Impel NeuroPharma Announces Publication of Pivotal Phase 3, Open-Label Stop 301 Study of INP104 (TRUDHESA™) for Treatment of Acute Migraine in the Journal Headache

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Study Shows TRUDHESA ™Was Well Tolerated and Delivered Rapid, Consistent Symptom Relief

Exploratory Patient-Reported Outcomes Data Indicated More Than One Third of Patients Experienced Pain Freedom and Two Thirds Had Pain Relief Two Hours Following TRUDHESA ™Administration

Among the 38 Percent of Patients Who Self-Reported Two-Hour Pain Freedom for Their First TRUDHESA™- Treated Attack, only 7.1 Percent and 14.3 Percent of Patients Reported Recurrence of Migraine at 24 and 48 hours post TRUDHESA™ Administration, Respectively

The U.S. FDA Has Accepted TRUDHESA ™for Review with a Target PDUFA Date of September 6, 2021

SEATTLE, Aug. 09, 2021 (GLOBE NEWSWIRE) -- Impel NeuroPharma (NASDAQ: IMPL), a late-stage biopharmaceutical company focused on the development and commercialization of transformative therapies for patients living with central nervous system (CNS) diseases who have high unmet medical needs, announced today that its pivotal Phase 3, open-label study, STOP 301, was published in the August 7, 2021 edition of *Headache: The Journal of Head and Face Pain*, the official journal of the American Headache Society. TRUDHESA™ (INP104) is dihydroergotamine mesylate (DHE) delivered directly into the vascular-rich upper nasal space using Impel's proprietary Precision Olfactory Delivery (POD®) technology for the treatment of acute migraine.

"We are proud to announce the publication of our pivotal data, which further reinforce the potential for TRUDHESA to be a differentiated, well-tolerated treatment that, subject to approval by the FDA, has the potential to deliver rapid and reliable symptom relief for patients with acute migraine," said Stephen Shrewsbury, M.D., Chief Medical Officer at Impel NeuroPharma. "We were particularly pleased to see that most patients reported that TRUDHESA was easy to use, and allowed them to return to normal activities of daily living faster compared with their previous treatment."

The publication, which can be found here, addresses the STOP 301 trial, which is an open-label study with the primary objective of assessing the long-term safety and tolerability of TRUDHESA in the acute treatment of migraine, with a specific focus on nasal mucosa and olfactory function. Exploratory objectives included efficacy assessments of migraine measures and a patient acceptability questionnaire.

"I am pleased to see pivotal data demonstrating that INP104 was both safe and tolerable with long-term use. This is welcome and important news to people living with migraine who have experienced inadequate relief with existing therapies and the physicians who treat them who are in need of new options," said Tim Smith, M.D., RPh, FACP, AQH, First Vice President, The National Headache Foundation, STOP 301 Principal Investigator and lead author of the publication. "Right now, there is a critical need for non-oral treatment options in particular because many patients living with migraine also have related gastrointestinal disorders and are often unable to achieve relief with oral routes of administration."

The New Drug Application (NDA) for INP104 was accepted for review by the U.S. Food and Drug Administration (FDA) in January 2021 and has a Prescription Drug User Fee Act (PDUFA) target action date of September 6, 2021. The FDA has conditionally accepted a trade name of TRUDHESA.

If approved by the FDA, TRUDHESA will become the first and only therapy to deliver DHE to the vascular-rich upper nasal space using the POD technology, a novel delivery system. Many current nasal delivery technologies – sprays, droppers, and pumps – may deliver less than five percent of the active drug to the upper nasal space.[1]

About STOP 301: [2]
STOP 301 is a pivotal Phase 3 open-label study that evaluated the safety, tolerability, exploratory efficacy, and patient acceptability of INP104 (TRUDHESA™). After a 28-day screening period—where patients kept a daily diary and were being treated with their established 'best' usual care—patients were given TRUDHESA to treat self-recognized migraine attacks.

The trial enrolled 360 patients at 36 sites in the United States who had a documented diagnosis of migraine with or without aura, with at least two attacks per month for the previous six months. In the trial, 354 patients received at least one dose of TRUDHESA and comprised the 24-week Full Safety Set. The Primary Safety Set was comprised of 185 patients who took an average of two or more treatments with TRUDHESA per 28-day period during the 24-week treatment period. During the 24-week study, 4,515 self-reported migraine attacks were treated with TRUDHESA. The study evaluated 6,332 doses of TRUDHESA over the full 52 weeks.

In the study, TRUDHESA exhibited a well-tolerated safety profile throughout the initial 24-week treatment period and the full 52-week treatment period, with no serious adverse events (AEs) related to study treatment reported. TRUDHESA-related treatment-emergent AEs were reported by 36.7 percent of patients, and 6.8 percent discontinued treatment due to AEs over 24 weeks. No new safety signals, including cardiovascular (CV) safety signals, were observed following treatment, though patients with a history of CV disease were excluded from the study. A Nasal Safety Review Committee reviewed the nasal safety data and suggested TRUDHESA may be safe and tolerable on the nasal mucosa. In addition, nausea—which is typically observed in intravenous (IV) formulations of DHE—was reported by 6.8 percent of patients.

The study also assessed patient-reported exploratory efficacy using patients' best usual care at baseline compared to TRUDHESA-treated attacks over 24 and 52 weeks. Pain freedom, the most bothersome symptom freedom, and pain relief at 2 hours post-TRUDHESA were self-reported in an eDiary, with almost half of patients reporting pain relief at one hour following INP104 administration, and efficacy of TRUDHESA was similar if patients

administered within 2 hours of migraine initiation or beyond. A low recurrence rate at 24 and 48 hours was also observed. Furthermore, there was a low rate of treatment discontinuation, with 74 percent of patients completing the 24-week period. Of those who completed 24 weeks, 73 entered the 28-week extension, and of those, 90.4 percent completed the study. The study found that 98 percent of patients with pain freedom had sustained pain freedom through 24 hours and 95 percent through 48 hours. Additionally, of the 38 percent of patients who self-reported two-hour pain freedom for their first TRUDHESA-treated attack, only 7.1 percent and 14.3 percent of patients self-reported recurrence of migraine at 24 and 48 hours post-TRUDHESA administration, respectively.

Exploratory endpoints included a patient acceptability questionnaire (PAQ) assessing the patient's impression of TRUDHESA usability and effectiveness. Most patients reported TRUDHESA was easy to use, and patients also reported faster and more consistent onset of effect with TRUDHESA than with their previous best usual care treatment. Compared with their previous treatment, the majority of patients reported that TRUDHESA kept their migraine from coming back for a longer time and allowed them to return to normal activities of daily living faster.

About Precision Olfactory Delivery Technology:
Impel's proprietary Precision Olfactory Delivery (POD®) technology is able to deliver a range of therapeutic molecules and formulations into the vascular-rich upper nasal space, believed to be a gateway for unlocking the previously unrealized full potential of these molecules. By delivering predictable doses of drug directly to the upper nasal space, Impel's precision performance technology has the goal of enabling increased and consistent absorption of drug, overriding the high variability associated with other nasal delivery systems, yet without the need for an injection. While an ideal target for drug administration, to date no technology has been able to consistently deliver drugs to the upper nasal space. By utilizing this route of administration, Impel NeuroPharma has been able to demonstrate blood concentration levels for its investigational therapies that are comparable to intramuscular (IM) administration and can even reach intravenous (IV)-like systemic levels quickly, which could transform the treatment landscape for CNS and other disorders. Importantly, the POD technology offers propellant-enabled delivery of dry powder and liquid formulations that eliminates the need for coordination of breathing, allowing for self- or caregiver-administration in a manner that may improve patient outcome, comfort, and potentially, compliance.

About Migraine and About the Acute Treatment of Migraine:
Migraine is a common and debilitating neurological disease characterized by recurrent episodes of severe head pain and associated with nausea, vomiting and sensitivity to light and sound.[3] Migraine affects approximately 36 million people in the United States.[4] Of the approximately 18 million diagnosed migraine patients, only four million are on prescription treatment.[5] While triptans account for almost 80 percent of migraine therapies, approximately 30 to 40 percent of patients do not respond adequately to triptans and up to 79 percent of the patients who do respond to triptans report being dissatisfied with their current treatment and willing to try a new therapy.[6,7,8] Further, evidence suggests that gastroparesis, delayed emptying of the stomach, is a prevalent feature in migraine that may delay or reduce the absorption of oral medications, including triptans, gepants and ditans. This means that acute medications can remain in the stomach for hours, delaying symptom relief, leading to loss of confidence (about future administration) and prolonged suffering for the current migraine attack.[9]

About TRUDHESA™:
Impel NeuroPharma is developing TRUDHESA with the goal to be a transformative new therapy for the acute treatment of migraine headaches. TRUDHESA aims to optimize dihydroergotamine mesylate (DHE) for fast and lasting whole migraine relief, regardless of when in the migraine attack it is administered, without an injection. Importantly, TRUDHESA is designed to deliver a lower dose of DHE compared to other nasally administered, FDA-approved and investigational products. This may enable patients to benefit from the established efficacy of DHE, without the undesired side effects that may be experienced with delivery to the lower nasal space.

TRUDHESA utilizes Impel’s propellant-enabled POD technology to conveniently and consistently deliver optimal doses of DHE deep into the vascular rich upper nasal space, an ideal target for efficient drug administration. This may be particularly important for the majority of patients with migraine who experience nausea and/or vomiting during an attack, which presents limitations for the use of oral therapies, including triptans, CGRP inhibitors and ditans as well as other non-specific medications used for the acute treatment of migraine.

About Impel NeuroPharma:
Impel NeuroPharma, Inc. is a late-stage pharmaceutical company focused on utilizing its proprietary technology to develop and commercialize transformative therapies for people suffering from diseases with high unmet needs, with an initial focus on diseases of the CNS. The Company's strategy is to rapidly advance its product candidate pipeline that pairs its proprietary Precision Olfactory Delivery (POD®) system with well-established therapeutics, including INP104 for the acute treatment of migraine, INP105 for the acute treatment of agitation in patients with autism, and INP107 for OFF episodes in Parkinson’s disease.

Cautionary Note on Forward-Looking Statements
This press release contains “forward-looking” statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, including, but not limited to, timing of approval of Impel’s NDA for INP104 (proposed trade name TRUDHESA™) and of Impel’s other regulatory submissions, timing of announcements of clinical results and clinical development activities of its product candidates, potential benefits and market opportunities of INP104 and its other product candidates and its cash runway. Forward-looking statements can be identified by words such as: “believe,” “may,” “will,” “potentially,” “estimate,” “continue,” “anticipate,” “intend,” “could,” “would,” “project,” “plan,” “expect” or the negative or plural of these words or similar expressions. These statements are subject to numerous risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including but not limited to, Impel’s ability to obtain and maintain regulatory approval of INP104 and its other product candidates, its ability to execute its commercialization strategy for INP104 its ability to develop, manufacture and commercialize its product candidates including plans for future development of its POD devices and plans to address additional indications for which Impel may pursue regulatory approval, whether results of preclinical studies or clinical trials will be indicative of the results of future trials, and the effects of COVID-19 on its clinical programs and business operations. Many of these risks are described in greater detail in Impel’s filings with the Securities and Exchange Commission. Any forward-looking statements in this press release speak only as of the date of this press release. Impel assumes no obligation to update forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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