LYRA THERAPEUTICS

Corporate Presentation

October 2024

Forward Looking Statement

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The words “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect,” and similar expressions are intended to identify forward-looking statements. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including statements regarding our focus on the two ongoing ENLIGHTEN Phase 3 trials evaluating LYR-210, our ongoing ENLIGHTEN 1 extension study and expectation for data in Q4 2024, our ongoing ENLIGHTEN 2 trial and our expectation for data in 1H 2025, whether LYR-210 if advanced would be positioned to align with current ENT practices, our cash runway into 2026 and plans to update investors regarding our cash runway, and our plans to evaluate potential strategic options to maximize shareholder value. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause the Company's actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: any potential financial or strategic option we pursue in order to maximize shareholder value may not result in the identification of a suitable transaction, or if one is identified and pursued, may not be completed on attractive terms, or at all; our ability to sublease or assign our three leaseholds, which represent significant operating costs; our incurrence of significant losses since inception and expectation to incur significant additional losses for the foreseeable future; our recurring losses from operations raise substantial doubt regarding our ability to continue as a going concern; our need for significant additional funding in order to complete development of and obtain regulatory approval for our product candidates and commercialize our products, if approved; the failure of our ENLIGHTEN 1 Phase 3 trial to meet its primary endpoint has made it more difficult for the Company to raise capital; we could be forced to delay, reduce, or eliminate our product development programs or commercialization efforts; following the failure of our ENLIGHTEN 1 Phase 3 trial evaluating LYR-210 for the treatment of chronic rhinosinusitis (CRS) to meet its primary endpoint, which was announced in May 2024, there is significant uncertainty about the Company’s ability to complete development of LYR-210 and our ability to obtain regulatory approval for LYR-210 is at least significantly delayed and may not be possible; our common stock may be delisted from The Nasdaq Global Market if we cannot regain compliance with Nasdaq’s continued listing requirements; our loss of key personnel significantly and adversely affects our ability to manufacture our product candidates, among other activities; we are no longer engaged in the manufacturing of our product candidates in-house; our business is highly dependent on the success of our most advanced product candidate, LYR-210; clinical trials required for our current product candidate and any future product candidates are expensive and time-consuming, their outcome is uncertain, and if our clinical trials do not meet safety or efficacy endpoints in these evaluations, or if we experience significant delays in these trials, our ability to commercialize our product candidates and our financial position will be impaired; any failure by a third party to conduct our pre-clinical or clinical trials according to good clinical practices and in a timely manner may delay or prevent our ability to seek or obtain regulatory approval for or commercialize our product candidates; even if LYR-210 receives marketing approval, it may fail to achieve market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success; if our collaborations are not successful, including with LianBio our product candidates may not reach their full market potential; our ability to manage our obligations under our license and other strategic agreements may divert management time and our limited resources, causing delays or disruptions to our business; our operating activities may be restricted by certain covenants in our license and strategic agreements, which could limit our development and commercial opportunities; failure to obtain marketing approval in international jurisdictions would prevent our products from being marketed in such jurisdictions; developments by competitors may render our products or technologies obsolete or non-competitive or may reduce the size of our markets; the successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and pricing policies; failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue; if we are unable to obtain, maintain, or adequately protect our intellectual property rights, we may not be able to compete effectively in our market; the impact of international terrorism, political unrest and wars on our business; and the impact of other events such as the COVID-19 pandemic may adversely impact our business and operations, including our clinical trials. These and other important factors discussed under the caption "Risk Factors" in the Company's Quarterly Report on Form 10-Q filed with the SEC on August 14, 2024 and its other filings with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While the Company may elect to update such forward-looking statements at some point in the future, it disclaims any obligation to do so, even if subsequent events cause its views to change.

This presentation also includes statistical and market data that we obtained from industry, publications and research, surveys and studies conducted by third parties or us. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. All of the market data used in this presentation involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. While we believe these industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data. The industry in which we operate is subject to a high degree of uncertainty, change and risk due to a variety of factors, which could cause results to differ materially from those expressed in the estimates made by the independent partners and by us.

Lyra’s product candidates, LYR-210 and LYR-220, have not been approved by FDA. This presentation is intended for the investor community only. Nothing herein is intended to promote the Company’s product candidates.

In connection with its previously announced reduction in workforce Lyra stopped manufacturing and commercialization efforts for LYR-210, as well as development efforts for LYR-220 in an effort to reduce operating expenses. Nevertheless, we anticipate that we will continue to incur expenses as we continue the two ongoing ENLIGHTEN Phase 3 clinical trials of LYR-210.

Company Overview

Clinical-stage biotechnology company developing long-acting, anti-inflammatory sinonasal implants for the treatment of chronic rhinosinusitis

- **Bioabsorbable sinonasal implant designed to deliver 6 months of continuous anti-inflammatory therapy**
- **Indication: Chronic rhinosinusitis (CRS)**
  - ~12% of the US population[1]
  - ~50% of patients fail medical therapy[2]
- **Pivotal Phase 3 trials ongoing**
- **Over 100 global patents issued and pending**

1) Summary Health Statistics Tables for U.S. Adults: National Health Interview Survey, 2018, Tables A-2b, A-2c; 2) Baguley et al. Int Forum Allergy Rhinol, 2014;4(7):525-3;

Chronic Rhinosinusitis (CRS): An “Unrecognized Epidemic”[1]

CRS Cardinal Symptoms[1]

- Nasal obstruction and congestion
- Facial pain and pressure
- Nasal discharge
- Reduced sense of smell

CRS in the United States Annually

~8M	CRS patients **treated**[2]
~4M	CRS patients **failing medical** management[3]
~1.4M	CRS patients **currently presenting to an ENT**[4]

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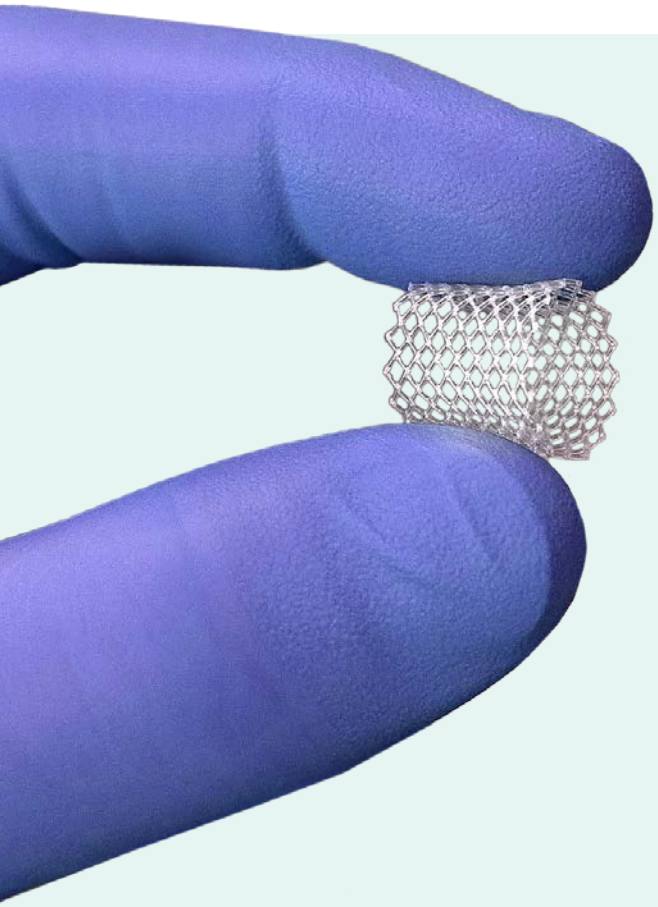
1) Tan BK et al. Am J Respir Crit Care Med, 2013;188(11):1275–7; 2) Jang et al. Otolaryngol Head Neck Surg, 2018; 3) Baguley et al. Int Forum Allergy Rhinol, 2014;4(7):525-32; 4) OM1 Real World Data Cloud (OM1, Inc, Boston, MA, US), 2015 – 4/2019. Analysis 9/2019

Lyra’s Proprietary Drug-Eluting Implant



Polymer-Drug Complex

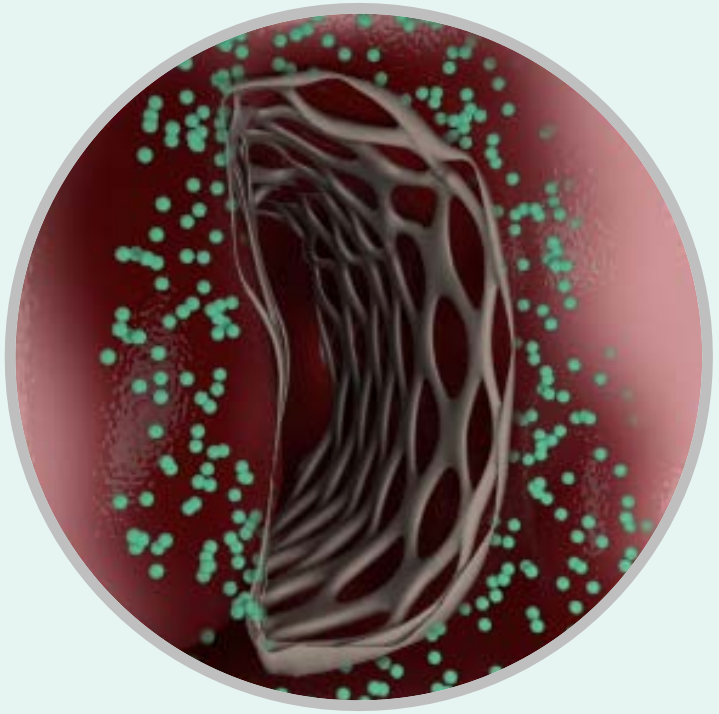
Designed to deliver 6 months of continuous, local drug therapy with a single placement

Engineered Elastomeric Matrix

Shape memory keeps implant in place

Bioabsorbable Mesh Scaffold

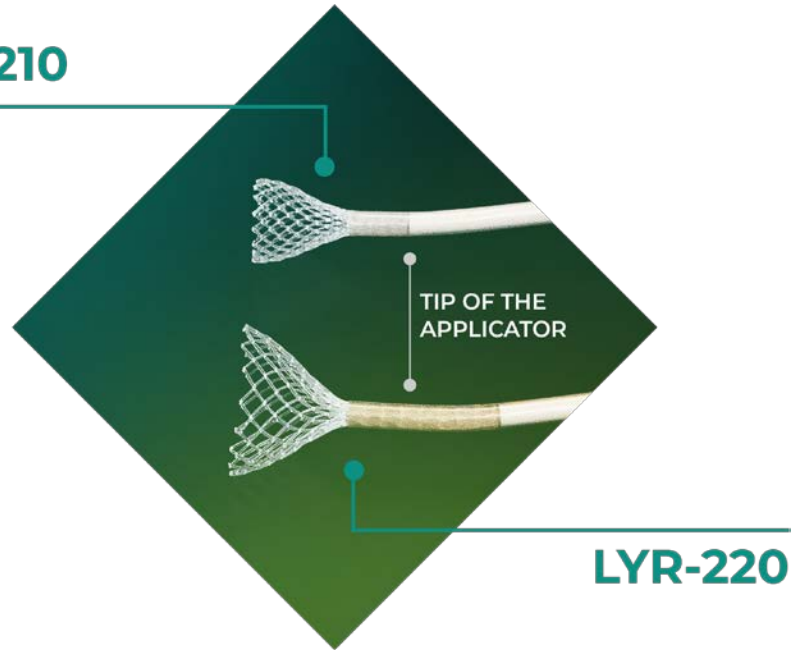
Maximizes surface area for drug release while maintaining underlying tissue function



Lyra's "Family" of CRS Product Candidates

LYR-210 and LYR-220 are designed to address the full spectrum of CRS patients where ENTs select size based on patient anatomy

Smaller dimension for patients with narrow anatomy (includes surgery naïve patients)



Larger dimension for patients with enlarged anatomy due to previous ethmoid sinus surgery

Lyra Pipeline

LYR-210 and LYR-220 are designed to address the full spectrum of CRS patients where ENTs select size based on patient anatomy

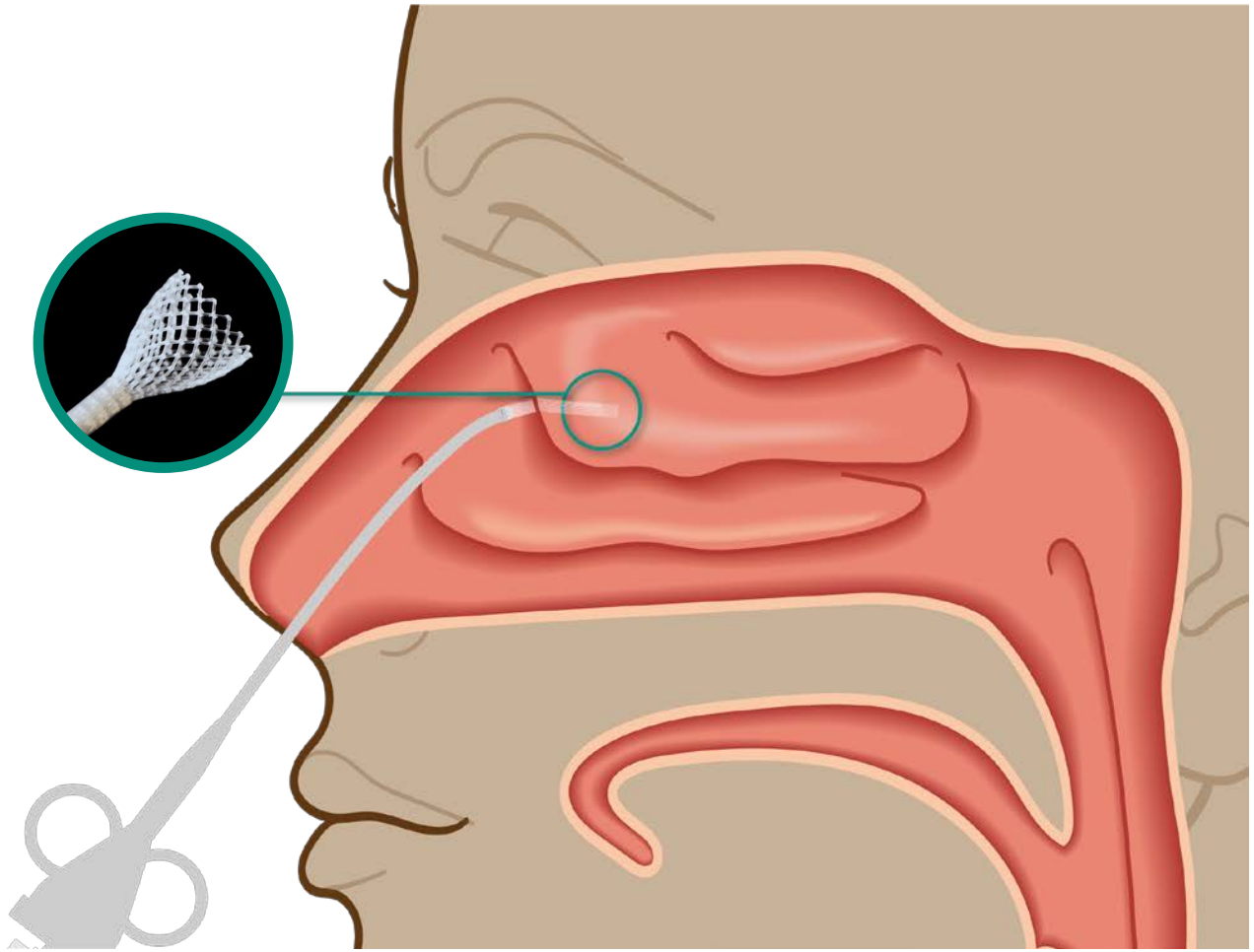
Candidate	CRS Patient Type	Phase 2	Phase 3
LYR-210 Long-acting Mometasone Furoate	Chronic Rhinosinusitis **Patients with Narrow Anatomy (Includes Surgically Naïve Patients)[1]**	**ENLIGHTEN 1 Trial**	
		ENLIGHTEN 2 Trial	
LYR-220 Long-acting Mometasone Furoate	Chronic Rhinosinusitis **Patients with Enlarged Anatomy due to Prior Sinus Surgery[1]**	**BEACON Phase 2 Trial**	

1) "Surgically naïve" and "sinus surgery" refer to ethmoid sinus surgery.

LYR-210 and LYR-220
Designed to be the New Standard of Care for CRS

Only product candidate designed to provide 6 months of CRS therapy with a single treatment

- FDA-approved API/steroid: Mometasone furoate
- Designed to provide continuous anti-inflammatory therapy
- Straightforward, office-based procedure with topical anesthesia
- Administered nasally via a single-use applicator
- Designed to be replaced every 6 months



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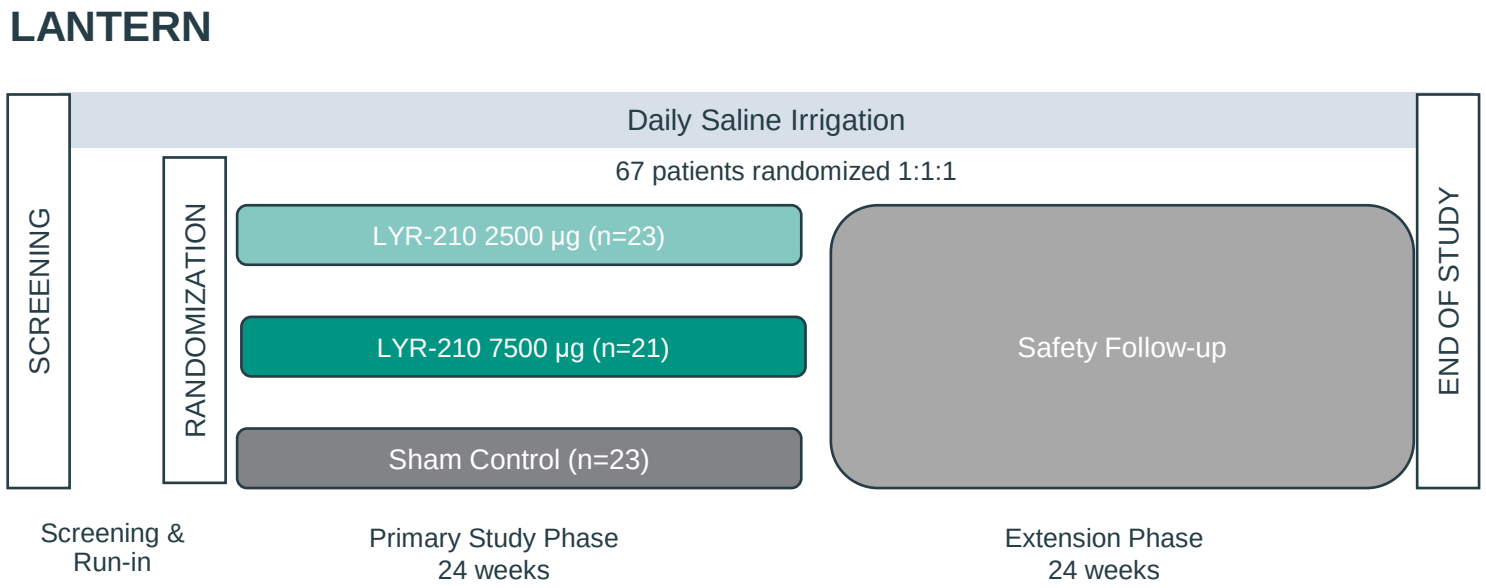
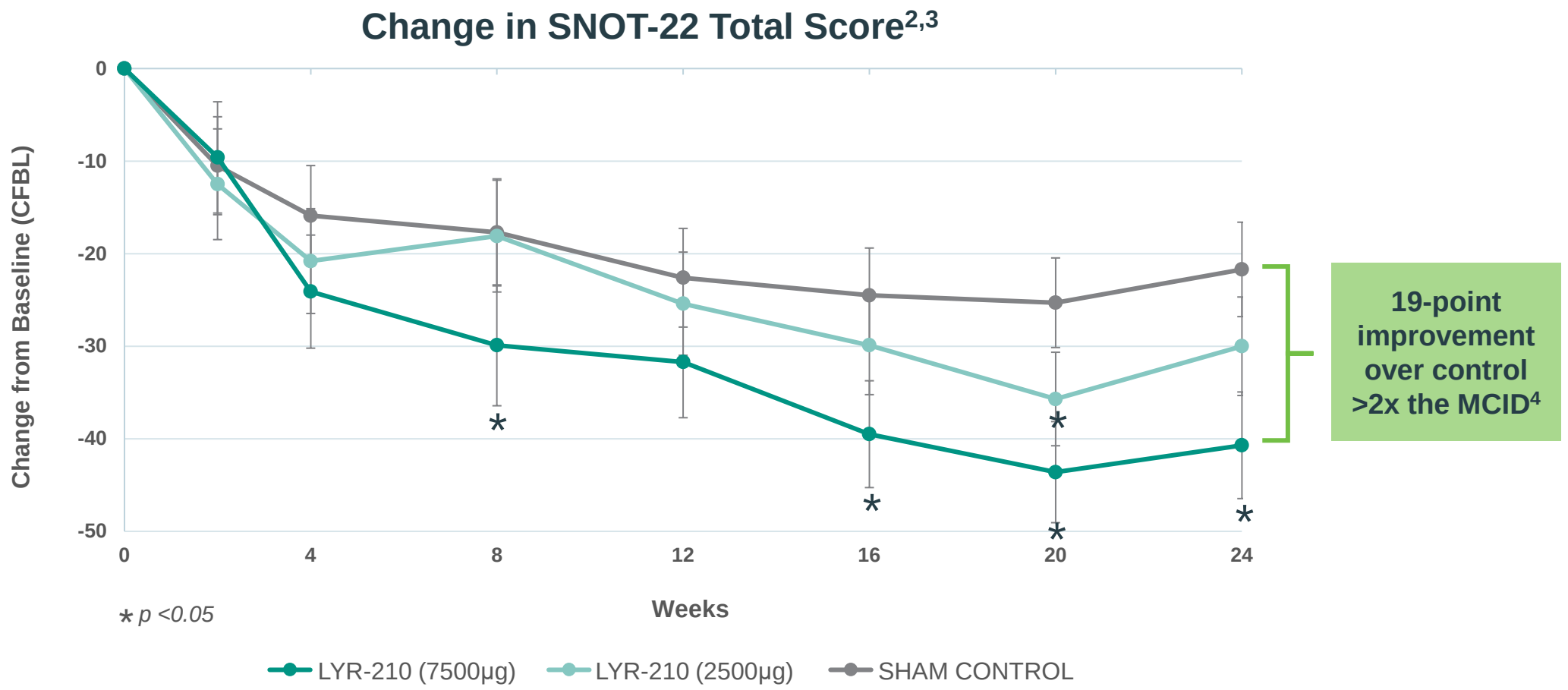
LANTERN Study Design
LYR-210 Phase 2 Clinical Trial in CRS Patients

- Multicenter, randomized, blinded, controlled, dose-ranging trial
- Adult CRS patients (polyp and non-polyp) who failed previous medical management and have not undergone FESS[1]
- **Primary endpoint:**
  - Change from baseline in 4 cardinal symptoms composite score (4CS) at Week 4[2,3]
- **Key secondary endpoints:**
  - SNOT-22[4]
  - Individual and composite cardinal symptom scores over 24 weeks



1) Functional endoscopic sinus surgery; 2) The study did not meet the primary endpoint at Week 4; however, the 7,500 ug dose group showed statistically significant improvements in 4CS over sham procedure control at weeks 16, 20, and 24. Due to COVID-19, study enrollment was curtailed at 67 patients (vs. 150 planned); 3) Four Cardinal Symptom Score is a composite of nasal blockage/obstruction, facial pain/pressure, nasal discharge and loss of sense of smell; 4) SinoNasal Outcome Test is a patient reported score from 0 – 110 based on symptoms; 5) NCT04041609

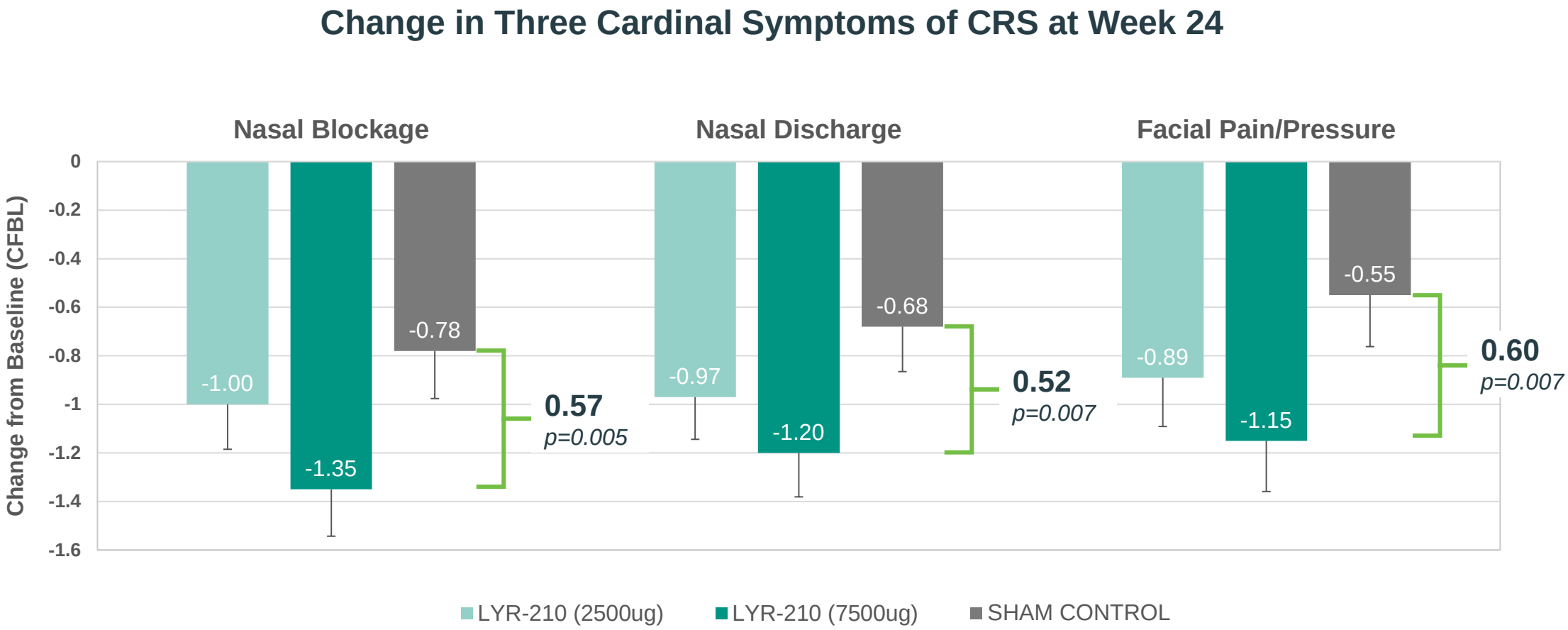
LANTERN Efficacy Results
Rapid and Durable Improvement in SNOT-22 Score over 24 Weeks[1]



Error bars represent standard error

1) Cervin A, et al. Long-acting implantable corticosteroid matrix for chronic rhinosinusitis: Results of LANTERN Phase 2 randomized controlled study. Int Forum AllergyRhinol. 2021;1-13; 2) SinoNasal Outcome Test is a patient reported score from 0 – 110 based on symptoms; 3) Data represents the least square mean. Missing data and data post use of rescue medication was imputed by LOCF method; 4) Minimum clinically important difference

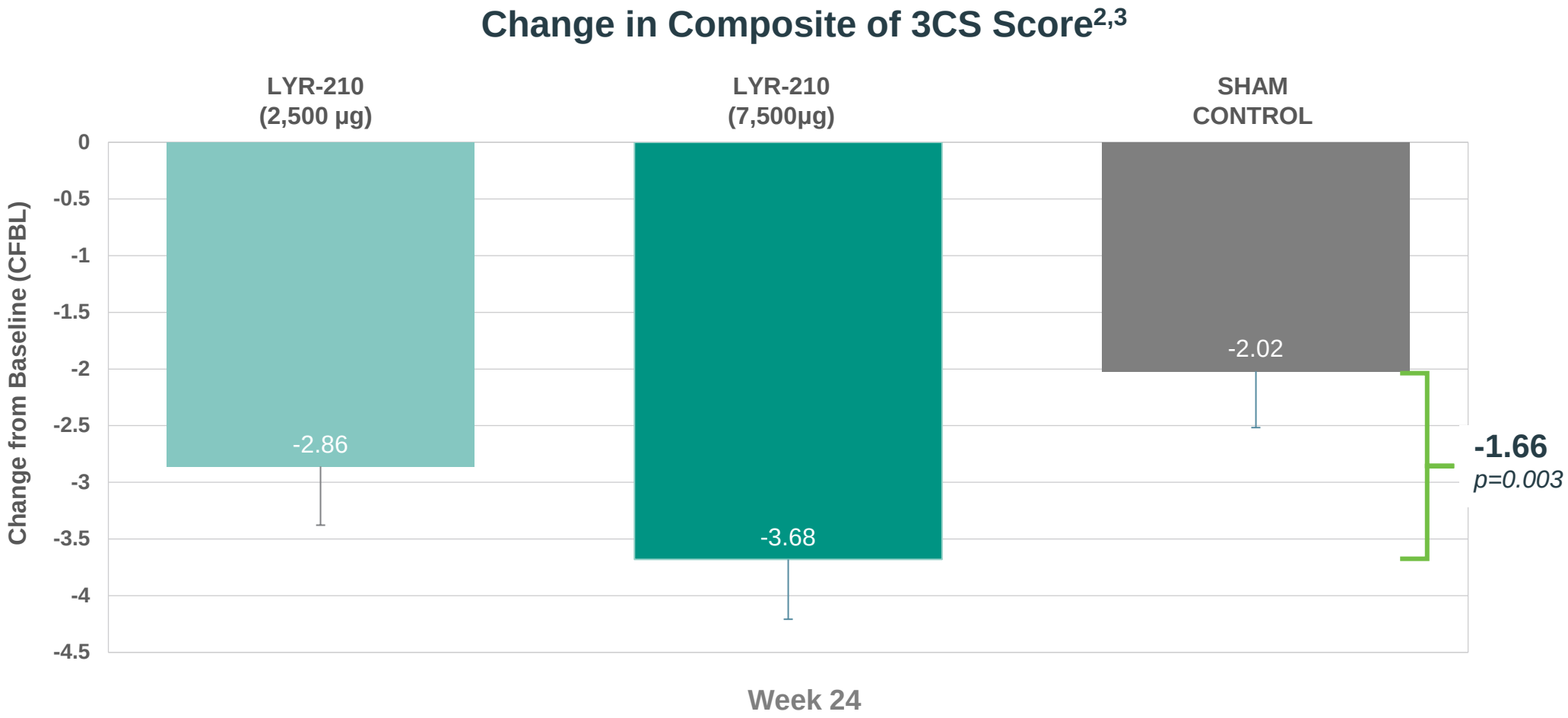
LANTERN Efficacy Results
Improvement Across Three Cardinal Symptoms of CRS[1]



Error bars represent standard error

1) Cervin A, et al. Long-acting implantable corticosteroid matrix for chronic rhinosinusitis: Results of LANTERN Phase 2 randomized controlled study. Int Forum AllergyRhinol. 2021;1-13

LANTERN Efficacy Results
Robust Effect in 3 Cardinal Symptom (3CS) Score at Week 24[1]

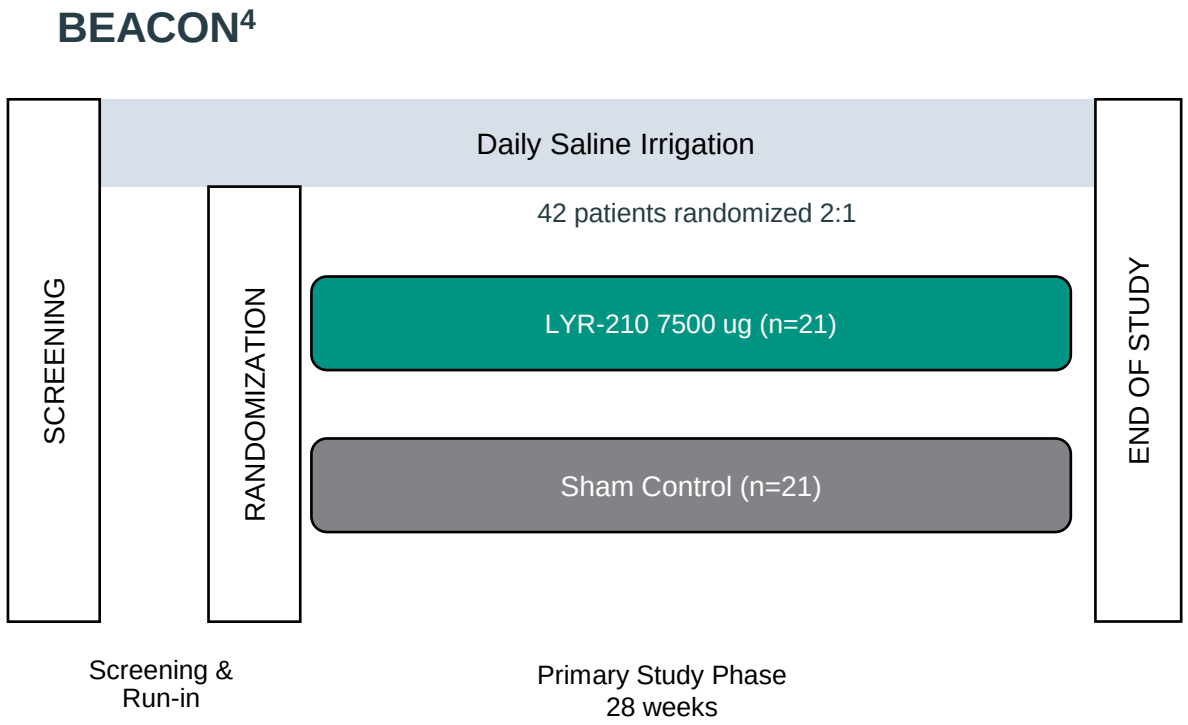


Error bars represent standard error

1) Cervin A, et al. Long-acting implantable corticosteroid matrix for chronic rhinosinusitis: Results of LANTERN Phase 2 randomized controlled study. Int Forum AllergyRhinol. 2021;1-13; 2) Mean change from baseline (CFBL) in the 7-day average score in the 3CS composite score of nasal blockage/obstruction, facial pain/pressure, and nasal discharge; 3) Post-hoc analysis; data represent LSM. P<0.05 is considered statistically significant to control.

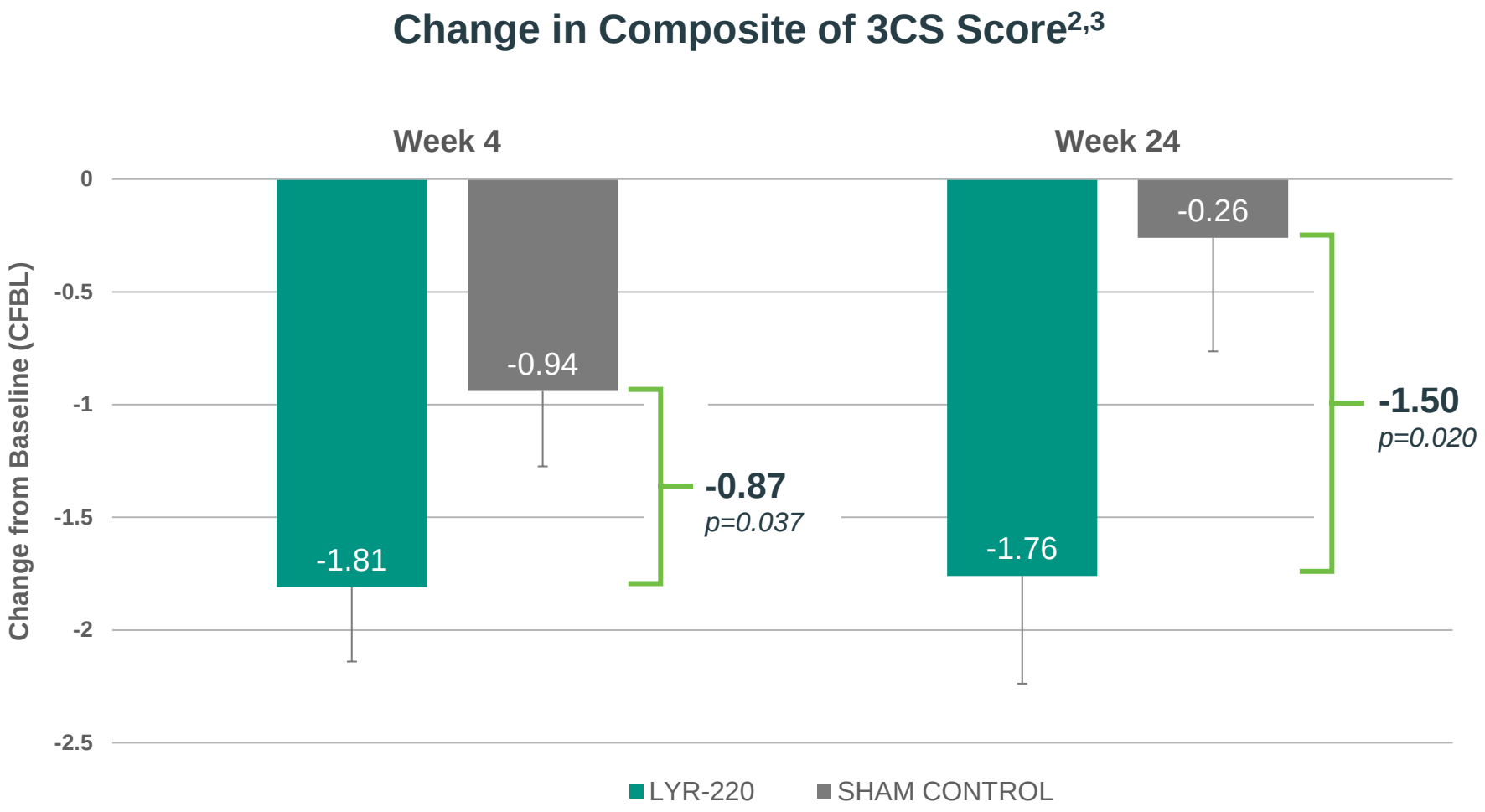
BEACON Study Design
LYR-220 Phase 2 Clinical Study

- Randomized, blinded, sham-controlled proof of concept study to assess safety and efficacy[1]
- Adult CRS patients (polyp and non-polyp) who have had a prior bilateral FESS and failed medical management
- **Primary endpoint – safety**
  - Product-related serious adverse events
- **Key efficacy endpoints**
  - 3CS Score[2]
  - SNOT-22[3]



1) Preceded by feasibility phase to choose matrix design; 2) Three Cardinal Symptom Score is as a composite of nasal blockage/obstruction, facial pain/pressure, and nasal discharge; 3) SinoNasal Outcome Test is a patient reported score from 0 – 110 based on symptoms; 4) NCT05035654

BEACON Efficacy Results
Robust Effect in 3 Cardinal Symptoms (3CS) Score - Weeks 4 and 24[1]

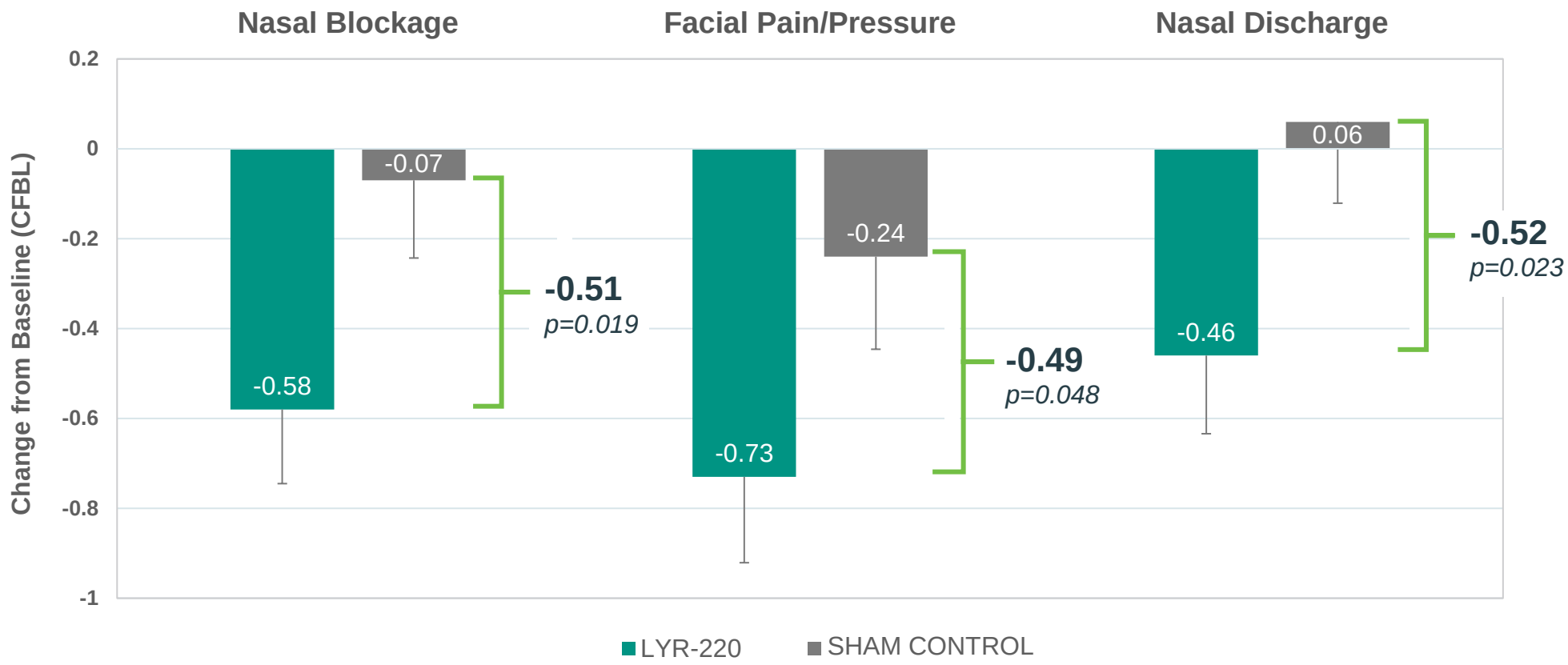


Error bars represent standard error

1) Data on file as of January 5, 2024; 2) Mean change from baseline (CFBL) in the 7-day average score in the 3CS composite score of nasal blockage/obstruction, facial pain/pressure, and nasal discharge; 3) Data represent least square means. Data post rescue was censored and imputed using patient's worst observed post-baseline score. P<0.05 is considered statistically significant to control.

BEACON Efficacy Results
Improvement Across Three Cardinal Symptoms of CRS[1]

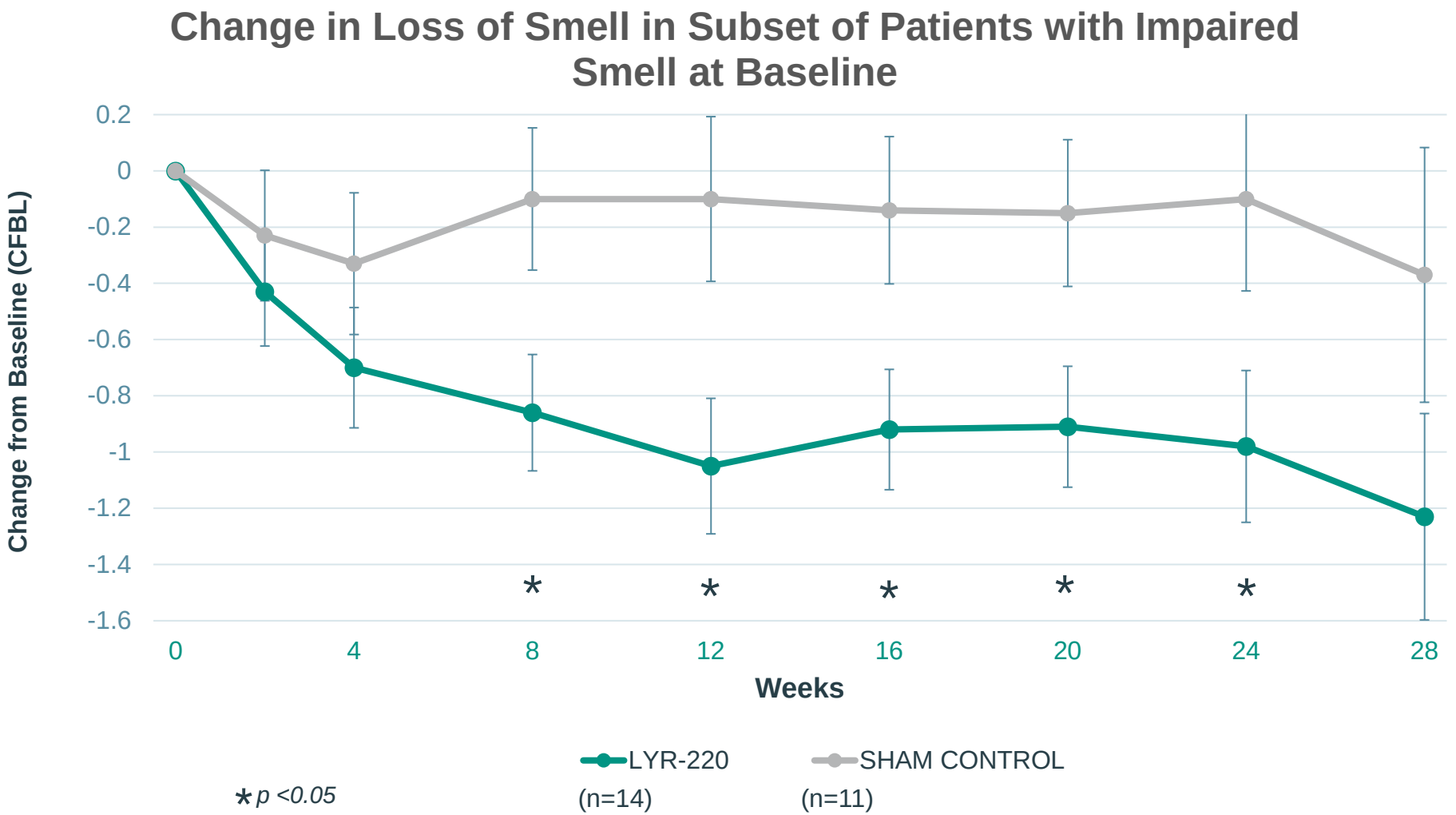
Change in Three Cardinal Symptoms of CRS at Week 24[2,3]



Error bars represent standard error

1) Data on file as of January 5, 2024; 2) Mean change from baseline (CFBL) in the 7-day average score in each individual CS of nasal blockage/obstruction, facial pain/pressure, and nasal discharge; 3) Data represent least square means. Data post rescue was censored and imputed using patient's worst observed post-baseline score. P<0.05 is considered statistically significant to control.

BEACON Efficacy Results
Improvement in Loss of Smell[1]



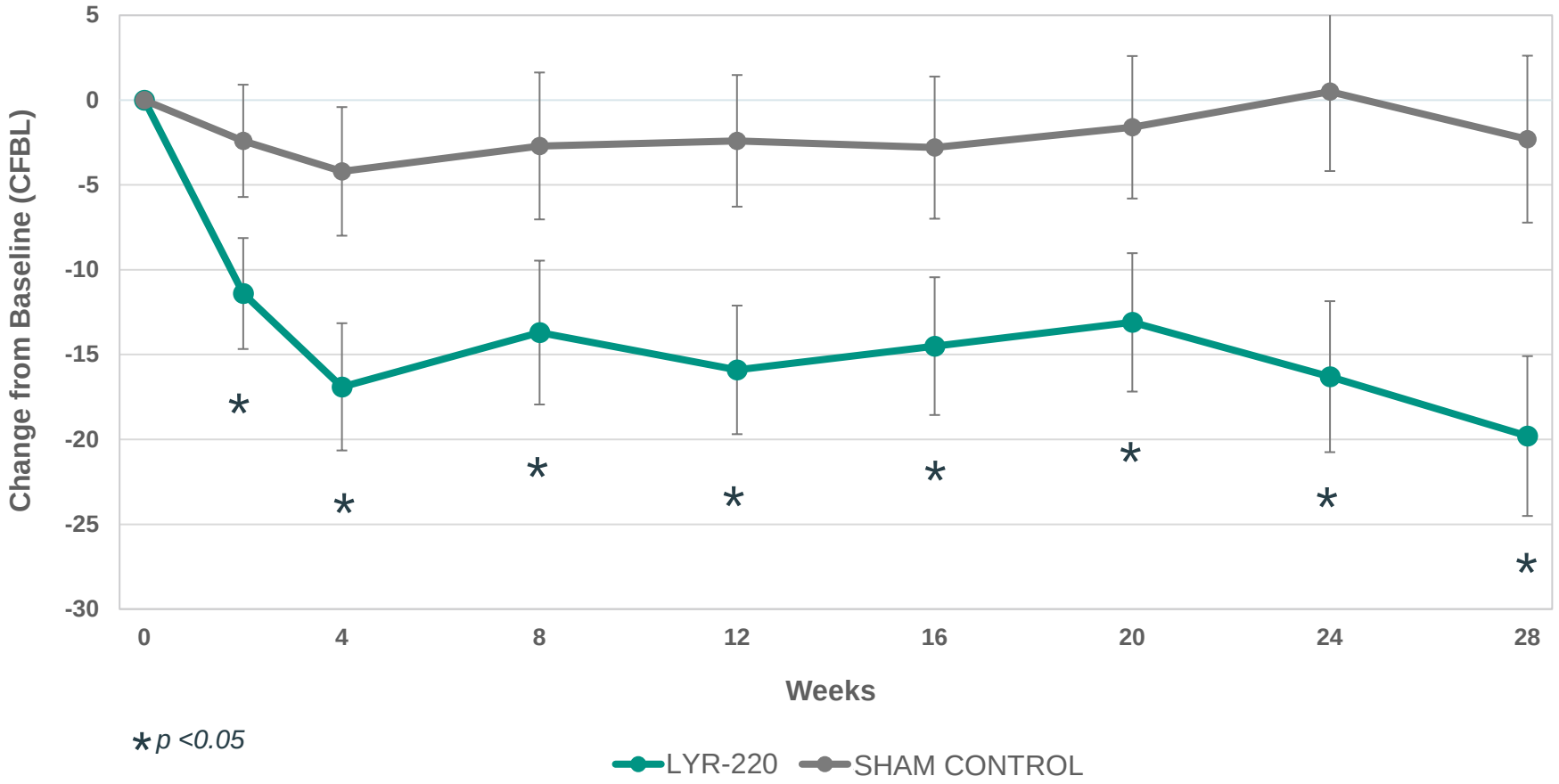
Statistically significant (0.87-point) improvement over control at week 24 (p=0.026)

∗ *p <0.05*

1) Data on file as of January 5, 2024.

BEACON Efficacy Results
Rapid and Durable Improvement in SNOT-22 Score over 28 Weeks[1]

Change in SNOT-22 Total Score[2,3]



Achieved 17-point improvement over control (1.9x the MCID[4]) as early as two weeks and through 28 weeks

Error bars represent standard error

1) Data on file as of January 5, 2024; 2) SinoNasal Outcome Test is a patient reported score from 0 – 110 based on symptoms; 3) Data represent the least square means. Data post rescue was censored and imputed using patient's worst observed post-baseline score. P<0.05 is considered statistically significant to control; 4)Minimum clinically important difference.

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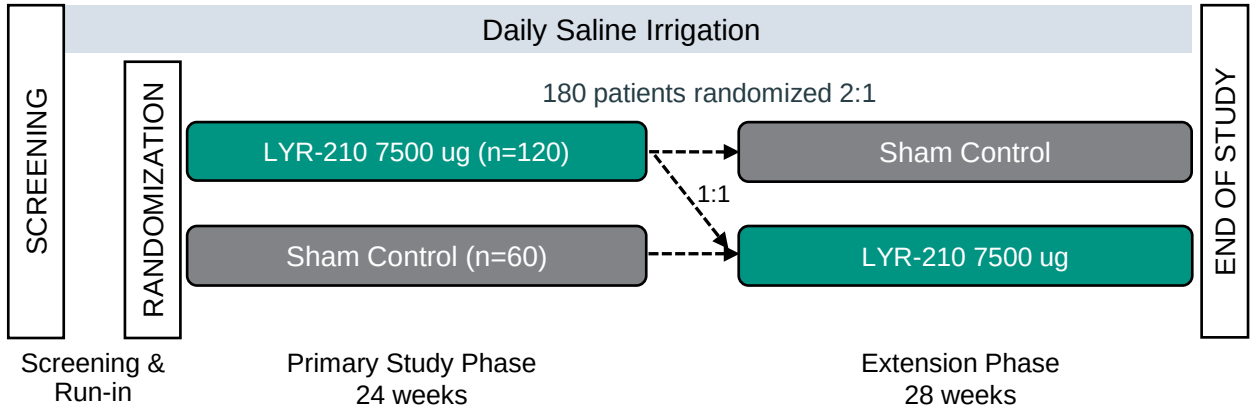
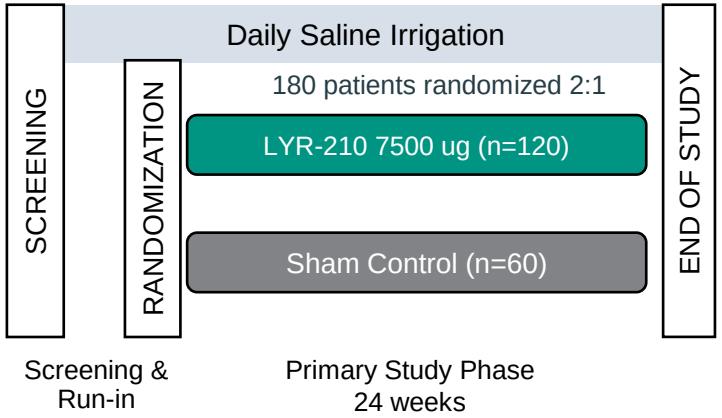
ENLIGHTEN Program Design
LYR-210 Ongoing Pivotal Phase 3 Program

- Two pivotal studies of ~180 subjects each
- Adult CRS patients each, without nasal polyps or with grade 1 nasal polyps, who have failed medical management[1]
- **Primary endpoint**
  - Change from baseline in 3CS[2] Score at Week 24 in patients without nasal polyps
- **Key secondary endpoints**
  - Individual cardinal symptoms
  - SNOT-22[3]
  - CT sinus opacification

ENLIGHTEN 1[4]



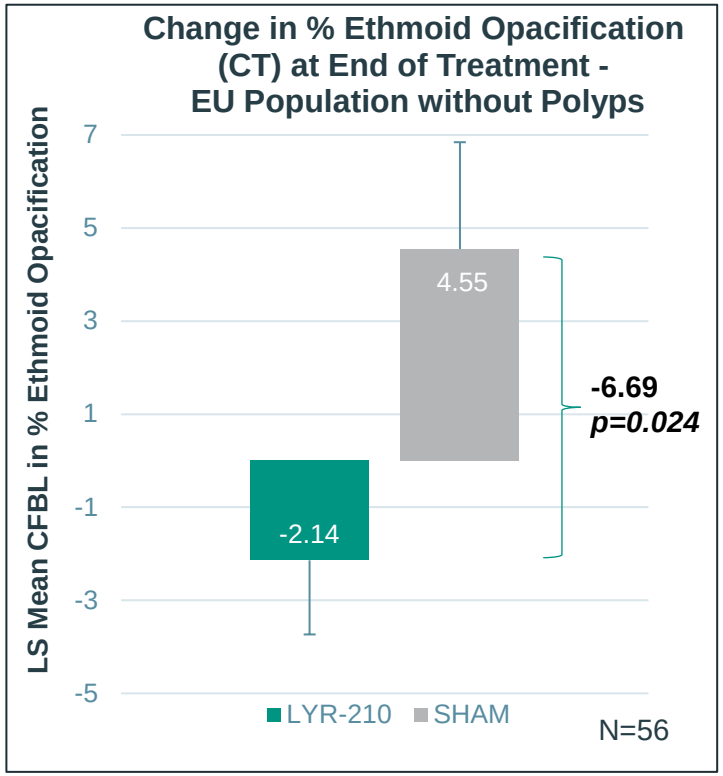
ENLIGHTEN 2[5]



1) Up to 30 patients with nasal polyps per study; study population represents 95% of CRS patients; 2) Three Cardinal Symptom Score is as a composite of nasal blockage/obstruction, facial pain/pressure, and nasal discharge; 3) SinoNasal Outcome Test is a patient reported score from 0 – 110 based on symptoms; 4) NCT05219968; 5) NCT05295459

ENLIGHTEN 1 Topline Results at 24 Weeks

- Primary readout as of May 6, 2024 and sub-group analyses as of August 14, 2024
  - Primary endpoint of Change from Baseline (CFBL) in 3CS Score at Week 24 in Patients Without Nasal Polyps was not met
    - *In the primary efficacy analysis, treatment with LYR-210 resulted in a mean (standard deviation; SD) improvement in the 3CS score of 2.13 (2.17) points, compared to 2.06 (2.14) points in the SHAM control group*[1]
  - Secondary endpoint of SNOT-22 score in the ITT population demonstrated a mean (SD) improvement relative to baseline in the LYR-210 treated patients of 20.2 (21.38) points compared to 15.70 (18.55) points in the SHAM control group[1]
  - Non-polyp patients in EU demonstrated objective improvement relative to the SHAM control[1] group in Percent Ethmoid Opacification by CT *(graph to right)*
  - In the polyp patient cohort[2], robust improvement in patient symptoms for LYR-210 treated patients relative to the SHAM control group[1] *(see data on slide 20)*
  - LYR-210 was generally well tolerated, with no product-related serious adverse events



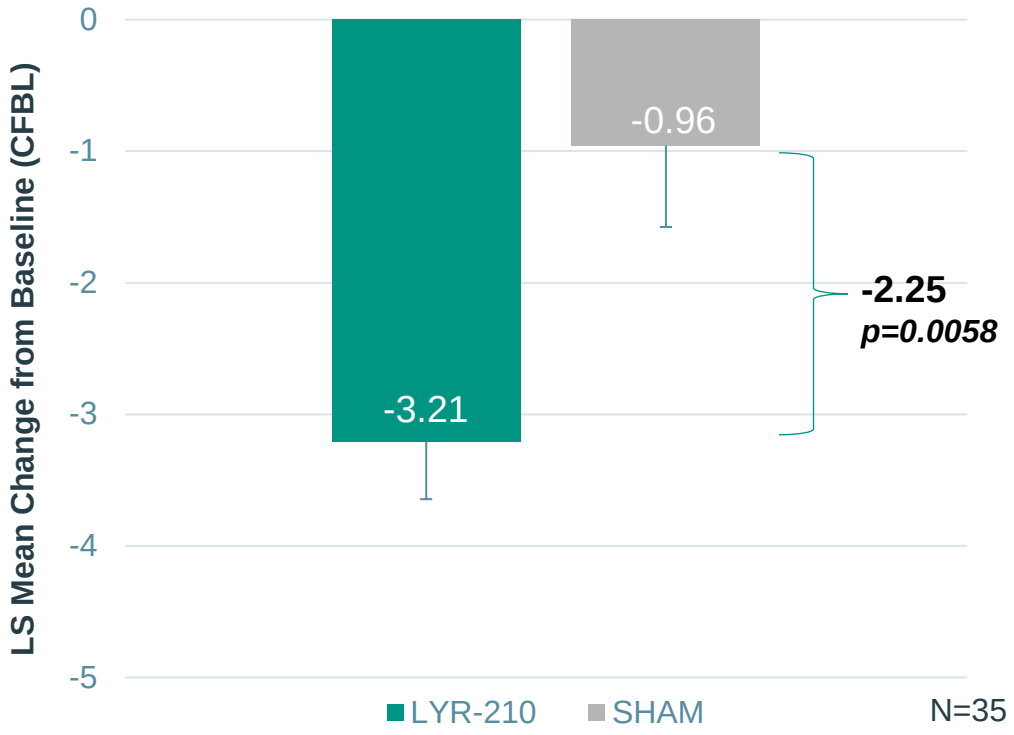
ENLIGHTEN 1 and 2 are ongoing with ENLIGHTEN 2 topline results expected in 1H 2025

1) SHAM patients received treatment in the form of a mock procedure that included decongestion followed by daily saline irrigation, potentially leading to improvements in their symptoms. 2) Polyps are an objective indicator of CRS disease; non-polyp is a heterogeneous CRS population which may have been enriched with more transient disease particularly in the US due to patient recruitment through advertising campaign.

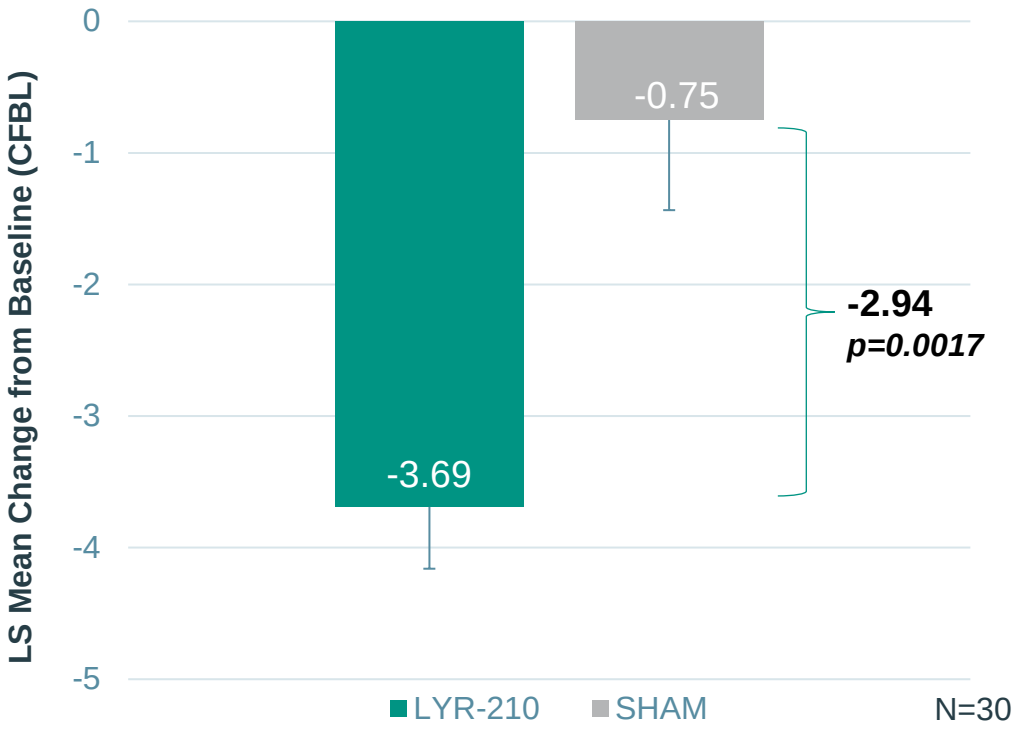
ENLIGHTEN 1: 3 Cardinal Symptoms in Polyp Patients at Week 24

Improvement observed in the three cardinal symptoms in polyp subgroup, and to a greater extent in those with at least moderate nasal congestion at baseline

Change in Composite of 3CS Score - All Polyp Patients[1]



Change in Composite of 3CS Score – Patients with Nasal Congestion Score ≥ 2 @ Baseline[1,2]

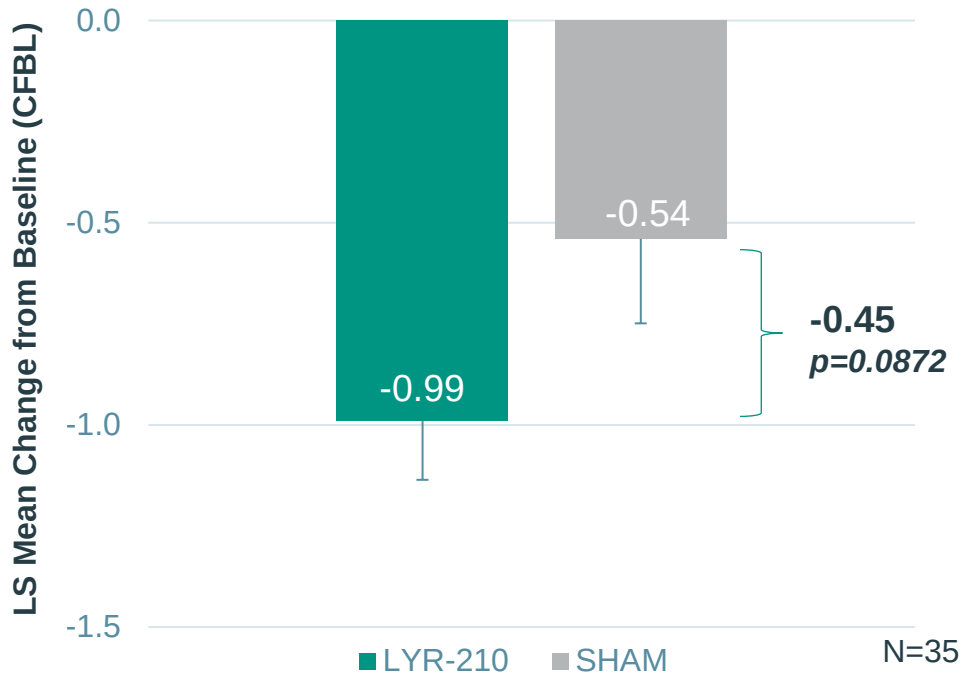


1) Data represent least square means; 2) Moderate to severe nasal congestion as assessed on a 0-3 scale.

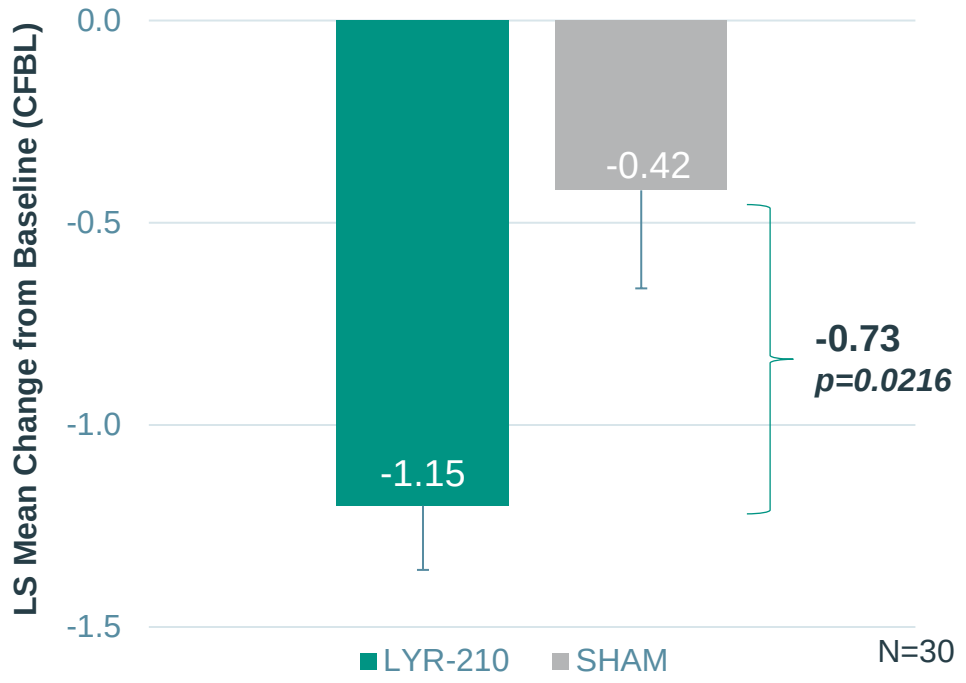
ENLIGHTEN 1: Nasal Congestion Score in Polyp Patients at Week 24

Nasal congestion scores improved in polyp patients with at least moderate nasal congestion at baseline

Change in Nasal Congestion Score – All Polyp Patients[1]



Change in Nasal Congestion Score – Patients ≥ 2 @ Baseline[1,2]



1) Data represent least square means; 2) Moderate to severe nasal congestion as assessed on a 0-3 scale.

LYR-210, if Advanced, Would Be Positioned To Align With Current ENT Practices

- Office-based procedure that ENTs are accustomed to performing
- Treatment option for patients who are unwilling to undergo surgery, allowing ENTs to serve more patients in their care
- Expected to fit into ENT practice reimbursement models

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Anticipated Milestones

LYR-210: ENLIGHTEN Phase 3 Program

✓ May 2024: Topline data from ENLIGHTEN 1

- Q4 2024: Extension study data from ENLIGHTEN 1
- 2H 2024: Complete enrollment in ENLIGHTEN 2
- 1H 2025: Topline data from ENLIGHTEN 2

Financial Profile

- Cash, cash equivalents and short-term investments of $67.5 million as of June 30, 2024
- 65.5 million common shares outstanding as of August 1, 2024

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