bluebirdbio®

Q3 Update Call

November 2, 2018

NASDAQ: BLUE

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.



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Making Hope
A Reality

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2022 Vision on Track

LentiGlobin TDT
Potential First Approval (2019)

Lenti-D CALD
Potential First Approval (2020)

LentiGlobin SCD
Data-Driven Acceleration

bb2121 Multiple Myeloma
Potential First Approval (2020)

2+ Products on the Market

2+ Programs Nearing Commercialization

4+ Additional Programs in the Clinic

Q3 2018 & Recent Highlights

TDT	• Filed MAA with the European Medicines Agency
SCD	• Plan to pursue accelerated development path for LentiGlobin
CALD	• Reached agreement with regulators for filing based on ALD-102 and ALD-103 • Updated data presented at SSIEM
BCMA	• In collaboration with Celgene, the clinical program evaluating bb2121 in earlier lines of MM is advancing, including the phase II MM-002 and phase III MM-003 trials
BLUE	• Announced strategic collaborations with Regeneron and Gritstone Oncology • Raised $600.6 million in equity financing • Ended Q3 with $2.0 billion in cash, cash equivalents and marketable securities
ASH	• 10 presentations across severe genetic diseases, oncology and preclinical pipeline

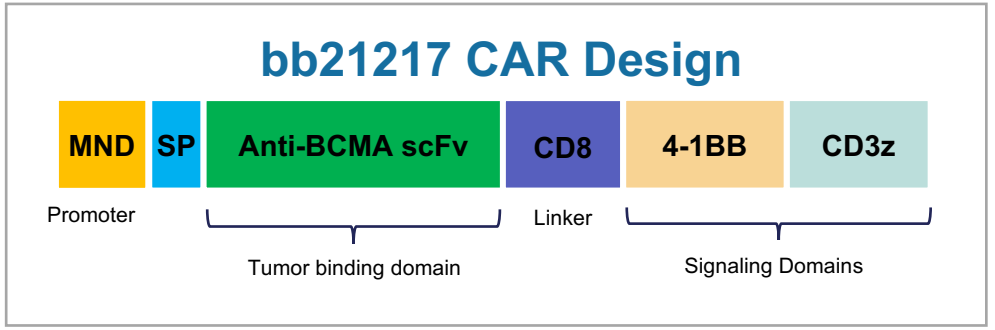
10 Presentations at ASH 2018

NORTHSTAR STUDY NORTHSTAR-2 STUDY NORTHSTAR-3 STUDY	LentiGlobin TDT	• **Northstar: Outcomes following study completion** • **Northstar-2: Updated results and first look: Northstar-3**
HGB-206	LentiGlobin SCD	• **HGB-206 Group C: Updated results** • HGB-206 Group A & B: Updated results w/ up to 33 months follow up • Real world evidence: U.S. population • HGB-205: Analysis of RBC properties in patients
CRB-402	bb21217 MM	• **First look: CRB-402 initial results in R/R multiple myeloma**
BCL11a	shRNA^{miR} SCD	• **First look: BCL11a shRNA initial results**
	Preclinical	• **First look: MegaTAL engineered T cells** • **NHP-based target validation with gene-edited hematopoietic stem cells**

**Bold indicates bluebird Oral Presentations*

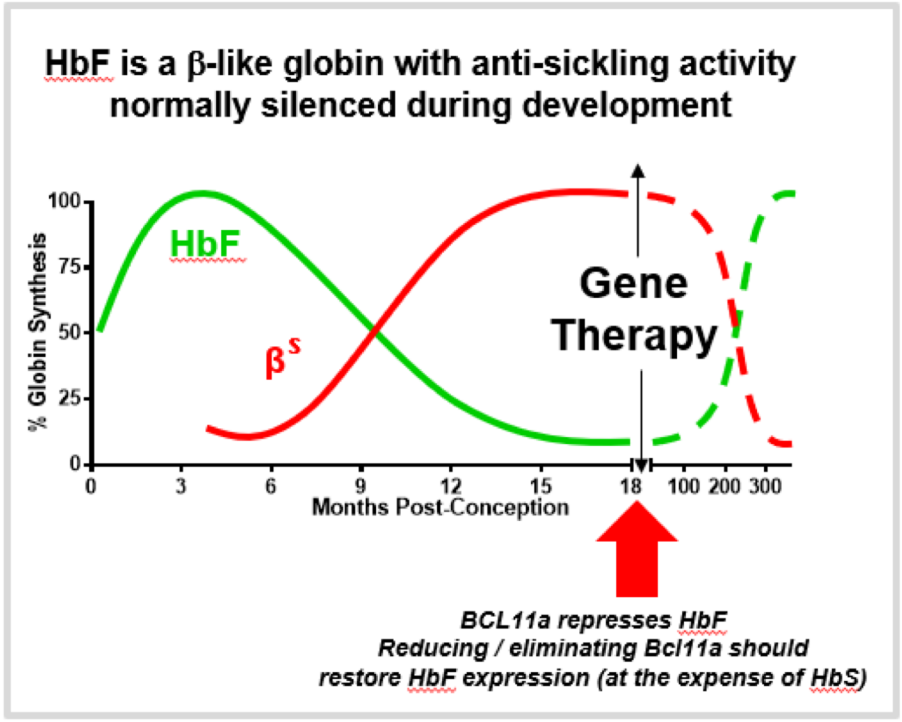
bb21217: Early Indication of CAR Durability

- Key bb21217 attributes based on preclinical studies:
  - Enrichment for memory-like T cells
  - Increased functional persistence and durability
  - Complete tumor elimination in a re-challenge model



- ASH 2018 Abstract Data
  - 8 patients treated at 150 x 10^6; median 9 prior lines of therapy
  - 6/7 evaluable patients responded
    - 1 sCR, 3 VGPR, 2PR
  - 3 of 3 evaluable patients were MRD negative
  - 2 of 2 at 6 months had detectable CAR vector copies
  - Safety comparable with known toxicities of CAR T cell therapies

Initial Proof of Concept: LVV Approach to Suppression of BCL11a in SCD

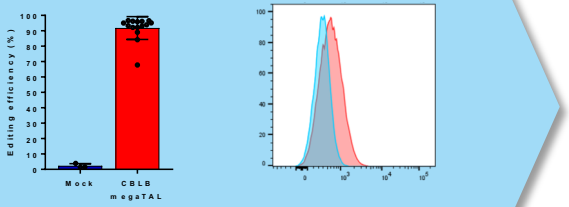


- As of July 28, 2018, one patient had received treatment with HSCs transduced with an LVV encoding the BCL11a shRNA^{miR}
- As of day 76:
  - Sustained Hb of >10 g/dL
  - 59.7% total HbF cells; 30% HbF as a fraction of all β-like globin
  - Notable absence of irreversibly sickled cells on peripheral smear
  - Low absolute reticulocyte count consistent with markedly reduced hemolysis Hb
- Safety profile consistent with myeloablative conditioning

CBLB Knock-out Enhances CAR-T Cell Anti-tumor Activity

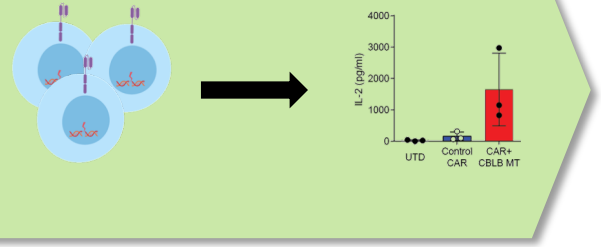
Novel Technology for Improving T Cell Function in Liquid and Solid Tumors

1



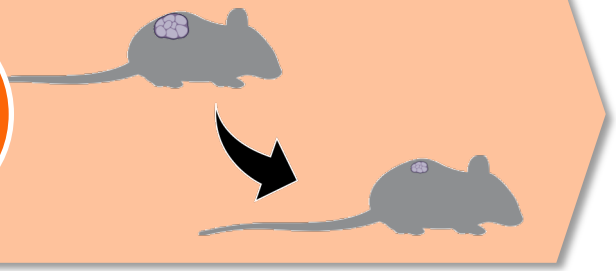
- CBLB megaTAL induces a high rate of gene editing and corresponding knockdown of CBLB protein levels

2



- CBLB megaTAL treatment enhances production of cytokines *in vitro* by CAR-T cells

3



- Genetic deletion of CBLB enhances anti-tumor activity of CAR-T cells in a mouse solid tumor xenograft model

LentiGlobin in SCD Development Strategy

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Advancing Innovative Endpoints for Sickle Cell Disease

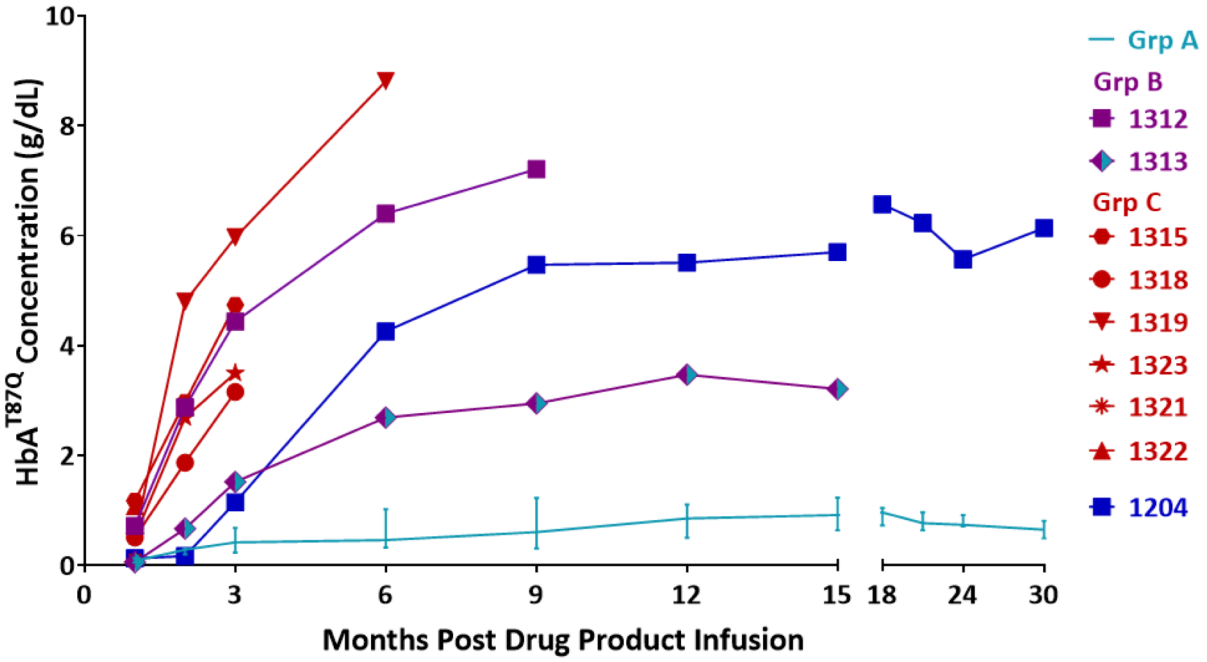
"Science and technology have evolved, and medical care delivery for patients with sickle cell disease has changed. The robust SCD drug development pipeline is poised to deliver new therapies to patients; however, there is general agreement that a timely discussion about endpoints is needed…"

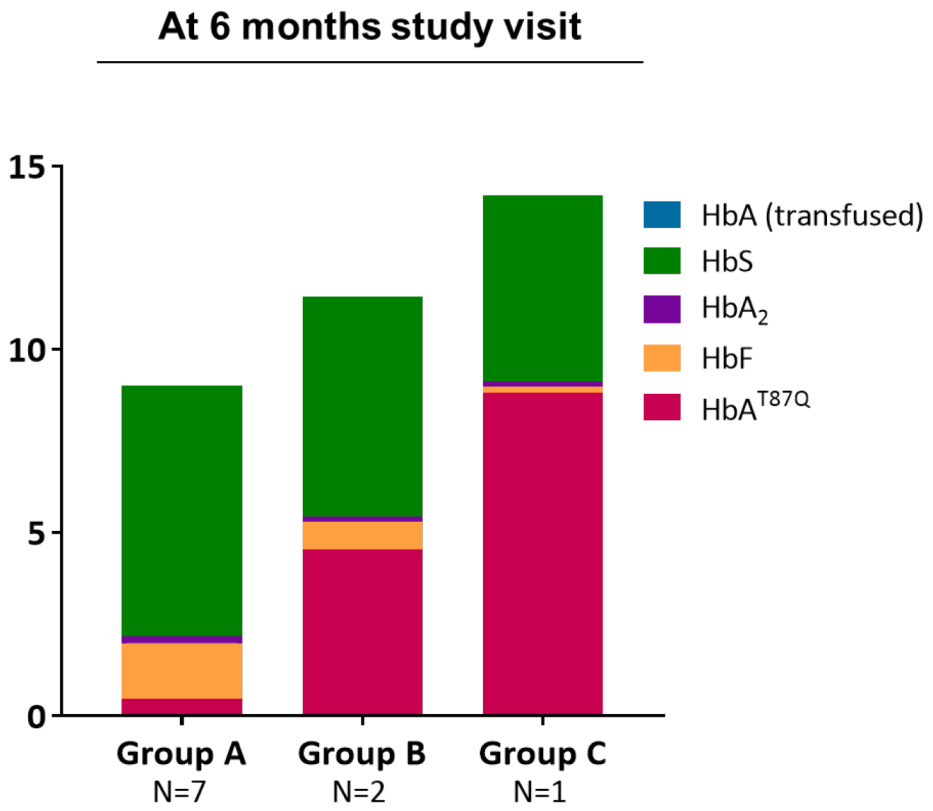
– FDA.gov

- Global annual birth incidence ~ 300,000 – 400,000
- High morbidity and early mortality
  - Mean age of death in U.S. is 44 years*
- FDA-ASH Sickle Cell Disease Clinical Endpoints Workshop, October 2018
  - FDA staff, SCD physician experts and SCD patient advocates engaged in dialogue on potential SCD trial endpoints, including for therapies with curative intent
  - Biological markers of disease, such as hematologic parameters, may provide useful surrogates for clinical benefit

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

Group C: Robust Improvements Underscore the Clinical Relevance of Hemoglobin Endpoints





For Group A patients, medians (min, max) depicted; Group A patients with month 30 study visit (N=2)

Data as of May 15, 2018 for HGB-206 and Sep 20, 2017 for pt 1204

Accelerated Development Plan Using Hemoglobin Primary Endpoint as a Surrogate for VOE Reduction

EXPANDED

Updated Primary Endpoints

Up to add'l 21 patients

Expanded age range

HGB-206 Group C

(Sickle Cell Disease, history of VOEs over 24 months)

Ongoing phase 1/2, single arm, multi-center, U.S. study
N=41 (Group C)

- Primary Endpoint: HbA^{T87Q} and Total Hb
- Key Secondary Endpoint:
  - Reduction in severe VOEs
- ≥ 12 years of age - ≤ 50 years of age

HGB-210

(Sickle Cell Disease, history of VOEs over 24 months)

Phase 3, single arm, multi-center, global study

- Primary Endpoint: HbA^{T87Q} and Total Hb
- Key Secondary Endpoint:
  - Reduction in severe VOEs

NEW

Planned for 2019

Additional Clinical Investigation in Other Patient Types and Ages Planned

2018 Milestones

TDT

- ✓ Northstar-2 (HGB-207) Updated Data
- ✓ Northstar (HGB-204) Updated Data
- ✓ MAA Filing in non-β0/β0 Genotypes
- • Northstar-3 (HGB-212) Early Data
- • Northstar-2 Updated Data

SCD

- ✓ HGB-206 Data
- ✓ Registration Strategy Update
- • HGB-206 Updated Data

MM

- ✓ CRB-401 bb2121 ASCO Data
- • Initiate 3rd Line Study*
- • CRB-402 bb21217 Early Data

CALD

- ✓ Starbeam (ALD-102) Updated Data

ASH 2018 Investor & Analyst Event

Monday, December 3 @ 8:00 p.m. PT - Hilton San Diego Gaslamp Quarter

Event to be webcast

*Conducted by Celgene