Impel NeuroPharma Announces First Subject Dosed in Phase 1 Trial Evaluating INP105 for the Treatment of Acute Agitation in Bipolar I Disorder and Schizophrenia

Study to Establish Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Olanzapine Delivered via Precision Olfactory Delivery (POD®) Device

SEATTLE, August 29, 2018 — Impel NeuroPharma, a Seattle-based, privately-held biopharmaceutical company focused on therapies for the treatment of central nervous system (CNS) disorders, today announced the first subject has been dosed in a Phase 1, randomized, double-blind, placebo-and-active controlled crossover study of their intranasal olanzapine product, INP105, dosed via Impel's proprietary Precision Olfactory Delivery, or POD®, intranasal delivery device. INP105 is being studied for the treatment of acute agitation in bipolar I disorder and schizophrenia.

The "SNAP 101" Trial (**S**afety and Tolerability of Intra**na**sal **P**OD-olanzapine) will evaluate the safety, tolerability and pharmacokinetic/pharmacodynamic (PK/PD) profile of INP105 at three ascending doses compared with two doses of Zyprexa® intramuscular (5 mg and 10 mg) and orally disintegrating Zyprexa Zydis® (10 mg) in 36 healthy volunteers. The aim of the SNAP 101 trial is to establish the safety and tolerability of INP105 while informing appropriate dosing for future studies based on the PK and PD profiles.

"The evolution of mental healthcare options and treatments in the US is a priority, and there is a specific unmet need for optimal treatments that could address acute agitation," said Jon Congleton, Chief Executive Officer of Impel NeuroPharma. "Our goal with INP105 is to provide an easy-to-administer, rapidly-acting medicine that addresses acute agitation with a therapy that can be used in both the hospital and home setting without an injection."

Acute agitation often manifests in patients with serious underlying mental health conditions such as bipolar I disorder or schizophrenia. Between 1.7 million and 7 million episodes of acute agitation have been reported to occur in US hospitals and emergency room settings each year.[1] An ideal medication for acute agitation, according to a 2005 expert consensus is easy-to-administer, non-traumatically administered,

provides rapid tranquilization without excessive sedation, has a swift onset of action with sufficient duration to prevent untimely recurrence and has low risk for adverse events and drug interactions.[2]

Further details of the SNAP 101 (INP105-101) study can be found on ClinicalTrials.gov.

About INP105
INP105 is a drug-device combination product being studied for the treatment of acute agitation associated with bipolar I disorder or schizophrenia. It is comprised of a novel nasal formulation of olanzapine and Impel's novel Precision Olfactory Delivery, or POD™, intranasal delivery device. The POD is a novel, simple-to-use device designed to deliver consistent and predictable doses of drug. INP105 delivers olanzapine to the richly-vascularized upper nasal cavity offering rapid, consistent and optimized bioavailability that can be administered by the patient or a caregiver. Olanzapine is the most commonly used treatment for acute agitation, but its use is limited to intramuscular injection and in a hospital setting. INP105 is intended to be suitable for use in the hospital emergency room setting as well as early in an episode where it could be self-administered in the patient's home or supportive care setting.

About Acute Agitation
Acute agitation is defined as excessive motor activity associated with a feeling of inner tension, often manifesting from a number of serious underlying mental health conditions such as bipolar I disorder or schizophrenia. Between 1.7 million and 7 million episodes of acute agitation have been reported, or estimated, to occur in US hospitals and emergency room settings each year. This places a huge burden on ERs, the healthcare systems and the friends and families of those afflicted and is responsible for many healthcare staff assaults and injuries. The historic approach of "restrain and sedate" is being abandoned in favor of less coercive, more compassionate, de-escalation approaches that include less invasive pharmacologic interventions.

About Impel NeuroPharma
Impel NeuroPharma, Inc., is a privately-held, Seattle-based biotechnology company devoted to creating life-changing, innovative therapies for central nervous system (CNS) diseases. Impel NeuroPharma is currently investigating INP104 (POD-DHE) for acute migraine headache, INP103 (POD-levodopa) for reversal of OFF episodes in Parkinson's disease, INP105 (POD-olanzapine) for acute agitation in schizophrenia and bipolar disorders as well as INP102 (POD-insulin) for Alzheimer's disease in a series of trials currently funded by the NIH.

Impel's products utilize its novel, nasal Precision Olfactory Delivery, or POD®, device technology, which is designed to deliver liquid or dry powder forms of drug to the upper nasal cavity in a consistent and predictable manner.

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[1] The Diagnosis and Management of Agitation. Edited by Scott L. Zeller, Kimberly D. Nordstrom and Michael P. Watson. Cambridge University Press 2017, Page 1.

[2] Allen MH, Currier GW, Hughes DH et al. *J Psychiatr Pract* 2005. 11(Suppl 1); 5-108