NEWS RELEASE

Aptinyx Reports Positive, Statistically Significant, Top-line Data From Phase 2 Study of NYX-783 in Patients With Post-Traumatic Stress Disorder

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Clinically meaningful and statistically significant improvement on CAPS-5 Arousal and Reactivity Score observed with NYX-783

Clinically meaningful improvement from baseline on CAPS-5 Total Score observed in 50 mg dose arm

Statistically significant separation of 50 mg from placebo achieved on multiple measures of responder rate on CAPS-5 Total Score

Observed safety and tolerability similar to placebo

Data support discussion with FDA and advancement into pivotal study

Conference call and webcast presentation tomorrow at 8:30 a.m. ET

EVANSTON, Ill.--(BUSINESS WIRE)-- Aptinyx Inc. (Nasdaq: APTX), a clinical-stage biopharmaceutical company developing transformative therapies for the treatment of brain and nervous system disorders, today announced positive results from the first Phase 2 study of its novel NMDA receptor modulator, NYX-783, in 153 patients with post-traumatic stress disorder (PTSD). In the Phase 2 study, NYX-783 demonstrated statistically significant and clinically meaningful efficacy results and a favorable adverse event and tolerability profile. Based on these results, the company expects to initiate a pivotal study in 2021.

“Post-traumatic stress disorder is one of the most complex and difficult-to-treat psychiatric conditions due to a host of debilitating symptoms,” said Murray Stein, MD, MPH, FRCPC, Distinguished Professor of Psychiatry and Public

Health and Vice Chair for Clinical Research in Psychiatry at the University of California San Diego and a consultant to Aptinyx. “It is encouraging to see such positive effects with NYX-783 in this study, especially given the relatively short duration of treatment. Although few drugs have shown efficacy in PTSD, this study of NYX-783 has demonstrated preliminary evidence of clinically meaningful effect along with excellent tolerability. These data position NYX-783 as a promising therapeutic candidate moving into further clinical development, which is welcomed news for the underserved patients currently living with PTSD.”

The primary objective of the first-in-patient study was achieved as both dose levels studied (10 mg and 50 mg once daily) demonstrated clinically meaningful and statistically significant improvement on the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) Arousal and Reactivity Score (p=0.040 and p=0.049 on 50 mg and 10 mg vs. placebo, respectively). This scale evaluates symptoms of PTSD such as hypervigilance, exaggerated startle response, irritability and aggression, reckless or self-destructive behaviors, and concentration and sleep disturbances. The resolution of such symptoms is highly relevant to the mechanism of action of NYX-783, which has been shown to enhance extinction learning.

Clinically meaningful improvement was also observed in the CAPS-5 Total Score within just four weeks in the 50 mg dose arm, which trended toward significance. In the intention-to-treat (ITT) population that completed Stage 1 at week four, 78% of subjects taking NYX-783 50 mg achieved a 30% improvement from baseline in the CAPS-5 Total Score, compared to 44% of subjects taking placebo (p=0.008). In the same population and time period, 50% of subjects taking NYX-783 50 mg achieved a 50% CAPS-5 Total Score improvement from baseline, compared to 26% of subjects taking placebo (p=0.044).

The improvements on the primary, clinician-administered CAPS-5 endpoints were concordant with improvements observed on multiple secondary and exploratory endpoints.

Across endpoints in the study, a clear dose response was evident with the 50 mg dose demonstrating more consistent effects than the 10 mg dose.

In the study, NYX-783 was well tolerated and exhibited a favorable adverse event profile.

“We are very pleased with these impressive results, which surpassed our expectations for this initial exploratory study and clearly indicate the strong potential of NYX-783 to rapidly and reliably address some of the most challenging symptoms of PTSD,” said Norbert Riedel, Ph.D., president and chief executive officer of Aptinyx. “People suffering from PTSD have immense unmet medical needs and the few existing therapeutic options offer limited benefit. We believe these results indicate that the mechanism of NYX-783, which modulates NMDA receptors to enhance extinction learning, addresses the putative underlying pathology of PTSD. We expect the data from this study will support discussion with the FDA and the initiation of a first pivotal study. In addition, these results

provide further clinical validation of our NMDA receptor modulation platform and reinforce our confidence in its therapeutic utility across our other clinical-stage programs in chronic pain and cognition."

Aptinyx plans to discuss these results on a conference call scheduled for 8:30 a.m. ET tomorrow. Additionally, the company plans to submit the detailed results from this study for publication and presentation at future scientific and medical meetings.

About the Phase 2 Exploratory Study of NYX-783 in PTSD

The Phase 2 exploratory study was a multi-center, placebo-controlled, double-blind, randomized, Sequential Parallel Comparison Design (SPCD) study of 153 patients with PTSD, as characterized by criteria set forth in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5).

In accordance with the SPCD design, the study was conducted in two, four-week sequential stages. No patient in the study received more than 4 weeks of NYX-783 treatment. Patients were randomly assigned to receive placebo, NYX-783 10 mg, or NYX-783 50 mg in Stage 1. Patients on placebo in Stage 1 were re-randomized in Stage 2 to again receive placebo, or start NYX-783 10 mg, or NYX-783 50 mg. All patients from Stage 1 as well as the patients in the placebo non-responder group at week 4 (defined as CAPS-5 total score >26 and a percent-reduction from baseline in CAPS-5 total score of <35% at week 4), in Stage 2 were combined for primary efficacy analysis. The primary endpoint of the study was the change in CAPS-5 Total Score and symptom domain sub-scores (Arousal and Reactivity, Negative Cognitions and Mood, Intrusions, and Avoidance) for Stage 1 and Stage 2, combined as weighted effects. In total, the Phase 2 study duration was ten to thirteen weeks overall, consisting of a screening period, two four-week treatment periods (Stage 1 and Stage 2), and a safety follow-up period.

Conference Call Information

To access the live conference call and webcast presentation, please dial (866) 939-3921 (U.S. Toll Free) or (678) 302-3550 (U.S. Toll) and refer to conference ID 49992933. A live audio and webcast presentation will be available on the Investors & Media section of Aptinyx's website at **https://ir.aptinyx.com**. A replay of the webcast will be archived on Aptinyx's website for 30 days following the event.

About Post-Traumatic Stress Disorder

Approximately eight and a half million people in the United States suffer from PTSD, which is characterized by intrusive symptoms, avoidance, negative alteration in cognition and mood, hyperarousal, and/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 seven 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 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 adverse event 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 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-783 and potential therapeutic effects of NYX-783, the timing and outcome of discussions with FDA and other regulatory agencies, expectations regarding the design, implementation, timing, and success of its future clinical studies of NYX-783, including whether they are

pivotal or would support registration, and expectations regarding its other NMDA receptor modulation platform development activities. Risks that contribute to the uncertain nature of the forward-looking statements include: the effect of COVID-19 on our business and financial results, including with respect to disruptions to our clinical trials, business operations, and ability to raise additional capital; 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; that positive results from a clinical study may not necessarily be predictive of the results of future or ongoing clinical studies; future clinical studies may fail to demonstrate adequate safety and efficacy of our product candidates, which would prevent, delay, or limit the scope of regulatory approval and commercialization; regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming, and inherently unpredictable; regulatory developments in the United States and foreign countries; the company's estimates regarding expenses, future revenue, and capital requirements; 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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