Voyager Therapeutics Announces New Data in Multiple Presentations at the American Society of Gene and Cell Therapy 2019 Annual Meeting

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Voyager's vectorized antibody program directed against tau demonstrates antibody distribution and expression levels in specific cell types that further facilitate studies with a vectorized antibody in animal models of disease

New TRACER™ system enables the rapid discovery of novel AAV capsids with the potential to penetrate the blood-brain barrier for cell-specific transduction after IV administration

Preclinical updates with VY-SOD102 for ALS-SOD1 support the potential benefit of suppressing SOD1 with a one-time intraparenchymal administration

CAMBRIDGE, Mass., April 29, 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 multiple data presentations at the American Society of Gene and Cell Therapy (ASGCT) taking place April 29-May 2, 2019, in Washington, D.C. New preclinical data at this year's ASGCT relate to Voyager's vectorized antibody program directed against tau for the potential treatment of Alzheimer's disease, its new TRACER™ system to discover adeno-associated virus (AAV) capsids with blood-brain barrier crossing and cell-specific transduction properties, as well as VY-SOD102 targeting a monogenic form of Amyotrophic Lateral Sclerosis (ALS) called SOD1.

"One of the major limitations of biologic therapies for the treatment of severe neurodegenerative diseases is the ability of those therapies to cross the blood-brain barrier," said Dinah Sah, Ph.D., chief scientific officer of Voyager. "At this year's ASGCT, we describe our efforts to address these limitations, including our vectorized antibody program directed against tau for the treatment of Alzheimer's disease as well as our newly developed TRACER system that allows for rapid evolution of novel AAV capsids that have the potential to cross the blood-brain barrier and target specific cells within the brain after systemic administration."

Vectorized antibodies directed against tau for the treatment of Alzheimer's disease

The use of therapeutic antibodies targeting various forms of tau to prevent, reduce, or slow the development of tau pathology is an important potential therapeutic strategy for Alzheimer's disease and other tauopathies. Because of the blood-brain barrier, only very low levels of antibody distribute to the brain from the systemic circulation after passive immunization, resulting in modestly reduced tau pathology in animal models.

Voyager's vectorized antibody approach aims to circumvent this limitation by delivering, with a potential one-time intravenous (IV) administration, the genes that encode for the production of therapeutic antibodies utilizing Voyager's novel blood-brain barrier penetrant AAV capsids. This approach could potentially result in higher levels of therapeutic antibodies in the brain compared with current systemic administration of antibodies.

Oral presentation title: "Cell Specific Transduction of a Vectorized Anti-Tau Antibody Using IV Dosing of a Blood Brain Barrier Penetrant AAV Capsid in Mice"

- In this study, a vectorized antibody consisting of a novel capsid, VOY101, and transgenes encoding an anti-tau antibody and either a cell-specific or ubiquitous promoter was delivered to C57BI/6J wild-type mice.
- This one-time IV administration of the vectorized antibody resulted in high anti-tau antibody distribution in the brain, particularly in the hippocampus, cortex and thalamus, four-weeks post dosing. Specifically, IV dosing using the VOY101 capsid and cell type-specific promoters resulted in anti-tau antibody expression in neurons and astrocytes at levels similar to those achieved with ubiquitous promoters.
- In a previous study conducted by Voyager, anti-tau antibody expression levels in the mouse central nervous system (CNS) after IV dosing of a vectorized antibody with a ubiquitous promoter were at least fifteen-fold higher than levels achieved with passive immunization.
- Results from the current study facilitate the evaluation of cell type-specific versus ubiquitous anti-tau antibody expression on efficacy in animal models of Alzheimer's disease to help define the target profile for a therapeutic vectorized antibody.

Voyager's TRACER System for Discovering Novel Gene Therapy Capsids

Robust delivery across the blood-brain barrier is one of the major limitations of current AAV gene therapies for CNS diseases. To address this, Voyager is discovering and developing novel AAV capsids that cross the blood-brain barrier after IV administration with improved transduction of the brain and spinal cord and enhanced cellular specificity. As part of that effort, Voyager scientists have developed a proprietary system called TRACER (Tropism Redirection of AAV by Cell Type-Specific Expression of RNA) to facilitate the selection of AAV capsids with blood-brain barrier crossing and cell-specific transduction properties for particular therapeutic applications.

Oral presentation title: "Targeted In Vivo Bio-Panning of AAV Capsid Libraries Using Cell Type-Specific RNA Expression"

- Voyager's TRACER system is a broadly-applicable, functional RNA-based AAV capsid screening platform that allows for rapid *in vivo* evolution of AAV capsids with cell-specific transduction properties in wild-type animals.

- Results presented at this year's ASGCT provide *in vivo* proof-of-concept for the TRACER system using libraries under the control of either the neuron-specific synapsin (SYN) promoter or the astrocyte-specific glial fibrillary acidic protein (GFAP) promoter to apply selective pressure for capsid variants that transduce the cell type of interest.

- Multiple capsid variants were identified with up to 1,000-fold improvement of CNS transduction in the mouse over AAV9 following IV administration after three rounds of selection. Voyager scientists are applying the TRACER system towards selecting AAV capsids with improved blood-brain barrier penetrant properties in the non-human primate.

VY-SOD102 for SOD1 ALS

VY-SOD102 is composed of an AAV capsid and a proprietary transgene that harnesses the RNA interference pathway to selectively knock down, or lower, levels of SOD1 mRNA in order to reduce levels of toxic, mutant SOD1 protein in the spinal cord. VY-SOD102 is administered by a novel delivery paradigm comprising a one-time infusion after laminectomy to the cervical region of the spinal cord. Preclinical data previously reported included extensive reductions of SOD1 mRNA throughout the spinal cord of the Göttingen mini-pig, which has a spinal cord similar in length and diameter to the human spinal cord. This novel delivery approach with VY-SOD102 reduced SOD1 mRNA in the spinal cord on average by 70% and 50% in the cervical and thoracic regions, respectively, both regions critical for respiratory function, and by 22% in the lumbar region.

Oral presentation title: "Intraparenchymal Spinal Cord Delivery of AAV Gene Therapy Provides Robust SOD1 Knockdown in Large Mammal Spinal Cord for the Treatment of SOD1-ALS"

- New data at this year's ASGCT demonstrated functional improvement and extended survival in a transgenic mouse model of ALS-SOD1.

- In G93A mice, intra-lumbar injections of VY-SOD102 delayed median disease onset, reduced median disease duration, and improved survival compared with vehicle control. Improvements in disease onset, disease duration and survival were also accompanied by improved hindlimb function as measured by delay to complete hindlimb paralysis compared with vehicle control.

- These efficacy and pharmacology studies in the G93A mouse model of ALS-SOD1 and Göttingen mini-pigs, respectively, support the use of VY-SOD102 with intraparenchymal spinal cord delivery as a novel approach for the treatment of ALS-SOD1.

- Preclinical pharmacology and toxicology studies are underway to support the potential filing of an investigational new drug (IND) application later this year.

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 wholly-owned and partnered 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, Alzheimer's disease, and other neurodegenerative diseases related to defective or excess aggregation of tau and alpha-synuclein proteins in the brain. Voyager has strategic collaborations with Sanofi Genzyme, AbbVie and Neurocrine Biosciences. Founded by scientific and clinical leaders in the fields of AAV gene therapy, expressed RNA interference and neuroscience, Voyager is headquartered in Cambridge, Massachusetts. For more information on Voyager, please visit the company's website at www.voyagertherapeutics.com or follow @VoyagerTx on Twitter and LinkedIn.

Voyager Therapeutics® is a registered trademark, and TRACER ™ is a trademark, of Voyager Therapeutics.

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, activities, goals and reporting of results of its preclinical programs and clinical trials and its research and development programs, the potential benefits and future operation of the collaboration agreements with Sanofi Genzyme, AbbVie and Neurocrine, including any potential future payments thereunder, 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 and its TRACER system, its ability to perform under existing collaborations with, among others, Sanofi Genzyme, AbbVie and Neurocrine and to add new programs to its pipeline, 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 such forward looking statements 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, those related to 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 and its TRACER system; Voyager's scientific approach and general development progress; the sufficiency of cash resources; the possibility

or the timing of the exercise of development, commercialization and license options under collaborations, 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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