Trevi Therapeutics Reports Positive Results from the Ph2b/3 PRISM Trial of Haduvio™ in the Treatment of Prurigo Nodularis

Haduvio (oral nalbuphine ER) demonstrated statistically significant results on the primary efficacy endpoint as measured by a 4-point reduction in the Worst Itch – Numerical Rating Scale (WI-NRS) (p=0.0157)

The trial also met key secondary endpoints, with a safety profile consistent with prior studies

Topline data will be presented by management and study investigator, Jennifer L Parish, MD, on a conference call and webcast on June 29, 2022, at 8:30 am EDT

NEW HAVEN, Conn., June 29, 2022 /PRNewswire/ -- Trevi Therapeutics, Inc. (Nasdaq: TRVI), a clinical-stage biopharmaceutical company developing an investigational therapy Haduvio™ (oral nalbuphine ER) for prurigo nodularis and chronic cough in idiopathic pulmonary fibrosis (IPF), today announced positive results from its Phase 2b/3 **P**ruritus **R**elief through **I**tch-**S**cratch **M**odulation (PRISM) trial of Haduvio in treating prurigo nodularis.

Trevi Therapeutics Ph2b/3 PRISM trial of Haduvio achieves statistical significance for the treatment of Prurigo Nodularis

"We are very pleased to announce the statistically significant results for Haduvio from the PRISM trial, the first and only oral therapy to demonstrate in a clinical trial a positive result in treating prurigo nodularis," said Jennifer Good, President and CEO of Trevi Therapeutics. "This positive trial in prurigo nodularis, along with the highly statistically significant data from the interim analysis of our Phase 2 trial in IPF chronic cough that we presented earlier this year, further supports our belief that Haduvio could potentially benefit patients across a broad range of refractory chronic pruritic and cough conditions."

Prurigo nodularis is a chronic disease characterized by severe pruritus and the presence of nodules, lesions, and excoriations. Chronic pruritus is a key contributing cause of prurigo nodularis and manifests in an itch-scratch cycle, which is difficult to disrupt. There are no approved therapies for prurigo nodularis where a large unmet need exists due to its impact on patients' quality of life, function, and emotional well-being.

"Prurigo nodularis is one of the most challenging dermatologic diseases for clinicians to manage," said Jennifer L Parish, MD, Dermatologist at Parish Dermatology and study investigator for the PRISM trial. "Patients suffer not only from the itching and the resulting excoriations, but many also suffer from anxiety often caused by the lack of effective treatments. It is exciting to see therapeutic options in development for this potentially devastating condition."

In the Phase 2b/3 PRISM trial, results comparing subjects randomized to Haduvio monotherapy (n=168) or placebo (n=176) showed:

- 25% of Haduvio subjects evaluated at week 14 met the primary endpoint of a 4-point reduction in WI-NRS from baseline compared to 14% of placebo subjects (p=0.0157).
- Haduvio subjects experienced significantly greater improvements in ItchyQoL vs. placebo (p=0.0002) at week 14, which was statistically significant across each of the three domains (symptoms, functional limitations, and emotions). ItchyQoL is used to measure how pruritus impacts a subject's quality-of-life.
- 55% of Haduvio subjects saw at least a 1-category improvement in the 5-point scale in their Prurigo Activity Scale (PAS) (pruriginous lesions with excoriations), vs. 38% on placebo (p=0.006) as evaluated at week 14.

"In this study, Haduvio demonstrated an early onset of effect to reduce itch, which we believe improved quality of life for the patient as well as the underlying skin healing," said Dr. Bill Forbes, Chief Development Officer at Trevi Therapeutics. "We believe the ability of Haduvio to work both centrally and peripherally helps to break the ingrained itch-scratch cycle, which leads to the difficulty in treating prurigo nodularis. We look forward to analyzing these data further, along with the open label extension data, to help inform continued development in this area of high unmet need."

The safety results of the trial were generally consistent with the known safety profile of Haduvio from previous trials. During the double-blind titration period (weeks 1-2) Treatment-Emergent Adverse Events (TEAE) were more common in the Haduvio-treated subjects (66.1%) vs. placebo-treated subjects (31.3%). During the 12-

week fixed-dose period, the occurrence of TEAEs were generally similar between Haduvio and placebo groups (48% Haduvio, 45% placebo). Discontinuations during the 14 weeks of the trial were 36.9% in Haduvio-treated subjects vs. 19.3% in placebo-treated subjects. During the 14-week double-blind portion of the PRISM trial, 8 subjects on Haduvio and 6 subjects on placebo experienced at least one treatment emergent Serious Adverse Event (SAE). None of the SAEs were considered by the investigator to be treatment-related. Adverse events most commonly observed with Haduvio were nausea, dizziness, headache, and constipation.

Conference Call Details
To participate in the live conference call by phone, please dial (888) 317 6003 (domestic) or (412) 317 6061 (international) and provide access code 8601030. A live audio webcast and presentation will be accessible from the 'Investors & News' section on the Company's website at www.trevitherapeutics.com. An archived replay of the webcast and the presentation will also be available for 60 days on the Company's website following the event.

About PRISM
The Phase 2b/3 **P**ruritus **R**elief through **I**tch **S**cratch-**M**odulation (PRISM) trial is a randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of Haduvio in prurigo nodularis. In the trial, subjects are randomized equally across two treatment groups (oral Haduvio 162 mg or placebo, twice daily including an initial 2-week blinded titration period). The primary endpoint of the trial is the proportion of subjects achieving a greater than or equal to 4-point improvement in the weekly mean Worst Itch Numerical Rating Scale (WI-NRS) score at Week 14 compared to baseline. Subjects that complete week 14 are eligible to roll into an additional 38-week open label extension trial. More information about the PRISM trial is available at www.clinicaltrials.gov: NCT03497975

About Trevi Therapeutics, Inc.
Trevi Therapeutics, Inc. is a clinical-stage biopharmaceutical company focused on the development and commercialization of the investigational therapy Haduvio for the treatment of prurigo nodularis and chronic cough in adults with idiopathic pulmonary fibrosis. These conditions share a common pathophysiology that is mediated through opioid receptors in the central and peripheral nervous systems.

Founded in 2011, Trevi Therapeutics is headquartered in New Haven, CT.

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 known to be critical mediators of itch, cough 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. Nalbuphine ER has been granted Fast Track designation by the FDA for the proposed indication of reduction of moderate to severe pruritus in adults with prurigo nodularis. 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, Trevi's business plans and objectives, including future plans or expectations for Trevi's product candidates; 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 our clinical trials and next steps in the development path for Trevi's product candidates in the United States and foreign countries; uncertainties regarding fast track designation and the effect such status could have on the regulatory review or approval process; 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 March 31, 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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