Aptinyx Presents Preclinical Data Demonstrating Robust Activity of NYX-783 on Alcohol-Seeking Behavior and Relapse-Like Behavior in Multiple Models of Alcohol Use Disorder

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EVANSTON, Ill., June 26, 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 the presentation of preclinical data on its novel NMDA receptor modulator, NYX-783, demonstrating that the product candidate robustly attenuated alcohol-seeking and relapse-like behavior in multiple models of alcohol use disorder. These studies were conducted in collaboration with the Medical University of South Carolina and data are being exhibited in a poster presentation today at the 42nd Annual Research Society on Alcoholism Scientific Meeting in Minneapolis, Minnesota.

“Given the increasingly recognized societal impact of substance abuse, and the lack of safe and effective therapies, we are very encouraged by the activity demonstrated by NYX-783 in these preclinical models of alcohol use disorder,” said Cassia Cearley, Ph.D., vice president of research at Aptinyx. “Together with the favorable safety and tolerability profile already demonstrated in a Phase 1 study, these data strongly support the development of NYX-783 in substance abuse conditions. With NYX-783 currently in Phase 2 development as a therapy for PTSD, the results from these preclinical studies support its potential to treat one of the more prevalent comorbidities associated with PTSD, and expand the potential indications in which the mechanism of NYX-783 may have relevance.”

In the studies being presented, behavior was assessed in two different models of alcohol use disorder in which animals were trained to self-administer ethanol through lever pressing. In the first model, an alcohol dependence model, alcohol dependence was induced in rats by exposing animals to ethanol vapor, with exposure to air used as a comparative control. After alcohol dependence was established, rats were dosed with either 0.1 mg/kg NYX-783, 6 mg/kg NYX-783, or vehicle one hour prior to the first extinction session. During the extinction sessions, animals were exposed to cues previously associated with alcohol intake, however lever pressing no longer resulted in alcohol delivery. Extinction was measured by the number of days to achieve elimination of alcohol-seeking behavior. Three weeks after extinction, rats were evaluated for relapse-like behavior after re-exposure to alcohol associated cues. In the second model, a stress-induced alcohol-seeking model, rats were exposed to a stressor prior to being trained to self-administer ethanol. Stress exposure increased alcohol-seeking behavior and rendered rats resistant to extinction of alcohol-seeking behavior. This approach models the influence of PTSD on substance abuse. Animals were then evaluated during and after the same extinction paradigm as described in the alcohol dependence model.

In both the alcohol dependence model and the stress-induced alcohol seeking model, animals dosed with NYX-783 prior to extinction demonstrated a significantly more rapid elimination of alcohol-seeking behavior as compared to vehicle ($p<0.0001$ *for both studies*). Animals dosed with NYX-783 prior to extinction also demonstrated significantly less relapse-like behavior when exposed to alcohol-associated cues in the alcohol dependence model ($p<0.001$) or stress-associated cues in the stress-induced alcohol-seeking model ($p<0.05$). In the stress-induced alcohol seeking model, animals that were only dosed with NYX-783 prior to re-exposure to the stress-associated cue also demonstrated significantly less relapse-like behavior when compared to vehicle-treated rats ($p<0.05$).

The data being presented support the continued evaluation of NYX-783 in human clinical studies and indicate that treatment with NYX-783 may be an effective approach to addressing alcohol abuse in patients with or without comorbid PTSD.

Poster Presentation Details:

Presentation Title: The Novel NMDAR Modulator NYX-783 Facilitates Extinction of Ethanol-seeking Behavior and Blocks Relapse-like Behavior Primed by Ethanol-associated Cues or Prior Stress in Rats (Poster Number: 039-732)
Authors: Cora Smiley (MUSC), Cassia Cearley, Ph.D. (Aptinyx), Justin T. Gass, Ph.D. (MUSC), M. Scott Bowers, Ph.D. (Aptinyx)
Presenter: M. Scott Bowers, Ph.D., Aptinyx
Poster Presentation: June 26th, 2019

About NYX-783
NYX-783 is a novel, oral NMDA receptor modulator currently in Phase 2 development for the treatment of post-traumatic stress disorder (PTSD). In preclinical studies of NYX-783, particularly strong results were observed in psychiatric models, models of fear extinction, and models of substance abuse. In a Phase 1 clinical study of NYX-783, ample central nervous system exposure was observed and the product candidate demonstrated a favorable safety and tolerability profile, with no serious adverse effects, across a wide dose range. The U.S. Food and Drug Administration has granted Fast Track designation to the development of NYX-783 for the treatment of PTSD.

About Alcohol Use Disorder
Alcohol use disorder is a chronic, relapsing condition characterized by compulsive alcohol use, loss of control over alcohol intake, and a negative emotional state when not using alcohol. Alcohol use disorder affects an estimated 16 million people in the United States. Currently, there are limited treatment options available for alcohol use disorder and the pharmacotherapies used often come with substantial side effects.

About Post-Traumatic Stress Disorder
More than eight million people in the United States suffer from PTSD, which is characterized by intrusive symptoms, avoidance, negative alteration in cognition and mood, hyperarousal, or arousal alterations following the experience of trauma. PTSD can result from various forms of trauma, including combat exposure, car accidents, sexual or other physical assault, abuse, natural disasters, and others. The lifetime prevalence of PTSD is approximately eight percent in the general population, but is much higher in populations at risk for exposure to trauma, such as military service members and first responders. In addition to the challenges associated with the direct symptoms, PTSD sufferers have a higher rate of suicide and

often struggle with simultaneous addiction, leading to an even greater social and economic burden of the disorder. Available therapeutic options are limited, including only two approved conventional SSRI antidepressants, which have limited efficacy, undesirable side effects, and target only the symptoms of PTSD, not the underlying disorder itself.

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.

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