August 2, 2022

Tonix Pharmaceuticals Receives Federal Grant from the National Institute on Drug Abuse (NIDA) to Advance Development of TNX-1300 as a Treatment for Cocaine Intoxication

There is No FDA-Approved Product for Cocaine Intoxication

TNX-1300 Has Been Granted Breakthrough Therapy Designation by the FDA

Phase 2 Single-Blind, Placebo-Controlled, Potential Pivotal Study Expected to Start in Fourth Quarter 2022, Pending FDA Agreement

CHATHAM, N.J., Aug. 02, 2022 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced that it has received a Cooperative Agreement grant from the National Institute on Drug Abuse (NIDA), part of the National Institutes of Health (NIH), to support development of TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, *i.v.* solution) for the treatment of cocaine intoxication. TNX-1300 is a recombinant enzyme that efficiently degrades and metabolizes cocaine. Cocaine intoxication refers to a state in which cocaine has deleterious effects on several body systems, especially the cardiovascular system. TNX-1300 demonstrated activity on reversing the physiological effects of *i.v.* cocaine challenge in people who use cocaine in a prior Phase 2a randomized, double-blind, placebo-controlled clinical study.[1]

The grant is intended to support continued development of TNX-1300 as a treatment for life threatening cocaine intoxication. In 2021, more than 24,900 individuals in the U.S. died from drug overdose deaths involving cocaine[2].

“This grant award underscores the unmet need for safe and effective treatments for cocaine intoxication and validates the progress we have achieved to date with TNX-1300,” said Seth Lederman, M.D., President and Chief Executive Officer of Tonix Pharmaceuticals. “Cocaine intoxication remains a serious issue in the U.S. where there is currently no specific pharmacotherapy indicated treatments. By targeting the cause rather than the symptoms of cocaine intoxication, we believe TNX-1300 may offer significant advantages to the current standard of care for cocaine intoxication.”

Tonix recently announced the design of a new single-blind, open-label, placebo-controlled, randomized Phase 2 clinical trial of TNX-1300 for the treatment of cocaine intoxication. The Phase 2 study, which has the potential to serve as a pivotal trial, is anticipated to start in the

fourth quarter of 2022, pending U.S. Food and Drug Administration (FDA) agreement. 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 research Tonix is pursuing is a bright light in our shared goal of reducing overdose deaths and harm as we continue to battle the crisis in substance use disorders in New Jersey and across the country, which has only been compounded by the pandemic. This targeted treatment could bring down healthcare costs and, most importantly, loss of life due to cocaine overdose,” said Representative Mikie Sherrill (NJ-11). “With this federal grant, Tonix will be able to move one step closer to FDA authorization and getting this potentially life-saving treatment into the hands of emergency room doctors and nurses, as well as EMS and other first responders. I am proud to have Tonix’s headquarters based here in NJ-11.”

“Tonix has been an incredible partner and job creator in Maryland, and I commend their efforts in fighting against the substance use disorder crisis that our nation continues to face. With over 100,000 Americans killed by drug overdoses just last year, we need to work together to curb the loss and set our sights on prevention, harm reduction, treatment and recovery. That starts with medical innovation in our own communities and reliable investment in our country's brightest leaders. This funding from the National Institute on Drug Abuse will do just that,” said Representative David Trone (MD-06).

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About TNX-1300

TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg,*i.v.* solution) is being developed under an Investigational New Drug (IND) application 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 temperature.[6] 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 a cocaine 50 mg *i.v.* challenge.[1]

About Cocaine Intoxication

Cocaine is an illegal recreational drug which is taken for its pleasurable effects and associated euphoria, as well as mental alertness, in some cases. 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 which reinforces the drug taking. With the continued use of cocaine,

however, intense cocaine cravings can occur, resulting in a high potential for continued use and addiction, as well as the risk of cocaine intoxication. Cocaine intoxication refers to the deleterious effects of cocaine 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. According to the U.S. Centers for Disease Control and Prevention (CDC), in 2021 the number of overdose death involving cocaine reached 24,900 individuals.[2] Also according to a recent report by the CDC, among all 2020 U.S. drug overdose deaths, approximately nearly 1 in 5 involved cocaine.[7] In 2020, Black Americans experienced the highest death rate for overdoses involving cocaine, at 14 per 100,000.[7]

References

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[7] *National Institute on Drug Abuse* https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates#:~:text=Overall%2C%20drug%20overdose%20deaths%20rose,overdose%20deaths%2(

About 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 mid-Phase 2 with a new potentially pivotal Phase 2 study expected to be initiated in the fourth quarter of 2022. TNX-1300 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 first half of 2023. Tonix's infectious disease pipeline consists of a vaccine in development to prevent smallpox and monkeypox, next-generation vaccines to prevent COVID-19, and a platform to make fully human monoclonal antibodies to treat COVID-19. TNX-801, Tonix's vaccine in development to prevent smallpox and monkeypox, also serves as the live virus vaccine platform or recombinant pox vaccine (RPV) platform for other infectious diseases. A Phase 1 study of TNX-801 is expected to be initiated in Kenya in the first half of 2023. Tonix's lead vaccine candidate for COVID-19 is TNX-1850, a live virus vaccines based on Tonix's recombinant pox live virus vector vaccine platform. A Phase 1 study of the COVID-19 vaccine is expected to be initiated in the second half of 2023.

**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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