Item 7.01 Regulation FD Disclosure.

Announcement of Preclinical Data

On June 8, 2021, NeuBase Therapeutics, Inc. (the “Company”) announced positive data from preclinical studies being conducted on the Company’s myotonic dystrophy type 1 and Huntington’s disease programs, and unveiled a new oncology program. A copy of the press release related to these data is furnished herewith as Exhibit 99.1 to this Current Report on Form 8-K (this “Current Report”). In connection with such announcement, the Company conducted a webcasted research and development day event to discuss these data with accompanying presentation materials. The presentation materials are furnished herewith as Exhibit 99.2. A replay of the event will be archived and accessible at https://ir.neubasetherapeutics.com/ for approximately thirty days following the conference call.

The information contained in this Item 7.01 of this Current Report, including Exhibits 99.1 and 99.2, is being furnished pursuant to Item 7.01 and shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, and it shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or under the Exchange Act, whether made before or after the date hereof, except as expressly set forth by specific reference in such filing to this Item 7.01 of this Current Report.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

<table>
<thead>
<tr>
<th>Exhibit No.</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>99.1</td>
<td>Press Release, dated June 8, 2021</td>
</tr>
<tr>
<td>99.2</td>
<td>Presentation Materials for Research and Development Day event held on June 8, 2021</td>
</tr>
</tbody>
</table>
Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

NEUBASE THERAPEUTICS, INC.
(Registrant)

Date: June 8, 2021

By: /s/ Sam Backenroth
Sam Backenroth
Chief Financial Officer
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 models

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 8, 2021 – 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\R 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. 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.


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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Ultra-precision genetic medicines

R&D DAY 2021

Drugging the genome to increase, decrease, or edit protein function to address base causality in disease

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

Certain statements contained in this presentation regarding matters that are not historical facts are forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995, known as the PSLRA. These include statements regarding management’s intentions, plans, beliefs, expectations or forecasts for the future, and, therefore, you are cautioned not to place undue reliance on them. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. NeuBase Therapeutics, Inc. (“NeuBase”) undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise, except to the extent required by law. NeuBase uses words such as “anticipates,” “believes,” “plans,” “expects,” “projects,” “future,” “intends,” “may,” “will,” “should,” “could,” “estimates,” “predicts,” “potential,” “continue,” “guidance,” and similar expressions to identify these forward-looking statements that are intended to be covered by the safe-harbor provisions of the PSLRA. Such forward-looking statements are based on NeuBase’s expectations and involve risks and uncertainties; consequently, actual results may differ materially from those expressed or implied in the statements due to a number of factors, including NeuBase’s plans to develop and commercialize its product candidates, including from the NT0100, NT0200 and NT0300 programs; the timing of initiation of NeuBase’s planned clinical trials; the timing of the availability of data from NeuBase’s clinical trials; the timing of any planned investigational new drug application or new drug application; NeuBase’s plans to research, develop and commercialize its current and future product candidates; the clinical utility, potential benefits and market acceptance of NeuBase’s product candidates; NeuBase’s commercialization, marketing and manufacturing capabilities and strategy; NeuBase’s ability to protect its intellectual property position; and NeuBase’s estimates regarding future revenue, expenses, capital requirements and need for additional financing and the impact of COVID-19 on us and our partners. New factors emerge from time to time and it is not possible for NeuBase to predict all such factors, nor can NeuBase assess the impact of each such factor on the business or the extent to which any factor or combination of factors may cause actual results to differ materially from those contained in any forward-looking statements. Forward-looking statements included in this presentation are based on information available to NeuBase as of the date of this presentation. NeuBase disclaims any obligation to update such forward-looking statements to reflect events or circumstances after the date of this presentation, except as required by applicable law. This presentation does not constitute an offer to sell, or the solicitation of an offer to buy, any securities.
A DIFFERENTIATED PLATFORM FOR THE DISCOVERY AND DEVELOPMENT OF NOVEL GENOME-TARGETED DRUGS

Proprietary genome-targeting platform
Target genes to increase proteins, decrease proteins or edit protein function with selectivity and tolerability

Address root causality
Our compounds are designed to address the underlying cause of rare and common diseases, including cancers

Broad therapeutic potential
Up to ~7,000 rare diseases affecting ~10% of global population¹
An estimated 1.9 million new cancer cases diagnosed and ~600,000 cancer deaths in the US alone in 2021²

Approaching clinical stage with an emerging pipeline
DM1 program expected to enter Phase 1/2 in 2022³, with HD and KRAS programs in pre-clinical development

¹Calendar year
**PIPELINE**

<table>
<thead>
<tr>
<th>Programs</th>
<th>Preclinical</th>
<th>IND</th>
<th>Clinical</th>
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<tbody>
<tr>
<td>Myotonic Dystrophy (DM1)</td>
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<td>CTG Repeats in DMPK Causing Splice Dysfunction and Haploinsufficiency</td>
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<td>Huntington’s Disease (HD)</td>
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<td>CAG Repeat in HTT Causing Polyglutamine Aggregates</td>
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<tr>
<td>Oncology</td>
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<tr>
<td>Point Mutations in KRAS (G12D and G12V) Driving many Tumors</td>
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**PATROL™ PLATFORM**

- **ON**
  - Gene Activation
  - Increase endogenous protein levels to address loss-of-function mutations\(^1\)

- **CHANGE**
  - Gene Editing
  - Edit proteins to address change-of-function mutations\(^2\)

- **OFF**
  - Gene Silencing
  - Decrease protein levels to address gain-of-function mutations\(^3\)

HOW WE DO IT

Ultra-high binding affinity compounds precisely target genes to address disease causing mechanisms


DRUG GENES TO ADDRESS BASE CAUSALITY IN SEVERE DISEASES

- A platform to address most causal mechanisms of disease
- Drug the genome (DNA or RNA) with allele selectivity
- Stable against degradation with enhanced biodistribution
- Modular synthesis with established peptide manufacturing
KEY TAKE-AWAYS FROM TODAY

Peptide nucleic acids have the potential to be best-in-class

**Myotonic dystrophy, type 1 (DM1)**
Functional rescue of myotonia after subcutaneous dosing positions us for 2022 IND
- Designed to maintain DMPK protein
- Patient-friendly route of administration

**Huntington’s disease (HD)**
Selective reduction of mutant huntingtin protein in the brain after subcutaneous dosing
- Potential for uniform brain distribution & whole-body solution
- Preferable route over intrathecal administration

**Oncology (KRAS)**
Allele-selective engagement of G12D and G12V in vitro, and tumor growth inhibition in vivo
- High-value oncology targets previously considered “undruggable”
- Four months from inception to proof-of-principle
PETER E. NIELSEN, PH.D.

- Full Professor, University of Copenhagen
- One of the inventors of peptide nucleic acid (PNA) (1991)
- Studied and developed this DNA mimic during the last 30 years in relation to chemistry, origin of life, molecular biology, and drug discovery
- Co-author of more than 400 scientific papers
- Co-inventor of more than 20 patents and patent applications
- Editor-in-Chief of the journal “Artificial DNA”
- Several national and international scientific prizes including the NovoNordic Foundation (1997), the Lundbeck Foundation (1997) and the Institute Curie Jeanne Loubaresse prize (2003)
PEPTIDE NUCLEIC ACIDS (PNA)
PNA dsDNA BINDING

- Nanomolar triplex affinity
- >100x higher than DNA
- Triplex >100x faster than invasion


PNA PROPERTIES: CHEMISTRY

- Oligomers are synthesized by conventional solid phase peptide chemistry
- Charge neutral, generally hydrophilic and water soluble
- Chemically and biologically stable

IN VIVO ADMINISTRATION AND PK

IV administration: $t_{1/2} \approx 30\text{min}$

SC administration: $t_{1/2} \approx 120\text{min}$

**WHY PNA: ADVANTAGES**

- Exquisite biological and chemical stability
- Robust and versatile chemistry
- Multiple modes of action for a specific indication
- Low inherent toxicity
- Unique technology allowing profound medicinal chemistry modification without jeopardizing receptor affinity/specificity
PREVIOUS CHALLENGES

- Cellular uptake/delivery
- Pharmacokinetics
- Formulation
- Therapeutic window

PATROL™ IMPROVES 1ST GEN PNA TO IMPART DRUG-LIKE PROPERTIES

<table>
<thead>
<tr>
<th>Scaffold Modifications</th>
<th>Delivery Domains</th>
<th>Base Modifications</th>
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<tbody>
<tr>
<td>Tunable for RNA or DNA targets</td>
<td>Efficient intracellular delivery</td>
<td>Tunable specificity and affinity</td>
</tr>
<tr>
<td>Tunable binding affinity</td>
<td>Tissue targeting</td>
<td>Tunable for RNA or DNA targets</td>
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<tr>
<td>ADME/Tox optimization</td>
<td>ADME/Tox optimization</td>
<td>Optimize biophysical properties</td>
</tr>
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</table>
WHY

Newest improved chemistry  Focused and scientific approach
New delivery technology  Globally recognized experts
Carefully selected indications & targets  IP generation

MYOTONIC DYSTROPHY TYPE 1 (DM1)
POTENTIAL TO BE BEST-IN-CLASS IN DM1

2021
Preclinical execution

Splice rescue in animal model
Functional rescue of myotonia in animal model
Activity via subcutaneous and intravenous routes
Whole-body solution designed to maintain DMPK levels

2022
on track for clinic

DM1 IS DEVASTATING WITH HIGH UNMET NEED

Most patients have myotonia (impaired muscle relaxation), muscle weakness and wasting, cardiac conduction defects, cognitive deficits and decreased lifespan.

70-80% of congenital onset patients require mechanical ventilation, with mortality rates between 15-20%.

DM1 is a dominantly inherited disease defined by a repeat expansion in the DMPK gene with severity defined by expansion size.

1 out of 20,000 are affected by DM1 globally.

0 currently approved therapies that alter the natural history of DM1.

References:
1. https://www.myotonic.org;
2. https://www.mda.org;
DISEASE PATHOGENESIS

Expanded CUG repeats in DMPK mRNA 3' UTR form toxic hairpins in the nucleus

- Hairpins form nuclear aggregates together with MBNL splice proteins
- Results in widespread mis-splicing of pre-mRNAs
- Produce altered proteins which are dysfunctional in adults

Adapted from Muangkaew and Vilaivan, Bioorg Med Chem Lett 2020; 30:127064

THERAPY DESIGNED TO RESTORE CORRECT SPlicing

- Therapy releases nuclear aggregates
- Designed to maintain DMPK mRNA and allow translation of mutant transcript

Adapted from Muangkaew and Vilaivan, Bioorg Med Chem Lett 2020; 30:127064
December 2020: splice rescue in patient cells, while maintaining DMPK protein levels, and *in vivo*

June 2021: functional rescue *in vivo* after systemic dosing

- Reduce nuclear aggregates in muscle
- Well tolerated at pharmacologically active doses
- Rescue:
  - Splicing defects across many transcripts, including muscle chloride channel
  - Muscle chloride channel protein expression
  - Myotonia (3 mg/kg subcutaneous dose)

**NUCLEAR INCLUSIONS ARE REDUCED IN HSA<sup>LR</sup> MUSCLE AFTER DOSING**

*29 mg/kg iv*
**MIS-SPlicing CORRECTED IN VIVO**

**Single Dose**
administered IV at 29 mg/kg in the HSA<sup>LR</sup> mouse

~75% splice correction observed in tibialis anterior at ~2 weeks after single dose

**Clcn1**
slice correction of myotonia-causing transcript.

![Graph showing mDSI](image)

- Day 13
- All mis-spliced transcripts
- Rescue of mis-splicing

**SKELETAL MUSCLE CHLORIDE CHANNEL (CLCN1) IS RESTORED IN VIVO**

![Western blotting](image)

- Healthy (channel present)
- Untreated (channel reduced)
- Treated (channel restored)

Clcn1 protein

Beta-actin loading control

- FVB background unaffected strain
- HSA<sup>LR</sup> affected

Single dose - 29mg/kg IV, western blotting from soleus muscle on day 20 after dosing
**FUNCTIONAL RESCUE OF MYOTONIA IN VIVO**

- **3mg/kg**
  - Dosed weekly x4 in the HSA LR mouse

- **Subcutaneous**
  - Route of administration

- ~70%
  - Reduction of myotonia at 35 days post first-dose
  - Via plantar flexor torque assay

---

**December 2020:** Splice rescue in patient cells, while maintaining DMPK protein levels, and *in vivo*

**June 2021:** Functional rescue *in vivo* after systemic dosing

- Reduce nuclear aggregates in muscle
- Well tolerated at pharmacologically active doses
- Rescue:
  - Splicing defects across many transcripts, including muscle chloride channel
  - Muscle chloride channel protein expression
  - Myotonia (3 mg/kg subcutaneous dose)

---

**KEY ADVANCEMENTS TOWARD THE CLINIC**
ON TRACK TO FIRST CLINICAL STUDY IN 2022

- Initiated CMC process research
- Initiate non-clinical toxicology
- Ongoing PK/ADME
- Pre-IND meeting

DR. ROBERT FRIEDLANDER
ROBERT FRIEDLANDER, M.D., M.A.

Currently

• Chairman, Walter E. Dandy Distinguished Professor, University of Pittsburgh Department of Neurological Surgery
• Co-Director, UPMC Neurological Institute
• Head, Cerebrovascular Neurosurgery
• Director, Complex Brain Surgery Program

Previously

• Professor, Harvard Medical School
• Vice-Chairman of Neurosurgery, Associate Director of Cerebrovascular Surgery, and Co-Director of the Neuroscience Research Center at the Brigham and Women’s Hospital in Boston

Honors & Awards

• National Academy of Medicine
• International Charcot Prize for Motor Neuron Diseases
• Award from the Academy of Neurological Surgeons
• H. Richard Winn Prize from the Society of Neurological Surgeons

Associations

• American Society for Clinical Investigation
• Association of American Physicians
• National Advisory Council of the National Institutes of Neurological Disorders and Stroke (NINDS)

HUNTINGTON’S DISEASE
**Previously:** selective mutant huntingtin protein knockdown in human patient cells

**June 2021:** Subcutaneous dosing crosses BBB and selectively knocks down mutant huntingtin protein in the mouse brain
- Knock-down achieved by targeting either RNA or DNA
- Well tolerated at pharmacologically active doses

**HUNTINGTON'S DISEASE (HD) IS SEVERE & INCURABLE**

- **100%** of patients carry a repeat expansion in the huntingtin (HTT) gene
- Long poly-glutamine tract in the protein cause cell death
- **Progressive neurodegeneration**
  - Movement disorder, mood disturbances, cognitive impairment and a whole-body disorder

- **41,000** HD cases in the US alone
- **>200,000** at risk from the disease in the US alone

**15-20 years** is life expectancy after diagnosis

---

**Primarily Known as a Progressive CNS Disease**

- Neuronal loss starts in the striatum and progresses to the cortex


**HD is also a Whole-Body Disease**

- Weight loss
- Muscle atrophy
- Glucose intolerance
- Osteoporosis
- Testicular atrophy
- Heart failure
- Cardiac abnormalities

Systemic administration of PATrOL™ has the potential to be a whole-body solution

**Pros:** Reaches all organs, easy to administer, low risk, low training requirement
NORMAL HUNTINGTIN IS WIDELY EXPRESSED AND IMPORTANT FOR:

- Cell signaling, transcriptional regulation, molecular trafficking, axonal transport
- Modulating brain-derived neurotrophic factor (BDNF) production
- Mitochondrial function
- Caspase inhibition

LOSS OF NORMAL HUNTINGTIN IN ANIMAL MODELS IS DETRIMENTAL

- Homozygous gene knock-out is embryonic lethal in mice
- Hemizygous mice demonstrate neurodegeneration in subthalamic nucleus and globus pallidus
- Postnatal protein reduction is detrimental

SYSTEMIC DOSING ENABLES A WHOLE-BODY SOLUTION

[Diagram showing untreated, intrathecal, intrastriatal, and systemic drug delivery to the body]
SIZE DIFFERENCES BETWEEN MOUSE AND HUMAN BRAIN

- Makes clinical translation of intrathecal administration results difficult

ALLELE-SELECTIVE KNOCK-DOWN IS IMPORTANT

- Maintenance of normal huntingtin function while eliminating toxic protein is ideal
SUBCUTANEOUS DOSING CROSSES BBB AND KNOCKS DOWN MUTANT HUNTINGTIN PROTEIN IN THE MOUSE BRAIN

\[ p < 0.05 \]

\[ \text{untreated} \] \quad \text{treated} \]

\[ \text{wtHTT} \quad \text{mHTT} \]

Adapted from Muangkaew and Vilaivan, Bioorg Med Chem Lett 2020; 30:127064

SUBCUTANEOUS DOSING CROSSES BBB AND KNOCKS DOWN MUTANT HUNTINGTIN PROTEIN IN THE MOUSE BRAIN

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Previously: selective mutant huntingtin protein knockdown in human patient cells

June 2021: Subcutaneous dosing crosses BBB and selectively knocks down mutant huntingtin protein in the mouse brain
- Knock-down achieved by targeting either RNA or DNA
- Well tolerated at pharmacologically active doses

HD PROGRAM: THE PATH FORWARD

- In vivo translational profiling
- Systemic dosing for CNS and whole-body solution
- Optimization of delivery and target engagement
- Patient-friendly subcutaneous route
**KRAS G12D & G12V MUTATIONS IN ONCOLOGY**

MUTATIONS IN THE RAS GENE FAMILY CAUSE 30% OF ALL CANCERS

<table>
<thead>
<tr>
<th>Normal KRAS protein is essential for normal function</th>
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<tbody>
<tr>
<td>KRAS mutations are the most common RAS mutations¹</td>
</tr>
<tr>
<td>G12D and G12V account for ~55% of all KRAS mutations</td>
</tr>
<tr>
<td>Our compounds targeting KRAS codon 12 mutations have potential to work against NRAS and HRAS</td>
</tr>
</tbody>
</table>

approved therapies for the 2 most prevalent RAS mutations

- New program initiated in 2021
- Allele-selective target engagement of KRAS G12D and G12V
- Target engagement of the genome and the transcriptome
- Tumor growth inhibition after intra-tumoral administration
- Reduction of downstream signaling validates target engagement
RNA TARGETING OF KRAS

- Engaging RNA to inhibit translation

Adapted from Muangkaew and Vilaivan, Bioorg Med Chem Lett 2020; 30:127064

IN VIVO TUMOR GROWTH INHIBITION VIA RNA TARGETING OF G12D MUTATION

G12D is the most prevalent mutation¹ accounting for 33% of KRAS mutations in patients

Inhibition of tumor growth after 0.3 mg/kg intra-tumoral injections into HPAFII heterozygous pancreatic cancer xenografts

8 days after first dose until statistically significant growth inhibition achieved

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

¹Papke B et al. ACS Pharmacology & Translational Science. 2021
IN VIVO MUTANT KRAS KNOCK-DOWN DECREASES DOWNSTREAM SIGNALING

Reduction in phosphorylation levels of multiple pathway members in oncogenic cascade

IN VIVO TUMOR GROWTH INHIBITION VIA RNA TARGETING OF G12V MUTATION

G12V is the second most prevalent mutation, accounting for 23% of KRAS mutations in patients

Inhibition of tumor growth after 0.3 mg/kg intra-tumoral injections into CAPAN-2 heterozygous pancreatic cancer xenografts

3 doses leads to prolonged tumor growth inhibition

Papke B et al. ACS Pharmacology & Translational Science. 2021
DNA TARGETING OF KRAS

- Engaging DNA to inhibit transcription

SELECTIVITY FOR G12D RAS PROTEIN KNOCK-DOWN VIA DNA TARGETING

- Evidence for invasion of dsDNA in vitro
- Inhibition of transcription of mutant allele
- ~90% of mutant protein knockdown relative to wild-type
KEY ADVANCEMENTS

• New program initiated in 2021
• Allele-selective target engagement of KRAS G12D and G12V
• Target engagement of the genome and the transcriptome
• Tumor growth inhibition after intra-tumoral administration
• Reduction of downstream signaling validates target engagement

KRAS PROGRAM: THE PATH FORWARD

- Optimization of tumor delivery & target engagement
- Select target tumor types
- In vivo translational profiling
- Power towards the clinic
KEY TAKE-AWAYS FROM TODAY

Peptide nucleic acids have the potential to be best-in-class

**Myotonic dystrophy, type 1 (DM1)**
Functional rescue of myotonia after subcutaneous dosing positions us for 2022 IND
- Designed to maintain DMPK protein
- Patient-friendly route of administration

**Huntington’s disease (HD)**
Selective reduction of mutant huntingtin protein in the brain after subcutaneous dosing
- Potential for uniform brain distribution & whole-body solution
- Preferable route over intrathecal administration

**Oncology (KRAS)**
Allele-selective engagement of G12D and G12V in vitro, and tumor growth inhibition in vivo
- High-value oncology targets previously considered “undruggable”
- Four months from inception to proof-of-principle

NEUBASE WELCOMES DR. ROJAS-CARO AND MOTESHAReI

*Sandra Rojas-Caro, M.D.*
Chief Medical Officer

*Kia MoteshaRei, Ph.D.*
Chief Business and Strategy Officer
DELIVERING ON THE PROMISE

Rapid execution
Company operating for 24 months & plans to be in the clinic next year

In vivo proof-of-principle
Functional and/or molecular rescue in 3 diseases & well tolerated at pharmacological doses

Three high value indications
Selection of 3 high value indications in wholly unmet patient needs

On track to the clinic in 2022
DM1 program expected to enter Phase 1/2 in 2022

neubase
A new class of ultra-precision genetic medicine

Drugging the genome to increase, decrease, or edit protein function to address base causality in disease