uniQure

Delivering Gene Therapy to Patients

Jefferies Global Healthcare Conference

New York, NY

June 1, 2015
Forward-looking statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements contained in this presentation reflect uniQure’s current views with respect to future events, and uniQure assumes no obligation to update any forward-looking statements except as required by applicable law.

These forward-looking statements include, but are not limited to, statements regarding the risk of cessation or delay of any of the ongoing or planned clinical studies and/or development of our product candidates, the risk of delay or failure to successfully commercialize or obtain further regulatory approval of Glybera, and the risk that our collaborations with Chiesi or our other collaboration partners will not continue or will not be successful. Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including, without limitation, risks associated with our clinical development activities, regulatory oversight, product commercialization, intellectual property claims, and the risks, uncertainties and other factors described under the heading “Risk Factors” in uniQure’s form 20-F and the prospectus dated February 5, 2014, both documents filed with the Securities and Exchange Commission. 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, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, except as required by law.
Most Advanced Gene Therapy Company

Broad portfolio and mature technology platform

- Near term clinical results in Hemophilia B, Sanfilippo B (MPSIII)
- > $2.3 bn BMS partnership for cardiovascular gene therapies
- Glybera first EU-approved gene therapy, via partner Chiesi
- Industrial scale, insect cell-based manufacturing platform
- Multiple preclinical programs in liver, CNS, CV diseases
- Strong next-generation vector + promoter partnerships

Leading fully integrated AAV-based gene therapy company
BMS Partnership
Largest gene therapy deal leveraging uniQure’s technology platform

The goal of advancing the promise of gene therapy for the millions of patients that suffer from heart failure

MULTIPLE CARDIOVASCULAR PROGRAMS
> Exclusive License for S100A1, a master regulator of heart function
> Up to 9 other targets (primarily CV)

KEY TERMS
> Near term commitment of $102 million
> Total milestone potential: > $2.3 billion
> Equity investments of up to 19.9%
> BMS funds all R&D
> BMS – Clinical development and commercialization
> QURE – CMC and manufacturing
> Tiered royalties up to double digits
Proprietary Manufacturing and Vector Know-How
The Core of Our Technology Platform

**LEADING MANUFACTURING CAPABILITIES**

**AMSTERDAM, NL (EU)**
- 2 x 50 L
- EMA approved facility

**LEXINGTON, MA (USA)**
- World's largest GT manuf facility
- 2 x 500 L (scalable to 2 x 2,000 L)
- GMP validation in 2H 2015

**PROPRIETARY INSECT CELL-BASED TECHNOLOGY**
- Enhanced proprietary replication process; Safe by design
- Highly scalable and cost efficient
- Attracting collaborations and partnerships

**STATE-OF-THE-ART VECTOR DESIGN**

Natural AAV Serotypes

- AAV1 (exclusive for LPLD/ muscle)
- AAV2 (public domain)
- AAV5 (exclusive for Liver/ CNS)
  (non-exclusive for CV)

Directed Evolution

Next-Gen AAV

Super-mutant vectors
Selected for potency, IP and FTO
Available by end of 2015
Pipeline Overview
Leveraging technology platform through partnerships

1st Approved Gene Therapy
GLYBERA EU / Other Select Regions
GLYBERA US / CANADA / ROW
HEMOPHILIA B EU / ROW
HEMOPHILIA A
MULTIPLE PRECLINICAL PROGRAMS
PARKINSON’S DISEASE (GDNF)
SANFILIPPO B
HUNTINGTON’S (miRNA)
MULTIPLE PRECLINICAL

CNS
CONGESTIVE HEART FAILURE (S100A1)
MULTIPLE PRECLINICAL CV PROGRAMS

Cardiovascular

Liver-Targeted

QURE Partnered
Life with Hemophilia
Frequent treatments to overcome spontaneous bleeds

- **WHAT IS HEMOPHILIA?**
  - Rare, genetic disease affecting males
  - Lack of / dysfunctional Factor IX or FVIII
  - Susceptible to spontaneous bleeds
  - Often affecting joints, leading to severe disabilities

- **SIGNIFICANT MEDICAL NEED**
  - Frequent infusions: painful, time-consuming
  - Challenging compliance
  - Despite treatment, risk for breakthrough bleeds

- **HUGE CHANGE IN QUALITY OF LIFE**

- **PREMIUM PRICING**
Standard of Care: Enzyme Replacement Therapy

Prophylactic Treatment: 2 – 3 infusions per week

Risk of Breakthrough Bleeds Below 5% Expression
Gene Therapy

No Risk of Spontaneous Bleeds, if Expression > 5% of Normal

Continuous Expression > 5% Reduces Risk of Breakthrough Bleeds

% Expression of normal

Disease Severity
- Mild
- Moderate
- Severe

5% Expression
AAV8/FIX for Hemophilia B

Single Intervention Reduces Need for Prophylactic Treatment\(^1\)


\(^1\) Third party trial conducted by St. Jude’s Children Research Hospital and UC London
Conclusion

**REMARKABLE PATIENT BENEFIT**

- Median duration post treatment: 3.2 years for all 10 patients
- Median annual bleeding episodes down > 90%: from 16.5 to 1.0 in high dose
- Factor IX concentrate units used in high dose patients down 96%

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Third party trial conducted by St. Jude’s Children Research Hospital and UC London

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(1) Third party trial conducted by St. Jude’s Children Research Hospital and UC London
AAV5/FIX Hemophilia B
Phase I/II Dose Escalation Study

**POPULATION**
- 10 patients (severe bleeding phenotype)
  - Severe (< 1% FIX) on prophylactic therapy
  - Moderate (≤ 2% FIX) on-demand therapy

**OBJECTIVES**
- Assess safety/tolerability
- Define FIX expression level

**KEY EFFICACY ASSESSMENTS**
- Factor IX activity
- FIX product consumption
- Annual bleeding rate
- Health related quality of life

**TIMELINES**
- Interim data expected in 2H 2015

**Dose (gc/kg)**
- **High** (2.0 × 10^{13})
- **Mid** (2.0 × 10^{12})
- **Low** (2.0 × 10^{11})

**St. Jude Study**
- AAV8 mammalian
- AAV5 insect cell

**QURE Ph I/II**
- uniQure

**5% Expression**

**FAST TRIAL EXECUTION BY CROSS REFERENCING DATA FROM PREVIOUS TRIALS**
- St. Jude FIX safety data
- Porphyria AAV5 safety data

**Notes**
- FAST TRIAL
- EXECUTION
- CROSS
- REFERENCE
- DATA
- FROM
- PREVIOUS
- TRIALS

** uniQure **
Best-in Class Hemophilia B Program
Validated AAV5 PoC (AIP Study) | Validated FIX PoC (St. Jude study)

**SAFETY FIRST**

**PREDICTABLE SAFETY PROFILE**
- No immune suppression/rescue medication required
- Pushed AAV5 human doses 10x higher than competitors

**DURABLE EXPRESSION**
- Unprecedented durability in humans
- Strong preclinical AAV5 data

**PREDICTABLE, DOSE LINEARITY**
- Clear relationship between dose and expression levels

**LOW NAB LEVELS**
- Negligible prevalence of neutralizing anti-AAV5 antibodies
Life with Sanfilippo B
Devastating deterioration of brain function in children

- WHAT IS SANFILIPPO?
  - Rare, autosomal recessive lysosomal storage disease (MPSIII)
  - Lack of NaGlu, enzyme required to break down glycosaminoglycan heparan sulfate
  - Leading to cognitive decline, maladaptive behavior

- SIGNIFICANT MEDICAL NEED
  - No treatment option available
  - Prevalence 1:200,000

- CLINICAL PH 1 WITH INSTITUT PASTEUR
  - Strong preclinical data
  - Read-out in 2H 2015
HEART FAILURE: A MULTI-BILLION DOLLAR MARKET OPPORTUNITY

> Western countries +20 million patients
> Single largest cause of hospitalizations, 5-year mortality >50%
> Huge unmet need for disease modifying agent

DE-RISKED GENE THERAPY PRODUCT DEVELOPMENT PROGRAM

> Leading CV experts in uniQure team (Prof. Most / Prof. Katus, Univ. of Heidelberg)
> uniQure’s validated manufacturing platform optimizes product safety, quality and scalability

STRONG VALUE ESTABLISHED

> Patent for the S100A1 gene – a master regulator of heart function
> Proof-of-concept in human-relevant pig model
  > Preclinical efficacy: 90% survival vs. 10% in placebo treated pigs
  > 6 month Troponin T, BNP biomarkers re-established to normal levels
Restoration of Overall Cardiac Function

S100A1: A Master Regulatory of Heart Function

Dysfunctional Heart

Heart Functions Regulated by S100A1

- Contractile Force
- Energy Supply
- Rhythm Stability
- Growth Control

Restored Heart Function
Best-in Class Program for Congestive Heart Failure

S100A1 – A Differentiated Approach to Cardiovascular Disease

**UPSTREAM GENE TARGET**
- S100A1: Master regulator of heart function
- Restores entire calcium network

**SPECIFIC PROMOTER**
- MLCV-2
- Specific activity cardiomyocyte-targeted expression

**VECTOR TECHNOLOGY**
- Cardiac tropism
- Desired gene copy/protein levels

**ADMINISTRATION/DELIVERY**
- Retrograde intravenous infusion
- High concentration and fast injection
1 Year Survival in Human Relevant Pig Model

S100A1 – Survival Data, Supported by Biomarkers

- **AAV9-S100A1** (90% Survival)
- **AAV9-luc/saline** (10% Survival)

**Survival Data, Supported by Biomarkers**

**Plasma BNP (pg/ml)**
- Sham
- AAV9-luc/sal
- AAV9-S100A1

**hsTnT (pg/ml)**
- Sham
- AAV9-luc/sal
- AAV9-S100A1

n=20 each group
Cash and Financial Overview
Ample Resources to Execute Our Plan

- **CASH BALANCE AS OF DECEMBER 31, 2014 = €53.2 MILLION**
  > 2014 cash used in operations/investing activities = €45.9 million
  > Closed follow-on offering on April 15, raising gross proceeds of $88.5 million

- **2015 CASH IMPACT OF BMS COLLABORATION**
  > $50 million upfront payment due at closing (May 2015)
  > ~$37 million from sale of 4.9% equity position at $33.84/share (June 2015)
  > $15 million guaranteed milestone on selection of next three targets (Q3 2015)
  > Commitment to purchase an additional 5.0% equity ownership at a 10% premium to market (2H 2015)

- **EXCLUDING IMPACT OF BMS TRANSACTION, 2015 CASH BURN EXPECTED TO BE €45-55 MILLION**
  > Phase 1/2 clinical study of AMT-060 in Hemophilia B
  > Preparing for initiation of Ph 4/ U.S. pivotal study of Glybera
  > GMP validation of Lexington facility
2015 A Breakthrough Year for uniQure

Multiple Near-term Catalysts

- HEMOPHILIA B HUMAN POC PRELIMINARY DATA
- CLINICAL DATA FROM SANFILIPPO B HUMAN TRIAL (LYSOSOMAL STORAGE DISORDER)
- MULTI- BILLION $ PARTNERSHIP WITH BMS ON CARDIOVASCULAR DISEASES AND BEYOND
- 1ST LAUNCH OF A GENE THERAPY PRODUCT IN THE WESTERN WORLD: GLYBERA
uniQure
The Leader in Gene Therapy