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NeuBase Therapeutics Announces Positive, Preclinical Data Validating its Novel Genetic Therapy PATrOL™ Platform

Demonstrates broad biodistribution, including across the blood-brain barrier into the central nervous system, and into skeletal muscle, in non-human primates ("NHPs") after systemic administration

Durable and therapeutically relevant drug concentrations achieved in NHPs after single intravenous dose

Potent cell-based activity and allele-specific enrichment in patient-derived cell lines

Platform validation data supports expansion of the therapeutic pipeline into new organ systems previously unreachable with first-generation antisense oligonucleotide technology

Management to hold a conference call today at 8 a.m. ET

PITTSBURGH, March 31, 2020 (GLOBE NEWSWIRE) -- NeuBase Therapeutics, Inc. (Nasdaq: NBSE) ("NeuBase" or the "Company"), a biotechnology company developing next-generation antisense oligonucleotide ("ASO") therapies to address genetic diseases, today announced positive preclinical data from its pharmacokinetics studies in non-human primates ("NHPs") and *in vitro* pharmacodynamics data in patient-derived cell lines. NeuBase believes these data validate the key advantages of the proprietary NeuBase peptide-nucleic acid ("PNA") antisense oligonucleotide (PATrOL™) platform and support the Company's decision to advance the development of its Huntington's disease ("HD") and myotonic dystrophy type 1 ("DM1") programs, as well as the potential expansion of its therapeutic pipeline into other indications.

Dr. George Church, professor of genetics at Harvard Medical School and member of the National Academy of Sciences, stated, "Given the activity and broad biodistribution observed in these studies and the potential for easier target definition, I believe the PATrOL™ technology may have a potent impact on the future of drug development and treatment of genetic diseases."

Non-Human Primate Pharmacokinetic Study

Quantitative whole-body autoradiography was performed on NHPs. A PATrOL™-enabled compound was radio-labeled, and the resulting material was injected into NHPs at 5 mg/kg via a bolus tail vein injection. At four hours, twelve hours, and seven days post-dosing, NHPs were sacrificed and sectioned into 40 µm slices. Slices were exposed to autoradiography imaging plates alongside a dilution series of radioactive PNA in whole blood. Upon imaging, the dilution series enabled an analysis of the amount of compound in each of the tissues. In addition, prior to sacrifice, whole blood, urine, and feces were

collected from the NHPs at specified timepoints. The major conclusions from this study include:

- Rapid uptake of compound out of the body's circulation after systemic intravenous administration, with a half-life in circulation of approximately 1.5 hours;
- Compound penetrates every organ system studied, including the central nervous system and skeletal muscle;

° Compound crosses the blood-brain barrier and into the key deep brain structures, including the caudate, supporting a key capability for the development of the Company's lead program in HD;
° Delivery of the compound to skeletal muscle, the primary organ system that is affected in DM1;
° Because both HD and DM1 have manifestations outside of the primary affected organ, the broad biodistribution of the compounds may enable a potential whole-body therapeutic solution in both indications.

- Therapeutically relevant doses persist for greater than one week in NHPs after single-dose injection;

° 96% of administered compound remained *in vivo* after a one-week period (latest timepoint tested);
° Redistribution over one week after administration between organ systems enriches concentrations in key brain regions up to two-fold, including in those deep brain structures most relevant for HD;
° Retention of ~90% of compound concentrations achieved in skeletal muscle over the course of one-week post-single-dose administration; and

- Sustained concentrations in many other key organ systems throughout the body may indicate the potential for durable therapeutic responses and an infrequent dosing cadence.

Patient-Derived Huntington's Cell Line Pharmacodynamic Studies

Multiple Huntington's disease candidate compounds were incubated with HD-derived cells and assayed for their toxicity and their ability to selectively knock down mutant huntingtin protein ("mHTT") expression by engaging with the CAG repeat expansion in the huntingtin ("*HTT*") gene transcript. Multi-well plates were seeded with cells and candidates were added to the culture at various concentrations. Cells were grown for three days and thereafter assayed for cell death. Cell pellets were also collected, lysed, and run on gradient SDS-PAGE gels. Following the transfer of the proteins to a membrane, the membrane was probed with anti-huntingtin and anti-beta-actin antibodies. Secondary antibodies were used to image the immunoblots. The beta-actin bands were used to normalize the amount of protein across the wells. The amounts of mutant and wild type huntingtin protein in treated cells were compared to untreated cells to determine the level of knockdown. The major conclusions from this study include:

- Activity in engaging target disease-causing transcripts and knocking-down resultant malfunctioning mHTT protein levels preferentially over normal HTT protein knock-down; and

- Dose limiting toxicities were not observed relative to a control either at or above the doses demonstrating activity in human cells *in vitro*.

In addition, PATrOL™ enabled compounds were generally well-tolerated *in vivo* after systemic administration, both after single dose administration in NHPs and multi dose administration in mice for over a month.

“We believe the PATrOL™ platform has the potential to create drugs that are easy for patients to take at infrequent intervals after they have tested positive for a genetic disease but before symptoms emerge,” said Dietrich Stephan, Ph.D., chief executive officer of NeuBase. “We believe the best way to effectively manage degenerative genetic diseases is to get ahead of the disease process, and we believe that can only be achieved with early diagnosis coupled with well-tolerated, effective, and easily administered therapies.”

Dr. Robert Friedlander, chief medical officer of NeuBase and member of the National Academy of Medicine, stated, **“**An allele specific approach that can be systemically administered and cross the blood brain barrier would be an ideal drug profile for many untreatable genetic diseases. I believe that NeuBase is moving towards realizing this goal.”

The intersection of the NHP pharmacokinetic data and the*in vitro* patient-derived pharmacodynamic data provides a roadmap to create a pipeline of therapeutic candidates which can reach target tissues of interest after systemic administration and achieve the desired activity at that dose. NeuBase believes the data from these studies support the advancement of the Company’s HD and DM1 programs into lead optimization and subsequent IND-enabling studies, as well as provide a roadmap for the future expansion of the Company’s therapeutic pipeline into other indications, including oncology.

Dr. Sam Broder, former Director of the National Cancer Institute of the National Institutes of Health and member of the National Academy of Sciences, stated, “I believe that the NeuBase strategy of targeting transcripts before they become dangerous mutant proteins has the potential to deliver a dramatic improvement in our collective capabilities to effectively treat a wide range of genetic diseases, including some of the most deadly cancers, by targeting driver mutations and accelerating immunotherapy capabilities.”

Conference Call

NeuBase Therapeutics, Inc. will discuss these data and next steps for development during a webcasted conference call with slides today, March 31, 2020, at 8:00 a.m. ET. The live and archived webcast of this presentation can be accessed through the IR Calendar page on the Investors section of the Company’s website, www.neubasetherapeutics.com. The dial-in details for the call are 877-451-6152 (domestic) or +1-201-389-0879 (international), and conference ID: 13701118. The archived webcasts will be available for approximately 30 days following the presentation date.

About NeuBase Therapeutics

NeuBase Therapeutics, Inc. is developing the next generation of gene silencing therapies with its flexible, highly specific synthetic antisense oligonucleotides. The proprietary NeuBase peptide-nucleic acid (PNA) antisense oligonucleotide (PATrOL™) platform is designed to permit the rapid development of targeted drugs, thereby potentially increasing

the treatment opportunities for the hundreds of millions of people affected by rare genetic diseases, including those that can only be treated through accessing of secondary RNA structures. Using PATrOL™ technology, NeuBase aims to first tackle rare, genetic neurological disorders.

Safe Harbor Statement under the Private Securities Litigation Reform Act of 1995

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act. These forward-looking statements include, among other things, statements regarding the Company's goals and plans and the Company's pharmacokinetics and pharmacodynamics studies. These forward-looking statements are distinguished by use of words such as "will," "would," "anticipate," "expect," "believe," "designed," "plan," or "intend," the negative of these terms, and similar references to future periods. These views involve risks and uncertainties that are difficult to predict and, accordingly, our actual results may differ materially from the results discussed in our forward-looking statements. Our forward-looking statements contained herein speak only as of the date of this press release. Factors or events that we cannot predict, including those described in the risk factors contained in our filings with the U.S. Securities and Exchange Commission, may cause our actual results to differ from those expressed in forward-looking statements. The Company may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in the forward-looking statements, and you should not place undue reliance on these forward-looking statements. Because such statements deal with future events and are based on the Company's current expectations, they are subject to various risks and uncertainties and actual results, performance or achievements of the Company could differ materially from those described in or implied by the statements in this press release, including: the Company's plans to develop and commercialize its product candidates; the Company's plans to commence clinical trials in Huntington's disease and myotonic dystrophy type 1 and to potentially expand the pipeline into other indications; the utility of the preclinical data generated in existing studies performed by the Company in determining the results of potential future clinical trials and of the potential benefits of the PATrOL™ platform technology; the timing of initiation of the Company's planned clinical trials; the timing of the availability of data from the Company's clinical trials; the timing of any planned investigational new drug application or new drug application; the Company's plans to research, develop and commercialize its current and potential future product candidates; the clinical utility, potential benefits and market acceptance of the Company's current and potential future product candidates; the Company's commercialization, marketing and manufacturing capabilities and strategy; the Company's ability to protect its intellectual property position; and the requirement for additional capital to continue to advance these product candidates, which may not be available on favorable terms or at all, as well as those risk factors in our filings with the U.S. Securities and Exchange Commission. Except as otherwise required by law, the Company disclaims any intention or obligation to update or revise any forward-looking statements, which speak only as of the date hereof, whether as a result of new information, future events or circumstances or otherwise.

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