

November 13, 2012



## Tonix Pharmaceuticals Presents Research Findings at the 2012 American College of Rheumatology Annual Scientific Meeting

NEW YORK, NY -- (MARKETWIRE) -- 11/13/12 -- Tonix Pharmaceuticals Holding Corp. (OTCQB: TNXP) ("TONIX" or "the Company"), a specialty pharmaceutical company developing novel treatments for challenging disorders of the central nervous system ("CNS"), including fibromyalgia ("FM") and post-traumatic stress disorder ("PTSD"), announced the presentation of detailed results from pre-clinical studies of cyclobenzaprine, the active ingredient of the Company's lead candidate, TNX-102 sublingual tablet ("TNX-102 SL"), at the 2012 American College of Rheumatology ("ACR") annual meeting being held in Washington, D.C.

The poster, entitled "Cyclobenzaprine (CBP) and Its Major Metabolite Norcyclobenzaprine (nCBP) Are Potent Antagonists of the Serotonin Receptor 2A, Histamine H1 and  $\alpha$ -Adrenergic Receptors: Mechanistic and Safety Implications for Treating Fibromyalgia Syndrome by Improving Sleep Quality," will be made available on the Company's website ([www.tonixpharma.com](http://www.tonixpharma.com)).

In *in vitro* receptor studies, both CBP and nCBP were shown to be potent antagonists of certain central nervous system receptors, including the serotonin 5-HT<sub>2A</sub> receptor, the histamine H<sub>1</sub> receptor, and the alpha-adrenergic 1<sub>A</sub> receptor (Table 1). Antagonists of 5-HT<sub>2A</sub> and H<sub>1</sub> are known to exert effects on sleep and sleep maintenance (Landolt HP, et al. (2009) Eur J Neurosci 29:1795-809; Monti JM. (2010) Drugs Today 46:183-93; and Owen RT. (2009) Drugs Today 45:261-7), and  $\alpha$ -adrenergic antagonists may have effects on sleep and sleep disturbances (Ouyang M, et al. (2004) J Neurophysiol 92(4):2071-82; [Carra MC](#), et al. (2010) Sleep 33:1711-6; and Thompson CE, et al. (2008) J Trauma Stress 21:417-20.)

Table 1: Cyclobenzaprine and Norcyclobenzaprine *In Vitro* Binding and Activity Data on Selected CNS Receptors

|                    | K <sub>i</sub> (nM) |      | IC <sub>50</sub> (nM) |             |
|--------------------|---------------------|------|-----------------------|-------------|
|                    | CBP                 | nCBP | CBP                   | nCBP        |
| 5-HT <sub>1A</sub> | 1100                | 76   | 5300†                 | 3200†       |
| 5-HT <sub>2A</sub> | 5.2                 | 13   | 230<br>99*            | 140<br>181* |
| 5-HT <sub>2B</sub> | 15                  | 12   | 100                   | 580         |
| 5-HT <sub>2C</sub> | 43                  | 43   | 444                   | 1220        |

|                        |     |     |             |             |
|------------------------|-----|-----|-------------|-------------|
| Adrenergic $\alpha_1A$ | 5.6 | 34  | 4.9         | 16          |
| Adrenergic $\alpha_1B$ | 9.1 | 11  | 530<br>144* | 790<br>173* |
| Adrenergic $\alpha_2B$ | 21  | 150 |             |             |
| Adrenergic $\alpha_2C$ | 25  | 48  |             |             |
| H <sub>1</sub>         | 1.3 | 5.9 | 5.2<br>2.7* | 16<br>6.1*  |
| M <sub>1</sub>         | 7.9 | 30  | 0.71<br>81* | 8.7<br>266* |
| M <sub>2</sub>         | 250 | 76  | 3.3         | 33          |

\*Functional analysis evaluated via  $\beta$ -arrestin signaling; all other analyses were performed via intracellular calcium mobilization.

†Agonist activity (EC<sub>50</sub>).

Bruce Daugherty, Ph.D., TONIX's Senior Director of Drug Development and the study's lead author, commented, "Through the use of modern analytical methods, we have advanced our understanding of how CBP and a major metabolite, nCBP, interact with receptors in the CNS. Importantly, our *in vitro* receptor binding studies show that the activity profile of the CBP metabolite, nCBP, on CNS receptors is similar to that of the parent drug. With this knowledge, we can further the development of TNX-102 SL to optimize the dose, delivery, and metabolism of cyclobenzaprine as a potential chronic treatment for bedtime use to improve sleep quality and manage chronic pain syndromes."

### **About Fibromyalgia**

Fibromyalgia is a common and complex CNS condition characterized by chronic diffuse musculoskeletal pain, increased pain sensitivity at multiple tender points, fatigue, abnormal pain processing and disturbed sleep, and often features psychological stress. Despite the fact that most FM patients suffer from poor sleep, there are no medications indicated for FM that work by improving sleep quality. It is estimated that five million people are suffering from FM in the U.S.

### **About PTSD**

PTSD is an anxiety disorder that can develop from seeing or experiencing a terrifying event or ordeal in which there was the threat or actual occurrence of grave physical harm. PTSD was once associated primarily with war veterans, but civilian PTSD can be triggered by serious accidents, natural or human-caused disasters, exposure to terrorist attacks, violent personal assaults or sexual abuse, or even sudden and major emotional losses. People with PTSD experience persistent symptoms that include strong and unwanted memories of the event, bad dreams, emotional numbness, intense guilt or worry, angry outbursts, feelings of anxiety, and avoiding thoughts and situations that are reminders of the trauma. The National Institute of Mental Health estimates that PTSD affects about 7.7 million American adults at some point during their lifetimes.

## **About TONIX**

TONIX is developing innovative prescription medications for challenging disorders of the central nervous system. The Company targets conditions characterized by significant unmet medical need, inadequate existing treatment options, and high dissatisfaction among both patients and physicians. TONIX's core technology improves the quality of sleep in patients with chronic pain syndromes, which is believed to translate into reductions in daytime pain. The Company's lead product candidate, TNX-102 SL, is a novel under-the-tongue tablet formulation of CBP, the active ingredient in two U.S. FDA-approved muscle relaxants, and is expected to enter a Phase 3 program in FM in early 2013. TNX-102 SL is an Investigational New Drug. An Investigational New Drug Application ("IND") has been filed with the U.S. Food and Drug Administration for TNX-102 for FM. TONIX is also exploring the utility of TNX-102 SL in a new bedtime treatment paradigm for PTSD. The Company has held a pre-IND meeting with FDA to discuss PTSD and is planning to file an IND for this indication in early 2013.

In a randomized, double-blind, placebo-controlled, eight-week Phase 2 trial, TONIX demonstrated that low-dose CBP given at bedtime resulted in a significant decrease in next-day pain and other core FM symptoms, as well as in a significant improvement in sleep quality (Moldofsky H et al. (2011) J Rheum 38:2653-2663). Legacy CBP products are widely used by FM patients, but are neither designed nor approved for this indication. TNX-102 SL has demonstrated faster systemic absorption relative to administration of the 5 mg CBP tablet in a Phase 1 comparative PK and safety study in healthy volunteers. In that study, TNX-102 SL 2.4 and 4.8 mg were generally well tolerated. There were no unexpected adverse events, with the exception of a mild, temporary numbness at the tongue experienced by less than one-third of the subjects that received TNX-102 SL tablets.

To learn more about the Company, please visit [www.tonixpharma.com](http://www.tonixpharma.com).

*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," "estimated" 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, substantial competition; our ability to continue as a going concern; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payer reimbursement; limited sales and marketing efforts and dependence upon third parties; and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. 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 filed with the SEC on March 30, 2012 and future periodic reports filed with the Securities and Exchange Commission. All of the Company'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 hereof.*

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