Trevi Therapeutics Announces Positive Results from Phase 2/3 Trial in Uremic Pruritus

Oral Nalbuphine ER trial achieved statistically significant results on the primary endpoint of reducing itch intensity and also demonstrated sustained duration of effect

New Haven, CT, September 10, 2015 – Trevi Therapeutics, Inc. ("Trevi" or the "Company"), a late-stage clinical development company developing oral Nalbuphine ER for chronic pruritus conditions, today announced statistically significant results from its Phase 2/3 trial for the treatment of moderate to severe uremic pruritus. Uremic pruritus is a persistent and debilitating itch in patients on dialysis that has been associated with increased mortality, and currently has no approved therapies in the United States or Europe. Nalbuphine ER has a dual mechanism of action, as it is a mu receptor antagonist and kappa receptor agonist, and both mechanisms have been separately shown to be effective in abolishing itch.

The multi-center, randomized, double-blind, placebo-controlled, parallel, three-arm study evaluated the safety and anti-pruritic efficacy of Nalbuphine ER tablets dosed twice-daily at 60mg and 120mg in approximately 370 patients on hemodialysis in the United States and Europe. Patients with a wide range of mean moderate-to-severe itch intensity, ranging from 4.5 to 10 on the ten-point Numerical Rating Score (NRS) scale, were enrolled to evaluate efficacy across a representative patient population for this chronic indication.

The study consisted of a titration period of two weeks, followed by a six-week blinded period on a fixed dose of drug or placebo and a wash-out period. At the end of the wash-out period, patients were eligible to roll over into a six-month open label extension study. The Company expects the open label extension study to be completed by year-end.

Patients receiving 120 mg of Nalbuphine ER (n=120) experienced a 3.5 point reduction in itch intensity from baseline, resulting in a highly statistically significant mean reduction in itch intensity as compared to placebo (p-value = 0.017). A statistically significant mean reduction for Nalbuphine ER compared to placebo was observed as early as one week following titration to the Nalbuphine ER fixed dose, and there was a statistically significant separation from placebo throughout the remaining blinded period. Sustained duration of drug effect continued to trend away from placebo through the 8th week of the study. On average, patients entered the study with a baseline mean NRS itch score of 6.9 (just under severe NRS score of 7), and at the end of the 8 week dosing period, average itch scores had been reduced to an NRS score of 3.4, which is considered mild on the NRS scale. Severe itch patients (those with NRS scores greater than or equal to 7) experienced on average an NRS score reduction of 4.5 points from baseline, (p-value=0.007). The 60 mg dose showed a numerically favorable reduction over placebo, but did not achieve statistical significance.

The secondary endpoints, the Skindex-10 Disease Domain and the Itch MOS Sleep index, provided confirmatory evidence of a favorable Nalbuphine ER effect on itching compared to placebo.

Only one serious adverse event was attributed to the drug in the study, with the most common adverse events being nausea, vomiting, dizziness and somnolence. However, the rates of these events quickly resolved and were approaching placebo rates after the first week of titration. Because of the challenging nature of the patient population, the company elected to put in place a Data Safety Monitoring Board ("DSMB") to oversee the safety of the study. The DSMB raised no issues that affected the continuation of the study.

Jennifer L. Good, Trevi's President and Chief Executive Officer, said, "We are pleased with the results of this robust trial. We studied drug effect over eight weeks of dosing at sites in both the U.S. and Europe, and demonstrated statistically significant results on the primary, protocol-specified endpoint: reduction in worst itch severity as recorded by NRS score. We believe Nalbuphine ER may be useful broadly in itch conditions, and look forward to the results from our ongoing Phase 2/3 trial in prurigo nodularis, which will report out in the first half of next year. "

Thomas R. Sciascia, M.D., Trevi's Chief Medical Officer, said, "This is a difficult patient population to study over an extended period of time because of multiple co-morbidities. There was strong patient and physician interest in both the blinded portion of the study as well as the ongoing six-month open label extension trial. We look forward to a discussion with both the FDA and the European Medicines Agency about next steps in our program."

About Trevi Therapeutics, Inc.

Trevi Therapeutics, Inc. is a late-stage clinical development company focused on developing Nalbuphine ER for chronic pruritus (itch). Pruritus develops in various dermatologic, metabolic, hematologic and neuropathic conditions. The Company is pursuing two conditions for clinical development: uremic pruritus and prurigo nodularis. Uremic pruritus is a persistent and debilitating itch in patients on dialysis that has been associated with increased mortality. Prurigo nodularis is a chronic dermatologic condition characterized by severely pruritic nodules on the skin that are independent of underlying etiology. There are no approved therapies in the U.S. or EU for either condition.

Nalbuphine ER is an oral extended release opioid with a dual mechanism of action, mu receptor antagonist and kappa receptor agonist, both of which have been shown in research to be effective in abolishing itch. Because of Nalbuphine ER's unique dual mechanism of action, which has shown efficacy in addressing pruritus in both animal studies and human clinical trials, the Company believes it can have broad utility in treating chronic pruritus.

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

For additional information, visit www.trevitherapeutics.com.
