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Tonix Pharmaceuticals Announces Poster Presentation Describing Discovery of Novel Next-Generation Oxytocin Analogues at the American Chemistry Society (ACS) Spring 2024 Meeting

Four Phase 2 investigator-initiated studies of TNX-1900 (intranasal potentiated oxytocin) are ongoing for pediatric obesity, binge eating disorder, bone health in autism and social anxiety disorder

TNX-2900 (intranasal potentiated oxytocin) is being developed under an IND as a treatment for Prader-Willi Syndrome, an Orphan Disease characterized by excessive eating

TNX-1900 and TNX-2900 may serve as novel neuroendocrine treatments for certain pain, eating and endocrine disorders

CHATHAM, N.J., March 21, 2024 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a biopharmaceutical company with marketed products and a pipeline of development candidates, today announces a poster presentation at the American Chemistry Society (ACS) Spring 2024 Meeting, held March 17-21, 2024, in New Orleans, Louisiana. A copy of the poster is available under the scientific presentations page of the Tonix website atwww.tonixpharma.com.

The poster presentation titled, *Oxytocin Analogs with Enhanced Craniofacial Antinociceptive Effects in Low Magnesium Formulations,* describes the discovery and characterization of novel oxytocin analogues that are candidate treatments for craniofacial pain, excessive eating (including Prader Willi Syndrome), and endocrinological conditions including bone health in autism and insulin resistance.

“Intranasal oxytocin has several potential therapeutic applications,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “Preclinical studies have shown that oxytocin, a hypothalamic peptide hormone, simultaneously reduces food intake and increases energy expenditure, leading to weight loss.[1-3] Intranasal oxytocin is well-tolerated and in published studies of adults, results in reduced caloric intake, increased fat burning and improved insulin sensitivity.[1-3]”

Dr. Lederman continued, “There is preclinical evidence that the activity of intranasal oxytocin is dependent on magnesium (Mg^{++}) concentration.[4-6] Our current intranasal oxytocin formulations of TNX-1900 and TNX-2900 contain Mg^{++} to augment the activity. We believe

the new oxytocin analogues described in the poster have enhanced binding to Mg^{++} and consequently their activity does not require Mg^{++} augmentation."

Four Phase 2 investigator-initiated studies of TNX-1900 are currently ongoing; three at the Massachusetts General Hospital (MGH) and one at the University of Washington. The Phase 2 'POWER' study at MGH is investigating the efficacy and safety of TNX-1900 as a novel therapeutic agent to induce weight loss and improve indicators of cardiometabolic risk in adolescent patients with obesity. The Phase 2 'STROBE' study at MGH is investigating the efficacy and safety of TNX-1900 as a novel therapeutic agent to reduce binge eating frequency in adults with binge-eating disorder. The Department of Defense (DoD)-funded Phase 2 'BOX' study at MGH is investigating the efficacy and safety of TNX-1900 as a novel therapeutic agent to improve bone health in children with autism spectrum disorder. In addition, a Phase 2 study at the University of Washington is investigating the potential role of TNX-1900 in enhancing vicarious extinction learning in social anxiety disorder, compared to healthy controls.

About TNX-1900 and TNX-2900

TNX-1900 and TNX-2900 (intranasal potentiated oxytocin) are proprietary formulations of oxytocin. TNX-1900 is in Phase 2 development under investigator-initiated INDs as a candidate for adolescent obesity, binge eating disorder, bone health in autism and social anxiety disorder. TNX-1900 is also planned for development in treating insulin resistance. TNX-2900 is in development as a treatment for Prader Willi Syndrome. TNX-2900 has received orphan drug designation from the U.S. Food and Drug Administration (FDA) and its IND has been cleared. In 2020, TNX-1900 was acquired from Trigemina, Inc. who had licensed the technology underlying the composition and method from Stanford University. TNX-1900 is a drug-device combination product, based on an intranasal actuator device that delivers oxytocin into the nasal cavity. 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. 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.[7] 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). Oxytocin has no recognized addiction potential. Oxytocin, when delivered via the nasal route, concentrates in the trigeminal system[1] resulting in binding of oxytocin to receptors on neurons in the trigeminal system. With TNX-1900 and TNX-2900, the addition of magnesium to the oxytocin formulation enhances oxytocin receptor binding[8] as well as its inhibitory effects on trigeminal neurons and resultant craniofacial analgesic effects, as demonstrated in animal models[9]. Intranasal oxytocin has been shown to be well tolerated in several clinical trials in both adults and children[10]. Targeted nasal delivery results in low systemic exposure and lower risk of non-nervous system, off-target effects. Tonix also has a license with the University of Geneva to use TNX-1900 for the treatment of insulin resistance and related conditions.

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.[11] 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.[12] In addition, oxytocin has potent effects in correcting behavioral characteristics of the neonatal *Magel2* knock-out mouse model for PWS and autism[13] and intriguing effects in a clinical trial of neonates with PWS.[14]

**Pitocin® is a trademark of Par Pharmaceutical, Inc.*

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

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Tonix Pharmaceuticals Holding Corp.*

Tonix is a biopharmaceutical company focused on developing, licensing and commercializing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's development portfolio is focused on central nervous system (CNS) disorders. Tonix's priority is to submit a New Drug Application (NDA) to the FDA in the second half of 2024 for Tonmya, a product candidate for which two positive Phase 3 studies have been completed

for the management of fibromyalgia. TNX-102 SL is also being developed to treat acute stress reaction as well as fibromyalgia-type Long COVID. Tonix's CNS portfolio includes TNX-1300 (cocaine esterase) a biologic designed to treat cocaine intoxication with Breakthrough Therapy designation. Tonix's immunology development portfolio consists of 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. Tonix also has product candidates in development in the areas of rare disease and infectious disease. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg for the treatment of acute migraine with or without aura in adults.

*Tonix's product development candidates are investigational new drugs or biologics and have not been approved for any indication. Tonmya™ is conditionally accepted by the U.S. Food and Drug Administration as the tradename for TNX-102 SL for the management of fibromyalgia.

Zembrace SymTouch and Tosymra are registered trademarks of Tonix Medicines. All other marks are property of their respective owners.

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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