Voyager Therapeutics Announces Additional Results from Phase 1b Trial of VY-AADC01 for Advanced Parkinson's Disease

April 25, 2017

Improved Functional and Quality of Life Data Presented at the American Academy of Neurology (AAN) Meeting in Boston, MA

Surgical Delivery Data Presented at the American Association of Neurological Surgeons (AANS) Meeting in Los Angeles, CA

CAMBRIDGE, Mass., April 25, 2017 (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 dose-dependent improvements in functional and quality of life measures from the Phase 1b trial of VY-AADC01 for advanced Parkinson's disease presented as part of an emerging (late-breaking) oral presentation at the AAN Annual Meeting. In addition, during a separate oral presentation at the AANS Annual Scientific Meeting, investigators presented results for maximizing coverage of the putamen during the surgical procedure for VY-AADC01.

"We are pleased that VY-AADC01 data were selected for oral presentation at major neurology and neurosurgery meetings," said Bernard Ravina, M.D., M.S., chief medical officer of Voyager Therapeutics. "In addition to the previously reported improvements in biomarkers and motor symptoms, investigators at the AAN meeting presented data on patients' improved function and quality of life. Motor fluctuations in advanced Parkinson's are debilitating and these function and quality of life results are key indicators of the potential clinical impact of a one-time treatment with VY-AADC01. Here, we were encouraged with the 9-point improvement in PDQ-39 total score, a patient reported outcome, in Cohort 2 at 12 months. In addition to these data at the AAN meeting, the data at the AANS meeting highlighted key advances in the neurosurgical techniques used to administer VY-AADC01 and increase the coverage of the putamen, the brain region that we are targeting with our gene therapy approach aimed at restoring patients' response to their levodopa medication."

VY-AADC01 data presented at the AAN Annual Meeting included previously reported motor symptom data from all 10 patients treated in Cohorts 1 and 2 at six months (five patients in each Cohort), and data from five patients in Cohort 1 and three patients in Cohort 2 who have reached 12 months of follow-up at the time of the interim results. In addition, investigators at the AAN meeting presented new functional and quality of life data as measured by the Unified Parkinson's Disease Rating Scale (UPDRS) Part II and Part IV, and the patient-reported 39-item Parkinson's Disease Questionnaire (PDQ-39) demonstrating dose-dependent and clinically meaningful improvements in these scores (Table 1).

Table 1. VY-AADC01 Phase 1b interim results on UPDRS-II, -IV, and PDQ-39 scores

Functional/Quality of Life Measure	Baseline score	Results at 12-months[1]
UPDRS-II (off-medication)	Cohort 1 (13.6) Cohort 2 (16.7)	Cohort 1 (0.2-point worsening, SD 3.7) vs. Cohort 2 (4.0-point improvement, SD 1.0)
UPDRS-IV total score	Cohort 1 (7.8) Cohort 2 (8.7)	Cohort 1 (1.2-point improvement, SD 1.9) vs. Cohort 2 (2.7-point improvement, SD 3.1)
PDQ-39 total score	Cohort 1 (18.2) Cohort 2 (12.3)	Cohort 1 (1.9-point improvement, SD 5.6) vs. Cohort 2 (9.2-point improvement, SD 5.5)

1) Cohort 1 baseline and 12-month data from 5/5 patients. Cohort 2 baseline and 12-month data from 3/5 patients. 2/5 patients in
Cohort 2 have not reached 12-month follow-up period at the time of the analysis

- The emerging (late-breaking) oral presentation at the AAN Annual Meeting will be presented during the Emerging Science Session taking place this evening from 5:45 p.m. to 6:30 p.m. EDT.

Data presented at the AANS Annual Scientific Meeting reviewed the evolution of the real-time MRI-guided surgical procedure during the clinical trial that resulted in increased coverage of the putamen, a region of the brain associated with motor function in Parkinson's disease. In addition to increased infusion volumes, these steps included modifications to the size of the cannula and position of infusion sites during surgery. As previously reported, these developments increased the average coverage of the putamen from 21% in Cohort 1, to 34% in Cohort 2, and 42% in Cohort 3.

- The oral presentation of these data at the AANS Meeting occurred on April 24, during the Stereotactic and Functional Surgery session from 2:00 p.m. to 5:30 p.m. PST.

About the Phase 1b Trial of VY-AADC01 for Advanced Parkinson's Disease

In advanced Parkinson's disease, the putamen is depleted of dopamine and of the enzyme aromatic L-amino acid decarboxylase (AADC) that is

responsible for converting levodopa to dopamine. VY-AADC01 is Voyager's gene therapy vector that contains the gene that encodes the AADC enzyme. The Phase 1b, open-label trial includes 15 patients with advanced Parkinson's disease and disabling motor fluctuations, treated with a single administration of VY-AADC01. The primary objective of the trial is to assess the safety and surgical coverage of ascending doses of VY-AADC01 in the putamen, a region of the brain associated with motor function in Parkinson's disease. The secondary objectives of the trial include the assessment of AADC expression and activity in the putamen measured by positron emission tomography (PET) using [^{18}F] fluorodopa (or ^{18}F-DOPA). In addition, changes in motor responses to levodopa are measured by a controlled intravenous infusion of levodopa and by measuring daily requirements for levodopa and related medications. Other secondary objectives include assessment of motor function as measured by the Unified Parkinson's Disease Rating Scale (UPDRS) and a patient-completed (Hauser) diary.

Conference Call Information

Voyager is hosting a breakfast event at the AAN conference today at 8:00 a.m. with KOL neurologists to discuss advanced Parkinson's disease. The event may be accessed live by dialing (877) 851-3834 for domestic callers or +1 (631) 291-4595 for international callers, and referencing conference ID number 5621646, or by audio webcast from the Investors & Media section of Voyager's website at www.voyagertherapeutics.com. The webcast will be archived for 30 days.

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 diseases of the CNS. 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 CNS diseases in need of effective new therapies, including advanced Parkinson's disease, a monogenic form of ALS, Friedreich's ataxia, Huntington's disease, 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," "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, ability to enter into new partnerships or collaborations, its expected cash, cash equivalents and marketable debt securities at the end of a fiscal year and anticipation for how long expected cash, cash equivalents and marketable debt 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-K 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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