LYRA THERAPEUTICS

Dedicated to transforming the lives of patients with debilitating chronic diseases through local, targeted drug therapy

INVESTOR PRESENTATION

OCTOBER 2021

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 clinical advancement and efficacy of LYR-210 and LYR-220 for the treatment of CRS and our expectations regarding the upcoming LYR-210 Phase 3 ENLIGHTEN program and LYR-220 Phase 2 BEACON program. 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 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; our 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 relies on third parties for the manufacture of materials for its research programs, pre-clinical studies and clinical trials; 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; 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 August 9, 2021 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

Working to disrupt the treatment paradigm for chronic diseases, starting with CRS

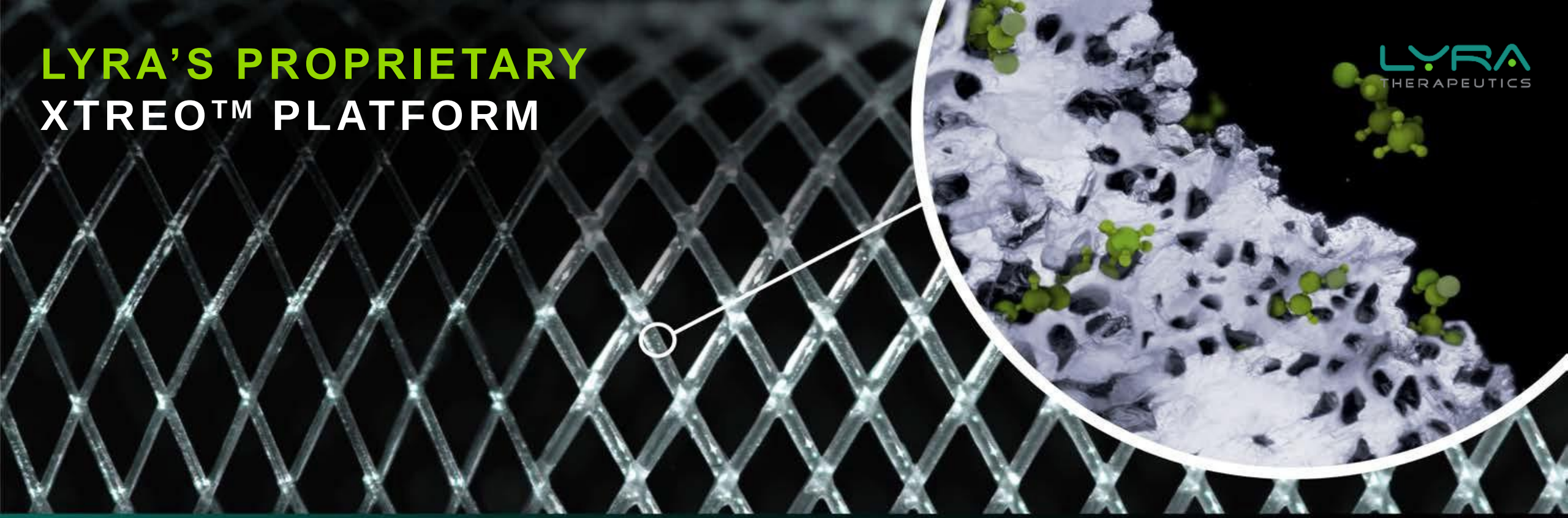
Proprietary XTreo™ platform delivers the RIGHT DRUG to the RIGHT PLACE for the RIGHT AMOUNT OF TIME to treat chronic diseases

Creating the standard of care for the millions of patients suffering from CRS and for which there is no approved therapeutic treatment

Achieved consistent, dramatic improvement in 3 clinical studies to date; Phase 3 program initiating ~YE'21

Poised to be the dominant player in this 14M U.S. patient, $6B opportunity

LYRA'S PROPRIETARY XTREO™ PLATFORM



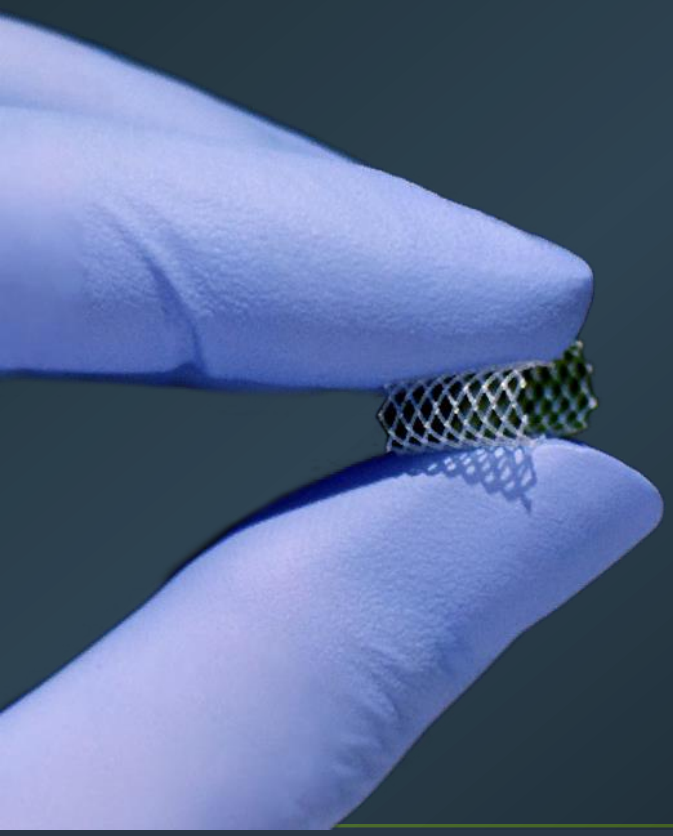
BIOCOMPATIBLE MESH SCAFFOLD

ENGINEERED ELASTOMERIC MATRIX

VERSATILE POLYMER-DRUG COMPLEX

XTREO™ PLATFORM

SUSTAINED TARGETED DRUG THERAPY

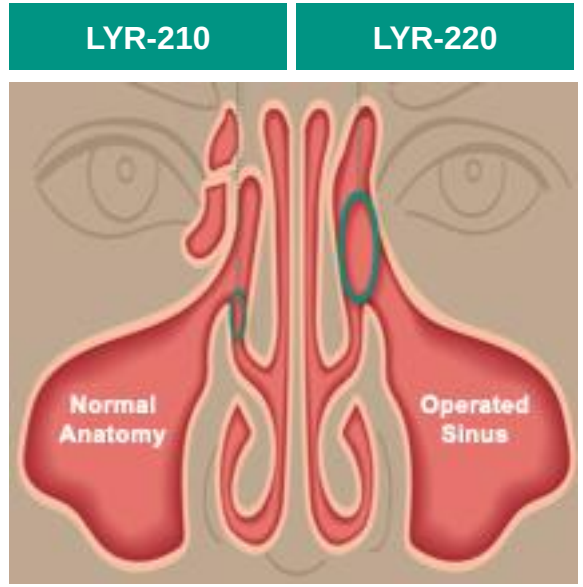


- Six months or more of local drug therapy
- Consistent daily dosing
- Shape memory keeps matrix in place
- Single non-invasive administration

DEVELOPMENT PIPELINE

LYR-210 and LYR-220: Designed to address the full spectrum of CRS patients

Candidate	CRS Patient Type	Phase 2	Phase 3	Next Milestone
LYR-210 Long-acting Mometasone Furoate	Chronic Rhinosinusitis **Patients with Surgically Naïve Anatomy**			**ENLIGHTEN** Phase 3 ~YE'21
LYR-220 Long-acting Mometasone Furoate	Chronic Rhinosinusitis **Patients with Post-Surgical Anatomy**			**BEACON** Phase 2 ~YE'21



WHAT IS CHRONIC RHINOSINUSITIS (CRS)?

Chronic Rhinosinusitis: The “Unrecognized Epidemic”[1]

CRS Cardinal Symptoms[1]

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

United States

~14M	CRS Prevalent Patients[2]
~8M	CRS Patients Treated by Physicians Annually[3]
~4M	CRS Patients Failing Medical Management Annually[4]
400K	Surgeries annually

1) Tan BK et al. Am J Respir Crit Care Med, 2013;188(11):1275–7; 2) Battacharrya. Ann Otol Rhinol Laryngol, 2011; Jul;120(7):423-7; 3) Jang et al. Otolaryngol Head Neck Surg, 2018; 4) Baguley et al. Int Forum Allergy Rhinol, 2014;4(7):525-32

MANY CRS PATIENTS FAIL CURRENT TREATMENTS

Current approaches do not control symptoms in the majority of patients

FIRST-LINE THERAPY
Medical Management

of patients fail medical management[1]

SECOND-LINE THERAPY
Surgical Treatments + Medical Management

65%
have recurrent CRS[2]

20%
elect revision surgery[3]

100%
require ongoing medical management[4]

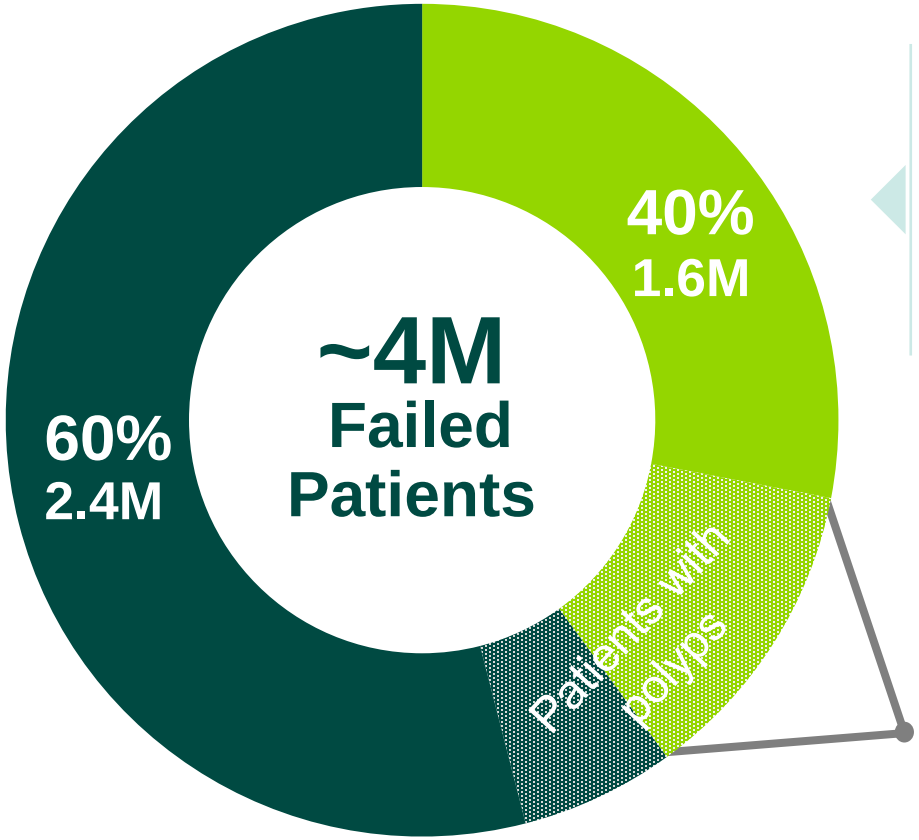
1) Young et al. Allergy Rhinol, 2012; 3:e8-e12; 2) Schaitkin et al. Laryngoscope, 1993; 103; 3) Stein et al. Laryngoscope,2018; 128(1): 31–36; 4) Rosenfeld et al. Otolaryngology–Head and Neck Surgery, 2015; 152(2S)

DEVELOPING SOLUTIONS FOR ALL CRS PATIENTS

LYR-210 and LYR-220 are designed for the full range of CRS patients treated by ENTs

LYR-210

CRS Patients with Surgically Naïve Anatomy



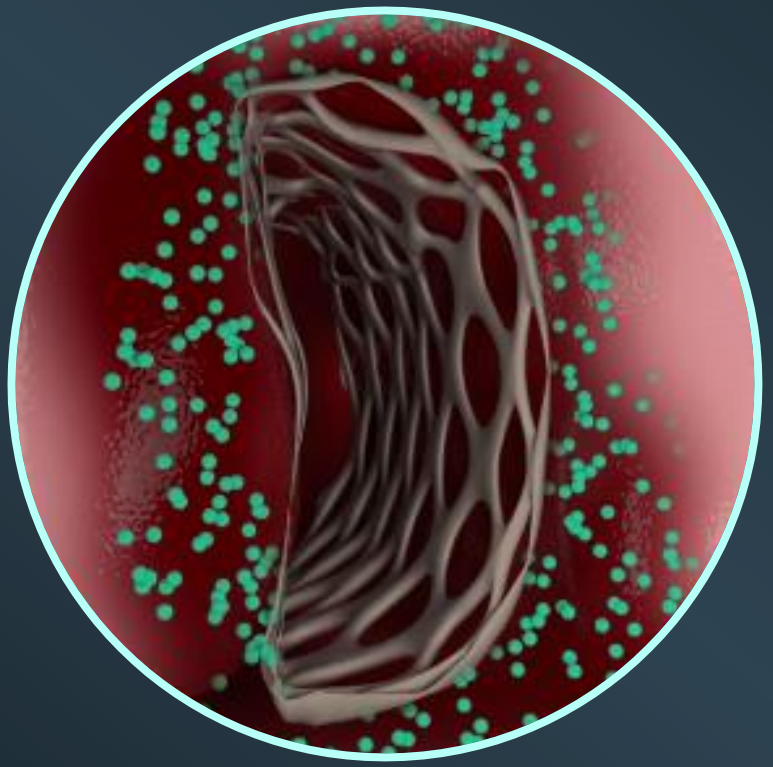
LYR-220

CRS Patients with Post-Surgical Anatomy

LYR-210: MEANINGFUL IMPROVEMENT IN CARE

NON-SYSTEMIC DELIVERY FOR MONTHS TO A BROAD PATIENT POPULATION

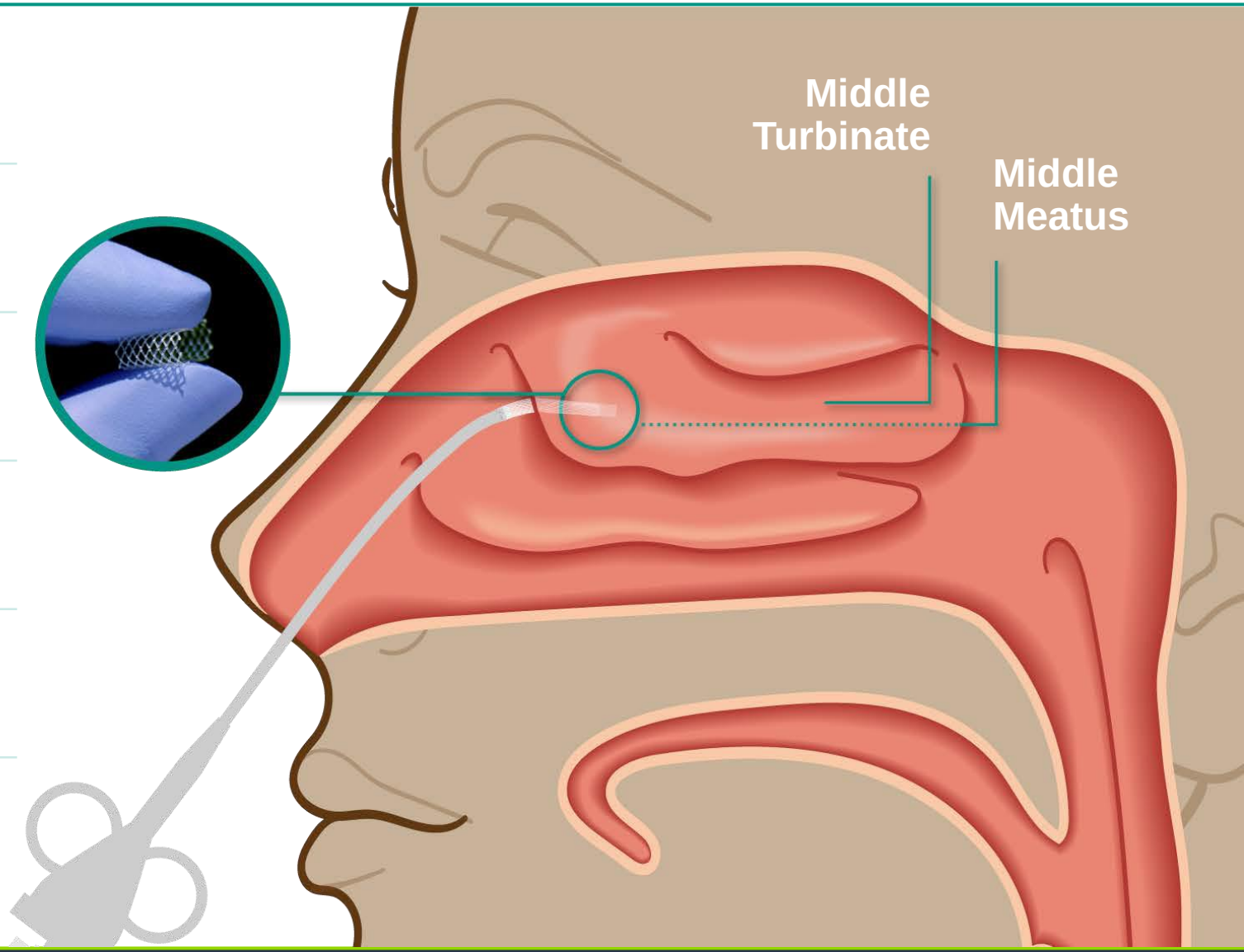
- **Local effect**
- **6-month continuous treatment with one application**
- **For non-polyp & polyp CRS**
- **Surgically naïve anatomy**
- **Requires no patient compliance**



LYR-210: DESIGNED TO BE THE GOLD STANDARD

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 treatment as an alternative to surgery
- Administered nasally via a single-use applicator
- Office-based procedure with topical anesthesia
- Not detectable by patients
- Designed to be replaced every 6 months

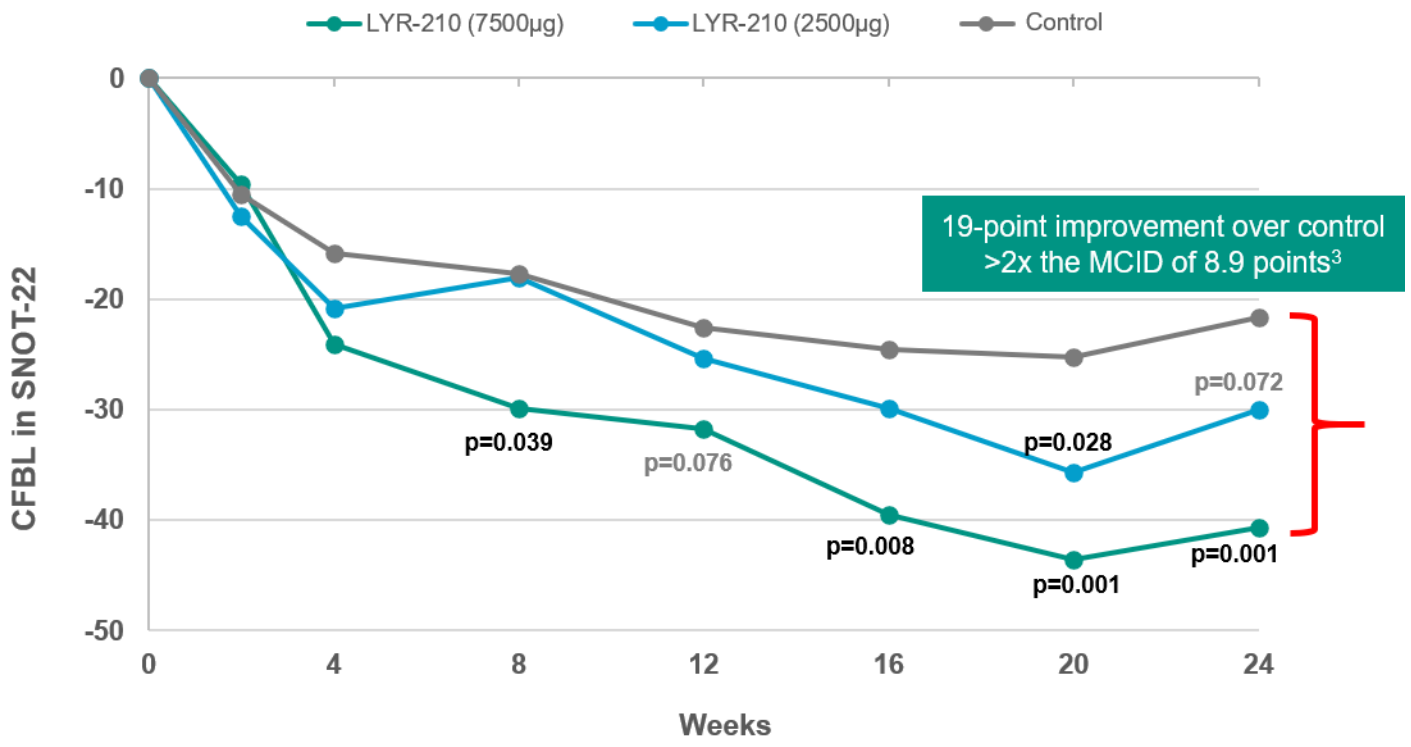


LYR-210

POSITIVE LANTERN PHASE 2 STUDY

- Rapid, durable and clinically meaningful results based on gold standard measurement
- >2X the MCID of 8.9 points relative to control
- 70% of patients in the 7500 mcg group improved ≥ MCID at week 4; 100% by week 24

SYMPTOM IMPROVEMENT BY SNOT-22[1,2]



Statistically Significant Improvement vs Control at 8, 16, 20 and 24 wks

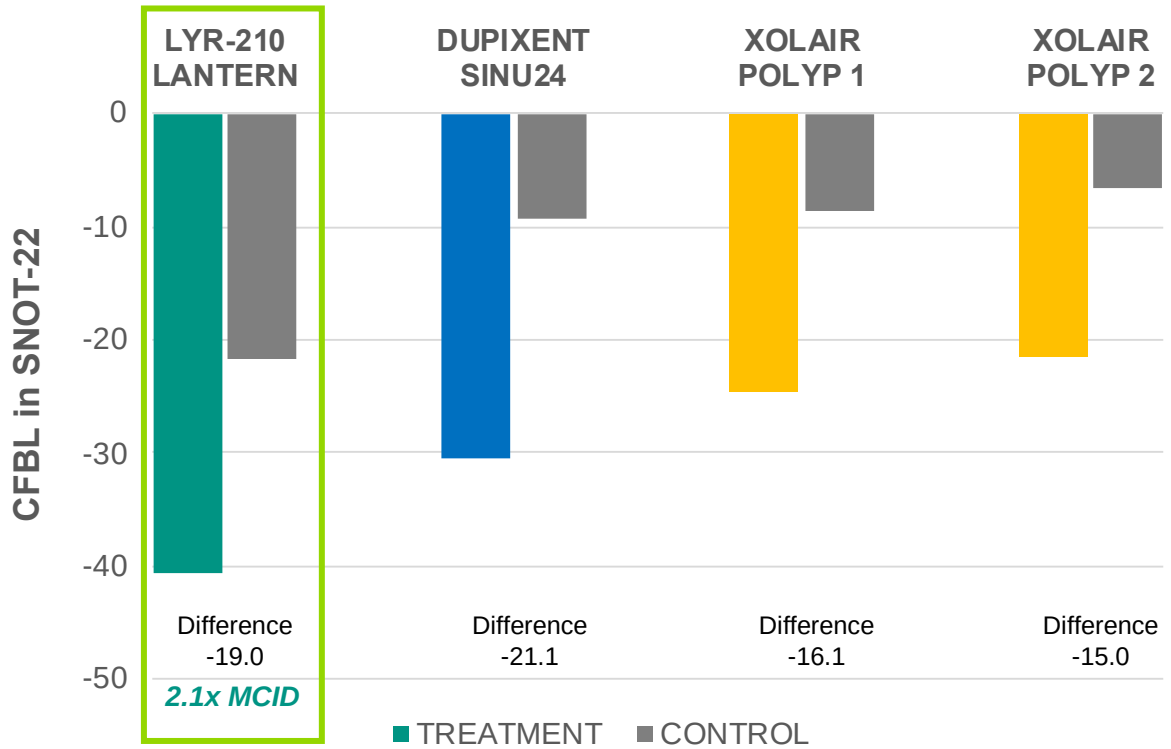
1) SinoNasal Outcome Test is a patient reported score from 0 – 110 based on symptoms; 2) Data represents the least square mean. Missing data and data post use of rescue medication was imputed by LOCF method; 3) Minimal clinically important difference

LYR-210

POSITIVE LANTERN PHASE 2 STUDY

- Performance is highly competitive
- >2X the MCID of 8.9 points relative to control
- Durable at week 24 without need for repeat dosing

SNOT-22 COMPARISON AT 24 WEEKS



*Data from separate trials with different inclusion/ exclusion criteria and patient populations

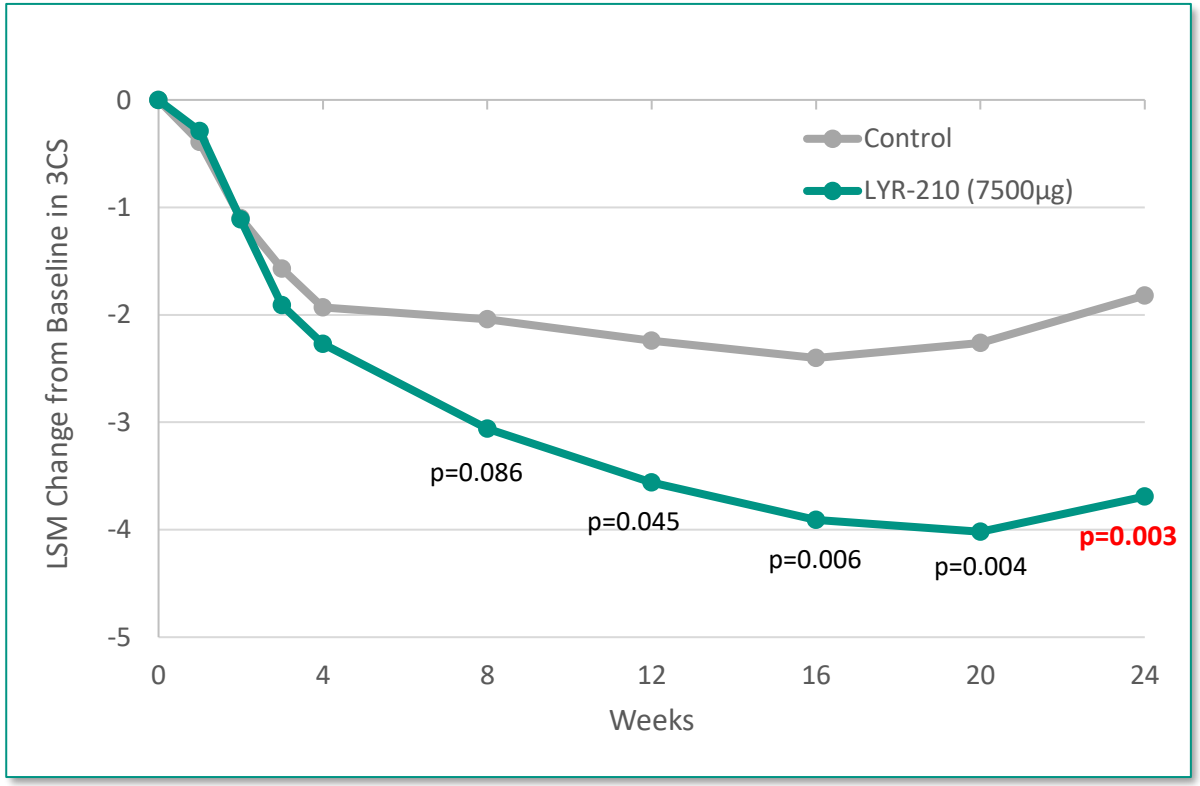
Sources:
XHANCE: Sindwani, et al., Am J Rhinol Allergy 2019, Vol. 33(1) 69–82; Lepard et al., J Allergy Clin Immunol, 2019;143:126-34
DUPIXENT: Bachert, et al., Lancet 2019; 394: 1638–50
XOLAIR: Gevaert et al, J Allergy Clin Immunol, 2020, 146(3), 595-605

LYR-210

POSITIVE LANTERN PHASE 2 STUDY

- Robust effect on 3 cardinal symptoms: highly statistically significant at week 24
- **6-month benefit from a single administration**
- **Showed benefit in both polyp and non-polyp patients**

SYMPTOM IMPROVEMENT BY COMPOSITE OF 3 CARDINAL SYMPTOMS[1,2]



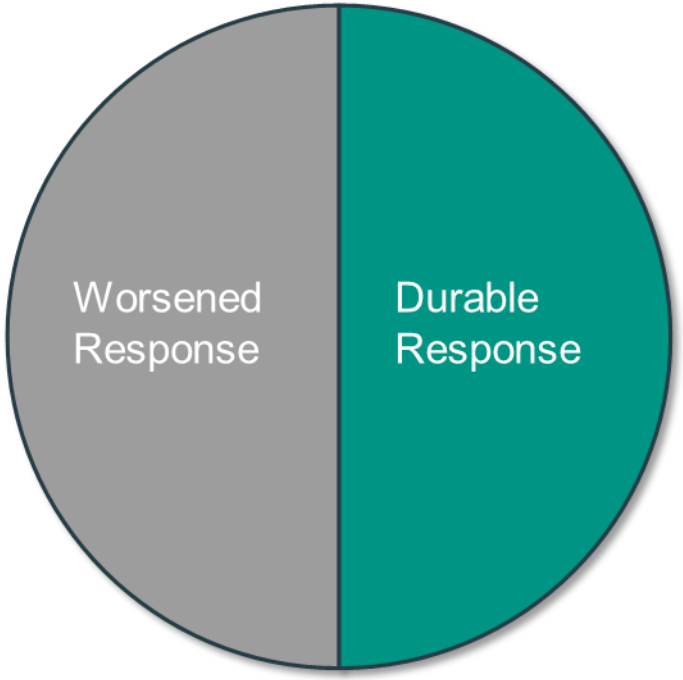
Statistically Significant Improvement vs Control at Weeks 12 - 24

1) Mean change from baseline (CFBL) in the 7-day average score in the 3CS composite score (nasal blockage, facial pain/pressure, and nasal discharge (anterior/posterior); 2) Data represents LSM. P<0.05 is considered statistically significant to control

TREATED PATIENTS EXPERIENCED A DURABLE RESPONSE UP TO 6-MONTHS AFTER REMOVAL

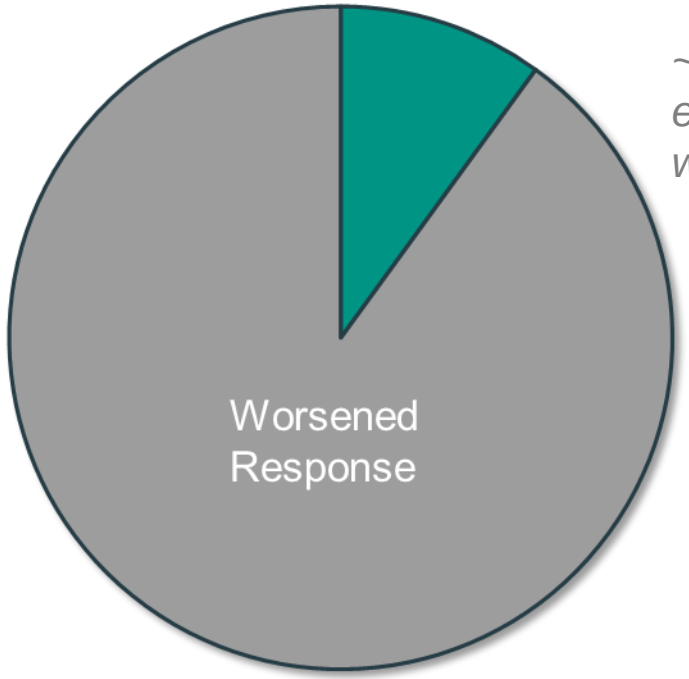
LANTERN Study: Long-term Outcomes (7500 µg)

LYR-210 (7500 µg)



~50% of patients experienced a durable response

Control



~90% of patients experienced a worsened response

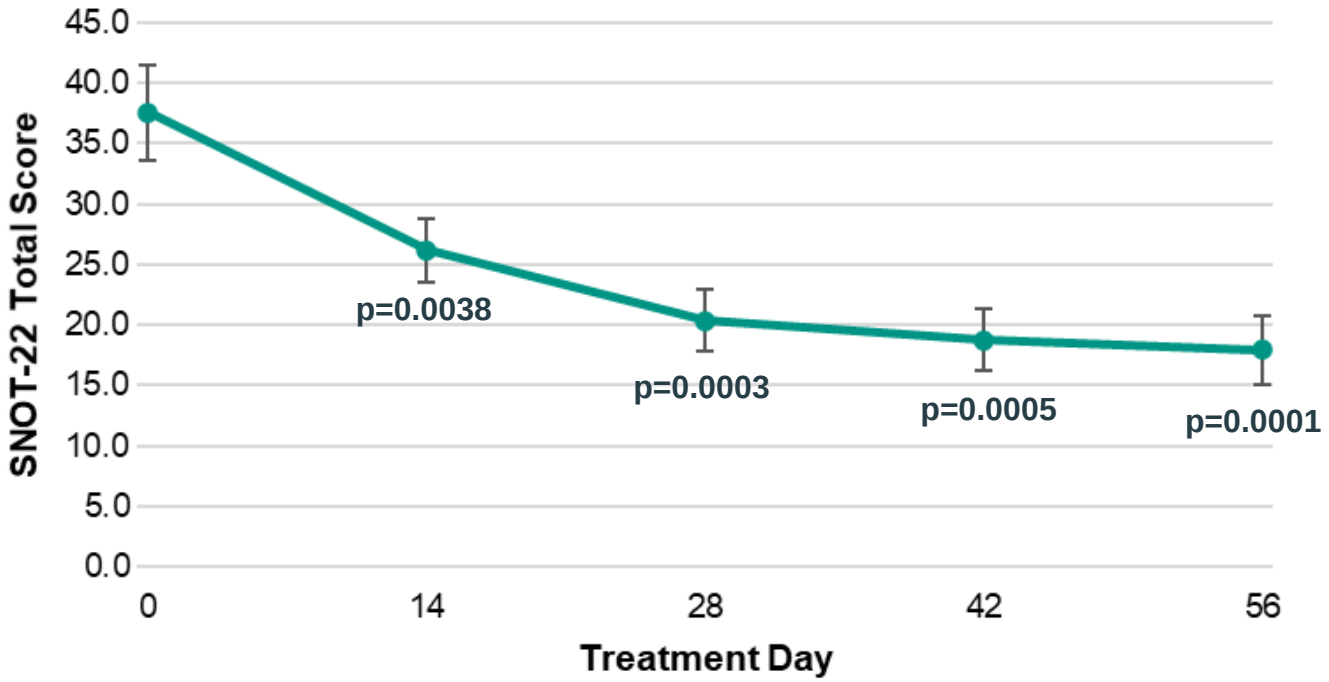
Worsened response = patients experiencing a worsening in 4CS scores from week 24 baseline (at ≥1 time points in the post-treatment period) and patients that required rescue treatment. Durable response = patients experiencing no worsening in 4CS scores from week 24 baseline throughout the post-treatment period. These percentages of patient responses in the post-treatment period represent trends. Analyses are not powered for statistical significance.

4CS = Composite score of 4 cardinal CRS symptoms (nasal blockage, facial pain/pressure, nasal discharge, and olfactory loss)

PHARMACOKINETIC STUDY: ACHIEVED CLINICALLY RELEVANT IMPROVEMENT IN SNOT-22 WITHIN 2 WEEKS

LYR-210 56-Day PK Study

SN0T-22 CRS Symptom Scores

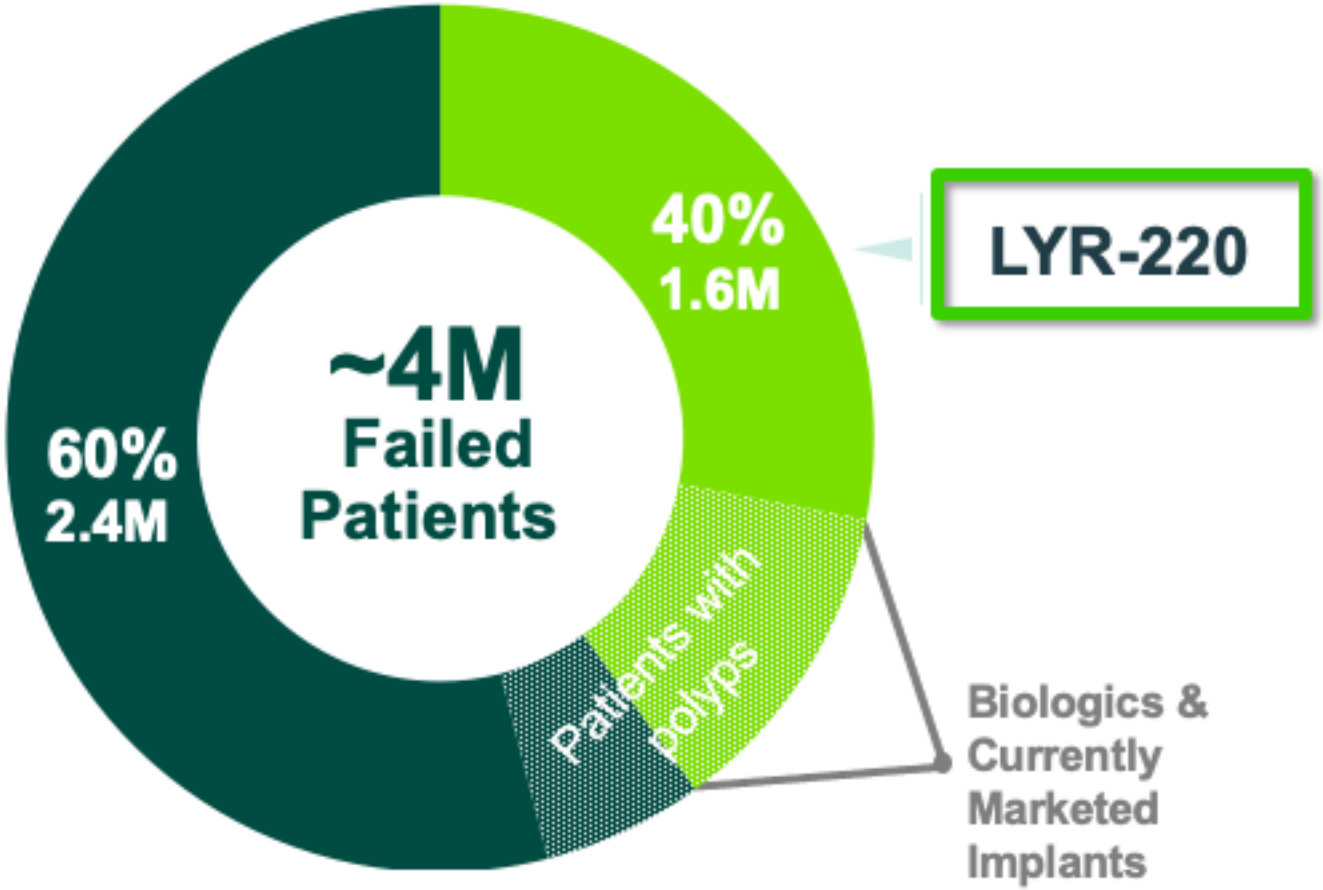


63% of patients improved beyond the threshold for surgery with a SNOT-22 score (< 20) on Day 56

38% of patients reported a “normal” SNOT-22 score (< 8) on Day 56

Data are represented as mean and standard error. n=24 patients. P-values represent statistical significance of SNOT-22 total scores relative to baseline. SNOT-22 = 22-item Sinonasal Outcome Test. MCID = 8.9 points

LYR-220 TARGETS CRS PATIENTS WITH POST-SURGICAL ANATOMY



- Scaled-up matrix for larger post-surgical anatomy
- Same drug dosing profile, kinetics and materials
- Enter the clinic around YE'21
- Regulatory path will leverage LYR-210

LYR-210 & LYR-220 MOVING INTO LATE-STAGE DEVELOPMENT

LYR-210 ENLIGHTEN
Phase 3 Program

Adult patients with CRS that have failed medical management and not had ESS

Primary Endpoint: 3 Cardinal Symptoms at 24 weeks

2:1 randomization: 7500µg, Control

~350 subjects split between two staggered studies; >95% power per study

Other Endpoints: SNOT-22, rescue treatments, sinus CT, QoL, PE

First Phase 3 trial to begin around YE'21

LYR-220 BEACON
Phase 2 Study

Adult patients with CRS that have failed medical management and had a total ESS

Primary Endpoint: safety & feasibility over 24 weeks

1:1:1 randomization: Design 1 7500µg, Design 2 7500µg, Control

~ 65 subjects in US & Australia

Other Endpoints: PK, SNOT-22, 3CS, rescue treatments, sinus CT, nasal biomarkers, QoL

Trial to begin around YE'21

EXCITEMENT IS BUILDING FOR LYR-210/220

KOL Perspectives

> I see LYR-210 as being somewhat of a whole change to my paradigm…I think it's exciting.

> [CRS] is not life-threatening, so the symptoms are the key… the fact that you're getting a SNOT-22 drop that is similar to what we can see in the range of sinus surgery and with oral steroids; that's excellent. I'm excited about that.

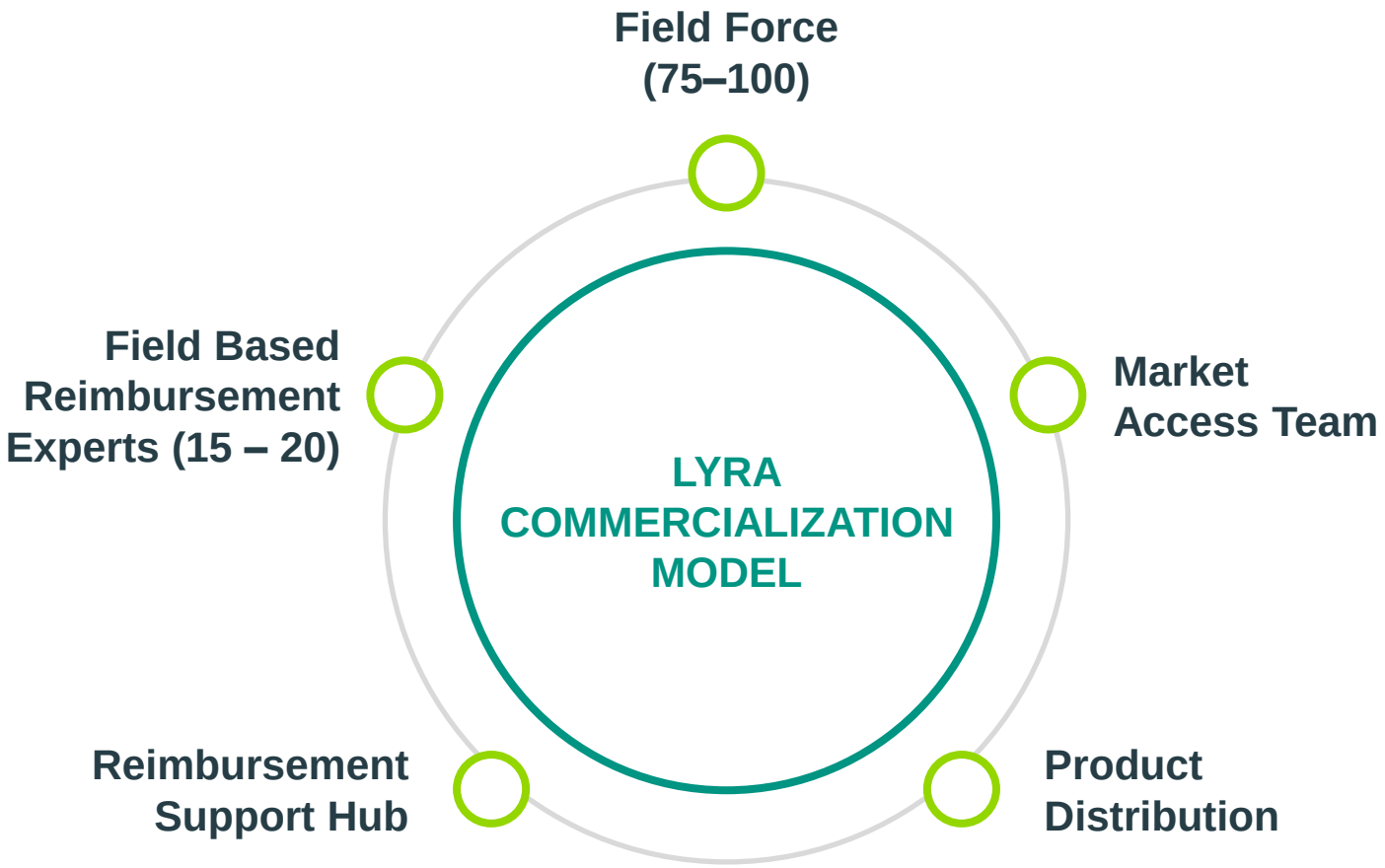
> The one thing that really caught my eye with the LANTERN data was how good the LYR-210 product performed compared to the biologics.

> It's not just simply polyps…all forms of chronic rhinosinusitis really requiring management of inflammation… steroids become much more important for us…But from a clinical standpoint and from a safety and efficacy standpoint, there's no doubt that a product like this is going to be far superior to take than the oral steroids.

LYR-210

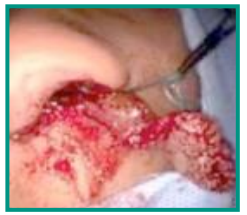
COMMERCIALIZATION STRATEGY

- Promote product awareness among ENTs and patients
- Secure broad payer coverage
- Ensure reimbursement confidence and facilitate processing of claims
- Limit product acquisition “hassle-factor”
- Efficient commercialization model



ATTRACTIVE PRICING ENVIRONMENT

Broad Range of Price Points for Existing Treatments

Merck Nasonex®	OptiNose Xhance®	Intersect ENT Sinuva®	Regeneron/Sanofi Dupixent®	Sinus Surgery
				
Steroid nasal spray (mometasone furoate, BID)	Steroid nasal spray (fluticasone, BID)	Short-term steroid stent for surgical relapse (mometasone furoate)	Monoclonal antibody for uncontrolled disease (anti-IL4, SQ injection)	Functional Endoscopic Sinus Surgery
Annual Price				
~$3,000	**~$6,000 to $11,000**	**~$10,000**	**~$36,000**	**Average ~$14,000**

Source: Product package inserts and IBM Micromedex RED BOOK

REIMBURSEMENT RATIONALE

Potential to fit well into ENT reimbursement models

Professional Fee

Office procedure

LYR-210/220 placed with nasal endoscopy

Leverage existing CPT codes
for placement and removal

Product Fee

Reimburse via a J-Code

Purchase through buy-and-bill or specialty pharmacy

5%–10% mark-up per unit

STRATEGIC PARTNERSHIP WITH LIANBIO

SUPPORTS GLOBAL COMMERCIALIZATION STRATEGY

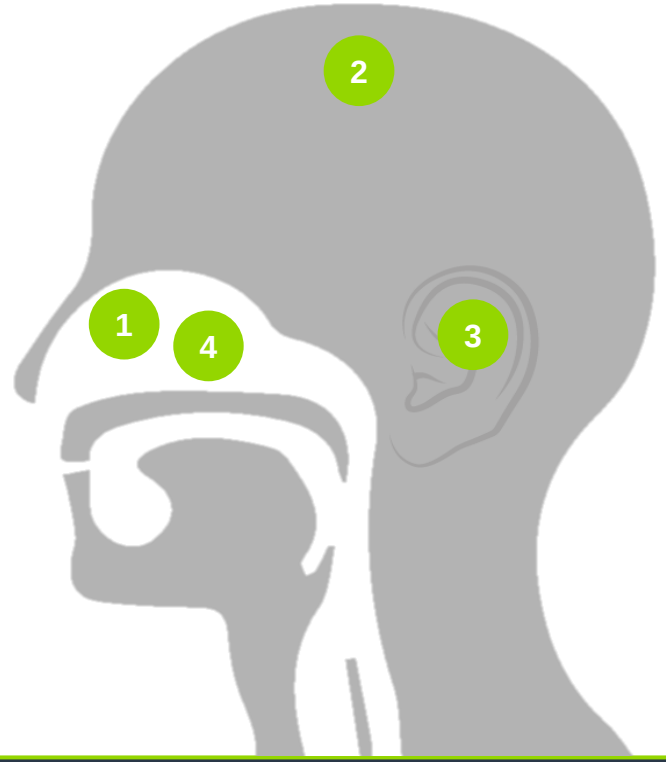
Lyra Therapeutics and LianBio ink strategic partnership and license agreement to develop and commercialize LYR-210 in Greater China, South Korea, Singapore and Thailand

- **$12 million** upfront; **$135 million** total potential milestones, tiered low double-digit royalties
- CRS prevalence of **88 million** patients in Greater China
- LianBio responsible for the **clinical development and commercialization** of LYR-210 in partnership territory
- Lyra **retains all rights** to LYR-210 in all other geographies
- Potential future collaboration on **LYR-220**

BROAD POTENTIAL FOR EXPANDED INDICATIONS

Lyra's XTreo™ platform has potential in other indications where long-term delivery would improve local bioavailability, enhance efficacy and safety

1. **Allergic Rhinitis**
2. **Nasal Delivery for CNS Disorders**
3. **Ear Conditions**
4. **Sinus-Related Rare Disorders**



WORKING TO DISRUPT THE TREATMENT PARADIGM FOR CHRONIC DISEASES, STARTING WITH CRS

Creating the standard of care for the millions of patients suffering from CRS and for which there is no approved therapeutic treatment

Poised to be the dominant player in $6B CRS opportunity

Multiple value-creating near-term milestones

- **PK and Long-term LANTERN safety to be presented at ARS Oct. ’21**
- **LYR-210 Phase 3 ENLIGHTEN study initiation ~YE’21**
- **LYR-220 Phase 2 BEACON study initiation ~YE’21**

Opportunities for Proprietary XTreo™ platform into new indications


LYRA
THERAPEUTICS