These slides and the accompanying oral presentation contain forward-looking statements and information. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify forward-looking statements. For example, all statements we make regarding the initiation, timing, progress and results of our preclinical and clinical studies and our research and development programs, our ability to advance product candidates into, and successfully complete, clinical studies, and the timing or likelihood of regulatory filings and approvals are forward looking. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These statements are also subject to a number of material risks and uncertainties that are described in our most recent quarterly report on Form 10-Q, as well as our subsequent filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.
Our Vision: Make Hope a Reality
Our Strategic Intent

- **Late Stage (LentiGlobin, Lenti-D)**
- **Big Near Term Opportunities (SCD, Multiple Myeloma)**
- **Severe Genetic Diseases**: Hematopoietic Stem Cells (HSCs)
- **Immunotherapy**: T Cells
- **Transformative Product Focus**
- **Best Team (350+) Great Partners**
- **"Tetris" R&D (Anti-Pure Play)**
- **Truly Integrated Platform**

**Lentiviral Gene Delivery** Pure, Potent, Reproducible, Scalable

**Global Manufacturing Platform** Virus and Drug Product

**Genome Editing Platform** MegaTALs
World-class Gene Therapy Platform and Integrated Global Capabilities

THE GENE THERAPY PRODUCT COMPANY

∞ | Patient Impact

2+ Products on the Market
2+ Programs Nearing Commercialization
4+ Additional Programs in the Clinic
How Do We Get There?

Data, Execution and Development in 2017

**DATA**
- CRB-401 Study Data (bb2121) @ ASCO
- Lenti-D CALD Update @ TBD
- Initiate HGB-212 Study of LentiGlobin

**EXECUTION**
- LentiGlobin, TDT Update @ EHA
- LentiGlobin, TDT and SCD Update @ ASH
- Preparations for TDT EU MAA Filing
- Confirm LentiD, CALD Clinical/Regulatory Path

**DEVELOPMENT**
- File Next Generation BCMA IND (bb21217)
- Advance & Further Validate Gene Editing Platform
CRB-401: All bb2121 Patients in Active Dose Cohorts Achieved an Objective Response, Duration up to 54 Weeks

bb2121 has induced durable and deepening responses in a heavily pre-treated population (median 7 prior therapies) with relapsed/refractory multiple myeloma, including:

- 100% ORR, 73% VGPR or better, 27% CR (at doses > 50 x 10⁶)
- MRD negative results in all evaluable patients (N=4)
- No disease progression in patients treated with doses > 50 x 10⁶, with 1 patient past 1 year and 8 patients past 6 months

To date, the safety profile of bb2121 has been manageable at all tested doses

- No DLTs
- The 2 reported events of grade 3 CRS resolved within 24 hours
- No grade 3/4 neurotoxicity reported
LentiGlobin Clinical Studies

**NORTHSTAR (HGB-204)**
- Phase 1/2 multicenter study; all genotypes
- All 18 patients treated, with ≥ 6 months follow-up
- 2 patients have completed 2-year analysis

**HGB-205 (TDT and SCD)**
- Phase 1/2 single-center study; all genotypes
- 4 TDT patients treated, with 11 – 33 months follow-up

**HGB-206 (Severe SCD)**
- Open label, multicenter, U.S. based study
- N=29 adults

**NORTHSTAR-2 (HGB-207)**
- Phase 3, global, multicenter study; non-β°/β° genotypes
- N=15 adults and adolescents, and N=8 pediatric patients
- *First study to use new manufacturing process*

**NORTHSTAR-3 (HGB-212)**
- Phase 3, multicenter, global study; β°/β° genotypes
- N=15 adults, adolescents and pediatric patients
- *Initiation planned for 2017*
Key Questions

**Transfusion-Dependent β-thalassemia (TDT): Northstar-2 and HGB-205**

- With our new manufacturing process in Northstar-2, are we able to consistently manufacture drug product (DP) with higher vector copy number (VCN) and proportion of transduced cells?

- How do the early results from Northstar-2...
  - Compare to the results seen in non-β⁰/β⁰ patients in HGB-204?
  - Read through to β⁰/β⁰ patients?
  - Read through to SCD patients?

- What can we learn from the HGB-205 TDT patients?

**Severe Sickle Cell Disease (SCD)**

- How do the data from the HGB-205 patients compare to ASH 2016 data?

- What does HGB-205 teach us regarding the potential impact of the protocol and manufacturing changes made in HGB-206?
A Phase 3 Study to Evaluate Safety and Efficacy of LentiGlobin Gene Therapy for Transfusion-Dependent β-thalassemia in Patients with non-β0/β0 Genotypes: The Northstar-2 (HGB-207) Trial

Mark C. Walters, Alexis Thompson, Suradej Hongeng, Janet L. Kwiatkowski, Franco Locatelli, John Porter, Martin Sauer, Adrian Thrasher, Isabelle Thuret, Evangelia Yannaki, Alexandria Petrusich, Mohammed Asmal
Gene Therapy for Transfusion-Dependent \(\beta\)-thalassemia (TDT)

- Autologous gene therapy aims to correct TDT without the immunologic risks of allogeneic HSCT
- In Northstar (HGB-204) and HGB-205 phase 1/2 studies
  - LentiGlobin BB305 gene therapy has eliminated transfusions in most patients with non-\(\beta^0/\beta^0\) genotypes
  - Patients with \(\beta^0/\beta^0\) genotypes had a median 63% reduction in transfusion volume following treatment

**Key finding:** Vector copy number (VCN) in drug product (DP) correlates with HbA\(^{T87Q}\) production
- DP VCN in HGB-204 study was 0.3 – 1.5 copies/cell
Northstar-2 (HGB-207) Study of LentiGlobin BB305 Gene Therapy

- Investigating efficacy and safety of LentiGlobin BB305 in adolescents and adults with TDT and non-β₀/β₀ genotypes
- Uses refined manufacturing process to yield higher DP VCNs
- Primary endpoint: proportion of patients who achieve “transfusion independence” (TI)
  - TI = maintain an average Hb ≥ 9 g/dL without RBC transfusions for ≥12 months

Data as of June 2, 2017
Current Status of Northstar-2 Study

Key enrollment criteria

• 12 to 50 years of age
• Non-β₀/β₀ genotype
• RBC requirement: ≥100 mL/kg/year (or ≥8 RBC transfusions/yr) for past 2 years
• Adequate organ function/performance status
• No previous stem cell transplant or gene therapy

First patient infused December 2016

Target: 15 treated patients (including ≥5 aged 12-17 years)

Consented N=16

Ineligible N=4*

Stem Cell Mobilization complete N=6

Drug Product Manufacturing and Release Complete N=6

Transplant Pending N=3

LentiGlobin Drug Product Infused N=3 (adult)

As of June 2, 2017
*reasons for ineligibility: 2 withdrew consent, 2 screen failure due to liver biopsy findings
Overview of the Northstar-2 Study Process

**Patient Treatment**
- Stem Cell Collection
  - Select CD34+ cells

**Centralized Manufacturing**
- Pre-infusion Conditioning
  - mobilization (with G-CSF/plerixafor) + apheresis
- Transduced Stem Cells Infused
  - Transduce using new manufacturing process
- Immune System Reconstitution
  - LentiGlobin BB305 manufacturing
  - busulfan myeloablation
  - Cryopreserve, test and release DP

**Follow-up**
- 2 years follow-up
  - Extension study (13 years)
  - Up to 15 years total follow-up
# Northstar-2 Patient Characteristics

*N=3 treated patients to date*

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>20</td>
<td>20</td>
<td>22</td>
</tr>
<tr>
<td>Gender</td>
<td>F</td>
<td>F</td>
<td>F</td>
</tr>
<tr>
<td>Genotype</td>
<td>β⁰/β⁺</td>
<td>β⁰/β⁺</td>
<td>IVS-I-5 (G&gt;C)</td>
</tr>
<tr>
<td>Pre-Treatment pRBC Transfusions (mL/kg/year)¹</td>
<td>162.5</td>
<td>192.9</td>
<td>158.7</td>
</tr>
<tr>
<td>Liver Iron Concentration (mg/g) (normal range &lt;1.1 mg/g)</td>
<td>18.8</td>
<td>19.6</td>
<td>1.4</td>
</tr>
<tr>
<td>Cardiac T2⁺ (msec) (normal range &gt;20 msec)²</td>
<td>42.5</td>
<td>45.3</td>
<td>36.3</td>
</tr>
<tr>
<td>Splenectomy</td>
<td>N</td>
<td>N</td>
<td>Y</td>
</tr>
</tbody>
</table>

Initial Safety Summary & Treatment-related Parameters

N=3 treated patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>VCN in Drug Product(^1)</td>
<td>2.9</td>
<td>2.4</td>
<td>3.2, 2.4</td>
</tr>
<tr>
<td>Vector positive cells</td>
<td>77%</td>
<td>53%</td>
<td>77%, 82%</td>
</tr>
<tr>
<td>CD34+ Cell Dose (x10^6/kg)</td>
<td>7.0</td>
<td>13.6</td>
<td>8.1</td>
</tr>
<tr>
<td>Busulfan AUC (μM*min)(^2)</td>
<td>4286</td>
<td>4337</td>
<td>4562</td>
</tr>
<tr>
<td>Neutrophil engraftment, study day(^3)</td>
<td>25</td>
<td>24</td>
<td>19</td>
</tr>
<tr>
<td>Platelet engraftment, study day(^4)</td>
<td>44</td>
<td>45</td>
<td>35</td>
</tr>
<tr>
<td>Follow up (months)</td>
<td>6</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

Grade ≥3 non-hematologic AEs \(^1,2\)

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow up</td>
<td>6 months</td>
<td>3 months</td>
<td>2 months</td>
</tr>
<tr>
<td>Adverse events</td>
<td>none</td>
<td>Hypotension (SAE; Grade 3)</td>
<td>Mucositis (Grade 3)</td>
</tr>
</tbody>
</table>

- No significant veno-occlusive disease (VOD) of the liver or infections post-treatment
- No drug product-related AEs

As of June 2, 2017
1. VCN: vector copy number (vector copies per diploid genome)
2. Estimated average daily busulfan exposure over four days
3. ANC ≥ 500 for 3 consecutive days
4. Unsupported platelet count ≥ 20,000/μL

As of June 2, 2017
1. Hematological values typically decreased post-transplant are not shown
2. All AEs are reported from Day -8 to date of last contact (2-6 months)
Improved Manufacturing Process Yields Higher Drug Product Vector Copy Number and Proportion of Transduced Cells

- DP VCN for initial 6 subjects manufactured in **Northstar-2** consistently higher than 18 subjects in Northstar
  - Northstar: median 0.7 (0.3 – 1.5)
  - Northstar-2 to date: **median 3.0** (2.4 – 4.0)

- Increased DP VCN in **Northstar-2** reflects higher proportion of transduced cells (% vector positive)
  - Northstar: median 32% (range 17% – 58%)
  - Northstar-2 to date: **median 77%** (range 53% – 90%)

* Samples from EU manufacturing pending vector positive analysis
First Patient Treated in Northstar-2 with 6 Months Follow-up has Achieved Normal Total Hemoglobin After Discontinuing Transfusions

Northstar

Medians in non-β⁰/β⁰ genotypes
(N=10)
(data as of Sept 2016)

Hemoglobin Concentration (g/dL)

Month 2 | Month 3 | Month 6
---|---|---
1.1 | 2.2 | 4.2

Northstar-2

Patient 1

Hemoglobin Concentration (g/dL)

Month 2 | Month 3 | Month 6
---|---|---
4.8 | 7.1 | 9.5

Last RBC transfusion: Day 33

* N=6 patients in Northstar study with HbE genotype
HbA$^{T87Q}$ in Patients Treated in Northstar-2 Match or Exceed HbA$^{T87Q}$ in Patients Achieving Early Transfusion Independence in Northstar

**VCN over time**

**HbA$^{T87Q}$ levels over time**

**Northstar-2**
- Patient 1
- Patient 2
- Patient 3

**Northstar (non-β0/β0 patients only)**
- DP lots for treated patients
- Transfusion independent
- Not yet TI evaluable

*Northstar data as of ASH 2016*
Northstar-2 Patient 2: Phenotypic Profile of CD34+ Cells is Atypical

Disproportionate number of lymphoid cells results in lower proportion of primitive stem cells available for transduction.

With the improved manufacturing process, the patient still achieved a transduced stem cell dose on par with transfusion independent HGB-204 patients.
Summary and Next Steps

Northstar-2 Summary

- The improved manufacturing process in Northstar-2 consistently yields higher DP VCNs and proportions of cells transduced.
- Initial results show that the 3 patients treated to date have achieved *in vivo* VCN and HbA\(^{T87Q}\) production as good or better than patients achieving transfusion independence in the first Northstar study.
- No LentiGlobin-related AEs reported in Northstar-2 with 2 - 6 months follow-up:
  - AE profile of LentiGlobin continues to appear similar to autologous HCT with myeloablative busulfan.
  - Data on vector insertion pattern with higher DP VCN is pending.

Next Steps

- **HGB-212**
  - \(\beta^0/\beta^0\) genotypes
- **Phase 3, multi-center, global study**
  - N=15 adults, adolescents and pediatric patients
  - **Initiation planned for 2017**
HGB-205: Transfusion-Dependent Thalassemia (TDT)
HGB-205: Study Status

Patients consented & enrolled N=8

Cell collection and drug product manufacture complete N=7

Conditioning and drug product infusion complete N=7

Ineligible N=1

Follow-up after drug-product infusion for 7 treated patients (4 TDT, 3 SCD)

Median: 23.4 months
range: 3.4 – 42.2 months

As of June 2, 2017
### HGB-205 TDT: Patient and Drug Product Characteristics and Safety

<table>
<thead>
<tr>
<th></th>
<th>1201</th>
<th>1202</th>
<th>1203</th>
<th>1206</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at Enrollment (yrs)</strong></td>
<td>18</td>
<td>16</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td><strong>Genotype</strong></td>
<td>β0/βE</td>
<td>β0/βE</td>
<td>homozygous IVS1 nt 110 G&gt;A</td>
<td>β0/βE</td>
</tr>
<tr>
<td><strong>Pre-Treatment pRBC Transfusions (mL/kg/yr)</strong></td>
<td>139</td>
<td>188</td>
<td>176</td>
<td>189</td>
</tr>
<tr>
<td><strong>VCN in Drug Product</strong></td>
<td>1.5</td>
<td>2.1</td>
<td>0.8</td>
<td>1.1</td>
</tr>
<tr>
<td><strong>CD34+ Cell Dose (x10⁶/kg)</strong></td>
<td>8.9</td>
<td>13.6</td>
<td>8.8</td>
<td>12.0</td>
</tr>
<tr>
<td><strong>Busulfan AUC (average, μM*min)</strong></td>
<td>4,967</td>
<td>5,212</td>
<td>4,670</td>
<td>4,930</td>
</tr>
<tr>
<td><strong>Follow-up (months)</strong></td>
<td>42.2</td>
<td>39.0</td>
<td>23.4</td>
<td>20.4</td>
</tr>
</tbody>
</table>

1=mean pRBC requirement per year, over the past 2 years prior to consent; 2=VCN = number of vector copies per diploid genome

- Adverse events generally consistent with myeloablative conditioning
- No drug-product related non-hematologic AEs or SAEs
- No replication competent lentivirus (RCL) detected to date
- No evidence of insertional mutagenesis
HGB-205 TDT: Stable Peripheral VCN Over Time and Durable HbA<sup>T87Q</sup> Production

VCN over Time

HbA<sup>T87Q</sup> Levels over Time
HGB-205 TDT: Consistent and Durable Transfusion Independence Up to 3.5 Years

*Hemoglobin (g/dL) at most recent study visit
+ Discontinued iron chelation and transitioned to therapeutic phlebotomy: Patients 1201 (started Aug. 2016), 1202 (started Nov. 2015), 1206 (started Oct. 2016)
HGB-205:
Sickle Cell Disease (SCD)
ASH 2016: 8% to 48% Anti-Sickling Hemoglobin at Last Follow Up

Data as of Sept 9, 2016 [HGB-205] and Nov 9, 2016 [HGB-206]
ASH 2016: Vector Copy Number (VCN) in Drug Product and Peripheral Blood

Vector copy number (VCN; per diploid genome)

VCN drop from drug product to peripheral blood in HGB-206

Peripheral blood VCN over time

Data as of Sept 9, 2016 [HGB-205] and Nov 9, 2016 [HGB-206]
Protocol and Process Changes to Potentially Improve Outcomes in SCD Patients

<table>
<thead>
<tr>
<th>Issue</th>
<th>Proposed Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoxic, inflamed marrow</td>
<td>Pre-harvest transfusions to reduce marrow inflammation, hypoxia</td>
</tr>
<tr>
<td>Inadequate myeloablation</td>
<td>Increased exposure to myeloablative agent</td>
</tr>
<tr>
<td>Low yield harvest</td>
<td>Additional changes to manufacturing process to increase cell dose</td>
</tr>
<tr>
<td>Poor transduction</td>
<td>New manufacturing process</td>
</tr>
<tr>
<td>Apheresis (vs. Bone Marrow)</td>
<td>Utilize Plerixafor for mobilization and collection</td>
</tr>
</tbody>
</table>
### HGB-205 SCD: Patient and Drug Product Characteristics

<table>
<thead>
<tr>
<th></th>
<th>1204</th>
<th>1207</th>
<th>1208</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at Enrollment (yrs)</strong></td>
<td>13</td>
<td>16</td>
<td>21</td>
</tr>
<tr>
<td><strong>Genotype</strong></td>
<td>βS/βS</td>
<td>βS/βS</td>
<td>βS/β0</td>
</tr>
<tr>
<td><strong>Busulfan AUC</strong> (average, μM*min)</td>
<td>4,841</td>
<td>5,022</td>
<td>5,447</td>
</tr>
<tr>
<td><strong>CD34+ Cell Dose (x10⁶/kg)</strong></td>
<td>5.6</td>
<td>4.7</td>
<td>3.0</td>
</tr>
<tr>
<td><strong>VCN in Drug Product¹</strong></td>
<td>1.0/1.2</td>
<td>0.7/1.0</td>
<td>0.8/0.5</td>
</tr>
<tr>
<td><strong>Follow-up</strong> (months)</td>
<td>31.7</td>
<td>6.1</td>
<td>3.4</td>
</tr>
<tr>
<td><strong>Neutrophil engraftment²</strong></td>
<td>Day + 38</td>
<td>+ 27</td>
<td>+32</td>
</tr>
<tr>
<td><strong>Platelet engraftment³</strong></td>
<td>Day + 92</td>
<td>+ 51</td>
<td>+39</td>
</tr>
</tbody>
</table>

1. VCN: number of vector copies per diploid genome; 2. Absolute neutrophil count [AUC] ≥ 500 cells/μL for 3 consecutive days; 3. Unsupported platelet count ≥ 50,000/µL for 3 consecutive measures.
HGB-205 SCD: Durable Effect in Patient 1204

Total Hb 12.4 g/dL

VCN 2.3

HbA (transfused)

HbA\textsuperscript{T87Q} 50%

HbS 48%

HbA\textsubscript{2} 2%

HbF <1%
HGB-205 SCD: Safety and Clinical Status in Severe SCD Patients

- Adverse events generally consistent with myeloablative conditioning
  - No drug-product related non-hematologic AEs or SAEs
  - No replication competent lentivirus (RCL) detected to date
  - No evidence of insertional mutagenesis

- Patient 1204
  - One episode of acute gastroenteritis at 30 months post-treatment, with vomiting and 2 days of fever up to 40°C, followed by a vaso-occlusive crisis (VOC) and was hospitalized
  - HbA^{T87Q} and peripheral blood VCN levels have remained stable (HbA^{T87Q} 6.1 g/dL, VCN 2.3 at 30 months)

- Patient 1207
  - Pre-treatment history of frequent episodes of VOC and acute chest syndrome (ACS) despite hydroxyurea prior to beginning regular transfusions. Experienced an episode of ACS 6 months post-treatment and was hospitalized. HbA^{T87Q} continues to increase with 1.8 g/dL at 6 months.
SCD: Transfused Patients Have More Stable VCN

* Dotted lines represent transfused patients
Data from transplant and other literature argue that as little as 3g/dL (~30%) of anti-sickling hemoglobin and gene marking as low as 20% could potentially achieve a disease-modifying effect.
HGB-205 SCD: Levels of Anti-sickling Hemogoblin (HbA$^{T87Q}$ + HbF) Above 30%
Evolution of LentiGlobin in SCD – More To Come at ASH 2017

HGB-206 Process 1

- **Transfusions** (Pre-Treatment)
  - No

- **Conditioning**
  - Low/Med

- **Total Cell Dose**
  - Low

- **Transduction** (VCN & % Transduced)
  - Low

HGB-205

- **Transfusions** (Pre-Treatment)
  - Yes

- **Conditioning**
  - High

- **Total Cell Dose**
  - Medium

- **Transduction** (VCN & % Transduced)
  - Medium

HGB-206 Updated Protocol

- **Transfusions** (Pre-Treatment)
  - Yes

- **Conditioning**
  - High

- **Total Cell Dose**
  - Medium

- **Transduction** (VCN & % Transduced)
  - High

HGB-206 (Apheresis)

- **Transfusions** (Pre-Treatment)
  - Yes

- **Conditioning**
  - High

- **Total Cell Dose**
  - High

- **Transduction** (VCN & % Transduced)
  - High

**Planned Cell Source Shift**

Cell Source: Bone Marrow

Cell Source: Apheresis

(Apheresis simplifies cell harvest and facilitates higher cell doses)
Closing
Key Questions

Transfusion-Dependent β-thalassemia (TDT): Northstar-2 and HGB-205

- With our new manufacturing process in Northstar-2, are we able to consistently manufacture drug product (DP) with higher vector copy number (VCN) and proportion of transduced cells?

- How do the early results from Northstar-2...
  - Compare to the results seen in non- $\beta^0/\beta^0$ patients in HGB-204?
  - Read through to $\beta^0/\beta^0$ patients?
  - Read through to SCD patients?

- What can we learn from the HGB-205 TDT patients?

Severe Sickle Cell Disease (SCD)

- How do the data from the HGB-205 patients compare to ASH 2016 data?

- What does HGB-205 teach us regarding the potential impact of the protocol and manufacturing changes made in HGB-206?
Bringing & Valuing Hope

We Must Make Hope a Reality

Go TRUE BLUE