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The Journal npj Schizophrenia Publishes the Results of the PRISMA-3 Study of the Efficacy and Safety of Doria® in Schizophrenic Patients

The results of the phase III pivotal clinical trial show that the once-monthly injectable antipsychotic Doria® furnishes a significant improvement in the symptomatology and severity of the illness in patients with acute exacerbation of schizophrenia.

Madrid – 27 November 2020 – Today, Laboratorios Farmacéuticos Rovi, S.A. (www.rovi.es) has announced the online publication of the results of the pivotal study PRISMA-3 on the efficacy and safety of Doria® in schizophrenic patients in the journal *npj Schizophrenia*[1].

Doria® (Risperidone ISM®) is a novel investigational antipsychotic for the treatment of schizophrenia with once-monthly injections which has been developed and patented by Laboratorios Farmacéuticos ROVI S.A. and which, as of the first injection, provides immediate and sustained plasmatic drug levels and does not require loading doses or supplementation with oral risperidone.

The results obtained in this study show that both doses (75 mg and 100 mg once a month) have achieved the prespecified primary and secondary efficacy endpoints for treatment of patients with acute exacerbation of schizophrenia. The primary efficacy endpoint, the PANSS total score (mean difference, CI: 95%), improved significantly

[1] Correll, C.U., Litman, R.E., Filts, Y. et al. Efficacy and safety of once-monthly Risperidone ISM® in schizophrenic patients with an acute exacerbation. npj Schizophr 6, 37 (2020). https://doi.org/10.1038/s41537-020-00127-y

with Risperidone ISM® 75 mg and 100 mg from the beginning until day 85, with adjusted differences of -13.0 (17.3 to -8-8; p <0.0001) and -13.3 (-17.6 to -8.9; p<0.0001), respectively. Significantly improved mean changes for the secondary endpoint, the CGI-S score, were also obtained for Risperidone ISM® in comparison with the placebo, -0.7 (-1.0 to -0.5; p<0.0001), for both doses. The significant statistical improvement for both efficacy results was observed as early as 8 days after the first injection. The most frequently reported treatment-emergent adverse events were increased blood prolactin (7.8%), headaches (7.3%), hyperprolactinemia (5%) and weight increase (4.8%). No important new or unexpected safety information was reported.

According to the authors of the article, Risperidone ISM® represents an effective therapeutic strategy in schizophrenic patients who are admitted to hospital with an acute episode with severe or moderate psychotic symptoms.

"We are very pleased with these results, since, not only do they prove that our ISM® technology works, but also because we believe that Doria® will be able to help cover an unmet medical need", said Dr. Ibón Gutierro, ROVI's Corporate R&D Manager. Likewise, Dr. Gutierro explained that "this study is proof that a schizophrenic patient with moderate to severe psychotic symptoms can also be treated with a long-acting injectable antipsychotic like Doria®".

On the basis of these positive results and the other data from the product, ROVI previously announced the commencement of the centralised procedure for registration with the European Medicines Agency (EMA) in January 2020. Likewise, at its Capital Markets Day held on 24 November, ROVI has just announced the filing of an NDA (New Drug Application), i.e. a registration dossier to obtain marketing authorisation in the USA, with the FDA (Food and Drug Administration).

About the PRISMA-3 study

The pivotal study PRISMA-3 is a multicenter, randomized, double-blind, placebo-controlled clinical trial to evaluate, after a period of 12 weeks, the efficacy and safety of once-monthly intramuscular injections of Risperidone ISM® in patients with acute exacerbation of schizophrenia[2].

[2] https://clinicaltrials.gov/ct2/show/NCT03160521

A total of 438 patients were included in the double-blind period of the study and were randomly allocated to receive Risperidone ISM® 75 mg or 100 mg or placebo. Slightly more than half of the participants (61%) were recruited in U.S. centers. At the beginning of the study, patients, of both sexes, were between 18 and 64 years old, were diagnosed with schizophrenia according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V) and presented with an acute exacerbation or relapse of the disease, confirmed by a PANSS total score between 80 and 120 and a CGI-S score greater than or equal to 4 ("moderately ill").

The prespecified primary efficacy endpoint in the study was the mean change at 12 weeks from baseline value in the PANSS total score, using a Mixed Effects Model with Repeated Measurements (MMRM), with the Hommel's closed-testing correction procedure for multiple tests. In addition, the study protocol prespecified as a key secondary efficacy endpoint the mean change in the CGI-S total score at 12 weeks compared to the baseline value.

Patients who successfully completed the double-blind period were offered to continue in a long-term, open-label 12-month extension phase with once-monthly injections of Risperidone ISM® (75 mg or 100 mg). New, clinically stable patients ("de novo" patients) have also been able to enter this open phase of the study. The objective of the study extension phase is to check the safety, tolerability and durability of the long-term Risperidone ISM® effect.[3].

About Schizophrenia

Schizophrenia is a chronic, serious, and disabling mental disorder that affects about 1% of the global population. Schizophrenia patients are characterized by a mixture of psychiatric symptoms, both positive (delusional ideas, hallucinations, disorganized language and behavior) as negative (affective flattening, speech poverty, abulia) in nature. The disease usually starts at a critical age for personal development, forcing patients in many cases to leave their educational or work activity, resulting in a great deal of suffering for the subjects and their family environment as well as representing an important loss for society at large. It is estimated that approximately 3% to 5% of total global health expenditure is devoted to schizophrenia.

[3] https://clinicaltrials.gov/ct2/show/NCT03870880

About the ISM® Technology

ISM® is a Technology Platform for the release of drugs patented by ROVI, which is based on the *in situ* formation of biodegradable matrices after the administration of a liquid carrier. Its unique characteristics allow to quickly obtain therapeutic levels of the medicine after its administration, without the need to for oral coadministration or additional booster or loading injections to achieve and maintain the levels in a predictable and sustained way, which has a greater likelihood of satisfying the patient's clinical needs.

About ROVI

ROVI is a pan-European pharmaceutical company specializing and engaging in the research, development, contract manufacturing and marketing of small molecules and biological specialties. The company, in a continuous international expansion process, has subsidiaries in Portugal, Germany, the United Kingdom, Italy France and Poland, and has a diversified marketing portfolio of more than 40 products, among which its flagship product, Bemiparin, which is already marketed in 56 countries all over the world, should be highlighted. Likewise, in 2017, ROVI commenced the marketing of its in-house developed enoxaparin biosimilar in Europe. ROVI continues to develop the ISM® Platform technology, a leading-edge line of research in the field of prolonged drug release with proven advantages. For more information, please visit www.rovi.es.

Forward-looking statements

This news release contains forward-looking statements. Such forward looking statements involve known and unknown risks, uncertainties and other factors which might cause the actual results, financial condition, performance, or achievements of ROVI or industry results, to be materially different from any future results, performance, or achievements expressed or implied by such forward looking statements. The statements in this press release represent ROVI's expectations and beliefs as of the date of this press release. ROVI anticipates that subsequent events and developments may cause these expectations and beliefs to change. However, while ROVI may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking

statements should not be relied upon as representing ROVI's expectations or beliefs as of any date subsequent to the date of this press release.