

Trevi Therapeutics Announces Positive Topline Results from the Phase 2b CORAL Trial of Haduvio in Patients with Idiopathic Pulmonary Fibrosis Chronic Cough

June 2, 2025

Haduvio met the primary endpoint with statistically-significant reductions in 24-hour cough frequency across all dose groups (108 mg BID $p<0.0001$; 54 mg BID $p<0.01$); a -43.3% placebo-adjusted change from Baseline was achieved at the 108 mg BID dose group

Patients saw a rapid reduction in 24-hour cough frequency at Week 2, the first time point measured

Haduvio was generally well-tolerated at all doses; discontinuation rates due to adverse events were similar in the Haduvio and placebo groups, 5.6% and 5.0%, respectively

Trevi plans to request an End-of-Phase 2 meeting with the FDA later this year and is planning to initiate the Phase 3 program in the first half of 2026

Company to host a conference call and webcast today at 8:30 a.m. ET and will be joined by the study's UK Lead Investigator, Professor Philip Molyneaux

NEW HAVEN, Conn., June 2, 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), is pleased to announce today positive topline results from its Phase 2b CORAL trial of Haduvio for the treatment of chronic cough in patients with IPF (N=165). The primary endpoint in the CORAL trial was achieved, demonstrating statistically significant reductions in 24-hour cough frequency across all dose groups at Week 6. The 108 mg BID, 54 mg BID and 27 mg BID dose groups achieved reductions from Baseline of 60.2% ($p<0.0001$), 53.4% ($p<0.0001$), and 47.9% ($p<0.01$), respectively, compared to a placebo reduction from Baseline of 16.9%¹. Statistically significant improvements were observed across secondary endpoints at Week 6 in the 108 mg BID and 54 mg BID dose groups.

"The CORAL trial is the first positive Phase 2b parallel group study for the treatment of chronic cough in patients with IPF, a significant milestone for patients and Trevi," said Jennifer Good, President and CEO of Trevi Therapeutics. "Chronic cough is one of the most debilitating comorbidities for patients with IPF, impacting an estimated 85% of these patients. There are no approved therapies for chronic cough in this population and with these data, Trevi is one step closer to addressing this unmet need."

"In my patients with IPF, chronic cough is one of the most challenging comorbidities I face clinically," said Philip Molyneaux, MD, Professor of Pulmonary Medicine at the Royal Brompton Hospital, London. "IPF treatments focus on slowing disease progression but have not shown benefit on chronic cough, which can lead to poor health outcomes and quality of life. I am excited about the CORAL data and the potential continued development of nalbuphine ER for this significant unmet need among IPF patients."

Primary Endpoint – Relative Change from Baseline in 24-hour Cough Frequency (coughs per hour) at Week 6

	Placebo ¹ (N=39)	Haduvio 27 mg BID (N=42)	Haduvio 54 mg BID (N=43)	Haduvio 108 mg BID (N=40)
Baseline 24-hour Cough Frequency (coughs/hour)	29.4	24.6	28.0	31.5
Relative Change from Baseline in 24-hour Cough Frequency at Week 6	-16.9 %	-47.9% ($p<0.01$)	-53.4% ($p<0.0001$)	-60.2% ($p<0.0001$)
Placebo-adjusted difference	-	-30.9 %	-36.5 %	-43.3 %

¹One placebo patient with an extreme outlier value at Week 6 was excluded from the modified intent-to-treat (mITT) population. Inclusion of the patient in the placebo group would have resulted in an increased cough frequency from Baseline in the placebo group and much greater placebo-adjusted differences.

The primary efficacy endpoint was the relative change in objective 24-hour cough frequency (coughs per hour) for the mITT population at the end of Week 6 versus Baseline for Haduvio compared to placebo. The mITT population consists of all randomized patients who received at least one dose of study drug or placebo.

Additional Trial Results

- A rapid reduction was seen in 24-hour cough frequency at Week 2 with Haduvio, the first time point measured.

- A 50% reduction in 24-hour cough frequency at Week 6 vs Baseline was seen in 65% of patients on 108 mg BID Haduvio ($p<0.001$), 63% of patients on 54 mg BID Haduvio ($p<0.001$) and 60% of patients on 27 mg BID Haduvio ($p<0.001$) dose groups, compared to 19% of placebo patients.
- A statistically-significant response was observed on the cough-severity numerical rating scale (CS-NRS), a secondary endpoint, at Week 6 on Haduvio in both the 108 mg BID and 54 mg BID dose groups. There was a mean reduction on a 0 – 10 scale of 3.0 points on the 108 mg BID ($p<0.05$), 3.2 points on the 54 mg BID ($p<0.01$) and 2.0 points on the 27 mg BID ($p=0.46$) dose groups compared to a 1.5-point reduction on placebo at Week 6.
- The 108 mg BID and 54 mg BID dose groups were statistically-significant ($p<0.01$) on the patient-reported outcome E-RS@: IPF Cough Subscale, a secondary endpoint, with mean relative change from Baseline of -42.4% and -43.1%, respectively at Week 6, compared to -23% for those on placebo at Week 6. The 27 mg BID dose group was not statistically-significant with a mean relative change from Baseline of -31.6%.

Discontinuation rates due to adverse events were similar in the combined Haduvio groups (5.6%) and placebo group (5.0%). The safety profile observed in the trial was generally consistent with the known safety profile of Haduvio from previous trials. The most common adverse events experienced included: nausea, vomiting, constipation, dizziness, headache, fatigue, somnolence, and dry mouth. Serious adverse events (all non-fatal) were reported for four patients (10.0%) in the placebo group and for two patients (1.6%) across all Haduvio doses combined.

James Cassella, Ph.D., Chief Development Officer of Trevi Therapeutics added, "We are very pleased with the findings from the CORAL trial, which continue to demonstrate the robust cough suppressant activity of nalbuphine ER. The study has provided critical dose-ranging data to inform the planning of our Phase 3 program. We intend to request an End-of-Phase 2 meeting with the FDA to discuss our plans for initiating the Phase 3 program for the treatment of chronic cough in patients with IPF. I would like to take the opportunity to thank the patients, investigators and site staff for moving research forward for these patients. We look forward to advancing development of this program."

Conference Call/Webcast

The Company will host a conference call and webcast to review the topline results today, June 2nd, 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 live 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 the CORAL Trial

The Phase 2b **Cough Reduction in IPF with Nalbuphine ER (CORAL)** trial was a double-blind, randomized, placebo-controlled, parallel-arm trial evaluating three doses of Haduvio (27 mg, 54 mg, and 108 mg twice daily) compared to placebo for the treatment of chronic cough in patients with IPF over a 6-week treatment period. 165 patients with IPF chronic cough were randomized 1:1:1:1 to one of three Haduvio doses or placebo with an initial 2-week titration period to the target dose followed by 4 weeks of fixed dosing. The primary efficacy endpoint for the trial was the relative change in 24-hour cough frequency (coughs per hour), as determined by an objective cough monitor, for the modified intent-to-treat (mITT) population at the end of Week 6 versus Baseline for Haduvio compared to placebo. The mITT population consisted of all patients who were randomized and received at least one dose of study drug or placebo.

About Idiopathic Pulmonary Fibrosis (IPF) Chronic Cough

Chronic cough is a highly prevalent condition in patients with IPF, impacting up to 85% of the IPF population. There are ~140,000 patients in the U.S. with IPF. 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.

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 of patients with IPF chronic cough and in patients with RCC. 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.

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 and timing 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 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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²Evaluating Respiratory Symptoms in Idiopathic Pulmonary Fibrosis as collected in the EXACT® (EXAcerbation of Chronic pulmonary disease Tool). EXACT© 2013, Evidera, Inc. All rights reserved.

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