Trevi Therapeutics to Present Final Data from Phase 2 Trial of Oral Nalbuphine Extended Release for Chronic Cough in IPF at BTS' Winter Meeting

Data from full set of subjects was statistically significant for the primary efficacy endpoint (p<0.0001)

Key secondary patient and clinician-reported outcomes supported positive primary endpoint

NEW HAVEN, Conn., Oct. 27, 2022 /PRNewswire/ -- Trevi Therapeutics, Inc. (Nasdaq: TRVI), a clinical-stage biopharmaceutical company developing an investigational therapy Haduvio™ (oral nalbuphine ER) for the treatment of serious chronic cough conditions, today announced data from the full set of subjects from CANAL, a phase 2 trial in idiopathic pulmonary fibrosis (IPF) chronic cough, will be presented as an oral presentation at the upcoming British Thoracic Society's (BTS) Winter Meeting 2022 taking place in London, United Kingdom.

BTS (British Thoracic Society) Winter Meeting 2022 (November 23-25)

Session:	Hot shots" – What's hot in cough?
Title:	S15 – Efficacy of oral nalbuphine extended release for the treatment of chronic cough in idiopathic pulmonary fibrosis: analysis of a phase 2 study
Location:	QEII Centre, Broad Sanctuary, Westminster, London, SW1P 3EE
Presentation**:**	**November 23, 8:45 AM CET**
Presenter:	Philip Molyneaux, MD, Faculty of Medicine, National Heart & Lung Institute, Imperial College London
Registration Details:	https://www.brit-thoracic.org.uk/education-and-events/winter-meeting/

"IPF places a high burden on patients and caregivers impacting over a million patients globally. Coughing spells can lead to significant fatigue, air hunger, and oxygen desaturation with a negative impact on quality of life for the patient. The results of the study demonstrate the potential of nalbuphine ER's central and peripheral mechanism of action to significantly reduce chronic cough in IPF and potentially improve the quality of life in afflicted patients," said Prof. Philip Molyneaux.

The CANAL (**C**ough **A**nd **NAL**buphine) trial was a Phase 2 double-blind, randomized, placebo-controlled, 2-treatment, 2-period crossover efficacy and safety study of nalbuphine ER for chronic cough in IPF. Statistically significant efficacy results from the full analysis set (N=38) were previously announced and showed the following:

- Nalbuphine ER subjects had a 76.1% reduction in 24hr cough frequency compared to a 25.3% of placebo subjects, a 50.8% placebo-adjusted change (p<0.0001).
- Reduction in 24-hour cough frequency was consistent with the reduction in daytime cough frequency.
- Key secondary endpoints on patient and clinician-reported outcomes were also statistically significant.
- In a post-hoc analysis, 97% of nalbuphine ER subjects had at least a 30% reduction in 24hr cough frequency compared to 35% of placebo subjects, signifying a clinically meaningful reduction in cough (p<0.0001).
- Subjects on nalbuphine ER experienced a statistically significant improvement as measured by their patient-reported outcomes compared to placebo over the 3-week treatment period in the EXACT2: Cough Frequency Score (p=0.001).

Safety and Tolerability Results:
The safety results of the trial were generally consistent with the known safety profile of nalbuphine ER 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 common adverse events observed during the trial were nausea, fatigue, constipation, dizziness, somnolence, vomiting, headache, anxiety and depression.

About Chronic Cough in Idiopathic Pulmonary Fibrosis
IPF is a serious, end-of-life disease. Chronic cough is one of the most common symptoms of IPF and has a significant impact on quality of life in these patients. There are estimated to be 140,000 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 often isn't affected by

antitussive therapy. Patients with chronic cough in IPF can cough up to 1,500 times per day, leading to increased feelings of fear and stress as it causes shortness of breath. Coughing spells or episodes lead to significant fatigue, an urge to breathe, low levels of oxygen in blood, and some patients also experience loss of bladder control. The social impact of chronic cough in IPF is increased because of limited exercise ability, reduced walking distance, and the need to use additional oxygen. Chronic cough in IPF may be an early clinical marker of disease activity that could potentially help to identify patients at high risk of progression and predict time to death or lung transplant. In addition, chronic cough in IPF may also contribute to enhanced activation of profibrotic mechanisms and disease worsening.

About the Ph2 CANAL Trial
The Phase 2 Cough And NALbuphine (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 was 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 oral therapy Haduvio™ (nalbuphine ER) for the treatment of serious chronic cough conditions. The Company has successfully completed a Phase 2 trial of Haduvio for the treatment of chronic cough in adults with idiopathic pulmonary fibrosis (IPF). Based on this positive data, Trevi plans to focus future clinical development on chronic cough conditions, including IPF, refractory chronic cough, and interstitial lung diseases (ILDs).

For more information, visit www.TreviTherapeutics.com and follow the company on Twitter and LinkedIn.

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 centrally and peripherally active and known to be critical mediators of cough, itch, 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 scheduled 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. 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 Trevi's business plans and objectives, including future plans or expectations for Trevi's product candidates and plans with respect to future 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; 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 Trevi's product candidates in the United States and foreign countries; 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; 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; as well as other risks and uncertainties set forth in the quarterly report on Form 10-Q for the quarter ended June 30, 2022 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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