



## IMPEL NEUROPHARMA ANNOUNCES PUBLICATION OF POSITIVE RESULTS OF SNAP 101 STUDY FOR INP105 FOR THE TREATMENT OF ACUTE AGITATION IN THE JOURNAL OF CLINICAL PSYCHIATRY

*Study Shows INP105 Achieves Rapid Absorption Which May Provide An Effective, Convenient, & Noninvasive Future Alternative for Treating Acute Agitation In the Home, Community, or Hospital Setting*

*INP105 is a Powder Formulation of Olanzapine, the Gold Standard Treatment for Acute Agitation, Delivered to the Upper Nasal Space in One-Tenth of a Second, Which Aims to Provide a More Compassionate Approach to De-escalating Agitation Episodes in Sensitive Patient Populations Such as Bipolar I Disorder, Schizophrenia and Autism*

*Agitation Episodes Related to Neuropsychiatric Disorders Account for 1.7 Million Visits to the Emergency Room in the US Each Year, Underscoring Need for an At Home, Self- or Caregiver-Administrated Option*

SEATTLE, June 30, 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 the publication of positive results from the SNAP 101 study (Safety and Tolerability of Intranasal POD-olanzapine), a Phase 1 double-blind, placebo/active-controlled study evaluating the safety, pharmacokinetic, and pharmacodynamic effects of INP105 in healthy adults in *The Journal of Clinical Psychiatry*. INP105 is comprised of a powder formulation of olanzapine targeting the upper nasal cavity using the Company's unique propellant-enabled POD<sup>®</sup> technology. Olanzapine is the most commonly used treatment for acute agitation, but its use is currently limited to intramuscular injection.

The published results from the study, which can be found [here](#), demonstrated that INP105 reached peak plasma levels ( $T_{max}$ ) approximately twice as fast as intramuscular olanzapine (Zyprexa<sup>®</sup>), and ten-times faster than orally-disintegrating tablets (ODT, Zyprexa Zydis<sup>®</sup>). Maximum and total plasma levels ( $C_{max}$  and AUC) were similar to intramuscular delivery of the same dose and exceeded the total plasma levels for ODT. Additionally, pharmacodynamic measures of sedation, including Visual Analogue Scale (VAS), the Agitation and Calmness Evaluation Scale (ACES) and Digit Symbol Substitution Test (DSST) all showed a robust statistical significance compared to placebo.

“Acute agitation often manifests in people living with serious mental health conditions, such as bipolar I disorder or schizophrenia, and places a significant burden on emergency rooms, the healthcare system, and the friends and families of those afflicted,” said Stephen Shrewsbury, M.D., Chief Medical Officer of Impel. “The results published today are encouraging for our INP105 clinical program, which is being developed to disrupt the acute agitation treatment landscape by safely, effectively and non-invasively delivering the preferred standard of care, olanzapine. Our goal is for INP105 to become the first viable and rapidly effective treatment option that allows patients, their caregivers, and providers the ability to treat agitation without the need for an injectable drug or requiring in-patient treatment.”



INP105 utilizes Impel's proprietary drug delivery POD technology system which targets the vascular rich upper nasal space and may enable rapid absorption and consistent drug bioavailability, with both powder and liquid formulations, supported by results from multiple clinical trials across Impel's pipeline. Unlike traditional nasal delivery systems, such as spray pumps, that predominantly deliver medicine to the lower nasal cavity which can lead to high variability and low overall absorption, INP105 is part of a suite of product candidates that utilize the POD technology and are designed to achieve rapid absorption with predictability, reliability and consistency.

Agitation episodes related to neuropsychiatric disorders account for approximately 1.7 million visits to the emergency room (ER) each year, placing a significant economic and resource burden on the healthcare system.<sup>1</sup> 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.<sup>2</sup> Such an optimal medication could be suitable for administration earlier during an agitation episode, possibly avoiding the need for ER attendance, as well as reduce the need for injected drugs and the associated risks of needlestick injuries and assaults on healthcare staff.

#### **About the SNAP 101 Study**

The "SNAP 101" study evaluated the safety, tolerability and pharmacokinetic/pharmacodynamic (PK/PD) profile of INP105 at three ascending doses compared with two doses of Zyprexa<sup>®</sup> intramuscular (5 mg and 10 mg) and orally disintegrating Zyprexa Zydis<sup>®</sup> (10 mg) in 36 healthy volunteers. The aim of the SNAP 101 study was to establish the safety and tolerability of INP105 while informing appropriate dosing for future studies based on the PK and PD profiles.

Further details of the SNAP 101 (INP105-101) study can be found on [ClinicalTrials.gov](https://clinicaltrials.gov).

#### **About INP105**

Impel NeuroPharma is currently developing INP105 with the goal to be a preferred choice for the safe and rapid treatment of acute agitation associated with bipolar I disorder, schizophrenia and autism. INP105 is comprised of an upper nasal formulation of olanzapine powder administered using Impel's propellant-enabled POD technology. Olanzapine is the most commonly used treatment for acute agitation, but its use is currently limited to intramuscular injection. Because INP105 is designed to be non-invasive, it has the potential to expand the treatment setting beyond the emergency room, such as inpatient treatment or community care facilities and the patient's home.

#### **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, schizophrenia or autism. Agitation episodes related to neuropsychiatric disorders account for 1.7 million visits to the emergency room (ER) in the US each year.<sup>1</sup> This places a significant burden on ERs, the healthcare system, 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.



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### **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, INP105 for acute agitation associated with schizophrenia, bipolar I disorder and autism, and INP107 for OFF episodes in Parkinson's disease. The Company has completed its Phase 3 clinical program for INP104 and is on track to submit a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) in the second half of 2020.

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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 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 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>1</sup> Allen MH, Currier GW, Hughes DH et al. *J Psychiatr Pract* 2005. 11(Suppl 1); 5-108

<sup>2</sup> The Diagnosis and Management of Agitation. Edited by Scott L. Zeller, Kimberly D. Nordstrom and Michael P. Watson. *Cambridge University Press* 2017, Page 1.