Quarterly Update & ASH 2017 Abstract Conference Call

November 1, 2017

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.

Objectives

Quarterly highlights

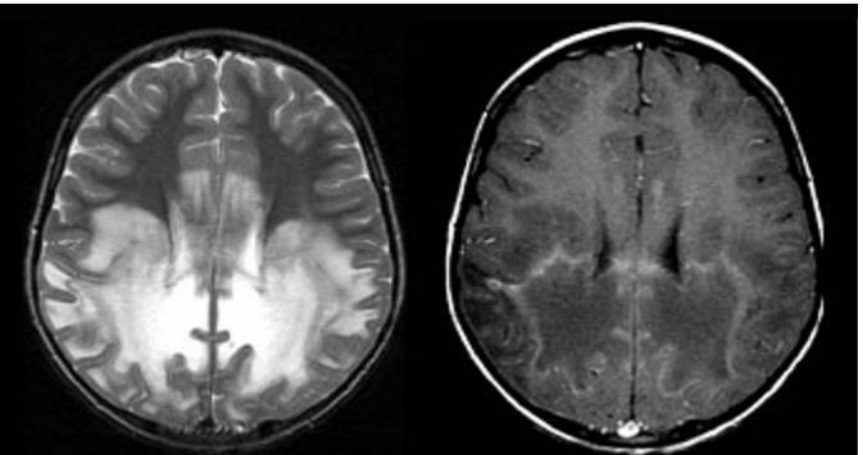
Review ASH 2017 abstracts

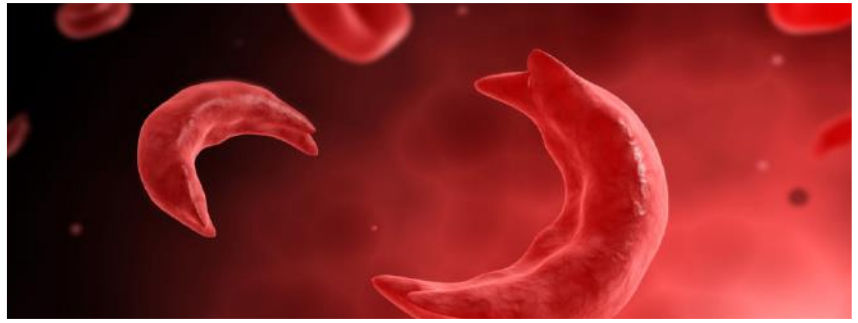
Two key questions:

- What is the relevance of the new data?
- What are expectations now, going into ASH?

Our Vision: **Make Hope a Reality**

OUR PATIENTS

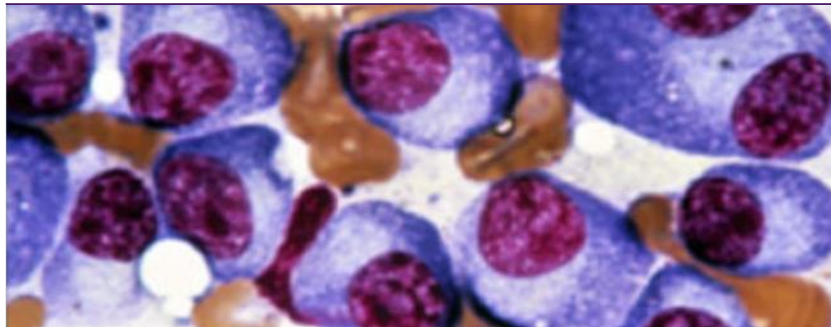




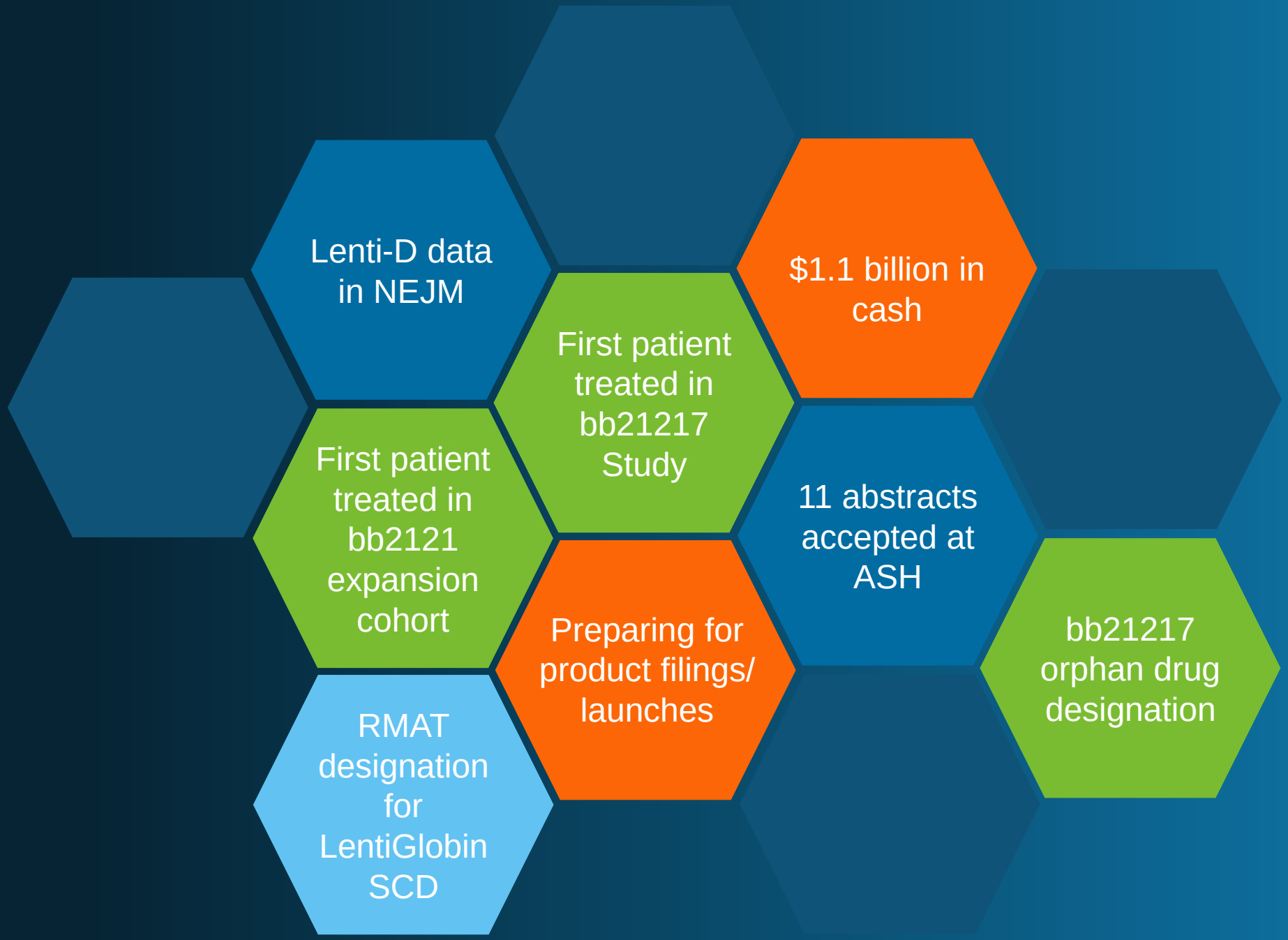
BLUE MOJO

TRUE BLUE

OUR PEOPLE



Third Quarter 2017 Highlights



ASH 2017: 11 Abstracts Accepted Across the Pipeline

TDT

HGB-207
(Northstar-2) non-β^0/β^0 genotypes using updated manufacturing process

HGB-204
(Northstar) update on all genotypes

HGB-205

SCD

HGB-206
2 patients treated under updated protocol

Plerixafor
Mobilization safety and cell processing in patients in HGB-206

HGB-205
Update on SCD patients

Multiple Myeloma (MM)

CRB-401
Update on anti-BCMA CAR T bb2121 in patients with relapsed/refractory MM

Other

5 preclinical presentations

shmiR (SCD)

megaTAL gene editing (2)

Immuno-Oncology (2)

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Summary of 2017 ASH Abstract Data in Northstar (HGB-204) and HGB-206 Studies

HGB-206

- Early data suggest positive impact of protocol and manufacturing process changes

Plerixafor Safety

- Plerixafor well tolerated and may enable increased cell doses with higher percentage of true stem cells
- Plerixafor mobilization implemented in HGB-206

NORTHSTAR STUDY

HGB-204

- Up to 3-year follow up data demonstrate durability of treatment and potential for improved outcomes over time

Transfusion-Dependent Thalassemia

NORTHSTAR STUDY — HGB-204	• Primary basis of EU filing • Original manufacturing process • All genotypes
HGB-205 — HGB-205	• Basis of EU filing (with Northstar) • Original manufacturing process
NORTHSTAR-2 STUDY — HGB-207	• Basis of US filing • Refined manufacturing process • non-β^0/β^0 genotypes
NORTHSTAR-3 STUDY — HGB-212	• β^0/β^0 genotypes • Refined manufacturing process • Study initiation planned in 2017

Northstar Update

Non-β^0/β^0 (n=10)

8 patients

- Transfusion free > 12 months (median 27.1 months; range 12.5 – 35.2 months)
- Hb level: 9.3 – 13.7 g/dL
- HbA^{T87Q} level: 3.6 – 9.6 g/dL

2 patients

- Annual transfusion volumes reduced by 30% and 94%
- Received lowest DP VCNs (0.3/0.4)

β^0/β^0 (n=8)

2 patients

- Transfusion free > 12 months
- Hb level: 9.0 and 10.2 g/dL
- HbA^{T87Q} level: 8.2 and 6.8 g/dL

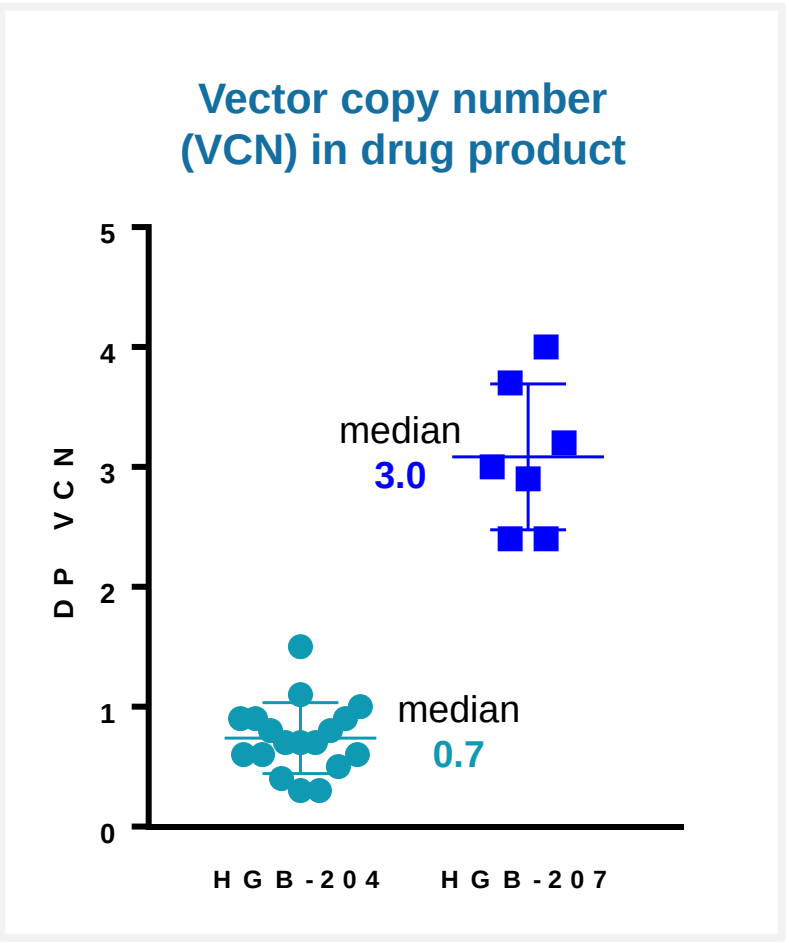
6 patients

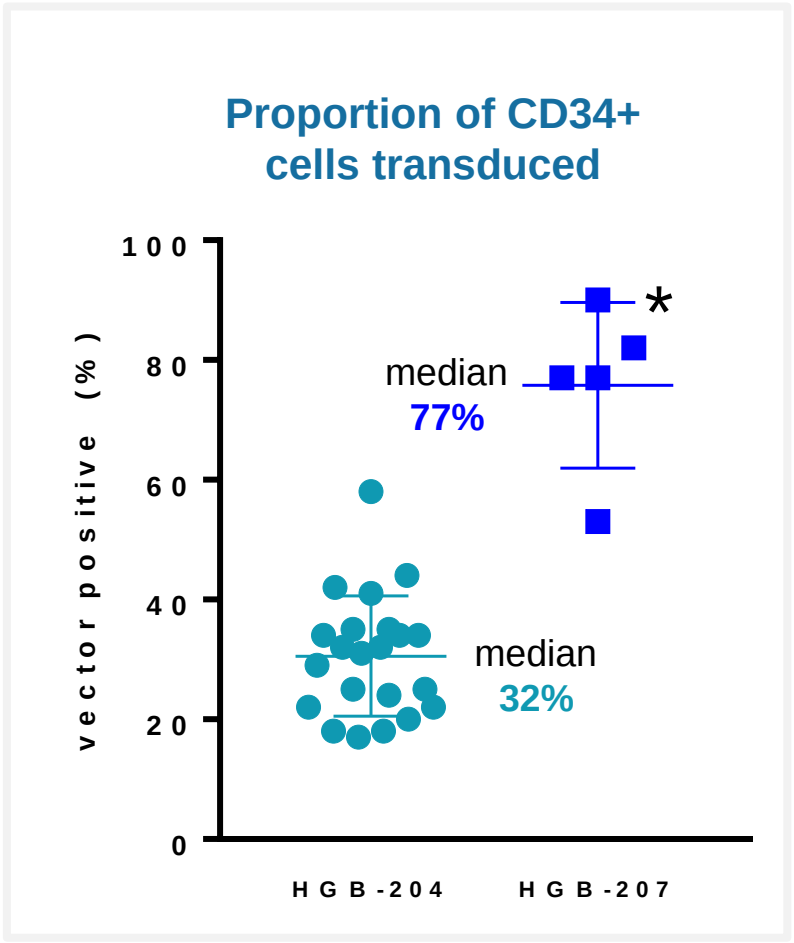
- Annual transfusion volumes reduced by 63% (median)

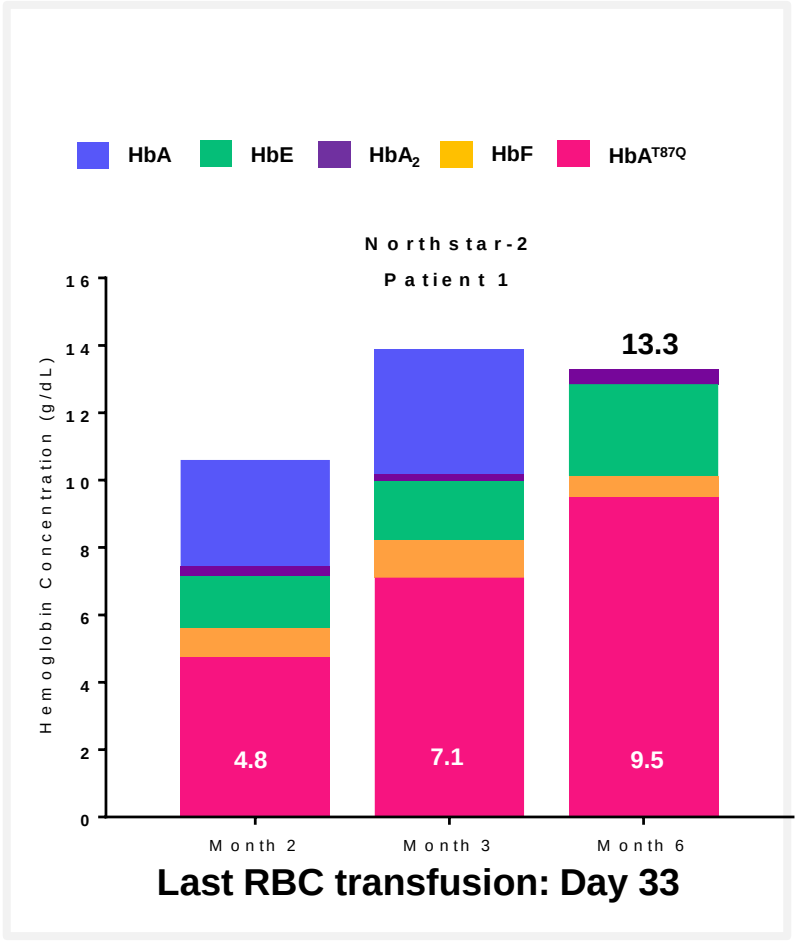
Safety profile consistent with autologous transplantation

Data as of June 2017

Northstar-2: EHA Data Showed the Promising Impact of the Refined Manufacturing Process







* Samples from EU manufacturing pending vector positive analysis

TDT Registration Strategy

General agreement with EU & US regulators on the registration path for LentiGlobin BB305 for the treatment of transfusion-dependent β-thalassemia

EU

Pursue **CONDITIONAL APPROVAL** in patients with non-β^0/β^0 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

ADAPTIVE PATHWAYS

PRIME

US

Pursue **approval** in adults and adolescents with non-β^0/β^0 genotypes based on data from ongoing pivotal HGB-207 trial

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

Submission for approval in β^0/β^0 patients to be based on planned HGB-212 study

BREAKTHROUGH THERAPY DESIGNATION

ORPHAN DRUG DESIGNATION

ASH 2017: Sickle Cell Disease Abstracts

TDT

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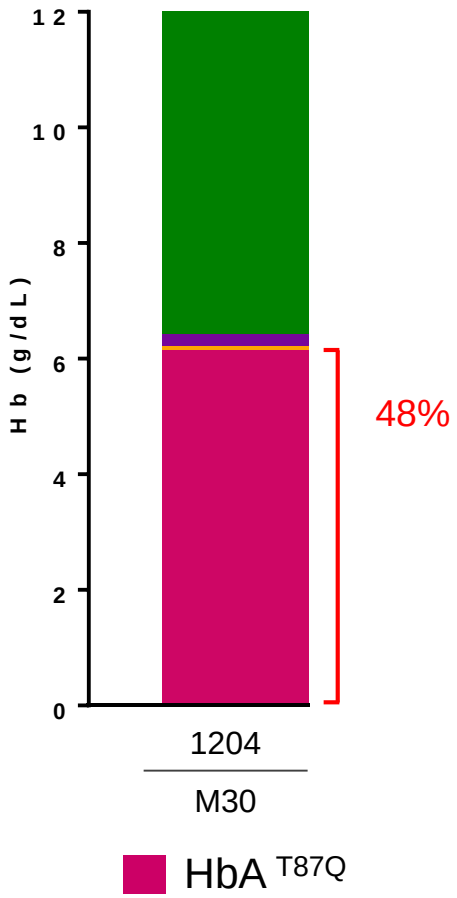
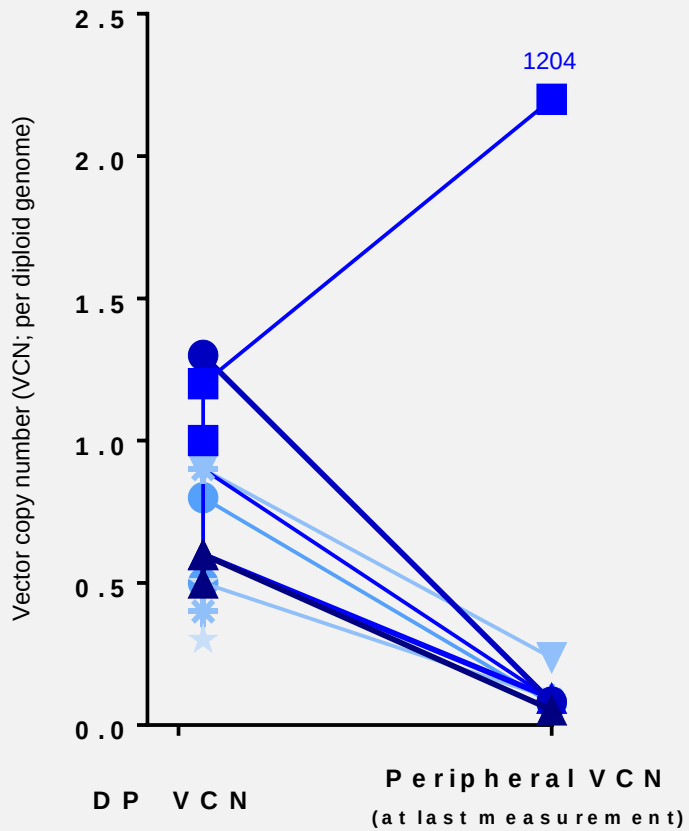
Understanding the Biology of SCD: Manufacturing and Protocol Improvements



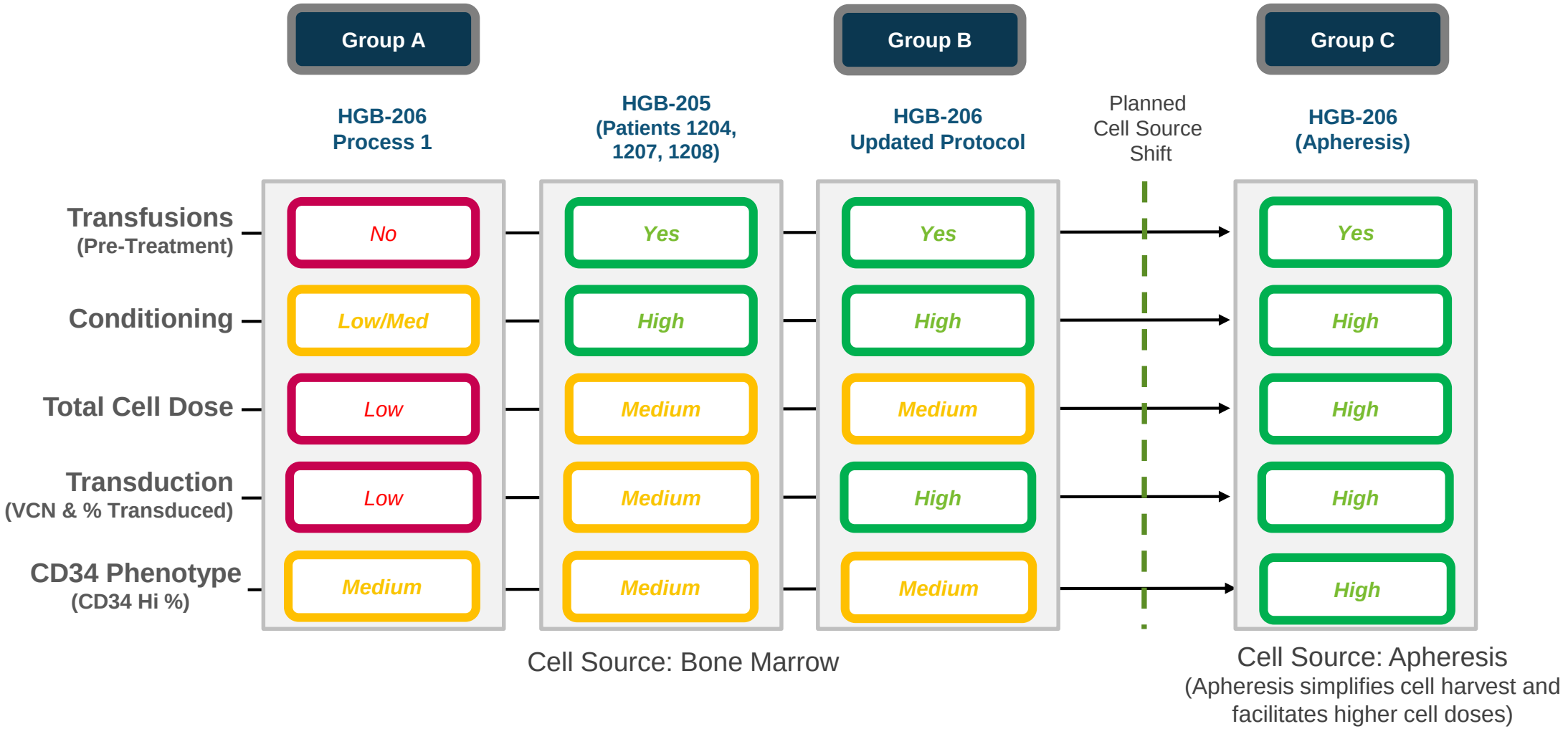
VCN drop from drug product to peripheral blood in HGB-206



Hypoxic, inflamed marrow	**Pre-harvest transfusions to reduce marrow inflammation, hypoxia**
Inadequate myeloablation	**Increased exposure to myeloablative agent**
Low yield harvest	**Additional changes to manufacturing process to increase cell dose**
Poor transduction	**New manufacturing process**
Apheresis (vs. bone marrow harvest)	**Utilize Plerixafor for mobilization and collection**

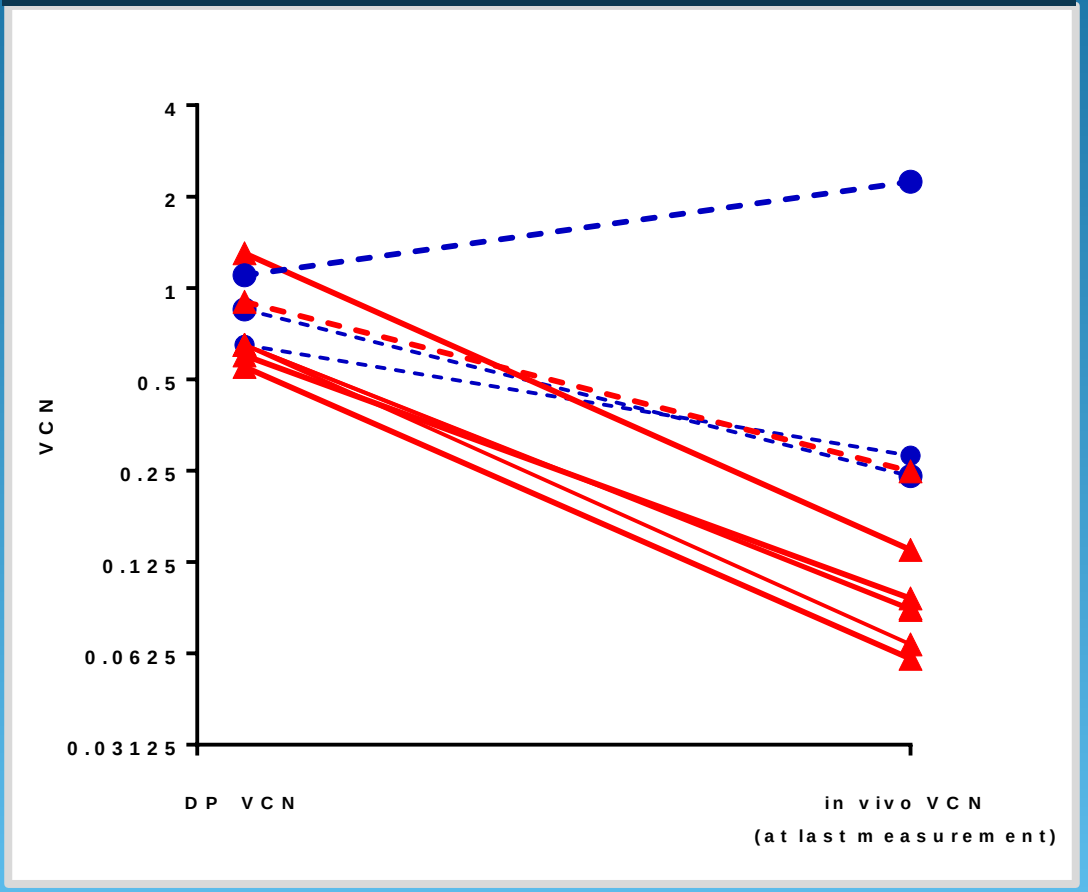
Data as of Sept 9, 2016 [HGB-205] and Nov 9, 2016 [HGB-206]

Evolution of LentiGlobin in SCD – New Early Data from Patients in Group B and Group C

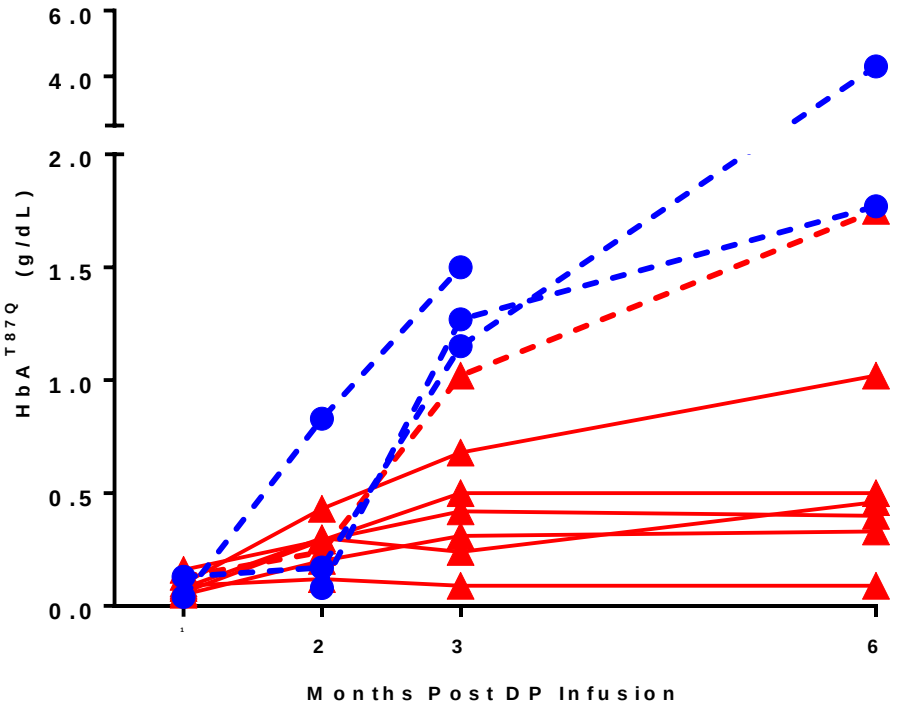


Group A + Additional Patients in HGB-205 Show Impact of Transfusions, Optimized Conditioning

In Vivo VCN

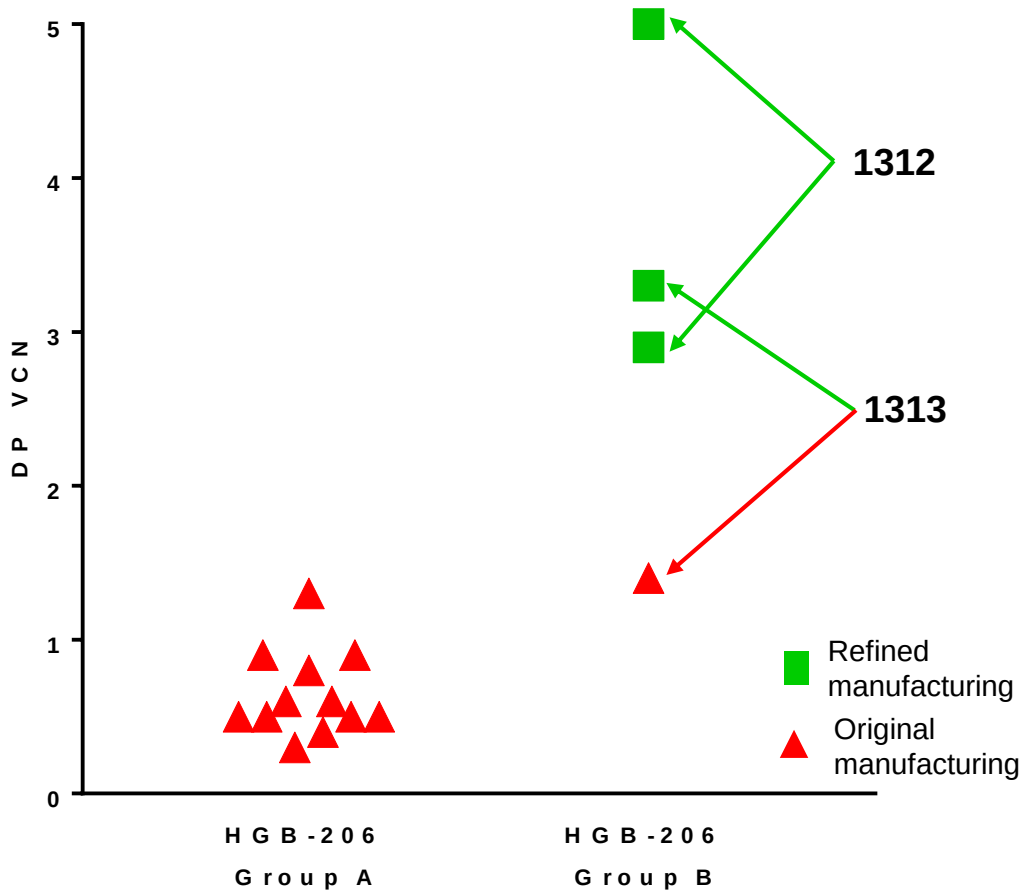


HbA^{T87Q}

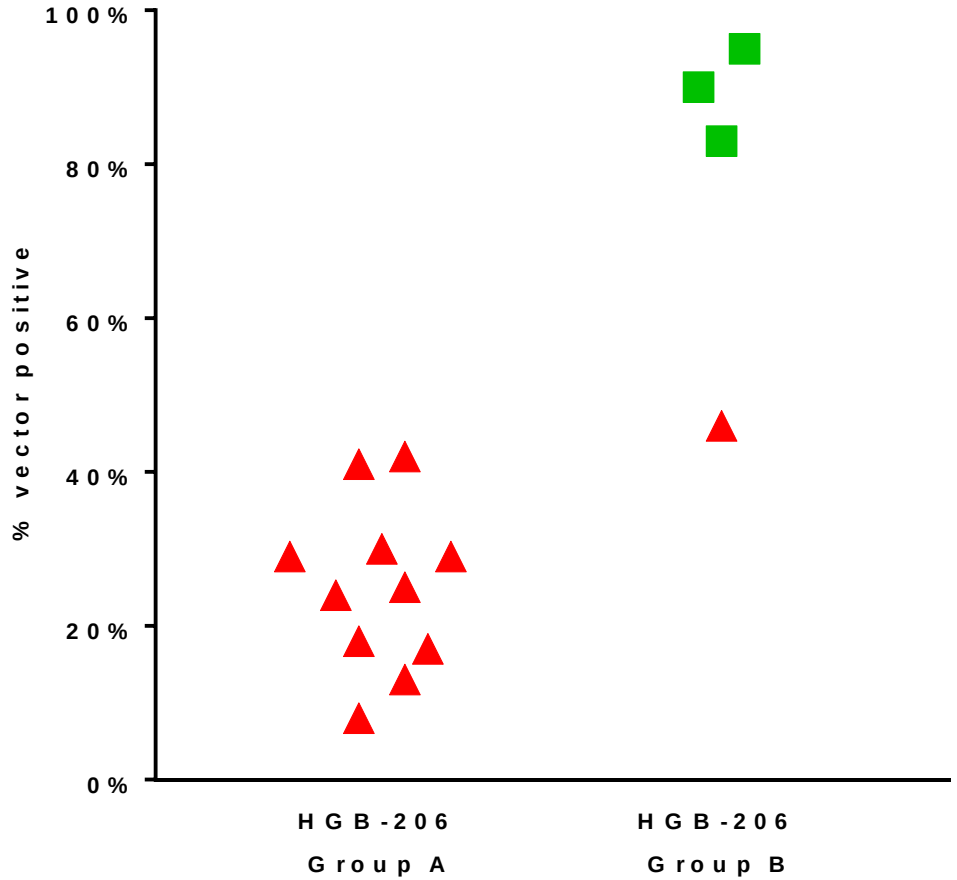


Group B: Early Data Indicates Impact of Process and Protocol Changes

Drug Product VCN



% Cells Transduced



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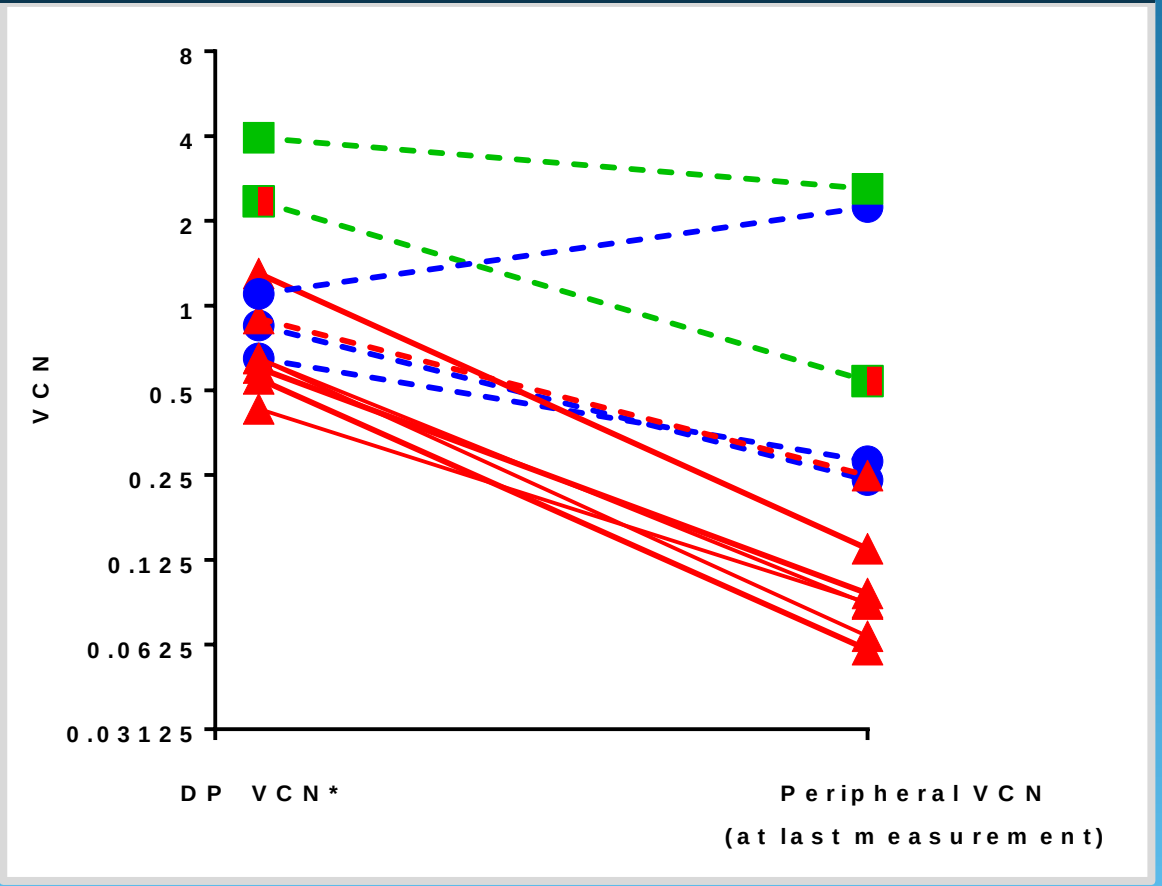
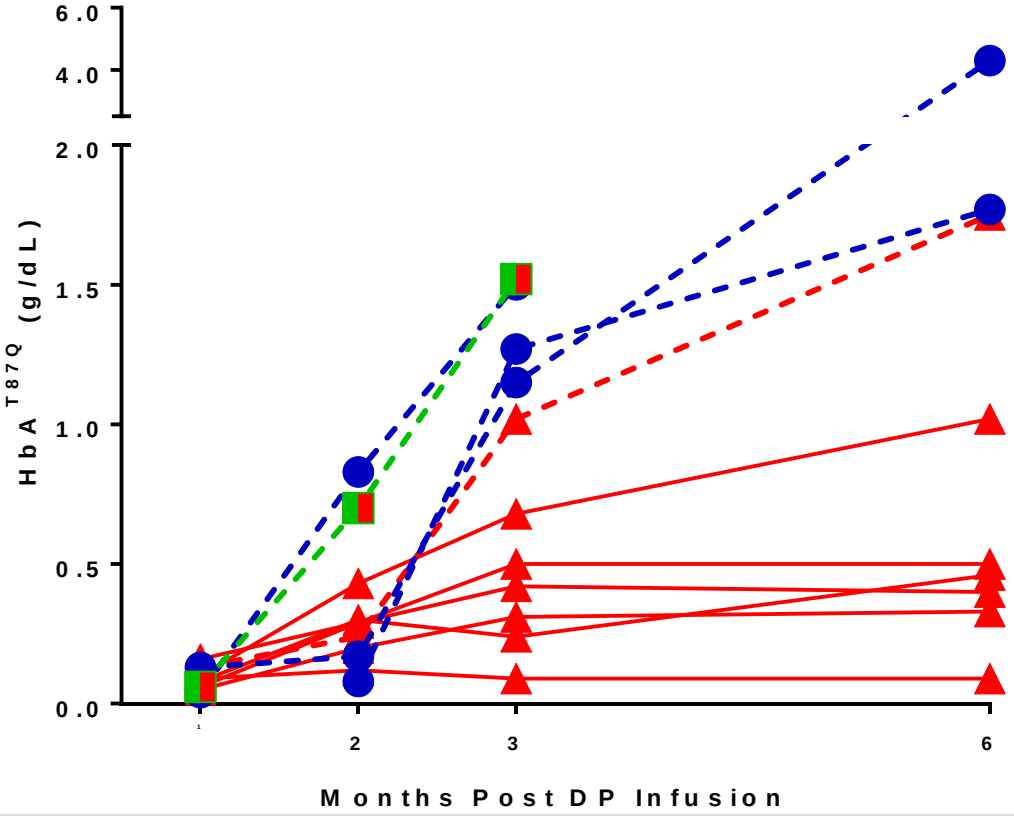
In Vivo VCN



HbA^{T87Q}



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

HbA^{T87Q} not available for patient 1312 at time of data cut

Initial Safety Assessment of Plerixafor Mobilization in 3 Patients

Results

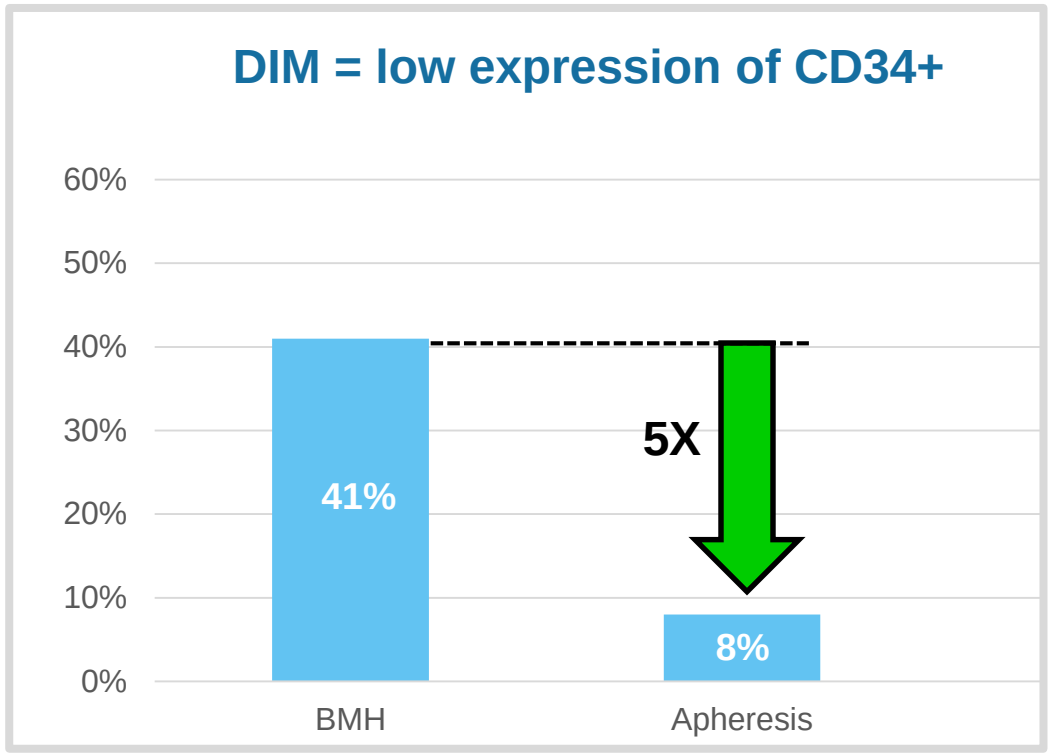
- **WELL TOLERATED** no dose limiting toxicities observed
- **CELL DOSE** trending higher than with BMH
- **CELL PHENOTYPE** may be more favorable than BMH
- Early drug product data to be shown at ASH (no *in vivo* data)

Cell Dose

- CD34+ cells/kg collected in single day of apheresis = **15.3**, **5.6**, and **9.0** x 10^6
  - For comparison, CD34+ cells/kg collected per BMH = **5.0 mean** (range 0.3 – 10.8) x 10^6 (n=21)

Plerixafor mobilization implemented in HGB-206

Cell Phenotyping Suggests Mobilization with Plerixafor May Yield Better Cell Dose



CD34^{dim} cells
- Express low levels of CD34
- Less likely to be primitive stem cells

mean DIM Cells

Plerixafor mobilized cells have 5-fold fewer CD34^{dim} cells than bone marrow harvested cells; suggests higher quality cell dose may be obtained

Summary of 2017 ASH Abstract Data in Northstar (HGB-204) and HGB-206 Studies

HGB-206

- Two subjects with severe sickle cell disease (SCD) treated under the amended study protocol with cells collected via bone marrow aspiration
- Early indication that changes to process and protocol yields improved DP VCN and in vivo peripheral VCN; expected to improve HbA^{T87Q} hemoglobin production

Plerixafor Safety

- Plerixafor was well tolerated and may enable increased cell doses with higher percentage of target primitive stem cells
- Acceptable toxicity profile with no dose-limiting toxicities observed
- Plerixafor mobilization has been implemented in HGB-206

NORTHSTAR STUDY HGB-204

- EU and US regulatory pathways on track
- Up to 3-year follow up data demonstrate durability of treatment and potential for improved outcome over time
- Safety profile consistent with autologous transplantation with no drug-product related adverse events

Additional ASH Abstracts

PRECLINICAL

Preclinical Evaluation of a Novel Lentiviral Vector Driving Lineage-Specific BCL11A Knockdown γ-Globin Induced and Simultaneous Repression of β-Globin for the Potential Treatment of Sickle Cell Disease

A novel TGF-β/interleukin receptor signal conversion platform that protects CAR/TCR T cells from TGF-β-mediated immune suppression and induces T cell supportive signaling networks

A Drug-Regulated CAR Platform (DARIC) Induces Effective and Reversible Tumor Control In Vivo Using Non-Immunosuppressive Rapamycin Dosing

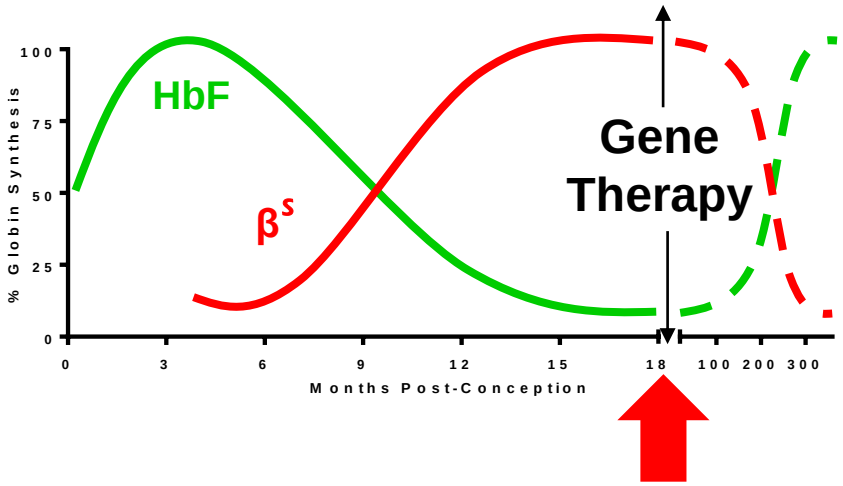
Gene Editing of TRAC Locus Utilizing megaTAL Nucleases Increases Expression of Transgenic TCRs Delivered via Lentiviral Vector-Mediated Gene Transfer

ROR1-directed chimeric antigen receptor T cell recognition of self-antigen is associated with acute toxicity, T cell dysfunction, and poor tumor control

Lentiviral Vector Approach to Suppression of BCL11a in SCD

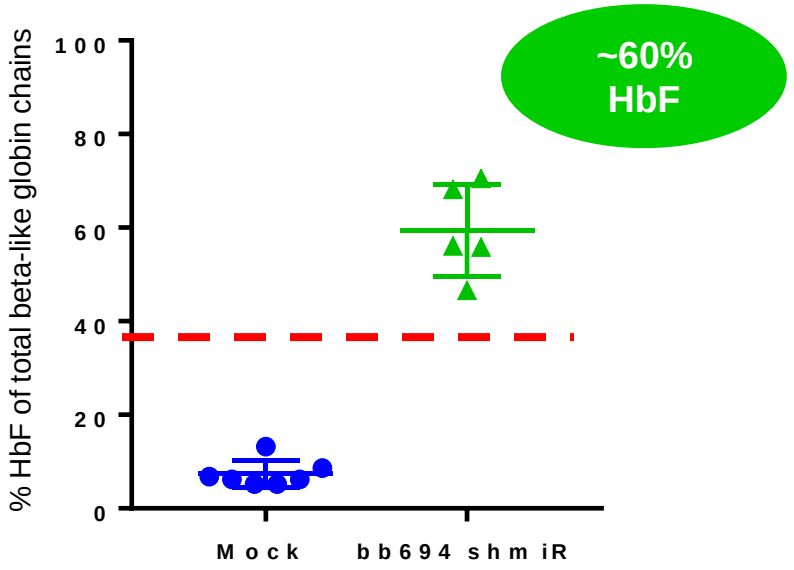
Forces expression of anti-sickling HbF with suppression of disease causing HbS

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



BCL11a represses HbF
Reducing / eliminating Bcl11a should restore HbF expression (at the expense of HbS)

Meta-analysis % HbF induction with BCL11a shRNA(miR)



- Transduced 70 - 81% of SCD HSCs → **HbF induction of 66-81%** (and suppression of HbS to 5-38%)
- Program and IP exclusively licensed from Boston Children's Hospital
- IND open (NCT03282656) and BCH investigator planning to advance into the clinic in H1 2018

Brendel et al J Clin Invest. (2016). PMID: 27599293, Abstract ID#:107681

Additional Clinical Study Data to be Presented at ASH

HGB-204

NORTHSTAR STUDY

Updated results in TDT using original manufacturing, including durability and transfusion-free time

HGB-205

HGB-205

Longer-term follow up on TDT and SCD

HGB-207

NORTHSTAR-2 STUDY

Updated data on 3 patients with TDT seen at EHA; early data from additional patients

HGB-206

HGB-206

Longer follow up on two Group B patients shown today; DP VCN data from patients in Group C at ASH

CRB-401

Additional ~6 months follow up on anti-BCMA CAR T therapy bb2121 in patients with R/R multiple myeloma reported at ASCO

Investor Event at ASH

Sunday, December 10
@ 8:00 pm ET
Omni Atlanta Hotel
Birch Room
Event to be webcast

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Q&A

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