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News Release

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New Data from the Phase 3b ESCAPE-TRD Study Show that Participants Receiving SPRAVATO®▼ (Esketamine Nasal Spray [NS]) Achieved Higher Response and Remission Rates, Increasing Over Time, Compared to those Receiving Quetiapine Extended-Release[1]

Findings presented at the 31st European Congress of Psychiatry (EPA 2023) confirm the importance of SPRAVATO® as a long-term therapeutic option for adults with treatment-resistant major depressive disorder[1]

BEERSE, BELGIUM, 27 March 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced further findings for SPRAVATO® (esketamine nasal spray [NS]) from the ESCAPE-TRD study. Data show that adults with treatment-resistant major depressive disorder (TRD) treated with esketamine NS achieved significantly* higher remission rates from Week 6 and response rates as early as Day 15 in the study, and at every subsequent time-point through Week 32, compared to adults treated with quetiapine extended-release (XR), when both were dosed as per their respective labels and used in combination with a continuing selective serotonin reuptake inhibitor (SSRI) or serotonin and norepinephrine reuptake inhibitor (SNRI).[1] The findings were presented

*Tested at a two-sided 0.05 significance level without adjustment for multiple testing.[1]

at the 31st European Congress of Psychiatry (EPA 2023) taking place from March 25 to March 28 in Paris, France, following earlier top line data from the study presented at the German Association for Psychiatry, Psychotherapy and Psychosomatics (DGPPN) Congress last year.[2]

Major depressive disorder (MDD) affects around 40 million people in the EU.[3] Approximately a 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]

"TRD is a major burden to the millions of people[3] impacted by the condition, as well as to their caregivers and healthcare systems," said Professor Andreas Reif, Principal Investigator for the ESCAPE-TRD study and Head of the Department of Psychiatry, Psychosomatic Medicine and Psychotherapy at University Hospital Frankfurt, Germany[†]."The ESCAPE-TRD study findings show us that using esketamine NS over the long-term provides clinically important improvements in remission rates in people with TRD, with treatment response increasing over time.[1] These data give those affected by TRD and their healthcare professionals reassurance and confidence that esketamine NS could have a meaningful impact in helping reduce the effect TRD has on their lives, and eventually enabling them to take a more active role in society."

ESCAPE-TRD is a long-term, comparative, randomised, open-label, rater-blinded phase 3b clinical study designed to evaluate the short- and long-term efficacy, safety and tolerability of flexibly-dosed esketamine NS compared with quetiapine XR, both in combination with a continuing SSRI or SNRI, in adults with TRD.[1,2,6] The study evaluated 676 adults aged 18-74 years with TRD, randomised to receive either esketamine NS (n=336) or quetiapine XR (n=340), both in combination with a continuing SSRI/SNRI.[1,6] TRD was defined as non-response to at least two consecutive adequately dosed treatments (including the ongoing treatment) during the current depressive episode.[1]

Findings presented at EPA 2023 showed that a significantly[*] higher proportion of participants in the esketamine NS arm achieved remission[‡] from Week 6 and at every

[†] Professor Andreas Reif has been a paid consultant to Janssen; he has not been paid for contributing to this press release

[*] Tested at a two-sided 0.05 significance level without adjustment for multiple testing.[1]

[‡] Remission was defined as Montgomery-Åsberg Depression Rating Scale [MADRS] total score ≤10. MADRS is a clinician-rated measure of depression severity[1]

subsequent time-point through Week 32 compared to the quetiapine XR arm.[1] At Week 32, 55 percent of patients in the esketamine NS arm achieved remission compared to 37 percent in the quetiapine XR arm.[1]

In addition, a significantly* greater proportion of participants in the esketamine NS arm versus the quetiapine XR arm experienced response§ from Day 15 and at every subsequent time-point through Week 32.[1] Notably, the absolute response rate at Week 8 in the esketamine NS arm was 55.4 percent vs 39.1 percent for quetiapine XR, rising to 75.5 percent vs 55.5 percent respectively at Week 32.[1]

Participants in the esketamine NS study arm also experienced a significantly* improved reduction of depressive symptoms, as measured by the Montgomery-Åsberg Depression Rating Scale (MADRS) vs quetiapine XR from Day 8, with an average difference over time in the least squares (LS) means total MADRS score change from baseline of −2.4.[1] MADRS is a clinician-rated measure of depression severity.[1]

"Today marks another major milestone in the treatment of TRD. With a third of people with MDD not responding to treatment and considered to be treatment-resistant[4], the data being presented today at EPA 2023 demonstrate that esketamine nasal spray may help a greater proportion of people living with TRD achieve response and remission over the long-term, compared to quetiapine extended-release.[1] We are hopeful that this news will be welcomed by people living with TRD, their caregivers and their healthcare providers," said Dr. Tamara Werner-Kiechle, EMEA Therapeutic Area Lead, Neuroscience and Pulmonary Hypertension, Janssen-Cilag GmbH, part of the Janssen Pharmaceutical Companies of Johnson & Johnson. "We are committed to bringing to life therapies to prevent and treat what can be a devastating disease and are confident that today's ESCAPE-TRD results, on top of those presented last year, show the potential of esketamine nasal spray in ending repeated treatments failures in a population that is often difficult to treat and providing positive outcomes for people impacted by TRD."

Safety findings demonstrated that the rate of treatment discontinuation due to treatment-emergent adverse events (TEAEs) were lower in the esketamine NS arm (4.2 percent versus the quetiapine XR arm (11.0 percent).[1] The most common TEAEs leading to treatment discontinuation in the esketamine NS arm were dizziness (0.6 percent vs

*Tested at a two-sided 0.05 significance level without adjustment for multiple testing.[1]

§ Response was defined as ≥50% improvement in MADRS total score from baseline or MADRS ≤10[1]

1.2 percent for quetiapine XR), dissociation (0.6 percent vs 0 percent for quetiapine XR) and vomiting (0.6 percent vs 0 percent for quetiapine XR).[1] In the quetiapine XR arm the most common TEAEs leading to treatment discontinuation were sedation (2.1 percent vs 0 percent for esketamine NS), weight increase (1.8 percent vs 0 percent for esketamine NS) and somnolence (1.5 percent vs 0 percent for esketamine NS).[1]

-ENDS-

NOTES TO EDITORS

About ESCAPE-TRD

ESCAPE-TRD is a randomised, open-label, rater-blinded, active-controlled, international, multicenter 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 SSRI or SNRI in subjects with TRD.[1]

676 adults were randomised to receive either esketamine NS (N=336) or quetiapine XR (N=340), both in combination with their current SSRI/SNRI.[1,2,6] 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.[2,6]

ESCAPE-TRD was conducted across 24 countries in Europe, Latin America, Africa and Asia.[6]

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.[3,7] TRD is 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.[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.[8] 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.[3,4,9,10]

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.[11,12,13]

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.[11,12,13] The decision to prescribe esketamine NS should be determined by a psychiatrist.[12]

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.[14,15] 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.[12,15]

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. 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.

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Janssen-Cilag International NV, the marketing authorisation holder for SPRAVATO®▼ in the EU, and Janssen-Cilag GmbH, are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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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, 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 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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[1] Reif A. et al., Esketamine nasal spray shows higher remission and response rates over 32 weeks of treatment compared with quetiapine extended-release in patients with treatment resistant depression: Results from ESCAPE-TRD, a randomised, phase IIIb clinical trial. Presented at EPA 2023, March 25-28. Poster PO0067

[2] Reif A. et al., Esketamine nasal spray improves short- and long-term outcomes compared with quetiapine extended release in patients with treatment resistant depression: First results from ESCAPE-TRD, a randomised, multi-centre phase IIIb clinical trial. Presented at DGPPN 2022, November 23-26. Poster P-01-04.

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[15] United Kingdom Electronic Medicines Compendium. Summary of Product Characteristics. Spravato 28 mg nasal spray. Janssen-Cilag Ltd. Last updated November 2022.