Making Hope A Reality – bluebird style
Forward Looking Statements

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.
Three Regulatory Filings Anticipated by End of 2019

- LentiGlobin TDT
  First Filing (2018)

- Lenti-D CALD
  First Filing (2019)

- LentiGlobin SCD
  Data-Driven Acceleration

- bb2121 Multiple Myeloma
  First Filing (2019)

2+ Products on the Market
2+ Programs Nearing Commercialization
4+ Additional Programs in the Clinic

∞ Patient Impact
Healthy Ecosystem for Transformative Gene Therapy

Regulatory Atmosphere

- Breakthrough Designation
- PRIME
- RMAT

Approvals

- TDT
- SCID
- CALD
- BCMA

Pricing / Reimbursement & Access

- Payer Engagement
- CMS Value-Based Payment Talk
- Alnylam Access Principles

Industry Validation

- Pfizer
- GSK
- Celgene
- Gilead
- Novartis

Healthy Ecosystem for Transformative Gene Therapy

- Scott Gottlieb, M.D. (FDA)
- Alex Azar (HHS)

Healthy Ecosystem for Transformative Gene Therapy

- Gilead/Kite Yescarta™
- bluebird bio
- Novartis KYMRIAH™
- Spark Luxturna™
- Juno

Healthy Ecosystem for Transformative Gene Therapy

- PATH TO PATIENTS
Our Focus. Our Imperatives.

**Execute & Deliver**
Operate with discipline, urgency and healthy paranoia

**Scale & Reach**
Expand organization and capabilities to bring products to patients globally

**Lead The Way**
Lever product engine, capabilities and resources to solve challenges and unleash opportunities

**Stay BLUE**
Beat the regression odds. Believe in the WHY and act accordingly.
Hopes & Dreams Becoming a Reality

1993
- Genetix Founded

2009/2010
- Science: CALD
- Nature: TDT
- Restart VC Investment
- Changed Name to bluebird bio

2013/2014
- Celgene CAR T partnership
- IPO
- Acquired Genome Editing Company

2015/2016
- TDT: Breakthrough & PRIME Designation
- SCD: RMAT Designation

2017
- BCMA: Breakthrough & PRIME Designation
- NEM: CALD & SCD
- Acquired Manufacturing Facility

CALD Starbeam (Oct. 2013)
TDT Northstar (March 2014)
SCD HGB-205 (Oct. 2014)
bb2121 for multiple myeloma (Feb. 2016)
Driving the Product Platform to Reality for Patients

Make & Scale It  Relentlessly Learn & Innovate

Deliver It  Relentlessly Learn & Innovate

Value It  Relentlessly Learn & Innovate

Lever It  Relentlessly Learn & Innovate
Make & Scale It: Focused on Transitioning from Development to Commercial

DEVELOPMENT

INNOVATE

Viral Vector
Virus Manufacturing
Drug Product

SCALE & DEPLOY

COMMERCIAL

Cambridge | Seattle | NC | EU

[Logos of various companies: apceth, novasep, brammer, Millipore Sigma, Lonza]
Deliver It: The Best Possible Provider, Payer and Patient Experience

**Patient Case Management, Navigation, & Services**

**Enabling Patients to Get To Treatment**
- Educating Patients and Families on Gene Therapy
- Multi Channel Stakeholder Engagement & Data Dissemination
- Referral Network Development

**Supporting Patients Through Treatment**
- Providing Patient Support Through Treatment Process
- Cell Traceability & Scheduling
- Drug Product Manufacturing with End to End Supply Chain
- Reimbursement Authorization

**Enabling Patients to Complete Treatment**
- Allow Patients to Participate in their Ongoing Care and Follow-Up
- Operationalize & Track
- Easy-to-Access Registry

**Key Outcome:**
- Treatment Prescribed
- Treatment Delivered & Patient Discharged
The value our products bring to patients should stand on its own for all stakeholders.
Value It: Quick Answer is Value Based Payment Over Time

**BLUE “VALUE” PRINCIPLES**

- Be focused on patient access to innovation
- Be creative and disruptive (if needed)
- Be flexible and share risk
- Be transparent and proactive with stakeholders
- Be proud
- Don’t do stupid short sighted stuff!

**CONSTRAINTS & AMBITIONS**

**UNMET NEED**

- Heighten awareness of true unmet need in terms of impact on life expectancy and cost

**VALUE EVIDENCE**

- Deliver credible and rigorous value platform arguments/data for value

**PAYMENT MODELS**

- “Free Up” system to recognize value over time
- “Buy time” to prove enduring value
- Fix cost density constraint
- Fix policy constraints (e.g., best price)
- Fix “portability of cure” concern
Lever It: Experience, Capabilities and Partnerships Driving Pipeline Expansion

Innovation & Capabilities
- Viral Vector Manufacturing
- Transduction Enhancements
- Plerixafor Mobilization
- PI3ki-based BCMA manufacturing

New Products & Pipeline
- bb21217 Phase 1
- shmiR Phase 1
- CAR Ts and TCRs Preclinical
- Gamma Delta T cells Preclinical
- MegaTALs Preclinical

Partnerships & Acquisitions
## Our Quest to Constantly Innovate Continues

<table>
<thead>
<tr>
<th>Product Candidates</th>
<th>Program Area</th>
<th>Preclinical</th>
<th>Phase 1/2</th>
<th>Phase 2/3</th>
<th>Rights/Partner</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lenti-D™ Drug Product</td>
<td>Cerebral ALD</td>
<td></td>
<td></td>
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<td>Worldwide</td>
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<tr>
<td>LentiGlobin® Drug Product</td>
<td>Transfusion-Dependent β-thalassemia (Phase 3)</td>
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<tr>
<td></td>
<td>Severe Sickle Cell Disease</td>
<td></td>
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<td>Worldwide</td>
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<tr>
<td>BCL11a shRNA(miR)*</td>
<td>Severe Sickle Cell Disease</td>
<td></td>
<td></td>
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<td>Worldwide</td>
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<td>Cancer</td>
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<td>Multiple Myeloma</td>
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<td>bb21217</td>
<td>Multiple Myeloma</td>
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<td>Celgene</td>
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<tr>
<td>Undisclosed Targets</td>
<td>Various Indications</td>
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<td>Worldwide</td>
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<tr>
<td>Early Research</td>
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<tr>
<td>Early Pipeline</td>
<td>Undisclosed + Gene Editing</td>
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<td></td>
<td>Worldwide</td>
</tr>
</tbody>
</table>

*Development is led by Boston Children’s Hospital*
2018 Milestones

**BY MID YEAR**

- TDT: Northstar-2 (HGB-207) Data
- MM: CRB-401 (bb2121) Data
- SCD: BCL11A shRNA Study Start

**BY END OF YEAR**

- TDT: EMA Filing in non-\(\beta^0/\beta^0\) Genotypes
- TDT: Northstar-3 (HGB-212) Data
- SCD: HGB-206 Data
- SCD: Registration Strategy Update
- MM: Initiate 3\(^\text{rd}\) Line Study*; bb21217 Data
- CALD: Starbeam (ALD-102) Data

$1.6 Billion Cash

Runway into 2021

49.4m shares outstanding as of 12/31/17

49.4m shares outstanding as of 12/31/17. Cash runway guidance is based on current assumptions as of the date thereof and does not include the effect of potential license and collaboration agreements, business combinations or asset acquisitions.

**Anticipated Clinical Data Updates**

*Bespoke Responsibility
Transfusion Dependent β-Thalassemia
Transfusion-dependent β-thalassemia

- Inherited blood disease that requires lifelong, frequent blood transfusions and iron reduction therapy

**STATUS**

- Majority of patients with non-β<sup>0</sup>/β<sup>0</sup> genotype are free of transfusions
- Refined manufacturing leading to robust increase in HbA<sup>T87Q</sup>
- 3+ years durability of effect in early studies

**NEXT STEPS**

- Anticipated first regulatory filing in EU in patients with non-β<sup>0</sup>/β<sup>0</sup> genotypes in 2018

“When I get blood, it is no less than a 14-hour day with transportation included. Getting blood is a lonely job for us thalassemia patients. Transfusion schedules are rigorous and a time consumer. I lose one day every two weeks.” – Laurice
Transfusion-Dependent Thalassemia

- **HGB-204**
  - Basis of EU filing
  - Original manufacturing process
  - All genotypes

- **HGB-205**
  - Basis of EU filing (with Northstar)
  - Original manufacturing process

- **HGB-207**
  - Basis of US filing
  - Refined manufacturing process
  - non-β⁰/β⁰ genotypes

- **HGB-212**
  - β⁰/β⁰ genotypes
  - Refined manufacturing process
  - First patient treated in November 2017
Northstar: 9/10 Patients with non-β^0/β^0 Genotypes and 2/8 with β^0/β^0 Genotypes are Free from Chronic RBC Transfusions

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Time from treatment to last transfusion</th>
<th>Time from last transfusion to last follow-up</th>
<th>Hb (g/dL) At last study visit</th>
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<tbody>
<tr>
<td>β^E/β^0</td>
<td></td>
<td>33.1</td>
<td>10.5</td>
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<tr>
<td>β^E/β^0</td>
<td></td>
<td>34.7</td>
<td>9.4</td>
</tr>
<tr>
<td>β^0/β^+</td>
<td></td>
<td>30.2</td>
<td>12.1</td>
</tr>
<tr>
<td>β^+/β^x*</td>
<td></td>
<td>29.0</td>
<td>12.6</td>
</tr>
<tr>
<td>β^E/β^0*</td>
<td></td>
<td>29.3</td>
<td>13.7</td>
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<tr>
<td>β^+/β^+</td>
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<td>19.1</td>
<td>9.8</td>
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<tr>
<td>β^E/β^0</td>
<td></td>
<td>18.1</td>
<td>9.6</td>
</tr>
<tr>
<td>β^E/β^0</td>
<td></td>
<td>15.9</td>
<td>10.2</td>
</tr>
<tr>
<td>β^E/β^0*†</td>
<td></td>
<td>14.7</td>
<td>8.4</td>
</tr>
<tr>
<td>β^0/β^0</td>
<td></td>
<td>16.7</td>
<td>10.2</td>
</tr>
<tr>
<td>β^0/β^0</td>
<td></td>
<td>15.7</td>
<td>10.3</td>
</tr>
</tbody>
</table>

Data as of September 21, 2017
Northstar: Hemoglobin Remains Stable in Patients Free from Chronic Transfusions Up to Three Years

*Patient 1118 is free from chronic RBC transfusions, however received a single transfusion at 13 months post-infusion during an acute viral illness.

Data as of September 21, 2017
Refined Manufacturing Process Yields Higher Drug Product Vector Copy Number and Proportion of Transduced Cells

Vector copy number (VCN) in drug product

- Median: 3.3 (min-max: 2.4-5.4) for HGB-204
- Median: 0.7 (min-max: 0.3-1.5) for HGB-207

Proportion of CD34+ cells transduced

- Median: 82% (min-max: 53-90%) for HGB-204
- Median: 32% (min-max: 17-58%) for HGB-207

Cell Phenotyping across TDT studies

- HGB-207 pt 2
- HGB-207
- HGB-204

* No of DP exceed number of patients since some patients were mobilized twice
* % LVV not available for 3 patients at time of analyses

Data as of December 1, 2017
Northstar-2: Higher Transduction Efficiency Translates to Robust HbA$^{T87Q}$ with 5 of 6 Patients Producing >6 g/dL HbA$^{T87Q}$ at 3 Months

Data as of October 13, 2017

Patients with at least 6 months follow-up:
Time from last transfusion and initiation of phlebotomy

- Phlebotomy
- Total Hb
- Time from treatment to last transfusion
- Time from last transfusion to data cut-off

Circles indicate females
General agreement with EU & US regulators on the registration path for LentiGlobin for the treatment of transfusion-dependent β-thalassemia

**EU**

Pursue **CONDITIONAL APPROVAL** in patients with non-β°/β° genotypes on the basis of data from ongoing Northstar (HGB-204) & HGB-205 studies, as well as available data from Northstar-2 (HGB-207) study

**US**

Pursue **approval** in adults and adolescents with non-β°/β° genotypes based on data from ongoing pivotal Northstar-2 (HGB-207) trial

**Pediatric population** to be included as a cohort of HGB-207, rather than separate study

Submission for approval in β°/β° patients to be based on ongoing Northstar-3 (HGB-212) study

**BREAKTHROUGH THERAPY DESIGNATION**

**ORPHAN DRUG DESIGNATION**
Severe Sickle Cell Disease
Severe Sickle Cell Disease

• Severe blood disorder that leads to anemia, frequent pain crises and shortened lifespan

STATUS

• Revised study protocol has yielded significant increase in anti-sickling hemoglobin

• Shift to plerixafor-based cell collection providing more and better cells; easier for patients

NEXT STEPS

• Complete 206 study

• Define clinical development and regulatory path

“I experienced my first sickle crisis requiring hospitalization at age 5. Since then I’ve endured hundreds of hospitalizations, blood transfusions and surgical procedures. Despite the devastating symptoms of sickle cell, I was determined to complete my educational goals.” - Lakiea

Source: Global Genes
First disease described at the molecular level; minimal progress in treatment in past 50 years

- Greater than 100,000 Americans affected, millions worldwide
- High morbidity and early mortality
  - Mean age of death in US is 44 years*
- Only 2 FDA-approved treatments
  - Symptom reduction only
  - Not universally effective
- Significant health disparity
- HLA-matched bone marrow transplant curative
  Limited by donor availability to less than 10% of patients

- Paulukonis et al, California's Sickle Cell Data Collection Cohort, 2005-2015* ASH 2017*

*Mean age of death in US is 44 years*
Understanding the Biology of SCD: Manufacturing and Protocol Improvements

Data as of Sept 9, 2016 [HGB-205] and Nov 9, 2016 [HGB-206]
Key Questions on Sickle Cell Disease Gene Therapy Efforts

1. Have the changes to the process and protocol improved *in vivo* VCN and HbA^{T87Q} production?

2. Can we improve patient experience by eliminating the need for bone marrow harvest?

3. Can mobilization with plerixafor allow us to yield more and better cells versus bone marrow?

4. What impact will the implementation of plerixafor have on clinical outcomes?
HGB-206: Evolution of LentiGlobin in SCD – New Early Data from Patients in Group B and Group C

**Group A**
- Bone Marrow: Original Protocol and Manufacturing Process
- Transfusions (Pre-Treatment): No
- Conditioning: Medium
- Total Cell Dose: Low
- Transduction (VCN & % Transduced): Low
- CD34 Phenotype (% CD34 Bright): Medium

**Group B**
- Bone Marrow: Modified Protocol and Mixed Manufacturing Process
- Transfusions (Pre-Treatment): Yes
- Conditioning: High
- Total Cell Dose: Medium
- Transduction (VCN & % Transduced): High
- CD34 Phenotype (% CD34 Bright): Medium

**Group C**
- Peripheral Blood: Modified Protocol and Refined Manufacturing Process
- Transfusions (Pre-Treatment): Yes
- Conditioning: High
- Total Cell Dose: High
- Transduction (VCN & % Transduced): High
- CD34 Phenotype (% CD34 Bright): High

**Planned Cell Source Shift**
- Group A: Cell Source: Bone Marrow
- Group B: Planned Cell Source Shift
- Group C: Cell Source: Apheresis
Enhancements to Manufacturing Lead to Improved Drug Product Characteristics

Vector Copy Number

% Transduced Cells

Data as of November 30, 2017
Process and Protocol Changes Lead to Higher Peripheral Blood Vector Copy Number (VCN) After Drug Product Infusion

- **Mean DP VCNs used for patients with >1 DP lot**
- **Data as of November 30, 2017**

**VCN in drug product and peripheral blood**

- **Peripheral blood VCN over time**

- **NEJM patient**

- **Group A**
- **HGB-205**
- **Group B 1313**
- **Group B 1312**

*Mean DP VCNs used for patients with >1 DP lot*

Data as of November 30, 2017
Improvements in Drug Product Characteristics and Protocol Improve HbA\textsuperscript{T87Q} Production

- 51\% HbA\textsuperscript{T87Q}
- Total Hb 12.6 g/dL

Higher DP VCN
Higher \textit{in vivo} VCN
Higher T87Q

Data as of November 30, 2017
Data with Plerixafor Mobilization and Apheresis Support Using Peripheral Blood for DP Manufacture

Key Findings in 7 Patients

• ACCEPTABLE SAFETY PROFILE no dose limiting toxicities observed

• CELL DOSE delivered higher than with bone marrow harvest

• CELL PHENOTYPE may be more favorable than BMH

Total CD34 cells collected per collection cycle

Median 5.0
(min-max: 0.3 – 10.8) x 10^6
CD34+ cells/kg

Median 10.4
(min-max: 5.1 – 20.0) x 10^6
CD34+ cells/kg

Plerixafor mobilization implemented in HGB-206
Group C: Shift to Apheresis May Further Improve Drug Product Characteristics

Vector Copy Number

% Transduced Cells

CD34+ cell count in DP

Data as of November 30, 2017
Process and Protocol Changes Lead to Higher Peripheral Blood Vector Copy Number (VCN) After Drug Product Infusion

*Mean DP VCNs used for patients with >1 DP lot

Data as of November 30, 2017
Improvements in Drug Product Characteristics and Protocol Improve HbA\textsuperscript{T87Q} Production

Data as of November 30, 2017
Most CD34+ Cells Collected Through Plerixafor Mobilization and Apheresis Have Desirable “Bright” Phenotype

* squares indicate cells transduced for research only

**SCD BM**
- Median 56.5, min-max 49.3-82.7

**SCD APH**
- Median 91.0, min-max 80.5-98.4

**TDT APH**
- Median 97.9, min-max 86.4-99.6
Mobilization and Apheresis Combined with Improved DP Transduction Raises Dose of Cells that Drive Long-Term Hemoglobin Production
Key Questions

Have the changes to the process and protocol improved \textit{in vivo} VCN and HbA$^{T87Q}$ production? ✔️

Can we improve patient experience by eliminating the need for bone marrow harvest? ✔️

Can mobilization with plerixafor allow us to yield more and better cells versus bone marrow? ✔️

What impact will the implementation of plerixafor have on clinical outcomes? 2018
“When I was diagnosed and realized that there was an empty pipeline... I knew I needed to do something — not only for myself and my family, but for everyone else with this ‘orphan cancer’. I desperately wanted my daughter to remember me and thought that if I lived for five years, maybe she would have memories of her mom.” - Kathy Giusti, Founder, MMRF

Multiple Myeloma (BCMA)

- A lethal blood cancer that often infiltrates the bone marrow causing anemia, kidney failure, immune problems and bone fractures

STATUS
- 94% ORR, 56% CR
- 89% VGPR or better
- Median PFS not reached with 40 weeks follow up

NEXT STEPS
- Complete pivotal study
- Initiate studies in earlier lines
- Anticipated US and EU filings in 2019
Despite Progress in Multiple Myeloma, There Remains a Need for New Therapies

“Despite the availability of these classes of drugs for the treatment of MM, a recent analysis of patients with relapsed and refractory MM (RRMM) who were double refractory to a PI and an IMiD or had relapsed after ≥3 prior lines of therapy, including the novel agents pomalidomide (third-generation IMiD) and carfilzomib (second-generation PI), showed a median overall survival (OS) of 8 months.”

Usmani, Blood 2016
### Current U.S. Standards of Care For Multiple Myeloma

#### 4th Line of Therapy

<table>
<thead>
<tr>
<th></th>
<th>Pomalyst and dex.</th>
<th>Daratumab</th>
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</thead>
<tbody>
<tr>
<td>(Pomalyst Product Monograph)</td>
<td>(Lancet 2016, Lonial, S)</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>452</td>
<td>106</td>
</tr>
<tr>
<td><strong>Inclusion Criteria</strong></td>
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<tr>
<td>≥2 prior therapies (including REVLIMID and bortezomib)</td>
<td></td>
<td>Previously treated with at least three lines of therapy (including proteasome inhibitors and immunomodulatory drugs), or were refractory to both proteasome inhibitors and immunomodulatory drugs</td>
</tr>
<tr>
<td>Relapsed and refractory multiple myeloma</td>
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<tr>
<td>Disease progression on or within 60 days of last therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prior Tx</strong></td>
<td>5 (2-14)</td>
<td>5 (2-14)</td>
</tr>
<tr>
<td><strong>CR Rate (%)</strong></td>
<td>&lt;1%</td>
<td>~3%</td>
</tr>
<tr>
<td><strong>ORR (%)</strong></td>
<td>23.5%</td>
<td>29%</td>
</tr>
<tr>
<td><strong>PFS (mos)</strong></td>
<td>3.6 months</td>
<td>3.7 months</td>
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![Tumor Cell Diagram](image-url)
CRB-401 Study Design and Status

3 + 3 Dose Escalation of CAR + T Cells

Cells Collected
N=24

Manufacturing success rate of 100%

Dosed
N=21

Clinical deterioration prior to infusion n=3

Evaluable for Response
N=21

Study Status (Escalation Phase)

Expansion Cohort Initiated in August 2017
12 additional patients have been collected and dosed in the Expansion Cohort as of 02 Nov 2017

Leukapheresis

Screening

Leukapheresis

manufacturing

bb2121

infusion

bb2121

flu (10 days) + release

 Screening

Day 0

Flu 30 mg/m²
Cy 300 mg/m²
Days -5,-4,-3

1st Response Assessment (Wk 4)

1200 x 10⁶ dose cohort no longer planned
Baseline Demographics, Clinical Characteristics and Treatment History from Dose Escalation

21 patients have received bb2121 as of the data cut-off of October 2, 2017
Median follow-up is 35 weeks (min, max: 6.6, 69)

<table>
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<tr>
<th>Parameter</th>
<th>Statistic</th>
<th>Dosed Patients (N = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Median (min, max)</td>
<td>58 (37, 74)</td>
</tr>
<tr>
<td>Male</td>
<td>n (%)</td>
<td>13 (62)</td>
</tr>
<tr>
<td>Time since diagnosis (years)</td>
<td>Median (min, max)</td>
<td>4  (1.3, 15.8)</td>
</tr>
<tr>
<td>ECOG PS¹</td>
<td>n (%)</td>
<td>10 (48)</td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>11 (52)</td>
</tr>
<tr>
<td>ISS² stage</td>
<td>n (%)</td>
<td>6  (29)</td>
</tr>
<tr>
<td>I</td>
<td></td>
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</tr>
<tr>
<td>II</td>
<td></td>
<td>11 (52)</td>
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<tr>
<td>III</td>
<td></td>
<td>4  (19)</td>
</tr>
<tr>
<td>High-risk cytogenetics</td>
<td>n (%)</td>
<td>9  (43)</td>
</tr>
<tr>
<td>del17p, t(4;14), t(14;16)</td>
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</table>

¹ECOG, Eastern Cooperative Oncology Groups Performance Status
²ISS, International Staging System
³SCT, Stem Cell Transplant

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Statistic</th>
<th>Dosed Patients (N = 21)</th>
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</thead>
<tbody>
<tr>
<td>Prior lines of therapy</td>
<td>Median (range)</td>
<td>7  (3, 14)</td>
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<tr>
<td>Prior autologous SCT³</td>
<td>n (%)</td>
<td>21 (100)</td>
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<td>Prior Therapies</td>
<td>Exposed, n (%)</td>
<td>Refractory, n (%)</td>
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<tr>
<td>Bortezomib</td>
<td>21 (100)</td>
<td>14 (67)</td>
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<tr>
<td>Carfilzomib</td>
<td>19 (91)</td>
<td>12 (57)</td>
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<tr>
<td>Lenalidomide</td>
<td>21 (100)</td>
<td>18 (86)</td>
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<tr>
<td>Pomalidomide</td>
<td>19 (91)</td>
<td>15 (71)</td>
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<tr>
<td>Daratumumab</td>
<td>15 (71)</td>
<td>10 (48)</td>
</tr>
<tr>
<td>Cumulative Exposure</td>
<td>Exposed, n (%)</td>
<td>Refractory, n (%)</td>
</tr>
<tr>
<td>Bort / Len</td>
<td>21 (100)</td>
<td>14 (67)</td>
</tr>
<tr>
<td>Bort / Len / Car</td>
<td>19 (91)</td>
<td>10 (48)</td>
</tr>
<tr>
<td>Bort / Len / Pom</td>
<td>19 (91)</td>
<td>12 (57)</td>
</tr>
<tr>
<td>Bort / Len / Car / Pom</td>
<td>18 (86)</td>
<td>9  (43)</td>
</tr>
<tr>
<td>Bort / Len / Car / Pom / Dara</td>
<td>15 (71)</td>
<td>6  (29)</td>
</tr>
</tbody>
</table>
Dose Escalation Select Treatment Emergent Adverse Events; Generally Well Tolerated

- No dose-limiting toxicities (DLTs) observed in dose escalation
- Cytopenias mostly related to Cy/Flu lymphodepletion
- Mortality: 3 deaths due to disease progression at $50 \times 10^6$ dose; 2 in patients treated at active doses in CR at the time of death (cardiac arrest, MDS)
- 14 patients experienced 1 or more SAEs: CRS* Grade 1-2 that required hospitalization per protocol (N=4); Pyrexia (N=2)

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Overall n (%)</th>
<th>Grade 3 or higher n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytokine release syndrome</td>
<td>15 (71)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Neurotoxicity²</td>
<td>5 (24)</td>
<td>0</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>18 (86)</td>
<td>18 (86)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>11 (52)</td>
<td>9 (43)</td>
</tr>
<tr>
<td>Anemia</td>
<td>14 (67)</td>
<td>12 (57)</td>
</tr>
</tbody>
</table>

Dose Escalation Patients (N = 21)

Reversible Grade 4 neurotoxicity followed by rapid myeloma response in patient from expansion cohort
- 46 y/o female with 11 prior lines of therapy – $450 \times 10^6$ CAR+ cells
- High tumor burden M spike = 8.03 g/dL, BMPC 90%
- History of subarachnoid hemorrhage prior to enrollment
- Low BCMA expression: BCMA 1% of malignant cells (IHC)

*CRS uniformly graded according to Lee et al., Blood 2014;124:188-195

¹Data cut-off of October 2, 2017
²Neurotoxicity includes the preferred terms: depressed level of consciousness, confusional state, bradypenia, somnolence
High Frequency of Deep and Durable Tumor Response in Active Dose Cohorts

- Median follow up of 40 weeks in active dose cohorts; PFS not yet reached
- 17/18 (94%) ORR at active doses
- 56% Complete Response Rate and 89% VGPR or better
- 9/10 evaluable patients MRD negative
- Durable ongoing responses over 1 year
- Responses continue to improve as late as month 15 (VGPR to CR)

Patient 12 died of cardiopulmonary arrest
Patient 4 died of MDS following discontinuation

- High Tumor Burden (>50% Bone Marrow Involvement)
56% of Patients Achieved a Complete Response; 94% Overall Response Rate

Dose Escalation: Cohorts ≥150 × 10⁶ CAR T Cells (N=18)
Median duration of follow up 40 weeks (min, max: 6.6, 69.1)

- Median Duration of Response not yet reached
- Median Progression Free Survival not yet reached
- 81% Progression Free Survival at 6 months
- 71% Progression Free Survival at 9 months

Objective Response Rate
Subjects Treated in Escalation – Cohorts ≥150 × 10⁶

Note: Objective Response defined as attaining Stringent Complete Response, Complete Response, Very Good Partial Response, or Partial Response. Including unconfirmed responses.
Relapsed and refractory MM
- ≥3 prior treatment regimens with ≥ 2 consecutive cycles each (unless PD was best response)
- Received prior IMiD®, PI and anti-CD38
- Refractory (per IMWG) to last treatment regimen

Endpoints
Primary: ORR
Key Secondary: CR, TTR, DOR, PFS, TTP, OS, Safety, bb2121 expansion and persistence, MRD (genomic and flow assays)
Exploratory: BCMA expression/loss, T cell immunophenotype, GEP in BM, HEOR

N = 80

bb2121 manufacturing

Apheresis

CAR T infusion*

Dose (x 10^6 CAR+ T cells)
- Range: 150-300

Flu (30 mg/m^2)  || |
Cy (300 mg/m^2)  |   |
Days -5, -4, -3 0

* Re-treatment allowed at PD for best response of ≥ SD
Advancing bb2121 into Earlier Lines of Multiple Myeloma

Comprehensive Clinical Plan in Earlier Lines to Begin in 2018

- Pivotal trial in late line open to enrollment
- Planned Ph III in 3rd line vs. Dara/Pom/dex
- Explore label expansion opportunity in 2nd line setting
- Opportunities for bb2121 in NDMM including high risk, TNE and TE vs. transplant

NDMM: Newly Diagnosed Multiple Myeloma
TNE: Transplant Non-Eligible
TE: Transplant Eligible
What’s Next…

**bb2121**
- Pivotal KarMMA trial now enrolling in the US, EU and Canada with anticipated launch in 2020
  - Target enrollment: 80
  - Primary endpoint: ORR
  - Dose range of 150 to 300 x 10^6 CAR T cells
- Celgene planning additional clinical studies to explore bb2121 in earlier lines of therapy
- Expansion cohort enrolling rapidly

**bb21217**
- Second generation anti-BCMA CAR T therapy – study actively enrolling
Changing the balance of T cell lineages with bb21217

T Cell Plasticity
Self Renewal
Long Lived

bb21217: Addition of PI3K inhibition for “younger” T cells
Cerebral Adrenoleukodystrophy

• Severe, often fatal neurological disease in boys

Status

• 15/17 patients hit the primary endpoint so far
• Newborn screening active in 5 states

Next Steps

• Expanding study to enroll total of 30 patients
• Anticipated filing in 2019

Ethan’s family spent nearly two years trying different medications and meeting with specialists to try and resolve his symptoms. Tragically, during this period, the ravaging effects of ALD were continuing to damage Ethan’s brain and adrenal glands.

Ethan Zakes 2000 - 2011

Source: Ethan Zakes Foundation

Lenti-D Treatment Halts CALD Disease Progression

15/17 patients (88%) alive and MFD-free at 24 months follow-up
- Exceeds pre-determined efficacy benchmark for the study MFD-free survival in 13/15 (76%)

Safety profile consistent with autologous transplantation
- No GvHD, no graft rejection

Two patients did not meet primary endpoint:
- Patient 2016: Withdrew due to radiographic progression, later underwent allogeneic transplant; subsequently died from complications of allo
- Patient 2018: Rapid disease progression early in the study; developed severe disabilities from CALD progression; died from complications unrelated to Lenti-D

Data as of August 25, 2017
Early Pipeline
Good Is Never Good Enough For Patients: BLUE Toolbox Strategy

**Product Engine**

- **Transduction**
  - v1.0: LentiGlobin
  - v2.0: LentiGlobin & Enhancers

- **Durability**
  - BCMA (bb2121)
  - BCMA & PI3Ki (bb21217)

**vFuture**

- LentiGlobin
  - Optimized severe genetic disease products
- Novel areas; autoimmune In vivo gene editing
- New & enhanced oncology products

**Areas of Focus**

- Autoimmune
- In vivo gene editing
- Optimized severe genetic disease products
- New & enhanced oncology products

**Transduction**

- HSC
- T Cell

**Durability**

- BCMA (bb2121)
- BCMA & PI3Ki (bb21217)
Lentiviral vector approach to suppression of BCL11a in SCD

HbF is a β-like globin with anti-sickling activity normally silenced during development.

- Transduced >80% of SCD HSCs → **HbF induction of 66-92%** (and suppression of HbS to 5-38%)
- Leverage understanding of sickle cell biology and advances to the manufacturing, cell source and patient management now deployed in HGB-206
- Program and IP licensed exclusively from Boston Children’s Hospital
- IND open and BCH investigator planning to advance into the clinic in H1 2018
Go TRUE BLUE

We Must
Make Hope a
Reality