

Trevi Therapeutics Concludes Enrollment for Phase 2 CANAL Trial in IPF Chronic Cough

Previously Announced Statistically Significant Interim Analysis Established Proof of Concept (p-value less than 0.0001)

Efficacy and Safety Data Expected on the Full Set of Subjects in Third Quarter 2022

NEW HAVEN, Conn., March 15, 2022 /PRNewswire/ -- [Trevi Therapeutics, Inc.](#) (Nasdaq: TRVI) is a clinical-stage biopharmaceutical company developing an investigational therapy Haduvio™ (nalbuphine ER). Today, Trevi announced that it concluded enrollment early for its Phase 2 Cough And NALbuphine (CANAL) trial for the treatment of chronic cough in idiopathic pulmonary fibrosis (IPF) patients following the [previously announced](#) statistically significant efficacy results from the interim analysis (N=26). The primary efficacy endpoint demonstrated a 77.3% reduction in daytime cough frequency from baseline with the use of Haduvio compared to a 25.7% reduction with placebo, demonstrating a 52% placebo-adjusted reduction in the geometric mean percent change in the daytime cough frequency (p<0.0001).

Trevi enrollment CANAL positive results	completes for Ph2 trial following interim analysis
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Because the trial achieved statistical significance in the interim analysis, sites were notified that they could enroll eligible subjects already in screening but that no additional recruitment was required. Approximately 40 subjects in total have been enrolled in the study. The Company continues to expect to report efficacy and safety on the full set of subjects in the third quarter of 2022.

Archived Interim Analysis Call Details

An archived replay of the interim analysis webcast and slide presentation that took place on February 24 are available on the 'Investors & News' section on the Company's website at www.trevitherapeutics.com.

Upcoming Meetings

The Company plans to participate at the following upcoming conferences and events:

- March 28-30: Maxim Group 2022 Virtual Growth Conference
- March 30, 8:00 a.m. – 9:00 a.m. ET: "Understanding the Seriousness of Chronic Cough in IPF Patients and Trevi's Latest Data." A webinar featuring Trevi management, along with insights from an IPF expert.
- April 11-14: 21st Annual Needham Virtual Healthcare Conference

About Chronic Cough in Idiopathic Pulmonary Fibrosis

IPF is a serious, end of life disease where cough is one of the most significant symptoms. There are estimated to be 130,000 IPF patients in the US and more than 1 million patients ex-US, where up to 85% of these patients experience 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 520 times per day, leading to increased feelings of anxiety as it induces breathlessness. Coughing spells or episodes lead to significant fatigue, air hunger, peripheral oxygen desaturation and some patients also experience cough-related urinary incontinence. 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 CANAL

The Phase 2 Cough And NALbuphine (CANAL) trial is 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 taking place in the United Kingdom. The study consists of 2 treatment periods of 3 weeks, with a washout period of 2 weeks after each treatment period. The primary efficacy endpoint is to evaluate 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 focused on the development and commercialization of the investigational therapy Haduvio to treat serious neurologically mediated conditions. Trevi is conducting a Phase 2b/3 clinical trial of Haduvio for the treatment of chronic pruritus

associated with prurigo nodularis (PN) and a Phase 2 trial for chronic cough in patients with idiopathic pulmonary fibrosis (IPF). These conditions share a common pathophysiology that is mediated through opioid receptors in the central and peripheral nervous systems.

Founded in 2011, Trevi Therapeutics is headquartered in New Haven, CT.

About Haduvio

Haduvio, an investigational therapy, is an oral extended-release (ER) formulation of nalbuphine. Nalbuphine is a mixed κ -opioid receptor agonist and μ -opioid receptor antagonist that has been approved and marketed as an injectable for pain indications for more than 20 years in the United States and Europe. The κ - and μ -opioid receptors are known to be critical mediators of itch, cough and certain movement disorders. Nalbuphine's mechanism of action may also mitigate the risk of abuse associated with μ -opioid agonists because it antagonizes, or blocks, μ -opioid receptors. Parenteral nalbuphine is not currently classified as a controlled substance by the DEA in the United States or by regulatory authorities in most of Europe. Trevi intends to propose Haduvio as the trade name for nalbuphine ER. Nalbuphine ER (Haduvio) is an investigational therapy that has been granted Fast Track designation by the FDA for the proposed indication of reduction of moderate to severe pruritus in patients with prurigo nodularis. Its safety and efficacy have not been evaluated by any regulatory authority.

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 the expected timing of reporting the full set of subjects' data from Trevi's Phase 2 CANAL trial of Haduvio in IPF subjects with chronic cough; Trevi's business plans and objectives, including future plans or expectations for Trevi's product candidates; 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, including with respect to the timing of reporting top-line data from both Trevi's Phase 2b/3 PRISM trial and Phase 2 CANAL trial; uncertainties regarding Trevi's ability to execute on its strategy; the risk that positive interim or top-line results from a clinical trial may not necessarily be predictive of the results of the completed trial or other future or ongoing clinical trials; potential regulatory developments in the United States and foreign countries; uncertainties regarding fast track designation and the effect such status could have on the regulatory review or approval process; uncertainties inherent in estimating Trevi's cash runway, future expenses and other financial results, including Trevi's ability to continue as a going concern, comply with its obligations under its loan facility and fund future operations; uncertainties regarding the scope, timing and severity of the COVID-19 pandemic, the impact of the COVID-19 pandemic on Trevi's clinical operations and actions taken in response to the pandemic; uncertainties regarding Trevi's ability to maintain its listing on the Nasdaq Global Market; as well as other risks and uncertainties set forth in the quarterly report on Form 10-Q for the quarter ended September 30, 2021 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.

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