RESOLVE: A Phase 1b/2 Study Evaluating the Safety, Efficacy, and Pharmacokinetics of EP-104GI in Adults with Eosinophilic Esophagitis

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BACKGROUND

- Eosinophilic esophagitis (EoE) is a chronic esophageal disease, characterized by local inflammation potentially leading to fibrosis [1]
- It is one of the most common causes of swallowing difficulties (dysphagia) and food impaction in adults [2]
- Increases in EoE prevalence highlight the need for new therapies
- Swallowed topical corticosteroids, including fluticasone propionate, are used in EoE, but their use may be limited by transient contact, class-related side effects and adherence challenges [4,5]

EP-104GI

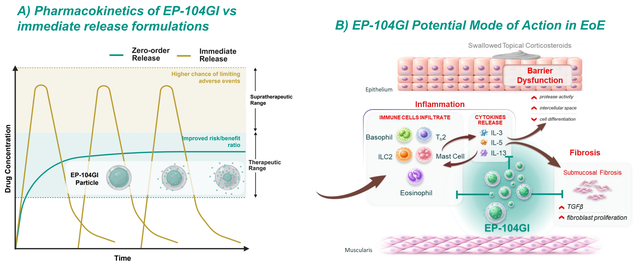

Figure 1. Pharmacokinetics and Mode of Action of EP-104GI in EoE

- EP-104GI is a novel long-acting submucosal fluticasone propionate microparticles formulation designed for local drug delivery, in sustained zero-order release [6,7] (Fig 1a)
- Local fluticasone release by EP-104GI has the potential to inhibit atopic cytokine release, immune cell infiltration and fibrotic remodelling progression (Fig 1b)

REFERENCES

1. Dellon et al. (2025) AJG 120(1):31-59 2. Furuta et al. (2015) NEJM 373:1640–1648 3. Thel et al (2025) CGH 2:272-280.e8. 4. Schoepfer et al. (2024) Inflamm Intest Dis. 9(1):199–209 5. Haasnoot et al. (2022) 1;117(9):1412-1418. 6. Główczewski et al. (2022) J Clin Med 11(5):1454. 7. Webb et al. (2024) AJG 119(10S):p S445-S446

RESOLVE (NCT05608681) is a Phase 1b/2 study evaluating EP-104GI in adults with EoE

PART 1: Dose Escalation

- **Part 1 is a dose-escalation Phase 1b trial to identify dose and pattern for further optimization**
- Participants received a single administration of EP-104GI at baseline with follow-up through 24 or 52 weeks (Fig 2)
- EP-104GI was administered as submucosal injections in the esophageal wall, in dose cohorts increasing in both the number of injections or per-injection dose to achieve total doses from 4 mg to 160 mg (Fig 3)
- Efficacy was assessed by peak eosinophil counts (PEC), EoE Histology Scoring System (EoEHSS), EoE Endoscopic Reference Score (EREFS) and Straumann Dysphagia Index (SDI)
- Primary endpoints included pharmacokinetics (PK), safety, and tolerability

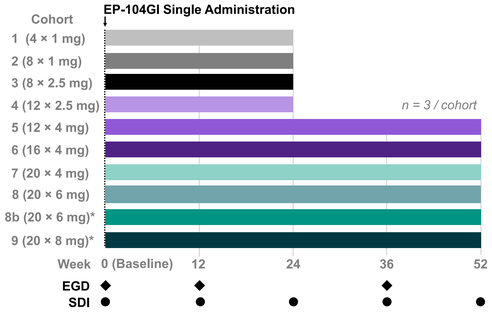

Figure 2. RESOLVE Part 1 Dose Escalation Design

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

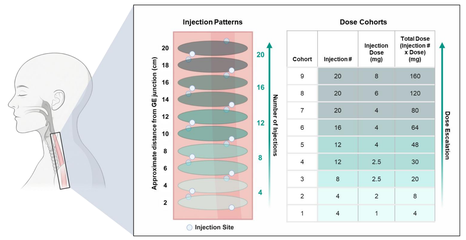

Figure 3. Injection Patterns in RESOLVE Part 1

PART 2: Dose Optimization

- **Part 2 is a randomized dose-optimization Phase 2 trial comparing 2 EP-104GI doses versus vehicle control**
- Participants receive a single administration at baseline and are followed for 52 weeks with a placebo crossover at Week 24 (Fig 4)
- Subjects are randomized 1:1:1 to EP-104GI 120 mg (20 × 6 mg), EP-104GI 160 mg (20 × 8 mg) or placebo (Fig 4)
- EP-104GI is delivered as 20 submucosal injections distributed along the length of the esophagus (Fig 5)
- Efficacy is assessed by esophageal inflammation and remodelling measures (PEC, EoEHSS, EREFS) and dysphagia symptom scores (SDI, Dysphagia Symptom Questionnaire [DSQ])
- Primary endpoint is the change from baseline in EoEHSS score

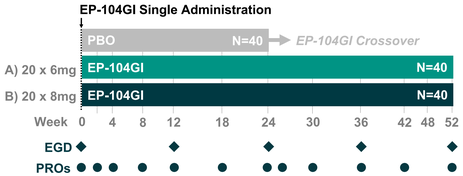

Figure 4. RESOLVE Part 2 Dose Optimization Design

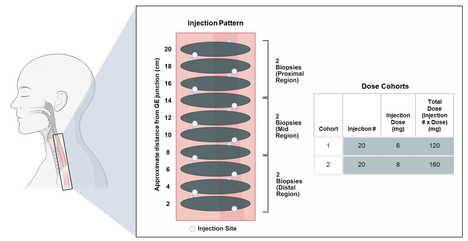

Figure 5. Injection Patterns in RESOLVE Part 2

Dose Selection

- Two doses were selected for dose-optimization in Phase 2
- Dose escalation proceeded until a total dose of 160 mg (20 × 8 mg) was achieved, without dose-limiting toxicity
- Safety review during dose escalation showed no serious adverse events, laboratory abnormalities of concern or signs of adrenal insufficiency
- Preliminary efficacy assessments suggested that greater histologic and symptom responses may be achievable at higher doses

CONCLUSION

The design of RESOLVE allowed the identification and investigation of appropriate doses and injection patterns for development of EP-104GI in the treatment of EoE

***Abbreviations**: AUC, Area Under The Curve; DSQ, Dysphagia Symptom Questionnaire;EGD, esophagogastroduodenoscopy; EoE, eosinophilic esophagitis; EoEHSS, EoE Histology Scoring System; EREFS, Eosinophilic Esophagitis Reference Score; GE, gastroesophageal; PBO, placebo; PEC, Peak Eosinophil Count; PK, pharmacokinetics; PRO, patient-reported outcome; SDI, Straumann Dysphagia Index.*