Trevi Therapeutics Announces the Initiation of its Phase 2b CORAL Clinical Trial of Haduvio™ for Chronic Cough in Idiopathic Pulmonary Fibrosis (IPF)

December 5, 2023

Expect to enroll approximately 160 subjects and study 3 doses of Haduvio against placebo

Primary efficacy endpoint is the relative change in 24-hour cough frequency of Haduvio versus placebo

NEW HAVEN, Conn., Dec. 5, 2023 /PRNewswire/ -- Trevi Therapeutics, Inc. (Nasdaq: TRVI), a clinical-stage biopharmaceutical company developing the investigational therapy Haduvio™ (oral nalbuphine ER) for patients with chronic cough in idiopathic pulmonary fibrosis (IPF), refractory chronic cough (RCC), and prurigo nodularis, today announced the initiation of its Phase 2b CORAL clinical trial evaluating three doses of Haduvio against placebo in approximately 160 IPF patients with chronic cough. This Phase 2b trial builds on the positive results from the Phase 2a CANAL trial, which demonstrated a statistically significant reduction in daytime cough frequency by 75.1%, a 52.5% difference from placebo (p<0.0001).

After Haduvio reduces daytime IPF chronic cough by 75.1% in Phase 2a trial, Trevi initiates Phase 2b trial

"We are thrilled to continue our development of Haduvio in IPF chronic cough patients building on the positive results from our Phase 2a CANAL trial," said David Clark, Chief Medical Officer of Trevi Therapeutics. "Chronic cough impacts up to 85% of IPF patients and is often one of the first signs of the disease. There are currently no approved therapies for chronic cough in IPF and it persists despite antifibrotic treatment. This cough is often reported by patients as one of the most bothersome aspects of IPF. Haduvio has the potential to reduce cough and improve quality of life through its novel mechanism of action, which affects both central brain and peripheral lung targets."

Phase 2b Trial Design: **CO**ugh **R**eduction in IPF with n**AL**buphine ER (CORAL)

The CORAL trial is a double-blind, randomized, placebo-controlled, parallel-arm trial evaluating three doses of Haduvio (27mg, 54mg and 108mg twice daily) against placebo in IPF patients with chronic cough. Approximately 160 IPF patients with chronic cough are expected to be randomized 1:1:1:1 to one of three Haduvio doses or placebo for a period of 6 weeks, which includes an initial 2-week titration to the target dose followed by 4 weeks of fixed dose administration.

The primary efficacy endpoint for the trial is the relative change in 24-hour cough frequency at the end of Week 6 versus baseline for Haduvio compared to placebo, as measured via an objective cough monitor. The trial will also explore secondary endpoints, including patient reported outcome measures for cough, dyspnea, and quality of life.

The protocol for the CORAL trial provides for a sample size re-estimation (SSRE) analysis once approximately 50% of the patients in the trial are evaluable for the primary endpoint. The SSRE is expected to occur in the second half of 2024, and topline data from the full trial are expected to be available in the first half of 2025 assuming there are no adjustments made to the sample size.

About Idiopathic Pulmonary Fibrosis (IPF) Chronic Cough

There are estimated to be 140,000 IPF patients in the US and more than 1 million patients ex-US. Up to 85% of these patients experience a chronic cough.

Patients with chronic cough in IPF can cough up to 1,500 times per day, leading to increased feelings of anxiety, fatigue, air hunger, and peripheral oxygen desaturation. The social impact of chronic cough in IPF further compounds limited exercise ability, reduced walking distance, and the need to use supplemental oxygen. In addition to the immediate impact on patients, chronic cough in IPF may be an early clinical marker of disease activity and patients at high risk of progression. It may also help predict time to death or lung transplant and contribute to enhanced activation of profibrotic mechanisms and disease worsening in IPF.

There are no approved therapies for the treatment of chronic cough in IPF.

About Trevi Therapeutics, Inc.

Trevi Therapeutics, Inc. is a clinical-stage biopharmaceutical company developing the investigational therapy Haduvio™ (oral nalbuphine ER) for patients with chronic cough in idiopathic pulmonary fibrosis (IPF), refractory chronic cough (RCC), and prurigo nodularis. Haduvio is a dual κ-opioid receptor agonist and μ-opioid receptor antagonist that works both centrally in the brain as well as peripherally in the lungs and has the potential for a synergistic antitussive effect to treat chronic cough.

The impact of chronic cough is significant and often leads to a decline in patients' social, physical, and psychological quality of life. In IPF, chronic cough may lead to worsening disease and may be associated with a higher risk of progression, death, or need for lung transplant. There are no approved therapies for the treatment of chronic cough in IPF and current treatment options provide minimal relief to patients. RCC affects up to 10% of the adult population and Haduvio's expansion into RCC has the potential to reach patients suffering from moderate to severe chronic cough. There are also no approved therapies for RCC in the US.

Parenteral nalbuphine is not scheduled by the U.S. Drug Enforcement Agency. Trevi intends to propose Haduvio as the trade name for oral nalbuphine ER. Its safety and efficacy have not been evaluated by any regulatory authority.

For more information, visit www.TreviTherapeutics.com and follow Trevi on X (formerly Twitter) and LinkedIn.

Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements are subject to risks and uncertainties and actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding Trevi's business plans and objectives, including future plans or expectations for Haduvio and plans and timing with respect to clinical trials, and other statements containing the words "believes," "anticipates," "plans," "expects," and similar expressions. Risks that contribute to the uncertain nature of the forward-looking statements include: uncertainties regarding the success, cost and timing of Trevi's product candidate development activities and ongoing and planned clinical trials; the risk that data from a clinical trial may not necessarily be predictive of the results of later clinical trials in the same or a different indication; uncertainties regarding Trevi's ability to execute on its strategy; uncertainties with respect to regulatory authorities' views as to the data from Trevi's clinical trials and next steps in the development path for Haduvio in the United States and foreign countries, including Trevi's ability to submit and get clearance of an IND and other regulatory filings on a timely basis; uncertainties inherent in estimating Trevi's cash runway, future expenses and other financial results, including Trevi's ability to fund future operations, including clinical trials, as well as other risks and uncertainties set forth in the quarterly report on Form 10-Q for the quarter ended September 30, 2023 filed with the Securities and Exchange Commission and in subsequent filings with the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made. Trevi undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Investor Contact
Katie McManus
Trevi Therapeutics, Inc.
203-304-2499
k.mcmanus@trevitherapeutics.com

Media Contact
Rosalia Scampoli
914-815-1465
rscampoli@marketcompr.com

SOURCE Trevi Therapeutics, Inc.