Aptinyx Initiates Phase 2 Clinical Studies Evaluating NYX-2925 in Two Chronic Pain Conditions

Evanston, Ill., August 1, 2017 – Aptinyx Inc., a clinical-stage biopharmaceutical company developing transformative therapies for challenging neurologic disorders, today announced the first subjects have been randomized in a Phase 2 clinical study evaluating the company's lead product candidate, NYX-2925, a novel modulator of the N-methyl-D-aspartate (NMDA) receptor, for neuropathic pain associated with diabetic peripheral neuropathy (DPN). Aptinyx has also initiated an exploratory Phase 2 study of NYX-2925 in subjects with fibromyalgia. The company is advancing its clinical program after observing favorable safety and pharmacokinetics of NYX-2925 in a recently completed Phase 1 study in healthy volunteers.

"The Phase 1 study clearly demonstrated that NYX-2925 has highly predictable pharmacokinetics and is well-tolerated at doses that far exceed anticipated therapeutic doses. Therefore, we have advanced NYX-2925 into Phase 2 development for neuropathic pain associated with diabetic peripheral neuropathy, a condition in which patients struggle to manage their pain effectively with currently available therapeutic options," said Torsten Madsen, M.D., Ph.D., chief medical officer of Aptinyx. "Our preclinical research also supports studying NYX-2925 in several other chronic pain conditions, including fibromyalgia."

A randomized, double-blind, parallel-group, placebo-controlled study will enroll approximately 300 subjects with type 2 diabetes experiencing neuropathic pain associated with DPN. Eligible subjects will be randomized to receive oral doses of either NYX-2925 or placebo once daily for four weeks. The primary endpoint of the study is the efficacy in neuropathic pain of NYX-2925 versus placebo at any of the multiple dose levels being studied. Secondary endpoints include assessment of the effects of NYX-2925 on pain characteristics, sleep interference, and psychological state, as well as further assessment of safety and tolerability. The study is enrolling subjects at approximately 35 centers in the U.S.

A second initiated Phase 2 study is evaluating NYX-2925 in subjects with fibromyalgia. Led by researchers at the University of Michigan and University of Cincinnati, the exploratory study is expected to enroll approximately 24 subjects. The primary objective of the study is to determine whether once-daily dosing of NYX-2925, over a two-week period, changes the markers of central pain processing in subjects with fibromyalgia, as assessed by neuroimaging methods. The study will also provide the first characterization of the safety of NYX-2925 in the fibromyalgia population and includes exploratory endpoints to understand the effects of NYX-2925 on multiple pain, fatigue, cognition, and sleep parameters. Two oral dosage strengths of NYX-2925 will be evaluated.

Aptinyx's completed randomized, double-blind, placebo-controlled, Phase 1 study evaluated the safety, tolerability, and pharmacokinetics of NYX-2925 in single-dose and multiple-dose cohorts of healthy volunteers. NYX-2925 was generally well-tolerated across all dose cohorts. There were no serious adverse events reported and no subjects discontinued due to adverse events. The results, along with modeling based on preclinical data, informed the dose levels that are being evaluated in the Phase 2 program.

About Neuropathic Pain and Fibromyalgia

Neuropathic pain, across various conditions, is estimated to affect 7% to 9% of the population in the United States. Individuals suffering from neuropathic pain, irrespective of the underlying disorder, are currently treated with a variety of therapies. These include antidepressants, anticonvulsants, and opioids—medications that offer inadequate efficacy for a large proportion of patients, are often poorly tolerated due to side effects, and in some cases are associated with abuse.

DPN is one of the largest neuropathic pain conditions, due to the 60% to 70% of people with diabetes who will develop the condition after chronically high glucose damages nerves and impairs transmission of information between the central nervous system and other parts of the body. Patients may experience sensory loss, leading to difficulties with balance, coordination, and walking.

Fibromyalgia is characterized by chronic, debilitating, and widespread musculoskeletal pain accompanied by symptoms of fatigue, affected sleep, memory, and mood problems. It is estimated that fibromyalgia affects between five million and 12 million people in the United States, or 2% to 5% of the American adult population. Women are more commonly diagnosed than men (female:male diagnosis ratio is 7:1) and prevalence increases with age.

About NYX-2925

Discovered by Aptinyx scientists leveraging the company's proprietary small-molecule chemistry platform, NYX-2925 is a novel, oral, small-molecule NMDA receptor modulator in clinical development as a therapy for neuropathic pain. NYX-2925 binds to a distinct, recently discovered site on the NMDA receptor to modulate NMDA-receptor channel opening and enhance synaptic plasticity. This mechanism is distinct from any other therapies, emerging or marketed, for neuropathic pain. NYX-2925 has demonstrated robust efficacy in preclinical models of numerous neuropathic pain conditions with a favorable safety profile. In a Phase 1 clinical study in healthy human subjects, NYX-2925 was well tolerated across a wide dose range, including dose levels well in excess of the expected therapeutic levels. The U.S. Food and Drug Administration has granted Fast Track designation to Aptinyx's development of NYX-2925 for the treatment of neuropathic pain associated with DPN. Two Phase 2 clinical studies of NYX-2925 are currently ongoing in subjects with painful DPN and in subjects with fibromyalgia.

About Aptinyx

Aptinyx Inc. is a clinical-stage biopharmaceutical company discovering and developing transformative therapies for challenging disorders of the brain and nervous system. Aptinyx has

a proven platform for discovery of novel compounds that work through a unique mechanism to modulate — rather than block or over-activate — NMDA receptors and enhance synaptic plasticity, the foundation of neural cell communication. Drugs that modulate NMDA receptors in this distinct way have both robust efficacy and exceptionally favorable safety. The company's lead drug candidate, NYX-2925, is in Phase 2 clinical development as a therapy for neuropathic pain, an area of significant unmet need. Aptinyx is also advancing additional compounds from its proprietary chemistry platform, which continues to generate a rich and diverse pipeline of small-molecule NMDA receptor modulators with the potential to treat an array of neurologic disorders. For more information, visit www.aptinyx.com.

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