Larimar Therapeutics Presents Additional Data from Phase 1 Studies and Phase 2 Dose Exploration Study Supporting the Nomlabofusp Clinical Program at ICAR 2024

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- *Treatment with nomlabofusp modified gene expression and lipid profiles in addition to increasing frataxin (FXN) levels in study participants with Friedreich's ataxia (FA)*
- *Modeling and simulation predict that, in most patients with FA, 50 mg of nomlabofusp administered daily is likely to achieve FXN levels that are ≥50% of levels observed in healthy controls and similar to mean FXN levels reported in asymptomatic heterozygous carriers*
- *Disease characteristics of adult participants in the nomlabofusp studies were representative of the broad population of adults with FA*
- *Relationships between tissue FXN levels and onset of disease and GAA repeat length observed at baseline in nomlabofusp clinical study participants were consistent with prior published studies*
- *Nomlabofusp program update expected mid-December 2024*

BALA CYNWYD, Pa., Nov. 18, 2024 (GLOBE NEWSWIRE) -- Larimar Therapeutics, Inc. (Larimar) (Nasdaq: LRMR), a clinical-stage biotechnology company focused on developing treatments for complex rare diseases, last week presented data from the Company's Phase 1 studies and the Phase 2 dose exploration study of nomlabofusp at the International Congress for Ataxia Research (ICAR) in London, U.K. Data from a total of 61 adults with FA who participated in these studies evaluating short-term (up to 28 days) subcutaneous administration of 25, 50, 75, and 100 mg nomlabofusp were further evaluated and presented in three posters during the conference (posters available in the Our Science section at www.larimartx.com).

"As our nomlabofusp program advances towards potential registration, we are continuing to evaluate the characteristics and activity of nomlabofusp. Using modeling and simulation based on the data collected from our completed clinical studies, long-term daily administration of 50 mg nomlabofusp was predicted to achieve tissue FXN levels in most patients similar to the average FXN levels observed in asymptomatic heterozygous carriers," said Carole Ben-Maimon, MD, President, and Chief Executive Officer of Larimar. "Importantly, in study participants with FA, gene expression and lipid profiles in buccal cells and plasma, respectively, were observed to improve directionally towards values seen in healthy controls, suggesting that nomlabofusp has the potential to affect downstream metabolic pathways that may be disrupted in patients with FA."

Dr. Ben-Maimon, continued, "As we move ahead with the development of nomlabofusp, it is important to consider the totality of the data observed to date. Nomlabofusp has shown dose dependent increases in tissue FXN levels as well as changes in gene expression and lipid profiles in the same study population. Our studies have included a broad population of adults with FA and will be expanding study participants to include children and adolescents with the initiation of our pediatric pharmacokinetic (PK) run-in trial later this year. With the ongoing open label extension study, we are collecting long-term safety, PK and FXN data with the intent of supporting a potential accelerated approval using FXN as a novel surrogate endpoint. Our Biologics License Application (BLA) submission remains targeted for the second half of 2025. We look forward to sharing a nomlabofusp program update in mid-December of 2024."

Dr. Rusty Clayton, Chief Medical Officer of Larimar added, "We were pleased that the relationships between tissue FXN levels and disease characteristics in patients with FA across our three completed investigational studies are representative of those in the broader FA population reported in the literature. Data from this representative population supports our dose prediction modeling and simulation designed to aid in our nomlabofusp dose selection for patients with FA across age groups and with different baseline characteristics. We look forward to further enhancing our model with data from our upcoming pediatric PK run-in study, as well as long-term data from our open label extension (OLE) study. Most importantly, the activity of nomlabofusp in participants from our Phase 2 study was encouraging, as it showed a trend towards normalization of dysregulated gene expression and lipid profiles identified by comparing profiles between patients with FA and healthy volunteers. We expect to build on these initial data with additional analyses of an expanded data set as we continue to advance our nomlabofusp development program."

Disease characteristics and tissue FXN concentrations in nomlabofusp clinical studies
FA is an autosomal recessive neurodegenerative disorder caused by GAA repeats in the FXN gene that result in FXN deficiency. The variable number of GAA repeats leads to a diverse spectrum of disease characteristics. Tissue FXN levels are known to correlate with age of onset and inversely correlate with the number of GAA repeats and rate of disease progression. The data presented at ICAR described the characteristics of and tissue FXN levels in adult participants in the nomlabofusp clinical studies.

- **Nomlabofusp study participants were representative of the broad population of adults with FA**
- Lower tissue FXN levels were associated with younger age of onset and more severe and rapidly progressive disease
- Relationships between disease characteristics and baseline buccal cell FXN levels were consistent with previous published

studies
- Baseline buccal cell FXN levels correlate with baseline skin cell FXN levels in adults with FA participating in nomlabofusp clinical studies

Prediction of skin FXN levels after nomlabofusp administration based on data from the Phase 1 studies and Phase 2 dose exploration studies
FXN deficiency is the root cause of FA, and based on the literature, on average patients with FA have 21%-35% of the mean tissue FXN levels observed in healthy controls, and asymptomatic heterozygous carriers on average have ~50% of the mean FXN levels in buccal cells observed in healthy controls. The modeling used the skin tissue FXN levels measured in the completed clinical studies evaluating short-term administration of nomlabofusp to predict the potential increase in skin FXN levels after long-term administration of nomlabofusp.

- Dose-dependent increases in nomlabofusp exposure and skin FXN levels were observed in adults with FA after short-term administration of 25, 50, 75 or 100 mg nomlabofusp
- **Daily administration of 50 mg nomlabofusp is predicted to achieve skin FXN levels >50% of healthy controls in most patients, which is similar to mean tissue FXN levels observed in asymptomatic heterozygous carriers**
- Prediction model will be further optimized with long-term administration data from the ongoing OLE and data from adolescents and children as it becomes available

Effect of nomlabofusp on plasma lipid profiles and tissue gene expression in adults with FA
Deficiency in the mitochondrial protein FXN results in metabolic dysfunction and abnormal gene expression and lipid profiles in patients with FA. This study evaluated the impact of short-term administration of nomlabofusp on gene and lipid profiles in patients with FA as part of an initial exploratory analysis.

- In subsets of identified genes and lipids, gene expression and triglyceride levels were altered in study participants with FA at baseline compared with values observed in healthy controls (gene expression measured from buccal cells and lipid profiling measured from plasma)
- **Improvement in gene expression and lipid profiles was observed in study participants with FA as post-treatment values trended towards values observed in normal controls, suggesting that nomlabofusp administration affects downstream metabolic pathways**
- Further evaluation of changes in gene expression and lipid profiles after treatment with nomlabofusp is ongoing, including following long-term administration in the OLE study

About Larimar Therapeutics
Larimar Therapeutics, Inc. (Nasdaq: LRMR), is a clinical-stage biotechnology company focused on developing treatments for complex rare diseases. Larimar's lead compound, nomlabofusp, is being developed as a potential treatment for Friedreich's ataxia. Larimar also plans to use its intracellular delivery platform to design other fusion proteins to target additional rare diseases characterized by deficiencies in intracellular bioactive compounds. For more information, please visit: https://larimartx.com.

Forward-Looking Statements
This press release contains forward-looking statements that are based on Larimar's management's beliefs and assumptions and on information currently available to management. All statements contained in this release other than statements of historical fact are forward-looking statements, including but not limited to statements regarding Larimar's ability to develop and commercialize nomlabofusp and other planned product candidates, Larimar's planned research and development efforts, including the timing of its nomlabofusp clinical trials, interactions and filings with the FDA, expectations regarding potential for accelerated approval or accelerated access and time to market and overall development plan and other matters regarding Larimar's business strategies, ability to raise capital, use of capital, results of operations and financial position, and plans and objectives for future operations.

In some cases, you can identify forward-looking statements by the words "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve risks, uncertainties and other factors that may cause actual results, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements. These risks, uncertainties and other factors include, among others, the success, cost and timing of Larimar's product development activities, nonclinical studies and clinical trials, including nomlabofusp clinical milestones and continued interactions with the FDA; that preliminary clinical trial results may differ from final clinical trial results, that earlier non-clinical and clinical data and testing of nomlabofusp may not be predictive of the results or success of later clinical trials, and assessments; that the FDA may not ultimately agree with Larimar's nomlabofusp development strategy; the potential impact of public health crises on Larimar's future clinical trials, manufacturing, regulatory, nonclinical study timelines and operations, and general economic conditions; Larimar's ability and the ability of third-party manufacturers Larimar engages, to optimize and scale nomlabofusp's manufacturing process; Larimar's ability to obtain regulatory approvals for nomlabofusp and future product candidates; Larimar's ability to develop sales and marketing capabilities, whether alone or with potential future collaborators, and to successfully commercialize any approved product candidates; Larimar's ability to raise the necessary capital to conduct its product development activities; and other risks described in the filings made by Larimar with the Securities and Exchange Commission (SEC), including but not limited to Larimar's periodic reports, including the annual report on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, filed with or furnished to the SEC and available at www.sec.gov. These forward-looking statements are based on a combination of facts and factors currently known by Larimar and its projections of the future, about which it cannot be certain. As a result, the forward-looking statements may not prove to be accurate. The forward-looking statements in this press release represent Larimar's management's views only as of the date hereof. Larimar undertakes no obligation to update any forward-looking statements for any reason, except as required by law.

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