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

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

Johnson & Johnson pivotal study of seltorexant shows statistically significant and clinically meaningful improvement in depressive symptoms and sleep disturbance outcomes

Seltorexant, an investigational first-in-class therapy, met all primary and secondary endpoints in pivotal Phase 3 study in patients with major depressive disorder (MDD) with insomnia symptoms, as presented at ASCP 2024

Approximately 60 percent of MDD patients on standard-of-care oral antidepressants experience residual insomnia symptoms[1], underscoring the high level of unmet need

Positive topline results for SPRAVATO® (esketamine) CIII nasal spray as a monotherapy were also presented, demonstrating rapid and sustained efficacy in treatment-resistant depression (TRD)

Titusville, New Jersey (May 29, 2024) – Johnson & Johnson announced today positive topline results from the pivotal Phase 3 MDD3001 clinical trial evaluating the efficacy and safety of seltorexant as an adjunctive treatment to baseline antidepressants in adult and elderly patients with major depressive disorder (MDD) with insomnia symptoms. Seltorexant is an investigational first-in-class selective antagonist of the human orexin-2 receptor being studied for the adjunctive treatment of MDD with insomnia symptoms. The findings will be presented at this year's American Society of Clinical Psychopharmacology (ASCP) Annual Meeting, which is being held from May 28-31 in Miami, Florida.

The Phase 3 randomized, double-blind, multicenter, placebo-controlled study achieved all primary and secondary endpoints, with seltorexant demonstrating both a statistically significant and clinically meaningful improvement in depressive symptoms based on the Montgomery-Asberg Depression Rating Scale (MADRS) total score at day 43, and improved sleep disturbance outcomes, in patients who had a prior inadequate response to SSRI/SNRI antidepressants alone. These results were observed in a patient population that was assessed to be moderately-to-severely depressed despite ongoing treatment with SSRI/SNRIs and suffered from significant sleep disturbance. Seltorexant was also safe and well-tolerated in the study, with similar rates of common adverse events seen in both trial arms, consistent with previous seltorexant clinical trials.

"Depression is a leading cause of disability worldwide and shares a strong link with sleep disturbances. In MDD, insomnia symptoms exacerbate the risk of depressive relapse, increase healthcare costs and impact quality of life, and it often goes under treated despite being one of the most common residual symptoms[2,3,4]," said Andrew Krystal, MD, Professor, Psychiatry, University of California, San Francisco Weill Institute for Neurosciences. "Seltorexant has the potential to fill a significant unmet need for new therapies to treat patients experiencing depression and insomnia, and most importantly, to improve outcomes and quality of life for these patients."

MDD is often accompanied by sleep disturbances such as insomnia or hypersomnia. With insomnia, patients may have trouble falling asleep, staying asleep, or getting good quality sleep. Approximately 60 percent of MDD patients on standard-of-care oral antidepressants experience residual insomnia symptoms.[1] Currently, no therapies are approved to treat MDD with insomnia symptoms.

"For nearly seven decades, Johnson & Johnson has delivered transformational treatments and solutions for people living with serious mental illness, and we are proud to present these data from our marketed and late-stage neuropsychiatry portfolios at ASCP," said Bill Martin, Ph.D., Global Therapeutic Area Head, Neuroscience. "As global leaders, we must continue to drive innovation in the treatment of depression, bringing new mechanisms of action and potentially first-in-class therapies to the millions of people living with mental health disorders."

DELIVERING RAPID AND SUSTAINED EFFICACY FOR TREATMENT-RESISTANT DEPRESSION (TRD)
Additional data presented at ASCP includes positive topline results from the placebo-controlled Phase 4 TRD4005 study of SPRAVATO® (esketamine) CIII nasal spray as a monotherapy in patients with TRD, which met both its primary and secondary endpoints. The randomized, double-blind, multicenter study showed SPRAVATO® provided rapid, statistically significant, and clinically meaningful improvement in depressive symptoms ~24 hours after the first dose and sustained through 4 weeks of treatment, as assessed by changes in MADRS total score.

The safety profile of SPRAVATO® monotherapy was consistent with the registration Phase 3 studies of TRD in combination with an oral antidepressant, and no new safety concerns were identified.

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

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

SPRAVATO® is approved by the U.S. Food and Drug Administration (FDA), in combination with an oral antidepressant, for adults with TRD and depressive symptoms in adults with MDD with suicidal thoughts or behaviors. With its approval in 2019, SPRAVATO® offered the first novel mechanism of action in decades for the treatment of MDD. To date, SPRAVATO® has been administered to more than 100,000 people living with challenging-to-treat forms of depression around the world.

Other accepted data at ASCP showcase our innovative data science usage in MDD research, including leveraging machine learning and similar measures that support our precision approach to neuropsychiatry. A complete listing of Company-sponsored abstracts can be viewed here.

ABOUT SELTOREXANT
Seltorexant, an investigational first-in-class therapy, is a selective antagonist of the human orexin-2 receptor currently being developed as an adjunctive treatment for adults with MDD with insomnia symptoms. Seltorexant selectively antagonizes the orexin-2 receptors, potentially improving mood and sleep symptoms associated with depression. When orexin-2 receptors are stimulated for too long or at inappropriate times, their activation can cause hyperarousal manifestations, including insomnia and excessive cortisol release, which may contribute to depression and insomnia.

ABOUT MDD3001
The Phase 3 MDD3001 study was a randomized, double-blind, multicenter, placebo-controlled study designed to compare the efficacy and safety of oral, once daily seltorexant 20 milligrams to that of placebo, adjunctive to background SSRI/SNRI, for improving depressive symptoms in adult and elderly patients with MDD with insomnia symptoms.

ABOUT MAJOR DEPRESSIVE DISORDER WITH INSOMNIA SYMPTOMS
MDD is one of the most common psychiatric disorders and leading causes of disability worldwide,[5] with an estimated 280 million people living with the disorder around the world.[6] MDD is often accompanied by sleep disturbances such as insomnia or hypersomnia, with approximately 60 percent of MDD patients experiencing insomnia symptoms despite being on an SSRI/SNRI.[1] Disturbed sleep and insomnia symptoms have a significant impact on a patient's quality of life and exacerbate the risk of depressive relapse and suicide.[2,4]

ABOUT SPRAVATO®
SPRAVATO® (esketamine) CIII nasal spray is approved by the U.S. Food and Drug Administration in combination with an oral antidepressant for adults with TRD and depressive symptoms in adults with major depressive disorder with acute suicidal ideation or behavior. It is the first novel mechanism of action in decades for the treatment of MDD. SPRAVATO® 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. To date, SPRAVATO® has been approved in 77 countries and administered to more than 100,000 patients worldwide.

ABOUT TRD4005
The Phase 4 TRD4005 clinical trial was a randomized, double-blind, multicenter, placebo-controlled study designed to evaluate the efficacy, safety, and tolerability of esketamine monotherapy at either 56 milligrams or 84 milligrams, administered bi-weekly, compared with placebo nasal spray in improving depressive symptoms in adult patients with TRD.

ABOUT TREATMENT-RESISTANT DEPRESSION
It is estimated that at least 30 percent of people living with MDD have treatment-resistant depression, which is defined as not responding to at least two or more different antidepressants of adequate dose and duration.[7] TRD has a significant negative impact, emotionally and functionally, on the individual and their loved ones, and has one of the highest economic burdens of all psychiatric disorders.[7]

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.

Johnson&Johnson

Media contact:
Caitlin Lormel
Johnson & Johnson
clormel@its.jnj.com
732-740-1701

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

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.
  - 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:**

Johnson&Johnson

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

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

- 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.

Johnson&Johnson

Media contact:
Caitlin Lormel
Johnson & Johnson
clormel@its.jnj.com
732-740-1701

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

- 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.

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

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

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 seltorexant and 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.

1. Emery PC, Wilson KG, Kowal J. Major depressive disorder and sleep disturbance in patients with chronic pain. Pain Res Manag. Jan-Feb 2014;19(1):35-41. doi: 10.1155/2014/480859
2. Chopra, A. (2023, December 1). Understanding the Relationship Between Insomnia Disorder and MDD. Psychopharmacology Institute. https://psychopharmacologyinstitute.com/section/understanding-the-relationship-between-insomnia-disorder-and-mdd-2765-5602
3. Chow W et al. Economic Burden Among Patients With Major Depressive Disorder: An Analysis of Healthcare Resource Use, Work Productivity, and Direct and Indirect Costs by Depression Severity. AJMC. 2019 Feb 2014. Link: https://www.ajmc.com/view/economic-burden-mdd
4. Taddei-Allen P. Economic Burden and Managed Care Considerations for the Treatment of Insomnia. 2020 Apr 12. Link: https://www.ajmc.com/view/economic-burden-and-managed-care-considerations-for-the-treatment-of-insomnia.
5. World Health Organization. "Depression: let's talk" says WHO, as depression tops list of causes of ill health. March 30, 2017. Accessed April 2024. Available at: https://www.who.int/news/item/30-03-2017--depression-let-s-talk-says-who-as-depression-tops-list-of-causes-of-ill-health
6. World Health Organization. Depressive disorder (depression). March 31, 2023. Accessed April 2024. Available at: https://www.who.int/news-room/fact-sheets/detail/depression
7. Zhdanava M, Pilon D, Ghelerter I, et al. The prevalence and national burden of treatment-resistant depression and major depressive disorder in the United States. *J Clin Psychiatry*. 2021;82(2):20m13699.