

News Release

MEDIA CONTACTS:

Kristina Chang
+1-201-213-4115
Kchang12@its.jnj.com

Greg Panico
+1-908-240-2011
GPanico1@its.jnj.com

INVESTOR CONTACTS:

Lesley Fishman
+1-732-524-3922

Christopher DelOrefice
+1-732-524-2955

Janssen Announces U.S. FDA Approval of SPRAVATO™ (esketamine) CIII Nasal Spray for Adults with Treatment-Resistant Depression (TRD) Who Have Cycled Through Multiple Treatments Without Relief

- SPRAVATO™ uses the first new mechanism of action in decades to treat major depressive disorder^{1,2,3}
- In short- and long-term clinical trials, those who received SPRAVATO™ and a newly initiated oral antidepressant achieved superior improvement in depression symptoms, and sustained improvement in their symptoms over time compared to adults who received a placebo and an oral antidepressant¹
- To support responsible use of the medication while ensuring patient access, SPRAVATO™ will launch with a controlled distribution model, including a comprehensive Risk Evaluation and Mitigation Strategy¹

TITUSVILLE, N.J., – (March 5, 2019) – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the U.S. Food and Drug Administration (FDA) has approved SPRAVATO™ (esketamine) CIII nasal spray for use in conjunction with an oral antidepressant in adults with treatment-resistant depression (TRD).¹ People who are currently struggling with major depressive disorder (MDD) are considered to have TRD if they have not responded adequately to at least two different antidepressants of adequate dose and duration in the current depressive episode.¹ It is estimated that approximately one-third of U.S. adults with MDD have TRD.⁴ SPRAVATO™ carries a Boxed WARNING regarding a Risk Evaluation and Mitigation Strategy (REMS) and the

risk of suicidal thoughts and behaviors in pediatric patients and young adults.¹ See below for Important Safety Information.

[Click to Tweet: #BREAKINGNEWS: FDA approves @JanssenUS antidepressant for treatment-resistant depression, marking first new mechanism of action for major depressive disorder in decades. Read full press release here: po.st/rFHeS9](#)

"It was hard to have any emotions, because I was just numb," said Robin P., an esketamine clinical trial patient. "When I began treatment with esketamine and my symptoms started to lift, I could see very clearly just how depressed I had been. I'm now able to appreciate a wider range of emotions than when I was depressed. My long-term goals have taken shape and actually seem attainable."

[Click to Tweet: Robin P., a person living with treatment-resistant #depression, talks about her treatment journey and how she's managing her symptoms. po.st/rFHeS9](#)

SPRAVATO™ was studied in a robust Phase 3 clinical trial program with more than 1,700 adults with TRD. In a short-term study, those who took SPRAVATO™ and an oral antidepressant experienced superior improvement in depression symptoms at four weeks, compared to those who received a placebo and an oral antidepressant.¹ In a long-term study, patients in stable remission taking SPRAVATO™ who continued treatment with the medicine were 51 percent less likely to relapse versus those who maintained a regimen of a placebo and an oral antidepressant.¹

In the clinical trials, the most common side effects of SPRAVATO™ when used along with an antidepressant taken by mouth included: dissociation, dizziness, nausea, sedation, spinning sensation, reduced sense of touch and sensation, anxiety, lack of energy, increased blood pressure, vomiting, and feeling drunk.¹

"Depression is a common and potentially debilitating illness that can have profound emotional, functional and economic impact on both those who suffer and their loved ones. The impact of depression is greatest for those who do not benefit from standard treatments," said Michael E. Thase,* M.D., a professor of psychiatry and director of the Mood and Anxiety Disorders Treatment and Research Program in the Perelman School of Medicine at the University of Pennsylvania, who served as a site principal investigator for the clinical trials. "In Phase 3 clinical trials, we saw this therapy provide sustained improvement to patients with treatment-resistant depression."

SPRAVATO™ uses the first new mechanism of action in decades to treat MDD.^{1,2,3} SPRAVATO™ works on the N-methyl-D-aspartate (NMDA) receptor, an ionotropic glutamate receptor in the brain. The medicine is administered as a nasal spray that is absorbed by the lining of the nasal passages and into the blood stream.¹

"SPRAVATO™ has the potential to change the treatment paradigm and offer new hope to the estimated one-third of people with major depressive disorder who have not responded to existing therapies," said Mathai Mammen, M.D., Ph.D., Global Head, Janssen Research & Development, LLC. "This unique and innovative medicine is a testament to Janssen's heritage of advancing solutions in neuroscience to heal minds and improve health outcomes."

Once SPRAVATO™ is determined as an appropriate treatment option, in accordance with the REMS, the patient will be treated at a certified treatment center that is trained to administer the medicine and address patient needs. SPRAVATO™ will not be dispensed directly to patients for home use. Instead, SPRAVATO™ will be self-administered by the patient under the direct observation of a healthcare provider. The healthcare provider will then observe the patient for treatment-emergent sedation, dissociation and blood pressure changes for at least two hours, until the patient is safe to leave. Patients should not drive or operate heavy machinery until the next day, following a restful sleep. All patients will be enrolled in the SPRAVATO™ REMS registry to further characterize the risks of serious adverse outcomes from sedation, dissociation, abuse and misuse, and to support safe use of this medicine.¹

With the approval of SPRAVATO™ comes a new way of treating TRD. Janssen is working quickly to educate and certify treatment centers in accordance with the REMS so healthcare providers can offer SPRAVATO™ to appropriate patients. Later this month, patients can visit www.SPRAVATO.com for a locator tool and to sign up to receive alerts when new treatment centers are available. More locations will be added over time as new treatment centers become certified.

Janssen CarePath offers a comprehensive support program that helps patients get started on SPRAVATO™ and stay on track. 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.

Please [click here](#) for full Prescribing Information.

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

About Treatment-Resistant Depression

Approximately one-third of people who have major depressive disorder (MDD) have not responded adequately to at least two different antidepressants of adequate dose and duration in the current depressive episode and are considered to have treatment-resistant depression (TRD).⁴ TRD is a chronic condition that places an ongoing emotional, functional, and economic burden on the individual, their loved ones, and society.⁵

Depression may lead to an inability to manage life's demands and maintain social connections, affecting all aspects of one's life, from school and employment, to relationships and overall quality of life.⁶ Treatment-resistant depression is associated with greater morbidity, higher healthcare costs, and various comorbid conditions.⁵

About the SPRAVATO™ Clinical Program

SPRAVATO™ was studied in five pivotal Phase 3 trials in more than 1,700 adults with TRD, including but not limited to a short-term study and one long-term maintenance study. SPRAVATO™ was also studied in four Phase 2 studies and 19 Phase 1 studies in patients with TRD and healthy volunteers. Patients who participated in the double-blind Phase 3 studies received SPRAVATO™ or a placebo in addition to a newly initiated oral antidepressant at the start of the treatment phase.¹

WHAT IS SPRAVATO™?¹

SPRAVATO™ is a prescription medicine, used along with an antidepressant taken by mouth, for treatment-resistant depression (TRD) in adults.

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 in children.

The U.S. FDA granted Breakthrough Therapy designation for SPRAVATO™ for treatment-resistant depression. Janssen is also investigating the medicine for a second indication, major depressive disorder with imminent risk for suicide.⁷ Janssen is currently conducting Phase 3 clinical studies for the second indication. Janssen submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for the esketamine treatment-resistant depression indication in October 2018 and anticipates approval later in 2019.

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.
- **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 and to patients enrolled in the program.
- **Increased risk of suicidal thoughts or actions.** SPRAVATO™ may cause worsening of depression and suicidal thoughts and behaviors, especially during the first few months of treatment and when the dose is changed. 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:**
 - attempts to commit suicide
 - thoughts about suicide or dying
 - worsening depression
 - other unusual changes in behavior or mood

SPRAVATO™ is not for use in children.

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.

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: dissociation, dizziness, nausea, sedation, spinning sensation, reduced sense of touch and sensation, anxiety, lack of energy, increased blood pressure, vomiting, and feeling drunk.

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.

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/JanssenGlobal. Janssen Pharmaceuticals, Inc. is one of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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™ (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 Janssen Pharmaceuticals, Inc., any of the other Janssen Pharmaceutical Companies of Johnson & Johnson 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 30, 2018, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," in the company's most recently filed Quarterly Report on Form 10-Q and in 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. Neither 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.

#

REFERENCES

- 1 SPRAVATO™ [Prescribing Information]. Titusville, N.J., Janssen Pharmaceuticals, Inc.
- 2 Duman RS. *F1000Research*. 2018;7:F1000.
- 3 Dubovsky SL. *Psychother and Psychosom*. 2018;87:129-139.
- 4 Rush AJ et al. *Am J Psychiatry*. 2006;163(11):1905-1917.
- 5 Mrazek DA et al. *Psychiatr Serv*. 2014;65(8):977-987.
- 6 Hofmann S et al. *Cogn Behav Ther*. 2017; 46(4): 265-286.
- 7 Johnson & Johnson Press Release. Esketamine Receives Breakthrough Therapy Designation from U.S. Food and Drug Administration for Major Depressive Disorder with Imminent Risk for Suicide. Available at: <https://www.jnj.com/media-center/press-releases/esketamine-recieves->

breakthrough-therapy-designation-from-us-food-and-drug-administration-for-major-depressive-disorder-with-imminent-risk-of-suicide. Accessed February 28, 2019.