uniQure

Leadership in Gene Therapy

August 2022

uniQure

Our mission is to deliver curative, one-time administered genomic medicines that transform the lives of patients.

inGENEuity through imagGENEation…

uniQure inGENEuity: our history of innovation

uniQure: A gene therapy pioneer with a >20-year history and deeply engrained culture of innovation across an increasingly validated platform

15 years of commercial-scale cGMP manufacturing capabilities

100+ patients across 8 clinical studies with >10 years of follow-up

World-class research and technical expertise

Leading portfolio of next-generation enabling technologies

inGENEuity: our history of innovation

uniQure: A gene therapy pioneer with a >20-year history and deeply engrained culture of innovation across an increasingly validated platform

First approved gene therapy in the world

First commercially licensed gene therapy manufacturing facility

First AAV-delivered gene silencing therapy for Huntington's disease to enter clinic

First AAV vector clinically demonstrated to be effective in patients with pre-existing NABs

inGENEuity: a case study in delivering value through innovation

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Leapfrogging hemophilia B with a first and best-in-class gene therapy

2015
Initiated Phase 1/2 study of AMT-060 with wtFIX transgene

2017
Announced transition to AMT-061 with AAV5/FIX-Padua transgene

2018
Initiated Ph 2b dose-confirmation study and Phase 3 pivotal study

2020
Completed dosing of 54 patients in Ph 3 pivotal study

2020
Announced $2 billion CSL license and collaboration agreement

2022
Submitted BLA and MAA

Re-imaGENEing our in-house manufacturing

Manufacturing for the future: Establishing larger scale and highly cost-effective capabilities to address more prevalent disorders

Consistency & Comparability from Discovery to Commercialization

	2L STR	50L STR	500L STR	1,000-10,000 STR
Status	Currently Deployed	Currently Deployed	Currently Deployed	Being Developed
Usage	Early research	Large animal studies	cGMP	cGMP

COGS

uniQure Re-imaGENEing our capabilities

Initiated construction of a second cGMP manufacturing facility in Amsterdam that will complement commercial manufacturing in Lexington, Massachusetts.

Amsterdam, NL
111,000 sq ft (~290 FTEs)

- Research
- Process Development
- Analytical Development
- Quality

cGMP Manufacturing
Coming in 2022

Lexington, MA
Increasing to ~100,000 sq ft (~200 FTEs)

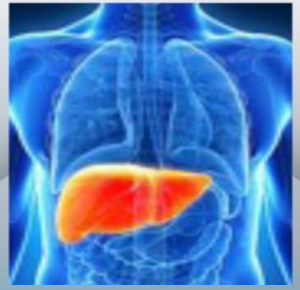
- Process Development
- Analytical Development
- Quality
- cGMP Manufacturing
- Research

uniQure: our focus

AAV Engine: Leveraging our leading technology platform to develop and commercialize products targeting the CNS, liver and heart/muscle

CNS

Liver



Heart/Muscle

AAV Technology Engine

Manufacturing & Enabling Tools

Our Research and Development Pipeline

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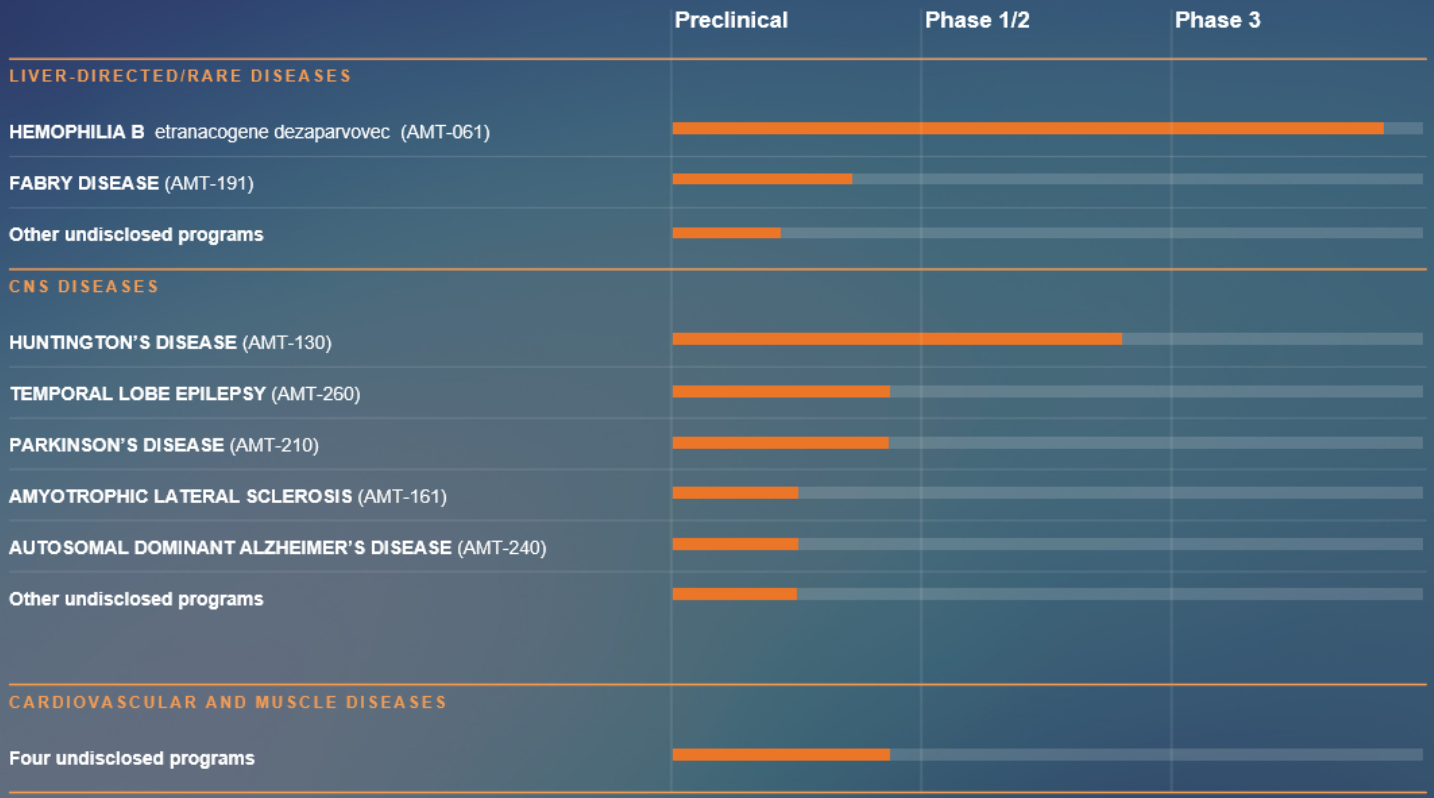

CSL Behring partnership ←

Proprietary programs ←

Bristol-Myers Squibb partnership ←

Re-imaGENEing the R&D pipeline

Doubling the pipeline in 5 years

5-year Pipeline Goals:

- **3-4 Phase 3 commercial programs**
- **5-8 Phase 1/2 programs**
- **7-12 preclinical programs**

Re-imaGENEing the R&D pipeline

Larger market opportunities built on validated targets and technologies

Key criteria:

- Best and/or first in class
- Human validation
- Leverage proven technologies
- Larger indications

Re-imaGENEing the R&D pipeline

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Significant cash runway to transform our pipeline

~$500M of cash on hand > Runway to mid-2024 2024

+$175M in near-term milestones > Extends runway into 1H 2025 2025

+$1.3B in potential other milestones + royalties > Extends runway into 2026 and beyond 2026+

Recent company progress & upcoming events

Hemophilia B	• Announced positive 78-week top-line data from HOPE-B pivotal trial • MAA and BLA regulatory filings accepted • Received $55 million in additional milestone payments from CSL Behring
Huntington's	• Announced 12-month data on lower-dose cohort in Phase I/II trial of AMT-130 • Enrolled a total of 36 patients in U.S. and European trials to date • Temporarily paused European higher-dose enrollment due to SUSAR events
Research Pipeline	• Announced new research programs in TLE, Parkinson's, Alzheimer's and ALS • Anticipate initiation of IND-enabling studies in TLE and Fabry in 2H22 • Additional research programs initiated in 2022
Manufacturing and Technology Platform	• Building out of 2nd cGMP facility in Amsterdam with 500-liter capacity • Completed process validation for etranacogene dezaparvovec • Lexington manufacturing GMP certification from EMA

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Hemophilia B

Etranacogene dezaparvovec
(AMT-161)

A global licensing deal with CSL Behring in hemophilia B

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

- $450M upfront payment received in 2Q 2021
- $1.6B in regulatory and commercial milestones
- Double-digit royalty payments up to low-twenties percentage of net product sales
- Reimbursement of certain remaining clinical and development costs

Collaboration 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 2021 with commercial sales in more than 100 countries

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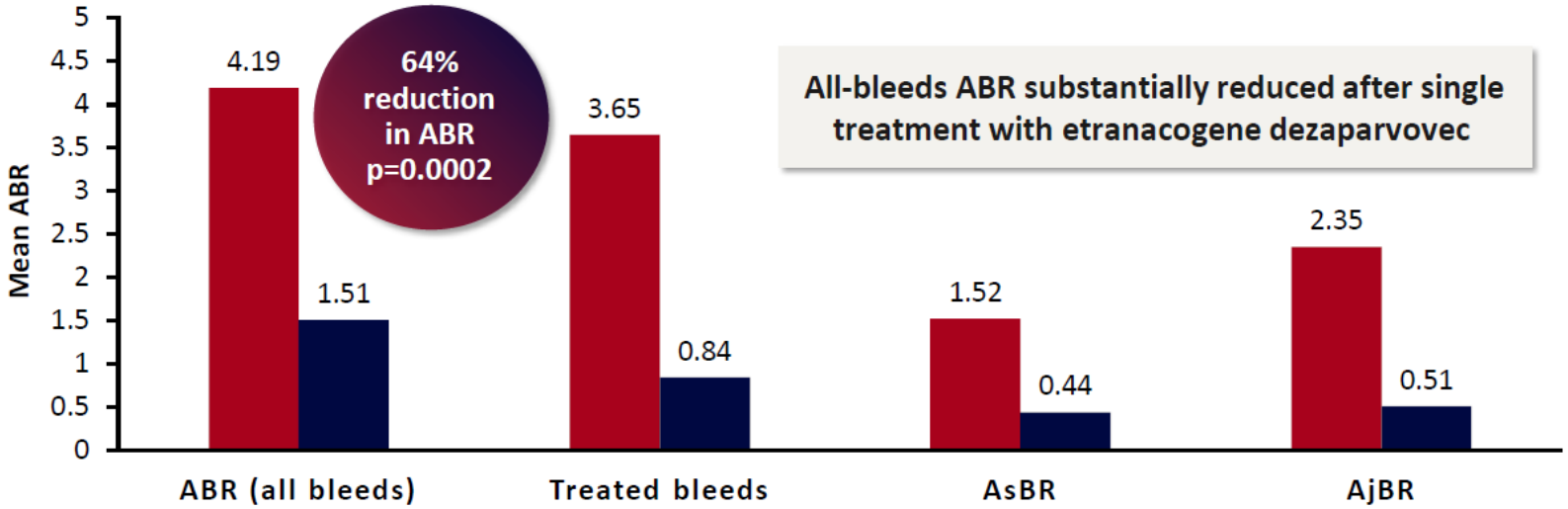
Overview of 78-week top-line data

- **Achieved primary endpoint** in HOPE B Pivotal trial
- Also achieved secondary endpoint demonstrating **statistical superiority** in reduction of bleeding rate compared to FIX replacement therapy
- Stable and durable FIX activity with **mean of 36.9% of normal at month 18**
- Clinical benefit demonstrated in patients with NAb titers of up to 678.2, a range expected to include **more than 95% of the general population**
- Generally **well-tolerated** with over 80% of adverse events considered mild

Primary endpoint of annualized bleeding rate (ABR) was statistically significant



Etranacogene dezaparvovec reduced ABR by **64%** and demonstrated **superiority to prophylaxis** in the lead-in period

One-sided p-value ≤0.025 for post-treatment/lead-in <1 is regarded as statistically significant.
ABR, annualized bleeding rate; AjBR, annualized joint bleeding rate; AsBR, annualized spontaneous bleeding rate.

Substantial reductions in FIX replacement and use of prophylaxis when compared with lead-in

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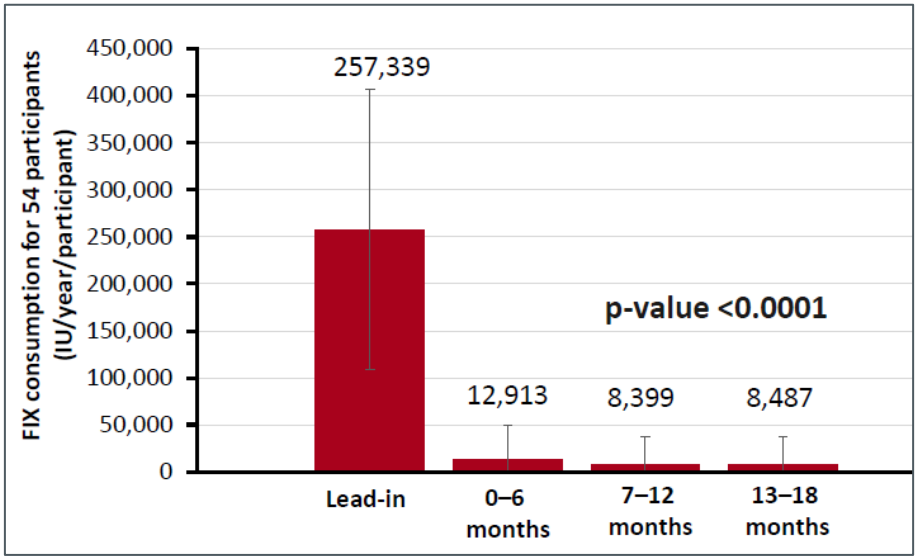
At 78 weeks follow-up, compared with the lead-in period

- **96.3%** (52/54) subjects **discontinued prophylaxis** and **remain prophylaxis-free**



Analyses include two subjects who remain on prophylaxis (1 subject received a partial infusion, 1 subject FIX expression remained <2%).
IU, international unit

Hemophilia B regulatory timeline

CSL Behring filled the BLA and MAA in the first half of 2022

- Granted Breakthrough Therapy Designation by FDA
  - BLA accepted in May 2022 under Priority Review
  - FDA does not expect an advisory panel
  - Approval expected as early as Q4 2022

- Granted access to Priority Medicines (PRIME) regulatory initiative by EMA
  - MAA validated in 1Q22
  - EMA will be conducting a standard review, with approval expected in Q1 2023

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Huntington's Disease

AMT-130

Two ongoing studies in the U.S., EU and UK

CT-AMT-130-01 (Phase Ia/II)
double-blind sham-controlled

HD GeneTRX1

44 Patients Total
22 Treated, 16 Control
26 Patients Enrolled

- ✓ Low-dose 6e12 AMT-130 (6 Drug, 4 Control)
- ✓ High-dose 6e13 AMT-130 (10 Drug, 6 Control)
- Surgical Expansion (12 Drug, 6 Control)

Crossover of eligible patients after 1 year following DSMB review

CT-AMT-130-02 (Phase Ib/II)
open-label

HD GeneTRX2

15 Patients Total
15 Patients Treated
10 Patients Enrolled

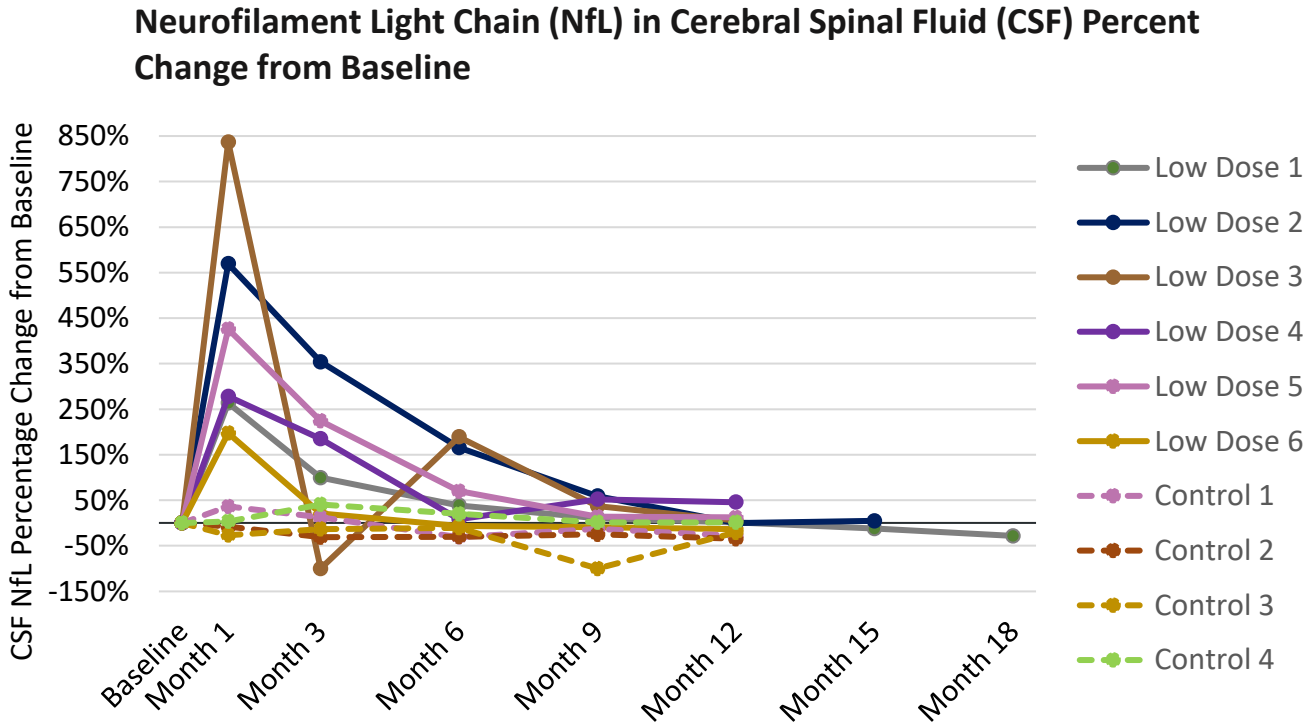
- ✓ Low-dose 6e12 AMT-130 (6 patients)
- High-dose 6e13 AMT-130 (9 patients)

uniQure Encouraging data from lower dose cohort in U.S. Ph I/II study

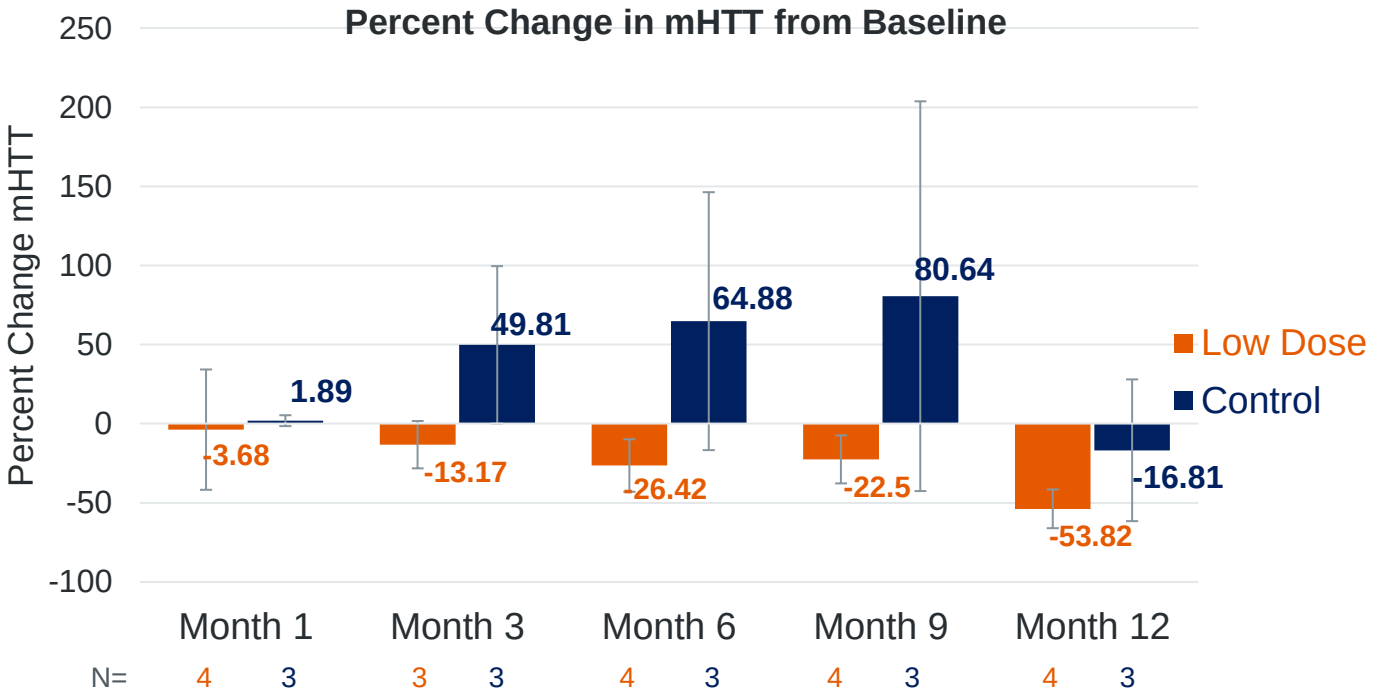
- **AMT-130 was generally well-tolerated at lower dose, with no reported adverse drug reactions or serious unexpected suspected adverse reactions**
- **CSF NfL increased as expected following surgical administration of AMT-130 and neared baseline at 12 months**
- **Trends in CSF mHTT support target engagement at the low dose of AMT-130**

As of time of database lock for analysis on 05.13.22

NfL levels near baseline at 12-months in treated patients



Declines in CSF mHTT support target engagement



August 8 Clinical Update

- SUSARs reported in 3 of 14 patients treated at higher dose
  - Two were treated at a single clinical site in Europe
  - The third patient was treated back in March in the U.S. and subsequently reclassified as a SUSAR
  - All three patients have fully or substantially recovered
- All events occurred within days of the procedures and appear related to post-op inflammation
- DSMB does not consider any of the events to be dose-limiting toxicity
- Enrollment at higher-dose temporarily and voluntarily postponed to complete investigation and implement additional post-operative monitoring procedures (expected in early Q4 2022)
- No impact on lower dose procedures
  - No SUSARs reported in 12 patients at lower dose with up to 2 years of follow-up
  - Cross-over of control patients in U.S. study will proceed and expected to take place this quarter
- No impact on planned data disclosures in 2023

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Acquisition of
Corlieve Therapeutics

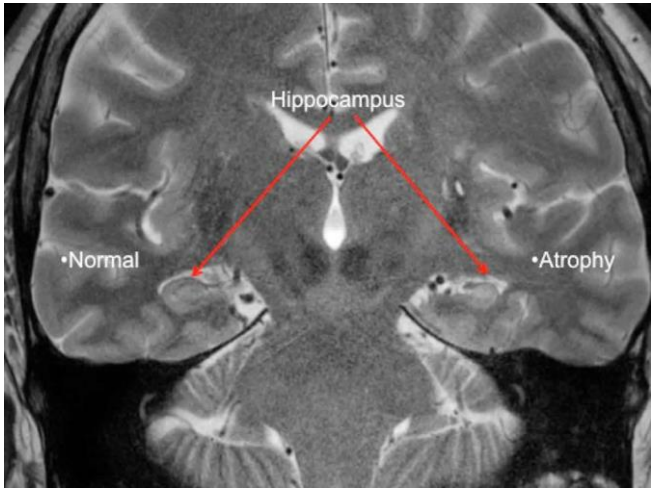
Acquisition of Corlieve Therapeutics

- **In June 2021, uniQure announced the acquisition of Corlieve Therapeutics and its gene therapy to treat refractory Temporal Lobe Epilepsy (rTLE)**

- **Highly compelling and strategic transaction:**
  - Expands uniQure's pipeline of transformational gene therapies
  - Strengthens uniQure's global leadership in miRNA silencing technology
  - Targets 1.3 million people with TLE, of which up to 800,000 are drug-resistant
  - Targets kainate receptors which play a critical role in TLE
  - Preclinical proof-of-concept demonstrating clear suppression of epileptic seizures
  - Clear development path with a rapid proof of concept
  - Diversifies our platform to include HEK293 mammalian cell manufacturing

Refractory temporal lobe epilepsy (TLE)

- TLE is the **most common type** of focal epilepsy
- TLE is associated with damage to the **temporal lobe and hyperexcitability of the hippocampus**
- It's often caused by brain injury, tumors or a prolonged febrile seizure
- TLE affects approximately 1.3 million people in the U.S. and Europe; **~400,000 patients are inadequately treated**
- Refractory TLE patients have a poor quality of life and a reduced lifespan
- The standard of care is lobectomy or laser tissue ablation but **only 1-2% of eligible patients undergo surgery**



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Near-term milestones

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Upcoming milestones

Hemophilia B	• U.S. approval by end of 2022/early 2023 • European approval by early 2023 • CSL commercial launch in early 2023 ($175 million milestones)
Huntington's	• Complete SUSAR investigation / resume higher-dose enrollment in Q4 2022 • Present 1-2 year data on 26 patients in U.S. Ph I/II in Q2 2023 • Present 1 year data on 6 patients in European low-dose cohort in 2023
Research Pipeline	• Submit IND for AMT-260 in rTLE mid-2023 • Submit IND for AMT-191 in Fabry disease mid-2023 • Initiate IND-enabling tox study for AMT-161 in ALS 2H 2023
Manufacturing and Technology Platform	• cGMP certification of Lexington facility by FDA and EMA • Complete build-out of cGMP facility in Amsterdam

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