Evaluation of LYR-220 Corticosteroid Matrices at Week 24 from the BEACON Study in CRS

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Disclosures

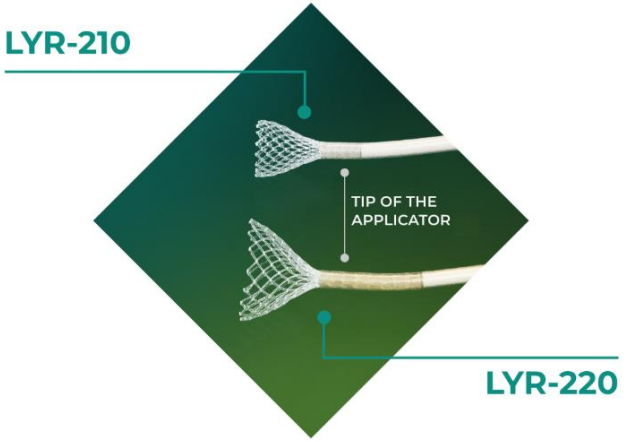
- BAS is the Lead Principal Investigator for the Phase 2 BEACON study, consultant for Lyra Therapeutics and Stryker, and VP of Development and Strategy for the ARS.
- RAO, MSM, SLS, and JR are principal investigators in the BEACON study. RAO and SLS are consultants for Lyra Therapeutics.
- RCK is Chief Clinical Advisor for Lyra Therapeutics.
- LB, MM, ES, ML, VB, and RN are employees of and have stock options at Lyra Therapeutics.
- Lyra Therapeutics is the sponsor of the BEACON study.

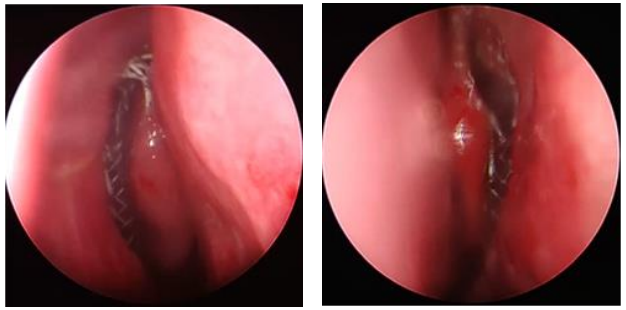
LYR-210 and LYR-220: Investigational Products for CRS

- Bioresorbable nasal matrix
- Designed to continuously deliver mometasone furoate (7500µg) over 24 weeks to the sinonasal passages
- Administered in a straightforward, in-office procedure

- LYR-220: For CRS patients with post-surgical anatomy
  - Phase 2 BEACON trial – Topline results presented today

- LYR-210: For CRS patients with unoperated sinuses
  - Phase 3 ENLIGHTEN trials ongoing





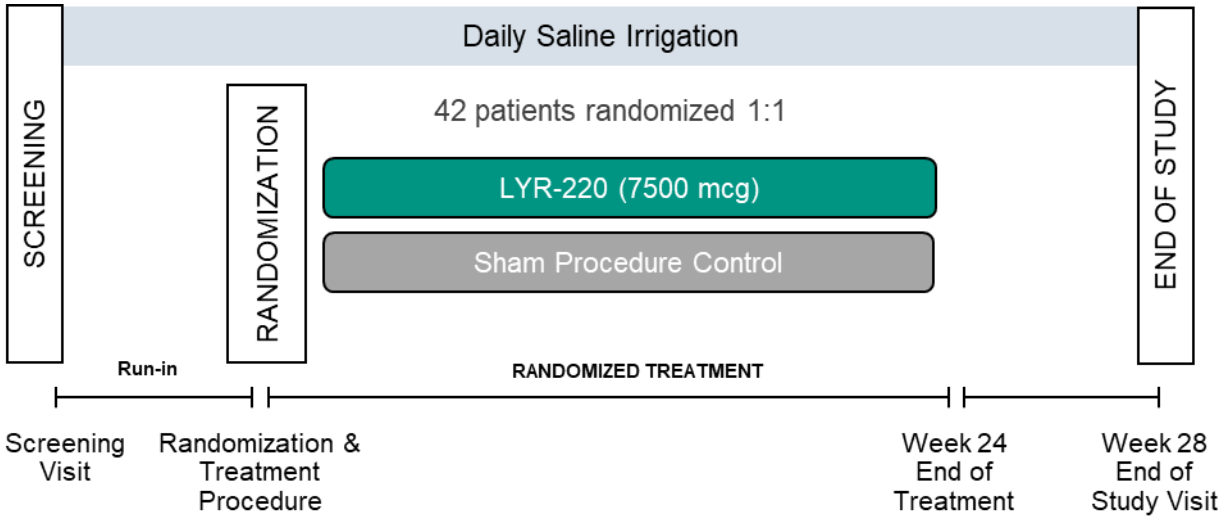
LYR-220 bilaterally placed in the ethmoid cavity of a patient with CRS

BEACON: Phase 2 Clinical Study of LYR-220

- **CRS patients (polyp and non-polyp)** who have had a prior bilateral ethmoidectomy
- Randomized, blinded, sham-controlled Phase II study to assess safety and efficacy of LYR-220*
- **Safety endpoint:**
  - Serious adverse events
- **Key efficacy endpoints:**
  - 3 cardinal symptoms (3CS)** scores
  - SNOT-22 scores

Clinicaltrials.gov ID: NCT05035654
*Preceded by feasibility phase to choose matrix design
**3 cardinal symptoms are defined as nasal blockage / obstruction, facial pain / pressure, and nasal discharge

BEACON Study Design



Note: Primary outcome measure was product-related serious adverse events

BEACON: Patient Disposition

Part 2	LYR-220 (n=21)	Sham (n=21)	Total (n=42)
Completed study treatment (*n, %*)	19 (90.5)	17 (81)	36 (85.7)
Discontinued early from treatment *(n, %)*	2 (9.5)	4 (19)	6 (14.3)
Withdrawal by subject	0	4 (19)	4 (9.5)
Adverse Event	1 (4.8)	0	1 (2.4)
Investigator decision	1 (4.8)	0	1 (2.4)

BEACON: Patient Demographics and Baseline Characteristics

	LYR-220 (n=21)	Sham (n=21)	Total (n=42)
Age in years (*mean, SD)*	48 (12.51)	55 (11.29)	**51 (12.35)**
Sex *(n, %)*			
Male	7 (33.3)	10 (47.6)	**17 (40.5)**
Female	14 (66.7)	11 (52.4)	**25 (59.5)**
Race *(n, %)*			
White	20 (95.2)	18 (85.7)	**38 (90.5)**
Black or African American	1 (4.8)	2 (9.5)	**3 (7.1)**
Baseline SNOT-22 Total Score (*mean, SD)*	56.1 (17.16)	50.0 (16.65)	**53.1 (16.9)**
Baseline 3CS Score (*mean, SD)*	6.4 (1.47)	6.8 (1.65)	**6.6 (1.56)**

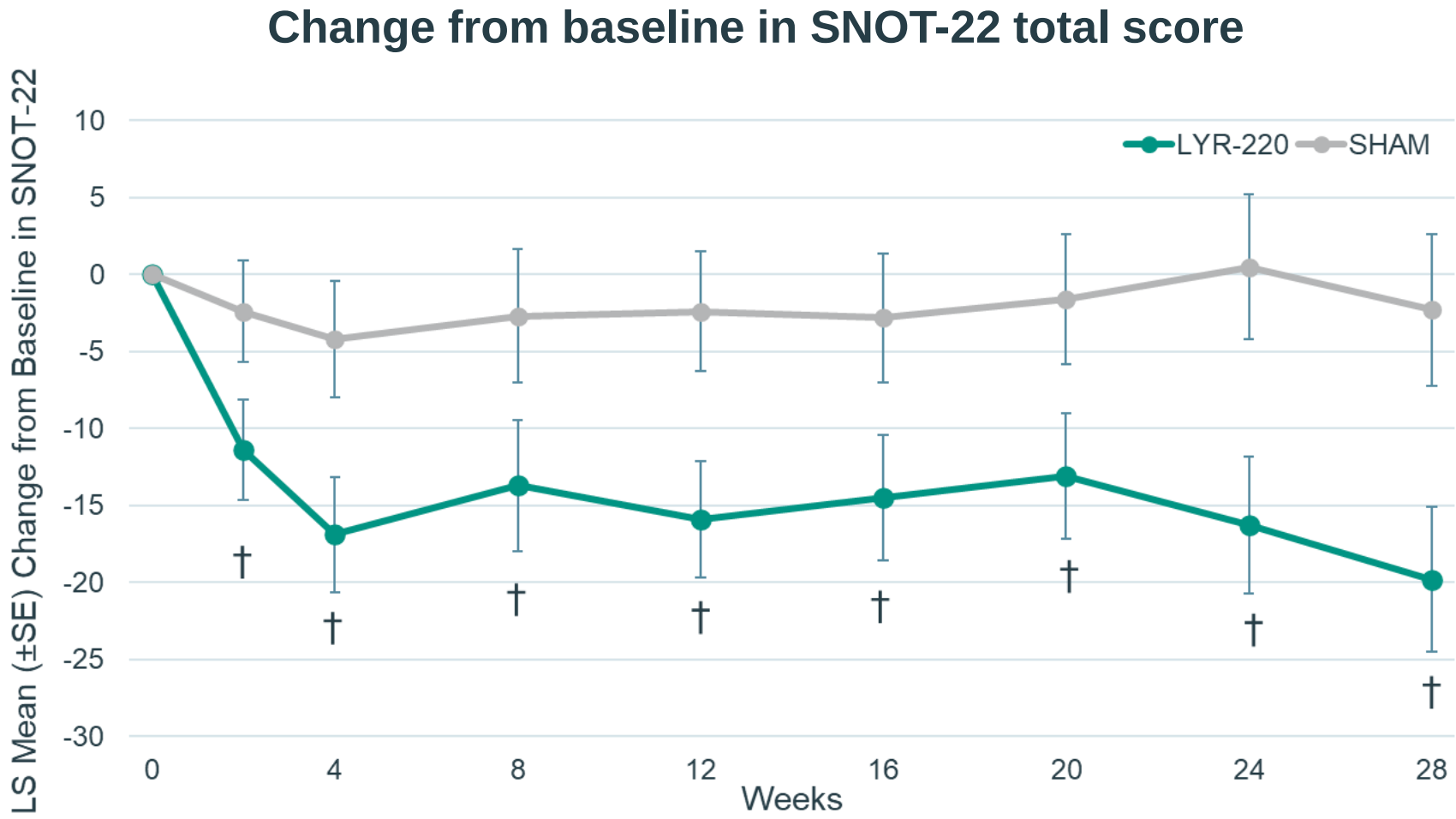
BEACON: No Serious Adverse Events

Adverse Events occurring in >2 subjects in any group

MedDRA Preferred Term	LYR-220 N=24*	SHAM N=21
Sinusitis	8 (33.3%)	4 (19%)
Acute sinusitis	6 (25%)	2 (9.5%)
Nasopharyngitis	4 (16.7%)	2 (9.5%)
Bronchitis	4 (16.7%)	0
Chronic sinusitis	2 (8.3%)	2 (9.5%)
Covid-19	3 (12.5%)	0
Upper respiratory tract infection	2 (8.3%)	1 (4.8%)

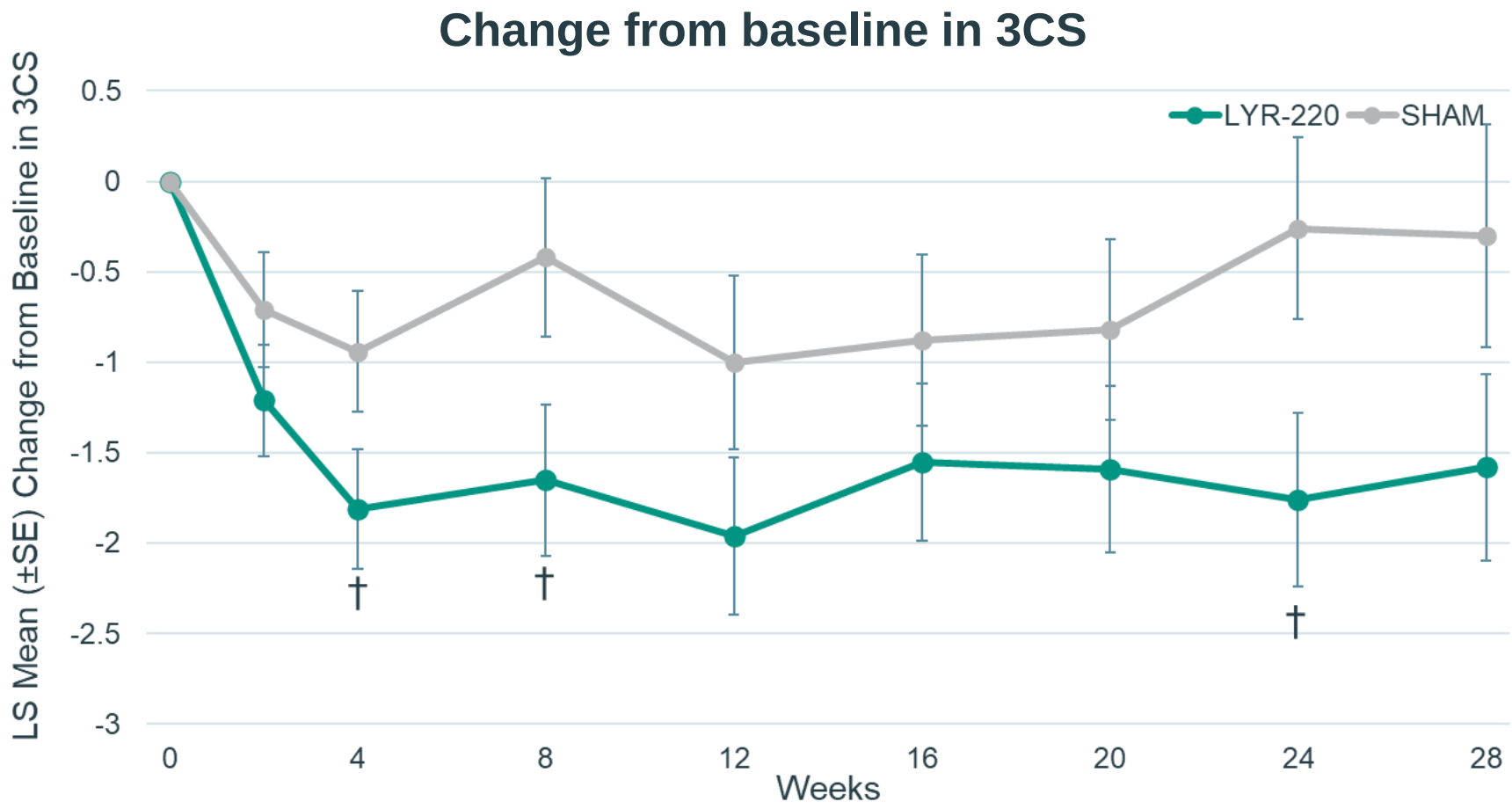
* Includes 3 subjects that received LYR-220-32 in Part 1 of the study

BEACON: Early and Sustained Improvement in SNOT-22



† p <0.05

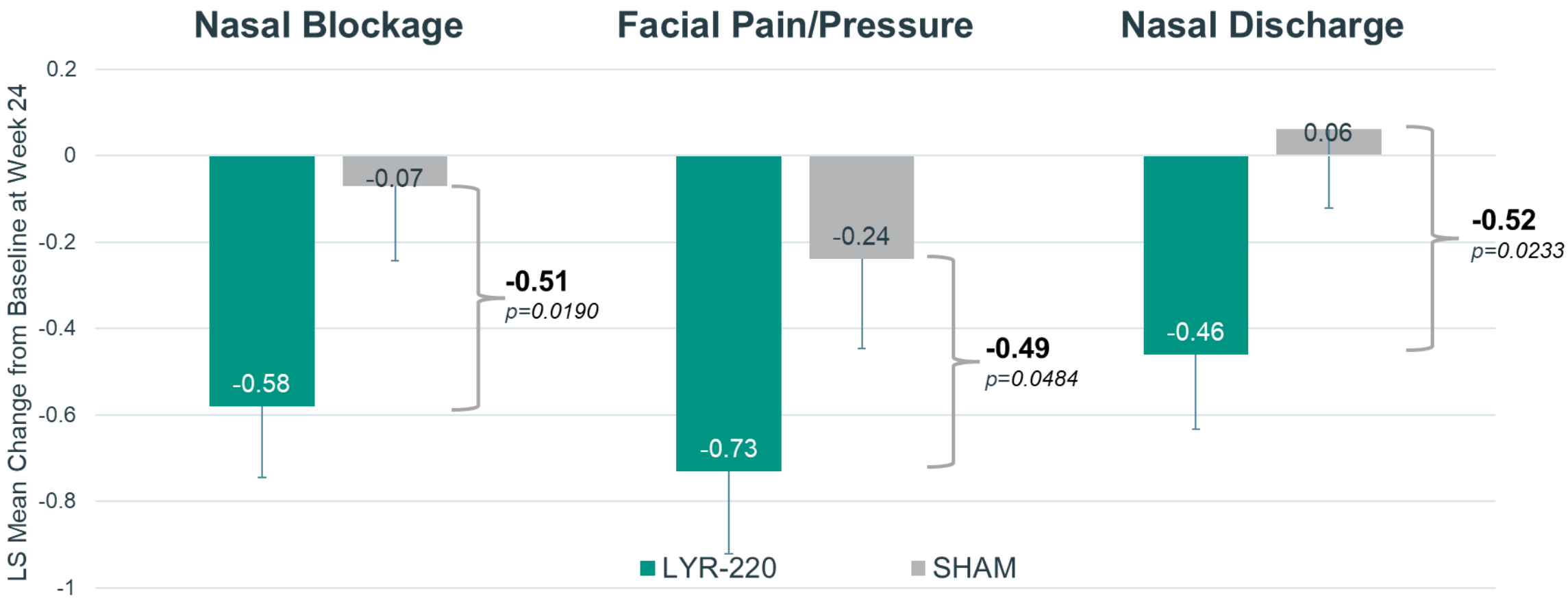
BEACON: Statistically Significant Improvements in 3CS



† p <0.05

3CS: 3 cardinal symptoms of CRS (nasal obstruction, nasal discharge, facial pain/pressure)

BEACON: Statistically Significant Improvements in Individual CS at Week 24



Error bars represent SE

BEACON Study Summary

- Achieved Primary Endpoint: No serious adverse events
- Statistically significant improvements in a composite of the 3CS (nasal obstruction, nasal discharge, facial pain/pressure) as early as week 4 (-0.87; p=0.037) and at week 24 (-1.50; p=0.02)
  - Statistically significant improvements for each individual cardinal symptom at week 24
- Clinically relevant and statistically significant improvements over sham in SNOT-22 as early as week 2 (-9.0; p=0.031) and at week 24 (-16.8; p=0.007)
- Improvements in SNOT-22 were sustained throughout the study and clinically meaningful with almost twice the MCID* at week 24 compared to sham (-16.8 points)

*MCID-minimal clinically important difference; 8.9 points