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neubase

NeuBase Therapeutics Announces Positive Preclinical In Vivo Data for PATrOL™-enabled Anti-gene for the Treatment of Myotonic Dystrophy Type 1

In vivo *data after single-dose IV administration demonstrate engagement with* DMPK *mRNA and broad rescue of mis-splicing across key transcripts*

Findings provide support for hypothesized mechanism of action of anti-gene, which is designed to not degrade the DMPK *transcript*

Data further validate the potential of the PATrOL™ platform to develop highly targeted therapies that increase, decrease or change causal protein function

NeuBase management to hold conference call and webcast today, December 16, at 8:00 a.m. EST

PITTSBURGH, Pa., Dec. 16, 2020 (GLOBE NEWSWIRE) -- NeuBase Therapeutics, Inc. (Nasdaq: NBSE) ("NeuBase" or the "Company"), a biotechnology company accelerating the genetic revolution using a new class of synthetic medicines, today announced positive *in vitro* and *in vivo* preclinical data for its PATrOL™-enabled anti-gene therapies for the treatment of myotonic dystrophy type 1 (DM1). These new data show that PATrOL-enabled Compound A can rapidly resolve mis-splicing without negatively impacting DMPK protein levels. They also support the potential of NeuBase's anti-gene approach to comprehensively treat the underlying cause of DM1.

"Despite the fact that the genetic basis of DM1 is well understood today, there is still an urgent need to find the first genetically-targeted, disease-modifying treatment option for affected patients," said Curt Bradshaw, Ph.D., Chief Scientific Officer of NeuBase. "DM1 is caused by a genetic mutation in the *DMPK* gene leading to mis-splicing of a broad spectrum of genes and DMPK protein insufficiency. A treatment option that addresses mis-splicing while retaining functional DMPK protein levels may be key to treating all aspects of DM1."

Dietrich A. Stephan, Ph.D., Chief Executive Officer of NeuBase, added, "Using our proprietary PATrOL platform, we have designed a first-in-class anti-gene candidate that selectively binds mutant *DMPK* mRNA and opens its hairpin secondary structure, as opposed to a mechanism of action that explicitly degrades the mutant and wild-type transcripts indiscriminately, making it a unique option for the treatment of DM1. These *in vitro* and *in vivo* data both support our hypothesized mechanism of action and demonstrate rapid and broad resolution of the mis-splicing that is the primary cause of DM1.

"This is the second set of positive data that we've announced in 2020 for our PATrOL-enabled therapies, which we believe serves as proof of concept that further validates our

technologic foundation. With a single unified platform, we believe we can increase, decrease or change protein function of potentially any nucleic acid target, unique among genetic medicine approaches. We are excited by the progress we have made and look forward to providing additional updates on our platform and pipeline of programs at an R&D day in the first half of 2021."

In vitro data highlights in DM1 patient-derived fibroblasts:

- Compound A traffics to the nucleus, engages and normalizes *DMPK* mRNA.
- Compound A rescues mis-splicing of two key DM1 dysregulated transcripts (*MBNL1* and *MBNL2)* within two days after initial treatment. Notably, induction of rescue continues to improve through day 9, the latest time point analyzed.
- Compound A significantly induces broad correction of global exon inclusion levels of mis-spliced transcripts.
  - Statistically significant improvement in global splicing as measured by the human differential splice inclusion (hDSI) statistic.
  - More than 175 dysregulated human transcripts achieved statistically significant improvement in splicing, many with completely normalized exon usage.
- DMPK protein levels remain unchanged 5 days after a single Compound A dose, supporting the hypothesized mechanism of action maintaining DMPK.

In vivo data highlights in the HSA^{LR} transgenic mouse model of DM1 that expresses high levels of mutant CUG-repeat-containing mRNA (*HSA*) in skeletal muscle:

- A single intravenous (IV) injection of 29 mg/kg of Compound A traffics to the nucleus and engages *HSA* mRNA within 24 hours in tibialis anterior (TA) skeletal muscle.
- A single intravenous (IV) injection of Compound A significantly induces broad correction of global exon inclusion levels of mis-spliced transcripts in HSA^{LR} TA skeletal muscle at day 13.
- Statistically significant improvement in global splicing as measured by the murine differential splice inclusion (mDSI) statistic.
  - More than 50 unique dysregulated murine transcripts achieved statistically significant improvement in splicing post-treatment, with many achieving complete normalization of appropriate exon usage.
- Compound A was well tolerated after single dose administration at the dose demonstrating activity *in vivo.*

DM1 is a rare, autosomal dominant repeat expansion disorder characterized by progressive muscle wasting and weakness. It also affects the central nervous system (CNS) and heart. DM1 is caused by CTG nucleic acid repeats in the *DMPK* gene that produce a hairpin structure in the transcribed *DMPK* mRNA. The hairpin structure sequesters critical splice regulators and results in the mis-splicing of multiple gene transcripts. Furthermore, the binding of splice regulators traps the mutant *DMPK* mRNA in the nucleus, resulting in DMPK protein haploinsufficiency, or half the level of protein that is needed for normal function, which is thought to exacerbate the CNS and cardiac symptoms that are characteristic of DM1 (as knock-out mice for *Dmpk* show both severe cardiac conduction defects as well as issues with neuronal cytoskeletal remodeling manifesting in aberrant long-term potentiation). The prevalence of DM1 is >5/100,000 in the general population. There are currently no

approved treatments for DM1.

Conference Call and Webcast Details

NeuBase Therapeutics, Inc. will discuss these data during a webcasted conference call with slides today, December 16, 2020, at 8:00 a.m. EST. To access the webcast, please click here. An archived recording of this presentation will be available following the call through the IR Calendar page on the Investors section of the Company's website, www.neubasetherapeutics.com.

About NeuBase Therapeutics, Inc.
NeuBase is accelerating the genetic revolution using a new class of synthetic medicines. NeuBase's designer PATrOL™ therapies are centered around its proprietary drug scaffold to address genetic diseases at the source by combining the highly targeted approach of traditional genetic therapies with the broad organ distribution capabilities of small molecules. With an initial focus on silencing disease-causing mutations in debilitating neurological, neuromuscular and oncologic disorders, NeuBase is committed to redefining medicine for the millions of patients with both common and rare conditions. To learn more, visit www.neubasetherapeutics.com.

Use of Forward-Looking Statements
This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act. 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 forward-looking statements include, among others, those related to the potential significance and implications of the Company's positive *in vitro* and *in vivo* preclinical data for its PATrOL™-enabled anti-gene therapies for the treatment of myotonic dystrophy. 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 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 timing of initiation of the Company's planned clinical trials; the risks that prior data will not be replicated in future studies; 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 future product candidates; the clinical utility, potential benefits and market acceptance of the Company's product candidates; the Company's commercialization, marketing and manufacturing capabilities and strategy; global health conditions, including the impact of COVID-19; 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 contained 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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