Lyra Therapeutics Reports Positive Results from the ENLIGHTEN 2 Phase 3 Trial of LYR-210 Achieving Statistically Significant Results for Primary and Key Secondary Endpoints in the Treatment of Chronic Rhinosinusitis (CRS)

June 2, 2025

- *ENLIGHTEN 2 trial met primary endpoint with LYR-210 demonstrating statistically significant improvement in the composite of the three cardinal symptoms (3CS) of CRS at 24 weeks (p=0.0078)*
- *ENLIGHTEN 2 trial also showed statistically significant improvement in key secondary endpoints in the full population of 3CS at 24 weeks (p=0.0209) and SNOT-22 score at 24 weeks (p=0.0101)*
- *Additionally, in pooled data from ENLIGHTEN 2 and ENLIGHTEN 1 trials in 64 CRS patients with nasal polyps, LYR-210 demonstrated a consistent positive trend over 24 weeks in multiple key efficacy endpoints*
- *Lyra plans to review the totality of the dataset from the ENLIGHTEN trials to evaluate next steps for pursuing an indication in non-polyp patients, as well as to continue development of LYR-210 in patients with nasal polyps*
- *Conference call to discuss trial results today at 8:30 a.m. ET*

WATERTOWN, Mass., June 02, 2025 (GLOBE NEWSWIRE) -- Lyra Therapeutics, Inc. (Nasdaq: LYRA) ("Lyra" or the "Company"), a clinical-stage biotechnology company developing long-acting, anti-inflammatory sinonasal implants for the treatment of chronic rhinosinusitis (CRS), today announced positive results from the ENLIGHTEN 2 Phase 3 clinical trial of LYR-210 in adult patients with CRS. The ENLIGHTEN 2 trial met its primary endpoint, with LYR-210 demonstrating statistically significant improvement compared to sham control in a composite of the three cardinal symptoms (3CS) of CRS (nasal obstruction, nasal discharge, facial pain/pressure) at week 24 (-1.13; p=0.0078) in patients without nasal polyps.

The ENLIGHTEN 2 trial also met the key secondary endpoints of 3CS at 24 weeks in the full population (i.e., patients with and without nasal polyps) (-0.90; p=0.0209) and in the clinically-validated SNOT-22 score at 24 weeks (-8.7; p=0.0101), with symptom improvement observed as early as week 4. Consistent with previous studies, LYR-210 was well-tolerated, with a safety profile similar to sham control.

The ENLIGHTEN program consists of two Phase 3 clinical trials, ENLIGHTEN 1 and ENLIGHTEN 2, to evaluate the efficacy and safety of LYR-210 for the treatment of CRS. While the ENLIGHTEN 2 trial met its primary endpoint and key secondary endpoints, the ENLIGHTEN 1 trial did not meet the primary endpoint or secondary endpoints, as previously reported in May 2024. Each ENLIGHTEN trial has enrolled approximately 180 CRS patients who have failed medical management and have not had prior ethmoid sinus surgery, randomized 2:1 to either LYR-210 (7500µg mometasone furoate) or sham control. The 24-week endpoints in the ENLIGHTEN trials assess LYR-210's long-acting therapeutic effect as a bioresorbable nasal implant designed to deliver six months of continuous anti-inflammatory medication to the sinonasal passages.

Results for Primary and Key Secondary Endpoints from ENLIGHTEN 2 Phase 3 Trial

Patients reported LYR-210 significantly improved important outcome measures on primary and key secondary endpoints:

- Statistically significant improvement compared to sham control in a composite of the 3CS of CRS at week 24 (-1.13; p=0.0078) in patients without nasal polyps.
- Statistically significant improvement in 3CS with LYR-210 compared to sham control at week 24 (-0.90; p=0.0209) in the full population (i.e., patients with and without nasal polyps)
- Statistically significant improvements in Sino-Nasal Outcome Test (SNOT-22) score with LYR-210 compared to sham control at week 24 (-8.7; p=0.0101)
    - Improvements in SNOT-22 were observed as early as week 4 with LYR-210 compared to sham control (-6.4; p=0.0456)
    - Improvements in SNOT-22 were sustained throughout the trial and were clinically meaningful, with more than twice the minimal clinically important difference observed at week 24 compared to baseline in the LYR-210 group (-22.4 points)
- Data evaluating computed tomography (CT) scans demonstrated numerical improvement in ethmoid sinus opacification in patients who received LYR-210, compared to sham control at week 20 (-2.15; p=0.1809). These data provide objective radiological evidence of improvement with LYR-210 treatment.
- LYR-210 patients showed no difference from sham patients in use of corticosteroid rescue medication; however, the LYR-210 patients had fewer endoscopic sinus surgeries compared to sham control.

LYR-210 was well tolerated, with no product-related serious adverse events in the ENLIGHTEN 2 trial. The most commonly reported adverse events included epistaxis, upper respiratory tract infection, chronic sinusitis, acute sinusitis, nasopharyngitis, COVID-19, and headache.

Results for CRS Patents with Nasal Polyps in Pooled Analysis from ENLIGHTEN 1 and ENLIGHTEN 2

Additionally, Lyra conducted a pooled data analysis of a total of 64 CRS patients with small nasal polyps (grade 1) from the ENLIGHTEN 1 and ENLIGHTEN 2 trials. The data demonstrated a consistent positive trend compared to sham control over 24 weeks in multiple endpoints:

- Improvement in 3CS with LYR-210 compared to sham control at week 24 (-1.13; p=0.0837), starting as early as week 4.
- Improvement in SNOT-22 score with LYR-210 compared to sham control at week 24 (-8.7; p=0.1331), starting as early as week 4.
- Improvements in percent ethmoid opacification with LYR-210 compared to sham control at week 20 (-6.07; p=0.1127).
- Improvements in nasal congestion score (NCS) with LYR-210 compared to sham control at week 24 for patients with moderate to severe NCS at baseline (-0.33; p=0.2159), starting as early as week 4.
- Improvements in nasal polyp score with LYR-210 compared to sham control at week 24 (-0.16; p=0.3494).

"We are thrilled to announce these positive results from our ENLIGHTEN 2 trial. We believe this has the potential to provide a path to advance LYR-210 to treat CRS, offering six months of therapy in a single administration for millions of patients who do not respond to standard CRS medical management. We will continue to review the totality of the dataset from the ENLIGHTEN trials to optimize our regulatory strategy," said Maria Palasis, Ph.D., President and CEO, Lyra Therapeutics. "Given these data we reported today, we plan to align with the FDA on a path forward for an NDA submission in patients without nasal polyps. As planned, we also analyzed the pooled data from ENLIGHTEN 2 and ENLIGHTEN 1 trials to treat CRS patients with nasal polyps, and we believe this positive data positions us to proceed with a development plan in patients with nasal polyps, based on our alignment in December 2024 with FDA on endpoints, inclusion criteria, patient population, background therapy, and assessments. Looking further ahead, we envision LYR-210 achieving its potential to benefit both non-polyp and polyp patients, positioning us to become a leader in CRS and validating our platform for future ENT indications."

"The positive results seen in the ENLIGHTEN 2 study are impressive and represent what could be a promising new treatment approach for the many CRS patients that I see every day in my practice who are underserved by limited therapies," said Zachary Soler, M.D., MSc, Professor in the Department of Otolaryngology-Head and Neck Surgery at the Medical University of South Carolina and coordinating Lead Investigator for the ENLIGHTEN 2 trial. "The more than 20-point improvement from baseline in SNOT-22 score after LYR-210 treatment represents a clinically meaningful improvement in patient symptoms."

"These positive results represent a significant milestone in advancing an innovative treatment to CRS patients who suffer from this chronic condition. It's a proud moment for us and a testament to the dedication of this team and our investigators in the development of this novel therapy," said Harlan Waksal, M.D., Executive Chairman, Lyra Therapeutics.

Results from the ENLIGHTEN 2 trial of LYR-210 are planned to be presented at the 71st Annual Meeting of the American Rhinologic Society, October 2025.

Conference Call and Webcast

Lyra Therapeutics will host a conference call and webcast to discuss results from the ENLIGHTEN 2 trial today, June 2, 2025, beginning at 8:30 a.m. ET. To join the audio call please register via this audio link, or to view the livestreamed webcast visit this webcast link. A replay of the webcast and presentation will be available following the conference call in "Events and Presentations" in the Investors section of Lyra's website for a limited time.

About LYR-210
LYR-210 is an investigational product candidate for the treatment of chronic rhinosinusitis (CRS) in patients who have failed current therapies and require further intervention. LYR-210 is a bioabsorbable nasal implant designed to be inserted in a simple, in-office procedure. LYR-210 is intended to deliver six months of continuous anti-inflammatory therapy, mometasone furoate, to the sinonasal passages to treat CRS.

About Lyra Therapeutics
Lyra Therapeutics, Inc. is a clinical-stage biotechnology company developing long-acting, anti-inflammatory sinonasal implants for the treatment of chronic rhinosinusitis (CRS). Lyra Therapeutics is developing therapies for CRS, a highly prevalent inflammatory disease of the paranasal sinuses which leads to debilitating symptoms and significant morbidities. LYR-210, the company's lead product, is a bioabsorbable nasal implant designed to be administered in a simple, in-office procedure and is intended to deliver six months of continuous anti-inflammatory drug therapy (7500µg mometasone furoate) to the sinonasal passages for the treatment of CRS with a single administration. LYR-210, which was evaluated in the ENLIGHTEN Phase 3 clinical program, is intended for patients with and without nasal polyps. The company's therapies are intended to treat the estimated four million CRS patients in the United States who fail medical management each year. For more information, please visit www.lyratx.com and follow us on LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The words "believe," "may," "will," "estimate," "envision," "continue," "anticipate," "intend," "expect," and similar expressions are intended to identify forward-looking statements. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including statements regarding our evaluation and investigation of the ENLIGHTEN 2 results and how they inform our path forward, our planned regulatory interaction and path for LYR-210, including alignment with the FDA and any planned regulatory submissions, our ability to design, implement and complete a new Phase 3 trial, the expected label for LYR-210, whether the pooled results from ENLIGHTEN 1 and 2 would support a path forward to a pivotal study in CRSwNP, our ability to correctly interpret FDA guidance received in December 2024 including on endpoints, inclusion criteria, patient population, background therapy, and assessments, whether LYR-210, if advanced, would be positioned to align with current ENT practices, and statements regarding the potential market opportunity for LYR-210, our participation in future events and presentations, and the timing of any of the foregoing. 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 Company's failure to meet its primary endpoint in its ENLIGHTEN 1 Phase 3 clinical trial; the fact the Company terminated the employment of approximately 87 employees following the announcement that it failed to attain the primary endpoint of its ENLIGHTEN 1 Phase 3 clinical trial; the fact that the Company

has incurred significant losses since inception and expects to incur additional losses for the foreseeable future; the Company's need for additional funding, which may not be available; the fact that the Company needs to conduct at least one additional phase 3 clinical trial; the Company's ability to continue as a going concern; the Company's limited operating history; the fact that the Company has no approved products; the fact that clinical trial data is subject to change until the completion of the applicable clinical study report; the fact that clinical trials required for the Company's product candidates are expensive and time-consuming, and their outcome is uncertain; effects of recently enacted and future legislation; the possibility of system failures or security breaches; effects of significant competition; the Company's reliance on third parties to conduct its preclinical studies and clinical trials; failure to obtain and maintain or adequately protect the Company's intellectual property rights; failure to retain key personnel; 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 6, 2025 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 press release. Any such forward-looking statements represent management's estimates as of the date of this press release. 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.

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