Voyager Therapeutics Presents Data Characterizing a Novel CNS Receptor and Demonstrating the Low-Dose Potential of TRACER™ Generated Capsid Families

10/11/22

- Data presented at European Society of Gene & Cell Therapy (ESGCT) Congress 2022 -

- Receptor findings support potential for human translation of Voyager's capsids and may help overcome barriers to CNS drug delivery -

CAMBRIDGE, Mass., Oct. 11, 2022 (GLOBE NEWSWIRE) -- Voyager Therapeutics, Inc. (Nasdaq: VYGR), a gene therapy company developing life-changing treatments and next-generation adeno-associated virus (AAV) capsids, today presented data on the discovery of a novel cell surface receptor identified as a binding receptor for a family of Voyager's next-generation TRACER AAV capsids. This receptor is expressed in human central nervous system (CNS) and brain endothelial cells, increasing the potential for the associated capsid family to translate into humans. In addition, Voyager presented preclinical data demonstrating the potential for ultra-low dosing with a separate next-generation TRACER capsid family. These and other data were presented by Voyager at the European Society of Gene & Cell Therapy (ESGCT) 29th Annual Congress in Edinburgh, Scotland.

"Our discovery of a binding receptor for one of our capsid families, along with the data showing the receptor to be highly conserved across multiple species including humans, increases our confidence that the preclinical data on gene therapies utilizing this capsid family may translate in human clinical trials," said Alfred Sandrock, Jr., M.D., Ph.D., Chief Executive Officer of Voyager. "In the longer term, this receptor could enable reverse engineering to further enhance our capsid discovery platform. In addition, we have begun experiments to explore whether we may be able to leverage this receptor to enable the delivery of modalities such as proteins and oligonucleotides across the blood-brain barrier – which, if successful, could constitute a new platform for CNS drug development."

Details of Voyager's presentations at ESGCT are as follows:

Identification of a Cell Surface Receptor Utilized by an Engineered BBB-Penetrant Capsid Family with Enhanced Brain Tropism in Non-Human Primates and Mice (Poster #P024)

- Voyager has identified a highly conserved membrane protein as the primary cell surface receptor responsible for improved CNS biodistribution for one of Voyager's novel TRACER capsid families.
- This capsid family has been demonstrated to cross the blood-brain barrier (BBB) in multiple species (mice and non-human primates [NHPs]) with ~50-fold improved penetrance over conventional AAV9. The newly identified receptor is highly conserved across mice, NHPs and humans, and data indicate that mouse and human receptor isoforms also bind and increase capsid transduction.
- The receptor has been shown to be expressed in primate and rodent CNS, particularly in brain endothelial cells, and experiments performed in mice suggest a strong correlation between receptor expression profile and capsid tropism.
- In summary, the data support the potential for the BBB-penetrating properties of this novel TRACER capsid family to translate to humans.

Dose-Response Evaluation of 9P801, an Engineered AAV Capsid with High BBB Penetration and CNS Transduction in Non-Human Primates (Poster #P015)

- In a dose-response NHP study, a next-generation TRACER capsid from another novel capsid family achieved high levels of BBB penetration and CNS target engagement when administered in the range of 2e12 VG/kg to 2e13VG/kg, which is 2% to 20% of the dose used in current approved intravenous gene therapies.
- Intravenous delivery of doses of 2e12 VG/kg and higher were sufficient to achieve widespread CNS transduction and supra-physiological mRNA expression of a model transgene.
- Expression in the liver and dorsal root ganglion (DRG) was confirmed to be at or near background levels at these low doses that achieve potentially therapeutically relevant transduction in the CNS.
- In summary, these data suggest that a next-generation TRACER capsid shows strong efficacy at well-tolerated doses, potentially addressing the narrow therapeutic windows and subsequent toxicity issues that have hampered the gene therapy field.

Evaluation of an Early, Late, Very Late Expressed Rep in a Recombinant Baculovirus to Produce a More Potent AAV-based Gene Therapeutic in Insect Cells (Poster #P065)

- Voyager investigated the asynchronous expression of AAV Replicase and Capsid genes in context of the insect cell line based baculovirus expression vector system. Earlier expression of Replicase correlated with increased transgene packaging and higher transduction potency of assembled AAV capsids.
- The findings underscore Voyager's efforts to produce more potent gene therapies and address the challenges of serving larger populations with an efficacious and affordable gene therapy product.

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 leading the next generation of AAV gene therapy to unlock the potential of the modality to treat devastating diseases. Proprietary capsids born from the Company's TRACER discovery platform are powering a rich early-stage pipeline of programs and may elevate the field to overcome the narrow therapeutic window associated with conventional gene therapy vectors across neurologic disorders and other therapeutic areas. voyagertherapeutics.com LinkedIn Twitter

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

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 Voyager's presentation of preclinical data on the discovery of a novel cell surface receptor identified as the binding receptor for a family of Voyager's next-generation TRACER AAV capsids; Voyager's presentation of preclinical data demonstrating the potential for ultra-low dosing with a next-generation TRACER capsid family; and Voyager's presentation of preclinical data demonstrating that earlier expression of Replicase correlated with increased transgene packaging and higher transduction potency of assembled AAV capsids 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, the continued development of Voyager's technology platforms, including Voyager's TRACER platform and Voyager's recombinant baculovirus manufacturing platform; the ability of Voyager to initiate and conduct preclinical studies in pre-clinical animal models; the ability for Voyager's next generation capsids to translate into humans; the ability for Voyager to attract and retain talented contractors and employees; the ability of Voyager to create and protect intellectual property; and the sufficiency of Voyager's cash resources.

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 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

Investors

Investors@vygr.com

Andrew Funderburk

afunderburk@kendallir.com

Media

Trista Morrison

tmorrison@vygr.com

Peg Rusconi

prusconi@vergescientific.com

Source: Voyager Therapeutics, Inc.