NEWS RELEASE

# Clinical Evaluation of Aptinyx's NYX-783 for Treatment of Opioid Use Disorder to Be Funded by $5.6 Million NIH Grant

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NIH HEAL Initiative grant, administered by NIDA, funds preclinical and clinical studies of NYX-783 in opioid use disorder

Preclinical studies demonstrate NYX-783 has promising activity and safety profile relevant to treatment of opioid use disorder, clearing path for funding and initiation of clinical evaluation

Phase 1 clinical study in individuals using opioids expected to begin later this year

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 the finalization of a $5.6 million grant under the National Institutes of Health (NIH) Helping to End Addiction Long-term (HEAL) Initiative, supporting the development of NYX-783 for the treatment of opioid use disorder (OUD). NYX-783 is an NMDA receptor positive allosteric modulator also in Phase 2b development by Aptinyx for the treatment of post-traumatic stress disorder (PTSD).

The research and development of NYX-783 in OUD is funded by the NIH HEAL Initiative grant, administered by the National Institute on Drug Abuse (NIDA), and awarded to researchers at Yale University School of Medicine. A Phase 1 clinical study of NYX-783 in individuals using opioids will be conducted by researchers at Yale and is expected to commence later this year.

“We are excited to be partnering with world-class researchers at Yale in this evaluation of NYX-783, funded by a prestigious and generous grant from NIDA through the NIH HEAL Initiative,” said Andy Kidd, M.D., president and chief executive officer at Aptinyx. “In preclinical studies to date, Aptinyx has shown that NYX-783 has promising

extinction learning activity in multiple models of psychiatric disorders, including PTSD and alcohol use disorder. Additional preclinical research has demonstrated NYX-783's potential as a treatment option for the millions of people struggling with opioid use disorder. We look forward to collaborating with our research partners at Yale on the initiation of a Phase 1 clinical study of NYX-783 in people who use opioids. The NIDA grant, secured by the experienced researchers at Yale, ensures this development program can be advanced in a manner that is capital efficient for Aptinyx."

The co-principal investigators for the evaluation of NYX-783 in OUD are Ralph DiLeone, Ph.D., professor of psychiatry and of neuroscience at Yale University School of Medicine, and Rajita Sinha, Ph.D., Foundations Fund endowed professor of psychiatry and of neuroscience and child study at Yale University School of Medicine. Under a research collaboration with Aptinyx, Dr. DiLeone's lab conducted preclinical studies testing NYX-783 in animal models of OUD. In these studies, NYX-783 showed positive effects in reducing oxycodone consumption and oxycodone-seeking behavior. The studies also demonstrated that NYX-783 has a strong and relevant safety profile (e.g., no respiratory depression when administered in combination with an opiate).

"We are pleased to continue our collaboration with Aptinyx for the evaluation of NYX-783 for the treatment of OUD," said Dr. DiLeone. "The data generated from our preclinical studies in models of OUD have laid a strong foundation for the potential of NYX-783 in promoting relapse prevention among patients with opioid use disorder. With the support of the NIDA grant, we look forward to translating these findings to clinical benefit in humans through this Phase 1 development program."

The Phase 1 study will be a randomized, double-blind, placebo-controlled study to assess the safety, tolerability, and pharmacokinetics of NYX-783 50 mg and 150 mg, in combination with oxycodone 15 mg and 30 mg, in individuals who use opioids. The primary outcome measures in the study will evaluate a variety of safety-related measures, including change in respiratory rate, oxygenation saturation, blood pressure, heart rate, and cardiac activity over three weeks. Secondary outcome measures will evaluate opiate withdrawal and symptom scales over three weeks. The study will be conducted at the Yale Interdisciplinary Stress Center through a research collaboration with Aptinyx.

"NYX-783 presents a compelling therapeutic approach to improving relapse prevention in patients with opioid use disorder," said Dr. Sinha, director of the Yale Interdisciplinary Stress Center. "Patients suffering from OUD experience emotional dysregulation that leads to harmful addictive behavior. NMDA receptor modulation has demonstrated an ability to affect synaptic plasticity and learning processes, both of which have been implicated in opiate addiction and the vulnerability to relapse. We look forward to moving this program into Phase 1 clinical development."

About Opioid Use Disorder

Opioid use disorder (OUD) is a chronic brain disease in which people continue to use opioids despite harms caused by their use. OUD affects nearly three million people in the United States and over 80,000 people died from overdoses involving opioids in 2021. Over-prescription of opioid pain killers, insufficient drug prescription controls, a rise in illicit heroin use, and the emergence of potent synthetic forms (e.g., fentanyl) have all contributed to the continuation of the opioid crisis and related overdose epidemic. While medication-assisted therapies for opioid users (e.g., methadone, buprenorphine, and naltrexone) are available, many with OUD remain treatment refractory and vulnerable to recurrent cycles of relapse and drug use.

About NYX-783

NYX-783 is a novel, oral, positive allosteric modulator of NMDA receptors in Phase 2b development for the treatment of post-traumatic stress disorder (PTSD) and in Phase 1 development for the treatment of opioid use disorder (OUD). In preclinical studies of NYX-783, particularly strong results were observed in models of psychiatric disorders, fear extinction, and substance use disorders. 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 across a wide dose range. In an exploratory Phase 2a study in patients with PTSD, patients receiving a 50 mg dose level of NYX-783 showed meaningful symptom improvements and rates of response. The U.S. Food and Drug Administration has granted Fast Track designation to the development of NYX-783 for the treatment of PTSD. Evaluation of NYX-783 for the treatment of OUD is being conducted by researchers at Yale University School of Medicine and funded by a $5.6 million grant under the National Institutes of Health (NIH) Helping to End Addiction Long-term (HEAL) Initiative.

## 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 multiple product candidates in clinical development in central nervous system indications, including cognitive impairment, post-traumatic stress disorder, and opioid use disorder. 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 therapeutic effects of NYX-783 and expectations regarding the design, implementation, timing, and success of the company’s planned clinical trials. 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; 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 in its other filings and reports with the United States 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.

Source: Aptinyx Inc.

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