Neurocrine Biosciences and Voyager Therapeutics Present New Long-Term Three-Year Data Demonstrating that One-Time Treatment with an Investigational Gene Therapy Showed Sustained Improvement in Motor Function in Patients with Parkinson's Disease

September 11, 2020

-- Data for Investigational Gene Therapy Treatment NBIb-1817 (VY-AADC) Presented at the MDS Virtual Congress 2020 --

- ***NBIb-1817 Treatment Showed Sustained Improvement in Motor Function, Including Greater "On" Time without Troublesome Dyskinesia and Reduction in Unified Parkinson's Disease Rating Scale (UPDRS) Part III Scores, and Reduction in the Amount of Medications Up to Three Years in Patients with Parkinson's Disease***

- ***14 of 15 Patients Treated with NBIb-1817 Continued to Experience an Improvement in Disease Staging after Three Years, as Assessed by the Modified Hoehn & Yahr Scale***

- ***Re-Initiation of Enrollment in Registrational RESTORE-1 Clinical Trial of NBIb-1817 Planned for Later this Year***

SAN DIEGO and CAMBRIDGE, Mass., Sept. 11, 2020 (GLOBE NEWSWIRE) -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) and Voyager Therapeutics, Inc. (Nasdaq: VYGR) today announced data from PD-1101, a Phase Ib open-label, three-year efficacy and safety study, demonstrating that a one-time treatment with investigational gene therapy, NBIb-1817 (VY-AADC), showed sustained improvement in motor function including greater "On" time without troublesome dyskinesia, reduction in Unified Parkinson's Disease Rating Scale (UPDRS) Part III scores, and reduction in the amount of medications in patients with Parkinson's disease. In the PD-1101 study, NBIb-1817 reduced average "Off" time by up to -1.91 hours and improved average "On" time without troublesome dyskinesia by up to +2.23 hours in patients with advanced Parkinson's disease after three years across three cohorts. In addition, 14 out of 15 patients treated with NBIb-1817 continued to show an improvement in disease staging after three years, as assessed by the modified Hoehn & Yahr scale. These new data, along with two-year data from another open-label Phase Ib trial, PD-1102, were presented today at the MDS Virtual Congress 2020, September 12–16, 2020 (www.mdscongress.org/Congress/Registration.htm).

In data from the three-year PD-1101 trial, the one-time treatment with NBIb-1817 showed sustained reduction in diary "Off" time by an average of -0.15 to -1.91 hours (baseline 4.28 to 4.93 hours) and improved diary "On" time without troublesome dyskinesia by an average of +0.26 to +2.23 hours (baseline 10.32 to 10.46 hours) across the cohorts as reported by 15 patients with advanced Parkinson's disease. NBIb-1817 also showed sustained improvement in motor function after three years, as measured by UPDRS Part III off medication scores, by -10.2 to -19.0 points (baseline 35.8 to 38.2 points) across the cohorts, per clinician assessment. Requirements for Parkinson's disease medications were also reduced in cohorts 2 and 3 (daily levodopa-equivalent dose reductions, average of -322.0 and -441.2 mg/day, respectively; baseline 1507.0 and 1477.0 mg/day, respectively). Two-year data from the PD-1102 trial for 7 patients showed that NBIb-1817 reduced diary "Off" time by an average of -3.2 hours and increased diary good "On" time by +2.1 hours (baselines 9.3 hours and 6.6 hours, respectively). In this study, NBIb-1817 showed sustained improvement in motor function after two years, with improved UPDRS Part III off medication scores of -12.0 points (baseline 34.4). Requirements for Parkinson's disease medications were also reduced (daily levodopa-equivalent dose reduction, average pf -439.5 mg/day; baseline 1500.9 mg/day). Preliminary safety data from both studies suggest that NBIb-1817 was well-tolerated, with no study drug-related serious adverse events (SAEs) reported. The most common adverse events reported were headache, hypoesthesia, and musculoskeletal pain (PD-1101), and upper respiratory tract infection, headache, nausea, and depression (PD-1102).

"It is promising to see that after three years, a single administration of one-time investigational gene therapy treatment NBIb-1817 showed sustained reduction in "Off" time, as well as improvement in "On" time without troublesome dyskinesia and other measures of motor function in patients with Parkinson's disease," said Chad Christine, M.D., primary author, a lead investigator of the study and Professor of Neurology at the University of California, San Francisco (UCSF) Weill Institute for Neurosciences. "Parkinson's disease patients' motor function would be expected to worsen over three years, making these results very encouraging. The standard of care for advanced Parkinson's disease has not significantly changed in decades and it is our hope that NBIb-1817 has the potential to become the first gene therapy for Parkinson's disease."

Parkinson's disease is a chronic, progressive and debilitating neurodegenerative disorder that affects approximately one million people in the U.S. and six million people worldwide. It is characterized by a loss of dopamine from neuronal degeneration, with a concomitant loss of the aromatic L-amino acid decarboxylase (AADC) enzyme required to synthesize dopamine in the brain, leading to associated impairment in motor, neuropsychiatric, and autonomic functions.

"We are pleased that the results from these studies show that one-time treatment with investigational NBIb-1817 may help restore the brain's ability to convert levodopa into dopamine," said Eiry Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences. "Our hope is that NBIb-1817 will help patients experience less "Off" time and more "On" time and improve motor symptom control. We plan to re-initiate enrollment in our registrational RESTORE-1 clinical trial with NBIb-1817 this year and look forward to further evaluating NBIb-1817 in patients with Parkinson's disease."

NBIb-1817 is an investigational recombinant adeno-associated viral serotype 2 vector encoding the gene for human AADC that is designed to help

produce the AADC enzyme in brain cells where it can convert levodopa to dopamine.

“We are encouraged by the congruence of long-term data, including clinician- and patient-reported clinical outcomes in our clinical studies,” said Omar Khwaja, M.D., Ph.D., Chief Medical Officer and Head of Research and Development at Voyager Therapeutics. “These results are promising and show that the approach has the potential to transform the treatment of Parkinson’s disease, and help improve the lives of patients and their families.”

Additional information about PD-1101 and PD-1102 will be available on demand for registered participants through October 1, 2020 on the MDS meeting website (www.mdscongress.org/Congress/Registration.htm).

- Christine CW, Richardson RM, Van Laar AD, et al. Three-Year Safety and Clinical Outcomes from the PD-1101 Trial of AADC Gene Therapy for Advanced Parkinson’s Disease
  Poster # 879: Update on Genetics of Movement Disorders, September 13, 2020, 10:30–12:30pm EST (10-minute prerecorded presentation)
- Factor SA, Van Laar AD, Richardson RM, et al. AADC Gene Therapy Administered via a Posterior Approach: 24-Month Results from the PD-1102 Trial in Advanced Parkinson’s Disease
  Poster # 889: Poster Tour, launches on-demand on September 11, 2020 8:00am EST (5-minute prerecorded presentation)

About Parkinson’s Disease and NBIb-1817 (VY-AADC)
Parkinson’s disease is a chronic, progressive and debilitating neurodegenerative disease that affects approximately one million people in the U.S. and six million people worldwide. It is characterized by a loss of dopamine and neuronal degeneration with a concomitant loss of the aromatic L-amino acid decarboxylase (AADC) enzyme required to synthesize dopamine in the brain, leading to associated impairment in motor, neuropsychiatric, and autonomic functions. Dopamine is a chemical “messenger” that is produced in the brain and is involved in the control of movement. It is made when AADC converts the chemical levodopa to dopamine. As Parkinson’s disease progresses, there is less AADC enzyme in parts of the brain where levodopa is converted to dopamine.

NBIb-1817 is an investigational recombinant adeno-associated viral (AAV) serotype 2 vector encoding the gene for human AADC that is designed to help produce the AADC enzyme in brain cells where it can convert levodopa to dopamine. NBIb-1817 is administered into the brain using intraoperative monitoring with magnetic resonance imaging (MRI)-facilitated targeted delivery.

About the RESTORE-1 Clinical Trial
Paused temporarily in April 2020 due to the COVID-19 pandemic, Neurocrine Biosciences and Voyager Therapeutics plan to re-initiate RESTORE-1, a Phase 2, randomized, placebo-surgery controlled, double-blinded, multi-center clinical trial, to evaluate the safety and efficacy of NBIb-1817 in patients who have been diagnosed with Parkinson's disease for at least four years and have at least three hours of “Off” time during the day as measured by a validated self-reported patient diary.

For more information about the RESTORE-1 clinical trial, including eligibility criteria, please visit clinicaltrials.gov and restore1study.com.

About the RESTORE-2 Clinical Trial
Preparations are ongoing for the RESTORE-2 global registrational trial that will include clinical sites within and outside the U.S.

About Neurocrine Biosciences and Voyager Therapeutics Strategic Collaboration
In 2019, Neurocrine Biosciences and Voyager Therapeutics entered into a strategic collaboration focused on the development and commercialization of gene therapy programs, VY-AADC for Parkinson’s disease and VY-FXN01 for Friedreich’s ataxia, as well as rights to two programs to be determined. This collaboration combines Neurocrine Biosciences’ expertise in neuroscience, drug development and commercialization with Voyager’s innovative gene therapy programs targeting severe neurological diseases.

About Neurocrine Biosciences
Neurocrine Biosciences is a neuroscience-focused, biopharmaceutical company with 28 years of experience discovering and developing life-changing treatments for people with serious, challenging and under-addressed neurological, endocrine and psychiatric disorders. The company's diverse portfolio includes FDA-approved treatments for tardive dyskinesia, Parkinson’s disease, endometriosis* and uterine fibroids*, with three pivotal and five mid-stage clinical programs in multiple therapeutic areas. Headquartered in San Diego, Neurocrine Biosciences specializes in targeting and interrupting disease-causing mechanisms involving the interconnected pathways of the nervous and endocrine systems. For more information, visit neurocrine.com, and follow the company on LinkedIn. *(*in collaboration with AbbVie)*

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 for which effective new therapies are needed, including Parkinson’s disease, Huntington’s disease, Friedreich’s ataxia, and other severe neurological diseases. For more information on Voyager, please visit the company’s website at **www.voyagertherapeutics.com** or follow **@VoyagerTx** on Twitter and **LinkedIn**.

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Neurocrine Biosciences Forward-Looking Statements
In addition to historical facts, this press release contains forward-looking statements that involve a number of risks and uncertainties. Among the factors and risks that could cause actual results to differ materially from those indicated in the forward-looking statements are risks that the product candidates licensed from Voyager may not obtain regulatory approval from the FDA or other regulatory agencies, or such approval may be delayed or conditioned; risks that development activities related to the product candidates licensed from Voyager may not be completed on time or at all; risks associated with the Company's dependence on Voyager for research, development and manufacturing activities; risks that ongoing or future clinical trials may not be successful or replicate previous clinical trial results, or may not be predictive of real-world results or of results in subsequent clinical trials; risks and uncertainties relating to competitive products and technological changes that may limit demand for product candidates licensed from Voyager; risks that the product candidates licensed from Voyager may be precluded from commercialization by the proprietary rights of third parties;

the impact of the COVID-19 pandemic and efforts to mitigate its spread on our business; risks and uncertainties associated with the scale and duration of the COVID-19 pandemic and resulting global, national, and local economic and financial disruptions; risk and uncertainties related to any COVID-19 quarantines, shelter-in-place and similar government orders that are currently in place or that may be put in place in the future, including the impact of such orders on our business operations and the business operations of the third parties on which we rely; risks related to the development of our product candidates; and other risks that are described in the Company's periodic reports filed with the Securities and Exchange Commission, including without limitation the Company's quarterly report on Form 10-Q for the quarter ended June 30, 2020. Neurocrine disclaims any obligation to update the statements contained in this press release after the date hereof.

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 Therapeutics makes regarding the potential impact or significance of the long-term medical data for patients treated in the PD-1101 and PD-1102 clinical trials; the re-initiation of RESTORE-1 Phase 2 clinical trial prior to year-end, the initiation of the RESTORE-2 Phase 3 clinical trial during the first half of 2021; the initiation, timing, progress, activities, goals and reporting of results of other activities associated with the PD program, and the potential benefits, timing and future operation of the collaboration with Neurocrine Biosciences 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, risks that ongoing or future clinical trials may not be successful or replicate previous clinical trial results, or may not be predictive of real-world results or of results in subsequent clinical trials; risks and uncertainties relating to competitive products and technological changes that may limit demand for product candidates now being evaluated in clinical trials; the impact of the COVID-19 pandemic and efforts to mitigate its spread on our clinical trials and our business generally; risks related to the initiation and conduct of preclinical studies and clinical trials; the sufficiency of preclinical and clinical data to support applications for additional studies and marketing approval of our PD drug development candidates; changes in expectations from the FDA and other regulatory authorities as to the requirements for obtaining product approvals; the decisions of the FDA and other regulatory authorities in response to applications we file in connection with our product candidates under our PD program and otherwise in our conduct of PD drug development activities; the priorities, capabilities, diligence and efforts of Neurocrine Biosciences, our collaboration partner for the PD program, and other collaborators and vendors supporting our PD program; and the commercial potential of PD product candidates that may be developed as part of our PD program. These statements are also subject to a number of material risks and uncertainties that are described in Voyager Therapeutics’ Annual Report on Form 10K, Voyager Therapeutics’ Quarterly Reports on Form 10-Q and other reports filed by Voyager Therapeutics with the Securities and Exchange Commission, as may be 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 Therapeutics 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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