Impel Pharmaceuticals to Present New Real-World Data for Trudhesa® at the 65th Annual Scientific Meeting of the American Headache Society

June 15, 2023

Real-World Assessment Suggests that Concomitant Preventive and Acute Medication Use Decreases in Patients Using Trudhesa

Additional Poster Underscores the Need for Non-Oral Treatment Options Given the Prevalence of Pre-Existing Gastrointestinal Disorders Among Those Prescribed Trudhesa

SEATTLE, June 15, 2023 (GLOBE NEWSWIRE) -- Impel Pharmaceuticals (NASDAQ: IMPL), a commercial-stage biopharmaceutical company with a mission to develop transformative therapies for people suffering from diseases with high unmet medical needs, today announced it will present new real-world data adding to the growing body of evidence supporting Trudhesa® (dihydroergotamine mesylate [DHE]) nasal spray (0.725 mg per spray) as an effective acute therapy for migraine management. The findings will be featured in two poster presentations during the 65th Annual Scientific Meeting of the American Headache Society (AHS), taking place June 15-18, 2023, in Austin, Texas.

Preliminary real-world findings from an assessment of medical and pharmacy claims data for patients with migraine who were treated with Trudhesa in the United States provide new evidence suggesting that concomitant preventive (with the exception of the anti-CGRP monoclonal antibody class) and acute medication use generally decreases in patients taking Trudhesa between the 12-month baseline and 90-day follow-up period. Importantly, an increase in antinausea medications was not observed following Trudhesa use, whereas these medications are commonly used with DHE administered intravenously.

“DHE has an established safety and efficacy profile, often providing long-lasting relief for even the toughest of migraine attacks. However, until Trudhesa, nasal delivery options couldn’t reach the upper nasal space, where DHE can be rapidly absorbed,” said Zubair Ahmed, M.D., a headache specialist and neurologist at the Cleveland Clinic. “Trudhesa has been an important addition to migraine care as it provides patients with the reliable relief of DHE in a new and easy-to-use delivery technology that can provide relief in as early as 15 minutes and, importantly, be administered at any point during an attack. This real-world evidence indicates that patients who respond to Trudhesa will likely continue to respond long-term, providing an additional benefit of potentially reducing the need for using daily oral concomitant preventative and acute medications.”

A second poster on real-world demographic and clinical characteristics, as well as baseline comorbidities among patients with migraine who were treated with Trudhesa, found that most patients were females between the ages of 36 and 45 years, and had comorbidities that include headache syndromes other than migraine, other neurological conditions, other pain disorders, sleep disorders, gastrointestinal (GI) disorders, and psychiatric disorders. In contrast to other epidemiological studies, in this real-world patient population, GI comorbidities were more common, which may be due to many of these patients not being able to achieve migraine relief with oral routes of administration.

“Through our ongoing research, we continue to find that Trudhesa has great potential for patients who don’t find the relief they are searching for from other preventative and acute options," said Sheena Aurora, M.D., Vice President Medical Affairs, Impel Pharmaceuticals. "We are pleased to share these new insights about Trudhesa use in the real-world setting with researchers and clinicians from around the world at the AHS Annual Meeting.”

All presentations will be accessible on the AHS website at www.americanheadachesociety.org. Following are the presentation details of Trudhesa data being presented:

- **Title:** “Real-World Assessment of Concomitant Medication Use in Patients Using INP104 in the United States” (**Poster** #P-161)
    - **Date & Time:** Friday, June 16, 12:35 – 1:50 p.m. Central Time (CT)
- **Title:** “Real-World Assessment of Baseline Demographic and Clinical Characteristics Among Patients Using INP104 in the United States” (**Poster** #P-160)
    - **Date & Time:** Saturday, June 17, 12:45 – 2:00 p.m. CT
- **Title:** “Safety of INP104 in Migraine Patients With Cardiovascular Risk Factors: Post Hoc Subgroup Analysis of the Phase 3 STOP 301 Study” (**Poster** #P-175)
    - **Date & Time:** Friday, June 16, 12:35 – 1:50 p.m. CT
- **Title:** “Assessment of the Potential for Drug-Drug Interactions Between INP104 and Gepants for Migraine Management” (**Poster** #P-17)
    - **Date & Time:** Friday, June 16, 12:35 – 1:50 p.m. CT
- **Title:** “A Cross-Sectional Survey of Prevailing Opinions from Headache Specialists Regarding Status Migrainosus Management” (**Poster** #P-04)

- **Date & Time:** Saturday, June 17, 12:45 – 2:00 p.m. CT

- **Title:** “Safety of Concomitant Triptan and INP104 Use From the Phase 3 STOP 201 Study in Migraine Patients” (**Poster** #P-174)
  - **Date & Time:** Saturday, June 17, 12:45 – 2:00 p.m. CT

Trudhesa uses Impel’s proprietary Precision Olfactory Delivery (POD ®) technology and is the first and only migraine nasal spray which delivers DHE – a proven, well-established migraine therapeutic – quickly to the bloodstream through the vascular-rich upper nasal space. Trudhesa bypasses the gut and reduces potential absorption issues, offering rapid, sustained, and consistent symptom relief without nausea commonly associated with injection or infusion DHE – even when administered hours after the onset of a migraine attack.

About Migraine

Approximately 31 million adults in the U.S. are living with migraine,[1] and there is a need for more treatment options. In a survey of nearly 4,000 U.S. patients using oral acute prescription medication for migraine, 96 percent said they were dissatisfied with at least one aspect of their treatment —including lack of sustained relief, inconsistent relief, and lack of relief from a rapid-onset attack. Nearly half (48%) said they can still have pain two hours after taking medication and 38 percent say their headache returns within 24 hours of getting relief.[2] Additionally, there is a need for non-oral routes of administration given the high prevalence of gastrointestinal issues among people with migraine.

About Trudhesa® (dihydroergotamine mesylate) Nasal Spray

Trudhesa® is approved by the FDA for the acute treatment of migraine with or without aura in adults in the U.S. Using Impel’s proprietary POD ® technology, Trudhesa gently delivers DHE[3] —a proven, well-established therapeutic—quickly to the bloodstream through the vascular-rich upper nasa space. Trudhesa bypasses the gut and potential absorption issues, offering the potential for rapid, sustained, and consistent relief without injection or infusion, even when administered hours after the start of a migraine attack.[4]

Trudhesa is a single use, drug-device combination product containing a vial of DHE (4 mg DHE in a 1 mL solution that is clear and colorless to faintly yellow) and a POD® device. Prior to initiation of Trudhesa, a cardiovascular evaluation is recommended. For patients with risk factors predictive of coronary artery disease who are determined to have a satisfactory cardiovascular evaluation, it is strongly recommended that administration of the first dose of Trudhesa take place in the setting of an appropriately equipped healthcare facility.

Trudhesa is designed to be self-administered. Once assembled, Trudhesa should be primed before initial use by releasing 4 sprays. A patient should use Trudhesa immediately after priming. The recommended dose of Trudhesa is 1.45 mg administered as two metered sprays into the nose (one spray of 0.725 mg into each nostril). The dose may be repeated, if needed, a minimum of 1 hour after the first dose. A patient should not use more than 2 doses of Trudhesa within a 24-hour period or 3 doses within a 7-day period. A patient should use or discard Trudhesa within 8 hours once the vial has been opened or the product has been assembled. A consumer assembly video is available on www.TRUDHESA.com and please refer to the Instructions for Use for more details.

The most common adverse reactions (incidence ≥2%) to Trudhesa were nasal congestion, nasal discomfort, nausea, product taste abnormal, and product package associated injury. For more information about Trudhesa and Full Prescribing Information, including BOXED WARNING, please visit, www.TRUDHESA.com.

About Impel Precision Olfactory Delivery (POD®) Technology

Impel’s proprietary 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 Pharmaceuticals 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 a broad range of 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.

About Dihydroergotamine Mesylate (DHE)

DHE was approved for the treatment of migraine in 1946[8] and has more than 70 years of therapeutic use.[3] Migraine treatment with DHE has demonstrated efficacy independent of when the treatment is initiated. Unlike other available treatments for migraine, DHE is known to bind to multiple receptors theorized to be implicated in migraine onset and duration.[5]

Trudhesa® Indication and Important Safety Information

Indication

Trudhesa® is used to treat an active migraine headache with or without aura in adults. Do not use Trudhesa to prevent migraine when you have no symptoms. It is not known if Trudhesa is safe and effective in children.

Important Safety Information

Serious or potentially life-threatening reductions in blood flow to the brain or extremities due to interactions between dihydroergotamine (the active ingredient in Trudhesa) and strong CYP3A4 inhibitors (such as protease inhibitors and macrolide antibiotics) have been reported rarely. As a result, these medications should not be taken together.

Do not use Trudhesa if you:

- Have any disease affecting your heart, arteries, or blood circulation.

- Are taking certain anti-HIV medications known as protease inhibitors (such as ritonavir or nelfinavir).
- Are taking a macrolide antibiotic such as clarithromycin or erythromycin.
- Are taking certain antifungals such as ketoconazole or itraconazole.
- Have taken certain medications such as triptans or ergot-type medications for the treatment or prevention of migraine within the last 24 hours.
- Have taken any medications that constrict your blood vessels or raise your blood pressure.
- Have severe liver or kidney disease.
- Are allergic to ergotamine or dihydroergotamine.

Before taking Trudhesa, tell your doctor if:

- You have high blood pressure, chest pain, shortness of breath, heart disease; or risk factors for heart disease (such as high blood pressure, high cholesterol, obesity, diabetes, smoking, strong family history of heart disease or you are postmenopausal, or male over 40); or problems with blood circulation in your arms, legs, fingers, or toes.
- You have or had any disease of the liver or kidney.
- You are taking any prescription or over-the-counter medications, including vitamins or herbal supplements.
- You are pregnant, planning to become pregnant or are nursing, or have ever stopped medication due to an allergy or bad reaction.
- This headache is different from your usual migraine attacks.

The use of Trudhesa should not exceed dosing guidelines and should not be used on a daily basis. Serious cardiac (heart) events, including some that have been fatal, have occurred following the use of dihydroergotamine mesylate, particularly with dihydroergotamine for injection, but are extremely rare.

You may experience some nasal congestion or irritation, altered sense of taste, sore throat, nausea, vomiting, dizziness, and fatigue after using Trudhesa.

Contact your doctor immediately if you experience:

- Numbness or tingling in your fingers and toes
- Severe tightness, pain, pressure, heaviness, or discomfort in your chest
- Muscle pain or cramps in your arms or legs
- Cold feeling or color changes in 1 or both legs or feet
- Sudden weakness
- Slurred speech
- Swelling or itching

The risk information provided here is not comprehensive. To learn more, talk about Trudhesa with your healthcare provider or pharmacist. The FDA-approved product labeling can be found at www.Trudhesa.com or 1-800-555-DRUG. You can also call 1-833-TRUDHESA (1-833-878-3437) for additional information.

About Impel Pharmaceuticals
Impel Pharmaceuticals is a commercial-stage pharmaceutical company developing transformative therapies for people suffering from diseases with high unmet medical needs. Impel offers treatments that pair its proprietary POD® technology with well-established therapeutics. In September 2021, Impel received U.S. FDA approval for its first product, Trudhesa® nasal spray, which is approved in the U.S. for the acute treatment of migraine with or without aura in adults. In addition to Trudhesa, the Company continues to address patient needs via licensing and partnerships.

Cautionary Note on Forward-Looking Statements
This press release contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, including, but not limited to, the potential clinical benefits of Trudhesa®, the market opportunities of Trudhesa within the migraine market, the speed of uptake and market growth of Trudhesa, the effectiveness of the Trudhesa sales force, the timing of announcements of clinical results and clinical development activities of Impel's product candidates, and Impel's cash runway. Forward-looking statements can be identified by words such as: "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "plan," "expect" or the negative or plural of these words or similar expressions. These statements are subject to numerous risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including but not limited to, Impel's ability to maintain regulatory approval of Trudhesa, its ability to execute its commercialization strategy for Trudhesa, its ability to develop, manufacture and commercialize its other product candidates including plans for future development of its POD® devices and plans to address additional indications for which Impel may pursue regulatory approval, whether results of preclinical studies or clinical trials will be indicative of the results of future trials, and the effects of COVID-19 on its clinical programs and business operations. Many of these risks are described in greater detail in Impel's filings with the Securities and Exchange Commission. Any forward-looking statements in this press release speak only as of the date of this press release. Impel assumes no obligation to update forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

 To learn more about Impel Pharmaceuticals, please visit our website at https://impelpharma.com.

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[1] R. B. Lipton, M. E. Bigal, M. Diamond, F. Freitag, M. L. Reed, W. F. Stewart. Migraine prevalence, Disease Burden, and the Need for Preventive Therapy. *Neurology* 2007;68;343-349 DOI: 10.1212/01.wnl.0000252808.97649.21

[2] Impel Neuropharma. (2020). INP104-301. Table 3.8.2.

[3] Smith TR.; Winner P.; Aurora SK.; Jeleva M.; Hocevar-Trnka J.; Shrewsbury SB.; STOP 301: A Phase 3, Open-Label Study Of Safety, Tolerability, And Exploratory Efficacy Of INP104, Precision Olfactory Delivery (POD®) Of Dihydroergotamine Mesylate, Over 24/52 Weeks In Acute Treatment Of Migraine Attacks In Adult Patients. *Headache*. 2021; 00: 1– 13. https://doi.org/10.1111/head.14184

[4] Aurora SK, et al. *J Headache Pain*. 2013;14(Suppl 1):P143.

[5] Impel Neuropharma. (2020). INP104-301. Table 3.3.6.