Trevi Therapeutics Announces the Initiation of its Phase 2a RIVER Clinical Trial of Haduvio™ for Refractory Chronic Cough

Expect to enroll 60 subjects across a broad range of cough frequencies

RIVER topline data expected in the second half of 2024

NEW HAVEN, Conn., Nov. 2, 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), refractory chronic cough (RCC), and prurigo nodularis, today announced the initiation of its Phase 2a RIVER clinical trial evaluating Haduvio in RCC patients. RCC affects up to 10% of adults worldwide and is defined by a cough that lasts >8 weeks and does not respond to therapy for an underlying condition. Topline data from the RIVER trial is expected in the second half of 2024.

"We are excited about the initiation of the RIVER study in refractory chronic cough," said Jennifer Good, President and CEO of Trevi Therapeutics. "Based on our positive data in IPF chronic cough, we believe Haduvio has the potential to provide therapy for severe cough across a broad range of cough frequencies through its differentiated central and peripheral mechanism of action. The RIVER study will not only enroll severe RCC subjects in the high cough frequency population, but also subjects with a moderate cough frequency, where a significant unmet need still exists."

Phase 2a Trial Design: **R**efractory Chronic Cough **I**mprovement **V**ia Nal **ER** (RIVER)
The RIVER trial is a double-blind, randomized, placebo-controlled, 2-period crossover study evaluating the safety and efficacy of Haduvio in reducing chronic cough in RCC subjects. Approximately 60 RCC subjects are expected to be randomized with a 1:1 stratification between those with 10-19 coughs/hour (moderate 24-hour cough frequency) and those with ≥20 coughs/hour (high 24-hour cough frequency). Each treatment period will last 21 days, separated by a 21-day washout period, and subjects on Haduvio will have the dose titrated from 27 mg once a day (QD) up to 108 mg twice a day (BID) across the 21-day dosing period.

The primary efficacy endpoint for the trial is the relative change in 24-hour cough frequency at Day 21 from treatment period baseline for Haduvio compared to placebo, as measured via an objective cough monitor. The study will also explore secondary endpoints, including patient reported outcome measures for cough and dyspnea.

About Refractory Chronic Cough (RCC)
Refractory chronic cough affects up to 10% of the adult population and is defined as a persistent cough lasting >8 weeks, despite treatment for an underlying condition. RCC is caused by cough reflex hypersensitivity in the central and peripheral nerves. It is highly disruptive and accompanied by a wide range of complications, ranging from urinary incontinence in females to sleep disruption and social embarrassment that causes significant social and economic burden for patients and those around them.

The most common causes of RCC are asthma, gastroesophageal reflux disease (GERD), non-asthmatic eosinophilic bronchitis, and upper airway cough syndrome or post-nasal drip. There are no approved therapies for RCC in the U.S., E.U., or U.K.

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), refractory chronic cough, 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 disease and may be associated with a higher risk of progression, death, or need for lung transplant.

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 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 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 June 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.

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