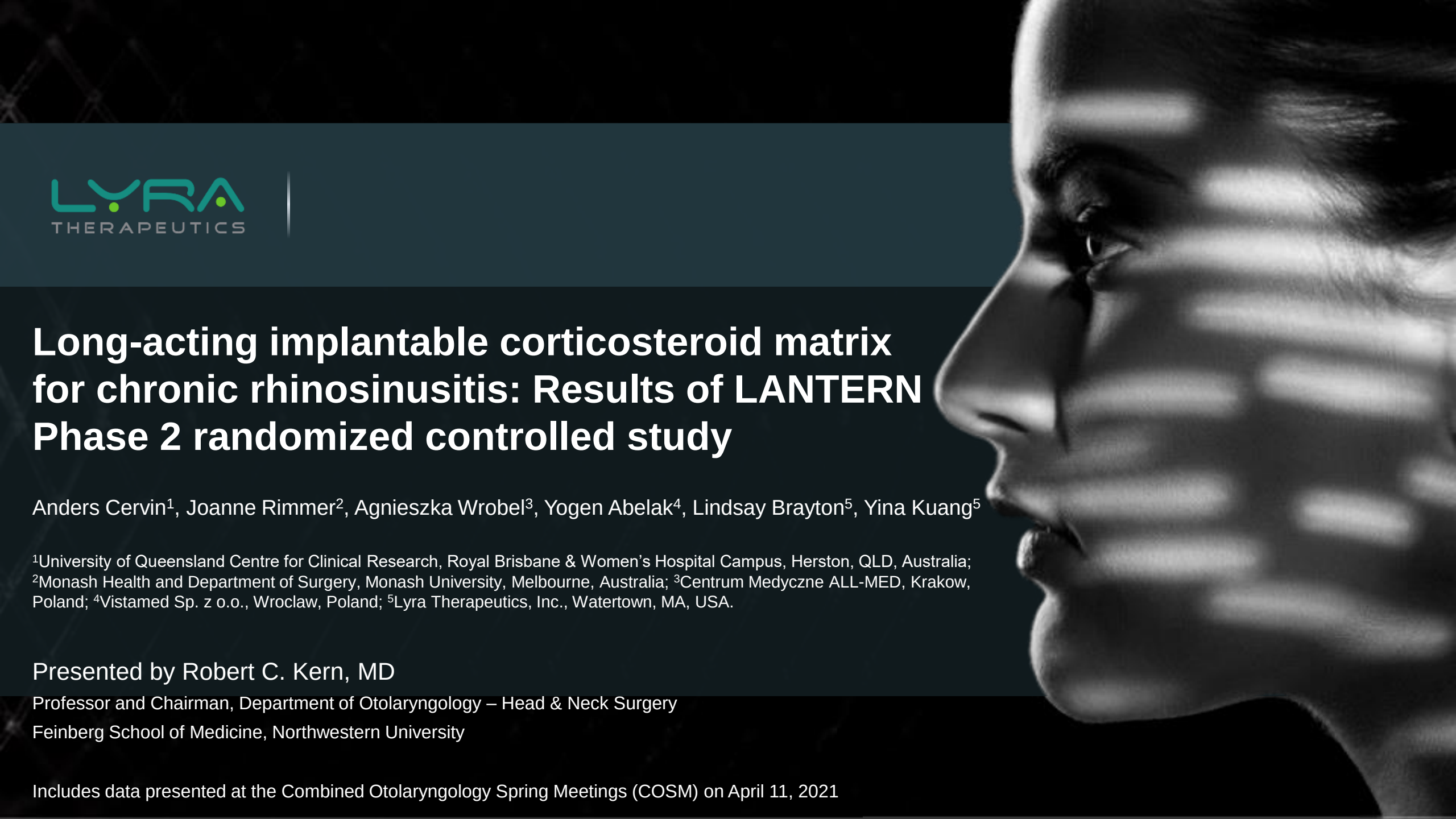

# Long-acting implantable corticosteroid matrix for chronic rhinosinusitis: Results of LANTERN Phase 2 randomized controlled study

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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.

# CHRONIC RHINOSINUSITIS (CRS)

## Topical steroids used to treat CRS are suboptimal[1,2]

- Limited ability to reach inflammation deep within the sinonasal passages
- Rapid clearance rates
- Poor patient compliance

## 40-60% of CRS patients fail medical management and become candidates for functional endoscopic sinus surgery[3]

- ~4 million CRS patients fail medical management annually in the U.S.[4]
- ~400,000 CRS patients undergo FESS annually in the U.S.[3]

## Novel therapeutic modalities are needed for CRS patients that fail medical management

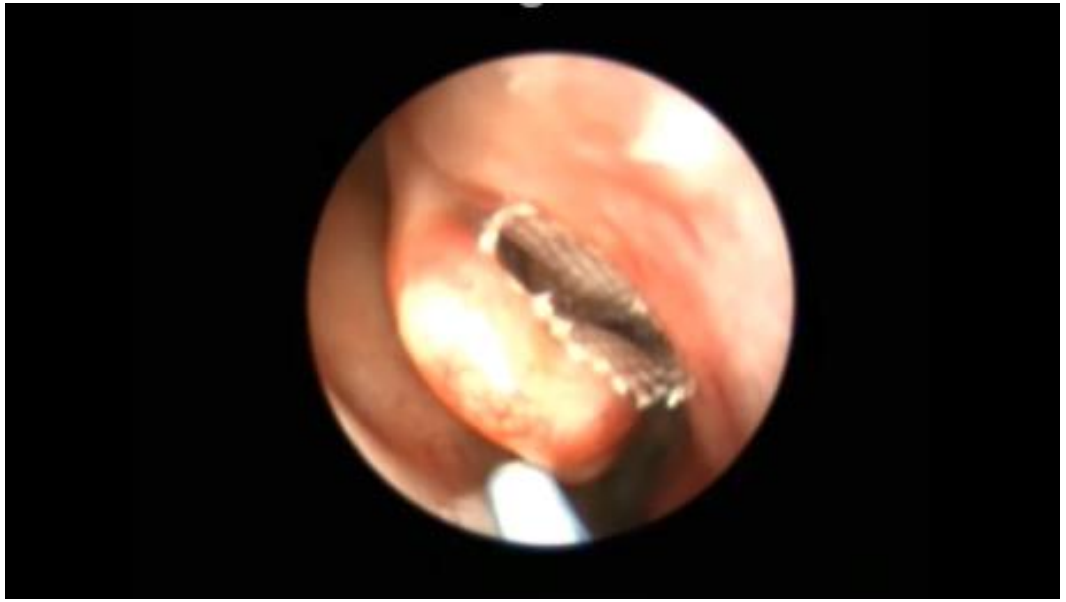
[1]Moeller W et al. *Rhinology*. Dec 2009;47(4):405-12. [2]Nabi S et al. *J Otolaryngol Head Neck Surg*. Apr 2012;41 Suppl 1:S49-55. [3]Young LC et al. *Allergy Rhinol (Providence)*. 2012;3(1):e8-e12.
[4]Baguley et al. Int Forum Allergy Rhinol, 2014;4(7):525-32

## LYR-210

# FOR CHRONIC RHINOSINUSITIS

- Being developed to provide sustained release of mometasone furoate deep in the middle meatus
- Adaptable mesh design conforms and adapts to patient's anatomy
- Designed to be administered in an otolaryngologist's office
- Designed to eliminate patient compliance issues

***LYR-210 is designed to provide 24 weeks of continuous anti-inflammatory therapy directly to the inflamed mucosa***

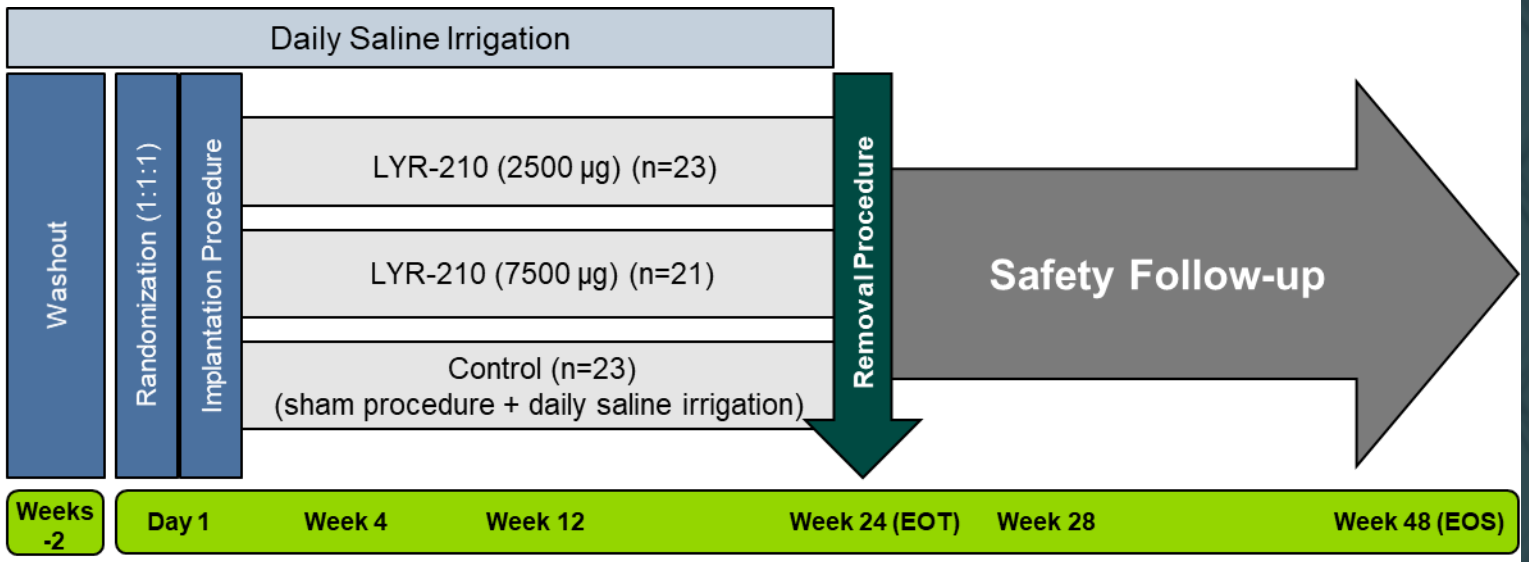


***In-office Placement of LYR-210***

# LANTERN PHASE 2 STUDY DESIGN

## Multicenter, randomized, blinded, controlled, dose-ranging trial

***LYR-210 was evaluated in adult subjects with CRS that failed previous medical management and have not undergone FESS***




***Due to COVID-19, study enrollment was curtailed to 67 total patients***

**Moderate-to-severe CRS**

- **Baseline SNOT-22: ~68**

**Approximately half had nasal polyps**

**Primary Endpoint:** Change in 4 cardinal symptoms composite score

**Secondary Endpoints include:**

- SNOT-22
- Symptom improvement over 24 weeks
- Reduction in inflammation (MRI)
- Time to first rescue treatment
- Adverse events

EOT = End of Treatment; EOS = End of Study

LYR-210

# LANTERN PHASE 2 STUDY

**Well-tolerated throughout the 24-week treatment period at both 2500µg and 7500µg doses**

## WELL-TOLERATED SAFETY PROFILE AT BOTH DOSES

**No treatment-related SAEs**

**Treatment-related AEs in more than 1 subject:**

- Epistaxis: 3 subjects in LYR-210 (2500µg) group
- Rhinitis: 3 subjects in LYR-210 (7500µg) group
- Rhinorrhea: 2 subjects in LYR-210 (2500µg) group
- Headache: 2 subjects in Control group

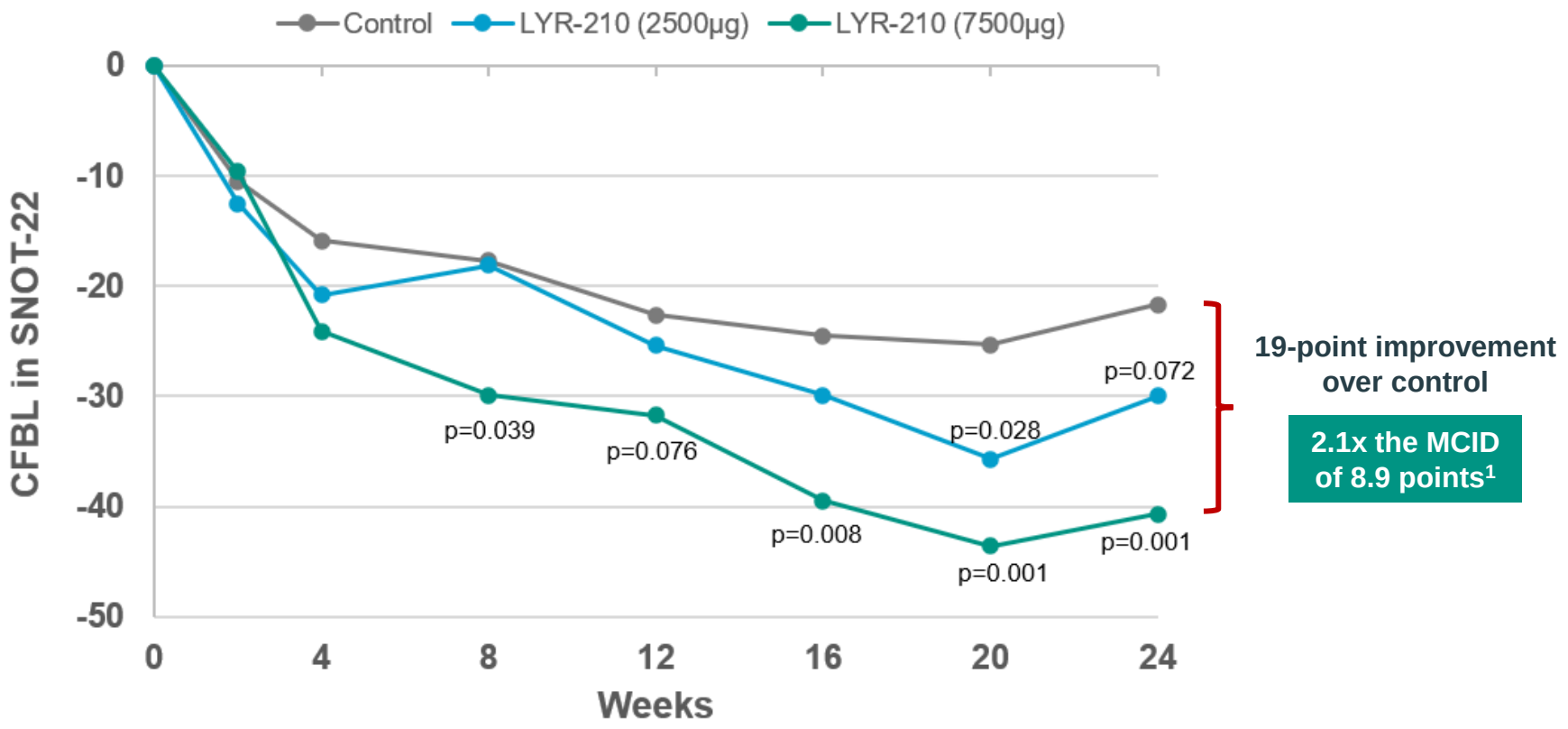
**All treatment-related AEs were mild or moderate apart from 1 event in LYR-210 (2500µg) group:**

- Increased viscosity of upper respiratory secretion

**Treatment-related AEs in Control and LYR-210 (7500µg) groups occurred at comparable rates**

# 22-ITEM SINO-NASAL OUTCOME TEST (SNOT-22)

***LYR-210 achieved rapid, durable and clinically meaningful improvement in SNOT-22 score over 24 weeks***



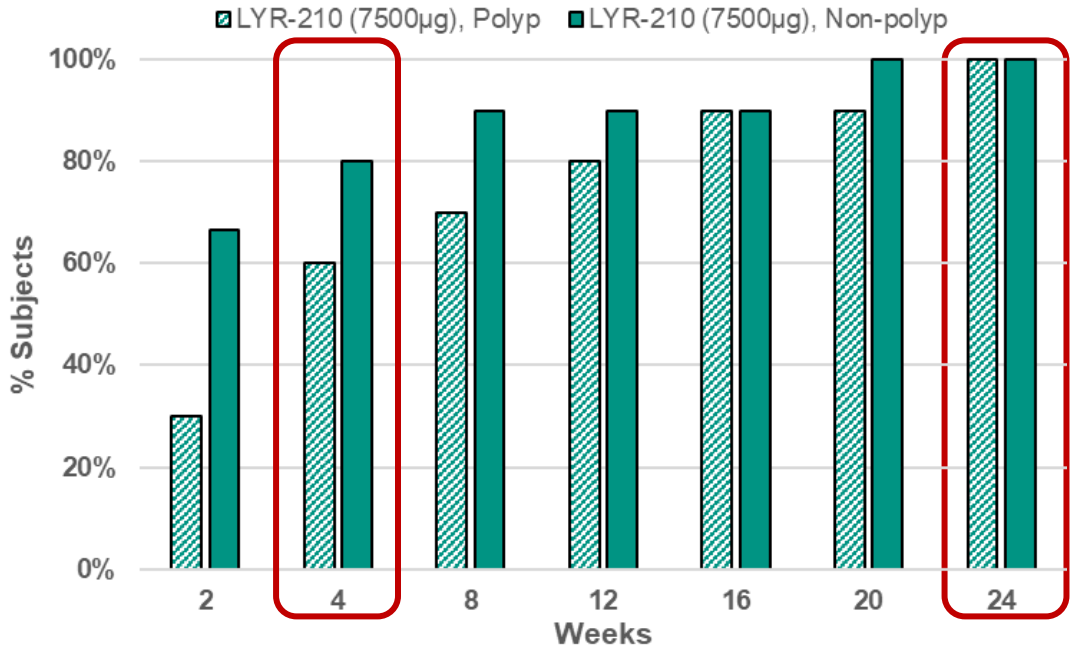

Mean change from baseline (CFBL) in SNOT-22 total score. Data represents LSM. P<0.05 is considered statistically significant to control.
MCID = Minimal Clinically Important Difference. [1]Hopkins et al., Clinical Otolaryngology 2009, 34, 447–454.

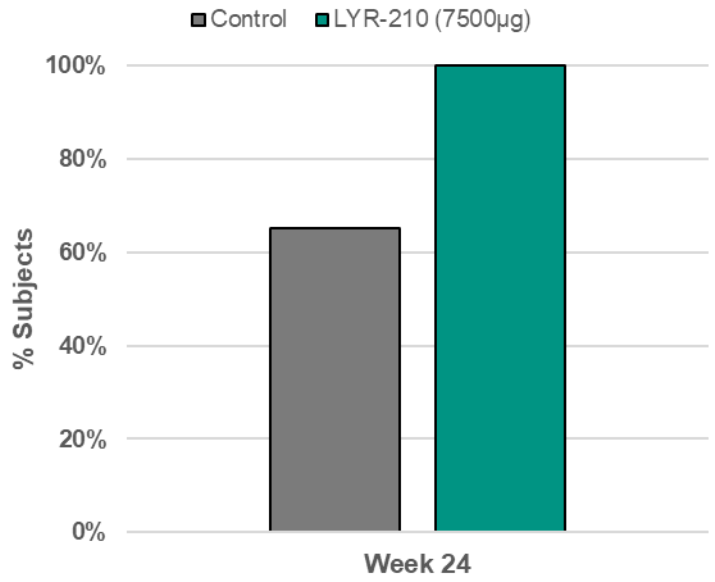
# SNOT-22 RESPONDER ANALYSIS

## % Subjects Achieved MCID in SNOT-22[1]

***100% of polyp and non-polyp CRS subjects administered LYR-210 (7500µg) achieved MCID by Week 24***

***Rapid onset and durable therapeutic response***



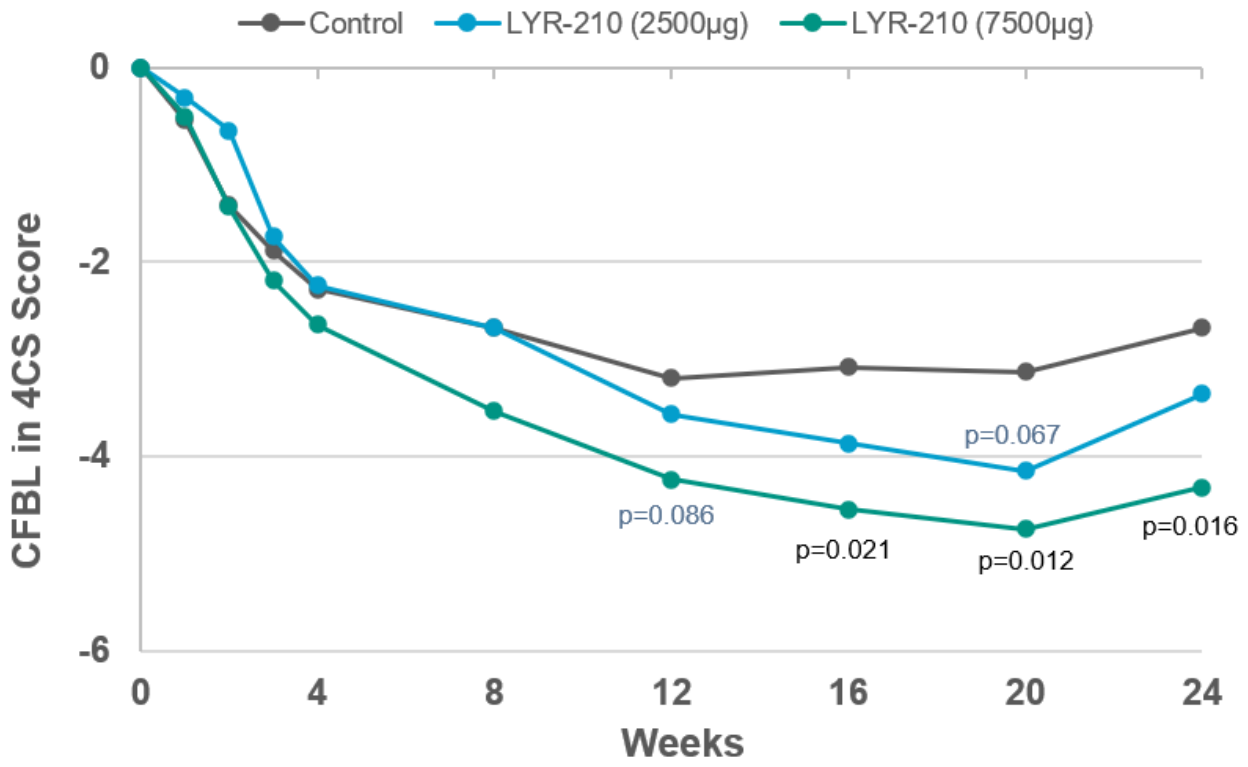

[1]*Data represents % of subjects that reported at least an 8.9-point decrease in the SNOT-22 total score as defined in Hopkins et al., Clinical Otolaryngology 2009, 34, 447–454.*

MCID = Minimal Clinically Important Difference. Left: Polyp vs. Non-polyp subjects administered LYR-210 (7500µg). Right: Total patients administered LYR-210 (7500µg) or nasal saline irrigation control at week 24.

# COMPOSITE OF 4 CARDINAL SYMPTOMS (4CS)

## Nasal Blockage, Facial Pain/Pressure, Nasal Discharge, and Loss of Smell

***LYR-210 (7500µg) achieved statistically significant improvement in the 4CS at 24 weeks and earlier compared to control***

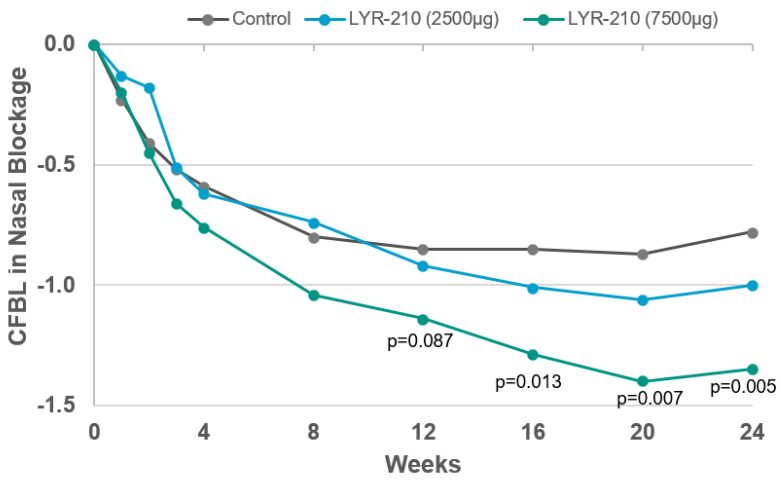



Mean change from baseline (CFBL) in the 7-day average score in the 4CS composite score (nasal blockage, facial pain/pressure, nasal discharge (anterior/posterior), and loss of smell). 4CS scale: 0-12. Data represents LSM. P<0.05 is considered statistically significant to control.

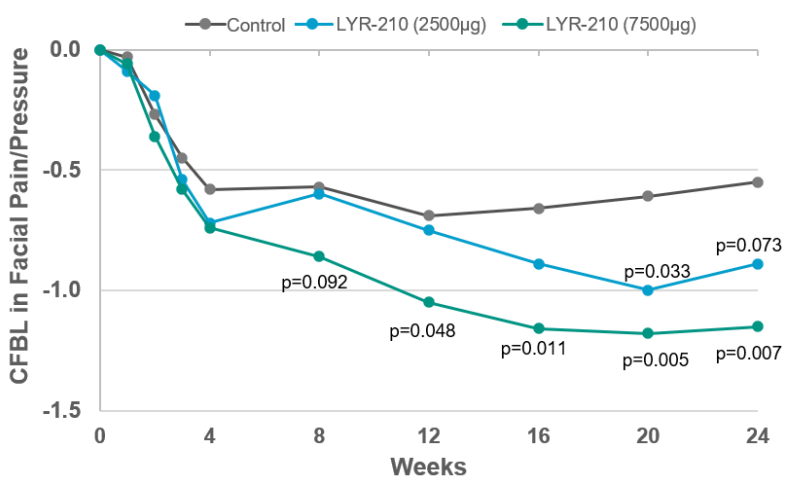
# CARDINAL SYMPTOMS OF CRS

## *LYR-210 achieved dose-dependent improvement in the cardinal symptoms of CRS*

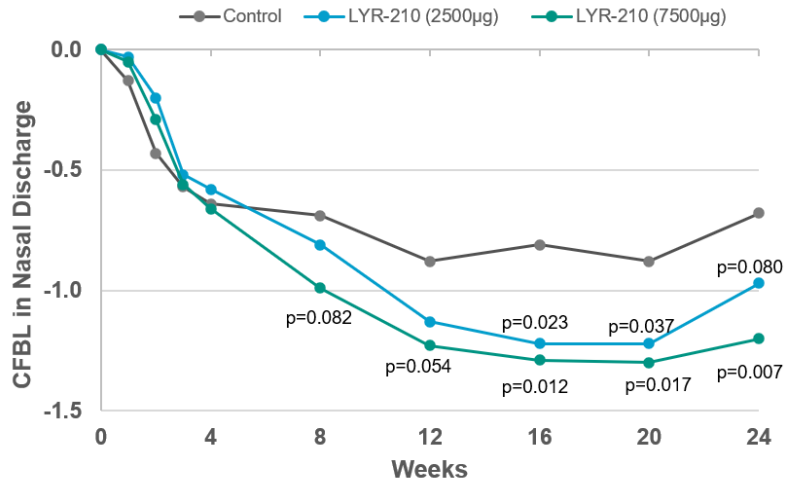
### Nasal Blockage




### Facial Pain/Pressure



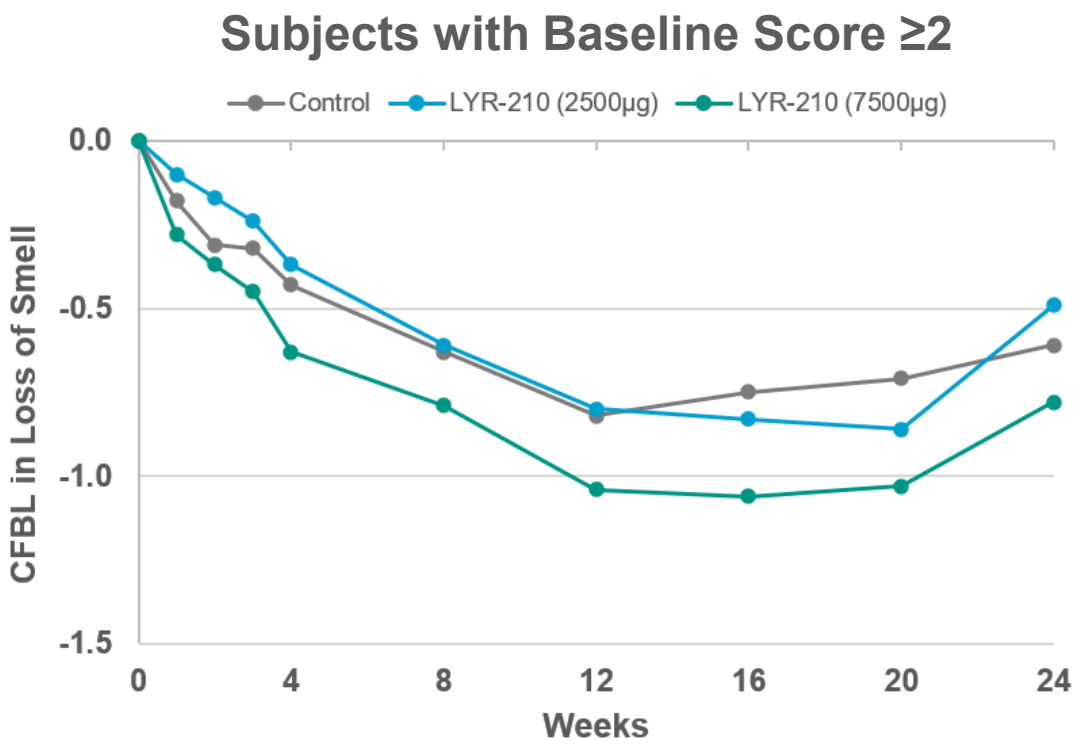

### Nasal Discharge




Mean change from baseline (CFBL) in the 7-day average score in nasal blockage, facial pain/pressure, or nasal discharge (anterior/posterior) for all patients. Data represents LSM.
P<0.05 is considered statistically significant to control.

# CARDINAL SYMPTOMS OF CRS

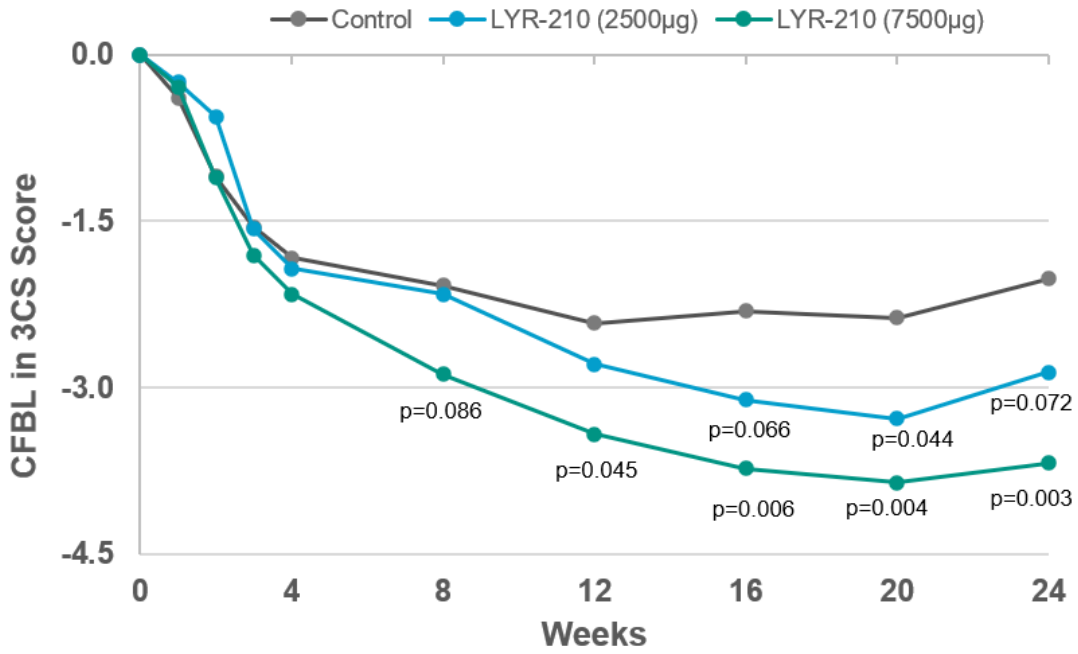
***LYR-210 (7500µg) was associated with a trend towards improvement in smell in patients with moderate-to-severe anosmia***




Mean change from baseline (CFBL) in the 7-day average score in loss of smell for patients with moderate-to-severe baseline anosmia (≥ 2 baseline score in loss of smell): LYR-210 (7500µg) (n=15 patients), LYR-210 (2500µg) (n=20 patients), control (n=20 patients). Data represents LSM. P<0.05 is considered statistically significant to control.

## Composite of 3 Cardinal Symptoms (3CS)

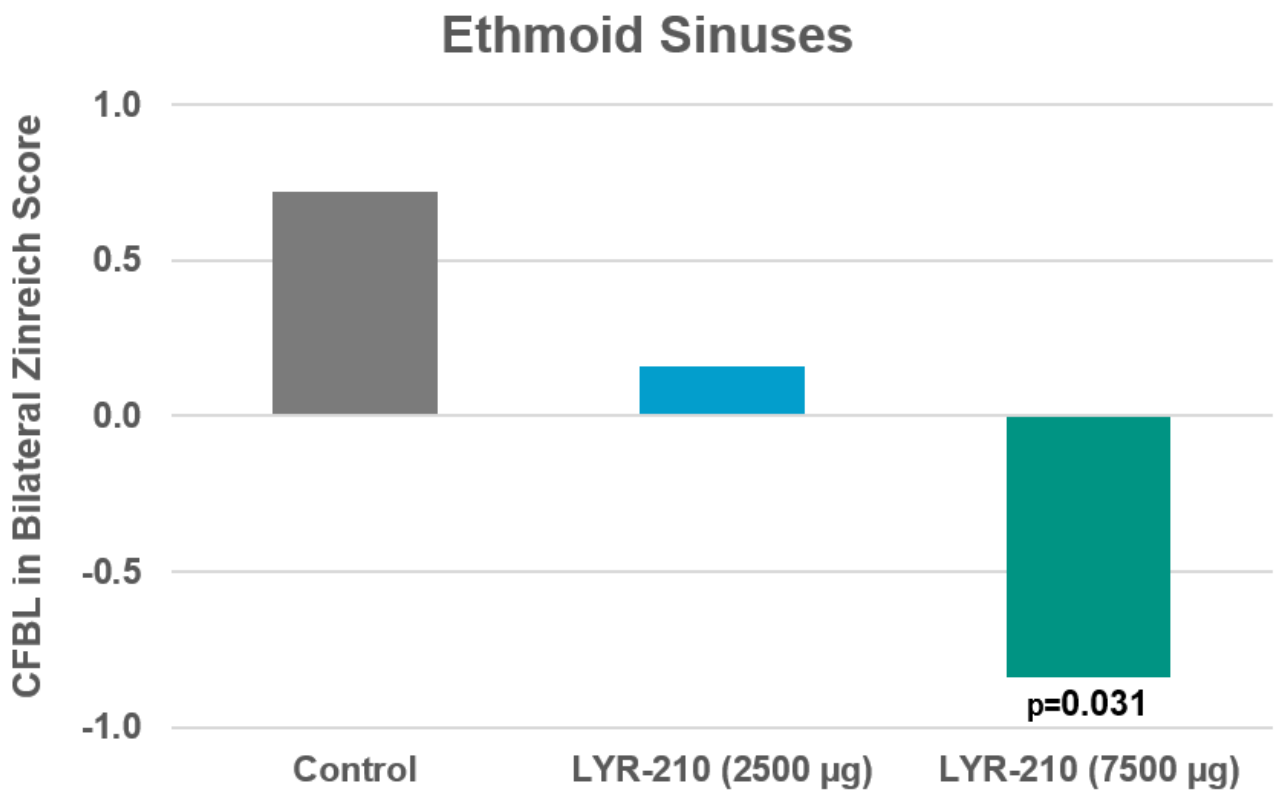
***Nasal Blockage, Facial Pain/Pressure, Nasal Discharge***




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)). Data represents LSM. P<0.05 is considered statistically significant to control.

# ETHMOID OPACIFICATION

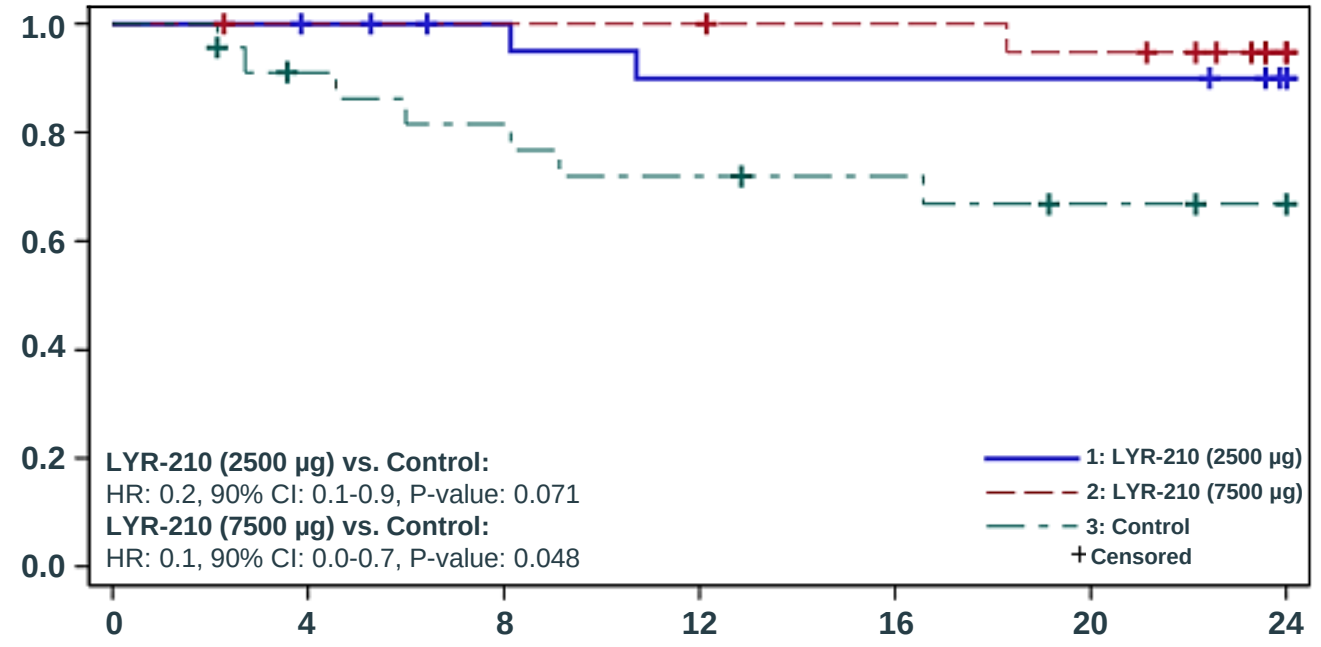
***LYR-210 improved bilateral ethmoid Zinreich (modified Lund-Mackay) scores at Week 24***




Mean change from baseline (CFBL) in the bilateral ethmoid Zinreich score (composite score of anterior ethmoid and posterior ethmoid Zinreich scores) at 24 weeks. Data represents mean. 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.

# CONCLUSIONS

- **LYR-210 achieved a rapid and durable dose-dependent improvement in the cardinal symptoms of CRS and SNOT-22 throughout 24 weeks in subjects independent of polyp status from a single administration**
- **LYR-210 decreased ethmoid opacification and need for rescue treatment**
- **LYR-210 provided up to 24 weeks of continuous local steroid treatment, eliminating issues of patient compliance in the clinical trial**
- **LYR-210 has the potential to represent a major step forward in the care for CRS patients who are facing surgery as their next treatment option**
- **Lyra Therapeutics, Inc. is advancing LYR-210 into a pivotal Phase 3 study**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