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NeuBase Therapeutics Demonstrates Functional Rescue in Myotonic Dystrophy Type 1 Model and Allele-Selective Inhibition of KRAS Mutations to Inhibit Tumor Growth

- *Data presented today at NeuBase's R&D Day show functional rescue of myotonic dystrophy type 1 (DM1) phenotype* in vivo *after subcutaneous dosing; positions program to enter the clinic in CY 2022*
- *Company also presented data demonstrating selective reduction of mutant huntingtin protein in the brain after subcutaneous dosing in zQ175 Huntington's disease mouse model*
- *Company unveiled new oncology program targeting* KRAS *G12D and G12V, the two most common and historically "undruggable"* KRAS *driver mutations; data show initial compounds are allele selective and inhibit tumor growth in* KRAS-*mutant tumor xenograft model*s
- *These three programs highlight the broad potential of NeuBase's PATrOL™ precision genetic medicine platform to scale across many diseases and address root causality via multiple mechanisms*

PITTSBURGH, June 08, 2021 (GLOBE NEWSWIRE) -- NeuBase Therapeutics, Inc. (Nasdaq: NBSE) ("NeuBase" or the "Company"), a biotechnology company accelerating the genetic revolution using a new class of precision genetic medicines, today announced positive new data and program updates for its development pipeline of PATrOL-enabled genetic medicines.

Dietrich A. Stephan, Ph.D., Chairman and CEO of NeuBase Therapeutics, said, "The data presented today from several programs in our pipeline highlight the unique potential of our PATrOL technology platform to generate new precision genetic medicines for a wide range of diseases with an incomparable flexibility to target distinctive gene dysfunctions. We successfully demonstrated that our platform can therapeutically modulate *in vivo* gene function at the DNA or RNA level with exquisite precision of target engagement in three different disease indications with different mechanisms of disease. These data show how we can utilize the PATrOL platform to design drug candidates to inhibit DNA transcription, RNA translation, and mutant protein production, as well as displace bound proteins to rescue mis-splicing."

Dr. Stephan continued, "We have made significant progress since our last data release, showing functional rescue in myotonic dystrophy type 1 after subcutaneous dosing, *in vivo* proof of concept in Huntington's disease with allele-selective mutant protein knock-down after getting compounds across the blood-brain barrier following systemic dosing, and initial

data for a new oncology program against historically 'undruggable' *KRAS* driver mutations. With this tremendous momentum building across our expanding development pipeline, we look forward to entering the clinic with our DM1 program in 2022 and continuing to evaluate diseases where our PATrOL platform can deliver significant therapeutic value."

DM1 Program Data Highlights

Experiments conducted in the HSA^{LR} transgenic mouse model of DM1, which express high levels of mutant CUG-repeat-containing mRNA in skeletal muscle, demonstrated molecular rescue *in vivo* after a single intravenous (IV) dose (29 mg/kg), which resulted in:

- ~75% splice correction of mis-spliced transcripts observed at ~2 weeks (p=<0.0001);
- Complete splice correction of chloride channel (*Clcn1*) in skeletal muscle, a transcript responsible for the myotonia phenotype;
- Restoration of Clcn1 protein in skeletal muscle;
- Reduction of nuclear inclusions at day 21; and
- Good tolerability at pharmacologically active doses.

Additional experiments using PATrOL-enabled compounds to treat DM1 showed a 70% reduction in myotonia 35 days post first-dose via plantar flexor torque assay (p=<0.05) *in vivo* after subcutaneous (SC) dosing (3 mg/kg dosed weekly x4). This functional rescue via SC administration was achieved at a significantly lower dose relative to the IV route.

Dr. Stephan stated, "We've delivered on several key advancements in our development program of PATrOL-enabled compounds to treat myotonic dystrophy type 1. These data show that the platform is capable of addressing the underlying genetic causes of DM1 after systemic dosing. In addition, these data demonstrate the ability of our candidates to achieve these effects using multiple systemic routes, including subcutaneous administration. We are continuing to advance our DM1 program and anticipate entering the clinic in calendar year 2022."

HD Program Data Highlights

Experiments conducted in the zQ175 Huntington's disease mouse model with 190 CAG repeats in exon 1 of *HTT* demonstrated that SC administration of PATrOL-enabled compounds:

- Crossed the blood-brain-barrier and reached target brain regions; and
- Selectively reduced mutant HTT protein (mHTT).

These results were achieved with PATrOL-enabled compounds designed to target the mutation at either the DNA or RNA level, and the compounds were generally well tolerated.

Robert Friedlander, M.D., M.A., Chairman of NeuBase's Scientific Advisory Board and Chairman and Professor of Neurosurgery at the University of Pittsburgh and UPMC, said, "NeuBase's Huntington's disease development program has made significant progress toward our target profile. We have advanced from showing mutant HTT protein knockdown in human patient cells to *in vivo* proof-of-concept after a patient-friendly subcutaneous administration. We achieved this reduction in *mHTT* by targeting the mutation at either the RNA or DNA level, which is one of the unique attributes of the PATrOL platform. In addition, we are focusing our efforts on systemic dosing routes, which offers the potential for uniform brain distribution, while also being a preferable route compared to intrathecal

administration."

New Program - KRAS Oncology Program Overview and Data Highlights
NeuBase's new oncology program targets *KRAS* G12D and G12V gene mutations, which are the two most common and historically "undruggable" *KRAS* driver mutations, together representing more than 50% of *KRAS*-driven tumors.[1] There are no approved therapies for *KRAS* G12D or G12V mutations. NeuBase designed novel PATrOL-enabled compounds to selectively engage with the mutant transcript at either the DNA or RNA level to inhibit downstream signaling and protein production.

Data from preclinical studies targeting *KRAS* G12D and G12V mutations demonstrated that PATrOL-enabled compounds targeting the mRNA achieved:

- Target engagement and selective inhibition of the mutant *KRAS* transcript *in vitro*;
- Inhibition of tumor growth *in vivo* in HPAFII heterozygous pancreatic cancer xenografts (G12D mutation, 0.3 mg/kg intra-tumoral injections x3);
- Reduction in phosphorylation levels of the downstream oncogenic signaling cascade, including MEK, ERK, and CREB (G12D mutation, 0.3 mg/kg intra-tumoral injections x3); and
- Prolonged tumor growth inhibition *in vivo* in CAPAN-2 heterozygous pancreatic cancer xenografts (G12V mutation, 0.3 mg/kg intra-tumoral injections x3).

Furthermore, PATrOL-enabled compounds targeting double-stranded DNA achieved *in vitro*:

- Target engagement at DNA level; and
- ~90% reduction in mutant *KRAS* transcript relative to the wild type ($p=<0.001$).

Curt Bradshaw, Ph.D., Chief Scientific Officer at NeuBase, said, "Expanding our research pipeline to include an oncology program has been a company goal, and we are pleased to announce today that we've moved from concept to *in vivo* proof-of-principle. Our new oncology program covers the most common *KRAS* mutations and are significant targets for the treatment of cancer. With our PATrOL-enabled compounds, we are developing an allele-selective approach, which we believe is critical to addressing this target as normal KRAS protein is essential for cellular function. This program exemplifies the potential of NeuBase's PATrOL platform to not only address but also precisely target different genetic drivers of disease to develop new disease-modifying medicines for many diseases that currently have no treatment options."

NeuBase R&D Day Details
NeuBase is hosting a virtual R&D Day for investors and analysts at 12:30 p.m. EDT today, June 8th. To register and attend the event or listen to the replay, click here.

About NeuBase Therapeutics
NeuBase is accelerating the genetic revolution by developing a new class of precision genetic medicines which can be designed to increase, decrease, or change gene function, as appropriate, to resolve genetic defects that drive disease. NeuBase's targeted PATrOL™ therapies are centered around its proprietary drug scaffold to address genetic diseases at the DNA or RNA level 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.

1. Papke B, et al. ACS Pharmacology & Translational Science. 2021.

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 updates provided on the Company's development pipeline, including the myotonic dystrophy type 1 (DM1) and Huntington's disease (HD) programs and an oncology program targeting high value genetic driver mutations, at an R&D Day in June 2021 and the prospects of the Company's proprietary PATrOL™ platform. 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 (the "SEC"), 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 SEC. 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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