Voyager Demonstrates ALPL Receptor-Mediated Blood-Brain Barrier Transport of Novel AAV Capsids in Molecular Therapy Publication

05/15/25

LEXINGTON, Mass., May 15, 2025 (GLOBE NEWSWIRE) -- Voyager Therapeutics, Inc. (Nasdaq: VYGR), a biotechnology company dedicated to leveraging genetics to treat neurological diseases, today announced the first peer-reviewed publication of data demonstrating the ability of alkaline phosphatase (ALPL) to transport a novel AAV capsid across the blood-brain barrier (BBB). The article, titled "Highly conserved brain vascular receptor ALPL mediates transport of engineered AAV vectors across the blood-brain barrier," was published in *Molecular Therapy* and can be accessed here.

"Understanding ALPL and its ability to mediate transport across the blood-brain barrier has been foundational to the evolution of our gene therapy programs, two of which are advancing towards IND filings this year with a partner," said Mathieu Nonnenmacher, Ph.D., Vice President of Gene Therapy at Voyager. "Building on our first-generation capsids, such as VCAP-102, which is featured in this paper, we have evolved next-generation capsids with even stronger brain transduction and liver de-targeting, as well as stealth capsids with immune-evading capabilities."

The *Molecular Therapy* paper outlines the generation of novel, cross-species AAV capsid VCAP-102, which demonstrates 20- to 400-fold increased gene transfer across multiple brain regions relative to AAV9 in both rodents and non-human primates (NHP), and the identification of ALPL as the primary receptor used by VCAP-102 to cross the BBB. In addition, the confirmation that the ALPL capsid family binds and demonstrates transcytosis with human ALPL in a cell barrier *in vitro* model suggests clinical translatability. As previously announced, Voyager presented next-generation and stealth-capsid data at the American Society of Gene & Cell Therapy's (ASGCT) 28th annual meeting. In multiple NHP studies utilizing a variety of payloads, a single intravenous 3e13 vg/kg dose of Voyager's second-generation CNS capsids transduced up to 98% of dopaminergic neurons in substantia nigra, up to 94% of motor neurons in the spinal cord, up to 66% of neurons in the thalamus, up to 43% of neurons in the motor cortex, and 87-99% of astrocytes broadly across brain regions.

"In addition to speeding the evolution of novel capsid families, we are leveraging our work with ALPL and other receptors to deliver diverse classes of non-viral candidates into the CNS," said Todd Carter, Ph.D., Chief Scientific Officer of Voyager Therapeutics. "We believe this multi-modality approach, encompassing both viral and non-viral CNS delivery, is critical to addressing unmet needs in neurological disease."

About the TRACER™ 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 novel AAV capsids to enable gene therapy. Voyager has leveraged TRACER to create multiple families of novel capsids that, following intravenous delivery in preclinical studies, harness the extensive vasculature of the central nervous system (CNS) to cross the blood-brain barrier and transduce a broad range of CNS regions and cell types. In cross-species preclinical studies (rodents and multiple non-human primate species), intravenous delivery of TRACER-generated capsids resulted in widespread payload expression across the CNS at relatively low doses, enabling selection of multiple development candidates in Voyager's wholly-owned and partnered gene therapy programs for neurologic diseases.

About Voyager Therapeutics
Voyager Therapeutics, Inc. (Nasdaq: VYGR) is a biotechnology company dedicated to leveraging the power of human genetics to modify the course of – and ultimately cure – neurological diseases. Our pipeline includes programs for Alzheimer's disease, Friedreich's ataxia, Parkinson's disease, amyotrophic lateral sclerosis (ALS), and multiple other diseases of the central nervous system. Many of our programs are derived from our TRACER™ AAV capsid discovery platform, which we have used to generate novel capsids and identify associated receptors to potentially enable high brain penetration with genetic medicines following intravenous dosing. Some of our programs are wholly owned, and some are advancing with partners including Alexion, AstraZeneca Rare Disease; Novartis Pharma AG; and Neurocrine Biosciences, Inc. For more information, visit http://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 "will," "anticipated," "expect," "believe," "anticipate," "potential," "may," or "continue," and other similar expressions are intended to identify forward-looking statements.

For example, all statements Voyager makes regarding Voyager's ability to advance its AAV-based gene therapy programs and non-viral CNS delivery programs, including the potential for Voyager's novel TRACER capsids to achieve desired results in humans, including neuronal and glial transduction across multiple brain regions, and ALPL-mediated transcytosis similar to the results demonstrated in rodents and NHPs; potential clinical translatability in humans; increased patient eligibility to receive AAV gene therapies; and expectations for advancement of gene therapy product candidates under the collaboration programs, including anticipated submission of IND filings and initiation of clinical trials in two partnered programs 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 and 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 continued development of Voyager's technology platforms, including Voyager's TRACER platform and its non-viral discovery platform; Voyager's scientific approach and program development progress, and the restricted supply and increased costs of critical research components; the development by third parties of capsid identification platforms that may be competitive to Voyager's TRACER capsid discovery platform; Voyager's ability to create and protect intellectual property rights associated with the TRACER capsid discovery platform, the capsids identified by the platform, and development candidates for Voyager's pipeline programs; the timing, initiation, conduct and outcomes of Voyager's preclinical and clinical studies; the availability of data from clinical trials; the expectations and decisions of regulatory authorities; the availability or commercial potential of product candidates under collaborations; the success of Voyager's product candidates; the willingness and ability of Voyager's collaboration partners to meet obligations under collaboration agreements with Voyager; the possibility or the timing of Voyager's receipt of program reimbursement, development or commercialization milestones, option exercise, and other

payments under Voyager's existing licensing or collaboration agreements; the ability of Voyager to negotiate and complete licensing or collaboration agreements with other parties on terms acceptable to Voyager and the third parties; the success of programs controlled by third-party collaboration partners in which Voyager retains a financial interest; the ability to attract and retain talented directors, employees, and contractors; and the sufficiency of Voyager's cash resources to fund its operations and pursue its corporate objectives.

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. All information in the 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.

Contacts
Trista Morrison, NACD.DC, tmorrison@vygr.com
Investors: Sarah McCabe, smccabe@jpa.com
Media: Brooke Shenkin, brooke@scientpr.com

Source: Voyager Therapeutics, Inc.