September 29, 2020

Tonix Pharmaceuticals Announces Plan to Complete the Phase 3 RELIEF Study of TNX-102 SL for Management of Fibromyalgia with Currently Enrolled Participants Based on Results of Interim Analysis

Topline Results of Full Study Expected Fourth Quarter 2020

RELIEF Study Protocol Was Formally Amended Mid-Study to Conform to FDA Guidance During COVID-19 Public Health Emergency

Currently Enrolled 503 Participants Represents More than Original Target of 470

Company is Currently Enrolling a Second Potential Pivotal Phase 3 Study (RALLY) of TNX-102 SL in Fibromyalgia, with Topline Data Expected Second Half of 2021

CHATHAM, N.J., Sept. 29, 2020 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, announced today the outcome of the pre-planned interim analysis for the Phase 3 RELIEF study of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) 5.6 mg for the management of fibromyalgia. An independent statistical team conducted the unblinded interim analysis of the primary endpoint of the first 50 percent of randomized participants who entered the 14-week study. Based on the interim results and the prespecified sample size re-estimation, the independent data monitoring committee (IDMC) made the non-binding recommendation that the trial continue to completion with the addition of 210 participants to the original sample size of 470 participants, which is the maximum number of participants that could be added under the interim statistical analysis plan. Based on this information, the Company plans to complete the study with the 503 currently enrolled participants and to report topline results in the fourth quarter of 2020. The Company remains blinded to the interim analysis results.

“We plan to complete the Phase 3 RELIEF study without adding new participants,” commented Seth Lederman, M.D., President and Chief Executive Officer. “We started enrolling RELIEF in December 2019 and continued to enroll and study fibromyalgia sufferers through the onset and progression of the COVID-19 pandemic. We made changes to the protocol to conform to the U.S. Food and Drug Administration’s (FDA’s) guidance on research during the COVID-19 public health emergency. We need to consider the possibility that the onset of the COVID-19 pandemic affected both the reporting and variability of fibromyalgia symptoms in the interim analysis cohort, or first half, of the RELIEF participants

in a way that was not anticipated prior to the pandemic. It is also possible that the second half of the RELIEF participants, enrolled after April 22, 2020, may have been affected by the ongoing nature of the pandemic, but differently than the first half which comprised the interim analysis cohort. The interim analysis plan did not contemplate any differences between the interim analysis cohort and subsequent cohort. The possibility that there are differences between the cohorts is the basis for our decision to complete the study without adding new participants, since the IDMC recommendation was based only on analysis of the interim analysis cohort. We believe that recruiting participants to the ongoing RALLY study is a more efficient use of resources than expanding the RELIEF study. Based on the prior Phase 2 and Phase 3 studies in fibromyalgia at a lower dose, we believe that TNX-102 SL has potential as a novel non-opioid, centrally-acting analgesic for the millions of U.S. adults suffering with fibromyalgia."

Dr. Lederman continued, "Fibromyalgia is a significant treatment market in which the annual sales of approved drugs grew to more than $9 billion before Cymbalta® and Lyrica® went off patent. The dollar value of the fibromyalgia drug market has since decreased because of generic substitution, but the number of sufferers has not. We believe many are dissatisfied with available drug treatments. Poor tolerability is often a reason why patients give up taking the currently approved drugs. As many as one-third of fibromyalgia patients end up on chronic opiates. TNX-102 SL has the potential to provide relief from the pain and dysfunction of fibromyalgia with good tolerability and without addictive potential. We look forward to assessing top-line data from RELIEF in the fourth quarter of 2020."

Tonix is currently enrolling into a second potentially pivotal Phase 3 trial, F306 or the RALLY study, to study TNX-102 SL for the management of fibromyalgia, with topline data expected in the second half of 2021. The trial design is very similar to the ongoing Phase 3 RELIEF study. The Company expects the FDA to require two positive registration-quality clinical studies to support marketing approval.

About Fibromyalgia

Fibromyalgia is a chronic pain disorder that is understood to result from amplified sensory and pain signaling within the central nervous system. Fibromyalgia afflicts an estimated 6-12 million adults in the U.S., and physicians and patients report common dissatisfaction with currently marketed products. Symptoms of fibromyalgia include chronic widespread pain, nonrestorative sleep, fatigue, and morning stiffness. Other associated symptoms include cognitive dysfunction and mood disturbances, including anxiety and depression. Individuals suffering from fibromyalgia struggle with their daily activities, have impaired quality of life, and frequently are disabled.

About the Phase 3 RELIEF and RALLY Studies

The RELIEF and RALLY studies are double-blind, randomized, placebo-controlled trials designed to evaluate the efficacy and safety of TNX-102 SL (cyclobenzaprine HCl sublingual tablets). The two-arm trials each targeted enrolling 470 participants at approximately 40 U.S. sites. For the first two weeks of treatment, there is a run-in period in which participants start on TNX-102 SL 2.8 mg (1 tablet) or placebo. After the first two weeks, all participants have the dose increased to TNX-102 SL 5.6 mg (2 x 2.8 mg tablets) or two placebo tablets for 12 weeks. The primary endpoint is daily diary pain severity score change (TNX-102 SL 5.6 mg vs. placebo) from baseline (using the weekly averages of the daily numerical rating scale

scores), analyzed by mixed model repeated measures with multiple imputation.

Additional details about the RELIEF study are available at clinicaltrials.gov (NCT04172831).

Additional details about the RALLY study are available at clinicaltrials.gov (NCT04508621).

About 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 immunology portfolio includes vaccines to prevent infectious diseases and biologics to address immunosuppression, cancer and autoimmune diseases. The CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead vaccine candidate, TNX-1800*, 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 data from animal studies of TNX-1800 in the fourth quarter of this year. TNX-801*, live horsepox virus vaccine for percutaneous administration, is in development to protect against smallpox and monkeypox and serves as the vector platform on which TNX-1800 is based. Tonix is also developing TNX-2300* and TNX-2600*, live replicating vaccine candidates for the prevention of COVID-19, but using bovine parainfluenza as the vector. Tonix's lead CNS candidate, TNX-102 SL**, is in Phase 3 development for the management of fibromyalgia. The Company expects topline data in the Phase 3 RELIEF study in the fourth quarter of 2020. Tonix is also currently enrolling participants in the Phase 3 RALLY study for the management of fibromyalgia using TNX-102 SL, and the results are expected in second half of 2021. TNX-102 SL is also in development for agitation in Alzheimer's disease and alcohol use disorder (AUD). Both programs are Phase 2 ready, and the AAD program has FDA Fast Track designation. Tonix's programs for treating addiction conditions also include TNX-1300* (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution), which is in Phase 2 development for the treatment of life-threatening cocaine intoxication and has FDA Breakthrough Therapy designation. TNX-601 CR** (tianeptine oxalate controlled-release tablets) is another CNS program, currently in Phase 1 development as a daytime treatment for depression while TNX-1900**, intranasal oxytocin, is in development as a non-addictive treatment for migraine and cranio-facial pain. Tonix's preclinical pipeline includes TNX-1600** (triple reuptake inhibitor), a new molecular entity being developed as a treatment for PTSD; TNX-1500* (anti-CD154), a monoclonal antibody being developed to prevent and treat organ transplant rejection and autoimmune conditions; and TNX-1700* (rTFF2), a biologic being developed to treat gastric and pancreatic cancers.

*TNX-1800, TNX-801, TNX-2300, TNX-2600, TNX-1300, TNX-1500 and TNX-1700 are investigational new biologics and have not been approved for any indication.

**TNX-102 SL, TNX-601 CR, TNX-1600 and TNX-1900 are investigational new drugs 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; 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 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.

Jessica Morris (corporate)
Tonix Pharmaceuticals
investor.relations@tonixpharma.com
(212) 980-9159

Travis Kruse (media)
Russo Partners
travis.kruse@russopartnersllc.com
(212) 845-4272

Peter Vozzo (investors)
Westwicke
peter.vozzo@westwicke.com
(443) 213-0505

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