bluebirdbio®

Making Hope A Reality – bluebird style

November, 2017

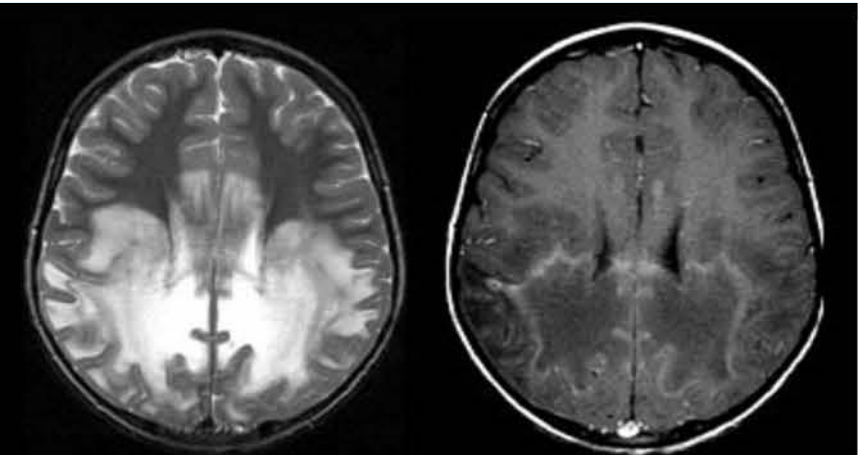
Nasdaq : BLUE

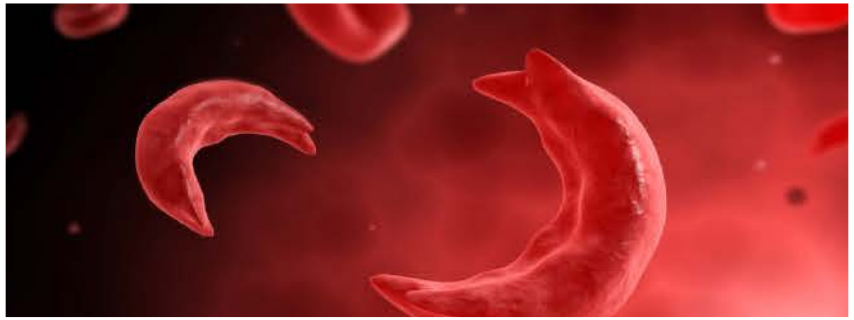
Forward Looking Statements

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.

Our Vision: **Make Hope a Reality**

OUR PATIENTS

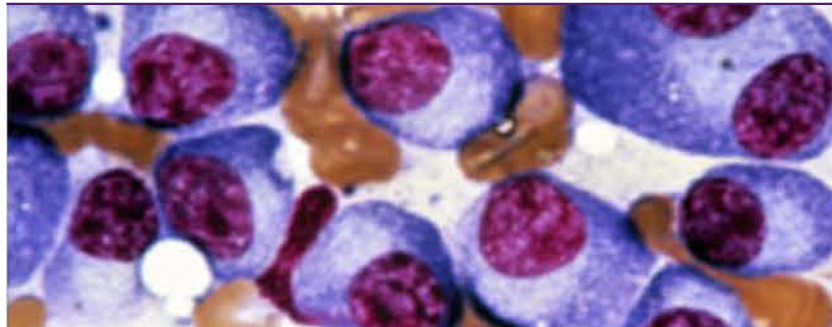




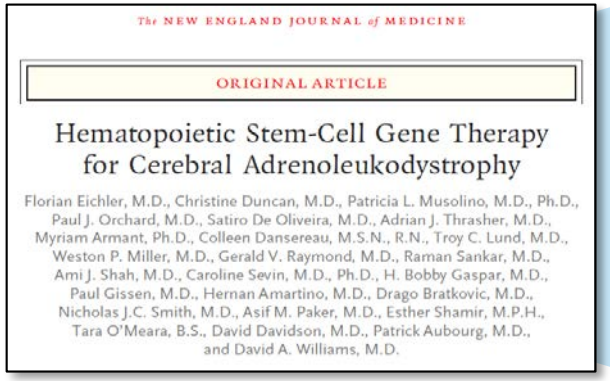
BLUE MOJO

TRUE BLUE

OUR PEOPLE



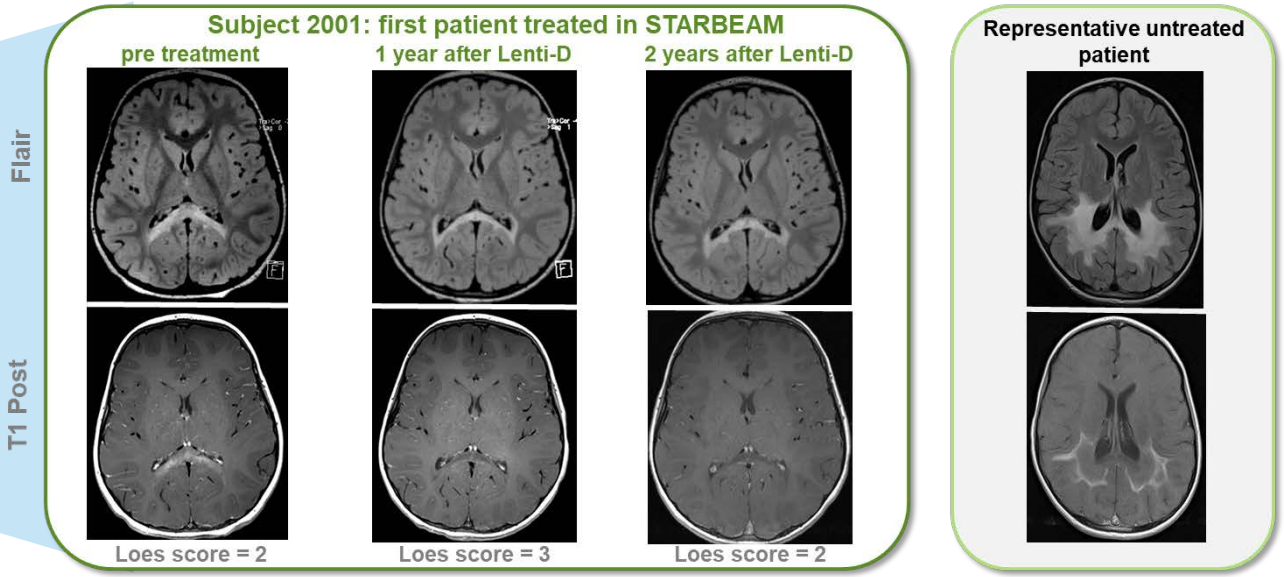
Neuroimaging outcomes demonstrate halting of disease progression after Lenti-D treatment


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hematopoietic Stem-Cell Gene Therapy for Cerebral Adrenoleukodystrophy

Florian Eichler, M.D., Christine Duncan, M.D., Patricia L. Musolino, M.D., Ph.D., Paul J. Orchard, M.D., Satiro De Oliveira, M.D., Adrian J. Thrasher, M.D., Myriam Armant, Ph.D., Colleen Dansereau, M.S.N., R.N., Troy C. Lund, M.D., Weston P. Miller, M.D., Gerald V. Raymond, M.D., Raman Sankar, M.D., Ami J. Shah, M.D., Caroline Sevin, M.D., Ph.D., H. Bobby Gaspar, M.D., Paul Gissen, M.D., Hernan Amartino, M.D., Drago Bratkovic, M.D., Nicholas J.C. Smith, M.D., Asif M. Paker, M.D., Esther Shamir, M.P.H., Tara O'Meara, B.S., David Davidson, M.D., Patrick Aubourg, M.D., and David A. Williams, M.D.



Data as of March 31, 2018

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

World-class Gene Therapy Platform and Integrated Global Capabilities

∞ | Patient Impact

2+ Products on the Market

2+ Programs Nearing Commercialization

4+ Additional Programs in the Clinic

bluebird Pipeline Overview

Product Candidates	Program Area	Preclinical	Phase 1/2	Phase 2/3	Rights/Partner
	CNS Diseases				
Lenti-D™ Drug Product	Cerebral ALD				Worldwide
	Rare Hemoglobinopathies				
LentiGlobin® Drug Product	Transfusion-Dependent ß-thalassemia			(Phase 3)	Worldwide
	Severe Sickle Cell Disease				Worldwide
BCL11a shRNA(miR)*	Severe Sickle Cell Disease				Worldwide
	BCMA				
bb2121	Multiple Myeloma				Celgene
bb21217	Multiple Myeloma				Celgene
	Oncology				
Viromed Target	Undisclosed				Worldwide excluding Korea
Medigene Targets	Undisclosed				Worldwide
	Research				
Early Pipeline	Undisclosed + Gene Editing				Worldwide

Development led by Boston Children's Hospital

COLLABORATORS

apceth BIOPHARMA

Boston Children's Hospital
Until every child is well

Lonza

medigene innovative immunotherapies

Celgene

Seattle Children's HOSPITAL · RESEARCH · FOUNDATION

ViroMed

How Do We Get There?

Data, Execution and Development in 2017

ASH 2017: 11 Abstracts Accepted Across the Pipeline

TDT

HGB-207
(Northstar-2) non-β^0/β^0 genotypes using refined 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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Transfusion Dependent β-Thalassemia

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Transfusion-Dependent Thalassemia

NORTHSTAR STUDY	HGB-204
HGB-205	HGB-205
NORTHSTAR-2 STUDY	HGB-207
NORTHSTAR-3 STUDY	HGB-212

- HGB-204
  - Primary 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-β^0/β^0 genotypes
- HGB-212
  - β^0/β^0 genotypes
  - Refined manufacturing process
  - Study initiation planned in 2017

Northstar (HGB-204) 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

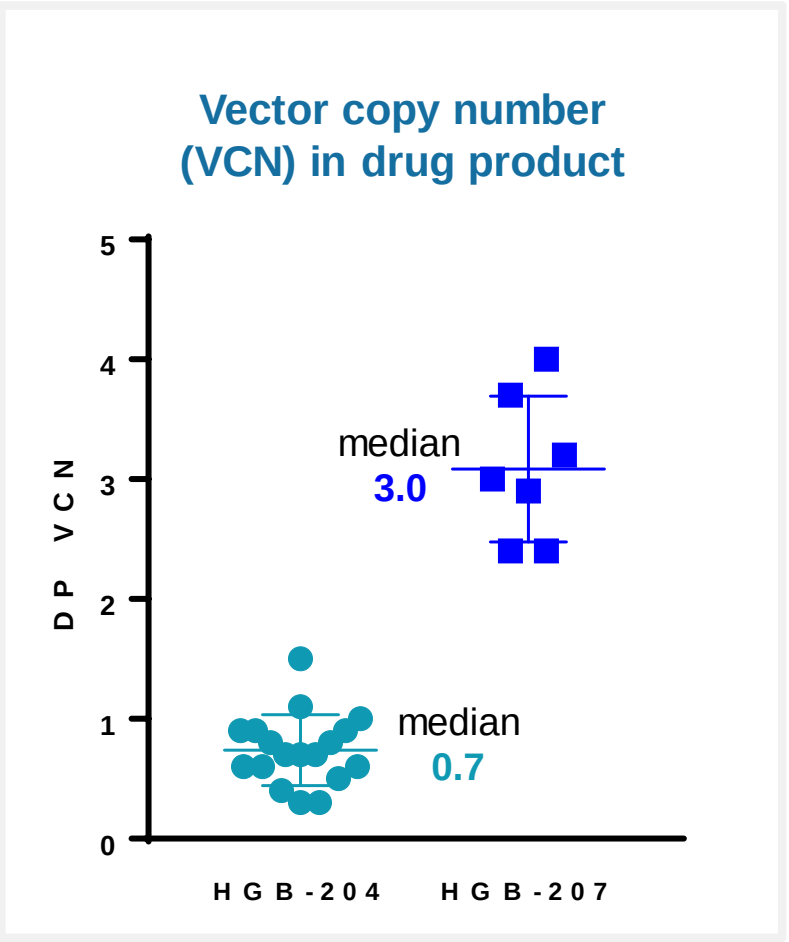
6 patients

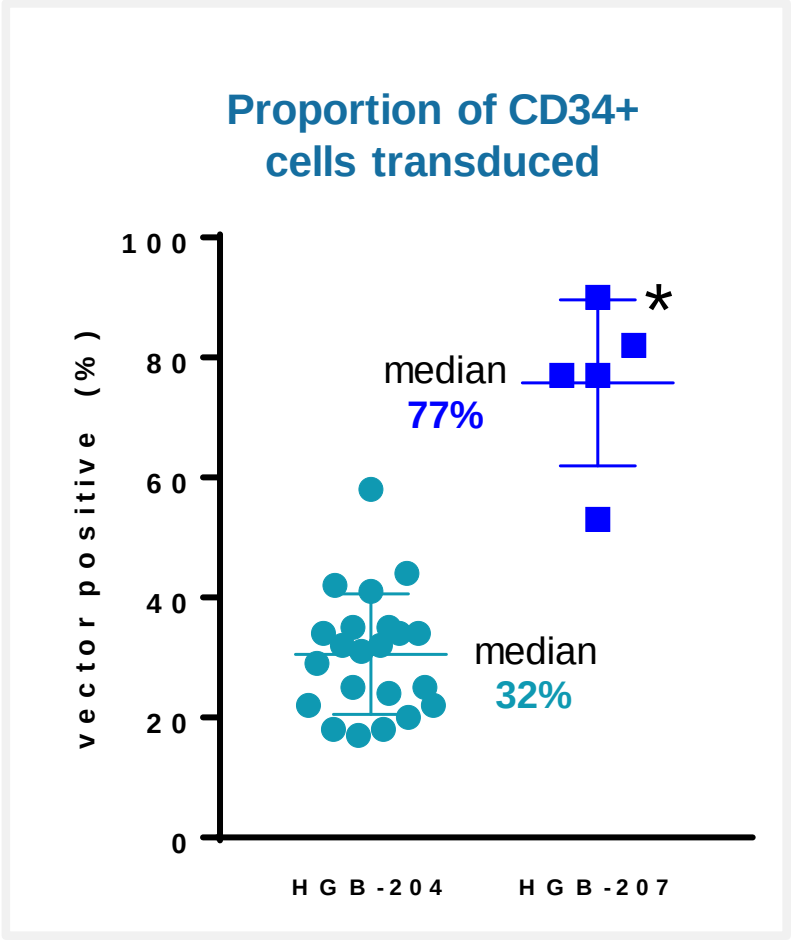
- Annual transfusion volumes reduced by 63% (median)

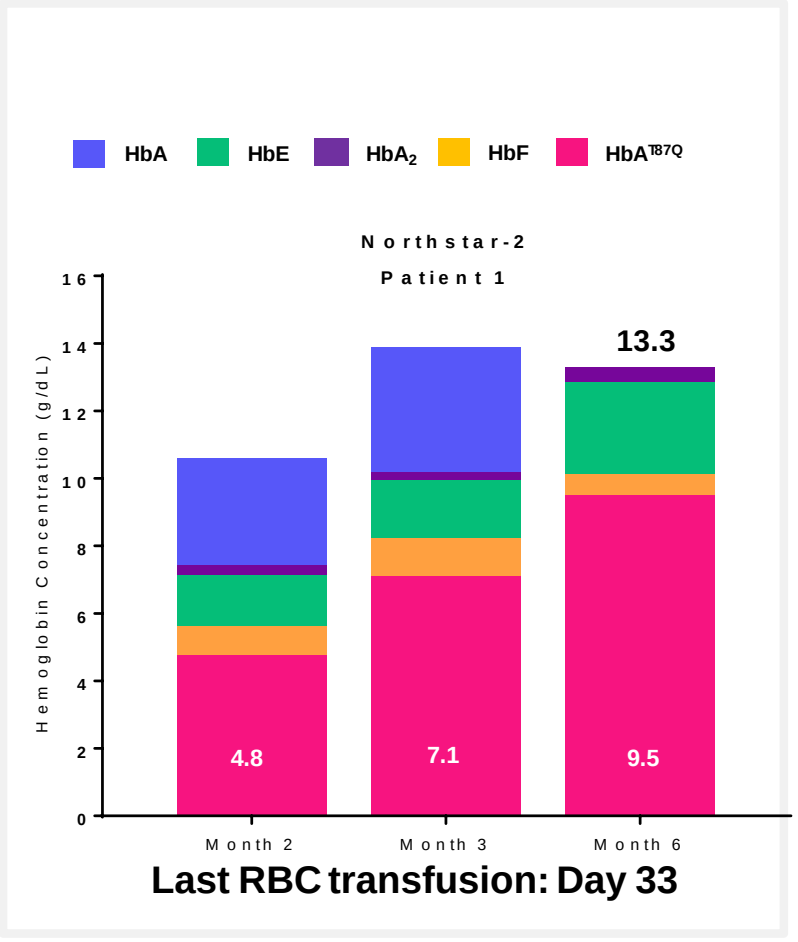
Safety profile consistent with autologous transplantation

Data as of June 2017

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



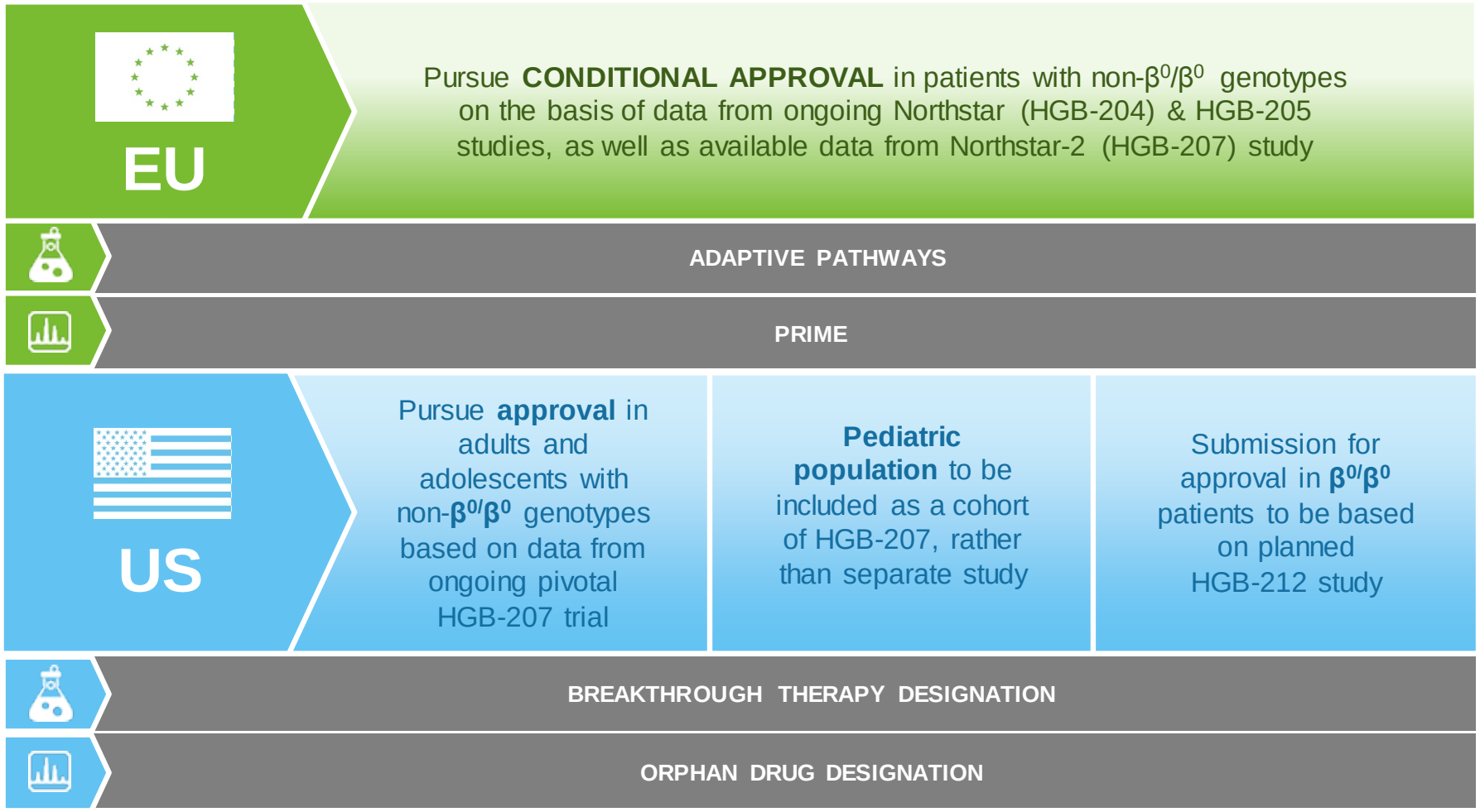




* Samples from EU manufacturing pending vector positive analysis

TDT Registration Strategy

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



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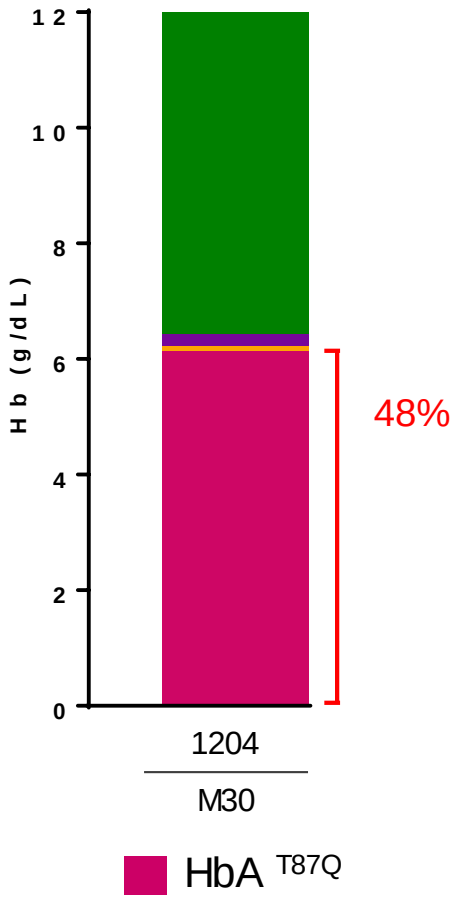
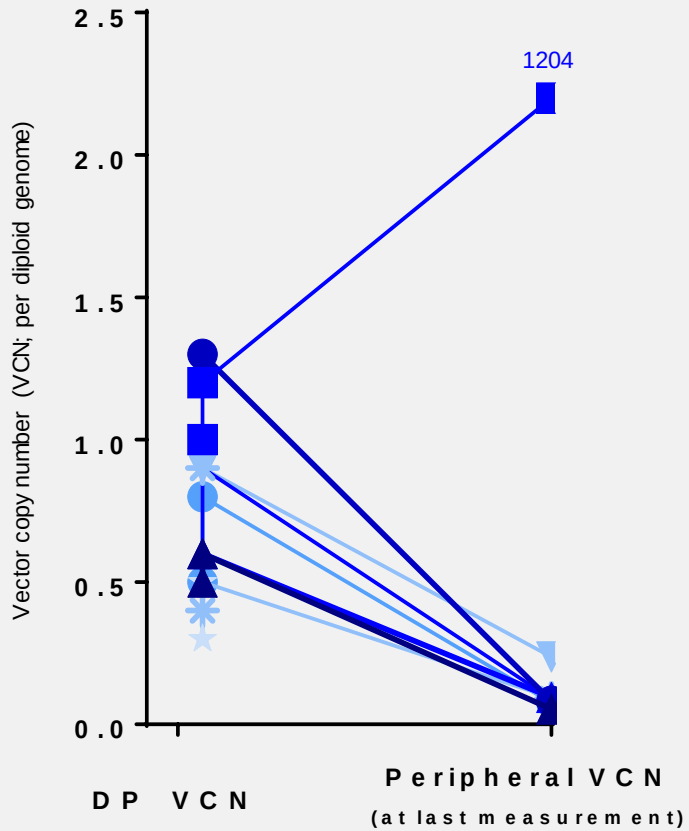
Severe Sickle Cell Disease

Nasdaq : BLUE

Understanding the Biology of SCD: Manufacturing and Protocol Improvements



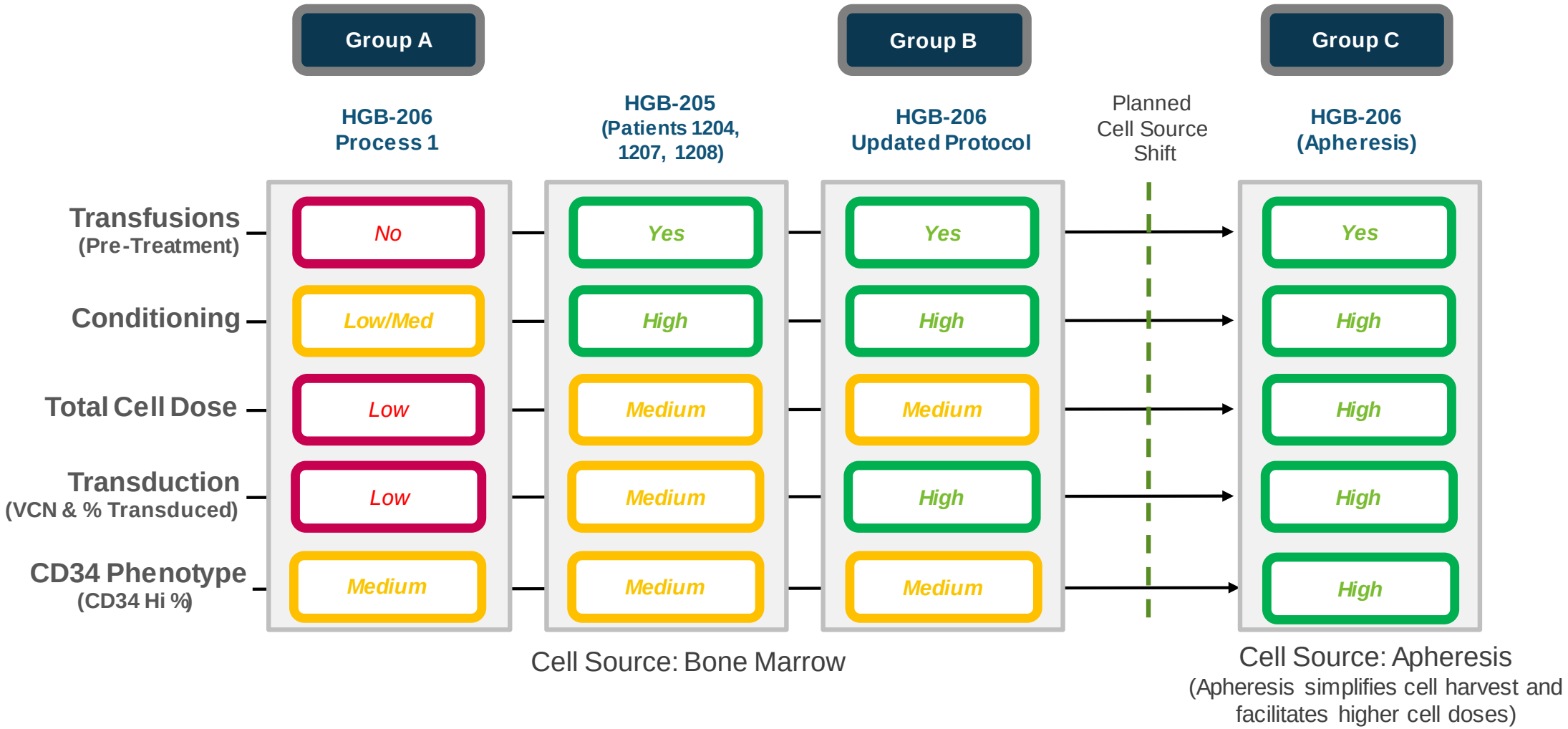
VCN drop from drug product to peripheral blood in HGB-206



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	Refined manufacturing process
Apheresis (vs. bone marrow harvest)	Utilize Plerixafor for mobilization and collection

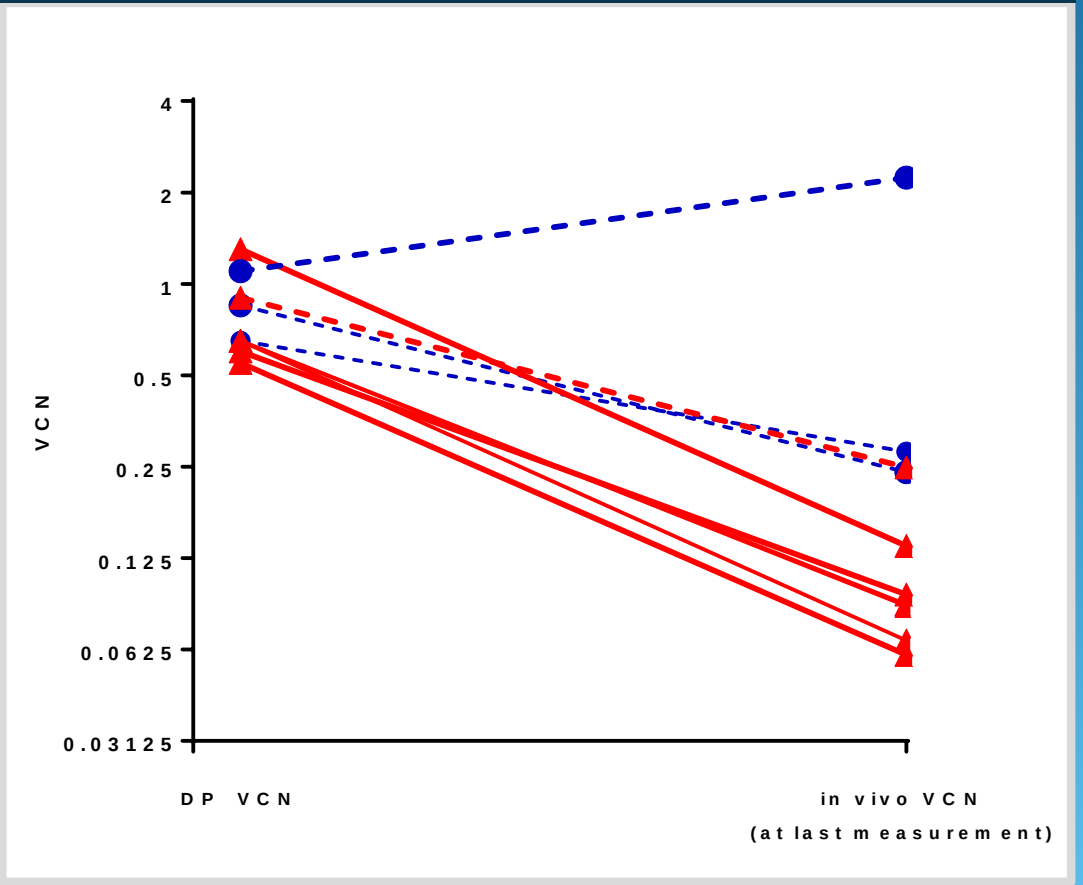
Data as of Sept 9, 2016 [HGB-205] and Nov 9, 2016 [HGB-206]

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

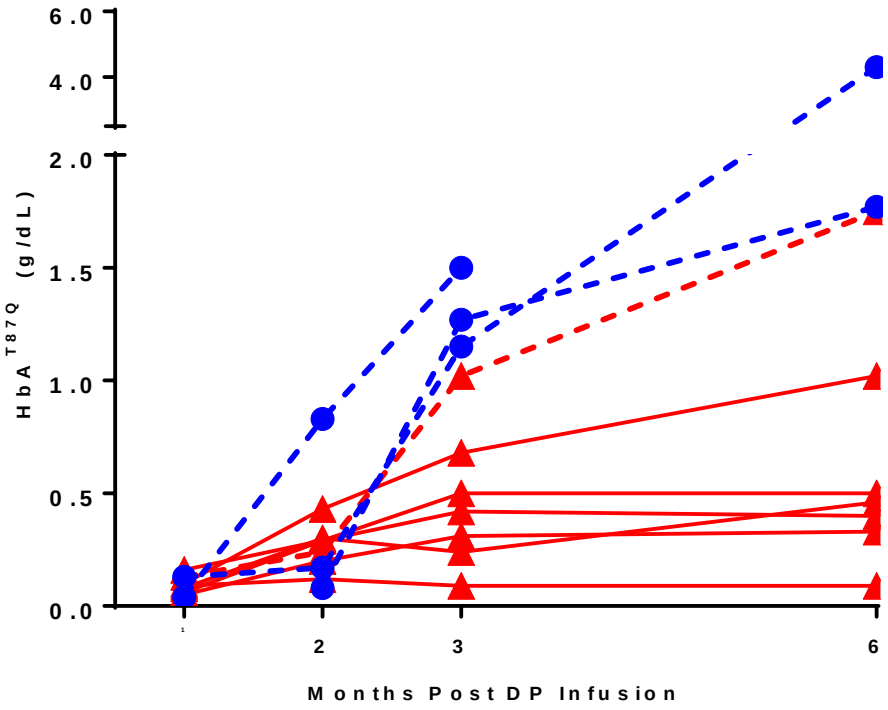


HGB-205 Show Impact of Transfusions, Optimized Conditioning

In Vivo VCN

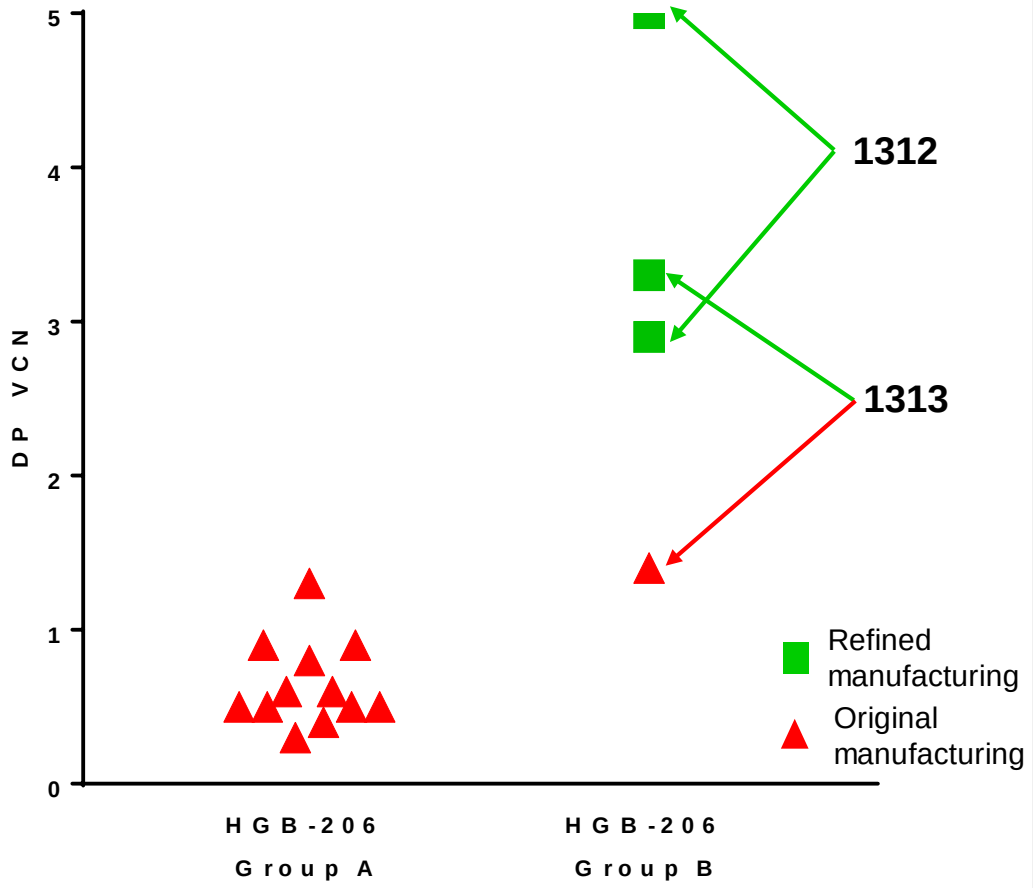


HbA^{T87Q}

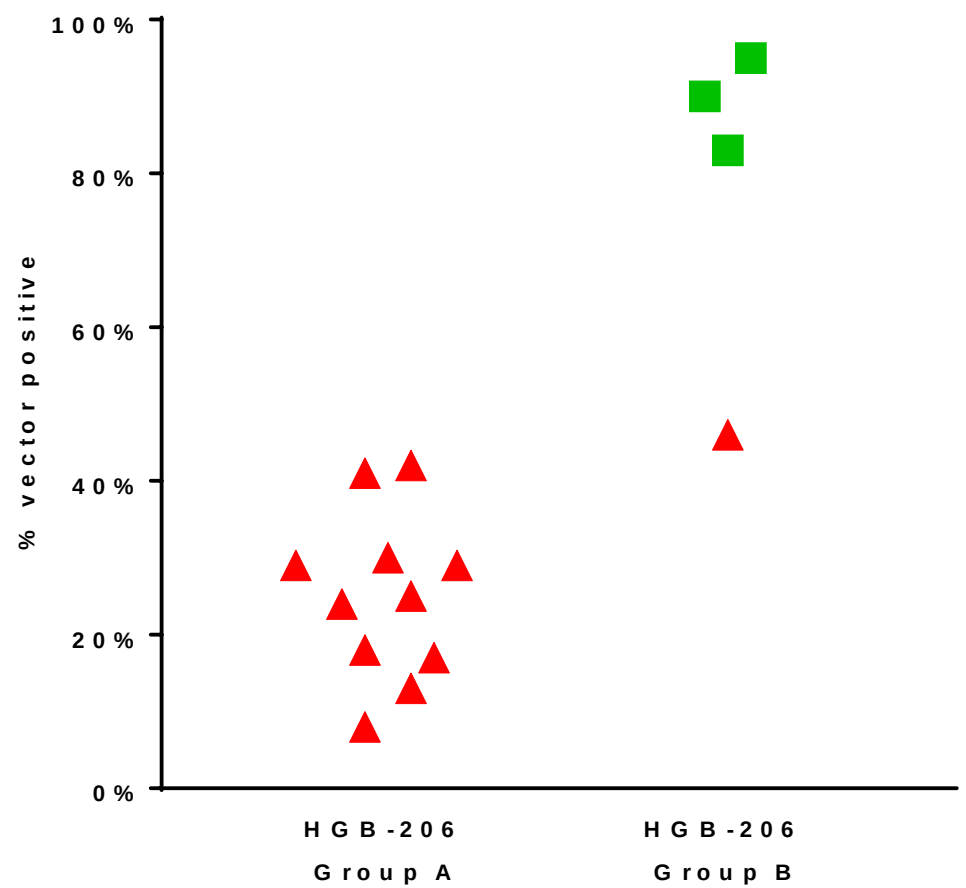


Group B: Early Data Indicates Impact of Process and Protocol Changes

Drug Product VCN



% Cells Transduced



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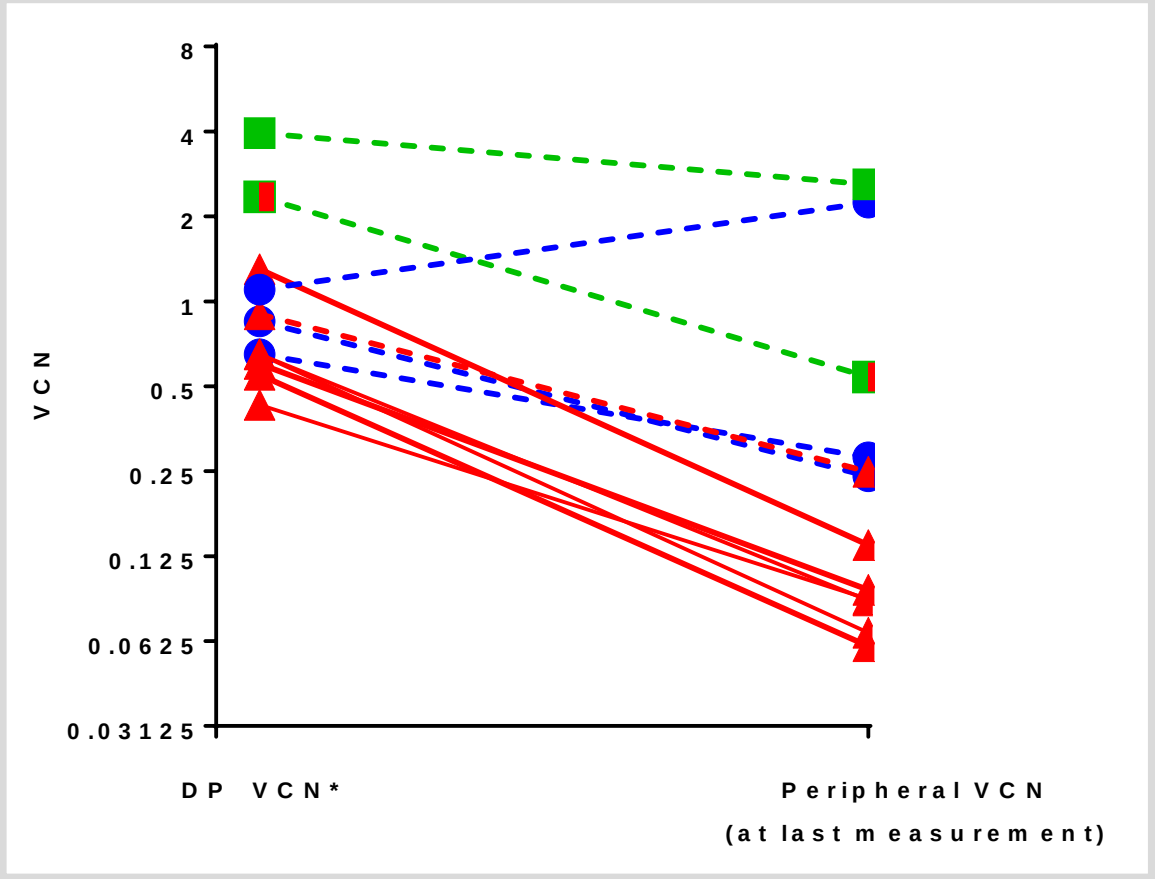
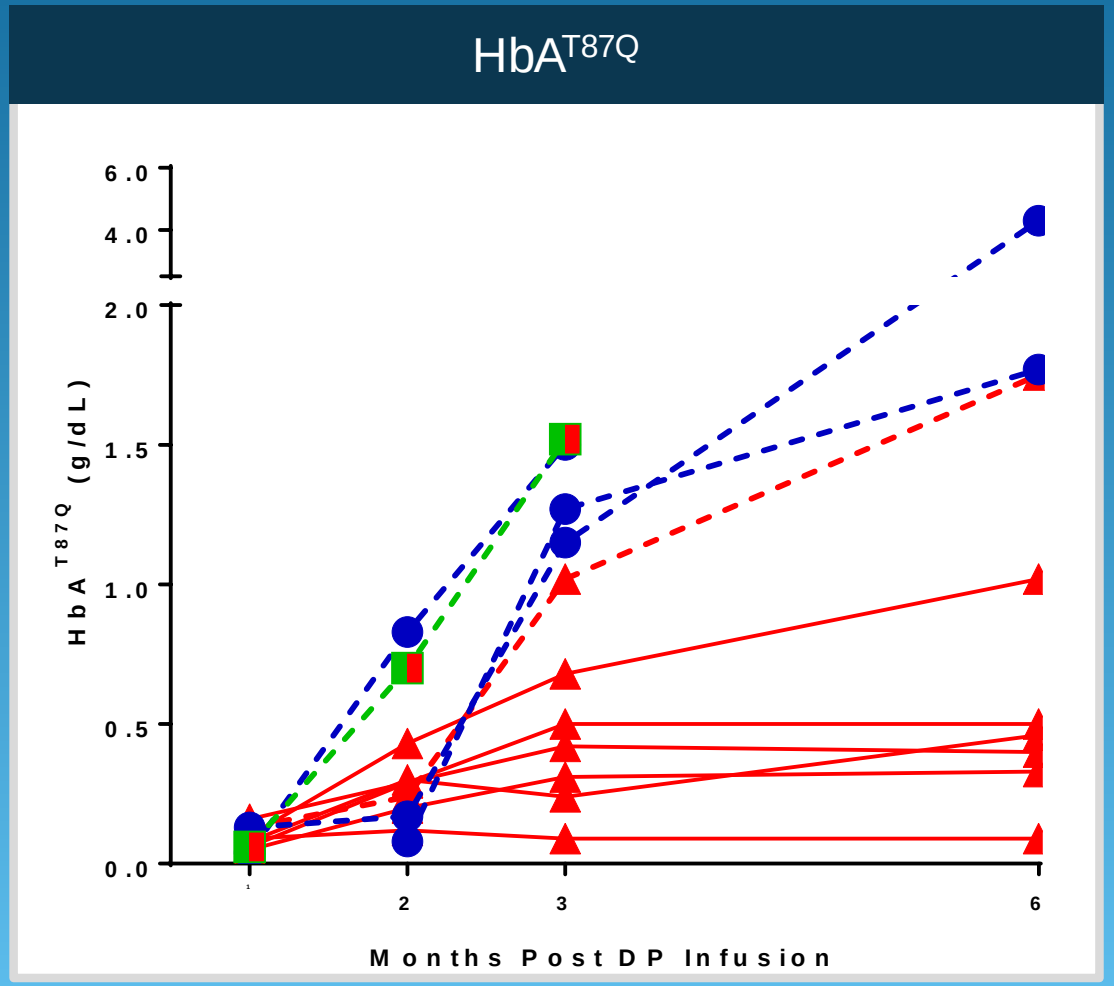
In Vivo VCN



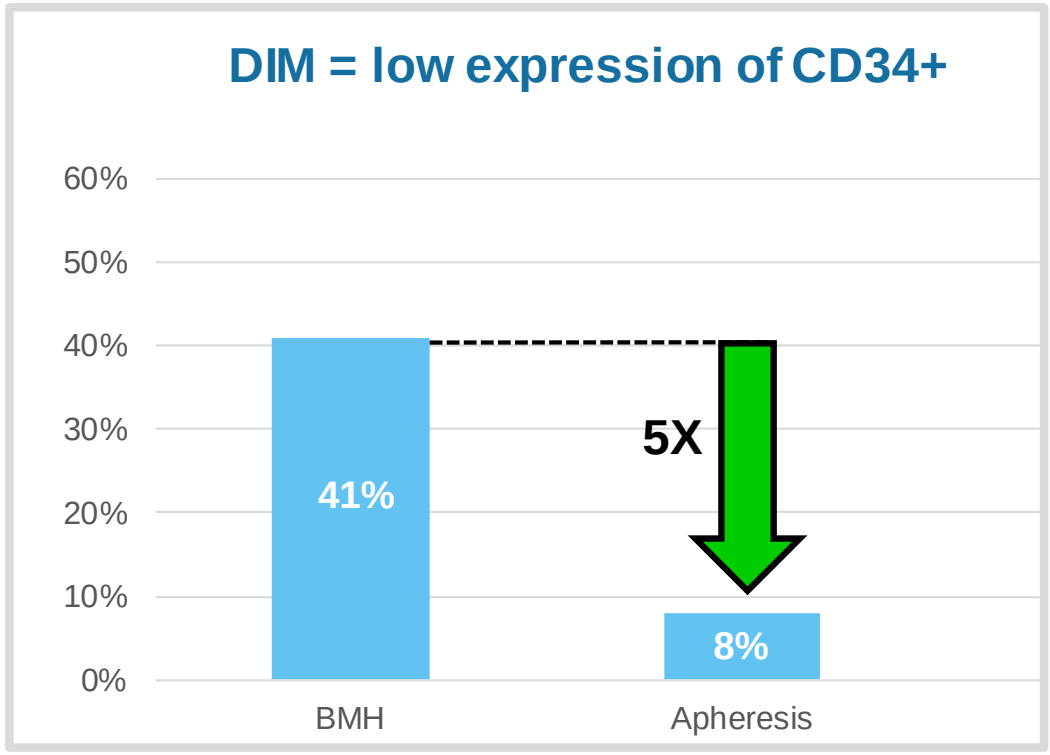
HbA^{T87Q}



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

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

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

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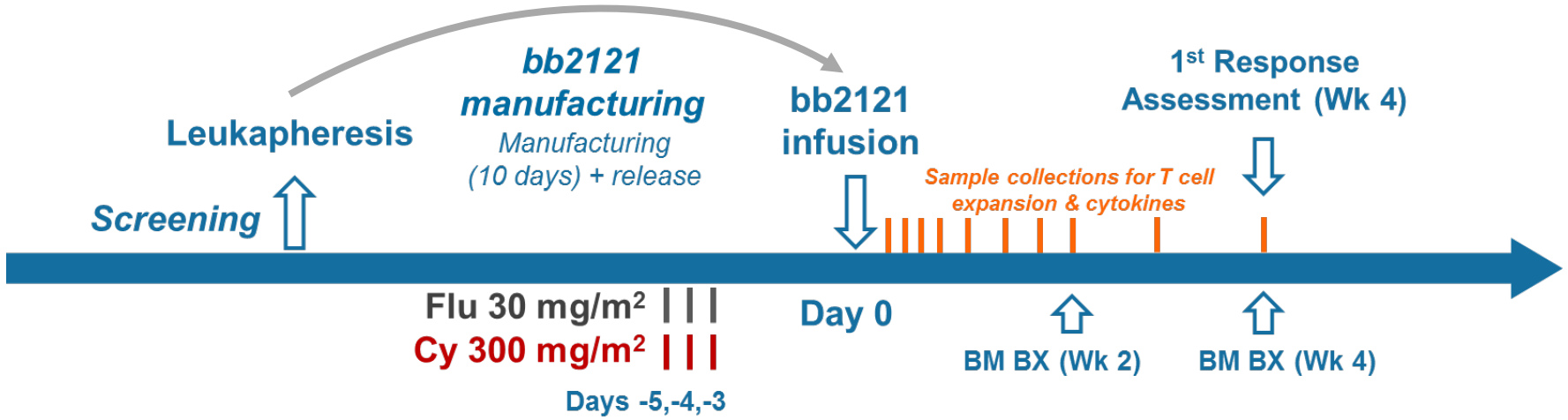
Multiple Myeloma

Nasdaq : BLUE

Multiple Myeloma Development – BCMA Targeted CARs (Chimeric Antigen Receptors)

bb2121	CRB-401	• Relapsed/refractory MM patients • Escalation complete; expansion ongoing • Pivotal start EOY 2017 / Early 2018 (Celgene)
bb21217	CRB-402	• Fast follower program – extend durability • Product design identical to 2121 • Manufactured in presence of PI3Ki

CRB-401 Open-label Phase 1 Clinical Study of bb2121



3 + 3 Dose Escalation Followed by Expansion Cohort

50×10^6 → 150×10^6 → 450×10^6 → 800×10^6 → $1200 \times 10^{6*}$

Escalation

- R/R MM ≥ 3 prior lines of therapy (incl. PI & imid) or double refractory (n=21)
- Measurable disease & ≥ 50% BCMA expression
- Adequate bone marrow, renal and hepatic function

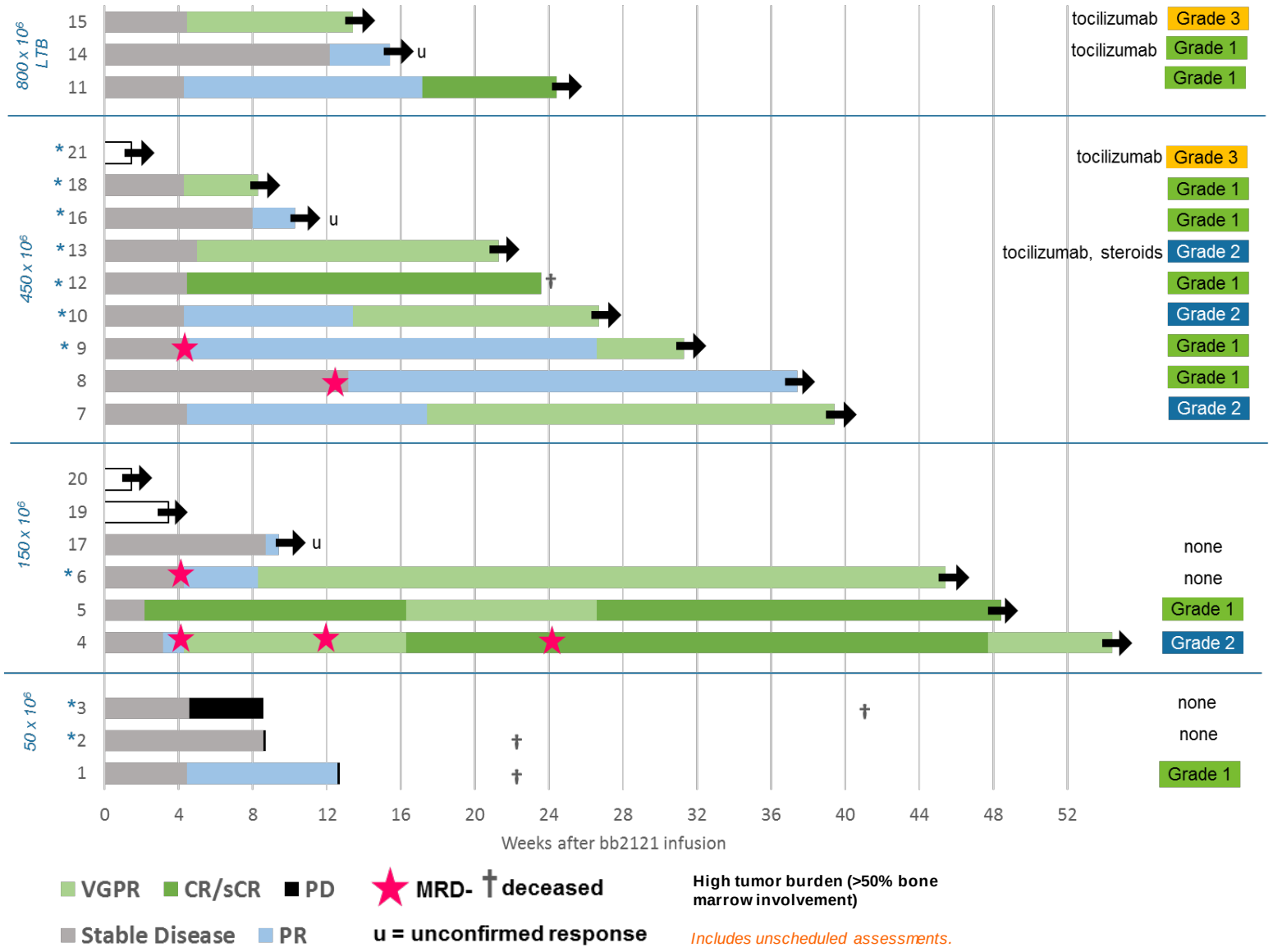
18 patients evaluated as of May 4, 2017

Expansion

- Dose 150-450 x 10^6
- No restrictions on BCMA expression levels
- N = ~20 patients

First patient treated Sept. 13, 2017

CRB-401: All bb2121 Patients in Active Dose Cohorts Achieved an Objective Response, Duration up to 54 Weeks



- **15/21 (71%) with cytokine release syndrome (CRS)**
  - 2 patients with Grade 3 CRS that resolved in 24 hours
  - 4 patients received tocilizumab, 1 (Grade 2 CRS) with steroids
  - CRS grade does not appear related to tumor burden
- **CRS-related symptoms mostly Grade 1-2**
- **No Grade 3/4 neurotoxicity**

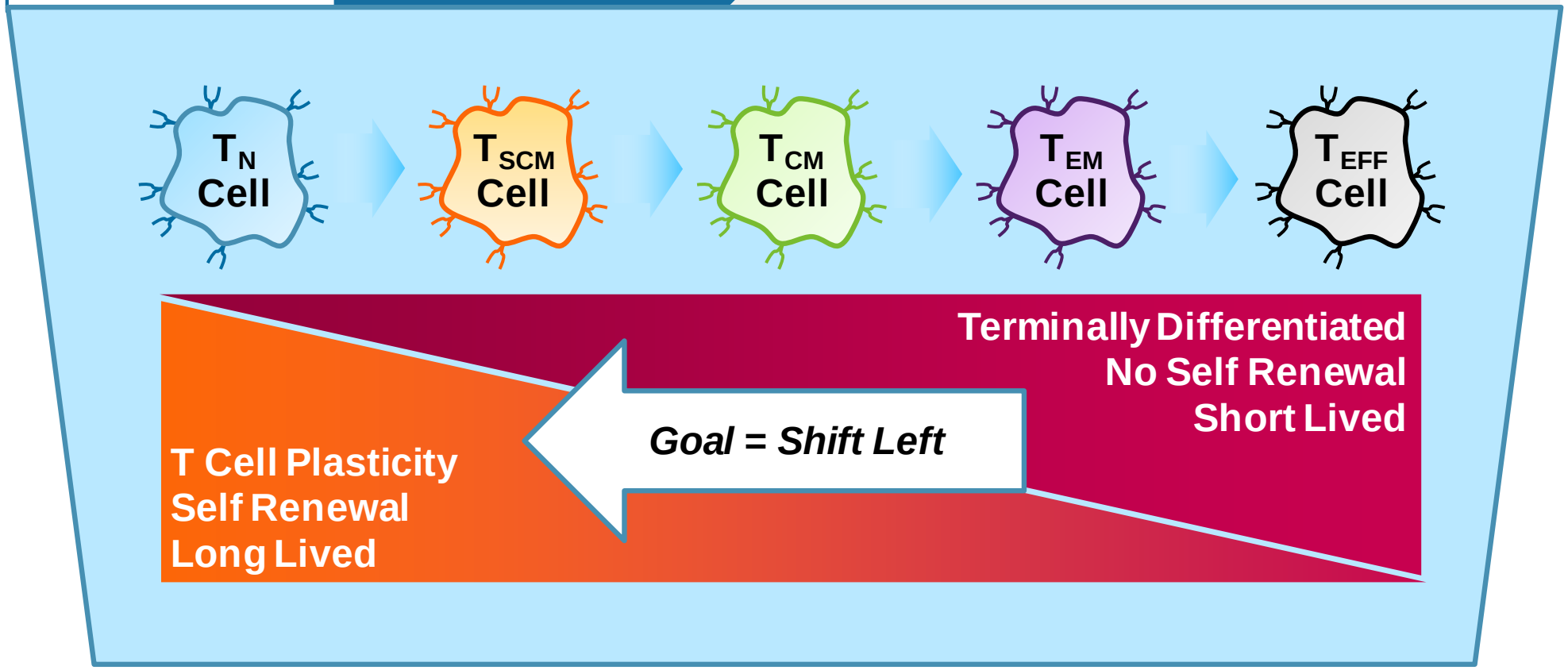
Data as of May 4, 2017

Fast Follower BCMA Program – Study Actively Enrolling

bb21217

CRB-402

- Goal – improve durability
- Product design identical to 2121
- Manufactured in presence of PI3Ki



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

Go TRUE BLUE

We Must Make Hope a Reality