September 23, 2024

Tonix Pharmaceuticals Announces Data Presentations on TNX-102 SL for Fibromyalgia at the 11th Global Conference on Pharmaceutics and Novel Drug Delivery Systems (PDDS 2024)

Presentations highlighted the proprietary formulation technology and pharmacokinetic properties of TNX-102 SL (sublingual cyclobenzaprine HCl)

Composition and methods patents based on the eutectic formulation of TNX-102 SL are expected to provide market exclusivity until at least 2034 in the U.S., E.U., Japan, China and other jurisdictions

U.S. FDA New Drug Application (NDA) submission on track for October 2024; Fast Track designation granted by FDA; 2025 PDUFA date for FDA decision on approval expected

Results from the confirmatory Phase 3 RESILIENT study of TNX-102 SL demonstrated statistically significant improvement in primary endpoint of fibromyalgia nociplastic pain and in all six key secondary endpoints, including sleep quality

CHATHAM, N.J., Sept. 23, 2024 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a fully-integrated biopharmaceutical company with marketed products and a pipeline of development candidates, announced data in two oral presentations and a poster presentation at the 11th Global Conference on Pharmaceutics and Novel Drug Delivery Systems (PDDS 2024), held September 19-21, 2024, in Rome, Italy. Copies of the Company's oral presentations and poster are available under the Scientific Presentations tab of the Tonix website at www.tonixpharma.com following the conference.

Prof. Marino Nebuloni, Director, Qualified Person, Redox Analytical Science Srl, in an oral presentation titled, "*Mannitol as Eutectic Forming Agent for Improved Sublingual Delivery of Cyclobenzaprine HCl,*" described the eutectic formation of cyclobenzaprine HCl and mannitol and how it provides a stable product that dissolves rapidly and delivers cyclobenzaprine by the transmucosal route efficiently into the bloodstream. The eutectic protects cyclobenzaprine HCl from interacting with the basifying agent that is also part of the formulation and required for efficient transmucosal absorption. The work described included studies by Giorgio Reiner and his team at APR Applied Pharma Research S.A. and the team at Tonix.

"Patents based on TNX-102 SL's eutectic composition and its properties have issued in the

U.S., E.U., Japan, China and many other jurisdictions around the world," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "The European Patent Office's Opposition Division maintained Tonix's European Patent EP 2 968 992 in unamended form after an Opposition was filed against it by a Sandoz subsidiary, Hexal AG. Hexal AG did not appeal that decision. Tonix had two pre-NDA meetings with the U.S. Food and Drug Administration (FDA) in the second quarter of 2024. The FDA granted TNX-102 SL Fast Track designation in July 2024. The FDA New Drug Application (NDA) submission is on track for October 2024, and a 2025 Prescription Drug User Fee Act (PDUFA) date for an FDA decision on approval is expected."

Bruce Daugherty, Ph.D., Executive Vice President, Research at Tonix Pharmaceuticals, in the second oral presentation titled, "*Pharmacokinetic Properties of TNX-102 SL, a Sublingual Formulation of Cyclobenzaprine Hydrochloride,*" outlined the clinical pharmacology of TNX-102 SL *via* single dose and multiple dosage administration. The formulation of TNX-102 SL was designed specifically for sublingual administration and transmucosal absorption for bedtime dosing to target disturbed sleep, while reducing the risk of daytime somnolence. Clinical pharmacokinetic studies indicated that the addition of a basifying agent was necessary for efficient transmucosal absorption. The addition of a basifying agent resulted in higher levels of exposure during the first 2 hours after dosing and resulted in deceased levels of the long-lived active metabolite, norcyclobenzaprine in both single dose and multiple dose studies, consistent with bypassing first pass hepatic metabolism. At steady state after 20 days of dosing TNX-102 SL, the dynamic peak level of cyclobenzaprine is higher than the background level of norcyclobenzaprine. In contrast, after 20 days of dosing oral cyclobenzaprine, the simulated peak level of cyclobenzaprine is lower than the simulated background level of norcyclobenzaprine. Tonix believes that TNX-102 SL's dynamic levels of cyclobenzaprine exceeding norcyclobenzaprine levels after steady state modeling of chronic dosing, contributes to the durability of its clinical benefits. Dr. Daugherty also presented evidence showing that cyclobenzaprine interacts as an antagonist at four different receptors in the brain, which are believed to play roles in sleep quality supporting the multi-functional mechanism of TNX-102 SL. The presentation also illustrated the prevalence of fibromyalgia and the unmet need for new treatments in the U.S., despite the availability of three FDA-approved drugs. In the Phase 3 RESILIENT study in fibromyalgia, TNX-102 SL met the pre-specified primary endpoint of significantly reducing daily pain as compared to placebo (p-value=0.00005). TNX-102 SL also demonstrated broad syndromal benefits with statistically significant improvement in all six pre-specified key secondary endpoints including those related to improving sleep quality, reducing fatigue, and improving patient global ratings and overall fibromyalgia symptoms and function. TNX-102 SL was well tolerated with an adverse event profile comparable to prior studies and no new safety signals were observed.

Dr. Lederman continued, "There remains a significant unmet need in fibromyalgia for an effective treatment given the frustrations with existing therapeutic options. TNX-102 SL has demonstrated it has the potential to provide broad-spectrum symptom relief in fibromyalgia as a once-daily treatment at bedtime. With the support of statistically significant results from two Phase 3 studies of TNX-102 SL in fibromyalgia, TNX-102 SL is potentially positioned to be the first new treatment option for fibromyalgia patients in 15 years."

Siobhan Fogarty, Executive Vice President, Product Development at Tonix Pharmaceuticals, in the poster presentation titled, "*The Importance of In Vitro Discriminatory Tests in the*

Development of a Sublingual Dosage Form of TNX-102 SL (Cyclobenzaprine HCl) Tablets," presented the development of *in vitro* techniques used to assess characteristics of the TNX-102 SL tablet including dissolution, "disintegration time" and a proprietary "wetting time" test. These *in vitro* tests assessed the impact of the particle size, excipient variation and compression force. The data presented indicate that a dissolution test does not discriminate between tablets made with intentional modifications to particle size, excipient content or compression strength. However, both "disintegration time" and "wetting time" are sensitive tests to discriminate differences in particle size, concentration of the excipient Pearlitol Flash and compression strength.

Dr. Lederman concluded, "The *in vitro* "disintegration time" and "wetting time" tests have supported an efficient clinical development process and provide a strategy to evaluate manufacturing processes and product uniformity going forward. The *in vitro* discriminatory tests have been utilized by Tonix in the scale-up, validation and launch preparation of TNX-102 SL at the contract drug manufacturing organization sites. Together, these data suggest that TNX-102 SL has the potential to address a significant unmet need for fibromyalgia patients."

About Redox - Analytical Science Srl

Redox is an independent CRO company headquartered in Monza, Italy with research and development activities and customer analytical support to pharmaceutical companies for more than 30 years. For more than 25 years the analytical activities have been certified by national and international agencies (European Medicines Agency, the Italian Medicines Agency (AIFA), FDA, etc.). One of its main activities is the development of new drug products in order to improve the pharmaceutical actions, in concert with improvement in the stability and reduction of the cost of the new drug substances. Several unique and sophisticated analytical techniques and equipment are used in support of these research and development strategies, focused on achieving optimal and effective pharmaceutical formulation in the shortest time frame. More than 30 professional people are dedicated to Redox's efforts and many of its projects are ongoing in collaboration with the pharmaceutical industry as well as with Italian and international universities.

Further information about Redox can be found at www.labredox.com.

About APR Applied Pharma Research S.A., a wholly-owned subsidiary of Relief Therapeutics Holding AG

APR Applied Pharma Research S.A., a wholly-owned subsidiary of Relief Therapeutics Holding AG, is a commercial-stage biopharmaceutical company committed to advancing treatment paradigms and delivering improvements in efficacy, safety, and convenience to benefit the lives of patients living with select specialty and rare diseases. Relief Therapeutics' portfolio offers a balanced mix of marketed, revenue-generating products, including the proprietary, globally patented Physiomimic™ and TEHCLO™ platform technologies and a targeted clinical development pipeline consisting of risk-mitigated assets focused in three core therapeutic areas: rare metabolic disorders, rare skin diseases and rare respiratory diseases. In addition, Relief Therapeutics is commercializing several legacy products via licensing and distribution partners. Relief Therapeutics' mission is to provide therapeutic relief to those suffering from rare diseases and is being advanced by an international team of well-established, experienced biopharma industry leaders with

extensive research, development and rare disease expertise. Relief Therapeutics is headquartered in Geneva, with additional offices in Balerna, Switzerland, Offenbach am Main, Germany and Monza, Italy. Relief Therapeutics is listed on the SIX Swiss Exchange under the symbol RLF.

Further information about APR can be found at www.relieftherapeutics.com or by following Relief Therapeutics on LinkedIn and Twitter.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a fully-integrated biopharmaceutical company focused on developing, licensing and commercializing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's priority is to submit a New Drug Application (NDA) to the FDA in October of 2024 for TNX-102 SL, a product candidate for which two statistically significant Phase 3 studies have been completed for the management of fibromyalgia. The FDA has granted Fast Track designation to TNX-102 SL for the management of fibromyalgia. TNX-102 SL is also being developed to treat acute stress reaction. Tonix recently announced the U.S. Department of Defense (DoD), Defense Threat Reduction Agency (DTRA) awarded it a contract for up to $34 million over five years in an Other Transaction Agreement (OTA) to develop TNX-4200 small molecule broad-spectrum antiviral agents targeting CD45 for the prevention or treatment of infections to improve the medical readiness of military personnel in biological threat environments. Tonix owns and operates a state-of-the art infectious disease research facility in Frederick, MD. The company's Good Manufacturing Practice (GMP)-capable advanced manufacturing facility in Dartmouth, MA was purpose-built to manufacture TNX-801 (live horsepox vaccine) for the prevention of mpox and other vaccines on the horsepox platform. The GMP suites are ready to be reactivated in case of a national or international emergency. Tonix's development portfolio is focused on central nervous system (CNS) disorders. Tonix's CNS portfolio includes TNX-1300 (cocaine esterase), a biologic in Phase 2 development designed to treat cocaine intoxication that has Breakthrough Therapy designation. Tonix's immunology development portfolio consists of 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. Tonix also has product candidates in development in the areas of rare disease and infectious disease. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg for the treatment of acute migraine with or without aura in adults.

*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, 2023, as filed with the Securities and Exchange Commission (the “SEC”) on April 1, 2024, 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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