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ASH 2019

december 9, 2019

LET'S
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THE STORY

forward-looking statements

These slides and the accompanying oral presentation contain forward-looking statements and information. The use of words such as "may," "might," "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 initiate or complete, clinical studies, the timing or likelihood of regulatory filings and approvals or the requirements that may be imposed, and the timing and likelihood of entering into contracts with payors for value-based payments over time or reimbursement approvals, and our commercialization plans for approved products 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.

today's agenda

LET'S
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THE SYSTEM

welcome	Nick Leschly *chief bluebird*
LentiGlobin for TDT data	Dave Davidson, M.D. *chief medical officer*
LentiGlobin for SCD data	Mohammed Asmal, M.D., Ph.D. *vice president, head of SGD clinical research*
bb21217 and KarMMa topline data	Dave Davidson, M.D. *chief medical officer*
Q&A	Chip Baird, *chief financial officer* Philip Gregory, D. Phil., *chief scientific officer* Alison Finger, *chief commercial officer*

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WE RECODE FOR LIFE

RADICAL CARE

We care in a way that's intense and truly sets us apart.

THIS IS PERSONAL

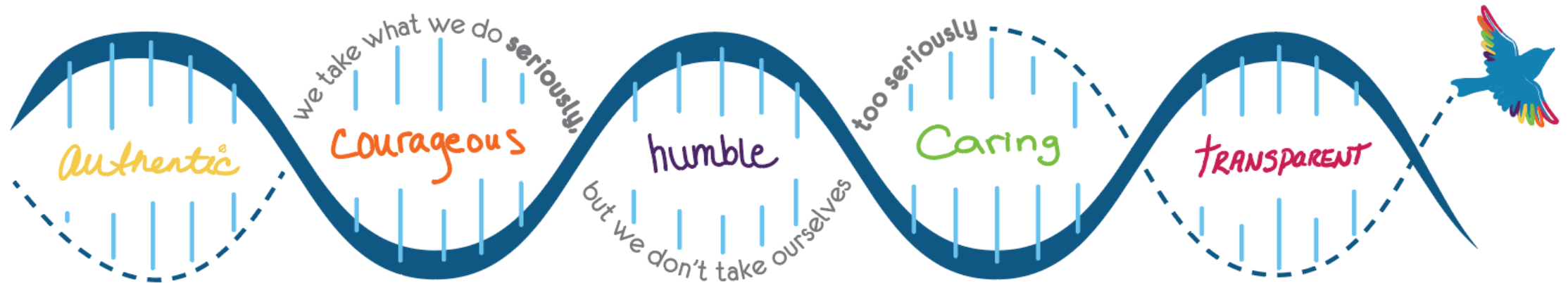Gene therapy is about saving lives one person at a time. And we are, each of us, personally all in.

PIONEERS WITH PURPOSE

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Key questions for today

LentiGlobin TDT	• Do the updated data in patients with non-β^0/β^0 genotypes reinforce the potential for patients to achieve and maintain transfusion independence (TI)? • Do the emerging data in patients with β^0/β^0 genotypes suggest that these patients may achieve TI?
LentiGlobin SCD	• With more patients and more follow up, are we continuing to see profound impact on important clinical manifestations of disease (VOEs, hemolytic anemia)? • Do the laboratory tools we have developed conclusively demonstrate that LentiGlobin for SCD changes the fundamental pathophysiology of the sickle RBC?
bb21217	• Does enriching bb21217 drug product for memory-like T cells translate to greater T cell persistence and longer durations of response?
ide-cel KarMMa	• Are KarMMa data supportive of ide-cel as a meaningful advance for patients and as a potential new standard of care for refractory multiple myeloma? • Is the program on track for 1H:2020 filing?

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Transfusion-Dependent β-Thalassemia (TDT)

- A severe, progressive, genetic disease that leads to severe anemia, lifelong transfusion dependence, unavoidable iron overload, serious comorbidities, and a shortened lifespan
- Global prevalence estimated at ~288,000[1]
- The U.S. prevalence of beta-thalassemia major is estimated to be at least 1,000 people[2,3]
- European prevalence is variable by country ranging from <1,000[4] patients in nonendemic countries, to ~6,500[5] patients in endemic countries

program overview

- EU approval granted June 2019
- U.S. rolling BLA submission to begin by YE 2019
- Studies ongoing:
  - Northstar-2 (HGB-207)
  - Northstar-3 (HGB-212)
  - Long-term follow-up: LTF-303

[1]Biffi A. Gene Therapy as a Curative Option for beta-Thalassemia. *N Engl J Med*. 2018;378(16):1551-1552.
[2]SayaniFA, Kwiatkowski JL. Increasing prevalence of thalassemia in America: implications for primary care. Ann Med. 2015;47(7):592-604.
[3]Centers for Disease Control and Prevention. Living with thalassemia. 2018; https://www.cdc.gov/features/international-thalassemia/index.html. Accessed May 11, 2018.
[4]CarioH, StahnkeK, Sander S, KohneE. Epidemiological situation and treatment of patients with thalassemia major in Germany: results of the German multicenter β-thalassemia study. Ann Hematol. 2000;79(1):7-12.
[5]AngelucciE, AntmenAB, LosiS, Burrows N, BartiromoC, Hu XH. Direct medical care costs associated with β-Thalassemia care in Italy. Blood. 2017;130(Suppl 1):92-5599.

Completed studies of LentiGlobin for TDT reinforce long term durability of clinical outcomes

HGB-204
Complete

- Up to 5 years follow-up with stable HbA^{T87Q} and total Hb
- 8/10 non-β^0/β^0; 3/8 β^0/β^0 remain TI as of data cut-off
- Reduction in liver iron content; cardiac iron remains stable in normal range as of data cut-off

HGB-205
Complete

- Stable HbA^{T87Q} and total Hb at up to 5+ years follow-up
- 3/4 non-β^0/β^0 remain TI as of data cut-off
- Substantial improvement in underlying dyserythropoiesis

HGB-207
non-β^0/β^0 genotypes

- 21/23 patients treated
- 9/10 patients achieved TI
- Total unsupported Hb is near-normal in most patients as of data cut-off
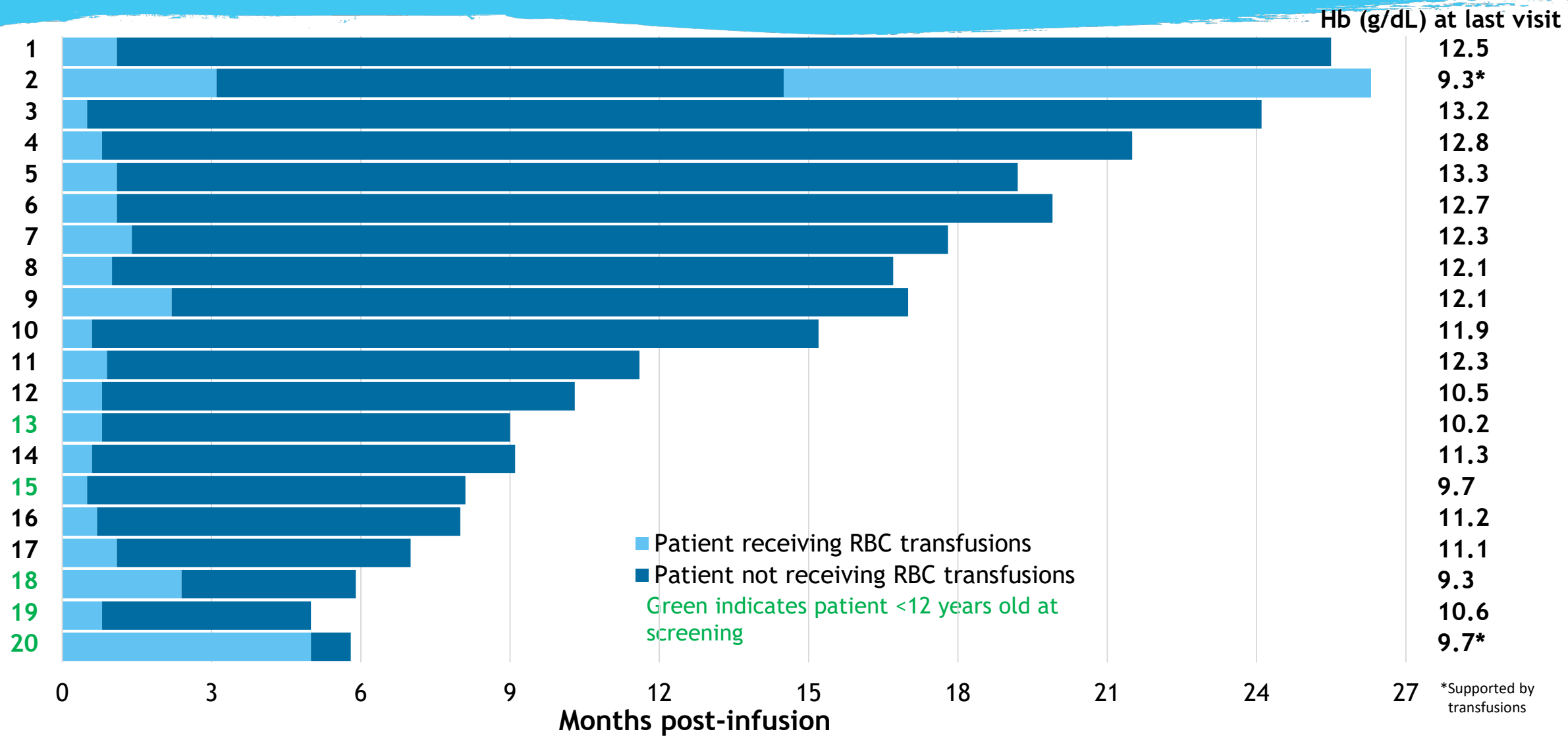
HGB-212
β^0/β^0 genotype or IVS-I-110 mutations
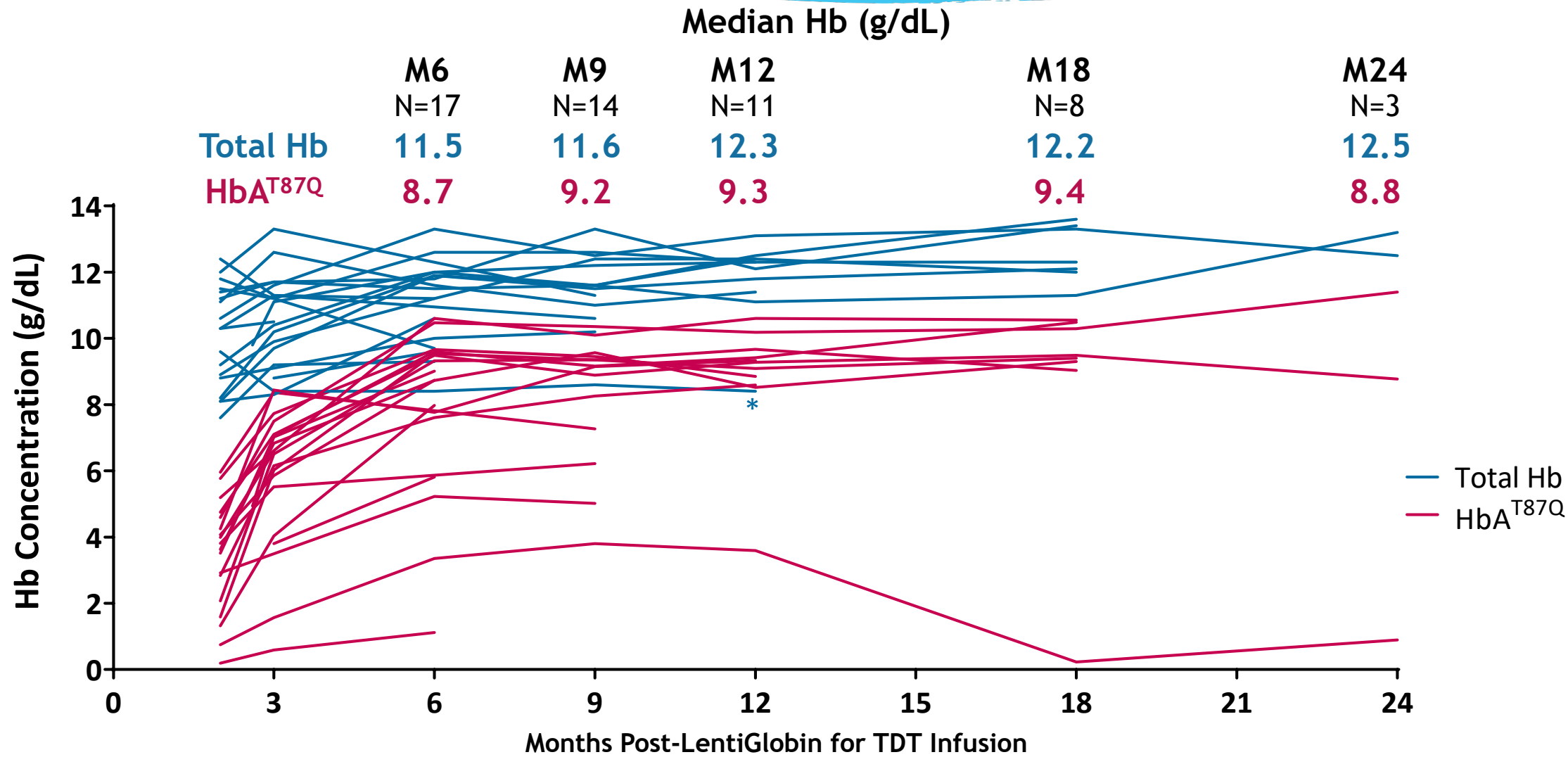
- 13/18 patients treated
- 2/2 patients achieved TI

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HGB-207: 90% (18/20) of patients with > 3 months follow-up are off pRBC transfusions

Hb (g/dL) at last visit

Patient	Hb (g/dL) at last visit
1	12.5
2	9.3*
3	13.2
4	12.8
5	13.3
6	12.7
7	12.3
8	12.1
9	12.1
10	11.9
11	12.3
12	10.5
13	10.2
14	11.3
15	9.7
16	11.2
17	11.1
18	9.3
19	10.6
20	9.7*

■ Patient receiving RBC transfusions
■ Patient not receiving RBC transfusions
Green indicates patient <12 years old at screening

Months post-infusion

*Supported by transfusions

The safety profile of LentiGlobin for TDT remains generally consistent with that of myeloablative busulfan conditioning.
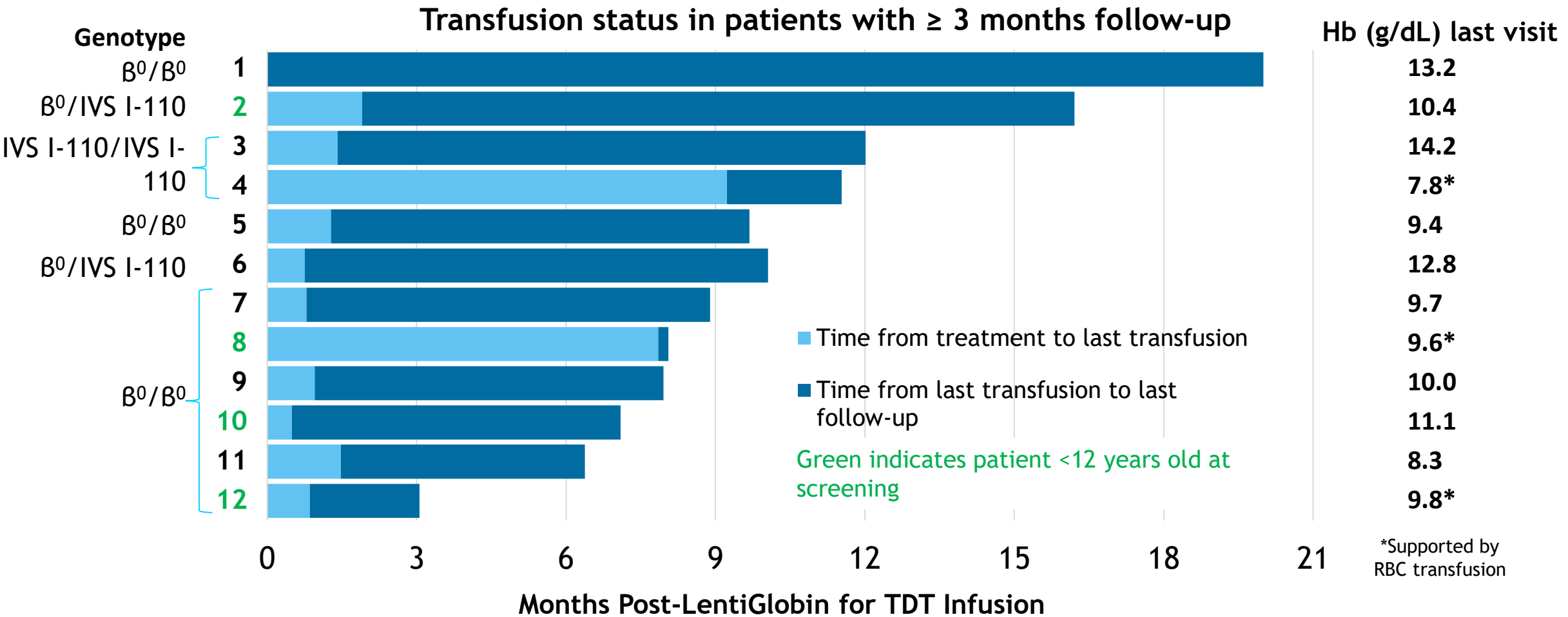
Data as of 12 June 2019   9

HGB-207: stable total Hb and gene therapy-derived HbA^{T87Q} in the majority of patients

Median Hb (g/dL)

	M6	M9	M12	M18	M24
	N=17	N=14	N=11	N=8	N=3
Total Hb	11.5	11.6	12.3	12.2	12.5
HbA^{T87Q}	8.7	9.2	9.3	9.4	8.8

Y-axis: Hb Concentration (g/dL)
X-axis: Months Post-LentiGlobin for TDT Infusion

Legend: Total Hb, HbA^{T87Q}

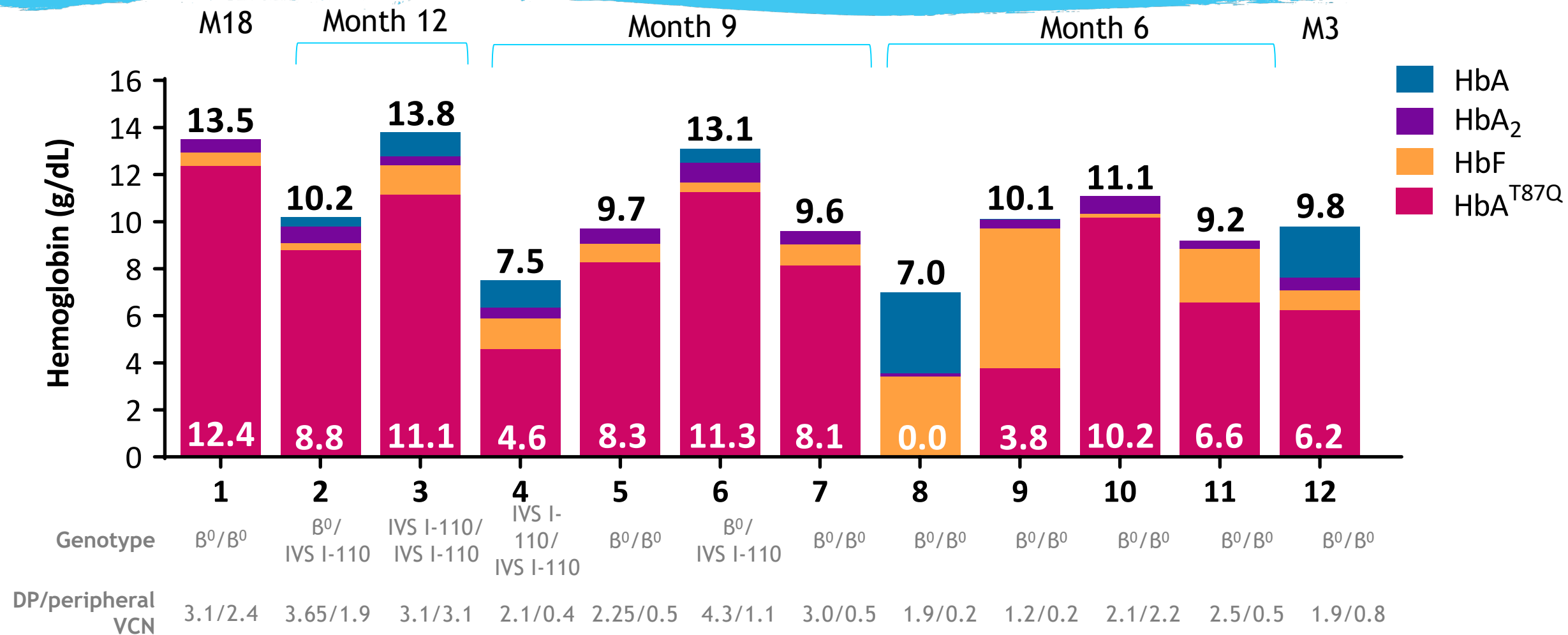HGB-207 utilized a range of manufacturing process conditions as the commercial manufacturing process was defined

*Last Hb before patient 2 restarted red blood cell transfusions. Hb, hemoglobin. Median total Hb values include Patient 2 who was on transfusions

Transfusion status in patients with ≥ 3 months follow-up

Genotype		Hb (g/dL) last visit
β^0/β^0	1	13.2
β^0/IVS I-110	2	10.4
IVS I-110/IVS I-110	3	14.2
	4	7.8*
β^0/β^0	5	9.4
β^0/IVS I-110	6	12.8
β^0/β^0	7	9.7
	8	9.6*
	9	10.0
	10	11.1
	11	8.3
	12	9.8*

■ Time from treatment to last transfusion

■ Time from last transfusion to last follow-up

Green indicates patient <12 years old at screening

*Supported by RBC transfusion

X-axis: 0, 3, 6, 9, 12, 15, 18, 21 — **Months Post-LentiGlobin for TDT Infusion**

Patients 1 and 2 achieved and maintained transfusion independence Weighted average Hb ≥ 9 g/dL without RBC transfusions for ≥ 12 months

Hb, hemoglobin; RBC, red blood cell

HGB-212: HbA^{T87Q} supports target total Hb in most patients with minimal endogenous HbA ≥ 3 months after treatment

HGB-212 utilized a range of manufacturing process conditions as the commercial manufacturing process was defined

The safety profile of LentiGlobin for TDT remains generally consistent with that of myeloablative busulfan conditioning

DP, drug product; Hb, hemoglobin; VCN, vector copy number

50+ patients treated across program for LentiGlobin in TDT

Completed HGB-204 and HGB-205 studies with up to 5+ years of data reinforce durability of treatment

90% of evaluable patients who do not have a β^0/β^0 genotype achieved TI in HGB-207 study

9 of 11 patients with at least 6 months of follow-up in HGB-212 did not receive a transfusion for more than 3 months as of last follow-up

Safety profile of LentiGlobin for TDT treatment is consistent with that of busulfan conditioning

Sickle Cell Disease (SCD)

- A serious, progressive, unpredictable, and debilitating genetic disease caused by abnormal sickle hemoglobin

- Results in chronic hemolytic anemia, repeated painful vaso-occlusive events and persistent vasculopathy that frequently leads to early morbidity and mortality

- Global annual birth incidence ~ 300,000 – 400,000[1,2]

- U.S. prevalence estimated at 72,000 – 100,000[3,4]

- Mean age of death in the U.S. is 44 years[5]

program overview

- Plan to pursue an accelerated development path based on hematological primary endpoint

- Phase 3 HGB-210 study to be open and enrolling patients by early 2020

- HGB-206 target enrollment achieved

[1]Kato GJ, Piel FB, Reid CD, et al. Sickle cell disease. *Nat Rev Dis Primers.* 2018;4:18010.
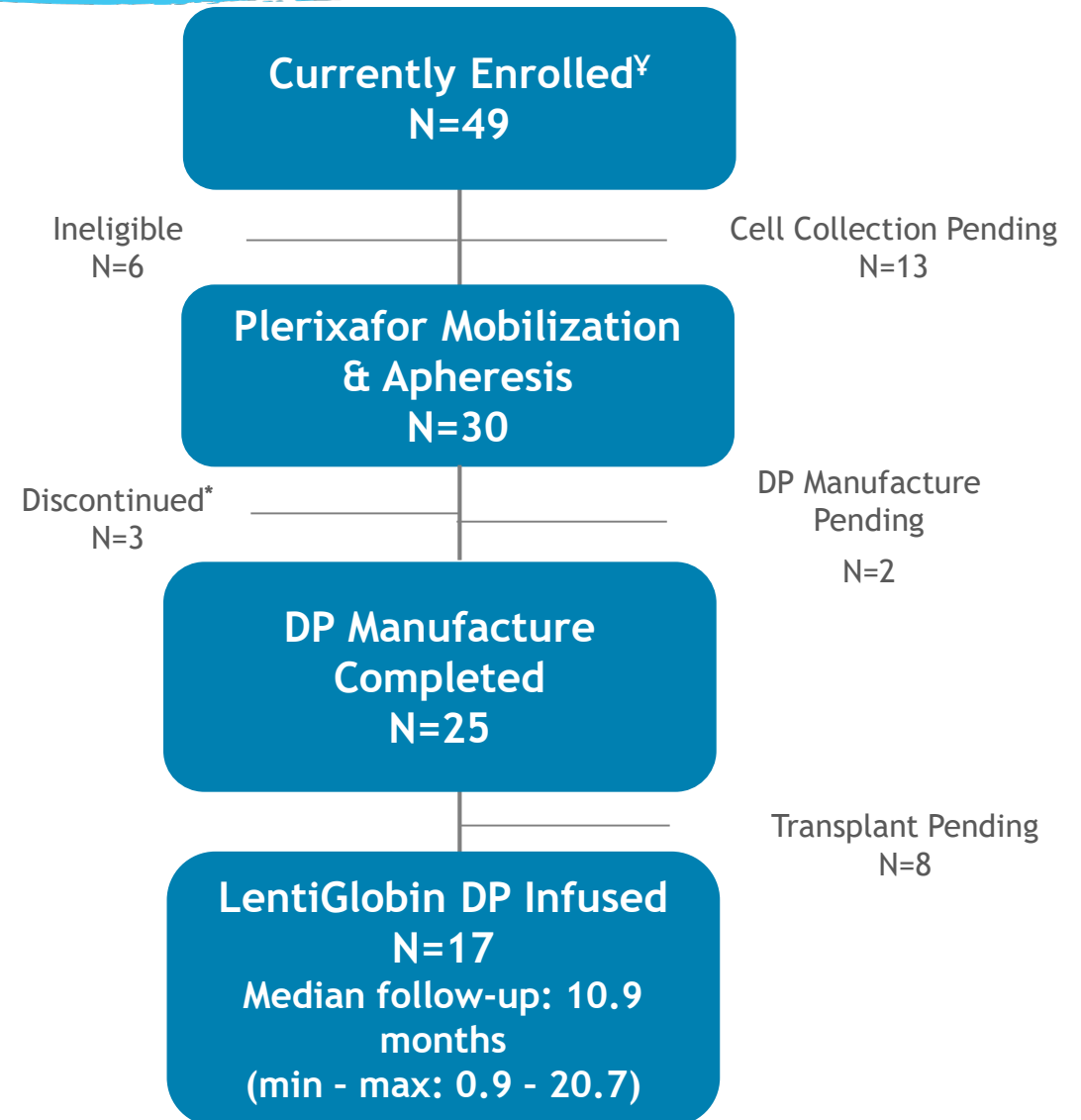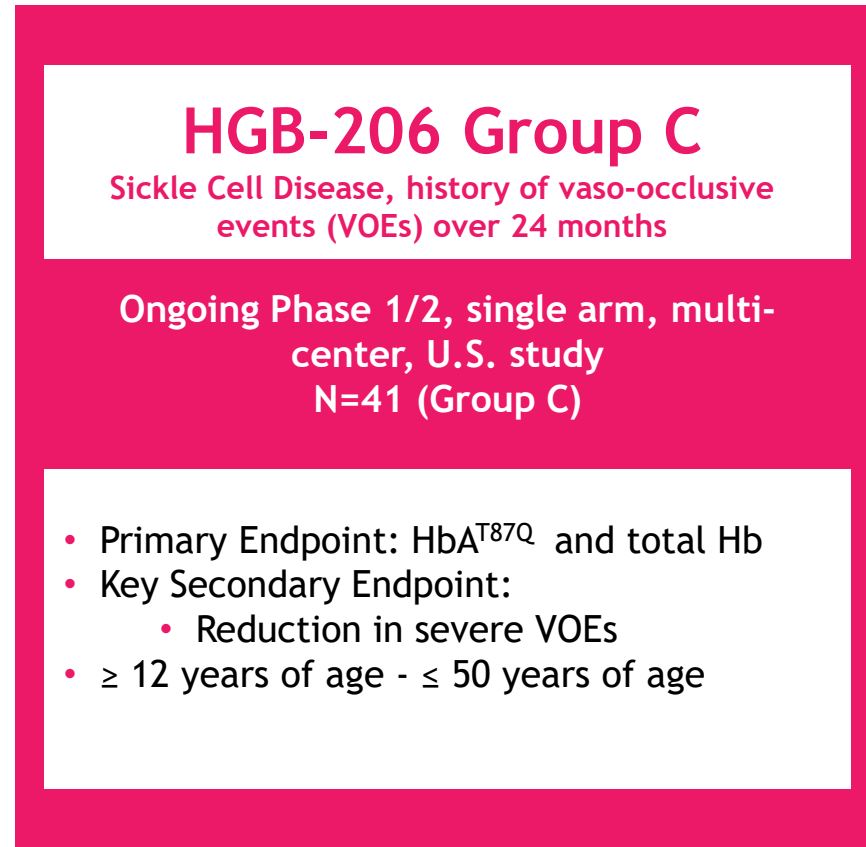[2]Piel FB, Patil AP, Howes RE, et al. Global epidemiology of sickle haemoglobin in neonates: a contemporary geostatistical model-based map and population estimates. *Lancet.* 2013;381(9861):142-151.
[3]Hassell KL. Population estimates of sickle cell disease in the U.S. *Am J Prev Med.* 2010;38(4 Suppl):S512-521.
[4]CDC Data and Statistics on Sickle Cell Disease. https://www.cdc.gov/ncbddd/sicklecell/data.html
[5]Paulukonis et al, California's Sickle Cell Data Collection Cohort, 2005-2015* ASH 2017*

# Expanding development program to evaluate LentiGlobin across SCD patient types and ages

HGB-206 Group C

Sickle Cell Disease, history of vaso-occlusive events (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

Currently Enrolled[¥]
N=49

Ineligible
N=6

Cell Collection Pending
N=13

Plerixafor Mobilization & Apheresis
N=30

Discontinued*
N=3

DP Manufacture Pending
N=2

DP Manufacture Completed
N=25

Transplant Pending
N=8

LentiGlobin DP Infused
N=17
Median follow-up: 10.9 months
(min – max: 0.9 – 20.7)

¥ Currently active, not recruiting

*1 withdrew consent, 1 discontinued due to investigator discretion, 1 mobilization failure; DP, drug product

Data as of 26 August 2019

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99% reduction in annualized rate of VOC + ACS in HGB-206 Group C patients with history of VOCs and ACS who had ≥ 6 months of follow-up
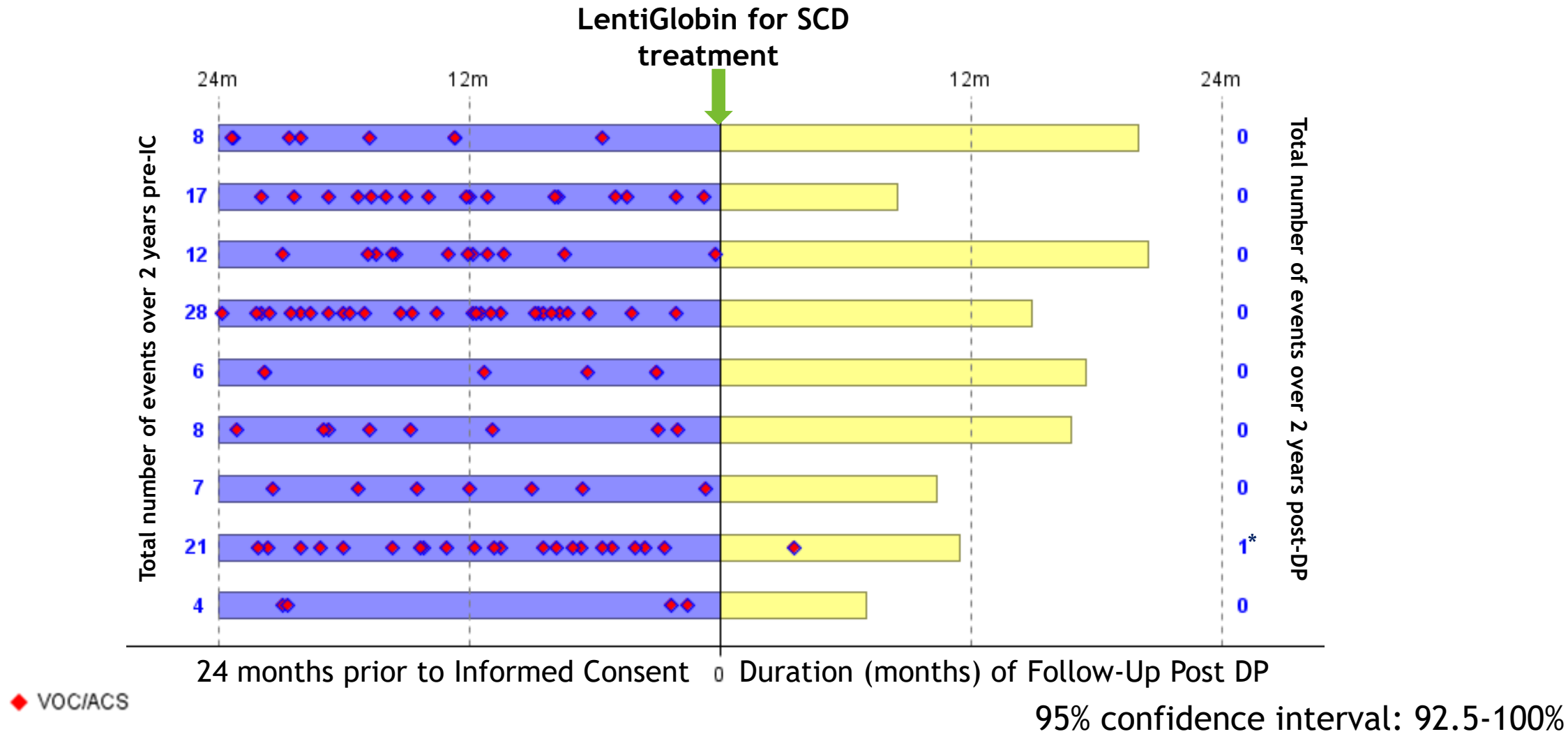

*As previously reported, 1 non-serious Grade 2 VOC was observed in 1 patient ~3.5 months post-LentiGlobin treatment

Investigator-reported adverse events of VOC or ACS are shown; *Patients with ≥ 4 VOC/ACS at baseline before Informed Consent and with ~ ≥ 6 months of follow-up post-DP infusion

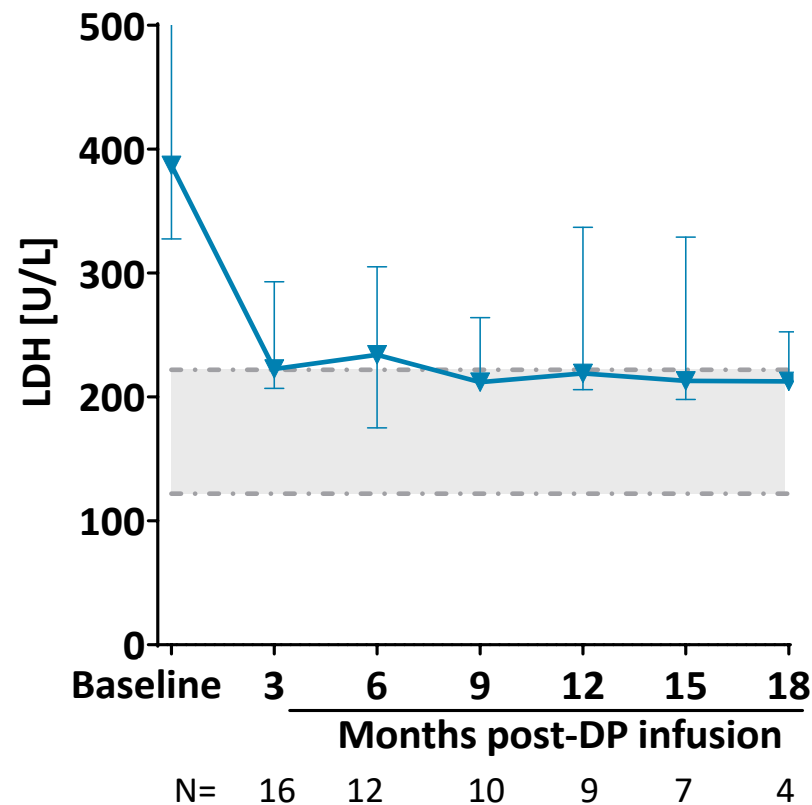ACS, acute chest syndrome; VOCs, vaso-occlusive crises; DP, drug product

95% confidence interval: 92.5-100%

Data as of 26 August 2019

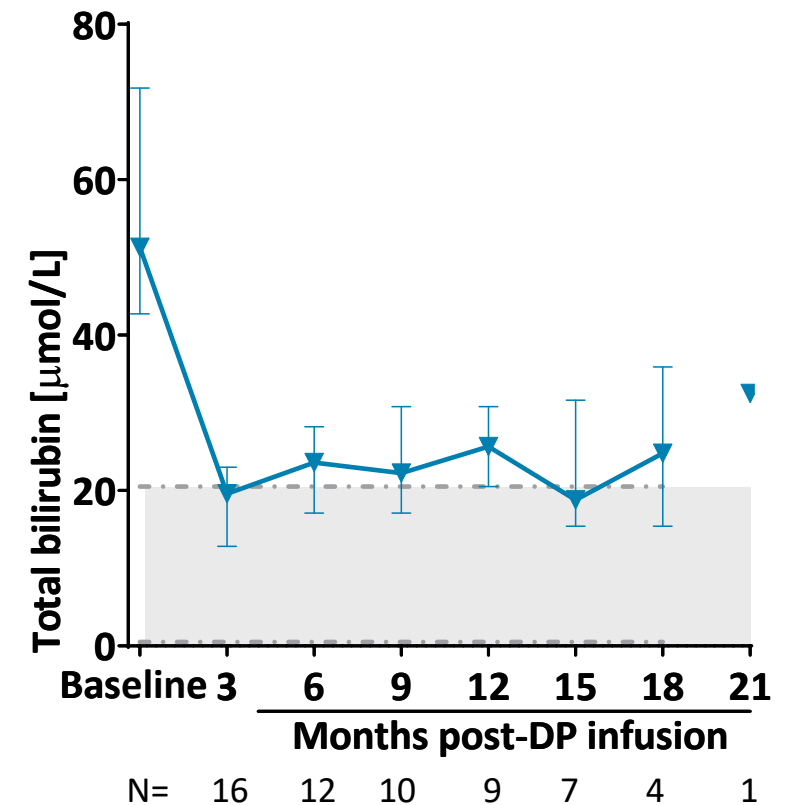# Improving key markers of hemolysis in HGB-206 Group C patients following treatment with LentiGlobin for SCD
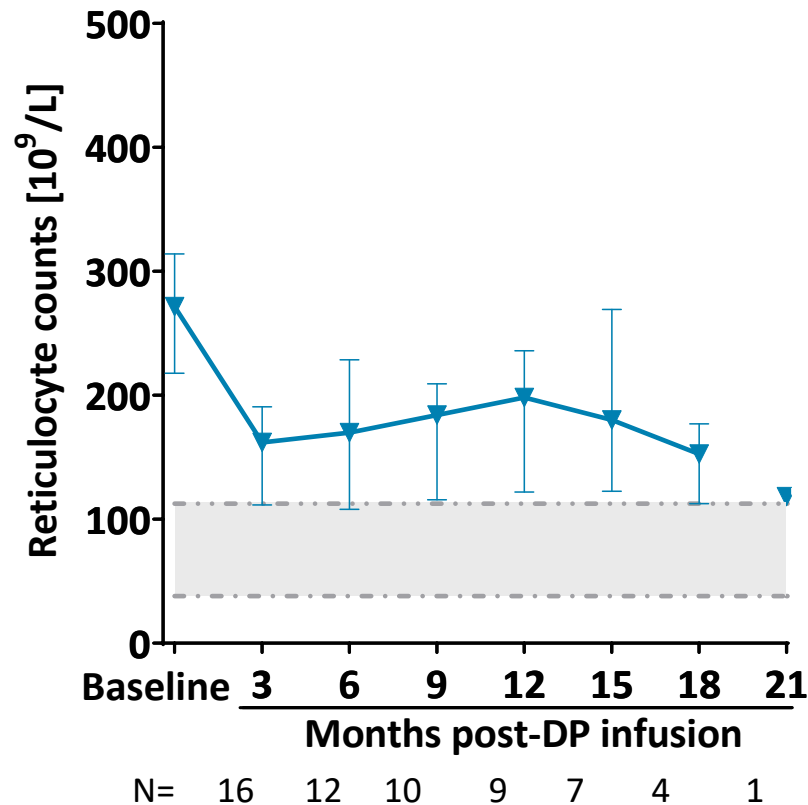
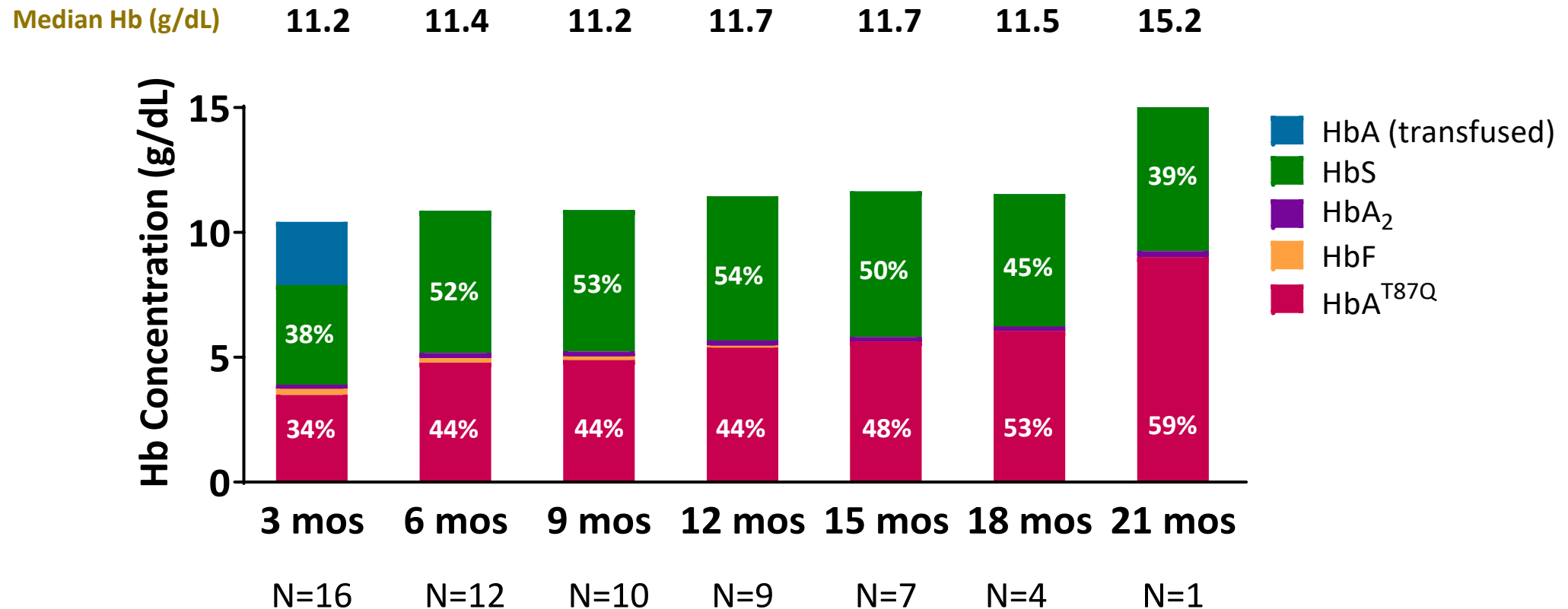

Median (Q1, Q3) depicted; Dot-dash lines denote lower and upper limits of normal values; *Number of patients with data available; †Total bilirubin at last follow-up remains > 2-fold lower than at screening

DP, drug product; LDH, lactate dehydrogenase
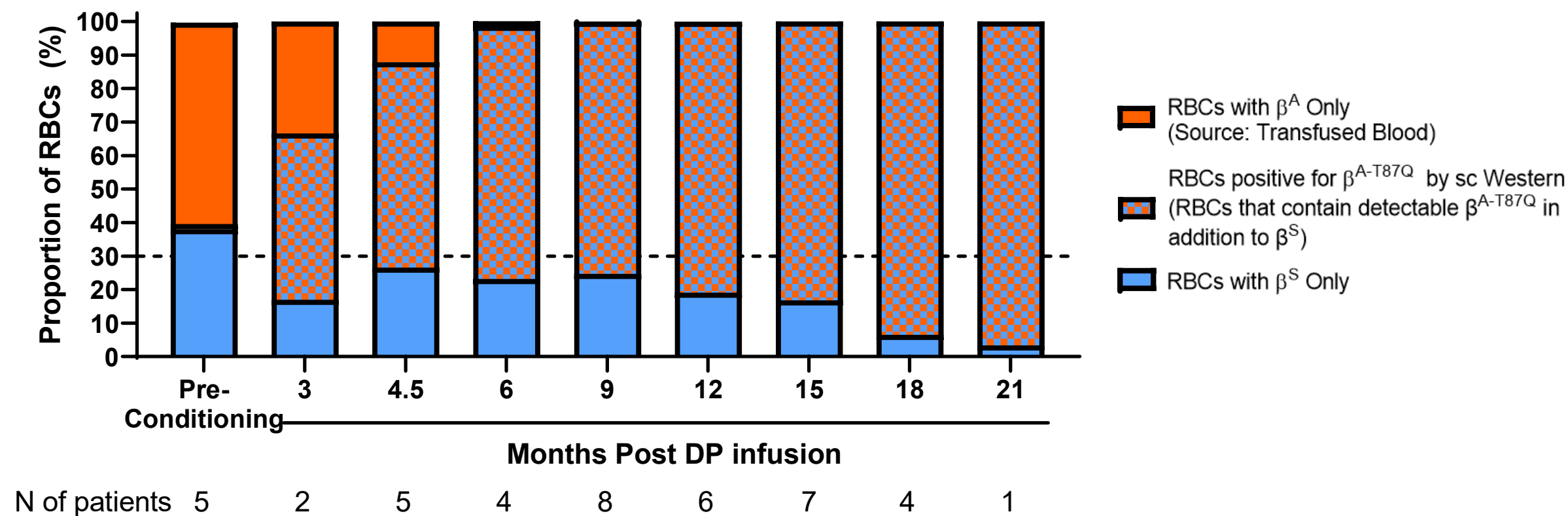
Data as of 26 August 2019

17

HGB-206 Group C patients at 6 months post-treatment produced consistent median levels of anti-sickling hemoglobin ranging from 44% - 59% (month 6-21)

Median Hb (g/dL): 11.2, 11.4, 11.2, 11.7, 11.7, 11.5, 15.2

Legend:
- HbA (transfused)
- HbS
- HbA_2
- HbF
- HbA^{T87Q}

3 mos (N=16), 6 mos (N=12), 9 mos (N=10), 12 mos (N=9), 15 mos (N=7), 18 mos (N=4), 21 mos (N=1)

- Median HbS ≤ 60% at ≥ 6 months post-LentiGlobin for SCD treatment
- Total Hb and HbA^{T87Q} ranged from 9.3 – 15.2 g/dL and 2.7 – 9.0 g/dL, respectively, at last visit in patients with ≥ 6 months of follow-up

% represents median Hb fraction as % of total Hb; Hb, hemoglobin

Data as of 26 August 2019

On average, ≥ 70% of RBCs from patients treated with LentiGlobin for SCD contain β^{A-T87Q} by month 6

- Exploratory single RBC western assay performed on samples from 15 patients in Group C

Legend:
- RBCs with β^A Only (Source: Transfused Blood)
- RBCs positive for β^{A-T87Q} by sc Western (RBCs that contain detectable β^{A-T87Q} in addition to β^S)
- RBCs with β^S Only

Y-axis: Proportion of RBCs (%)

X-axis: Months Post DP infusion — Pre-Conditioning, 3, 4.5, 6, 9, 12, 15, 18, 21

N of patients: 5, 2, 5, 4, 8, 6, 7, 4, 1

Mean is depicted - if N=1, data show technical replicates; *Pre-conditioning sample does not contain any β^{A-T87Q}, signal is due to error rate of multiples
DP, drug product; RBCs, red blood cells; sc, single cell

Data as of 26 August 2019

Exploratory assays: high concentrations of β^A-T87Q achieved at the cellular level result in reduced propensity to sickle

Propensity to sickle decreases over time post-gene therapy with LentiGlobin for SCD; Group C similar to trait
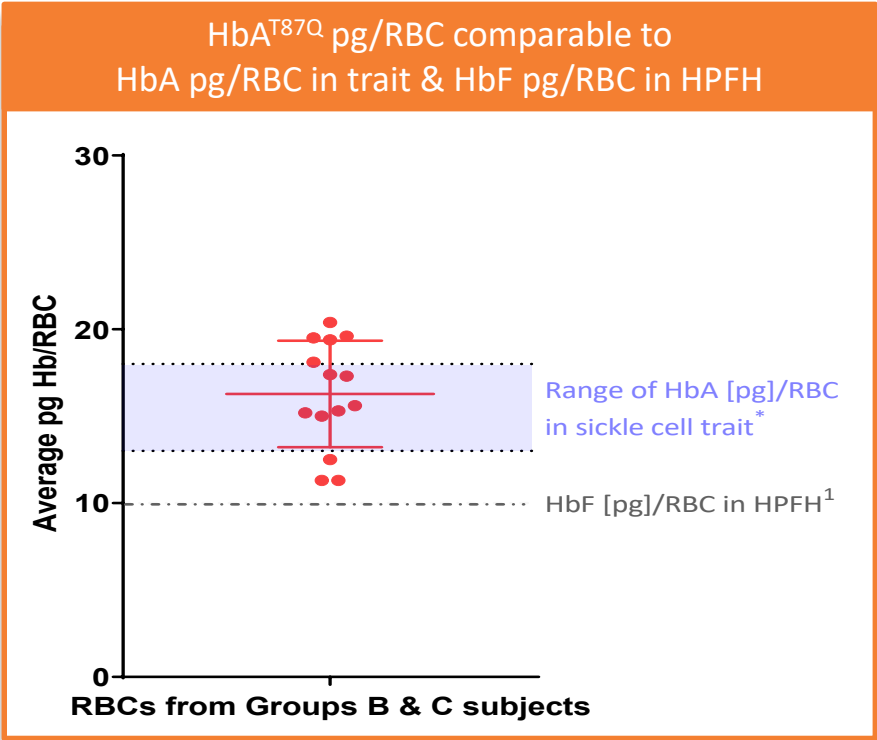
Average pg Hb/RBC = (% HbA^T87Q of total Hb/% RBCs containing β^A-T87Q) x MCH
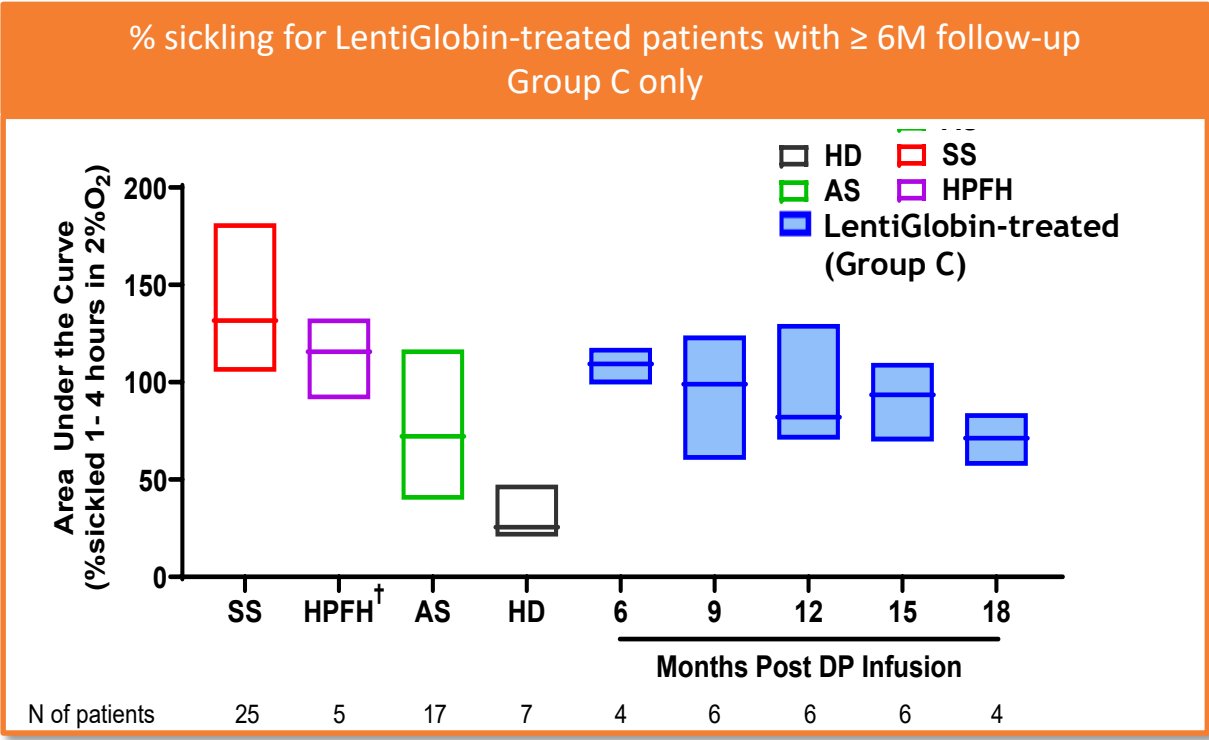
HGB-206 Group C: safety profile post-DP infusion generally consistent with myeloablative single-agent busulfan conditioning

Non-hematologic Grade ≥ 3 AEs Post-DP infusion in ≥ 2 patients*	N = 17 n (%)
Febrile neutropenia	10 (58.8)
Stomatitis	9 (52.9)
Increased blood bilirubin	3 (17.6)
Upper abdominal pain	2 (11.8)
Increased alanine aminotransferase	2 (11.8)
Increased aspartate aminotransferase	2 (11.8)
Nausea	2 (11.8)
Premature menopause	2 (11.8)
Serious AEs Post-DP infusion in ≥ 2 patients	N = 17 n (%)
Nausea	2 (11.8)
Vomiting	2 (11.8)

- Safety profile post-DP infusion is generally consistent with myeloablative single-agent busulfan conditioning
- No DP-related adverse events
- No cases of veno-occlusive liver disease
- No graft failure or deaths reported
- No vector-mediated RCL
- No evidence of clonal dominance
- No further cases of MDS have been observed across studies of LentiGlobin†▪

*Hematologic AEs commonly observed post-transplantation have been excluded
†As of June 2019 (HGB-205); 12 Jun 2019 (HGB-204, HGB-207), and 30 Sep 2019 (HGB-212)
▪One patient in Group A was reported to have MDS at ASH 2018. There was no evidence of LVV-mediated oncogenesis and the MDS SAE was considered unlikely related to LentiGlobin gene therapy.
AE, adverse event; DP, drug product; RCL, replication competent lentivirus

Notable impact on underlying pathophysiology of SCD

99% reduction in annualized rate of VOC + ACS in Group C patients with history of VOCs and ACS who had ≥ 6 months of follow-up, with no reports of ACS or serious VOCs at up to 21 months post-treatment

Continued improvement in key markers of hemolysis in Group C patients as of the data cut-off date

Group C patients at 6 months post-treatment produced consistent median levels of anti-sickling hemoglobin ranging from 44% - 59%

Continue to pursue an accelerated development path based on hematological primary endpoint

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ACS, acute chest syndrome; VOCs, vaso-occlusive crises

multiple myeloma

- An incurable type of blood cancer that arises from antibody producing cells in the bone marrow, resulting in anemia, kidney failure, infections and skeletal fractures.
- Second most common hematologic cancer[1,2]
- In 2018, MM was diagnosed in nearly 160,000 patients worldwide and over 31,000 patients in the US. It is estimated that over 130,000 patients in the US are living with this disease.

BCMA program overview

- **ide-cel (bb2121):**
   - U.S. BLA submission planned for 1H:2020
    - KarMMa-2 and KarMMa-3 studies in earlier lines of therapy open and enrolling; Phase 1 study in newly-diagnosed multiple myeloma starting in 2019
- **bb21217 CRB-402** Phase 1 study underway

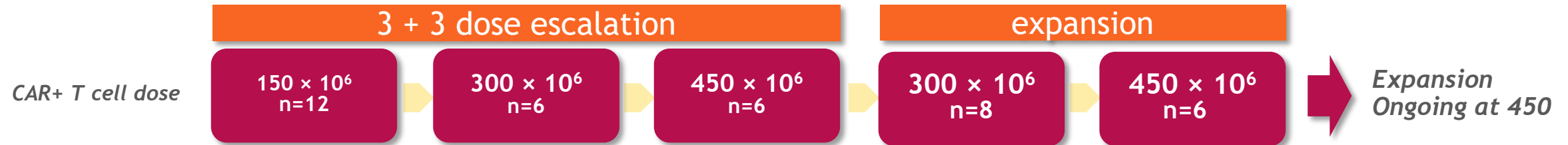[1]NCI SEER. https://seer.cancer.gov/statfacts/html/mulmy.html. Accessed June 5, 2019.
[2] Bray F, et al. *CA Cancer J Clin*. 2018;68(6):394-424

bb21217: PI3K inhibition during manufacturing drives increase in long-lived, memory-like T cells
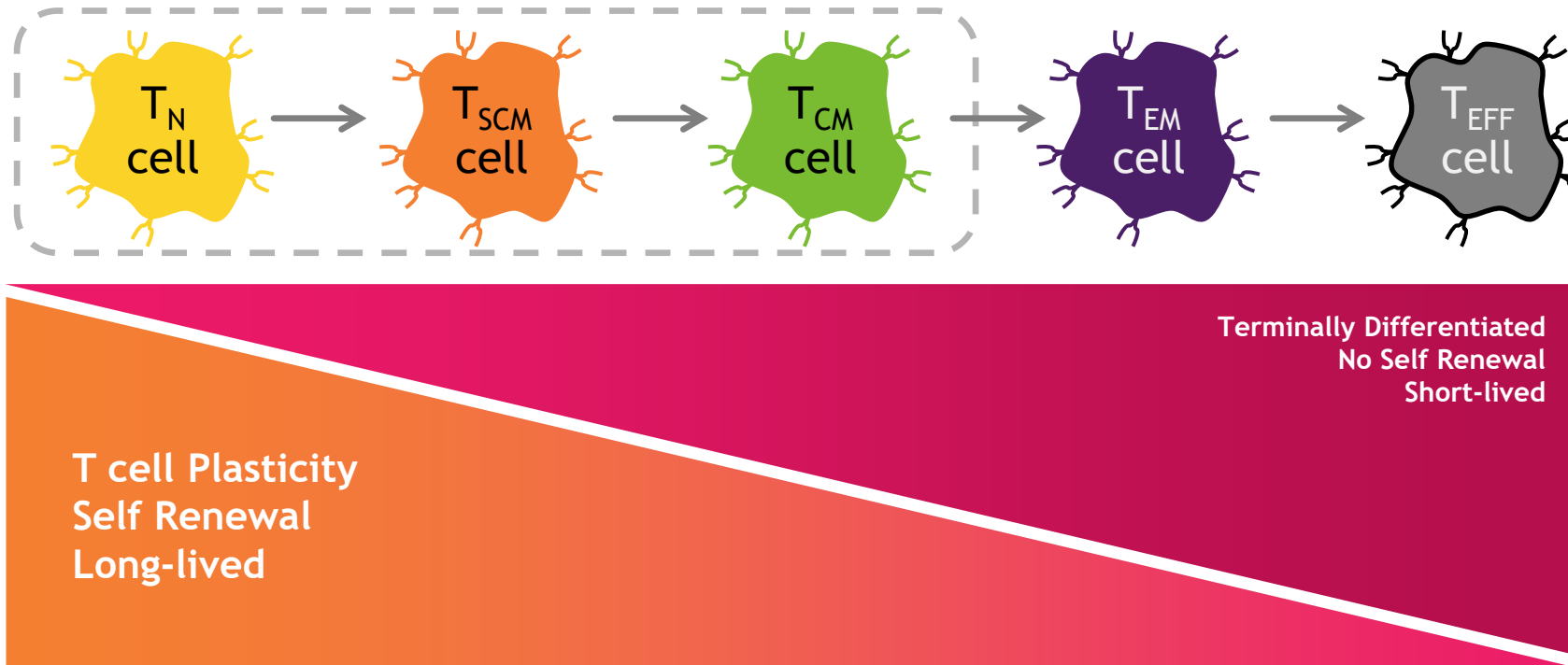
Hypothesis: Increasing long-lived, memory-like T cell subsets in the drug product may result in enhanced persistence of functional anti-BCMA CAR T cells _in vivo_

Phase 1 dose-escalation study in heavily pretreated and refractory patient population continues to enroll

CAR+ T cell dose

3 + 3 dose escalation			expansion	
150×10^6 n=12	300×10^6 n=6	450×10^6 n=6	300×10^6 n=8	450×10^6 n=6

Expansion Ongoing at 450

N ≈ 74
- R/R MM
- ≥3 prior regimens
- Prior IMiD and PI required
- In escalation only ≥50% BCMA expression required
- In expansion only αCD38 exposure and refractory to last line required

- **Primary endpoints:** AEs, DLTs
- **Other endpoints:** Response[c], PFS, OS, MRD, CAR+ T cell expansion and persistence

Manufacturing Success Rate 100%*

*3 patients required
1 re-manufacturing run

BCMA, B-cell maturation antigen; IMiD, immunomodulatory imide drugs; MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; R/R, relapsed/refractory. [c]Per International Myeloma Working Group Criteria.

Baseline patient characteristics and treatment history

Characteristic	bb21217-Treated (N=38)
Median (min, max) age, y	62 (33, 74)
Male, n (%)	21 (55)
Time since initial diagnosis, y Median (min, max)	5.5 (1.0, 13.5)
ECOG PS, n (%) 0 1 2	12 (32) 24 (63) 2 (5)
ISS stage[a], n (%) I II III Unavailable	11 (29) 7 (18) 10 (26) 10 (26)
High-risk cytogenetics, n (%) del(17p), t(4;14), t(14;16) Unknown	13 (34) 1 (3)

Characteristic		bb21217-Treated (N=38)	
Median (min, max) no. prior regimens[b]		6 (3, 17)	
Prior autologous SCT, n (%) 0 1 >1		7 (18) 22 (58) 9 (24)	
Prior therapies, n (%)		Exposed	Refractory
IMiD agent	Any	38 (100)	30 (79)
	Lenalidomide	38 (100)	30 (79)
	Pomalidomide	35 (92)	22 (58)
PI	Any	38 (100)	33 (89)
	Bortezomib	36 (95)	21 (55)
	Carfilzomib	32 (84)	25 (66)
αCD38 antibodies	Any	36 (95)	29 (76)
	Daratumumab	35 (92)	28 (74)
Cumulative	PI/IMiD	38 (100)	29 (76)
	PI/IMiD/αCD38 antibodies	36 (95)	24 (63)

ECOG PS, Eastern Cooperative Oncology Groups performance status; IMiD, immunomodulatory imide drugs; ISS, International Staging System; mAb, monoclonal antibody; PI, proteasome inhibitor; SCT, stem cell transplantation.
[b]Number of antimyeloma regimens, including autologous SCT.

Data as of 4 September 2019

Safety profile consistent with CAR T experience

Grade 3/4 AEs in >2 Patients[a], n (%)	Grade 3/4 (N=38)
Neutropenia	31 (82)
Leukopenia	21 (55)
Thrombocytopenia	21 (55)
Anemia	19 (50)
Lymphopenia	13 (34)
Hypophosphatemia	8 (21)
Infection[b]	7 (18)
Hyponatremia	5 (13)
Febrile neutropenia	4 (11)

	N	Grade, n (%)					Total all grades
		1	2	3	4	5	
CRS							
150×10^6	12	4 (33)	3 (25)	1 (8)	0	0	8 (67)
300×10^6	14	4 (29)	3 (21)	0	0	0	7 (50)
450×10^6	12	4 (33)	5 (42)	0	0	1 (8)	10 (83)
Neurotoxicity							
150×10^6	12	1 (8)	1 (8)	0	1 (8)	0	3 (25)
300×10^6	14	1 (7)	2 (14)	1 (7)	0	0	4 (29)
450×10^6	12	1 (8)	0	1 (8)	0	0	2 (17)

- CRS[c] occurred in 25 patients (66%)
  - Median (min, max) time to onset was 3 d (1, 20)
  - Generally adequately managed with tocilizumab (n=10) and tocilizumab plus corticosteroids (n=4)
  - 1 fatal CRS event associated with grade 3 neurotoxicity at the 450×10^6 dose occurred after 15 days of follow-up

- Neurotoxicity[d] of grade 3 or higher occurred in 3 patients
  - 2 grade 3 events and 1 previously reported grade 4 event
  - Median (min, max) time to onset of neurotoxicity was 7 d (3, 24)

- 7 grade 3/4 infections reported

- 19 patients (50%) experienced ≥1 SAE

AE, adverse event, SAE, serious AE, CMV, cytomegalovirus
[a]AEs and SAEs after first documented progression are excluded
[b]Includes SOC infections and infestations, one case each of anal abscess, bacteraemia, CMV colitis, device related infection, escherichiabacteraemia, pneumococcal bacteraemia, pneumococcal sepsis and pneumonia; CRS, cytokine release syndrome;. [c]CRS uniformly graded according to Lee et al., *Blood* 2014;124:188-195 occurring after bb21217 infusion and before disease progression. [d]Events selected as CAR T neurotoxicity on the case report form occurring within 90 days after bb21217 infusion.

Data as of 4 September 2019

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To date, no progression in patients with confirmed response at the 300 x 10^6 and 450 x 10^6 dose cohorts; mDOR of 11.1 months at 150 x 10^6 dose
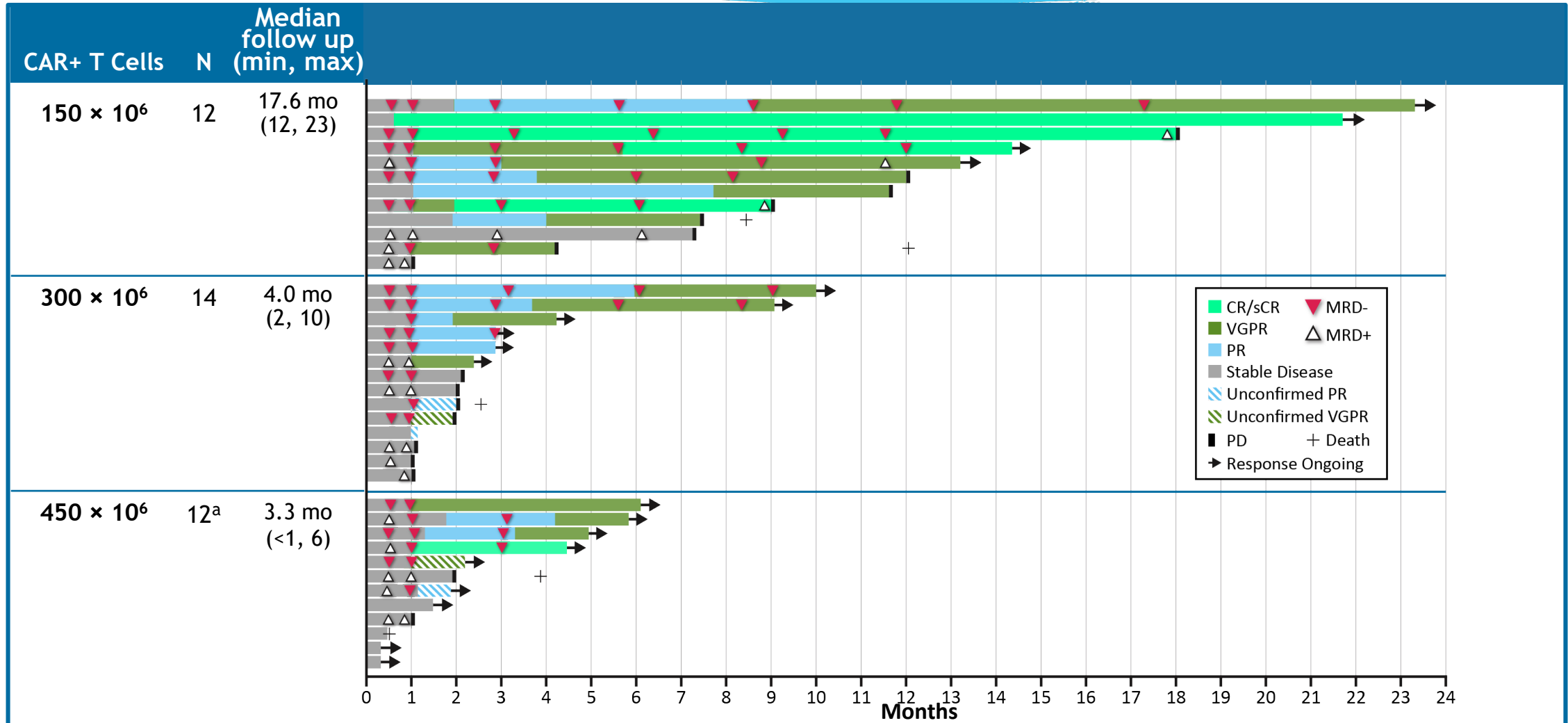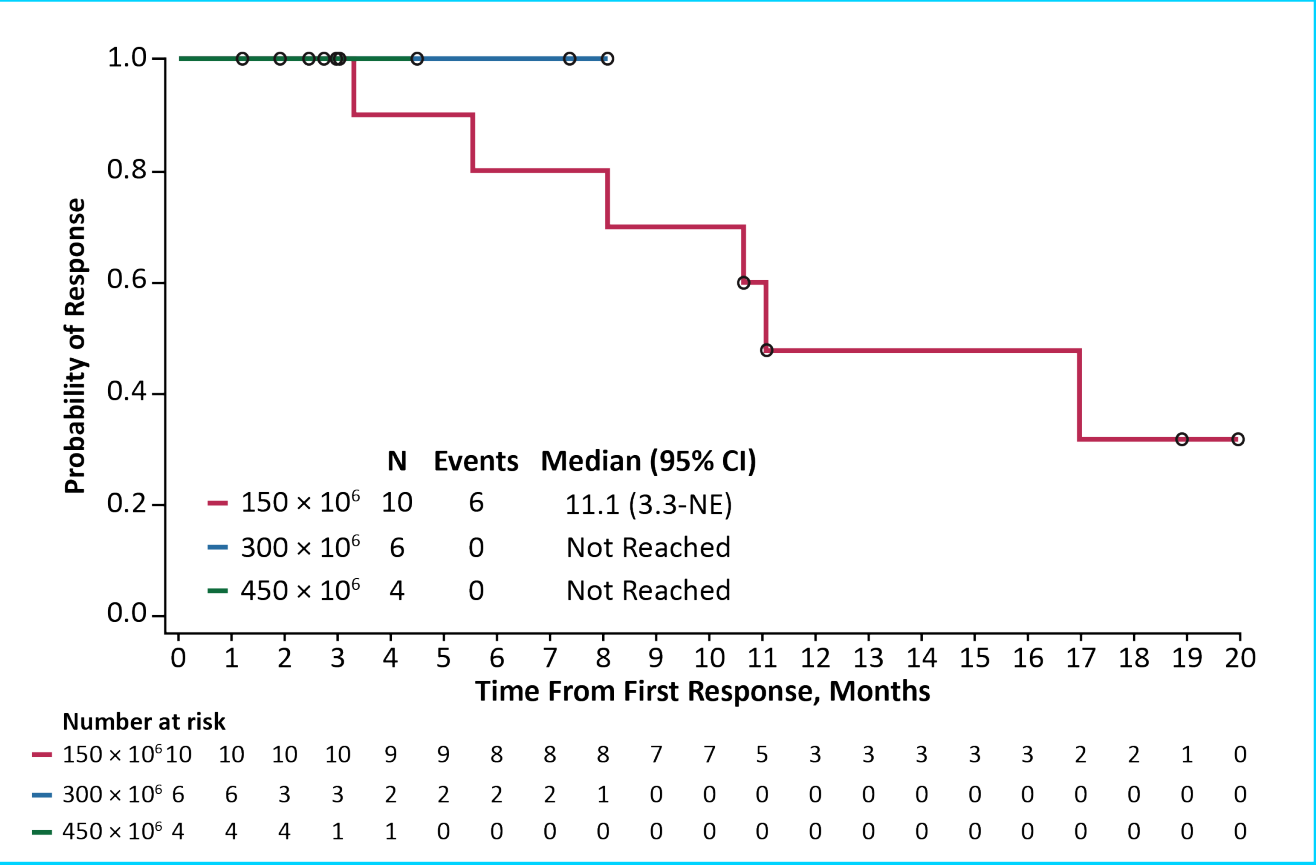

CR, complete response; MRD, minimal residual disease; PD, progressive disease; sCR, stringent complete response; VGPR, very good partial response.
[a] One patient ongoing at the time of the data extraction missed their 2-month visit and another was in VGPR but is reported as a PR owing to a missed assessment.

Confirmed responses across dose cohorts

CAR+ T Cells:	150 × 10⁶ (n=12)	300 × 10⁶ (n=14)	450 × 10⁶ (n=7)
Median follow-up (min, max)	17.6 mo (12, 23)	4.0 mo (2, 10)	3.3 mo (<1, 6)
Confirmed response[a], n (%)			
sCR/CR	4 (33)	0	1 (14)
VGPR	6 (50)	4 (29)	2 (29)
PR	0	2 (14)	1 (14)
Total	**10 (83)**	**6 (43)**	**4 (57)**
Median time to first response (min, max), mo	1.0 (1.0, 1.9)	1.0 (1.0, 1.0)	1.2 (1.0, 1.8)
MRD status in bone marrow[b]			
Evaluable responders, n	7	6	4
MRD negative, n	7	5	4

confirmed response duration by dose[a]

	N	Events	Median (95% CI)
150 × 10⁶	10	6	11.1 (3.3-NE)
300 × 10⁶	6	0	Not Reached
450 × 10⁶	4	0	Not Reached

Number at risk

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
150 × 10⁶	10	10	10	10	9	9	8	8	8	7	7	5	3	3	3	3	3	2	2	1	0
300 × 10⁶	6	6	3	3	2	2	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0
450 × 10⁶	4	4	4	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

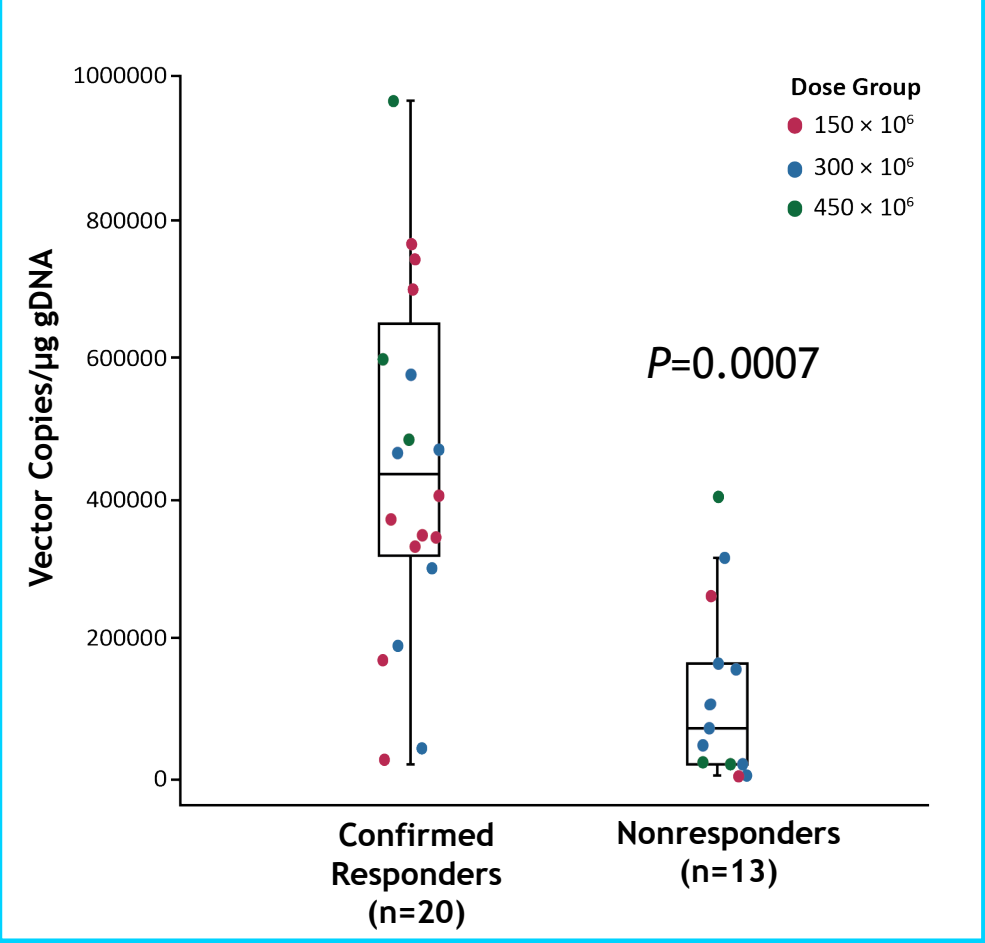Probability of Response vs Time From First Response, Months

DOR, duration of response; MRD, minimal residual disease; NE, not estimable; PD, progressive disease; PR, partial response; sCR/CR, stringent complete response/complete response; VGPR, very good partial response.
[a]Patients with ≥2 months of follow up or PD/death within 2 months. Response confirmed by a consecutive response of the same category or better.
[b]Patients with ≥PR and ≥1 valid post-baseline MRD assessment by Adaptive next-generation sequencing. 150x10⁶ dose 6 neg at 10⁻⁶ and 1 neg at 10⁻⁵, 300x10⁶ dose 4 neg at 10⁻⁶ and 1 at 10⁻⁵, 450x10⁶ 2 neg at 10⁻⁶ and 2 at 10⁻⁵.
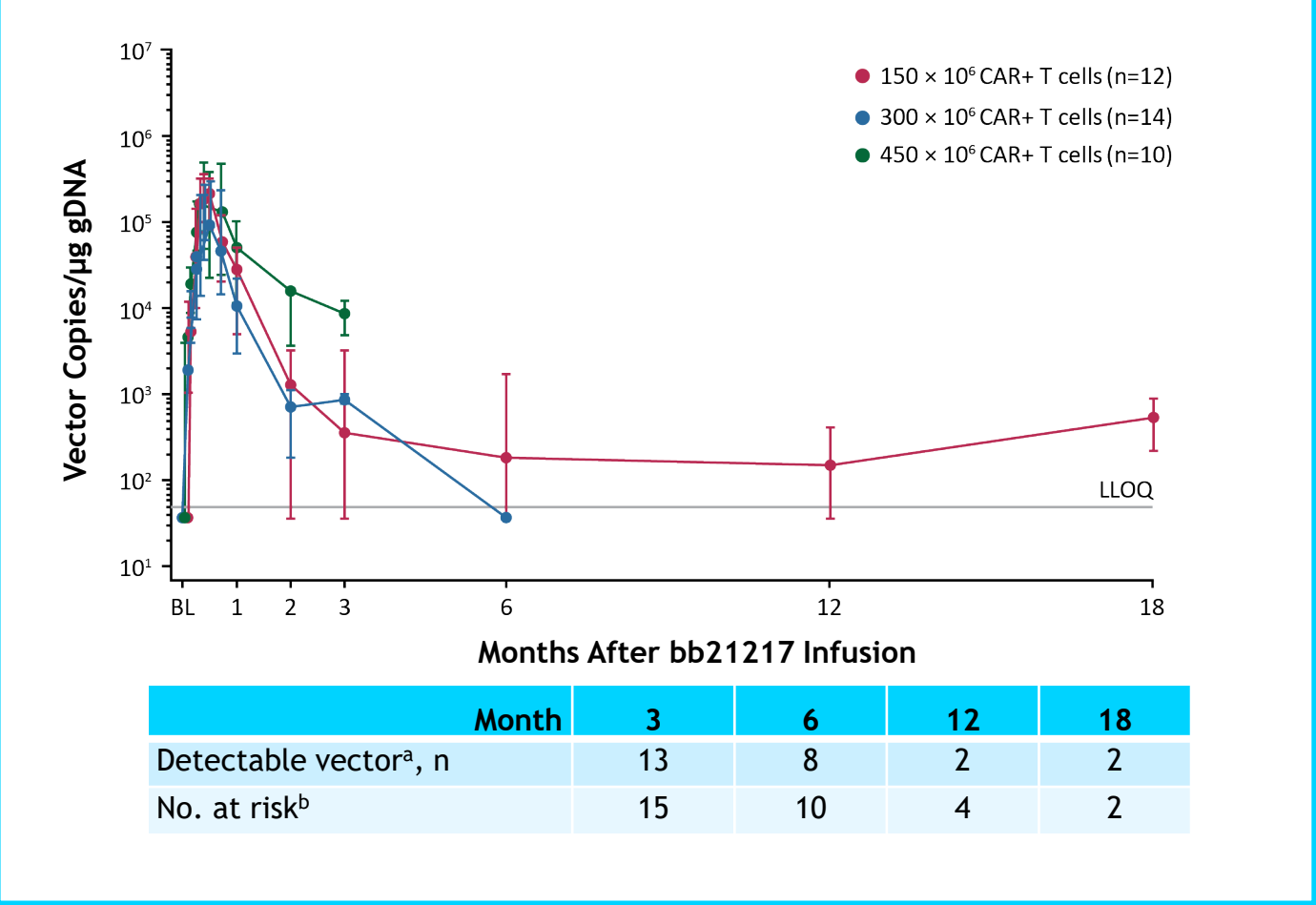
Data as of 4 September 2019

Confirmed responders show increased CAR T cell expansion and durable persistence

peak VCN by response

Vector Copies/µg gDNA

Dose Group
- 150 × 10^6 (pink)
- 300 × 10^6 (blue)
- 450 × 10^6 (green)

P=0.0007

Confirmed Responders (n=20)

Nonresponders (n=13)

median VCN over time by dose

Vector Copies/µg gDNA

- 150 × 10^6 CAR+ T cells (n=12)
- 300 × 10^6 CAR+ T cells (n=14)
- 450 × 10^6 CAR+ T cells (n=10)

LLOQ

Months After bb21217 Infusion

| Month	3	6	12	18
Detectable vector[a], n	13	8	2	2
No. at risk[b]	15	10	4	2

P value based on a 2 sided Wilcoxon rank sum test.

BL, baseline; gDNA, genomic DNA; IQR, interquartile range; LLOQ, lower limit of quantification; VCN, vector copy number. [a] includes detectable but not measurable. [b] includes VCN data for patients until PD, includes 1 patient who received subsequent chemotherapy before progression. Error bars for median VCN represent IQR
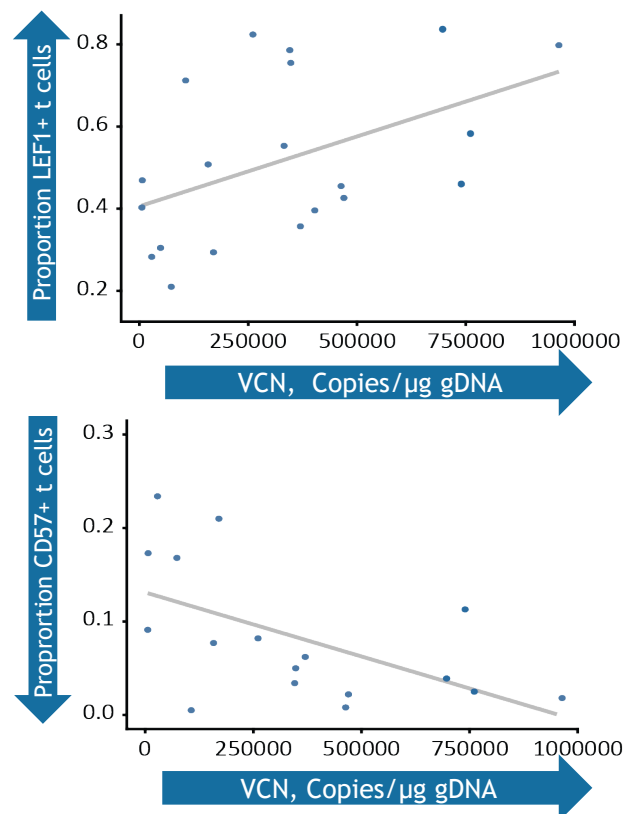
Data as of 4 September 2019

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Enrichment for memory-like T cells is associated with robust CAR T expansion and lack of progression by month 6

- Patients with a higher proportion of memory-like T cells in bb21217 drug product have significantly better peak expansion
- A higher proportion of memory-like T cells is associated with numerically less progression by M6
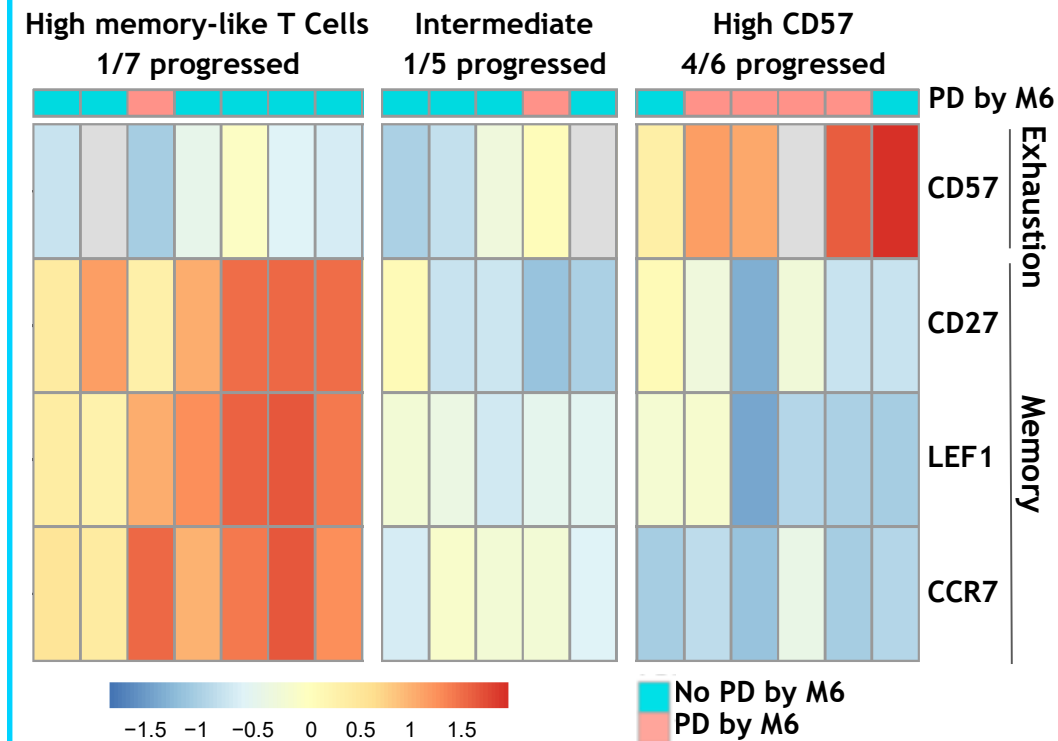

bb21217 drug product enriched for memory-like T cells
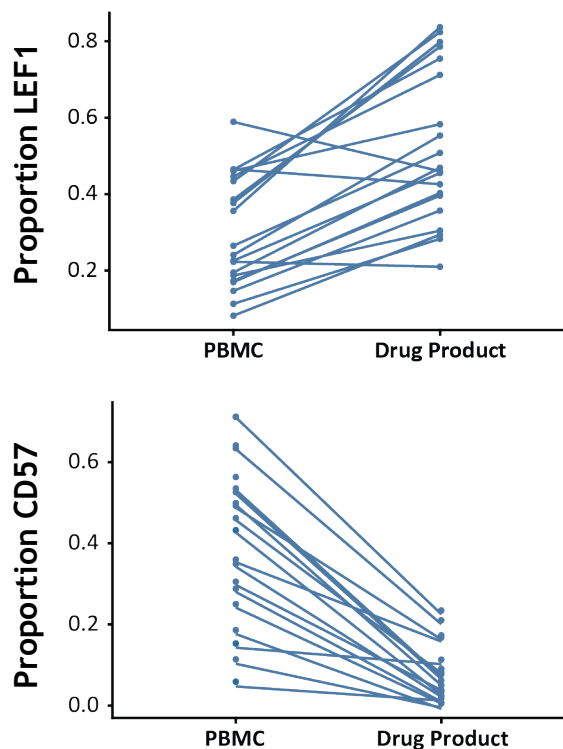
memory-like T cells associated with peak CAR T expansion

memory-like T cells in drug product associated with lack of progression at M6[a]

High memory-like T Cells 1/7 progressed

Intermediate 1/5 progressed

High CD57 4/6 progressed

No PD by M6
PD by M6

M6, month 6; PBMC, peripheral blood mononuclear cell in apheresis product; PD, progressive disease; VCN, vector copy number. [a] Responding Patients with biomarker data who had either PD or a month 6 visit confirming absence of PD, 1 patient with continued stable disease at M6 included.

Emerging data supports memory T cell hypothesis

Safety profile consistent with known toxicities of CAR T cell therapies

Confirmed responses achieved across all doses

Detectable CAR T cells at 18 months for patients remaining in response with greater than 20 months follow up

Demonstrated association between enrichment in 21217 manufacturing process and robust CAR T cell expansion

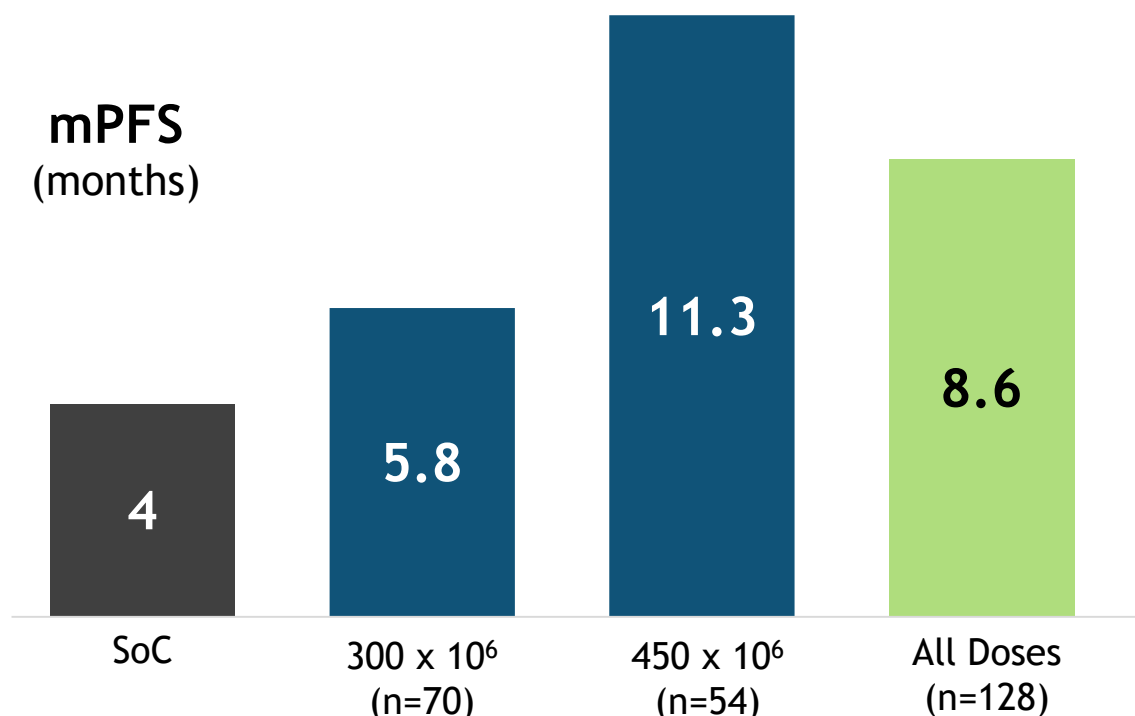Dose escalation is complete. Continue to evaluate safety and efficacy at recommended phase 2 dose of 450 x 10^6 dose

KarMMa topline data readout

ide-cel (bb2121): positive pivotal data

mPFS
(months)

	150 x 10⁶ CAR+ T cells (N=4)	300 x 10⁶ CAR+ T cells (N=70)	450 x 10⁶ CAR+ T cells (N=54)	All Doses (N=128)
ORR, n (%)	2 (50.0)	48 (68.6)	44 (81.5)	94 (73.4)
CR/sCR, n (%)	1 (25.0)	20 (28.6)	19 (35.2)	40 (31.3)
Median DoR, mo	---	9.9	11.3	10.6

- **Heavily pretreated population**
  - 94% refractory to anti-CD38, 84% triple refractory
  - All patients were refractory to their last treatment (progression during or within 60 days of last therapy)

- **Deep and durable responses across dose levels**
  - mPFS of >11mo at the 450 x 10⁶ dose
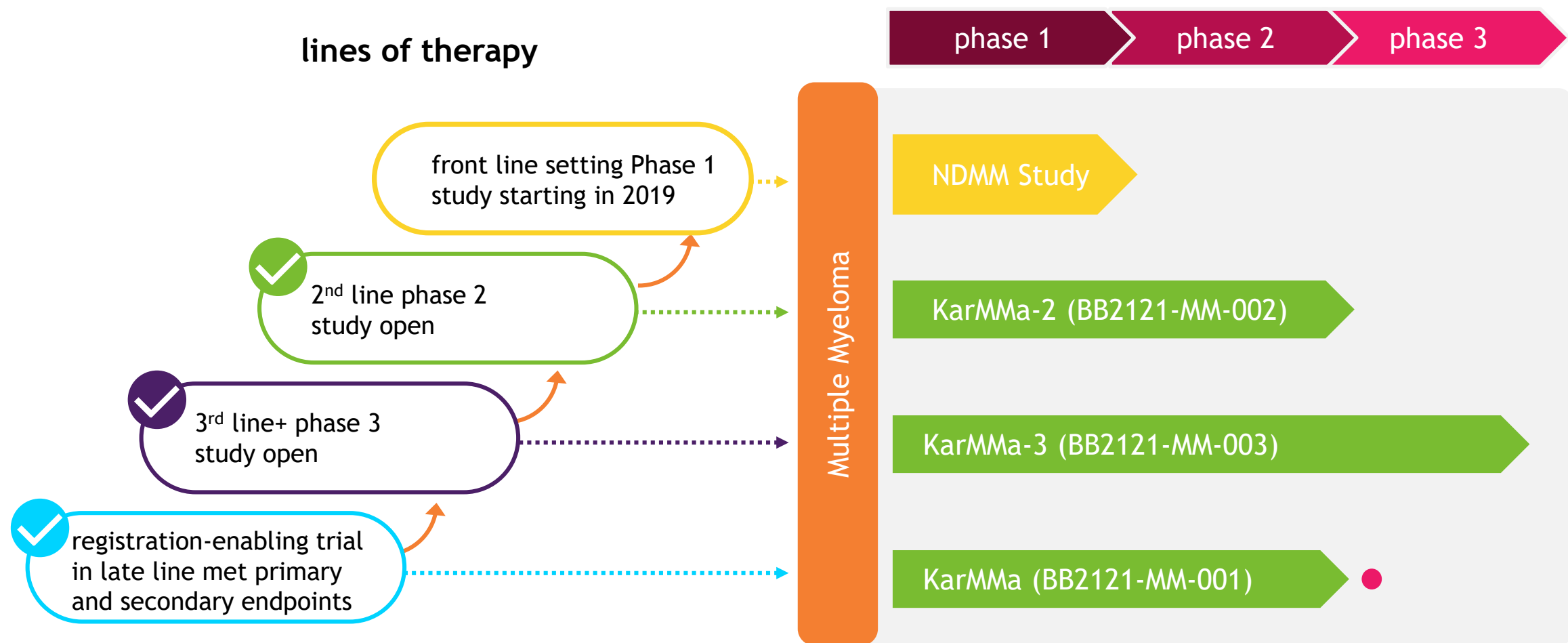 - Durability is consistent across doses

- **Safety consistent with the Ph1 data**
  - Gr ≥ 3 CRS and iiNT were reported in <6% of subjects at each target dose
  - CRS and iiNT of any grade occurred in 83.6% and 18% of patients, respectively

iiNT: investigator identified neurotoxicity
Ide-cel is being developed in collaboration with Bristol-Myers Squibb

Advancing ide-cel (bb2121) into earlier lines of multiple myeloma

lines of therapy

phase 1	phase 2	phase 3

Multiple Myeloma

front line setting Phase 1 study starting in 2019
→ NDMM Study

2nd line phase 2 study open
→ KarMMa-2 (BB2121-MM-002)

3rd line+ phase 3 study open
→ KarMMa-3 (BB2121-MM-003)

registration-enabling trial in late line met primary and secondary endpoints
→ KarMMa (BB2121-MM-001)

● Planned 1H:2020 regulatory submission

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closing

bbb at ASH 2019:

LentiGlobin TDT	• Patients achieving and maintaining TI across genotypes • Launch progressing in EU
LentiGlobin SCD	• Clinical impact underscored by impact on underlying disease • Program gradually expanding
bb21217	• Indication of hypothesis bearing out • Further investigation underway
ide-cel (bb2121)	• Topline data support 1H:2020 regulatory submission • Development path in earlier lines of therapy progressing

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