IMPEL NEUROPHARMA ANNOUNCES U.S. FOOD & DRUG ADMINISTRATION ACCEPTANCE OF NEW DRUG APPLICATION FOR INP104 FOR THE ACUTE TREATMENT OF MIGRAINE

FDA Conditionally Accepts Trade Name, TRUDHESA™, Pending Approval of the NDA, and Sets PDUFA Goal Date of September 6, 2021

Company's Lead Candidate is Based on Impel's Proprietary Precision Olfactory Delivery (POD®) Technology, and is the First and Only Delivery System to Explore the Vascular-Rich Upper Nasal Space as a Therapeutically Viable Treatment Pathway

SEATTLE, January 20, 2021 — Impel NeuroPharma, a late-stage biopharmaceutical company, today announced that the U.S. Food and Drug Administration (FDA) has accepted for review the company's 5O5(b)(2) New Drug Application (NDA) for INP104 for the acute treatment of migraine headaches with or without aura in adults. INP104 is dihydroergotamine mesylate (DHE) delivered directly into the vascular-rich upper nasal space using Impel's proprietary Precision Olfactory Delivery (POD®) technology. If approved, INP104 will be marketed under the trade name, TRUDHESA™, in the U.S. and will become the first and only therapy to utilize the POD technology, a novel delivery system that specifically targets the vascular-rich upper nasal space.

"The FDA's acceptance of our submission package for TRUDHESA™ marks another important step in our journey to bring an important new treatment option to patients who, despite recent treatment advances, are still in need of a fast, effective, and consistently reliable relief from their migraine," said Adrian Adams, chairman and chief executive officer of Impel NeuroPharma. "Our proprietary POD® technology has the potential to unlock the therapeutic viability of a previously untapped treatment pathway – the vascular-rich upper nasal space. We are hopeful that patients with migraine who are still in search of an acute treatment that is both non-oral and on-demand will have access to such an option later this year and look forward to working closely with the FDA as it completes its review of our application."

The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date of September 6, 2021, which reflects a standard 10-month review period and is consistent with the review timeline for a 505(b)(2) NDA submission.

Impel is focused on the development and commercialization of transformative therapies for patients living with central nervous system (CNS) disorders with high unmet medical needs, and TRUDHESA™ is the Company's first therapeutic candidate to be submitted for U.S. regulatory review.

The NDA submission for TRUDHESA™ is supported by safety results from the pivotal Phase 3 STOP 301 study, in which more than 5,650 migraine attacks were treated over 24 or 52 weeks. The study met its primary objectives, with no new safety signals or concerning trends in nasal safety findings observed for TRUDHESA™ following delivery of DHE to the upper nasal space. For the 24-week Full Safety Set (FSS) (n=354), the majority of treatment-emergent adverse events (TEAEs) were mild and transient in nature. The most frequently reported TEAEs, (≥5%) during the entire 24-week period were nasal congestion

(16.7%), nausea (7.9%), nasal discomfort (5.4%), and abnormal taste (5.1%). No cardiac TEAEs were observed, and no significant changes in mean heart rate were observed over 24 weeks of treatment. No drug-related serious adverse events (SAEs) were observed over the entire 52-week study. Exploratory patient-reported efficacy data in the FSS (n=354) observed that 66.3% of patients reported pain relief, 38% of patients reported pain freedom, and 52% had freedom from their most bothersome migraine symptom (MBS) at two hours following their first dose of TRUDHESA™. In 85% of reported migraine attacks, patients did not report use of rescue medication. Initial onset of pain relief as early as 15 minutes was reported by 16.3% of patients, which continued to improve over time. The STOP 301 study is one of the largest longitudinal studies of DHE to date.

About STOP 301:

The Phase 3 STOP 301 study enrolled 360 patients at 36 sites in the U.S. who had a documented diagnosis of migraine headaches with or without aura, with at least two attacks per month for the previous six months. 354 patients received at least one dose of TRUDHESA™ and comprised the Full Safety Set. 185 patients who took an average of two or more treatments of TRUDHESA™ 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%]), adverse events (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 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 Treatment of Acute Attacks 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.[1] Migraine affects approximately 39 million people in the U.S.[2] Of the approximately 19 million diagnosed migraine patients, only four million are on prescription treatment.[3] While triptans account for almost 70% of therapies used for the acute treatment of migraine therapies, approximately 30 to 40% of patients do not respond

adequately to triptans and up to 79% of the patients who do respond to triptans report being dissatisfied with their current treatment and willing to try a new therapy.[4]

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 oral medications can remain in the stomach for hours, delaying symptom relief, leading to loss of confidence (about future administration) and prolonged suffering during the current migraine attack.[5]

About Impel NeuroPharma:
Impel NeuroPharma, Inc. is a privately held, Seattle-based biopharmaceutical company focused on developing transformative therapies for people living with CNS and other 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 TRUDHESA™ for the acute treatment of migraine, INP107 for OFF episodes in Parkinson's disease, and INP105 for acute agitation associated with schizophrenia, bipolar I disorder and autism.

About Precision Olfactory Delivery or POD® Technology:
Impel's proprietary Precision Olfactory Delivery (POD®) system 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 is designed to enable increased and consistent absorption of drug, with the potential to outperform the high variability associated with other nasal delivery systems.

While an ideal target for drug administration, to date no other system has been developed to 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 many 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. IMPEL, POD and the IMPEL Logo are registered trademarks of Impel NeuroPharma, Inc. To learn more about Impel NeuroPharma, please visit our website at http://impelnp.com.

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