

Trevi Therapeutics Announces Positive Topline Results from Human Abuse Potential Study of Oral Nalbuphine

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Statistically significant lower "Drug Liking" for the 81mg and 162mg doses of oral nalbuphine vs. butorphanol covering our clinical dose range

Company to host a conference call and webcast today at 5:00 p.m. ET

NEW HAVEN, Conn., Dec. 3, 2024 /PRNewswire/ -- [Trevi Therapeutics, Inc.](#) (Nasdaq: TRVI), a clinical-stage biopharmaceutical company developing the investigational therapy Haduvio™ (oral nalbuphine ER) for the treatment of patients with chronic cough in idiopathic pulmonary fibrosis (IPF) and refractory chronic cough (RCC), today announced positive results from the human abuse potential (HAP) study of oral nalbuphine.

The HAP study was a randomized, double-blind, double-dummy, active and placebo controlled five-way crossover study in recreational drug users. The study's primary endpoint was the peak effect (E_{max}) for "Drug Liking" ("at this moment"), assessed on a bi-polar, 100-point visual analog scale (VAS). The VAS scale for this endpoint ranges from strong disliking (0) – to neither like nor dislike (50) – to strong liking (100). Oral nalbuphine was analyzed across three different doses (ranging from a low dose to a suprathreshold dose) for its "Drug Liking" compared to the active comparator, intravenous (IV) butorphanol, and placebo. Topline results demonstrated a statistically significant lower "Drug Liking" for the clinical doses of oral nalbuphine (81mg and 162mg) compared to 6mg IV butorphanol. The suprathreshold dose of oral nalbuphine (486mg) was numerically lower than the 6mg IV butorphanol for "Drug Liking" but the results were not statistically significant.

Primary Endpoint*

	Placebo (N=52)	IV butorphanol 6mg (N=52)	Oral nalbuphine 81mg (N=52)	Oral nalbuphine 162mg (N=52)	Oral nalbuphine 486mg (N=52)
Mean E_{max} for "Drug Liking"	51.8	82.3	71.2	74.5	81.1
P-value for difference vs butorphanol 6mg IV	p<0.0001	-	p<0.0001	p=0.0008	p=0.3221

*All analyses performed were on the Modified Completer Population, which was prespecified in the statistical analysis plan for the primary endpoint.

Secondary Endpoints

	Placebo (N=52)	IV butorphanol 6mg (N=52)	Oral nalbuphine 81mg (N=52)	Oral nalbuphine 162mg (N=52)	Oral nalbuphine 486mg (N=52)
Mean E_{max} for "Take Drug Again"	53.4	62.8	71.0	67.3	64.2
Mean E_{max} for "I Feel High"	3.4	77.6	35.6	39.3	59.2
Mean E_{max} for "I Feel Good"	2.7	71.9	40.3	40.8	61.0

Secondary endpoints included pharmacodynamic markers and patient reported outcomes, which were generally consistent with the primary endpoint. No serious adverse events were reported in the study.

"We're very pleased with our study results," said James Cassella, Ph.D., Chief Development Officer of Trevi Therapeutics. "The positive butorphanol drug liking effect versus placebo demonstrates the validity and robustness of our study design. Our clinical program has studied doses ranging from 27mg to 162mg and we believe these results are consistent with the known profile of nalbuphine. We look forward to reporting data from our two ongoing chronic cough studies in IPF and RCC, two conditions where patients continue to have a significant unmet need."

[Jack Henningfield](#), Ph.D., Vice President, Research, Health Policy and Abuse Liability at Pinney Associates added, "Nalbuphine is currently unscheduled in the U.S. and has been for several decades. It has remained unscheduled because of its years of experience with little evidence of diversion, abuse, or contribution to overdose deaths. This experience, coupled with these HAP results, continues to support the conclusion that nalbuphine extended-release has potential to address an important health need without the public safety risks posed by the opioids that are often prescribed for chronic cough."

The results of the HAP study will be included in the 8-factor analysis of the abuse potential of nalbuphine for nalbuphine ER that would be submitted as part of any new drug application (NDA) submission to inform scheduling considerations.

The Company will host a conference call and webcast to review the topline results today, December 3rd, at 5:00 p.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 the Human Abuse Potential Study for Oral Nalbuphine

The HAP study was conducted in two parts. The first part of the study characterized various IV butorphanol doses in order to select a dose to be studied as the comparator. The second part of the HAP study being reported in this release was a randomized, double-blind, double-dummy, active and placebo-controlled five-way crossover study. The U.S. Food and Drug Administration, or FDA, agreed to the comparator (butorphanol), comparator route of administration (IV to mimic intranasal exposure), comparator dose (6mg), and nalbuphine doses. This study compared the likeability of three doses of oral nalbuphine with 6mg of IV butorphanol using various drug-liking scales, including the primary endpoint, which measured the peak effect for "Drug Liking" assessed using a bi-polar visual analog scale. Safety and physiological measures, pharmacokinetic data, and abuse-related adverse events were also evaluated.

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 among approximately 140,000 IPF patients in the U.S., with up to 85% of IPF patients experiencing chronic cough. The impact of chronic cough is significant with some IPF patients coughing up to 1,500 times per day and 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 IPF and current off-label treatment options provide minimal benefit to patients.

Refractory chronic cough affects approximately 2-3 million adults in the U.S. and is caused by cough reflex hypersensitivity in both 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 burdens for patients and those around them. Haduvio is being developed for the treatment of moderate to severe RCC. There are also no approved therapies for RCC in the U.S.

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, expectations regarding the abuse potential of Haduvio, 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, 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 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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