LYRA THERAPEUTICS

Corporate Presentation

December 2023

Disclaimer

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including statements regarding the Company's cash runway into the first quarter of 2025, the Company's pipeline of product candidates, the enrollment and success of the ENLIGHTEN Phase 3 program, the timing for reporting top line data from the Company's clinical trials, the Company's ability to manufacture its product candidates in-house, the safety and efficacy of the Company's product candidates and the outcome of the Phase 2 BEACON trial. 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: the fact that the Company has incurred significant losses since inception and expects to incur additional losses for the foreseeable future; the Company's need for additional funding, which may not be available; the Company's limited operating history; the fact that the Company has no approved products; the fact that the Company's product candidates are in various stages of development; the fact that the Company has never scaled up an in-house manufacturing facility for clinical or commercial use; or the fact that the Company may not be successful in its efforts to identify and successfully commercialize its product candidates; the fact that clinical trials required for the Company's product candidates are expensive and time-consuming, and their outcome is uncertain; the fact that the FDA may not conclude that certain of the Company's product candidates satisfy the requirements for the Section 505(b)(2) regulatory approval pathway; the Company's inability to obtain required regulatory approvals; effects of recently enacted and future legislation; the possibility of system failures or security breaches; effects of significant competition; the fact that the successful commercialization of the Company's 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 achieve market acceptance; product liability lawsuits; the fact that the Company must scale its in-house manufacturing capabilities or rely on third parties for the manufacture of materials for its research programs, pre-clinical studies and clinical trials and commercial supply; the Company's reliance on third parties to conduct its preclinical studies and clinical trials; the Company's inability to succeed in establishing and maintaining collaborative relationships; the Company's reliance on certain suppliers critical to its production; failure to obtain and maintain or adequately protect the Company's intellectual property rights; failure to retain key personnel or to recruit qualified personnel; difficulties in managing the Company's growth; effects of natural disasters, terrorism and wars; the fact that the global pandemic caused by COVID-19 could adversely impact the Company's business and operations, including the Company's clinical trials; the fact that the price of the Company's common stock may be volatile and fluctuate substantially; significant costs and required management time as a result of operating as a public company and any securities class action litigation. 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 November 7, 2023 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 presentation. Any such forward-looking statements represent management's estimates as of the date of this presentation. 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.

Company Overview

Clinical-stage biotechnology company developing innovative therapies for the localized treatment of chronic rhinosinusitis

- **Bioresorbable nasal implant designed to deliver 6 months of continuous anti-inflammatory therapy to the site of disease**
- **Indication: Chronic rhinosinusitis (CRS)**
  - ~12% of the US population[1]
  - ~50% of patients fail medical therapy[2]
- **Pivotal Phase 3 trials ongoing for lead candidate LYR-210**
- **Patent protection through 2036**

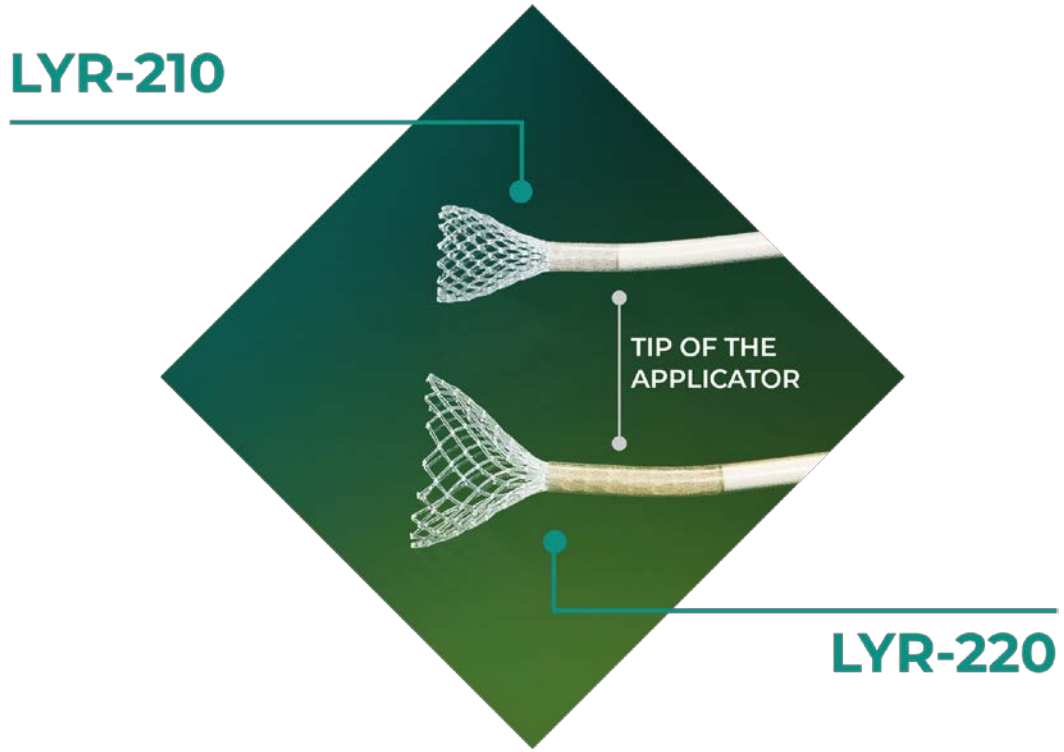
1) Summary Health Statistics Tables for U.S. Adults: National Health Interview Survey, 2018, Tables A-2b, A-2c; 2) Baguley et al. Int Forum Allergy Rhinol, 2014;4(7):525-3;

Lyra's Proprietary Drug-Eluting Implants

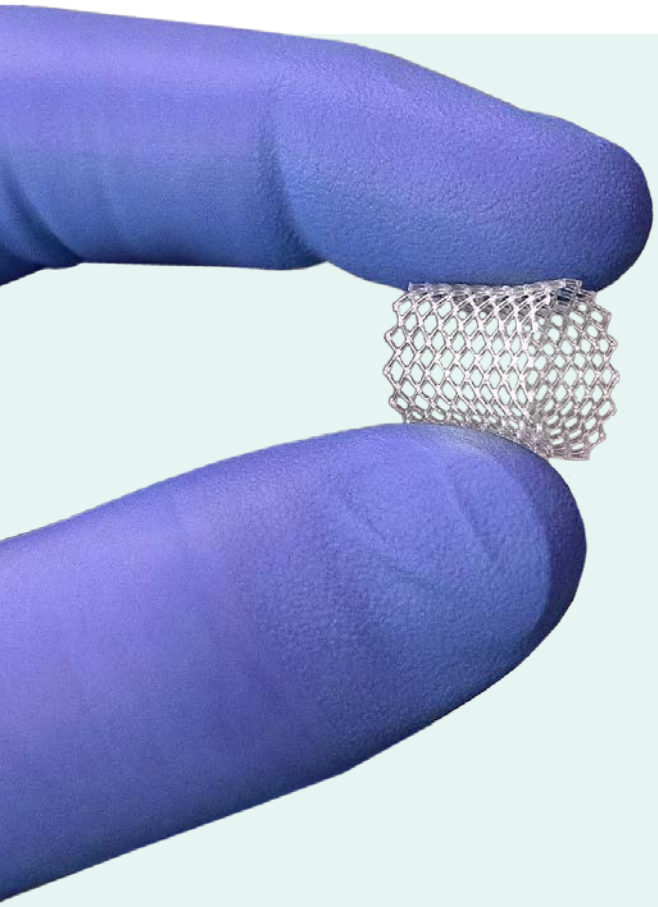
Biocompatible Mesh Scaffold
Maximizes surface area for drug release while maintaining underlying tissue function

Engineered Elastomeric Matrix
Adapts to target anatomy

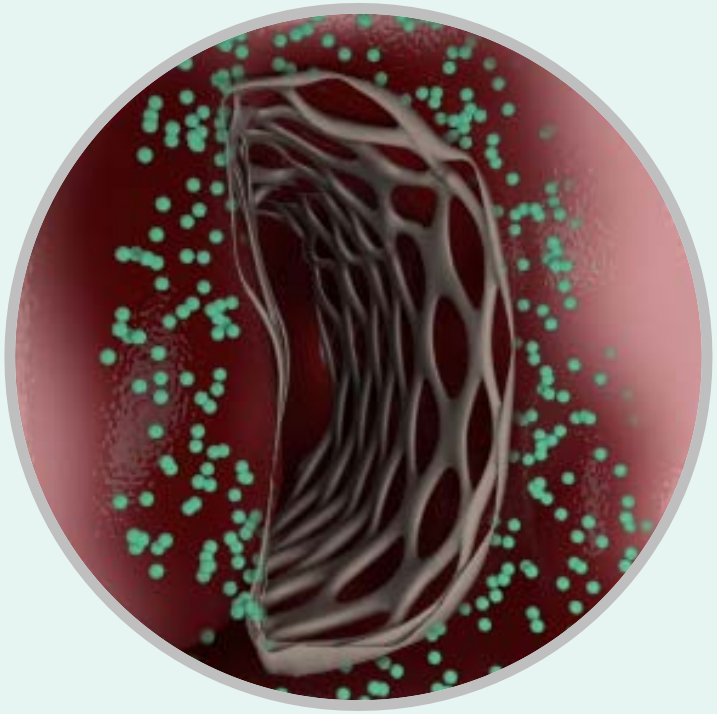
Versatile Polymer-Drug Complex
Continuous drug release for long-term dosing



Lyra's Proprietary Drug-Eluting Implant



- Designed to deliver 6 months of continuous, local drug therapy with a single placement
- Shape memory keeps matrix in place



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

CRS Cardinal Symptoms[1]

- Nasal obstruction and congestion
- Facial pain and pressure
- Nasal discharge
- Olfactory loss

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]

60% surgically naïve[5, 6]

40% had prior sinus surgery[5, 6]

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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; 5) Biocom Consulting ENT Quantitative Market Research – June 2019; 6) “Surgically naïve” and “sinus surgery” refer to ethmoid sinus surgery.

Lyra Pipeline

LYR-210 and LYR-220 are designed to address the full spectrum of CRS patients

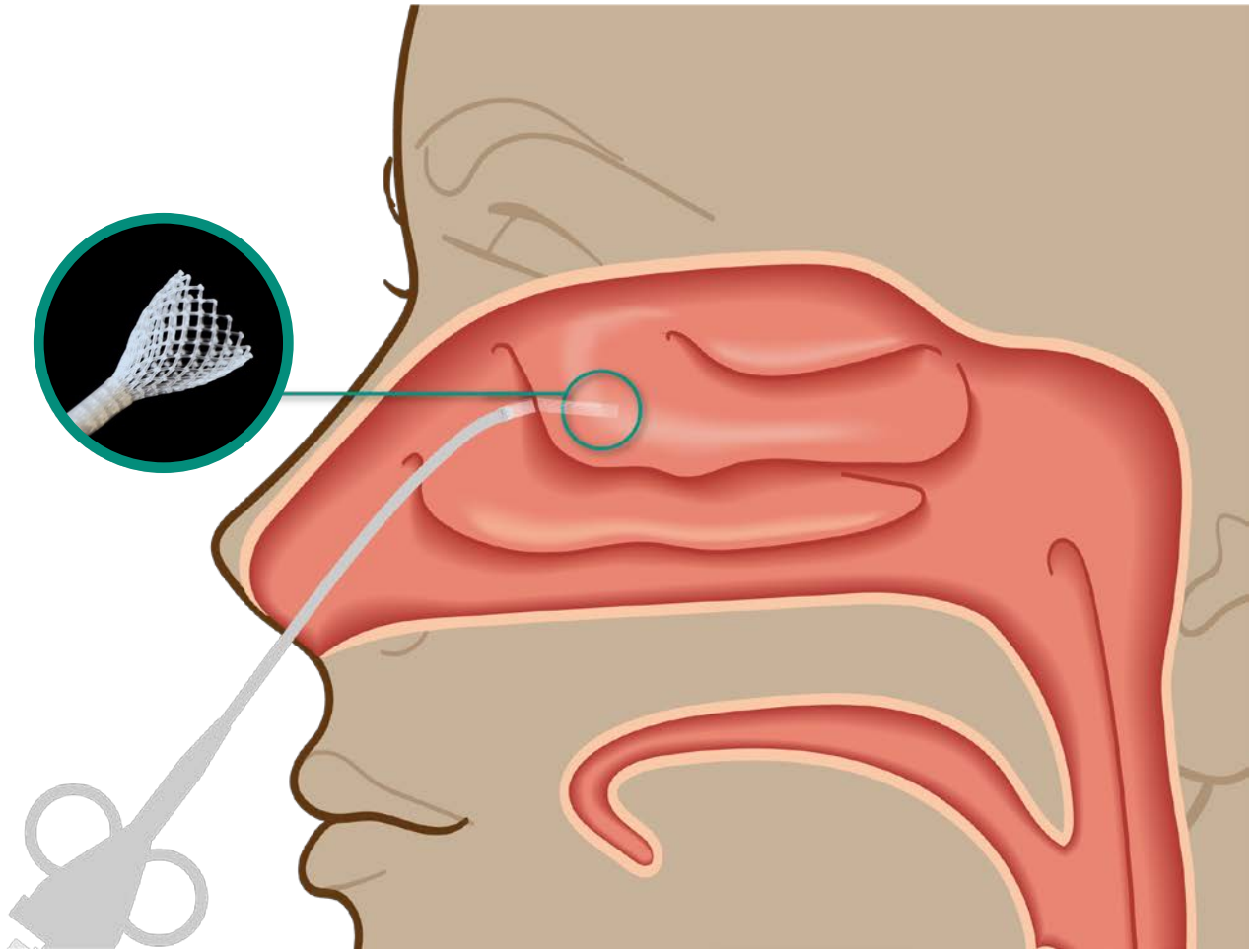
Candidate	CRS Patient Type	Phase 2	Phase 3
LYR-210 Long-acting Mometasone Furoate	Chronic Rhinosinusitis **Patients with Surgically-Naïve Anatomy[1]** **ENLIGHTEN Phase 3 Program**		
LYR-220 Long-acting Mometasone Furoate	Chronic Rhinosinusitis **Patients with Post-Surgical Anatomy[1]** **BEACON Phase 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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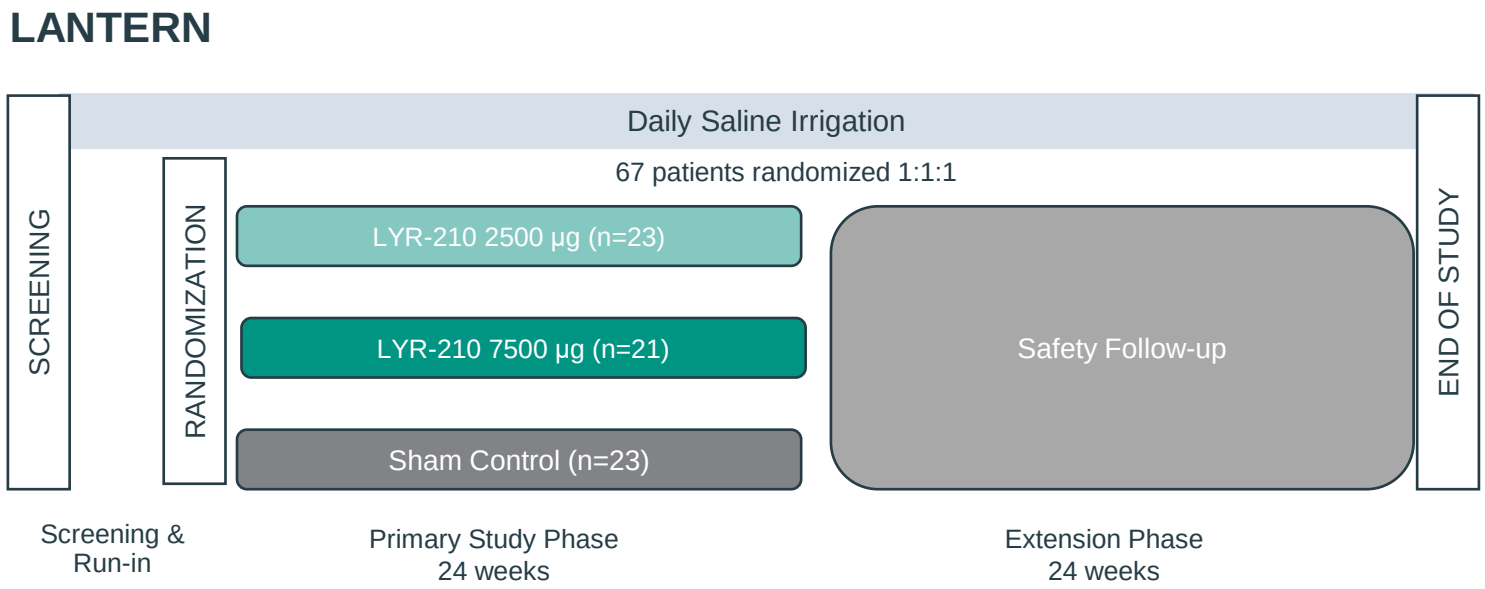
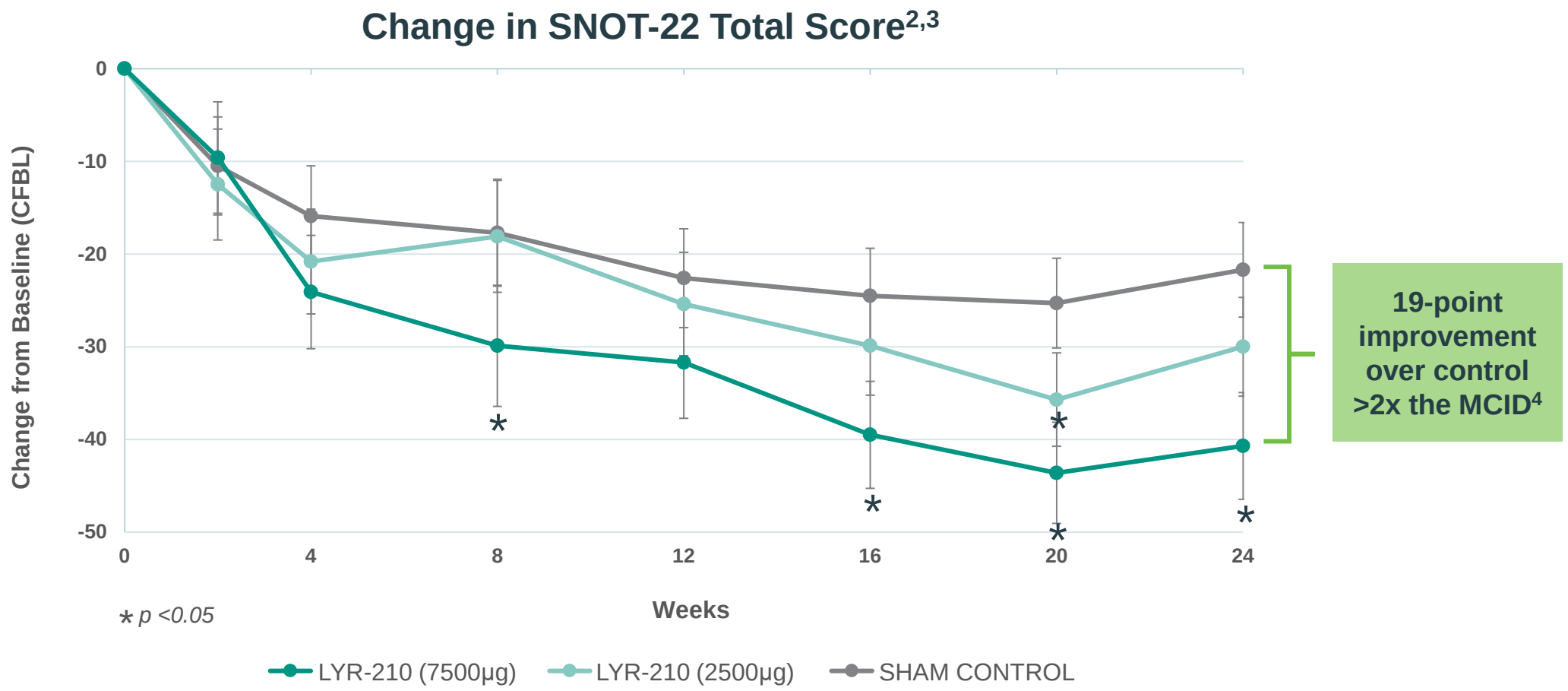
LANTERN Study Design
LYR-210 Phase 2 Clinical Trial in CRS Patients

- Multicenter, randomized, blinded, controlled, dose-ranging trial
- Adult CRS patients 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

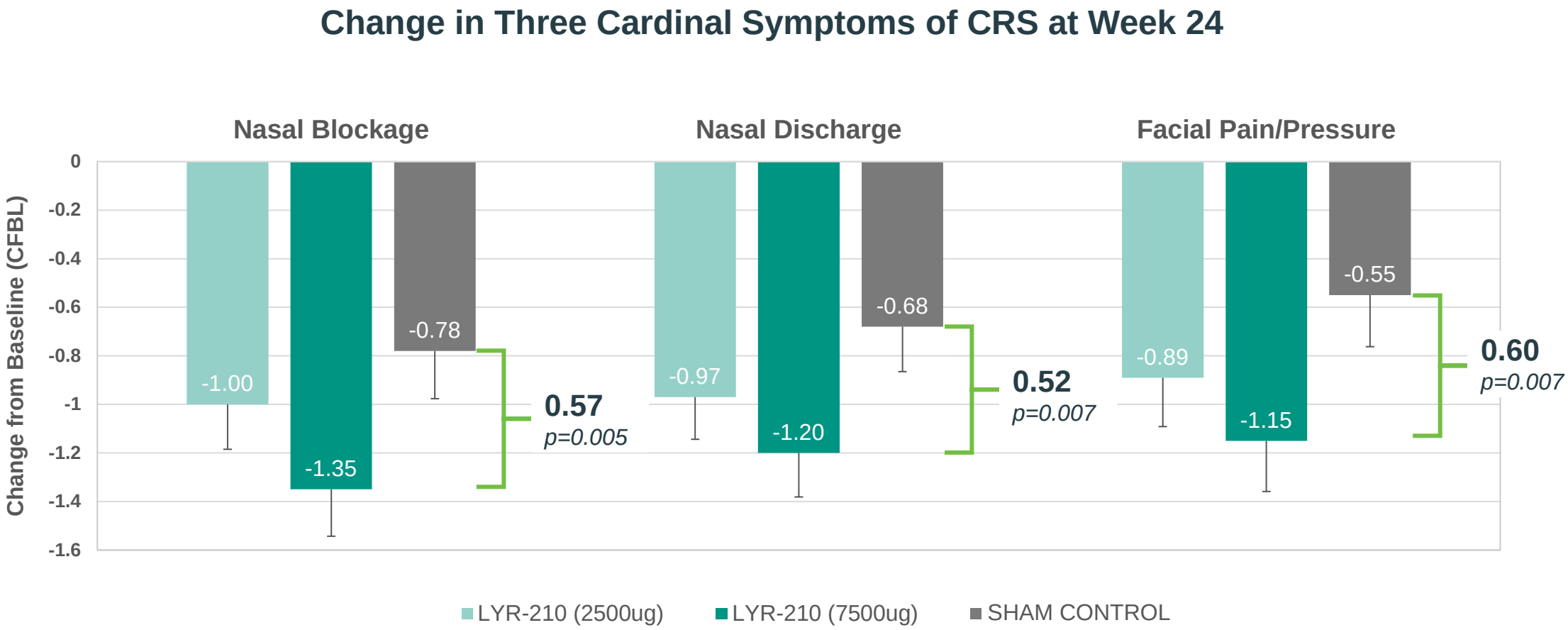
LANTERN Efficacy Results
Rapid and Durable Improvement in SNOT-22 Score over 24 Weeks[1]



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]



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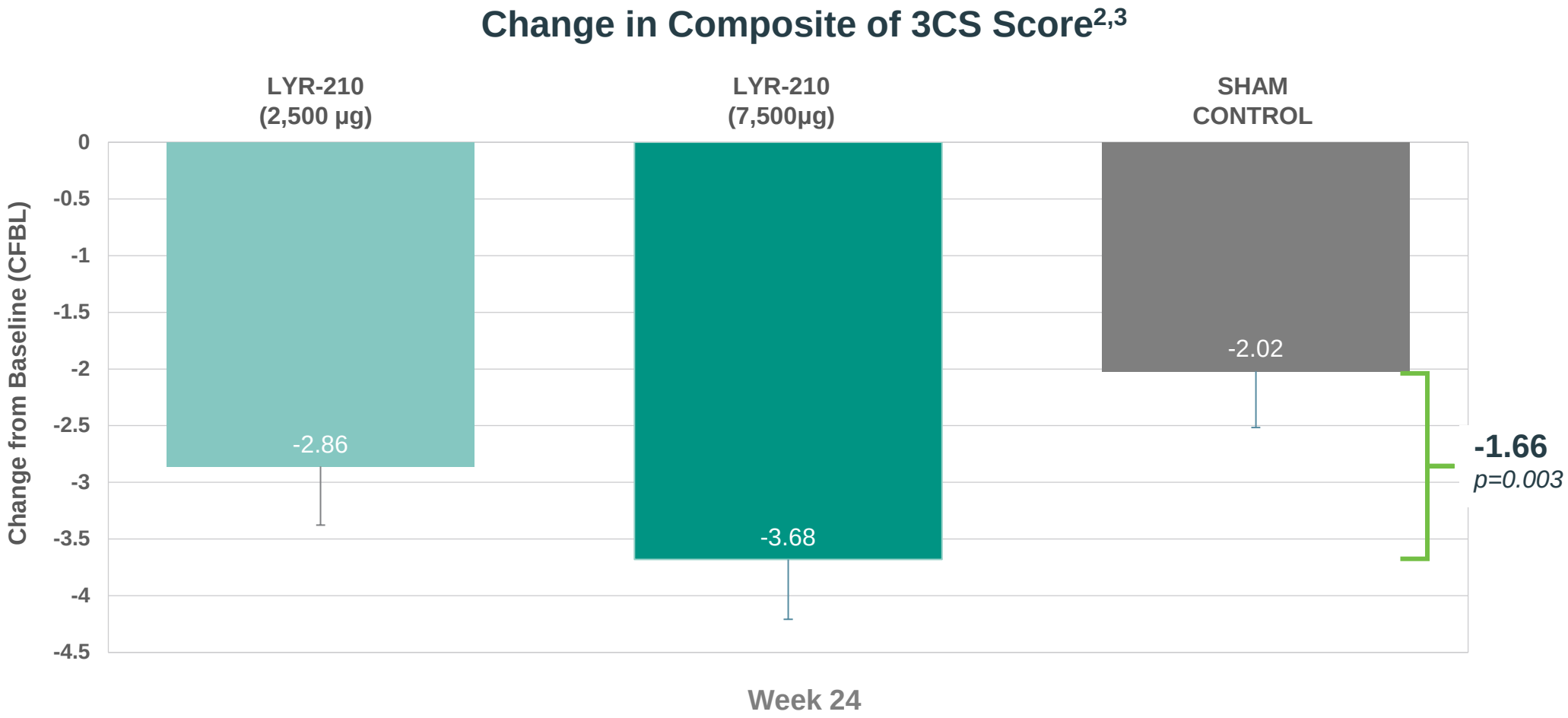
1) Cervin A, et al. Long-acting implantable corticosteroid matrix for chronic rhinosinusitis: Results of LANTERN Phase 2 randomized controlled study. Int Forum AllergyRhinol. 2021;1-13

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



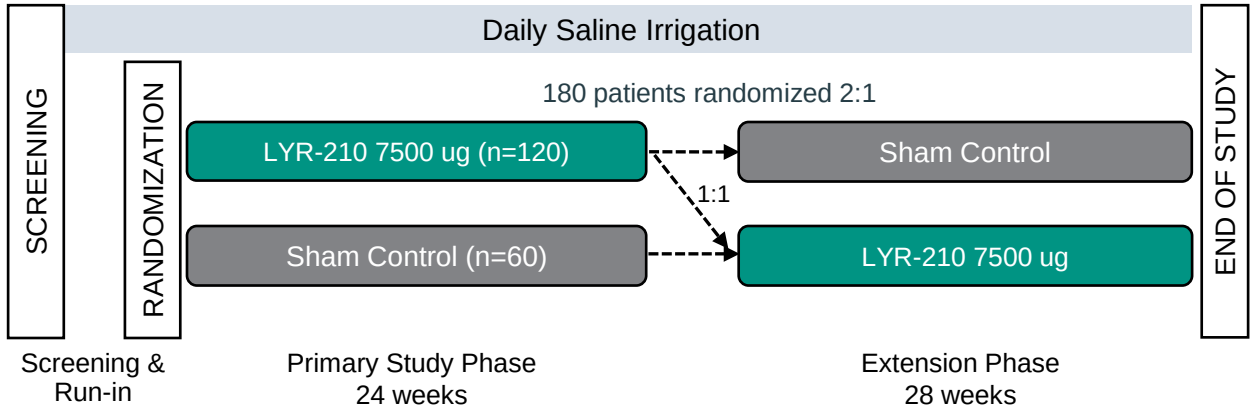
Error bars represent standard error

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.

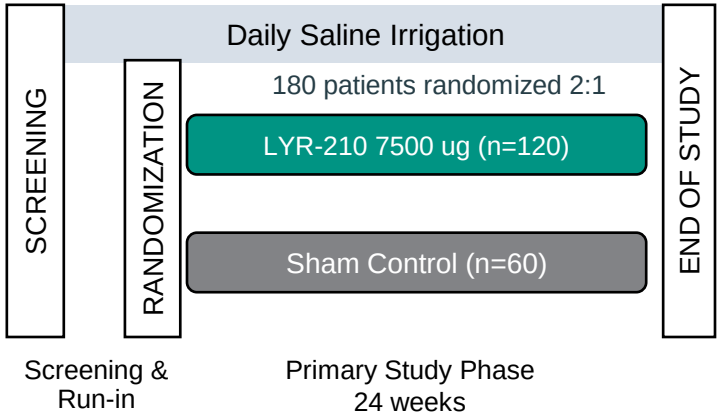
ENLIGHTEN Program Design
LYR-210 Ongoing Pivotal Phase 3 Program

- 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 I[4]



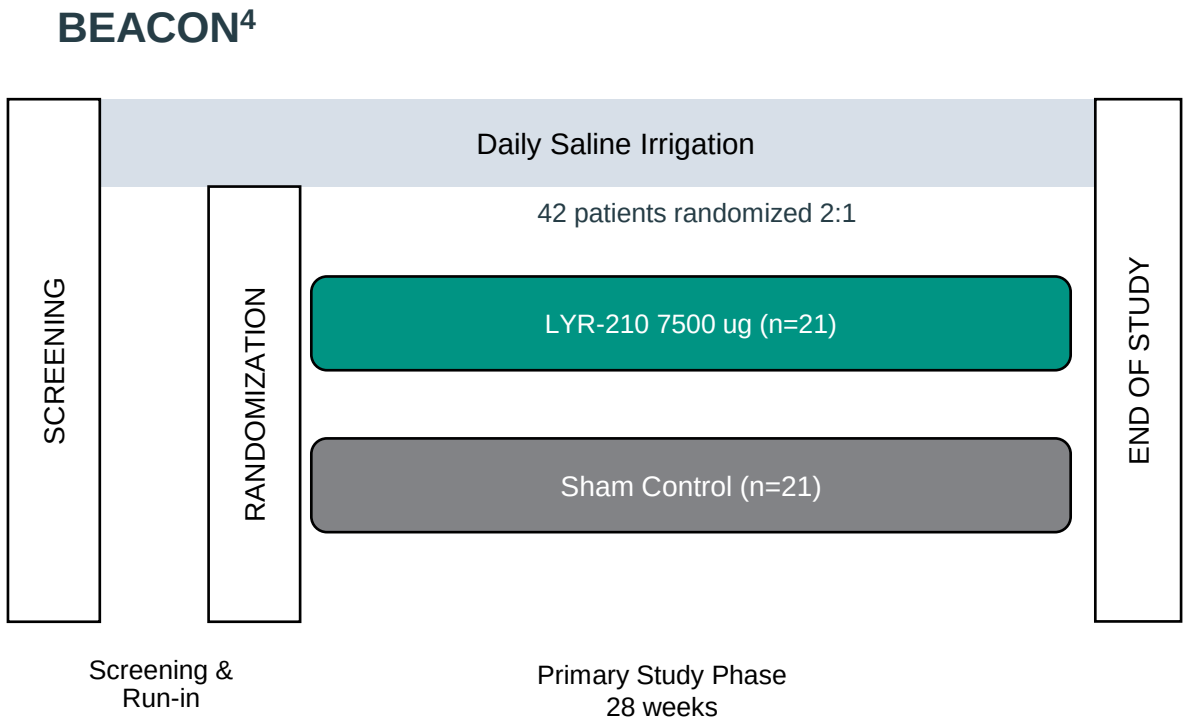
ENLIGHTEN II[5]



1) Limit of 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

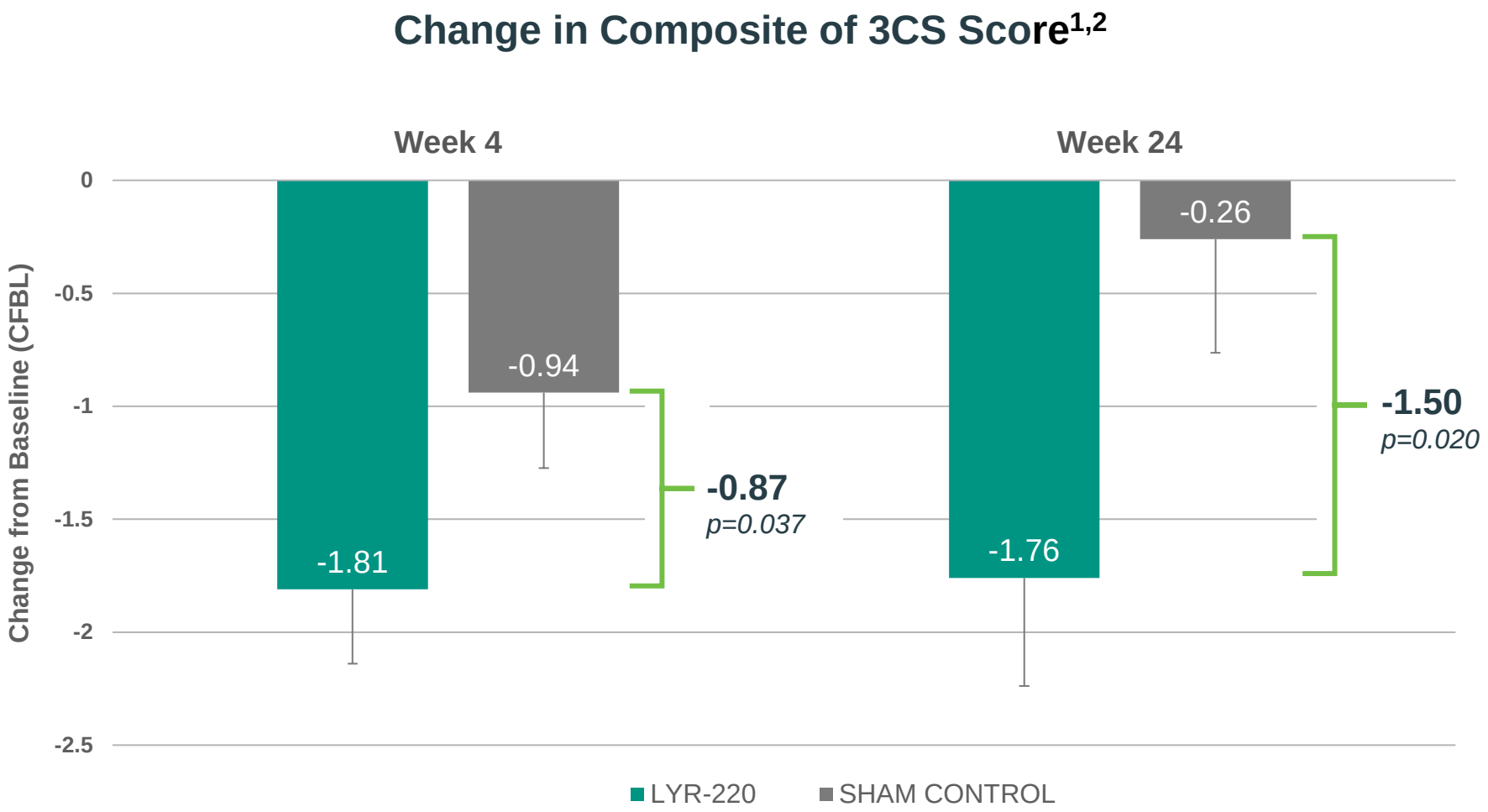
BEACON Study Design
LYR-220 Phase 2 Clinical Study

- Randomized, blinded, sham-controlled proof of concept study to assess safety and efficacy[1]
- Adult CRS patients 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

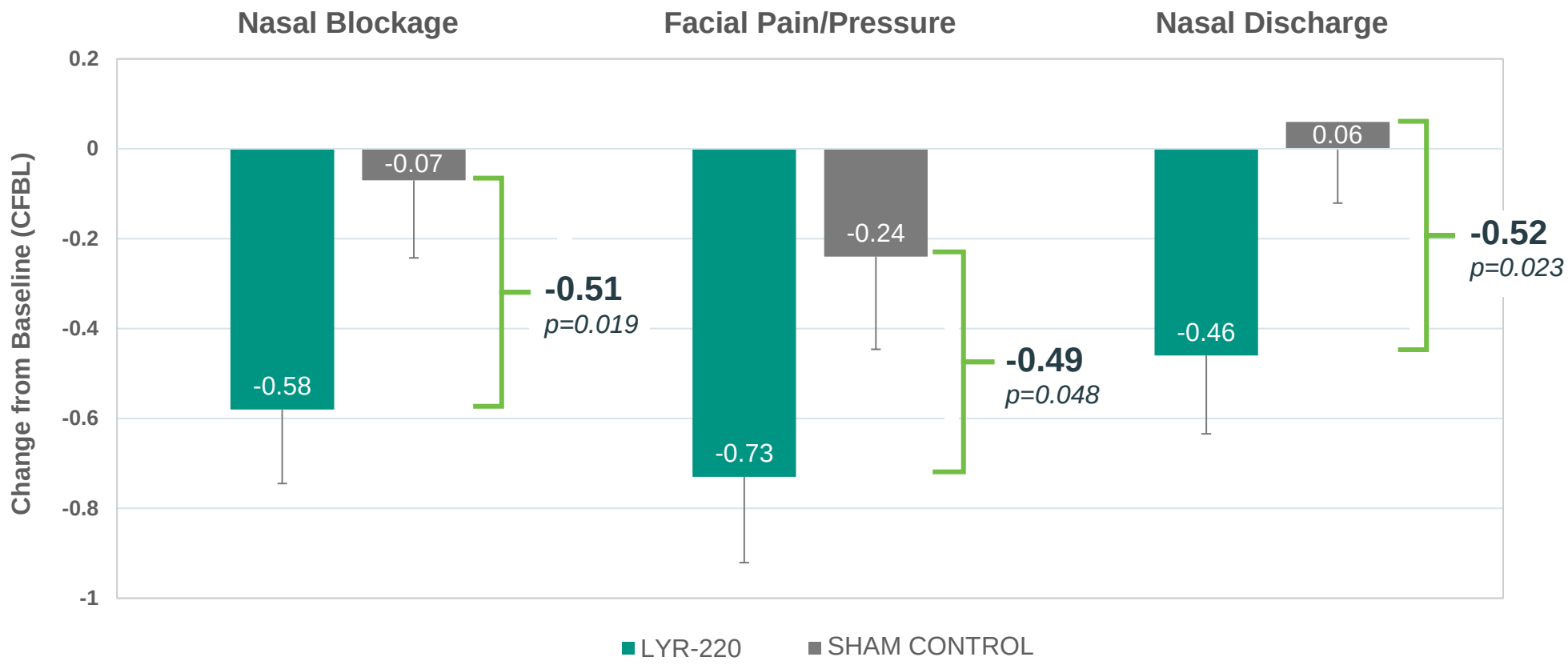


Error bars represent standard error

1) 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;
2) 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

Change in Three Cardinal Symptoms of CRS at Week 24[1,2]

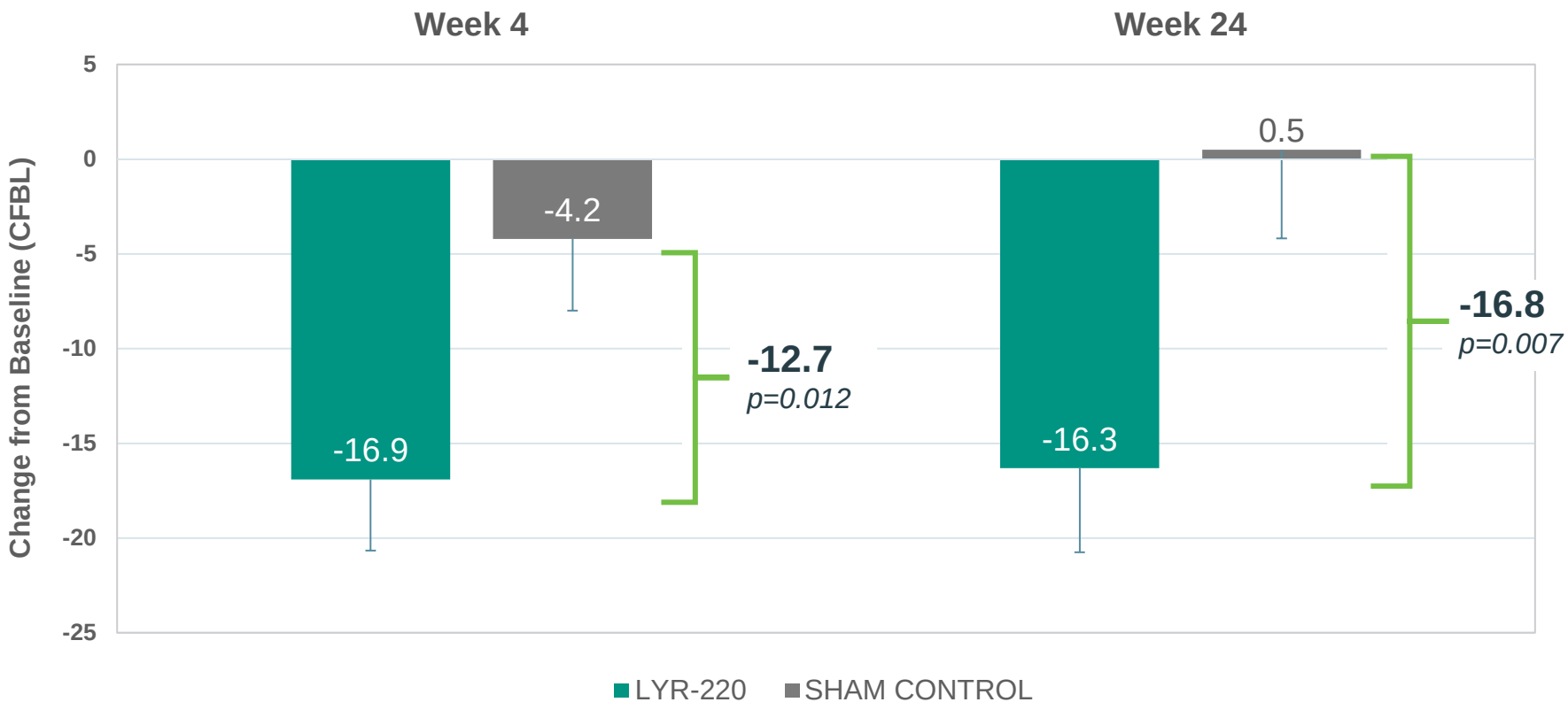


Error bars represent standard error

1) 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;
2) 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
Robust Effect in Composite SNOT-22 Score at Weeks 4 and 24

Change in SNOT-22 Total Score[1,2]



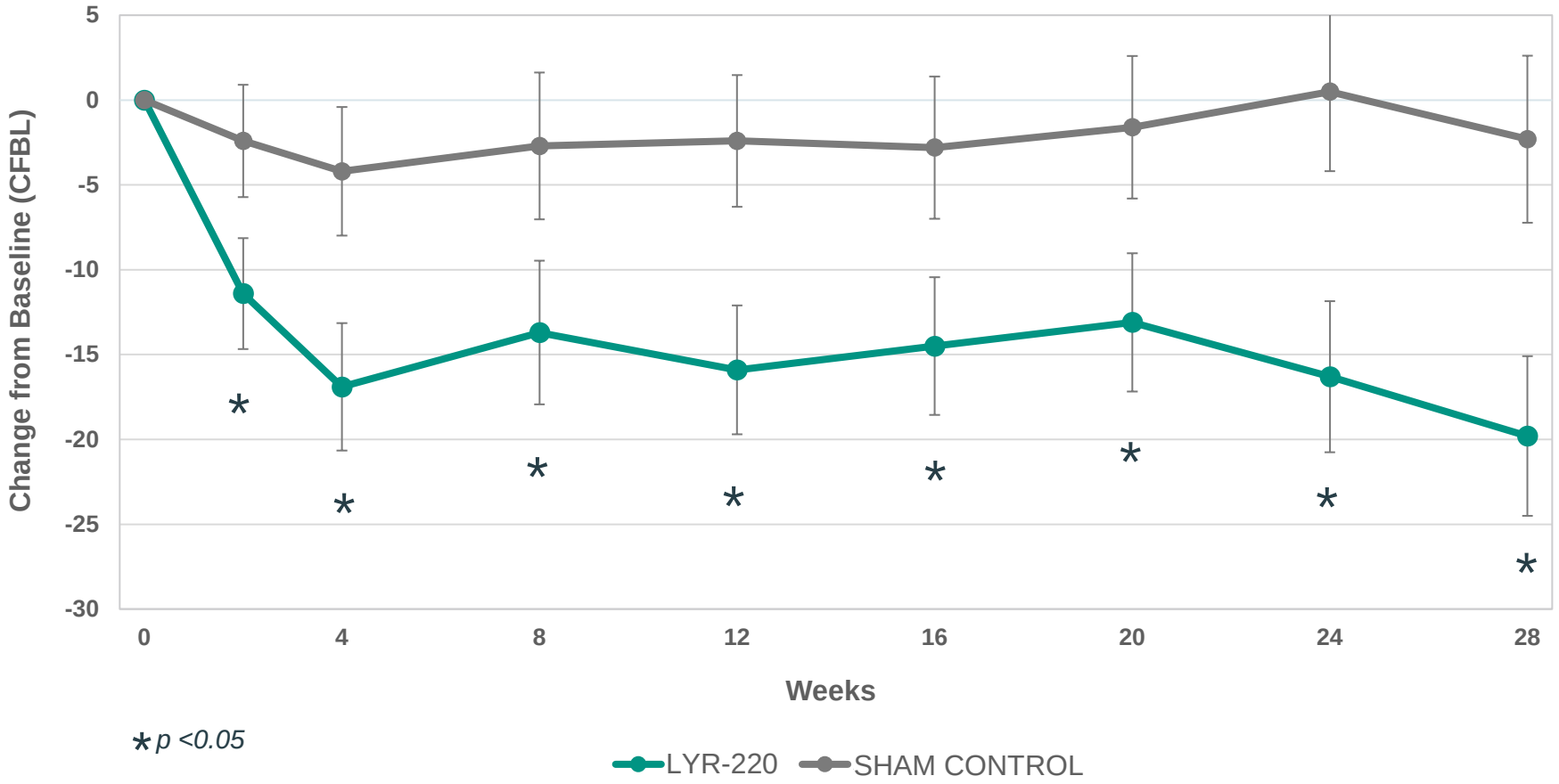
~17-point improvement over control 1.9x the MCID[3]

Error bars represent standard error

1) SinoNasal Outcome Test is a patient reported score from 0 – 110 based on symptoms; 2) 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 3) Minimum clinically important difference.

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

Change in SNOT-22 Total Score[1,2]



Achieved improvement greater than MCID[3] as early as two weeks and through 28 weeks

Error bars represent standard error

1) SinoNasal Outcome Test is a patient reported score from 0 – 110 based on symptoms; 2) 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; 3) Minimum clinically important difference.

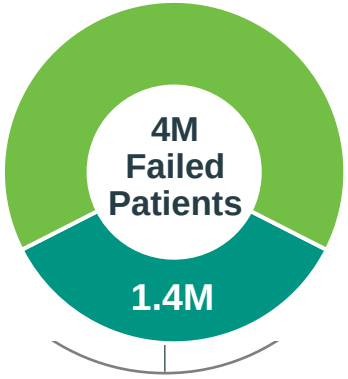
LYRA Product Candidates, if Approved, are Expected To Align With Current ENT Practices

- 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

Targeted Go-to-Market Strategy

Targeted Patient & Physician Base

Highly Accessible Patients



1.4M failed CRS patients actively seek care from ENT annually[1]

Specialist Physicians

2,500 ENTs perform ~90% of CRS procedures[2]

Specialty Field Force

Anticipate 20-40 sales reps & 3-5 medical science liaisons based on current estimates

1) OM1 Real World Data Cloud (OM1, Inc, Boston, MA, US), 2015 – 4/2019. Analysis 9/2019; 2) IQVIA In-Office Medical Claims Data, June 2021.

Anticipated Milestones

LYR-210: ENLIGHTEN Phase 3 Program

- ✓ Mid-2023: Complete enrollment in ENLIGHTEN I
- 1H 2024: Topline pivotal data from ENLIGHTEN I
- 2H 2024: Extension study data from ENLIGHTEN I
- 2H 2024: Complete enrollment in ENLIGHTEN II

LYR-220: BEACON Phase 2 Program

- ✓ Early 2023: Complete enrollment
- ✓ September 2023: Topline data
- 2024: End of Phase 2 meeting

Financial Profile

- Cash, cash equivalents and short-term investments of $102.6 million as of September 30, 2023
- On October 2, 2023, the Company sold an aggregate of 3,017,568 shares of common stock under the ATM Sales Agreement, at a weighted average price of $3.71 per share, which generated net proceeds of $10.9 million. These net proceeds were not included in cash and cash equivalents or short-term investments as of September 30, 2023
- 52.6 million common shares outstanding as of November 1, 2023

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