December 7, 2020

Tonix Pharmaceuticals Announces Positive Phase 3 RELIEF Study Results for TNX-102 SL 5.6 mg in Fibromyalgia

New 5.6 mg Dose Achieved Statistically Significant Pain Reduction Over Placebo at Week 14 (Primary Endpoint, p=0.01)

TNX-102 SL Generally Well Tolerated with Adverse Event Profile Comparable to Prior Studies; No New Safety Signals Observed

Approximately 90% of Those Affected by Fibromyalgia are Women; 95% of Participants in the RELIEF Study were Women

Company to Host Conference Call Today at 8:30 a.m. EST

CHATHAM, N.J., Dec. 07, 2020 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced that TNX-102 SL (cyclobenzaprine HCl sublingual tablets) met its pre-specified primary endpoint, significantly reducing daily pain compared to placebo (p=0.01) in participants with fibromyalgia in the Phase 3 RELIEF study (Table 1). TNX-102 SL is a novel, non-opioid, centrally-acting analgesic, taken once daily at bedtime, being developed for the management of fibromyalgia. RELIEF was a 14-week randomized, double-blind, placebo-controlled trial of TNX-102 SL 5.6 mg, in which 503 participants with fibromyalgia were randomized in a 1:1 ratio across 39 U.S. sites. All participants received one tablet of TNX-102 SL (2.8 mg) or placebo for the first two weeks, which was increased to two tablets of TNX-102 SL (5.6 mg) or placebo for the remaining 12 weeks.

“Tonix is dedicated to improving the lives of the millions suffering from fibromyalgia, approximately 90% of whom are female, and the results of the RELIEF trial bring new hope to this community,” said Seth Lederman, M.D., President and Chief Executive Officer of Tonix Pharmaceuticals. “TNX-102 SL at 5.6 mg showed statistically significant and clinically meaningful improvement on the primary endpoint of reducing daily pain, as well as showed activity in key secondary endpoints of improving sleep and reducing fatigue. One of the biggest challenges in drug development is finding a dose that balances efficacy and tolerability. We are pleased with the consistent effects of TNX-102 SL 5.6 mg on the primary endpoint of daily pain as well as the tolerability of this dose in the RELIEF study. We are also pleased at the activity shown on all of the fibromyalgia specific, pre-specified secondary endpoints. We look forward to the results of the currently enrolling, second potential pivotal Phase 3 study, RALLY, for which we expect to report topline data in the second half of 2021. Based on the long term safety exposure data we have already collected, the mature stage of our Good Manufacturing Practice (GMP) manufacturing processes and the established product stability at 36 months, we believe that upon achieving positive results from the

currently enrolling RALLY study, we may potentially be in a position to submit a New Drug Application (NDA) for TNX-102 SL for fibromyalgia to the U.S. Food and Drug Administration (FDA) in 2022. Additionally, we believe that our commercial manufacturing is on track to supply the U.S. market in 2022."

Table 1. Results of Primary and Secondary Endpoints

Outcome Measure at Week 14	Intent-to-Treat Analysis	P-value[1]
Primary Endpoint		
Daily Pain Diary, NRS	Mean Change (Primary Analysis)[2]	0.010*
Key Secondary Endpoints		
Non-specific		
Patient Global Impression of Change	Proportion "Much" or "Very Much Improved"	0.058 (LR)
Fibromyalgia Syndrome-Related		
FIQ-R Symptom Domain	Mean Change	0.007#
FIQ-R Function Domain	Mean Change	0.009#
PROMIS Fatigue	Mean Change	0.018#
Daily Sleep Quality Diary, NRS	Mean Change	<0.001#
PROMIS Sleep Disturbance	Mean Change	<0.001#

Abbreviations: FIQ-R = Fibromyalgia Impact Questionnaire - Revised; PROMIS = Patient-Reported Outcomes Measurement Information System; LR = Logistic Regression (missing data considered non-responders);

NRS = Numeric Rating Scale

* statistically significant at p<0.0452

nominally significant at p<0.0452

[1]Analysis by Mixed Model Repeated Measures with Multiple Imputation unless otherwise indicated.

[2]Primary endpoint analysis for FDA approvals of Cymbalta® and Lyrica® in fibromyalgia.

"These results support the proposed mechanism in which TNX-102 SL targets disturbed sleep in fibromyalgia and that improved sleep quality leads to improvement of fibromyalgia at the syndromal level," continued Dr. Lederman. "The sleep disorder specific to fibromyalgia has been called 'non-restorative' sleep. Dr. Harvey Moldofsky, Professor emeritus of Psychiatry and Medicine at the University of Toronto, founding Director of the University of Toronto Center for Sleep and Chronobiology, and Member of the Tonix Scientific Advisory Board, first recognized the central role of non-restorative sleep in the pathogenesis of fibromyalgia[3,4]. Our program is based on the subsequent pioneering work of Dr. Iredell W. Iglehart III, Assistant Professor of Medicine, part-time, Division of Rheumatology, Johns

Hopkins School of Medicine, and Member of the Tonix Scientific Advisory Board, who recognized that a sleep-focused cyclobenzaprine treatment protocol had the potential to target non-restorative sleep and lead to improvement of fibromyalgia at the syndromal level[5]. Transforming this treatment paradigm into a potential product with the clinical activity described in the RELIEF study depended on the invention of the Protectic® and Angstro® technologies. These technologies are integral to TNX-102 SL, which is a sublingual tablet designed for transmucosal delivery of cyclobenzaprine with distinctive pharmacokinetic properties that include bypassing first-pass hepatic metabolism. Teams led by Giorgio Reiner at APR Applied Pharma Research S.A. and Professor Marino Nebuloni and Patrizia Colombo at Redox Analytical Science Srl invented and developed these underlying technologies in collaboration with Tonix."

"I'm pleased that TNX-102 SL has demonstrated statistically significant treatment effects on fibromyalgia pain," said Dr. Harvey Moldofsky. "These results validate the mechanism that improving sleep quality can lead to syndromal effects on fibromyalgia. The sublingual formulation of TNX-102 SL for transmucosal absorption showed promise at the 2.8 mg dose in two prior studies, but now that the 5.6 mg dose has shown consistent efficacy, we are encouraged in the outcome of future studies."

"TNX-102 SL has the potential to be a new non-addictive, non-opiate analgesic for the management of fibromyalgia which is particularly important given that fibromyalgia is a chronic pain condition," said Gregory Sullivan, M.D., Chief Medical Officer of Tonix. "Approximately one third of fibromyalgia patients resort to opiates out of desperation and because of dissatisfaction with available therapies. Cyclobenzaprine, the active ingredient of TNX-102 SL, has no recognized potential for addiction. Based on our previous discussions with FDA, we expect to submit an NDA without new addiction liability studies. TNX-102 SL could potentially offer fibromyalgia patients, who have multiple disabling fibromyalgia symptoms, a first-line monotherapy with broad symptom relief, and the compliance advantage of being administered once-a-day (at bedtime)."

[3]Moldofsky H et al, Psychosom Med 1975;37:341-51.
[4]Moldofsky H and Scarisbrick P. Psychosom Med 1976;38:35-44.
[5]Iglehart IW. 2003; US Patent 6,541,523.

SUMMARY OF TOPLINE RESULTS OF THE RELIEF STUDY

The RELIEF study included a pre-specified interim analysis that was conducted in September 2020. Due to the inclusion of the potential to stop for success for this interim analysis, positive results required a two sided p-value of 0.0452 for both primary and secondary endpoints. Based on interim results, 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 was the maximum number of participants that could be added under the interim statistical analysis plan. Given this information, the Company decided to complete the study with the 503 enrolled participants and not to add additional participants. The first cohort of the study was enrolled between December 2019 and April 2020 at a time when the COVID-19 pandemic struck the U.S. Due to the pandemic, the Company modified the protocol in accordance with FDA guidelines to ensure patient safety and minimize risk in enrolling the first cohort. The modification allowed sites to conduct remote study visits for select cases in which the

COVID-19 pandemic made on-site visits unsafe or otherwise not possible. The second cohort was enrolled between last week of April and July 2020 and, by this time, the sites' COVID-19-related safety procedures for participants' attendance at clinic visits had become routine. At the time of the interim analysis in September 2020, there were only 15 participants still active in the study, all of whom completed their last visit by the end of October 2020.

In analyzing the efficacy endpoints, a sequential test procedure was applied to the primary and six key secondary efficacy endpoints such that each endpoint had to meet statistical significance (below a two-sided 0.0452 p-value) in order for the subsequent endpoints to be considered for statistical significance.

The RELIEF study achieved statistical significance on the pre-specified primary efficacy endpoint: change from baseline in the weekly average of daily diary pain severity numerical rating scale (NRS) scores for TNX-102 SL 5.6 mg (LS mean [SE]: -1.9 [0.12] units) versus placebo (-1.5 [0.12] units), analyzed by mixed model repeated measures with multiple imputation (LS mean [SE] difference: -0.4 [0.16] units, p=0.010, Table 1).

The statistically significant improvement in pain is further substantiated when diary pain was analyzed by another standard statistical approach, a 30 percent responder analysis, with 46.8% on active and 34.9% on placebo having a 30 percent or greater reduction in pain (logistic regression; odds ratio [95% CI]: 1.67 [1.16, 2.40]; p=0.006).

The key secondary efficacy endpoints, in sequential order, were: (1) Patient Global Impression of Change (PGIC) (responder analysis); (2) FIQ-R symptom domain score (mean change); (3) FIQ-R function domain score (mean change); (4) PROMIS Sleep Disturbance instrument T-score (mean change); (5) PROMIS Fatigue instrument T-score (mean change); and (6) daily diary NRS assessment of sleep quality (mean change). The responder analysis of PGIC trended for a greater proportion of responders (rating of "very much improved" or "much improved" at Week 14) to TNX-102 SL of 37.5% compared with placebo of 29.4% , but the result did not achieve statistical significance (logistic regression; odds ratio [95% CI]: 1.44 [0.99, 2.10]; p=0.058). Therefore, because of the sequential test waterfall, the remaining key secondary endpoints only could be considered nominally significant at best.

"The results on Patient Global Impression of Change or PGIC were unexpected based on results from the prior studies. PGIC is a general measure of patient self-assessed benefit that is not tied to any specific symptom of fibromyalgia. In two prior studies of TNX-102 SL at 2.8 mg in fibromyalgia, PGIC met statistical significance in both. We speculate that the ongoing COVID-19 pandemic might have affected the participants' sense of well-being and confounded the PGIC measure," said Dr. Sullivan. "The five other key secondary endpoints all resulted in nominal p-values of less than 0.02."

Consistent with the proposed mechanism that TNX-102 SL acts in fibromyalgia through improving sleep quality, TNX-102 SL showed nominal improvement of sleep by several measures. For the daily diary sleep quality ratings, TNX-102 SL (-2.0 [0.12] units) compared to placebo (-1.5 [0.12] units) was nominally significant (LS mean difference: -0.6 [0.17] units; p<0.001). For the PROMIS Sleep Disturbance instrument, TNX-102 SL was also nominally significant over placebo on T-scores (LS mean difference: -2.9 [0.82] units; p<0.001). The effect sizes on the diary sleep ratings and PROMIS Sleep Disturbance instrument were 0.31 and 0.32, respectively. Fatigue is another cardinal symptom of fibromyalgia. TNX-102 SL

showed nominal improvement over placebo on the PROMIS Fatigue instrument T-scores (-1.8 [0.76] units; p=0.018).

The syndromal activity of TNX-102 SL was studied by the Fibromyalgia Impact Questionnaire – Revised (FIQ-R). TNX-102 SL showed nominal improvement over placebo in both the symptom domain (-4.3 [1.60] units; p=0.007) and function domain (-4.4 [1.69] units; p=0.009).

SAFETY RESULTS OF THE PHASE 3 RELIEF STUDY

In the RELIEF study, TNX-102 SL was similarly well tolerated as in Phase 2 BESTFIT and Phase 3 AFFIRM studies which both studied TNX-102 SL at a lower dose of 2.8 mg daily. There were no new safety signals observed in the RELIEF study at the 5.6 mg daily dose. Among participants randomized to the TNX-102 SL and placebo arms, 82.3% and 83.5%, respectively, completed the 14-week dosing period. As expected based on prior TNX-102 SL studies, administration site reactions are the most commonly reported adverse events and were higher in the TNX-102 SL treatment group, including rates of tongue/mouth numbness , pain/discomfort of tongue/mouth, taste impairment, and tongue/mouth tingling (Table 2). Tongue/mouth numbness or tingling and taste impairment were local effects nearly always temporally related to dose administration and transiently expressed (<60 minutes) in most occurrences. The only systemic treatment-emergent adverse events that occurred at a rate of 5.0% or greater in either arm was somnolence/sedation at 5.6% in the TNX-102 SL arm, which was consistent with known side effects of marketed oral cyclobenzaprine. Adverse events resulted in premature study discontinuation in 8.9%of those who received TNX-102 SL compared with 3.9%of placebo recipients. There were a total of 7 serious adverse events in the study, none of which were deemed related to investigational product; 5 in placebo arm, and 2 in TNX-102 SL arm. Of the 2 in the TNX-102 SL arm, one was a motor vehicle accident with multiple bone fractures, and the other was a pneumonia secondary to an infection.

Table 2. Treatment-Emergent Adverse Events at Rate of 5% or Greater in Either Treatment Arm

	TNX-102 SL (N=248)		**Placebo (N=255)**		**Total (N=503)**	
Administration Site Reactions	**N**	**%**	**N**	**%**	**N**	**%**
Oral numbness	43	17.3	2	0.8	45	8.9
Oral pain/discomfort	29	11.7	5	2.0	34	6.8
Taste impairment	16	6.5	1	0.4	17	3.4
Oral tingling	14	5.6	1	0.4	15	3.0
Systemic Adverse Events	**N**	**%**	**N**	**%**	**N**	**%**
Somnolence/Sedation	14	5.6	3	1.2	17	3.4

Conference Call Information

Tonix Pharmaceuticals will host a live conference call and webcast with slides today at 8:30 a.m. Eastern Time to discuss the topline results of this clinical trial. The call can be accessed by dialing (866) 896-2215 (U.S. and Canada) or (617) 401-8110 (international) and

referencing conference ID 9045217. Callers should dial in approximately 10 minutes prior to the start of the call. A question and answer session with the Tonix management team will follow the company's remarks. Individuals can participate in an interactive Q&A session by submitting pertinent questions via the webcast platform. To access the live webcast or the replay, visit the investor page of the Company's website at https://ir.tonixpharma.com/ir-events. The webcast will be recorded and available on the Company's website for 90 days.

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., approximately 90% of whom are women. 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. Physicians and patients report common dissatisfaction with currently marketed products.

About TNX-102 SL

TNX-102 SL is a patented sublingual tablet formulation of cyclobenzaprine hydrochloride which provides rapid transmucosal absorption and reduced production of a long half-life active metabolite, norcyclobenzaprine, due to bypass of first-pass hepatic metabolism. As a multifunctional agent with potent binding and antagonist activities at the serotonin-2A, alpha-1 adrenergic, histamine-H1, and muscarinic-M1 receptors, TNX-102 SL is in clinical development as a daily bedtime treatment for fibromyalgia, PTSD, alcohol use disorder and agitation in Alzheimer's disease. The U.S. Patent and Trademark Office (USPTO) has issued United States Patent No. 9636408 in May 2017, Patent No. 9956188 in May 2018, Patent No. 10117936 in November 2018, Patent No. 10,357,465 in July 2019, and Patent No. 10736859 in August 2020. The Protectic™ protective eutectic and Angstro-Technology™ formulation claimed in these patents are important elements of Tonix's proprietary TNX-102 SL composition. These patents are expected to provide TNX-102 SL, upon NDA approval, with U.S. market exclusivity until 2034/2035.

About the Phase 3 RELIEF and RALLY Studies

The RELIEF and RALLY studies are double-blind, randomized, placebo-controlled phase 3 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 completed RELIEF study are available at clinicaltrials.gov (NCT04172831).

Additional details about the ongoing 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 CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. The immunology portfolio includes vaccines to prevent infectious diseases and biologics to address immunosuppression, cancer and autoimmune diseases. In addition to fibromyalgia, Tonix's lead CNS candidate, TNX-102 SL**, is in development for the treatment of 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 which 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 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 efficacy data from animal studies of TNX-1800 in the first quarter of 2021. TNX-801*, live horsepox virus vaccine for percutaneous administration, is in development to protect against smallpox and monkeypox. 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.

About APR Applied Pharma Research s.a.

APR is an independent pharma company headquartered in Switzerland with subsidiaries in Italy and Germany focused, since more than 25 years, in the development and commercialization of products intended to improve the quality of life of patients and families affected with rare or debilitating diseases. APR leverages many years of experience in developing patented drug delivery technologies, which are then applied to develop innovative therapeutic solutions.

Further information about APR Applied Pharma Research can be found atwww.apr.ch

About Redox - Analytical Science srl

Redox is an independent CRO company headquartered in Monza- Italy with R&D activities and customer analytical support to pharmaceutical companies for more than 30 years. From more than 25 years the analytical activities have been certified by national and international agencies (European Medicines Agency, the Italian Medicines Agency (AIFA), FDA, and etc). One of the main activities is the development of new drug products in order to improve the pharmaceutical actions and at the same time improve the stability and reducing the cost of the new drug substance. Several unique and sophisticated analytical techniques and equipment are used in support to research and development strategies with the focus to reach the best and effective pharmaceutical formulation in a short time frame. More than 30 professional people are dedicated to our efforts and many projects are ongoing in collaboration with the pharmaceutical industry as well as with Italian and international Universities.

Further information about Redox can be found atwww.labredox.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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