# Voyager Therapeutics Initiates Third Cohort in Ongoing Phase 1b Clinical Trial of VY-AADC01 in Advanced Parkinson's Disease

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**Phase 1b Study On Track to Report Six-Month Safety, Motor Function, and Biomarker Data from Cohorts 1 and 2 by Year-End 2016**

CAMBRIDGE, Mass., Aug. 09, 2016 (GLOBE NEWSWIRE) -- Voyager Therapeutics, Inc. (NASDAQ:VYGR), a clinical-stage gene therapy company developing life-changing treatments for severe diseases of the central nervous system (CNS), today announced dosing of the first patient in the third cohort of the ongoing Phase 1b open-label trial of VY-AADC01 in patients with advanced Parkinson's disease following a recent meeting of the trial's data and safety monitoring board.

"We are pleased with the progress of this ongoing Phase 1b trial and the initiation of the planned third cohort in this trial of up to 20 patients," said Bernard Ravina, MD, MS, vice president of clinical development at Voyager Therapeutics. "Along with assessing safety, the goal of this open-label trial is to explore ascending dose levels and optimal delivery of VY-AADC01 in patients with advanced Parkinson's disease. We remain on track to deliver six-month data on safety, motor function and biomarkers from patients in Cohort 1 and 2, as well as preliminary data from some patients in Cohort 3 by the end of this year. We will report longer-term safety and clinical data as we continue to advance the program next year."

**About the Phase 1b Study of VY-AADC01 in Advanced Parkinson's Disease**

Patients enrolled in Cohorts 1 and 2 received a single administration of VY-AADC01 at a total dose up to of $7.5 \times 10^{11}$ vector genomes (vg) and $1.5 \times 10^{12}$ vg, respectively. Patients enrolling in Cohort 3 (up to five patients) will receive up to a three-fold higher total dose ($4.5 \times 10^{12}$ vg) than Cohort 2. A final, additional cohort (Cohort 4) could increase the total dose six-fold higher than Cohort 2.

The primary objective of the study is to assess the safety at ascending dose levels of VY-AADC01. Secondary objectives include an assessment of the surgical coverage of the putamen and the assessment of aromatic L-amino acid decarboxylase (AADC) expression and activity in the putamen before and after VY-AADC01 treatment using 18-fluorodopa and positron emission tomography (PET). Changes in patients' sensitivity to levodopa treatment will be measured by assessing their motor function in response to an intravenous infusion of levodopa, their doses of levodopa, and related medications pre- versus post-treatment with VY-AADC01. Clinical motor symptoms including patients' off-time, or the time when medication is no longer providing benefit with regard to mobility, slowness, and stiffness, will be measured using a validated patient diary developed to assess Parkinson's disease motor symptoms. Additional tests will measure patients' motor symptoms including use of the Unified Parkinson's Disease Rating Scale (UPDRS), as well as tests of cognitive function, mood, and quality of life. These primary and secondary objectives will be measured systematically from baseline over a 36-month period post-treatment, with PET scans and intravenous levodopa infusions at six months after treatment. Additional details about the Phase 1b study can be found using the following link: https://clinicaltrials.gov/ct2/show/NCT01973543?term=AADC&rank=2

**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 disease arises 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 aromatic L-amino acid decarboxylase (AADC) enzyme. Neurons in the substantia nigra release dopamine into the putamen where the receptors for dopamine reside. In advanced Parkinson's disease, the neurons in the substantia nigra degenerate and the enzyme AADC is markedly reduced, which limits the brain's ability to convert oral levodopa to dopamine [4]. The neurons in the putamen do not degenerate in Parkinson's disease [5],[6]. VY-AADC01, comprised of the adeno-associated virus-2 capsid and a cytomegalovirus promotor to drive AADC transgene expression, is designed to deliver the AADC gene directly into the putamen where the 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.

[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

**About Voyager Therapeutics**

Voyager Therapeutics is a clinical-stage gene therapy company developing life-changing treatments for severe diseases of the CNS. Voyager is committed to advancing the field of AAV (adeno-associated virus) gene therapy through innovation and investment in vector engineering and optimization, manufacturing and dosing and delivery techniques. The Company's pipeline is focused on severe CNS diseases in need of effective new therapies, including advanced Parkinson's disease, a monogenic form of amyotrophic lateral sclerosis (ALS), Friedreich's ataxia, Huntington's disease, spinal muscular atrophy (SMA), 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," "expect," "plan," "anticipate," "believe," "estimate," "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 expected cash, cash equivalents and marketable securities at the end of the fiscal year and anticipation for how long expected cash, cash equivalents and marketable securities will last, and the timing or likelihood of its regulatory filings and approvals, 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-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.

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