Aptinyx Reports Positive Top-line Data from Phase 2 Study of NYX-2925 in Patients with Fibromyalgia, Demonstrating Significant Effects on Both Biomarkers and Patient-Reported Pain

June 10, 2019

NYX-2925 demonstrated statistically significant effects on a range of neuroimaging biomarkers and patient-reported outcomes, including pain scores

Neuroimaging biomarkers correlated with patient-reported pain improvements

NYX-2925 was well tolerated with no serious adverse events reported

Conference call today at 8:30 a.m. ET

EVANSTON, Ill., June 10, 2019 (GLOBE NEWSWIRE) -- Aptinyx Inc. (Nasdaq: APTX), a clinical-stage biopharmaceutical company developing transformative therapies for the treatment of brain and nervous system disorders, today announced positive top-line results from a 23-patient, single-blind, sequential design Phase 2 study of its novel NMDA receptor modulator, NYX-2925, in patients with fibromyalgia. Administration of NYX-2925 resulted in statistically significant effects on the primary endpoint, brain activity biomarkers associated with central pain processing, measured using advanced imaging techniques. Statistically significant and clinically meaningful improvements were also observed on secondary patient-reported endpoints, including pain scores, the Revised Fibromyalgia Impact Questionnaire (FIQR), and other fibromyalgia symptom scales. The brain activity biomarkers and improvements in patient-reported pain were correlated. Based on these results, the company will begin enrollment in a larger, 12-week, randomized, placebo-controlled study in patients with fibromyalgia in the second half of 2019, which will evaluate patient-reported outcomes as the primary endpoint.

“The statistically significant effects on both pain-related brain activity and patient-reported clinical measures elegantly demonstrates that NYX-2925 is acting in the brain to alter pain processing, leading to pain alleviation,” said Norbert Riedel, Ph.D., president and chief executive officer of Aptinyx. “The results of this study reinforce what we observed in patients with advanced painful diabetic peripheral neuropathy in our recent Phase 2 DPN study, in which NYX-2925 greatly alleviated the centralized pain that is predominant in these patients. The consistency of these data confirms our confidence in advancing NYX-2925 as a treatment for chronic pain. We look forward to initiating follow-up studies in both painful DPN and fibromyalgia later this year.”

Summary of Top-line Study Results

Primary Endpoint Findings – Neuroimaging Biomarkers
Fibromyalgia is associated with increased overall levels of glutamate/glutamine (Glx) in certain brain regions and studies have shown a correlation between pain severity and these higher Glx levels. Placebo administration did not result in significant differences from baseline in any of the neuroimaging biomarkers. Compared to placebo, administration of NYX-2925 resulted in statistically significant reductions of Glx levels in these key pain-regulating brain regions, including the dorsal anterior cingulate cortex at rest ($p<0.05$) and the posterior insular cortex following an evoked pain stimulus ($p<0.05$). This Glx reduction in the posterior insular cortex correlated with reductions in clinical pain ($p<0.05$). NYX-2925 administration also resulted in reduced connectivity between brain regions that are known to be associated with the processing of centralized chronic pain.

Secondary Endpoint Findings – Patient-Reported Outcomes
Significant clinical improvements on key symptoms of fibromyalgia were observed following treatment with NYX-2925 (week 6) compared to baseline (week 0) and placebo (week 2). NYX-2925 resulted in statistically significant improvements across multiple patient-reported clinical measures, including:

- Average daily pain score: 1.09-point reduction from baseline ($p=0.0027$) and 0.66-point reduction vs. placebo ($p=0.0072$) on a scale ranging from 0 to 10
- Worst daily pain score: 0.98-point reduction from baseline ($p=0.0169$) and 0.61-point reduction vs. placebo ($p=0.0360$) on a scale ranging from 0 to 10
- Total FIQR score: 9.6-point reduction from baseline ($p=0.0085$) and 6.3-point reduction vs. placebo ($p=0.0135$) on a scale ranging from 0 to 100
- $PROMIS_{FM}$ Fatigue Profile total score: 5.4-point reduction from baseline ($p=0.0081$) and 5.6-point reduction vs. placebo ($p=0.0049$) on a scale ranging from 16 to 80

In addition, trends of improvement were observed on the other clinical measures evaluated in the study. Together, the effects on the clinical measures demonstrate improvements across a broad range of fibromyalgia symptoms with NYX-2925.

Across all patients in the study, NYX-2925 was well tolerated with no serious adverse events reported.

“The results with NYX-2925 are compelling and compare very favorably with the effects of approved fibromyalgia drug treatments we previously evaluated in separate and similar studies,” said Daniel Clauw, M.D., professor of anesthesiology, medicine (rheumatology), and psychiatry at the University of Michigan and an investigator in the study. “The activity demonstrated by NYX-2925 on these pre-specified imaging markers indicates that it is acting in a manner that is relevant in addressing the type of centralized pain evident in patients with fibromyalgia, as well as other chronic pain disorders. It is notable that, despite the small number of patients in the study, the effects on these clinical assessments of pain and other symptoms

were also statistically significant."

Lesley Arnold, M.D., professor of psychiatry and behavioral neuroscience at the University of Cincinnati and an investigator in the study, commented, "Knowing the challenges these patients face and the limited therapeutic options, it is very encouraging to see these results on both imaging and clinical measures. The therapeutic potential indicated by these findings highlights the importance of advancing NYX-2925 in development as a therapy for patients suffering from fibromyalgia. These data meaningfully inform further clinical development, and I look forward to working with Aptinyx as the team moves into its next Phase 2 study."

The company plans to submit the detailed results from this study for publication and presentation at future scientific and medical meetings.

Conference Call Information
Aptinyx will host a conference call and webcast today at 8:30 a.m. ET to discuss the top-line results from the study. The conference call can be accessed by dialing 866-930-5579 (domestic) or +1-409-216-0606 (international) and using conference ID 3093727. A live webcast of the call will be available on the Investors & Media section of Aptinyx's website at https://ir.aptinyx.com. The archived webcast will be available approximately two hours after the conference call and for 30 days thereafter.

About the Phase 2 Fibromyalgia Study
The study was a single-blind, placebo-controlled study to assess the efficacy and safety of daily oral administration of NYX-2925 in 23 female patients with a confirmed diagnosis of fibromyalgia (NCT03249103). In a sequential manner, but blinded to the patient, all patients received daily doses of placebo, 20 mg NYX-2925, and 200 mg NYX-2925 for two weeks each. At baseline and during each two-week treatment period, patients underwent a series of functional magnetic resonance imaging (fMRI) scans, combined with proton magnetic resonance spectroscopy (^{1}H-MRS), to measure key brain activity and neurochemistry biomarkers known to be associated with perception and processing of centralized chronic pain. The study's primary endpoint was the evaluation of changes in these specific biomarkers. Imaging data analysis was performed by analysts who were blinded to treatment sequence. Secondary endpoints included several patient-reported assessments to evaluate the effects of NYX-2925 on fibromyalgia symptoms. These patient-reported outcomes included average daily pain and worst daily pain measured using the 10-point Numeric Rating Scale (NRS), the impact of patients' fibromyalgia on daily living measured by the Revised Fibromyalgia Impact Questionnaire (FIQR), scores on the Patient Reported Outcomes Measurement Information System Fibromyalgia ($PROMIS_{FM}$) scale, pain severity and impact on functioning measured by the Brief Pain Inventory (BPI), mood and anxiety measured by the Hospital Anxiety and Depression Scale (HADS), and cognitive impairment measured using the Multidimensional Inventory of Subjective Cognitive Impairment (MISCI).

At baseline, patients in the study had a mean average daily pain score of 5.3 on the NRS, which has a range from 0 to 10 (where 0 = no pain and 10 = worst pain imaginable) and had a mean baseline total FIQR score of 54.4 (this scale has a maximum score of 100, with higher scores indicating worse fibromyalgia). Based on these scores, the patients in the study were considered to have moderate-to-severe fibromyalgia.

About Fibromyalgia
Fibromyalgia is a chronic condition associated with widespread pain and tenderness, as well as general fatigue. Fibromyalgia is considered by many to be a condition that is largely mediated in the central nervous system, given that fibromyalgia sufferers often present without a direct peripheral insult or injury. People suffering from fibromyalgia also often experience sleep disruption, depressed mood, and cognitive impairment. It is estimated that, in the United States, fibromyalgia affects more than 5 million people. Currently, there are only three FDA-approved pharmacologic treatments for fibromyalgia, but they have limited efficacy and burdensome side effects in many patients.

About NYX-2925
NYX-2925 is a novel oral NMDA receptor modulator currently in Phase 2 clinical development for the treatment of chronic pain. In clinical studies, NYX-2925 has been shown to have activity that affects central pain processing, resulting in alleviation of pain and other symptoms associated with chronic pain conditions. In preclinical models of numerous neuropathic pain conditions, NYX-2925 has shown robust activity with a favorable tolerability profile. In Phase 1 and Phase 2 clinical studies, NYX-2925 has exhibited a favorable safety and tolerability profile across a wide dose range. 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.

About Aptinyx
Aptinyx Inc. is a clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of proprietary synthetic small molecules for the treatment of brain and nervous system disorders. Aptinyx has a 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. The company has three product candidates in clinical development in central nervous system indications, including chronic pain, post-traumatic stress disorder, and cognitive impairment associated with Parkinson's disease. Aptinyx is also advancing additional compounds from its proprietary discovery 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**.**

Forward-Looking Statements
Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding the company's business plans and objectives, including future plans or expectations for NYX-2925, therapeutic effects of the company's product candidates, expectations regarding the design, implementation, timing, and success of its current and planned clinical studies, and expectations regarding its uses and sufficiency of capital. Risks that contribute to the uncertain nature of the forward-looking statements include: the success, cost, and timing of the company's product candidate development activities and planned clinical studies; the company's ability to execute on its strategy; positive results from a clinical study may not necessarily be predictive of the results of future or ongoing clinical studies; regulatory developments in the United States and foreign countries; as well as those risks and uncertainties set forth in the company's most recent Annual Report on Form 10-K and subsequent filings with the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made. Aptinyx undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Investor & Media Contact:
Nick Smith
Aptinyx Inc.
ir@aptinyx.com or corporate@aptinyx.com
847-871-0377

Source: Aptinyx Inc.

Source: Aptinyx Inc.