Supernus Announces FDA Approval of ONAPGO™ (apomorphine hydrochloride) for Parkinson's Disease

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- ***ONAPGO is the first and only subcutaneous apomorphine infusion device for the treatment of motor fluctuations in adults with advanced Parkinson's disease***
- ***ONAPGO is a wearable subcutaneous infusion device that provides continuous treatment during the waking day for more consistent control of OFF time***
- ***ONAPGO will be available in the U.S. in second quarter 2025***

ROCKVILLE, Md., Feb. 04, 2025 (GLOBE NEWSWIRE) -- Supernus Pharmaceuticals, Inc. (Nasdaq: SUPN), a biopharmaceutical company focused on developing and commercializing products for the treatment of central nervous system (CNS) diseases, announced today that the U.S. Food and Drug Administration (FDA) approved ONAPGO (apomorphine hydrochloride) injection, formerly known as SPN-830, as the first and only subcutaneous apomorphine infusion device for the treatment of motor fluctuations in adults with advanced Parkinson's disease (PD). Supernus will make ONAPGO available in the second quarter of 2025 with a support team of experts, including a robust nurse education program, and access support at launch.

"Continuous subcutaneous apomorphine infusion already has a proven and established 30-year history in Europe, where it has helped deliver more consistent control of motor fluctuations for thousands of patients," said Rajesh Pahwa, M.D., Laverne and Joyce Rider Professor of Neurology at the University of Kansas School of Medicine, Director of the Movement Disorder Program at The University of Kansas Health System, and a clinical trial investigator for ONAPGO. "In a clinical trial in Europe, patients treated with ONAPGO experienced a significant reduction in daily OFF time and a similar significant increase in GOOD ON time. Today's approval of ONAPGO means patients in the U.S. who are not responding well to their current treatment regimen, including levodopa, will now have the option of using a small and lightweight wearable device to deliver a continuous infusion without the need for an invasive surgical procedure."

The approval is based on results from a Phase 3, 12-week, multicenter, parallel-group, double-blind, randomized, placebo-controlled study (N=107) evaluating the efficacy and safety of ONAPGO. The primary efficacy endpoint was the mean change in total daily OFF time assessed from baseline to the end of the 12-week treatment period based on patient diaries. The key secondary endpoints were the mean change in daily GOOD ON time, which was defined as ON time without troublesome dyskinesia, and Patient Global Impression of Change (PGIC).[1]

"ONAPGO represents a novel approach for adults with Parkinson's disease who are experiencing motor fluctuations," said Jack Khattar, President and CEO of Supernus Pharmaceuticals. "Supernus' significant experience in CNS has fueled the success of more than eight widely recognized products in CNS and other therapeutic categories. The addition of ONAPGO demonstrates our continued commitment to developing novel alternatives to manage Parkinson's disease and other neurological conditions."

"As Parkinson's disease progresses, levodopa treatment often becomes less effective at delivering consistent motor control in part due to GI dysmotility, variable absorption of oral medication, and the resulting pulsatile stimulation of dopamine pathways in the brain," said Stuart Isaacson, M.D., Director of Parkinson's Disease and Movement Disorders Center of Boca Raton, Florida, and a clinical trial investigator for ONAPGO. "With ONAPGO, the continuous infusion of apomorphine directly stimulates postsynaptic dopamine receptors with no metabolic conversion needed. In addition, the subcutaneous delivery of apomorphine bypasses the GI tract and enters the brain, which can allow for more predictable symptom improvement."

"As the motor symptoms of Parkinson's disease worsen over time, patients report alternating states between ON when their medication is working, and OFF when it's not working optimally," said Andrea Merriam, CEO of the Parkinson & Movement Disorder Alliance. "These on-again, off-again changes are disruptive and can happen at any time, which is why consistent daily control of OFF time is key to improving how patients feel and move. For many, continuous treatment options like ONAPGO can help to make days with Parkinson's more predictable."

About the Phase 3 Study
During the Phase 3 study, ONAPGO significantly reduced the amount of daily OFF time at 12 weeks from baseline (p=0.0114), with ONAPGO-treated patients (n=53) experiencing a 2.6-hour reduction compared to placebo (n=51) with 0.9 hours. The reduction in daily OFF time was accompanied by a similar significant increase in daily GOOD ON time (2.8 hours for ONAPGO-treated patients compared to 1.1 hours for the placebo group; p=0.0188).[1]* In addition, numerically greater improvements in daily OFF time and daily GOOD ON time were seen as early as week 1 and were maintained throughout all measured timepoints. Additionally, ONAPGO-treated patients more frequently reported improvement in their state of general health compared with placebo-treated patients (PGIC: 79% vs. 24%; p<0.0001). The most common adverse events (≥10% incidence) were infusion-site nodule, nausea, somnolence, infusion-site erythema, dyskinesia, headache, and insomnia.[1]

About Parkinson's disease
Nearly one million people in the U.S. and more than 10 million people worldwide are living with Parkinson's disease, a progressive and chronic neurodegenerative disorder that can cause tremors, muscle rigidity, and difficulty with movement and balance. Patients may also experience dyskinesia, involuntary movements that can significantly interfere with daily activities.[2] The disease impacts the central nervous system (e.g., the brain and spinal cord) and the peripheral nervous system, the network of nerves that support the limbs and the organs of the body (e.g., GI system including digestion, respiration, heart function, and blood pressure).[3] While there is no known cure for PD, there are treatments available to help reduce symptoms.[4] Patients treated with mainstay regimens may experience periods of GOOD ON time when medication treatment is working well, or OFF time when oral levodopa no longer provides symptom benefit and motor symptoms return.[5] PD is the second most common neurodegenerative

disorder of aging and the most common movement disorder.[6]

USE
ONAPGO is a prescription medicine used to treat motor fluctuations (OFF episodes) in adults with advanced Parkinson's disease (PD). It is not known if ONAPGO is safe and effective in children.

IMPORTANT SAFETY INFORMATION
Do not take ONAPGO if you are:

- taking certain medicines to treat nausea (ondansetron, granisetron, dolasetron, palonosetron) and alosetron. People taking ondansetron with apomorphine had very low blood pressure and lost consciousness (blacked out).
- allergic to apomorphine or to any ingredients in ONAPGO including sulfite. Sulfites can cause severe, life-threatening allergic reactions, especially in people with asthma.

Call your healthcare provider or get emergency help right away if you have any of the following symptoms of severe life-threatening allergic reaction:

- hives • itching • rash • swelling (eyes, tongue, lips, or mouth) • chest pain • throat tightness • trouble breathing or swallowing.

Before you start using ONAPGO, tell your healthcare provider about all of your medical conditions, including:

- difficulty staying awake during the daytime • dizziness, fainting spells, or low blood pressure • asthma
- allergies to any medicines containing sulfites • heart problems • a history of stroke or other brain problems
- kidney problems • liver problems • a mental problem called a major psychotic disorder • drinking alcohol • if you are pregnant or plan to become pregnant, or breastfeeding or plan to breastfeed. It is not known if ONAPGO will harm your unborn baby or pass into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription (over-the-counter) medicines, vitamins, and herbal supplements. ONAPGO and certain other medicines may affect each other and cause serious side effects.

- If you take nitroglycerin under your tongue (sublingual) while using ONAPGO, your blood pressure may decrease and cause dizziness. If possible, lie down before taking it and then try to continue lying down for at least 45 minutes after.

What should I avoid while using ONAPGO?

- **Do not** drink alcohol. It can increase your chance of developing serious side effects.
- **Do not** take medicines that make you sleepy.
- **Do not** drive, operate machinery, or do other dangerous activities until you know how ONAPGO affects you.
- **Do not** change your position too fast, get up slowly from sitting or lying. ONAPGO can lower blood pressure and cause dizziness or fainting.

What are the possible side effects of ONAPGO?
ONAPGO may cause serious side effects, including:

- **blood clots**. Infusing ONAPGO into a vein (intravenous) can cause blood clots. **Do not** infuse ONAPGO in your vein.
- **nausea and vomiting are common**. May be serious or severe. Your healthcare provider may prescribe medicine (trimethobenzamide) to help decrease nausea/vomiting. Follow your healthcare provider's instructions on how to take/when to stop this medicine.
- **sleepiness or falling asleep during the day is common and may be serious**. Some people may get sleepy during the day or fall asleep without warning while doing everyday activities such as talking, eating, or driving.
- **dizziness is common and may be serious**. ONAPGO can lower your blood pressure and cause dizziness. Dizziness can happen when treatment is started or when the dose is increased. **Do not** get up too fast from sitting or lying down, especially if you have been sitting or lying down for a long time.
- **falls**. Changes that can happen with PD, and effects of some PD medicines, including ONAPGO, as well as trimethobenzamide, can increase your risk of falling.
- **infusion site reaction is common and may be serious**. Reactions and infections including infusion site nodules, redness, bruising, swelling, rash, and itching may happen
- **hallucinations or psychotic-like behavior**. ONAPGO can cause/worsen psychotic-like behavior including hallucinations (seeing or hearing things that are not real), confusion, excessive suspicion, aggressive behavior, agitation, delusional beliefs (believing things that are not real), and disorganized thinking.
- **sudden uncontrolled movements (dyskinesia) are common and may be serious**. Some people with PD may get sudden, uncontrolled movements after treatment with some PD medicines. ONAPGO can cause/make dyskinesia worse.
- **low red blood cells (hemolytic anemia)**. Tell your healthcare provider if you have: become pale, fast heartbeat, feel more tired or weaker than usual, skin or eyes look yellow, chest pain, shortness of breath or trouble breathing, dark-colored

urine, fever, dizziness, or confusion.

- **strong (intense) urges**. New or increased gambling urges, sexual urges, and other intense urges have been reported.
- **heart problems**. If you have shortness of breath, fast heartbeat, or chest pain, call your healthcare provider or get emergency help right away.
- **serious heart rhythm changes (QT prolongation)**. Tell your healthcare provider right away if you have a change in your heartbeat (a fast or irregular heartbeat), or faint.
- **allergic reaction.** Tell your healthcare provider or get medical help right away if you get hives, itching, rash, swelling of the eyes and tongue, or trouble breathing.
- **tissue changes (fibrotic complications)**. Some people have had changes in the tissues of their pelvis, lungs, and heart valves when taking medicines called non-ergot derived dopamine agonists like ONAPGO.
- **prolonged painful erections (priapism)**. May occur. If you have an erection that lasts more than 4 hours, call your healthcare provider or go to the nearest hospital emergency room right away.

Other common side effects of ONAPGO include headache and trouble falling asleep or staying asleep (insomnia).

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088. Patients and care partners must receive complete instructions on the proper use of ONAPGO. Please see Patient Information and Patient Instructions for Use and talk to your healthcare provider.

ONAPGO (apomorphine hydrochloride) injection, for subcutaneous use, is available in a 98 mg/20 mL (4.9 mg/mL) apomorphine hydrochloride solution.

References

[1]ONAPGO. Package insert. Supernus Pharmaceuticals, Inc. **Efficacy results from the analysis of data from the TOLEDO study using the FDA's preferred methodology, mixed-effects model for repeated measures (MMRM), as required for the submission of the New Drug Application. The results confirmed the statistical significance of the primary outcome.*

[2]Parkinson's Foundation. Understanding Parkinson's. Parkinson's Foundation. 2024. Accessed December 2024. https://www.parkinson.org/understanding-parkinsons.

[3]American Parkinson Disease Association. Peripheral neuropathy and Parkinson's disease. 2020. Accessed December 2024. https://www.apdaparkinson.org/article/peripheral-neuropathy-parkinsons-disease/.

[4]World Health Organization. Parkinson disease. 2023. Accessed December 2024. https://www.who.int/news-room/fact-sheets/detail/parkinson-disease.

[5]Isaacson S, Pagan F, Lew M, Pahwa R. Should "on-demand" treatments for Parkinson's disease OFF episodes be used earlier? *Sci Direct.* 2022;8:100161.

[6]Mhyre TR, Boyd JT, Hamill RW, Maguire-Zeiss KA. Parkinson's disease. Subcell Biochem. 2012;65:389–455. doi:10.1007/978-94-007-5416-4_16.

About Supernus Pharmaceuticals, Inc.

Supernus Pharmaceuticals is a biopharmaceutical company focused on developing and commercializing products for the treatment of central nervous system (CNS) diseases.

Our diverse neuroscience portfolio includes approved treatments for attention-deficit hyperactivity disorder (ADHD), dyskinesia in Parkinson's disease (PD) patients receiving levodopa-based therapy, hypomobility in PD, epilepsy, migraine, cervical dystonia, and chronic sialorrhea. We are developing a broad range of novel CNS product candidates including new potential treatments for hypomobility in PD, epilepsy, depression, and other CNS disorders.

For more information, please visit www.supernus.com.

Forward-Looking Statements

This press release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements do not convey historical information but relate to predicted or potential future events that are based upon management's current expectations. These statements are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. In addition to the factors mentioned in this press release, such risks and uncertainties include, but are not limited to, the Company's reporting on preliminary and exploratory open label clinical study on SPN-820, the Company's ability to sustain and increase its profitability; the Company's ability to raise sufficient capital to fully implement its corporate strategy; the implementation of the Company's corporate strategy; the Company's future financial performance and projected expenditures; the Company's ability to increase the number of prescriptions written for each of its products and the products of its subsidiaries; the Company's ability to increase its net revenue; the Company's ability to commercialize its products and the products of its subsidiaries including ONAPGO; the Company's ability to enter into future collaborations with pharmaceutical companies and academic institutions or to obtain funding from government agencies; the Company's product research and development activities, including the timing and progress of the Company's clinical trials, and projected expenditures; the Company's ability to receive, and the timing of any receipt of, regulatory approvals to develop and commercialize the Company's product candidates including SPN-820; the Company's ability to protect its intellectual property and operate its business without infringing upon the intellectual property rights of others; the Company's expectations regarding federal, state and foreign regulatory requirements; the therapeutic benefits, effectiveness and safety of the Company's product candidates including SPN-820; the accuracy of the Company's estimates of the size and characteristics of the markets that may be addressed by its product candidates; the Company's ability to increase its manufacturing capabilities for its products, including ONAPGO, and product candidates including SPN-820; the Company's projected markets and growth in markets; the Company's product formulations and patient needs and potential funding sources; the Company's staffing needs; and other risk factors set forth from time to time in the Company's filings with the Securities and Exchange Commission made pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended. The Company undertakes no obligation to update the information in this press release to reflect events or circumstances after the date hereof or to reflect the occurrence of anticipated or unanticipated events.

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