Voyager Therapeutics Provides Updates for VY-AADC Clinical Program for Parkinson's Disease

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Voyager to increase the size of RESTORE-1 Phase 2 trial and to conduct a similarly-sized RESTORE-2 Phase 3 trial

VY-AADC clinical program updates incorporate FDA feedback from Type B meeting

CAMBRIDGE, Mass., Jan. 07, 2019 (GLOBE NEWSWIRE) -- Voyager Therapeutics, Inc. (NASDAQ: VYGR), a clinical-stage gene therapy company focused on developing life-changing treatments for severe neurological diseases, today announced an update to its VY-AADC clinical program for Parkinson's disease. In December 2018, the Company held a Type B meeting with the U.S. Food and Drug Administration (FDA) to discuss the overall development program for VY-AADC. Based on the meeting discussion and subsequent written feedback from the FDA, Voyager plans to submit a revised trial protocol that will include an increase in the target number of patients in the RESTORE-1 Phase 2 trial, resulting in 75 to 100 total patients in the trial, and to conduct a staggered-parallel Phase 3 trial (RESTORE-2) of similar size and design to RESTORE-1. These updates incorporate guidance from the FDA from the Type B meeting to conduct two adequate and well-controlled clinical trials for a large patient population such as Parkinson's disease.

"Our recent meeting with the FDA was informative and helps to clarify the expected regulatory pathway for VY-AADC," said Andre Turenne, president and chief executive officer of Voyager Therapeutics. "We look forward to continuing to engage with the FDA and other regulators as we advance our clinical development program and our work to bring VY-AADC to patients in need."

About the RESTORE-1 and RESTORE-2 clinical trials of VY-AADC for Parkinson's Disease

The RESTORE-1 Phase 2 trial is currently enrolling patients who have been diagnosed with Parkinson's disease for at least four years, are not responding adequately to oral medications, and have at least three hours of OFF time during the day as measured by a validated self-reported patient diary. Patients who meet the eligibility criteria are randomized (1:1) to one-time administration of VY-AADC or placebo surgery.

The primary efficacy endpoint of RESTORE-1 is ON time without troublesome dyskinesia, or good ON time, as measured by a validated self-reported patient diary at 12 months. In addition, Voyager will continue to follow patients on a blinded basis beyond 12 months to obtain additional safety data and to assess the durability of the potential beneficial effects. Secondary endpoints include diary OFF time, other motor function and quality of life measures from the United Parkinson's Disease Rating Scales (UPDRS-II,-III scores), the Parkinson's Disease Questionnaire (PDQ-39), and patient's global function as measured by the proportion of participants with improvement on the Clinical Global Impression (CGI) score. The trial will also measure non-motor symptoms from the Non-Motor Symptom Scale (NMSS), as well as safety. Biomarker data include measurements of the coverage of the specific region of the brain (putamen) targeted with VY-AADC and measurements of AADC enzyme expression and activity in the putamen measured by positron emission tomography (PET) using fluorodopa F-18. Changes in patients' daily doses of oral levodopa and related medications will also be recorded.

Voyager expects RESTORE-1 will take approximately 15 to 21 months to enroll. Voyager plans to begin enrolling patients in RESTORE-2 in both active Phase 2 sites and additional sites globally in the first half of 2020. Voyager anticipates that, if positive, results from RESTORE-1 and RESTORE-2 could potentially form the basis for submission of a biologics license application (BLA) to the FDA for VY-AADC for the treatment of Parkinson's disease.

For additional information regarding Voyager's RESTORE-1 Phase 2 clinical trial with its gene therapy VY-AADC for the treatment of Parkinson's disease, please use the following link or email Voyager at clinicaltrials@vygr.com.

About Voyager's VY-AADC Gene Therapy for Parkinson's Disease

VY-AADC is an investigational gene therapy product 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 produce the AADC enzyme to convert levodopa into dopamine. With this approach, VY-AADC has the potential to durably enhance the conversion of levodopa to dopamine and provide clinically meaningful improvements by restoring motor function in patients and improving symptoms following a single administration.

Voyager recently initiated the Phase 2 RESTORE-1 trial in patients who have been diagnosed with Parkinson's disease for at least four years, are not responding adequately to oral medications, and have at least three hours of OFF time during the day as measured by a validated self-reported patient diary.

For additional information regarding Voyager's RESTORE-1 Phase 2 clinical trial with its gene therapy VY-AADC for the treatment of Parkinson's disease, please use the following link or email Voyager at clinicaltrials@vygr.com.

The FDA granted Regenerative Medicine Advanced Therapy (RMAT) designation for VY-AADC for the treatment of Parkinson's disease in patients with motor fluctuations that are refractory to medical management. RMAT designation is an expedited program for the advancement and approval of regenerative medicine products, including gene therapy products. RMAT designation was granted based on clinical data from the Phase 1b trial with VY-AADC in patients with Parkinson's disease. During this trial, one-time administrations of VY-AADC demonstrated robust and durable improvements in patients' motor function along with substantial reductions in use of daily oral levodopa and other Parkinson's disease medications. Infusions of VY-AADC have been well-tolerated in this trial with no vector-related serious adverse events reported to date.

About Parkinson's Disease

Parkinson's disease is a chronic, progressive and debilitating neurodegenerative disease that affects approximately 1,000,000 people in the U.S. [1] and

seven to 10 million people worldwide[2]. 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 and the enzyme needed to convert levodopa to dopamine in this region of the brain, the putamen, leads to the motor symptoms associated with Parkinson's disease including tremors, slow movement or loss of movement, rigidity, and postural instability. Additional motor symptoms during the advanced stages of the disease include falling 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 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 levodopa to dopamine [4]. The intrinsic neurons in the putamen, however, do not degenerate in Parkinson's disease [5,6].

About Voyager Therapeutics

Voyager Therapeutics is a clinical-stage gene therapy company focused on 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. Voyager's pipeline focuses on severe neurological diseases in need of effective new therapies, including Parkinson's disease, a monogenic form of ALS called SOD1, Huntington's disease, Friedreich's ataxia, neurodegenerative diseases related to defective or excess aggregation of tau protein in the brain including Alzheimer's disease and severe, chronic pain. Voyager has strategic collaborations with Sanofi Genzyme and AbbVie. 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.

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 laws. The use of words such as "may," "might," "will," "would," "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 initiate, enroll and complete, clinical trials, the potential clinical utility of its product candidates, its ability to continue to develop its gene therapy platform, its ability to develop manufacturing capability for its products and successfully transition its manufacturing process, its ability to perform under existing collaborations with, among others, Sanofi Genzyme and AbbVie and to add new programs to its pipeline, its ability to enter into new partnerships or collaborations, the sufficiency of its cash resources and the regulatory pathway of, and the timing or likelihood of its regulatory filings and approvals for, any of its product candidates, 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. Such risks and uncertainties include, among others, the initiation and conduct of preclinical studies and clinical trials; the availability of data from clinical trials; the expectations for regulatory communications, submissions and approvals; the continued development of the gene therapy platform; Voyager's scientific approach and general development progress; and the availability or commercial potential of Voyager's product candidates. 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 subsequent 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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[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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