Voyager Therapeutics Prioritizes Pipeline and Reports Second Quarter 2022 Financial and Operating Results

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Pipeline prioritizes tau antibody for Alzheimer's disease and gene therapies for GBA1 Parkinson's disease and SOD1 ALS, each program employing efficient paths to human proof of biology

Targeting development candidate selection for priority programs in 2022 and H1 2023

Cross species transduction for multiple capsids and characterization of the receptor for a leading capsid support human translation potential of TRACER™ capsids

Catherine J. Mackey, Ph.D., appointed to Board of Directors

Strong balance sheet and disciplined financial approach expected to maintain cash runway into 2024

Conference call at 4:30 p.m. ET today

CAMBRIDGE, Mass., Aug. 04, 2022 (GLOBE NEWSWIRE) -- Voyager Therapeutics, Inc. (Nasdaq: VYGR), a gene therapy and neuroscience company developing life-changing treatments and next-generation adeno-associated virus (AAV) capsids, today unveiled its prioritized therapeutic pipeline and reported second quarter 2022 financial and operating results.

“I’m excited to announce our updated portfolio strategy that prioritizes programs targeting lead indications in Alzheimer’s disease, GBA1 Parkinson’s disease, and SOD1 ALS,” said Alfred W. Sandrock, Jr., M.D., Ph.D., chief executive officer of Voyager. “We believe our highly differentiated approaches against well-validated CNS targets leveraging Voyager’s breakthrough TRACER capsids can lead to the development of new therapeutic options for these devastating diseases. In addition, we believe each of these targets has a clear path to human proof of biology that should allow us to further progress these programs in an efficient manner.”

Dr. Sandrock continued, “The recent characterization of a receptor for one of our most promising TRACER capsids, along with the preclinical cross-species transduction data we presented at ASGCT for several or our capsids, increase our confidence that our capsids may cross the blood-brain barrier in humans. On the partnership front, we believe that our Pfizer and Novartis TRACER capsid collaborations are going well with option exercise decisions upcoming in Q4 2022 and Q1 2023, respectively, and we are optimistic about the potential for similar transactions in the future.”

Prioritized Pipeline Focused on Programs with Efficient Path to Human Proof of Biology

- Following an in-depth internal review process, Voyager has prioritized pipeline programs for its development. This review identified a compelling opportunity for each prioritized program based on the following criteria: high unmet medical need, target validation, efficient path to human proof of biology, robust preclinical pharmacology, and strong commercial potential. Voyager is evaluating partnering opportunities for its other programs.

Prioritized pipeline programs include:

- *GBA1 gene replacement* to treat Parkinson’s disease patients with GBA1 mutations
  - Mutations in glucocerebrosidase 1 (GBA1), the gene encoding the lysosomal enzyme glucocerebrosidase (GCase), are the most common genetic risk factor for synucleinopathies such as Parkinson’s disease and dementia with Lewy bodies. Voyager believes restoring GCase activity may attenuate progression and potentially slow neurodegeneration. Voyager anticipates delivering GBA1 (utilizing a blood-brain barrier (BBB)-penetrant, CNS-tropic AAV capsid discovered by the TRACER (Tropism Redirection of AAV by Cell-type-specific Expression of RNA) capsid discovery platform) via intravenous (IV) delivery to enable widespread distribution to multiple affected brain regions and to avoid the need for more invasive approaches.
  - Voyager believes the measurement of the GCase substrates such as glucosylsphingosine as cerebrospinal fluid (CSF) biomarkers will facilitate efficient clinical demonstration of proof of biology.
  - At the American Society of Gene and Cell Therapy (ASGCT) 25th Annual Meeting in May, Voyager presented preclinical data demonstrating CNS target engagement and delivery of therapeutically relevant levels of the lysosomal enzyme GCase (encoded by GBA1) in a GBA loss of function mouse model, as well as sustained expression for ≥3 months following IV administration.

- A non-human primate (NHP) capsid evaluation study is currently underway. Voyager intends to select a development candidate in the first half of 2023, to initiate a dose range finding study in NHPs in the second half of 2023, and to initiate GLP toxicology studies in 2024. Voyager anticipates an IND filing in 2025 but is actively reviewing options to accelerate the program.

- *SOD1 gene silencing* to treat amyotrophic lateral sclerosis (ALS) caused by the superoxide dismutase 1 (SOD1) mutation

  - Voyager believes that a therapeutic combining a highly potent siRNA construct with a CNS-tropic, BBB-penetrant capsid discovered by Voyager's TRACER platform allowing for IV delivery may enable broad CNS knockdown of SOD, potentially slowing the decline of functional ability. Voyager believes a Phase 1 clinical trial to demonstrate reduction in SOD1 in CSF and neurofilament light chain in plasma will provide evidence of target engagement and the attenuation of motor neuron loss, respectively.
  - At the ASGCT meeting, Voyager presented preclinical data demonstrating robust SOD1 knockdown in all levels of the spinal cord and significant improvements in motor performance, body weight, and survival in an SOD1-ALS mouse model following IV delivery of a vectorized siRNA using a mouse BBB-penetrant capsid.
  - A NHP capsid evaluation study is currently underway. The Company intends to select a development candidate in 2022, complete an NHP dose range finding study in 2023, initiate GLP toxicology studies in the first half of 2024 and file an IND in 2024.

- *Tau antibody program* – Voyager is developing novel antibodies that selectively target pathological tau to address Alzheimer's disease (AD)
  - Voyager has maintained a long-standing focus on developing novel and complementary approaches to disrupt the progression of tau pathology believed to be central to multiple neurodegenerative diseases. Collectively, its passive and vectorized anti-tau antibodies have differentiated properties, including improved targeting of specific regions of the tau protein that could offer an improved profile compared to first generation approaches.
  - Reduction of toxic tau aggregates may slow disease progression and cognitive decline in these diseases. Voyager believes its antibody targeting the C-terminus is highly differentiated from other approaches. Further, Voyager believes that following the clearance of an Investigational New Drug (IND) application, clinical assessments utilizing positron emission tomography (PET) imaging of human tau, together with measurements of plasma and CSF biomarkers have the potential to enable an efficient and accelerated demonstration of human proof of biology.
  - At the recent Alzheimer's Association International Conference, Voyager presented data for its novel anti-tau antibodies, targeting the mid-domain and C terminus with high affinity and showing favorable biophysical characteristics and strong activity in preclinical studies. In the P301S seeding-propagation tauopathy mouse model, Voyager's C-terminal targeting anti-tau antibody blocked the seeding/propagation of filamentous tau and demonstrated substantial reduction of induced tau pathology.
  - Humanization of the murine antibody is currently underway. Voyager intends to nominate a lead antibody development candidate in the first half of 2023, to initiate GLP toxicology studies in the second half of 2023 and to file an IND in the first half of 2024.
  - Voyager also plans to explore vectorized delivery utilizing its BBB-penetrant TRACER capsids with its anti-tau antibody.

Receptor Identified for TRACER AAV Capsid; AAV9- and AAV5-Derived TRACER Capsids Demonstrate Enhanced Brain Transduction Across NHPs and Rodents

- Voyager announced today that it has identified the receptor for one of its most promising TRACER AAV capsids. The Company has confirmed that those capsids can bind to the human isoform of the receptor, which is expressed in brain endothelial cells and other CNS cell types. Voyager believes that characterization of this receptor-capsid interaction increases the probability that the related capsid will cross the BBB in humans. Voyager intends to share data on this finding at an upcoming scientific conference.
- At the ASGCT meeting, Voyager presented new preclinical data on several families of novel capsids from its TRACER capsid discovery platform.
  - Voyager presented preclinical results for an AAV9-derived capsid, VCAP-102, which demonstrated 50-fold better transduction in mice and 60-fold better transduction in NHPs versus conventional AAV9 capsids following IV administration. Voyager believes demonstrating equivalent cross-species functionality is critical to increasing a capsid's potential for translation into humans. The study also demonstrated that VCAP-102 and other TRACER capsids showed preferential tropism for glial cells in mice, which may facilitate addressing CNS indications that would benefit from non-neuronal cell transduction.
  - Voyager also presented preclinical data for an AAV5-derived capsid with enhanced CNS transduction across species. AAV5 capsids have a reduced prevalence of pre-existing neutralizing antibodies, but conventional AAV5 capsids do not allow sufficient BBB-penetration to be used for gene therapies targeting the CNS. Voyager's AAV5-derived capsid showed 20-fold higher brain transduction and five-fold higher spinal cord transduction

compared to conventional AAV9 in NHPs. Modified capsids showed improved transduction in multiple CNS regions and cell types in NHPs, together with partial de-targeting from the dorsal root ganglia.

- Voyager continues to perform screening campaigns with its TRACER platform to identify additional proprietary AAV9- and AAV5-derived capsids and to refine already identified capsids to target or de-target multiple tissue and cell types. These capsids offer the potential to broaden the therapeutic window substantially and to enable gene therapies in a wide range of diseases based on enhanced tissue/cell tropisms that allow for lower doses and with lower off-target effects or toxicities.
    - Studies are currently underway to assess gene expression and therapeutic index at order-of-magnitude lower doses, and Voyager intends to share the results at an upcoming scientific conference.
- Initial option exercise decision of the license agreements with Pfizer and Novartis for TRACER AAV capsids are expected by October 2022 and March 2023, respectively.

Catherine J. Mackey, Ph.D., Appointed to Board of Directors

- In July, Voyager announced the appointment of Catherine J. Mackey, Ph.D. to its Board of Directors. Dr. Mackey is a seasoned life science executive with more than thirty years of operational experience highlighted by her tenure as Senior Vice President, Global Research & Development, for Pfizer. Dr. Mackey, who will join Voyager's Board on August 15, has been designated as a Class I director with a term ending as of the 2025 annual meeting of Voyager shareholders. Dr. Mackey has also been appointed to the Board's Audit Committee and Science and Technology Committee.

Second Quarter 2022 Financial Results

- **Collaboration Revenues:** Voyager had collaboration revenue of $0.7 million for the second quarter of 2022, compared to $1.4 million for the same period in 2021. The decrease in collaboration revenue was due to a reduction of Voyager's research activities within the collaboration with Neurocrine.
- **Net Loss:** Net loss was $19.1 million for the second quarter of 2022, compared to a net loss of $30.1 million for the same period of 2021. The decrease in net loss resulted primarily from a decrease in R&D expenses and G&A expenses.
- **R&D Expenses:** Research and development expenses were $12.5 million for the second quarter of 2022, compared to $19.5 million for the same period in 2021. The decrease in R&D expenses was primarily a result of lower employee-related costs and lower clinical spend related to the Huntington's disease program, as well as lower facilities costs.
- **G&A Expenses:** General and administrative expenses were $7.6 million for the second quarter of 2022, compared to $10.4 million for the same period in 2021. The decrease in G&A expenses was primarily a result of lower employee-related costs, as well as lower facilities costs.
- **Cash Position:** Cash, cash equivalents and marketable securities as of June 30, 2022, were $148.1 million.

Financial Guidance

- Voyager expects that its cash, cash equivalents, and marketable securities, together with amounts expected to be received as reimbursement for development costs under the Neurocrine collaboration, will be sufficient to meet Voyager's planned operating expenses and capital expenditure requirements into 2024.

Participation in Upcoming Investor Conferences

- BTIG Healthcare Conference, New York City, NY, August 8, 2022
- Wedbush Healthcare Conference, Virtual, August 9, 2022
- Canaccord Genuity Healthcare Conference, Boston, MA, August 10, 2022
- Wells Fargo Healthcare Conference, Boston, MA, September 7, 2022
- RW Baird Healthcare Conference, New York City, NY, September 14, 2022

Conference Call

The Voyager Therapeutics leadership team will host a conference call and webcast today at 4:30 p.m. ET to discuss Voyager's prioritized therapeutic pipeline and to provide second quarter 2022 financial and operating results. To access the call, please dial 1-833-634-2276 (domestic) or 1-412-902-4144 (international) and ask for the Voyager Therapeutics earnings call. A live webcast of the call will also be available on the Investors section of the Voyager website at ir.voyagertherapeutics.com, and a replay will be available at the same link approximately two hours after its completion. The replay will be available for at least 30 days following the conclusion of the call.

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 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.

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 Voyager's TRACER capsid 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.

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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 participation in future scientific conferences; Voyager's ability to continue to identify and develop proprietary capsids from its TRACER capsid discovery platform with increased transgene expression, increased blood-brain barrier penetration and increased biodistribution compared to conventional AAV9 and AAV5 capsids; Voyager's ability to utilize its novel proprietary capsids in its own product development programs; Voyager's ability to attract parties to license its novel proprietary capsids or to participate with Voyager in research and development collaborations utilizing its novel proprietary capsids; Voyager's ability to advance its AAV-based gene therapy programs; the preclinical and clinical development and regulatory status of the Company's product candidates; Voyager's ability to develop its tau antibody program; the size of potential markets for Voyager's product candidates; Voyager's scientific approach, including its ability to demonstrate efficient clinical proof-of-biology and/or proof-of-mechanism for its programs; Voyager's ability to perform its obligations under its respective license option agreements with Novartis and Pfizer; Voyager's entitlement to receive upfront, option exercise, milestone and royalty-based fees from Novartis and Pfizer under the respective license option agreements; Voyager's ability to maintain its current partnerships and collaborations and to enter into new partnerships or collaborations; the timing and suitability of Dr. Mackey's election to Voyager's Board of Directors; Voyager's anticipated financial results, including the receipt by Voyager of revenues or reimbursement payments from collaboration partners; and Voyager's ability to generate sufficient cash resources to enable it to continue to identify and develop proprietary capsids from its TRACER capsid discovery platform 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 final acceptance by the organizers of upcoming scientific conferences; the ability of Voyager scientists to effectively deliver their presentations at upcoming scientific conferences; the ability of Dr. Mackey to perform her duties as member of the Board; Voyager's ability to manage the financial and human resources challenges arising from the COVID-19 health crisis; the continued development of various technology platforms, including Voyager's TRACER platform; the development by third parties of capsid identification platforms that may be competitive to Voyager's TRACER capsid discovery platform; Voyager's scientific approach and general development progress; Voyager's ability to attract and retain talented contractors and employees to continue the development of the TRACER capsid discovery platform and the identification of proprietary capsids; Voyager's ability to create and protect intellectual property rights associated with the TRACER capsid discovery platform and the capsids identified by the platform; the response of the FDA and other regulators to Voyager's regulatory submissions and communications; the ability to attract and retain talented contractors and employees, including key scientists and business leaders; the ability to create and protect intellectual property; Voyager's ability to perform its obligations under its license option agreements and its counterparties' respective abilities to perform their obligations under such agreements; the sufficiency of cash resources; the initiation, timing, conduct, and outcomes of Voyager's preclinical studies and clinical trials; the possibility or the timing of the exercise of development, commercialization, license and other options under the Pfizer and Novartis license option agreements and other collaborations; the ability of Voyager to negotiate and complete licensing or collaboration agreements on terms acceptable to Voyager and third parties; 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. 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.

Selected Financial Information
($ amounts in thousands, except per share data)
(Unaudited)

	Three Months Ended June 30,	
Statement of Operations Items:	**2022**	**2021**
Collaboration revenue	$ 712	$ 1,357
Operating expenses:		
Research and development	12,527	19,505
General and administrative	7,552	10,437
Total operating expenses	20,079	29,942
Operating loss	(19,367)	(28,585)
Total other income	280	(1,535)
Net loss	$ (19,087)	$ (30,120)

Net loss per share, basic and diluted	$ (0.50)	$ (0.80)
Weighted-average common shares outstanding, basic and diluted	38,298,426	37,581,381

Selected Balance Sheet Items	**June 30, 2022**	**December 31, 2021**
Cash, cash equivalents, and marketable securities	$ 148,056	$ 132,539
Total assets	$ 188,605	$ 193,855
Accounts payable and accrued expenses	$ 8,403	$ 11,524
Deferred revenue	$ 94,883	$ 42,096
Total stockholders' equity	$ 60,052	$ 95,055

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