uniQure

A Global Leader in Gene Therapy

Corporate Presentation
November 2020

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Forward-looking Statements

This presentation contains forward-looking statements. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “goal,” “intend,” “look forward to,” “may,” “plan,” “potential,” “predict,” “project,” “should,” "will,” “would” and similar expressions. Forward-looking statements are based on management's beliefs and assumptions and on information available to management only as of the date of this presentation. These forward-looking statements include, but are not limited to, statements regarding the development of our gene therapies, the success of our collaborations, and the risk of cessation, delay or lack of success of any of our ongoing or planned clinical studies and/or development of our product candidates. Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including, without limitation, risks associated with collaboration arrangements, our and our collaborators’ clinical development activities, regulatory oversight, development of product candidates, product commercialization and intellectual property claims, as well as the risks, uncertainties and other factors described under the heading "Risk Factors" in uniQure’s Annual Report on Form 10-K filed on March 2, 2020 and Quarterly Report on Form 10-Q filed on October 27, 2020. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements, and we assume no obligation to update these forward-looking statements, even if new information becomes available in the future.

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Key highlights & near-term catalysts

Hemophilia B	• Global licensing agreement with CSL Behring announced in June • Topline FIX data from fully enrolled HOPE-B pivotal study in late 2020 • BLA submission anticipated in 2021
Huntington's	• First four sentinel patients enrolled in Phase I/II study • Positive DSMB meeting in September 2020; next one expected early 2021 • Early imaging/biomarker data in late 2021
Spinocerebellar Ataxia Type 3 (SCA3)	• IND-enabling studies initiated in 3Q of 2020 • Submit IND application in 2021
Manufacturing	• Continue to increase manufacturing scale and capacity • Conduct manufacturing process validation for EtranaDez (AMT-061) in 2020

Global leadership in AAV manufacturing

Large-scale AAV Manufacturing

- Based in Lexington, MA, expanded to 80,000 ft^2
- Proprietary 3rd generation insect cell, baculovirus
- Demonstrated 500L stirred-tank production
- Scalable up to 2 x 2,000L
- Strong intellectual property position

Potential Benefits

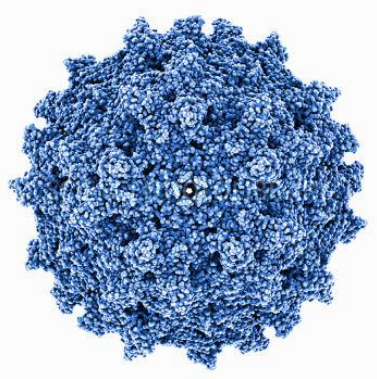
- Control and flexibility
- Consistent process from small-scale to large-scale
- Highly scalable, cost-effective
- High-volume capacity
- Consistent, stable, high-quality product

Leveraging AAV5: a potentially best-in-class vector

AAV5 – Clinically demonstrated tolerability and clinical effects observed to date

- Long-term follow-up data demonstrating safety and tolerability
- ~75 patients have received AAV5 across 5 clinical studies[1]
- Observed clinical effects in the liver and brain
- Low avidity of pre-existing neutralizing antibodies (NAbs)
- Favorable immunogenicity profile for systemic, intravenous delivery
- No confirmed T-cell-mediated immune responses to capsid

AAV5 Vector



[1] uniQure clinical trials in Hemophilia B, Sanfilippo B and Acute Intermittent Porphyria

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Hemophilia B

Etranacogene dezaparvovec (AMT-061)

A global licensing deal with CSL Behring in hemophilia B

- One of the largest gene therapy deals announced to date
- CSL Behring is an ideal strategic partner with extensive commercial expertise in hemophilia that best positions uniQure to provide EtranaDez to the greatest number of global patients as quickly as possible
- Strategically positions uniQure to focus on aggressively advancing its pipeline of gene therapy candidates, anchored by AMT-130 in Huntington's
- ~$720M pro forma cash provides runway into 2H 2024 to fund pipeline expansion, invest in technology innovation and scale manufacturing capabilities

A global licensing deal with CSL Behring in hemophilia B

The transaction is a historic collaboration in gene therapy and hemophilia, with uniQure eligible to receive more than $2B in total economics

- $450M upfront payment
- $1.6B in regulatory and commercial milestones
- Double-digit royalty payments up to low-twenties percentage of net product sales
- Full reimbursement of uniQure's clinical and regulatory costs

A global licensing deal with CSL Behring in hemophilia B

Partnership enables uniQure to leverage CSL Behring's world-class global hemophilia commercial infrastructure

- Hemophilia is a well-established, specialized and highly competitive global market
- CSL Behring has been a leader in bleeding disorders for more than 30 years
- Deep, long-standing relationships with hemophilia communities worldwide
- One of the broadest product portfolios in hematology and thrombosis
- $1B+ in hemophilia sales in 2019
- Commercial sales in more than 100 countries

Hemophilia B: significant financial burden and unmet medical needs

Disease prevalence: ~6,000 patients in the United States[1] and ~14,000 patients in Europe[2]

Clinical burden

Lifelong bleeding risk with current standard of care and accrual of **joint damage**[3]

Patient burden

Cumbersome treatment with adherence issues, **quality of life** and pain[3]

Economic burden

~$610,000 annual cost of factor IX replacement therapy for severe patients in the US[4]

Societal burden

>$20 million lifetime cost per severe patient in the US[5]

1. US CDC/ATHN Hemophilia community count, March 2019. 2. Estimated based on population in Europe and prevalence reported in Iorio et al. Ann Intern Med. 2019. doi: 10.7326/M19-1208.
3. VandenDriessche T and Chuah MK. Hum Gene Ther. 2017;28(11):1013-1023. 4. Noone et al. American Society of Hematology annual meeting 2019, Poster 2118. 5. uniQure internal data, cost including factor therapy and medical costs

Etranacogene dezaparvovec (AMT-061)

Key Treatment Features

- Demonstrated ability to increase FIX activity to therapeutic levels
- No bleeding events post-treatment
- No replacement therapy for bleeds outside surgery
- No requirement of immunosuppression
- No exclusion of patients with pre-existing NAbs

Key Safety Features

- Well-tolerated with no serious adverse events related to treatment
- No inhibitor development

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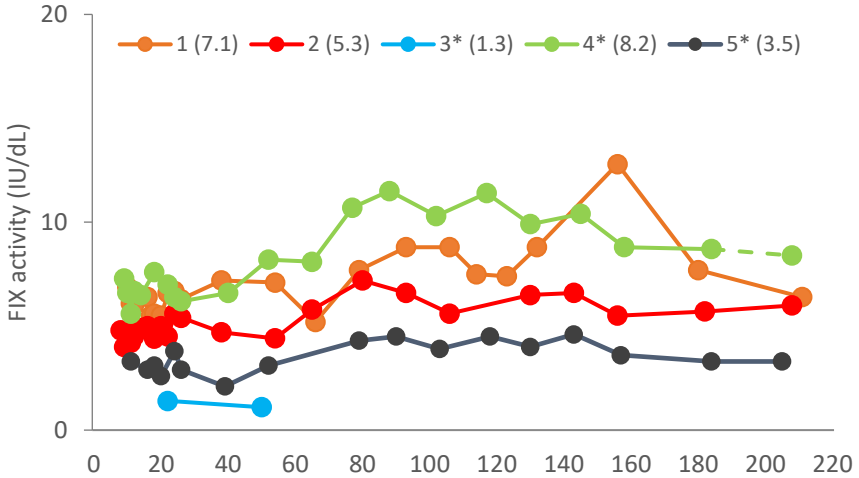
AMT-060: sustained dose-dependent increases in FIX activity

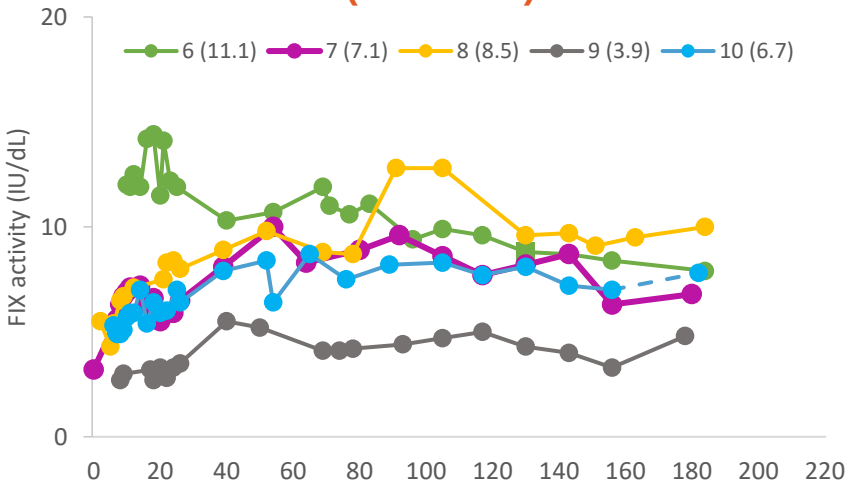
Cohort 1

Mean FIX activity (95% CI): 5.1 (1.6 – 8.6)



Cohort 2

Mean FIX activity (95% CI): 7.5 (4.2 – 10.7)



Weeks following AMT-060 treatment

Values in parentheses represent mean FIX activity over time. Only values at least 10 days after last FIX concentrate administration are included. FIX prophylaxis was continued after AMT-060 and tapered between Weeks 6 and 12. *Patients 3, 4 and 5 retrospectively tested positive for AAV5 neutralizing antibodies using the luciferase-based assay. Dashed line indicates sample collection occurred after the data cut (09Oct2019). Values after the data cut (Patient 4, year 3.5; Patient 10, year 4) are not included in calculations of mean FIX activity. FIX, factor IX; CI, confidence interval; IU, international units

Etranacogene dezaparvovec: Phase 2b sustained FIX activity in the functionally curative range

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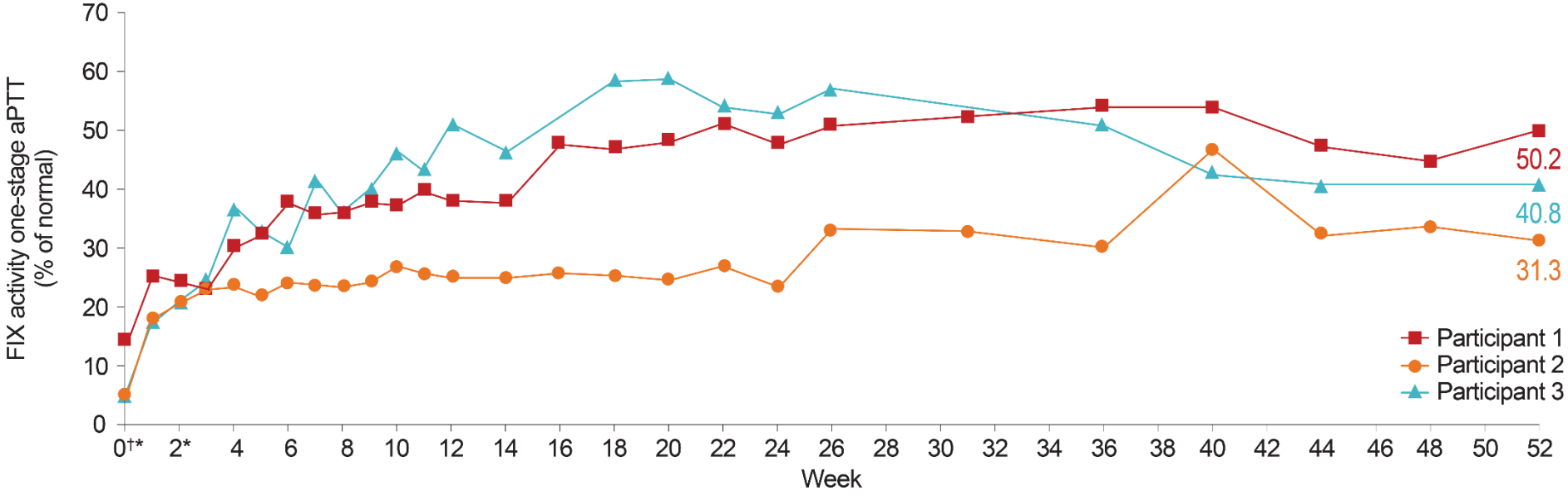
Mean FIX activity at 1 year: 41% of normal



FIX activity measured by a one stage clotting assay conducted in a central lab. aPTT, activated partial thromboplastin time

Etranacogene dezaparvovec (EtranaDez): HOPE-B Phase III pivotal study

- Targeted dosing achieved: 54 patients treated as of March 26
- Severe and moderately-severe Hemophilia B patients
- Open label, single-dose, multi-center, multi-national trial
- Patients with AAV5 neutralizing antibodies not excluded
- Patients served as their own control; 6-month lead-in to establish baseline
- Study objectives:
  - Increase FIX activity
  - Reduce frequency of bleeding episodes
  - Decrease use of FIX replacement therapy
  - Assess efficacy and safety

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Huntington's Disease

AMT-130

Huntington's disease: prevalence and overview

- Patient population[1]:
  - ~25,000 patients in United States
  - ~25,000 patients in Europe
- Underreported due to lack of treatment options
- Disease stage prevalence[2]:
  - 30.5% Early stage
  - 35.5% Middle stage
  - 34.0% Late stage

- Autosomal dominant neurodegenerative disorder
- Expansion of CAG trinucleotide huntingtin (HTT) exon1
- No disease-modifying therapies available

1 Neuroepidemiology 2016;46:144–153
2 Journal of Medical Economics. 2013 Aug;16(8):1043-50

AMT-130: major gene therapy opportunity

- No treatments available
- Strong preclinical data
- Near-term goal: Complete 1st dose cohort of Phase I/II study

- One-time administration of disease-modifying therapy
- Proprietary miQURE™ silencing platform
- Demonstrated strong knockdown at sites of pathology – striatum and cortex
- Demonstrated restoration of neuronal function in diseased animal model
- Silences both full-length mHTT protein and highly toxic exon1 fragments
- No direct miRNA toxicity and no off-target effects
- No expected immune-related toxicity
- Potential to be first gene therapy to market

AMT-130: extensive preclinical validation

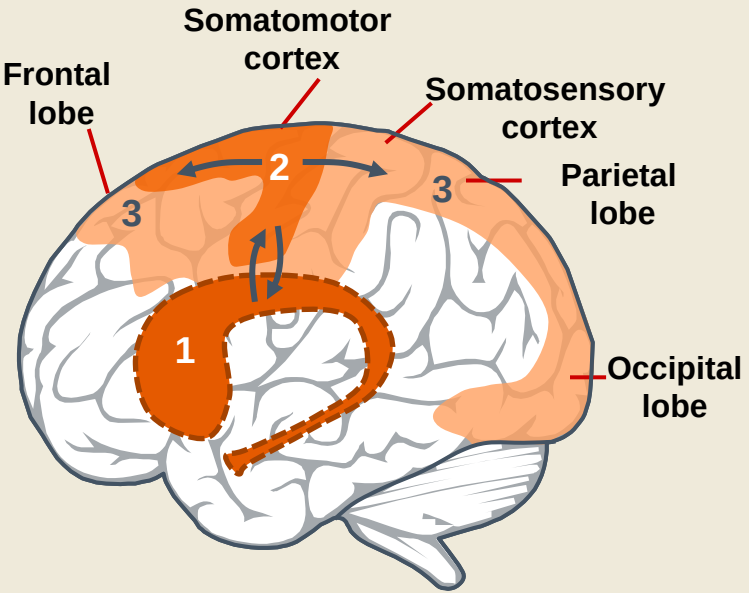
Model	Efficacy	Safety	Distribution
Cultured human neurons	✓	✓	
Rodents (HD rat[4]) (4 types HD mouse[3])	✓	✓	
NHP (Non-human primate[1])	✓	✓	✓
Pig (tgHD Minipig[2])	✓	✓	✓

Recent publications

1. Samaranch L, *et al. Gene Ther* 2017;24:253-261;
2. Evers M, *et al. Mol Ther* 2017;5(Suppl. 1):247;
3. Spronck EA, *et al. Hum Gene Ther* 2017;28:A78;
4. Miniarikova J, *et al. Gene Therapy* 2017;24:630-639
5. Evers MM et al. Mol Ther. 2018;26(9):2163-2177
6. Spronck EA et al. Mol Ther Methods Clin Dev. 2019 Mar 16;13:334-343
7. Keskin S et al. Mol Ther Methods Clin Dev. 2019 Oct 4;15:275-284
8. Caron NS et al. Nucleic Acids Res. 2019 Nov 20. pii: gkz976. doi: 10.1093/nar/gkz976

Huntington's disease: expected progression of brain pathology

- The striatum is the primary site of pathology
- Premanifest stage: atrophy spreads and cortical thinning occurs
- Motor symptoms manifest as atrophy increases



The shading and arrows indicate the progression of pathology. Darker shading represents earlier onset.

Figure adapted from Brundin P, *et al. Nat Rev Mol Cell Biol* 2010;11:301-7.

1. McColgan P, Tabrizi SJ. Eur J Neurol. 2018;25(1):24-34; 2.Tabrizi SJ, et al. Lancet Neurol 2009;8(9):791-801;
3. Nopoulos PC, et al. Neurobiol Dis 2010;40(3):544-54

AMT-130: well-tolerated and widespread distribution in the non-human primate (NHP) brain

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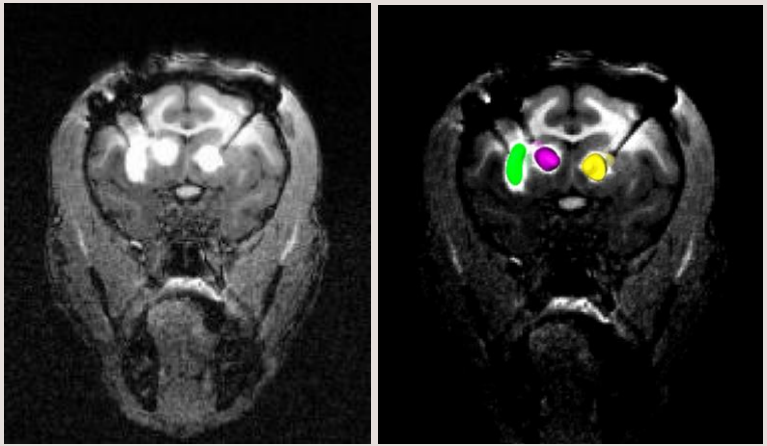
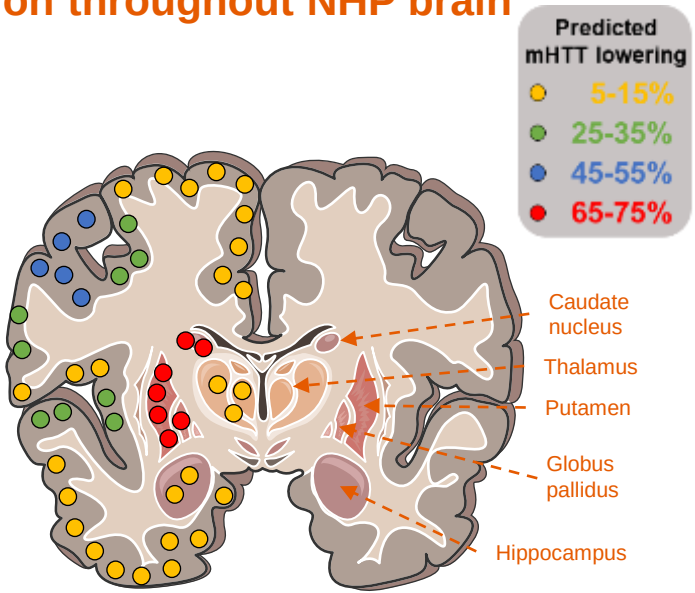
NHP MRI-guided frontal convection-enhanced delivery



No procedure-related neurological symptoms following infusion into the striatum

Distribution throughout NHP brain

Putaminal delivery AAV5-GFP



uniQure, data on file. MRI, magnetic-resonance imaging

Samaranch L. et al, Gene Ther. 2017 Apr;24(4):253-261. Figure 3

AMT-130: strong reduction of mutant HTT in the minipig brain

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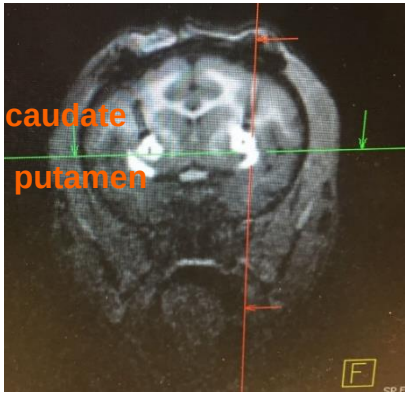
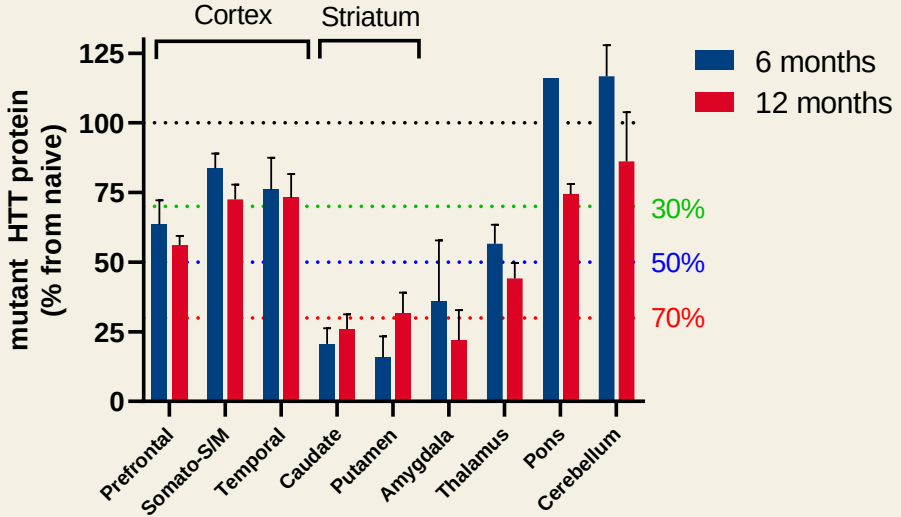
Libechov transgenic (tgHD) minipigs:

- Lifespan: 12-20 years
- Body weight: 50-140 kg
- Brain weight: 90-100 g
- Highly developed immune system

MRI-guided Convection-enhanced delivery



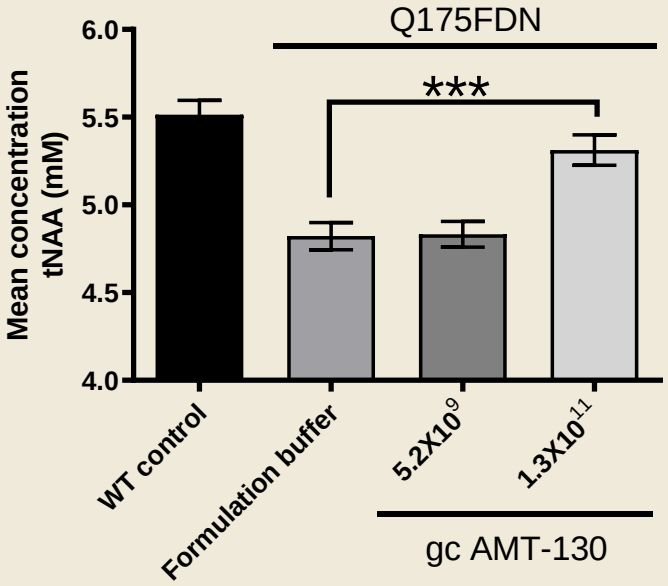
Comparable mutant huntingtin protein knockdown at 6 and 12 months



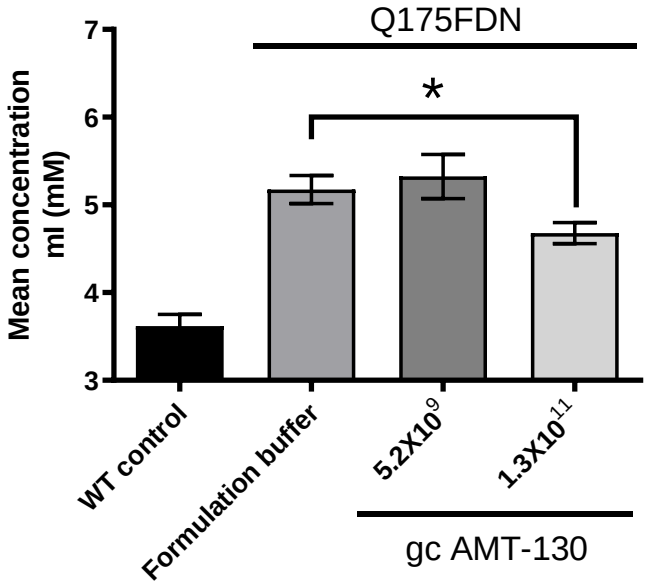
Bars represent average ± SEM of n=3-4 animals/group

AMT-130: neuropathology in diseased mouse model

N-Acetyl Aspartate (tNAA)
Neuronal integrity marker



Myo-Inositol (MI)
Gliosis marker



Leavitt BR, Vallès. et al., Manuscript in preparation

AMT-130: full-length and exon1 HTT lowering in striatum and cortex in diseased mouse model

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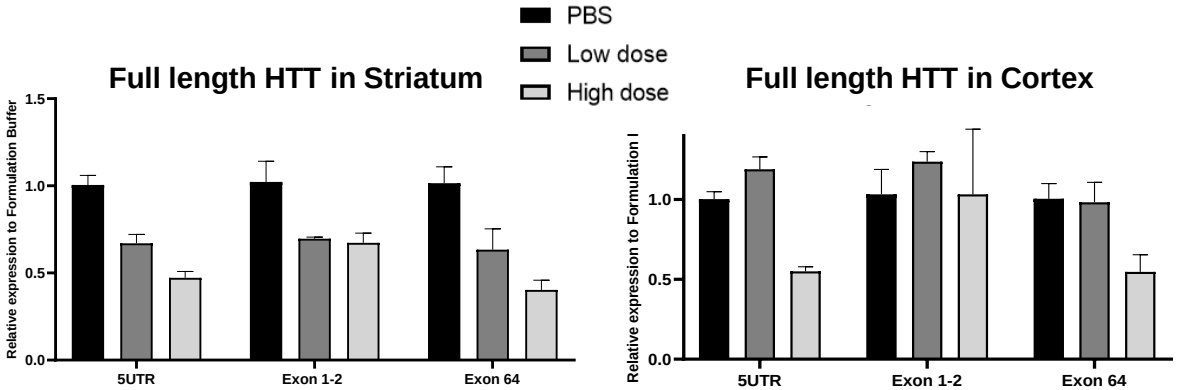
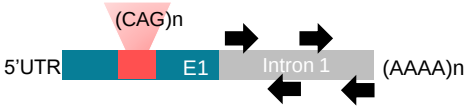
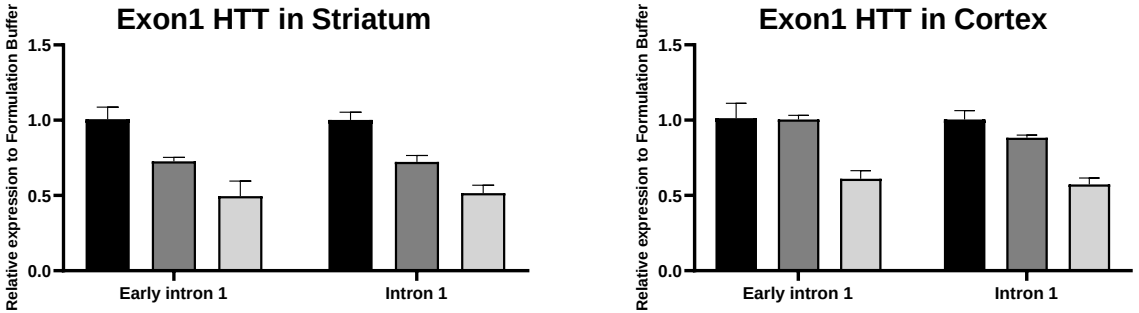
Full-length HTT mRNA



Exon-1 HTT mRNA





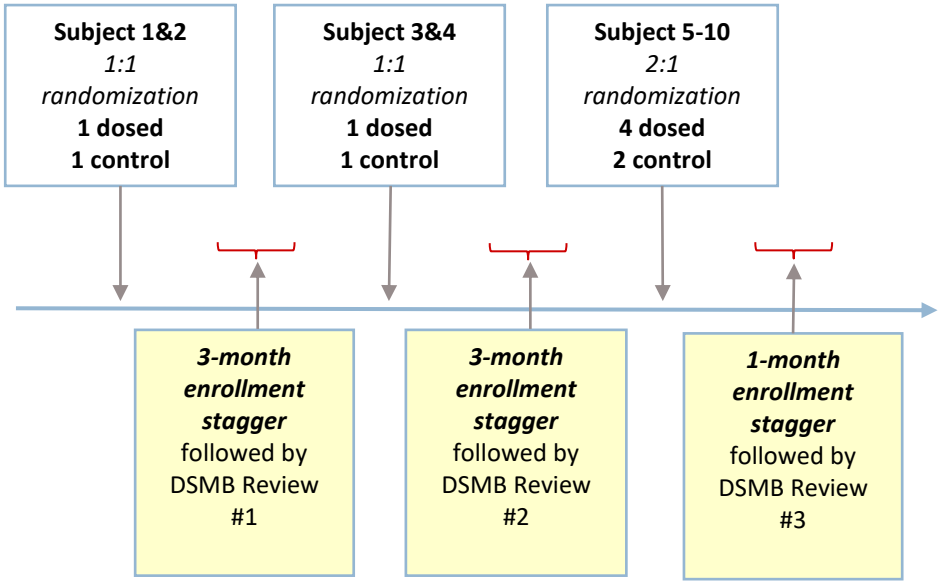
AMT-130: Phase I/II clinical trial

Study Overview

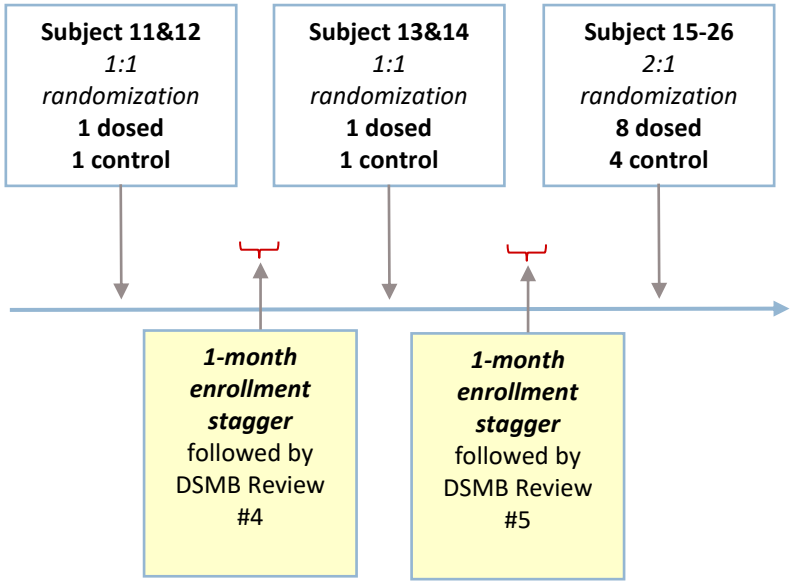
- Objectives: assess safety, tolerability and efficacy
- Multicenter, randomized, double-blinded study
- Controlled with imitation surgery
- Two dose cohorts with a total of 26 patients
- Early manifest patients
- 18-month follow-up (5 years for treated patients)

AMT-130: Phase I/II clinical trial design

Cohort 1: 10 patients (6 dosed, 4 control)



Cohort 2: 16 patients (10 dosed, 6 control)



AMT-130: Phase I/II efficacy endpoints

Biomarkers

- NF-L (neurofilament light)
- mHTT in CSF
- Other exploratory markers

Clinical Parameters*

- Total motor score
- Total functional capacity

Imaging (MRI and MRS)

- Measures of neural function
- Striatal volume (atrophy)

Quantitative Motor Function

- Finger, hand and foot tapping
- Grasping and lifting (chorea)

*Unified Huntington's Disease Rating Scale

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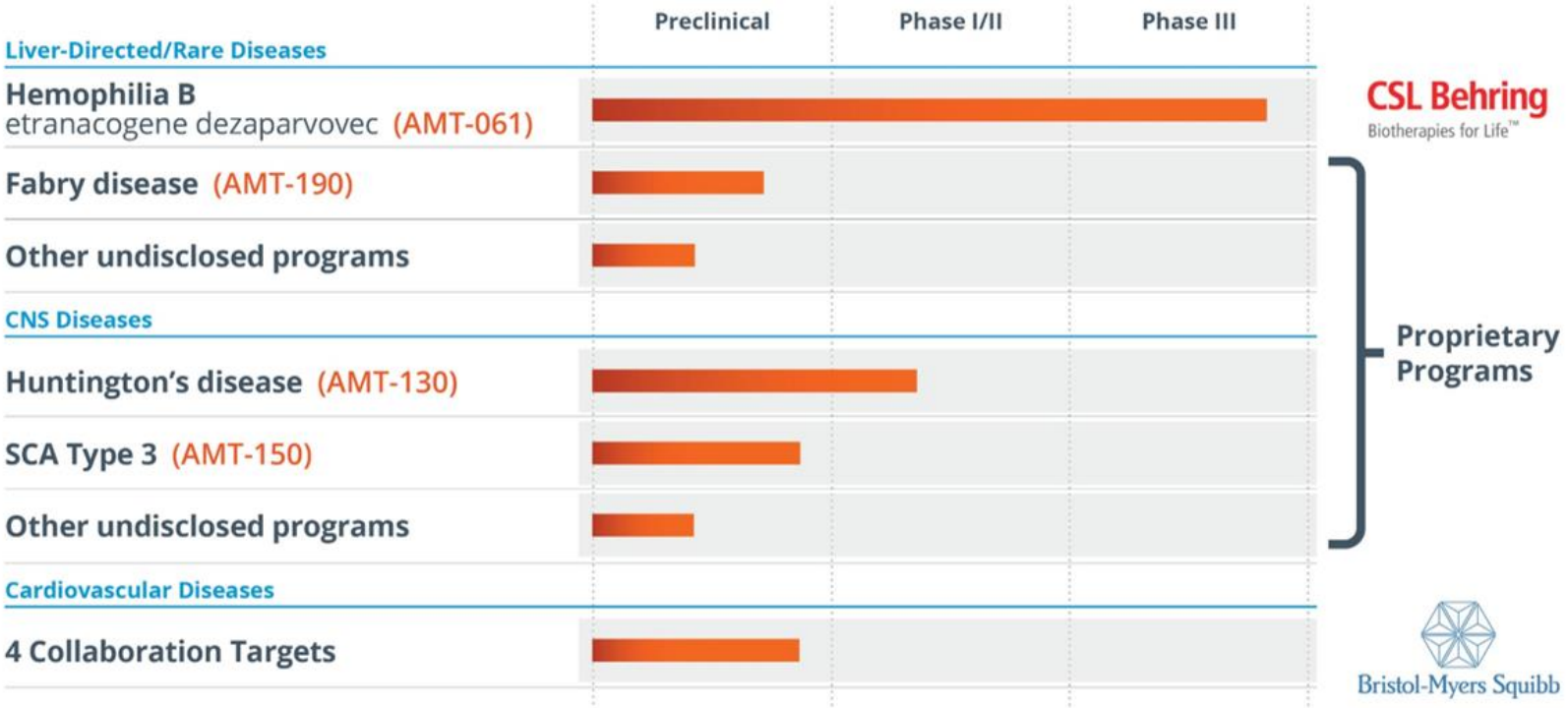
Research Pipeline

Our proprietary pipeline



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