Voyager Therapeutics Announces Interim Phase 1b Surgical Results for VY-AADC01 in Advanced Parkinson's Disease

June 22, 2016

Data Presented at the 20th International Congress of Parkinson's Disease & Movement Disorders in Berlin, Germany

VY-AADC01 Continues to Demonstrate Safety with Increasing Coverage of Targeted Regions of the Brain

Phase 1b Study On Track to Report Interim Motor Symptom and Biomarker Data by Year-End 2016

CAMBRIDGE, Mass., June 22, 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 reported interim surgical results from an ongoing Phase 1b study of VY-AADC01 in patients with advanced Parkinson's disease as a poster presentation at the 20th International Congress of Parkinson's Disease and Movement Disorders (ICPDMD) in Berlin, Germany.

"The interim surgical data from the Phase 1b study presented at this year's conference demonstrate the continued safety of VY-AADC01 in all 10 patients treated from Cohorts 1 and 2 of the ongoing dose escalation trial," said Bernard Ravina, MD, MS, vice president of clinical development at Voyager Therapeutics. "Importantly, the use of real-time, intra-operative MRI-guided delivery allowed the surgical teams to visualize the delivery of VY-AADC01, administer higher infusion volumes, and achieve greater coverage of the putamen, the brain region that we are targeting with our gene therapy program. Increased infusion volumes of VY-AADC01 in Cohort 2 resulted in a higher average coverage of the overall putamen of 34% compared to 21% in Cohort 1. This is substantially greater coverage of the putamen than has been achieved in previous gene therapy trials using a similar vector, and represents an important threshold based on preclinical studies. Obtaining sufficient coverage of the putamen with VY-AADC01 is a key step towards potentially improving patients' response to levodopa, the standard of care treatment for Parkinson's disease, and will allow us to begin to more fully assess the impact of VY-AADC01 on patients' motor symptoms from the top-line results of this study expected later this year."

About the Phase 1b study

The Phase 1b, open-label study will include up to 20 patients with advanced Parkinson's disease and disabling motor fluctuations, treated with a single administration of VY-AADC01. The primary objective of the study is to assess the safety and surgical coverage of the putamen at ascending dose levels of VY-AADC01. Secondary objectives include 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. 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 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

Five patients enrolled in Cohort 1 in this study received a single administration of VY-AADC01 at a concentration of 8.3×10^{11} vector genomes per milliliter (vg/ml) using an infusion volume of up to 450 µL per putamen, or up to 900 µL per patient, for a total dose of 7.5×10^{11} vg. Five patients enrolled in Cohort 2 received a single administration of VY-AADC01 at a concentration of 8.3×10^{11} vg/ml, using an infusion volume of up to 900 µL per putamen, or up to 1,800 µL per patient, for a total dose of 1.5×10^{12} vg. Following a planned meeting of the data and safety monitoring board, investigators may begin dosing a third cohort this summer. Cohort 3 patients will receive similar infusion volumes (up to 900 µL per putamen) of VY-AADC01 to Cohort 2 but three-fold higher vector genome concentrations. A final, additional cohort (Cohort 4) could increase the vector genome concentration 6-fold higher than Cohort 2.

VY-AADC01 Phase 1b surgical data presented at this year's ICPDMD

Patients enrolled in Cohorts 1 and 2 were on average 58 years of age (range: 47-70) and had Parkinson's disease for approximately 10 years (range: 5-17). Patients were candidates for surgical intervention due to disabling motor complications despite treatment with optimal antiparkinsonian medication and experienced on average 5 hours (range: 3-9) per day of off-time.

Previously reported surgical data from Cohort 1 patients revealed an average coverage of the overall putamen with VY-AADC01 of approximately 21% (range 17-25%). Surgical data presented at this year's ICPDMD from Cohort 2 patients revealed a higher average coverage of the overall putamen of 34% (range 25-38%). This includes data from recently dosed patients 9 and 10, who had an overall putamen coverage of 32% and 37%, respectively.

The surgical procedure was successfully completed in all 10 patients and infusions of VY-AADC01 have been well-tolerated with no treatment-related serious adverse events (SAEs). Nine of the 10 patients were discharged from the hospital one to two days following surgery. As previously reported, one patient experienced two SAEs; a pulmonary embolism or blood clot in the lung, and related heart arrhythmia or irregular heartbeat. The patient was treated with an anti-coagulant and the symptoms associated with the SAEs have completely resolved. Investigators determined that this was

related to immobility during the surgical procedure and a subsequent formation of a blood clot. Magnetic resonance imaging compatible measures have been added to prevent blood clots and no subsequent events have been observed following implementation of these measures.

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 7 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, difficulty with speech and swallowing, with patients often requiring 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 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 central nervous system. 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.

Investor Relations:
Matt Osborne
Head of Investor Relations & Corporate Communications
857-259-5353
mosborne@vygr.com

Media:

Katie Engleman
Pure Communications, Inc.
910-509-3977
Katie@purecommunicationsinc.com

Voyager Therapeutics