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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.

AGENDA

12:30	Welcome and Overview	**Curt Bradshaw, Ph.D.** Chief Scientific Officer
12:45	Peptide Nucleic Acids	**Peter Nielsen, Ph.D.** Scientific Advisory Board
1:00	Myotonic Dystrophy, Type 1 (DM1)	**Dietrich Stephan, Ph.D.** Chairman, CEO and founder
1:15	Huntington's Disease (HD)	**Robert Friedlander, M.D.** Scientific Advisory Board
1:30	Oncology (KRAS G12D and G12V)	**Dani Stoltzfus, Ph.D.** Head of Chemistry Division
1:45	Summary and Q&A	**The NeuBase Team**

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

Broad therapeutic potential

Up to ~7,000 rare diseases affecting ~10% of global population[1]; An estimated 1.9 million new cancer cases diagnosed and ~600,000 cancer deaths in the US alone in 2021[2]

Address root causality

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

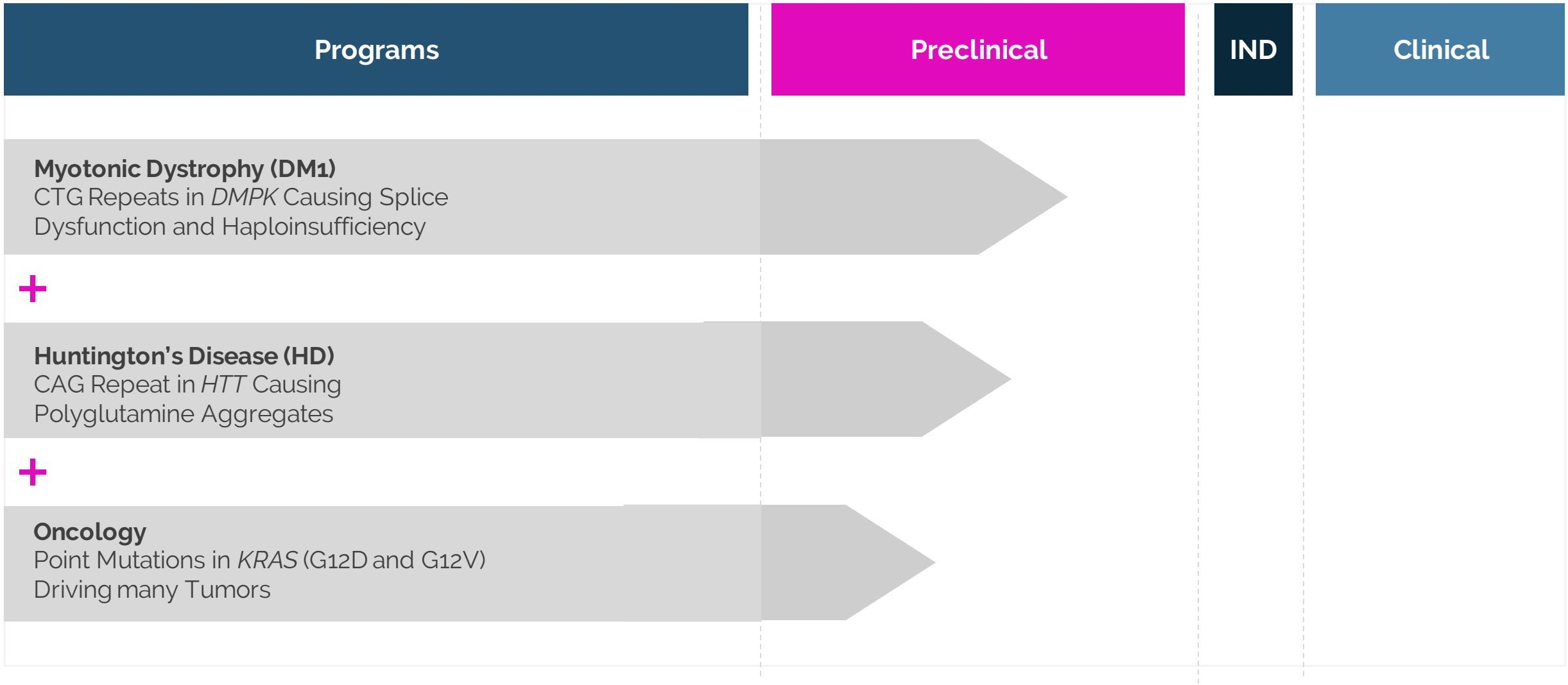
Approaching clinical stage with an emerging pipeline

DM1 program expected to enter Phase 1/2 in 2022[1], with HD and KRAS programs in pre-clinical development

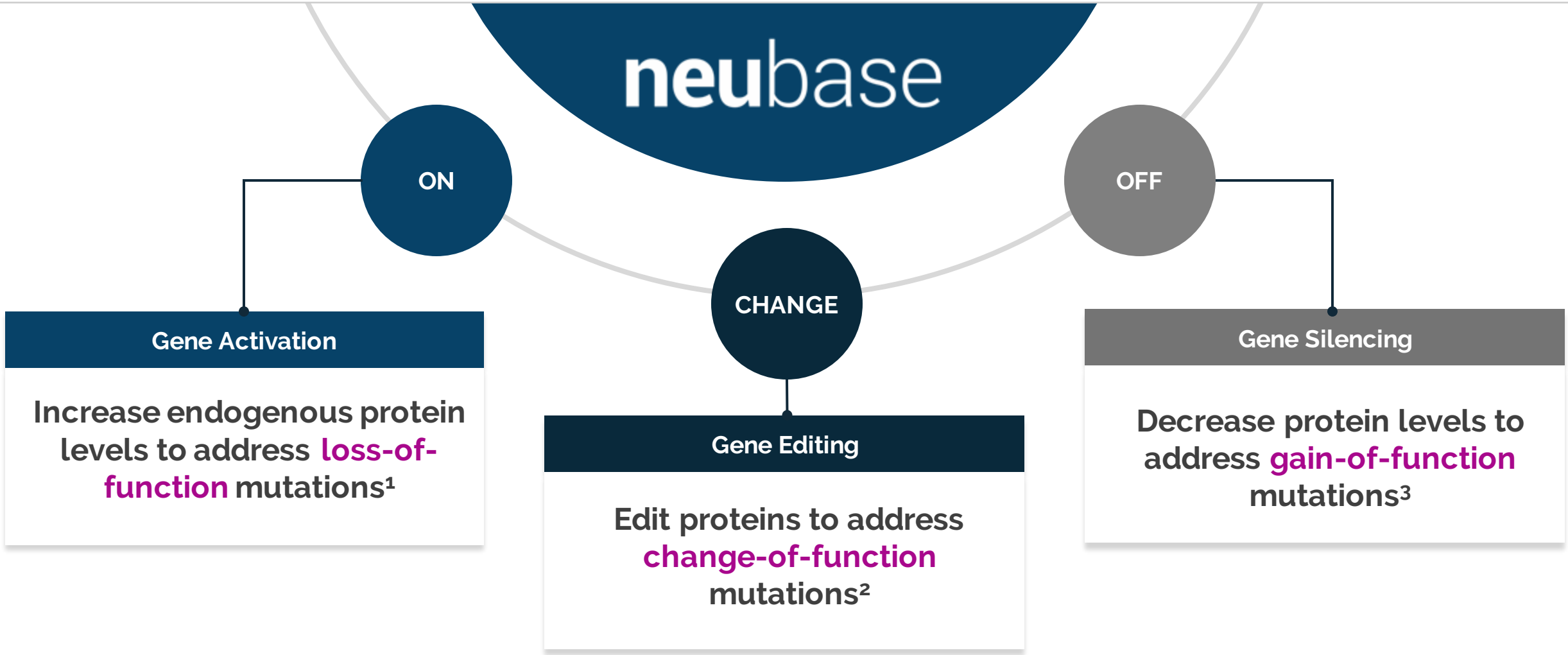
[1]https://globalgenes.org/; [2]www.cancer.org

[1]Calendar year

PIPELINE



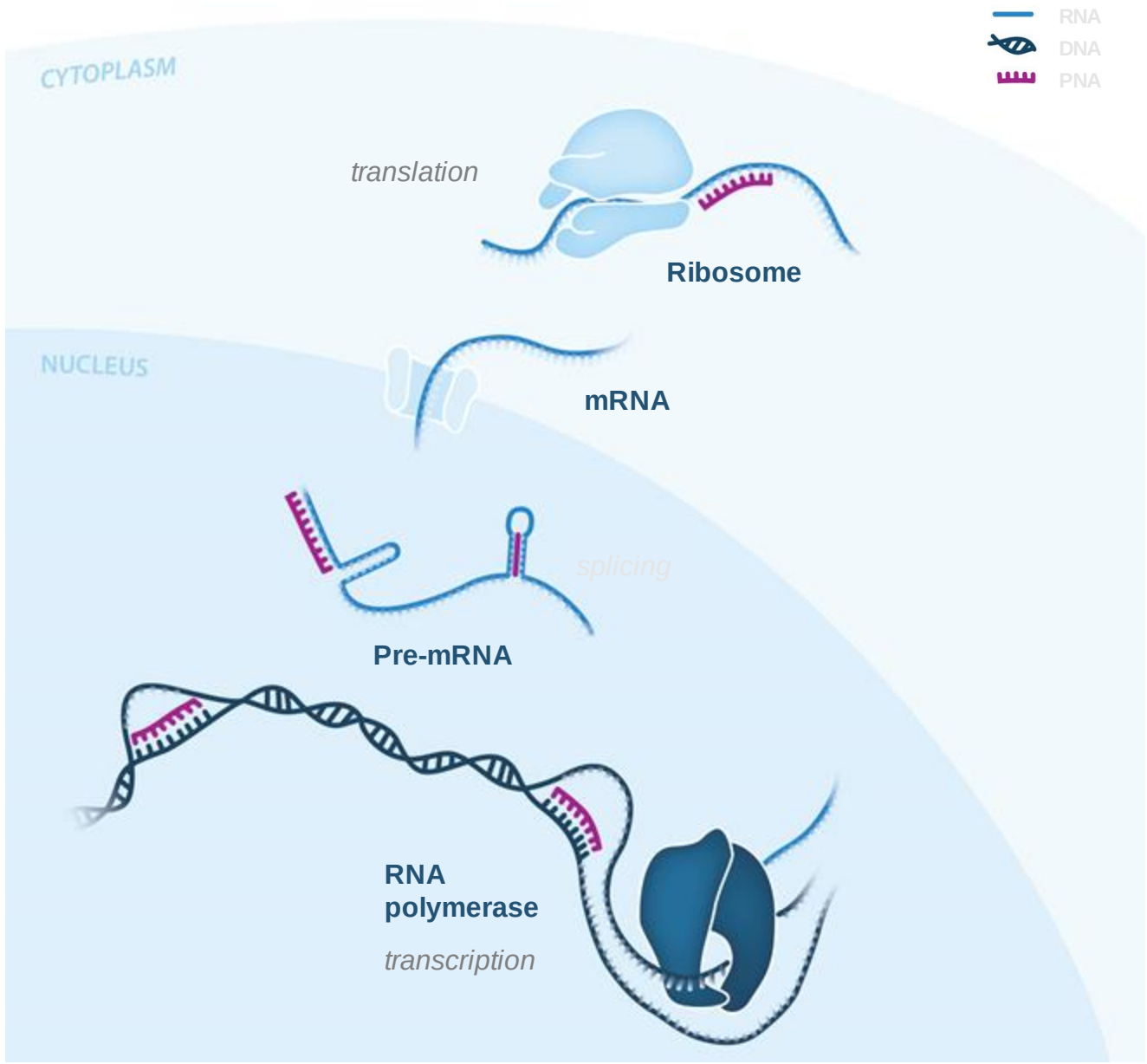
PATROL™ PLATFORM



[1]Wang G *et al. Nucleic Acids Res*. 1999;27(13):2806-2813; [2]Ricciardi AS *et al. Nat Commun*. 2018;9(1):2481; [3]Thomas SM *et al. ACS Chem Biol*. 2013;8(2):345-352

HOW WE DO IT

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



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

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[1] 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

[1]Calendar year

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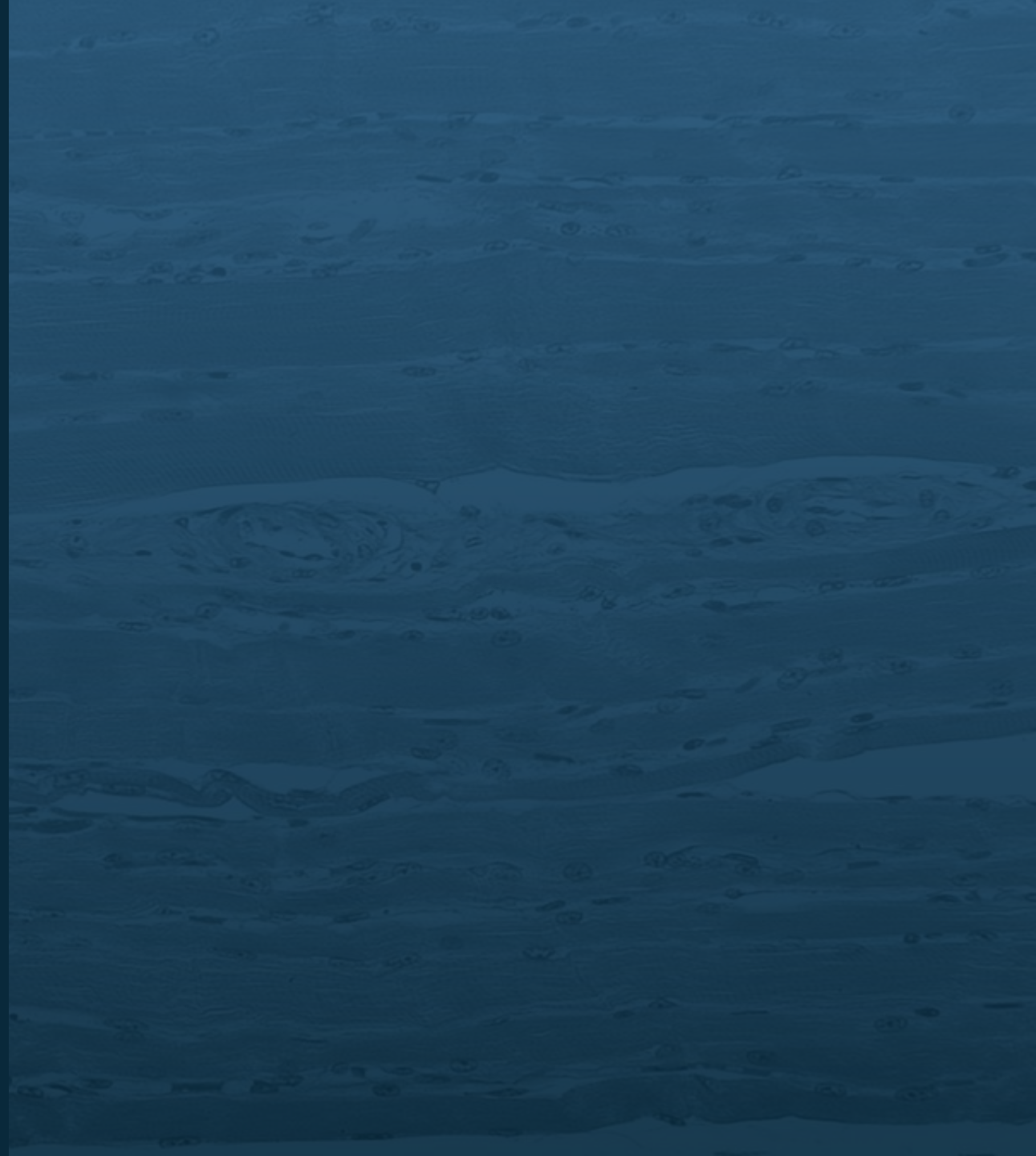
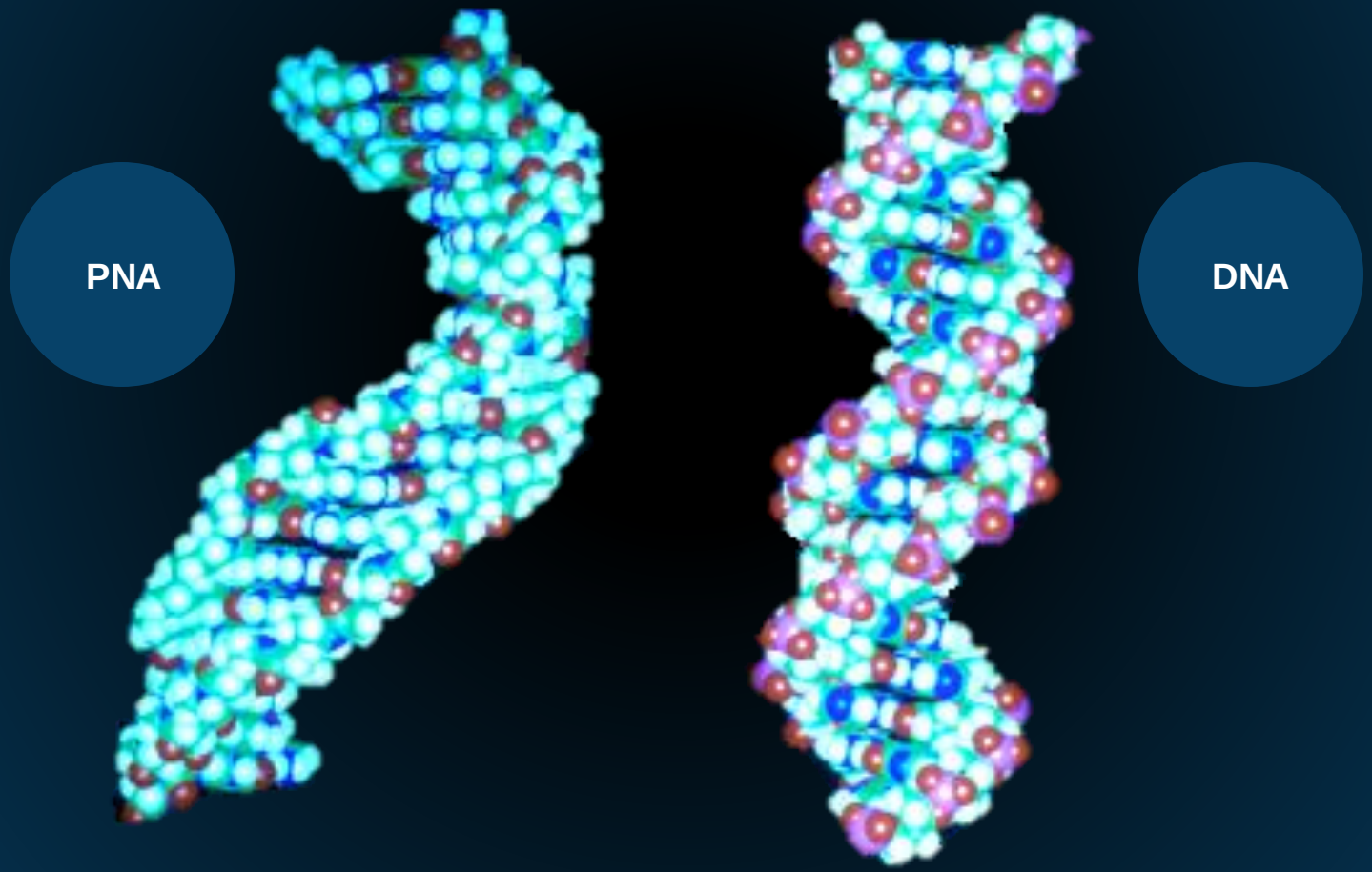
PROF. PETER NIELSEN



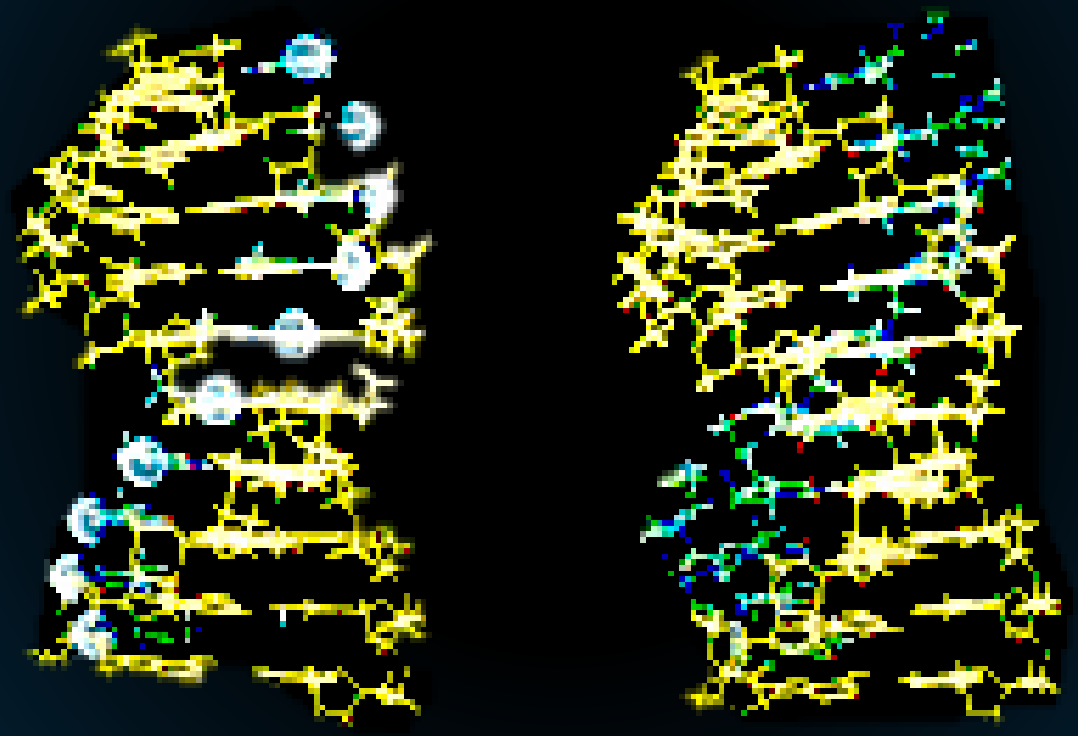
PETER E. NIELSEN, PH.D.

- 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)

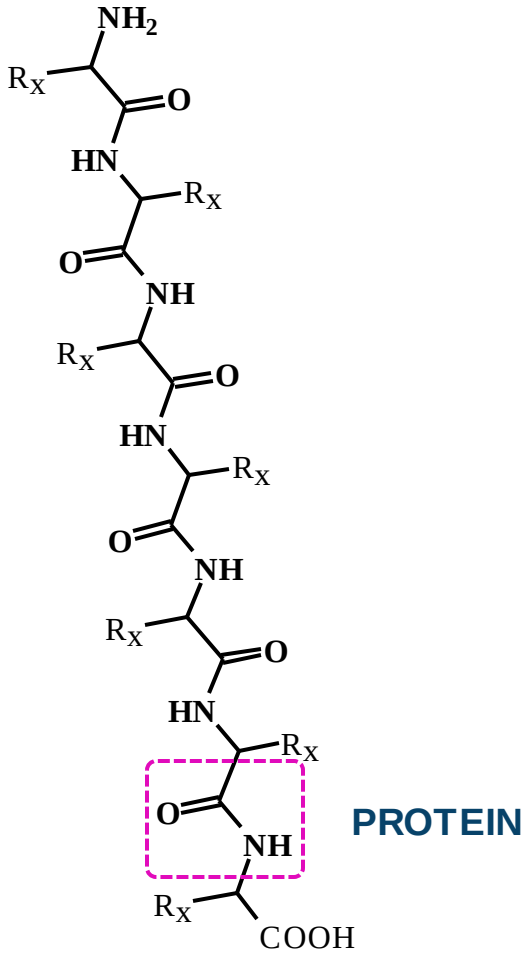
30 YEARS OF PNA

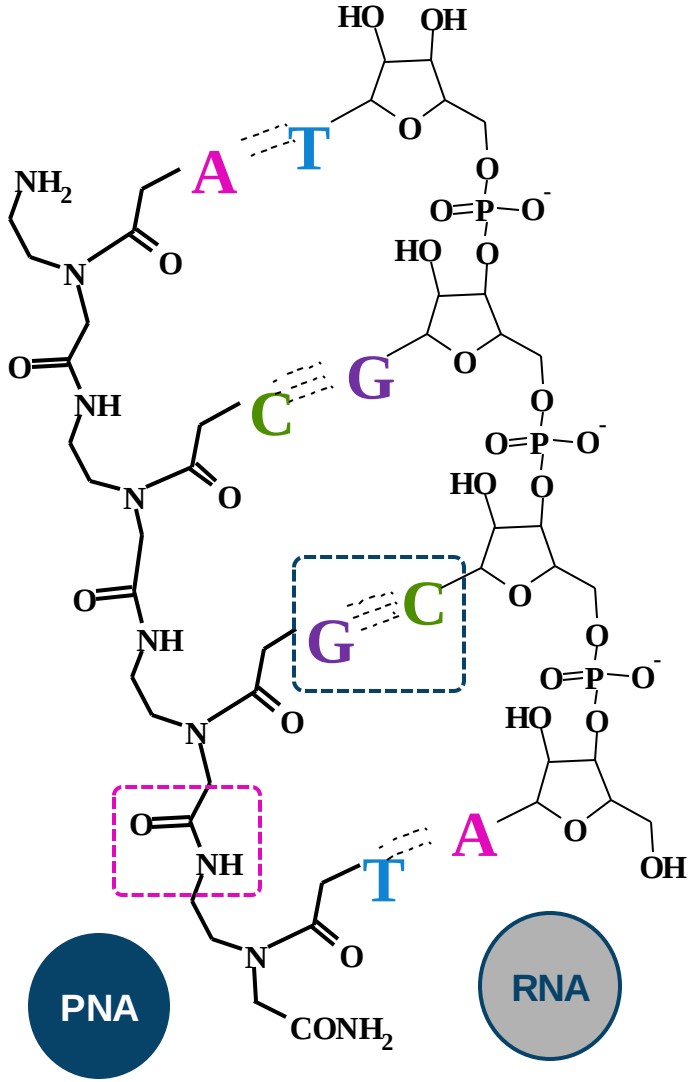


PNA DESIGN



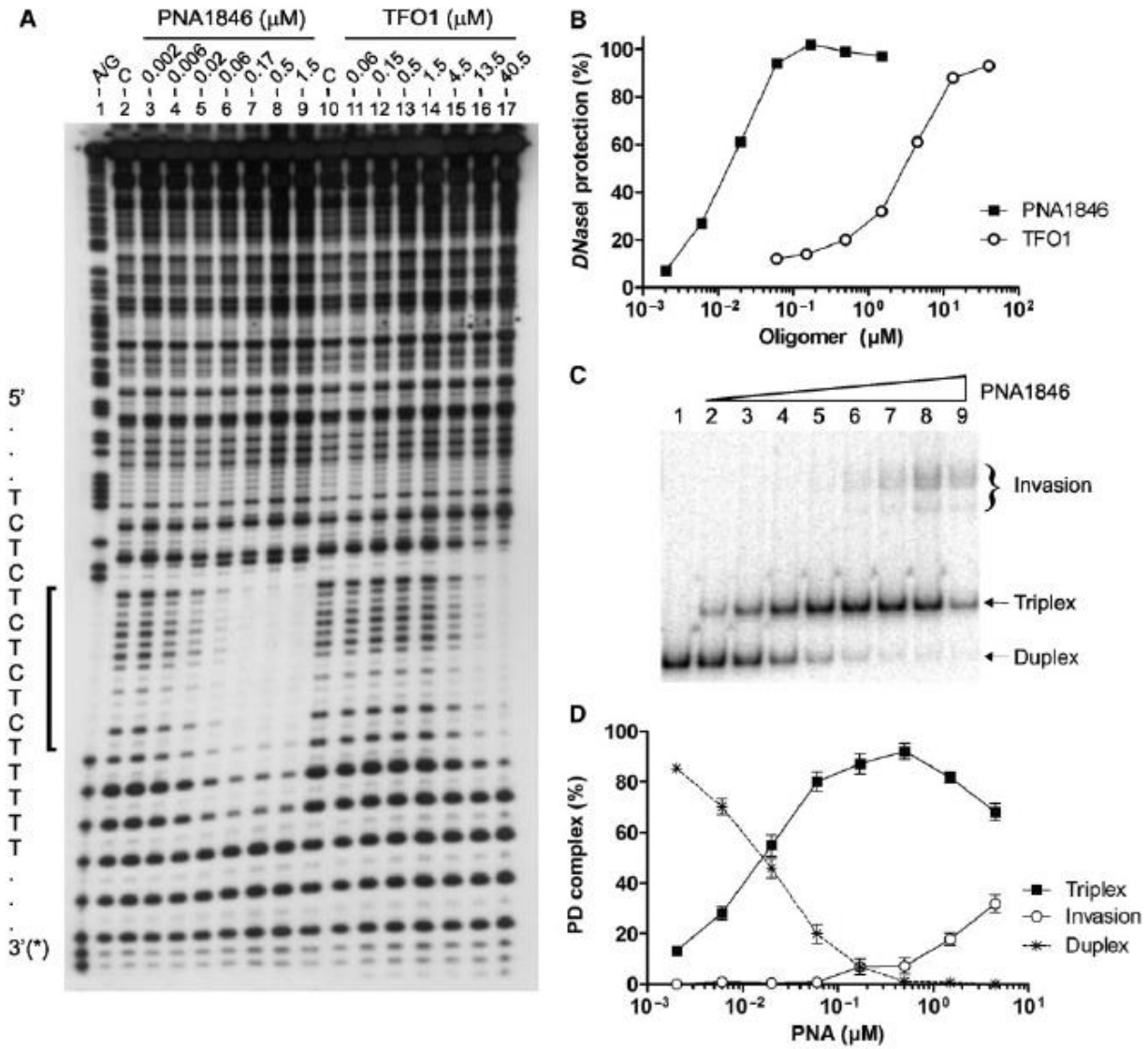
PEPTIDE NUCLEIC ACIDS (PNA)





PNA DSDNA BINDING

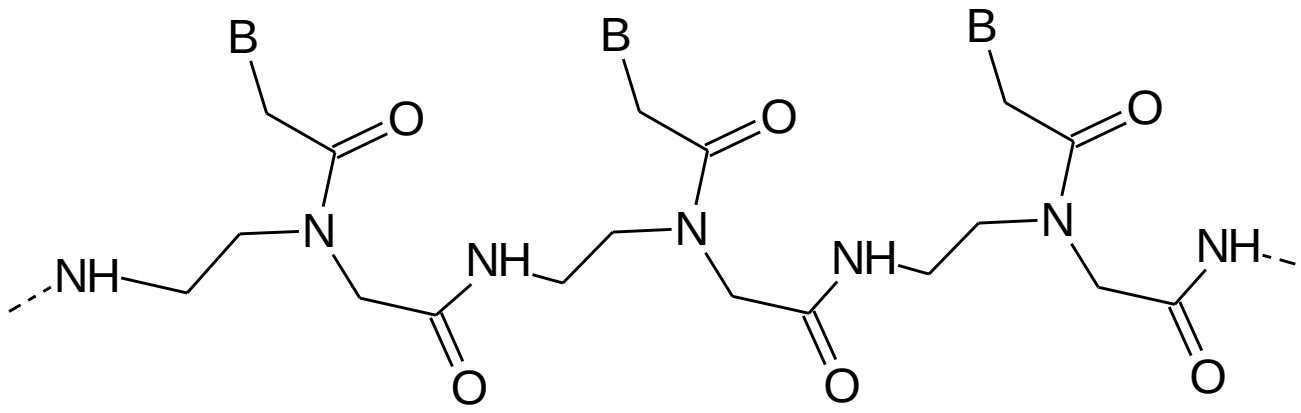
- Nanomolar triplex affinity
- >100x higher than DNA
- Triplex >100x faster than invasion



Hansen ME *et al*. *Nucleic Acids Res*. 2009;37(13):4498-4507

PNA PROPERTIES: CHEMISTRY

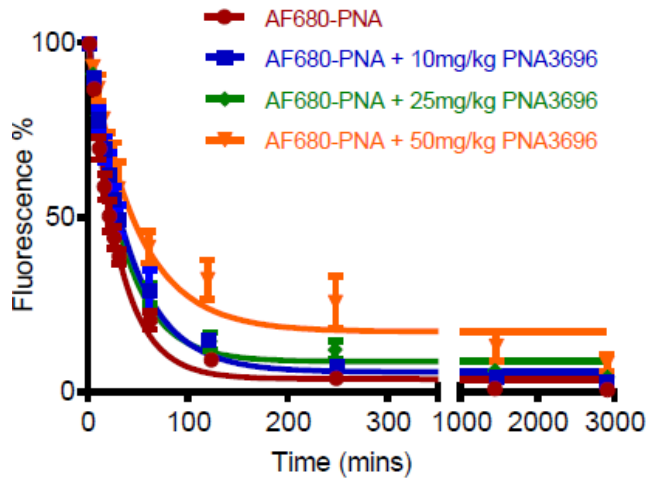
- Oligomers are synthesized by conventional solid phase peptide chemistry
- Charge neutral, generally hydrophilic and water soluble
- Chemically and biologically stable

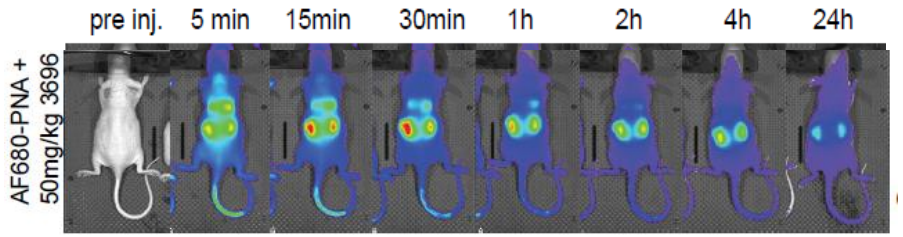


Egholm M *et al*. *J Amer Chem Soc* 1992 *114* (5), 1895-1897; Christensen L *et al*. *J Pept Sci*. 1995;1(3):175-183; Demidov VV *et al*. *Biochem Pharmacol*. 1994;48(6):1310-1313

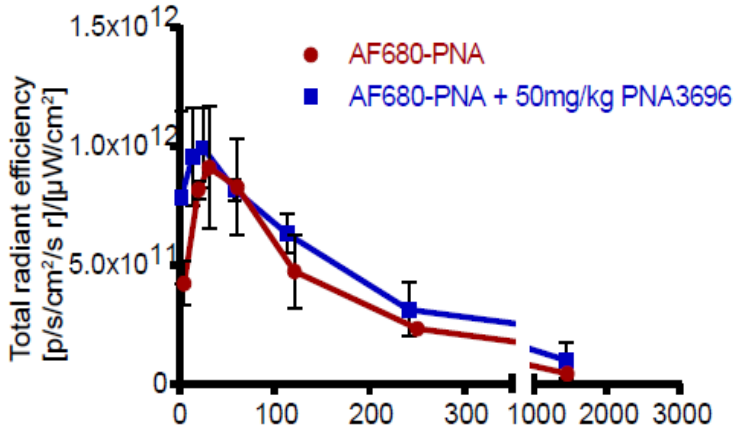
IN VIVO ADMINISTRATION AND PK

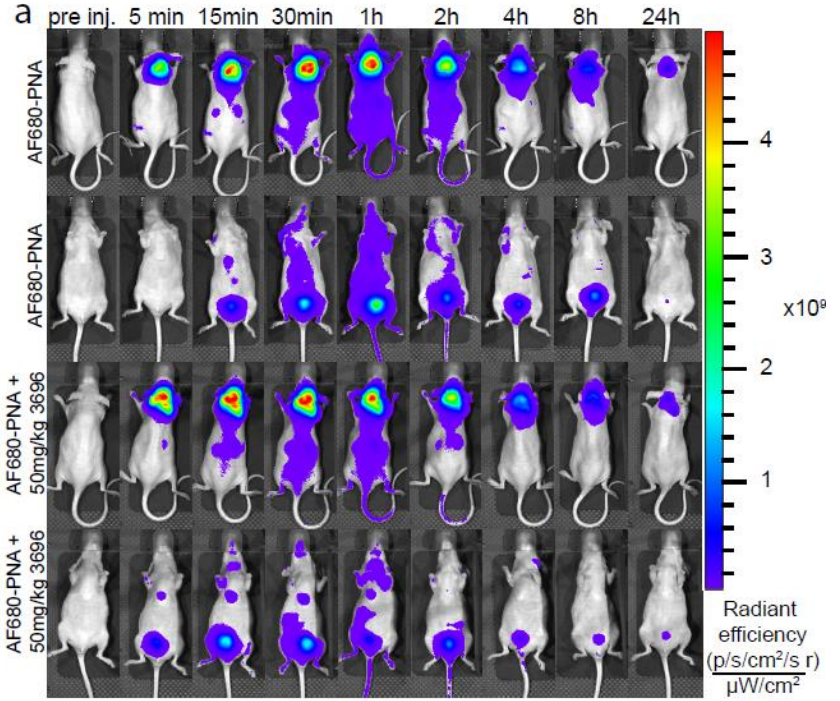
IV administration: $t_{½}$ 30min





SC administration: $t_{½}$ 120min



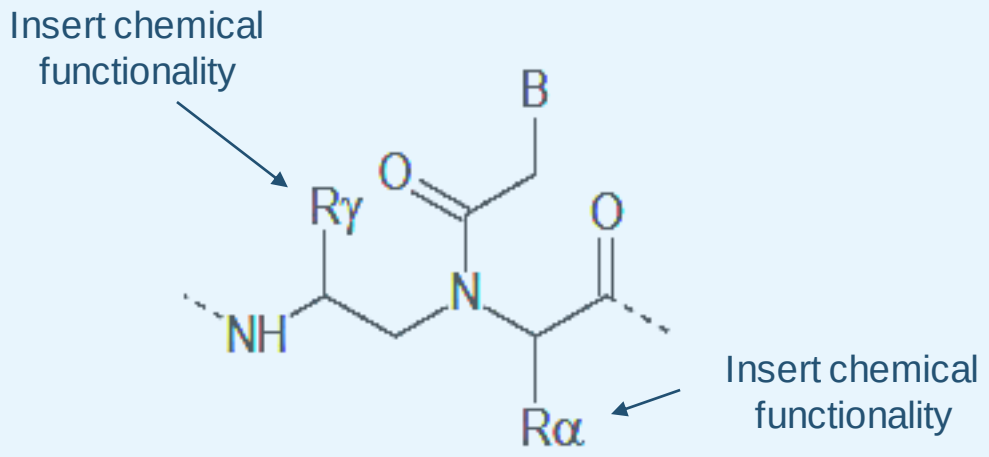


Brolin *et al*. *Nucleic Acid Ther*, 2020. doi: 10.1089/nat.2020.0856

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

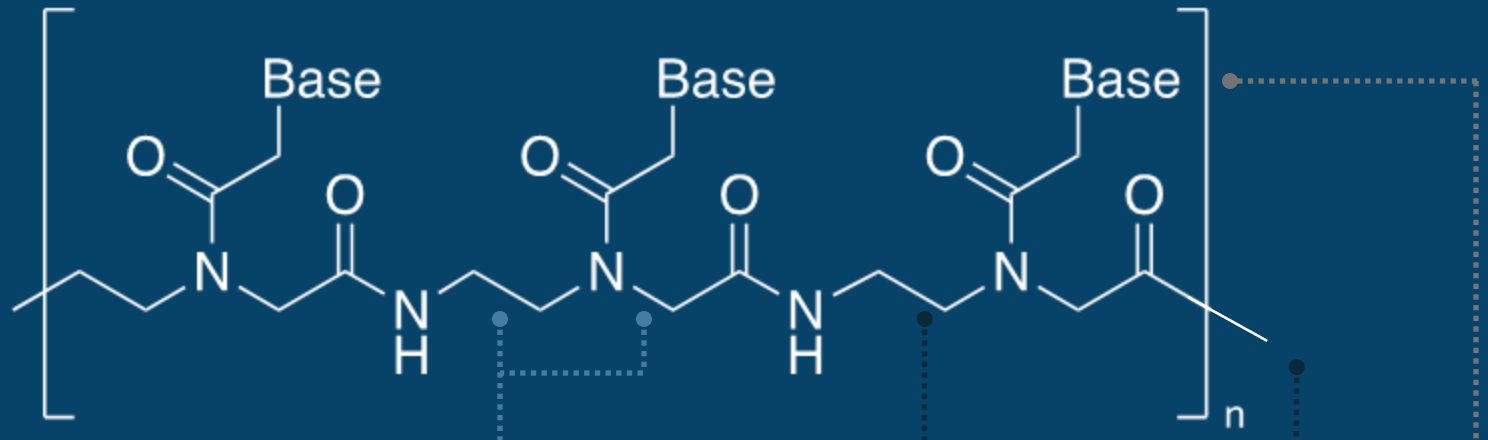
Functional backbone decoration



PREVIOUS CHALLENGES

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

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



Scaffold Modifications

- Tunable for RNA or DNA targets
- Tunable binding affinity
- ADME/Tox optimization

Delivery Domains

- Efficient intracellular delivery
- Tissue targeting
- ADME/Tox optimization

Base Modifications

- Tunable specificity and affinity
- Tunable for RNA or DNA targets
- Optimize biophysical properties

WHY

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

MYOTONIC DYSTROPHY TYPE 1 (DM1)

POTENTIAL TO BE BEST-IN-CLASS IN DM1

2021

Preclinical execution[1]

- 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[1]

[1]Calendar year

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[1]

70-80%

of congenital onset patients require mechanical ventilation, with mortality rates between 15-20%[2]

DM1 is a dominantly inherited disease defined by a repeat expansion in the *DMPK* gene with severity defined by expansion size[3]

1 out of 20,000

are affected by DM1 globally[4]

0

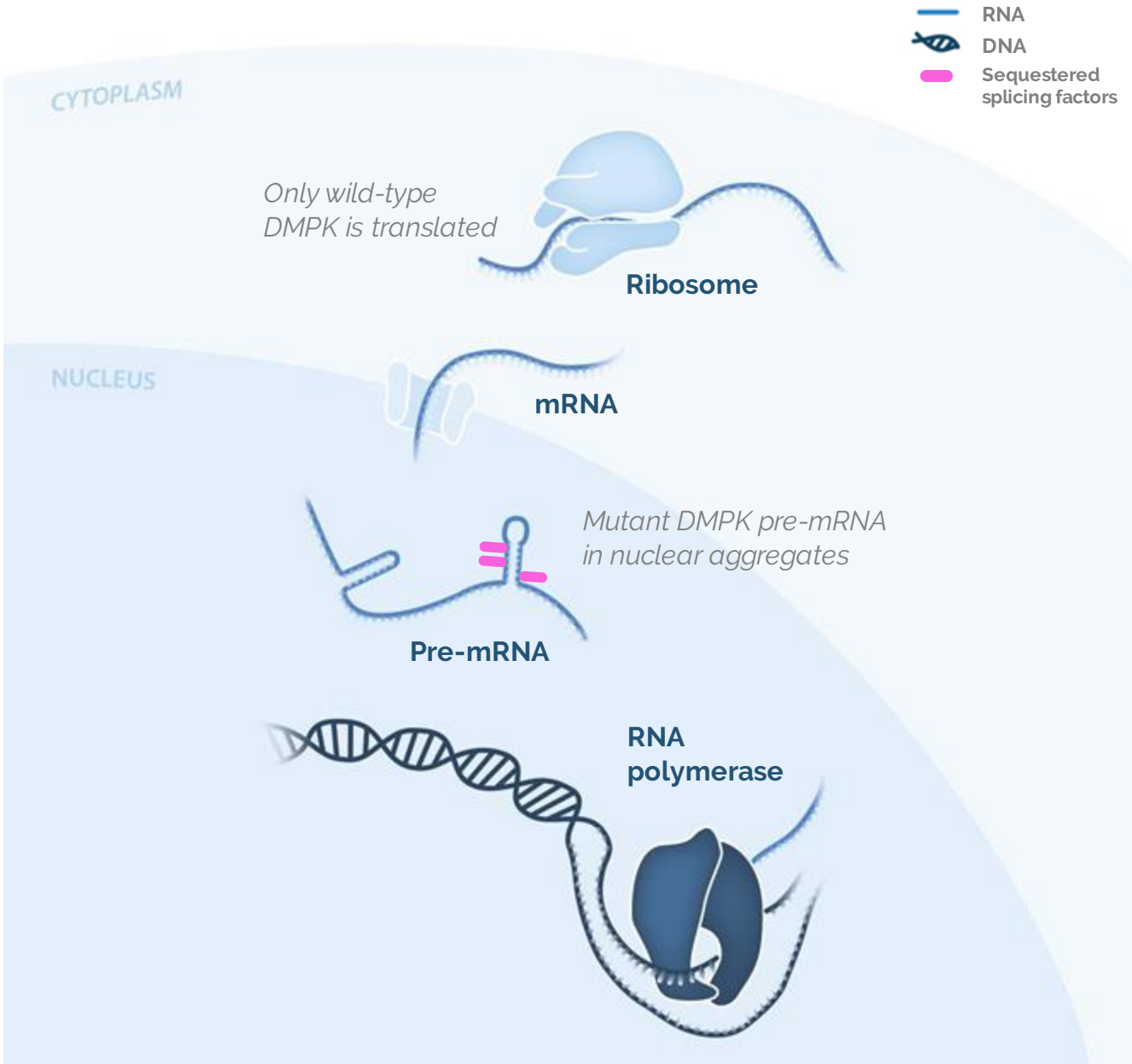
currently approved therapies that alter the natural history of DM1

[1]https://www.myotonic.org; [2]https://www.mda.org; [3]Mahadevan M et al. *Science*. 1992 Mar 6;255(5049):1253-5. [4]Bird TD. 1999 Sep 17 In: Adam MP *et al*., editors. GeneReviews®; 1993-2021. Metrics are approximate.

DISEASE PATHOGENESIS

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

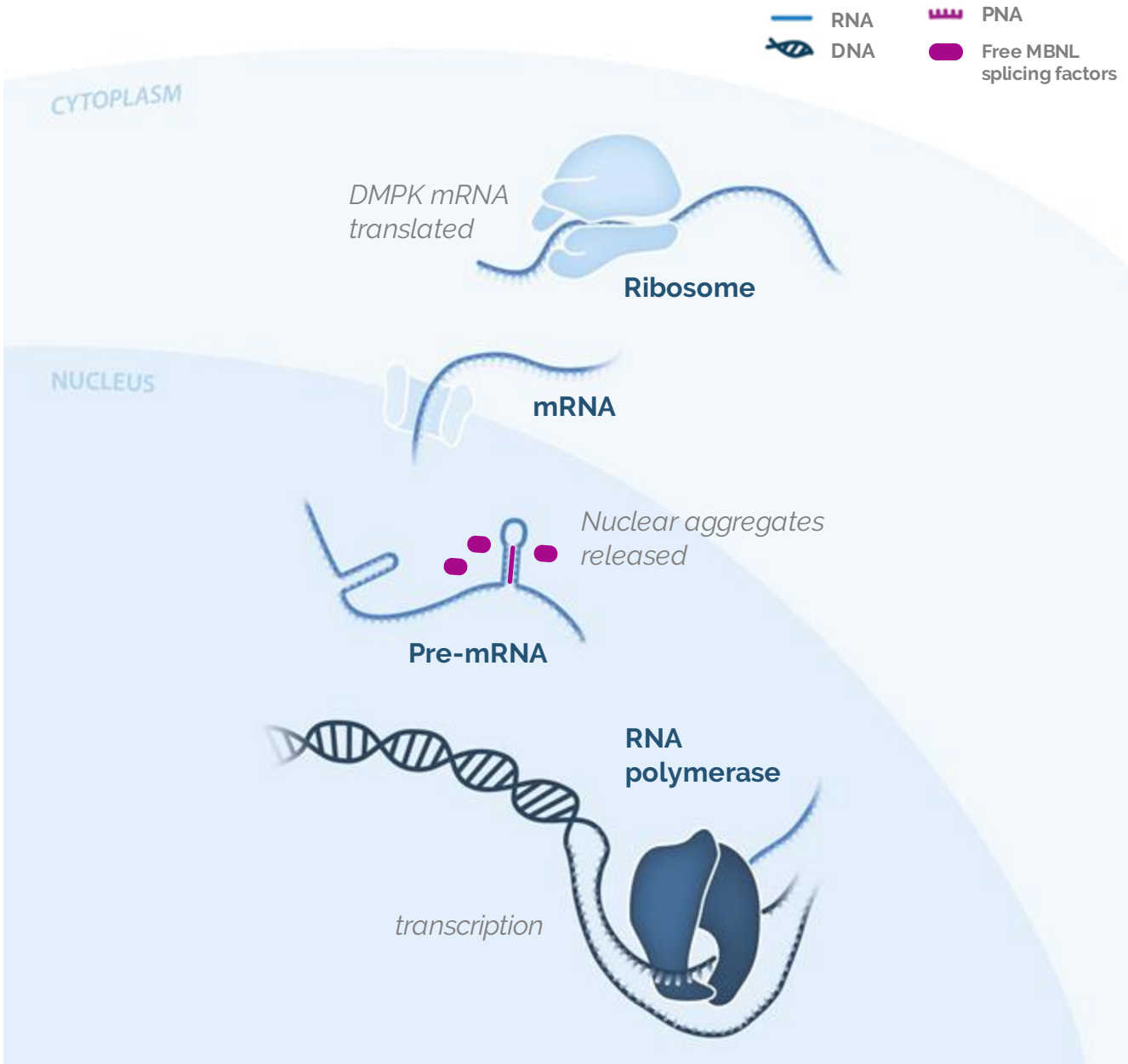
- Hairpins form nuclear aggregates together with MBNL splice proteins
- Results in widespread mis-splicing of pre-mRNAs
- Produce altered proteins which are dysfunctional in adults



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

KEY ADVANCEMENTS TOWARD THE CLINIC

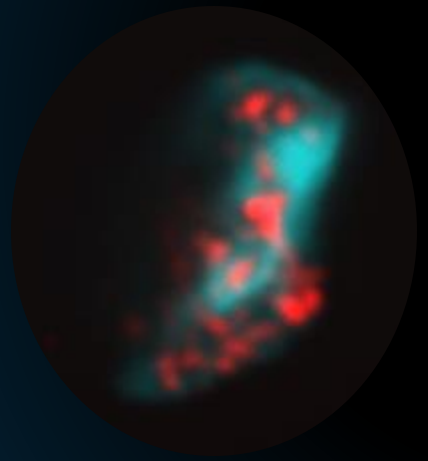
December 2020: splice rescue in patient cells, while maintaining DMPK protein levels, and *in vivo*

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

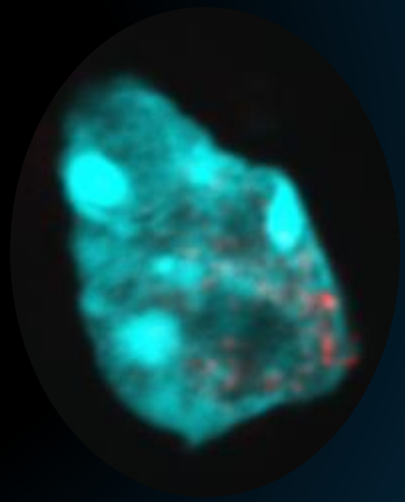
- Reduce nuclear aggregates in muscle
- Well tolerated at pharmacologically active doses
- Rescue:
  - Splicing defects across many transcripts, including muscle chloride channel
  - Muscle chloride channel protein expression
  - Myotonia (3 mg/kg subcutaneous dose)

NUCLEAR INCLUSIONS ARE REDUCED IN HSA^{LR} MUSCLE AFTER DOSING

Vehicle



Single Dose*, Day 21



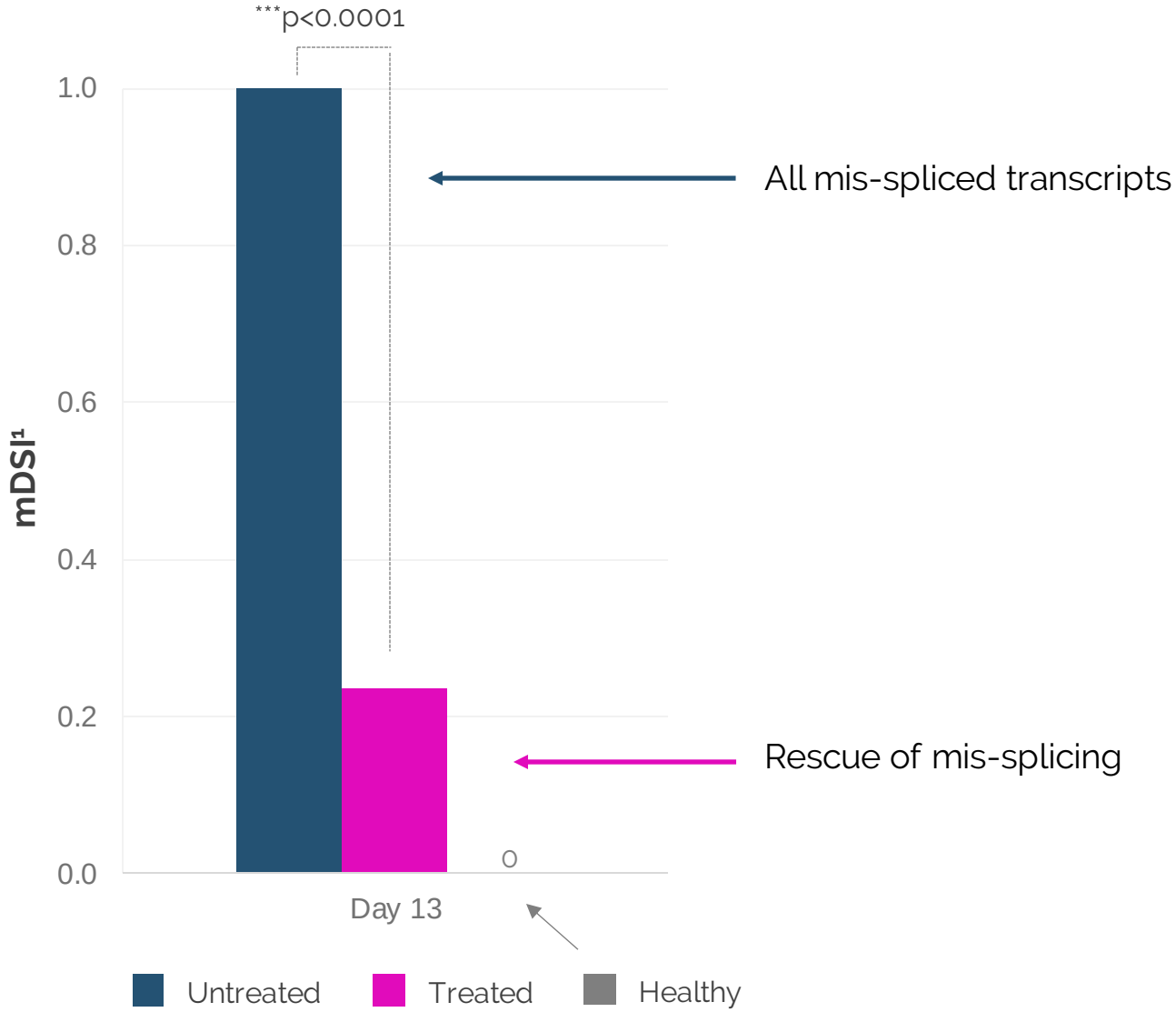
*29 mg/kg iv

MIS-SPLICING CORRECTED *IN VIVO*

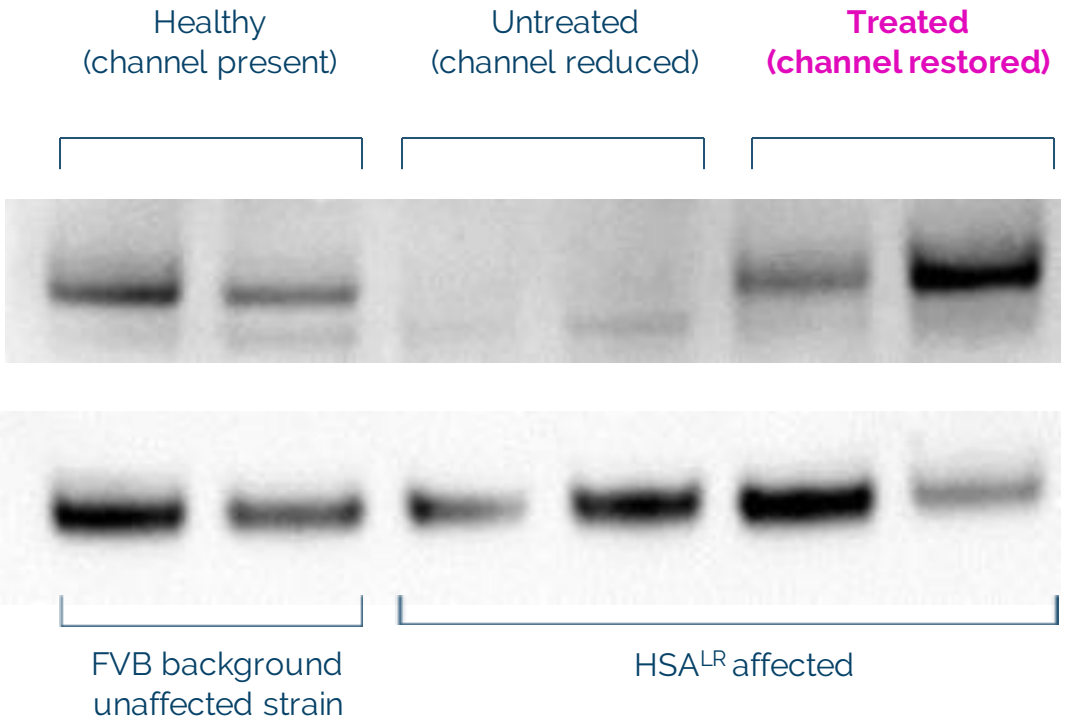
Single Dose
administered IV at 29 mg/kg in the HSA^{LR} mouse

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

Clcn1
splice correction of myotonia-causing transcript



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



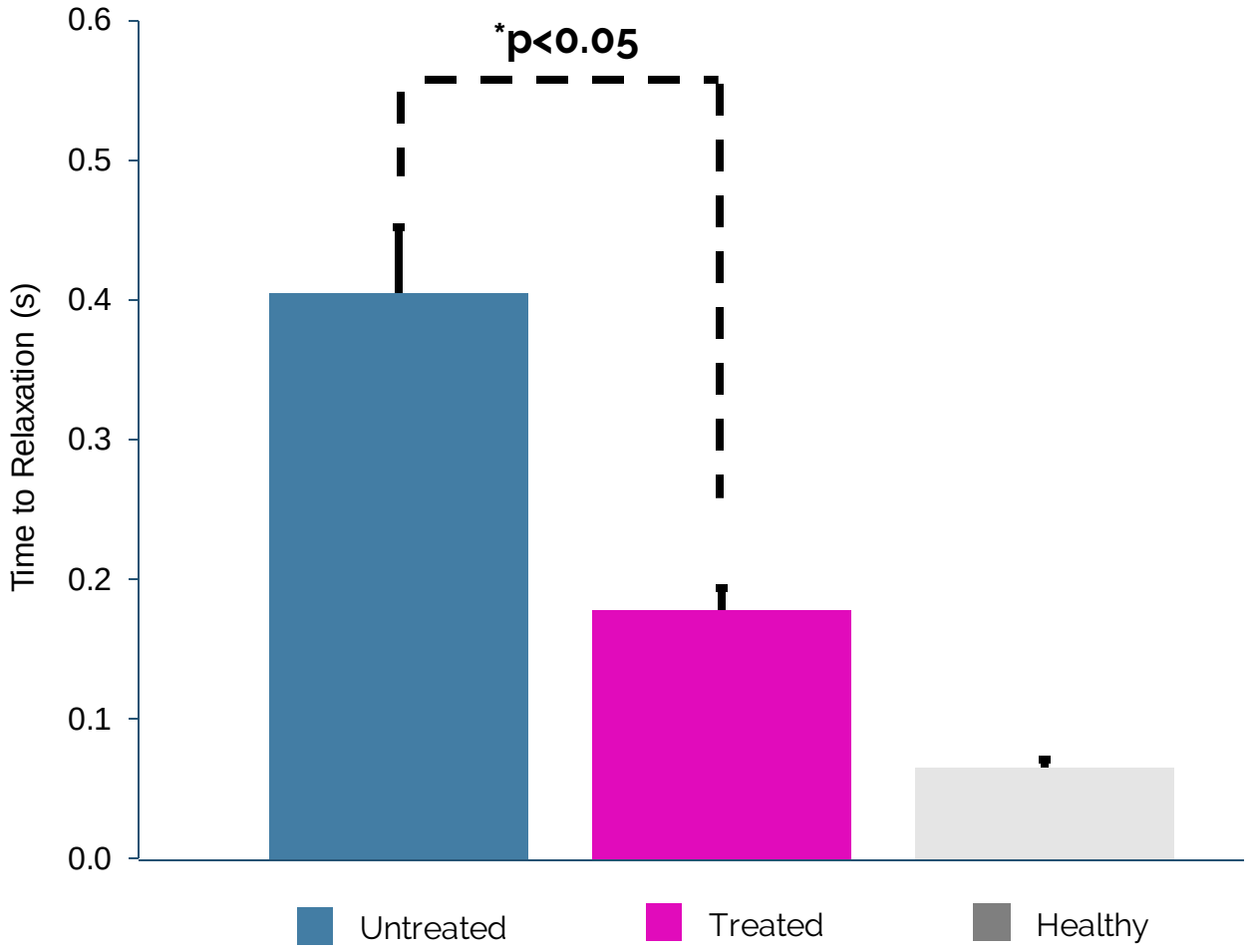
Single dose = 29mg/kg IV, western blotting from soleus muscle on day 20 after dosing

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



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ON TRACK TO FIRST CLINICAL STUDY IN 2022[1]

Initiated CMC process research

Initiate non-clinical toxicology

Ongoing PK/ADME

Pre-IND meeting

CLINIC

[1]Calendar year

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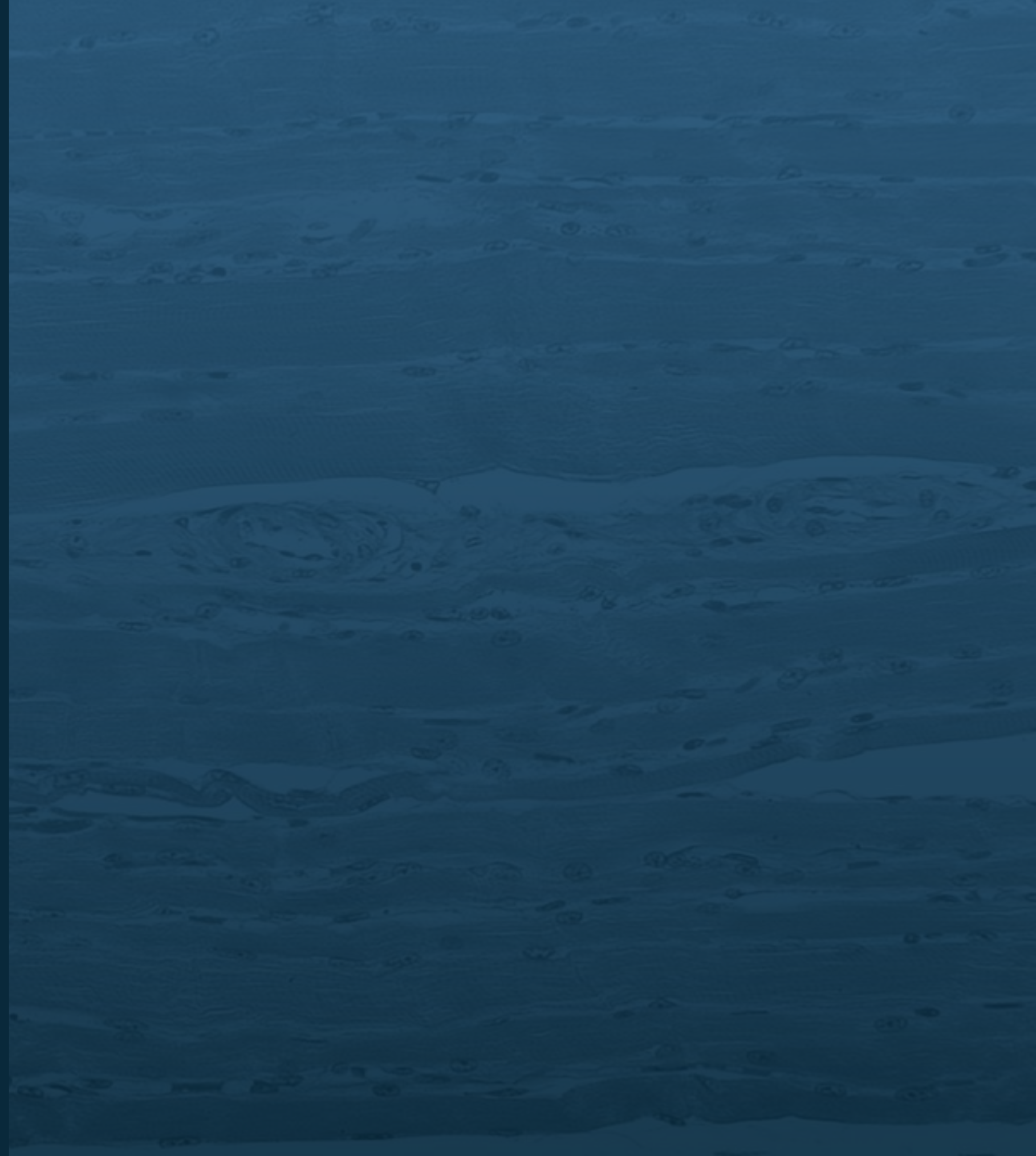
DR. ROBERT FRIEDLANDER



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

KEY ADVANCEMENTS

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[1]

Long poly-glutamine tract in the protein cause cell death

Progressive neurodegeneration

movement disorder, mood disturbances, cognitive impairment and a whole-body disorder

0

approved disease modifying therapies

15-20 years

is life expectancy after diagnosis[2]

41,000

HD cases in the US alone[3]

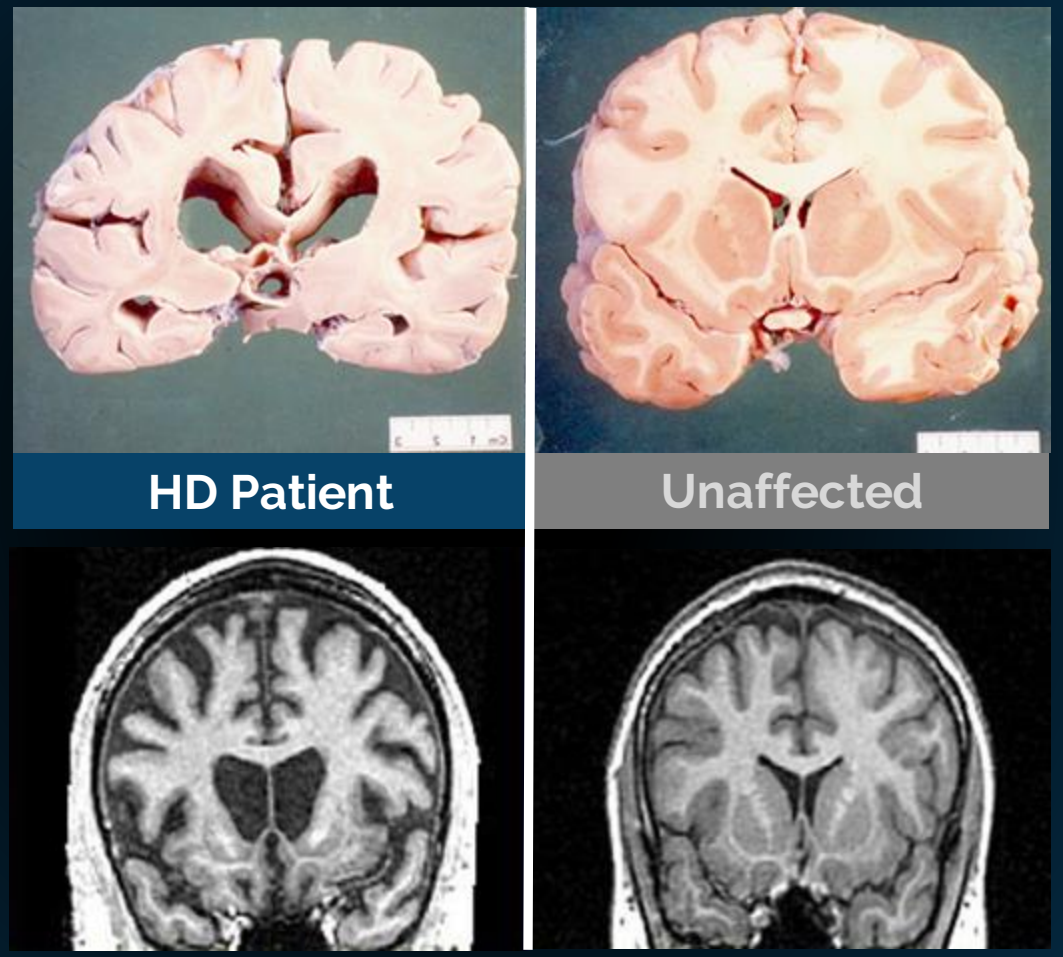
>200,000

at risk from the disease in the US alone[4]

[1]Pringsheim T *et al. Mov Disord*. 2012 Aug;27(9):1083-91; [2]Solberg OK *et al. J Huntington's Disease* 2018; 7(1): 77-86. [3]Yohrling G *et al. Neurology*. April 14, 2020; 94. [4]https://rarediseases.org. Metrics are approximate.

PRIMARILY KNOWN AS A PROGRESSIVE CNS DISEASE

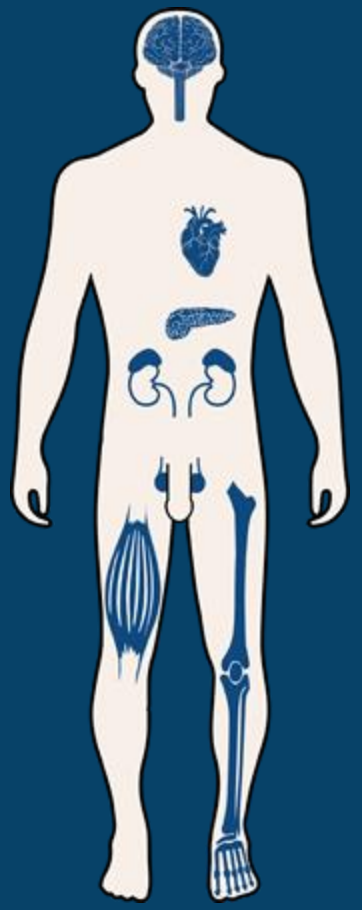
- Neuronal loss starts in the striatum and progresses to the cortex



Harper PS. *Huntington's disease.* London: W.B. Saunders, 1991

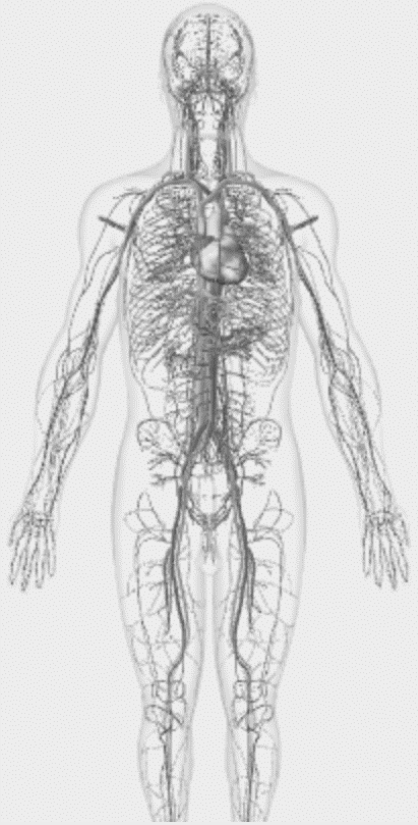
HD IS ALSO A WHOLE-BODY DISEASE

- 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



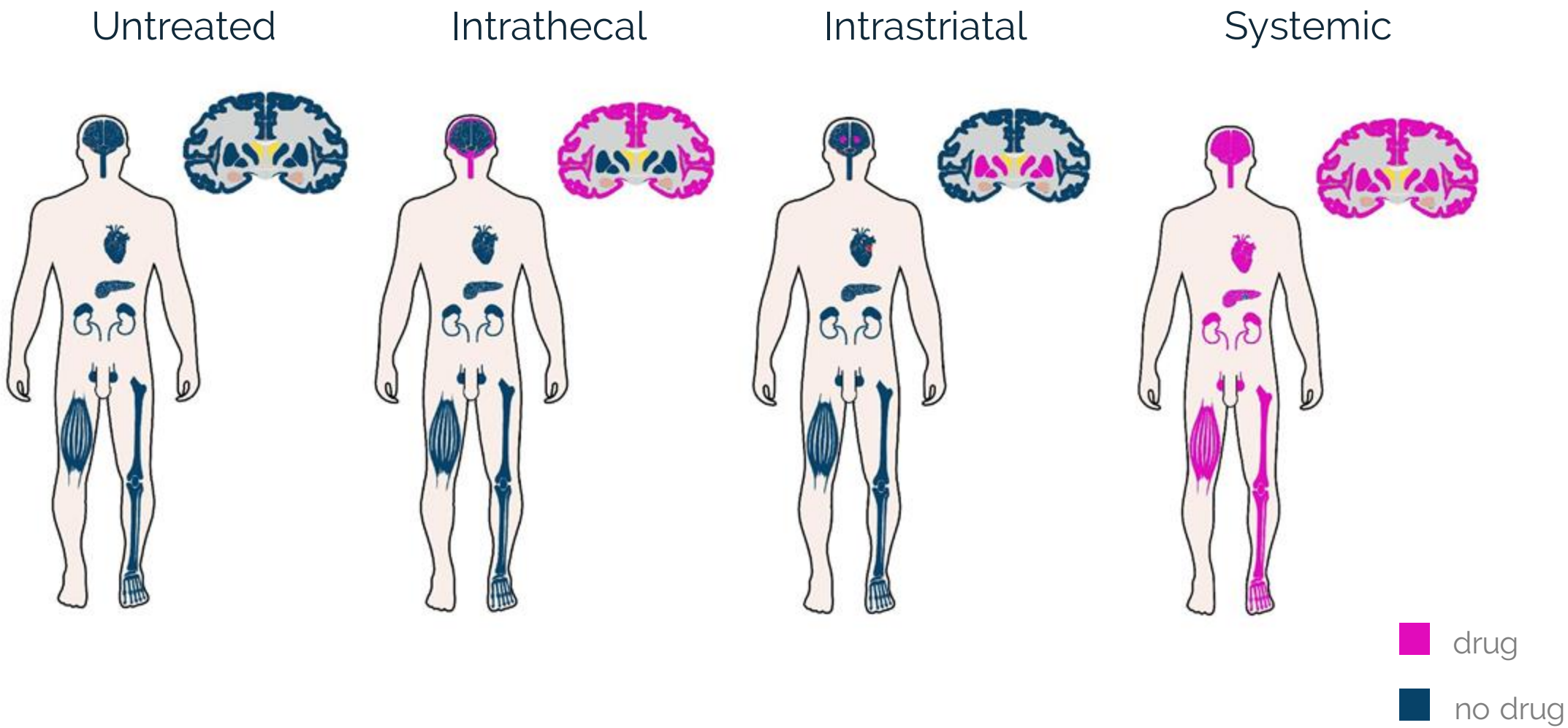
NORMAL HUNTINGTIN IS WIDELY EXPRESSED AND IMPORTANT FOR:

- 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

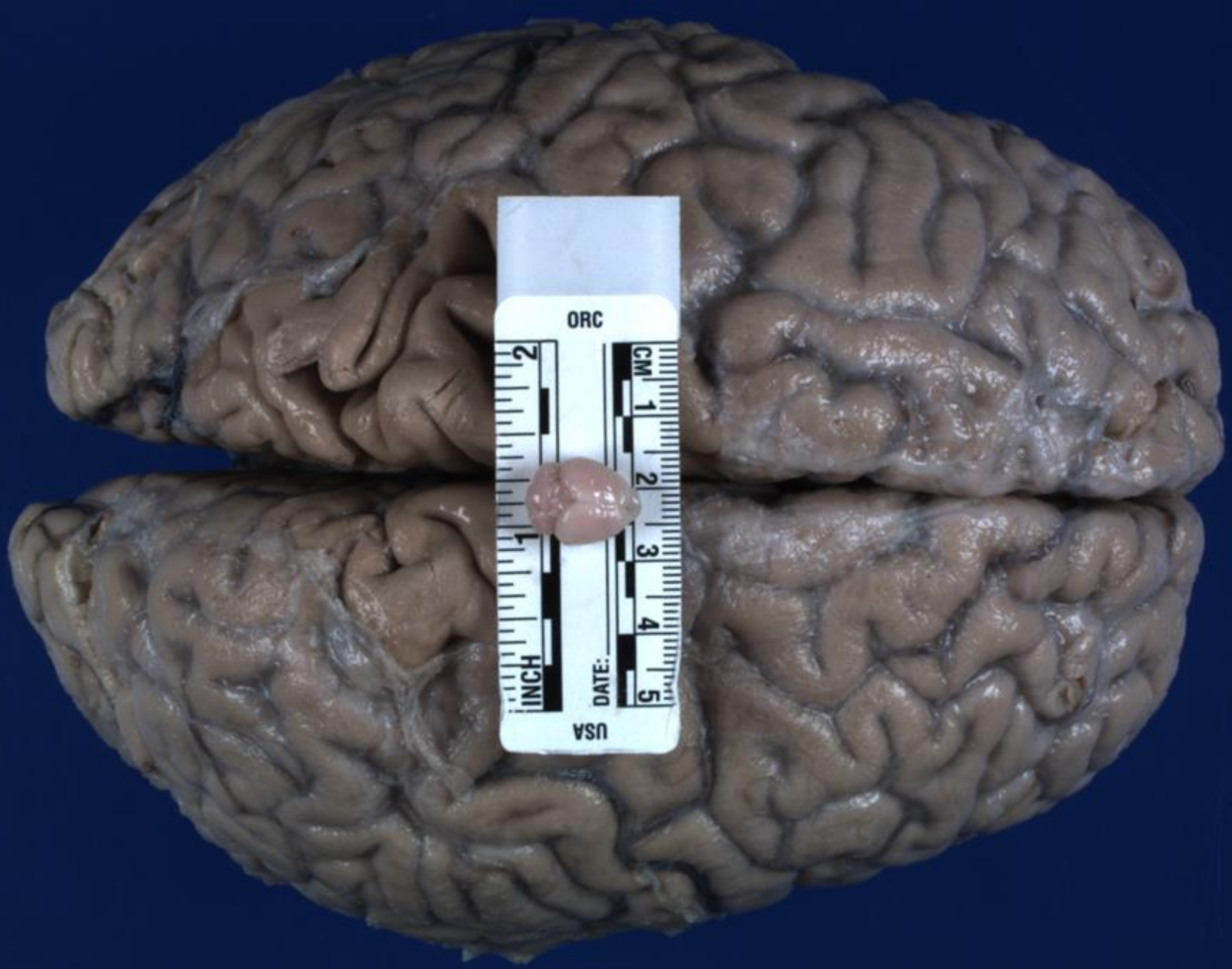
- Homozygous gene knock-out is embryonic lethal in mice
- Hemizygous mice demonstrate neurodegeneration in subthalamic nucleus and globus pallidus
- Postnatal protein reduction is detrimental

SYSTEMIC DOSING ENABLES A WHOLE-BODY SOLUTION



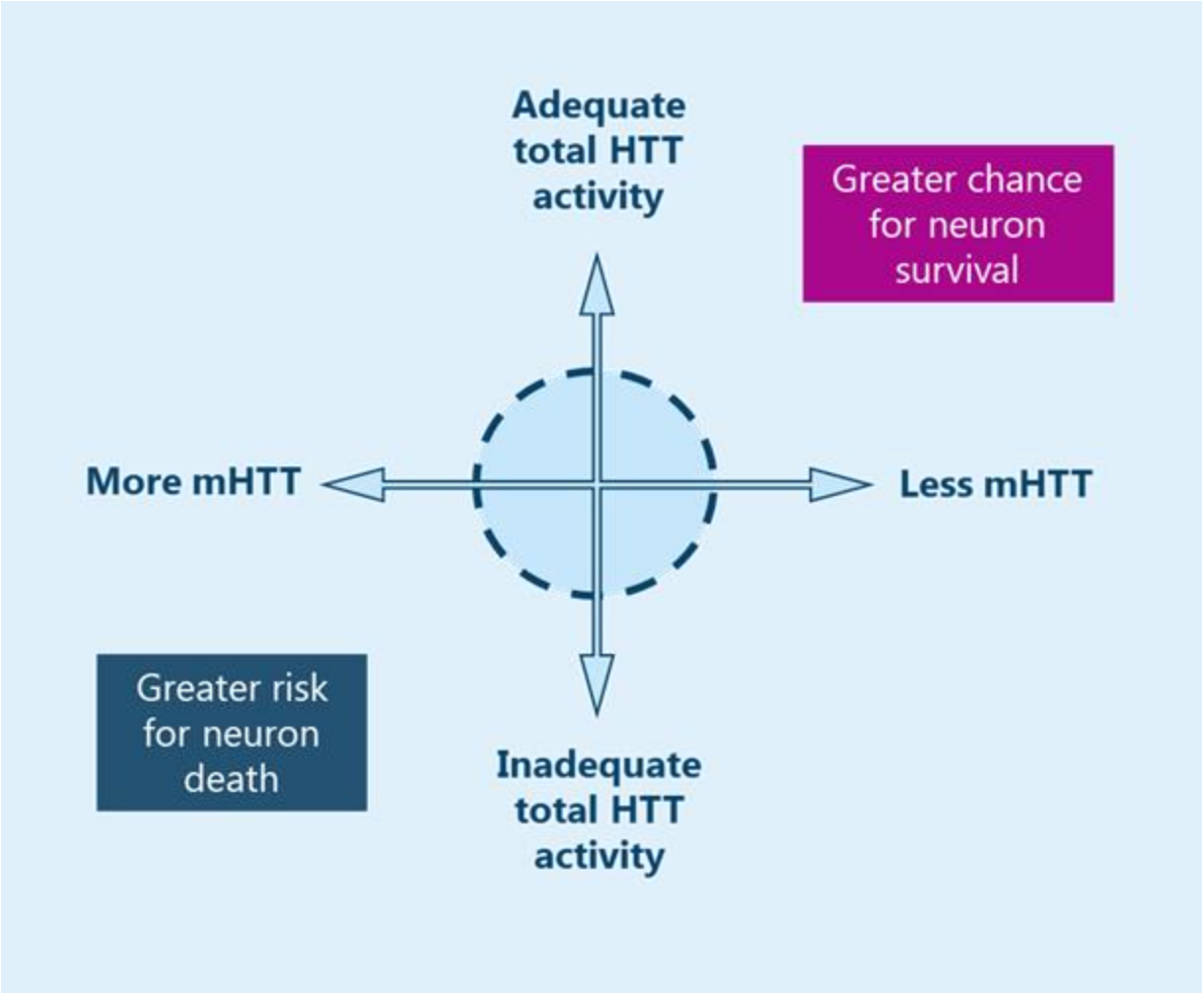
SIZE DIFFERENCES BETWEEN MOUSE AND HUMAN BRAIN

- Makes clinical translation of intrathecal administration results difficult

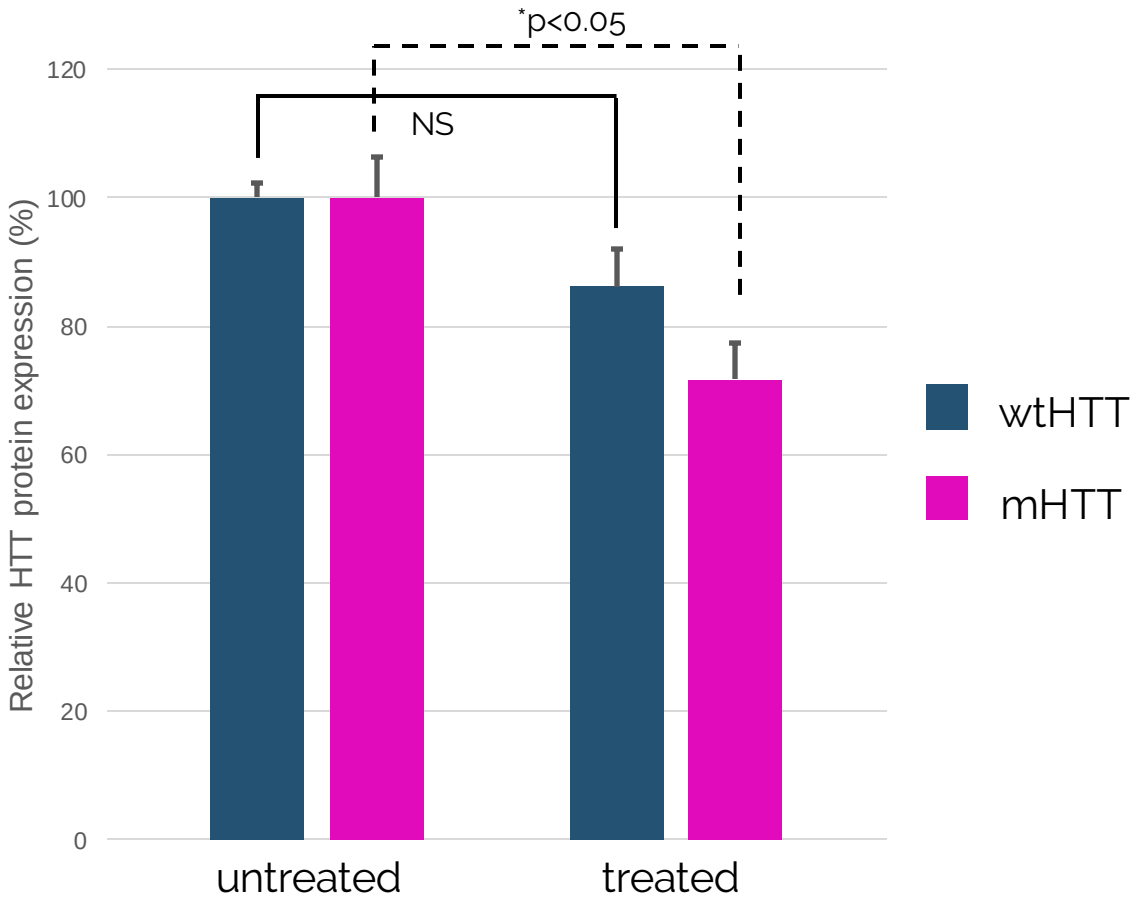


ALLELE-SELECTIVE KNOCK-DOWN IS IMPORTANT

- Maintenance of normal huntingtin function while eliminating toxic protein is ideal

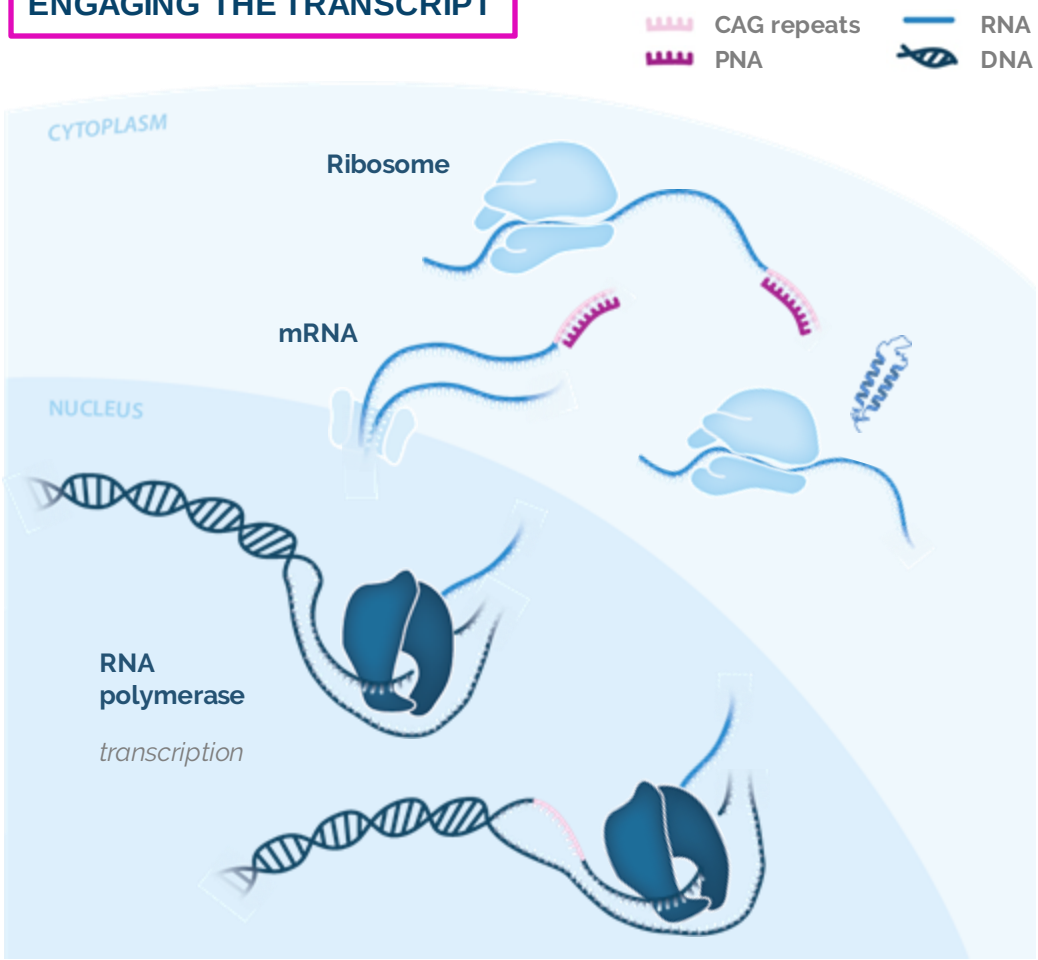


SUBCUTANEOUS DOSING CROSSES BBB AND KNOCKS DOWN MUTANT HUNTINGTIN PROTEIN IN THE MOUSE BRAIN[1]



[1]zQ175 mouse model with 190 CAG repeats in exon 1 of *HTT*; 60 mg/kg subcutaneous dose day 1 & 4; sacrifice day 7

ENGAGING THE TRANSCRIPT



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

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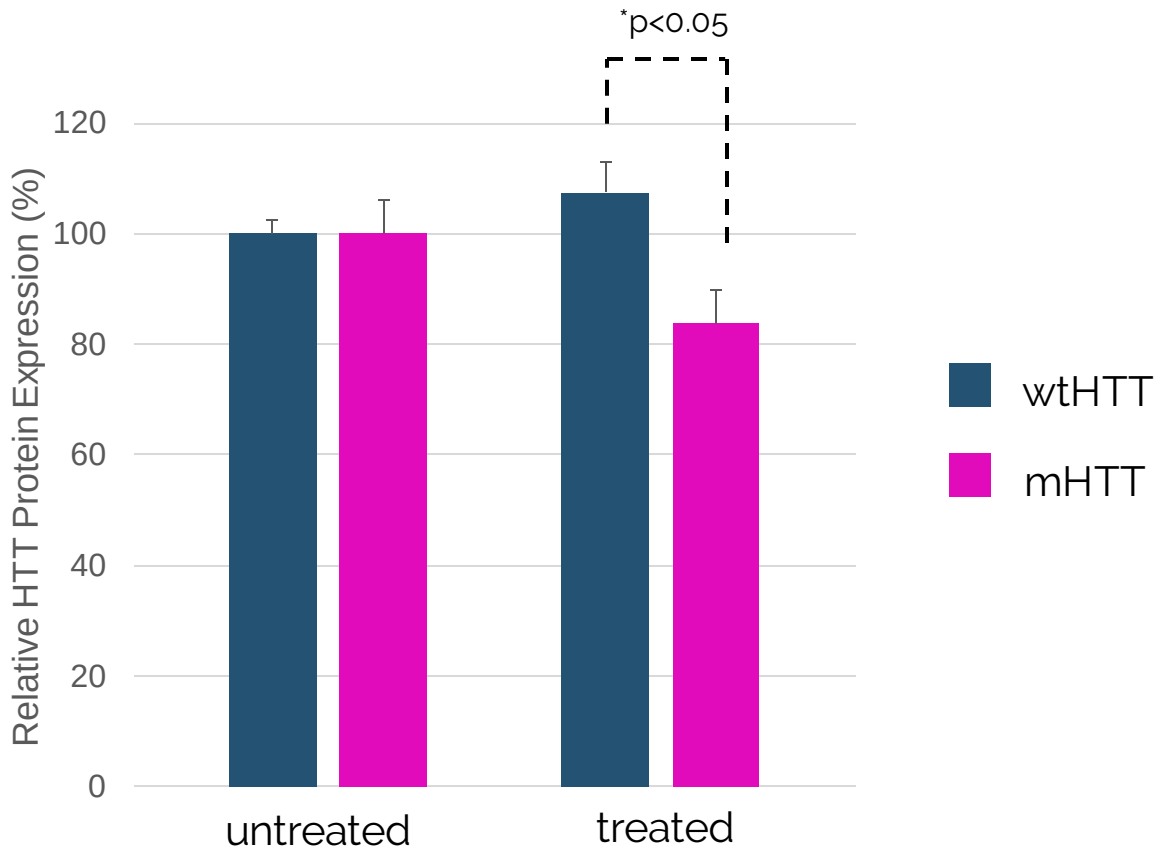
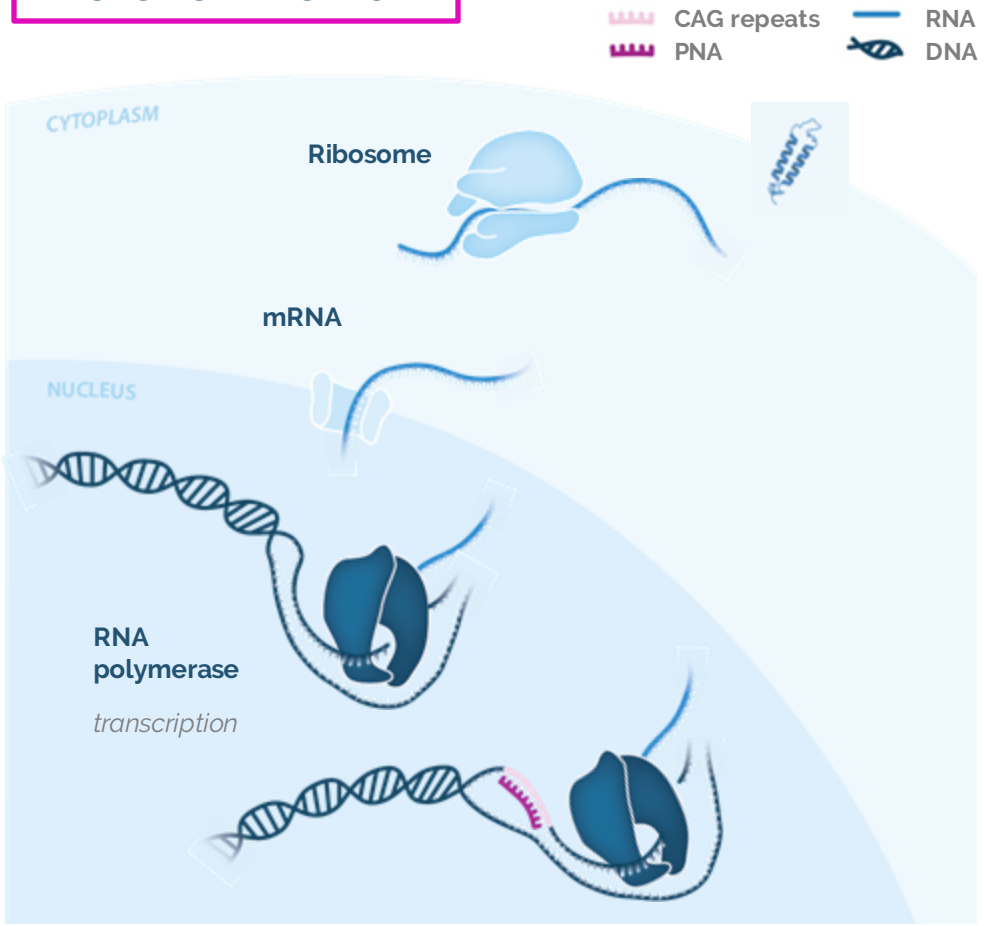


ENGAGING THE GENOME



[1]zQ175 mouse model with 190 CAG repeats in exon 1 of *HTT*; 30 mg/kg subcutaneous dose day 1 & 4; sacrifice day 7

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

KEY ADVANCEMENTS

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

***RAS*-driven cancers are common, severe and largely untreatable**

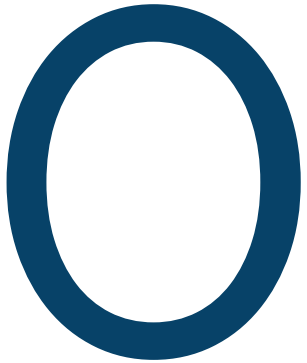
KRAS mutations are the most common *RAS* mutations[1]

G12D and G12V account for ~55% of all KRAS mutations

Our compounds targeting *KRAS* codon 12 mutations have potential to work against *NRAS* and *HRAS*

Normal KRAS protein is essential for normal function

[1]Papke B *et al. ACS Pharmacology & Translational Science*. 2021. Metrics are approximate.



approved therapies for the 2 most prevalent *RAS* mutations

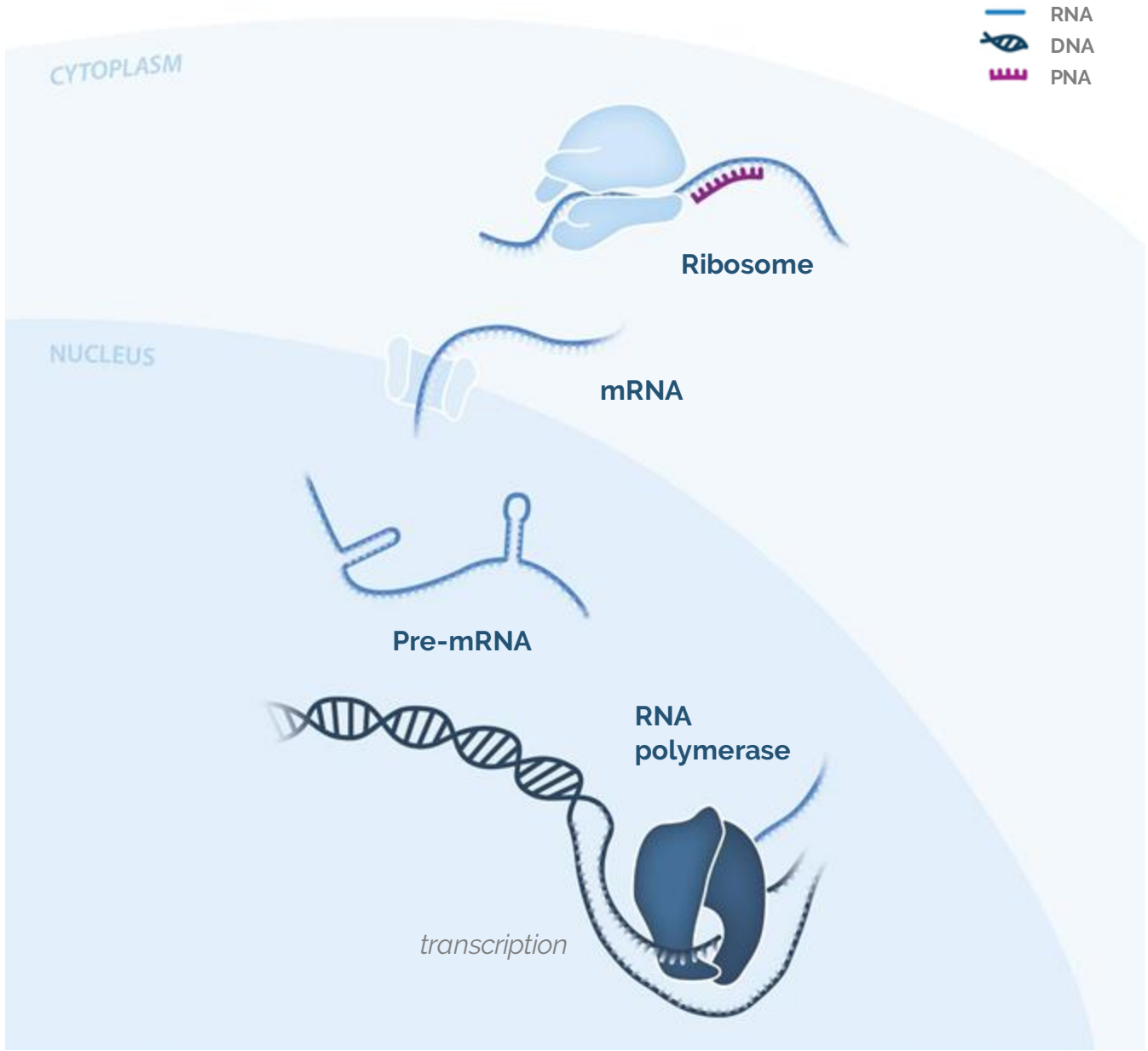
https://www.cancer.gov/research/key-initiatives/ras/about

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

RNA TARGETING OF *KRAS*

- Engaging RNA to inhibit translation



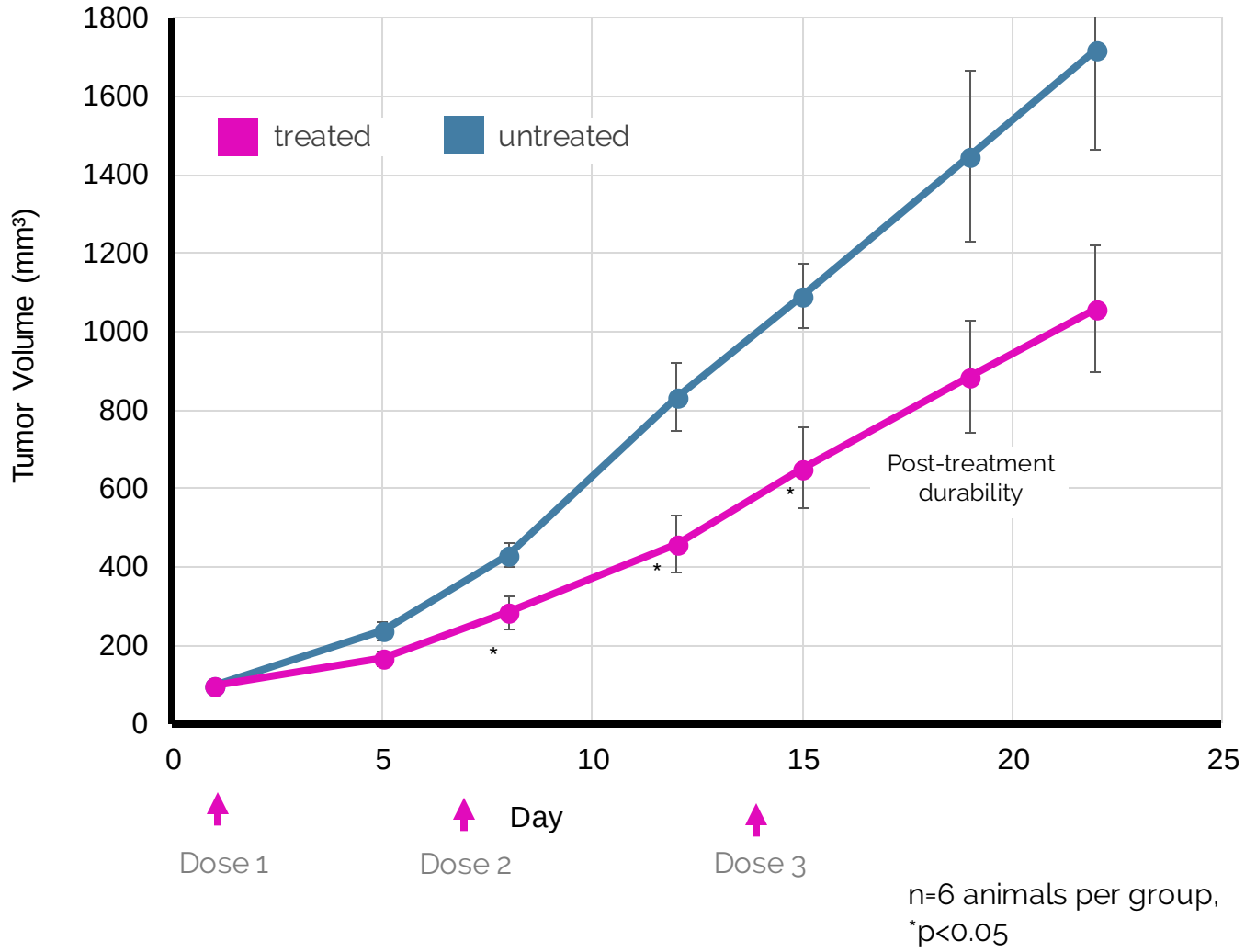
Adapted from Muangkaew and Vilaivan, *Bioorg Med Chem Lett* 2020; 30:127064

IN VIVO TUMOR GROWTH INHIBITION VIA RNA TARGETING OF G12D MUTATION

G12D is the most prevalent mutation[1]
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

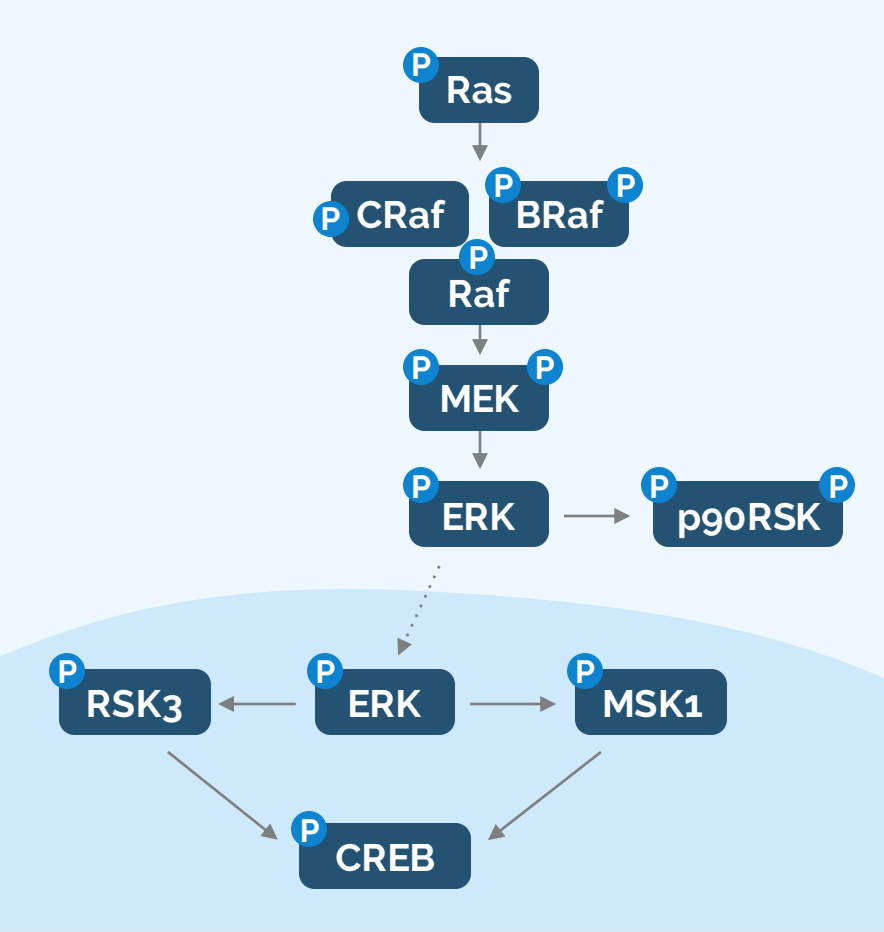


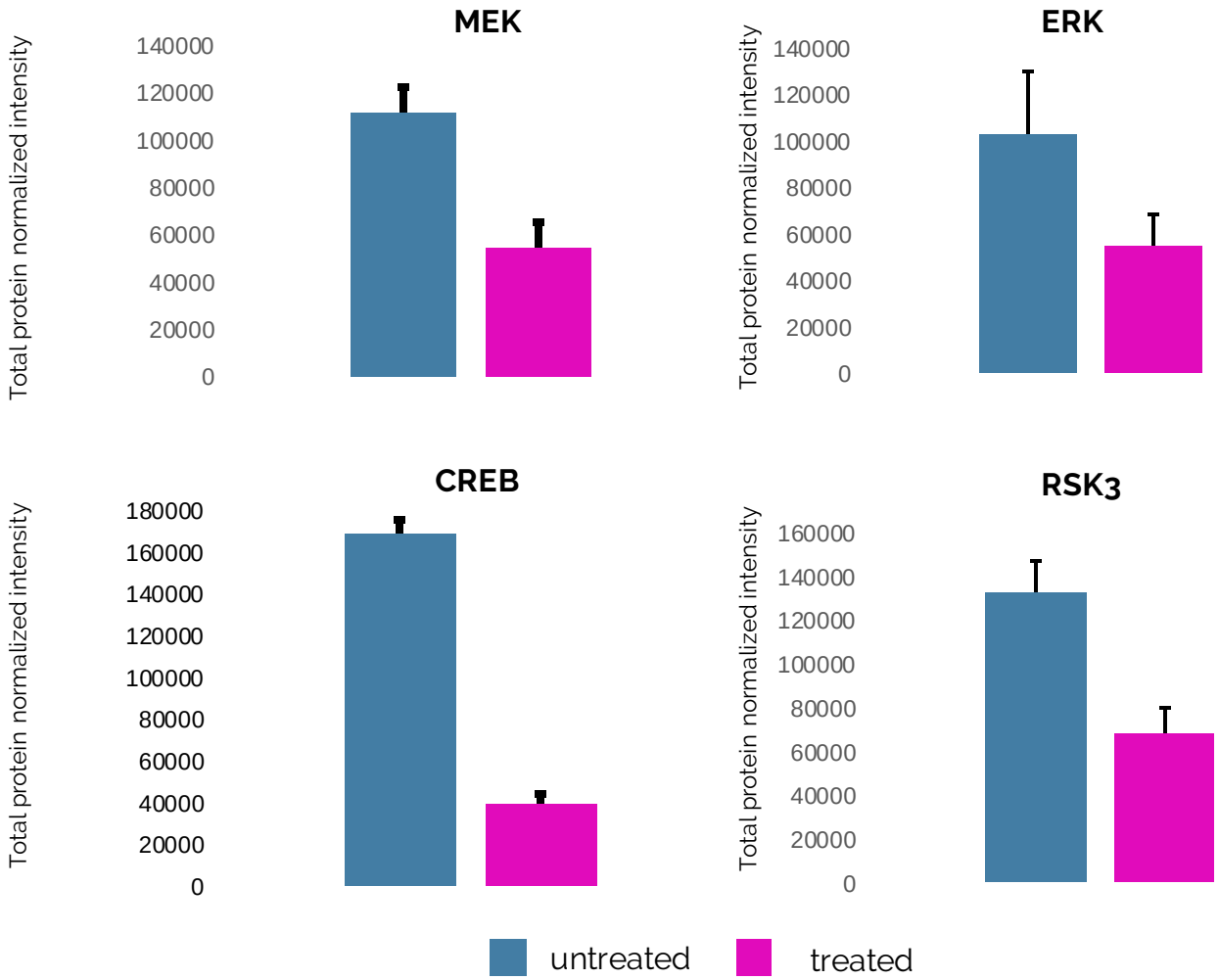
n=6 animals per group,
*p<0.05

[1]Papke 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



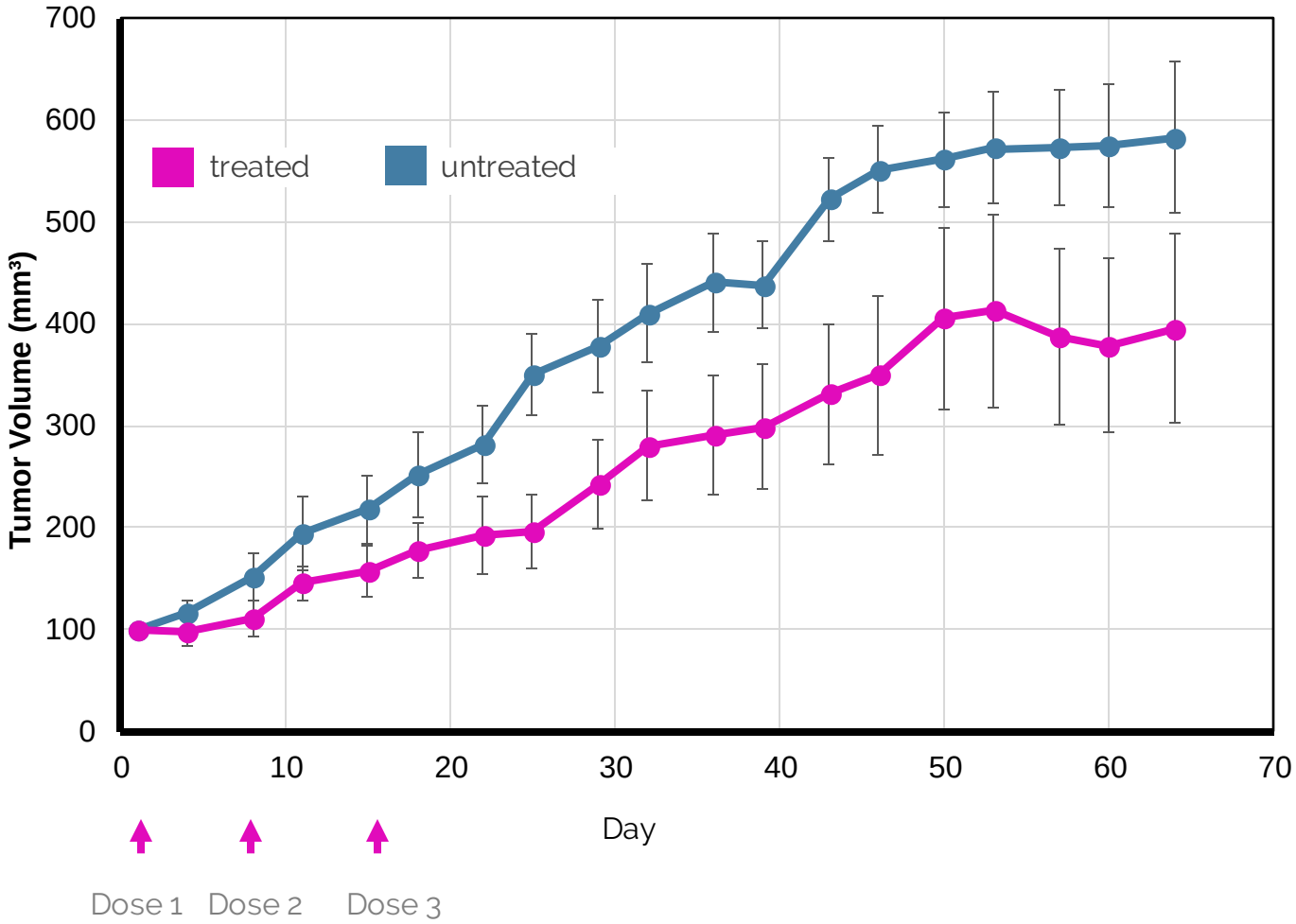


IN VIVO TUMOR GROWTH INHIBITION VIA RNA TARGETING OF G12V MUTATION

G12V is the second most prevalent mutation[1]
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

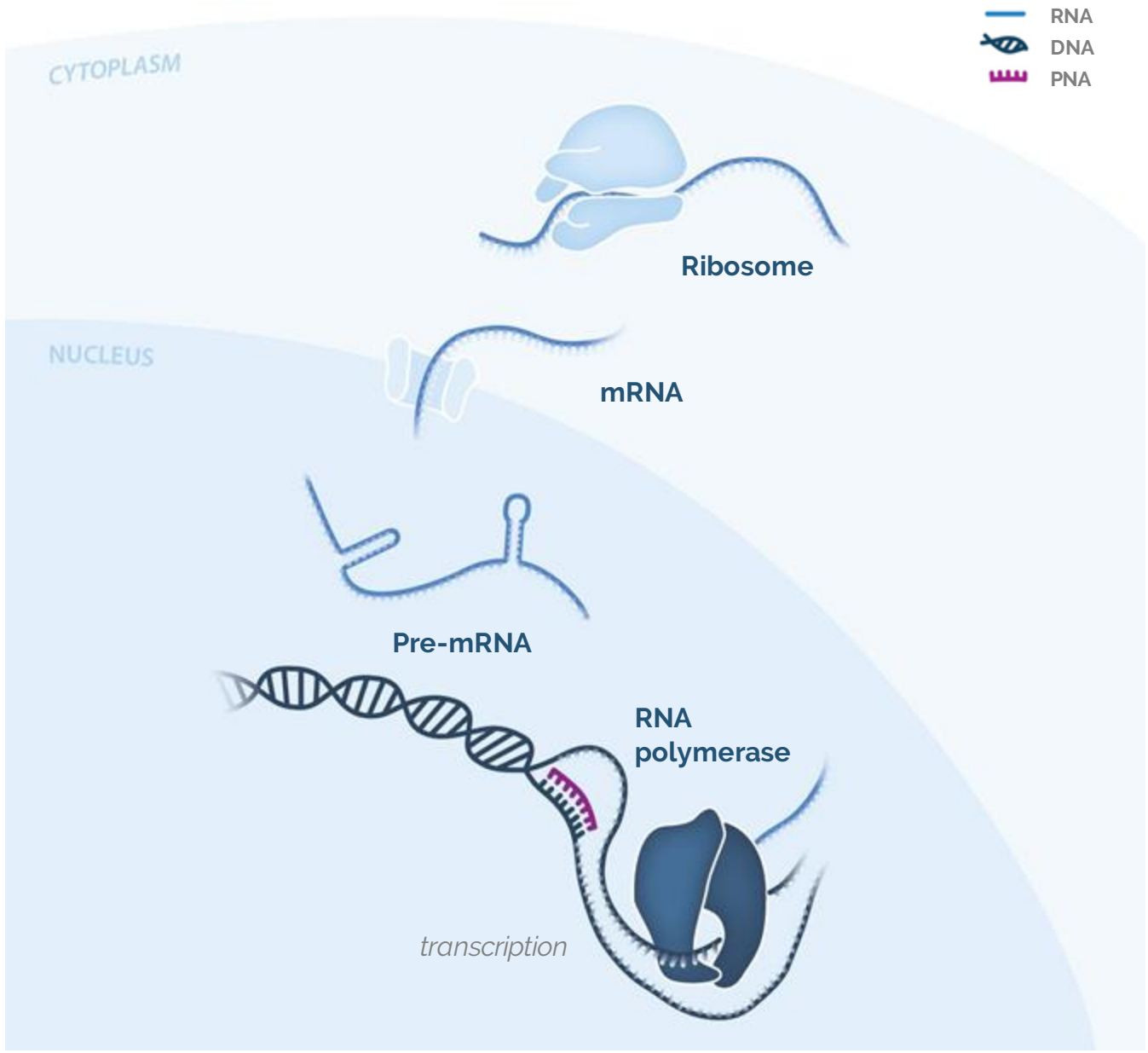


n=6 animals per group

[1]Papke B *et al. ACS Pharmacology & Translational Science*. 2021

DNA TARGETING OF *KRAS*

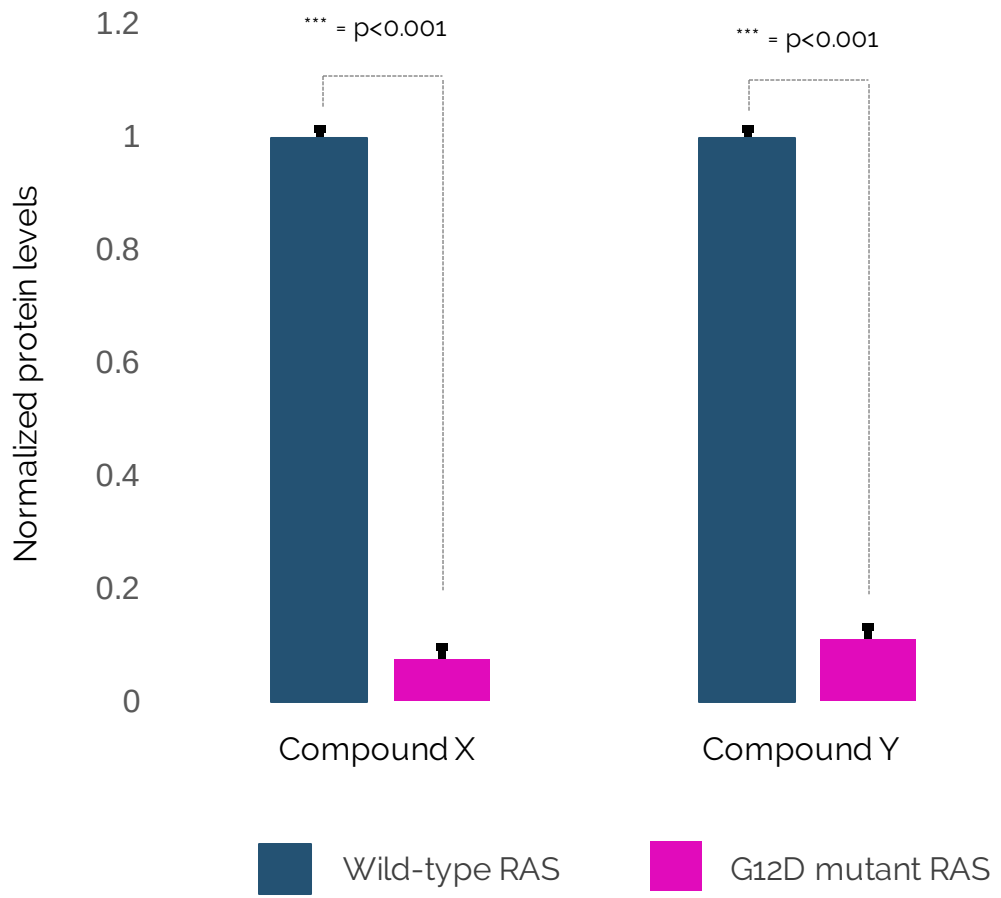
- Engaging DNA to inhibit transcription



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

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[1] 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

[1]Calendar year

NEUBASE WELCOMES DRS. 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[1]

[1]Calendar year

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