Johnson&Johnson

NEWS RELEASE

Johnson & Johnson seeks U.S. FDA approval of SPRAVATO® (esketamine) as the first and only monotherapy for adults with treatment-resistant depression

7/22/2024

Phase 4 SPRAVATO® monotherapy data shows rapid improvement in depressive symptoms at ~24 hours, sustained through at least 4 weeks

Monotherapy submission builds on more than a decade of research, 31 clinical trials and more than five years of real-world use that reinforce the safety and efficacy of SPRAVATO®

TITUSVILLE, N.J., July 22, 2024 /PRNewswire/ -- Johnson & Johnson (NYSE: JNJ) announced today the submission of a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) seeking approval of SPRAVATO® (esketamine) CIII nasal spray as a monotherapy for adults living with treatment-resistant depression (TRD). Nearly 30 percent of the estimated 280 million people worldwide living with major depressive disorder (MDD) have TRD,[1] which occurs when there is an inadequate response to two or more oral antidepressants during the same depressive episode.

"Many patients living with challenging-to-treat depression spend far too long cycling through multiple treatments that don't effectively resolve their symptoms, which can cause a significant functional and emotional burden on patients and their loved ones," said Bill Martin, PhD, Global Therapeutic Area Head, Neuroscience, Johnson & Johnson Innovative Medicine. "We're pleased to build on the more than a decade of research reinforcing the safety and efficacy of SPRAVATO® and look forward to working with the FDA to bring this innovative treatment to patients as a monotherapy option."

The submission is supported by positive results from the Phase 4 TRD4005 study that evaluated the efficacy, safety and tolerability of SPRAVATO® administered as a monotherapy. The randomized, double-blind, multicenter, placebo-controlled study showed a rapid change in Montgomery-Asberg Depression Rating Scale (MADRS) total score as early as 24 hours after the first SPRAVATO® dose and sustained through at least 4 weeks of treatment. The safety profile of SPRAVATO® monotherapy was consistent with the existing body of clinical data in combination with an oral antidepressant, and no new safety concerns were identified.[2]

SPRAVATO® is approved by the FDA, in combination with an oral antidepressant, to treat adults with TRD and depressive symptoms in adults with MDD with acute suicidal ideation or behavior. To date, SPRAVATO® has been approved in 77 countries and administered to more than 100,000 people worldwide.

IMPORTANT SAFETY INFORMATION

What is SPRAVATO® (esketamine) CIII nasal spray?

SPRAVATO® is a prescription medicine, used along with an antidepressant taken by mouth to treat:

- Adults with treatment-resistant depression (TRD)
- Depressive symptoms in adults with major depressive disorder (MDD) with suicidal thoughts or actions

SPRAVATO® is not for use as a medicine to prevent or relieve pain (anesthetic). It is not known if SPRAVATO® is safe or effective as an anesthetic medicine.

It is not known if SPRAVATO® is safe and effective for use in preventing suicide or in reducing suicidal thoughts or actions. SPRAVATO® is not for use in place of hospitalization if your healthcare provider determines that hospitalization is needed, even if improvement is experienced after the first dose of SPRAVATO®.

It is not known if SPRAVATO® is safe and effective in children.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about SPRAVATO®?
SPRAVATO® can cause serious side effects, including:

- Sedation and dissociation. SPRAVATO® may cause sleepiness (sedation), fainting, dizziness, spinning sensation, anxiety, or feeling disconnected from yourself, your thoughts, feelings, space and time (dissociation).
  - Tell your healthcare provider right away if you feel like you cannot stay awake or if you feel like you are going to pass out.
  - Your healthcare provider must monitor you for serious side effects for at least 2 hours after taking SPRAVATO®. Your healthcare provider will decide when you are ready to leave the healthcare setting.
- Respiratory depression was observed with the use of SPRAVATO®; additionally, there were rare reports of respiratory arrest.

o Your healthcare provider must monitor you for serious side effects for at least 2 hours (including pulse oximetry) after taking SPRAVATO®. Your

healthcare provider will decide when you are ready to leave the healthcare setting.

- Abuse and misuse. There is a risk for abuse and physical and psychological dependence with SPRAVATO® treatment. Your healthcare provider should check you for signs of abuse and dependence before and during treatment with SPRAVATO®.
  - Tell your healthcare provider if you have ever abused or been dependent on alcohol, prescription medicines, or street drugs.
  - Your healthcare provider can tell you more about the differences between physical and psychological dependence and drug addiction.
- SPRAVATO® Risk Evaluation and Mitigation Strategy (REMS). Because of the risks for sedation, dissociation, respiratory depression and abuse and misuse, SPRAVATO® is only available through a restricted program called the SPRAVATO® Risk Evaluation and Mitigation Strategy (REMS) Program. SPRAVATO® can only be administered at healthcare settings certified in the SPRAVATO® REMS Program. Patients treated in outpatient healthcare settings (e.g., medical offices and clinics) must be enrolled in the program.
- Increased risk of suicidal thoughts and actions. Antidepressant medicines may increase suicidal thoughts and actions in some people 24 years of age and younger, especially within the first few months of treatment or when the dose is changed. SPRAVATO® is not for use in children.
  - Depression and other serious mental illnesses are the most important causes of suicidal thoughts and actions. Some people may have a higher risk of having suicidal thoughts or actions. These include people who have (or have a family history of) depression or a history of suicidal thoughts or actions.
- How can I watch for and try to prevent suicidal thoughts and actions in myself or a family member?
  - Pay close attention to any changes, especially sudden changes, in mood, behavior, thoughts, or feelings, or if you develop suicidal thoughts or actions.
  - Tell your healthcare provider right away if you have any new or sudden changes in mood, behavior, thoughts, or feelings.
  - Keep all follow-up visits with your healthcare provider as scheduled. Call your healthcare provider between visits as needed, especially if you have concerns about symptoms.
- Tell your healthcare provider right away if you or your family member have any of the following symptoms, especially if they are new, worse, or worry you:
  - Suicide attempts
  - Worsening depression
  - Thoughts about suicide or dying
  - Other unusual changes in behavior or mood

Do not take SPRAVATO® if you:

- have blood vessel (aneurysmal vascular) disease (including in the brain, chest, abdominal aorta, arms and legs)
- have an abnormal connection between your veins and arteries (arteriovenous malformation)
- have a history of bleeding in the brain
- are allergic to esketamine, ketamine, or any of the other ingredients in SPRAVATO®.

If you are not sure if you have any of the above conditions, talk to your healthcare provider before taking SPRAVATO®.

Before you take SPRAVATO®, tell your healthcare provider about all of your medical conditions, including if you:

- have heart or brain problems, including:
  - high blood pressure (hypertension)
  - slow or fast heartbeats that cause shortness of breath, chest pain, lightheadedness, or fainting
  - history of heart attack
  - history of stroke
  - heart valve disease or heart failure
  - history of brain injury or any condition where there is increased pressure in the brain

- have liver problems
- have ever had a condition called "psychosis" (see, feel, or hear things that are not there, or believe in things that are not true).
- are pregnant or plan to become pregnant. SPRAVATO® may harm your baby. You should not take SPRAVATO® if you are pregnant.
    - Tell your healthcare provider right away if you become pregnant during treatment with SPRAVATO®.
    - If you are able to become pregnant, talk to your healthcare provider about methods to prevent pregnancy during treatment with SPRAVATO®.
    - There is a pregnancy registry for women who are exposed to SPRAVATO® during pregnancy. The purpose of the registry is to collect information about the health of women exposed to SPRAVATO® and their baby. If you become pregnant during treatment with SPRAVATO®, talk to your healthcare provider about registering with the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or online at **https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/antidepressants/.**
- are breastfeeding or plan to breastfeed. You should not breastfeed during treatment with SPRAVATO®.

Tell your healthcare provider about all the medicines that you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. Taking SPRAVATO® with certain medicine may cause side effects.

Especially tell your healthcare provider if you take central nervous system (CNS) depressants, psychostimulants, or monoamine oxidase inhibitors (MAOIs) medicines. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

How will I take SPRAVATO®?

- You will take SPRAVATO® nasal spray yourself, under the supervision of a healthcare provider in a healthcare setting. Your healthcare provider will show you how to use the SPRAVATO® nasal spray device.
- Your healthcare provider will tell you how much SPRAVATO® you will take and when you will take it.
- Follow your SPRAVATO® treatment schedule exactly as your healthcare provider tells you to.
- During and after each use of the SPRAVATO® nasal spray device, you will be checked by a healthcare provider who will decide when you are ready to leave the healthcare setting.
- You will need to plan for a caregiver or family member to drive you home after taking SPRAVATO®.
- If you miss a SPRAVATO® treatment, your healthcare provider may change your dose and treatment schedule.
- Some people taking SPRAVATO® get nausea and vomiting. You should not eat for at least 2 hours before taking SPRAVATO® and not drink liquids at least 30 minutes before taking SPRAVATO®.

- If you take a nasal corticosteroid or nasal decongestant medicine take these medicines at least 1 hour before taking SPRAVATO®.

What should I avoid while taking SPRAVATO®?

Do not drive, operate machinery, or do anything where you need to be completely alert after taking SPRAVATO®. **Do not** take part in these activities until the next day following a restful sleep. See **"What is the most important information I should know about SPRAVATO®?"**

What are the possible side effects of SPRAVATO®?

SPRAVATO® may cause serious side effects including:

See **"What is the most important information I should know about SPRAVATO®?"**

Increased blood pressure. SPRAVATO® can cause a temporary increase in your blood pressure that may last for about 4 hours after taking a dose. Your healthcare provider will check your blood pressure before taking SPRAVATO® and for at least 2 hours after you take SPRAVATO®. Tell your healthcare provider right away if you get chest pain, shortness of breath, sudden severe headache, change in vision, or seizures after taking SPRAVATO®.

Problems with thinking clearly. Tell your healthcare provider if you have problems thinking or remembering.

Bladder problems. Tell your healthcare provider if you develop trouble urinating, such as a frequent or urgent need to urinate, pain when urinating, or urinating frequently at night.

The most common side effects of SPRAVATO® when used along with an antidepressant taken by mouth include:

- feeling disconnected from yourself, your thoughts, feelings and things around you
- dizziness
- nausea
- feeling sleepy
- spinning sensation
- decreased feeling of sensitivity (numbness)
- feeling anxious
- lack of energy
- increased blood pressure
- vomiting
- feeling drunk
- feeling very happy or excited

If these common side effects occur, they usually happen right after taking SPRAVATO® and go away the same day.

These are not all the possible side effects of SPRAVATO®.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see full **Prescribing Information**, including Boxed WARNINGS, and **Medication Guide** for SPRAVATO® and discuss any questions you may have with your healthcare provider.

cp-170363v3

ABOUT JOHNSON & JOHNSON

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and where solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity.

Learn more at **http://www.jnj.com** or at **www.janssen.com/johnson-johnson-innovative-medicine**. Follow us at **@JNJInnovMed**.

Janssen Research & Development, LLC and Janssen Biotech, Inc. are both Johnson & Johnson companies.

CAUTIONS CONCERNING FORWARD-LOOKING STATEMENTS

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of SPRAVATO®. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, Janssen Biotech, Inc., and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products, and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of healthcare products and services; changes to applicable laws and regulations, including global healthcare reforms; and trends toward healthcare cost

containment. A further list and descriptions of these risks, uncertainties, and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 31, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the U.S. Securities and Exchange Commission. Copies of these filings are available online at **www.sec.gov**, **www.jnj.com**, or on request from Johnson & Johnson. None of Janssen Research & Development, LLC, Janssen Biotech, Inc. nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

Media contact:

Caitlin Lormel
Johnson & Johnson
clormel@its.jnj.com
732 740 1701

Investor contact:

Raychel Kruper
Johnson & Johnson
investor-relations@its.jnj.com

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