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Tonix Pharmaceuticals Announces Trial Design of New Phase 2 Clinical Study of TNX-1300 for Cocaine Intoxication

New Trial Design is Single-Blind, Placebo-Controlled, Potential Pivotal Study, Pending FDA Agreement

Expected to Include Women Based on Reproductive Toxicology Studies, Pending FDA Agreement

Planning to Include Patients Who Have Received Naloxone to Increase Enrollment

CHATHAM, N.J., June 27, 2022 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced the design of a new Phase 2 clinical trial of TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, *i.v.* solution) for the treatment of cocaine intoxication. This new protocol has the potential to serve as a pivotal trial. TNX-1300 is a recombinant enzyme that efficiently degrades and metabolizes cocaine in cocaine users, as demonstrated in a prior Phase 2a randomized, double-blind, placebo-controlled clinical study, providing support of the use of TNX-1300 as a treatment for cocaine intoxication.¹ The Company plans to submit the new protocol to the U.S. Food and Drug Administration (FDA).

A positive Phase 2a study of volunteer cocaine users in a controlled laboratory setting has been previously completed. TNX-1300 has been granted Breakthrough Therapy designation by the FDA. As a biologic and new molecular entity, TNX-1300 is eligible for 12 years of U.S. market exclusivity upon approval by the FDA, in addition to expected patent protection through 2029.

"The design of the new Phase 2 trial has the potential to serve as a pivotal trial," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "There are approximately 505,000 emergency room visits annually involving cocaine use, with approximately 61,000 of the visits involving detox services to treat cocaine overdose. In 2020, about 19,447 overdose deaths involving cocaine occurred in the U.S.² We believe that TNX-1300 has the potential to be a new treatment option for the substantial morbidity and mortality caused by cocaine intoxication."

"The new study replaces the Phase 2 open-label trial with TNX-1300 for cocaine intoxication originally expected to start in the second quarter of 2022, which was designed to evaluate feasibility of enrollment," said Gregory Sullivan, M.D., Chief Medical Officer of Tonix Pharmaceuticals. "We expect to be able to include women in this study, pending FDA

agreement, since we have now completed the required reproductive toxicology studies in which no incidents of toxicity were observed. Additionally, we will now admit patients into the study who might have received naloxone due to the intoxication symptoms they are presenting. Based on our learnings from the feasibility study, excluding patients who had received naloxone at the time of intoxication was a hindrance to enrollment. Both of these changes in the new protocol should improve our ability to enroll appropriate patients in a more timely manner.”

Currently there is no specific pharmacotherapy indicated for cocaine intoxication, a state characterized by acute agitation, hyperthermia, tachycardia, arrhythmias and hypertension, with the potential life-threatening sequelae of myocardial infarction, cerebrovascular accident, rhabdomyolysis, respiratory failure and seizures. Patients are currently managed only by supportive care for the adverse effects of cocaine overdose on the cardiovascular and central nervous systems. By targeting the cause rather than the symptoms of cocaine intoxication, the Company believes TNX-1300 may offer significant advantages to the current standard of care for cocaine overdose.

The Phase 2 trial is a single-blind, open-label, placebo-controlled, randomized study comparing the safety of a single 200 mg dose of TNX-1300 to standard of care alone for the treatment of signs and symptoms of acute cocaine intoxication in approximately 60 emergency department patients presenting with cocaine intoxication. During the treatment period, subjects assigned to receive TNX-1300 will receive a single IV injection of TNX-1300 administered over 2 minutes or less; whereas subjects assigned to receive standard of care alone will receive a single IV saline injection over 2 minutes or less. Both groups will be observed according to the site's emergency department protocol. For both study arms, signs and symptoms of cocaine intoxication will be assessed at pre-determined time points after treatment (30 minutes and then at 60, 90, 120, 180, and 240 minutes). After randomization, blood samples will be drawn at specific time points. The primary endpoint of the study is reduction of systolic blood pressure associated with acute cocaine intoxication identified at study baseline comparing TNX-1300 and standard of care after 60 minutes. A variety of secondary endpoints will be measured, including reduction of circulating cocaine, cocaethylene and ecgonine methyl ester levels after at multiple post-baseline timepoints. Safety assessments will consist of incidence and severity of treatment-emergent adverse events, adverse events of special interest, 12-lead ECGs, and vital signs.

About TNX-1300

TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, *i.v.* solution) is being developed under an Investigational New Drug application (IND) for the treatment of cocaine intoxication. TNX-1300 is a recombinant protein enzyme produced through rDNA technology in a non-disease-producing strain of *E. coli* bacteria. Cocaine esterase (CocE) was identified in bacteria (*Rhodococcus*) that uses cocaine as its sole source of carbon and nitrogen and that grows in soil surrounding coca plants.³ The gene encoding CocE was identified and the protein was extensively characterized.³⁻⁶ CocE catalyzes the breakdown of cocaine into metabolite ecgonine methyl ester and benzoic acid. Wild-type CocE is unstable at body temperature, so targeted mutations were introduced in the CocE gene and resulted in the T172R/G173Q double-mutant CocE, which is active for approximately 6 hours at body temperature⁷. In a Phase 2 study, TNX-1300, at 100 mg or 200 mg *i.v.* doses, was well tolerated and rapidly reduced cocaine effects after cocaine 50 mg *i.v.* challenge.¹

About Cocaine Intoxication and Overdose

Cocaine is an illegal recreational drug which is taken for its pleasurable effects and associated euphoria. Pharmacologically, cocaine blocks the reuptake of the neurotransmitter dopamine from central nervous system synapses, resulting in the accumulation of dopamine within the synapse and an amplification of dopamine signaling and its role in creating positive feeling. With the continued use of cocaine, however, intense cocaine cravings occur resulting in a high potential for abuse and addiction (dependence), as well as the risk of cocaine intoxication. Cocaine intoxication refers to the deleterious effects on several body systems, especially those involving the cardiovascular system. Common symptoms of cocaine intoxication include tachyarrhythmias and elevated blood pressure, either of which can be life-threatening. As a result, individuals with known or suspected cocaine intoxication are sent immediately to the emergency department, preferably by ambulance in case cardiac arrest occurs during transit. There are approximately 505,000 emergency room visits for cocaine abuse each year in the U.S., of which 61,000 require detoxification services. According to the National Institute on Drug Abuse, in 2020 the number of overdose death involving cocaine reached 19,447 individuals.² According to a recent report by the U.S. Centers for Disease Control and Prevention,⁷ among all 2019 U.S. drug overdose deaths, approximately nearly 1 in 5 involved cocaine. In 2019, Black Americans experienced the highest death rate for overdoses involving cocaine, at 10.7 per 100,000.⁸

References

- ¹ [Nasser AF, Fudala PJ, Zheng B, Liu Y, Heidbreder C.](#) A randomized, double-blind, placebo-controlled trial of RBP-8000 in cocaine abusers: pharmacokinetic profile of rbp-8000 and cocaine and effects of RBP-8000 on cocaine-induced physiological effects. *J Addict Dis.* 2014;33(4):289-302.
- ² National Institute on Drug Abuse (NIDA) National Institute on Drug Abuse - <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>; accessed June 19, 2022
- ³ [Bresler MM, Rosser SJ, Basran A, Bruce NC.](#) Gene cloning and nucleotide sequencing and properties of a cocaine esterase from *Rhodococcus* sp. strain MB1. *Appl Environ Microbiol.* 2000. 66(3):904-8.
- ⁴ [Larsen NA, Turner JM, Stevens J, Rosser SJ, Basran A, Lerner RA, Bruce NC, Wilson IA.](#) Crystal structure of a bacterial cocaine esterase. *Nat Struct Biol.* 2002. 9(1):17-21.
- ⁵ [Turner JM, Larsen NA, Basran A, Barbas CF 3rd, Bruce NC, Wilson IA, Lerner RA.](#) Biochemical characterization and structural analysis of a highly proficient cocaine esterase. *Biochemistry.* 2002. 41(41):12297-307.
- ⁶ [Gao D, Narasimhan DL, Macdonald J, Brim R, Ko MC, Landry DW, Woods JH, Sunahara RK, Zhan CG.](#) Thermostable variants of cocaine esterase for long-time protection against cocaine toxicity. *Mol Pharmacol.* 2009. 75(2):318-23.
- ⁷ <https://www.cdc.gov/drugoverdose/deaths/other-drugs.html>; accessed June 19, 2022

⁸ Kariisa M, Seth P, Scholl L, Wilson N, Davis NL. Drug overdose deaths involving cocaine and psychostimulants with abuse potential among racial and ethnic groups – United States, 2004-2019. *Drug Alcohol Depend.* 2021 Oct 1;227:109001. doi: 10.1016/j.drugalcdep.2021.109001. Epub 2021 Aug 28. PMID: 34492555.

Tonix Pharmaceuticals Holding Corp. *

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia with a new Phase 3 study launched in the second quarter of 2022 and interim data expected in the first quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition. Tonix expects to initiate a Phase 2 study in Long COVID in the third quarter of 2022. TNX-1300 (cocaine esterase) is a biologic designed to treat cocaine intoxication that is Phase 2 ready and has been granted Breakthrough Therapy Designation by the FDA. TNX-1900 (intranasal potentiated oxytocin), a small molecule in development for chronic migraine, is expected to enter the clinic with a Phase 2 study in the second half of 2022. Tonix's rare disease 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 portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is a humanized monoclonal antibody targeting CD40-ligand being developed for the prevention of allograft and xenograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 is expected to be initiated in the second half of 2022. Tonix's infectious disease pipeline consists of a vaccine in development to prevent smallpox and monkeypox called TNX-801, next-generation vaccines to prevent COVID-19, and a platform to make fully human monoclonal antibodies to treat COVID-19. Tonix's lead vaccine candidates for COVID-19 are TNX-1840 and TNX-1850, which are live virus vaccines based on Tonix's recombinant pox live virus vector vaccine platform.

**All of Tonix's product 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; delays and uncertainties caused by the global COVID-19 pandemic; 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, 2021, as filed with the Securities and Exchange Commission (the "SEC") on March 14, 2022, 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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