Johnson&Johnson

NEWS RELEASE

SPRAVATO® (esketamine) approved in the U.S. as the first and only monotherapy for adults with treatment-resistant depression

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Following U.S. FDA Priority Review, approval is based on data demonstrating SPRAVATO® alone met its primary endpoint at 4 weeks and led to rapid and superior improvement in depressive symptoms compared to placebo as early as 24 hours[1]

SPRAVATO® alone showed a rapid and superior improvement vs. placebo in the Montgomery-Asberg Depression Rating Scale (MADRS) total score, with numerical improvements across all 10 MADRS items seen at day 28 in a post-hoc analysis[2]

Monotherapy data adds to well-established clinical efficacy and real-world safety profile of SPRAVATO®

TITUSVILLE, N.J., Jan. 21, 2025 /PRNewswire/ -- Johnson & Johnson (NYSE: JNJ) announced today the U.S. Food and Drug Administration (FDA) approval of a supplemental New Drug Application (sNDA) for SPRAVATO® (esketamine) CIII nasal spray, making this innovative treatment the first and only monotherapy for adults living with major depressive disorder (MDD) who have had an inadequate response to at least two oral antidepressants.

MDD is one of the most common psychiatric disorders, with an estimated 21 million adults in the U.S. living with the disease. About one-third of adults will not respond to oral antidepressants alone, which has a significant negative impact on the quality of life of those affected. MDD has a high economic burden, with nearly half of it attributable to treatment-resistant depression (TRD).[3,4,5]

"Treatment-resistant depression can be very complicated, especially for patients who do not respond to oral

antidepressants or cannot tolerate them. For too long, healthcare providers have had few options to offer patients much-needed symptom improvement," said Bill Martin, Ph.D., Global Therapeutic Area Head, Neuroscience, Johnson & Johnson Innovative Medicine. "SPRAVATO® is now available as a standalone treatment, meaning patients may experience improvements in depressive symptoms as early as 24 hours and at 28 days – without the need for daily oral antidepressants."

This approval, which was granted following FDA Priority Review, is supported by positive results from the randomized, double-blind, multicenter, placebo-controlled study in which SPRAVATO® alone showed a rapid and superior improvement in Montgomery-Asberg Depression Rating Scale (MADRS) total score vs. placebo. In a post-hoc analysis, SPRAVATO® demonstrated numerical improvements across all 10 MADRS items at day 28.[2] At week 4, 7.6% of patients taking placebo and 22.5% of patients taking SPRAVATO® achieved remission (MADRS total score ≤ 12).[1] The safety profile of SPRAVATO® as a standalone treatment was consistent with the existing body of clinical and real-world data when used in conjunction with an oral antidepressant, and no new safety concerns were identified.

Because of the risks of serious adverse outcomes resulting from sedation, dissociation, respiratory depression, abuse, and misuse, to facilitate safe and appropriate use, SPRAVATO® is only available through a restricted program called the SPRAVATO® Risk Evaluation and Mitigation Strategy (REMS) Program.

"For more than six years, I've seen firsthand the real-world impact SPRAVATO® can have on patients' lives," said Gregory Mattingly, M.D., President, Midwest Research Group and Founding Partner, St. Charles Psychiatric Associates. "Now that it is also available as a monotherapy, healthcare providers have the freedom to further personalize treatment plans based on individual needs, so patients can experience the efficacy of SPRAVATO® in as little as 24 hours, through day 28, without the need for a daily oral antidepressant."

SPRAVATO® is unique and works by targeting glutamate, which is the most abundant excitatory neurotransmitter in the brain.[6] The mechanism by which esketamine exerts its antidepressant effect is unknown.

Backed by more than a decade of research and almost six years of real-world evidence, SPRAVATO® has proven to be a transformational treatment option for many patients with TRD by reducing depression symptoms in as little as 24 hours and reducing the time to relapse for patients who stay on treatment. To date, SPRAVATO® has been administered to more than 140,000 patients worldwide.

ABOUT TREATMENT-RESISTANT DEPRESSION

Depression is a common mental health disorder that impacts an estimated 280 million people worldwide.[3] In the U.S., approximately 21 million adults have had at least one major depressive episode. Approximately one-third of adults with MDD will not respond to oral antidepressants alone and are considered to have treatment-resistant

depression (TRD), which is defined as inadequate response to two oral medications.[4,5] TRD has a significant negative impact on the lives of those affected and has one of the highest economic burdens of all psychiatric disorders.[5] Patients often cycle through multiple oral medications, waiting 4-6 weeks for potential relief. After trying their third oral antidepressant, approximately 86% of patients do not achieve remission.[7]

ABOUT SPRAVATO®

SPRAVATO® (esketamine) CIII nasal spray is approved by the U.S. Food and Drug Administration alone or in conjunction with an oral antidepressant for adults with MDD when they have inadequate response to at least two oral antidepressants (TRD) and depressive symptoms in adults with major depressive disorder with acute suicidal ideation or behavior in conjunction with an oral antidepressant. It is a non-selective, non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor and is believed to work differently by acting on a pathway in the brain that affects glutamate. The mechanism by which esketamine exerts its antidepressant effect is unknown. To date, SPRAVATO® has been approved in 77 countries and administered to more than 140,000 patients worldwide.

IMPORTANT SAFETY INFORMATION

What is SPRAVATO® (esketamine) CIII nasal spray?

SPRAVATO® is a prescription medicine used:

- with or without an antidepressant taken by mouth, to treat adults with treatment-resistant depression (TRD)
- with an antidepressant taken by mouth, to treat 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, dissociation, and respiratory depression. SPRAVATO® may cause sleepiness (sedation), fainting, dizziness, spinning sensation, anxiety, or feeling disconnected from yourself, your thoughts, feelings, space and time (dissociation), breathing problems (respiratory depression and respiratory arrest)
  - 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.
- Abuse and misuse. There is a risk for abuse and misuse with SPRAVATO®, which may lead to physical and psychological dependence. Your healthcare provider should check you for signs of abuse, misuse, and dependence before and during treatment.
  - 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 (such as 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, or if you develop suicidal thoughts or actions.
  - 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 or get emergency help right away if you or your family member have any of the following symptoms, especially if they are new, worse, or worry you:
  - thoughts about suicide or dying
  - suicide attempts
  - new or worse depression
  - new or worse anxiety
  - feeling very agitated or restless
  - panic attacks
  - trouble sleeping (insomnia)
  - new or worse irritability
  - acting aggressive, being angry or violent
  - acting on dangerous impulses
  - an extreme increase in activity and talking (mania)
  - 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 unborn 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. SPRAVATO® passes into your breast milk. 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® 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
- headache
- 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 Johnson & Johnson at 1-800-526-7736, or to the 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.

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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 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.innovativemedicine.jnj.com**. Follow us at **@JNJInnovMed**. Janssen Research & Development, LLC and Johnson & Johnson International (Singapore) Pte. Ltd. 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.

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