

Trevi Therapeutics Announces Positive Topline Results from the Phase 2a RIVER Trial of Haduvio in Patients with Refractory Chronic Cough

March 10, 2025

Haduvio met the primary endpoint with a statistically-significant reduction ($p < 0.0001$) in 24-hour cough frequency with a 57% placebo-adjusted change from baseline

Haduvio showed similar efficacy in patients with moderate or severe cough counts ($p < 0.0001$)

Haduvio is the first and only therapy to show a statistically-significant reduction in chronic cough across both RCC and IPF patients

Patient reported and other secondary outcomes were statistically significant and consistent with the primary endpoint

Company to host a conference call and webcast today at 8:30 a.m. ET and will be joined by key opinion leader, Professor Jacky Smith

NEW HAVEN, Conn., March 10, 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 refractory chronic cough (RCC), is pleased to announce today positive topline results from its Phase 2a RIVER trial of Haduvio for the treatment of patients with RCC (N=66). 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 ($p < 0.0001$).

"I am happy to share these robust positive results from our Phase 2a RIVER trial in refractory chronic cough which has been a difficult-to-treat indication with no approved therapies in the U.S.," said Jennifer Good, President and Chief Executive Officer of Trevi Therapeutics. "The RIVER trial demonstrated that Haduvio was highly effective, and worked quickly at the lowest dose tested across a broad range of cough counts. These results, coupled with our existing IPF chronic cough results, are further evidence of the effectiveness of Haduvio's central and peripheral KAMA mechanism in treating these difficult neurological cough conditions which are so disruptive to patients' lives."

James Cassella, Ph.D., Chief Development Officer of Trevi Therapeutics added, "The results from the RIVER trial were highly statistically significant with consistent outcomes across the primary and analyzed secondary endpoints as well as for patients with moderate or severe baseline cough frequency. We look forward to advancing development of nalbuphine ER in the hopes of providing relief for the significant unmet need for these chronic cough patients. Based on these results, we plan to discuss next steps with the FDA and anticipate initiating the next study after we receive their input. Thank you to all the patients and investigators who contributed to our trials and continue to advance clinical research to find a treatment for chronic cough."

"I am excited to see the positive results from the Phase 2a RIVER trial and the potential role nalbuphine ER could have in therapy for RCC patients," said Professor Jacky Smith, Professor of Respiratory Medicine at the University of Manchester. "RCC significantly impacts patients' lives both physically and psychologically, resulting in chest pain, urinary incontinence, depression, exhaustion, dizziness and much more. Therapies are desperately needed as patients continue to suffer from this debilitating disease."

The Phase 2a **Refractory Chronic Cough Improvement Via Nalbuphine ER (RIVER)** trial was a randomized, double-blind, placebo-controlled, two-treatment, two-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.

Primary Endpoint

	Change from Baseline in 24-hour Cough Frequency at Day 21
Haduvio 108 mg BID	-67 %
Placebo BID	-10 %
Difference from placebo	57% ($p < 0.0001$)

Additional Endpoints

- Haduvio demonstrated a statistically-significant reduction in 24-hour cough frequency of 66% in the severe cough (20+ coughs/hour) subgroup ($p < 0.0001$) and 68% in the moderate cough (10-19 coughs/hour) subgroup ($p < 0.0001$).
- 84% of Haduvio patients had at least a 30% reduction in 24-hour cough frequency vs. baseline, as compared to 29% of placebo patients, a difference of 55% ($p < 0.0001$).
- A statistically-significant reduction in 24-hour cough frequency, as measured by an objective cough monitor, was seen as early as Day 7 (27 mg BID) for patients on Haduvio ($p < 0.0001$).
- Patients on Haduvio experienced a statistically-significant improvement in patient reported outcomes compared to placebo as early as Day 7 (27 mg BID) in the Cough Severity Visual Analog Scale and the Patient-Reported Cough Frequency.
- The safety results of the trial were generally consistent with the known safety profile of Haduvio from previous trials. The most common adverse events experienced included: constipation, nausea, somnolence, headache, dizziness, and fatigue and there were no treatment emergent serious adverse events.

Conference Call

The Company will host a conference call and webcast to review the topline results today, March 10th, at 8:30 a.m. ET. The live webcast, including audio and presentation slides, will be accessible at the time of the meeting and can be [accessed here](#). To participate in the conference call by phone, please dial (877) 870 4263 (domestic) or (412) 317 0790 (international) and ask to join the Trevi Therapeutics call. No code is necessary for access. An archived replay of the webcast will also be available for 30 days on the Company's website following the event.

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 refractory chronic cough (RCC). Haduvio acts on the cough reflex arc both centrally and peripherally as a kappa agonist and a mu antagonist (KAMA), which are opioid receptors that play a key role in controlling cough hypersensitivity. Nalbuphine is not currently scheduled by the U.S. Drug Enforcement Agency.

Chronic cough is highly prevalent in IPF patients, impacting up to 85% of the IPF population. There are ~140,000 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 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 with respect to clinical trials and clinical data, 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 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, as well as other risks and uncertainties set forth in Trevi's quarterly report on Form 10-Q for the quarter ended September 30, 2024 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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