Three Recent Preclinical Publications Highlight NMDA Receptor Activation Facilitated by Aptinyx's NYX-2925

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Data published across three peer-reviewed journals elucidate novel mechanism leading to enhanced synaptic plasticity

EVANSTON, Ill., Sept. 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 that preclinical data from the company's novel NMDA receptor modulator, NYX-2925, has been published in three scientific journals. The published data demonstrate the effects of NYX-2925 on NMDA receptor trafficking *in vitro* and on sleep, mood, and EEG biomarkers in rodent models. Taken together, these data provide key insights into the mechanism of NYX-2925 and its enhancement of synaptic plasticity processes in the brain.

"The data published in these journals are reflective of our in-depth understanding of the activity of NYX-2925, garnered through evaluations across numerous molecular and behavioral preclinical models," remarked Norbert Riedel, Ph.D., president and chief executive officer of Aptinyx. "NYX-2925 and other compounds in our pipeline are highly selective to the NMDA receptor and exhibit a unique modulatory mechanism of action on this receptor. We are very pleased to have these data published across these high-caliber peer-reviewed journals to enhance the understanding of this novel mechanism, which is highly relevant in the treatment of chronic centralized neuropathic pain as well as other neurologic conditions caused by aberrant synaptic plasticity processes."

The first publication is titled "*NYX-2925 induces metabotropic NMDAR signaling that enhances synaptic NMDAR and AMPAR*" and has been published in the Journal of Neurochemistry. The data published in this paper detail the NYX-2925 treatment-mediated increases in NMDA receptor GluN2B trafficking and long-term potentiation-related signaling. The findings demonstrate the facilitation of synaptic plasticity processes resulting from administration of different concentration levels of NYX-2925.

The second publication is titled "*NMDAR activation regulates the daily rhythms of sleep and mood*" and has been published in Sleep. The data presented in this paper demonstrate the positive activity exhibited by NYX-2925 on various elements of sleep architecture. Administration of NYX-2925 enhanced sleep quality, as measured by an increase in the non-REM component of sleep. NYX-2925 facilitated an increase in sleep-bout duration and decreased drowsiness during wake, as measured by delta power. NYX-2925 also reversed sleep deprivation-induced deficits in a learning task and improved mood. Aptinyx has also conducted a translational sleep study in humans based on these observations on sleep parameters and NYX-2925 demonstrated significant effects on multiple sleep measures, including an increase in non-REM sleep, in that study as well. NMDA receptor-dependent synaptic plasticity processes are critical for sleep regulation and disrupted sleep is known to occur in a number of disorders, including chronic pain. These data support continued exploration of the effect of positive NMDA receptor modulation on sleep quality and associated downstream behavioral changes in both preclinical and clinical models.

The third publication is titled "*A translational EEG-based approach to assess modulation of long-lasting NMDAR-dependent synaptic plasticity*" and has been published in Psychopharmacology. Oral administration of NYX-2925 enhanced alpha power, increased NMDA receptor-dependent auditory LTP, and facilitated NMDA receptor-dependent mismatch negativity. The published studies are the first *in vivo* demonstration of the long-lasting effects of positive NMDA receptor modulation on synaptic plasticity processes using non-invasive EEG techniques. Aptinyx has also conducted a translational EEG study in healthy human volunteers in which NYX-2925 was shown to facilitate mismatch negativity and enhance synaptic plasticity, demonstrating that the mechanistic activity observed preclinically is consistent with the activity observed in the human brain.

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 Phase 1 and Phase 2 clinical studies, NYX-2925 has exhibited a favorable safety and tolerability profile across a wide dose range. In preclinical models of numerous neuropathic pain conditions, NYX-2925 has shown robust activity with a favorable tolerability profile. 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, 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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