Voyager Therapeutics Announces Publication of Vectored Anti-Tau Monoclonal Antibody Study in The Journal of Neuroscience

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Single Administration of AAV-Vectored Anti-Tau Monoclonal Antibody Markedly Reduced Tau Pathology in Preclinical Model

Voyager Optimizing the Delivery of Anti-Tau Monoclonal Antibodies with its Proprietary VY-TAU01 Preclinical Program

CAMBRIDGE, Mass., Jan. 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 the publication of new preclinical data highlighting markedly reduced tau pathology including neurofibrillary tangles and neurodegeneration following treatment with a single dose of an adeno-associated virus (AAV) vector designed to administer a tau monoclonal antibody, PHF1, to the hippocampus of mutant tau transgenic mice. Scientists at Voyager, including Wencheng Liu, Ph.D., and Steven Paul, M.D., president and chief executive officer of Voyager, working in collaboration with colleagues at Weill Cornell Medical College, carried out the study and published the results in a recent issue of the Journal of Neuroscience[1].

"Using AAV vectors to deliver monoclonal antibodies directly to the brain represents an innovative approach to potentially treating various neurodegenerative disorders, such as frontotemporal dementia, progressive supranuclear palsy, or Alzheimer's disease, compared with systemically infusing repeated, high doses of antibodies, very little of which actually crosses the blood-brain barrier," said Steven Paul, M.D., president and chief executive officer of Voyager. "With the misfolded pathological tau protein implicated in the progression of several neurodegenerative diseases, we demonstrated that a single injection of an AAV vector to deliver an anti-tau antibody resulted in very high antibody expression in hippocampal and cortical neurons and reduced tau pathology by up to 90% in a robust tauopathy animal model as compared to 40-50% reductions in tau pathology reported by others using weekly, systemic infusions of anti-tau antibodies for several months. One of our ongoing efforts at Voyager, VY-TAU01, employs a similar approach and we are excited to continue to develop this program directed against tau, as well as to explore this approach with other antibodies directed at other misfolded proteins implicated in neurodegenerative disorders."

About the Study and Voyager's Monoclonal Antibody VY-TAU01 Program

In healthy individuals, tau is an abundant soluble cytoplasmic protein that binds to microtubules to promote microtubule stability and function.[2,3] In Alzheimer's disease (AD) and other tauopathies, tau aggregates and becomes hyper-phosphorylated, forming insoluble tau-containing neurofibrillary tangles (NFTs).[4,5] The progressive spread of tau pathology along distinct anatomical pathways in the brain closely correlates with disease progression and severity in a number of tauopathies, including AD, frontotemporal lobar degeneration (FTD), Pick's disease, progressive supranuclear palsy (PSP), and corticobasal degeneration. Because the extent of tau pathology in AD and other tauopathies closely correlates with the severity of neurodegeneration, synapse loss, and cognitive deficits, attempts to prevent, reduce, or slow the development of tau pathology have become prominent therapeutic strategies for AD and related tauopathies.[6,7,8]

In previous preclinical studies, despite high, weekly or biweekly infusions of anti-tau monoclonal antibodies (20–45 mg/kg weekly cumulative dose) administered for 3–6 months, only very low levels of antibody reach the brain parenchyma from the systemic circulation resulting in modestly reduced tau pathology of ~40–50%.[9,10,11] This incomplete and modest reduction in tau pathology following treatment with very high and frequent systemic doses of these antibodies may pose therapeutic challenges in humans with various tauopathies.

To address these limitations, investigators in this study injected an AAV vector containing a tau monoclonal antibody, PHF1, previously shown to reduce tau pathology following passive immunization.[9,11] Stereotactic injections administered bilaterally were administered to the hippocampus of a mutant tau transgenic P301S mouse tauopathy model that develops severe age-dependent tau pathology and neurodegeneration. A single, intracerebral dose of the AAVrh.10-vectored PHF1 antibody resulted in ~50-fold higher level of PHF1 antibody measured in the brain than that observed following a single systemic dose of the monoclonal antibody at 45 mg/kg[9] and a marked reduction (up to 90%) in hippocampal insoluble pathological tau species and neurofibrillary tangles compared with mice treated with an AAV-IgG control vector. In addition, the hippocampal atrophy observed in untreated P301S mice was fully rescued by treatment with the AAV-vectored PHF1 antibody.

"These preclinical studies provide proof of principle in a robust animal model that AAV vectors can be used to deliver monoclonal antibodies to misfolded pathological proteins like tau to increase brain antibody levels beyond what can be achieved by traditional passive immunization and to potentially enhance their therapeutic effects," added Dr. Paul. "Moreover, AAV vectors can be used to achieve both high intracellular as well as extracellular levels of these monoclonal antibodies and recent work has suggested that intraneuronal tau antibodies can facilitate the clearance and degradation of pathological tau.[12] With the VY-TAU01 program, using a variety of proprietary AAV capsids and routes of administrations, scientists at Voyager are optimizing the delivery of monoclonal antibodies directed against tau and other misfolded proteins to potentially treat a variety of neurodegenerative disorders."

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 adeno-associated virus (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," "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 a 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 Quarterly 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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