Voyager Therapeutics Presents Robust, Multi-Species Results from Preclinical Studies of IV-Delivered, TRACER™-Generated Novel Capsids at the ASGCT 26th Annual Meeting

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Oral presentation features further evaluation of second-generation capsids, demonstrating increased transduction in several brain areas across multiple non-human primate species

CAMBRIDGE, Mass., May 18, 2023 (GLOBE NEWSWIRE) -- Voyager Therapeutics, Inc. (NASDAQ: VYGR), a biotechnology company dedicated to breaking through barriers in gene therapy and neurology, presented data today validating the ability of novel capsids generated through its TRACER™ capsid discovery platform to consistently demonstrate desirable features such as improved blood-brain barrier penetration and increased transgene expression in multiple areas of the brain compared to conventional AAV capsids, as well as cross-species translation. These results are being presented at the American Society of Gene and Cell Therapy (ASGCT) 26th Annual Meeting, taking place May 16-20, 2023, in Los Angeles.

“These data demonstrate that our TRACER capsid discovery platform is able to generate brain-penetrant capsids in a highly reproducible manner,” said Todd Carter, Chief Scientific Officer of Voyager Therapeutics. “Further, the cross-species tropism observed in a range of non-human primates and the characterization of a receptor expressed in humans increase our confidence that these capsids may translate in human clinical trials and may enable gene therapies for neurologic diseases.”

TRACER AAV Capsid Discovery Platform

Directed evolution of an AAV9 library identifies a capsid variant with enhanced brain tropism and liver de-targeting in non-human primates and mice following systemic administration (Oral Presentation)

- As first disclosed at the ASGCT 2022 meeting, the novel, TRACER-derived capsid VCAP-102 has demonstrated CNS tropism across mice and non-human primates (NHPs).
- In a new study in marmosets, intravenous administration of VCAP-102 resulted in 450-fold higher transgene expression compared to a conventional AAV9 benchmark capsid, achieving greater than 50% cell transduction in multiple areas of the brain at a dose of 2E12 vg/kg.
- Further evaluation following intravenous administration of VCAP-102 in African green monkeys showed transduction across diverse brain areas including the frontal, motor, temporal and cerebellar cortexes; putamen; caudate; and hippocampus regions, with 38-fold to 186-fold increases in these brain regions compared to a conventional AAV9 benchmark capsid. In these studies, VCAP-102 demonstrated de-targeting of the dorsal root ganglia (DRG) and liver. VCAP-102 showed similar transduction of both neurons and astrocytes.
- The iterative evolution of the VCAP-102 capsid resulted in a second generation of capsids with further improvement in BBB-penetrance and liver de-targeting relative to VCAP-102 in cynomolgus macaques.

Discovery and characterization of novel cross-species BBB-penetrant capsids (Scientific Symposia)

- Building on preliminary results shared at the ESGCT 2022 meeting, ongoing findings further confirm the direct and specific binding interactions of the TRACER-generated capsid VCAP-102 with a novel receptor that is expressed in human central nervous system (CNS) and brain endothelial cells.
- Additional research is being conducted to determine if this receptor can be leveraged for the non-viral CNS delivery of a range of therapeutic molecules including antibodies, oligonucleotides and lipid nanoparticles. Work to identify receptors to additional TRACER-derived capsid families is also underway.

Stepwise evolution of the AAV5-derived capsid VCAP-100 identifies novel variants with improved CNS transduction and liver de-targeting following systemic injection (#464)

- Scientists evolved surface regions of VCAP-100, an AAV5-derived capsid that was previously reported to have improved CNS tropism in rodents and NHPs following systemic administration. This evolution resulted in multiple hits including one family of VCAP-100 derivatives that displayed more than a two-log improvement in liver de-targeting and improved brain transduction in NHPs relative to the parental sequence.

An evolved AAV variant with enhanced brain and spinal cord tropism and translation across primate species (#1393)

- Researchers identified a new capsid called VCAP-103, which demonstrated enhanced brain and spinal cord transduction in

marmosets and African green monkeys. When further evaluated in cynomolgus macaques, VCAP-103 demonstrated a robust improvement over conventional AAV9, with at least 20-fold higher viral genome biodistribution and transgene RNA expression across the brain and the spinal cord.

GBA-1 Gene Therapy Program

Development of AAV-GBA1 gene replacement therapy via single-IV-delivery with a blood brain barrier penetrant AAV capsid (#695)

- Multiple optimized GBA1 transgenes were administered via single, intravenous doses using a blood-brain barrier-penetrant AAV capsid in a GBA1 loss-of-function mouse model, and they were found to deliver therapeutically relevant levels of the lysosomal enzyme GCase, restore GCase activity, reduce neurofilament light chain and reduce motor impairment. Additionally, in a non-human primate study, administration of a reporter transgene via single, intravenous doses using two novel BBB-penetrant AAV capsids demonstrated substantially improved biodistribution and gene expression compared to conventional AAV9 in the Putamen and Substantia Nigra, two areas of the brain that are affected in Parkinson's disease.

Technical Operations

Effects of transgene size on self-complementary rAAV vectors (#1626)

- Studies demonstrated that transgene size can have different impacts on the transduction efficiency of self-complementary (scAAV) DNA vectors in different manufacturing systems, which could help inform optimal approaches to manufacturing.

rAAV produced by Sf9-baculovirus system shows different product quality profile throughout the production cycle (#394)

- Studies demonstrated that variations in the infection of Sf9 cells used to manufacture rAAV can impact productivity and product quality, which could help inform optimal approaches for rAAV production.

About the TRACER™ AAV Capsid Discovery Platform
Voyager's TRACER™ (Tropism Redirection of AAV by Cell-type-specific Expression of RNA) capsid discovery platform is a broadly applicable, RNA-based screening platform that enables rapid discovery of AAV capsids with robust penetration of the blood-brain barrier and enhanced central nervous system (CNS) tropism in multiple species, including non-human primates (NHPs). TRACER generated capsids have demonstrated superior and widespread gene expression in the CNS compared to conventional AAV capsids as well as cell- and tissue-specific transduction, including to areas of the brain that have been traditionally difficult to reach. Separate results have demonstrated the enhanced ability of certain capsids to target cardiac muscle and to de-target the dorsal root ganglia. Voyager is expanding its library of AAV capsids optimized to deliver diverse therapeutic payloads to address a broad range of CNS and other diseases. As part of its external partnership strategy, Voyager has established multiple collaboration agreements providing access to its next-generation TRACER capsids to potentially enable its partners' gene therapy programs to treat a variety of diseases.

About Voyager Therapeutics
Voyager Therapeutics (Nasdaq: VYGR) is a biotechnology company dedicated to breaking through barriers in gene therapy and neurology. The potential of both disciplines has been constrained by delivery challenges; Voyager is leveraging cutting-edge expertise in capsid discovery and deep neuropharmacology capabilities to address these constraints. Voyager's TRACER AAV capsid discovery platform has generated novel capsids with high target delivery and blood-brain barrier penetration at low doses, potentially addressing the narrow therapeutic window associated with conventional gene therapy delivery vectors. This platform is fueling alliances with Pfizer Inc., Novartis and Neurocrine Biosciences as well as multiple programs in Voyager's own pipeline. Voyager's pipeline includes wholly-owned and collaborative preclinical programs in Alzheimer's disease, amyotrophic lateral sclerosis (ALS), Parkinson's disease, and Friedreich's Ataxia, with a focus on validated targets and biomarkers to enable a path to rapid potential proof-of-biology. For more information, visit www.voyagertherapeutics.com.

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 participation of scientists associated with Voyager making presentations at ASGCT 2023, and the presentations of data at ASGCT 2023; Voyager's ability to continue to identify and develop proprietary capsids from its TRACER AAV capsid discovery platform with increased transgene expression, blood-brain barrier penetration, and biodistribution compared to conventional AAV5 and AAV9 capsids and the ability to target or de-target certain cells or tissues; the potential for capsids generated by Voyager's TRACER capsid discovery platform to have a positive impact for gene therapy development and the treatment of patients with medical conditions; the ability to broaden the application of Voyager's TRACER capsid discovery platform and establish human proof-of-concept across a range of serious diseases; and the potential to leverage the novel receptor expressed in human CNS and brain endothelial cells for the non-viral CNS delivery of a range of therapeutic molecules including antibodies, oligonucleotides and lipid nanoparticles, are forward looking statements.

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, a decision by the organizers of ASGCT 2023 not to allow the submissions presenting Voyager research to be presented notwithstanding prior acceptance of the submissions; the ability of Voyager scientists to effectively deliver their presentations at ASGCT 2023; the continued development by Voyager of various technology platforms, including the TRACER capsid discovery platform; and Voyager's scientific approach and general development progress.

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. All information in this press release is as of the date of this press release, and any forward-looking statement speaks only as of the date on which it was made. Voyager undertakes no obligation to publicly update or revise this information or any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

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