Impel NeuroPharma presents data from INP104 clinical program in acute migraine at the 2020 American Headache Society (AHS) virtual annual scientific meeting

Four Scientific Poster Presentations Support the Potential of INP104 to Fulfill Key Unmet Needs and If Approved, Become a Transformative New Therapeutic Option for Acute Migraine

Additional Data from STOP 301, the Company’s Pivotal Phase 3 Study of INP104 for Acute Migraine, Found Majority of Patients Reported INP104 Easy to Use and Preferred Over Current Acute Therapy

Impel NeuroPharma Plans to Submit a New Drug Application (NDA) in the Second Half of 2020

SEATTLE, June 15, 2020 — Impel NeuroPharma, a late-stage biopharmaceutical company focused on the development and commercialization of transformative therapies for patients living with central nervous system (CNS) disorders with high unmet medical needs, today announced that data for four scientific abstracts are being presented as part of the 2020 American Headache Society (AHS) Virtual Annual Scientific Meeting.

“Impel NeuroPharma is excited to present additional findings from our pivotal Phase 3 STOP 301 study, which further illustrates INP104’s potential to become an important new option for patients in the treatment of acute migraine,” said Stephen Shrewsbury, M.D., Chief Medical Officer of Impel. “In addition to the STOP-301 study meeting its primary safety objectives, the majority of participants reported at the end of 24 and 52 week periods that they found Impel’s proprietary POD® delivery device to be easy to use and carry, and allowed them to return to normal activities faster than previous acute medications. These insights, coupled with positive signals emerging from our exploratory efficacy analyses, suggest INP104 has the potential to become a valuable option in delivering the gold standard, DHE, for use at home by patients; especially for those who need whole migraine relief – regardless of when in the migraine attack it is administered – or those who need an alternative to oral therapy given the increased recognition of the link between migraine and gastrointestinal issues.”

The posters are available online and posters accompanied by audio presentations can be accessed on the AHS meeting website at: www.eventscribe.com/2020/AHSAnnual.

Poster Presentations:

- Patient Acceptability of a Novel Upper Nasal Delivery System for Dihydroergotamine Mesylate Using the Precision Olfactory Delivery (POD®) Device - Results From the Open-label STOP 301 Trial; Presenting Author: Stephen B. Shrewsbury, M.D., Chief Medical Officer, Impel NeuroPharma
  - Results suggest that delivery of DHE to the upper nasal space may provide an effective, consistent, and well-tolerated alternative to acute oral and injectable treatments for migraine, while providing the reliable efficacy, speed, and potency of the long-established DHE molecule.
• When Pills Don’t Work: Disorders of Gastric Motility in Migraine; Presenting Author: Linda Nguyen, M.D., Clinical Associate Professor, Medicine, Gastroenterology & Hepatology at Stanford University.
  o A review of the current state of scientific evidence that exists for linking migraine with disorders of gastric motility suggests this comorbidity is important for patients who experience gastrointestinal symptoms and do not have relief from migraine symptoms using an oral abortive treatment.

• Does Dihydroergotamine Treat the “Whole Migraine”?; Presenting Author: Sheena K. Aurora, M.D., Vice President, Medical Affairs – Migraine at Impel NeuroPharma.
  o Data from review of comparative pharmacology of acute treatments for migraine describe how DHE is able to exert a greater influence than single receptor agonists/antagonists over the pathophysiology of the migraine cycle due to its widespread pharmacological activity.

• Impact and Burden of Episodic, Acute Migraine (I-BEAM): A Patient Experience Study; Presenting Author: Stephen B. Shrewsbury, M.D., Chief Medical Officer, Impel NeuroPharma
  o This market research study further demonstrates the unmet needs of patients living with migraine, with respondents describing their ideal medication to be: (1) fast acting (15-30 mins) (2) long-lasting (12-24h) (3) providing complete or near complete relief (4) can be taken any time during the migraine and (5) with few/no side effects. Minor side effects are acceptable as a tradeoff for increased speed and efficacy.

Further analysis of STOP 301 data is ongoing and will be submitted for future publication or presentation. Impel NeuroPharma plans to submit a New Drug Application in the second half of 2020.

About STOP 301:
The Phase 3 STOP 301 study 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. 354 patients received at least one dose of INP104 and comprised the Full Safety Set. 185 patients who took an average of two or more treatments with INP104 per 28-day period during the 24-week treatment period comprised the Primary Safety Set. Of those enrolled, 74% (n=262) of patients completed the 24-week treatment period. Reasons for treatment discontinuation included withdrawal by subject (n=25 [7.1%]), AEs (n=24 [6.8%]), lack of efficacy (n=21 [5.9%]), lost to follow-up (n=11 [3.1%]), non-compliance/protocol violation (n=5 [1.4%]), and physician’s decision (n=1 [0.3%]). A subset of 73 patients continued into a 28-week treatment extension period to 52 weeks total, of which 90% completed.

About INP104:
Impel NeuroPharma is currently developing INP104 with the goal to be a transformative new therapy for acute migraine. INP104 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, INP104 is designed to deliver a lower dose of dihydroergotamine mesylate (DHE) compared to FDA-approved and investigational products in development via the nose. 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.
INP104 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, particularly 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 acute migraine medications.

**About Acute 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. Of the approximately 19 million diagnosed migraine patients, only four million are on prescription treatment. While triptans account for almost 70 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.

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.

**About Impel NeuroPharma:**
Impel NeuroPharma, Inc. is a privately held, Seattle-based biopharmaceutical company focused on developing transformative therapies for people living with central nervous system (CNS) disorders with high unmet medical needs. The Company is rapidly advancing a late-stage product pipeline that optimizes the effectiveness of proven treatments for neurological conditions, including INP-104 for acute migraine, INP-107 for OFF episodes in Parkinson’s disease, and INP-105 for acute agitation associated with schizophrenia, bipolar I disorder and autism.

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**About Precision Olfactory Delivery or POD® 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 enables increased and consistent absorption of drug, overriding the high variability associated with other nasal delivery systems.

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 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.

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iii Data on file
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