FDA Approves Tonmya for Fibromyalgia

The U.S. Food and Drug Administration has approved Tonmya (TNX-102 SL), a sublingual formulation of cyclobenzaprine HCl for the treatment of adults with fibromyalgia. This marks the first new drug approval for fibromyalgia in over 15 years, offering a much-needed option for patients. Tonmya is designed to target two core aspects of the condition-nonrestorative sleep and chronic pain-making it a significant advancement in the management of fibromyalgia.

The FDA is expected to assign the NDA a Prescription Drug User Fee Act (PDUFA) target action date in a Day 74 Letter. At that time, the FDA will also communicate to Tonix whether Priority Review has been granted. TNX-102 SL was granted Fast Track designation for fibromyalgia by the FDA in July of 2024. Fast Track is designed to expedite FDA review of important new drugs to treat serious conditions and fill an unmet medical need.

"The FDA's acceptance of our NDA represents another step forward as we pursue our goal of delivering the first member of a new class of medicines for the management of fibromyalgia, a condition affecting over 10 million adults in the U.S.," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "The fibromyalgia community, comprised of patients and their families and support groups, has been waiting for a new drug for over 15 years. Analysis of insurance claims in the U.S., commissioned by Tonix, have shown that 18 months after diagnosis, fibromyalgia patients were more likely to be prescribed addictive opioids than all three of the FDA-approved drugs combined."

Dr. Lederman continued, "We look forward to working closely with the FDA throughout the NDA review period with the goal of bringing TNX-102 SL to the market to address the significant unmet needs of the fibromyalgia community as quickly as possible. Furthermore, this is an important milestone as we advance our commercial preparations in anticipation of a potential approval in 2025 with an accomplished commercial leadership team already in place, supporting our marketed products 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."

The NDA is supported by data from two 14-week double-blind, randomized, placebo-controlled Phase 3 clinical trials evaluating the safety and efficacy of TNX-102 SL as a bedtime treatment for fibromyalgia. The first Phase 3 trial, RELIEF, of TNX-102 SL 5.6 mg in fibromyalgia, completed in December 2020, met its pre-specified primary endpoint of significantly reducing daily pain compared to placebo ($p=0.010$). In the confirmatory Phase 3 RESILIENT study in fibromyalgia, completed in December 2023, TNX-102 SL again met the pre-specified primary endpoint of significantly reducing daily pain compared to placebo ($p =0.00005$). In both trials, TNX-102 SL was generally well tolerated with an adverse event profile comparable to prior studies and with no new safety signals observed. In both pivotal studies, the most common treatment-emergent adverse event was tongue or mouth numbness at the administration site, which was temporally related to dosing, self-limited, never rated as severe, and rarely led to study discontinuation (one participant in each study). Excluding COVID-19, systemic adverse events in each of the two studies was lower than 4.0%. Tonix believes the submitted dossier contains the requisite safety and efficacy data from two adequate and well-controlled studies to support NDA approval.

About Fibromyalgia

Fibromyalgia is a common chronic pain disorder that is understood to result from amplified sensory and pain signaling within the central nervous system, called central sensitization. Brain imaging studies have localized the functional disorder to the brain's insula and anterior cingulate cortex. Fibromyalgia afflicts more than 10 million adults in the U.S., the majority of whom are women. Symptoms of fibromyalgia include chronic widespread pain, non-restorative sleep, fatigue, and brain fog (or cognitive dysfunction). Other associated symptoms include mood disturbances, including depression, anxiety, headaches and abdominal pain or cramps. Individuals suffering from fibromyalgia often struggle with their daily activities, have impaired quality of life, and frequently are disabled. Physicians and patients report common dissatisfaction with currently marketed products. Fibromyalgia is now recognized as the prototypic nociplastic syndrome. Nociplastic pain is the third primary type of pain in addition to nociceptive pain and neuropathic pain.

Many patients present with pain syndromes that are a spectrum of mixtures of the three primary types of pain. Nociplastic syndromes are associated with central and peripheral sensitization. Fibromyalgia can occur without any identifiable precipitating event. However, many fibromyalgia cases follow one or more precipitating event(s) including: post-operative pain, acute or chronic nociceptive or neuropathic pain states; recovery from an infectious illness; a cancer diagnosis or cancer treatment; a metabolic or endocrine stress; or a traumatic event. In the cases of recovery from an infectious illness, fibromyalgia is considered an Infection-Associated Chronic Condition. In addition to fibromyalgia cases associated with other conditions or stressors, the U.S. National Academies of Sciences, Engineering, and Medicine, has concluded that fibromyalgia is a diagnosable condition that can occur after recovery from COVID-19 in the context of Long COVID. Fibromyalgia is also recognized as a Chronic Overlapping Pain Condition, which is a group of related conditions including, chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME), irritable bowel syndrome, endometriosis, low back pain, post-concussive syndrome (also known as mild traumatic brain injury), chronic Lyme Disease, chronic diabetic neuropathy and chronic post-herpetic neuralgia.

About TNX-102 SL

TNX-102 SL is a centrally acting, non-opioid investigational drug, designed for chronic use. The tablet is a patented sublingual formulation of cyclobenzaprine hydrochloride developed for bedtime dosing for the management of fibromyalgia. Cyclobenzaprine potently binds and acts as an antagonist at four different post-synaptic neuroreceptor subtypes: serotonergic-5-HT2A, adrenergic-α1, histaminergic-H1, and muscarinic-M1-cholinergic receptors. Together, these interactions are believed to target the non-restorative sleep characteristic of fibromyalgia that was identified by Professor Harvey Moldofsky in 1975. Cyclobenzaprine is not associated with risk of addiction or dependence.

The TNX-102 SL tablet is based on a eutectic formulation of cyclobenzaprine HCl and mannitol that provides a stable product which 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. 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 and provide market protection into 2034. 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.

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 relative to oral cyclobenzaprine, TNX-102 SL results in higher levels of exposure during the first 2 hours after dosing and 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.

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