Impel NeuroPharma Announces U.S. FDA Approval of TRUDHESA™ (Dihydroergotamine Mesylate) Nasal Spray for the Acute Treatment of Migraine

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TRUDHESA Is the First and Only Therapeutic to Use POD technology to Deliver Dihydroergotamine Mesylate (DHE) to the Vascular-Rich Upper Nasal Space

TRUDHESA Is Well Tolerated and Delivers Rapid, Sustained and Consistent Symptom Relief for the Acute Treatment of Migraine

Commercial Launch of TRUDHESA is Planned for Early October 2021

Impel to Host Investor Call on Tuesday, September 7, 2021 at 8:30 a.m. ET

SEATTLE, Sept. 03, 2021 (GLOBE NEWSWIRE) -- Impel NeuroPharma, Inc. (NASDAQ: IMPL), a commercial-stage biopharmaceutical company developing transformative therapies for people suffering from diseases with high unmet medical needs, with an initial focus on the central nervous system, today announced that the U.S. Food and Drug Administration (FDA) approved TRUDHESA™ (dihydroergotamine mesylate) nasal spray (0.725 mg per spray) for the acute treatment of migraine with or without aura in adults. TRUDHESA was previously known as INP104.

Using Impel's proprietary Precision Olfactory Delivery (POD®) technology, TRUDHESA gently delivers dihydroergotamine mesylate (DHE)—a proven, well-established therapeutic—quickly to the bloodstream through the vascular-rich upper nasal space.[1] TRUDHESA bypasses the gut and potential absorption issues, offering rapid, sustained, and consistent symptom relief without injection or infusion, even when administered hours after the onset of a migraine attack.[2] The Commercial launch of TRUDHESA is planned for early October 2021.

"We are delighted with the approval of TRUDHESA and are proud to offer the millions of Americans with migraine a non-oral, acute treatment option that may provide rapid, sustained, and consistent relief, even when taken late into a migraine attack," said Adrian Adams, Chairman and Chief Executive Officer of Impel NeuroPharma. "The approval of TRUDHESA marks the culmination of more than a decade of research and advanced engineering to pair the proven efficacy of DHE with our innovative POD technology. We are grateful for all the patients and investigators who participated in our clinical trials and who were instrumental in bringing this needed advancement to the migraine community."

The New Drug Application for TRUDHESA included the results of the Phase 3, open-label, pivotal safety study, STOP 301, which is the largest longitudinal study ever conducted with DHE using nasal spray delivery.[3] More than 5,650 migraine attacks were treated over 24 or 52 weeks during the study. The primary objective of the study was to assess the safety and tolerability of TRUDHESA. Exploratory objectives included efficacy assessments of migraine measures and a patient acceptability questionnaire. In the trial, TRUDHESA was generally well tolerated and exploratory efficacy findings showed it provided rapid, sustained, and consistent symptom relief. Unlike some oral acute treatments that need to be taken within one hour of attack onset to be most effective, STOP 301 reported TRUDHESA offered consistent efficacy even when taken late into a migraine attack.[4]

"Many of my patients need more from their migraine treatment, and TRUDHESA offers a non-oral, fast-acting, reliable option that overcomes many current medication challenges," said Stephanie J. Nahas-Geiger, MD, MSEd, Associate Professor in the Department of Neurology, and Program Director of the Headache Medicine Fellowship Program, Thomas Jefferson University. "Its upper nasal delivery circumvents the GI tract and common phenomena associated with migraine, such as nausea and gastroparesis, that can impact the effectiveness of oral treatments. And, importantly, it is a self-administered, single dose that can be taken anytime during a migraine attack, so patients don't need to worry about missing the opportunity to benefit from using TRUDHESA within a certain timeframe. I think patients will be very receptive to this treatment, because it pairs the long-proven benefits of DHE with a patient-friendly delivery system."

There were no serious TRUDHESA-related treatment-emergent adverse events (TEAEs) observed in the STOP 301 study and the majority of TEAEs were mild and transient in nature.[4] Some of the most frequently reported TRUDHESA-related TEAEs (≥2%) during the entire 52-week study period were nasal congestion (17.8%), nausea (6.8%), nasal discomfort (6.8%), abnormal olfactory test (6.8%) and vomiting (2.7%).[5]

In the STOP 301 study, patient-reported exploratory efficacy findings reported that more than a third of patients (38%) had pain freedom,[6] two-thirds (66%) had pain relief,[7] and more than half (52%) had freedom from their most bothersome migraine symptom[8] at two hours after their first dose of TRUDHESA. For one in six patients (16%), pain relief started as early as 15 minutes.[7] Of patients who were pain free at two hours, 93 percent were still pain free at 24 hours,[11] and 86 percent were still pain free through two days.[9] The great majority of patients (84%) reported that TRUDHESA was easy to use[10] and preferred it over their current therapy.[11]

"Migraine is a disease that impacts the whole body and is the second leading cause of disability," [12] said Kevin Lenaburg, executive director, Coalition for Headache and Migraine Patients (CHAMP), which represents 12 national headache and migraine patient advocacy groups. "Historically there have not been enough effective treatments for treating migraine attacks, especially treatments that are not oral medicines, which can be challenging due to nausea, vomiting and other GI symptoms that can occur during a migraine. We welcome an important new treatment that combines the long-established efficacy of DHE with a non-oral, innovative delivery system that allows patients to self-administer wherever they are and at any point within a migraine attack."

TRUDHESA will be available through Trudhesa™ Direct, a hassle-free pharmacy partnership and copay program. The digital pharmacy fulfilment partners, Phil Inc. and Carepoint Pharmacy, will provide electronic prescribing and automatic enrollment in the patient savings program for eligible, commercially insured patients without the need for a paper copay card. The pharmacy partners will provide a customized and seamless patient experience. Once the pharmacy receives the e-prescription, patients will be notified via digital communications that their prescription has been processed and receive their medication via convenient, free, home delivery. For more information, please visit, www.TRUDHESA.com.

Conference Call Information

Impel NeuroPharma will host a live conference call and webcast on Tuesday, September 7, 2021 at 8:30 a.m. ET to discuss the FDA's approval of TRUDHESA. The conference call may be accessed by dialing 877-295-2648 (domestic) or 470-495-9487 (international) and referring to conference ID 4387746. A live webcast of the event will be available on the Investors section of the Impel NeuroPharma website at https://investors.impelnp.com/. A replay of the webcast will be available on the Impel NeuroPharma website following the event.

About Migraine and The Importance of Non-Oral Acute Treatment Options

Approximately 31 million adults in the U.S. are living with migraine,[13,14] which is characterized by recurrent episodes of moderate to severe head pain and associated with nausea, vomiting and sensitivity to light and sound. Migraine is the second most common cause of disability in the world and the most common cause of disability among young women.[14]

In a 2017 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.[15]

The high prevalence of related GI conditions among people with migraine may require alternative routes of medication delivery. Evidence suggests 80 percent of people with migraine experience gastroparesis, delayed emptying of the stomach, which may delay or reduce the absorption of oral medications.[16,17] Additionally, more than 70 percent of people with migraine experience nausea and nearly 30 percent experience vomiting.[3] The American Headache Society guidelines recommend a non-oral therapy for patients who have limited or no response to oral medicine.[18]

About TRUDHESA™ (dihydroergotamine mesylate) Nasal Spray

TRUDHESA™ (dihydroergotamine mesylate) nasal spray (0.725 mg per spray) is approved by the U.S. Food and Drug Administration for the acute treatment of migraine with or without aura in adults in the U.S. Using Impel's proprietary Precision Olfactory Delivery (POD®) Technology, TRUDHESA gently delivers dihydroergotamine mesylate (DHE)—a proven, well-established therapeutic[19]—quickly to the bloodstream through the vascular-rich upper nasal 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.[20]

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.

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 Dihydroergotamine Mesylate (DHE)

Dihydroergotamine Mesylate (DHE) was approved for the treatment of migraine in 1946[18] and has more than 70 years of therapeutic use.[18] Migraine treatment with DHE has demonstrated efficacy independent of when the treatment is initiated.[9] Unlike other available treatments for migraine, DHE is known to bind to multiple receptors theorized to be implicated in migraine onset and duration.[9]

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 NeuroPharma

Impel NeuroPharma, Inc. is a commercial-stage biopharmaceutical company developing transformative therapies for people suffering from diseases with high unmet medical needs, with an initial focus on diseases of the central nervous system. Impel offers and is developing treatments that pair its proprietary Precision Olfactory Delivery (POD®) technology with well-established therapeutics. In addition to TRUDHESA™ (dihydroergotamine mesylate) nasal spray, which is approved in the United States for the acute treatment of migraine with or without aura in adults, impel is also developing INP105 for the acute treatment of agitation and aggression in patients with autism, and INP107 for OFF episodes in Parkinson's disease.

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 timing of commercial availability of TRUDHESA, and the timing of announcements of clinical results and clinical development activities of Impel's product candidates. 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.

Contact:
Lance Buckley
twelvenote, a division of Lippe Taylor Group
lbuckley@lippetaylor.com
917-439-2241

A Media Snippet accompanying this announcement is available by clicking on the image or link below:

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