

**Implications For Future Research and How the POD technology Will Improve the Human Condition:**

The proprietary POD technology has the potential to transform treatment of many diseases with unmet needs. POD's novel approach to nasal delivery for the treatment of migraine substantiates its ability to overcome critical shortcomings of existing treatment mechanisms by depositing medicines directly and consistently to the vascular-rich upper nasal space where they can be readily absorbed. Clinical research currently underway is exploring the use of this technology to deliver important therapeutic molecules for the treatment of agitation in persons with autism spectrum disorder.

This promise for the utility of the POD technology for new indications began to be borne out in a recently completed Phase 1 clinical trial in the treatment of acute agitation associated with autism spectrum disorder (INP105). As noted in [The Journal of Clinical Psychiatry](#), the POD technology successfully delivered olanzapine in dry powder form to establish and maintain peak plasma levels twice as fast as commercially available intramuscular administration, and 10 times faster than orally disintegrating tablets. These finding suggests the POD technology may help deliver an ideal pharmacological rescue treatment for acute agitation in these cases. The current armamentarium of tools lacks INP105's non-invasive route of administration, rapid onset, adequate duration and good tolerability.

Between 1.7 million and 7 million episodes of acute agitation have been reported, or estimated, to occur in U.S. hospitals and emergency room settings each year. [Referenced Here](#), Pg 1] The most effective means of rapidly de-escalating these traumatic patient experiences today is through injection of antipsychotics, which are primarily used in emergency rooms and inpatient treatment facilities and which may require the use of patient restraints. Noninvasive treatments such as oral formulations of antipsychotics and benzodiazepines are limited by their slow onset of action. Oral medications also tend to be spit out by agitated patients, rendering them ineffective and underscoring the need for new treatment options.

Impel reported their first quarter 2022 earnings on May 16, 2022. To-date, Trudhesa continues a strong trajectory with approximately 16,750 prescriptions generated since launch, through April 2022 (111% percent growth from December 31, 2021, through March 31st, 2022). To-date, based on third-party data, we believe Trudhesa accounts for approximately 5% of new branded acute migraine prescriptions (NBRx) among Impel's 2,000 Super Target prescribers.

We are pleased to see continued strong growth and momentum with Trudhesa, supported by favorable market access coverage and positive physician and patient feedback. Trudhesa has garnered around five percent of new branded acute migraine prescriptions in our Super Target population in only six months since launch, and with 35-45% of Trudhesa patients being switched from or added to gepants, we believe Trudhesa is filling a significant unmet need in the post-triptan market

The potential for use of the POD technology in related treatment health is substantial. The POD technology can deliver both liquid and dry powder formulations of therapeutics. It can be modified to accommodate formulation and molecular structure of a wide range of medical compounds, the POD device has demonstrated the ability to deliver certain peptide and protein-based drugs that do not readily cross the blood-brain barrier. This capability opens the door to a wide array of potential investigational programs across many diseases.

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