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# Tonix Pharmaceuticals Licenses Technology for Treating Prader-Willi Syndrome, a Rare Genetic Eating Disorder, from the French National Institute of Health and Medical Research (Inserm)

***Expands Proprietary Uses of Tonix's Potentiated Oxytocin for Intranasal Administration***

***Disorder Stunts Growth of Newborns and, Paradoxically, Can Cause Excessive Hunger During Childhood and Beyond***

CHATHAM, N.J., Feb. 11, 2021 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced an agreement whereby Tonix has licensed technology using oxytocin-based therapeutics for the treatment of Prader-Willi syndrome and non-organic failure to thrive disease from Inserm. The licensing agreement has been negotiated and signed by Inserm Transfert, the private subsidiary of Inserm, on behalf of Inserm (the French National Institute of Health and Medical Research), Aix-Marseille Université and Centre Hospitalier Universitaire of Toulouse.

The co-exclusive license allows Tonix to expand its intranasal potentiated oxytocin development program to a new indication. The new program at Tonix has the designation TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. The patents covering the technology are expected to provide market exclusivity for the co-licensees in the U.S. and Europe through 2031, which exclusivity could be extended after marketing authorization by a Supplemental Protection Certificate in Europe or a Patent Term Extension in the U.S., independent of other Tonix-held patents covering the formulation and oxytocin potentiation technologies for intranasal administration.

"Prader-Willi syndrome is a rare genetic disorder of failure to thrive in infancy and uncontrolled appetite and obesity in childhood and adulthood with no approved treatments available," said Tonix's President and Chief Executive Officer, Seth Lederman, M.D. "With the license from Inserm Transfert, we have the opportunity to expand our ongoing efforts with intranasal potentiated oxytocin to this new indication. Since Prader-Willi syndrome is an orphan disease that occurs in approximately one in 15,000 births, we plan at the appropriate time to submit an application to the U.S. Food and Drug Administration for Orphan Drug and Fast Track designations for TNX-2900."

Prader-Willi syndrome results in physical, mental and behavioral problems. A key feature of

Prader-Willi syndrome in infants is a lack of suckling and poor muscle strength which leads to malnutrition and failure to thrive. However, paradoxically in children and adults, the key feature of Prader-Willi syndrome is a constant sense of hunger (hyperphagia), which leads to severe obesity. Intranasal oxytocin improves suckling in newborn animals but also suppresses feeding behaviors in adult animal models. 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.

**About Prader-Willi Syndrome**

Prader-Willi syndrome is recognized as the most common genetic cause of life-threatening childhood obesity[1] and affects males and females with equal frequency and all races and ethnicities. The hallmarks of Prader-Willi syndrome are lack of suckling in infants and, in children and adults, severe hyperphagia, an overriding physiological drive to eat, leading to severe obesity and other complications associated with significant mortality. There is currently no approved treatment for either the suckling deficit in babies or the obesity and hyperphagia in older children associated with Prader-Willi syndrome.

[1]Foundation for Prader-Willi Research (fpwr.org).

**About TNX-2900* and Tonix's Potentiated Oxytocin Platform**

TNX-2900 is based on Tonix's patented intranasal potentiated oxytocin formulation. Tonix is also developing a different intranasal formulation and device, designated TNX-1900, for prophylaxis of chronic migraine and for the treatment of insulin resistance and related conditions. Oxytocin is a naturally occurring human hormone that acts as a neurotransmitter in the brain. It was originally approved by the U.S. Food and Drug Administration (FDA) as Pitocin®**, an intravenous infusion or intramuscular injection drug, for use in pregnant women to induce labor. An intranasal form of oxytocin was marketed in the U.S. by Novartis to assist in the production of breast milk as Syntocinon®*** (oxytocin nasal 40 units/ml), but the product was withdrawn, and the New Drug Application (NDA) has been discontinued. TNX-2900 and TNX-1900 are in the pre-Investigational New Drug (IND) stage and have not been approved for any indication.

*TNX-2900 is an investigational new drug and has not been approved for any indication.

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

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

**About TNX-1900* (Intranasal Potentiated Oxytocin)**

TNX-1900 is based on a proprietary potentiated formulation of oxytocin and is currently being developed as a candidate for prophylaxis of chronic migraine and for the treatment of insulin resistance and related conditions.

***TNX-1900 for Migraine:*** In clinical and preliminary research, it has been observed that low oxytocin levels in the body can lead to increase in headache frequency, and that increased oxytocin levels can relieve headaches. Oxytocin, when delivered via the nasal route, results in enhanced binding of oxytocin to receptors on neurons in the trigeminal system, inhibiting

transmission of pain signals. Intranasal oxytocin has been well tolerated in several clinical trials in adults and children. Intranasal oxytocin has been shown to block calcitonin gene-related peptide (CGRP) release in animals, a pathway known to be critical to the pathogenesis of migraine attacks. TNX-1900 is believed to interrupt pain signals at the trigeminal ganglia by suppressing electrical impulses, a potentially different activity than drugs that just block CGRP. Migraine attacks are caused, in part, by the release of CGRP from pain-sensing nerve cells that are part of the trigeminal system. Targeted delivery results in low systemic exposure and lower risk of non-nervous system, off-target effects which could potentially occur with systemic CGRP antagonists. For example, CGRP has roles in dilating blood vessels in response to ischemia, including in the heart. Tonix believes 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. TNX-1900 is also believed to provide augmented analgesia in the treatment of pain, relative to oxytocin.

***TNX-1900 for Insulin Resistance:*** Tonix recently acquired the exclusive license to develop TNX-1900 for the treatment of insulin resistance and related conditions from the University of Geneva. The license allows Tonix to expand its intranasal potentiated oxytocin development program into cardiometabolic syndromes, which include insulin resistance, impaired glucose tolerance, obesity, diabetes management and related metabolic complications. The patents covering the technology are expected to provide Tonix market exclusivity in the U.S. and Europe through 2031 which exclusivity could be extended after marketing authorization by a Supplemental Protection Certificate in Europe or a Patent Term Extension in the U.S., independently of other Tonix-held patents covering the formulation and potentiation technologies related to TNX-1900. The University of Geneva technology is based on the discovery that oxytocin administration in an animal model of obesity improved lipid metabolism by increasing lipolysis and fatty acid-β-oxidation in adipose tissue accompanied by improvements in glucose intolerance and insulin resistance, independent of food intake[1]. A number of studies have shown that intranasal oxytocin has effects on insulin resistance and weight[2-4],". Intranasal oxytocin has been reported to improve glucose homeostasis, improve pancreatic β-cell responsivity, decrease energy-induced and reward-induced eating, and support cognitive control of food choices.[2-9]

*TNX-1900 is an investigational new drug and has not been approved for any indication.

[1]Deblon N, et al. (2011) *PLoS ONE* 6(9): e25565. doi:10.1371/journal.pone.0025565

[2]Lawson EA. (2017) *Nat Rev Endocrinol.* 13(12):700-709. doi: 10.1038/nrendo.2017.115. PMID: 28960210

[3]Olszewski PK, et al. (2017) *Curr Opin Endocrinol Diabetes Obes*. 24(5):320-325. doi: 10.1097/MED.0000000000000351. PMID: 28590323.

[4]Ding C, et al. (2019) *Obes Rev*. 2019 Jan;20(1):22-40. doi: 10.1111/obr.12757. PMID: 30253045.

[5]Lawson EA, et al. (2015) *Obesity*. 23:950–956. DOI: 10.1002/oby.21069 PMID: 25865294

[6]Klement, J et al. (2017) Diabetes 66(2) 264-271; DOI: 10.2337/db16-0569

[7]Ott V, et al. (2013) *Diabetes*. 62:3418–3425. DOI: 10.2337/db13-0663 PMID: 23835346

[8]Thienel M, et al. (2016) *Int J Obes*. 40(11):1707-1714. DOI: 10.1038/ijo.2016.149 PMID: 27553712

[9]Striepens N, et al. (2016) *Human Brain Mapp*. 37(12):4276–4285. DOI: 10.1002/hbm.23308 PMID: 27381253

**About Inserm Transfert**

Inserm Transfert, the private subsidiary of the French National Institute of the Health and Medical Research (Inserm), is responsible for value creation of Inserm innovations in human health and promotes long-term technology transfers in line with international best practices. Inserm Transfert SA was founded in 2000, and manages, under a Public Service Management Contract (Délégation de Service Public), the entire promotion and transfer of knowledge emerging from the Inserm research laboratories to the industrial world, from invention disclosure to industrial partnerships and startups incorporation. Inserm Transfert also offers services relating to setting up and managing national, European and international projects, as well as supporting the technology transfer of clinical research and health data/databases. In 2009, Inserm Transfert and Inserm established an investment fund to finance proofs of concept. In 2005, Inserm Transfert Initiative, a dedicated seed money fund for life sciences, was created. Since 2017 a pathway for pre-entrepreneurship supports researchers/inventors that aspire to become involved in entrepreneurship. www.inserm-transfert.com

**Tonix Pharmaceuticals Holding Corp.**

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing small molecules and biologics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is primarily composed of central nervous system (CNS) and immunology product candidates. The CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL[1], is in mid-Phase 3 development for the management of fibromyalgia, and positive data on the RELIEF Phase 3 trial were recently reported. The Company expects interim data from a second Phase 3 study, RALLY, in the second quarter of 2021[2] and topline data in the fourth quarter of 2021. The immunology portfolio includes vaccines to prevent infectious diseases and biologics to address immunosuppression, cancer, and autoimmune diseases. Tonix's lead vaccine candidate, TNX-1800[3], is a live replicating vaccine based on the horsepox viral vector platform to protect against COVID-19, primarily by eliciting a T cell response. Tonix expects efficacy data from animal studies of TNX-1800 in the first quarter of 2021. TNX-801[3], live horsepox virus vaccine for percutaneous administration, is in development to protect against smallpox and monkeypox.

[1]TNX-102 SL is an investigational new drug and has not been approved for any indication.
[2]Pending submission and agreement from FDA on statistical analysis plan.
[3]TNX-1800 and TNX-801 are investigational new 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 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, 2019, as filed with the Securities and Exchange Commission (the “SEC”) on March 24, 2020, and periodic reports filed with the SEC on or after the date thereof. All 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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