October 4, 2023

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

New patent expected to expire in 2036

Proof of concept data from Phase 2 study for prevention of migraine headache expected in early December 2023

CHATHAM, N.J., Oct. 04, 2023 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a clinical-stage biopharmaceutical company, announced today that the European Patent Office (EPO) issued European Patent No. 3242676 to the Company on October 4, 2023. The patent, entitled "Magnesium-Containing Oxytocin Formulations and Methods of Use", claims methods and compositions for treating pain, including migraine headaches, using intranasal magnesium-containing oxytocin formulations. This patent, excluding possible patent term extensions, is expected to provide Tonix with market exclusivity in the member states of the European Patent Office until 2036. The U.S. Patent and Trademark Office (USPTO) has previously issued U.S. Patents No. 9,629,894 and 11,389,473 which are expected to provide market exclusivity in the U.S. until 2036.

In August 2023, Tonix announced it completed enrollment in its proof-of-concept Phase 2 PREVENTION study of TNX-1900 (intranasal potentiated oxytocin) for the prevention of migraine headache in chronic migraineurs with a total of 88 patients enrolled. The Company expects topline results from this trial in early December 2023.

"We believe this European patent combined with the U.S. issuance provides a strong patent position for TNX-1900 as we move forward in clinical development for the treatment of chronic migraine," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "With a differentiated formulation including magnesium, which Tonix has shown to potentiate the action of oxytocin at oxytocin receptors in animal models, we believe TNX-1900 has the potential to help those chronic migraine sufferers by engaging and stimulating oxytocin receptors in the trigeminal ganglia. By expanding our patent coverage in Europe, we are ensuring the IP protection of this unique approach."

In addition to Tonix's patents that protect certain uses including treating migraine, Tonix has licensed patents from INSERM, the French national health and medical research institute, that claim methods of treating feeding disorders with onset during neonatal development, specifically Prader Willi syndrome and non-organic failure to thrive (NOFTT), using oxytocin (EP 2575853, US8853158 and US9125862) and licensed patents from University of Geneva that claim methods of treating insulin resistance using oxytocin (US9101569 and

EP2571511).

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 an increase 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 the 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 releasing of the 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], its effects on trigeminal neurons, and its 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.

1. https://www.mayoclinic.org/diseases-conditions/migraine-headache/symptoms-causes/syc-20360201
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

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 enrollment of a potentially confirmatory Phase 3 study in the third 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. Enrollment in a Phase 2 proof-of-concept study has been completed, and topline results were reported in the third quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets) is a once-daily oral formulation being developed as a treatment for major depressive disorder (MDD), that completed enrollment in a Phase 2 proof-of-concept study in the third quarter of 2023, with topline results expected in early November of 2023. TNX-4300 (estianeptine) is a single isomer version of TNX-601, small molecule oral therapeutic in preclinical development to treat MDD, Alzheimer's disease and Parkinson's disease. Relative to tianeptine, estianeptine lacks activity on the μ-opioid receptor while maintaining activity in the rat Novel Object Recognition test in vivo and the ability to activate PPAR-β/δ and neuroplasticity in tissue culture. TNX-1900 (intranasal potentiated oxytocin), is in development for preventing headaches in chronic migraine, and has completed enrollment 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. 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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