**Exhalation Delivery System With Fluticasone (EDS-FLU) for Chronic Rhinosinusitis (CRS): Integrated NAVIGATE I and NAVIGATE II Results**

**BACKGROUND**

- CRS is a high-prevalence condition characterized by chronic mucosal inflammation of the nose and paranasal sinuses; most CRS patients fall into subtypes based on the presence or absence of nasal polyps (CRSsNP and CRSsNP, respectively).
- The overall detrimental impact of CRS on quality of life (QoL) has been measured to be similar in magnitude to other serious diseases, such as CHF, COPD, and Parkinson’s disease.

**RESULTS**

- EDS-FLU has been extensively studied. This includes 2 pivotal, phase 3, randomized, fluticasone-controlled trials (NAVIGATE I and II) in CRSsNP.1,2 Studied patients were moderate to severe, and most had previously been treated with steroids and/or surgery. Results of both trials demonstrate that EDS-FLU produced statistically and clinically significant improvements in objective endoscopic assessments and in subjective, patient-reported symptom scores (on all defining symptoms), compared with EDS-placebo. These treatment benefits are further supported by clinically significant improvements in QoL, functioning, and disease severity. In this analysis, we present integrated efficacy and safety results from NAVIGATE I and II.

- **EDS-FLU** has been developed by (MOA) based on a new drug delivery system with a unique nasal valve actuation (NVA). The EDS MOA is described here: http://www.optinose.com/.

- **NAVIGATE I and II** are similarly designed, randomized, double-blind, parallel-group, multicenter, placebo-controlled trials with a 16-week, double-blind phase followed by an 8-week, active-treatment, extension phase in which all patients received EDS-FLU 372 µg. All treatment was BID (Figure 2).

**METHODS**

- The 186 and 372 µg doses were selected for further clinical development and commercialization and are reported here.

- **EDS-placebo comparator** was “active” in the sense that twice-daily saline may offer therapeutic benefit in CRS.

- Eligible patients were ≥ 18 years old, with a polyp grade of 1 to 3 in each of the nasal cavities and moderate to severe symptoms of nasal congestion/obstruction at entry. The comparator in both trials was an EDS-placebo delivering a saline-like deep nasal “lavage” BID using an EDS.

- For this integrated analysis, data were pooled by treatment group.

- Coptitomy endpoints: reduction of mean 7-day instantaneous morning (AM) nasal congestion/obstruction scores at week 4; reduction in total polyps grade at week 16 (using a nasal polyp grading scale of 0.3–9 per nostril), then summed, measured via nasendoscopy.

**CONCLUSIONS**

- In an integrated analysis of 2 large trials in CRSsNP, patients with moderate to severe symptoms, including those with a history of prior steroid use and/or surgery, EDS-FLU reduced subjective and objective evidence of inflammation (symptoms of CRS and polyp grade).

- Secondary outcomes were consistent with the primary outcomes, demonstrating broad, clinically significant improvement in multiple signs and symptoms of the disease, as well as in various functional, physical, and emotional domains related to QoL.

- Longer treatment with EDS-FLU produced greater improvement (measured by SNOT-22 and polyp regression), with polyp elimination rates (in at least 1 nostril) increasing through at least 6 months.

- All tested doses were effective; however, the highest dose produced the largest effect size and fastest onset of action.

- The safety/tolerability of EDS-FLU in these trials was consistent with expectations for topically-acting intranasal steroid.

- These 2 large, 24-week studies demonstrate that EDS-FLU may be an important new tool in maximizing medical management of diseases characterized by chronic nasal inflammation, such as CRSsNP.

---

**Table 2: Baseline Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>EDS-FLU (n=181)</th>
<th>Placebo (n=180)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior INS treatment for CRSwNP (past 10 y), n (%)</td>
<td>149 (92.5)</td>
<td>146 (91.3)</td>
<td>.53 (.32)</td>
</tr>
<tr>
<td>Day-7 morning nasal obstruction, at time of rating (0-3), mean score (SD)</td>
<td>2.3 (0.42)</td>
<td>2.2 (0.39)</td>
<td>.22 (.073)</td>
</tr>
<tr>
<td>Biennial endoscopic nasal polyp score, mean (SD)</td>
<td>3.8 (1.01)</td>
<td>3.9 (1.00)</td>
<td>3.8 (0.96)</td>
</tr>
</tbody>
</table>

**Figure 3. LS Mean Change In Core Symptom Scores at Week 4**

**Figure 4. LS Mean Change In Polyp Grade Score**

**Figure 5. LS Mean Change In SNOT-22 Score**

---

1. Leopold D, Elkayam D, Messina J, Gonzalez-Koalk C, Djupesland P, Mahmoud R. NAVIGATE II: a randomized double-blind trial of fluticasone propionate delivered with an inhaler, shown to deposit drug deep (posteriorly and superiorly) in regions affected by chronic inflammation, in endoscopic observation, where the sinuses drain and ventilate and polyps originate (Figure 5). EDS-FLU contains fluticasone propionate (22mcg) alcohol free. The EDS MOA is described here: http://www.optinose.com/.


