Voyager Therapeutics Announces Clinical Trial Update with VY-AADC01 for Advanced Parkinson's Disease

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VY-AADC01 Successfully Administered to the First Patient Using a New, Posterior Surgical Delivery Approach

CAMBRIDGE, Mass., June 26, 2017 (GLOBE NEWSWIRE) -- Voyager Therapeutics, Inc. (NASDAQ:VYGR), a clinical-stage gene therapy company developing life-changing treatments for severe neurological diseases, today announced dosing of the first patient in a Phase 1 trial aimed at further optimizing the surgical delivery of VY-AADC01 for advanced Parkinson's disease. This planned Phase 1 trial explores a posterior (i.e., back of the head) surgical delivery approach, compared to Cohorts 1-3 from a separate, ongoing Phase 1b trial that used a transfrontal (i.e., top of the head) surgical delivery approach, into the putamen, a specific region of the brain targeted by Voyager's gene therapy program. A posterior approach could better align the infusion of VY-AADC01 with the anatomical structure of the putamen to potentially reduce the total procedure time and increase the total coverage of the putamen. The administration of VY-AADC01 with this posterior approach was well-tolerated by the patient. No serious adverse events were reported and the patient was discharged from the hospital the day after surgery.

"We are excited to successfully dose the first patient with this new surgical delivery approach," said R. Mark Richardson, M.D., Ph.D., Director of Epilepsy and Movement Disorders Surgery at the University of Pittsburgh Medical Center and an investigator in the trial. "Reducing the number of bilateral surgical infusions from two with the transfrontal approach to one with the posterior approach is likely to reduce the total procedure time for this innovative program to treat advanced Parkinson's disease."

"Along with the potential to reduce the procedure time, this approach may also increase the coverage of the brain region we are targeting with VY-AADC01," said Bernard Ravina, M.D., chief medical officer at Voyager. "Preliminary total procedure time and putaminal coverage data from this trial that continues to enroll will be available during the third quarter of 2017 and will help inform the design of the pivotal Phase 2-3 program planned to initiate during late 2017."

About Parkinson's Disease and VY-AADC01

Parkinson's disease is a chronic, progressive and debilitating neurodegenerative disease that affects approximately 700,000 people in the U.S. [1] and seven to 10 million people worldwide[2]. It is estimated that up to 15% of the prevalent population with Parkinson's disease, or approximately 100,000 patients in the U.S., have motor fluctuations that are refractory, or not well-controlled, with levodopa. While the underlying cause of Parkinson's disease in most patients is unknown, the motor symptoms of the disease arise from a loss of neurons in the midbrain that produce the neurotransmitter dopamine. Declining levels of dopamine in this particular region of the brain leads to the motor symptoms associated with Parkinson's disease including tremors, slow movement or loss of movement, rigidity, and postural instability. Motor symptoms during the advanced stages of the disease include falling, gait freezing, and difficulty with speech and swallowing, with patients often requiring the daily assistance of a caregiver.

There are currently no therapies that effectively slow or reverse the progression of Parkinson's disease. Levodopa remains the standard of care treatment, with its beneficial effects on symptom control having been discovered over 40 years ago[3]. Patients are generally well-controlled with oral levodopa in the early stages of the disease, but become less responsive to treatment as the disease progresses. Patients experience longer periods of reduced mobility and stiffness termed off-time, or the time when medication is no longer providing benefit, and shorter periods of on-time when their medication is effective.

The progressive motor symptoms of Parkinson's disease are largely due to the death of dopamine neurons in the substantia nigra, a part of the midbrain that converts levodopa to dopamine, in a single step catalyzed by the enzyme AADC. Neurons in the substantia nigra release dopamine into the putamen where the receptors for dopamine reside. In advanced Parkinson's disease, neurons in the substantia nigra degenerate and the enzyme AADC is markedly reduced in the putamen, which limits the brain's ability to convert oral levodopa to dopamine [4]. The intrinsic neurons in the putamen, however, do not degenerate in Parkinson's disease [5,6]. VY-AADC01, comprised of the adeno-associated virus-2 capsid and a cytomegalovirus promoter to drive AADC transgene expression, is designed to deliver the AADC gene directly into neurons of the putamen where dopamine receptors are located, bypassing the substantia nigra neurons and enabling the neurons of the putamen to express the AADC enzyme to convert levodopa into dopamine. The approach with VY-AADC01, therefore, has the potential to durably enhance the conversion of levodopa to dopamine and provide clinically meaningful improvements in motor symptoms following a single administration.

About Voyager Therapeutics

Voyager Therapeutics is a clinical-stage gene therapy company developing life-changing treatments for severe neurological diseases. Voyager is committed to advancing the field of AAV gene therapy through innovation and investment in vector engineering and optimization, manufacturing and dosing and delivery techniques. The company's pipeline focuses on severe neurological diseases in need of effective new therapies, including advanced Parkinson's disease, a monogenic form of ALS, Huntington's disease, Friedreich's ataxia, frontotemporal dementia, Alzheimer's disease and severe, chronic pain. Voyager has broad strategic collaborations with Sanofi Genzyme, the specialty care global business unit of Sanofi, and the University of Massachusetts Medical School. Founded by scientific and clinical leaders in the fields of AAV gene therapy, expressed RNA interference and neuroscience, Voyager Therapeutics is headquartered in Cambridge, Massachusetts. For more information, please visit www.voyagertherapeutics.com. Follow Voyager on LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995 and other federal securities law. The use of words such as “may,” “might,” “will,” “should,” “could,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “undoubtedly,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify forward-looking statements. For example, all statements Voyager makes regarding the initiation, timing, progress and reporting of results of its preclinical programs and clinical trials and its research and development programs, its ability to advance its AAV-based gene therapies, into, and successfully complete, clinical trials, its ability to continue to develop its product engine, its ability to add new programs to its pipeline, its ability to develop manufacturing capability for its products, its ability to enter into new partnerships or collaborations, and the timing or likelihood of its submissions and filings with and approvals from the FDA and other regulatory authorities, are forward looking. All forward-looking statements are based on estimates and assumptions by Voyager’s management that, although Voyager believes to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that Voyager expected. These statements are also subject to a number of material risks and uncertainties that are described in Voyager’s most recent Annual Report on Form 10-K and Quarterly Report on 10-Q filed with the Securities and Exchange Commission, as updated by its future filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. Voyager undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

[1] Willis et al, *Neuroepidemiology*.2010;34:143–151

[2] www.pdf.org/en/parkinson_statistics

[3] Poewe W, et al, *Clinical Interventions in Aging*.2010;5:229-238.

[4] Lloyd, *J Pharmacol Exp Ther*. 1975;195:453-464, Nagatsu, *J Neural Transm Suppl*.2007

[5] Cold Spring Harb Perspect Med 2012;2:a009258

[6] Braak et al, *Cell Tissue Res*.2004;318:121-134

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