



Corporate Presentation

January 2025



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 ongoing ENLIGHTEN 2 Phase 3 trial evaluating LYR-210, our expectation for data in Q2 2025 for ENLIGHTEN 2, our ability to raise money to fund a pivotal trial for LYR-210, our ability to design, implement and complete that new phase 3 trial successfully (even if we obtain the requisite funding), our ability to correctly interpret FDA guidance received in December 2024, whether LYR-210, if advanced, would be positioned to align with current ENT practices, and statements regarding the potential market opportunity for LYR-210 to treat polyp patients.

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 continuing 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 initiate and complete another phase 3 trial for LYR-210, our need for significant additional funding, our ability 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; 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 LYR-210 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 our collaboration with LianBio, our product candidates may not reach their full market potential; developments by competitors may render our products or technologies obsolete or non-competitive or may reduce the size of our markets; the 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 November 12, 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.

Neither Lyra's most advanced product candidate, LYR-210, nor its pipeline product candidate, LYR-220, have been approved by FDA.

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 ongoing ENLIGHTEN Phase 3 clinical trial 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)**
 - Approximately 12% of the US population¹
 - Approximately 50% of patients fail medical therapy²
- **ENLIGHTEN Phase 3 program ongoing**
 - Efficacy signal observed in cohort with nasal polyps in ENLIGHTEN 1, despite not meeting primary endpoint in non-polyps
 - ENLIGHTEN 2 readout expected in Q2 2025
- **Planning Phase 3 study in polyp patients³**

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



CRS Cardinal Symptoms¹



Nasal obstruction and congestion



Nasal discharge



Facial pain and pressure



Reduced sense of smell

CRS in the United States Annually

~8M

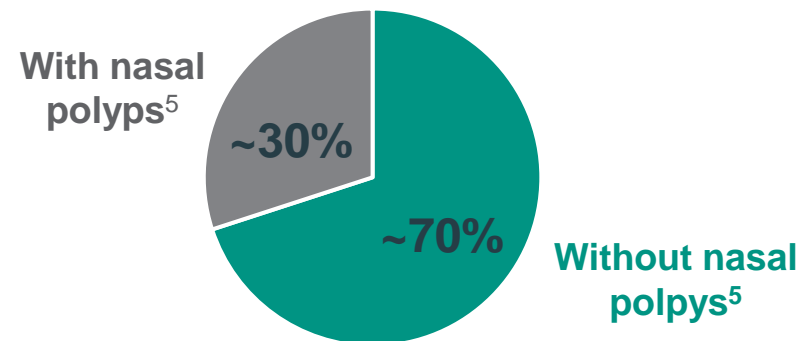
CRS patients treated²

~4M

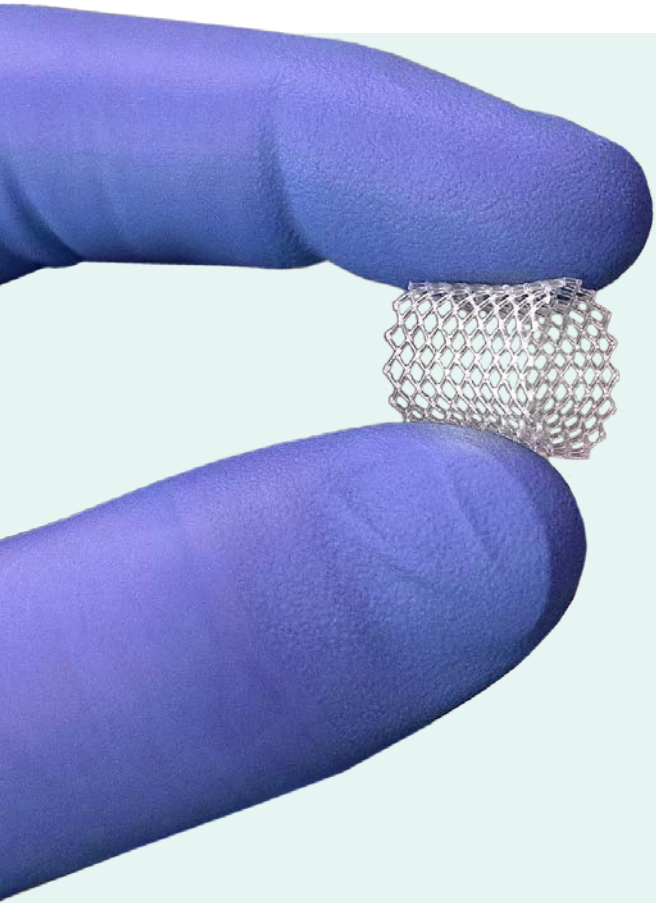
CRS patients failing medical management³

~1.4M

CRS patients currently presenting to an ENT⁴



Lyra's Proprietary Drug-Eluting Implant



Polymer-Drug Complex

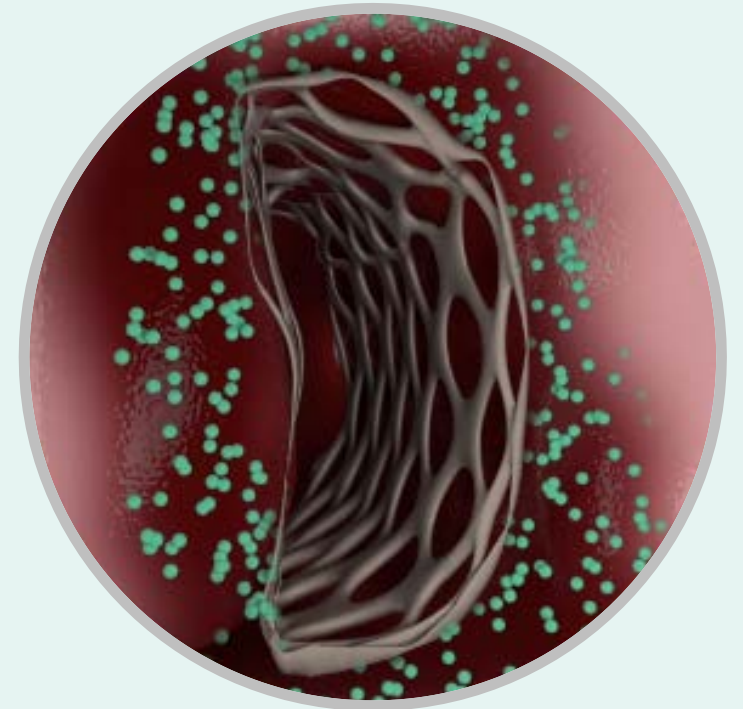
Designed to deliver 6 months of continuous, local drug therapy with a single placement

Engineered Elastomeric Matrix

Shape memory keeps implant in place

Bioabsorbable Mesh Scaffold

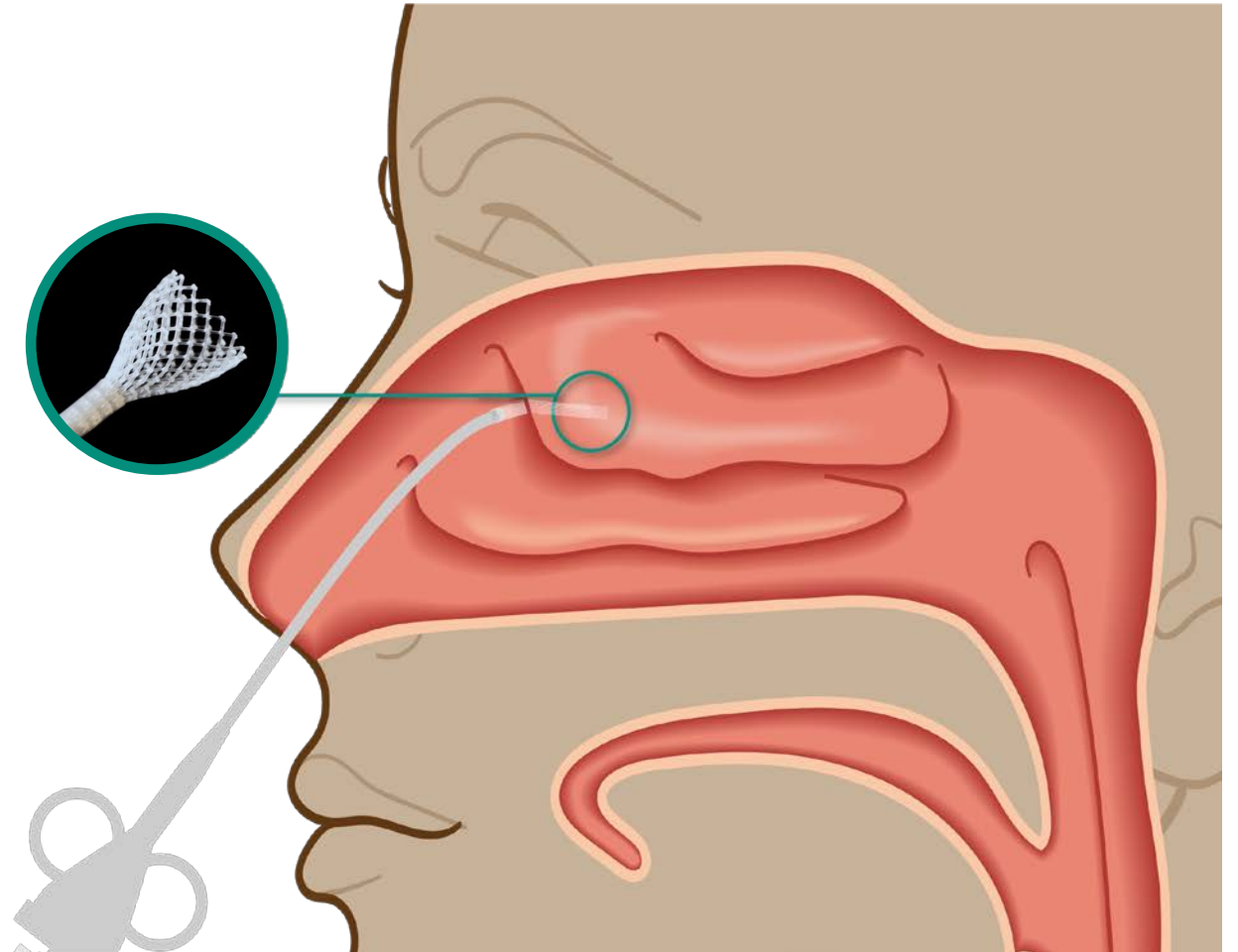
Maximizes surface area for drug release while maintaining underlying tissue function



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 steroid: Mometasone furoate
- Designed to provide continuous anti-inflammatory therapy
- Straightforward, office-based procedure with topical anesthesia
- Administered nasally via a single-use applicator
- Two product candidates are designed to address the diverse anatomy of both pre and post surgical patients
- Potential opportunity as surgical products to improve outcomes post sinus surgery



Summary of Clinical Studies

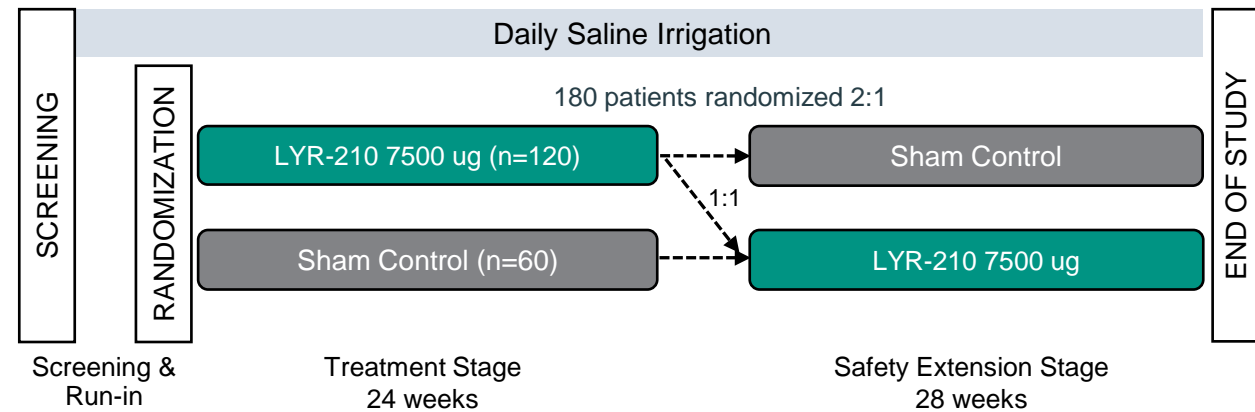
Candidate	Phase 1	Phase 2	Phase 3	Status
LYR-210 (Small diameter)	Phase 1 (n=20)			Complete
	PK Study (n=24)			Complete
	LANTERN Dose-Ranging Phase 2 Study (n=67)			Complete
	ENLIGHTEN 1 Study for CRS (n=190)			Complete
	ENLIGHTEN 2 Study for CRS (n=180)			Ongoing
	Pivotal Study for CRS with polyps (n=206) ¹			Planned
LYR-220 ² (Large diameter)	BEACON Phase 2 Study (n=48)			Complete

ENLIGHTEN Program Design

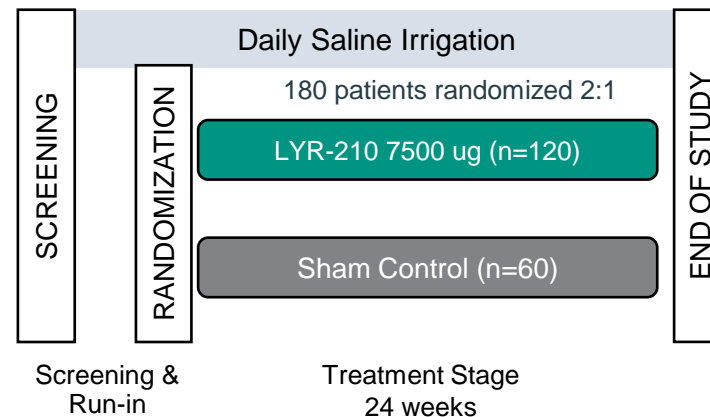
LYR-210 Ongoing Phase 3 Program

- Two phase 3 studies of ~180 subjects each
- Adult CRS patients without nasal polyps or with nasal polyps, who have failed medical management¹
- **Primary endpoint**
 - Change from baseline in 3CS² Score at Week 24 in patients without nasal polyps
- **ENLIGHTEN 1 complete**
- **ENLIGHTEN 2 fully enrolled and readout expected Q2 2025**

ENLIGHTEN 1³

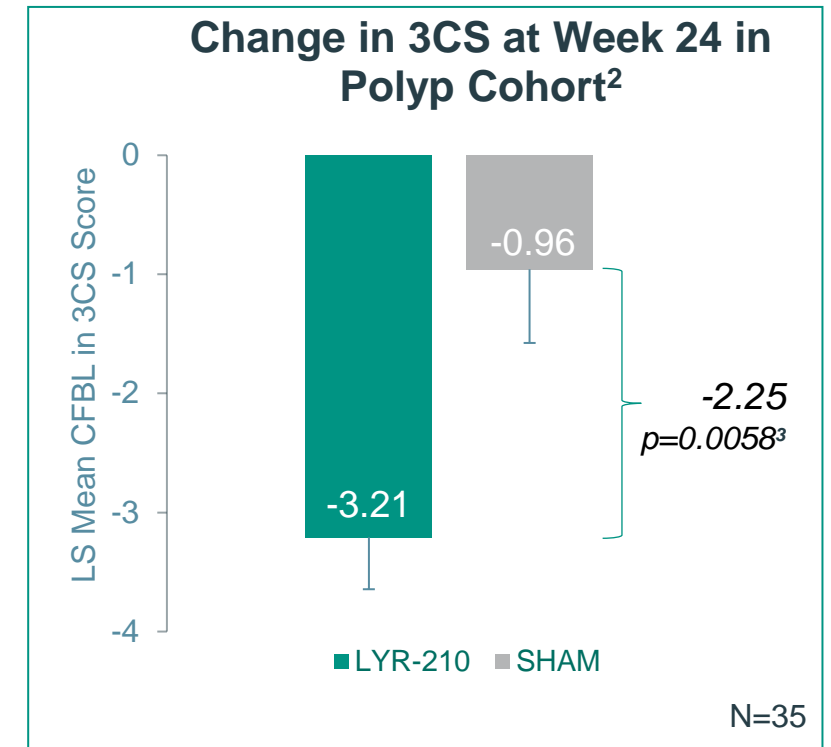


ENLIGHTEN 2⁴



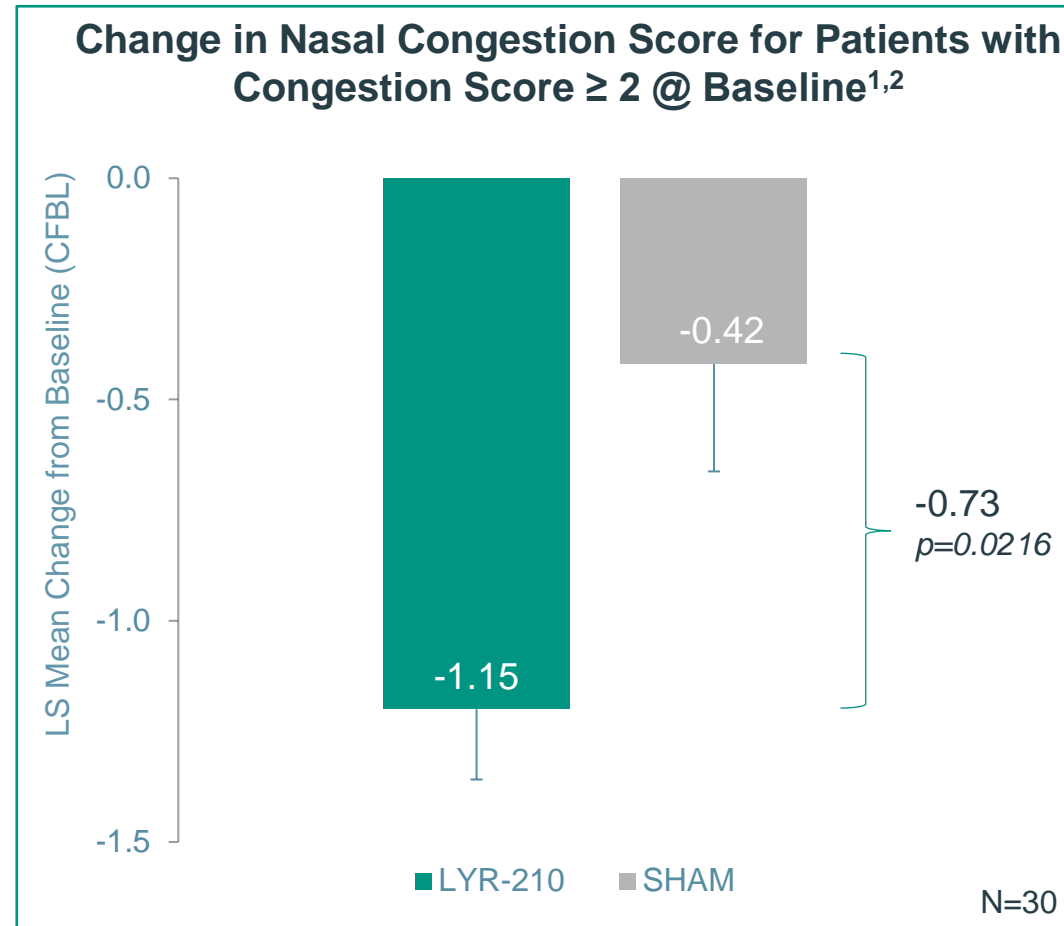
ENLIGHTEN 1 Treatment Stage Results

- **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 group¹
- **LYR-210 was generally well tolerated, with no product-related serious adverse events**
- **In the polyp cohort², robust improvement in patient symptoms for LYR-210 treated patients relative to the SHAM control group was observed**
 - Improvement of 2.25 points ($p=0.0058$)³ in 3CS score relative to sham control at 24 weeks in patients with Nasal Polyps



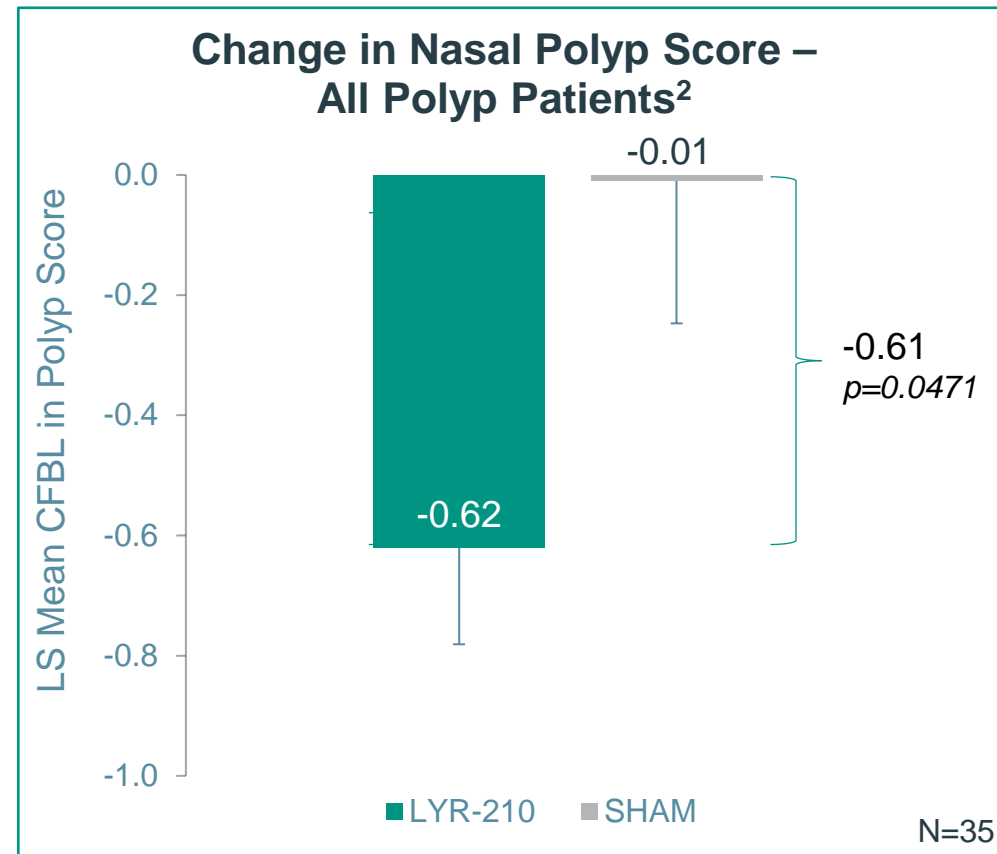
ENLIGHTEN 1 Polyp Cohort: Nasal Congestion Score at 24 Weeks

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



ENLIGHTEN 1 Polyp Cohort: Evaluation of Polyp Size

Reduction in Polyp Size at week 24 in the nasal polyp cohort in ENLIGHTEN 1 despite inclusion of patients with only small polyps¹



CFBL = Change from baseline

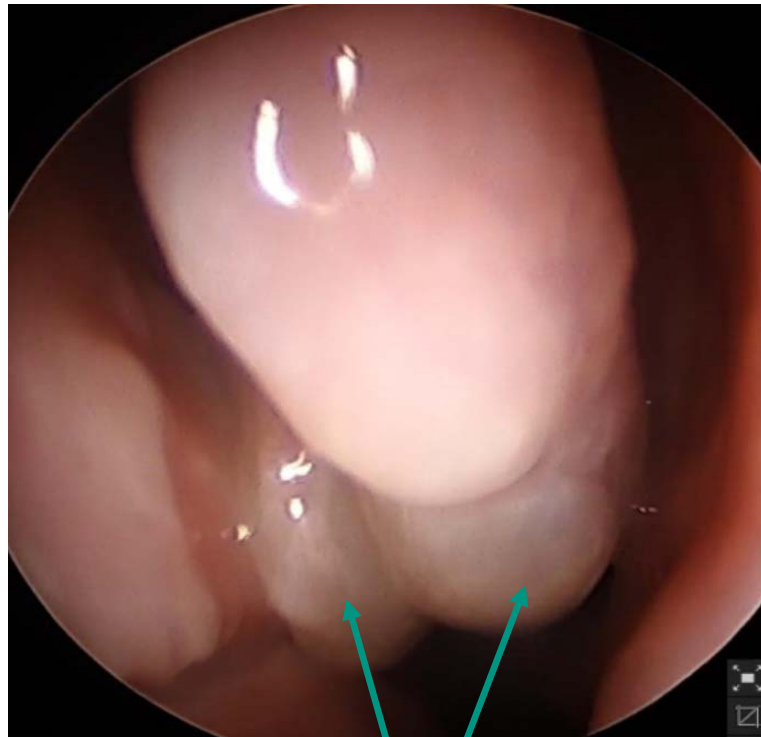
1) ENLIGHTEN 1 included Grade 1 nasal polyps.

2) Polyp scores were determined post-hoc by an independent blinded reviewer using a standard polyp grading scale (FDA Guidance for Industry: Chronic Rhinosinusitis With Nasal Polyps: Developing Drugs for Treatment). Nasal polyp score is the sum of polyp grades on each side of the nose.

ENLIGHTEN 1 Polyp Cohort: In-Office Endoscopic Evaluation

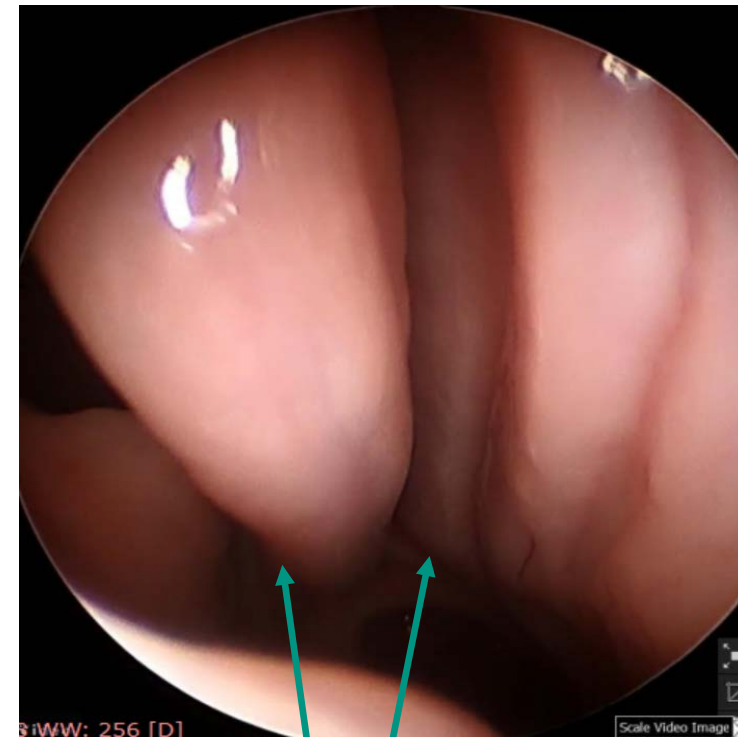
Visual improvement in nasal polyps and mucosa after LYR-210 treatment

Day 1 (before LYR-210 treatment)



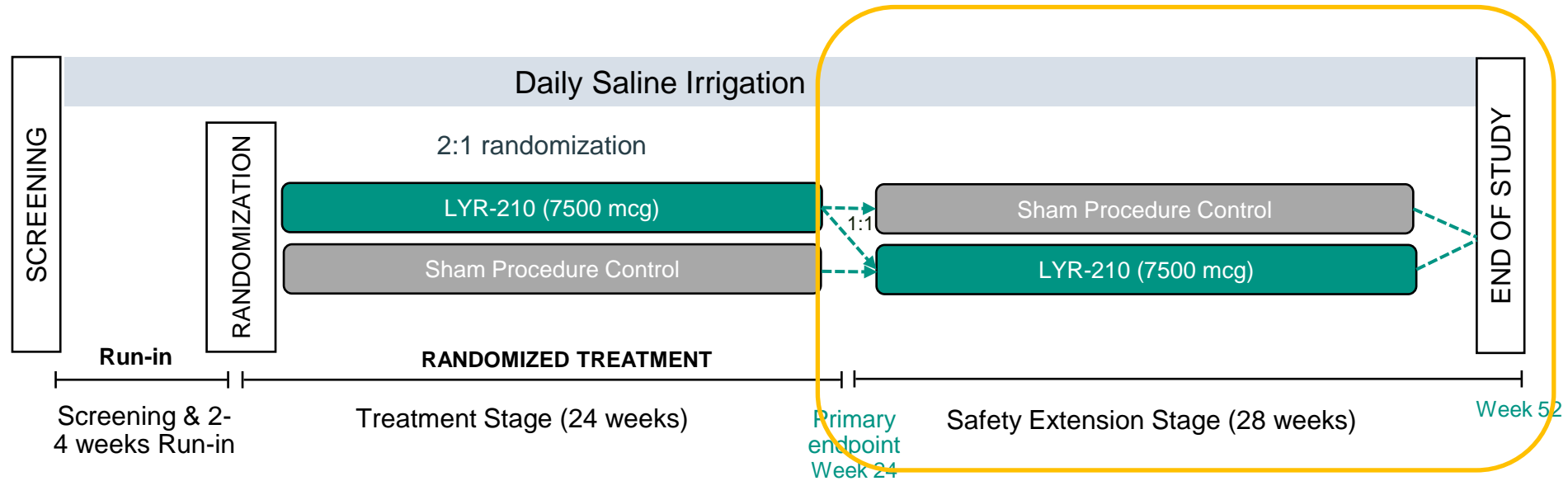
Polypoid tissue

Week 24 (after LYR-210 treatment)



Polypoid tissue greatly diminished

ENLIGHTEN 1: Extension Stage (Week 24 through Week 52)

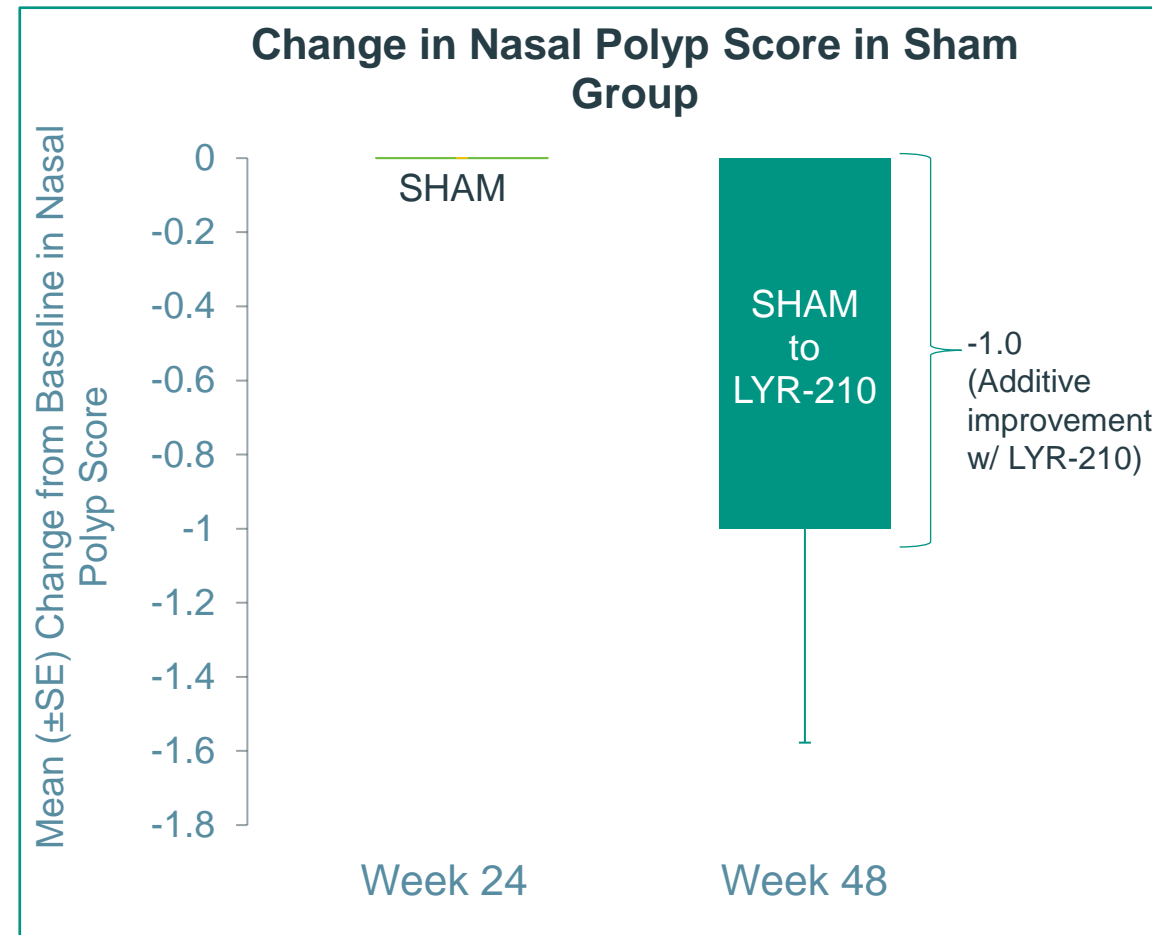
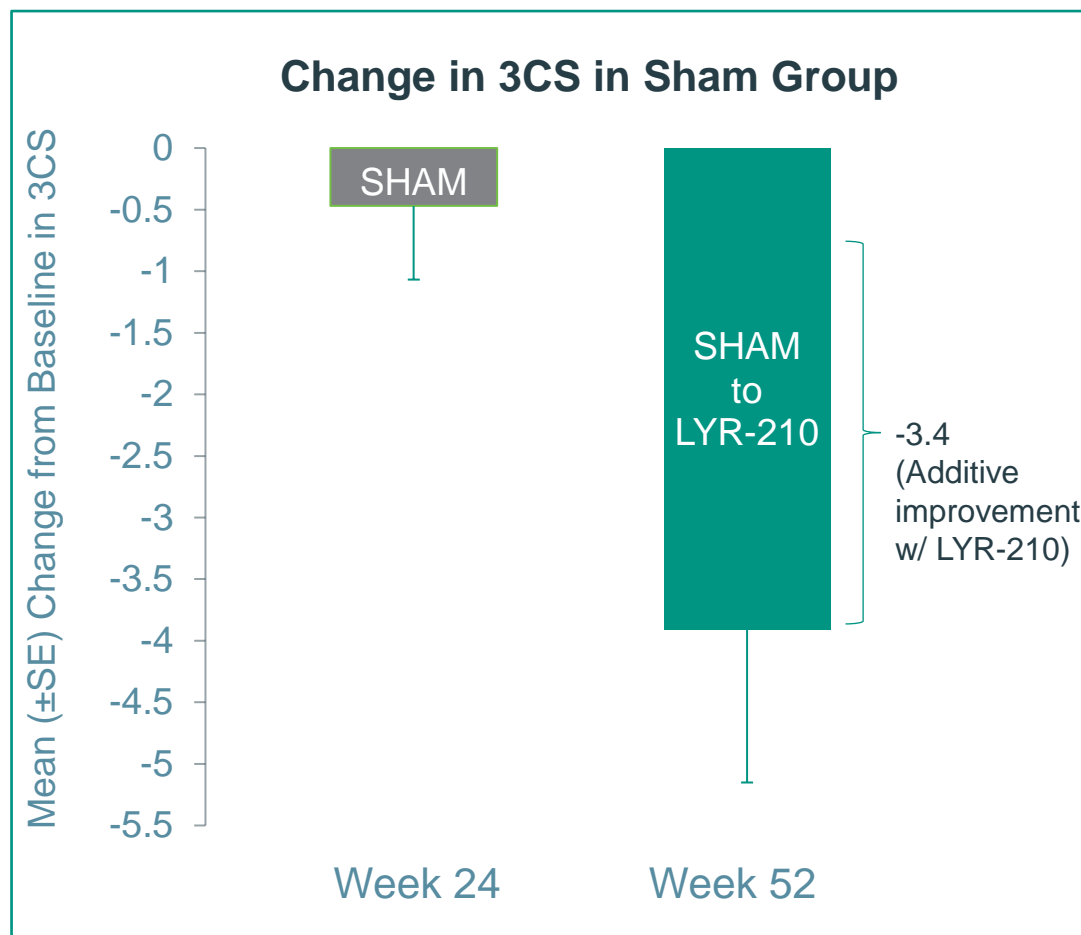


In the extension stage, patients were re-allocated to three different treatment groups:

- **Sham to LYR-210:** All sham group patients received LYR-210 treatment in the extension to provide additional patients exposed to LYR-210 for the safety dataset
- **LYR-210 to LYR-210:** Half of the LYR-210 group patients received a second LYR-210 treatment to evaluate safety of repeat treatment
- **LYR-210 to Sham:** The other half of the LYR-210 group received a sham treatment to assess durability of effect of LYR-210 treatment

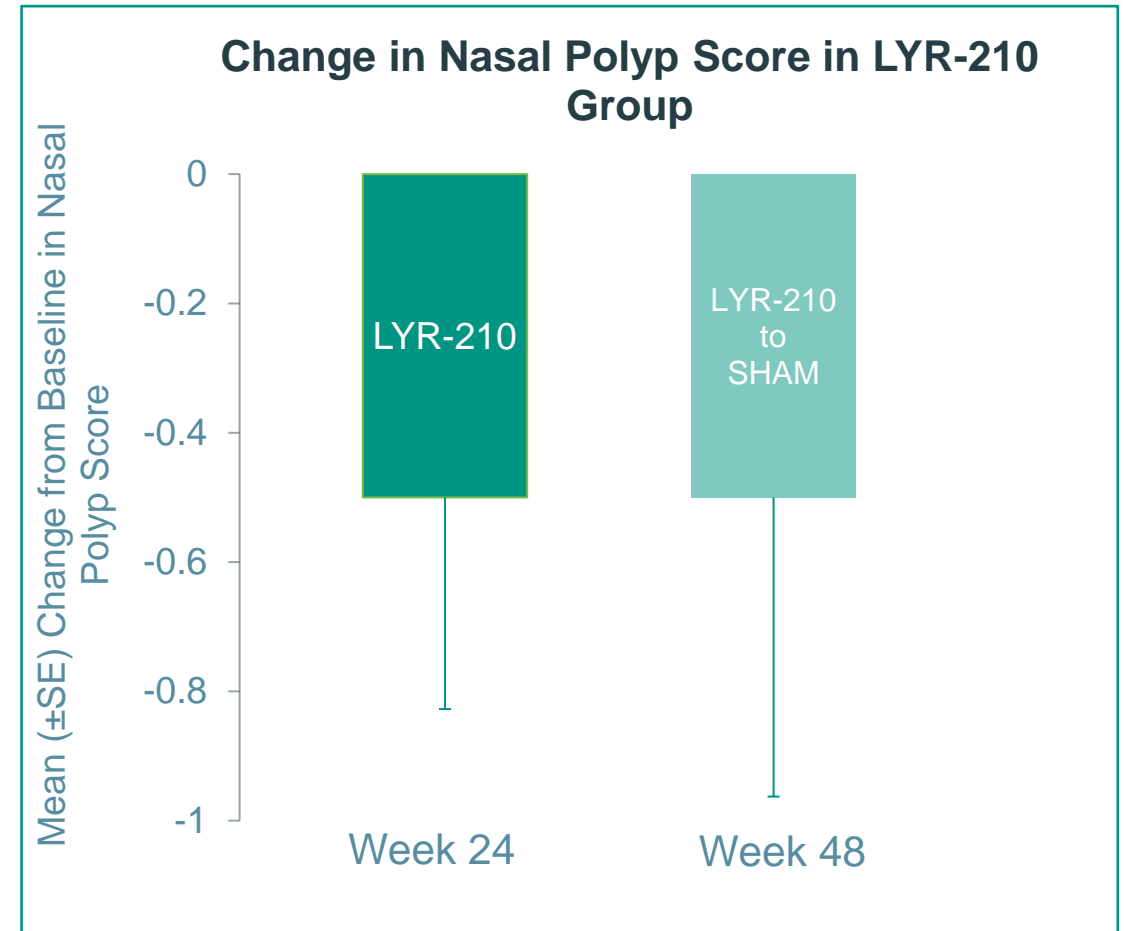
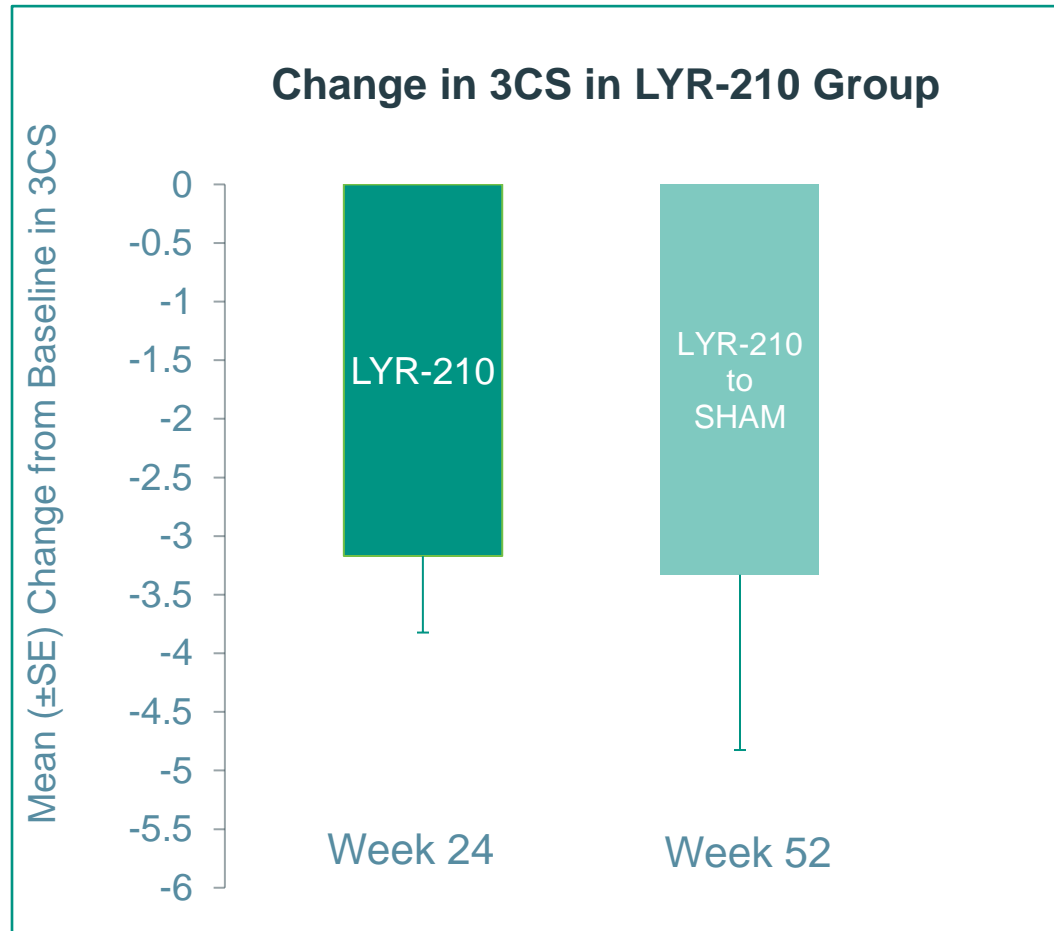
Extension Stage Polyp Cohort: Sham Polyp Patients Crossing Over to LYR-210

Sham patients that crossed over to LYR-210 treatment exhibited improvement in both their symptoms and polyp size



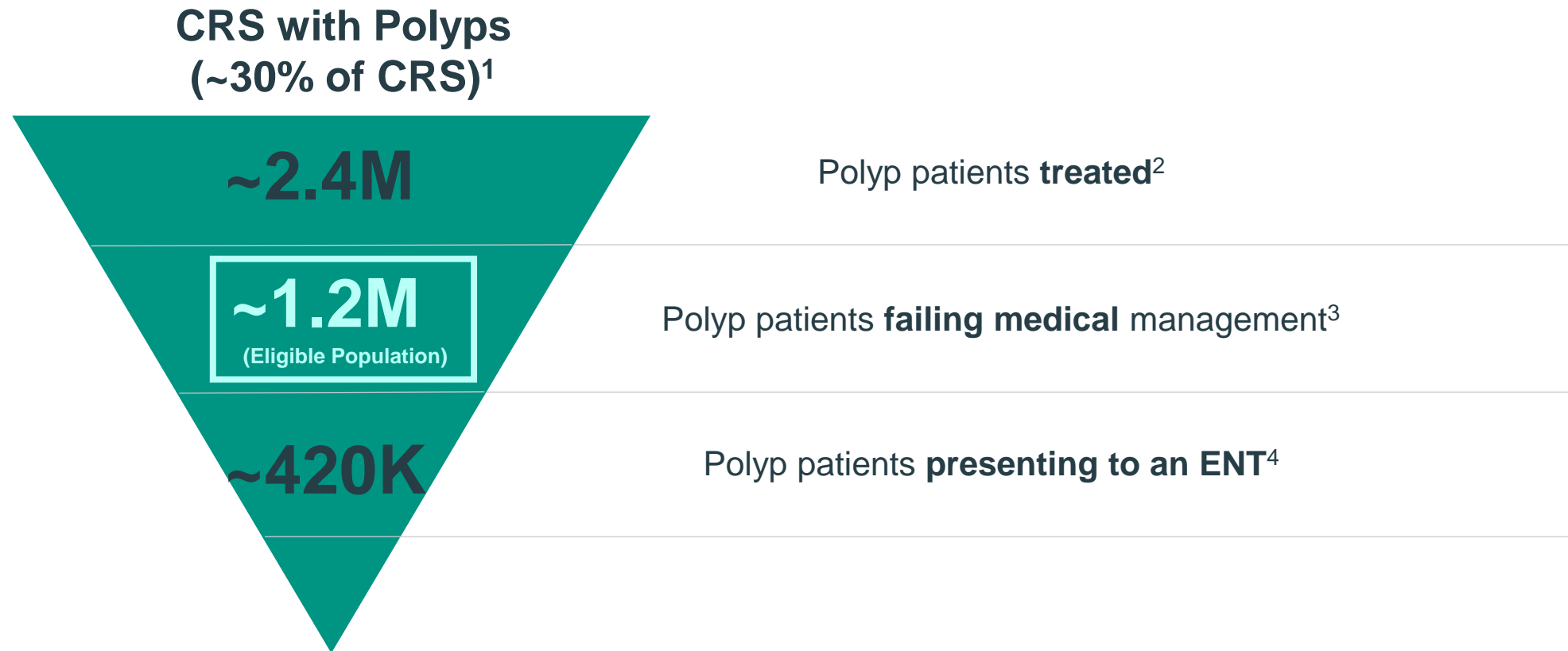
Extension Stage Polyp Cohort: LYR-210 Polyp Patients Crossing Over to Sham

LYR-210 polyp patients that crossed over to Sham demonstrated a durable response out to one year



Annual Incidence of CRS With Polyps in the U.S.

Polyp patients represent ~30% of CRS patients in the U.S. with over 1M annually being possible candidates for a potential Lyra polyp product¹



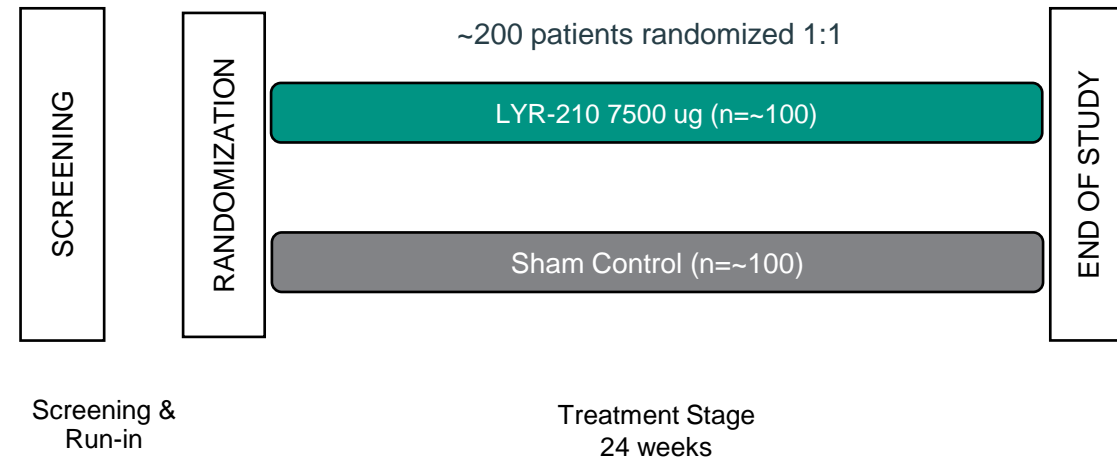
Planned Phase 3 Clinical Trial for CRS with Nasal Polyps¹

Received FDA feedback in December 2024 on study design for CRS with nasal polyps

- Safety dataset would be sufficient along with data from ENLIGHTEN and LANTERN, subject to no further additional safety concerns being identified
- Alignment on endpoints, inclusion criteria, patient population, background therapy, and assessments

- Potential pivotal study of ~200 subjects
- Adult CRS patients with nasal polyps, with or without prior ethmoid sinus surgery and who have failed medical management²
- **Co-primary endpoints³**
 - Change from baseline in Nasal Congestion Score (NCS) at Week 24
 - Change from baseline in Nasal Polyp Score (NPS) at Week 24

Phase 3 Study



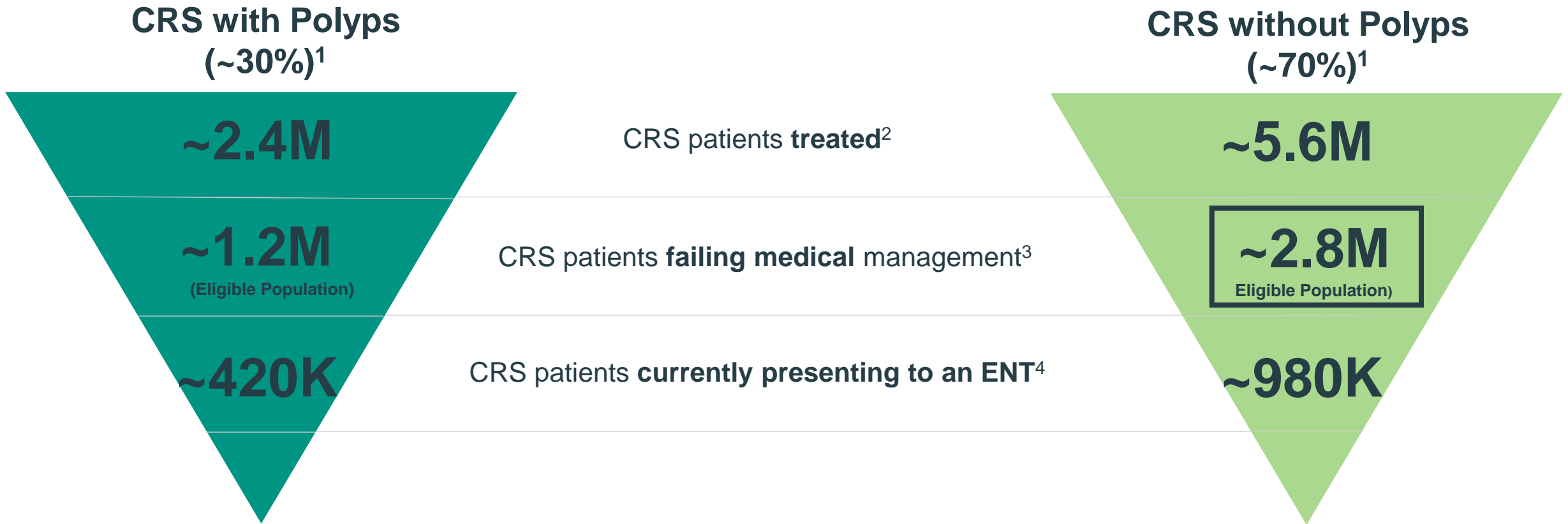
ENLIGHTEN 1 Outcomes in Non-polyp Patients

- **Although non-polyp patients showed a 2-point improvement from baseline in 3CS, a separation from the sham control group was not seen**
 - Treatment effect observed in European cohort, but not in the US cohort
 - Blinded post-hoc analysis demonstrated a signal in non-polyp CRS patients with endoscopic evidence of edema (evidence of inflammation)
 - Sham control patients that received crossover LYR-210 treatment in the Extension Stage demonstrated additional treatment benefit with LYR-210
- **Non-polyp is a heterogeneous CRS population which may have been enriched with more transient disease, particularly in the US cohort**

We expect data from the currently ongoing ENLIGHTEN 2 trial to provide further insight into the efficacy of LYR-210 in non-polyp patients

Annual Incidence of CRS Without Polyps in the U.S.

Both polyp and non-polyp CRS includes ~4M eligible patients for Lyra products



Note: Clinical development for LYR-00 is currently paused.

1) Biomedical Insights Market Sizing Assessment 2020;; 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

Key Milestones

- ✓ May 2024: Topline data from ENLIGHTEN 1
- ✓ Q4 2024: Extension study data from ENLIGHTEN 1
- ✓ 2H 2024: Complete enrollment in ENLIGHTEN 2
- 2Q 2025: Topline data from ENLIGHTEN 2
- Est. 2H 2025: Initiate Polyp Pivotal Trial¹

Financial Profile

- Cash, cash equivalents and short-term investments of \$51.6 million as of September 30, 2024
- 65.5 million common shares outstanding as of September 30, 2024

LYRA

THERAPEUTICS

