December 4, 2023

Tonix Pharmaceuticals Announces IND Clearance by the FDA for Phase 2 Trial of TNX-2900 for the Treatment of Prader-Willi Syndrome, the Most Common Genetic Cause of Life-Threatening Childhood Obesity

TNX-2900 is a proprietary magnesium-potentiated formulation of intranasal oxytocin, a naturally occurring hormone that reduces appetite and eating

Preclinical data show magnesium-potentiation increases the potency of exogenous oxytocin

Formulations of intranasal oxytocin without magnesium have reported inconsistent results in clinical trials of Prader Willi Syndrome[1,2]

CHATHAM, N.J., Dec. 04, 2023 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a biopharmaceutical company with marketed products and a pipeline of development candidates, today announced the U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application to support clinical development of TNX-2900 (intranasal potentiated oxytocin), a proprietary magnesium (Mg^{2+})-enhanced formulation of intranasal oxytocin, to treat Prader-Willi syndrome (PWS) in children and adolescents. TNX-2900 for the treatment of PWS was granted Orphan Drug designation by the FDA in 2022.

The Phase 2 study approved by the IND is a dose-finding study involving approximately 36 PWS patients divided into four groups with approximately nine PWS patients per group. One group will receive placebo and three groups will receive different dosage regimens of TNX-2900. Tonix intends to seek a partner to advance TNX-2900 for PWS in clinical development.

“We are pleased that TNX-2900 is cleared for clinical studies for the treatment of PWS in children and adolescents as there remains a significant need for new therapies, particularly for PWS hyperphagia, which currently has no approved treatments,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “PWS is the most common genetic cause of life-threatening childhood obesity.[3,4] We believe adding Mg^{2+} to the formulation has the potential to improve intranasal oxytocin’s therapeutic action.”

The IND application for TNX-2900 was supported by preclinical data demonstrating that

Mg^{2+} enhances the potency of oxytocin. Oxytocin is a naturally-occurring hormone that reduces appetite and eating and regulates hunger, anxiety and prosocial behavior. PWS is a genetic disorder associated with abnormalities of the oxytocin system[5]. Several previous clinical studies in PWS of intranasal oxytocin without Mg^{2+}-potentiation have shown trends toward improvement, but the results have been inconsistent.[1,2] Tonix believes that Mg^{2+}-potentiation of intranasal oxytocin in PWS may improve consistency in clinical trials because in animal studies Mg^{2+}-potentiation appears to eliminate the high-dose suppression of oxytocin's inverted "U"-shaped dose response.[6]

Gregory Sullivan, M.D., Chief Medical Officer of Tonix Pharmaceuticals added, "Recent reports show Mg^{2+} is necessary for oxytocin to fully activate the oxytocin receptor.[3,6] Oxytocin has potent effects in adult mice correcting behavioral characteristics of the *Magel2* knock-out mouse model for PWS and autism.[4] Oxytocin has many potential therapeutic roles in reducing appetite, eating, weight, migraine pain and autistic spectrum behaviors. Tonix recently completed enrollment in a Phase 2 study of TNX-1900, a related Mg^{2+}-potentiated intranasal oxytocin candidate, for the prevention of migraine headaches, and is also studying TNX-1900 through external collaborations for the treatment of obesity in adolescents, binge eating disorder, bone health in autism, and social anxiety disorder."

About Prader-Willi Syndrome (PWS)
PWS is recognized as the most common genetic cause of life-threatening childhood obesity and affects males and females with equal frequency and all races and ethnicities. PWS results from the absence of expression of a group of genes on the paternally acquired chromosome 15. The hallmarks of PWS are lack of suckling in newborns and, in children and adolescents, severe hyperphagia, an overriding physiological drive to eat, leading to severe obesity and other complications associated with significant mortality. A systematic review of the morbidity and mortality as a consequence of hyperphagia in PWS found that the average age of death in PWS was 22.1 years.[7] There is no approved medication to treat poor feeding in newborns or hyperphagia in children and adolescents with PWS. Given these serious or life-threatening manifestations of these conditions, there is a critical need for effective treatments to decrease morbidity and mortality, improve quality of life, and increase life expectancy in people with PWS. Oxytocin has potent effects in adult mice correcting behavioral characteristics of the *Magel2* knock-out mouse model for PWS and autism.[4] In addition, oxytocin has potent effects in correcting behavioral characteristics of the neonatal *Magel2* knock-out mouse model for PWS and autism[8] and intriguing effects in a clinical trial of neonates with PWS.[9]

About TNX-2900 and Tonix's Potentiated Oxytocin Platform
TNX-2900 is based on Tonix's patented intranasal potentiated oxytocin formulation intended for use by adults and adolescents. Tonix's patented potentiated oxytocin formulation is believed to increase specificity for oxytocin receptors relative to vasopressin receptors as well as to enhance the potency of oxytocin. Tonix is also developing a different intranasal formulation, designated TNX-1900, for prophylaxis of chronic migraine as well as for adolescent obesity, binge eating disorder, bone health in autism and social anxiety disorder. Oxytocin is a naturally occurring human hormone that acts as a neurotransmitter in the brain. Oxytocin is believed to be more than 600 million years old and is present in vertebrates including mammals, birds, reptiles, amphibians and fish.[10,11] It was originally approved by

the U.S. Food and Drug Administration as Pitocin®*, an intravenous infusion or intramuscular injection drug, for use in pregnant women to induce labor. An intranasal formulation of oxytocin is marketed in some European countries to assist in the production of breast milk as Syntocinon®** (oxytocin nasal 40 units/ml). **Pitocin® is a trademark of Par Pharmaceutical, Inc.*

***Syntocinon® is a trademark of BGP Products Operations GmbH*

Citations

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Tonix Pharmaceuticals Holding Corp.*

Tonix is a biopharmaceutical company focused on commercializing, developing, discovering and licensing therapeutics to treat and prevent human disease and alleviate suffering. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg under a transition services agreement with Upsher-Smith Laboratories, LLC from whom the products were acquired on June 30, 2023. Zembrace SymTouch and Tosymra are each indicated for the treatment of acute migraine with or without aura in adults. Tonix's development portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS development portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead development CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia, having completed the clinical phase of a potentially confirmatory Phase 3 study in the fourth quarter of 2023, with topline data expected in late December 2023. TNX-102 SL is also being developed to treat fibromyalgia-type Long COVID, a chronic post-acute COVID-19 condition, and topline results were reported in the third quarter of 2023. TNX-1900 (intranasal potentiated oxytocin), is in development as a preventive treatment in chronic migraine, and enrollment has completed in a Phase 2 proof-of-concept study with topline data expected in early December 2023. TNX-1900 is also being studied in binge eating disorder, pediatric obesity and social anxiety disorder by academic collaborators under investigator-initiated INDs. TNX-1300 (cocaine esterase) is a biologic designed to treat cocaine intoxication and has been granted

Breakthrough Therapy designation by the FDA. A Phase 2 study of TNX-1300 is expected to be initiated in the fourth quarter of 2023. Tonix's rare disease development portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan Drug designation by the FDA. Tonix's immunology development portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is a humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) being developed for the prevention of allograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 was initiated in the third quarter of 2023. Tonix's infectious disease pipeline includes TNX-801, a vaccine in development to prevent smallpox and mpox. TNX-801 also serves as the live virus vaccine platform or recombinant pox vaccine platform for other infectious diseases, including TNX-1800, in development as a vaccine to protect against COVID-19. During the fourth quarter of 2023, TNX-1800 was selected by the U.S. National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID) Project NextGen for inclusion in Phase 1 clinical trials. The infectious disease development portfolio also includes TNX-3900 and TNX-4000, which are classes of broad-spectrum small molecule oral antivirals.

*Tonix's product development candidates are investigational new drugs or biologics and have not been approved for any indication.

This press release and further information about Tonix can be found at www.tonixpharma.com.

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimate," "expect," and "intend," among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to the failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; risks related to the failure to successfully market any of our products; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2022, as filed with the Securities and Exchange Commission (the "SEC") on March 13, 2023, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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