Trevi Therapeutics Announces Publication of Positive Data from the CANAL Trial in IPF Chronic Cough in NEJM Evidence

Nalbuphine ER resulted in a rapid and marked reduction in recorded daytime cough among patients suffering from IPF-related cough

The mean change in 24-hour objective cough frequency was similar in patients with concomitant anti-fibrotic therapy and without concomitant anti-fibrotic therapy

NEW HAVEN, Conn., May 22, 2023 /PRNewswire/ -- Trevi Therapeutics, Inc. (Nasdaq: TRVI), a clinical-stage biopharmaceutical company developing the investigational therapy Haduvio™ (oral nalbuphine ER) for difficult to treat patients with chronic cough in idiopathic pulmonary fibrosis (IPF), other chronic cough indications, and prurigo nodularis, today announced the positive results from the Phase 2 CANAL trial in adults with IPF chronic cough has been published in *NEJM Evidence*.

Toby Maher, M.D., Ph.D., Professor of Clinical Medicine, Keck School of Medicine, University of Southern California, and the national corresponding investigator on the trial, said, "*The publication of these Phase 2 results in NEJM Evidence demonstrates the potential clinical benefit of targeting both the central and peripheral mechanisms of chronic cough with nalbuphine ER for adults with idiopathic pulmonary fibrosis. Every day in my clinical practice, I see the devastating impact of chronic cough on the lives of individuals with IPF. This challenging and debilitating symptom urgently requires effective treatments. We would like to thank all the investigators, study staff, and patients who participated in the CANAL trial.*"

Access publication here: https://evidence.nejm.org/doi/full/10.1056/EVIDoa2300083

The safety results of the CANAL trial were generally consistent with the known safety profile of Haduvio from previous trials. There were two serious adverse events reported during the trial, neither of which was considered by the investigator to be treatment related. The most frequently reported treatment emergent adverse events associated with Haduvio in the CANAL trial were nausea, fatigue, dizziness, vomiting, constipation, and somnolence.

About IPF

There are estimated to be 140,000 IPF patients in the US and more than 1 million patients ex-US, with up to 85% of these patients experiencing chronic cough. There are no approved therapies for the treatment of chronic cough in IPF, and the cough is often refractory to antitussive therapy. Patients with chronic cough in IPF can cough up to 1,500 times per day, leading to increased feelings of anxiety as it induces breathlessness. Coughing spells or episodes lead to significant 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. The chronic cough in IPF may be an early clinical marker of disease activity, identify patients at high risk of progression, predict time to death or lung transplant, and may also contribute to enhanced activation of profibrotic mechanisms and disease worsening in IPF.

About the CANAL Trial

The Phase 2 **C**ough **A**nd **NAL**buphine (CANAL) trial was a double-blind, randomized, placebo-controlled, 2-treatment, 2-period crossover efficacy and safety study of nalbuphine ER for chronic cough in patients with IPF that was conducted in the United Kingdom. The study consisted of 2 treatment periods of 3 weeks, with a washout period of 2 weeks after each treatment period. The primary efficacy endpoint evaluated the effect of nalbuphine ER tablets on the mean daytime cough frequency at day 22 compared to placebo as measured by an objective cough monitor. More information about the CANAL trial is available at www.clinicaltrials.gov: NCT04030026

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

a synergistic anti-tussive 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. There are no approved therapies for the treatment of chronic cough in IPF and current treatment options provide minimal relief to patients. In IPF, chronic cough may lead to worsening fibrosis and may be associated with a higher risk of progression, death, or need for lung transplant.

Parenteral nalbuphine is not scheduled by the US DEA. Trevi intends to propose Haduvio as the trade name for nalbuphine ER. Its safety and efficacy have not been evaluated by any regulatory authority.

For more information, visit www.TreviTherapeutics.com and follow the Company on 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 future clinical trials, expectations regarding Trevi's uses and sufficiency of capital, 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 positive data from a clinical trial may not necessarily be predictive of the results of future 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; as well as other risks and uncertainties set forth in the quarterly report on Form 10-Q for the quarter ended March 31, 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.
