



Data in Parkinson's Disease Model in Non-human Primates Demonstrate Reversal of Cognitive Deficits with Novel NMDA Receptor Modulator, NYX-458

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EVANSTON, Ill., April 03, 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 positive preclinical data on its novel NMDA receptor modulator, NYX-458, demonstrating reversal of cognitive deficits in a non-human primate model of Parkinson's disease. The data were presented last week at the 14th International Conference on Alzheimer's & Parkinson's Diseases in Lisbon (AD/PD™) Portugal.

"With up to half of all people with Parkinson's disease experiencing cognitive impairment and very few therapeutic options addressing these cognitive deficits, the unmet need in Parkinson's cognitive impairment is immense," said Norbert Riedel, Ph.D., president and chief executive officer at Aptinyx. "The benefits observed in this highly translatable disease model demonstrate the potential for NYX-458 to be a much-needed improvement in treating these cognitive symptoms. It is highly encouraging that administration of NYX-458 was able to restore cognitive performance in this study – on some measures, back to healthy baseline levels – and we are eager to initiate a Phase 2 study in patients with Parkinson's disease later this year."

In the study, healthy non-human primates were trained on a battery of cognitive tests that are components of the Cambridge Neuropsychological Test Automated Battery (CANTAB) to establish a baseline level of performance. The CANTAB is often used in human clinical studies to assess levels of cognitive performance. Once the baseline cognitive performance was established, a neurotoxin called MPTP was administered chronically at low doses to deplete dopaminergic neurons and induce cognitive deficits similar to those experienced by people with Parkinson's disease. Once a stable deficit was established, the non-human primates received a single dose of vehicle (placebo) and showed no improvement in cognitive performance. Following the placebo period, the primates were given a single dose of NYX-458 and assessed on the cognitive tests.

Administration of NYX-458 resulted in rapid, robust, and long-lasting improvements in cognitive performance across the battery of tests. In the Variable Delayed Response (VDR) assay, an assessment of attention and working memory, the effects observed were statistically significant ($p < 0.05$) on day one following a single administration of NYX-458 and remained significant at day twenty-one. NYX-458 was also shown to induce statistically significant cognitive improvements following a second course of MPTP dosing that was administered to deplete additional dopaminergic neurons and re-induce cognitive deficits. In the Simple Discrimination Reversal (SDR) assay, an assessment of cognitive flexibility or the ability to switch from thinking about one concept to another, administration of NYX-458 resulted in statistically significant improvements in discrimination reversal ($p < 0.05$). The robust improvements observed on cognitive performance were consistent across the battery of cognitive tests, were maintained with daily oral administration of NYX-458, and endured for approximately three months after dosing was discontinued.

A separate study evaluated the effects of NYX-458 on motor symptoms and on the anti-parkinsonian effects of levodopa. Such assessments are critical in the development of a pharmacotherapy for Parkinson's disease cognitive impairment, as it is important to ascertain whether the therapy adversely influences motor symptoms and whether it interferes with the benefits of levodopa, which is the standard of care. In this study, a separate cohort of non-human primates was dosed with high doses of MPTP and levodopa in order to cause Parkinson's-like motor impairments and levodopa-induced dyskinesia. After motor impairments were established, the non-human primates were dosed with NYX-458 and assessed on scales measuring activity, Parkinsonian disability, and dyskinesia. Administration of NYX-458, either as a monotherapy or in combination with levodopa, did not result in any adverse effects on motor symptoms and did not interfere with the anti-parkinsonian effects of levodopa on the evaluated scales. These results further reinforce the suitability of NYX-458 as a potential treatment for cognitive impairment due to Parkinson's disease and support its further development. Across both studies, no evident tolerability issues were observed with NYX-458.

"These are impressive data in a model that closely replicates the types of cognitive deficits seen in Parkinson's disease," said Jay Schneider, Ph.D., professor of pathology, anatomy, and cell biology at Thomas Jefferson University who worked with the research organization, Atuka Inc., on the conduct of the studies. "We have evaluated many different compounds and mechanisms in this model and the benefits exhibited by NYX-458 are among the most compelling I have seen. This model is highly translatable to the human condition – there are many similarities in the types of cognitive deficits expressed in this model and in Parkinson's patients – and a drug that has worked in this model has shown cognitive benefits in the clinic. Based on these results, it will certainly be interesting to evaluate this compound in patients to determine whether the cognitive benefits observed in this model can be replicated in patients."

The data presented indicate that NYX-458's novel modulation of NMDA receptors may be a highly effective approach to addressing the cognitive impairment associated with Parkinson's disease, without worsening motor symptoms or interfering with levodopa therapy.

Aptinyx is completing a Phase 1 study evaluating the safety, tolerability, pharmacokinetics, and CNS exposure of NYX-458 and expects to report data from that study in the first half of 2019. Based on the robust activity observed in various models of cognition, learning, and memory across rats and non-human primates, Aptinyx plans to initiate a Phase 2 study in people with Parkinson's disease in the second half of 2019.

About NYX-458

NYX-458 is a novel, oral NMDA receptor modulator currently in Phase 1 clinical development for the treatment of cognitive impairment associated with Parkinson's disease. In preclinical studies in rodents and non-human primates, NYX-458 has demonstrated rapid, robust, and enduring positive effects on cognitive performance. A Phase 1 study evaluating the safety, tolerability, pharmacokinetics, and CNS exposure of NYX-458 is ongoing and Aptinyx expects to report data from the study in the first half of 2019.

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 trials, expectations regarding its preclinical development activities, 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; 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.

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