NEWS RELEASE

Aptinyx Provides Update on NYX-783 Development Program for the Treatment of Post-Traumatic Stress Disorder

6/15/2021

Finalizes design for Phase 2b program, which remains on track to commence in 4Q 2021

Corrects statistical analysis from previous exploratory Phase 2 study—no impact on study conclusions or future clinical development plans

EVANSTON, Ill.--(BUSINESS WIRE)-- Aptinyx Inc. (Nasdaq: APTX), a clinical-stage biopharmaceutical company developing transformative therapies for the treatment of nervous system disorders, today announced that it has finalized the design of its Phase 2b program for NYX-783 in patients with post-traumatic stress disorder (PTSD) after having received the minutes from its recent Type C meeting with the U.S. Food and Drug Administration (FDA). The company expects to initiate the Phase 2b program in the fourth quarter of 2021. Aptinyx also announced that, in its preparation for Phase 2b, it identified a statistical error made by the contract research organization (CRO) that performed the statistical analysis of the previously completed exploratory Phase 2 study in PTSD. Accordingly, the company is providing updated statistical analysis for the exploratory Phase 2 study, which has no impact on the study conclusions.

“We are pleased to be moving forward with Phase 2b development of NYX-783 in PTSD and believe that its mechanism of enhancing extinction learning through NMDA receptor modulation has the potential to address the putative underlying pathology of PTSD,” said Norbert Riedel, Ph.D., chief executive officer of Aptinyx. “Upon identifying the error in statistical analysis made by the CRO in our previous study, we have moved quickly to reanalyze and release revised statistical analysis. It is important to note that the revised analysis does not impact our conclusions from that study, our confidence in the efficacy and safety profile of NYX-783, or our next steps in its clinical development. We look forward to advancing NYX-783 into Phase 2b starting in the fourth quarter of this

year."

NYX-783 Phase 2b Program Overview

The Phase 2b program will consist of two separate studies to evaluate NYX-783 at two dose levels: 50 mg (Study 1) and 150 mg (Study 2). The 50 mg dose performed best in the previous Phase 2 exploratory study and the 150 mg dose has been selected to evaluate the effects of a higher dose level. Study 1 is expected to commence as planned in the fourth quarter of 2021 and Study 2 is expected to commence in the first quarter of 2022.

The studies will be multi-center, placebo-controlled, double-blind, randomized, parallel design studies in patients with moderate to severe PTSD, as characterized by criteria set forth in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5). The studies will enroll a broad and representative group of patients who have experienced various types of trauma, including both military-related and civilian PTSD. Patients with a wide range of time since trauma will be included, with stratification of enrollment to ensure balanced representation of time since trauma in the study treatment groups. Patients enrolled in the studies will not be taking concomitant PTSD medication or undergoing specific forms of trauma-focused psychotherapy.

The primary efficacy endpoint of each study will be the change from baseline in the Clinician-Administered PTSD Scale for the DSM-5 (CAPS-5) Total score. Key secondary endpoints in both studies will include various measures of global impression of severity and improvement (CGI-S, CGI-I, PGI-S, PGI-I).

In Study 1, approximately 300 patients will be randomized into one of two treatment arms: placebo or NYX-783 50 mg administered orally once daily. The study will comprise a 1- to 4-week screening period, a 10-week treatment period, and a follow-up evaluation period.

In Study 2, approximately 300 patients will be randomized into one of two treatment arms: placebo or NYX-783 150 mg administered orally once daily. The other design parameters of Study 2 will be consistent with those of Study 1.

These Phase 2b studies are designed to be well-positioned for consideration as registration-supportive, taking into account guidance received in the recent Type C meeting with the FDA.

Revised Statistical Analysis for Phase 2 Exploratory Study of NYX-783

In the process of completing its in-depth data analysis to prepare for and finalize the design of the Phase 2b program for NYX-783, the company identified a statistical modeling error made by the CRO that performed the statistical analysis of the previously completed exploratory Phase 2 study. The error resulted from an incorrect analysis of variance in the mixed model for repeated measures (MMRM) statistical model. While there were no

changes to the numerical improvements from baseline, the revised MMRM p-values are higher than previously reported in October 2020. The CRO confirmed the error in late May and reported the updated statistical analysis to the company in June.

The statistical analysis plan (SAP) for the completed exploratory study pre-specified a one-sided $p<0.1$ as the threshold for statistical significance. As previously described, the results from Stage 1 of the two-stage study are most informative for future development.

There is no impact on the following study calculations or conclusions, which are not derived from the MMRM:

- On the CAPS-5 Total score, the 50 mg group demonstrated a clinically meaningful 15.7-point (43%) mean improvement from baseline in Stage 1.
- On the CAPS-5 Total score, 74% of patients receiving 50 mg in Stage 1 achieved a Clinically Reliable Change (≥13-point improvement from baseline) vs. 43% of patients receiving placebo (p=0.01).
- When accounting for imbalances in patients' time since trauma, the 50 mg group demonstrated a statistically significant separation from placebo on the percent change from baseline on the CAPS-5 Total score in Stage 1 (p=0.03).
- A favorable adverse event and tolerability profile was observed across the study.

The following study calculations have higher p-values than previously reported, but each remains below the significance threshold pre-specified in the SAP:

- On the CAPS-5 Arousal & Reactivity score, for the 50 mg dose vs. placebo in Stage 1, the revised p-value is p=0.019 (previously reported as p=0.004) and in Stages 1 + 2 combined, the revised p-value is p=0.071 (previously reported as p=0.040).
- On the CAPS-5 Negative Cognitions and Mood score, for the 50 mg dose vs. placebo in Stage 1, the revised p-value is p=0.096 (previously reported as p=0.049).
- On the HADS-Anxiety scale, for the 50 mg dose vs. placebo in Stage 1, the revised p-value is p=0.045 (previously reported as p=0.018).

The following table shows the updated statistical analysis for the 50 mg group—which performed best in the exploratory Phase 2 study and will be evaluated in the upcoming Phase 2b program—compared to placebo.

	Previously Reported			Revised Analysis		
Endpoint	Stage 1 (week 4) p-value vs. Placebo	Stage 2 (week 4) p-value vs. Placebo	Stage 1 & Stage 2 Combined P-Value vs. Placebo	Stage 1 (week 4) p-value vs. Placebo	Stage 2 (week 4) p-value vs. Placebo	Stage 1 & Stage 2 Combined P-Value vs. Placebo
CAPS-5 Total	0.119	>0.2	0.161	0.173	>0.2	0.212
CAPS-5 Arousal & Reactivity	0.004	0.1307	0.040	0.019	0.204	0.071
CAPS-5 Neg. Cognitions & Mood	0.049	>0.2	0.138	0.096	>0.2	0.189
CAPS-5 Intrusions	>0.2	>0.2	>0.2	>0.2	>0.2	>0.2
CAPS-5 Avoidance	0.143	>0.2	>0.2	0.201	>0.2	>0.2
PCL-5	0.099	>0.2	0.170	0.144	>0.2	0.206
HADS-A	0.018	>0.2	0.166	0.045	>0.2	0.216
CGI-S	0.175	>0.2	>0.2	0.216	>0.2	>0.2
CAPS-5 Total - % Change	0.060	>0.2	0.141	0.105	>0.2	0.191
CAPS-5 Arousal & Reactivity - % Change	0.003		0.047	0.015		0.086
CAPS-5 Neg. Cog. & Mood - % Change	0.036		0.154	0.079		0.208
CAPS-5 Intrusions - % Change			>0.2			>0.2
CAPS-5 Avoidance - % Change			>0.2			>0.2
CAPS-5 Total - % Change (with Time Since Trauma)	0.032			0.032		
CAPS-5 Total - Clinically Reliable Change	0.010			0.010		

Note to table: Endpoints in this exploratory study were assessed with a pre-specified one-sided alpha of p<0.1, LSM calculated using MMRM.

The company has published updated tables in its investor presentation, available in the Investors & Media section of Aptinyx's website at **ir.aptinyx.com**, and in an 8-K filed today with the U.S. Securities and Exchange Commission (SEC).

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. 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** or follow Aptinyx on Twitter @Aptinyx.

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, and 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 studies, 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; the accuracy of the company’s CROs’ analysis of resulting data from the company’s past, current and future clinical studies and the impact, if any, on the company’s development timelines; 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; 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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