Larimar Therapeutics Announces FDA Clearance to Initiate the 25 mg Cohort of a Phase 2 Dose Exploration Trial of CTI-1601 in Friedreich's Ataxia Patients

September 14, 2022

- *Initiation of the Phase 2 trial is expected in Q4 2022, with top-line data expected in 2H 2023*
- *Company management hosting webcast and conference call today at 8:30 a.m. ET*

BALA CYNWYD, Pa., Sept. 14, 2022 (GLOBE NEWSWIRE) -- Larimar Therapeutics, Inc. ("Larimar") (Nasdaq: LRMR), a clinical-stage biotechnology company focused on developing treatments for complex rare diseases, today announced that the U.S. Food and Drug Administration (FDA) has cleared the initiation of the 25 mg cohort of a Phase 2, four-week, placebo-controlled, dose exploration trial of CTI-1601 in Friedreich's ataxia (FA) patients. In a written communication to Larimar, the FDA indicated it was lifting its full clinical hold on the CTI-1601 program and imposing a partial hold. The design of the upcoming Phase 2 trial is identical to the design proposed by Larimar, with the exception of a requirement for the FDA to review data from the 25 mg cohort prior to escalating the dose in the second cohort. Larimar expects to begin the Phase 2 trial in Q4 2022, with top-line data expected in 2H 2023.

"We thank the FDA for their engagement and are pleased with their decision to clear CTI-1601's return to the clinic," said Carole Ben-Maimon**,** MD, President and Chief Executive Officer of Larimar. "Given the strength of our Phase 1 data and the urgent need for a disease-modifying FA therapy, we believe today's news is an important event for not only Larimar, but for the entire FA community. We are now working expeditiously to initiate our Phase 2 dose exploration trial next quarter. We anticipate that the results of this trial will provide crucial safety, pharmacokinetic, and pharmacodynamic data that will inform the design of future studies."

The CTI-1601 program was placed on a clinical hold by the FDA following the Company's notification to the agency of 3 mortalities out of a total of 34 animals in a 26-week non-human primate (NHP) toxicology study designed to support extended dosing of patients with CTI-1601. All 3 of these NHPs were in the study's two highest dose groups and all NHPs in the two lower dose groups survived to the end of the study. The FDA's decision to allow the upcoming CTI-1601 Phase 2 trial to proceed follows Larimar's submission of a complete response with detailed analyses from Larimar's NHP toxicology studies and Phase 1 clinical trials.

Larimar's upcoming Phase 2 trial is designed to further characterize CTI-1601's safety, pharmacodynamic (PD), and pharmacokinetic (PK) profiles to provide information about the preferred long-term dose and dose regimen. Eligible patients will include ambulatory and non-ambulatory individuals with FA who are at least 18 years old. Patients may be CTI-1601 treatment naïve or have previously participated in Larimar's Phase 1 single- or multiple ascending dose trials.

Patients enrolled into the Phase 2 trial will be randomized 2:1 to receive CTI-1601 or placebo. The trial is designed to enroll approximately 24 – 30 total patients across two cohorts, with the first cohort of 12 – 15 patients evaluating a 25 mg dose of CTI-1601. Patients will receive CTI-1601 or placebo daily via subcutaneous injections for the first 14 days, and then every other day until day 28. Key endpoints will include safety assessments, measures of frataxin levels and other PD markers (e.g., lipid profiles and gene expression data) in peripheral tissues, as well as PK assessments. Dose escalation to 50 mg in the second cohort will be contingent on the FDA's agreement based on its review of the data from the trial's first cohort, and on the review by the trial's independent data monitoring committee.

Nancy M. Ruiz, MD, Chief Medical Officer of Larimar, added, "Our Phase 2 dose exploration trial is designed to build upon the positive findings of our previously completed multiple ascending dose trial. In the multiple ascending dose trial, daily subcutaneous injections of 50 mg of CTI-1601 increased frataxin levels in the buccal cells of FA patients, with the levels achieved exceeding those we would expect to see in phenotypically normal heterozygous carriers. This was a promising finding, as FA is caused by insufficient frataxin production and frataxin levels in buccal cells have been shown to correlate with neurological function in patients. By exploring extended daily dosing at 25 mg before potentially escalating to 50 mg in our upcoming trial, we aim to determine if lower doses for a longer period of time can also drive relevant increases in peripheral frataxin, allowing us to better understand CTI-1601's minimum effective dose. In addition, two weeks of daily dosing followed by two weeks of every-other-day dosing will provide valuable data to support the PK/PD models that will help inform the design of subsequent studies."

Previously completed Phase 1 single- and multiple-ascending dose (MAD) clinical trials evaluated the safety, PK, and PD profiles of CTI-1601 administered subcutaneously at doses up to 100 mg daily for up to 13 days. No serious adverse events, important medical events, or treatment-related severe adverse events were reported in the trials. The most common adverse events were mild and moderate injection site reactions, which all resolved without intervention. Except for injection site reactions, the number and severity of adverse events did not increase with increasing exposure to CTI-1601. Data from cohorts 2 and 3 of the MAD trial also showed that subcutaneous injections of 50 or 100 mg of CTI-1601, administered daily for at least seven days, resulted in frataxin levels in buccal cells that were at or in excess of those that would be expected in phenotypically normal heterozygous carriers. Cohort 1 of the MAD trial, which evaluated a 25 mg dose, explored a daily dosing regimen for only four days. In contrast, the 25 mg cohort of the upcoming Phase 2 trial will explore 14 days of daily dosing followed by 14 days of every-other-day dosing.

Conference Call and Webcast

Larimar will host a conference call and webcast today, September 14, 2022, at 8:30 a.m. ET. To access the webcast, please visit this link to the event. To participate by phone please dial 1-877-407-9716 (domestic) or 1-201-493-6779 (international) and refer to conference ID 13732889. Following the

live event, the archived webcast will be available on the "Investors" page of the Larimar website.

About CTI-1601
CTI-1601 is a recombinant fusion protein intended to deliver human frataxin to the mitochondria of patients with Friedreich's ataxia who are unable to produce enough of this essential protein. CTI-1601 has been granted Rare Pediatric Disease designation, Fast Track designation and Orphan Drug designation by the U.S. Food and Drug Administration (FDA), Orphan Drug Designation by the European Commission, and a PRIME designation by the European Medicines Agency.

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, CTI-1601, 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 Larimar's expectations regarding its ability to resolve the partial clinical hold imposed by the FDA related to CTI-1601, Larimar's ability to develop and commercialize CTI-1601 and other planned product candidates, Larimar's planned research and development efforts, including the timing of its CTI-1601 clinical development plan and other matters regarding Larimar's business strategies, 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, Larimar's ability to successfully engage with the FDA and satisfactorily respond to requests from the FDA for further information and data regarding the CTI-1601 clinical trial including the FDA review of data from cohort one from the Phase 2 dose escalation trial and FDA's agreement to escalate the dosing in cohort two, the timing and outcomes of Larimar's interactions with the FDA concerning the partial clinical hold, the success, cost and timing of Larimar's product development activities, nonclinical studies and clinical trials, including CTI-1601 clinical milestones; that preliminary clinical trial results may differ from final clinical trial results, that earlier non-clinical and clinical data and testing of CTI-1601 may not be predictive of the results or success of later clinical trials, and assessments; the ongoing impact of the COVID-19 pandemic on Larimar's future clinical trials, manufacturing, regulatory, nonclinical study timelines and operations, and the potential impact of the Russian invasion of Ukraine on Larimar's ability to raise additional capital and general economic conditions; Larimar's ability and the ability of third-party manufacturers Larimar engages, to optimize and scale CTI-1601's manufacturing process; Larimar's ability to obtain regulatory approvals for CTI-1601 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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