

# Trevi Therapeutics Announces Additional Analyses from Phase 2a RIVER Trial of Haduvio in Patients with Refractory Chronic Cough

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*Results of analyses presented at an investor meeting during the American Thoracic Society 2025 International Conference*

NEW HAVEN, Conn., May 20, 2025 /PRNewswire/ -- [Trevi Therapeutics, Inc.](#) (Nasdaq: TRVI), a clinical-stage biopharmaceutical company developing the investigational therapy Haduvio™ (oral nalbuphine ER) for the treatment of chronic cough in patients with idiopathic pulmonary fibrosis (IPF) and in patients with refractory chronic cough (RCC), today announced additional analyses from the Phase 2a RIVER trial of Haduvio for the treatment of patients with RCC (N=66). In March 2025, the Company [announced positive topline results](#), where Haduvio met the primary endpoint with a statistically-significant reduction in the objective 24-hour cough frequency of 67% from baseline and 57% on a placebo-adjusted basis ( $p < 0.0001$ ).

"We continue to evaluate the full results from the Phase 2a RIVER trial and remain impressed with both the magnitude and consistency of effect of nalbuphine ER in this trial. We are looking forward to the results from our Phase 2b trial in IPF patients with chronic cough to finalize the development path forward for both indications," said James Cassella, Ph.D., Chief Development Officer of Trevi Therapeutics.

## Additional Analyses:

- Responder analyses of 24-hour cough frequency reduction at 30%, 50%, and 75% thresholds were statistically significant for patients on Haduvio across all doses.
- Patients on Haduvio experienced a statistically-significant improvement ( $p < 0.0001$ ) in the patient-reported Leicester Cough Questionnaire at Day 21 (108 mg BID).
- There were no significant treatment period effects from the crossover design for the primary efficacy analysis of relative change from baseline in 24-hour cough frequency.
- Similar to previous studies, adverse events for patients on Haduvio were more frequently observed following initial exposure to the drug at 27 mg BID in the first week and diminished over time despite dose escalation to 108 mg BID.
- Discontinuations primarily occurred in the first two weeks of Haduvio dosing and were mostly related to adverse events, typically central nervous system and gastrointestinal in nature.

The additional analyses were presented as part of a KOL panel discussion which took place during the American Thoracic Society's 2025 International Conference. [Click here to see the additional analyses slide set.](#)

## About the Phase 2a RIVER Trial

The Phase 2a [RIVER](#) trial was a randomized, double-blind, placebo-controlled, two treatment period, crossover study designed to evaluate the efficacy, safety, and tolerability of Haduvio for the treatment of patients with RCC. Each treatment period lasted 21 days, separated by a 21-day washout period. During the Haduvio treatment period, patients were titrated with assessments at 27 mg twice daily (BID), 54 mg BID and 108 mg BID, with objective cough and other assessments at each dose. The primary endpoint of the trial was the mean change in 24-hour cough frequency, as determined by an objective cough monitor, for the full analysis set (FAS) population at Day 21. The FAS population included all patients who received at least one dose of study drug and have objective cough count data on both Baseline and Day 21 in at least one treatment period.

## About Refractory Chronic Cough (RCC)

Refractory chronic cough has no approved therapies in the U.S. and is defined as a persistent cough lasting >8 weeks despite treatment for an underlying condition (i.e., asthma, gastroesophageal reflux disease, non-asthmatic eosinophilic bronchitis, and upper airway cough syndrome or post-nasal drip) and includes unexplained chronic cough. RCC affects ~2-3 million patients in the U.S. and is caused by cough reflex hypersensitivity in both the central and peripheral nerves. It is a highly debilitating disease 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 burdens for patients and those around them.

## About Trevi Therapeutics, Inc.

Trevi Therapeutics, Inc. is a clinical-stage biopharmaceutical company developing the investigational therapy Haduvio™ (oral nalbuphine extended-release) for the treatment of chronic cough in patients with idiopathic pulmonary fibrosis (IPF) and in patients with refractory chronic cough (RCC). Haduvio is the first and only investigational therapy to show a statistically significant reduction in cough frequency in clinical trials with IPF chronic cough patients and RCC patients. Haduvio acts on the cough reflex arc both centrally and peripherally as a kappa agonist and a mu antagonist (KAMA), targeting opioid receptors that play a key role in controlling chronic cough. Nalbuphine is not currently scheduled by the U.S. Drug Enforcement Agency.

Chronic cough is a highly prevalent condition in IPF patients, impacting up to 85% of the IPF population. There are ~150,000 U.S. IPF patients and the impact of chronic cough is significant with patients coughing up to 1,500 times per day. This consistent cough and any associated damage may lead to worsening disease, a higher risk of progression, death, or need for lung transplant.

Chronic cough also 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 patients with IPF and current off-label treatment options provide minimal benefit to patients.

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](http://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 clinical data, 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 clinical trials; the risk that positive 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; 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 March 31, 2025 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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