Efficacy and Pharmacokinetic Results From Ongoing Dose Escalation in RESOLVE, a Phase 1b/2a Study of EP-104GI (Extended-Release Fluticasone Propionate Intra-Esophageal Injection) for Eosinophilic Esophagitis

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Introduction

Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease characterized by inflammation, influx of eosinophils and esophageal remodeling. EP-104GI is an investigational long-acting fluticasone propionate (FP) injectable suspension being developed as a first-in-class treatment for EoE. EP-104GI consists of polymer-coated crystals of FP that release at a pre-defined rate via diffusion at the injection site, reducing peak concentrations while prolonging the therapeutic window (Fig 1).

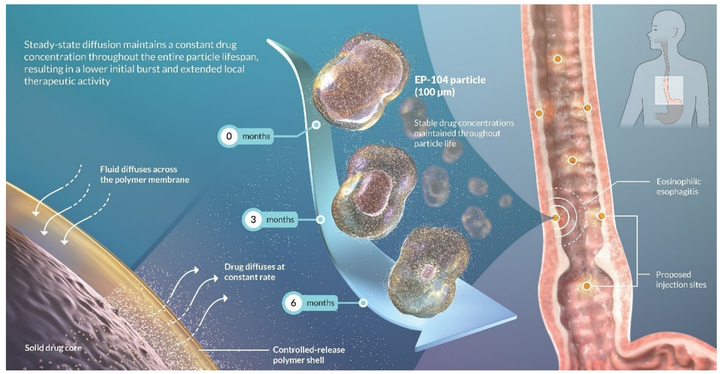

Figure 1: Mechanism of action of EP-104GI

Aim & Methods

RESOLVE (NCT05608681): Phase 1b/2a, multicenter, open-label, dose-escalation study in adults with histologically confirmed active EoE.

- Single dose via 4-20 injections into the esophageal wall.
- Dose escalations increase the dose per site and/or number of sites in cohorts of 3 patients.
- Participants in cohorts 1-4 were assessed for up to 24 weeks (subsequent cohorts will be assessed for 52 weeks).

Assessments:

- Esophageal biopsies: Peak Eosinophil Count (PEC) and Eosinophilic Esophagitis Histology Scoring System (EoEHSS)
- Patient-reported symptom outcomes (PROs): Likert scales scoring 0-10.
- Safety and pharmacokinetics.

JH, AM, MMK, CD, VP: employees of Eupraxia Pharmaceuticals. **ED:** Research funding: Adare/Ellodi, Allakos, Arena/Pfizer, AstraZeneca, Eupraxia, Ferring, GSK, Meritage, Miraca, Nutricia, Celgene/Receptos/BMS, Regeneron, Revolo, Shire/Takeda Consultant: Abbott, Abbvie, Adare/Ellodi, Aimmune, Akesobio, Alfasigma, ALK, Allakos, Amgen, Apollo, Aqilion, Arena/Pfizer, Aslan, AstraZeneca, Avir, Biorasi, Calypso, Celgene/Receptos/BMS, Celldex, Eli Lilly, EsoCap, Eupraxia, Dr. Falk Pharma, Ferring, GSK, Gossamer Bio, Holoclara, Invea, Knightpoint, Landos, LucidDx, Morphic, Nexstone Immunology/Uniquity, Nutricia, Parexel/Calyx, Phathom, Regeneron, Revolo, Robarts/Alimentiv, Salix, Sanofi, Shire/Takeda, Target RWE, Upstream Bio Educational grant: Allakos, Aqilion, Holoclara, Invea. **HHK:** advisory board and speaker's bureau for Sanofi. **AJB:** received research funding from Nutricia, Thelial, Sanofi/Regeneron, SST, and Dr. Falk Pharma and received speaker and/or consulting fees from Laborie, Medtronic, BMS, Dr. Falk Pharma, Calypso Biotech, Eupraxia, Aqilion, Alimentiv, Sanofi/Regeneron, Reckitt and AstraZeneca. **NG:** nothing to declare.

Results from Cohorts 1-4

- Mild-moderate AEs; none related to EP-104GI (Table 1).
- Glucose levels stable post-dose (Fig 2).
- Serum cortisol levels within normal range (Fig 2).
- No symptoms of adrenal insufficiency.
- Plasma FP concentrations show a low initial peak and increasing exposure with dose.

Cohort 1 (4 mg total dose)		Cohort 2 (8 mg total dose)		Cohort 3 (20 mg total dose)		Cohort 4 (30 mg total dose)	
Event	Severity	Event	Severity	Event	Severity	Event	Severity
Pain after endoscopy	Mild*	Post-procedural tightness in throat	Mild*	Worsening of migraine	Mild	Nausea	Mild
Left occipital lymphadenopathy	Mild			Vaginal candidiasis	Mild	Infected rash – upper back	Mild
Nausea	Mild*			Chest Pain	Moderate		
Stomach bug	Mild			Sinus infection	Mild		
Chest pain	Moderate*			Viral gastroenteritis	Moderate		
Back pain	Moderate						

* At least possibly related to injection procedure

Note: All AEs unlikely related or unrelated to EP-104GI. Black borders indicate AEs experienced by the same patient

Table 1: Treatment emergent adverse events (verbatim term) after a single dose of EP-104GI

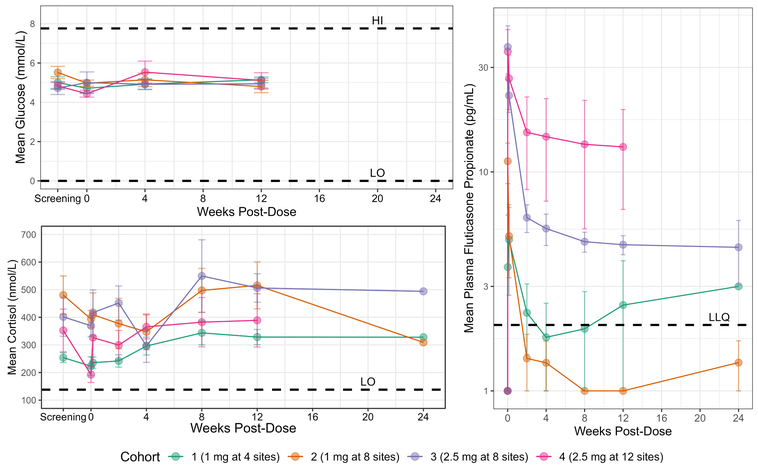

Figure 2: Mean serum cortisol, glucose, and serum fluticasone propionate

- By 12 weeks post-dose, 10/11 patients with available data showed decrease from baseline in SDI by 2 to 6 points or 25% to 100% (Fig 3).
- Of 11 patients with data available at Week 12, mean PEC scores at injection-area sites and EoEHSS composite grade and stage were reduced in 7 patients (Table 2).
- Data from 4 biopsy sites with the greatest decrease from baseline (of 16 assessed), showed a mean reduction in PEC of 67% at 12 weeks in cohort 4.

Cohort		Mean change in EoEHSS Composite Grade	Mean change in EoEHSS Composite Stage	Mean change in PEC
1[a]	1 mg at 4 sites (4 mg)	0.08 (15%)	0.10 (18%)	98 (109%)
2	1 mg at 8 sites (8 mg)	-0.13 (-20%)	-0.11 (-18%)	-51 (-34%)
3[b]	2.5 mg at 8 sites (20 mg)	-0.02 (-7%)	-0.06 (-15%)	-13 (-18%)
4	2.5 mg at 12 sites (30 mg)	-0.24 (-37%)	-0.26 (-39%)	1 (2%)

[a] One patient was lost to follow-up prior to Week 12 [b] One patient had a PEC of zero at baseline

Table 2: Week 12 mean change from baseline in EoEHSS composite grade and stage, and peak eosinophil count at injection sites

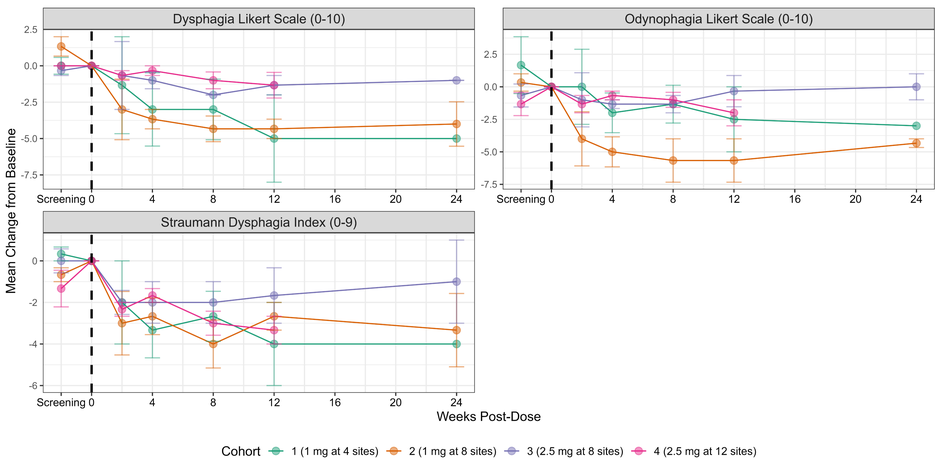

Figure 3: Mean change from baseline in patient reported outcomes

Conclusion

- These initial results indicate novel diffusion-based localized delivery of FP via EP-104GI injection into the esophagus is feasible and safe.
- Side-effects typically associated with swallowed/topical corticosteroids could be avoided with EP-104GI.
- Efficacy data suggest symptom outcomes and histologic response improve at higher doses of EP-104GI.
- Persistence of plasma FP and maintained reduction in symptom scores support the potential for at least 6 months interval between injections.
- The treatment interval may be further extended at the higher doses to be investigated; recruitment in this study is ongoing.