bluebirdbio®

Making Hope A Reality – bluebird style

September 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.



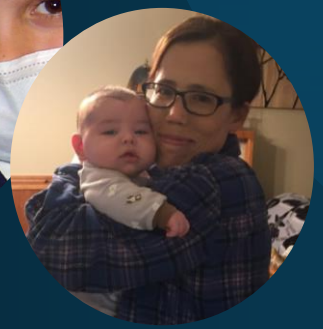
trueblue

Making Hope
A Reality

bluemojo







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

Leading the Way in Gene & Cell Therapy

Our Integrated Platforms

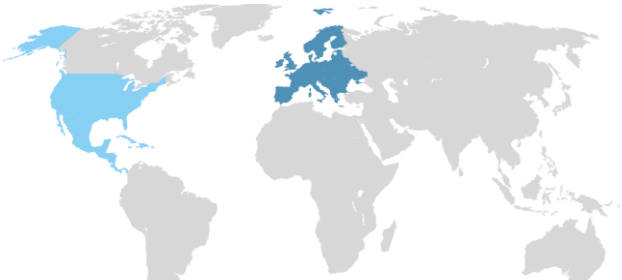
Gene Therapy · Cell Therapy · Gene Editing

Our Clinical Programs

Lenti-D™
LentiGlobin®

bb2121
bb21217

650+ Global bluebirds



Cambridge | Seattle | Durham | Zug

Regulatory Designations

RMAT *Regenerative Medicine Advanced Therapy*

ODD *Orphan Drug Designation*

BTD *Breakthrough Therapy Designation*

PRIME *PRIority MEdicines*

3 Potential regulatory approvals by end of 2020

Strategic Partnerships

REGENERON · gritstone ONCOLOGY · Boston Children's Hospital · medigene · TC BIOPHARM · Celgene

Manufacturing

apceth BIOPHARMA · novasep · brammer bio · Lonza · MilliporeSigma

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

Toolbox

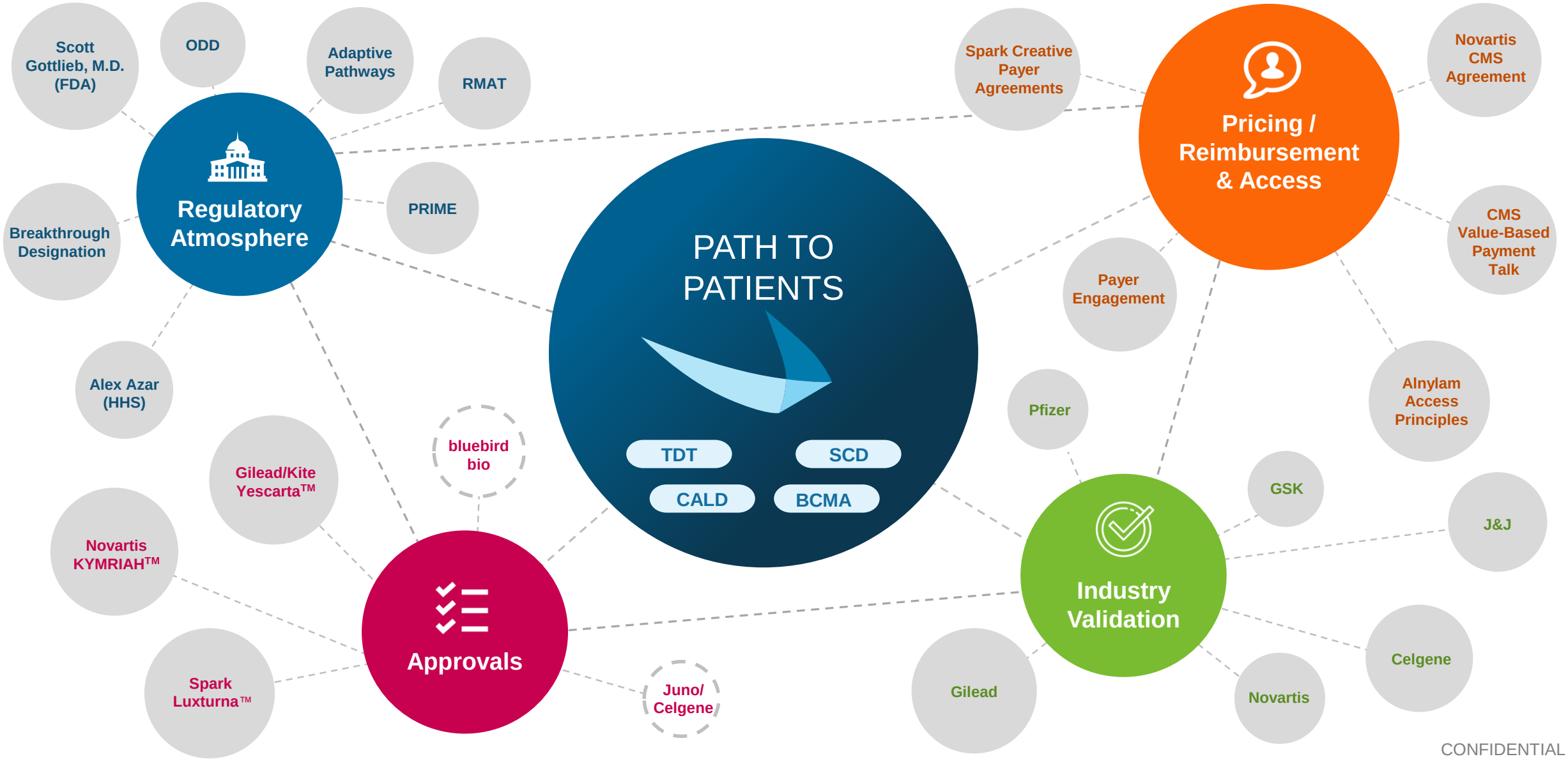
Lentiviral Gene Delivery

- Reproducible
- Scalable

Genome Editing Platform

- megaTALs
- homing endonucleases

Healthy Ecosystem for Transformative Gene Therapy



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

HOPE

REALITY 2022

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

2017

- BCMA: Breakthrough & PRIME Designation
- SCD: RMAT Designation
- *NEJM:* CALD & SCD
- Acquired Manufacturing Facility

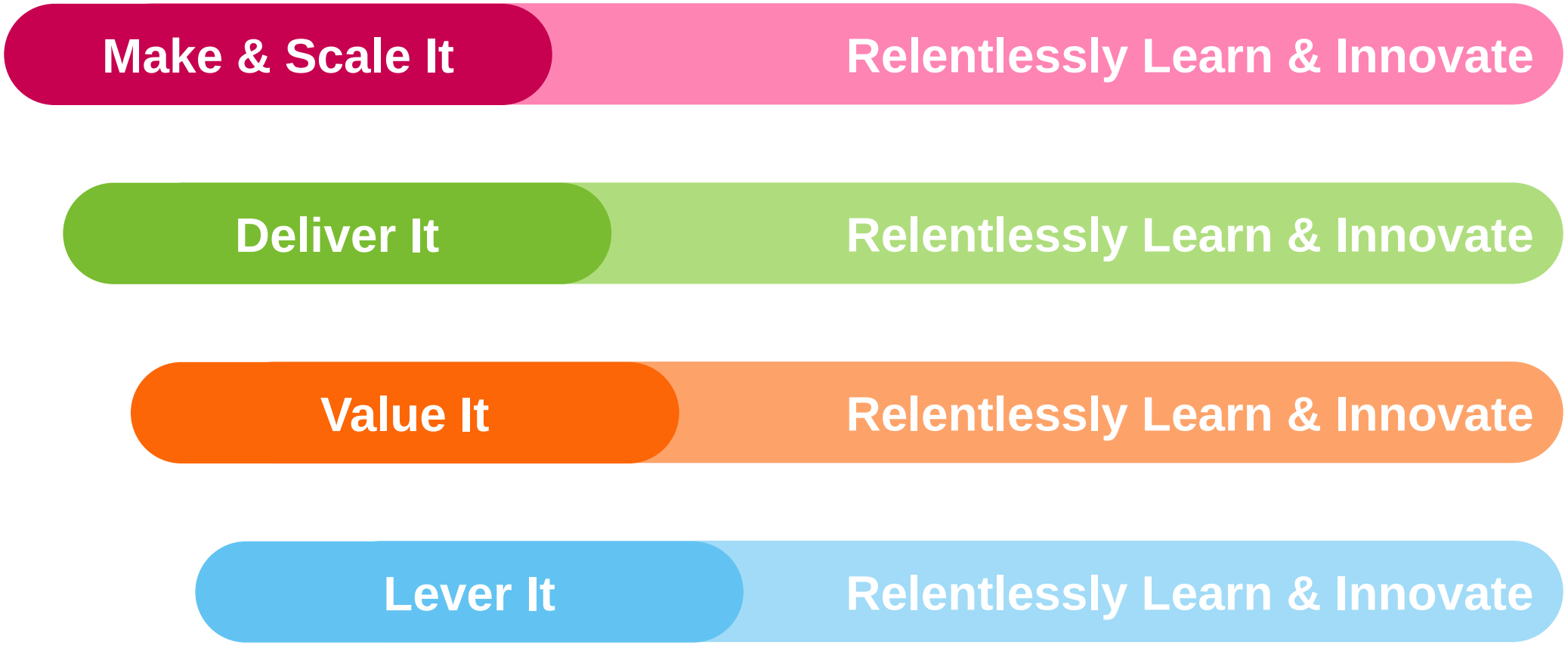
CALD Starbeam (Oct. 2013)

TDT Northstar (March 2014)

SCD HGB-205 (Oct. 2014)

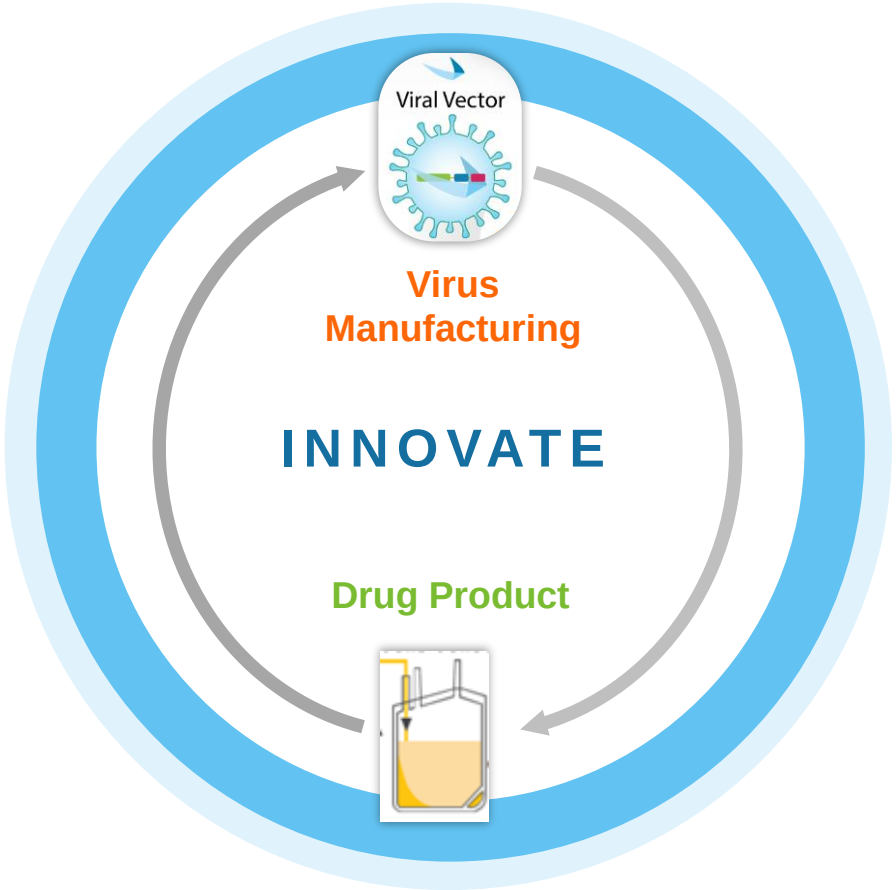
bb2121 for multiple myeloma (Feb. 2016)

Driving the Product Platform to Reality for Patients



Make & Scale It: Focused on Transitioning from Development to Commercial

DEVELOPMENT

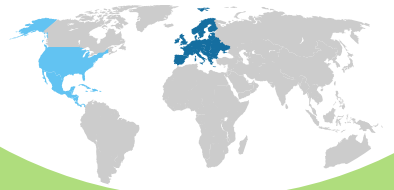


SCALE & DEPLOY

COMMERCIAL

Cambridge | Seattle | NC | EU

apceth BIOPHARMA · novasep passion & smart processes · Lonza · brammer bio · MilliporeSigma

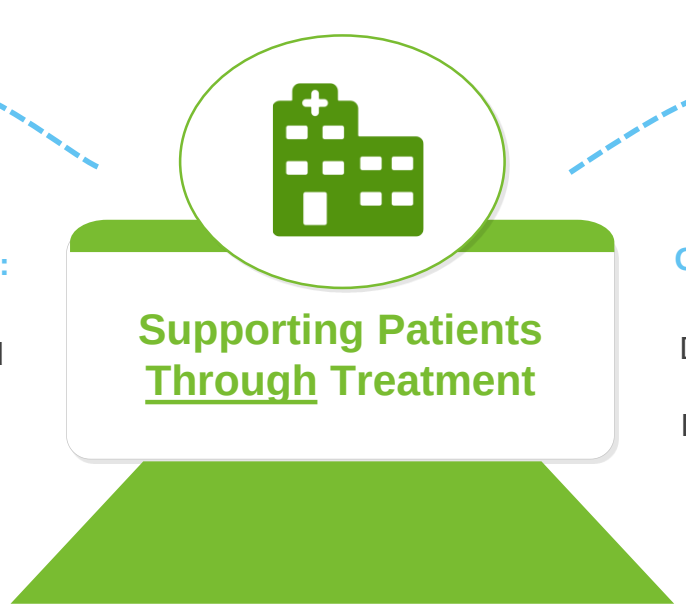


Deliver It: The Best Possible Provider, Payer and Patient Experience

Enabling Patients to Get To Treatment

- Educating Patients and Families on Gene Therapy
- Multi Channel Stakeholder Engagement & Data Dissemination
- Referral Network Development

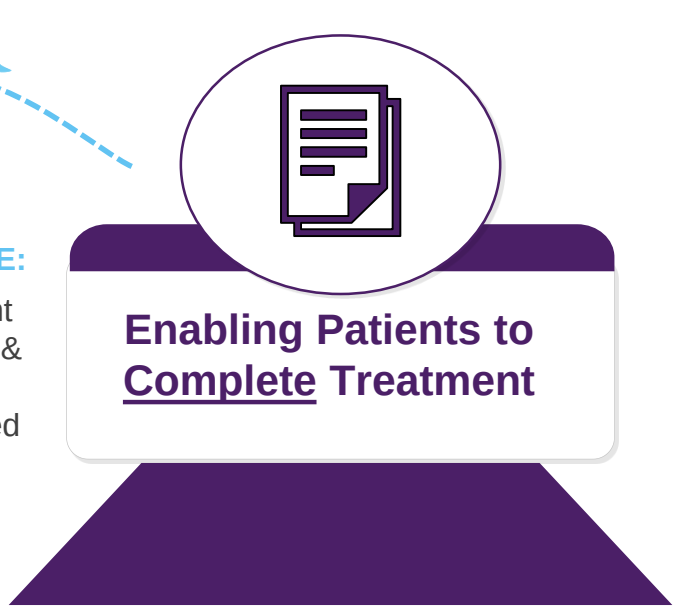
KEY OUTCOME: Treatment Prescribed



Supporting Patients Through Treatment

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

KEY OUTCOME: Treatment Delivered & Patient Discharged



Enabling Patients to Complete Treatment

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

Patient Case Management, Navigation, & Services

Value It: Time to Get It Right

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

Partnerships & Acquisitions

TC BIOPHARM

medigene innovative immunotherapies

Boston Children's Hospital Until every child is well

Celgene

PREGENEN

New Products & Pipeline

- bb21217 *Phase 1*
- shmiR *Phase 1*
- CAR Ts and TCRs *Preclinical*
- Gamma Delta T cells *Preclinical*
- MegaTALs *Preclinical*

Build the CORE… and Build Both RIGHT & LEFT

Pipeline Build

In-house capabilities and expertise

Business Development

Academic Partnerships

Infrastructure Build

bluebird RTP: LVV manufacturing

CMO partnerships

Company growth: 650+ birds and funded for success

Commercial and Launch Build

EU presence – Medical, Market Access, Commercial

COE network

Payer engagement

Our Quest to Constantly Innovate Continues

Product Candidates	Program Area	Preclinical	Phase 1/2	Phase 2/3	Rights/Partner
	Severe Genetic Diseases				
Lenti-D™ Drug Product	Cerebral ALD				Worldwide
LentiGlobin® Drug Product	Transfusion-Dependent ß-Thalassemia			(Phase 3)	Worldwide
	Severe Sickle Cell Disease				Worldwide
BCL11a shRNA(miR)*	Severe Sickle Cell Disease				Worldwide
	Cancer				
bb2121	Multiple Myeloma				Celgene
bb21217	Multiple Myeloma				Celgene
Undisclosed Targets	Various Indications				Worldwide
	Early Research				
Early Pipeline	Undisclosed + Gene Editing				Worldwide

*Development is led by Boston Children's Hospital

COLLABORATORS

Boston Children's Hospital
Until every child is well™

REGENERON

gritstone ONCOLOGY

Celgene

TC BIOPHARM

medigene innovative immunotherapies

1st Half 2018 Flashback - Path to Patients Full Steam Ahead

TDT

- @EHA: 7/8 patients in 207 reaching normal/near normal total hemoglobin by 6 months
- **MAA filing on track for 2018 – with Accelerated Assessment**

CALD

- @SSIEM: 15/17 patients with 24 months follow up alive and free from MFDs; additional 12 patients treated with no MFDs to date*
- **Breakthrough Designation and PRIME**

SCD

- @EHA: Group C patients showing rapid and consistent anti-sickling HbA^{T87Q} expression
- Anticipated update on development plan by EOY

Multiple Myeloma

- @ASCO: 95% ORR at doses above 150; 50% CR Rate; Media PFS of 11.8 months
- **KarMMa dose range increased (Celgene)**

**These patients have not yet reached 24 months of follow up*

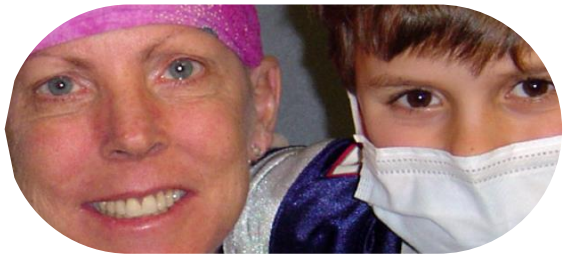
2018 Milestones

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
- • 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

*Conducted by Celgene

Transfusion Dependent β-Thalassemia

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“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

TDT Registration Strategy

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^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 Northstar-2 (HGB-207) trial

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

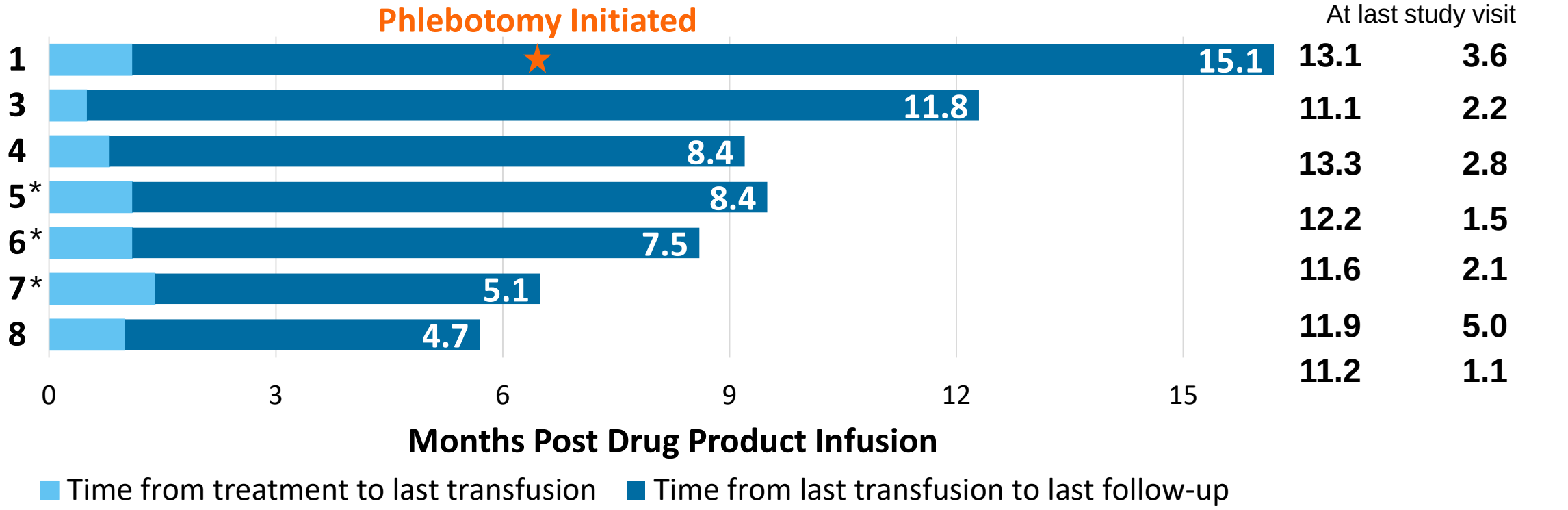
Submission for approval in **β^0/β^0** patients to be based on ongoing Northstar-3 (HGB-212) study

BREAKTHROUGH THERAPY DESIGNATION

ORPHAN DRUG DESIGNATION

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

First treated patient achieved transfusion independence and has begun phlebotomy



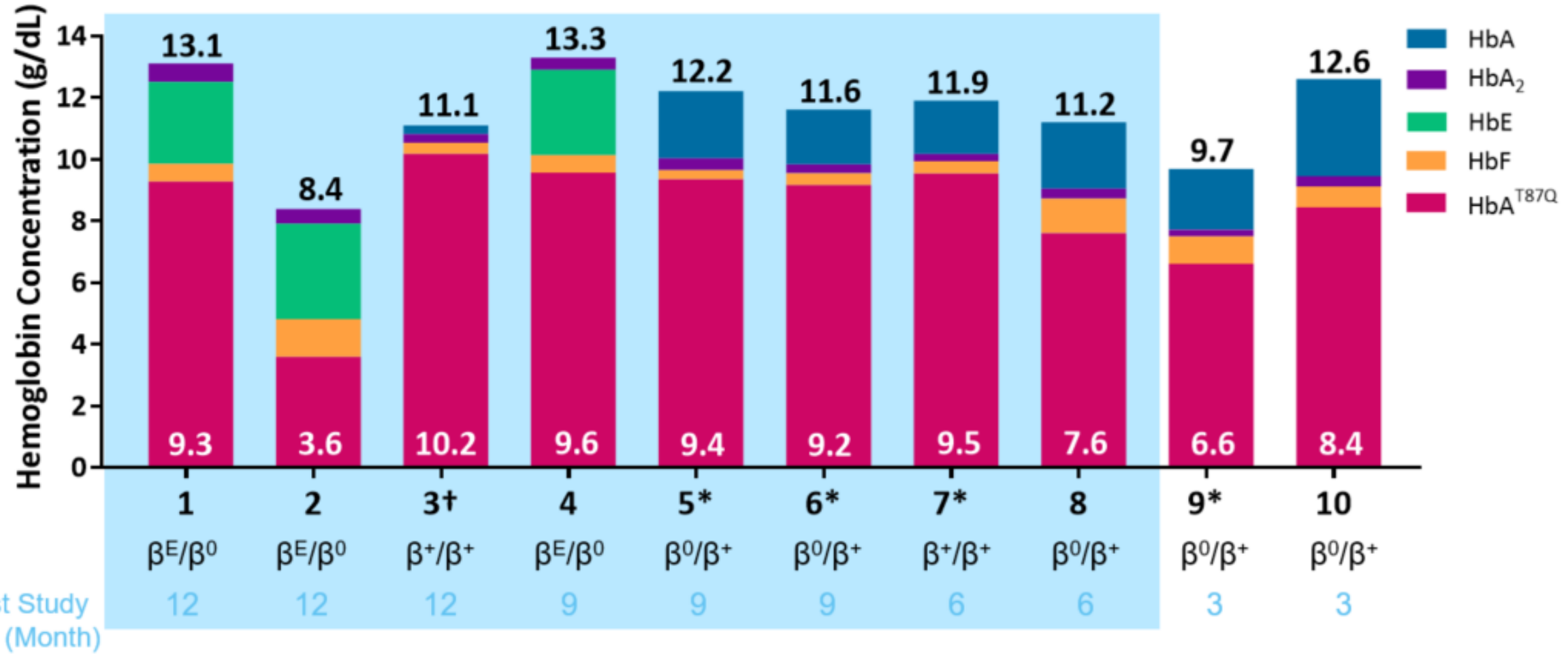
	Hb (g/dL)	Peripheral VCN
	At last study visit	
1	13.1	3.6
3	11.1	2.2
4	13.3	2.8
5*	12.2	1.5
6*	11.6	2.1
7*	11.9	5.0
8	11.2	1.1

- 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

Data as of 15 May 2018

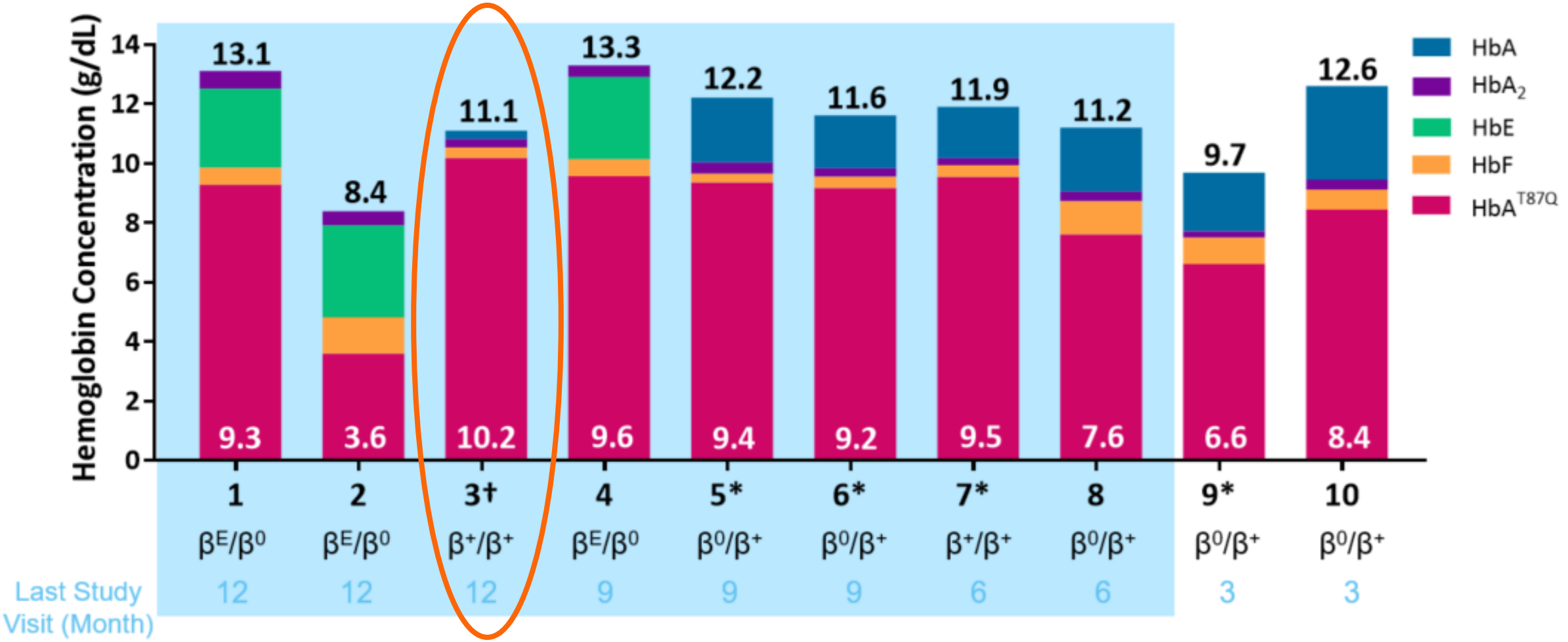
HGB-207: 7/8 Patients are Producing ≥ 7.6 g/dL of HbA^{T87Q} by 6 Months



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

Data as of 15 May 2018

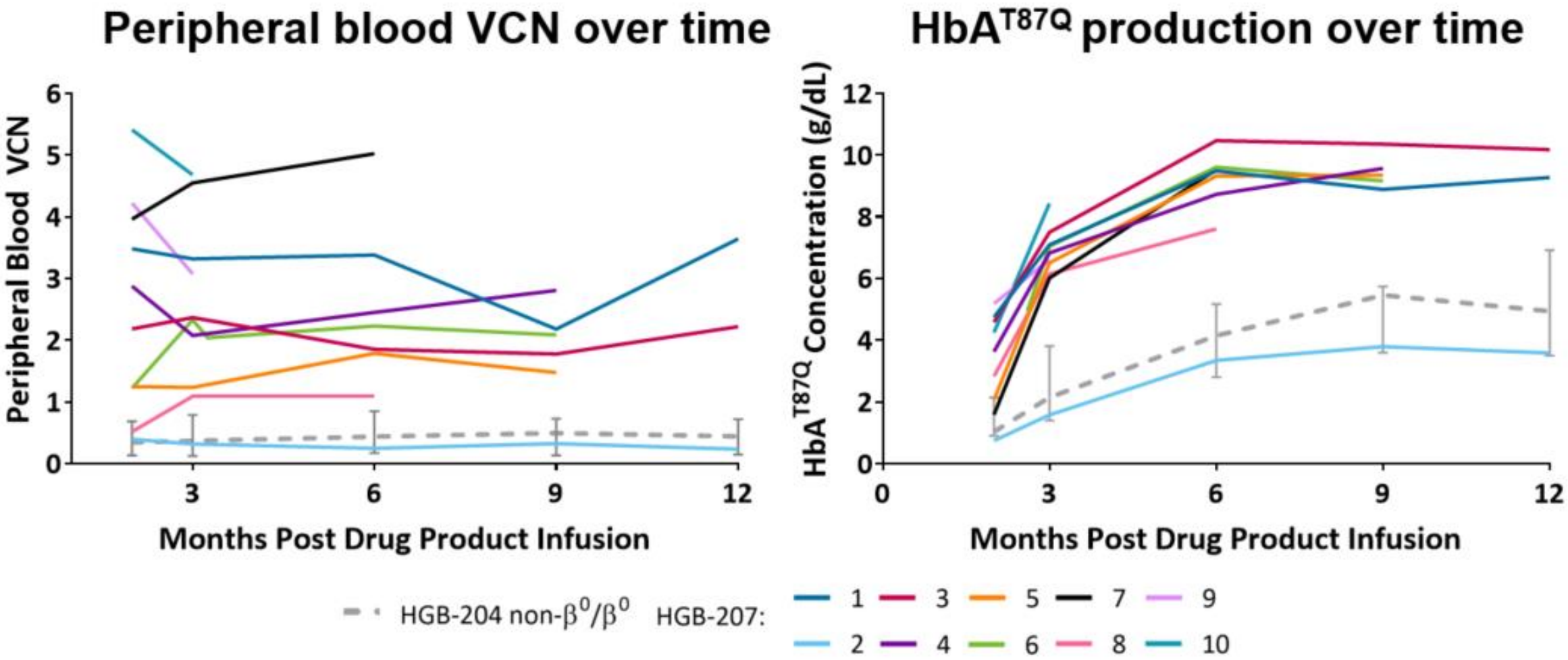
HGB-207: 7/8 Patients are Producing ≥ 7.6 g/dL of HbA^{T87Q} by 6 Months



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

Data as of 15 May 2018

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

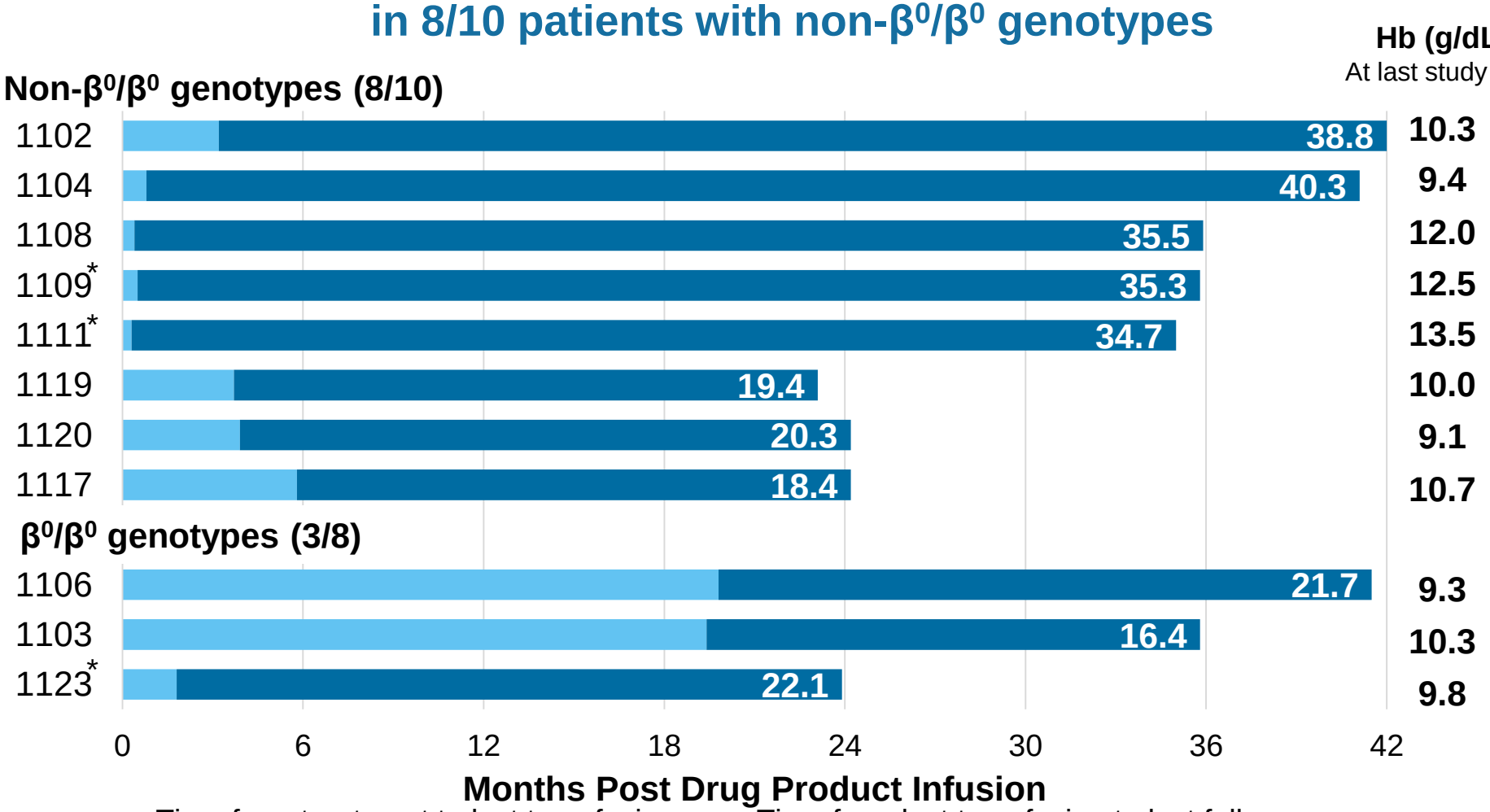


For 204 non-β^0/β^0 patients, medians (Q1, Q3) depicted

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



Hb (g/dL)
At last study visit

10.3
9.4
12.0
12.5
13.5
10.0
9.1
10.7
9.3
10.3
9.8

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

Data as of 7 March 2018

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

Severe Sickle Cell Disease

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"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

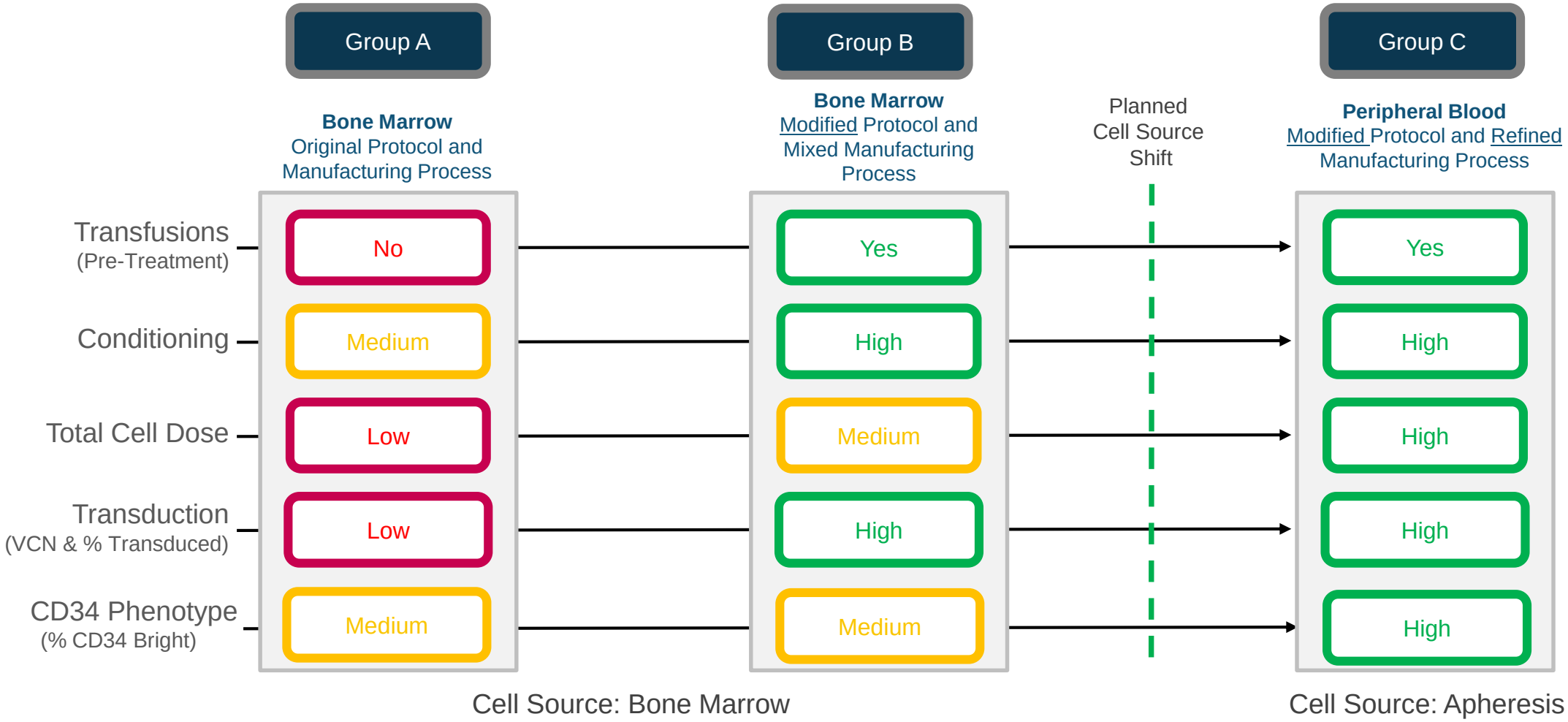
UNMET NEED

- 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

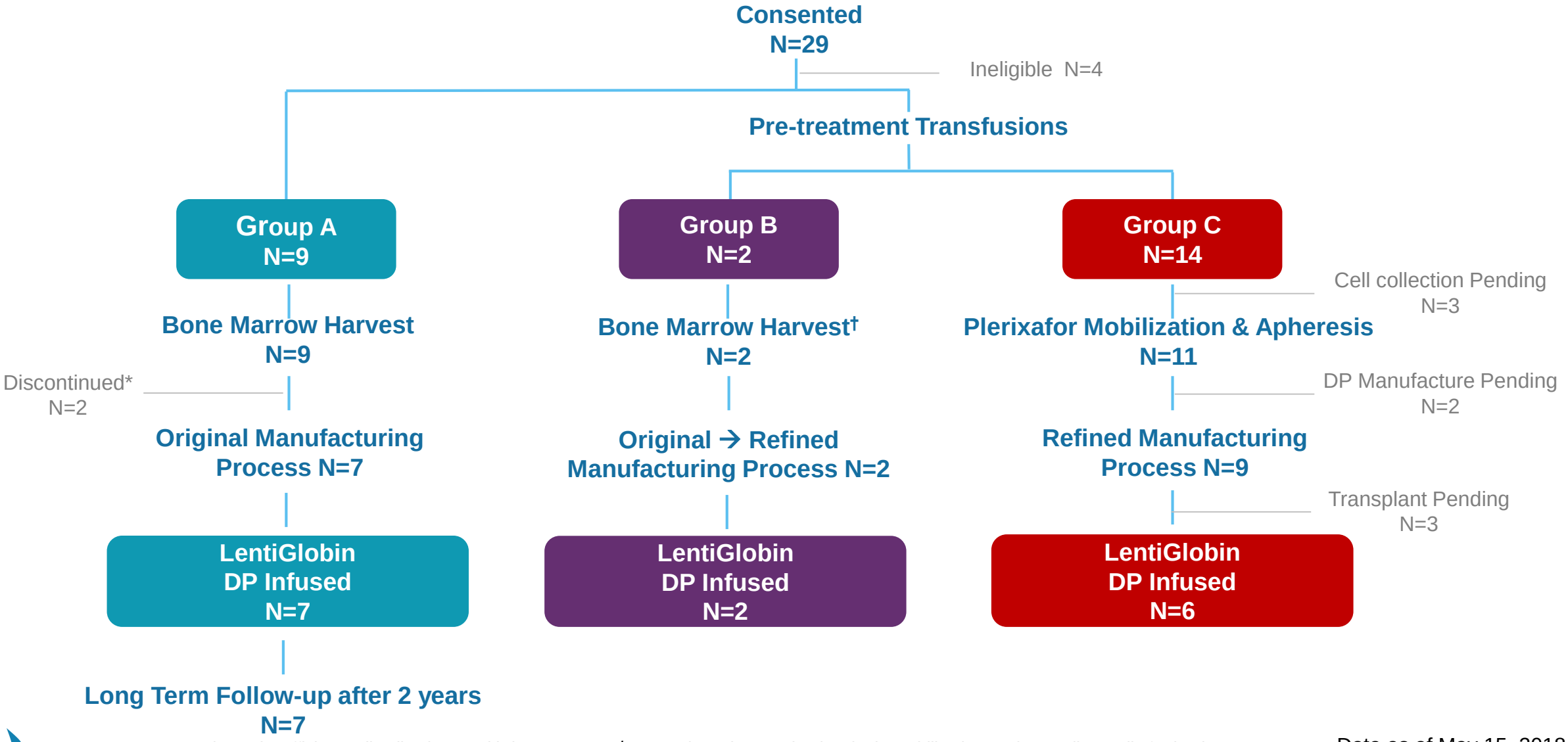
EPIDEMIOLOGY

- 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*

Data as of May 15, 2018

HGB-206: Patient Characteristics

N=22 Patients Who Started Cell Collection

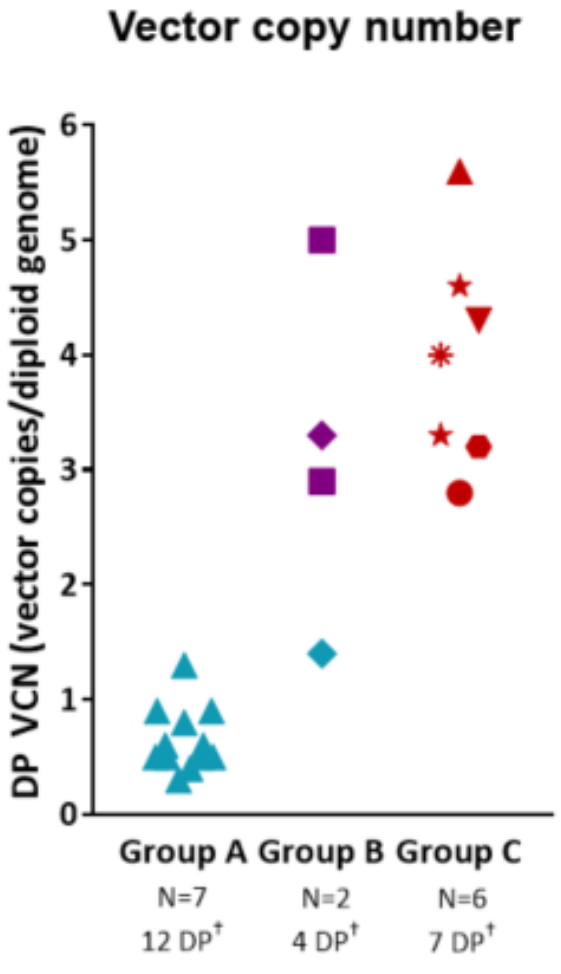
Parameter	Group A N=9	Group B N=2	Group C N=11
Age at consent median (min – max), years	**26** (18 – 43)	**24.5** (22 – 27)	**25** (18 – 35)
Gender	**2 Female**	**0 Female**	**5 Female**
Genotype β^S/β^S	**9**	**2**	**11**
Prior SCD History **No. of patients** **No. of events**, median (min – max)			
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**

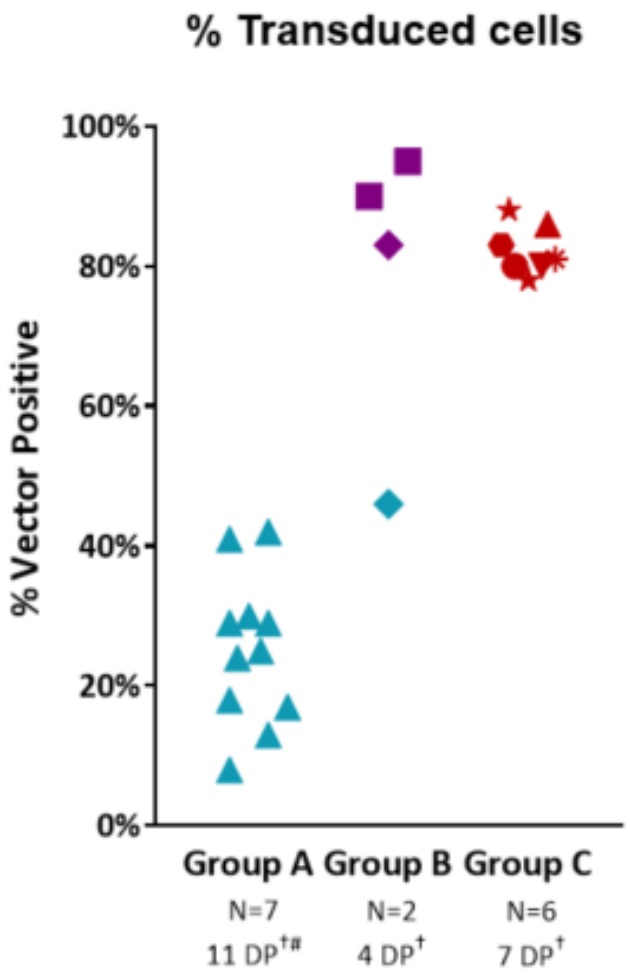
*Within 2 years prior to informed consent, or initiation of regular transfusions in case of VOCs; †Median Annualized values in patients with ≥2 events/year (for VOCs), or ≥1 events/year with at least one episode in the year before informed consent or initiation of regular transfusions (for ACS)

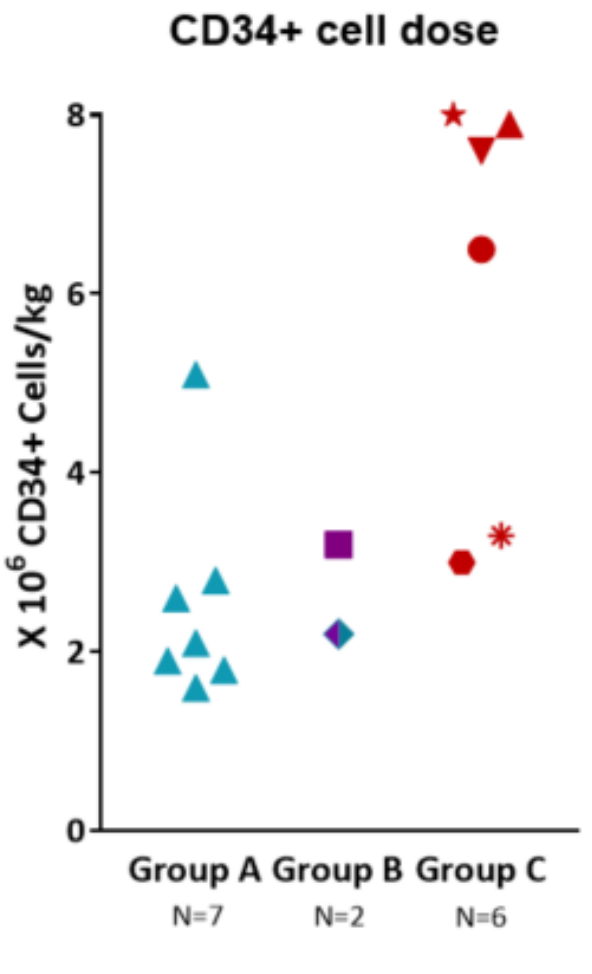
ACS, acute chest syndrome; VOC, vaso-occlusive crisis, TRJV, Tricuspid regurgitant jet velocity

Data as of May 15, 2018

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







LentiGlobin manufacturing process
(HSC source)

Original
(BM)

Rfined
(BM)

Refined
(PB)

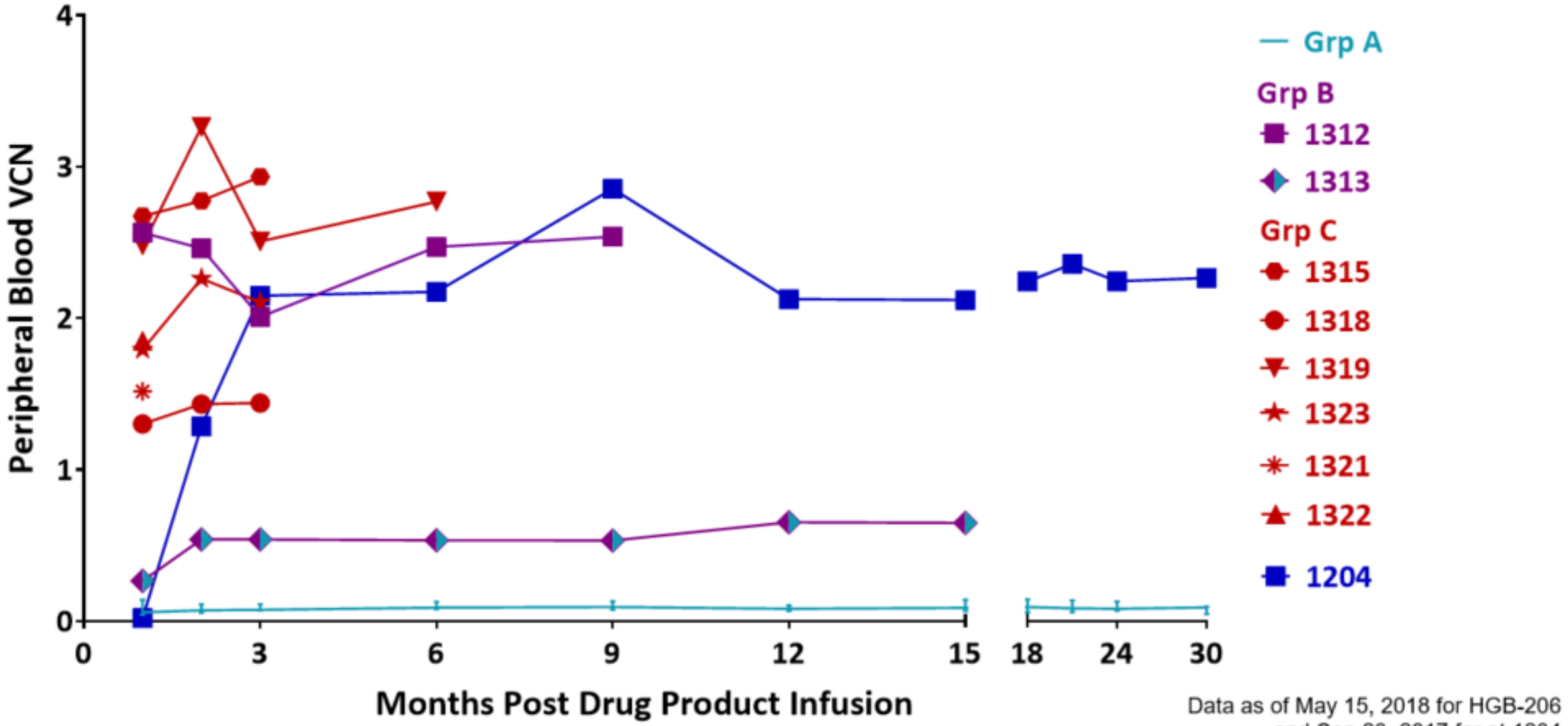
Median	0.6	3.1	4.0	25	87	81	2.1	2.7	7.1

† 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.

Data as of May 15, 2018

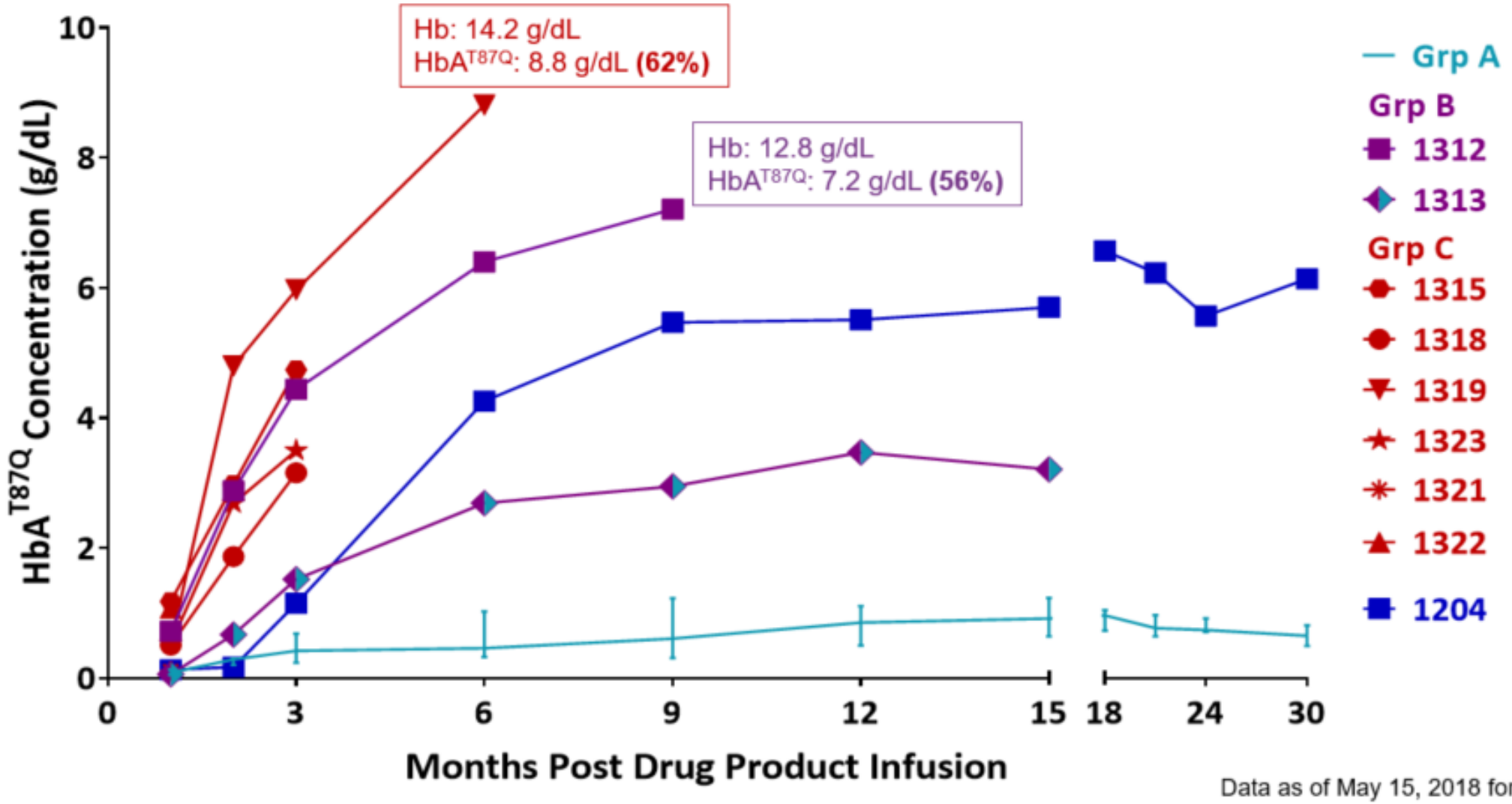
Peripheral Blood VCN is Higher in Patients in Group B and C



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

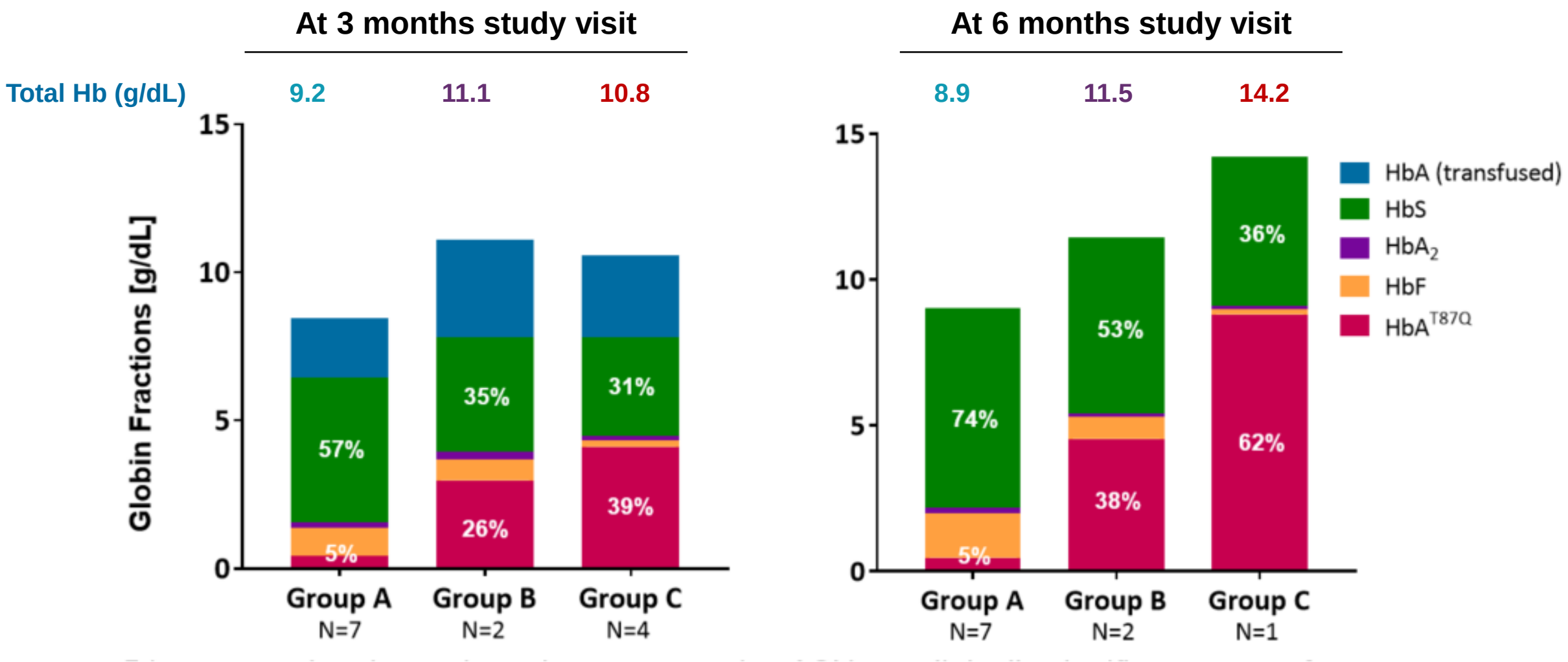
Patients in Group B and C Demonstrate Higher HbA^{T87Q} Production



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

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

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

Multiple Myeloma

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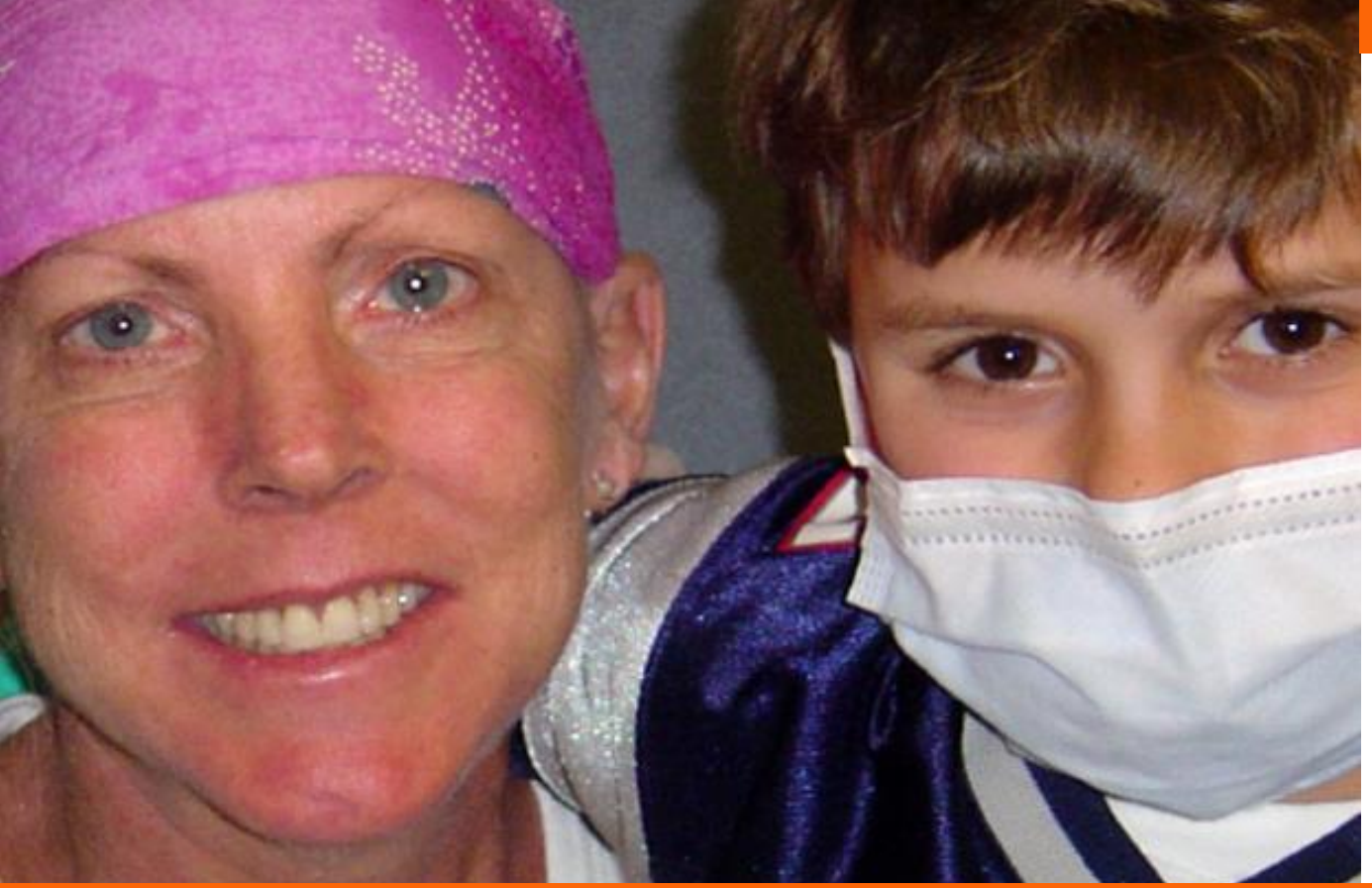


"When I was diagnosed and realized that there was an empty pipeline… I knew I needed to do something — not only for myself and my family, but for everyone else with this 'orphan cancer'. I desperately wanted my daughter to remember me and thought that if I lived for five years, maybe she would have memories 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

UNMET NEED

- Despite the availability of new therapies, remains incurable

EPIDEMIOLOGY

- U.S. incidence: ~30,000
- ~12,000 deaths/year in the U.S.

CRB-401 Data at ASCO 2018 - Baseline Demographics and Clinical Characteristics

Parameter	Escalation (N=21)	Expansion (N=22)
Median (min, max) follow-up, d	345 (46, 638)	87 (29, 184)
Median (min, max) age, y	58 (37, 74)	65 (44, 75)
Male, n (%)	13 (62)	16 (73)
Median (min, max) time since diagnosis, y	4 (1, 16)	6 (1, 36)
ECOG PS,[1] n (%)		
0	10 (48)	6 (27)
1	11 (52)	16 (72)
High-risk cytogenetics, n (%)		
del(17p), t(4;14), t(14;16)	8 (38)	9 (41)

ECOG, Eastern Cooperative Oncology Groups performance status; ISS, international staging system; NA, not available. [1]Data at screening presented.
Data cutoff: March 29, 2019

CRB-401 Data at ASCO 2018 - Heavily Pretreated Patient Population

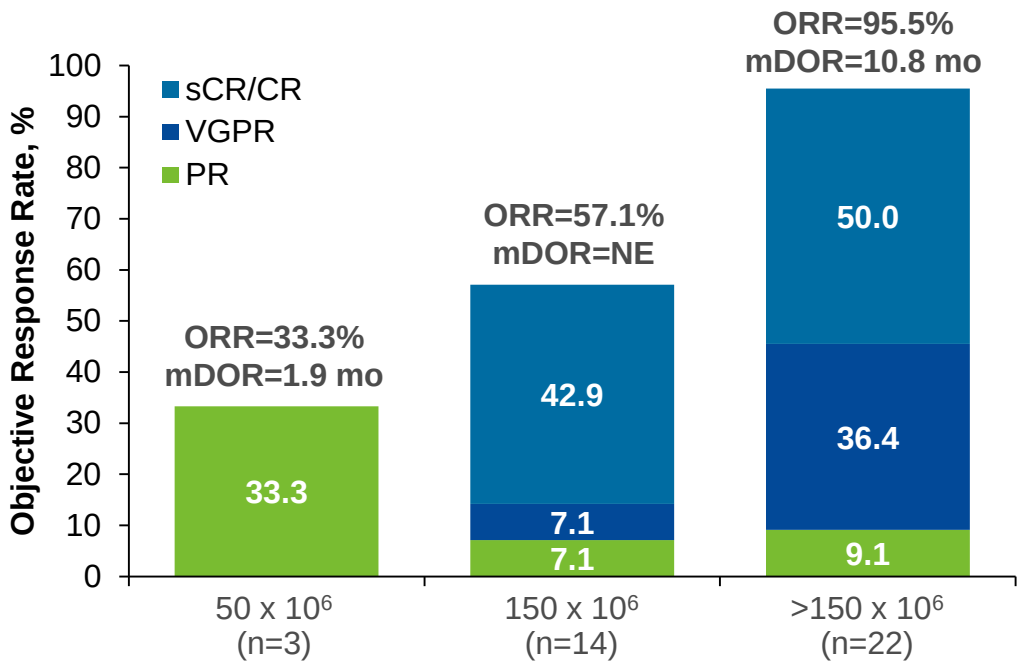
Parameter	Escalation (N=21)	Expansion (N=22)
Median (min, max) prior regimens	7 (3, 14)	8 (3, 23)
Prior autologous SCT, n (%)	21 (100)	19 (86)
0	0	3 (14)
1	15 (71)	14 (64)
>1	6 (29)	5 (23)

	Escalation (N=21)		Expansion (N=22)	
Parameter	**Exposed**	**Refractory**	**Exposed**	**Refractory**
Prior therapies, n (%)				
Bortezomib	21 (100)	14 (67)	22 (100)	16 (73)
Carfilzomib	19 (91)	12 (57)	21 (96)	14 (64)
Lenalidomide	21 (100)	19 (91)	22 (100)	18 (82)
Pomalidomide	19 (91)	15 (71)	22 (100)	21 (96)
Daratumumab	15 (71)	10 (48)	22 (100)	19 (86)
Cumulative exposure, n (%)				
Bort/Len	21 (100)	14 (67)	22 (100)	14 (64)
Bort/Len/Car/Pom/Dara	15 (71)	6 (29)	21 (96)	7 (32)

SCT, stem cell transplant. Data cut-off: March 29, 2018.

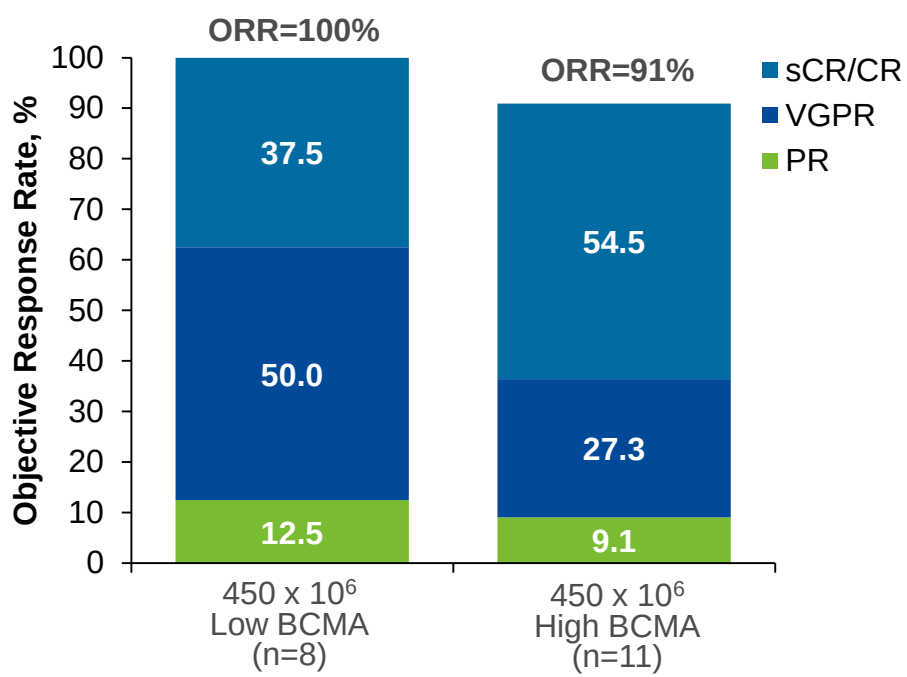
CRB-401 Data at ASCO 2018 - Tumor Response: Dose-related and Independent of Myeloma BCMA Expression Levels

Tumor Response By Dose[1]



Median follow-up (min, max), d	84 (59, 94)	87 (36, 638)	194 (46, 556)

Tumor Response By BCMA Expression[1]



Median follow-up (min, max), d	168 (121, 184)	311 (46, 556)

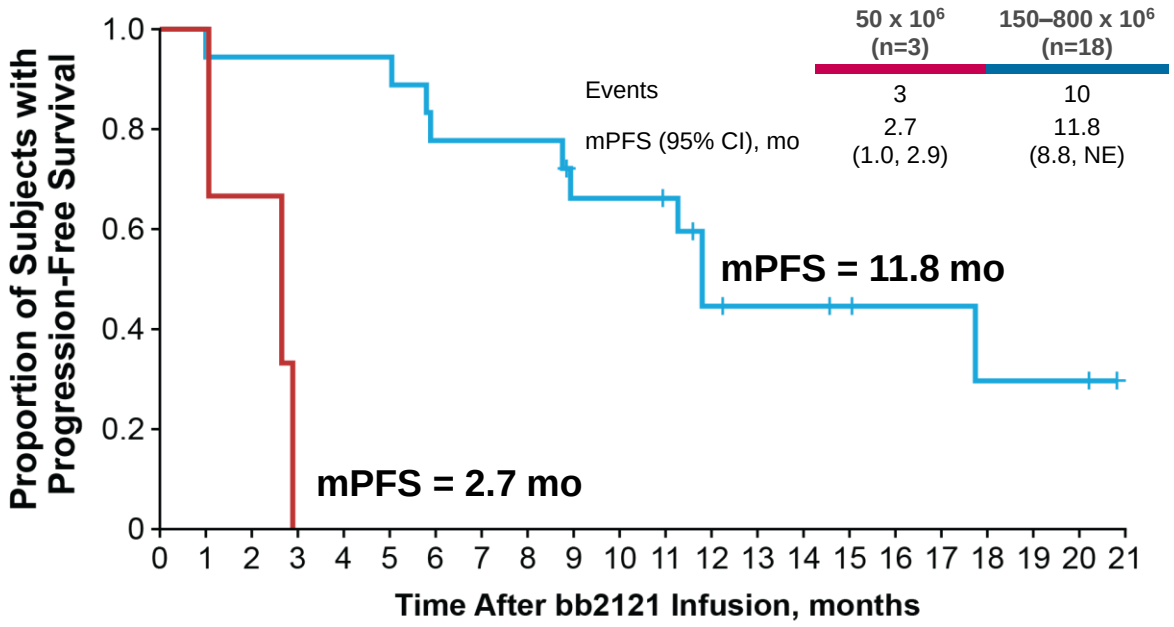
- 80.6% ORR across active dose cohorts (150-800 x 10^6)

CR, complete response; mDOR, median duration of response; ORR, objective response rate; PD, progressive disease; PR, partial response; sCR, stringent CR; VGPR, very good partial response. Data cut-off: March 29, 2018. [1]Patients with ≥2 months of response data or PD/death within <2 months. ORR is defined as attaining sCR, CR, VGPR, or PR, including confirmed and unconfirmed responses. Low BCMA is <50% bone marrow plasma cells expression of BCMA; high BCMA is defined as ≥50%.

CRB-401 Data at ASCO 2018 - Hitting the Mark for Progression Free Survival

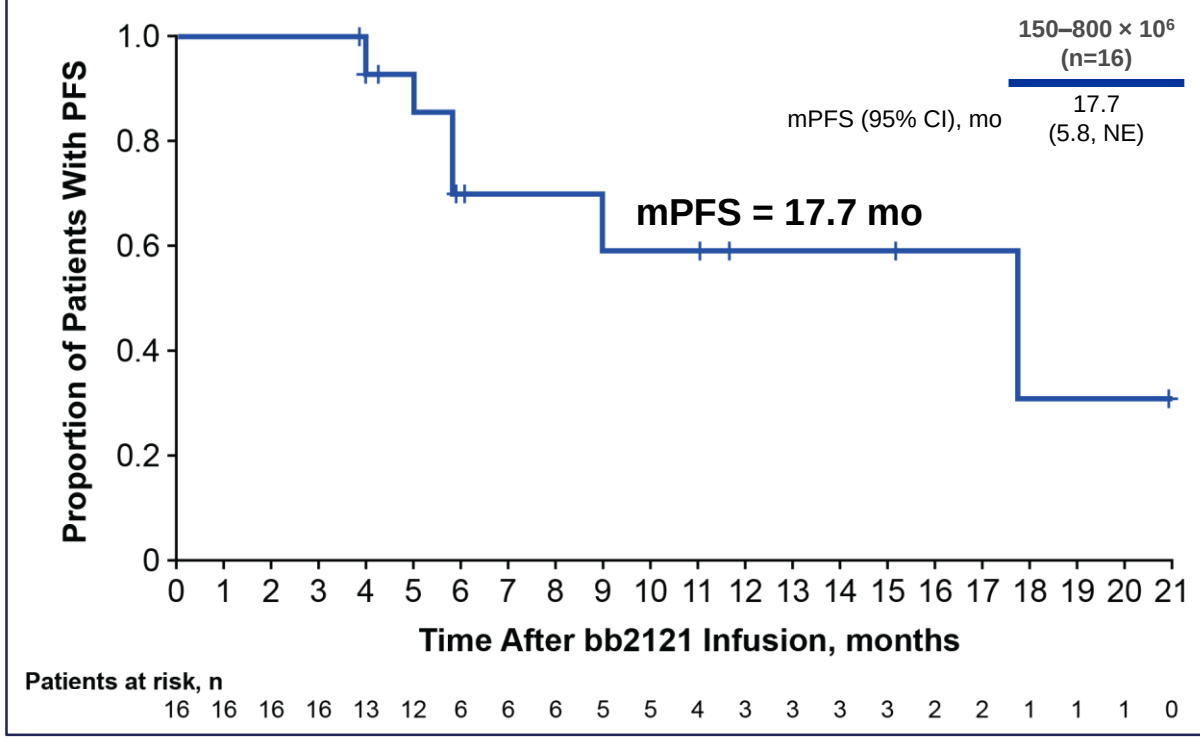
- mPFS of 11.8 months at active doses (≥150 x 10^6 CAR+ T cells) in 18 subjects in dose escalation
- mPFS of 17.7 months in 16 responding subjects from all study cohorts who are MRD-negative

PFS at Inactive (50 x 10^6) and Active (150–800 x 10^6) Dose Levels[1]



Data cut-off: March 29, 2018. Median and 95% CI from Kaplan-Meier estimate. NE, not estimable.
[1]PFS in dose escalation cohort.

PFS in MRD-Negative Responders
Escalation and Expansion Cohorts



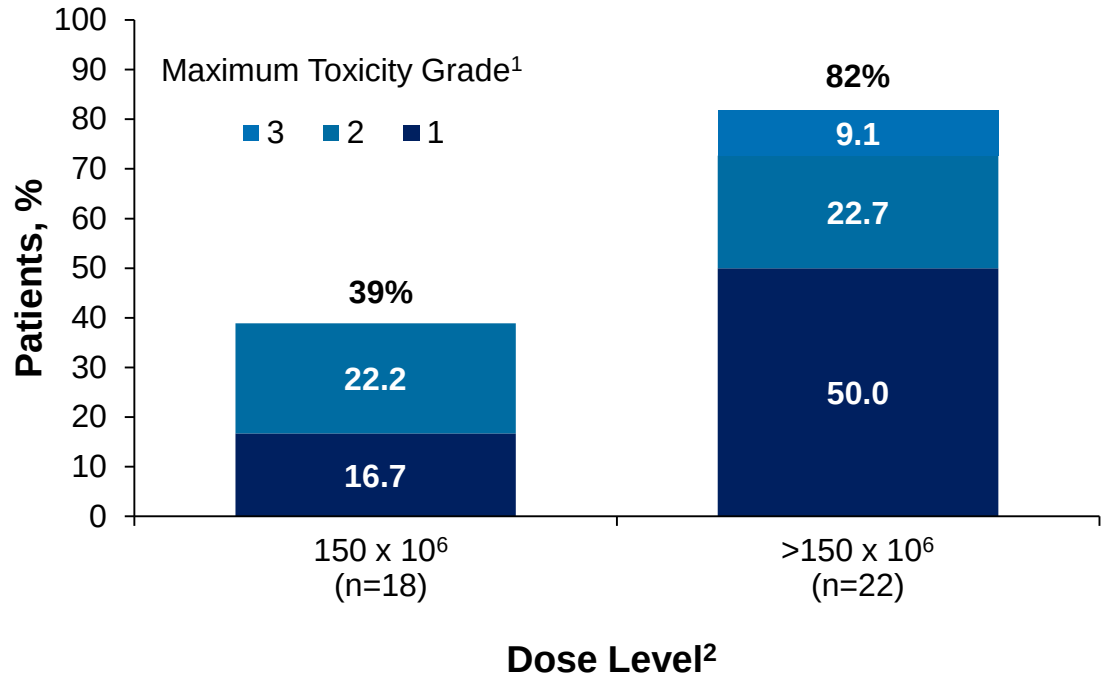
PFS progression-free survival; MRD, minimal residual disease.
Includes patients treated with <50 x 10^6 CAR T cells who were MRD-negative at >1 postbaseline time point

CRB-401 Data at ASCO 2018 - bb2121 Continues to be Generally Well-Tolerated; No New Safety Signals

CAR T Treatment-Emergent Adverse Events
All Infused Patients (N=43)

TEAE, n (%)	Overall	Grade ≥3
Cytokine release syndrome[1]	27 (63)	2 (5)
Neurotoxicity[2]	14 (33)	1 (2)
Neutropenia	35 (81)	34 (79)
Thrombocytopenia	26 (61)	22 (51)
Anemia	24 (56)	19 (44)
Infection[3]		
Overall	26 (61)	9 (21)
First Month	10 (23)	2 (5)

Cytokine Release Syndrome By Dose Level



- No grade 4 CRS events
- No fatal CRS or neurotoxicity events
- Patients with a CRS event, 63%

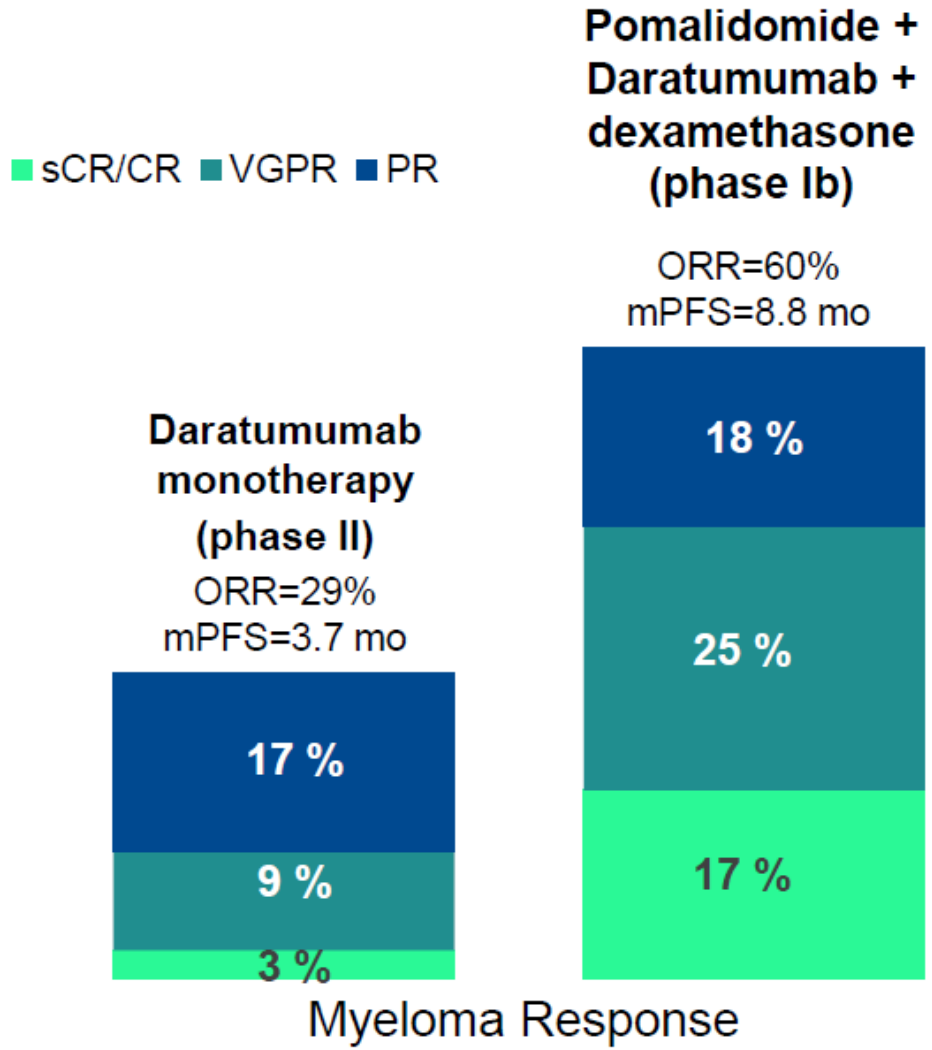
Data cut-off: March 29, 2018. NE, not estimable.[1]CRS uniformly graded per Lee et al., *Blood* 2014;124:188-195. [2]Events occurring in first 28 d and including dizziness, bradyphrenia, somnolence, confusional state, nystagnmus, insomnia, memory impairment, depressed level of consciousness, neurotoxicity, lethargy, tremor and hallucination. [3]Includes the SOC Infections and Infestations. Events observed in >10% include upper respiratory tract infection and pneumonia. [4]Includes patients treated with active doses (150–800 × 10^6 CAR+ T cells; N=40). Median and 95% CI from Kaplan-Meier estimate. [5]Time from first bb2121 infusion to the first grade ≤2 event after day 32.

Response to Current Standard of Care in Late Line RRMM

Current standard of care in RRMM after two or more lines of therapy:

	Dara	PDd	bb2121
Phase	II	I	I
N	106	103	43
Eligibility	≥ 3 prior lines Pom allowed Dara-naive	≥ 2 prior lines Pom-naïve Dara-naive	≥ 3 prior lines Pom allowed Dara allowed
Median prior lines	5	4	7

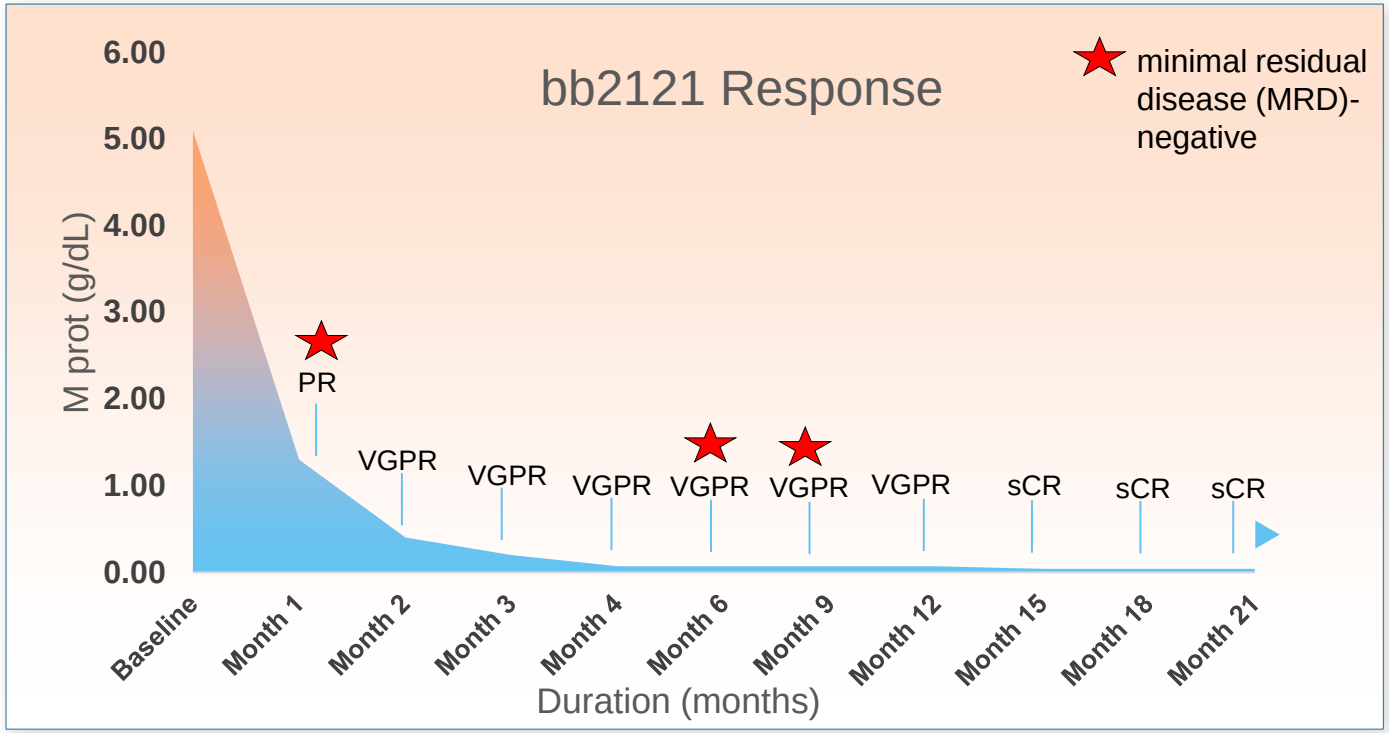
PDd=Pomalidomide + Daratumumab +dexamethasone.
Pom=Pomalidomide; Dara=Daratumumab



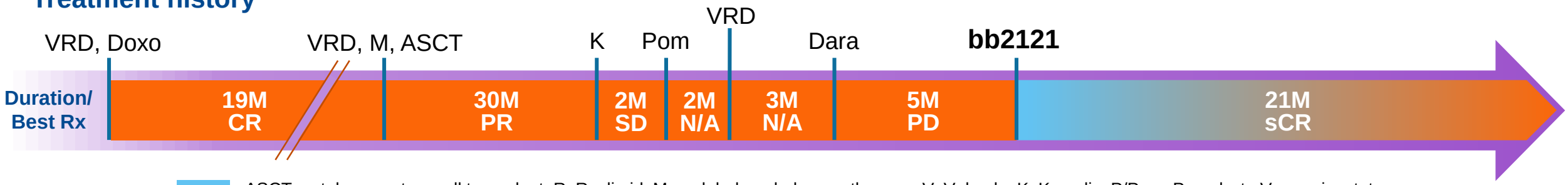
Chari, A. Blood 2017

bb2121 Patient Case: 21 Months in sCR

General Information	
Age & Gender	52 year old Male
Dose group	150x10^6
Tumor Burden	High
High Risk Cytogenetics (based on FISH)	No
Number of prior regimens	6
Initial diagnosis	May, 2010
BCMA% (prescreen, baseline)	60, 75



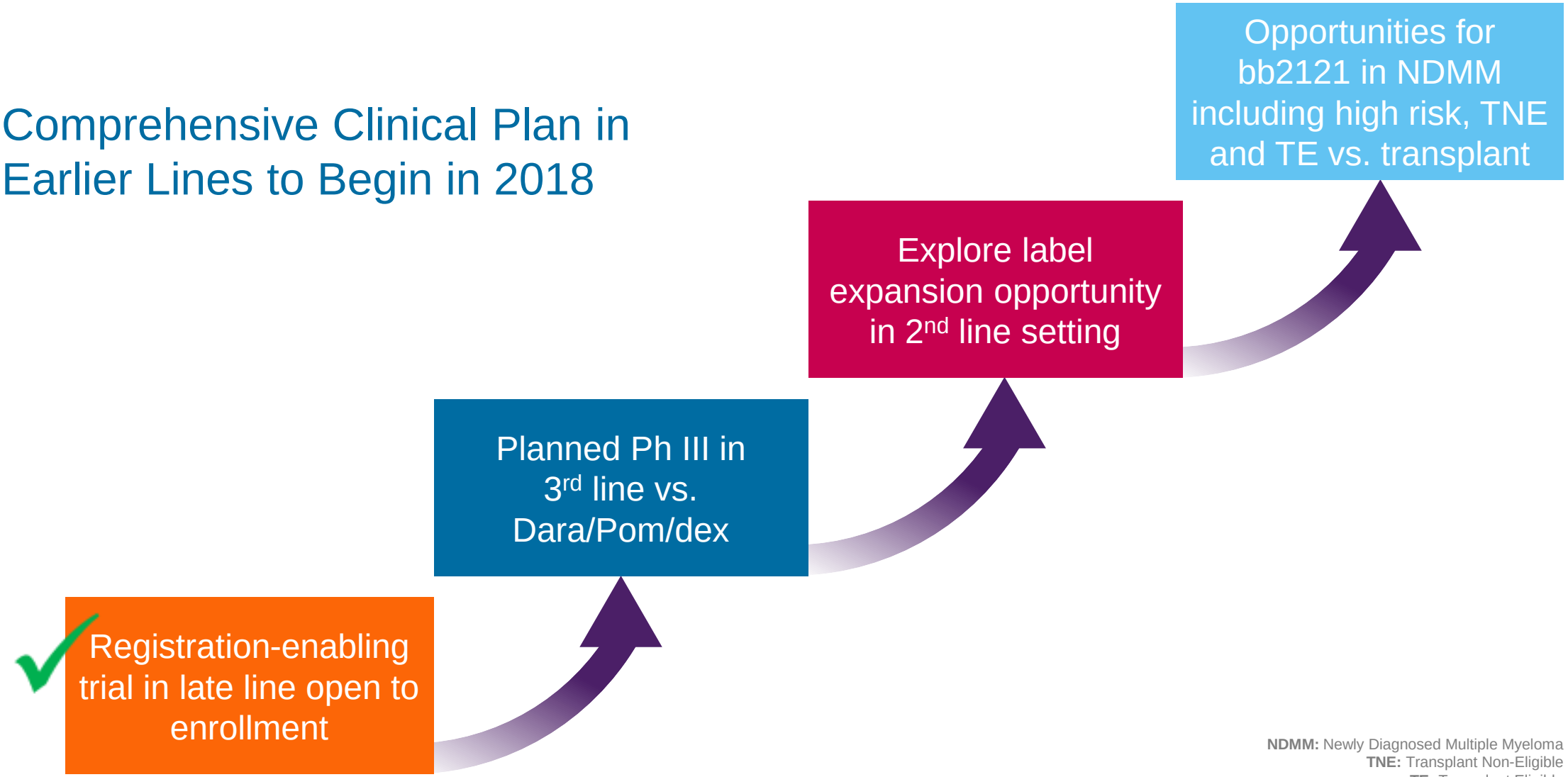
Treatment history



KEY ASCT: autologous stem cell transplant, R: Revlimid, M: melphalan, d: dexamethasone, V: Velcade, K: Kyprolis, P/Pom: Pomalyst, Vor: vorinostat, Dara: daratumumab, Doxo:Doxorubicin

Advancing bb2121 into Earlier Lines of Multiple Myeloma

Comprehensive Clinical Plan in Earlier Lines to Begin in 2018



NDMM: Newly Diagnosed Multiple Myeloma
TNE: Transplant Non-Eligible
TE: Transplant Eligible

Key Takeaways from CRB-401 Presented at ASCO

Efficacy?	• 95.5% ORR in doses above 150M cells. • 50% CR rate at doses above 150M cells.
Durability?	• 11.8 months median PFS in dose-escalation active doses. • 17.7 months median PFS in MRD(-) patients with response (escalation and expansion).
BCMA? MRD?	• Consistent responses across BCMA expression levels. • 16/16 responding, MRD-evaluable patients were MRD negative.
Safety?	• No new safety signals (G3/G4 CRS or Neurotox).
Path forward?	• KarMMa amendment raised high end of dose range to 450 based on observed dose-response and acceptable safety profile. Potential approval on track for 2020. Earlier line development plan advancing.

Cerebral Adrenoleukodystrophy

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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

Cerebral Adrenoleukodystrophy

- Severe, often fatal neurological disease in boys

UNMET NEED

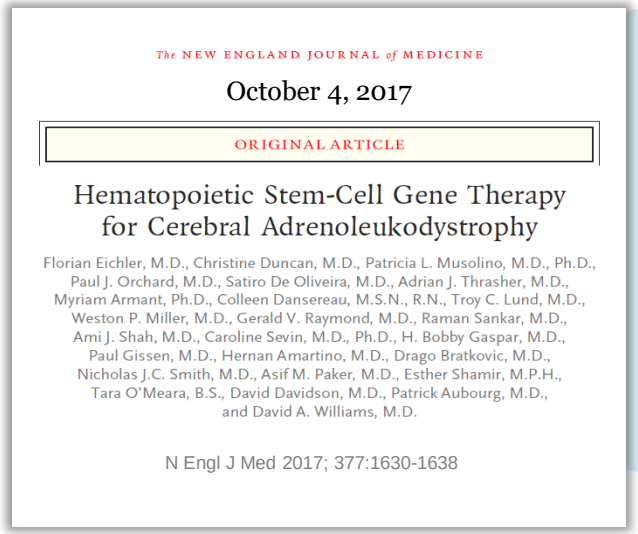
- Treatment limited to allo-HSCT
- Sometimes severe treatment-related risks and complications, especially when donor is not a matched sibling

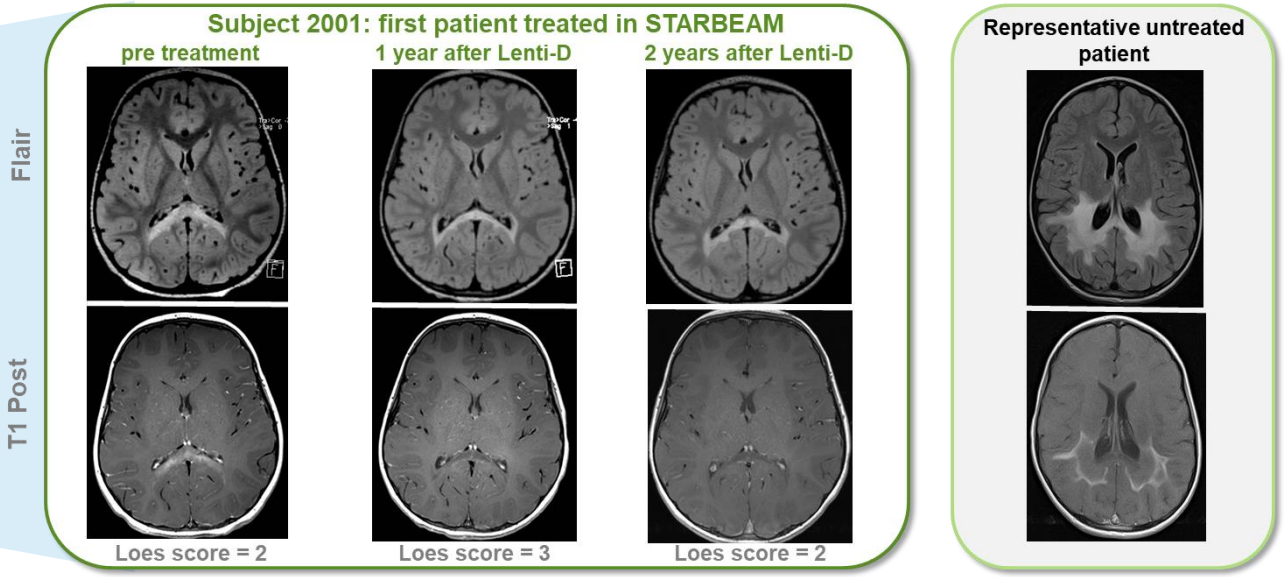
EPIDEMIOLOGY

- Global incidence of ALD: 1 in ~21,000 newborns
- Cerebral form develops in ~40% of affected boys

[1]Salzman, R., Kemp, S. (2017, December 06) Newborn Screening. Retrieved from http://adrenoleukodystrophy.info/clinical-diagnosis/newborn-screening

Lenti-D Treatment Halts CALD Disease Progression





15/17 patients (88%) alive and MFD-free at 24 months follow-up; all patients continue to be MFD-free as of April 25, 2018

- Exceeds pre-determined efficacy benchmark for the study MFD-free survival in 13/15 (76%)

12 additional patients treated in Starbeam study

- No MFDs reported as of April 25, 2018; median follow-up for this additional cohort of patients is 4.2 months (0.4 – 11.7 months)

Safety profile consistent with autologous transplantation

- No GvHD, no graft rejection

Two patients did not meet primary endpoint:

- Patient 2016: Withdrew
- Patient 2018: Rapid disease progression early in the study

Data as of April 25, 2018

Recent Collaborations

bluebirdbio®

Science-Driven and Highly Complementary Partnership

Science: Best-in-class technology platforms joining forces to crush cancer

Culture: Science- and patient-focused companies with a willingness to push boundaries of novel technologies

Structure: Aligned and streamlined operating model to enable flexible research and decision making

Investment: All-in mindset driving shared and enhanced funding for R&D efforts

BLUE remains BLUE: Clear value proposition through product rights, shared funding and capabilities

Engaging the Right Target with the Optimal Target Binder

VELOCISUITE®

REGENERON

VELOCIGENE®	*…target validation at unprecedented pace and precision*
VELOCIMOUSE®	*…rapid generation of genetically engineered mice*
VELOCIMMUNE®	*…fully human antibodies through immunization*
VELOCIMAB®	*…rapid identification & preclinical testing of target specific antibodies*
VelociT	*…fully human T cell receptors from an engineered mouse*
VELOCIHUM	*…immunodeficient mouse platform - study of human cells & tumors*

Pick Great Targets

Fully Human CARs

Identify Human TCRs

Better Models

Partnership Highlights

Research

- Five-year research collaboration
- Refreshable list of **six** targets
- Access to Regeneron *VelociSuite*® Platform technologies
- Leveraging bluebird expertise in cell biology and vector technology
- Brings together two science driven organizations with synergistic technology and expertise

Development

- bluebird leads R&D managed by a Joint Steering Committee
- bluebird retains significant product rights; Regeneron receives milestone payments and royalties
- Regeneron can opt-in to multiple products to become 50/50 partners
- Joint late-stage development and commercialization allocated between bluebird and Regeneron or future partners on a regional basis

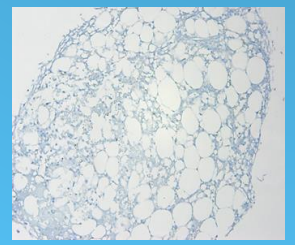
Funding

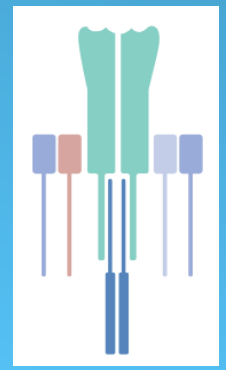
- Share costs equally through pre-IND research and into Phase 1/2 development
- For 50/50 collaboration products, development and commercialization costs (by region) are shared equally
- bluebird funds development and commercialization of its wholly-owned products
- $100 million equity investment by Regeneron in BLUE - 420,000 shares at $238.10 per share or a 59% premium*

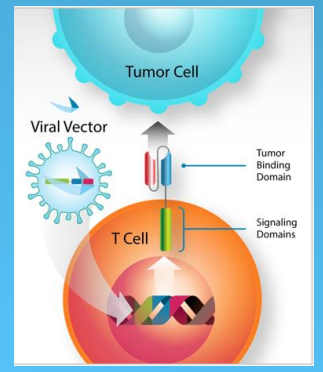
**Premium of approximately $37 million will be used to cover part of Regeneron's share of research costs; bluebird intends to use the balance of the proceeds to support its research activities in the collaboration.*

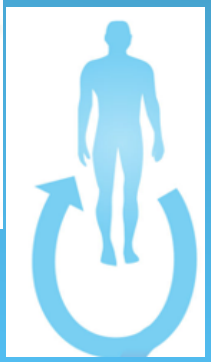
Gritstone Complements bluebird's Approach to Generating Novel Therapeutics for Oncology

Patient biopsy	Tumor targets	TCR	Cell therapy	Patient therapy
gritstone: Routine clinical biopsy	gritstone: Mass spec validation of expressed tumor targets in patients and sequencing of tumor transcriptome **Select patients with target** Validate 10 targets	Medigene, Regeneron, gritstone: Identify TCR sequences which bind to validated tumor targets	bluebird: Generate TCR cell therapy targeting validated tumor antigens using patient's white blood cells	bluebird: Genetically engineered patient cells infused back into patient









Early Pipeline

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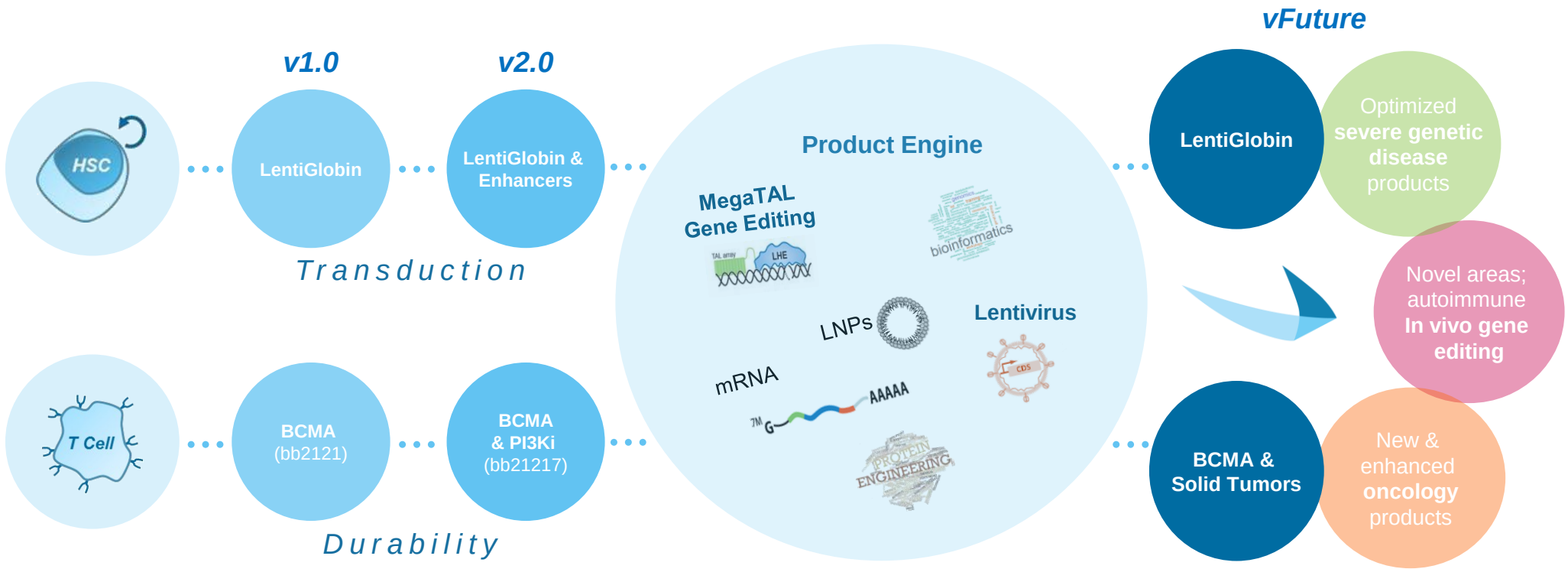
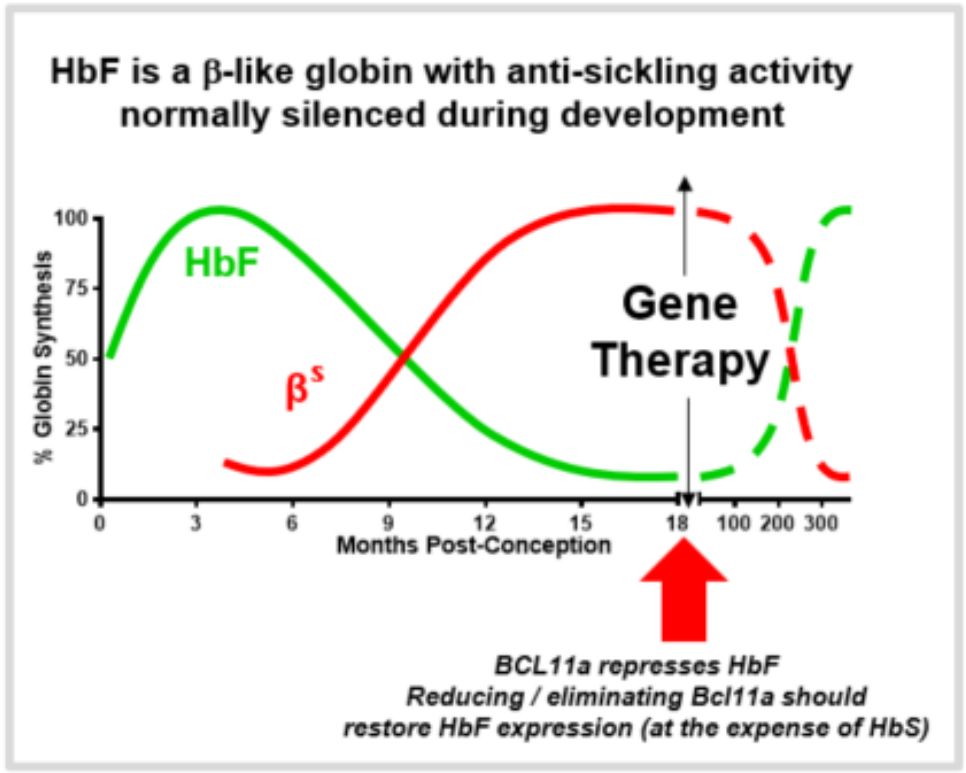
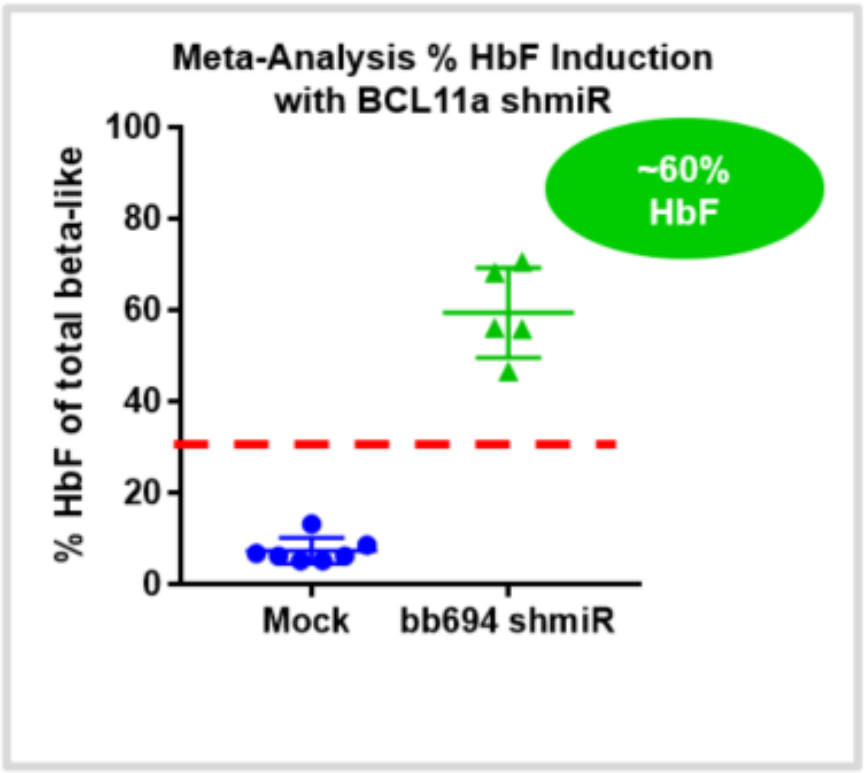
Good is Never Good Enough for Patients: BLUE Toolbox Strategy



Lentiviral Vector Approach to Suppression of BCL11a in SCD





- 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
- Clinical study underway

Go TRUE BLUE

We Must Make Hope a Reality