Delivering Gene Therapy to Patients

Jefferies Gene Editing/Therapy Summit
Matthew Kapusta, Interim Chief Executive Officer
OCTOBER 11, 2016
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 2014 Annual Report on Form 20-F filed with the Securities and Exchange Commission on April 7, 2015 and its 2015 Annual Report on Form 20-F filed with the Securities and Exchange Commission on April 4, 2016. 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.
This is uniQure. Pursuing the promise of gene therapy – single treatments with potentially curative results to transform the lives of patients.
A leader in gene therapy

3 therapeutic franchises with established clinical proof-of-concept in 2 indications

- Liver / Metabolism
  - Lead program in Hemophilia B

- CNS Disorders
  - Lead program in Sanfilippo B

- Cardiovascular Disease
  - Bristol-Myers Squibb collaboration
AAV5 - uniQure’s proprietary and proven vector

- Validated delivery technology
- Successfully and safely treated 20 patients in 3 clinical studies
- Lowest prevalence of pre-existing antibodies
- Successful delivery in liver and brain tissues
- Initial efficacy established in Hemophilia B and Sanfilippo B
- Applicable to a wide variety of indications
Leading baculovirus manufacturing platform

**FEATURES**
- 3rd generation insect cell, baculovirus
- Amsterdam: EU-approved facility
- Lexington: scalable to 2 x 2000L
- Ready for commercial scale-up
- IP protected process

**BENEFITS**
- Control process through commercialization
- Highly scalable, cost-effective
- Adaptable to every project
- High volume capacity
- Consistent, stable, high-quality products
Liver / Metabolism
Gene Therapy
Portfolio
### Goal of gene therapy in Hemophilia B

**Goal – Shift patients from severe to mild disease**

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>FIX activity</th>
<th>Spontaneous bleeding</th>
<th>Bleeding with minor trauma</th>
<th>Bleeding with major trauma/surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>severe</td>
<td>&lt;1%</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>moderate</td>
<td>1-5%</td>
<td>rare</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>mild</td>
<td>5-40%</td>
<td>very rare</td>
<td>no</td>
<td>no</td>
</tr>
</tbody>
</table>


- ~29,000\(^1\) hemophilia B patients worldwide
- On-demand cost of FIX replacement ~$300,000/patient/year\(^2\)
- Mild hemophiliacs require substantially less FIX replacement

\(^1\)Annual Global Survey 2014, World Federation of Hemophilia (2015)
\(^2\)Gene Therapy for Hemophilia: Addressing the Coming Challenges of Affordability and Accessibility, Molecular Therapy (2013)
Significant clinical benefit with FIX of approximately 5%

N=377 on demand Hem A patients - UMC, Utrecht

AMT-060: Validated AAV5 capsid

AAV5 – clinically proven, safe vector with potential for greater patient access

- AAV5 serotype: high liver tropism
- Lowest prevalence of pre-existing anti-AAV5 neutralizing antibodies in the general population

Safely tested in human clinical trials

1 year follow-up
8 patients with acute intermittent porphyria
Wide dose range 5x10^{11} to 1.8x10^{13} gc/kg

AAV5 differentiated from other wild-type vectors

Lowest prevalence of pre-existing antibodies

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2 D'Avola et al. Journal of Hepatology 2016; doi: http://dx.doi.org/10.1016/j.jhep.2016.05.012
3 Boutin et al. Human Gen Ther 2010; 21(6):704-12
FIX gene – the only gene cassette with clinically proven multi-year durability

- Demonstrated safety and durable FIX activity up to 4 yrs\(^1\)
- Wild type FIX gene, codon optimized
- Tested in more than 20 patients
- Resulted in improvement in bleeding phenotype
- Corresponds to a meaningful reduction in FIX usage
- LP1 liver specific promoter
- High dose (2x10\(^{12}\) gc/kg) mean FIX activity: 5.1%

Reduction in annual factor use\(^1\)

- All patients (n=10): 92%
- High dose (n=6): 96%

\(^1\)Nathwani et al. NEJM 2014; 371:1994-2004
Inclusion Criteria

- Older than 18 Years
- Severe (<1% FIX) or moderate-severe (FIX<2%) levels
- On prophylactic or on-demand rFIX
- Severe bleeding (>4 bleeds/year or arthropathy)
Demographics and baseline characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>35</td>
<td>54</td>
<td>72</td>
<td>69</td>
<td>71</td>
</tr>
<tr>
<td>Phenotype (FIX activity)</td>
<td>Severe (1%)</td>
<td>Severe (&lt;1%)</td>
<td>Severe (&lt;1%)</td>
<td>Moderate-severe (1.5%)</td>
<td>Severe (&lt;1%)</td>
</tr>
<tr>
<td>FIX prophylaxis (prescribed dose)</td>
<td>Once weekly 4,000 IU</td>
<td>Once weekly 2,000 IU</td>
<td>Once weekly 2,000 IU</td>
<td>Twice weekly 4,000 IU</td>
<td>Twice weekly 4,000 IU</td>
</tr>
<tr>
<td>Total bleedings 1 year prior to screening (spontaneous)</td>
<td>7 (2)</td>
<td>12 (9)</td>
<td>22 (16)</td>
<td>17 (7)</td>
<td>15 (15)</td>
</tr>
<tr>
<td>Arthropathy</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Prior Hepatitis C infection</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

- No screen failures due to pre-existing anti-AAV5 neutralizing antibodies
- Older population (4/5 patients >50 years)
- Frequent bleeding episodes despite 1-2x/week FIX prophylaxis (before treatment with AMT-060)
- Advanced joint disease (4/5 with multiple target joints)
Low-dose cohort: FIX activity up to 39 weeks

Consistent, stable FIX Activity – Patients off Prophylactic rFIX

Mean FIX activity up to 39 weeks: 5.4% (95% CI 5.0–5.8)

* Average of all values measured at least 10 days after last rFIX administration
Before AMT-060, usage is calculated as prescribed prophylaxis + on demand FIX
After AMT-060, usage is calculated from end of protocol-specified prophylaxis tapering period
Based on patient reported outcomes up to the data cut-off (22 July 2016)

Low-dose cohort: Annualized mean total usage of FIX

~80% reduction in total FIX usage after treatment with AMT-060

Before vs After AMT-060
up to 39 weeks of follow up

- Pre- AMT-060
- Post AMT-060

Annualized mean FIX units usage

<table>
<thead>
<tr>
<th></th>
<th>All patients (n=5)</th>
<th>Excluding Pt. 3 (n=4)</th>
</tr>
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<tbody>
<tr>
<td>Decrease in IUs used (mean)</td>
<td>267,351</td>
<td>319,809</td>
</tr>
</tbody>
</table>

75% decrease in usage
82% decrease in usage

Decrease in IUs used (mean)
AMT-060 has been safe and well-tolerated

Adverse Events

2 serious adverse events (SAEs) occurred

- **Patient 1**: mild, transient elevation of ALT; responsive to tapering prednisolone (60 mg/day start dose) without loss of FIX activity
  - No recurrence and no T-cell activation
- **Patient 3**: self-limiting fever in first 24 hours post-AMT-060

Immuno-geneticity

- No evidence of sustained AAV5 capsid-specific T-cell activation
  - 1 patient had transient T-cell activation slightly above positive threshold (only at 1 time point)
  - Patient did not have elevation in ALT
- As expected, all patients developed anti-AAV5 antibodies after week 1
- No patient developed FIX inhibitors

ALT, alanine aminotransferase; FIX, Factor IX
AMT-060: Next steps in Hemophilia B

1. Initiation of high-dose cohort
2. Low-dose cohort data presented
3. Second dose cohort data presentation in late 2016
4. Establish regulatory pathway for approval
5. Initiate pivotal trial in EU and U.S.
CNS Gene Therapy Portfolio
Goal – attenuated disease course

- 2,000 treatable patients in major markets (1: 350,000 births)
- No treatment for these patients currently available

- 30-month study ongoing in 4 patients
- 12-month data recently presented

Next steps:
- 2,000 treatable patients in major markets (1: 350,000 births)
- No treatment for these patients currently available

Market

Data to Date

Status

Next Steps

- Safety confirmed
- Proof of concept of gene therapy established
- Continuing improvement in cognitive development promising

- Read-out of 30-month data in 1Q 2017
Goal - reduction of mutant aggregating huntingtin to decrease toxic burden

- Worldwide prevalence of 2.71 in 100,000
- EU/US 5.70 in 100,000
- No treatment available

- Non-clinical safety toxicology studies ongoing

- Lead selection completed
- Pre-clinical proof of concept for AMT-130 established in peer-reviewed publication

- Initiate first-in-man study

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1Pringsheim et al. Mov. Disord. (2012)
Cardiovascular Program
Landmark gene therapy deal leveraging uniQure’s technology platform

Exclusive license for S100A1 gene therapy program for chronic heart failure

- Up to 10-target collaborations providing exclusive rights to BMS in CV disease
- Leverage BMS clinical and commercial expertise in CV disease
- $140 million received to date
- $2.3 billion in potential milestones
- Up to double-digit royalties
- All R&D paid by BMS; with QURE exclusive manufacturer
- BMS has 9.9% stake in uniQure; Warrants to own up to 19.9%
A leader in gene therapy

1. Robust discovery engine and strong product pipeline
2. Lead program, AMT-060, with Ph I/II POC
3. Established commercial-grade manufacturing
4. Proven, proprietary AAV vector platform
5. Strategic collaboration with BMS in CV disease
6. Strong cash position with €166M ($184M) at end of 2Q16
uniQure