LYR-210 Sinonasal Implants for Chronic Rhinosinusitis (CRS): Results from the Phase 3 ENLIGHTEN 2 Study

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LYR-210 improves symptoms and QOL in patients with CRS

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Zachary Soler, MD, is a consultant for Lyra Therapeutics, Optinose, and Regeneron and Medical Director for Healthy Humming.

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Brent A. Senior, MD, is a consultant for Lyra Therapeutics, Neurent, Smith and Nephew and Stryker.

Abby Dudek, Misun Lee, PhD, and Vineeta Belanger, PhD are employees of Lyra Therapeutics.

LYR-210 Drug-Eluting Sinonasal Implant

- LYR-210: For CRS patients who have failed medical management and require further intervention

Polymer-Drug Complex
Designed to deliver 6 months of continuous, local drug therapy with a single placement

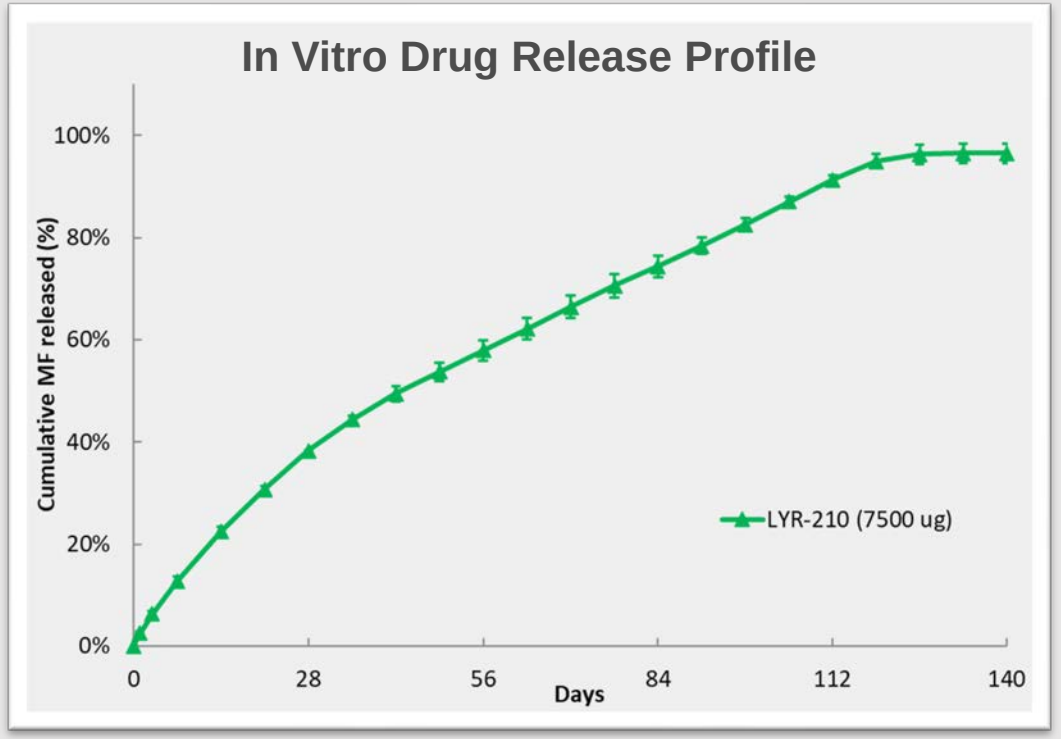
Designed to Deliver SUSTAINED Dosing over 24 weeks
Mometasone Furoate (7500µg)

Engineered Elastomeric Matrix
Shape memory intended to keep implant in place

Bioabsorbable Mesh Scaffold
Designed to maximize surface area for drug release while maintaining underlying tissue function

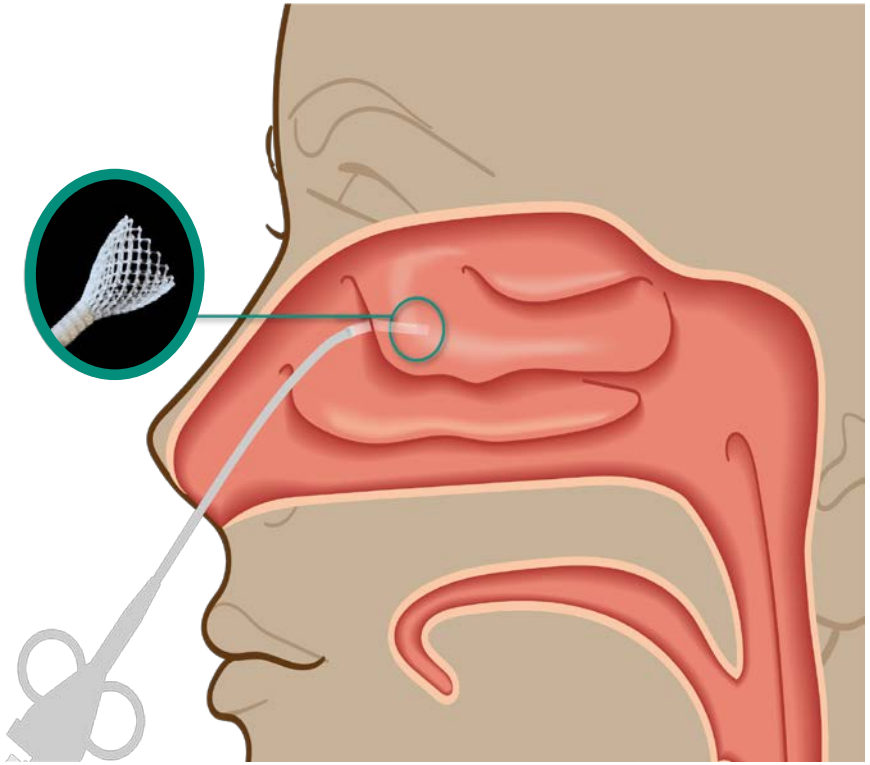
In-Office Procedure
Administered nasally via a single use applicator

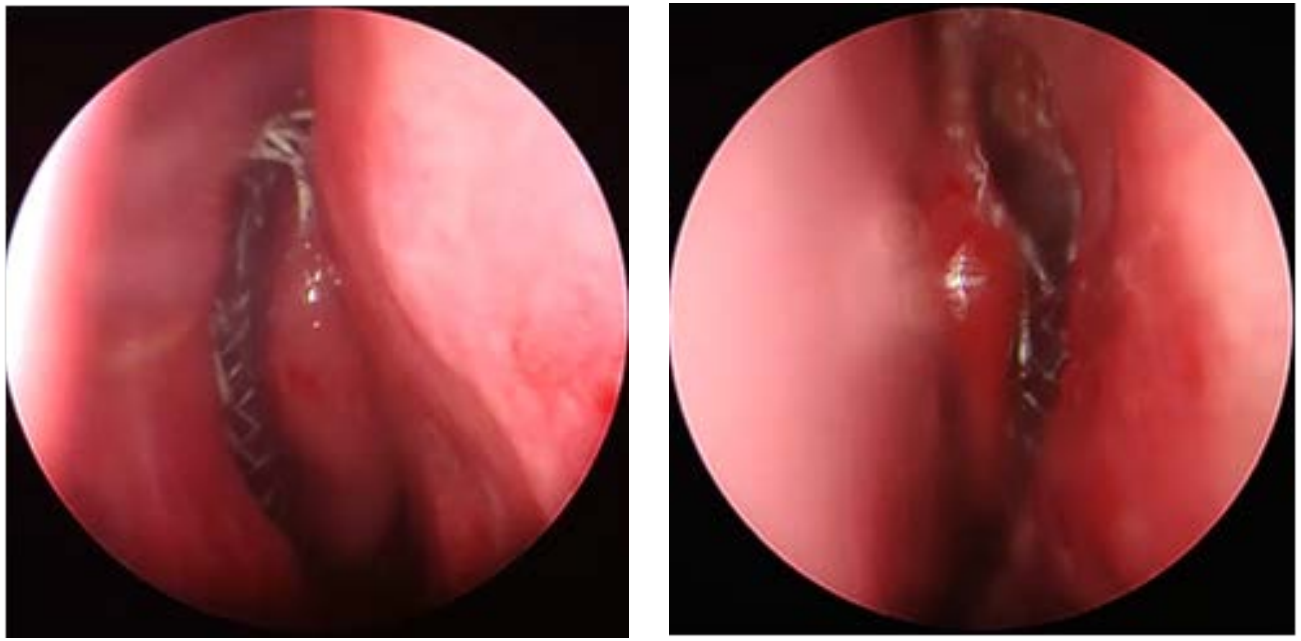
Safe and Effective
Demonstrated in Phase 2 LANTERN trial



Dissolution conditions: 37 C in PBS/2% SDS

In-Office Placement of LYR-210





LYR-210 bilaterally placed in the middle meatus of a patient with CRS

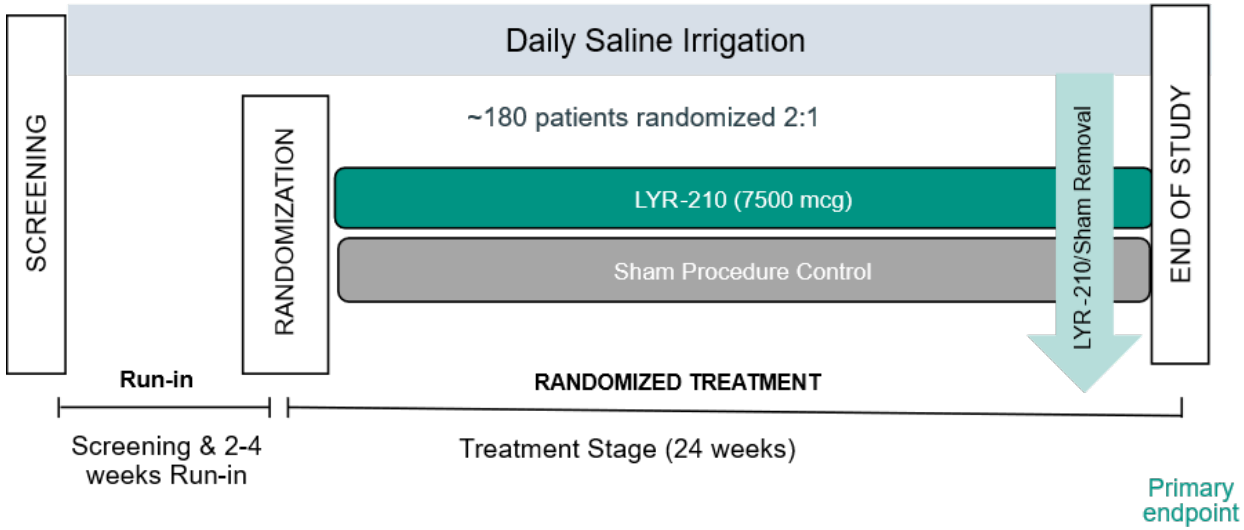
ENLIGHTEN 2: Pivotal Phase 3 Trial

- 24-week, multi-center, randomized, sham-controlled, blinded trial
- Adult CRS patients who failed prior medical management and have not previously undergone ethmoid sinus surgery.
- Non-polyp and a subset of 29 polyp grade 1
- 172 patients randomized 2:1 to LYR-210 or Sham procedure
- ***All patients were required to be on daily saline irrigation***

- **Primary endpoint:**
  - Change from baseline (CFBL) in the weekly average composite score of the 3 cardinal symptoms (3CS) at Week 24 in patients without nasal polyps.
    (3CS; nasal blockage/obstruction/congestion, anterior/posterior nasal discharge, and facial pain/pressure)

- **Key Secondary endpoints**:
  - CFBL in the weekly average composite score of 3CS at Week 24.
  - CFBL in the SNOT-22 total score at Week 24.
  - CFBL in the percent opacification of the ethmoids at Week 20, as determined by 3-D volumetric CT analysis.
  - Rescue treatment requirement through Week 24.

ENLIGHTEN 2 Study Design



Clinicaltrials.gov ID: NCT05295459

Participant Baseline Characteristics

ITT Analysis Set (N=172)	LYR-210 (n=111)	Sham (n=61)
Age in years (mean, SD)	50 (15.5)	49 (13.0)
Sex (n, %) Male Female	 65 (58.6%) 46 (41.4%)	 31 (50.8%) 30 (49.2%)
Race (n, %) White Black or African American	 94 (84.7%) 9 (8.1%)	 51 (83.6%) 5 (8.2%)
Region (n, %) North America European Union	 63 (56.8%) 48 (43.2%)	 31 (50.8%) 30 (49.2%)
Without Nasal Polyps (n, %)	94 (84.7%)	49 (80.3%)
Baseline 3CS Score (mean, SD)	6.5 (1.3)	7.2 (1.4)
Baseline SNOT-22 Score (mean, SD)	56.2 (17.4)	58.8 (22.2)
Baseline % Ethmoid Opacification Volume (**CT – 3D Volumetric**) (mean, SD)	45.3 (19.3)	45.7 (18.0)

Most Frequent Adverse Events (≥5% of participants)

Favorable safety profile with no product-related serious adverse events reported

Safety Analysis Set (Preferred Term[1])	LYR-210 (n=112*) n (%)	Sham (n=60*) n (%)
Any treatment-emergent adverse events (TEAEs)	68 (60.7%)	26 (43.3%)
Epistaxis[2]	18 (16.1%)	1 (1.7%)
Upper respiratory tract infection	10 (8.9%)	5 (8.3%)
Chronic sinusitis	8 (7.1%)	6 (10.0%)
Acute sinusitis	10 (8.9%)	2 (3.3%)
Nasopharyngitis	7 (6.3%)	4 (6.7%)
COVID-19	5 (4.5%)	4 (6.7%)
Headache	6 (5.4%)	3 (5.0%)

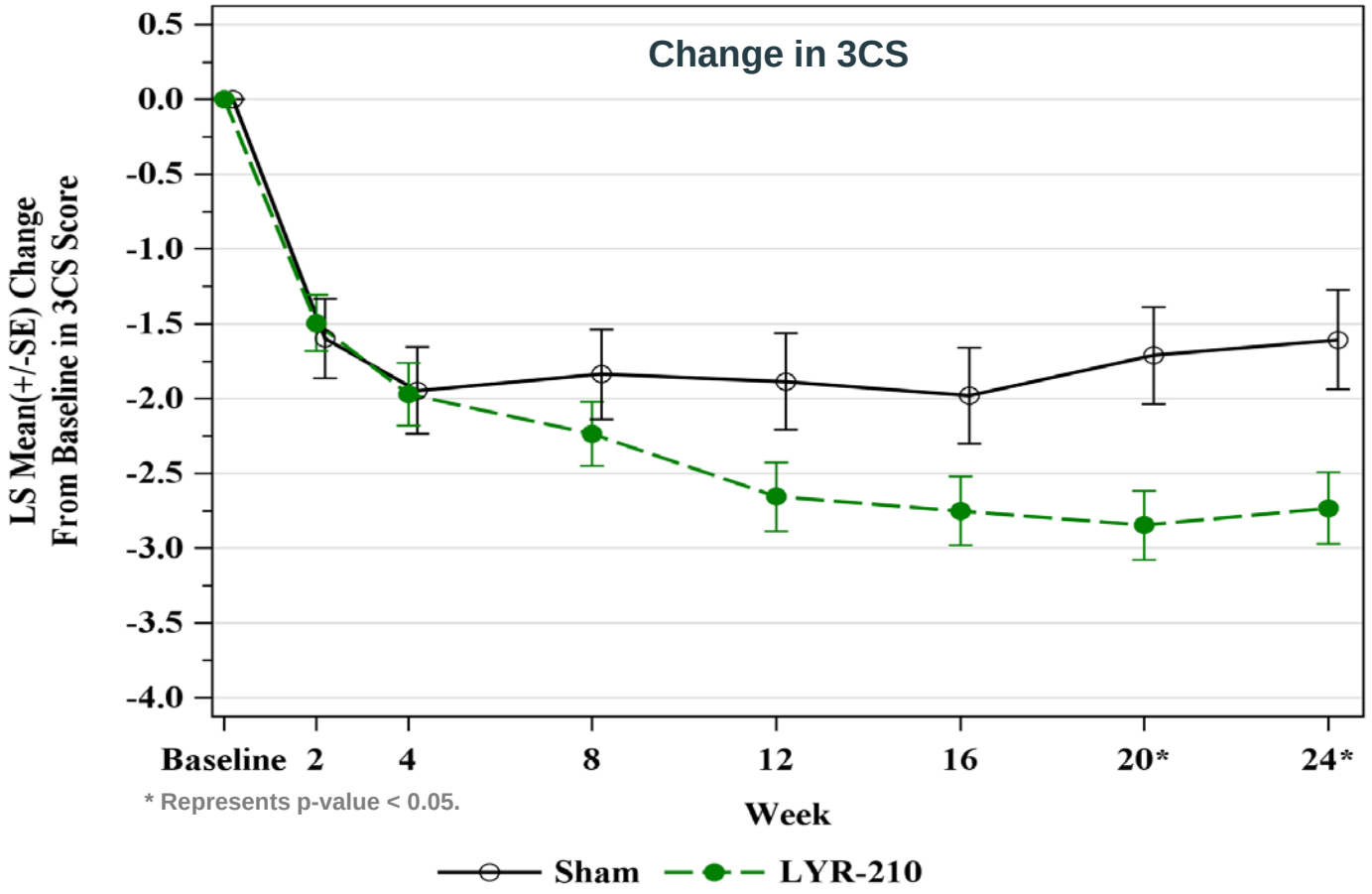
*One participant randomized to sham was inadvertently administered LYR-210. In the safety analysis set, participants were analyzed according to the treatment received.

1) Events coded to a standard term using MedDRA coding dictionary.
2) Any event with terms such as blood-tinged mucus, nosebleed, etc. are coded to this preferred term and does not indicate a clinical nosebleed requiring intervention.

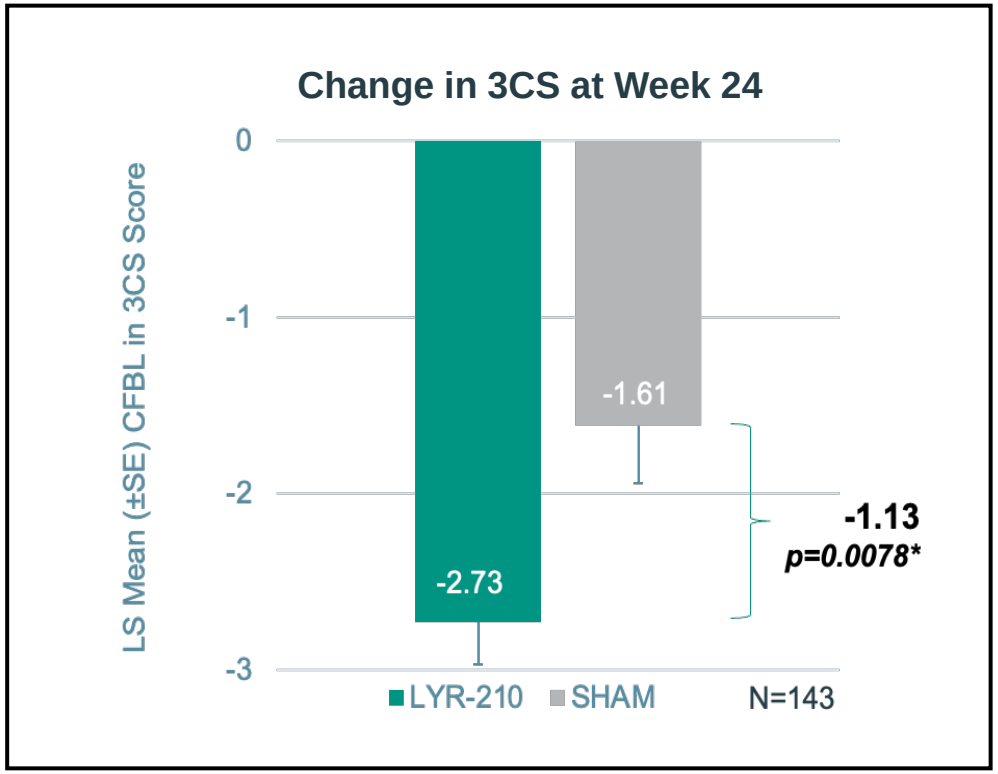
Primary Endpoint: Change from Baseline in 3CS at Week 24

[patients without nasal polyps]

- The primary endpoint was met with statistically significant improvement in 3CS at 24 weeks
- Consistent improvement over Sham control observed as early as Week 8



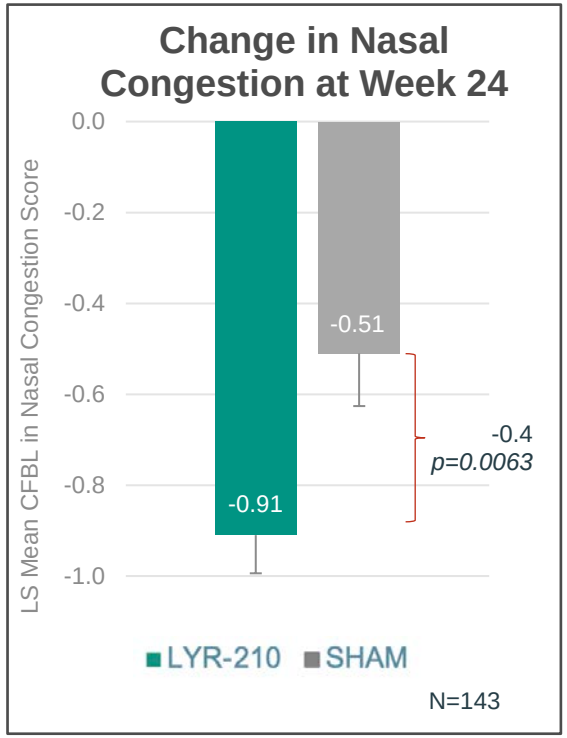
* Represents p-value < 0.05.

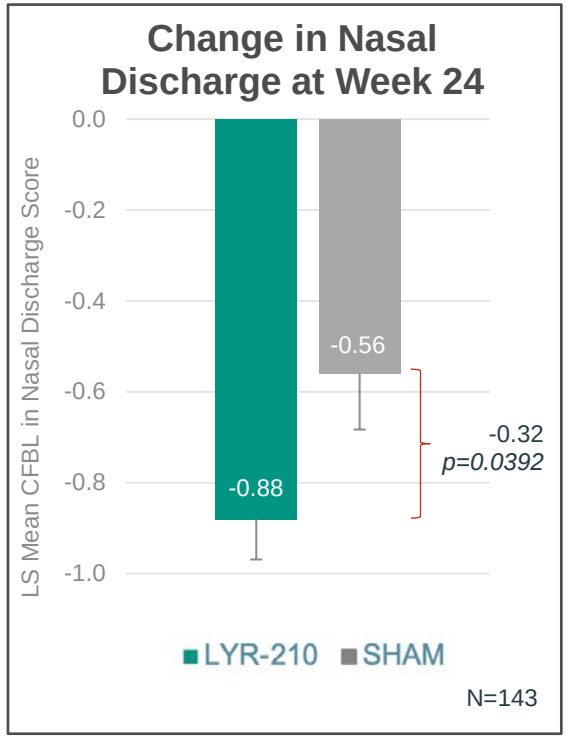


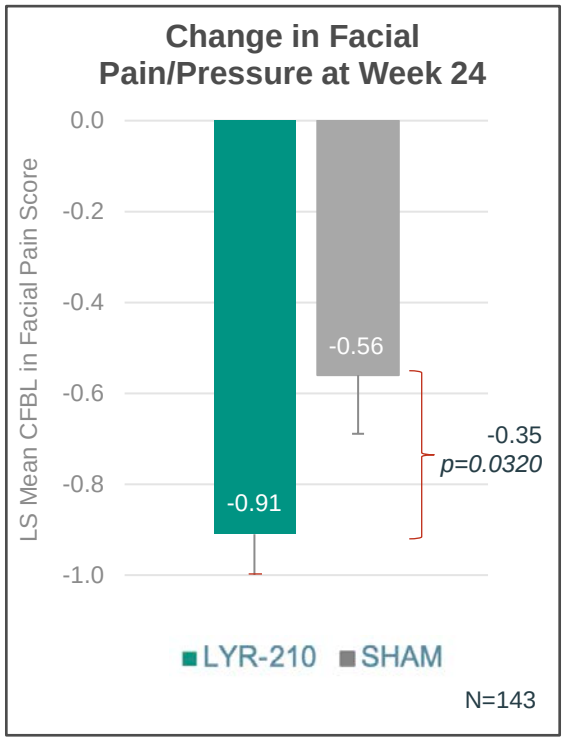
* Statistically significant

Individual Cardinal Symptoms
[patients without nasal polyps]

- **Consistent improvement observed in all 3 individual components of 3CS in patients without nasal polyps**



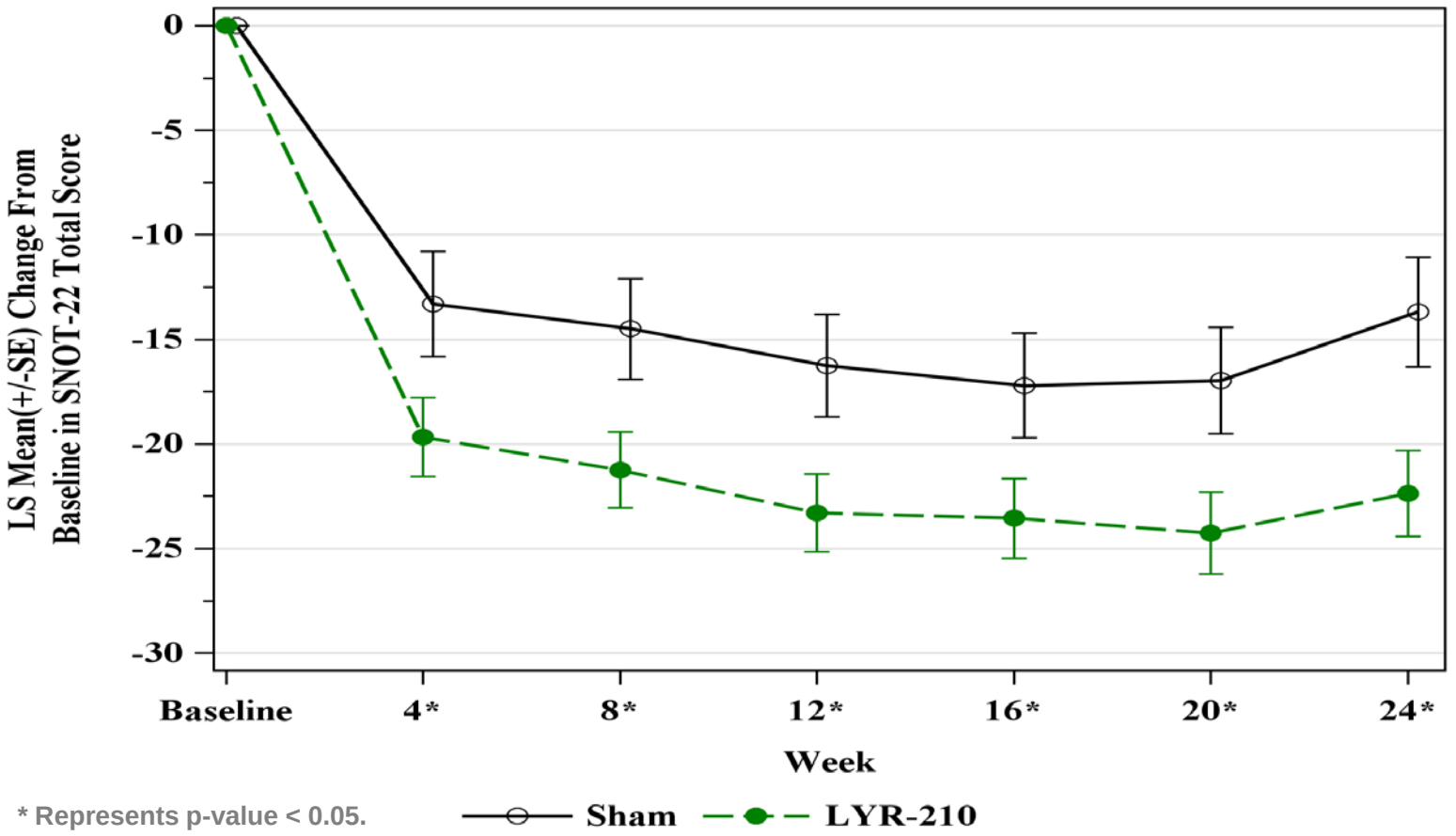




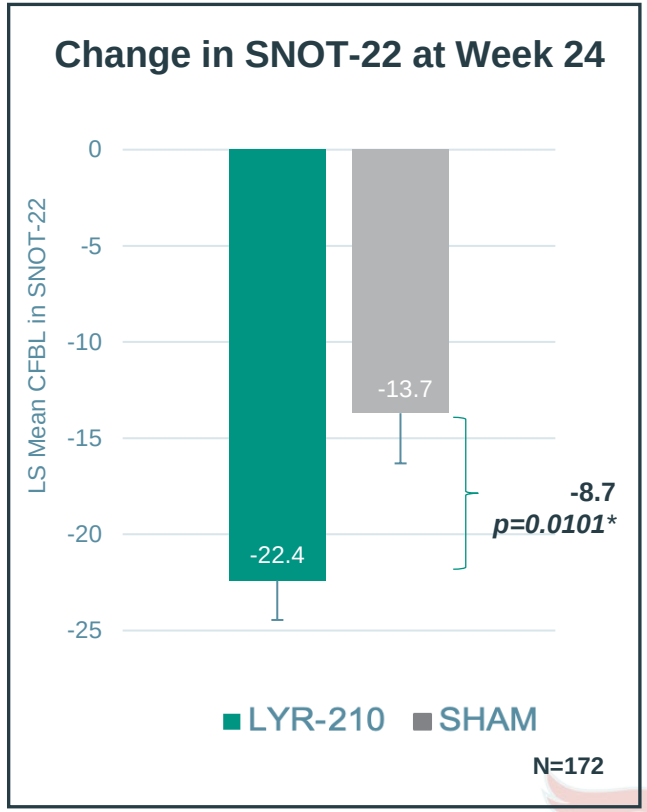
Change from Baseline in SNOT-22

[patients with or without nasal polyps]

- Statistically significant improvement in SNOT-22 score at 24 weeks, with robust improvement starting at Week 4
- LYR-210 group improved by 22.4 points – more than 2-fold the MCID

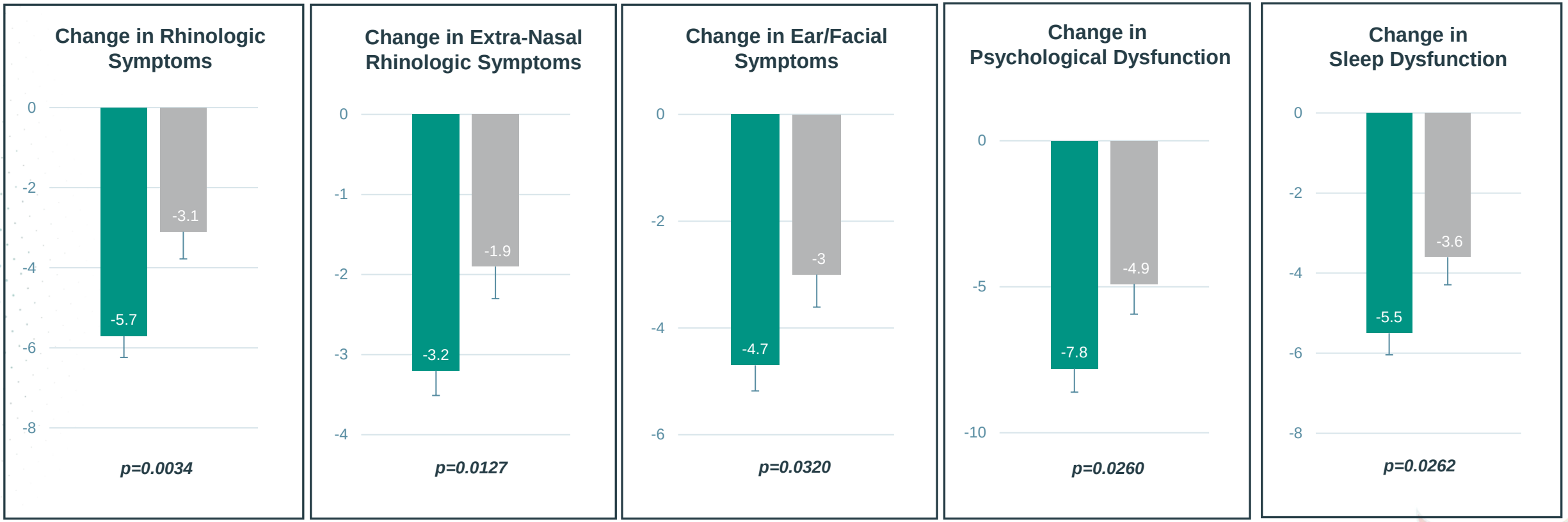


* Represents p-value < 0.05.



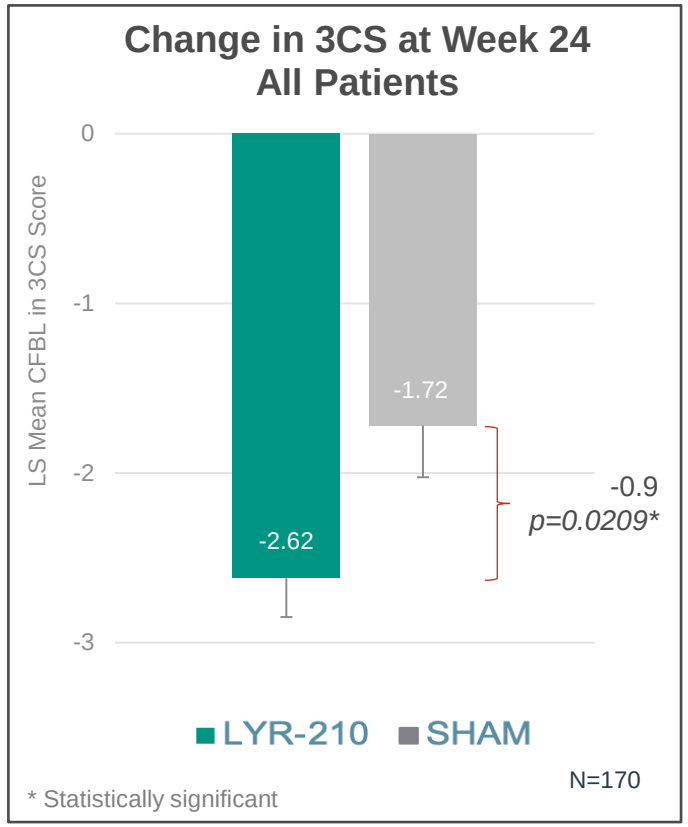
Change from Baseline in SNOT-22 Subdomain Scores
[patients with or without nasal polyps]

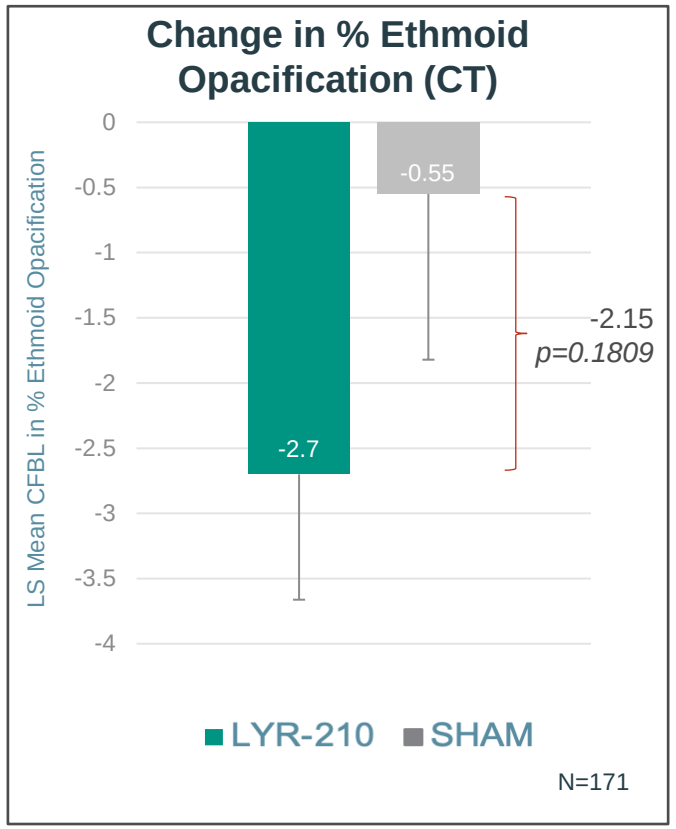
- **LYR-210 showed improvements over sham in all subdomains of SNOT-22**



Improvement over Sham in Other Key Secondary Endpoints

- CFBL in 3CS in the overall population (polyp and non-polyp participants) showed statistically significant improvement over Sham control
- CFBL in the % ethmoid opacification by 3D volumetric analysis of CT demonstrated a numerical improvement over Sham, despite a low threshold for disease severity on CT for inclusion into the study

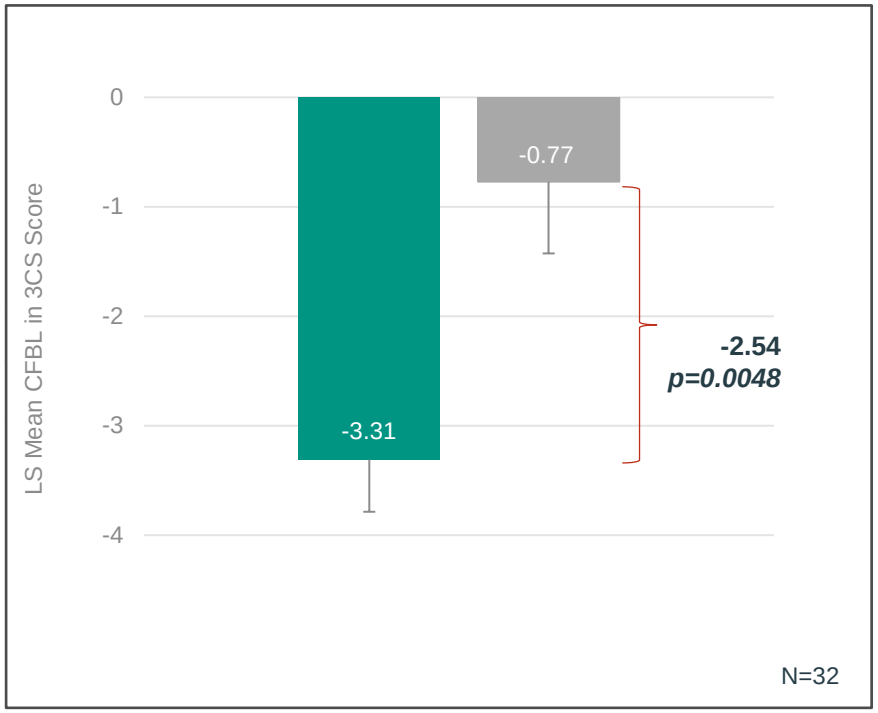




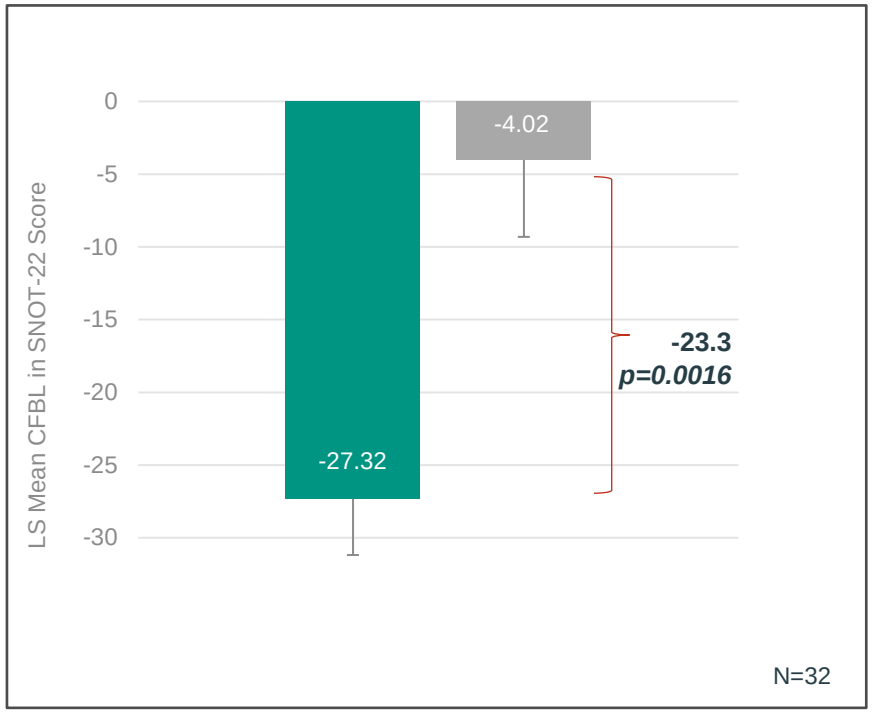
Large Treatment Effect in 3CS and SNOT-22 Observed in Patients with Higher CT Disease

CRS without Nasal Polyps with Baseline Ethmoid Opacification >25%*

Change in 3CS



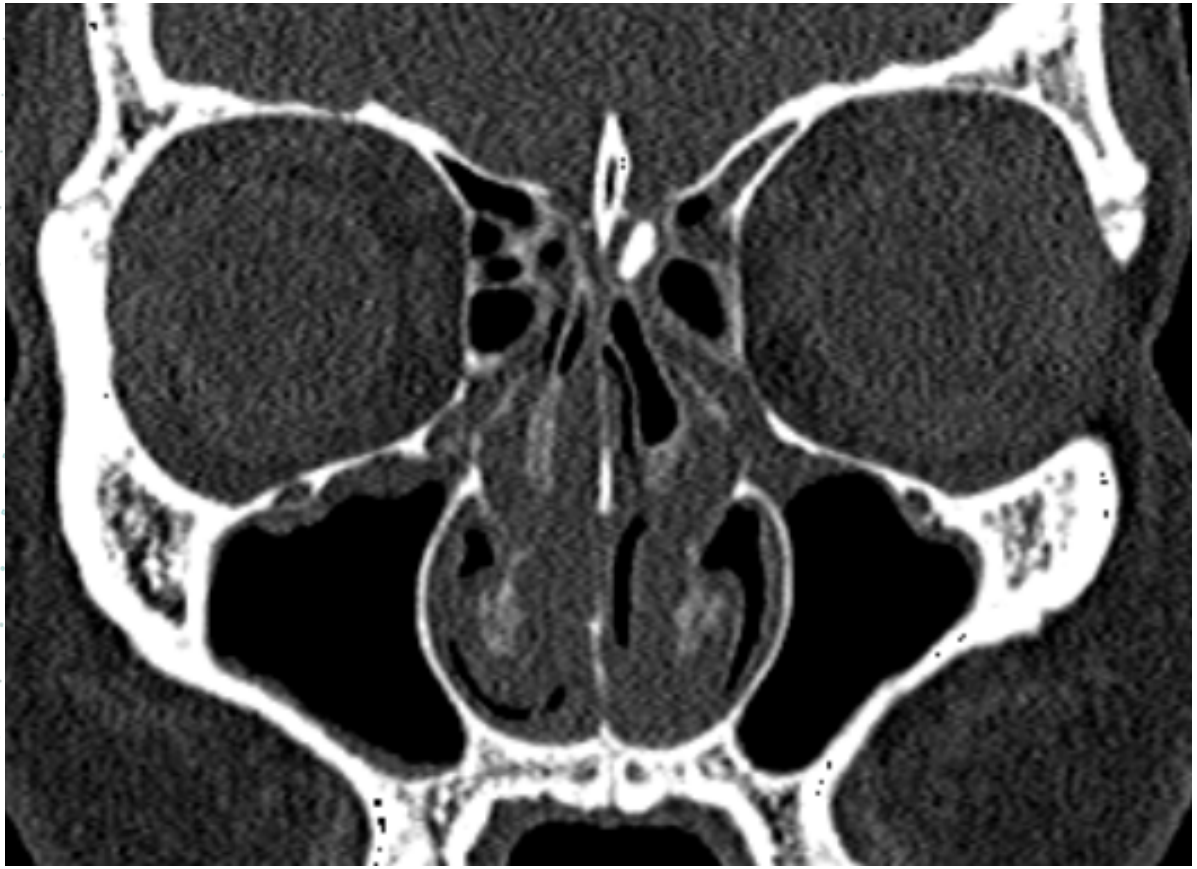
Change in SNOT-22



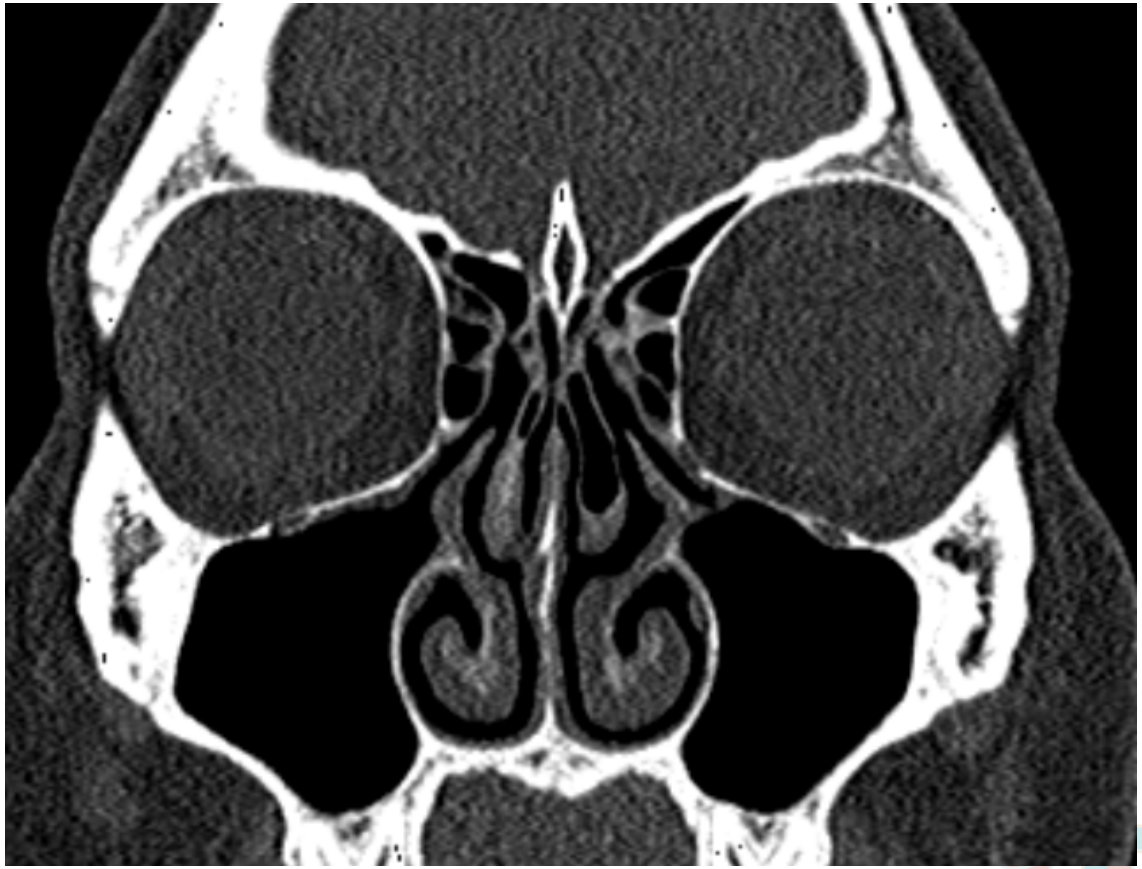
* Baseline average Zinreich Score >=2

CT of LYR-210 group Participant Pre and Post Treatment

Screening



Week 20



Summary of ENLIGHTEN 2 Results

- **ENLIGHTEN 2 study met its primary endpoint**
  - Statistically significant improvement over sham in 3CS at Week 24 in the primary population of CRS patients without nasal polyps, with improvement observed as early as Week 8.
  - Improvements observed in all 3 individual cardinal symptoms
- **Key secondary endpoints of change in 3CS and SNOT-22 in the full study population were also met**
  - Demonstrated statistically significant results in 3CS at Week 24
  - Demonstrated statistically significant results in SNOT-22 at Week 24
    - Improvement in SNOT-22 observed as early as Week 4 and sustained through Week 24
    - Clinically meaningful improvement, with almost twice the minimal clinically important difference observed at Week 24 (-22.4 points)
    - Improvements observed in all sub-domains of SNOT-22
- **Numerical improvement in key secondary endpoint of change in % ethmoid opacification (CT)**
- **Well tolerated with no product-related serious adverse events reported in the study**
- **Even larger improvements in 3CS and SNOT-22 seen in patients with higher baseline ethmoid disease**