LYRA THERAPEUTICS

Creating precisely tuned medicines so patients can breathe freely

JUNE 2021

INVESTOR PRESENTATION

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 lead product candidate LYR-210, the presentation of results relating to the Company's Phase 2 LANTERN clinical trial for LYR-210 and the Company's plans to initiate a pivotal Phase 3 study for LYR-210 in CRS for both non-polyp and 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: 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; 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 May 11, 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.

INVESTMENT SUMMARY

Working to disrupt the treatment paradigm for intranasal drug delivery, starting with CRS

Only Product Candidate To Provide Up To Six Months of Chronic Rhinosinusitis (CRS) Symptom Relief From A Single Treatment in Clinical Testing

- Positive LANTERN Phase 2 Results for LYR-210, presented April 2021
- 100% had clinically meaningful symptom improvement at Week 24 (7500 mcg)

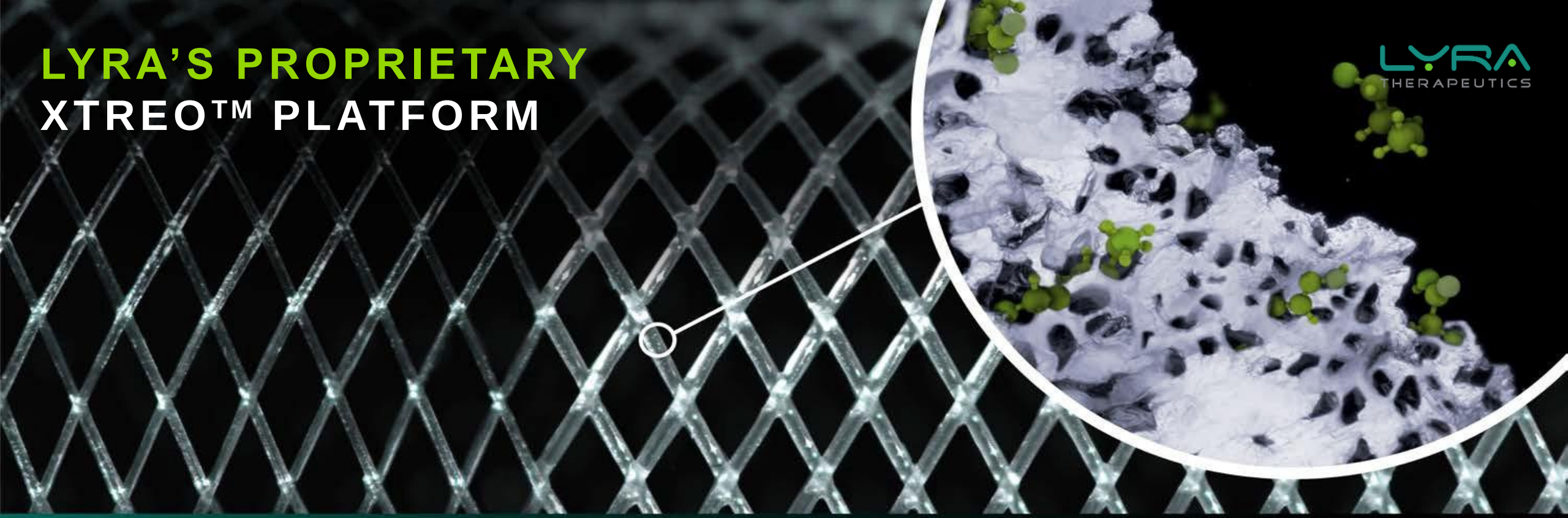
14M CRS Patients in U.S.; A $6BN Addressable Market

- No FDA approved medicines for non-polyp (90% of pre-surgical CRS patients)

Pivotal trial planned for 2021

- Initiation of pivotal Phase 3 program planned for end 2021
- Multiple potential expansion opportunities; LYR-220 expected to enter clinic in 2021

LYRA'S PROPRIETARY XTREO™ PLATFORM



BIOCOMPATIBLE MESH SCAFFOLD

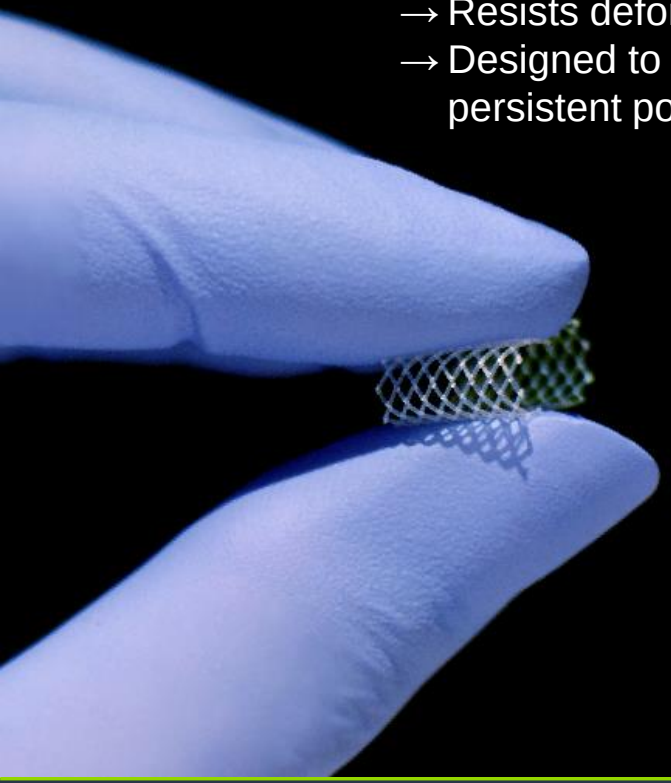
ENGINEERED ELASTOMERIC MATRIX

VERSATILE POLYMER-DRUG COMPLEX

ENGINEERED ELASTOMERIC MATRIX
ADAPTS TO NASAL ANATOMY

Shape-memory

→ Adaptive elastic tension
→ Resists deformation
→ Designed to maintain persistent positioning



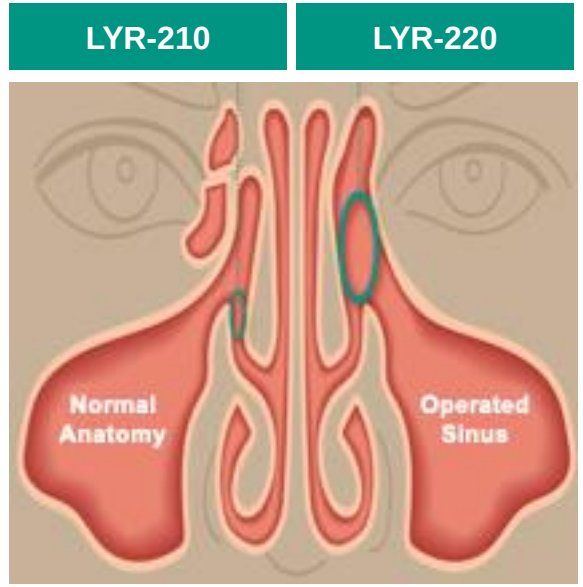
Designed to be Self-retaining

→ Exerts outward retention force at the target location
→ Designed to remain in place as tissue remodels

DEVELOPMENT PIPELINE

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

Candidate	Pre-clinical	Phase 1	Phase 2	Phase 3	Next Milestone
LYR-210 Long-acting Mometasone Furoate	Chronic Rhinosinusitis **Surgically Naïve Patients**		POSITIVE LANTERN PHASE 2 RESULTS PRESENTED APRIL 2021 at COSM VIRTUAL		End of Phase 2 FDA Meeting Mid 2021
LYR-220 Long-acting Mometasone Furoate	Chronic Rhinosinusitis **Operated Patients**				Enter Clinic End 2021



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

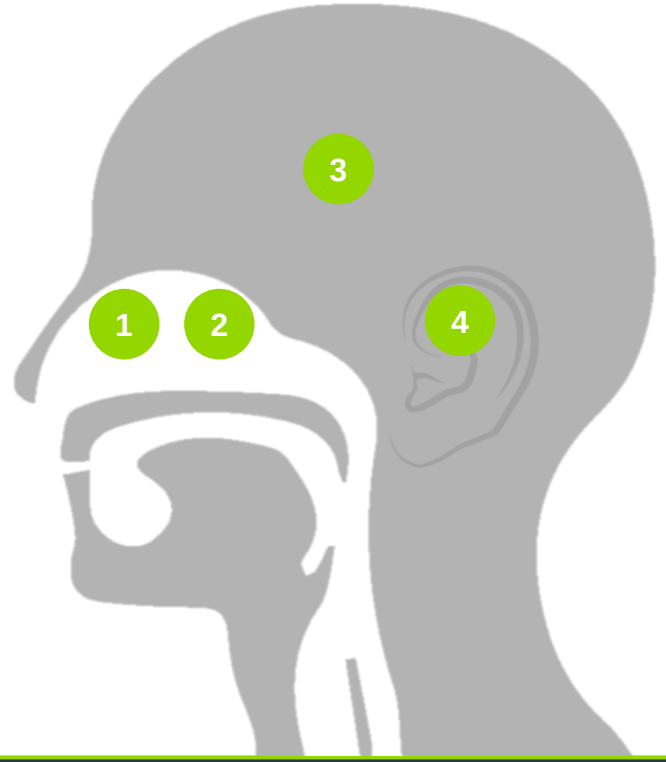
- **$12 million** upfront; **$135 million** total potential milestones, tiered low double-digit royalties
- CRS prevalence of **88 million** patients in Greater China
- LianBio responsible for the **clinical development and commercialization** of LYR-210 in partnership territory
- Lyra **retains all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

WITH POTENTIAL FOR EXPANSION INDICATIONS

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

Potential Expansion Indications:

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



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]

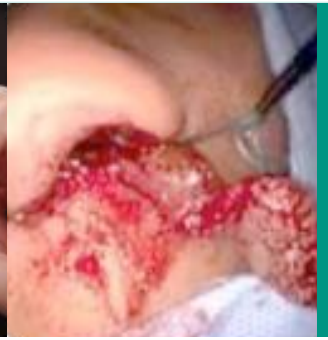
1) Tan BK et al. Am J Respir Crit Care Med, 2013;188(11):1275–7; 2) Battacharrya. Ann Otol Rhinol Laryngol, 2011; Jul;120(7):423-7; 3) Jang et al. Otolaryngol Head Neck Surg, 2018; 4) Baguley et al. Int Forum Allergy Rhinol, 2014;4(7):525-32

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]

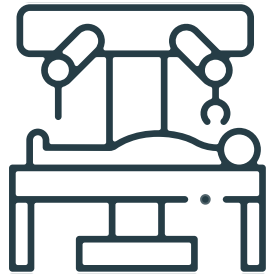
1) Young et al. Allergy Rhinol, 2012; 3:e8-e12; 2) Schaitkin et al. Laryngoscope, 1993; 103; 3) Stein et al. Laryngoscope,2018; 128(1): 31–36; 4) Rosenfeld et al. Otolaryngology–Head and Neck Surgery, 2015; 152(2S)

A $6BN MARKET OPPORUNITY

An unmet need for better treatment options exists for millions of CRS patients

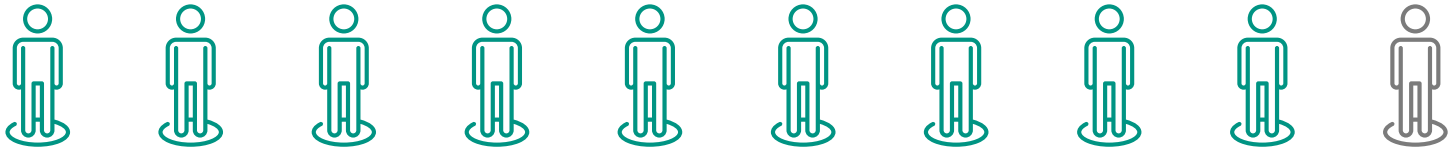
4M

fail medical management



400K

get surgery[1]



Up to 90%

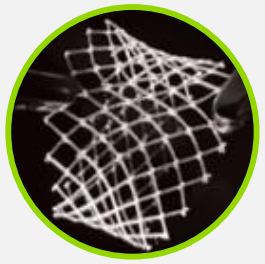
of patients are left with suboptimal treatment options

1) Young, L. Cet al. Allergy & Rhinology, 2012; 3(1), 8–12

DEVELOPING SOLUTIONS FOR ALL ENT CRS PATIENTS

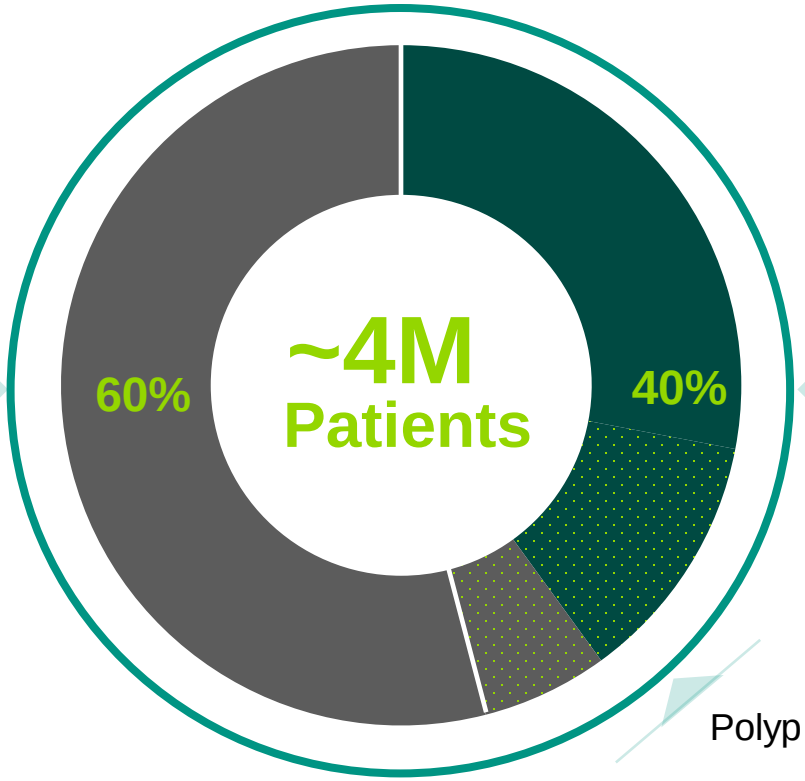
LYR-210 and -220 are designed for the full range of CRS patients treated by ENTs

For Surgically Naïve CRS Patients



LYR-210

Mometasone Furoate

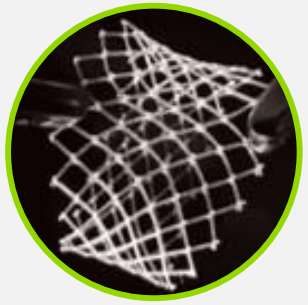


For Operated CRS Patients

LYR-220

XL

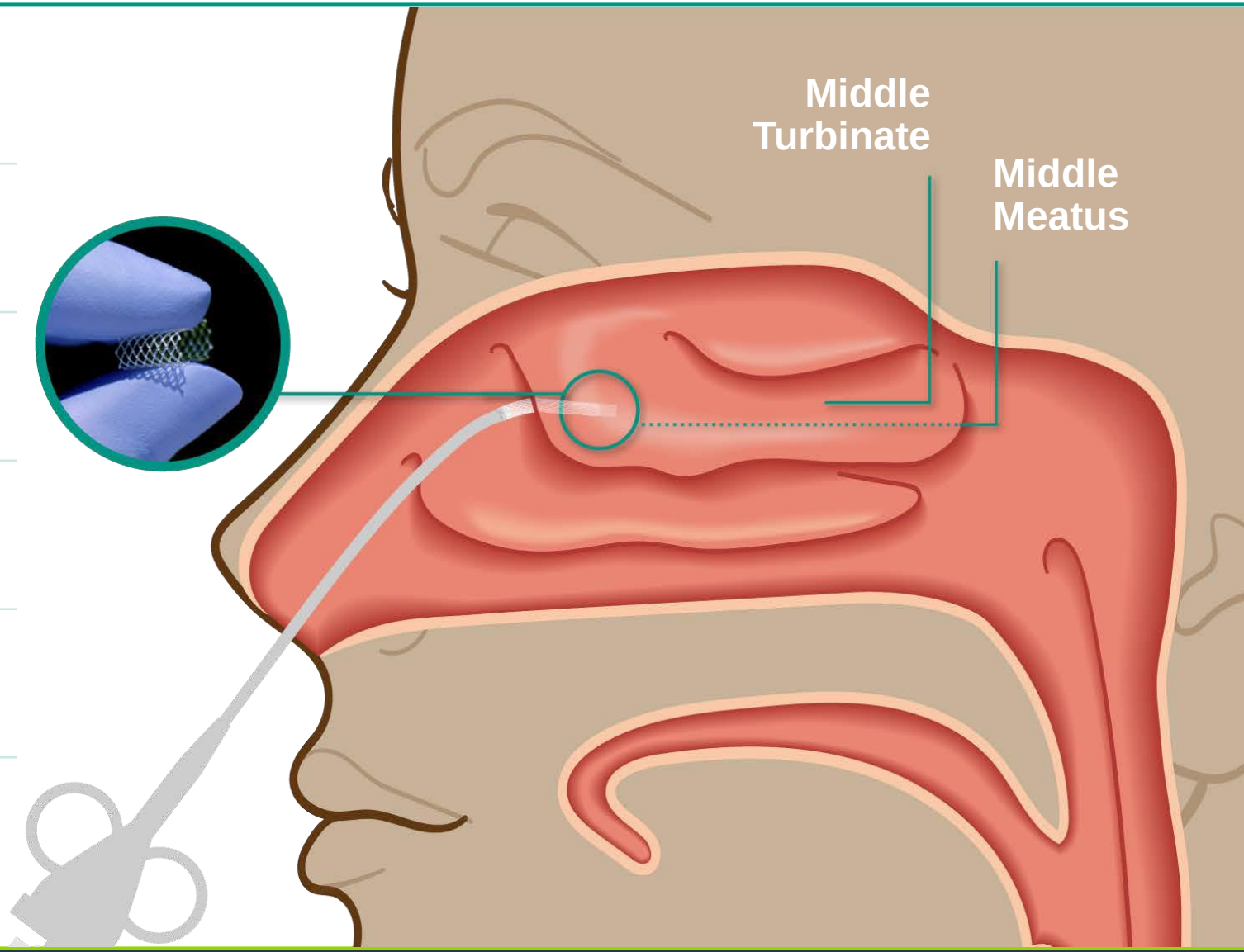
Mometasone Furoate



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



TRIAL SUMMARY

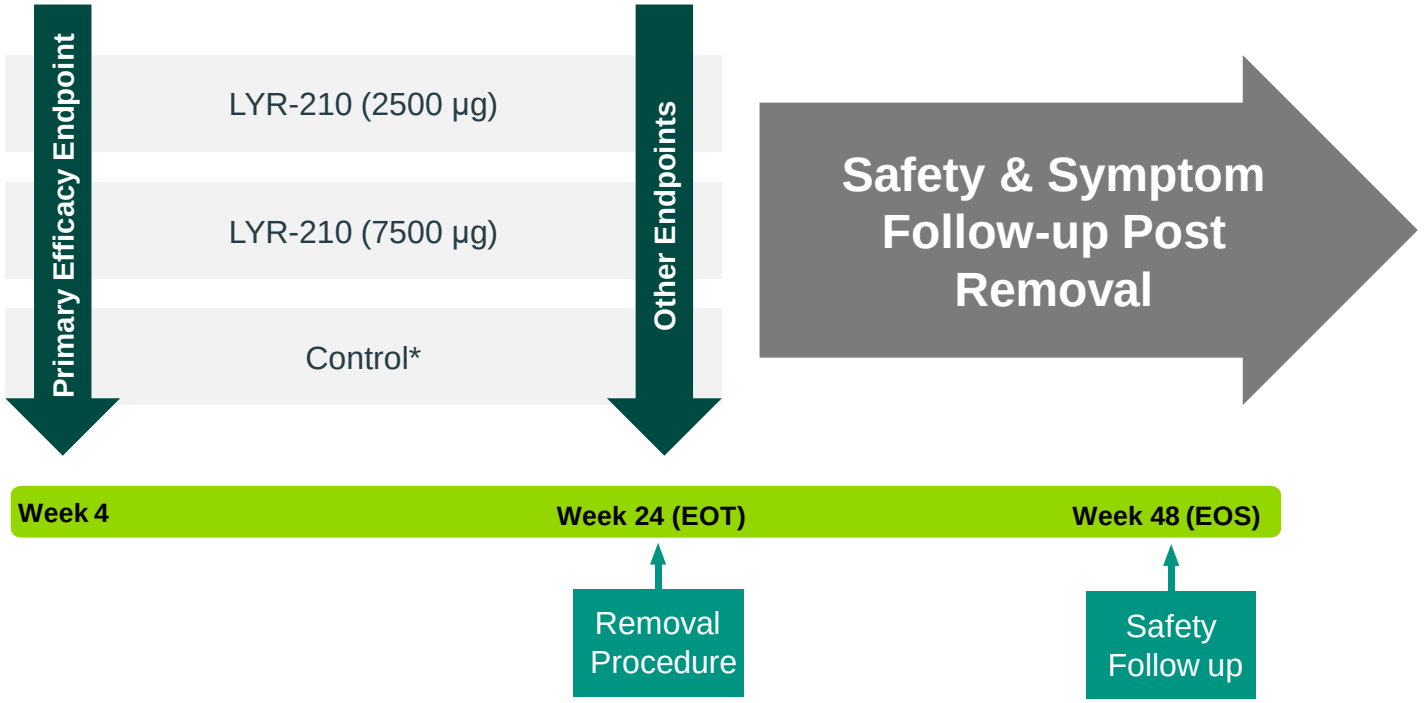
POSTIVE LANTERN PHASE 2 RESULTS

Positive Phase 2 results position Lyra to move forward to pivotal Phase 3 program

- **Rapid onset:** patients started feeling better quickly
- **Lasting effect:** patients experienced up to six months of symptom relief
- **Competitive profile** vs existing treatments
- **Positive safety profile** and well tolerated

LANTERN PHASE 2 STUDY

Randomized, Patient Blinded, Controlled, Dose-ranging



- Enrollment curtailed at 67 due to COVID-19
  - 110 - 150 planned
  - 1:1:1 randomization
- Evaluated efficacy in adult subjects with CRS who have failed medical management as an alternative to surgery
- 14 sites in Europe, Australia, New Zealand

EOT = End of Treatment, EOS = End of Study
*Control = Sham procedure followed by daily saline irrigation

ACCEPTED CLINICAL MEASURES OF EFFICACY

LANTERN Phase 2 Study Endpoints

SinoNasal Outcome Test (SNOT-22)

- Global instrument widely used by ENTs
- Gold standard validated CRS-specific instrument
- 22 patient reported questions (0-5 scale, total = 110)
- Minimal clinically important difference (MCID) of -8.9[1]

Cardinal Symptom Assessment

- Preferred by FDA for regulatory approval in CRS
- Sponsor plans to select 2-4 cardinal symptoms:
  - Obstruction congestion
  - Nasal discharge
  - Facial pain/pressure
  - Loss of sense of smell
- No minimal clinical importance difference (MCID) established

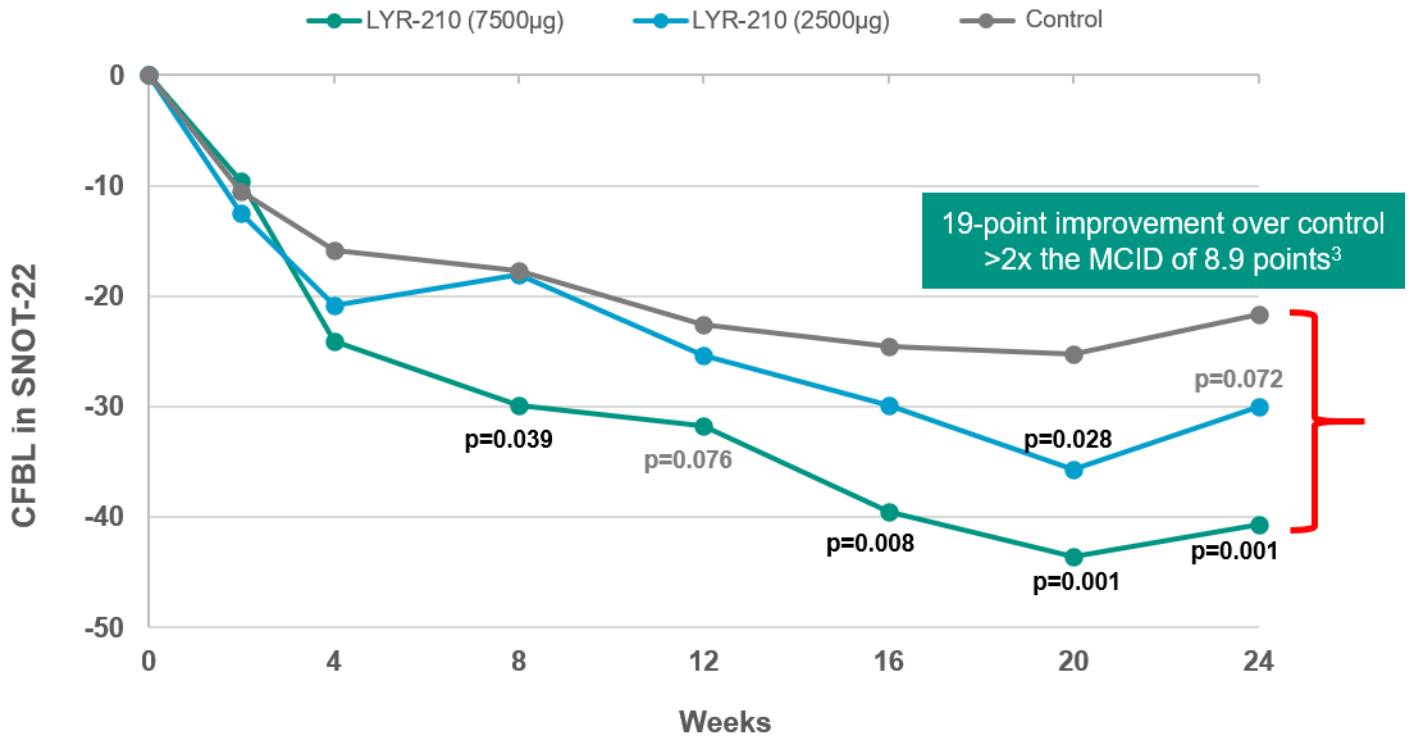
1) Hopkins C et al. Clin. Otolaryngol. 2009, 34, 447–454

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] THE CLINICAL GOLD STANDARD



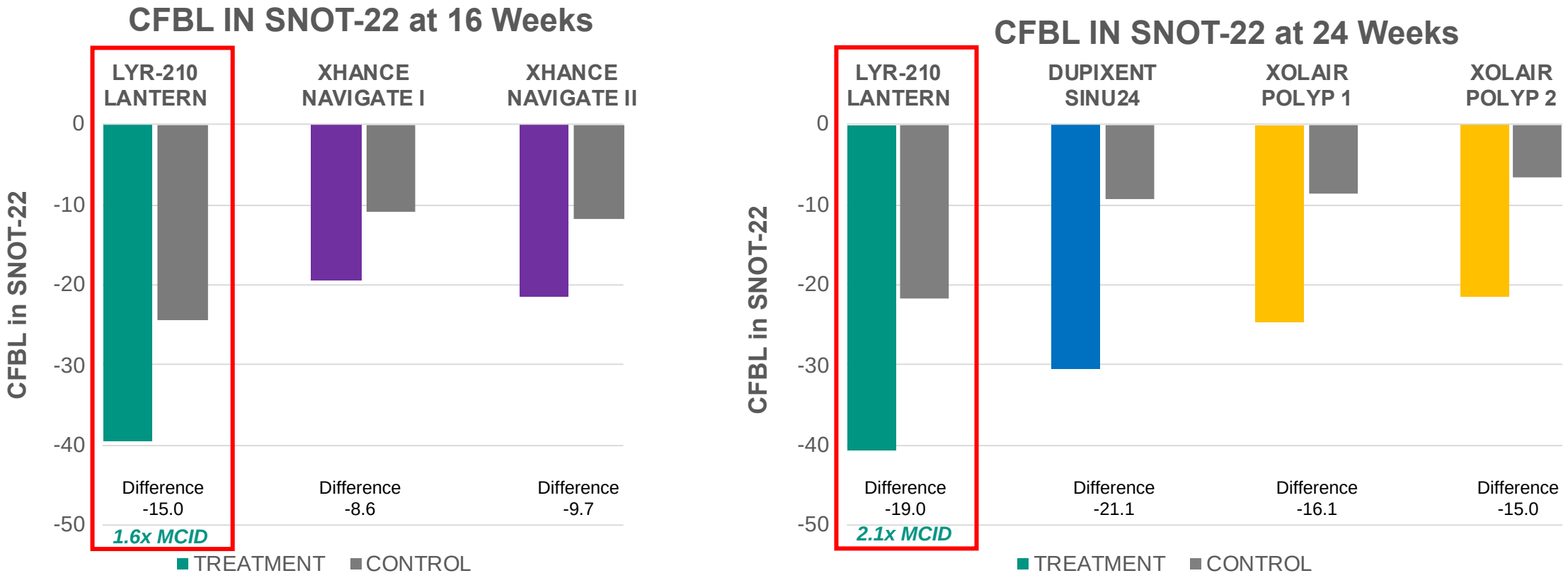
Statistically Significant Improvement vs Control at 8, 16, 20 and 24 wks

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 PERFORMANCE IS HIGHLY COMPETITIVE

SNOT-22 Score Comparison*

*Absolute change of ~**40 points** and **clinically meaningful** (>8.9 points) difference relative to control for 7500 mcg dose*



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

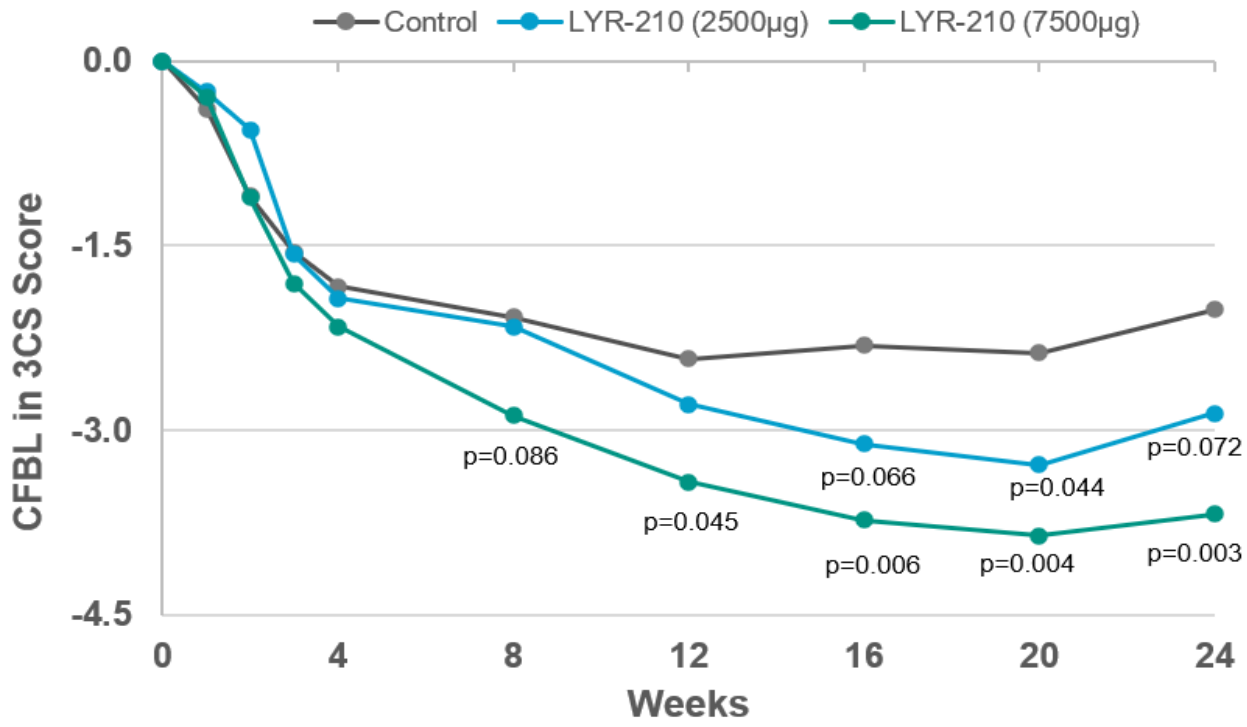
Sources:
XHANCE: Sindwani, et al., Am J Rhinol Allergy 2019, Vol. 33(1) 69–82; Lepard et al., J Allergy Clin Immunol, 2019;143:126-34
DUPIXENT: Bachert, et al., Lancet 2019; 394: 1638–50
XOLAIR: Gevaert et al, J Allergy Clin Immunol, 2020, 146(3), 595-605

LYR-210

POSITIVE LANTERN PHASE 2 STUDY

- Rapid symptom improvement that becomes more pronounced over 24 weeks
- Found 6-month benefit from a single administration
- Showed benefit in both polyp and non-polyp patients

DOSE DEPENDENT SYMPTOM IMPROVEMENT BY 3CS[1,2]

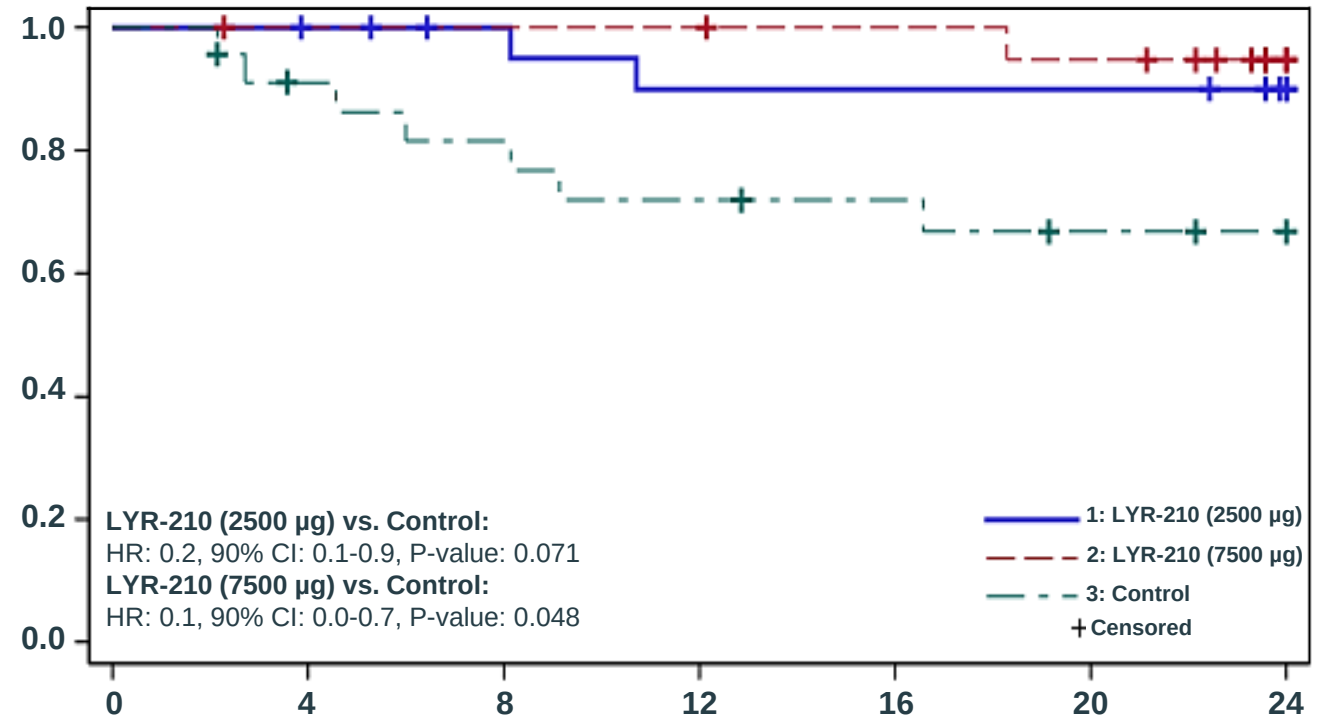


Statistically Significant Improvement vs Control at Weeks 12 - 24

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

TIME TO FIRST RESCUE TREATMENT USE

LYR-210 decreased the need for rescue treatment



Number of Patients at Risk:

1: LYR-210 (2500 µg)	23	22	20	18	18	18	15
2: LYR-210 (7500 µg)	21	20	20	20	19	18	12
3: Control	23	19	17	15	14	12	11

Time to first rescue treatment use over 24 weeks. Event is rescue treatment used. Patients who did not achieve the event were censored at the end of treatment date or at the early termination date. LYR-210 (7500µg) (n=1 patient), LYR-210 (2500µg) (n=2 patients), saline irrigation control (n=7 patients) used rescue treatment over the 24-week treatment period.

LYR-210

SAFETY & TOLERABILITY

Well-tolerated throughout the 24-week treatment period at both doses

WELL-TOLERATED SAFETY PROFILE AT BOTH DOSES

No treatment-related SAEs

Treatment-related AE's in more than 1 subject:

- Epistaxis: 3 subjects at 2500 mcg
- Rhinitis: 3 subjects at 7500 mcg
- Rhinorrhea: 2 subjects at 2500 mcg
- Headache: 2 subjects in control

All treatment-related AEs mild or moderate apart from one event:

- Increased viscosity of upper respiratory secretion at 2500 mcg

Treatment-related AE's in control and 7500 mcg groups occurred at comparable rates

BUILDING A COMPLETE CRS SOLUTION FOR ENTs

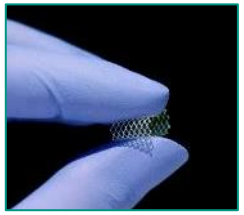
LYR-210's potential advantages over existing treatments are compelling and many

COMMERCIAL SUMMARY

- **Huge market opportunity:** $6BN in the U.S.
- **Product profile:**
  - Meaningfully differentiated
  - Appeals to physicians, patients and payers
- **Accessible market**: Efficient commercialization model

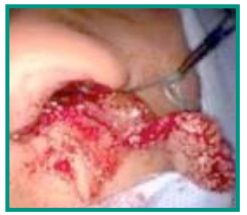
POTENTIAL COMPETITIVE ADVANTAGES

Non-systemic, easy compliance, 6-months via one application, for polys and non-polyps

	OptiNose Xhance®	Regeneron/Sanofi Dupixent®	Intersect ENT Sinuva®	LYR-210/220
				
	Steroid nasal spray (fluticasone, BID)	Monoclonal antibody for uncontrolled disease (anti-IL4, SQ injection)	Short-term steroid stent for surgical relapse (mometasone furoate)	**6-mo continuous intranasal steroid therapy**
Local effect	✓	✗	✓	✓
Requires no patient compliance	✗	✗	✓	✓
For non-polyp and polyp CRS	✗	✗	✗	✓
6-month continuous treatment with one application	✗	✗	✗	✓

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

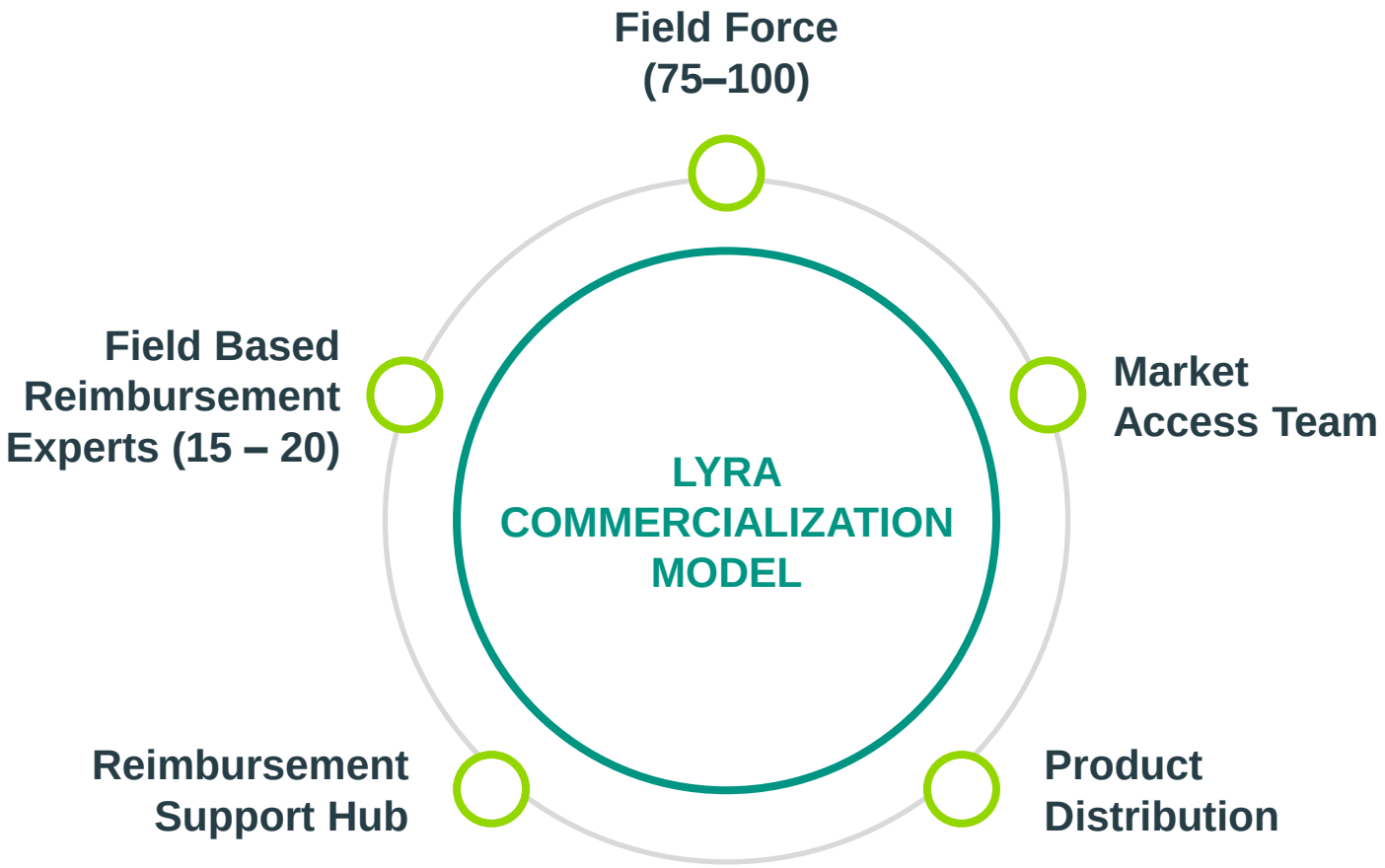
Reimburse via a J-Code

Purchase through buy-and-bill or specialty pharmacy

5%–10% mark-up per unit

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”



UPCOMING MILESTONES

- **End of Phase 2 FDA Meeting for LYR-210 – Q2 2021**
- **LYR-210 Pharmacokinetic Trial Results – Q2 2021**
- **Initiation of LYR-220 Phase 2 – year end 2021**
- **Initiation of LYR-210 Phase 3 – year end 2021**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