Media Contact:

Greg Panico
609-730-3061 (office)
908-240-2011 (mobile)

Investor Contact:

Christopher DelOrefice
732-524-2955 (office)

Lesley Fishman
732-524-3922 (office)

Janssen Submits Esketamine Nasal Spray New Drug Application to U.S. FDA for Treatment-Resistant Depression

If approved, esketamine nasal spray would provide the first new mechanism of action in 30 years to treat this debilitating mental illness[1,2]

TITUSVILLE, N.J., September 4, 2018 – The Janssen Pharmaceutical Companies of Johnson & Johnson (Janssen) today announced the submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for esketamine nasal spray. Janssen is seeking FDA approval of esketamine for treatment-resistant depression in adults.

Esketamine is an investigational, rapidly acting antidepressant that works differently than currently available therapies for major depressive disorder. Through glutamate receptor modulation, esketamine is thought to help restore connections between brain cells in people with treatment-resistant depression.

"Of the nearly 300 million people who suffer from major depressive disorder worldwide, about one-third do not respond to currently available treatments.[3,4] This represents a major unmet public health need," said Mathai Mammen, M.D., Ph.D., Global Head, Janssen Research & Development, LLC. "We are committed to working with the FDA to bring this new treatment option to U.S. patients with treatment-resistant depression and to the medical community."

The NDA is based on five pivotal Phase 3 studies of esketamine nasal spray in patients with treatment-resistant depression: three short-term studies, one withdrawal maintenance of effect study, and one long-term safety study. Data from these studies demonstrate that

treatment with esketamine nasal spray plus a newly initiated oral antidepressant compared to placebo nasal spray plus a newly initiated antidepressant was associated with rapid reduction of depressive symptoms and delayed time to relapse of symptoms of depression.[5,6] The long-term safety study showed that the esketamine doses studied were generally tolerated, with no new safety signals with dosing up to 52 weeks, compared to data from the short-term esketamine studies.[7] The short-term esketamine Phase 3 study in adults with treatment-resistant depression included a newly initiated oral antidepressant in both the control and placebo groups.[5]

"Esketamine has been shown to target critical aspects of glutamate-mediated synaptic plasticity, thereby bringing about rapid and sustained improvement in people with treatment-resistant depression," said Husseini K. Manji, MD, Global Head, Neuroscience Therapeutic Area, Janssen Research & Development, LLC.

Synaptic plasticity refers to the strength of information that flows through synapses, the spaces where neurons, cells in the brain, are connected.

Esketamine nasal spray will be self-administered by patients under the supervision of health care professionals.

The U.S. FDA granted Breakthrough Therapy Designations for esketamine nasal spray for treatment-resistant depression and for a second indication, major depressive disorder with imminent risk for suicide.[8] Janssen is currently conducting Phase 3 clinical studies for the second indication.

Janssen plans to submit a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for the esketamine treatment-resistant depression indication later in 2018.

More information on the esketamine Phase 3 study results can be accessed via the following links:

- https://www.janssen.com/new-phase-3-data-show-esketamine-nasal-spray-demonstrated-rapid-improvements-depressive-symptoms
- https://www.janssen.com/long-term-phase-3-study-shows-esketamine-nasal-spray-plus-oral-antidepressant-delayed-time-relapse

About Treatment-Resistant Depression
Major depressive disorder affects nearly 300 million people of all ages globally and is the leading cause of disability worldwide. People with depression, including major depressive disorder, suffer from a serious, biologically based disease which has a significant negative impact on all aspects of life, including quality of life and function.[3] Although currently available antidepressants are effective for many of these patients, about one-third do not respond to treatment.[4] Patients who have not adequately responded to at least two different antidepressant treatments for their current depressive episode are considered to have treatment-resistant depression.

About the Janssen Pharmaceutical Companies of Johnson & Johnson
At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science.

We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at http://www.janssen.com/. Follow us at www.twitter.com/JanssenUS and www.twitter.com/JanssenGlobal. Janssen Research & Development, LLC 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 of esketamine 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 Research & Development, LLC, 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; competition, including technological advances, new products and patents attained by competitors; challenges to patents; manufacturing difficulties and delays; changes in behavior and spending patterns or financial distress 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 description 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, 2017, including under 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, including under the caption "Cautionary Note Regarding Forward-Looking Statements", 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 undertake to update any forward-looking statement as a result of new information or future events or developments.

[1]Duman RS. Ketamine and rapid-acting antidepressants: a new era in the battle against depression and suicide. F1000Research. 2018;7:F1000 Faculty Rev-659. doi:10.12688/f1000research.14344.1.
[2]Dubovsky SL. What Is New about New Antidepressants? *Psychotherapy and Psychosomatics*. 2018;87(3):129-139. doi:10.1159/000488945.
[3]World Health Organization. Depression. Available at: http://www.who.int/mediacentre/factsheets/fs369/en/. Accessed June 2018.
[4]National Institute of Mental Health. Questions and Answers about the NIMH Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study — Background. Available at: https://www.nimh.nih.gov/funding/clinical-research/practical/stard/backgroundstudy.shtml. Accessed May 2018.
[5]V Popova, EJ Daly, M Trivedi, K Cooper, R Lane, P Lim, C Mazzucco, D Hough, ME Thase, RC Shelton, P Molero, E Vieta, M Bajbouj, H Manji, WC Drevets, JB Singh. Randomized, Double-Blind Study of Flexibly Dosed Intranasal Esketamine Plus Oral Antidepressant Versus Active Control in Treatment-Resistant Depression. Poster presented at: 2018 Annual Meeting of the American Psychiatric Association (APA); May 2018; New York, New York.
[6]EJ Daly, M Trivedi, A Janik, H Li, Y Zhang, X Li, R Lane, P Lim, AR Duca, D Hough, ME Thase, J Zajecka, A Winokur, I Divacka, A Fagiolini, WJ Cubala, I Bitter, P Blier, RC Shelton, P Molero, H Manji, WC Drevets, JB Singh. A Randomized Withdrawal, Double-blind, Multicenter Study of Esketamine Nasal Spray Plus an Oral Antidepressant for Relapse Prevention in Treatment-resistant Depression. Poster presented at: American Society of Clinical Psychopharmacology; May 2018; Miami, Florida.
[7]E Wajs, L Aluisio, R Morrison, EJ Daly, R Lane, P Lim, R Holder, G Sanacora, AH Young, S Kasper, AH Sulaiman, C Li, J Paik, H Manji, D Hough, WC Drevets, JB Singh. Long-Term Safety of Esketamine Nasal Spray Plus an Oral Antidepressant in Patients with Treatment-Resistant Depression: Phase 3, Open Label Safety and Efficacy Study (SUSTAIN-2). Poster presented at: The American Society of Clinical Psychopharmacology Meeting; May 2018; Miami, Florida.

[8]Janssen 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 May 2018.