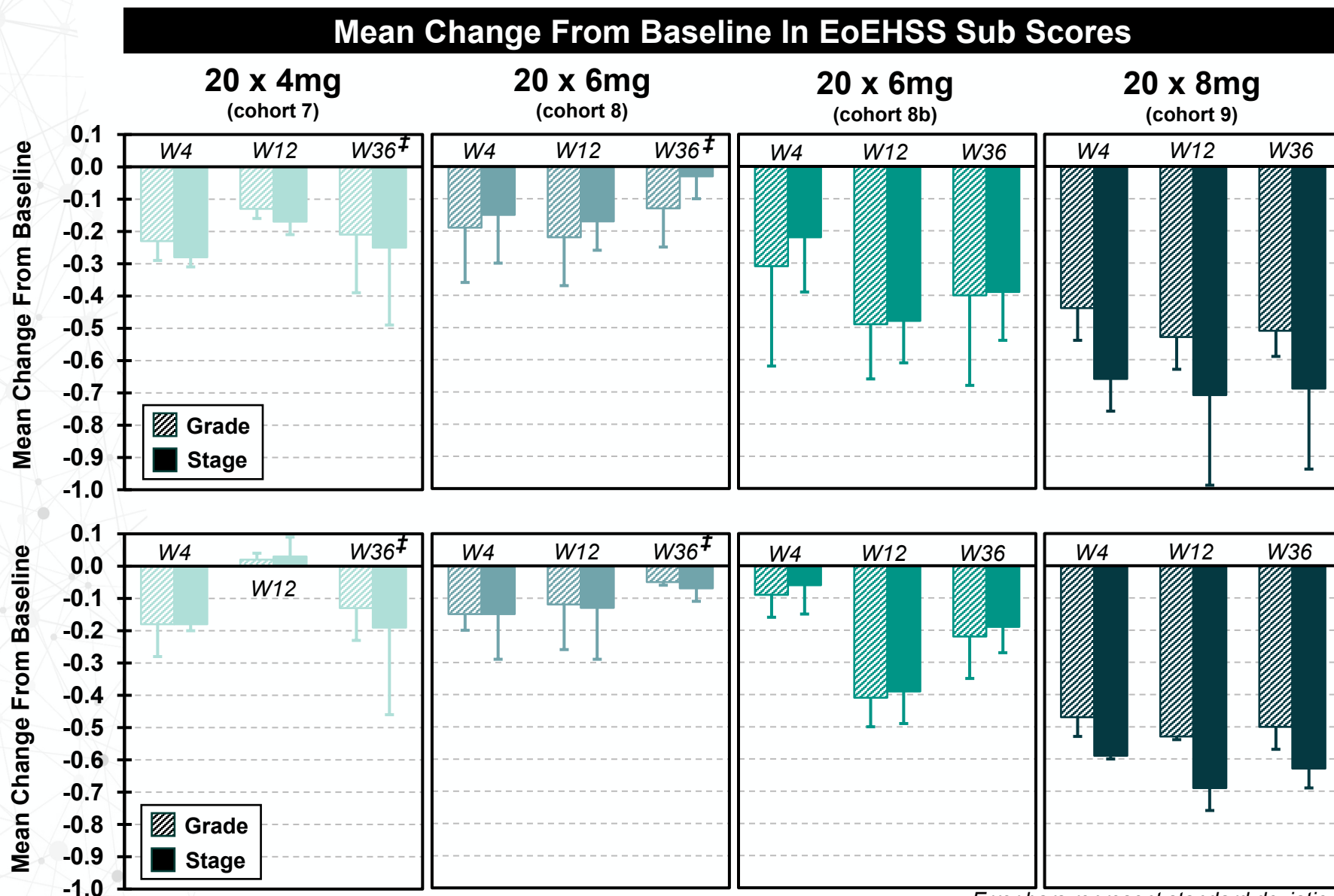
n=3/cohort, except for ‡: n=2

# EoEHSS Sub Scores After EP-104GI Administration

- Overall improvements in both inflammatory and structural sub scores observed over 36 weeks
- Largest improvements for 20x6mg (8b) and 20X8mg (9), as per EoEHSS score

Inflammatory

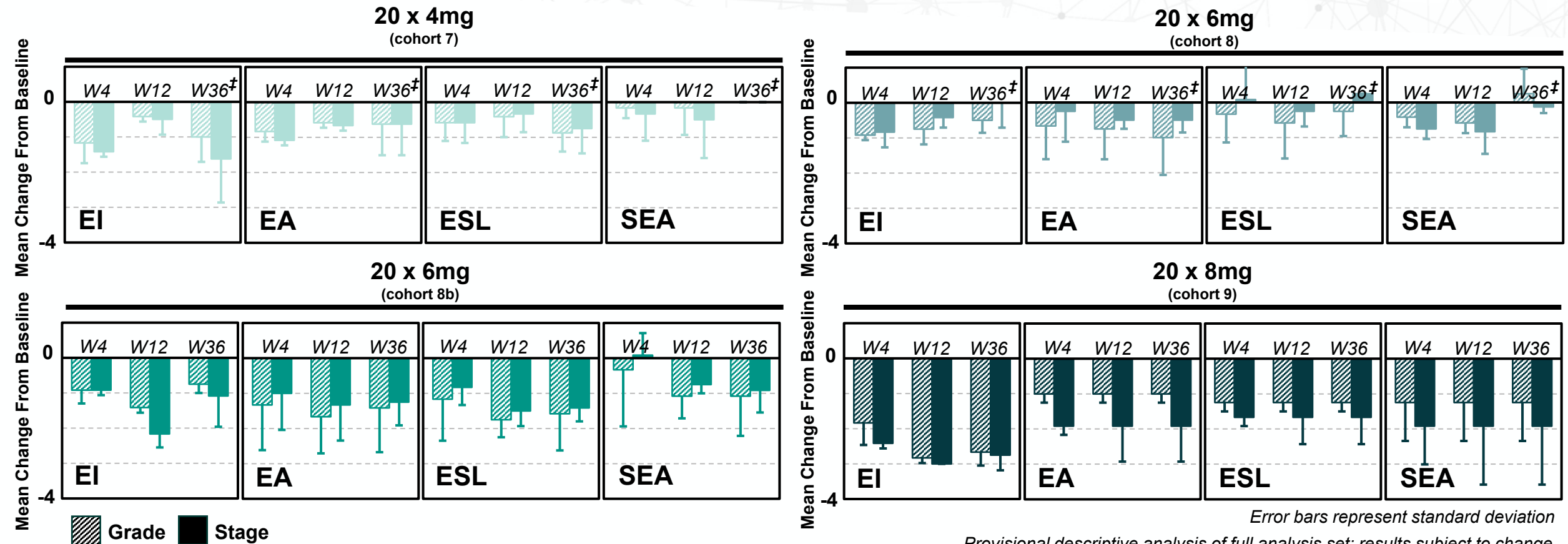
Architectural



Error bars represent standard deviation  
Provisional descriptive analysis of full analysis set; results subject to change  
n=3/cohort, except for ‡: n=2

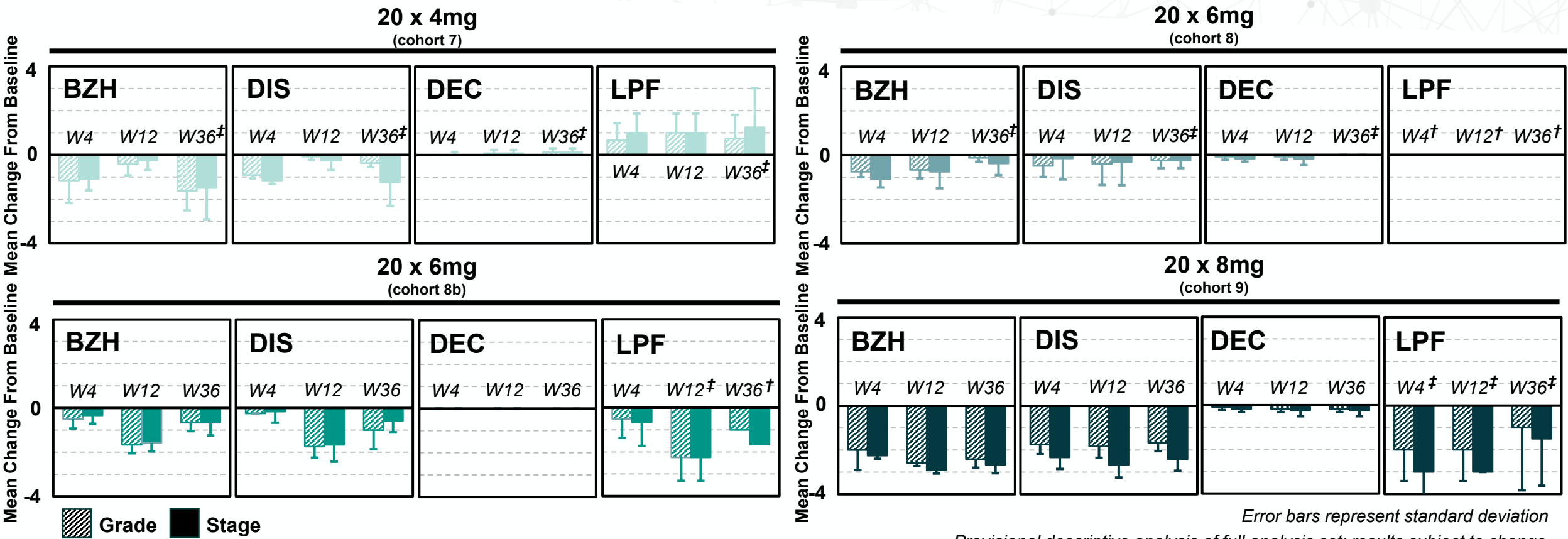
# EoEHSS Inflammatory Features After EP-104GI Administration

- Eosinophil-dependant features (inflammation (EI), abscesses (EA) and surface layering (ESL)) show numerical improvements over 36 weeks following a single EP-104GI administration
- Surface epithelial alteration (SEA) demonstrate more pronounced improvement in cohorts 20x6mg (8b) and 20x8mg (9) relative to other cohorts



# EoEHSS Structural Features After EP-104GI Administration

- Basal Zone Hyperplasia (BZH) and Dilated Interstitial Space (DIS) show the most consistent improvements across all four doses
- Lamina Propria Fibrosis (LPF) saw improvements in cohorts 20x6mg (8b) and 20x8mg (9)



Error bars represent standard deviation  
Provisional descriptive analysis of full analysis set; results subject to change  
n=3/cohort, except for †: n=1, ‡: n=2

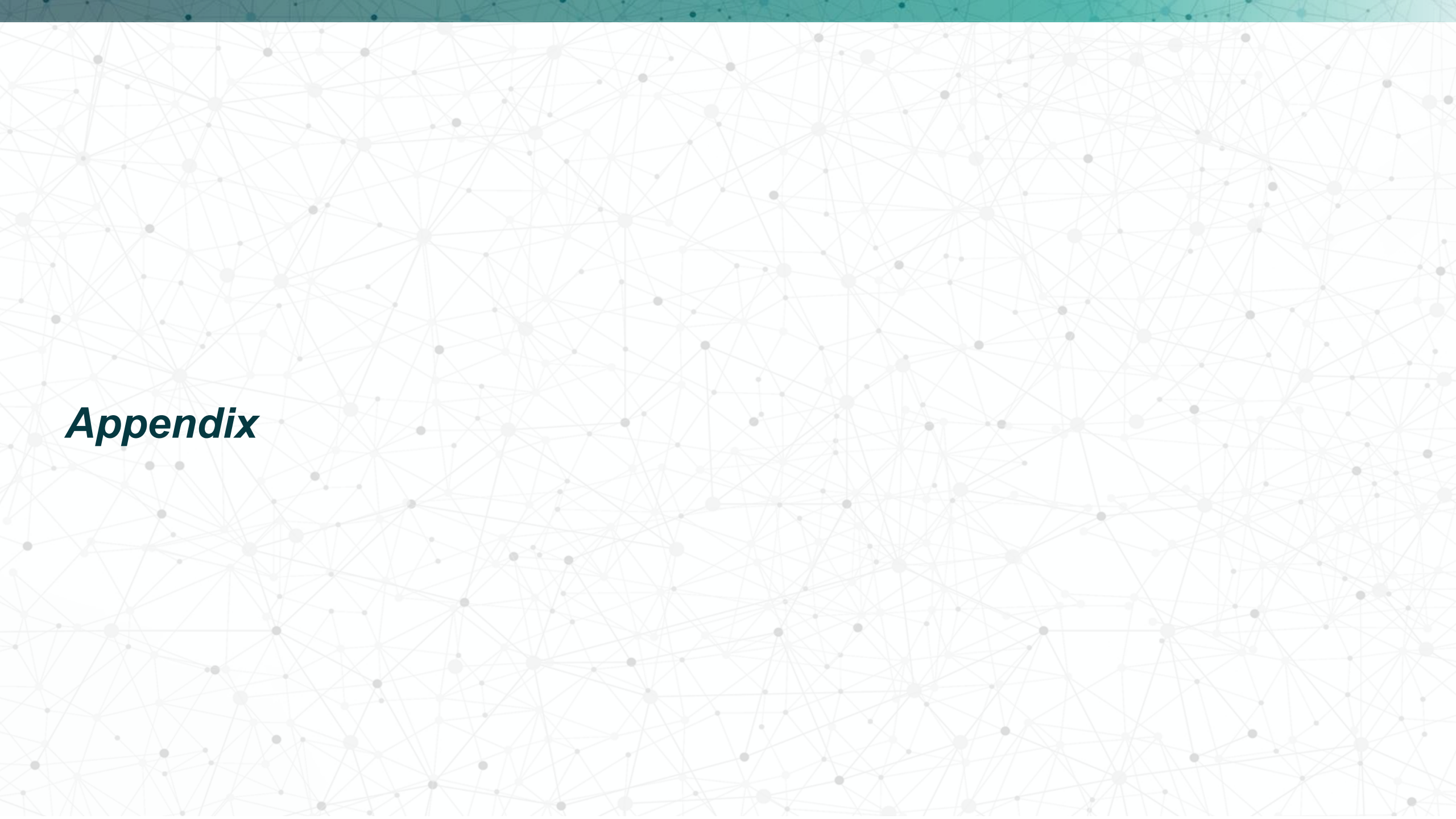
# Conclusions – Phase 1b Part of RESOLVE

Dose escalation of EP-104GI has been safe, and well tolerated to date, with no signs of dose-limiting toxicities or treatment-related adverse events.

These results demonstrate consistent long-term improvements from baseline in eosinophilic and non-eosinophilic features of EoE histopathology following a single EP-104GI administration.

Study limitations include small cohort numbers, lack of placebo control and open-label design.

Provisional results support selection of EP-104GI 20 x 6 mg & 20 x 8 mg dose regimens for optimization in the ongoing, blinded, placebo-controlled, randomized phase 2 portion of the RESOLVE trial.

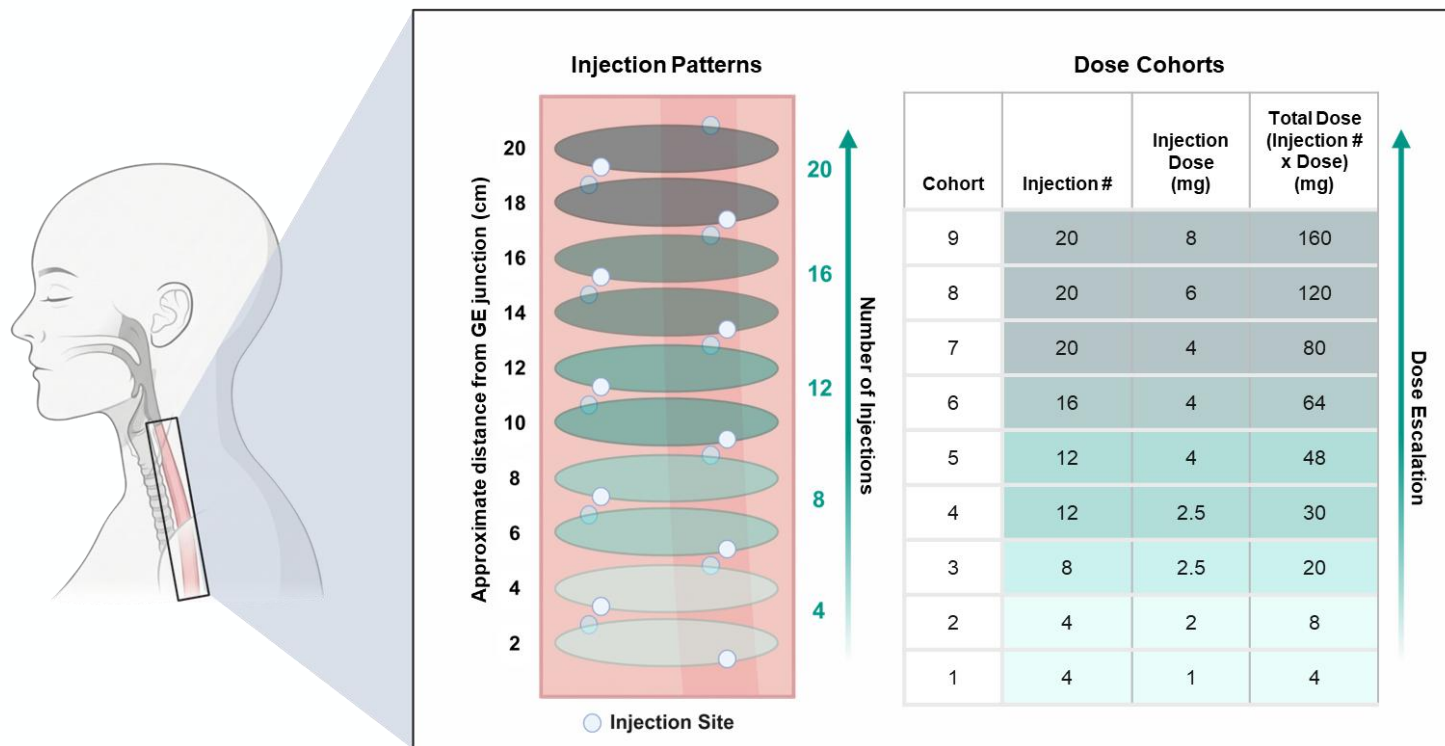


# ***Appendix***

# EP-104GI is Administered in a Single Procedure, at Baseline

- EP-104GI was injected in the esophagus submucosa during endoscopy with a through-the-scope injector
- Injected in alternating quadrants in levels separated by 2 cm
- EP-104GI was injected in dose cohorts in escalating:
  - number of sites (4, 8, 12, 16, 20)
  - or
  - dose per site (1, 2.5, 4, 6, 8 mg)

## EP-104GI Injection Patterns in Phase 1b Dose Escalation in RESOLVE



# EoEHSS Score & Sub Scores Baseline Values *(mean ±sd)*

|            |       | 4 x 1mg    | 8 x 1mg    | 8 x 2.5mg  | 12 x 2.5mg | 12 x 4mg   | 16 x 4mg   | 20 x 4mg   | 20 x 6mg   | 20 x 6mg    | 20 x 8mg   |
|------------|-------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|
|            |       | (cohort 1) | (cohort 2) | (cohort 3) | (cohort 4) | (cohort 5) | (cohort 6) | (cohort 7) | (cohort 8) | (cohort 8b) | (cohort 9) |
| EoEHSS     | Grade | 0.55 ±0.04 | 0.60 ±0.08 | 0.32 ±0.24 | 0.65 ±0.06 | 0.51 ±0.07 | 0.50 ±0.15 | 0.54 ±0.06 | 0.42 ±0.25 | 0.64 ±0.18  | 0.57 ±0.02 |
|            | Stage | 0.54 ±0.03 | 0.66 ±0.12 | 0.45 ±0.35 | 0.73 ±0.13 | 0.62 ±0.14 | 0.61 ±0.20 | 0.56 ±0.11 | 0.46 ±0.26 | 0.59 ±0.16  | 0.72 ±0.14 |
| Sub scores |       |            |            |            |            |            |            |            |            |             |            |
| EoEHSS-i   | Grade | 0.46 ±0.07 | 0.61 ±0.06 | 0.32 ±0.28 | 0.60 ±0.09 | 0.49 ±0.09 | 0.44 ±0.17 | 0.47 ±0.05 | 0.36 ±0.24 | 0.65 ±0.23  | 0.54 ±0.10 |
|            | Stage | 0.43 ±0.06 | 0.61 ±0.20 | 0.42 ±0.36 | 0.68 ±0.17 | 0.60 ±0.21 | 0.53 ±0.32 | 0.51 ±0.14 | 0.35 ±0.25 | 0.58 ±0.14  | 0.71 ±0.28 |
| EoEHSS-a   | Grade | 0.65 ±0.02 | 0.58 ±0.11 | 0.32 ±0.18 | 0.71 ±0.04 | 0.55 ±0.11 | 0.58 ±0.15 | 0.63 ±0.08 | 0.48 ±0.26 | 0.63 ±0.14  | 0.60 ±0.11 |
|            | Stage | 0.67 ±0.04 | 0.72 ±0.05 | 0.50 ±0.33 | 0.78 ±0.09 | 0.64 ±0.09 | 0.69 ±0.08 | 0.62 ±0.08 | 0.58 ±0.27 | 0.62 ±0.18  | 0.73 ±0.04 |

# EoEHSS Features Baseline Values (mean ±sd)

|                               |       | 4 x 1mg    | 8 x 1mg    | 8 x 2.5mg  | 12 x 2.5mg | 12 x 4mg   | 16 x 4mg   | 20 x 4mg   | 20 x 6mg    | 20 x 6mg    | 20 x 8mg   |
|-------------------------------|-------|------------|------------|------------|------------|------------|------------|------------|-------------|-------------|------------|
|                               |       | (cohort 1) | (cohort 2) | (cohort 3) | (cohort 4) | (cohort 5) | (cohort 6) | (cohort 7) | (cohort 8)  | (cohort 8b) | (cohort 9) |
| Inflammatory Features         |       |            |            |            |            |            |            |            |             |             |            |
| Eosinophilic Inflammation     | Grade | 2.67 ±0.58 | 3.00 ±0.00 | 2.00 ±1.73 | 3.00 ±0.00 | 2.83 ±0.29 | 2.83 ±0.29 | 3.00 ±0.00 | 2.177 ±0.88 | 2.83 ±0.29  | 3.00 ±0.00 |
|                               | Stage | 3.00 ±0.00 | 3.00 ±0.00 | 2.00 ±1.73 | 3.00 ±0.00 | 2.83 ±0.29 | 2.75 ±0.43 | 3.00 ±0.00 | 2.08 ±1.59  | 2.67 ±0.58  | 3.00 ±0.00 |
| Eosinophilic Abscesses        | Grade | 1.17 ±0.29 | 1.17±0.29  | 0.83 ±1.04 | 1.17 ±0.29 | 0.83 ±0.29 | 0.75 ±0.66 | 1.00 ±0.25 | 0.83 ±1.01  | 1.75 ±1.15  | 1.00 ±0.25 |
|                               | Stage | 1.00 ±0.00 | 1.50 ±0.50 | 1.00 ±1.00 | 1.67 ±0.58 | 1.50 ±0.87 | 1.25 ±1.39 | 1.25 ±0.50 | 0.58 ±0.38  | 1.58 ±0.88  | 1.92 ±1.01 |
| Eosinophil Surface Layering   | Grade | 1.17 ±0.76 | 2.00 ±1.00 | 0.67 ±0.76 | 1.67 ±0.76 | 1.00 ±0.50 | 0.83 ±0.76 | 0.92 ±0.58 | 0.58 ±1.01  | 1.92 ±0.76  | 1.25 ±0.25 |
|                               | Stage | 0.83 ±0.29 | 1.67 ±0.76 | 1.17 ±1.26 | 2.00 ±0.87 | 1.33 ±0.58 | 1.08 ±1.13 | 0.83 ±0.52 | 0.25 ±0.43  | 1.67 ±0.38  | 1.67 ±0.76 |
| Surface Epithelial Alteration | Grade | 0.50 ±0.87 | 1.17 ±0.29 | 0.33 ±0.58 | 1.33 ±0.58 | 1.17 ±1.04 | 0.83 ±0.88 | 0.67 ±1.15 | 0.75 ±0.50  | 1.25 ±0.90  | 1.25 ±1.09 |
|                               | Stage | 0.33 ±0.58 | 1.17 ±1.15 | 0.83 ±1.44 | 1.50 ±0.87 | 1.50 ±1.32 | 1.33 ±1.38 | 1.00 ±1.73 | 1.25 ±1.32  | 1.00 ±0.50  | 1.92 ±1.66 |
| Structural Features           |       |            |            |            |            |            |            |            |             |             |            |
| Basal Zone Hyperplasia        | Grade | 2.83 ±0.29 | 2.67 ±0.29 | 1.50 ±1.32 | 2.83 ±0.29 | 2.67 ±0.29 | 2.58 ±0.72 | 3.00 ±0.00 | 2.00 ±1.00  | 2.50 ±0.87  | 2.67 ±0.14 |
|                               | Stage | 3.00 ±0.00 | 3.00 ±0.00 | 2.00 ±1.73 | 3.00 ±0.00 | 3.00 ±0.00 | 2.83 ±0.29 | 3.00 ±0.00 | 2.50 ±0.87  | 2.50 ±0.87  | 3.00 ±0.00 |
| Dilated Intercellular Space   | Grade | 3.00 ±0.00 | 2.50 ±0.87 | 1.33 ±0.29 | 2.83 ±0.29 | 2.33 ±0.58 | 2.25 ±0.75 | 3.00 ±0.00 | 2.08 ±0.88  | 2.75 ±0.25  | 2.42 ±0.52 |
|                               | Stage | 3.00 ±0.00 | 3.00 ±0.00 | 2.33 ±1.15 | 3.00 ±0.00 | 2.83 ±0.29 | 2.75 ±0.43 | 3.00 ±0.00 | 2.42 ±1.01  | 2.67 ±0.58  | 3.00 ±0.00 |
| Dyskeratotic Epithelial Cells | Grade | 0.00 ±0.00 | 0.00 ±0.00 | 0.00 ±0.00 | 0.33 ±0.58 | 0.00 ±0.00 | 0.08 ±0.14 | 0.00 ±0.00 | 0.08 ±0.14  | 0.00 ±0.00  | 0.17 ±0.14 |
|                               | Stage | 0.00 ±0.00 | 0.00 ±0.00 | 0.00 ±0.00 | 0.50 ±0.87 | 0.00 ±0.00 | 0.17 ±0.29 | 0.00 ±0.00 | 0.17 ±0.19  | 0.00 ±0.00  | 0.25 ±0.25 |
| Lamina Propria Fibrosis       | Grade | 2.25 ±1.06 | 1.75 ±0.35 | 2.00       | 2.67 ±0.58 | 1.00 ±1.41 | 2.44 ±0.51 | 1.50 ±1.50 | 1.50 ±2.12  | 3.00 ±0.00  | 1.67 ±1.15 |
|                               | Stage | 2.25 ±1.06 | 3.00 ±0.00 | 3.00       | 3.00 ±0.00 | 1.50 ±2.12 | 3.00 ±0.00 | 1.17 ±1.61 | 1.50 ±2.12  | 3.00 ±0.00  | 3.00 ±0.00 |