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Tonix Pharmaceuticals Announces Issuance of U.S. Patent Covering Potentiated Intranasal Oxytocin (TNX-1900) for the Treatment of Pain

New patent expected to expire in 2036

Phase 2 Study for Prevention of Migraine Headache Expected to Start Second Half 2022

CHATHAM, N.J., Aug. 01, 2022 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a clinical-stage biopharmaceutical company, announced today that the United States Patent and Trademark Office (USPTO) issued U.S. Patent 11,389,473 to the Company on July 19, 2022. The patent, entitled "Magnesium-Containing Oxytocin Formulations and Methods of Use" claims methods and compositions for treating pain, including that incident to migraine headaches, using intranasal magnesium-containing oxytocin formulations. This patent, excluding possible patent term extensions, is expected to provide Tonix with U.S. market exclusivity until January 2036.

In late 2021, Tonix received Investigational New Drug (IND) clearance from the U.S. Food and Drug Administration (FDA) to support the initiation of a Phase 2 study of TNX-1900 (intranasal potentiated oxytocin) for the prevention of migraine headache in chronic migraineurs. The Company continues to expect to begin enrollment in the Phase 2 study during the second half of 2022.

“The USPTO’s issuance of this patent is an important milestone in protecting our expanding central nervous system therapeutic portfolio,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “An estimated four million individuals in the United States suffer from chronic migraine. We believe that by engaging and stimulating oxytocin receptors in the trigeminal ganglia, TNX-1900 has the potential to help those chronic migraine sufferers. TNX-1900 contains magnesium, which Tonix has shown potentiates the action of oxytocin at oxytocin receptors in animal models.”

About Migraine

Migraine is a neurological condition that manifests in throbbing headache, often on one side of the head, that lasts at least four hours. It can also be accompanied by nausea, vomiting, visual disturbances, and sensitivity to bright light, strong smells, and loud noises[1]. Epidemiological studies indicate that globally, approximately 1.2 billion individuals suffer from migraines annually.[2] In the U.S., approximately 39 million Americans suffer from migraines and among these individuals, approximately four million experience chronic migraines (15 or

more headache days per month).[2]

About TNX-1900

TNX-1900 (intranasal potentiated oxytocin) is a proprietary formulation of oxytocin in development as a candidate for prophylaxis of chronic migraine and for the treatment of craniofacial pain, insulin resistance and related conditions. 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 nose. Oxytocin is a naturally occurring human hormone that acts as a neurotransmitter in the brain. Oxytocin has no recognized addiction potential. It has been observed that low oxytocin levels in the body can lead to increases in migraine headache frequency, and that increased oxytocin levels can relieve migraine headaches. Certain other chronic pain conditions are also associated with decreased oxytocin levels. Migraine attacks are caused, in part, by the activity of pain-sensing trigeminal nerve cells which, when activated, release of calcitonin gene-related peptide (CGRP) which binds to receptors on other nerve cells and starts a cascade of events that is believed to result in headache. Oxytocin when delivered via the nasal route, concentrates in the trigeminal system[3] resulting in binding of oxytocin to receptors on neurons in the trigeminal system, inhibiting transmission of pain signals and the release of CGRP.[4] Blocking CGRP release is a distinct mechanism compared with CGRP antagonist and anti-CGRP antibody drugs, which block the binding of CGRP to its receptor. With TNX-1900, the addition of magnesium to the oxytocin formula enhances oxytocin receptor binding[5] as well as its effects on trigeminal neurons and craniofacial analgesic effects in animal models[7]. Intranasal oxytocin has been shown to be well tolerated in several clinical trials in both adults and children[6]. Targeted nasal delivery results in low systemic exposure and lower risk of non-nervous system, off-target effects, which could potentially occur with systemic CGRP antagonists such as anti-CGRP antibodies[8]. For example, CGRP has roles in dilating blood vessels in response to ischemia, including in the heart. We believe nasally targeted delivery of oxytocin could translate into selective blockade of CGRP release in the trigeminal ganglion and not throughout the body, which could be a potential safety advantage over systemic CGRP inhibition. In addition, daily dosing is more quickly reversible, in contrast to monthly or quarterly dosing, as is the case with anti-CGRP antibodies, giving physicians and their patients greater control. We intend to initiate a Phase 2 study of TNX-1900 in chronic migraine in the second half of 2022. We also plan to develop TNX-1900 for treatment of episodic migraine, craniofacial pain and insulin resistance. Tonix has a license with the University of Geneva to use TNX-1900 for the treatment of insulin resistance and related conditions.

About TNX-2900

TNX-2900 is another intranasal potentiated oxytocin-based therapeutic candidate, being developed for the treatment of Prader-Willi syndrome, or PWS. The technology for TNX-2900 was licensed from the French National Institute of Health and Medical Research. PWS, an orphan condition, is a rare genetic disorder of failure to thrive in infancy, associated with uncontrolled appetite later in childhood.

[1]https://www.mayoclinic.org/diseases-conditions/migraine-headache/symptoms-causes/syc-

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[2]Burch et al., Migraine: Epidemiology, Burden, and Comorbidity, Neurol Clin 37 (2019) 631–649.
[3]Yeomans DC, et al. Transl Psychiatry. 2021. 11(1):388.
[4]Tzabazis A, et al. Cephalalgia. 2016. 36(10):943-50.
[5]Antoni FA and Chadio SE. Biochem J. 1989. 257(2):611-4.
[6]Yeomans, DC et al. 2017. US patent US2017368095
[7]Cai Q, et al., Psychiatry Clin Neurosci. 2018. Mar;72(3):140-151.
[8]MaassenVanDenBrink A, et al. Trends Pharmacol Sci. 2016. 37(9):779-788

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 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. TNX-601 ER (tianeptine hemioxalate extended-release tablet) is being developed as an antidepressant in the U.S., with a Phase 2 study expected to be initiated in first quarter of 2023 pending IND clearance. 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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