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News Release

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New Safety Data Suggests SPRAVATO®▼ (Esketamine Nasal Spray) is More Tolerable and Effective Compared to Quetiapine Extended-Release (XR) in Adults with Treatment-resistant Major Depressive Disorder[1,2]

- *The new safety data is from the ESCAPE-TRD Phase 3b study[1]*
- *Additional findings from this study showed esketamine NS demonstrated a significant increase in the proportion of patients achieving remission and response compared to quetiapine XR, based on the patient-reported Patient Health Questionnaire (PHQ-9)[2]*

BEERSE, BELGIUM, 8 October 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced further findings for SPRAVATO® (esketamine nasal spray [NS]) from the ESCAPE-TRD study. Data on treatment-emergent adverse events (TEAEs) suggest a more favourable tolerability profile in adults with treatment-resistant major depressive disorder (TRD) receiving esketamine NS than quetiapine XR. Across all reported TEAEs experienced with esketamine NS, 92.1 percent were transient and resolved the same-day vs 12.1 percent of TEAEs experienced with quetiapine XR.[1] The findings were presented at the 36th European College of Neuropsychopharmacology Congress (ECNP 2023) taking place from 7 October to 10 October in Barcelona, Spain.

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While more TEAEs were observed with esketamine NS than with quetiapine XR, a greater proportion of esketamine NS-treated patients (82.6 percent) reported a TEAE that resolved same-day day vs quetiapine XR patients (15.5 percent).[1] Fewer esketamine NS-treated patients (53.6 percent) reported a TEAE that persisted for more than one day vs quetiapine XR-treated patients (74.7 percent) and TEAEs leading to treatment discontinuation were more frequent with quetiapine XR (11.0 percent) than with esketamine NS (4.2 percent).[1]

"From a clinician's perspective, each decision for treating a patient is based on a thorough evaluation of the treatment's benefits and risks, with patient safety being of paramount importance," said Professor Eduard Vieta, Investigator for the ESCAPE-TRD study and Head of the Psychiatry and Psychology Service of the Hospital Clínic de Barcelona, Spain.[*] "The findings from the ESCAPE-TRD study give confidence to healthcare professionals treating those living with TRD. It is important to have treatment options that are less likely to lead to discontinuation for a patient population that is, by its very definition, difficult to treat."

Major depressive disorder (MDD) affects nearly 40 million people in Europe.[3] Approximately one-third of people who experience MDD do not respond to treatment and are considered to have TRD – a term for people living with MDD who have cycled through two or more antidepressant treatments within the current depressive episode without experiencing symptomatic relief.[4,5]

Patients Report Superior Efficacy with Esketamine NS vs Quetiapine XR

In addition, patients enrolled in the ESCAPE-TRD study reported treatment effectiveness, using the nine-item patient health questionnaire (PHQ-9) scale. PHQ-9 is a widely used and effective tool for the detection of depression, and for monitoring its severity.[6]

Findings presented at ECNP 2023 showed that esketamine NS significantly increased the proportion of patients achieving, and shortened time to, PHQ-9 remission versus quetiapine XR, with patients being 1.21 times as likely to experience remission at Week 32.[2] From the patients' perspective of their own symptoms, esketamine NS showed superior short and long-term efficacy in TRD compared to quetiapine XR.[2]

Significantly more patients in the esketamine NS arm achieved PHQ-9 defined remission (56.8 percent versus 43.3 percent [$p<0.001$]) at Week 8, with numbers increasing by Week 32 (68.9 percent versus 57.2 percent [$p<0.01$], respectively) compared to patients

[*] Professor Eduard Vieta has been a paid consultant to Janssen; he has not been remunerated for contributing to this press release

in the quetiapine XR arm.[2] These findings were consistent with results of the primary endpoint analysis, which showed a significantly higher remission rate measured using the clinician-rated Montgomery-Äsberg Depression Rating Scale (MADRS) in the esketamine NS arm versus the quetiapine XR arm.[7]

"In addition to the previously published clinician-rated efficacy data from the ESCAPE-TRD study, the patient rated PHQ-9 data further confirms the favourable efficacy of esketamine NS compared to quetiapine XR, and we're proud to be providing options to patients in a therapeutic area that has seen few developments in recent years." said Dr Tamara Werner-Kiechle, EMEA Therapeutic Area Lead, Neuroscience and Pulmonary Hypertension, Janssen-Cilag GmbH, a Johnson & Johnson company. "Patient experience is increasingly recognised for its important role in driving improved patient outcomes and treatment experiences. That's why results like these really matter, especially for people impacted by TRD who often face treatment failure."

The 2023 ECNP data announcement follows the recent *New England Journal of Medicine* publication of the primary manuscript of the ESCAPE-TRD Phase 3b study, demonstrating the superior efficacy of esketamine NS compared to quetiapine XR in achieving remission at Week 8, and remaining relapse-free through Week 32 for patients with TRD.[7]

-ENDS-

NOTES TO EDITORS

About ESCAPE-TRD

ESCAPE-TRD is a randomised, open-label, rater-blinded, active-controlled, international, multicentre phase 3b clinical study designed to evaluate the efficacy, safety and tolerability of flexibly-dosed esketamine NS compared with quetiapine XR, both in combination with a continuing selective serotonin reuptake inhibitor (SSRI) or serotonin–norepinephrine reuptake inhibitor (SNRI) in subjects with TRD.[7,8]

676 adults were randomised to receive either esketamine NS (N=336) or quetiapine XR (N=340), both in combination with their current SSRI/SNRI.[7,8] The duration of the treatment period was up to a maximum of 32 weeks for all participants. Phases of the study were: an up-to-14-day screening phase, a treatment phase which included an 8-week acute phase and a 24-week maintenance phase, and a 2-week safety follow-up following the last dose of study intervention.[7,8]

The ESCAPE-TRD study was conducted across 24 countries in Europe, Latin America, Africa and Asia.[8]

About treatment-resistant major depressive disorder (TRD)

Depression affects nearly 40 million people of all ages in Europe and is one of the leading causes of disability worldwide.[3,9] TRD is a term for people living with major depressive disorder (MDD) who have cycled through two or more antidepressant treatments within the current depressive episode without experiencing symptomatic relief.[5] Approximately a third of people who suffer from MDD do not respond to treatment and are considered to have TRD.[4] TRD is a chronic condition that places an ongoing emotional, functional, and economic burden on the individual, their loved ones, and society.[10] The long-term nature of TRD means the condition has a greater patient and societal burden when compared to non-treatment-resistant MDD, including health-related quality of life (HRQoL), higher comorbidity, reduced functionality and increased use of health resources.[3,4,11,12]

About esketamine nasal spray (NS)

As an antagonist of the N-methyl-D-aspartate (NMDA) glutamate receptor, esketamine NS has a different mechanism of action and drug administration compared to other approved depression treatments.[13-15]

Esketamine NS is self-administered, under the direct supervision of a healthcare professional, through a single-use nasal spray device, for the treatment of patients within the licensed indications.[14,15] The decision to prescribe esketamine NS should be determined by a psychiatrist.[14]

Esketamine NS was authorised by the European Commission in December 2019 for use in combination with a SSRI or SNRI in adult patients with treatment-resistant major depressive disorder who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode.[16,17] It was also approved in February 2021 for co-administered use with oral antidepressant therapy in adults with a moderate to severe episode of major depressive disorder, as acute short-term treatment, for the rapid reduction of depressive symptoms, which according to clinical judgement constitute a psychiatric emergency.[14,17]

Important safety information

Adverse events should be reported.▼ This medicinal product is subject to additional monitoring and it is therefore important to report any suspected adverse events related to this medicinal product according to the local Summary of Product Characteristics

(SmPC). See Section 4.8 of your local SmPC to find specific reporting guidelines. For non-EU countries, please refer to your local SmPC.

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 & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

Learn more at www.janssen.com/emea.
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Janssen-Cilag International NV, the marketing authorisation holder for SPRAVATO®▼ in the EU, and Janssen-Cilag GmbH, are Johnson & Johnson companies.

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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 product development. 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 materialise, actual results could vary materially from the expectations and projections of Janssen-Cilag International NV, Janssen-Cilag Limited, Janssen-Cilag GmbH, 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 behaviour and spending patterns of purchasers of healthcare 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 January 1, 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 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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