



Teva and MedinCell Announce Positive Results for Registration Trial of Investigational Extended-Release Subcutaneous Injectable Risperidone for Patients with Schizophrenia

Study met its primary efficacy endpoint of delaying time to relapse

PARSIPPANY, N.J., TEL AVIV & PARIS, January 7, 2021 – Teva Pharmaceutical Industries Ltd. (NYSE and TASE: TEVA) and MedinCell (Euronext: MEDCL) today announced positive results for study TV46000-CNS-30072 (the RISE study – The Risperidone Subcutaneous Extended-Release Study), a Phase 3 clinical trial designed to evaluate the efficacy of TV-46000/mdc-IRM (risperidone extended-release injectable suspension for subcutaneous use) as a treatment for patients with schizophrenia. Trial enrollment was open to patients 13-65 years of age. In the RISE study, patients treated with the investigational subcutaneous risperidone injection either monthly (q1M) (n=183) or once every two months (q2M) (n=179) experienced a statistically significant delay in time to relapse versus placebo (n=181), the study's primary endpoint, with $p < 0.0001$ for each comparison. The investigational subcutaneous risperidone injection q1M and q2M demonstrated a reduction of 80.0% and 62.5% in the risk to relapse compared to placebo, respectively.

“Schizophrenia is a chronic, progressive and severe mental disorder in which every relapse has the potential to cause cognitive and psychosocial loss, worsen long-term outcomes, and increase the overall burden for patients, caregivers, families, and the healthcare system. We are encouraged by the results of the RISE study, which demonstrated a marked delay in time to relapse for patients in both the monthly and once-every-two months treatment groups,” said Christer Nordstedt, MD, PhD, Senior Vice President, Head of Specialty Clinical Development at Teva. “We look forward to sharing more detailed results from the RISE study at future scientific conferences, in peer-reviewed publications as well as exploring options for a potential NDA submission using the currently available clinical data.”

No new safety signals have been identified that are inconsistent with the known safety profile of other risperidone formulations. The second of Teva’s Phase 3 studies (TV46000-CNS-30078 – the SHINE study) evaluating the long-term safety and tolerability of the investigational subcutaneous risperidone injection across 331 patients is ongoing. Interim results align with the safety findings of the RISE study.

“Long-acting injectables (LAI) for schizophrenia are considered to be an innovative treatment option that we believe will make a meaningful difference, yet they tend to be underutilized and only introduced late in the course of the disease,” said Christophe Douat, CEO at MedinCell. “The results of the RISE study are promising and point to the potential for risperidone to be a subcutaneously administered treatment option for patients with schizophrenia.”

Teva will continue to lead the clinical development and regulatory process and be responsible for commercialization of this candidate treatment, with MedinCell eligible for development milestones, royalties on net sales and future commercial milestones.

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About Risperidone Extended-Release Injectable Suspension for Subcutaneous Use

The extended-release subcutaneous risperidone injection is an investigational once-monthly or once-every-two-months injectable formulation of the well-characterized and widely used atypical antipsychotic risperidone for the treatment of schizophrenia. The investigational subcutaneous risperidone injection utilizes a novel polymer delivery platform that allows the product to be delivered subcutaneously. The polymer delivery platform, in combination with risperidone, allows for control of the rate and duration of drug release and a range of dosing options. The investigational subcutaneous risperidone injection has been studied extensively in non-clinical and clinical studies, including a global Phase 3 clinical development program with two pivotal studies evaluating investigational subcutaneous risperidone injection in schizophrenia: The RISE Study (TV46000-CNS-30072) and the SHINE Study (TV46000-CNS-30078). No new safety signals have been identified that are inconsistent with the known safety profile of other risperidone formulations.

About TV46000-CNS-30072 (The RISE Study – The Risperidone Subcutaneous Extended-Release Study)

The RISE study was a multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy of risperidone extended-release injectable suspension for subcutaneous use as a treatment in patients (ages 13-65 years) with schizophrenia. 544 patients were randomized to receive a subcutaneous injection of risperidone either q1M or q2M, or placebo in a 1:1:1 ratio. The primary endpoint was time to impending relapse.

About TV46000-CNS-30078 (The SHINE Study)

The second of Teva’s Phase 3 studies; designed to evaluate the long-term safety and tolerability of the investigational subcutaneous risperidone injection administered q1M or q2M for up to 56 weeks in 331 patients (ages 13-65 years) with schizophrenia. The primary endpoint is the frequency of all adverse events, including serious adverse events. This study is continuing; interim results align with the safety findings of the RISE study (TV46000-CNS-30072).

About Schizophrenia

Schizophrenia is a chronic, progressive and severely debilitating mental disorder that affects how one thinks, feels and acts.¹ Patients experience an array of symptoms, which may include delusions, hallucinations, disorganized speech or behavior and impaired cognitive ability.¹ Approximately 1% of the world’s population will develop schizophrenia in their lifetime,² and 3.5 million people in the U.S. are currently diagnosed with the condition.³ Although schizophrenia can occur at any age,² the average age of onset tends to be in the late teens to the early 20s for men, and the late 20s to early 30s for women.⁴ The long-term course of schizophrenia is marked by episodes of partial or full remission broken by relapses that often occur in the context of psychiatric emergency and require hospitalization.²

¹ Patel, K. R., Cherian, J., Gohil, K., & Atkinson, D. (2014). Schizophrenia: overview and treatment options. *P & T: a peer-reviewed journal for formulary management*, 39(9), 638–645.

² Biagi, E., Capuzzi, E., Colmegna, F., Mascarini, A., Brambilla, G., Ornaghi, A., Santambrogio, J., & Clerici, M. (2017). Long-Acting Injectable Antipsychotics in Schizophrenia: Literature Review and Practical Perspective, with a Focus on Aripiprazole Once-Monthly. *Advances in therapy*, 34(5), 1036–1048.

³ SARDAA. About Schizophrenia. Available at: <https://sardaa.org/resources/about-schizophrenia/>. Accessed December 2020.

⁴ NAMI. About Mental Illness: Schizophrenia. Available at: <https://www.nami.org/About-Mental-Illness/Mental-Health-Conditions/Schizophrenia>. Accessed December 2020.

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Approximately 80% of patients experience multiple relapses over the first five years of treatment,⁵ and each relapse carries a biological risk of loss of function, treatment refractoriness, and changes in brain morphology.^{6, 7} Patients are often unaware of their illness and its consequences, contributing to treatment nonadherence, high discontinuation rates,⁵ and ultimately, significant direct and indirect healthcare costs from subsequent relapses and hospitalizations.^{8,9}

About Teva

Teva Pharmaceutical Industries Ltd. (NYSE and TASE: TEVA) has been developing and producing medicines to improve people’s lives for more than a century. We are a global leader in generic and specialty medicines with a portfolio consisting of over 3,500 products in nearly every therapeutic area. Around 200 million people around the world take a Teva medicine every day and are served by one of the largest and most complex supply chains in the pharmaceutical industry. Along with our established presence in generics, we have significant innovative research and operations supporting our growing portfolio of specialty and biopharmaceutical products. Learn more at www.tevapharm.com.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 regarding long-acting injectable risperidone for patients with Schizophrenia, which are based on management’s current beliefs and expectations and are subject to substantial risks and uncertainties, both known and unknown, that could cause our future results, performance or achievements to differ significantly from that expressed or implied by such forward-looking statements. Important factors that could cause or contribute to such differences include risks relating to:

- our ability to successfully compete in the marketplace, including: that we are substantially dependent on our generic products; consolidation of our customer base and commercial alliances among our customers; the increase in the number of competitors targeting generic opportunities and seeking U.S. market exclusivity for generic versions of significant products; competition for our specialty products, especially COPAXONE®, our leading medicine, which faces competition from existing and potential additional generic versions, competing glatiramer acetate products and orally-administered alternatives; the uncertainty of commercial success of AJOVY® or AUSTEDO®; competition from companies with greater resources and capabilities; delays in launches of new products and our ability to achieve expected results from investments in our product pipeline; ability to develop and commercialize biopharmaceutical products; efforts of pharmaceutical companies to limit the use of generics, including through legislation and regulations and the effectiveness of our patents and other measures to protect our intellectual property rights;

⁵ Emsley, R., & Kilian, S. (2018). Efficacy and safety profile of paliperidone palmitate injections in the management of patients with schizophrenia: an evidence-based review. *Neuropsychiatric disease and treatment*, 14, 205–223.

⁶ Emsley, R., Chiliza, B., Asmal, L. et al. (2013) The nature of relapse in schizophrenia. *BMC Psychiatry* 13, 50.

⁷ Andreasen, N. C., et al. (2013). Relapse duration, treatment intensity, and brain tissue loss in schizophrenia: a prospective longitudinal MRI study. *The American journal of psychiatry*, 170(6), 609–615.

⁸ Pennington, M., & McCrone, P. (2017). The Cost of Relapse in Schizophrenia. *PharmacoEconomics*, 35(9), 921–936.

⁹ Jin, H., & Mosweu, I. (2017). The Societal Cost of Schizophrenia: A Systematic Review. *PharmacoEconomics*, 35(1), 25–42.

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- our substantial indebtedness, which may limit our ability to incur additional indebtedness, engage in additional transactions or make new investments, may result in a further downgrade of our credit ratings; and our inability to raise debt or borrow funds in amounts or on terms that are favorable to us;
- our business and operations in general, including: uncertainty regarding the magnitude, duration, and geographic reach of the COVID-19 pandemic and its impact on our business, financial condition, operations, cash flows, and liquidity and on the economy in general; our ability to successfully execute and maintain the activities and efforts related to the measures we have taken or may take in response to the COVID-19 pandemic and associated costs therewith; effectiveness of our restructuring plan announced in December 2017; our ability to attract, hire and retain highly skilled personnel; our ability to develop and commercialize additional pharmaceutical products; compliance with anti-corruption sanctions and trade control laws; manufacturing or quality control problems; interruptions in our supply chain, including due to potential effects of the COVID-19 pandemic on our operations and business in geographic locations impacted by the pandemic and on the business operations of our suppliers; disruptions of information technology systems; breaches of our data security; variations in intellectual property laws; challenges associated with conducting business globally, including adverse effects of the COVID-19 pandemic, political or economic instability, major hostilities or terrorism; significant sales to a limited number of customers; our ability to successfully bid for suitable acquisition targets or licensing opportunities, or to consummate and integrate acquisitions; our prospects and opportunities for growth if we sell assets; and potential difficulties related to the operation of our new global enterprise resource planning (ERP) system;
- compliance, regulatory and litigation matters, including: our ability to successfully defend against the U.S. Department of Justice criminal charges of Sherman Act violations; increased legal and regulatory action in connection with public concern over the abuse of opioid medications in the U.S. and our ability to reach a final resolution of the remaining opioid-related litigation; costs and delays resulting from the extensive governmental regulation to which we are subject or delays in governmental processing time due to modified government operations due to the COVID-19 pandemic, including effects on product and patent approvals due to the COVID-19 pandemic; the effects of reforms in healthcare regulation and reductions in pharmaceutical pricing, reimbursement and coverage; governmental investigations into S&M practices; potential liability for patent infringement; product liability claims; increased government scrutiny of our patent settlement agreements; failure to comply with complex Medicare and Medicaid reporting and payment obligations; and environmental risks;
- other financial and economic risks, including: our exposure to currency fluctuations and restrictions as well as credit risks; potential impairments of our intangible assets; potential significant increases in tax liabilities; and the effect on our overall effective tax rate of the termination or expiration of governmental programs or tax benefits, or of a change in our business;

and other factors discussed in this press release, in our Quarterly Reports on Form 10-Q for the first, second and third quarters of 2020 and in our Annual Report on Form 10-K for the year ended December

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31, 2019, including in the sections captioned "Risk Factors" and "Forward Looking Statements." Forward-looking statements speak only as of the date on which they are made, and we assume no obligation to update or revise any forward-looking statements or other information contained herein, whether as a result of new information, future events or otherwise. You are cautioned not to put undue reliance on these forward-looking statements.

About MedinCell

MedinCell is a clinical stage pharmaceutical company that develops a portfolio of long-acting injectable products in various therapeutic areas by combining its proprietary BEPO® technology with active ingredients already known and marketed. Through the controlled and extended release of the active pharmaceutical ingredient, MedinCell makes medical treatments more efficient, particularly thanks to improved compliance, i.e. compliance with medical prescriptions, and to a significant reduction in the quantity of medication required as part of a one-off or chronic treatment. The BEPO® technology makes it possible to control and guarantee the regular delivery of a drug at the optimal therapeutic dose for several days, weeks or months starting from the subcutaneous or local injection of a simple deposit of a few millimeters, fully bioresorbable. Based in Montpellier, MedinCell currently employs more than 130 people representing over 25 different nationalities.

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