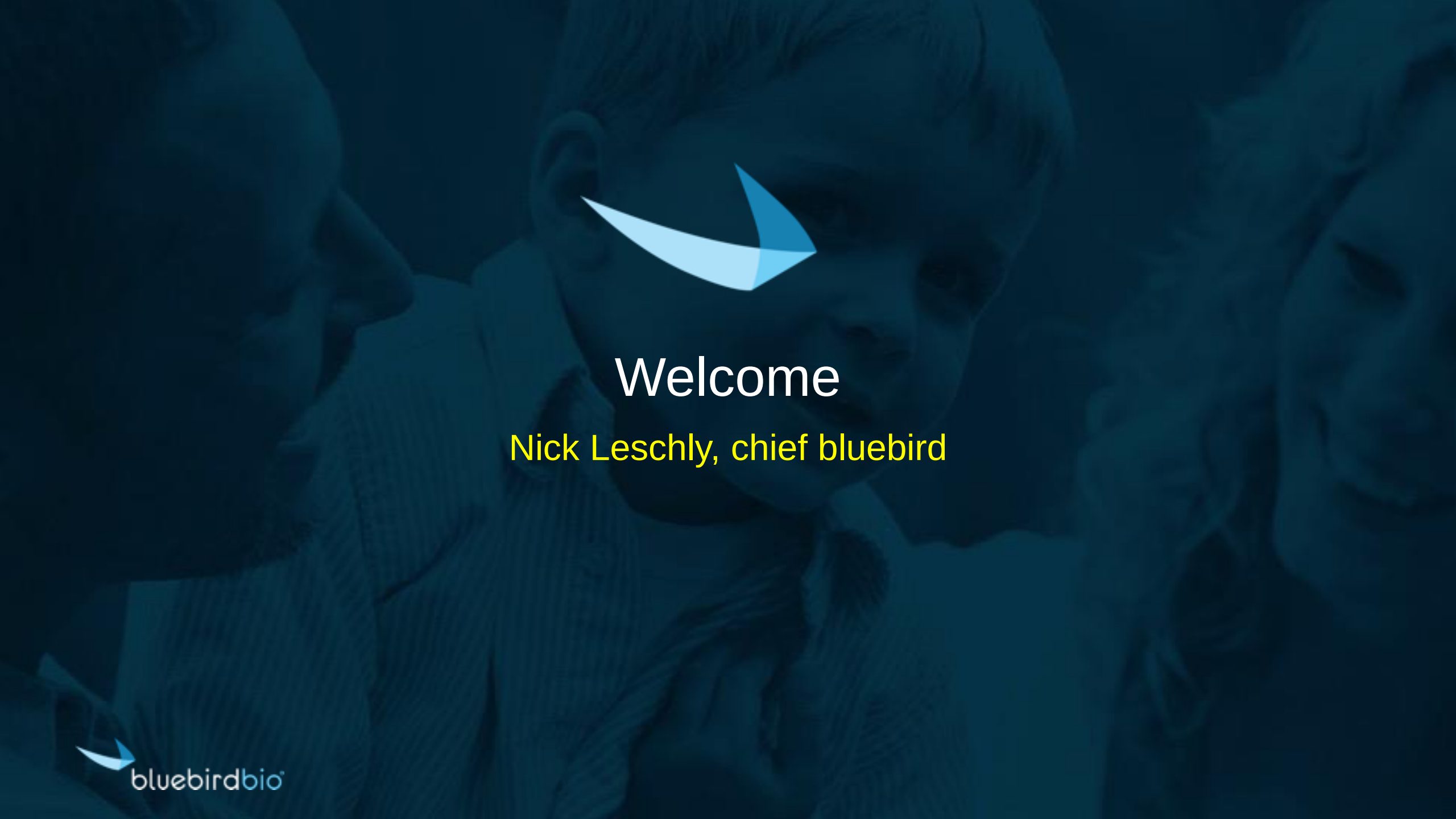
EHA Analyst & Investor Webcast

June 15, 2018

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.



Welcome

Nick Leschly, chief bluebird

bluebirdbio






Making Hope A Reality




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

Key Takeaways

LentiGlobin TDT

- Transfusion-dependent β-thalassemia (TDT) MAA filing on track for 2018
- HGB-207: 7/8 patients reaching normal/near normal total hemoglobin by 6 months
- HGB-204: 8/10 non-β^0/β^0 patients achieve and maintain TI for up to 3+ years

LentiGlobin SCD

- Group C (n=6) patients showing rapid and consistent anti-sickling HbA^{T87Q} expression
  - At 3 months (n=4) all patients have ≥ 30% HbA^{T87Q}
  - At 6 months (n=1) patient has 62% HbA^{T87Q}; total Hgb of 14.2 g/dL
- No new safety findings in patients treated with plerixafor

BLUE 2018 & Beyond

- Commercial readiness and implementation underway
- Early and late-stage clinical programs tracking
- Building for next phase of growth: innovation engine and commercialization

LentiGlobin TDT Data Update

David Davidson, M.D., chief medical officer

bluebirdbio

“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 β-Thalassemia (TDT)

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

UNMET NEED

- Treatment of underlying disease limited to allo-HSCT, primarily only for pediatric patients with sibling donor matches
- Sometimes severe treatment-related risks and complications
- Requires comprehensive care throughout life

EPIDEMIOLOGY

- Global prevalence ~ 288,000
- Global incidence ~ 60,000

Transfusion-Dependent β-Thalassemia

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

- Basis of EU filing
- Original manufacturing process
- All genotypes

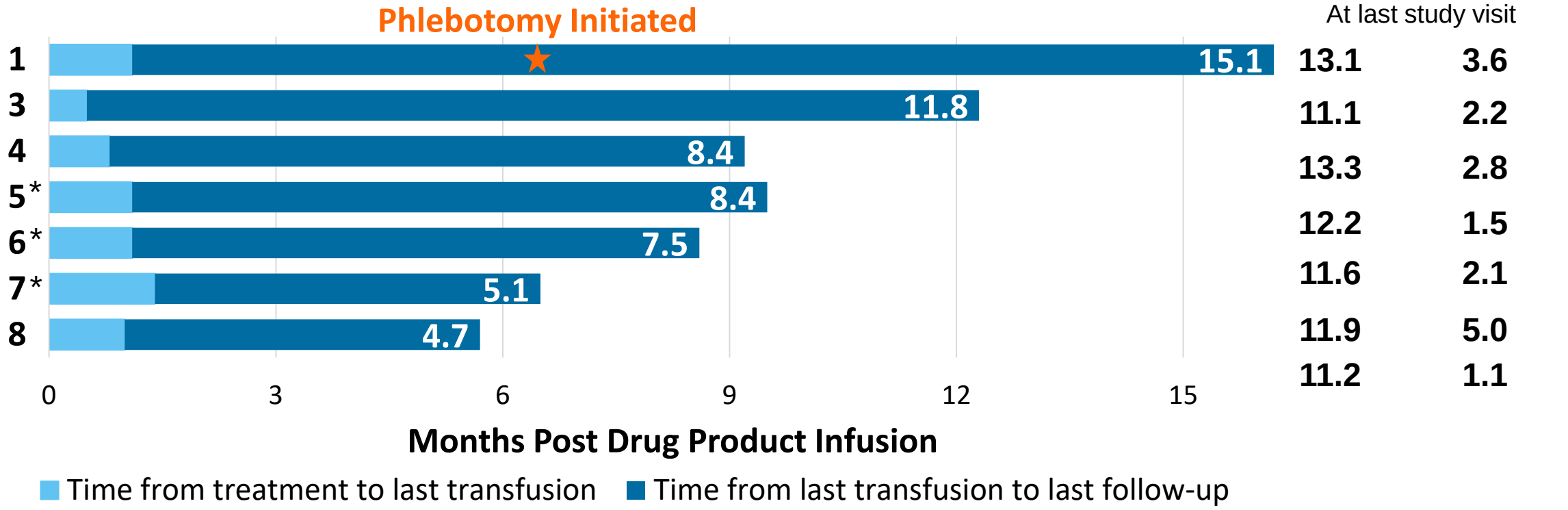
- Basis of EU filing (with Northstar)
- Original manufacturing process

- Basis of EU and U.S. filings
- Refined manufacturing process
- Non-β^0/β^0 genotypes

- β^0/β^0 genotypes
- Refined manufacturing process
- First patient treated in November 2017
- **First pediatric patient treated April 2018**

HGB-207: 7/8 Patients with ≥ 6 Months Follow-up are Transfusion Free

First treated patient achieved transfusion independence and has begun phlebotomy

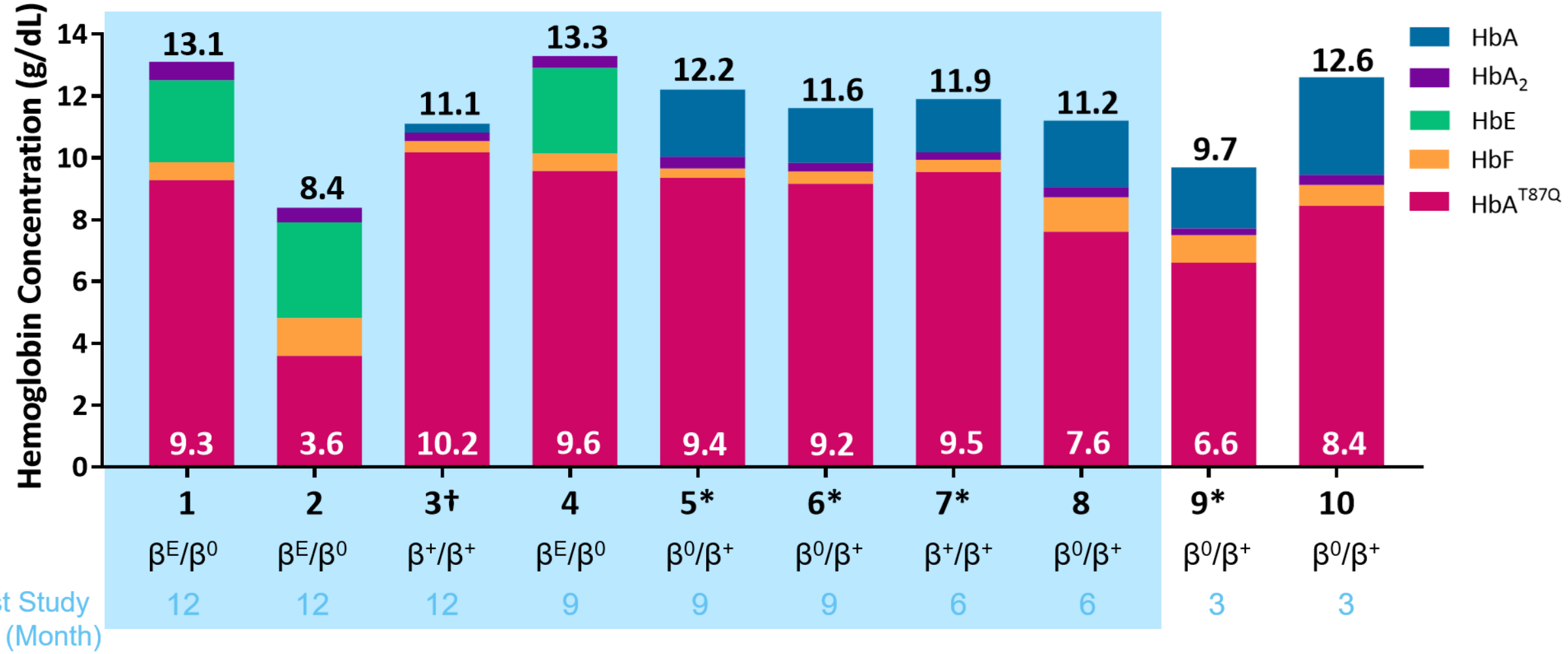


	Hb (g/dL)	Peripheral VCN
	At last study visit	
1	13.1	3.6
3	11.1	2.2
4	13.3	2.8
5*	12.2	1.5
6*	11.6	2.1
7*	11.9	5.0
8	11.2	1.1

- Patient 2 was free from chronic transfusions for 11 months, however received a transfusion following DP infusion due to low Hb; patient had a peripheral VCN of 0.2

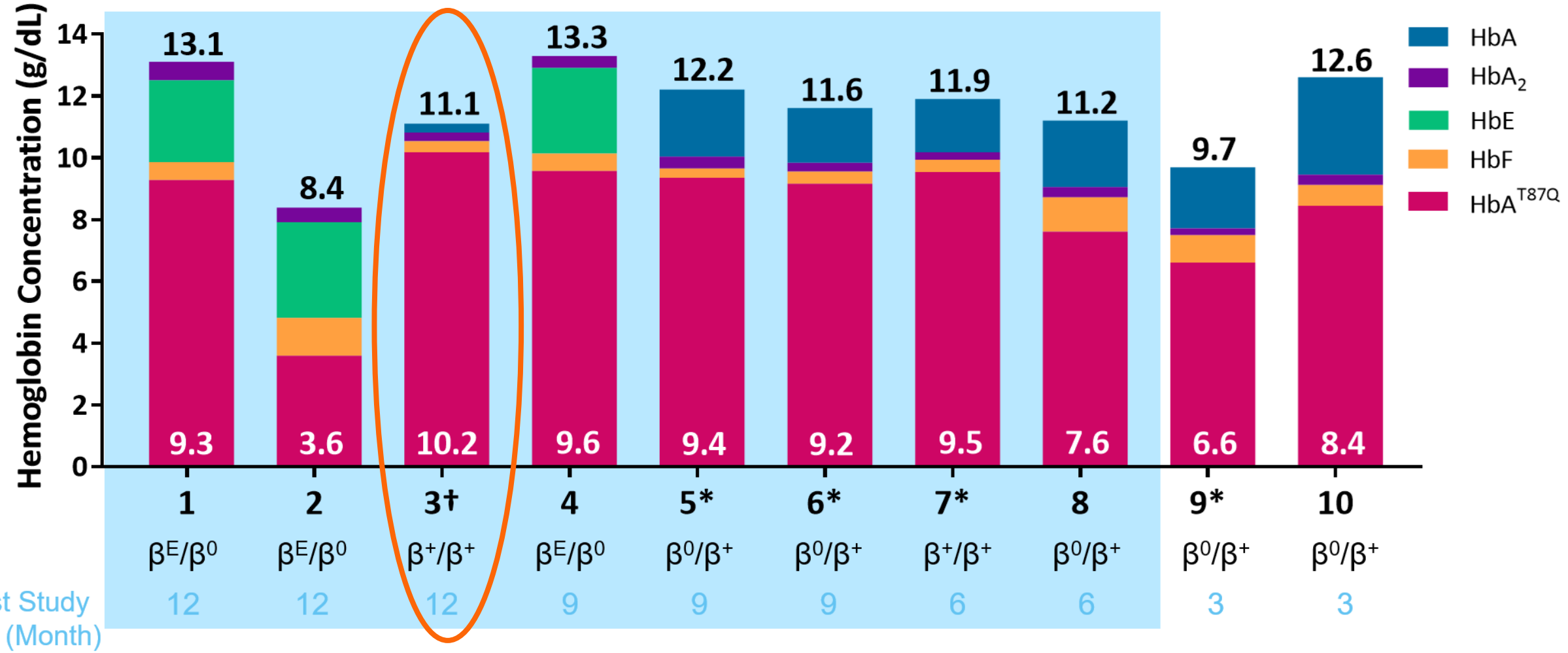
*Indicates male patients; Transfusion independence is defined as the weighted average Hb ≥9 g/dL without any RBC transfusions for ≥12 months; Hb, hemoglobin; VCN, vector copy number

HGB-207: 7/8 patients are producing ≥ 7.6 g/dL of HbA^{T87Q} by 6 months



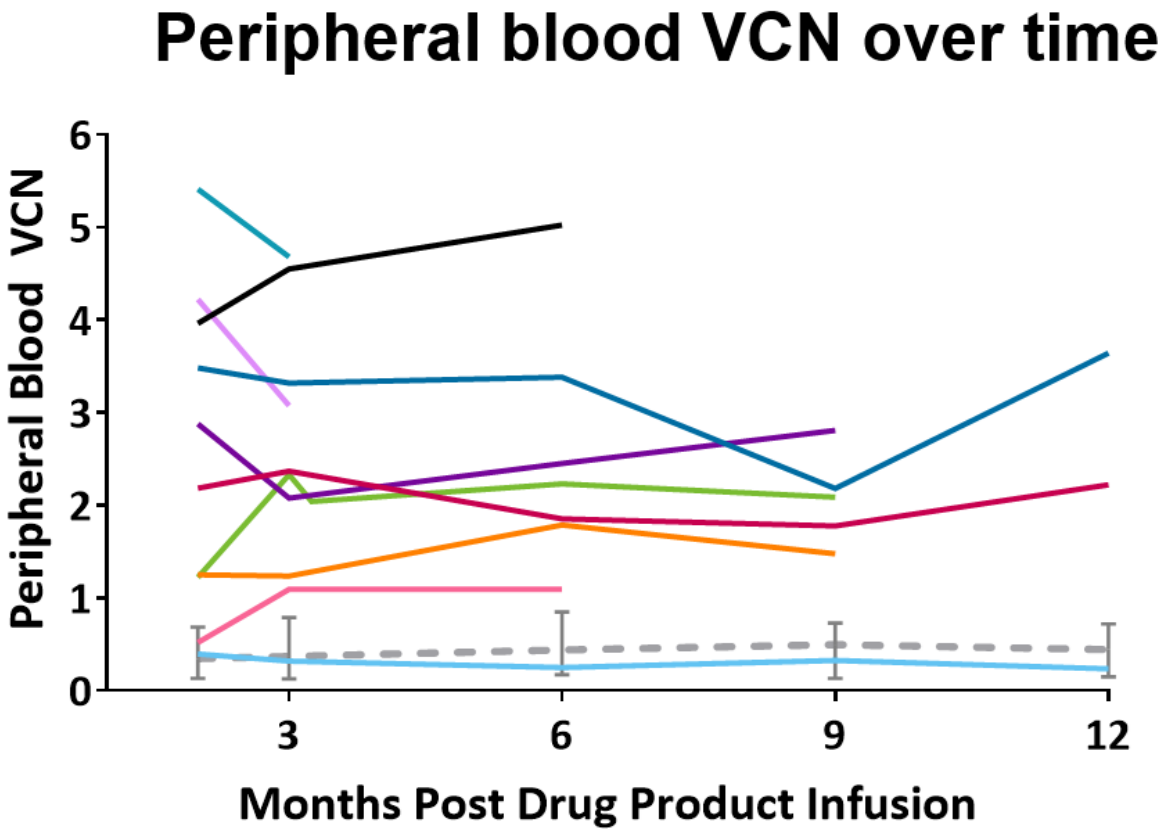
* Indicates male patients; †Patient is homozygous for severe IVS-1-5 β-globin mutation

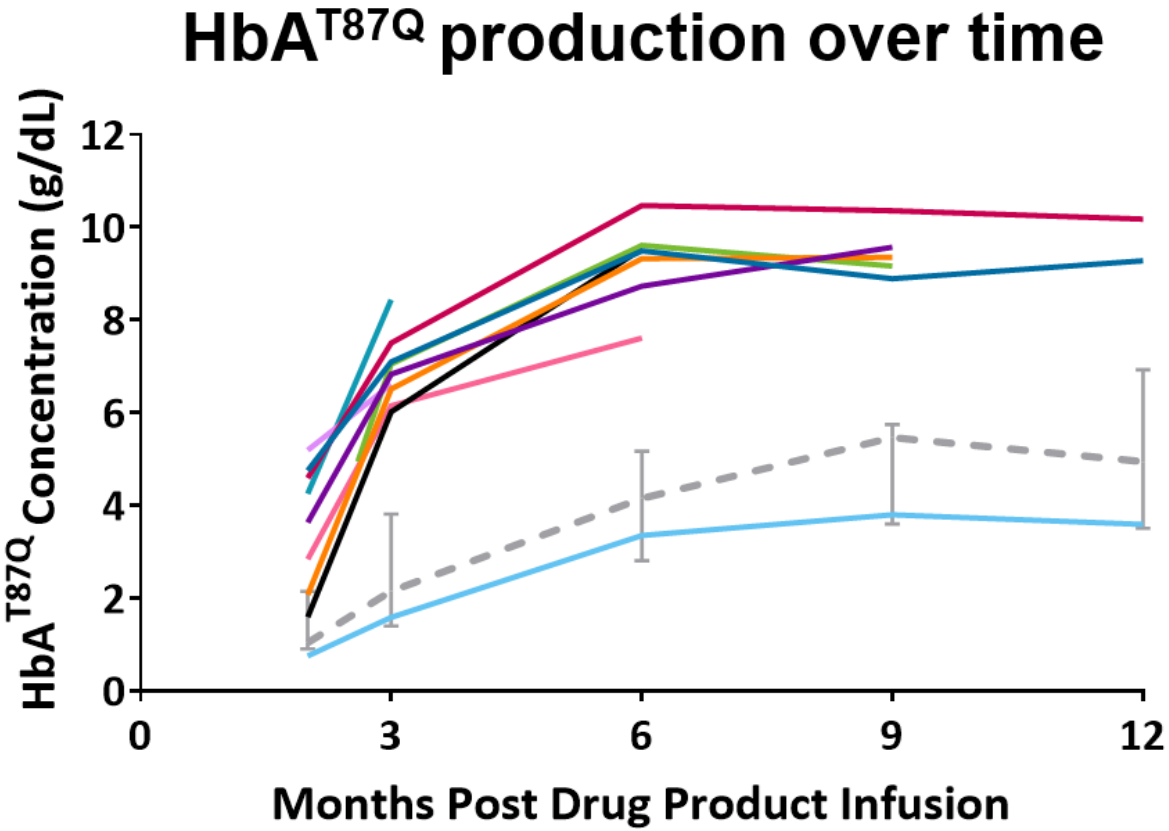
HGB-207: 7/8 patients are producing ≥ 7.6 g/dL of HbA^{T87Q} by 6 months



†Patient is homozygous for severe IVS-1-5 β-globin mutation

Peripheral Blood VCN and HbA^{T87Q} Production Over Time





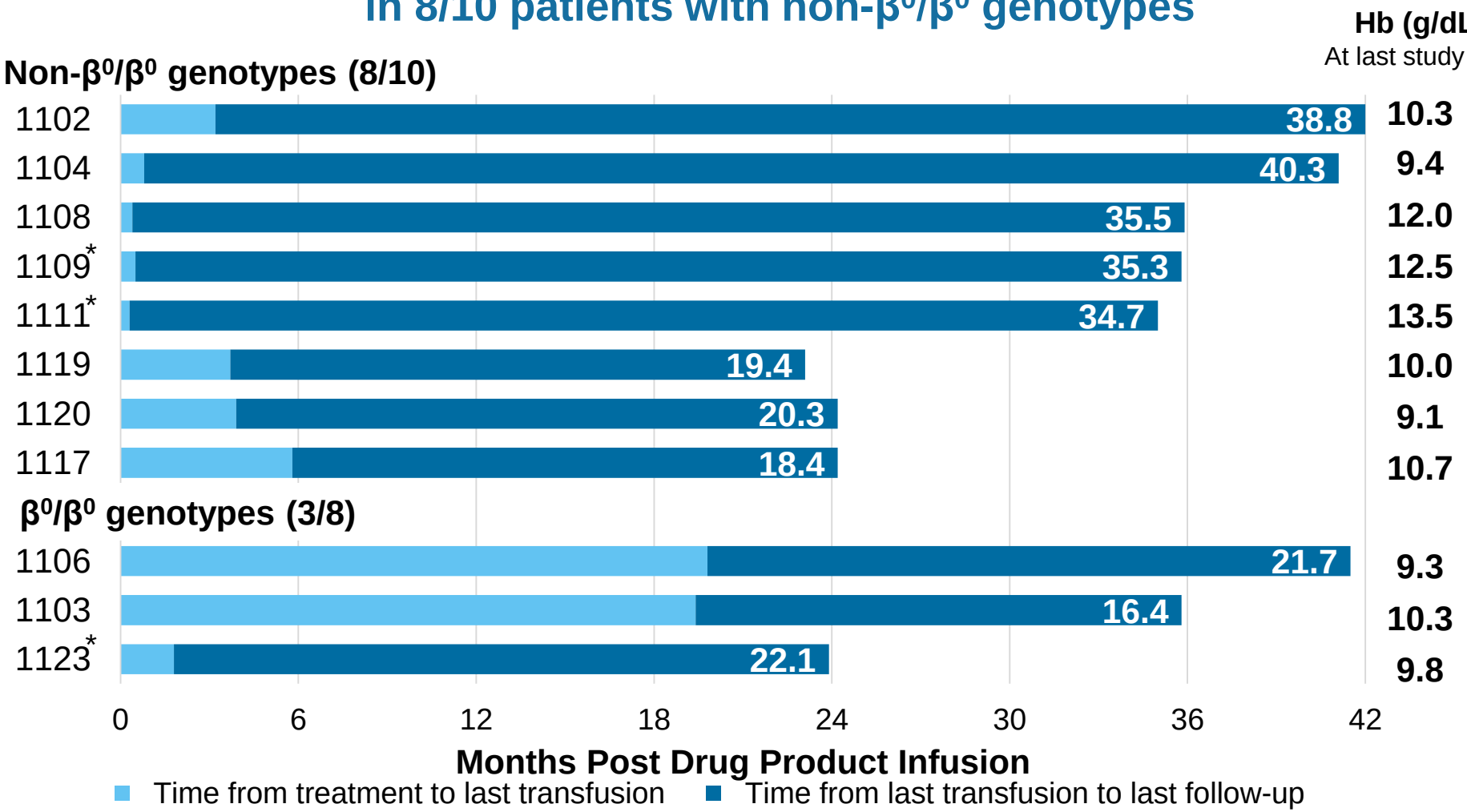
HGB-204 non-β^0/β^0 HGB-207: 1 3 5 7 9 2 4 6 8 10

For 204 non-β^0/β^0 patients, medians (Q1, Q3) depicted

Data as of 15 May 2018 (HGB-207) and 7 Mar 2018 (HGB-204)

HGB-204: 8/10 Patients with Non-β⁰/β⁰ Genotypes Achieve and Maintain Transfusion Independence

Median duration of transfusion independence to date of 33 months in 8/10 patients with non-β⁰/β⁰ genotypes



Transfusion Independence

Non-β⁰/β⁰ genotypes (8/10)
80% achieved TI for 16+ to 38+ months

β⁰/β⁰ genotypes (2/8)
25% achieved TI for 14+ and 16+ months

Reduction in Transfusion Volume

Non-β⁰/β⁰ genotypes (2/10)
27% and 82%

β⁰/β⁰ genotypes (5/8)
Median 53%
(min – max: 8% – 74%)

*Indicates male patients; Transfusion independence is defined as the weighted average Hb ≥9 g/dL without any RBC transfusions for ≥12 months

LentiGlobin Safety Profile is Generally Consistent with Myeloablative Conditioning

HGB-204

- No grade ≥ 3 DP-related AEs
- One SAE of asymptomatic wild-type HIV infection was reported 23 months after DP infusion and was considered not related to LentiGlobin
- Two SAEs of VOD

HGB-207

- One grade 1 abdominal pain event was considered possibly related to LentiGlobin
- Two SAEs of VOD extended hospitalization following DP infusion
  - Events occurred on Day +23 and Day +34
  - Both patients were treated with defibrotide
  - Both events have resolved

No graft failure

No deaths

No vector-mediated replication competent lentivirus

No early evidence of clonal dominance

AE, adverse event; DP, drug product; HIV, human immunodeficiency virus; SAE, serious adverse event, VOD, veno-occlusive liver disease

Data as of 15 May 2018

LentiGlobin SCD Data Update

bluebirdbio

"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

Sickle Cell Disease (SCD)

- Severe blood disorder that causes anemia, frequent pain crises, and shortened lifespan

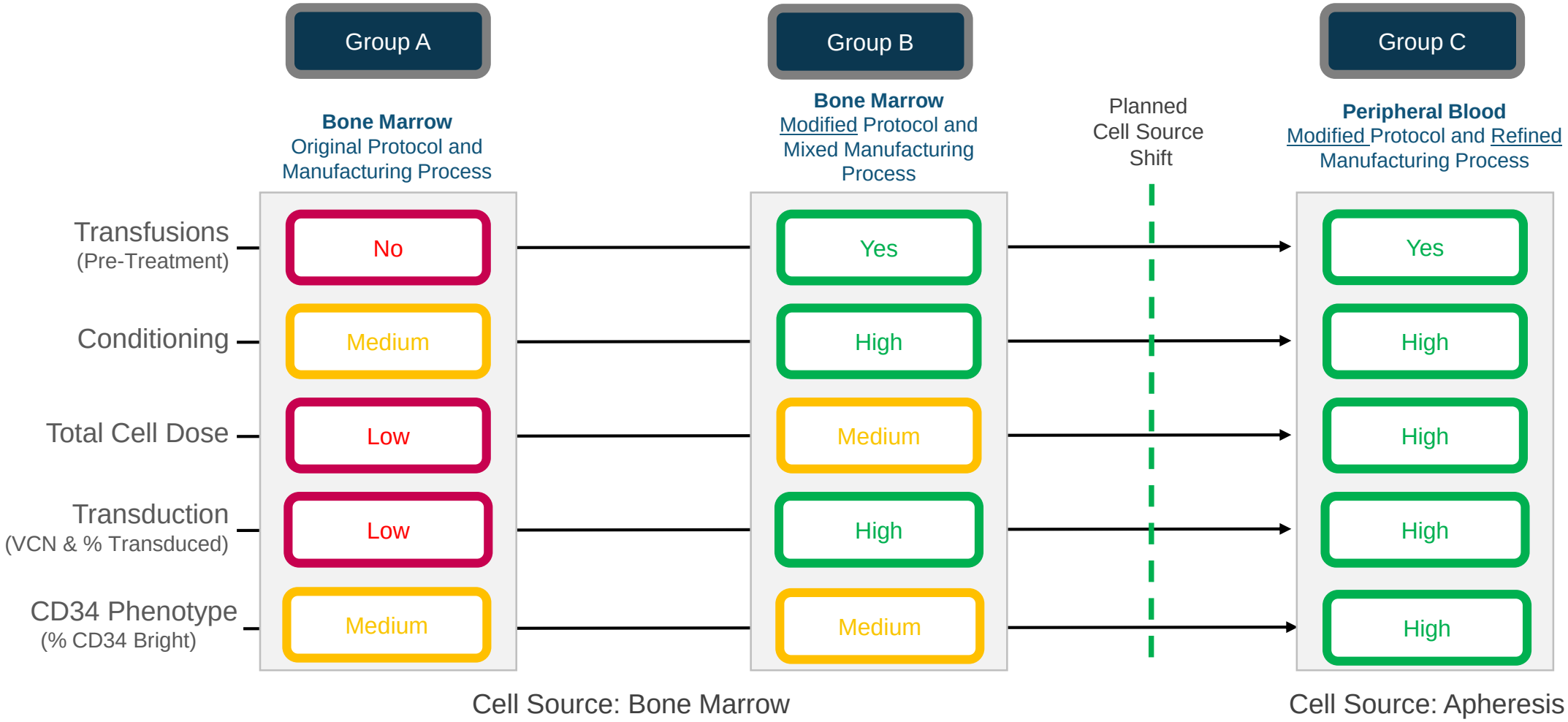
UNMET NEED

- High morbidity; early mortality; with median age of death in the 5th decade
- Treatment of underlying disease limited to allo-HSCT, primarily recommended only for pediatric patients with matched sibling donors
- 15-20% of patients with SCD may have HLA-identical sibling donor
- Substantial treatment-related risks and complications

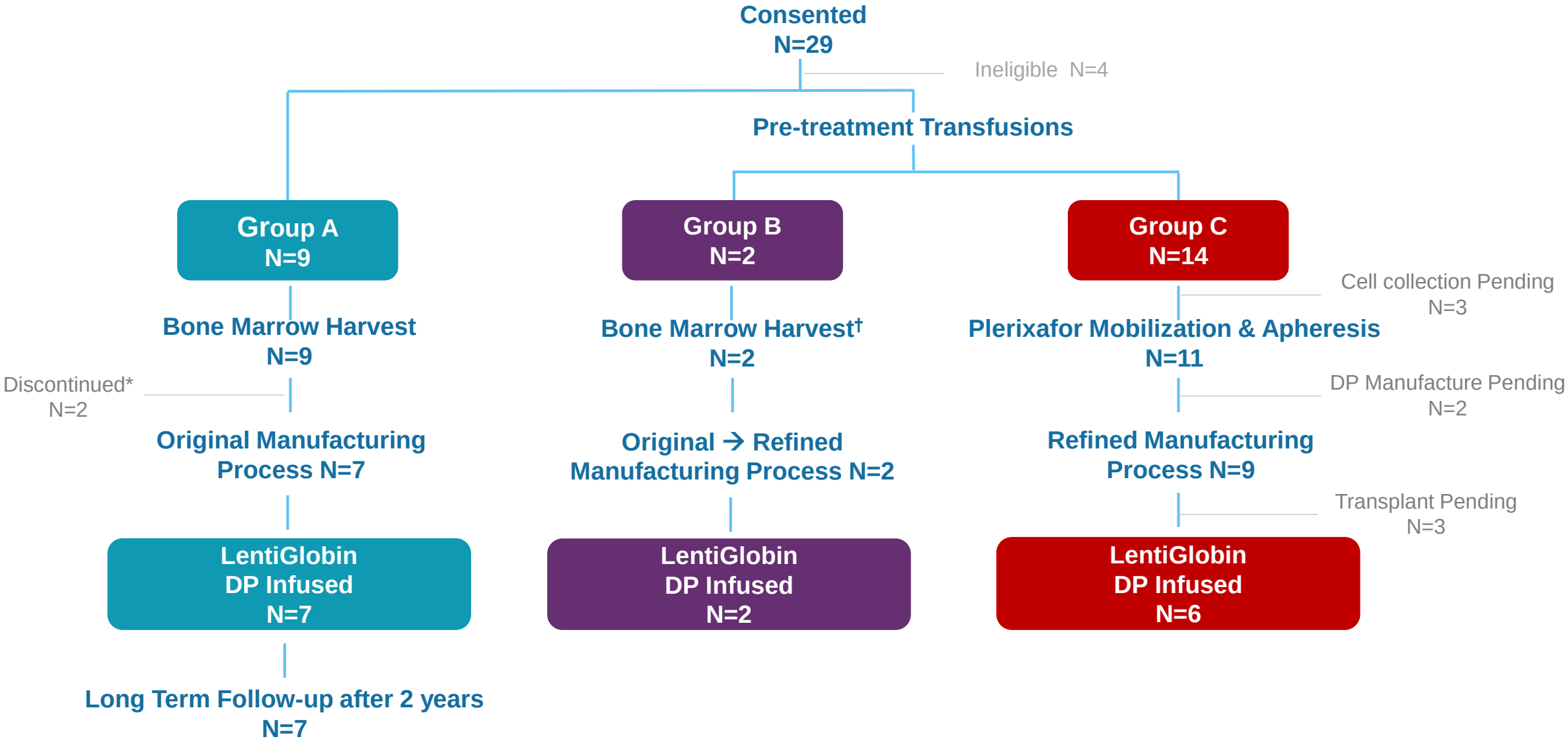
EPIDEMIOLOGY

- U.S. prevalence ~ 100,000; EU prevalence ~ 113,000
- Global annual birth incidence ~ 300,000 – 400,000

HGB-206: Evolution of LentiGlobin in SCD



HGB-206: Study Disposition



** 1 due to insufficient cell collection, 1 withdrew consent; †One patient also received a single mobilization cycle to collect cells for back-up*

HGB-206: Patient Characteristics

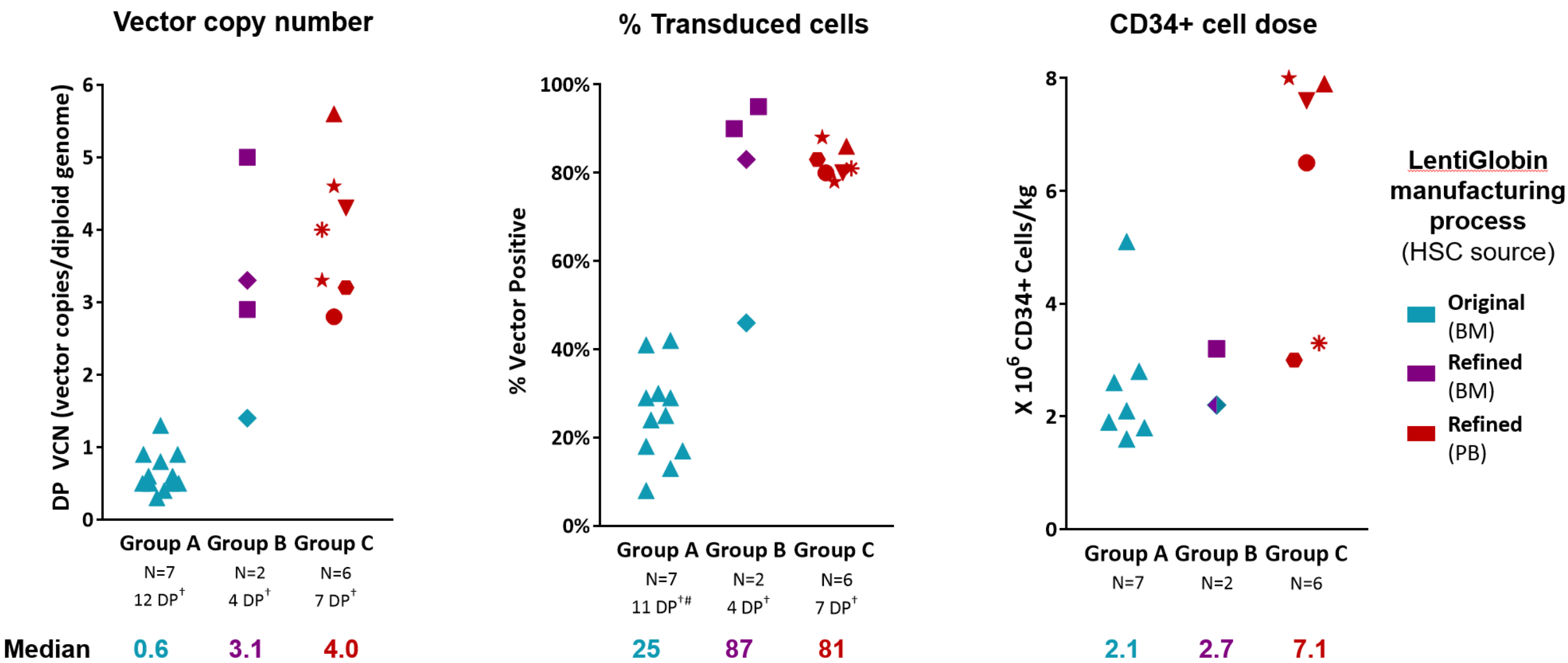
N=22 Patients Who Started Cell Collection

Parameter	Group A N=9	Group B N=2	Group C N=11
Age at consent median (min – max), years	**26** (18 – 43)	**24.5** (22 – 27)	**25** (18 – 35)
Gender	**2 Female**	**0 Female**	**5 Female**
Genotype β^S/β^S	**9**	**2**	**11**
Prior SCD History **No. of patients** **No. of events**, median (min – max)			
Hydroxyurea use	**5**	**2**	**6**
Recurrent VOCs[*,†]	**7** **4.5** (2.0 – 27.5)	**2** **10.0** (2.5 – 17.5)	**6** **7.5** (4.0 – 14.0)
Acute chest syndrome[*,†]	**1** **1**	**1** **1**	**2** **1** (1 – 1)
Any history of stroke	**2**	**0**	**3**
Regular pRBC transfusions before study entry	**1**	**0**	**7**
TRJV >2.5 m/s[*]	**1**	**0**	**0**

*Within 2 years prior to informed consent, or initiation of regular transfusions in case of VOCs; †Median Annualized values in patients with ≥2 events/year (for VOCs), or ≥1 events/year with at least one episode in the year before informed consent or initiation of regular transfusions (for ACS)

ACS, acute chest syndrome; VOC, vaso-occlusive crisis, TRJV, Tricuspid regurgitant jet velocity

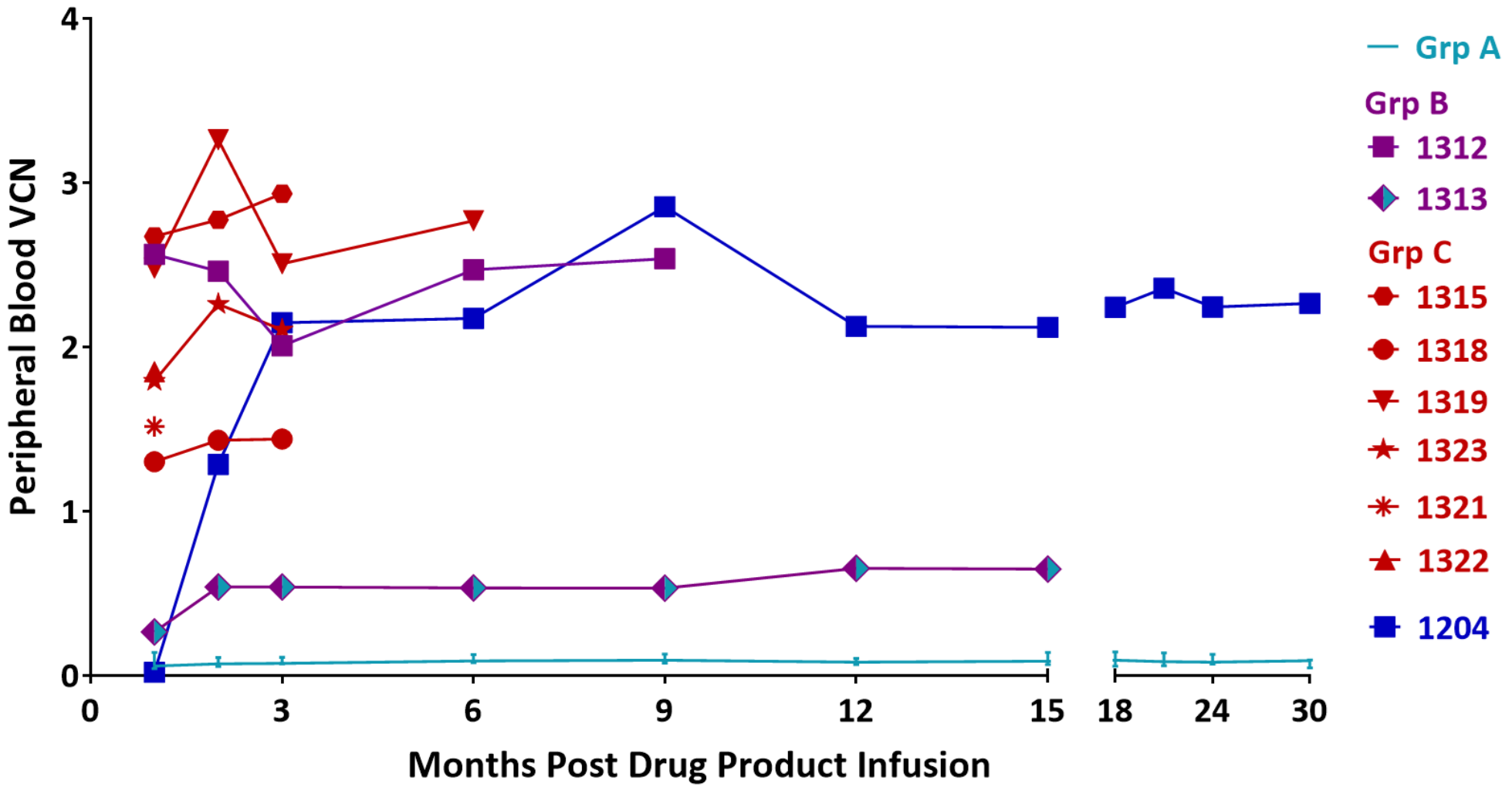
Refinements to Manufacturing and Cell Harvest Lead to Improved Drug Product Characteristics



† Number of DP exceeds number of patients since some patients were harvested or mobilized more than once; # % Transduced cells not available for 1 DP at time of analyses; Grey line indicates median

BM, bone marrow; HSC, hematopoietic stem cell; Med, median; PB, peripheral blood.

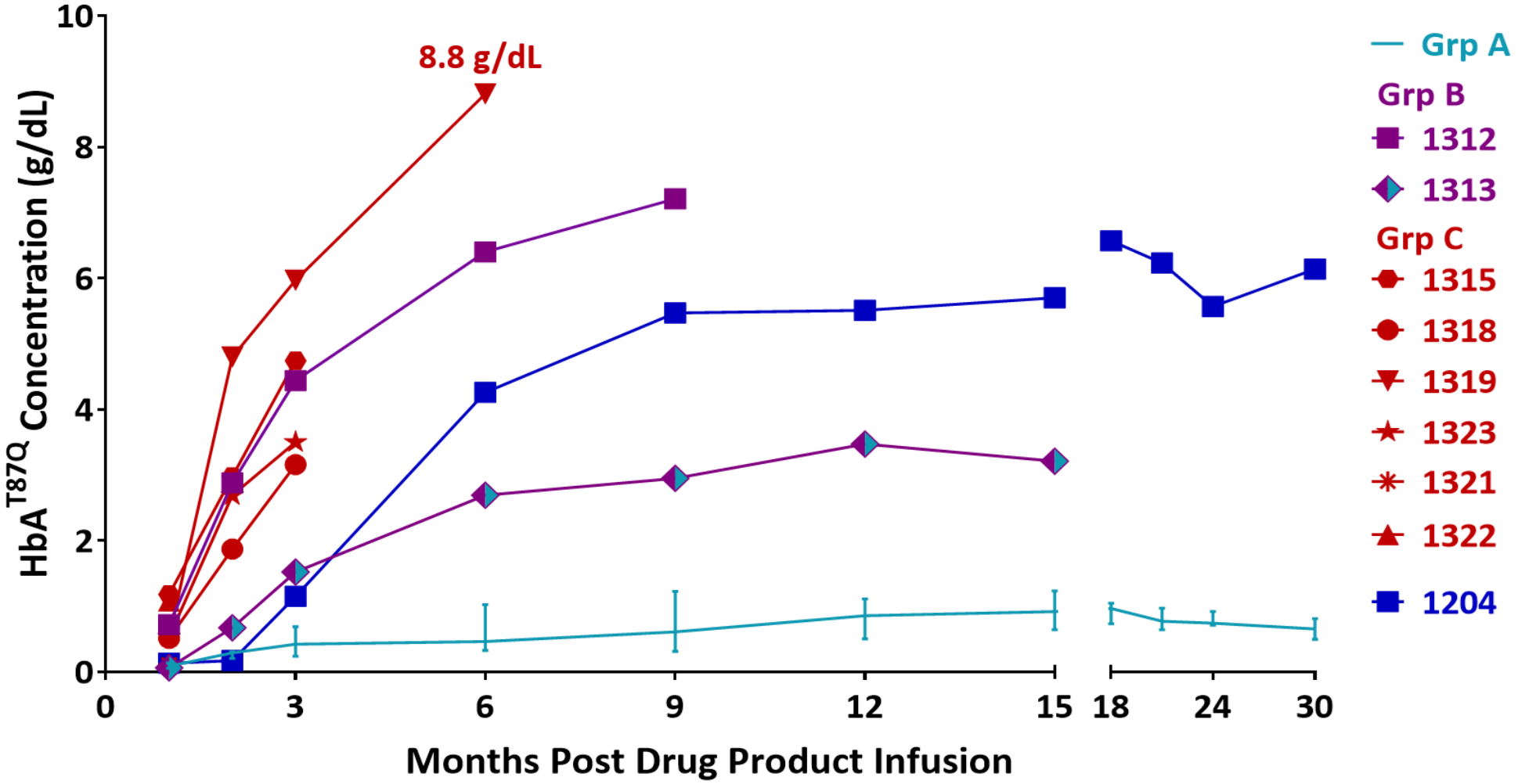
Peripheral Blood VCN is Higher in Patients in Group B and C



For Group A patients, medians (min, max) depicted; Group A patients with month 30 study visit (N=3)

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

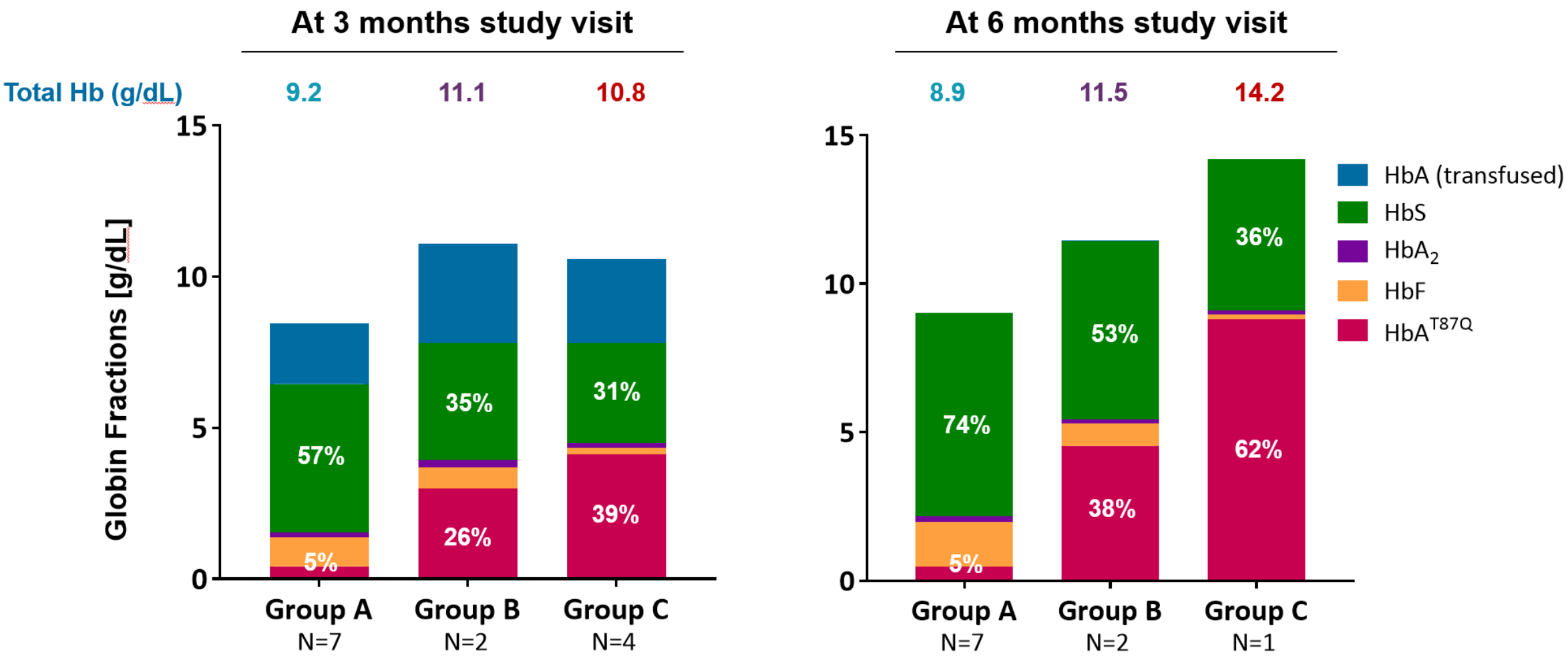
Patients in Group B and C Demonstrate Higher HbA^{T87Q} Production



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

All Group C Patients Above 30% Anti-Sickling Hemoglobin by 3 Months



- 5 incremental patients since data presented at ASH; no clinically significant new safety events

Median for DP-infused patients depicted, except for Group C at 6 months given N=1

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

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Closing

Nick Leschly, chief bluebird

bluebirdbio

Leaders in Gene & Cell Therapy

Our Integrated Platforms

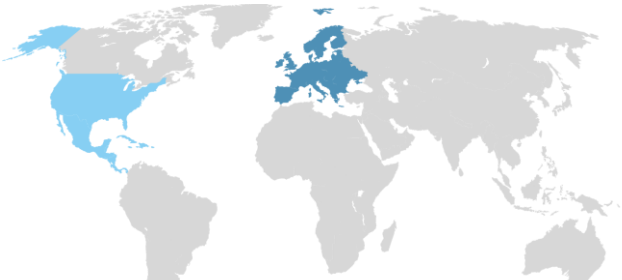
Gene Therapy | Cell Therapy | Gene Editing

Our Clinical Programs

Lenti-D™
LentiGlobin®

bb2121
bb21217

500+ bluebirds



Cambridge | Seattle | Durham | Zug

Regulatory Designations

RMAT *Regenerative Medicine Advanced Therapy*

ODD *Orphan Drug Designation*

BTD *Breakthrough Therapy Designation*

PRIME *PRIority MEdicines*

3 Regulatory filings planned by end of 2019

Strategic Partnerships

Boston Children's Hospital — Until every child is well
medigene
TC BIOPHARM
Celgene

Manufacturing

apceth BIOPHARMA
novasep passion & smart processes
brammer bio
Lonza
MilliporeSigma

Toolbox

Lentiviral Gene Delivery
- Reproducible
- Scalable

Genome Editing Platform
- megaTALs
- homing endonucleases

9 Active Treatment Studies

Starbeam STUDY

CRB-401

KarMMa™*

CRB-402

HGB-205

HGB-206

BCL11a**

NORTHSTAR-2 STUDY

NORTHSTAR-3 STUDY

*Led by Celgene, **Led by BCH

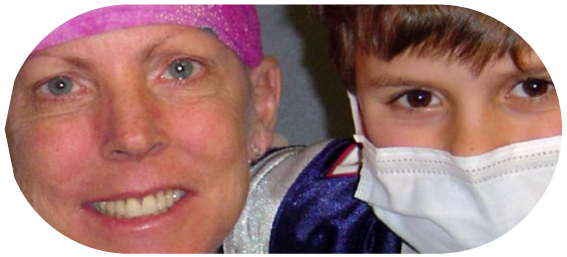
Stay Tuned…

TDT

- ✓ Northstar-2 (HGB-207) Updated Data
- ✓ Northstar (HGB-204) Updated Data
- • MAA Filing in non-β^0/β^0 Genotypes
- • Northstar-3 (HGB-212) Early Data
- • Northstar-2 Updated Data

SCD

- ✓ HGB-206 Data
- • Registration Strategy Update



MM

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

CALD

- • Starbeam (ALD-102) Updated Data

*Conducted by Celgene


Q&A
bluebirdbio