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 press release. 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, 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 14, 2018. 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.
Our mission: To deliver curative gene therapies that aim to transform the lives of patients.
We are focused on three key areas, each with proof-of-concept:

- **Hemophilia B**
  - AMT-061
  - AAV5 with FIX-Padua transgene

- **Huntington’s Disease**
  - AMT-130
  - Demonstrated strong, widespread lowering of mHTT

- **Cardiovascular Disease**
  - AMT-126
  - Bristol-Myers Squibb research collaboration
Several milestones across key programs

| Hemophilia B (AMT-061)                      | • Treat ~3 patients to confirm dose of $2 \times e^{13} \text{ gc/kg}$  
|                                            | • Initiate enrollment of AMT-061 pivotal trial  
|                                            | • Announce clinical data (FIX activity) from initial ~3 patients  

| Huntington’s disease (AMT-130)             | • Complete IND-enabling GLP safety study  
|                                            | • Submit IND/CTA for Phase I/II study  
|                                            | • Initiate Phase I/II study  

| Cardiovascular disease (AMT-126)           | • Conduct heart function study of AMT-126 in diseased minipigs  
|                                            | • Initiate IND-enabling GLP safety study of AMT-126  
|                                            | • Initiate nonclinical/preclinical studies with additional targets  

Large-scale AAV Manufacturing Capability

- Based in Lexington, MA
- 3rd generation insect cell, baculovirus
- Scalable up to 2 x 2000L
- Ready for commercial scale-up

Benefits

- Control process through commercialization
- Highly scalable, cost-effective
- High-volume capacity
- Consistent, stable, high-quality products
# Strong intellectual property on manufacturing

<table>
<thead>
<tr>
<th>Patent Family</th>
<th>Priority Date</th>
<th>Technology</th>
<th>Current Legal Status Patents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Upstream: AAV Production</strong></td>
<td></td>
<td></td>
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<tr>
<td>P104</td>
<td>20 Oct 2005</td>
<td>Improved infectivity</td>
<td>First published WO2007/046703. Granted in the US, Europe, Australia, Canada, Japan, China, Hong Kong</td>
</tr>
<tr>
<td>P105</td>
<td>21 June 2006</td>
<td>Improved Stability (Overlapping Rep78/52)</td>
<td>First published WO2007/148971. Granted in the US, Europe, Australia, China, Israel, Japan, Korea, Russia</td>
</tr>
<tr>
<td>P107</td>
<td>26 July 2007</td>
<td>Low Impurities</td>
<td>First published WO2009/038462. Granted in the US, Australia, Russia, Japan, China, Eurasia, Mexico, New Zealand, S. Africa</td>
</tr>
<tr>
<td>P108</td>
<td>19 Feb 2008</td>
<td>Dual Baculovirus Infection (Rep and Cap on the same Bac)</td>
<td>First published WO2009/10496. Granted in the US, Australia, China, Hong Kong, Israel, Russia</td>
</tr>
<tr>
<td>P117</td>
<td>11 Mar 2010</td>
<td>Improved productivity, low impurities and empty capsids</td>
<td>First published WO2011/112089</td>
</tr>
<tr>
<td>P124</td>
<td>10 Mar 2014</td>
<td>Improved AAV5 capsid produced in insect cells</td>
<td>First published WO2015/137802</td>
</tr>
<tr>
<td><strong>Downstream: Chromatography</strong></td>
<td>P104, 105, 107</td>
<td>See above</td>
<td>Claims include chromatography steps</td>
</tr>
<tr>
<td><strong>Downstream: Baculoviral filtration</strong></td>
<td>P113</td>
<td>08 Sep 2011</td>
<td>Baculoviral filtration (Potential regulatory requirement)</td>
</tr>
</tbody>
</table>
Leveraging AAV5: a potentially best-in-class vector for systemic delivery

AAV5 – Clinically demonstrated tolerability and outcomes

- Data from 22 patients in 3 clinical studies\(^1\)
- Demonstrated clinical outcomes in the liver and brain
- Lowest prevalence of pre-existing neutralizing antibodies\(^2\)
- Favorable immunogenicity profile for systemic, intravenous delivery
- No confirmed T-cell-mediated immune responses to capsid

\(^1\) Clinical trials in Hemophilia B, Sanfilippo B and Acute Intermittent Porphyria
\(^2\) Boutin et al 2014
AAV5: potential for broader patient access

### Assay development

- **Number of individuals screened**: 98
- **Number of individuals Positive (%)**: 2 (2%)

### Phase 1/2 screening

- **Number of individuals screened**: 10
- **Number of individuals Positive (%)**: 0 (0%)

* Boutin et al. Hum Gene Ther (2010); 21:704-12

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**Phylogenetic tree of AAV**

AAV5 has the least conserved capsid sequence (Only 50-67% homology with other serotypes)

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**Boutin et al.**
Hemophilia B
AMT-061
Leon was diagnosed with HEMOPHILIA B when he was a toddler.

Told he would need replacement therapy for the rest of his life.
Treated with uniQure investigational gene therapy.

Discontinued replacement therapy and enjoying an active life with his daughter Jersey.
Current market opportunity

- Estimated ~10,000 patients with hemophilia B in U.S.\(^1\) and EU5\(^2\)

- Up to 60% of hemophiliacs have a severe or moderately-severe phenotype (< 2% of normal FIX)

- Standard of care for severe hemophiliacs is a chronic, prophylactic FIX replacement therapy\(^3\)

- Estimated annual cost of prophylactic infusions is $500K - $775K\(^4\)

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\(^1\) WFH Global Survey 2016 (published in Oct 2017)

\(^2\) Global Data Epidemiology Forecast to 2024 (report Dec 2015)

\(^3\) Srivastava 2013

\(^4\) Published WAC prices of IDELVION®, BENEFIX, ALPROLIX®
January 2017

Breakthrough Therapy Designation
U.S. Food & Drug Administration (FDA)

April 2017

PRIME Designation
European Medicines Agency (EMA)
Goal of hemophilia B Gene Therapy

- Long-term safety, including favorable immunogenicity profile
- Predictable, sustained and potentially curative increases in FIX activity
- Significant reductions in bleeding rates and FIX replacement therapy
- Broad patient eligibility

Padua: expresses a protein with a single amino acid substitution that has been shown to have a ~6 to 7-fold increase in FIX activity compared to the wild-type FIX protein
Pivotal study:

- Open label, single-dose, multi-center, multi-national trial
- Approximately 50 patients with severe and moderately-severe hemophilia B
- Patients with AAV5 antibodies will not be excluded
- Patients will serve 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

Dose-confirmation study:

- To be conducted in parallel to 6-month lead-in of pivotal study
- Approximately 3 patients to receive a single dose of 2 x e13 gc/kg
- Approximately 6-week follow-up period to observe FIX activity and confirm dose
AMT-061: anticipated FIX activity in humans

COHORT 1
(5 x 10^{12} gc/kg)

Cohort 2
(2 x 10^{13} gc/kg)

NOTE: Anticipated FIX activity for AMT-061 based on computer simulations using actual data from AMT-060 Phase I/II patients and AMT-061 nonclinical animal data. Error bars represent 95% confidence intervals.
<table>
<thead>
<tr>
<th>Regulatory</th>
<th>Clinical</th>
<th>Manufacturing</th>
<th>Intellectual Property</th>
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<tbody>
<tr>
<td>• Submitted IND amendment for the dose-confirmation study</td>
<td>• Anticipate initiating lead-in for pivotal trial in Q3 2018</td>
<td>• Completed comparability protocol</td>
<td>• Acquired patent family — exclusive use of Padua-FIX in gene therapy</td>
</tr>
<tr>
<td></td>
<td>• Plan to start dosing patients in dose-confirmation study in early Q3 2018</td>
<td>• Full quality release of clinical material for dose confirmation study</td>
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</tr>
<tr>
<td></td>
<td>• Site identification, IRB submissions and contracting underway</td>
<td>• Clinical production underway for pivotal study</td>
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Huntington’s disease: A devastating disorder

- A rare, inherited neurodegenerative disease that leads to:
  - Loss of muscle coordination
  - Behavioral abnormalities
  - Cognitive decline
- Results in complete physical and mental deterioration over time
- Disease caused by expansion of CAG trinucleotide in exon 1 of a multifunctional gene coding for protein (mHTT)
- No therapies available to delay onset or slow progression
- Estimated ~63,000 HD patients in the U.S. and EU5

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1 Pringsheim et al. Mov. Disord. 2012
2 Global Data Epidemiology Forecast to 2024, December 2015 report and review by Roos in J Orphanet Rare Dis 2010
uniQure

AMT-130: Orphan drug designation

September 2017

Orphan Drug Designation
U.S. Food & Drug Administration (FDA)

January 2018

Orphan Medicinal Product Designation
European Medicines Agency (EMA)
AMT-130: approach to treating Huntington’s disease

AMT-130 gene therapy for Huntington’s disease (HD)

- Non-selective **knockdown of huntingtin protein** (HTT) in the brain
- Utilizes **proprietary miRNA** that binds to and degrades HTT mRNA
- **One-time injection** in the striatum, the primary affected structure in HD
- AAV5 has been shown to have **widespread distribution in brain, including cortex**
- MRI-guided stereotactic administration directly into **deep structures of brain**
- **Demonstrated preclinical PoC** in multiple small and large animal models
- AMT-130 **leverages same manufacturing platform** and process used for AMT-061
Therapeutic Targeting

- mHTT primarily leases to damage in the striatum, and in later stage disease, in parts of the cortex

- Therapeutic targeting of the areas involved in the disease:
  - Striatum (caudate nucleus and putamen)
  - Globus pallidus
  - Cortex (Sensorimotor)

- Lowering of HTT in other brain areas (or systemically) is not expected to contribute to a meaningful therapeutic effect

Huntington’s Disease Pathway

Penetration throughout brain

Vector genome copies per µg DNA

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

1 Lower Limit of Detection
Two-way ANOVA with Tukey's multiple comparison test, * p<0.05, ** p<0.01, *** p<0.001
AMT-130: status and next steps

Current Status

• Pre-clinical proof of concept for AMT-130
• Nonclinical safety toxicology studies ongoing
• Granted Orphan Drug Designation by FDA
• Granted Orphan Medicinal Drug Designation by EMA

Next Steps

• Submit IND for AMT-130 in 2H 2018
• Begin first-in-human clinical study
Cardiovascular Disease
Collaboration with Bristol-Myers Squibb

Overview

- Up to 10 targets focused on CV disease
- 4 of 10 targets designated thus far
- $140 million received to date
- $2.3 billion in potential milestones
- Up to double-digit royalties
- All R&D paid by BMS
- QURE is exclusive manufacturer
- BMS has global commercial rights
- BMS has 8% equity stake in uniQure
- BMS has warrants to acquire up to 19.9%
Targeting S100A1: a master regulator of heart function

**CHF Market**
- 5.7 million patients in US\(^1\)
- 50% die within 5 years\(^1\)
- $31 billion cost per year\(^2\)

**Current Status**
- Demonstrated DNA delivery and dose expression of S100A1 expression in large animal model
- Validated clinically acceptable administration technique
- Initiated preclinical heart function study in diseased minipigs
- Successful manufacturing of AMT-126 in Lexington, MA

**Next Steps**
- Data on heart function study in 2H 2018
- Initiate IND-enabling tox study
- Initiate Phase I/II trial

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\(^1\) Mozzafarian D, Benjamin EJ, Go AS, et al. 2016
\(^2\) Kochanek KD, Xu JQ, Murphy SL, Miniño AM, Kung HC. 2011
Several milestones across key programs

<table>
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<th>Program</th>
<th>Milestones</th>
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