Voyager Therapeutics Announces Positive Longer-Term Data for VY-AADC for Parkinson's Disease

11/07/18

One-time treatment with VY-AADC demonstrates durable improvements in motor function at 18 months and beyond from ongoing Phase 1b trial

CAMBRIDGE, Mass., Nov. 07, 2018 (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 positive longer-term results from the open-label, dose-escalating Phase 1b trial of VY-AADC demonstrating sustained improvements in patients' motor function. Patients in the two highest dose cohorts (Cohorts 3 and 2) experienced mean improvements in diary on-time without troublesome dyskinesia (good ON time) of 1.7 hours per day at 18 months and 2.7 hours per day at two years, respectively.

Having selected a dose for the Phase 2 trial between the two highest dose cohorts from the Phase 1b trial, Voyager performed a combined analysis of the outcomes from the ten patients in Cohorts 2 and 3. This combined analysis demonstrated an increase from baseline in good ON time of 2.4 hours per day at 12 months, the timepoint for the primary endpoint in the Phase 2 trial, and 2.6 hours per day at 18 months, the latest timepoint measured for both cohorts. Of the combined ten patients in Cohorts 2 and 3, seven patients would be eligible for the Phase 2 trial based on limits in severity of dyskinesia and minimum OFF time at baseline. For these seven patients, the Phase 2 trial relevant group, the improvements in good ON time were 2.8 hours at 12 months and 2.5 hours at 18 months. These results were achieved with clinically meaningful and sustained reductions in daily oral levodopa and related medications.

"The longer-term results from the Phase 1b trial provide an additional indication that VY-AADC treatment increases AADC enzyme levels, improves responses to levodopa, and increases time in the ON state, an important benefit for patients with Parkinson's disease," said Chad Christine, M.D., Professor of Neurology, University of California, San Francisco and Investigator in the Phase 1b trial of VY-AADC. "These results are very encouraging, and I look forward to the advancement of VY-AADC into the Phase 2 clinical trial."

VY-AADC Motor Function Results from the Phase 1b Trial

The Phase 1b, open-label, dose-escalation trial included 15 patients with advanced Parkinson's disease and disabling motor fluctuations, despite treatment with optimal anti-parkinsonian medications. Patients enrolled in the Phase 1b trial were, on average, 58 years of age with a Parkinson's disease diagnosis for an average of 10 years.

At baseline, patients' average good ON time was 10.5 hours and average OFF time was 4.6 hours. At baseline, patients were treated with optimal levels of multiple dopaminergic medications including, in many cases, amantadine for the treatment of dyskinesia, or uncontrolled or involuntary movements. On average, patients were receiving 1,526 mg of oral levodopa equivalent antiparkinsonian medications per day at baseline.

Today's results included data from all 15 patients treated in Cohorts 1, 2 and 3 (five patients in each Cohort) with data from patients in Cohort 1 at three years (as an update from four of five patients at three years as previously reported), Cohort 2 at two years and Cohort 3 at 18 months (Table 1).

Table 1: VY-AADC Mean Improvement in Good ON Time per Normalized 16-Hour Day

Good ON time: hour improvement from baseline (SE)	**Baseline**	**12-months**	**18-months**	**2-years**	**3-years**
Cohort 1, n=5	**10.5** (1.0)	**1.6** (0.4)	n/a [1]	**2.3** (0.4)	**2.1** (0.6)
Cohort 2, n=5	**10.6** (0.8)	**3.3** (0.6)	**3.5** (1.1)	**2.7** (1.4)	-
Cohort 3, n=5	**10.3** (0.7)	**1.5** (0.5)	**1.7** (1.1)	-	-
Cohorts 2-3, n=10	**10.5** (0.5)	**2.4** (0.5)	**2.6** (0.8)	-	-
Cohorts 2-3 and Phase 2 trial eligible, n=7	**10.1** (0.5)	**2.8** (0.6)	**2.5** (1.0)	-	-

(1) Protocol amended to include 18-month data collection after Cohort 1 reached this timepoint

One-time administration of VY-AADC resulted in reduced daily doses of oral levodopa and related medications. This included a 42.5% (standard error [SE], 5.7%) reduction from baseline for Cohort 3 at 18 months, a 21.2% (10.6%) reduction from baseline for Cohort 2 at two years, and a 14.7% (17.3%) increase from baseline for the low-dose Cohort 1 at three years.

Measured against the unmet disease burden at baseline, which is the time patients record as OFF time and ON time with troublesome dyskinesia, VY-AADC reduced this combined time by 46% from baseline at 12 months and 47% at 18 months for Cohorts 2 and 3 combined. Similar reductions were observed in the seven of ten patients who would have been eligible for the Phase 2 trial (Table 2).

Table 2: VY-AADC Mean Reduction in OFF Time and ON Time with Troublesome Dyskinesia

OFF time and ON time w/ troublesome dyskinesia hour per day (SE)	**Baseline**	**12-months**	Mean % change from baseline (1)	**18-months**	Mean % change from baseline

					(1)
Cohorts 2-3, n=10	**5.5** (0.5)	**-2.4** (0.5)	-46%	**-2.6** (0.8)	-47%
Cohorts 2-3 and Phase 2 trial eligible, n=7	**5.9** (0.5)	**-2.8** (0.6)	-46%	**-2.5** (1.0)	-39%

(1) Mean % change from baseline is calculated as the mean of all individual patient's percent change from baseline

Infusions of VY-AADC have been well-tolerated in all 15 patients treated in these Cohorts with no reported vector-related serious adverse events (SAEs) and fourteen of the 15 patients were discharged from the hospital within two days following surgery.

Voyager has identified 24 clinical trial sites (including neurosurgical and neurology patient referral and management sites) for participation in the Phase 2 randomized, placebo-controlled trial. Institutional review board approvals, site activation and patient screening efforts are underway. Voyager expects to announce when the first patient has been dosed.

For additional information regarding this Phase 2 clinical trial, please email Voyager at: clinicaltrials@vygr.com.

About Parkinson's Disease and VY-AADC

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 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, 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 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-AADC, 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-AADC, therefore, 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.

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 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 broad strategic collaborations with Sanofi Genzyme, the specialty care global business unit of Sanofi, AbbVie, 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.

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.

[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

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

Media:

Sheryl Seapy
W2O Group
949-903-4750
sseapy@w2ogroup.com

Voyager Therapeutics, Inc.