

News Release

MEDIA CONTACT:

Kaitlin Meiser
+1-908-938-3209
KMeiser3@its.jnj.com

INVESTOR CONTACT:

Jennifer McIntyre
+1-732-524-3922

Janssen Announces U.S. FDA Approval of SPRAVATO® (esketamine) CIII Nasal Spray to Treat Depressive Symptoms in Adults with Major Depressive Disorder with Acute Suicidal Ideation or Behavior

- SPRAVATO® is the first and only approved antidepressant medication shown to begin improving depressive symptoms with the first dose in this challenging to treat patient population
- Approval is based on Phase 3 data showing SPRAVATO® reduced depressive symptoms in as little as four hours in some patients, with symptom improvement maintained through the four-week treatment period

TITUSVILLE, N.J. – (August 3, 2020) – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that the U.S. Food and Drug Administration (FDA) has approved the supplemental new drug application (sNDA) for SPRAVATO® (esketamine) CIII nasal spray, taken with an oral antidepressant, to treat depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior.¹ SPRAVATO® is the first and only approved medicine that has been shown to reduce depressive symptoms within 24 hours,¹ providing a new option for significant symptom relief until a longer-term, comprehensive treatment plan can take effect.

The effectiveness of SPRAVATO® in preventing suicide or in reducing suicidal ideation or behavior has not been demonstrated. Use of SPRAVATO® does not preclude the need for hospitalization if clinically warranted, even if patients experience improvement after an initial dose of SPRAVATO®. SPRAVATO® carries a Boxed Warning regarding a Risk Evaluation and Mitigation Strategy (REMS) and the risk of suicidal thoughts and behaviors. See below for Important Safety Information. SPRAVATO® will be made available at REMS certified treatment centers. Janssen is working to responsibly educate and certify treatment centers in accordance with the REMS so healthcare providers can offer SPRAVATO® to appropriate patients.

[Click to Tweet:](#) #BREAKINGNEWS: FDA approves a new indication for @JanssenUS medicine for depressive symptom improvement in adults with major depression and suicidal behavior. Read full announcement here: <https://ctt.ec/7yfjG+>

Depression is the leading cause of disability worldwide and the condition most frequently associated with suicide.² MDD is a serious disease that causes a significant, negative impact on the way people think, feel and act.³ Symptoms and severity vary by person and may include persistent feelings of sadness, hopelessness or tension; changes in sleep or appetite; difficulty concentrating or performing activities of daily living; lack of interest; and/or thoughts of harming themselves.³

“Many people who live with depression know all too well the feeling of desperation. If that major depression progresses to active suicidal thoughts, it’s crushing, and they need options to help change the trajectory of their acute depressive episode,” said Theresa Nguyen, Chief Program Officer, Mental Health America. “Traditional oral antidepressants need weeks or more to take effect, so the availability of a medicine that can begin providing relief within a day is potentially life changing.”

The sNDA approval is based on two identical Phase 3 clinical trials in which SPRAVATO® plus comprehensive standard of care demonstrated a significant, rapid reduction of depressive symptoms within 24 hours, with some patients starting to respond as early as four hours. SPRAVATO® plus comprehensive standard of care led to a 15.9 and 16.0 point decrease on the Montgomery-Åsberg Depression Rating Scale (MADRS), a tool used to assess severity of depressive symptoms, in the two trials at 24 hours after the first dose of study medication. This compared to a reduction of 12.0 and 12.2 points in the placebo plus comprehensive standard of care group. The comprehensive standard of care included initial hospitalization, a newly initiated or optimized oral antidepressant and twice-weekly treatment visits for four weeks, during which patients received SPRAVATO® 84 mg or placebo nasal spray.^{4,5}

Both the SPRAVATO® and placebo groups continued to improve between four hours and 25 days, with 41 percent and 43 percent of the SPRAVATO® plus comprehensive standard of care group achieving clinical remission of depression (minimal or no symptoms) compared with 34 percent and 27 percent in the placebo groups, by the end of the double-blind period, in the two trials, respectively.^{4,5}

“It is astonishing to me that despite what we know about the risk of serious suicidal ideation in the context of major depression, patients with suicidal ideation have previously been excluded from nearly all studies examining antidepressant treatment efficacy. There is an immense need for high quality evidence showing effective and rapid antidepressant action in this population,” said Gerard Sanacora,* Ph.D., M.D., Director, Yale Depression Research Program, Co-Director, Yale New Haven Hospital Interventional Psychiatry Service, and esketamine clinical trial investigator. “The clinical trials supporting this new indication provide compelling evidence that esketamine may offer clinicians a new way to provide support to patients quickly in the midst of an urgent depressive episode and help set them on the path to remission.”

In the two Phase 3 trials, improvement in the severity of suicidality at 24 hours was measured using a standardized global scale. The treatment difference between the two groups was not statistically significant on this key secondary endpoint. Both SPRAVATO® and placebo in combination with comprehensive standard of care showed a similar reduction on this measure.^{4,5}

The safety profile observed in the trials was consistent with previous studies of SPRAVATO® in treatment-resistant depression (TRD), adding to the established body of safety and efficacy evidence. The most common side effects included dissociation (feeling disconnected from yourself, your thoughts, feelings, space and time), dizziness, sedation (sleepiness), increased blood pressure, hypoesthesia, vomiting, euphoric mood and vertigo.¹

With this new indication, SPRAVATO® can be prescribed to treat depressive symptoms in two MDD subpopulations of adults with high unmet need:

- TRD, which the FDA approved on March 5, 2019, and
- MDD with acute suicidal ideation or behavior.¹

A full course of treatment for the new indication is twice weekly for four weeks, after which evidence of therapeutic benefit should be evaluated to determine need for continued treatment. Please [click here](#) for the full Prescribing Information.

“People living with major depression need more options to meet their most critical needs, and we’re proud to help redefine how we treat ongoing and acutely worsening depressive symptoms,” said Bill Martin, Global Therapeutic Area Head, Neuroscience,

Janssen Research & Development, LLC. "SPRAVATO can now help patients with challenging to treat depression find significant and swift relief from debilitating depressive symptoms, offering those living with this serious mental health condition the possibility of a better future."

Once SPRAVATO® is determined as an appropriate treatment option, in accordance with the REMS, patients will be treated at a certified treatment center trained to administer the medicine and address their needs. Janssen will educate healthcare providers and payers on this updated label to ensure appropriate patients are evaluated and the full course of treatment is delivered in a safe, appropriate and controlled manner for patients to receive the maximum treatment benefit.

For patients who need help getting started on SPRAVATO® and staying on track, [Janssen CarePath](#) offers a comprehensive support program. Janssen CarePath provides information on insurance coverage, potential out-of-pocket costs and treatment support, and identifies options that may help make treatment more affordable, including the Janssen CarePath Savings Program for commercially insured patients who are eligible. Those who don't have commercial or private health insurance, or who aren't eligible for the Janssen CarePath Savings Program, can visit [JanssenPrescriptionAssistance.com](#) for more information about other resources that may help with their out-of-pocket medication costs.

**Dr. Sanacora has received research support from Janssen and has served as a paid consultant to the company.*

About SPRAVATO®

SPRAVATO® (esketamine) CIII nasal spray is a non-selective, non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor – an ionotropic glutamate receptor. It has a novel mechanism of action, meaning it works differently than currently available therapies for major depressive disorder (MDD).

SPRAVATO® is approved in the United States, in conjunction with an oral antidepressant, to treat adults with treatment-resistant depression (TRD) and depressive symptoms in adults with MDD with acute suicidal ideation or behavior. SPRAVATO® has been submitted for health authorities' review for TRD and adults with MDD who have current suicidal ideation with intent in other markets around the world, including Europe. The FDA granted Breakthrough Therapy Designation to esketamine nasal spray for TRD in November 2013 and for MDD with imminent risk for suicide in August 2016.

About the SPRAVATO® Risk Evaluation & Mitigation Strategy (REMS)

A REMS program is in place to ensure the safety of all patients who are treated with SPRAVATO®. SPRAVATO® is available only through a restricted distribution program called the SPRAVATO® REMS. The goals of the REMS are to mitigate the risks of serious adverse outcomes resulting from sedation and dissociation caused by SPRAVATO® administration, and abuse and misuse of SPRAVATO®, by:

- Ensuring SPRAVATO® is only dispensed and administered to patients in medically supervised healthcare settings that monitor these patients
- Ensuring pharmacies and healthcare settings that dispense SPRAVATO® are REMS certified
- Ensuring each patient is informed about serious adverse outcomes from dissociation and sedation and the need for monitoring
- Enrolling all patients who receive treatment in an outpatient healthcare setting in a REMS registry to further characterize the risks and support safe use

About the Phase 3 Studies^{4,5}

ASPIRE I and ASPIRE II evaluated the efficacy and safety of SPRAVATO® in addition to a comprehensive standard of care in adult patients with major depressive disorder who had active suicidal ideation with intent. This is the first global clinical program to study this severely ill patient population, who have been typically excluded from antidepressant clinical trials, addressing a great unmet need. Patients were defined as

those with major depression and active suicidal thoughts with intent. Every patient was treated with a comprehensive standard of care in both trials to safely and ethically conduct the studies. The comprehensive standard of care included initial hospitalization, a newly initiated or optimized oral antidepressant and twice-weekly treatment visits for four weeks.

The primary efficacy endpoint of the double-blind, randomized, placebo-controlled, multicenter studies was a reduction in depressive symptoms at 24 hours after the first dose, as measured by the Montgomery-Åsberg Depression Rating Scale (MADRS). The MADRS scale is a tool used to assess severity of depressive symptoms, allowing clinicians to evaluate 10 symptoms on a six-point scale to produce a total score of up to 60 points. A secondary efficacy endpoint measured improvement in severity of suicidality as measured by the revised Clinical Global Impression of Severity of Suicidality (CGI-SS-r), a seven-point scale developed by clinical experts that is a measure of the severity of suicidality as judged by the clinician's global impression.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenUS. Janssen Pharmaceuticals, Inc. is one of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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.

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.
- **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, 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 or 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?**
 - 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 have any of the following symptoms, especially if they are new, worse, or worry you:**
 - Suicide attempts
 - thoughts about suicide or dying
 - worsening depression
 - 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
- decreased feeling of sensitivity (numbness)
- feeling anxious
- lack of energy
- increased blood pressure
- vomiting
- spinning sensation
- 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.**

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Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding SPRAVATO® (esketamine) CIII nasal spray. 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 OPCO, any of the other Janssen Pharmaceutical Companies 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 health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care 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 29, 2019, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the 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 the Janssen Pharmaceutical Companies 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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