LYRA THERAPEUTICS

Creating precisely tuned medicines so patients can breathe freely

CORPORATE PRESENTATION

JANUARY 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 lead product candidate LYR-210, the presentation of top-line 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:

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INVESTMENT SUMMARY

Disrupting the treatment paradigm for intranasal drug delivery, starting with CRS

Developing Long-Acting Intranasal Implants for CRS

- Only therapy to achieve a benefit as much as six months after a single treatment
- 14M Chronic Rhinosinusitis (CRS) patients in U.S.; $6B addressable market
- No FDA approved medicines for non-polyp (70-90% of CRS patients)

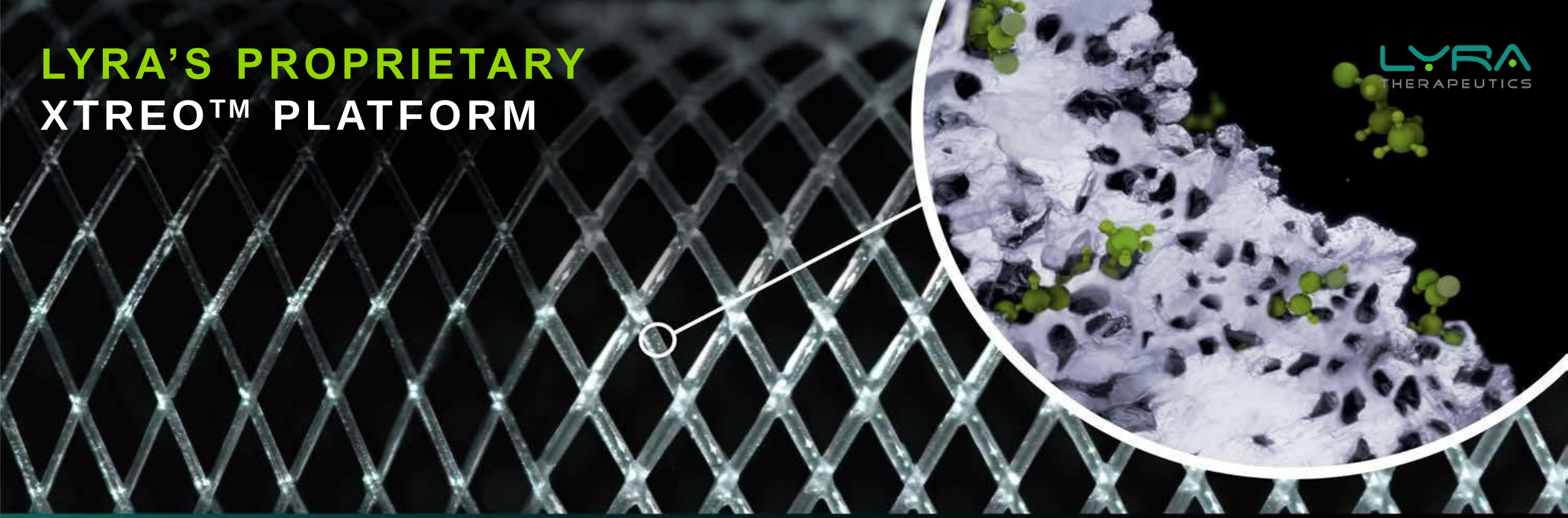
Positive LANTERN Phase 2 Results for LYR-210 Announced 4Q 2020

- Rapid, durable, and clinically meaningful symptom improvement
- 100% had clinically meaningful symptom improvement at Week 24 (7500 mcg)
- First implant to demonstrate benefit in both polyps & non-polyps
- Supports pathway to regulatory submission for pivotal trial in 2021

Potential Multiple Expansion Opportunities through XTreo™ Platform

- LANTERN supports XTreo as a tunable, long-acting, local, drug delivery platform
- LYR-220, for CRS patients with prior sinus surgery, expected to enter clinic in 2021

LYRA'S PROPRIETARY XTREO™ PLATFORM



BIOCOMPATIBLE MESH SCAFFOLD

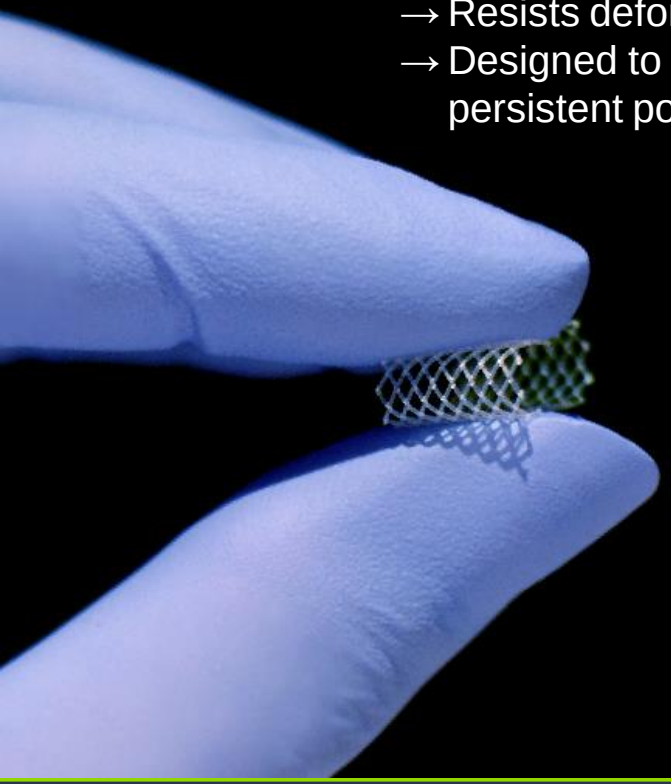
ENGINEERED ELASTOMERIC MATRIX

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

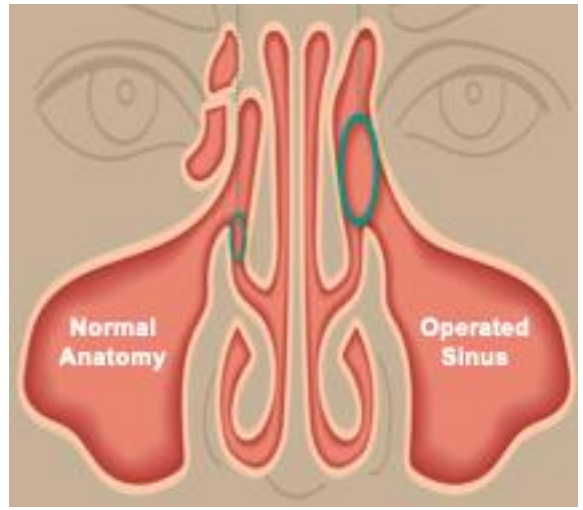
→ Exerts outward retention force at the target location
→ Designed to remain in place as tissue remodels

FOCUSED INITIAL 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**				End of Phase 2 FDA Meeting Mid 2021
LYR-220 Long-acting Mometasone Furoate	Chronic Rhinosinusitis **Operated Patients**				Enter Clinic End 2021

LYR-210 | **LYR-220**

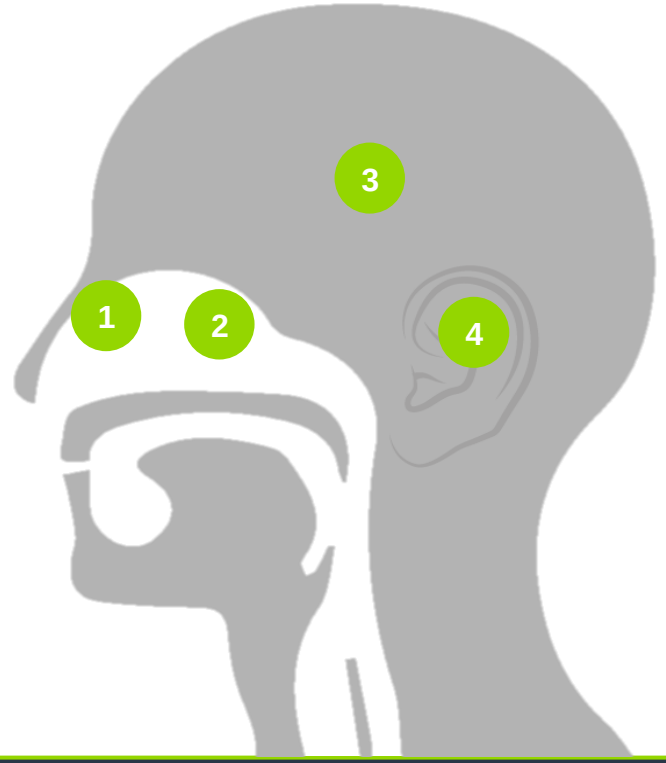


WITH POTENTIAL FOR EXPANSION INDICATIONS

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



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]

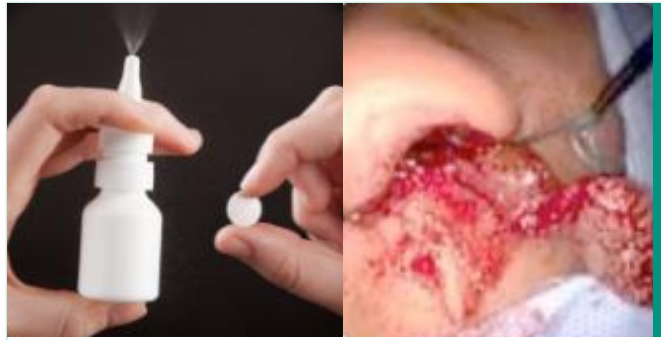
1) Tan BK et al. Am J Respir Crit Care Med, 2013;188(11):1275–7; 2) Battacharrya. Ann Otol Rhinol Laryngol, 2011; Jul;120(7):423-7; 3) Jang et al. Otolaryngol Head Neck Surg, 2018; 4) Baguley et al. Int Forum Allergy Rhinol, 2014;4(7):525-32

CHRONIC RHINOSINUSITIS

Current treatments do not control CRS 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]

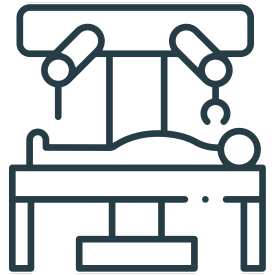
1) Young et al. Allergy Rhinol, 2012; 3:e8-e12; 2) Schaitkin et al. Laryngoscope, 1993; 103; 3) Stein et al. Laryngoscope,2018; 128(1): 31–36; 4) Rosenfeld et al. Otolaryngology–Head and Neck Surgery, 2015; 152(2S)

CHRONIC RHINOSINUSITIS

An unmet need for better treatment options exists for most patients

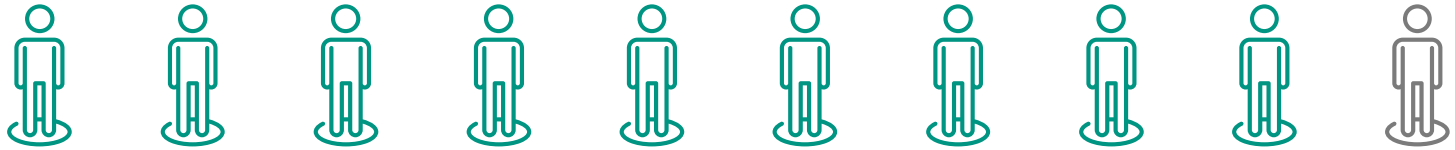
4M

fail medical management



400K

get surgery[1]



Up to 90%

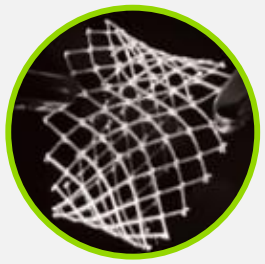
of patients are left with suboptimal treatment options

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

LYR-210 & LYR-220

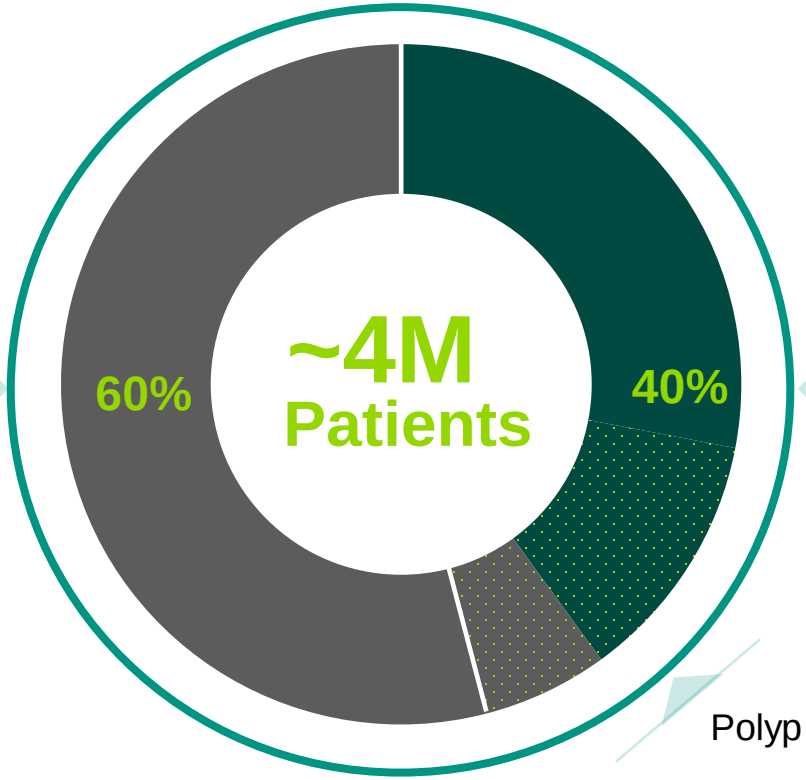
Designed for the full range of CRS patients treated by an ENT regardless of polyp status

For Surgically Naïve CRS Patients



LYR-210

Mometasone Furoate

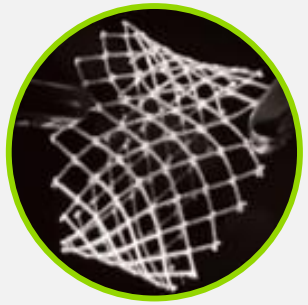


For Operated CRS Patients

LYR-220

XL

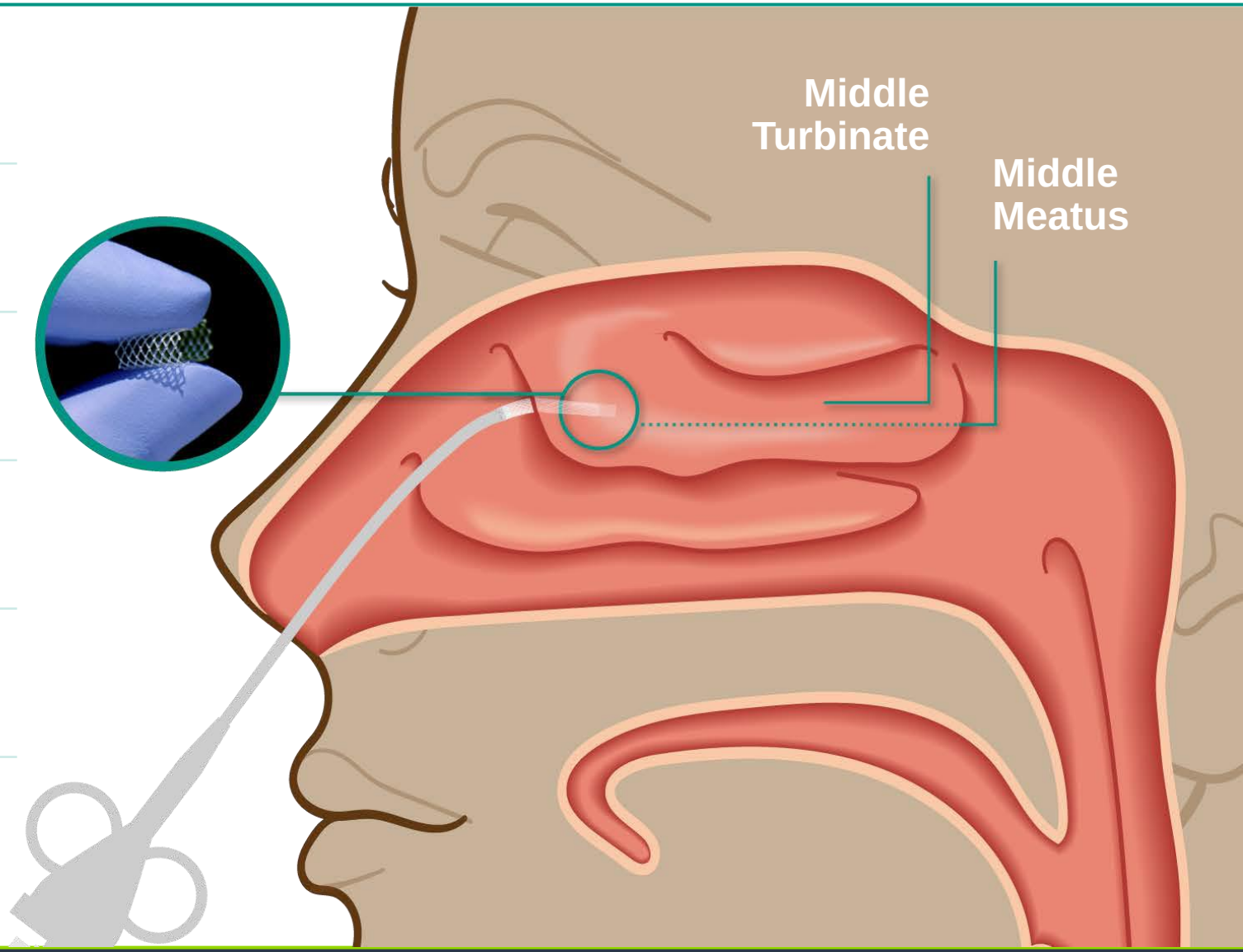
Mometasone Furoate



LYR-210

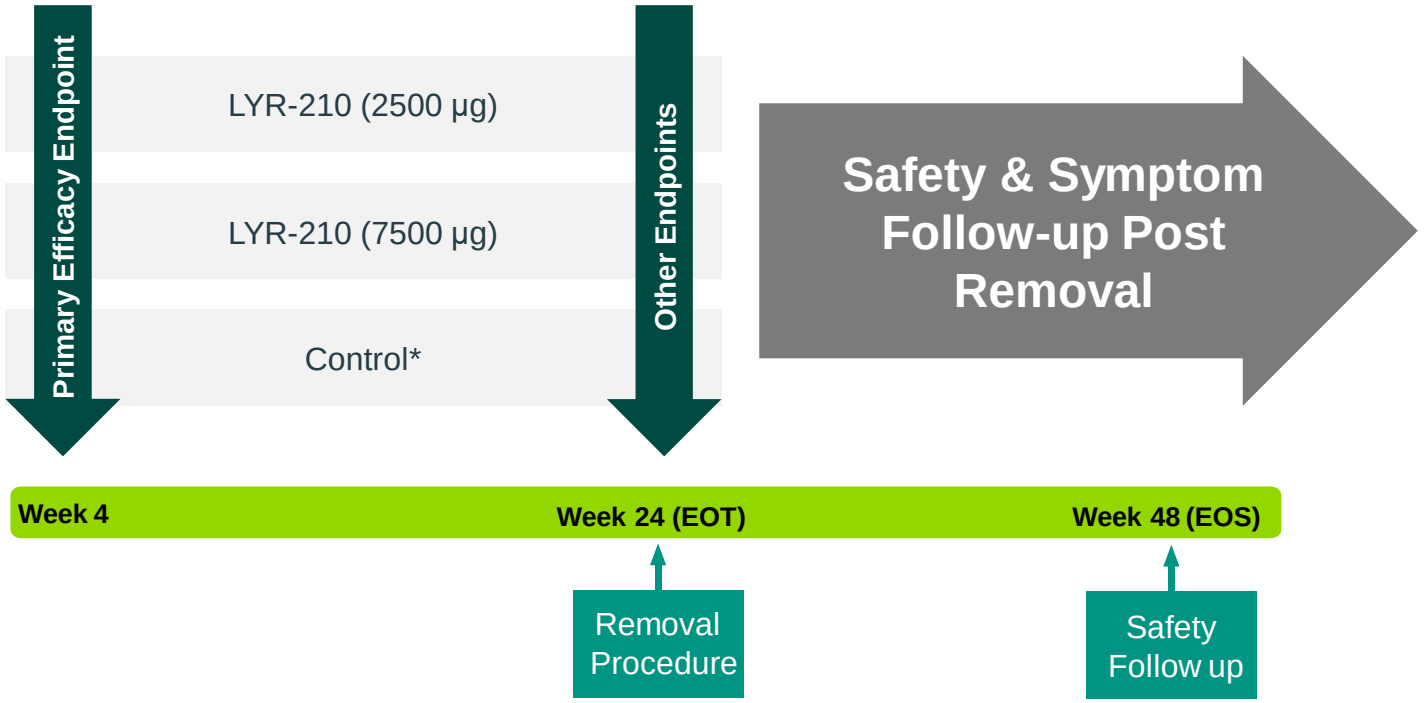
Only product candidate designed to provide 6 months of CRS therapy with a single treatment

- 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



LANTERN PHASE 2 STUDY

Despite COVID-19, we believe LANTERN significantly de-risked the Phase 3 pivotal study



LANTERN results support selection of dose and timing of the primary symptomatic endpoint for Phase 3

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

Randomized, 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
- 16 sites in Europe, Australia, New Zealand

LYR-210

LANTERN PHASE 2 STUDY

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

LANTERN PHASE 2 STUDY

Significant benefit observed along regulatory and clinical measures of efficacy

SinoNasal Outcome Test (SNOT-22)

- Global instrument widely used by ENTs in practice
- 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

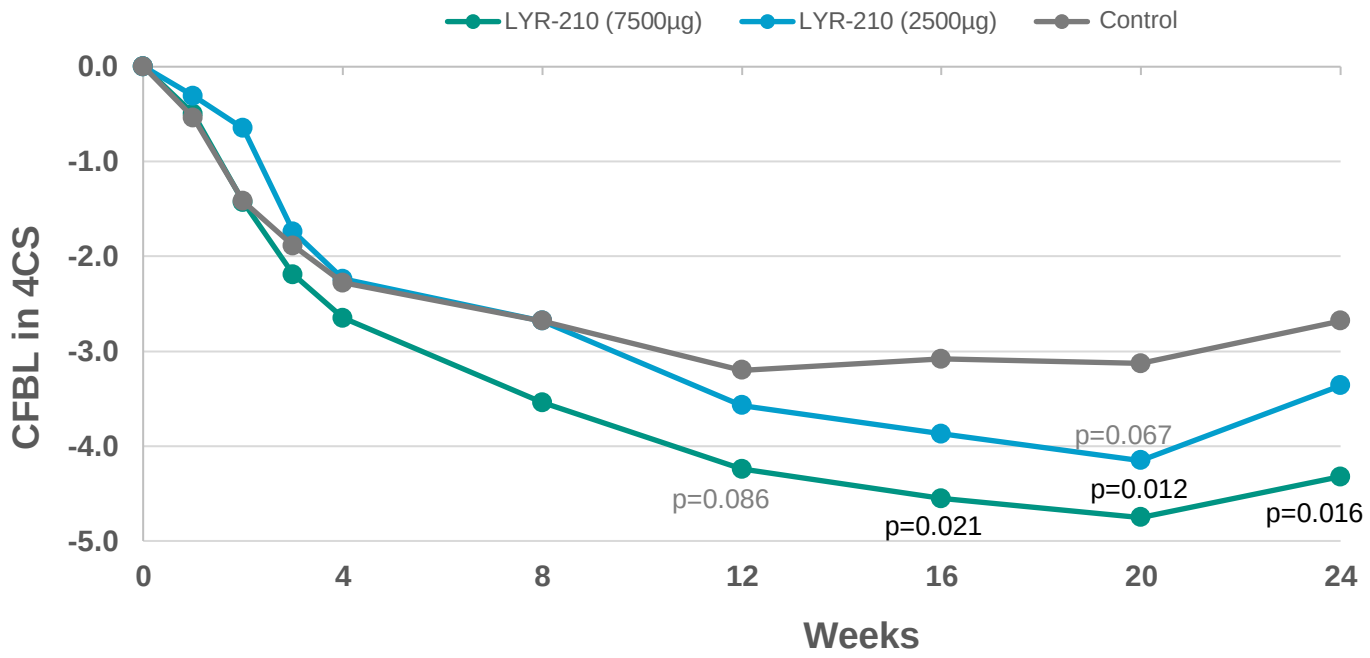
1) Hopkins C et al. Clin. Otolaryngol. 2009, 34, 447–454

LYR-210

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 4CS[1,2]



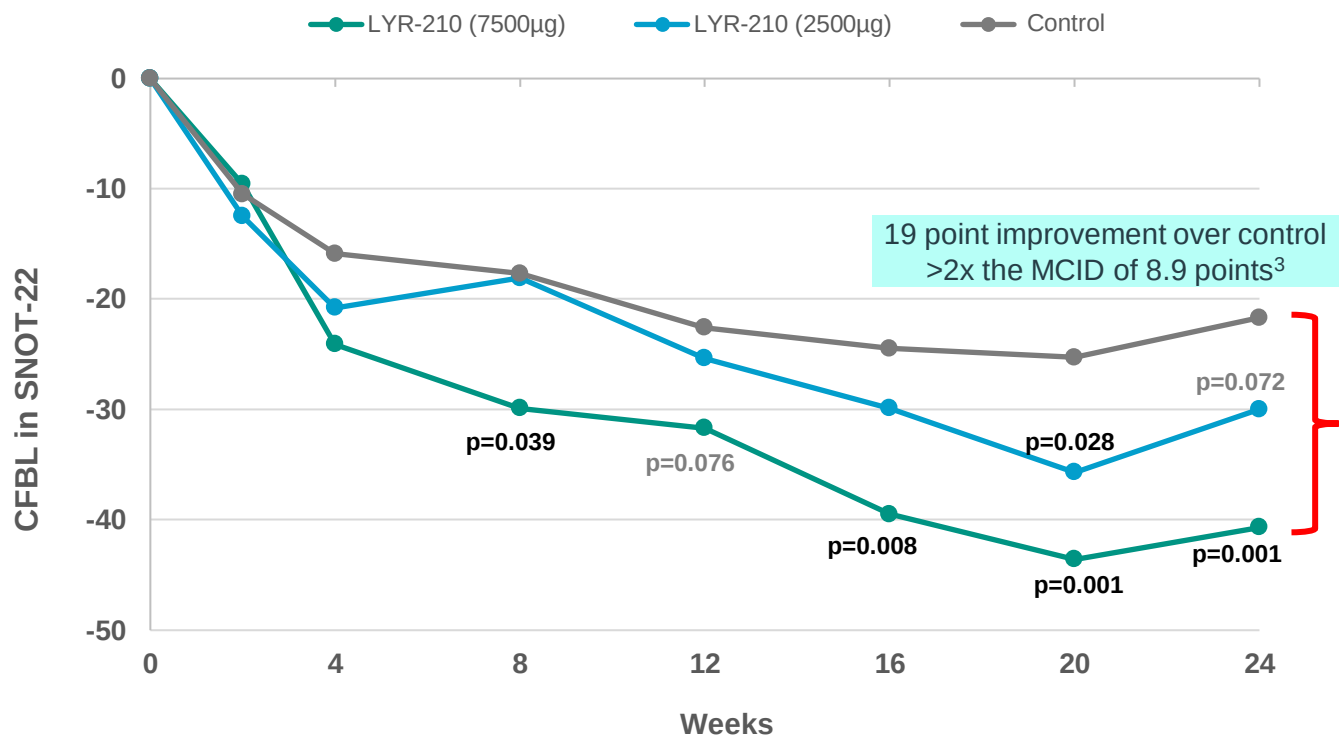
1) 4 cardinal symptom score includes nasal obstruction/congestion, rhinorrhea, facial pain/pressure and anosmia (score of 0-12 based on 7-day average symptom score); 2) Data represents the least square mean. Missing data and data post use of rescue medication was imputed by LOCF method

LYR-210

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

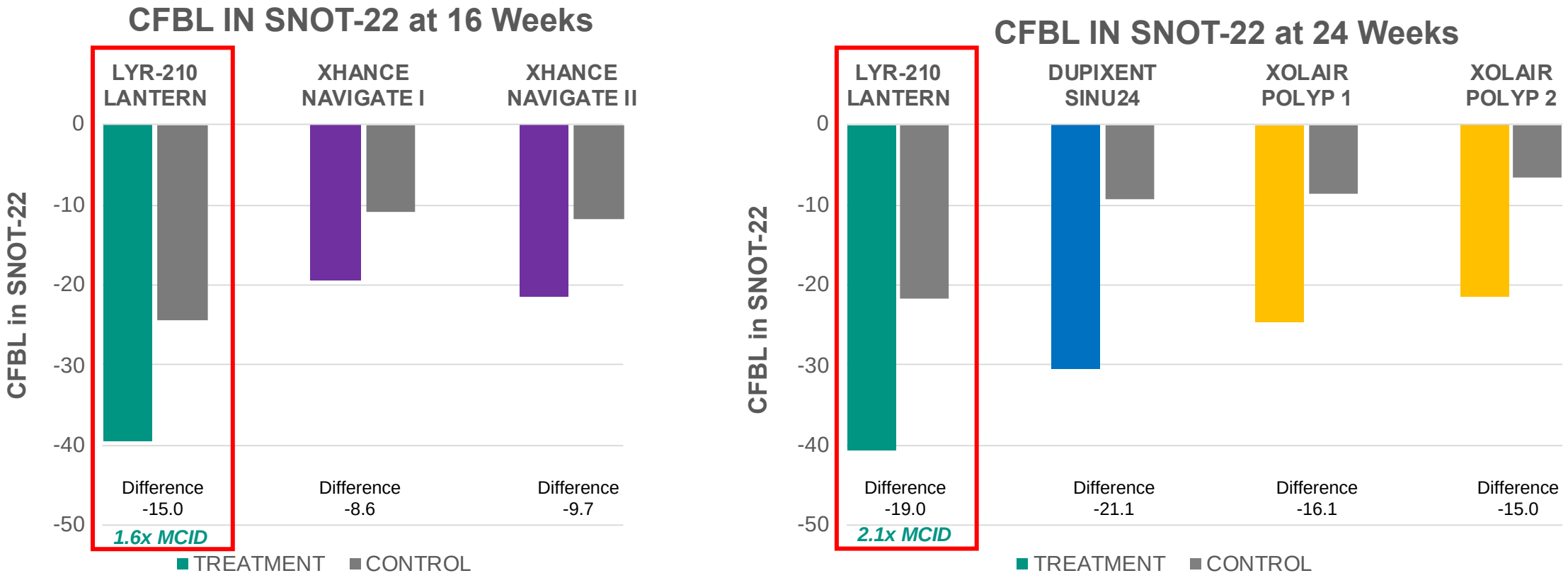


1) SinoNasal Outcome Test is a patient reported score from 0 – 110 based on symptoms; 2) Data represents the least square mean. Missing data and data post use of rescue medication was imputed by LOCF method; 3) Minimal clinically important difference

SNOT-22 SCORE COMPARISON*

LYR-210 performance is highly competitive

*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

PATH FORWARD

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

Expectations for Phase 3

- Single Phase 3 study with 7500 mcg dose
- 300 – 350 patients, US-centric
- Timing of primary symptomatic endpoint consistent with recent approved products

LYR-210 Expected Milestones

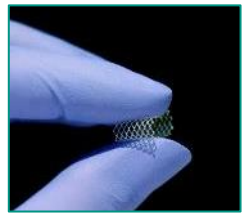
2021

1 Q	2 Q	3 Q	4 Q
	• End of Ph2 FDA Meeting		• LYR-220 Phase 2 start

Timing of Symptomatic Endpoints of Products Approved for CRS with Polyps

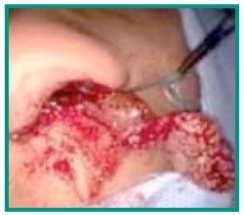
COMMERCIAL: LYR-210/220

Competitive comparison indicates potential advantages

	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	✗	✗	✗	✓

COMMERCIAL: CURRENT THERAPY PRICING

Broad range of price points provides pricing flexibility for LYR-210

	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

COMMERCIAL: LYR-210/220

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

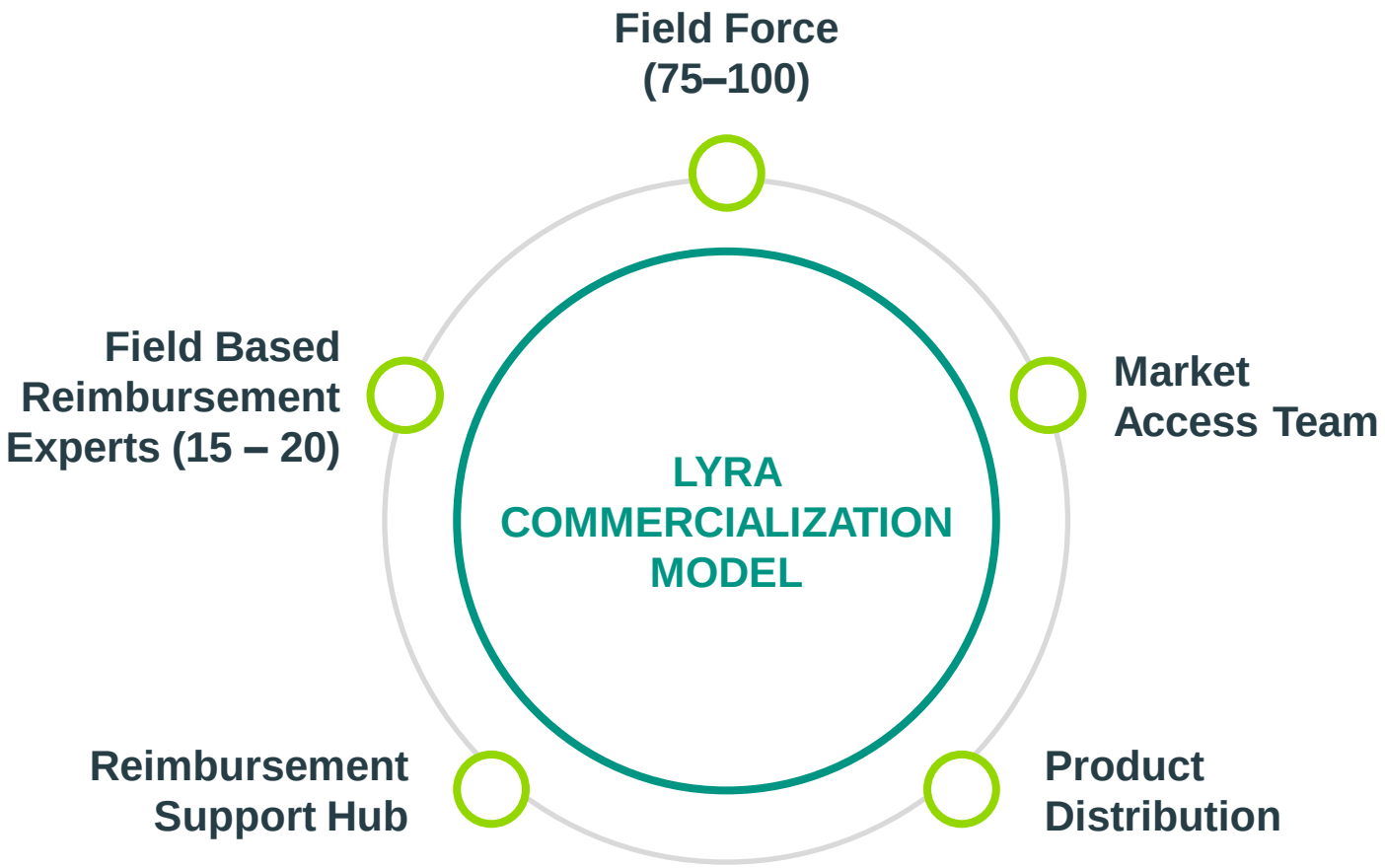
Reimburse via a J-Code

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”



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