ADDITIONAL DISCLOSURE DATA FOR SWITZERLAND

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Date: *17 August 2020*

Swiss marketing authorisation data

Swiss Marketing Authorisation number: 67103

Swiss Marketing Authorisation date: 25 February 2020

Name of the preparation: Spravato – 28 mg – nasal spray

Name of active pharmaceutical ingredient: Esketamine (JNJ-54135419-AAC)

Clinical trial data

1. **Clinical trial identification**

Protocol No.: 54135419SUI3002

Title of Study: A Double-blind, Randomized, Placebo-controlled Study to Evaluate the Efficacy and Safety of Intranasal Esketamine in Addition to Comprehensive Standard of Care for the Rapid Reduction of the Symptoms of Major Depressive Disorder, Including Suicidal Ideation, in Adult Subjects Assessed to be at Imminent Risk for Suicide

Study Name: ASPIRE II

EudraCT Number: 2016-003992-23

NCT No.: NCT03097133

2. **Protocol change history**

Protocol and Global Amendments:

Original Protocol, 08 December 2016

Amendment-1, 20 April 2017 – substantial

Amendment-2, 31 January 2018 – substantial

3. Clinical trial investigators and study centres

Principal Investigator*:* Siegfried Kasper, MD

Study Centres: Countries and number of sites in each country in which the study was conducted: Argentina (4), Austria (2), Belgium (2), Brazil (5), Canada (1), Czech Republic (2), France (5), Lithuania (2), Poland (4), Spain (3), Turkey (4), and United States (13)

4. Medication used

Test Product, Dose and Mode of Administration, Batch No.: Esketamine nasal spray was supplied as a solution of esketamine hydrochloride (16.14% weight/volume; equivalent to 14% weight/volume esketamine base) in a nasal spray pump (device), which delivered 16.14 mg esketamine hydrochloride (14 mg esketamine base) per 100-µL spray. Each individual nasal spray device contained a total of 28 mg (ie, 2 sprays). Esketamine batch numbers were: 160663, 161330, 502228, 170116, 160885, 170676, 161747, and 170677.

Reference Therapy, Dose and Mode of Administration, Batch No.: Intranasal placebo was supplied as a solution of water for injection with a bittering agent (0.001 mg/mL denatonium benzoate). The placebo solution was provided in matching nasal spray devices, each containing 2 sprays. Intranasal placebo batch numbers were: 160665, 502264, 161165, 161515, and 162284A.

5. Study population

Number of participants – planned: 224

Number of participants – analysed: 230

6. Summary and conclusion

- Results from the primary efficacy analysis in this study in subjects with major depressive disorder (MDD) assessed to be at imminent risk for suicide showed that esketamine nasal spray 84 mg plus comprehensive standard clinical care, including optimized antidepressant treatment and initial hospitalization, demonstrated a clinically meaningful and statistically significant benefit compared with placebo plus standard of care treatment as assessed by improvements in Montgomery-Asberg Depression Rating Scale (MADRS) total score at 24 hours after the first dose of study agent. Furthermore, between Day 1, 4 hours after the first dose, and Day 25, improvements in montgomery-asberg depression rating scale MADRS total score numerically favored treatment with esketamine plus standard of care over placebo plus standard of care.

- Although subjects in both treatment groups showed improvement from baseline in severity of suicidality as measured by the clinical global impression-severity of suicidality-revised (CGI-SS-R) scale, the difference between treatment groups in the changes from baseline was not statistically significant 24 hours after the first dose of study agent in the key secondary efficacy analysis.
- Esketamine nasal spray 84 mg plus standard of care treatment was safe and tolerated. The adverse events reported in this study were generally consistent with the safety profile of esketamine observed in previous studies in subjects with MDD assessed to be at imminent risk for suicide and those with treatment-resistant depression. Overall, there were no new or unexpected safety concerns noted with the administration of esketamine during this study.

7. Results reporting

Date of Clinical Trial Report: 29 August 2019

Prepared by: Janssen Research & Development, LLC

Publication(s) Reference(s):

Ionescu D, Fu DJ, Qiu X, Lane R, Lim P, Kasper S, Hough D, Drevets W, Manji H, Canuso C; et al. Esketamine Nasal Spray for Rapid Reduction of Depressive Symptoms in Patients with Major Depressive Disorder Who Have Active Suicide Ideation with Intent: Results of a Phase 3, Double-Blind, Randomized Study (ASPIRE II)". The International Journal of Neuropsychopharmacology. In press.

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