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Tonix Pharmaceuticals Outlines New Statistical Method to Analyze Future PTSD Studies at the 3rd Annual Neuropsychiatric Drug Development Summit

Increasing Placebo Responses in PTSD Drug Trials Raise Questions About Current Methods of Measuring or Analyzing PTSD Symptom Change Over Time

The U.S. 21st Century Cures Act Provides Direction on New Statistical Analyses Using Simulations

Tonix Plans to Study TNX-102 SL in a New Phase 3 PTSD Trial in Kenya

CHATHAM, N.J., Nov. 12, 2020 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, announced today that Seth Lederman, M.D., President and Chief Executive Officer of Tonix Pharmaceuticals, outlined a new statistical method to analyze future Posttraumatic Stress Disorder (PTSD) drug studies and presented a retrospective analysis using the new method of the Phase 3 HONOR study (P301) of TNX-102 SL (cyclobenzaprine HCl sublingual tablets), for the treatment of military-related PTSD at the 3rd Annual Neuropsychiatric Drug Development Summit today.

“The paradox that confounds modern PTSD studies is that the placebo response has increased over time, even as we and others have striven to improve study methods and data quality,” said Dr. Lederman. “In many studies, the placebo response has increased to the point where it has become very difficult for the treatment arm to be successful in a randomized placebo-controlled PTSD clinical trial. The measurements of PTSD placebo improvement in randomized clinical trials using the Clinician Administered PTSD Scale for DSM-5 (CAPS-5) are inconsistent with what is known about the natural history of PTSD. In real world settings, PTSD patients do not dramatically improve without treatment like they appear to do in randomized clinical trials. Therefore, an opportunity and need exist to improve upon the measurement of PTSD symptoms in trials or the analysis of the data from trials. The 2017 21st Century Cures Act provides direction to the U.S. Food and Drug Administration (FDA) and to sponsors that new data analyses and particularly simulations should be used to improve clinical trial design and data analysis.”

The proposed new statistical method, called Randomization Honoring Non-Parametric Combination of Tests (RHNPCOT), was applied to a retrospective analysis of the Phase 3 HONOR study and showed a nominal p-value of 0.03 compared to the p-value of the prospective primary analysis of 0.6 in TNX-102 SL’s treatment benefit at Week 12 as

measured by change from baseline in the CAPS-5.

Dr. Lederman added, “The RHNPCOT statistical method addresses key goals of the 21st Century Cures Act as a potential path forward in PTSD drug development and testing. It respects the actual randomization method of the study, preserves information from the 20 distinct items of the CAPS-5, efficiently uses data, and brings the analysis of CAPS-5 more into line with the patient self-reported outcome measure, Patient Global Impression of Change (PGIC). The PGIC has particular importance because it measures how study participants themselves rate how they feel and because it is not tied to any theoretical disease construct. We have requested that FDA consider RHNPCOT as an exploratory outcome in our completed, but still blinded Phase 3 RECOVERY (P302) PTSD study. We expect to unblind the RECOVERY study before year end. Exploratory analysis of RECOVERY by RHNPCOT will provide additional information about the utility of the method. We plan to propose RHNPCOT as a primary analysis for future PTSD studies.”

In other psychiatric conditions, the placebo response is growing faster in the U.S. than in other countries[1,2]. Tonix is planning a Phase 3 PTSD study of TNX-102 SL in Kenya, expected to initiate in the third quarter of 2021, and will focus on studying police. The primary site for this multi-center study is Moi University School of Medicine in Eldoret, Kenya. The study was planned and the agreements negotiated when Dr. Lukoye Atwoli was Professor and Dean at Moi University School of Medicine. Dr. Atwoli was the principal investigator of the planned study before being recently recruited to be Dean of Aga Khan University Medical College East Africa based in Nairobi, the Capital of Kenya.

Dr. Atwoli, now Professor of Psychiatry and Dean at Aga Khan University Medical College stated, “We in Kenya are very excited to be setting up the plans for a clinical trial to evaluate a treatment for PTSD in our region. This kind of research is not common in our part of the world. We believe there are opportunities to improve care in our population, but also to bolster the ability of our young researchers to carry out that kind of work. We are grateful to Tonix for supporting us and look forward to a long-term collaboration.”

Dr. Lederman stated, “PTSD knows no borders. We are impressed with the clinical trial capabilities at Moi University and several other sites in Kenya. We look forward to working with Dr. Atwoli and other experts to perform a study of TNX-102 SL on PTSD in Kenyan police.”

An archived replay of Dr. Lederman’s presentation will be available on the IR Events tab of the Investors section of the Tonix website at www.tonixpharma.com.

About the 3rd Neuropsychiatric Drug Development Summit

The 3rd Annual Neuropsychiatric Drug Development Summit focuses on unravelling the complexities of developing clinically transformative neuropsychiatric drugs. With an emphasis on depressive disorders, schizophrenia, addiction and PTSD, this meeting provides a platform for thought leaders to have open reflections and share competitive knowledge. The meeting will put the spotlight on innovations in clinical trial design, defining better clinical endpoints and the emergence of the next generation of anti-psychotics.

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 and the first quarter of 2021. TNX-801*, live horsepox virus vaccine for percutaneous administration, is in development to protect against smallpox and monkeypox. 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 PTSD, agitation in Alzheimer's disease (AAD) and alcohol use disorder (AUD). The PTSD program is in Phase 3 development while AAD and AUD are Phase 2 ready. 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.

[1]Gopalakrishnan, M *et al. J Clin Psychiatry*. 2020; 81(2):19r12960
[2]Laughren, TP *J Clin Psychiatry*. 2020; 81(2):19com13110

*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; 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 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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