



## IMPEL NEUROPHARMA PRESENTS DATA FROM PIVOTAL PHASE 3 REGISTRATION STUDY OF INP104 FOR THE TREATMENT OF ACUTE MIGRAINE AT 2020 MIGRAINE TRUST VIRTUAL SYMPOSIUM

*66.3% of Patients Reported Pain Relief Within Two Hours of Treatment with Rapid Uptake via the Upper Nasal Space Resulting in Onset of Relief as Early as 15 Minutes for Some Patients*

*Data Suggest Use of Impel's Proprietary Precision Olfactory Delivery (POD®) Technology with DHE May Offer Convenience, Clinical Benefit for Acute Migraine Patients*

SEATTLE, October 8, 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 it has presented patient-reported outcomes data from the Company's pivotal Phase 3, open-label study "STOP 301" of INP104 (dihydroergotamine mesylate) or DHE using the company's proprietary POD technology, for the treatment of acute migraine in an oral presentation at the Migraine Trust Virtual Symposium (MTIS) to be held from October 3-9, 2020.

"Despite several recent approvals, there remains a significant need for acute treatments that provide early and sustained relief, are easy to use and well tolerated," said Stephen Shrewsbury, M.D., Chief Medical Officer at Impel NeuroPharma. "The response between the safety and efficacy results from STOP-301 combined with the patient-reported tolerability, acceptability and exploratory efficacy results are encouraging and provide further evidence that INP104, the first and only product designed to deliver DHE to the vascular-rich upper nasal space using our proprietary POD technology, may offer a promising treatment option for the acute treatment of migraine."

In the trial, 360 adult patients with migraine were enrolled in a 28-day screening period, during which they received "best usual care." Over a period of 24 weeks, patients were permitted to self-administer up to three doses of INP104 nasally per week (1.45 mg). Among participants, there were 4,515 reported migraines. Within two hours of receiving their first dose of INP104, 38% of all patients reported freedom from migraine pain, 52% had freedom from their most bothersome migraine symptom (MBS) and 66.3% experienced pain relief. About 84% of patients reported INP104 easy to use and preferred it over their current therapy.

Additionally, sustained pain freedom through 24 hours was also reported in the majority of patients with 98.4% of patients remaining relapse-free of their migraine after using INP104 for 24 weeks. The most common treatment-emergent adverse events (TEAEs) were nasal congestion (15.0%), nausea (6.8%), nasal discomfort and unpleasant taste (5.1% each) with all other TEAEs being reported by less than 3% of participants. There were no treatment related Serious AEs, cardiac TEAEs or deaths.

The oral presentation and additional INP104 posters accompanied by audio presentations can be accessed on the MTIS 2020 meeting website at: <https://virtual.mtis2020.org/>



- **Abstract 229:** A Long Term, Open Label Study of Safety and Tolerability of Precision Olfactory Delivery of DHE In Acute Migraine (Stop 301): Clinical Results; Presenting Author: Sheena Aurora, M.D., Vice President of Medical Affairs, Impel NeuroPharma
- **Abstract 230:** Patient Acceptability of a Novel Upper Nasal Delivery System for DHE – Using The Precision Olfactory Delivery (POD®) Device (INP104); Presenting Author: Stephen B. Shrewsbury, M.D., Chief Medical Officer, Impel NeuroPharma
- **Abstract 231:** Does Dihydroergotamine Treat The “Whole Migraine”? Presenting Author: Sheena Aurora, M.D., Vice President of Medical Affairs, Impel NeuroPharma
- **Abstract 232:** When Pills Do Not Work: Gastroparesis in Migraine; Presenting Author: Sheena Aurora, M.D., Vice President of Medical Affairs, Impel NeuroPharma

#### **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 of 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.<sup>i</sup> Migraine affects approximately 39 million people in the United States.<sup>ii</sup> Of the approximately 19 million diagnosed migraine



patients, only four million are on prescription treatment.<sup>iii</sup> 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.<sup>iv</sup>

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.<sup>v</sup>

#### **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 INP104 for acute migraine, INP107 for OFF episodes in Parkinson's disease, and INP105 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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<sup>i</sup> Mayo Clinic. [Migraine Symptoms & Causes](#). Last Accessed February 3, 2020.

<sup>ii</sup> Migraine Research Foundation. [Migraine Facts](#). Last Accessed February 3, 2020.

<sup>iii</sup> Data on file

<sup>iv</sup> Data on file

<sup>v</sup> Aurora S, et al. *Cephalalgia*. 2013; 33:408-415; Tokola RA et al. *Br J Clin Pharmacol*. 1984. 18:867-871; Volans GN. *Clin Pharmacokinet*. 1978 3:313-318