LYRA THERAPEUTICS

Creating precisely tuned medicines so patients can breathe freely

LYR-210 & LYR-220 CLINICAL PROGRAMS

KEY OPINION LEADER EVENT

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.

Zachary Soler, MD, MSc

Associate Professor of Otolaryngology at Medical University of South Carolina (MUSC) and practicing Otolaryngologist at the MUSC Sinus Center

Randall A. Ow, MD, FACS, FARS, FAAOA, FAPCR

Otolaryngologist at Sacramento Ear, Nose & Throat and President and Chief Medical Officer of DaVinci Research

Dr. Robert Kern, MD

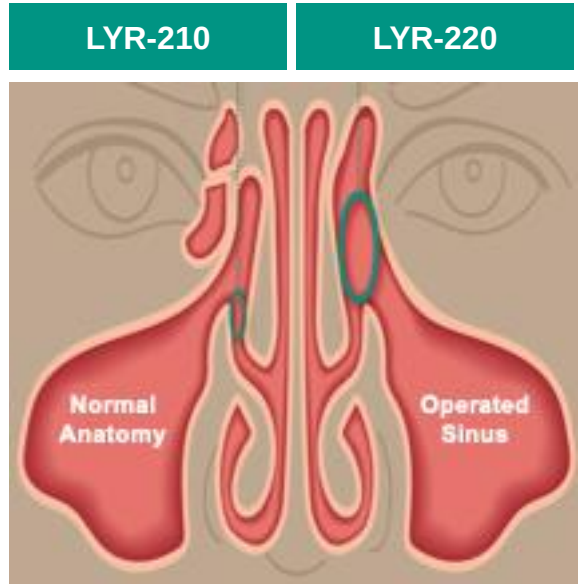
CMO of Lyra and the George A. Sisson Professor and Chair, Department of Otolaryngology – Head and Neck Surgery, Northwestern University Feinberg School of Medicine

WELCOME & AGENDA

Overview of Lyra's CRS Pipeline	**Maria Palasis, PhD, President & CEO**
LYR-210 LANTERN Ph2 6-mo follow-up data	**Zachary Soler, MD, MSc**
LYR-210 PK study	**Randall A. Ow, MD, FACS, FARS, FAAOA, FAPCR**
LYR-210 Ph3 ENLIGHTEN & LYR-220 Ph2 BEACON	**Robert Kern, MD, Chief Medical Officer**
Q&A	

LYR-210 & 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 Initiate ~YE'21
LYR-220 Long-acting Mometasone Furoate	Chronic Rhinosinusitis **Patients with Post-Surgical Anatomy**			**BEACON** Phase 2 Initiate ~YE'21

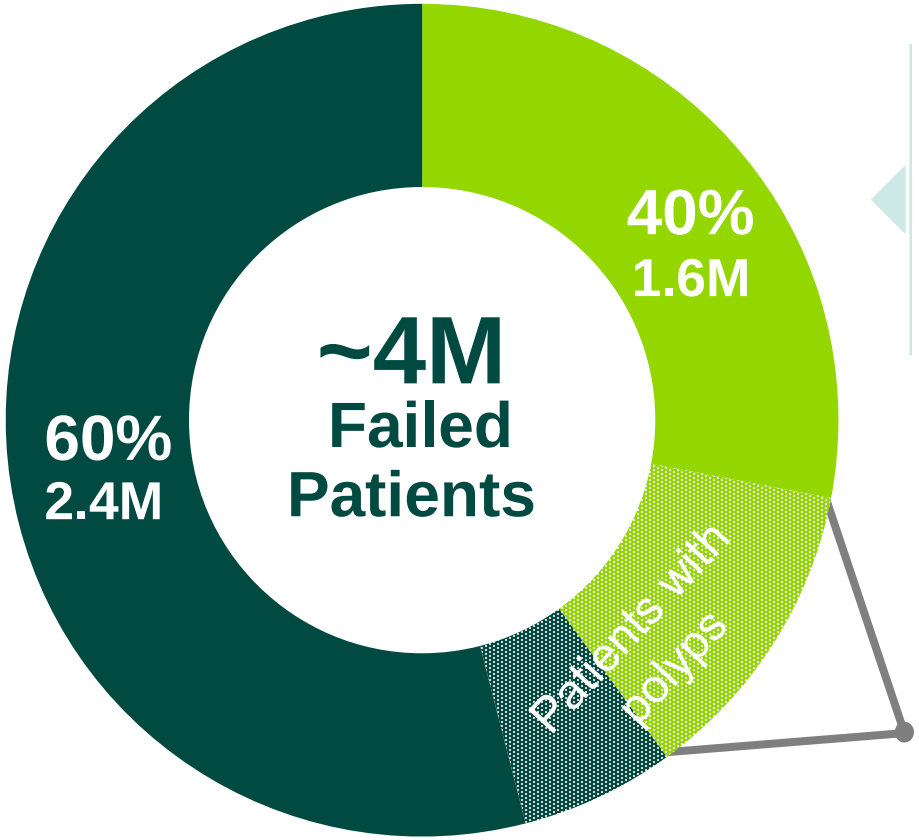


DEVELOPING SOLUTIONS FOR ALL CRS PATIENTS

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



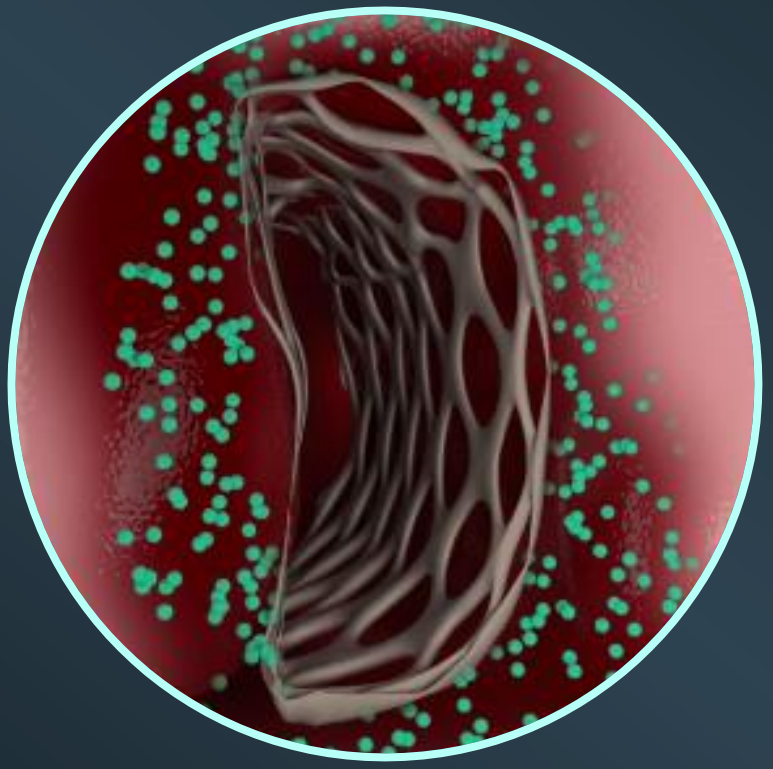
LYR-220

CRS Patients with Post-Surgical Anatomy

LYR-210/220: 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**
- **Agnostic to surgical status**
- **Requires no patient compliance**



LANTERN TRIAL 6-MONTH POST-TREATMENT OUTCOMES

Zachary Soler, MD, MSc

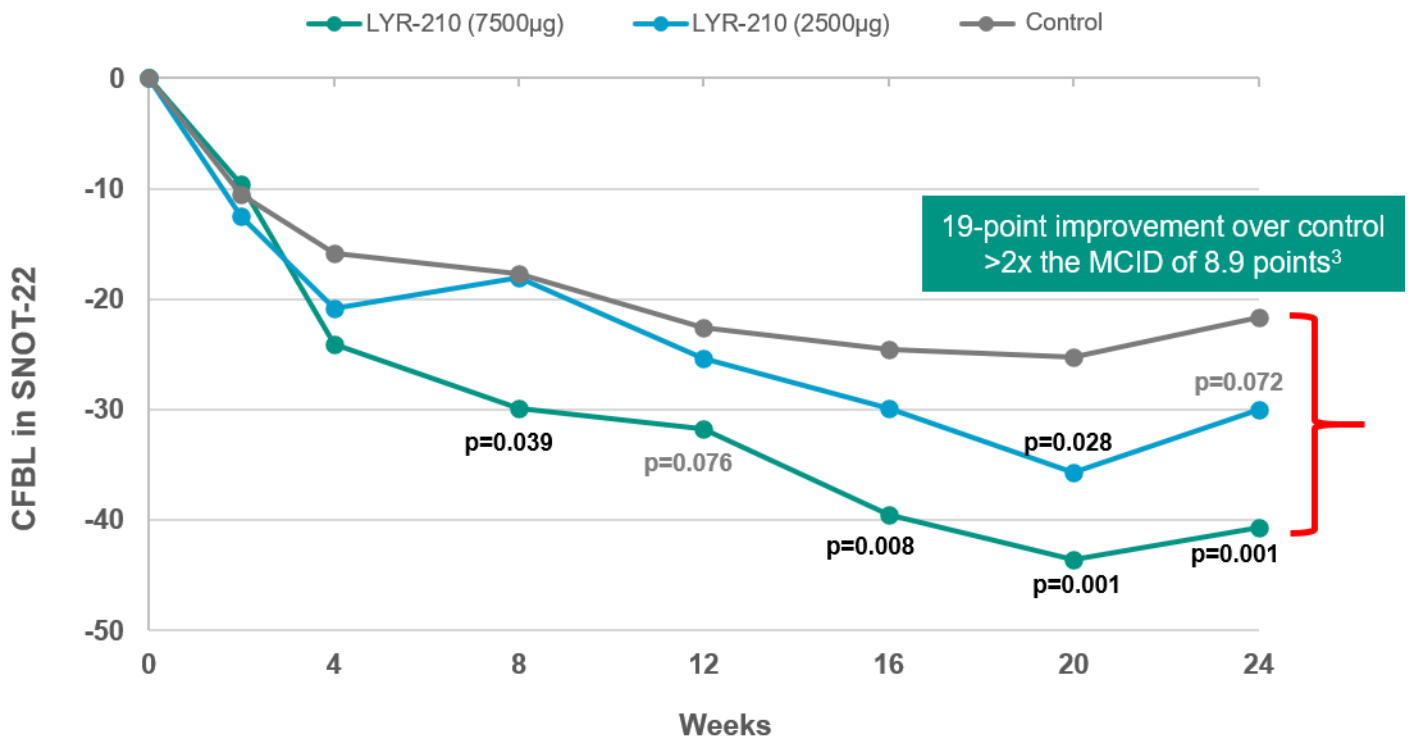
Associate Professor of Otolaryngology at Medical University of South Carolina (MUSC) and practicing Otolaryngologist at the MUSC Sinus Center

LYR-210

POSITIVE LANTERN PHASE 2 STUDY

- Rapid and clinically meaningful results based on clinical gold standard
- 40 point improvement ≥ than surgery or biologics
- >2X the MCID of 8.9 points relative to control

SYMPTOM IMPROVEMENT BY SNOT-22[1,2]



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

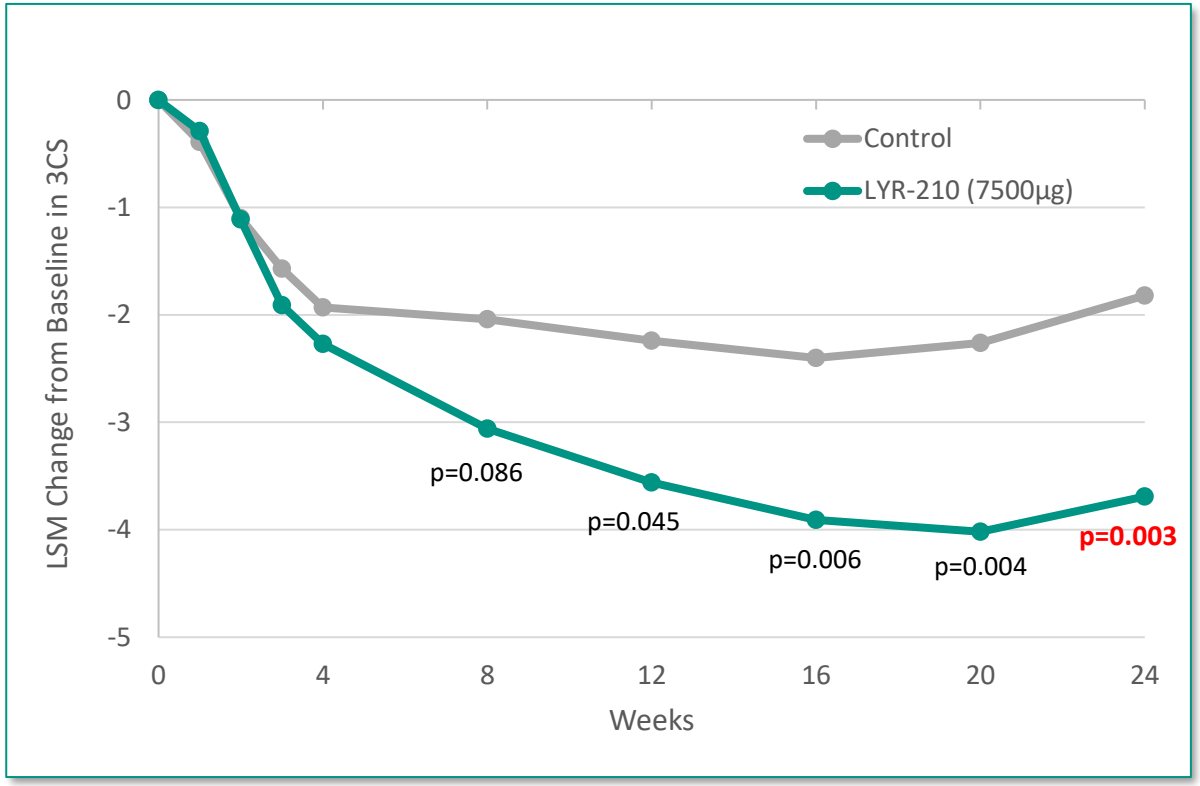
1) SinoNasal Outcome Test is a patient reported score from 0 – 110 based on symptoms; 2) Data represents the least square mean. Missing data and data post use of rescue medication was imputed by LOCF method; 3) Minimal clinically important difference

LYR-210

POSITIVE LANTERN PHASE 2 STUDY

- 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]

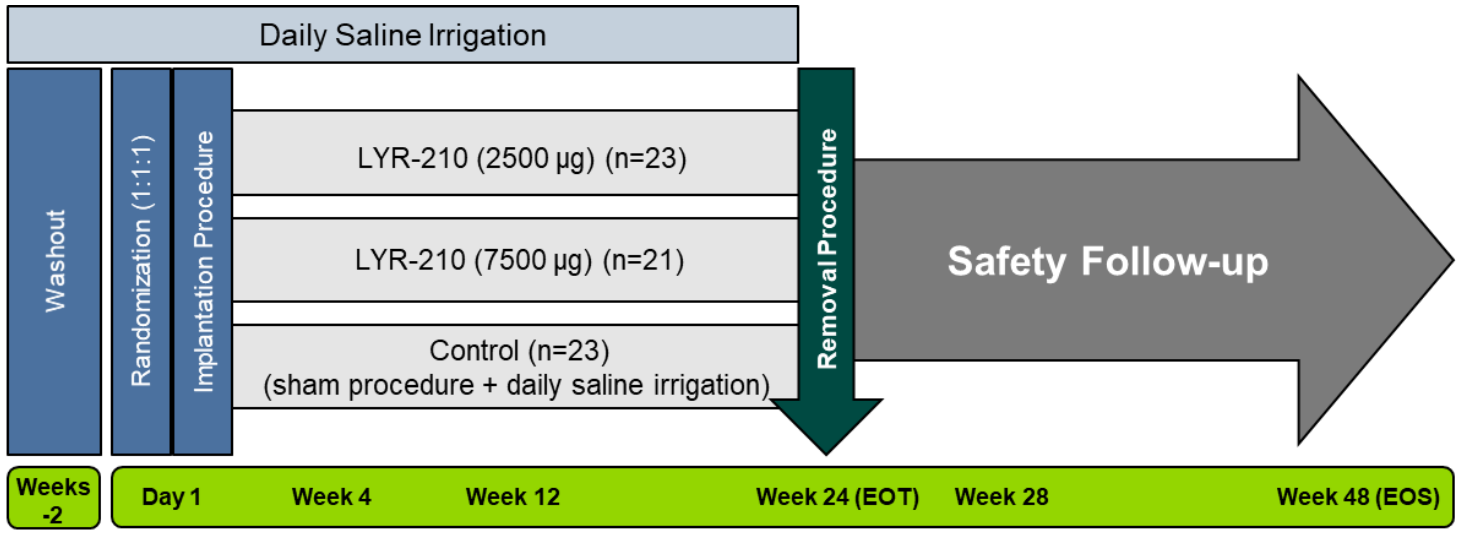


Statistically Significant Improvement vs Control at Weeks 12 - 24

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

LANTERN PHASE 2 STUDY DESIGN AND POST-TREATMENT EVALUATION

Multicenter, randomized, controlled, dose-ranging study



Study population: *Surgically naïve adults with moderate-to-severe CRS who failed previous medical management*

Post-Treatment Period: Weeks 24-48

Objective:

- Assess long-term safety post-removal

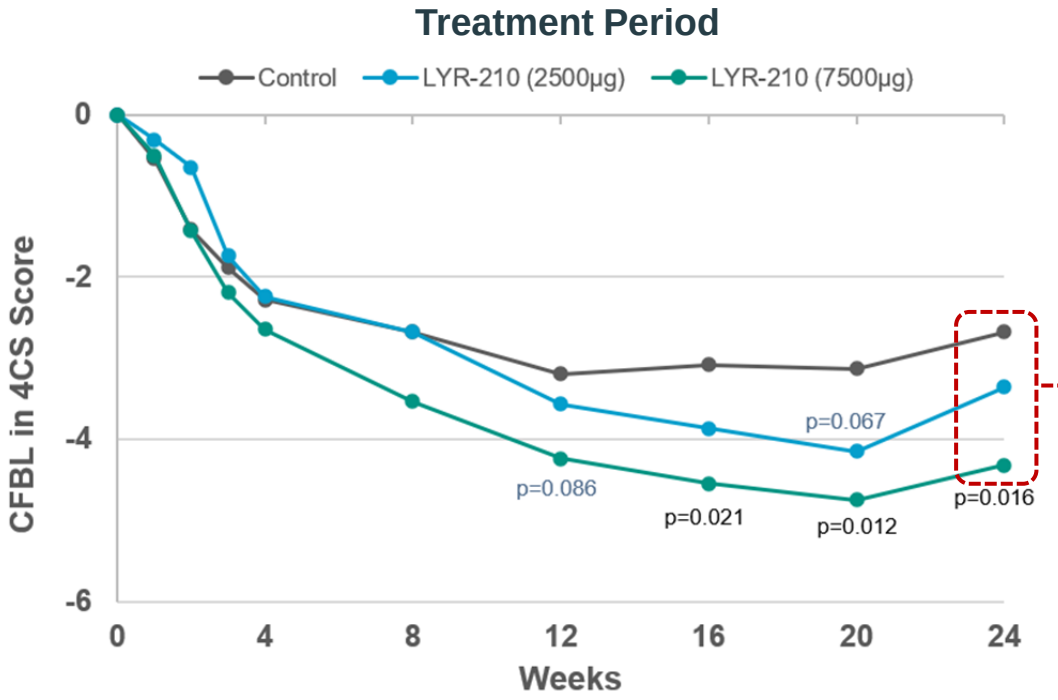
Clinical assessments included:

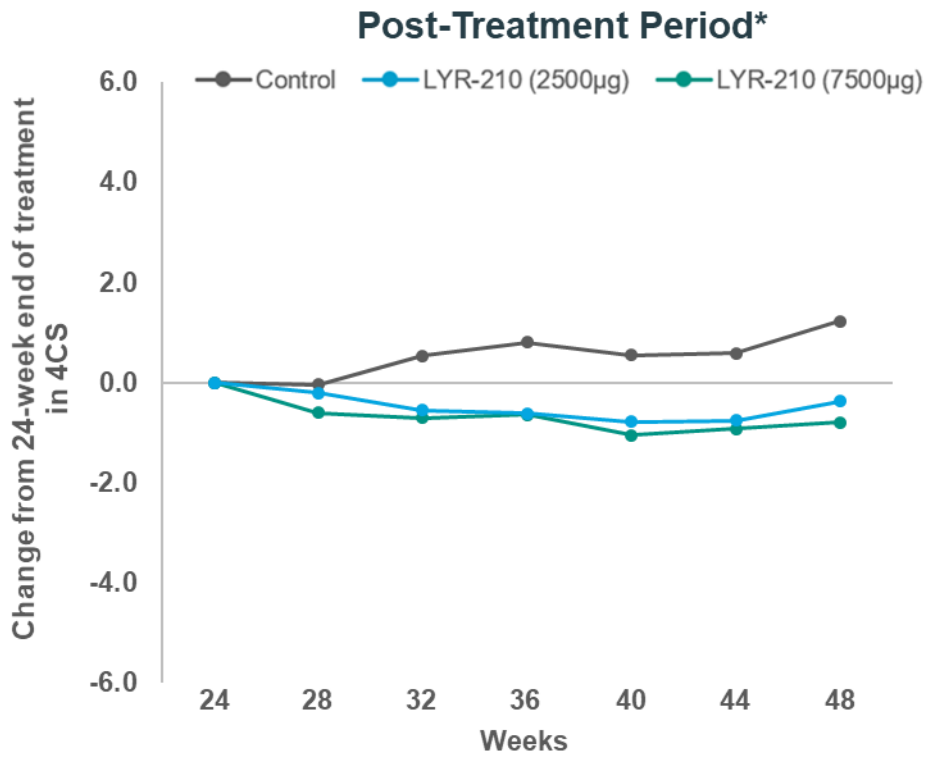
- Safety
- Rescue treatment use
- Cardinal symptom scores

EOT = End of Treatment. EOS = End of Study.

LASTING TREATMENT EFFECT POST-REMOVAL OF LYRA-210

4 Cardinal Symptom Composite Score (4cs)





Source: Cervin A, et al. [published online ahead of print, 2021 Sep 17]. Int Forum Allergy Rhinol. 2021;10.1002/alr.22883.

~73% mean compliance with daily nasal saline irrigation throughout the Post-Treatment Period

***Excluded from Post-Treatment Period Analysis:** Patients with missing data in the post-treatment period and patients who received rescue treatment prior to completing 80% of the post-treatment follow-up.

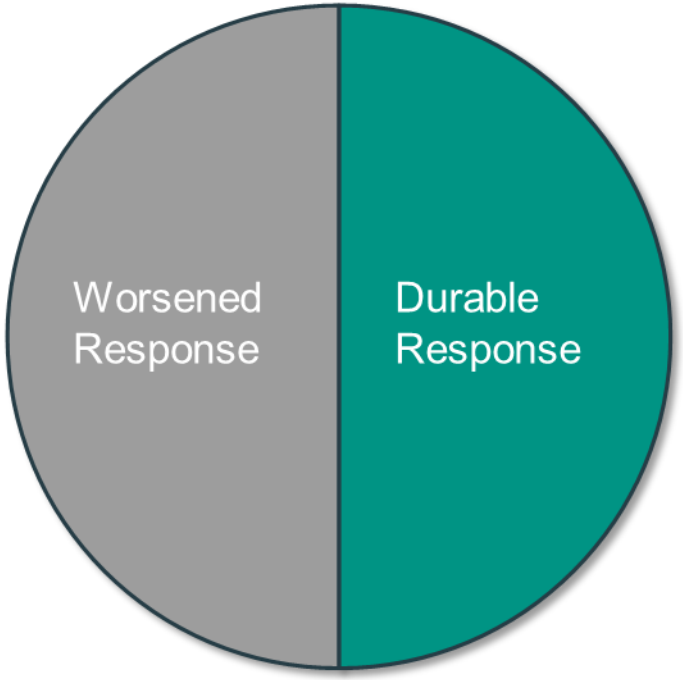
The analysis herein is not powered to detect statistically significant differences in outcomes. (Lyra Therapeutics, Inc., data on file)

CFBL = Change From Baseline. 4CS = Composite score of 4 cardinal CRS symptoms (nasal blockage, facial pain/pressure, nasal discharge, olfactory loss); (0-3 for each, 12-point scale).

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

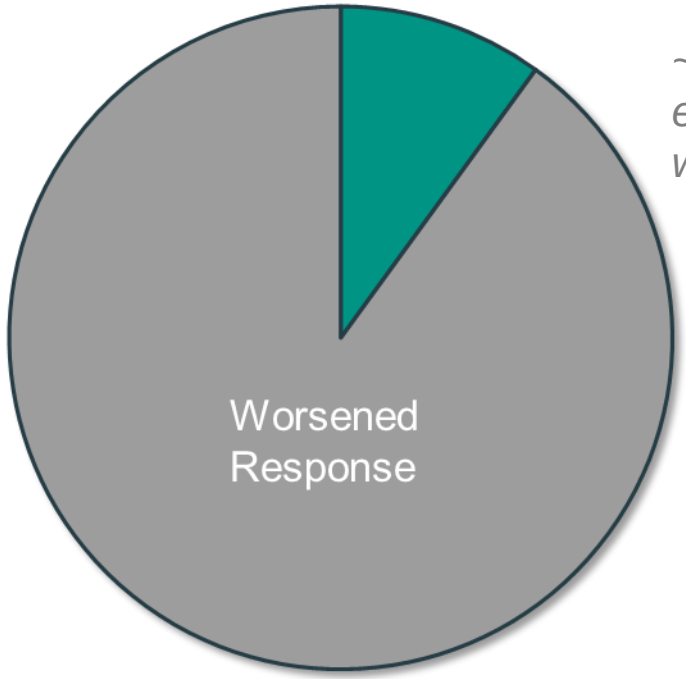
LANTERN Study: Long-term Outcomes (7500 µg)

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)

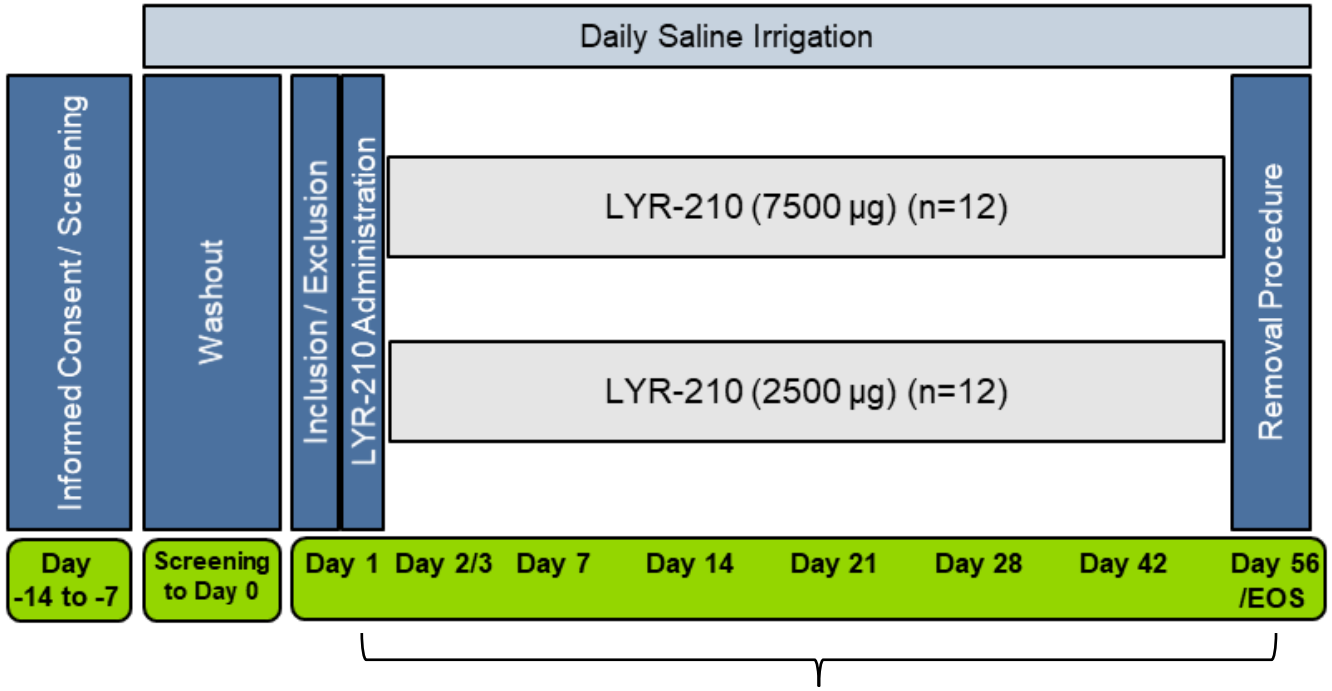
Randall A. Ow, MD, FACS, FARS, FAAOA, FAPCR

Otolaryngologist at Sacramento Ear, Nose & Throat and President and Chief Medical Officer of DaVinci Research

LYR-210 PK TRIAL DATA

PHARMACOKINETIC (PK) CLINICAL STUDY

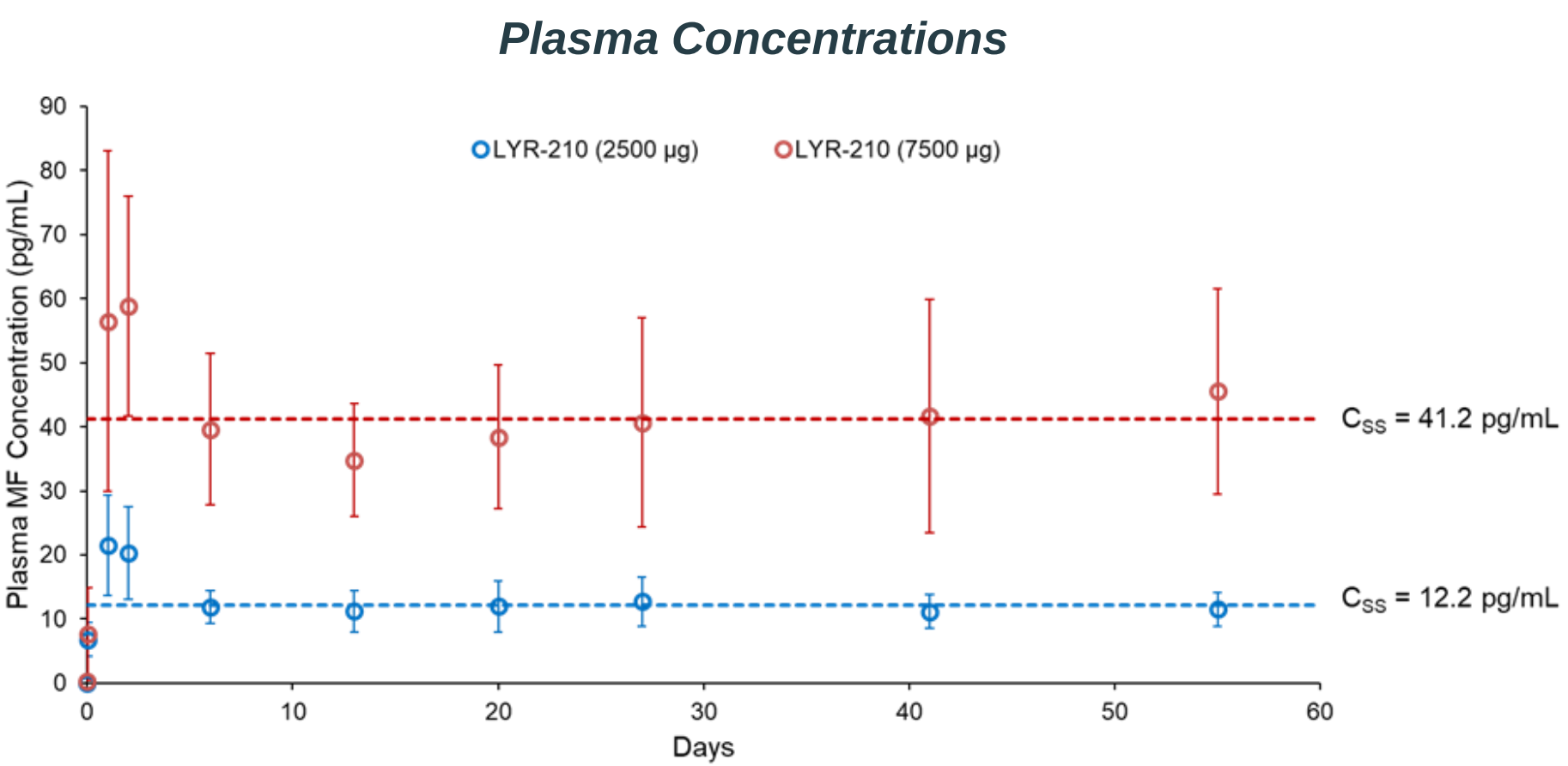
Study Objective: To characterize the PK profiles of LYR-210 (7500µg) and LYR-210 (2500µg) for up to 56 days.



- Open-label, multicenter study
- 24 enrolled subjects, 4 U.S sites
- Study Population: Adults with CRS who have not undergone sinus surgery
- 100% placement success

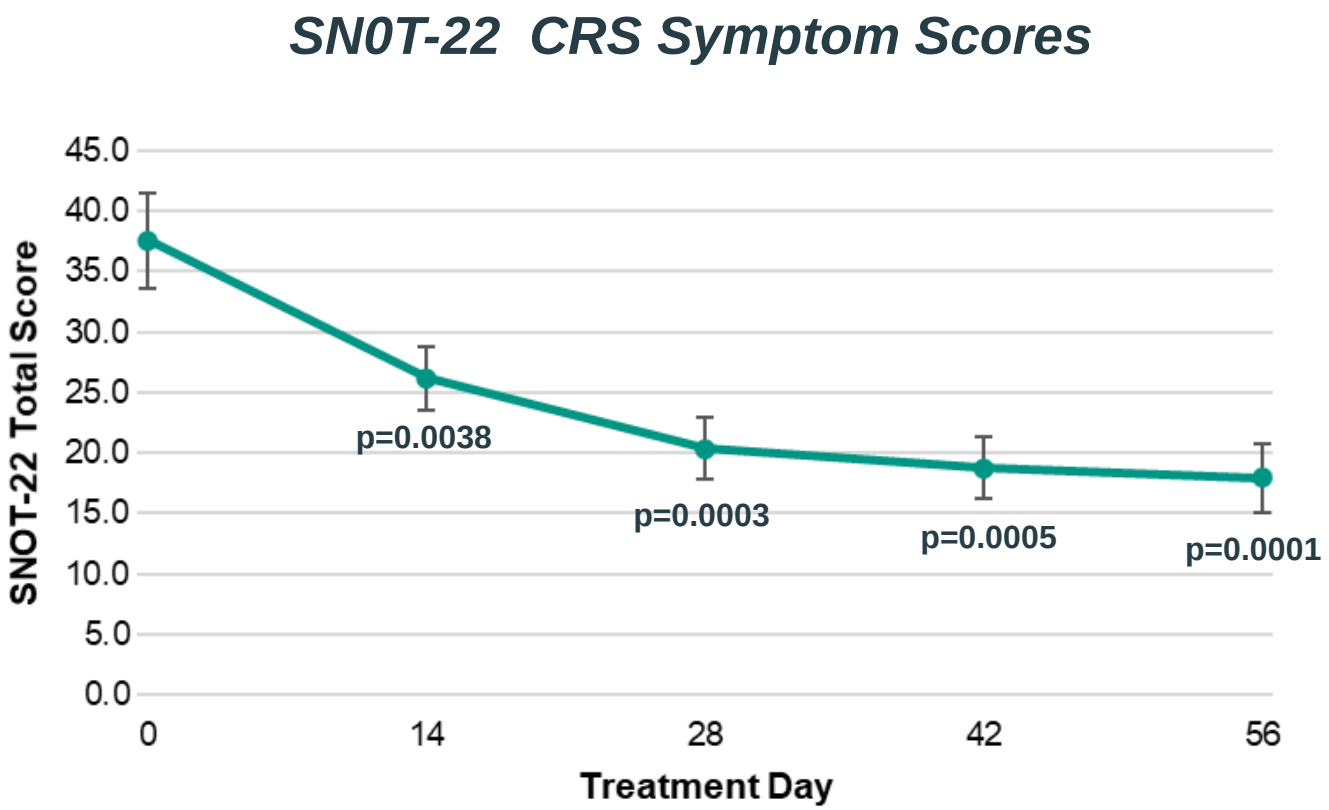
EOS = End of Study. MF = Mometasone Furoate.

LYR-210 DELIVERED A CONSTANT DAILY DOSE OF MF OVER 56 DAYS WITHOUT A DRUG BURST



Data are represented as mean and standard deviation. C_{ss} = Steady State Concentration. MF = Mometasone Furoate.

LYR-210 ACHIEVED CLINICALLY RELEVANT IMPROVEMENT IN SNOT-22 WITHIN 2 WEEKS



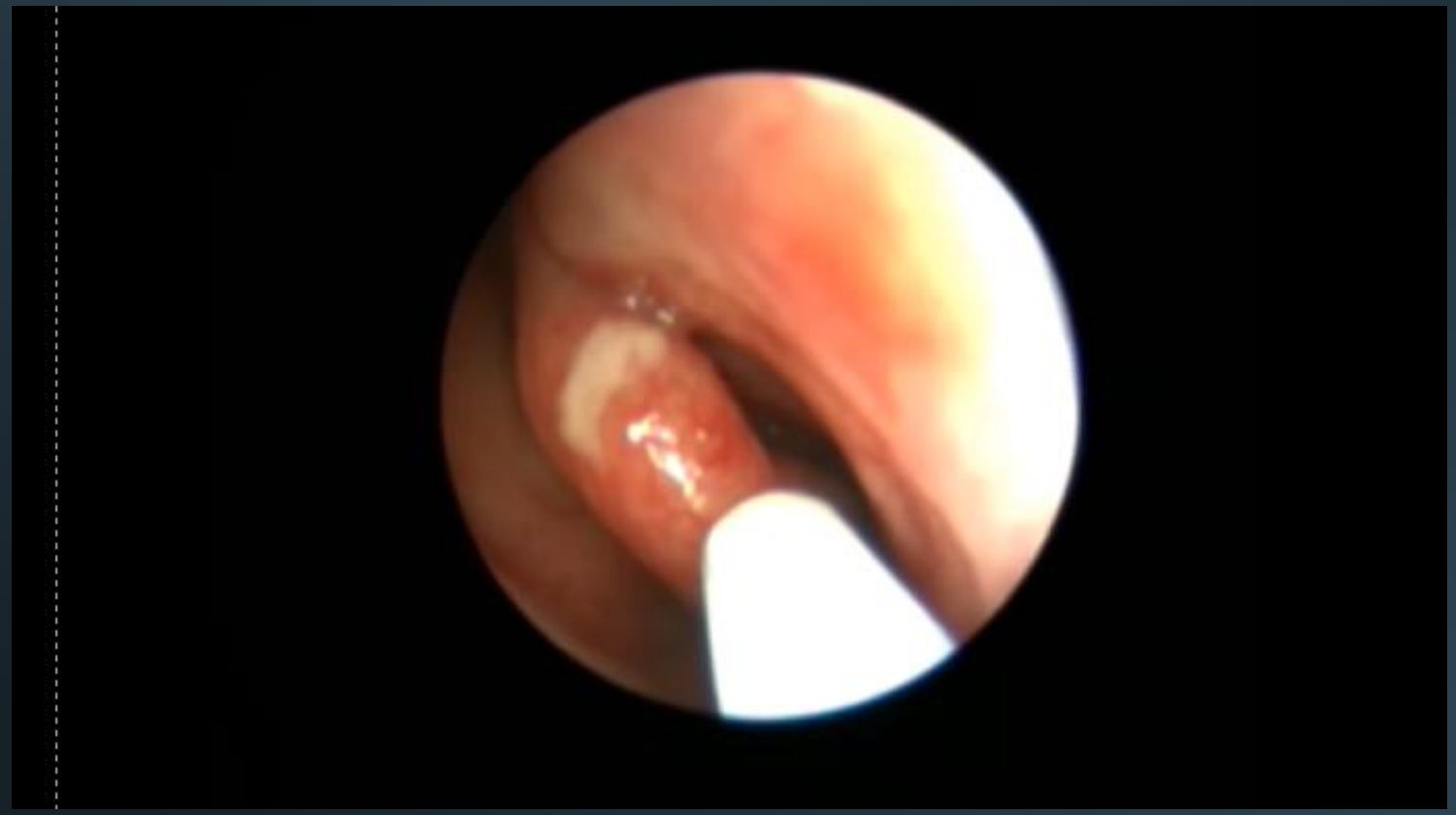
63% of patients improved beyond the threshold for surgery with a SNOT-22 score (< 20) on Day 56

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.

IN-OFFICE PLACEMENT OF LYR-210

- Simple, office-based placement and removal
- Dynamically conforms to the patient's nasal anatomy
- Well-tolerated by patients



LYR-210 PHASE 3 ENLIGHTEN PROGRAM

Dr. Robert Kern, MD

CMO of Lyra and the George A. Sisson Professor and Chair, Department of Otolaryngology – Head and Neck Surgery, Northwestern University Feinberg School of Medicine

PHASE 3 PROGRAM ON TRACK TO START YE'21

LYR-210 Phase 3 ENLIGHTEN 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

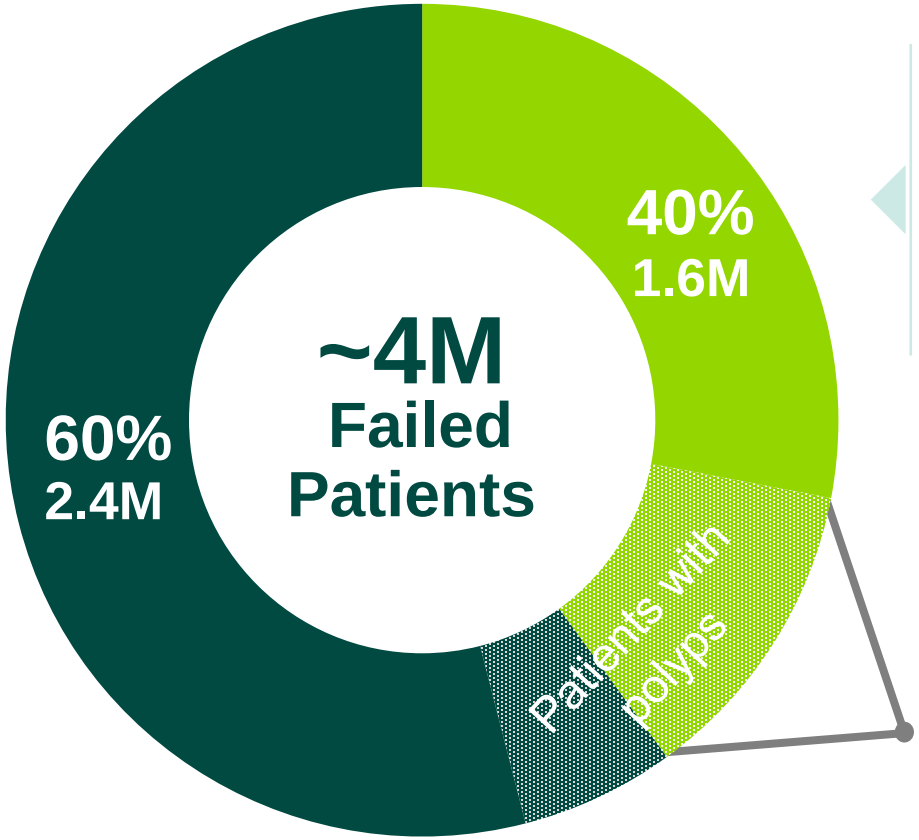
First Phase 3 trial to begin around YE'21

LYR-220

LYRA THERAPEUTICS

LYR-220 TARGETS 1.6M CRS PATIENTS WITH POST-SURGICAL ANATOMY

- Designed for post-surgical patients' ongoing medical management
- Scaled-up matrix for larger cavity of post-surgical anatomy
- Same drug dosing profile, kinetics and materials as LYR-210
- Regulatory path will leverage LYR-210 data



LYR-220

CRS Patients with Post-Surgical Anatomy

PH 2 BEACON STUDY ON TRACK TO START NEXT MONTH

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

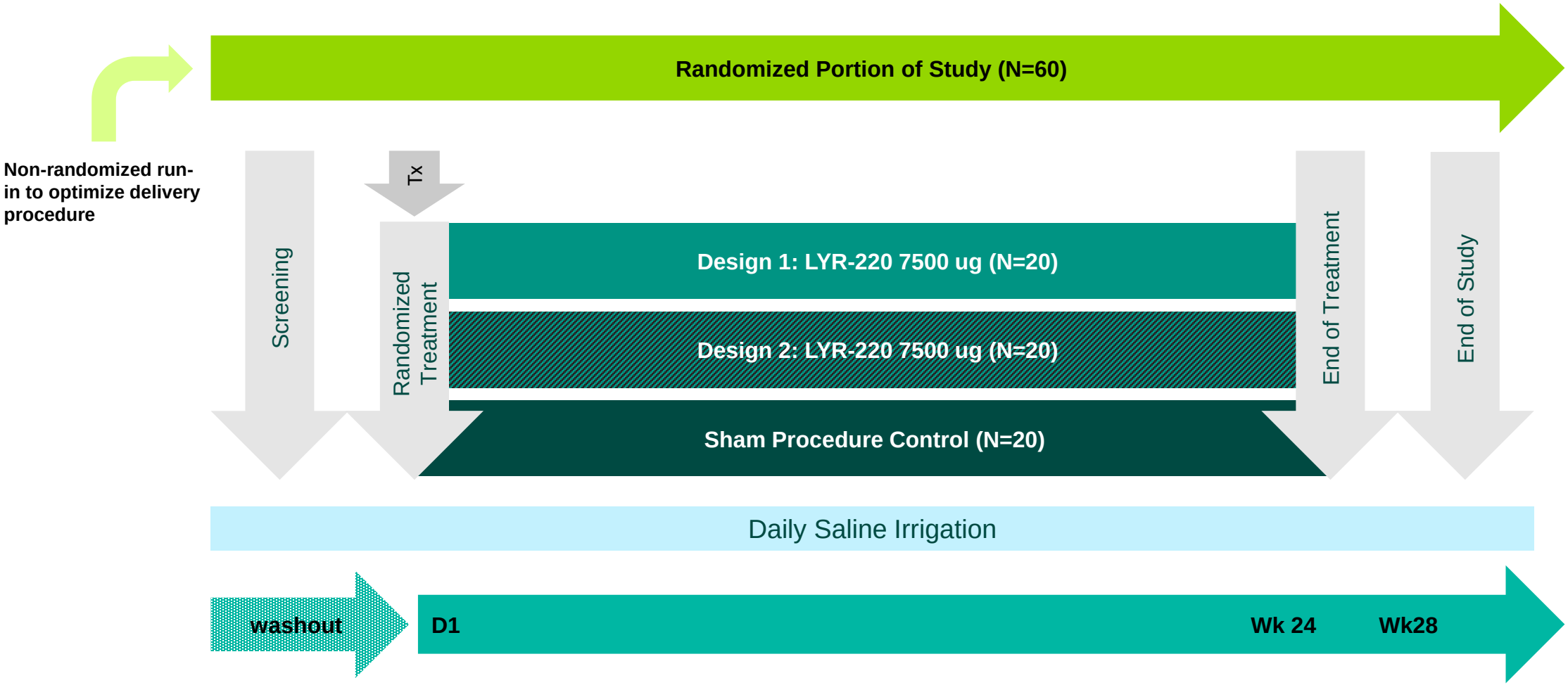
1:1:1 randomization: Design 1 7500µg, Design 2 7500µg, Control

~65 subjects in US & Australia

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

Trial to begin around Nov'21

BEACON PHASE 2 STUDY WILL EVALUATE 2 7500UG DESIGNS



Source:

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KOL Q&A


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