bluebirdbio®
recode for life™

ready to recode

company presentation

october 2019

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, the timing or likelihood of regulatory filings and approvals, 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.

potential catalysts

by end of year

ZYNTEGLO (autologous CD34+ cells encoding $\beta^{A\text{-}T87Q}$ globin gene)

- Initiation of U.S. BLA Rolling Submission
- Northstar-2 and Northstar-3 Data Update

LentiGlobin SCD

- HGB-210 Study Start
- HGB-206 Group C Data Update

ide-cel (bb2121) MM

- KarMMa Data*

bb21217 MM

- CRB-402 Data Update

cash position as of June 30, 2019

$1.54B

cash runway into 2022

*Driven by Celgene/BMS

WE RECODE FOR LIFE

RADICAL CARE

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

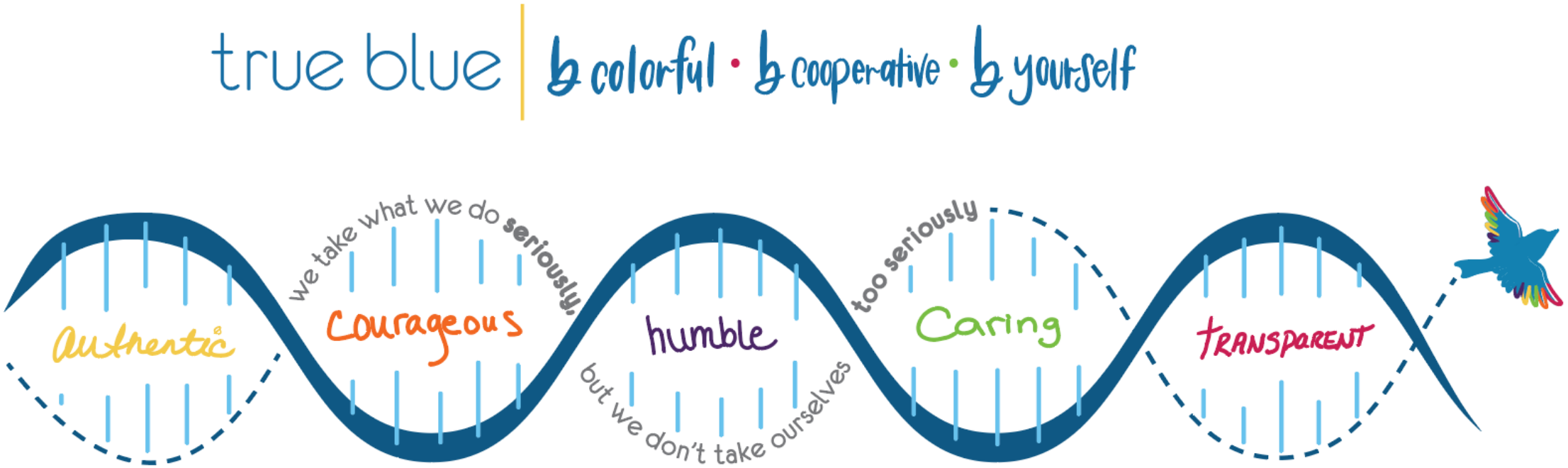
THIS IS PERSONAL

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

PIONEERS WITH PURPOSE

We're exploring new frontiers for the sake of patients.

we live by our non-negotiables



our 2022 vision - just got bolder

LentiGlobin TDT
2019 EU Approval
2020 U.S. Potential Approval

LentiGlobin SCD
2022 Potential Filing/Approval

Lenti-D CALD
2021 Potential Approval

ide-cel (bb2121)
Multiple Myeloma
2020 Potential Approval

4 Products on the Market

5+ Clinical Programs

1-2 INDs Per Year Beginning 2020

LET'S
RECODE
THE SYSTEM

Keeping it Focused on the Patient: Living with TDT

- **Potentially fatal genetic disease caused by mutations in the β-globin gene that result in reduced or absent hemoglobin**
- **Despite advances in iron management, TDT patients suffer from serious complications and organ damage caused by excess iron**
- **TDT patients have a lifelong challenge and currently rely on chronic treatments that accumulate in costs over decades**

LAURICE'S EXPERIENCE:

- Hemoglobin of 6.9 g/dL growing up [normal range for females: 12.1-15.1 g/dL][1]
- Congestive heart failure at 9 and 25
- Splenectomy at 10, tonsillectomy at 13, gall bladder removal at 22
- Severe osteoporosis
- Chronic pain
- Under care of PCP, cardiologist, hematologist, endocrinologist, and a pain specialist
- Lost many friends with TDT

1. National Institutes of Health (NIH). *Hemoglobin*. https://medlineplus.gov/ency/article/003645.htm.

TDT – Initial Launch Focus

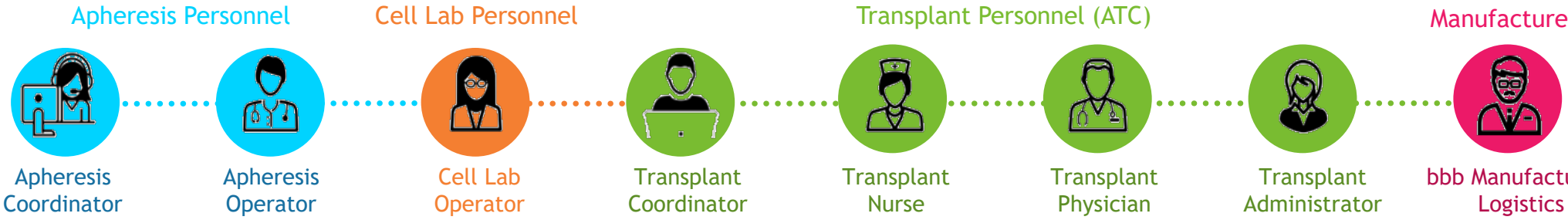
	EU Anticipated 1st Indication Patients* non-β^0/β^0; age ≥12; no matched related donor	Estimated total TDT Patients	Trial Site in Country?	Patient concentration
Germany	80-100	200-350	Yes	6 centers see ~50% of patients
Italy	2,000-2,200	6,500-7,500	Yes	73 centers see ~80% of patients
UK	200-300	500-600	Yes	15 centers see ~75% of patients
France	100-150	400-500	Yes	6 centers see ~50% of patients

EST TOTAL TDT:
3,500-4,000

EST TOTAL TDT:
1,400-1,500

*Numbers represent addressable patient population

preparing to serve patients in Europe



launch expectations

1. Optimal patient experience through a seamless delivery network
2. Steady country by country launch with progressive build
3. Get the model right for long term success
4. Advance value-based payment over time reimbursement

1 drug product manufacturing

Munich, Germany

9 qualified treatment centers at country launch

3 - Germany
4 - Italy
2 - UK
4 - France (in 2020)*

*Will support future launches in 2020+

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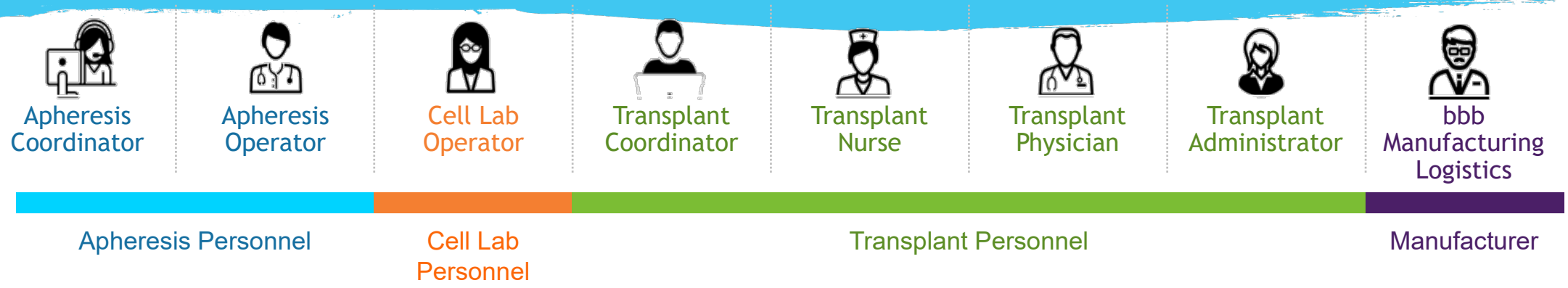
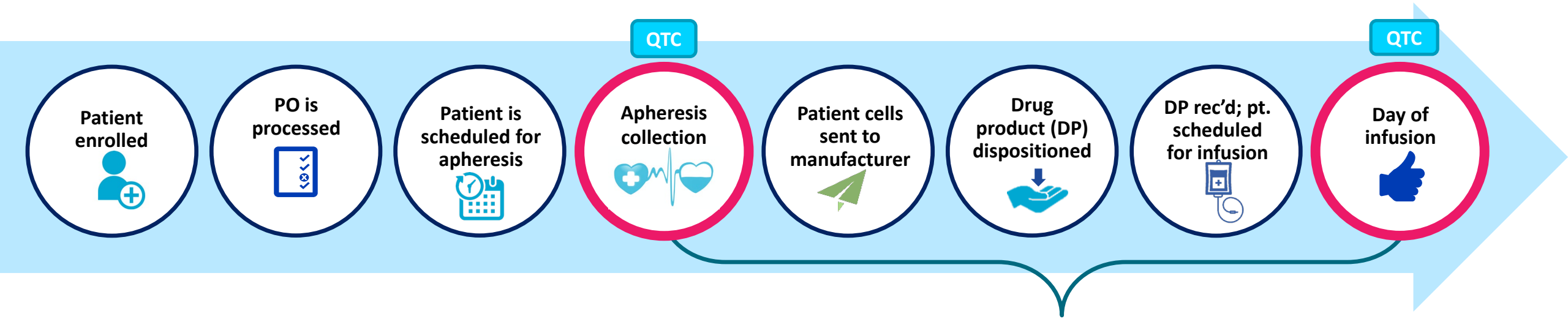
The Patient Journey is an Organizing Framework for bluebird QTC Support





bluebird bio system in place to support steps in patient treatment pathway

6-8 weeks from apheresis to infusion in TDT

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A system NOT setup for one-time potentially curative treatments

CNBC

"The debate over price is fundamentally a debate over access. Gene therapies and other treatments that can cost millions of dollars can still be a relative bargain for what they give patients and society if they're able to cure a disease that would severely limit or even end life."

Scott Gottlieb, M.D. Former FDA Commissioner

HEALTH PAYER INTELLIGENCE

"While … therapies that are in the pipeline offer the promise of dramatic health improvements, their upfront costs are significant, which makes it **imperative that we work together to find creative, value-based payment approaches that tie reimbursement level to both short-term and long-term efficacy."**

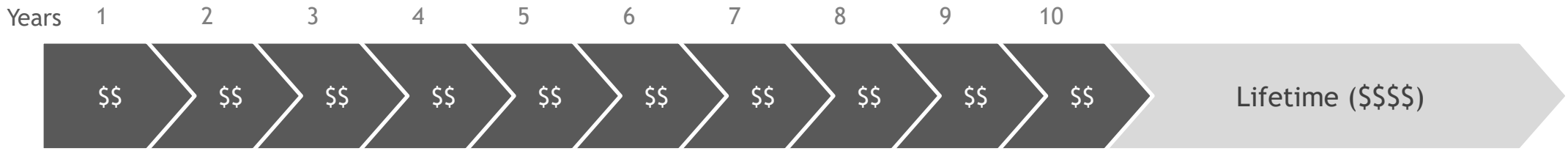
Michael Sherman, M.D.
Harvard Pilgrim Chief Medical Officer

FiercePharma

"Gene therapy either works or it doesn't… **If the product succeeds, it should be reimbursed at a robust level**, because the pharmaco-economics over the course of time are extremely positive. **If it doesn't work, the payer, whether it's public or private, shouldn't have to bear the burden. We're moving in that direction."**

Peter Pitts
Former FDA Assistant Commissioner

TRADITIONAL CHRONIC FOR LIFE MODEL



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Our commitment to recode the status quo

BLUE VALUE PRINCIPLES

- Focus on patient innovation and access
- Creative and disruptive
- Flexible and share risk
- Transparent, proud and proactive
- Don’t do silly short-sighted stuff

&

Unapologetically fund & reward innovation that matters

Focus on **real value** delivered to the patient & system

Don’t truncate value because it’s a one-time potentially curative treatment

Don’t price at what you can get away with or what the market can bear

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Our approach – VALUE-BASED PAYMENT over time based on OUTCOME

	OBJECTIVE	STRATEGIC APPROACH
1	FAIR VALUE RECOGNITION	✓ *Lifetime cost-effectiveness timeframe* ✓ *Base value only on patient QOL and Life Extension*
2	SHARED RISK	✓ *Pay ONLY IF the treatment works* ✓ *Put UP TO 80% of the price at risk based on success*
3	PER PATIENT AFFORDABILITY	✓ *Spread payments over UP TO A FIVE YEAR period* ✓ *NO PRICE INCREASES above CPI*
4	HEALTH SYSTEM AFFORDABILITY	✓ *NO COST after payment period (vs. for life)* ✓ *Recode system to catalyze change*

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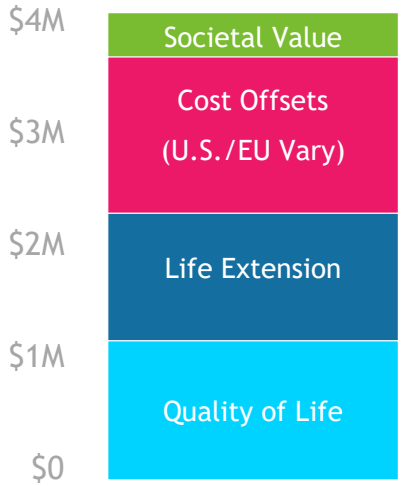
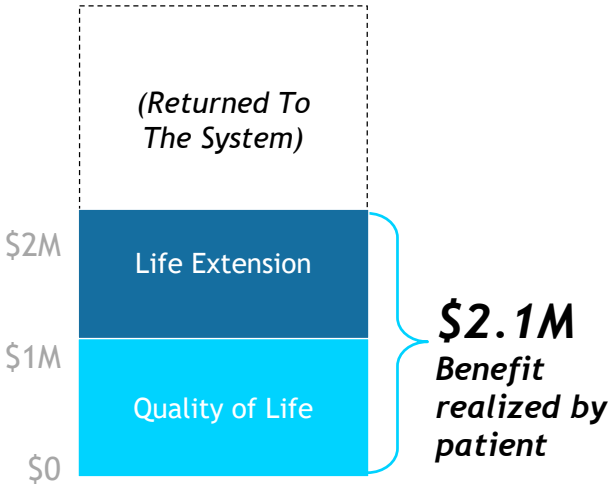
What has (and has not) gone into assessing the value of ZYNTEGLO®?

We measure the value of ZYNTEGLO based on impact on patients:
Life extension and quality of life improvements*

Traditional
All Inclusive Calculation



ZYNTEGLO
Intrintic Value



ZYNTEGLO
Actual Price Considerations

- The expected lifelong clinical benefits of ZYNTEGLO drive its intrinsic value
- The resulting cost offsets are returned to the healthcare system
- The ZYNTEGLO payment model protects health care systems from bearing the cost of ineffective therapy
- ZYNTEGLO is a good health care investment and is cost-effective when considering a range of accepted thresholds in Europe

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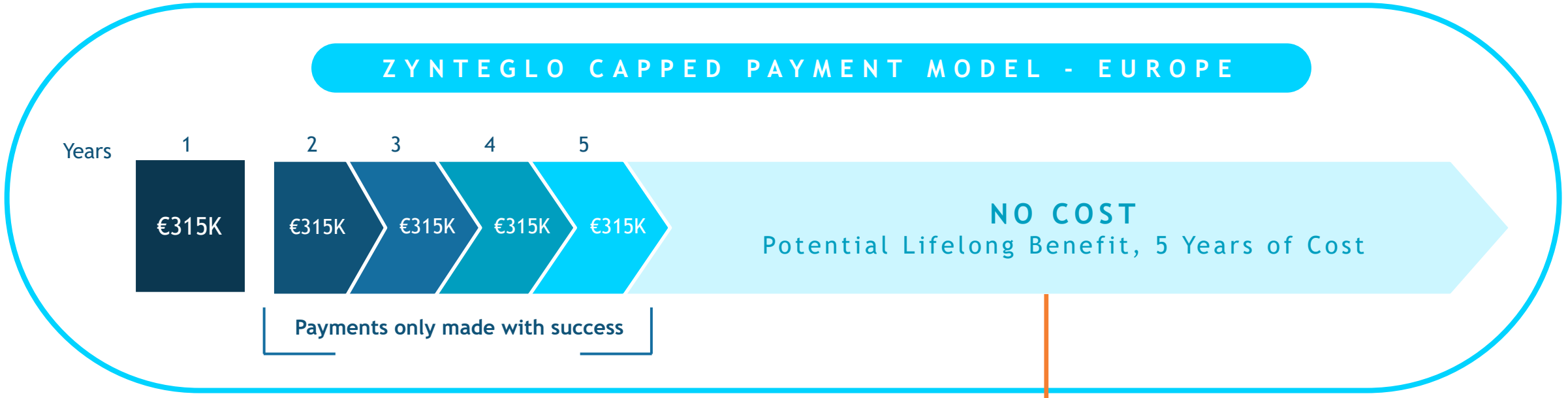
*We have quantified the impact on patient quality of life, survival, treatment cost and society using established health economic modeling techniques.

ZYNTEGLO® payment and pricing: value & outcome based, 5 year cap @ risk



- ✓ First Year Payment: €315K*
- ✓ Five Year Total Payment With 100% Success: €1.575M

A one-time treatment expected to deliver lifelong benefit with 5 years of cost versus continual, lifelong treatment and cost

*Based on exchange rate of 1 Euro = $1.13196 USD on June 12, 2019, First Year Payment in USD terms is: $356,567; Five Year Total Payment With 100% Success: $1,782,837

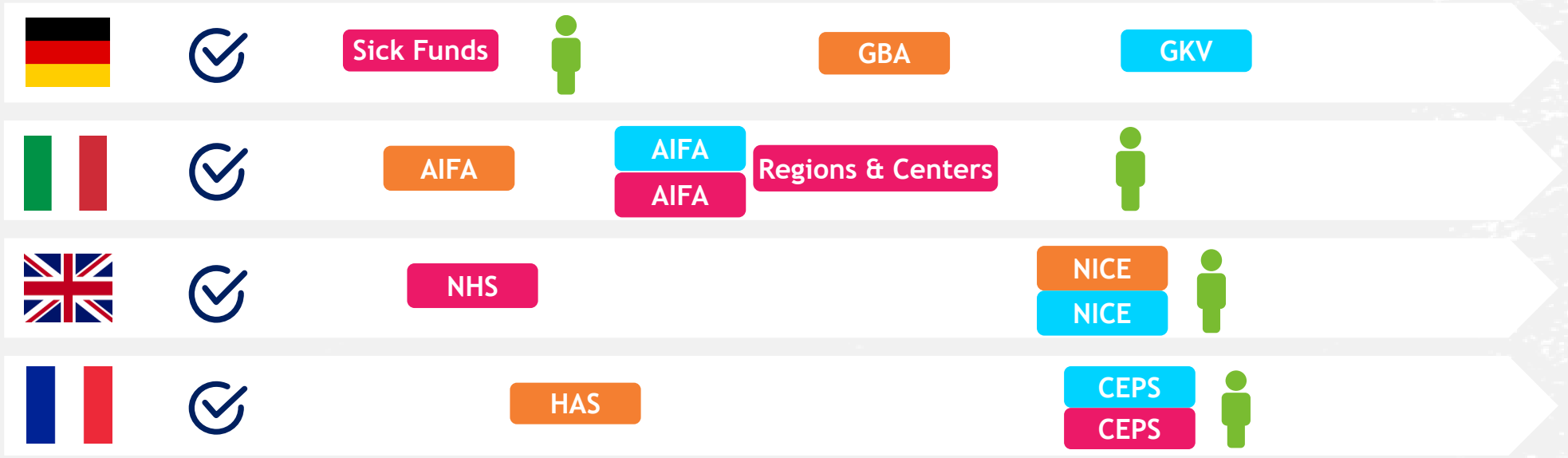
What are next steps and how is launch readiness progressing?

EC Decision

- Team in place; completing set-up and working to activate QTCs
- Actively engaging payers
- Progressing forward with dossier submissions
- Working in collaboration with EMA to finalize commercial drug product specifications and manufacturing parameters

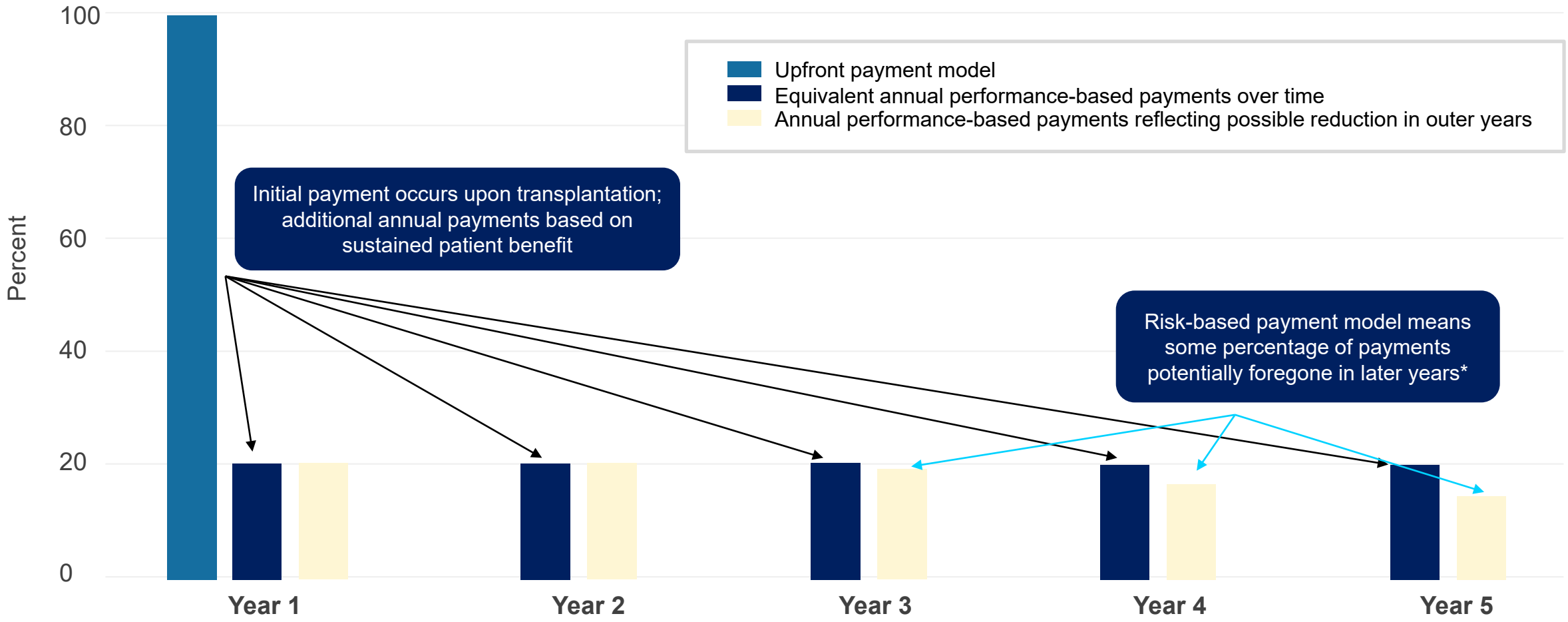
Each Journey is Different

Country-by-Country Recoding Will Play Out Over Time



Recoding the Payment Model

Payment Modeling Scenarios



*Illustrative reduction in payments

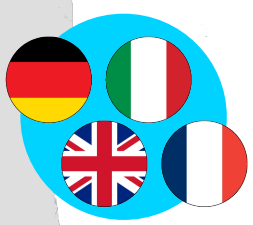
BLUE style commercial success factors

In the near-term, product revenue is not the most telling indicator on European TDT launch progress

- Payment models may vary by country
- Focus on establishing the commercial model and operations for the long-term

Performance metrics that we will be tracking and sharing

QTC contracts in place



Pricing approval by country

Commercial patient infusions

Learnings and local market insights to inform continuous innovation

Transfusion-Dependent β-Thalassemia (TDT)

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

program overview

- CHMP positive opinion granted on March 29
- EU approval granted June 2019
- General regulatory agreement with FDA for BLA filing
- Studies ongoing:
  - Northstar-2 (HGB-207)
  - Northstar-3 (HGB-212)
- Long-term follow-up: LTF-303

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conditional approval granted in EU for patients with TDT and non-β^0/β^0 genotypes

Gene therapy for patients 12 years and older with transfusion-dependent β-thalassemia (TDT) who do not have a β^0/β^0 genotype, for whom hematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte antigen (HLA)-matched related HSC donor is not available

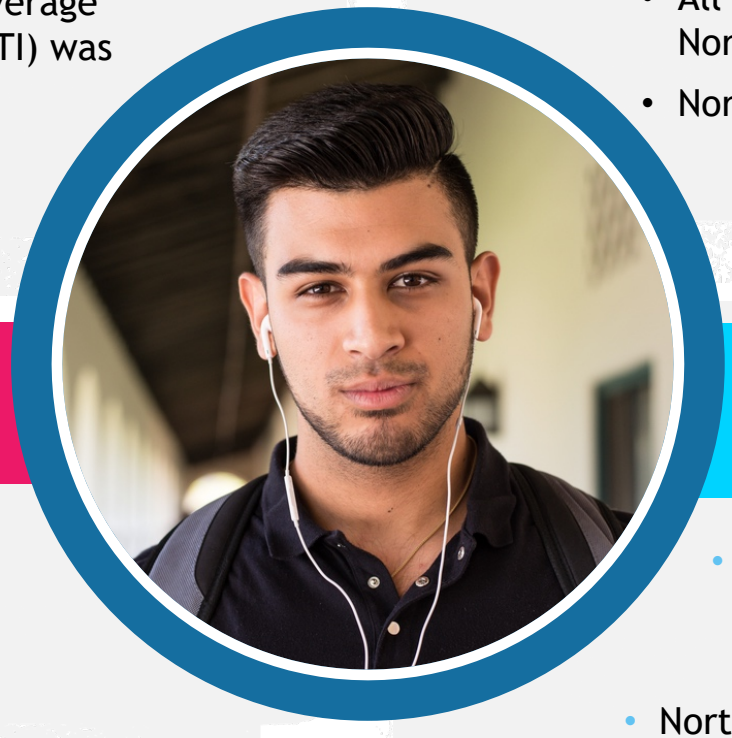
ZYNTEGLO® is the first and only one-time therapy for TDT now approved in the EU for people with TDT and non-β^0/β^0 genotypes

ZYNTEGLO has the potential to increase total Hb to normal levels

- Northstar-2 (HGB-207): Median weighted average total Hb during transfusion independence (TI) was 12.4 g/dL (n=4)

Following engraftment and achievement of TI, the effects of ZYNTEGLO are expected to be lifelong

- All non- β^0/β^0 patients in Northstar (HGB- 204) and Northstar-2 who achieved TI, maintained TI
- Northstar: TI maintained up to 3.8 years
  - Northstar: Reduction in iron overload seen at 4 years (n=4)



The majority of evaluable patients achieved TI

- Northstar and HGB-205: 11/14 patients with non-β^0/β^0 genotypes achieved TI
- Northstar-2: 4/5 patients achieved TI

Gene therapy derived Hb (HbA^{T87Q}) supports total Hb production soon after infusion

- Northstar-2: Median total hemoglobin at 6 months: 11.9g/dL; HbA^{T87Q} was 9.5 g/dL (n=11)
- Northstar, non-β^0/β^0 patients: Median 6 month Hb was 9.7 g/dL; HbA^{T87Q} was 4.7 g/dL (n=10)

Full Indication: Gene therapy for patients 12 years and older with transfusion-dependent β-thalassemia (TDT) who do not have a β^0/β^0 genotype, for whom hematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte antigen (HLA)-matched related HSC donor is not available

Data as of 13 December 2018

broad TDT clinical development program continues

NORTHSTAR STUDY	HGB-204 *Complete*	• Original manufacturing process • All genotypes • N=18
HGB-205	HGB-205 *Complete*	• Original manufacturing process • N=4
NORTHSTAR-2 STUDY	HGB-207	• Refined manufacturing process • Non-β^0/β^0 genotypes • N=23
NORTHSTAR-3 STUDY	HGB-212	• β^0/β^0 genotypes • Refined manufacturing process • N=15

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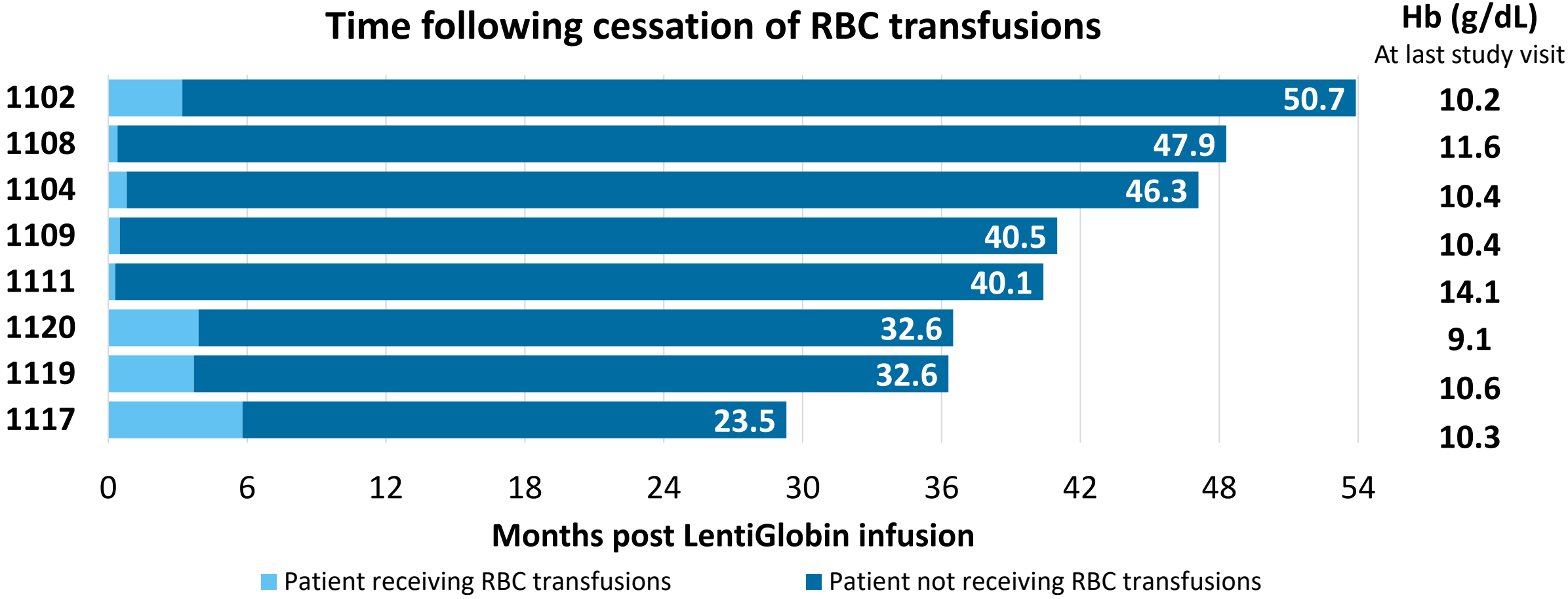
HGB-204: 8/10 patients with non-β^0/β^0 genotypes achieved transfusion independence

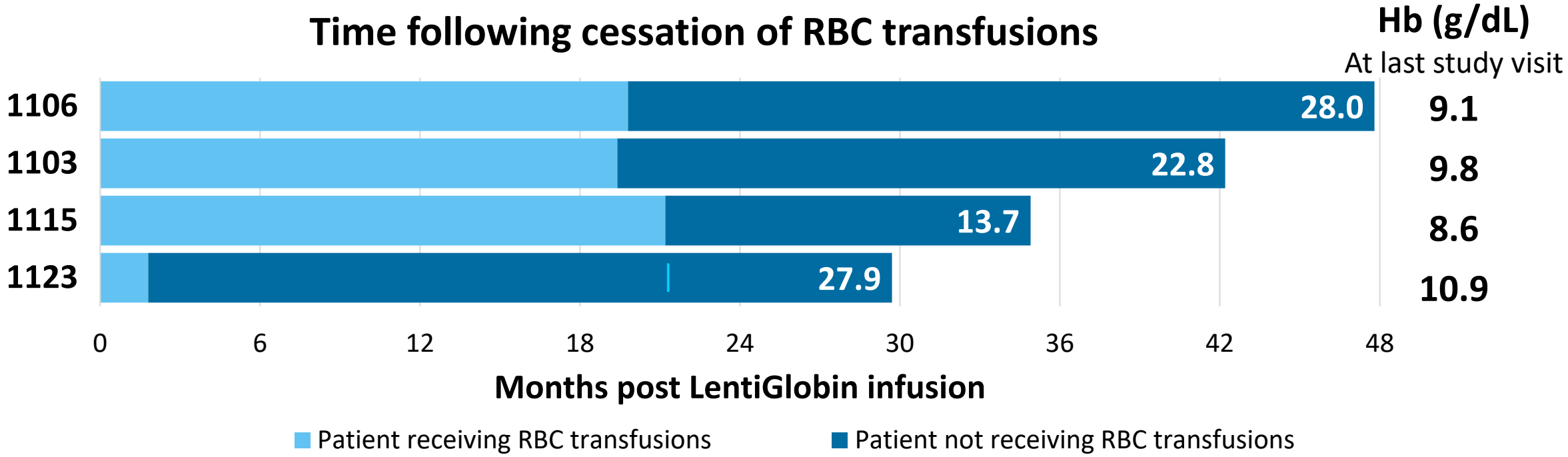


Median duration of TI: 38.0 months (min – max: 21.2 – 45.3 months); responses are ongoing
Median weighted average Hb during TI: 10.3 g/dL (min – max: 9.3 – 13.2 g/dL)

Definitions: Hb, hemoglobin; RBC, red blood cell; TI, transfusion independence (weighted average Hb ≥ 9 g/dL without RBC transfusions for ≥ 12 months)

Data as of 13 December 2018

HGB-204: 4/8 patients with β^0/β^0 genotypes have been transfusion free for > 12 months



3/8 patients with β^0/β^0 genotypes have achieved transfusion independence
(weighted average Hb ≥ 9 g/dL without any red RBC transfusions for ≥ 12 months)

Median duration of TI: 16.4 months (min – max: 16.1 – 20.8 months)
All responses are ongoing

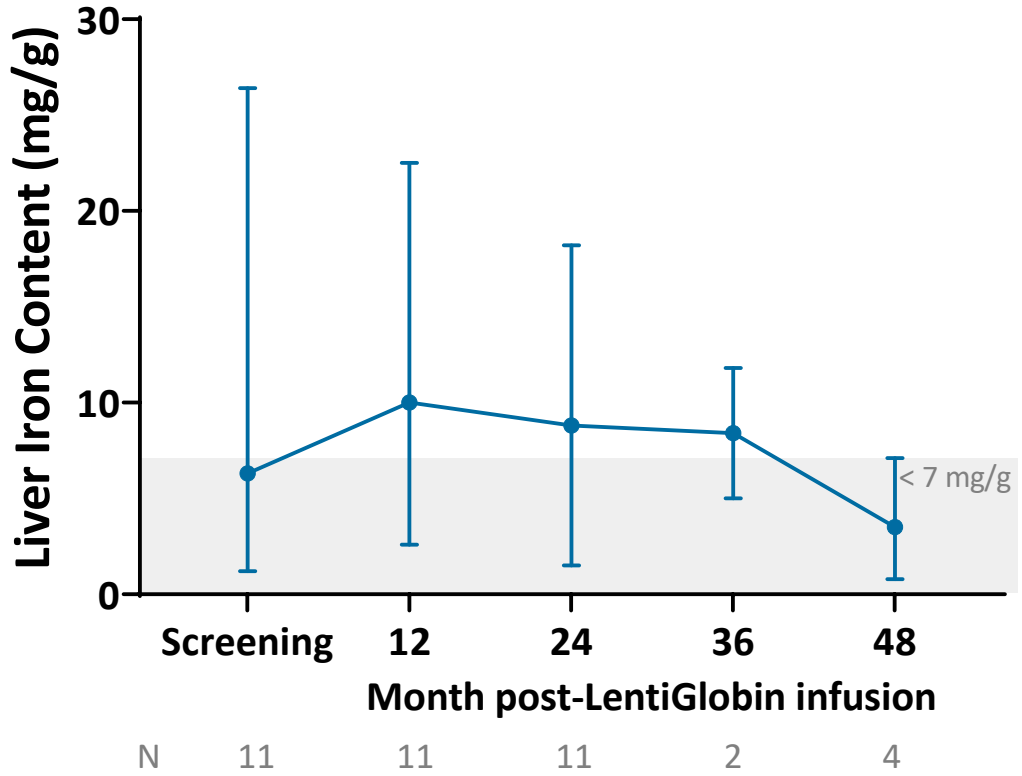
Median weighted average Hb during TI: 9.9 g/dL (min – max: 9.5 – 10.1 g/dL)

| Patient had a single transfusion for an acute event of cat scratch disease. Hb, hemoglobin; RBC, red blood cell; TI, transfusion independence

HGB-204: liver iron concentration decreased in patients who achieved transfusion independence

56% median reduction in LIC between baseline and M48 with re-initiation of iron chelation

(min – max: 38% – 83%; N=4)



Patients re-initiated iron chelation therapy a median of 13 months after LentiGlobin infusion (min – max: 2 – 15 months)

Medians (min, max) depicted
Definitions: LIC, liver iron concentration; M, month

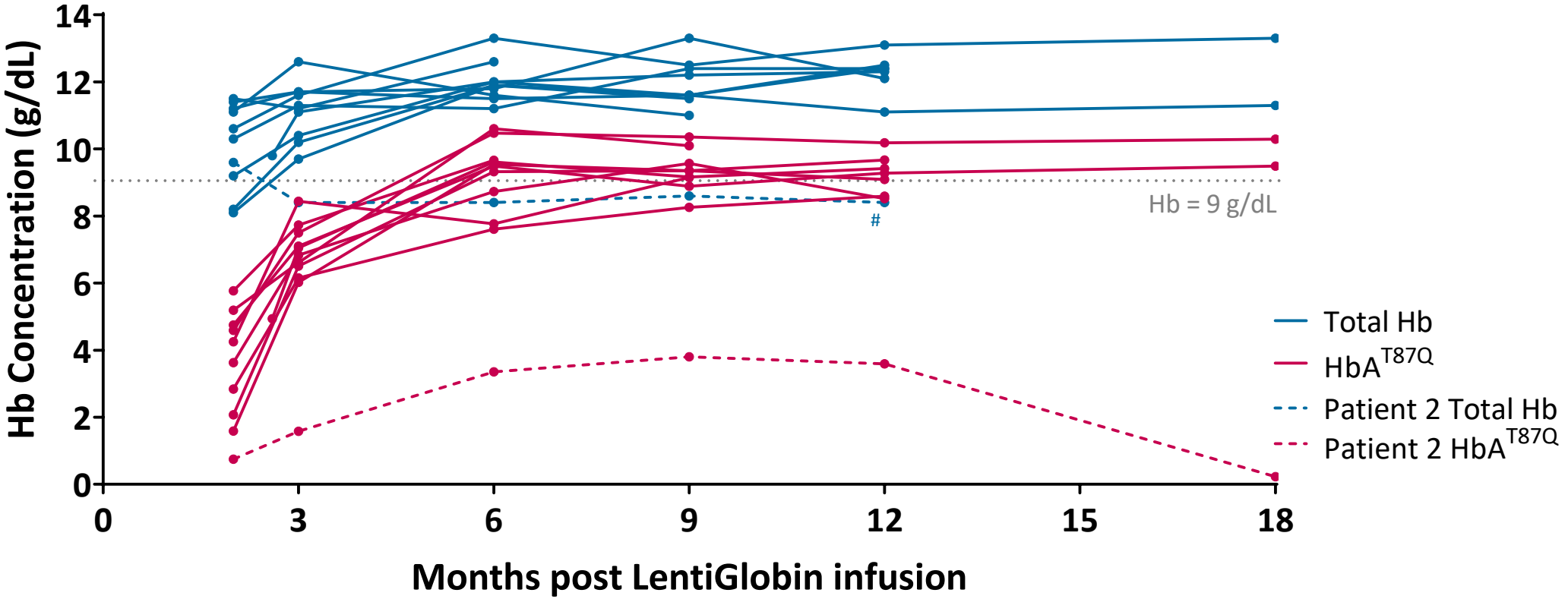
Data as of 13 December 2018

HGB-207: stable total Hb and gene therapy-derived HbA^{T87Q} in 10/11 patients with ≥ 6 months follow-up

NORTHSTAR-2 STUDY

Median Hb in patients free from transfusions at last study visit (g/dL)

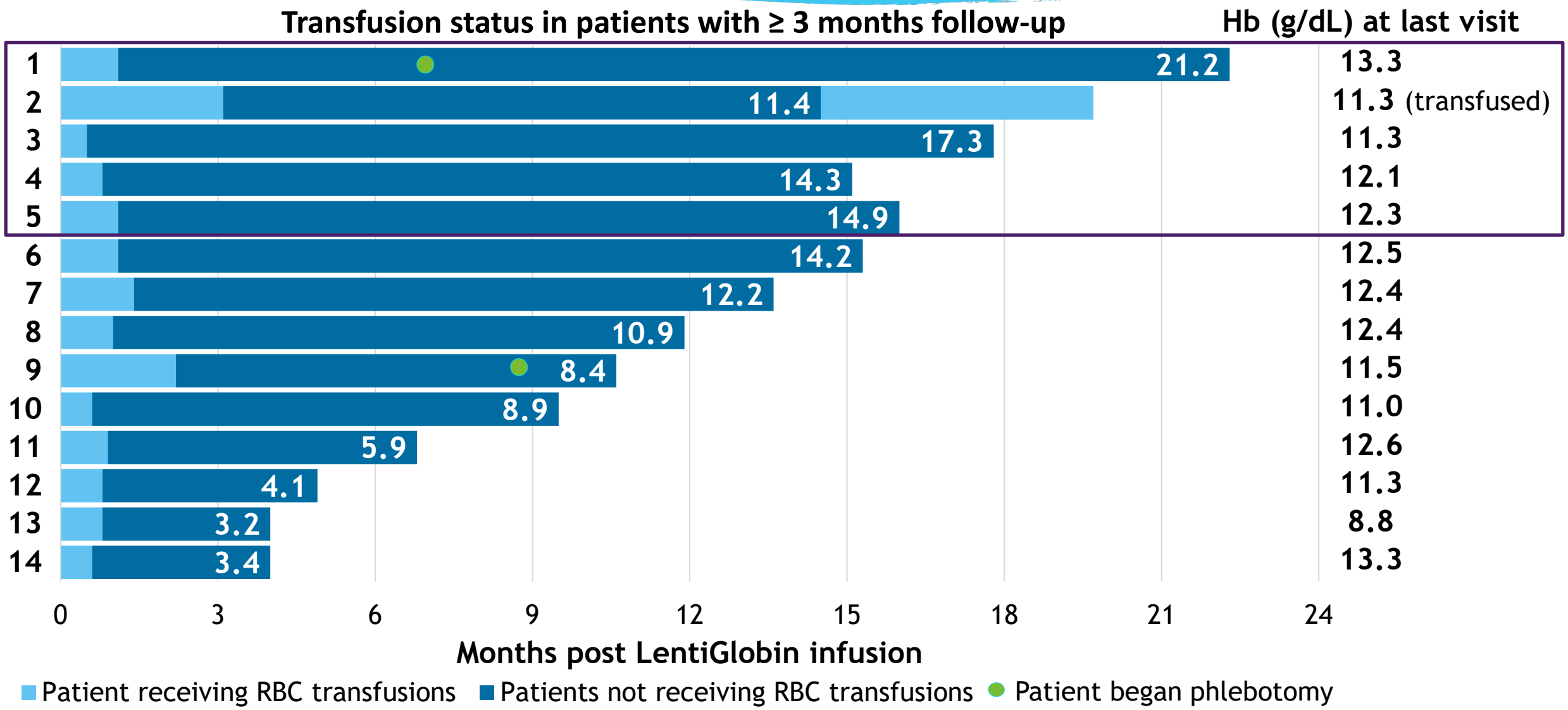
	M6 (n=10)	M9 (n=9)	M12 (n=7)	M18 (n=2)
Total Hb	11.9	11.6	12.4	12.3
HbA^{T87Q}	9.5	9.4	9.3	9.9



#Last Hb before patient restarted red blood cell transfusions
Definitions: Hb, hemoglobin

Data as of 13 December 2018

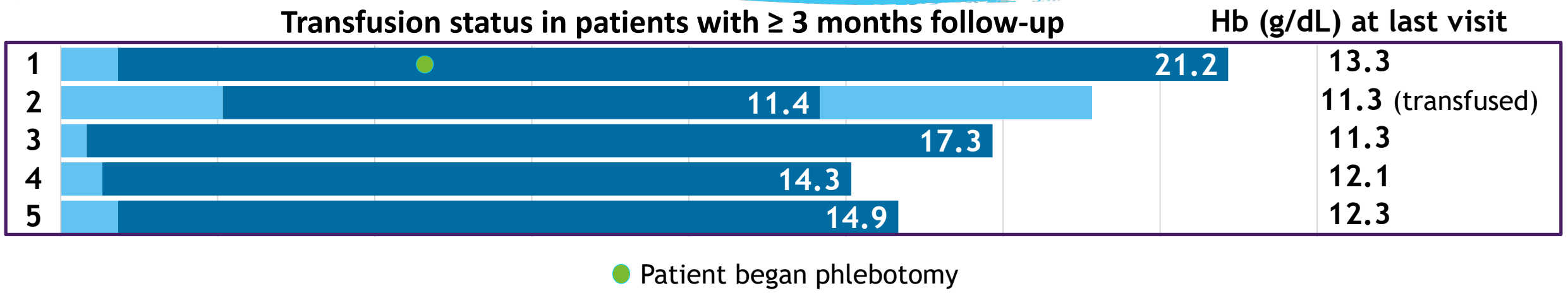
HGB-207: 8.8 – 13.3 g/dL total Hb in patients who have stopped RBC transfusions for ≥ 3 months (n=13)



Definitions: Hb, hemoglobin; RBC, red blood cell

Data as of 13 December 2018

HGB-207: 4/5 (80%) evaluable patients achieved the primary endpoint of transfusion independence

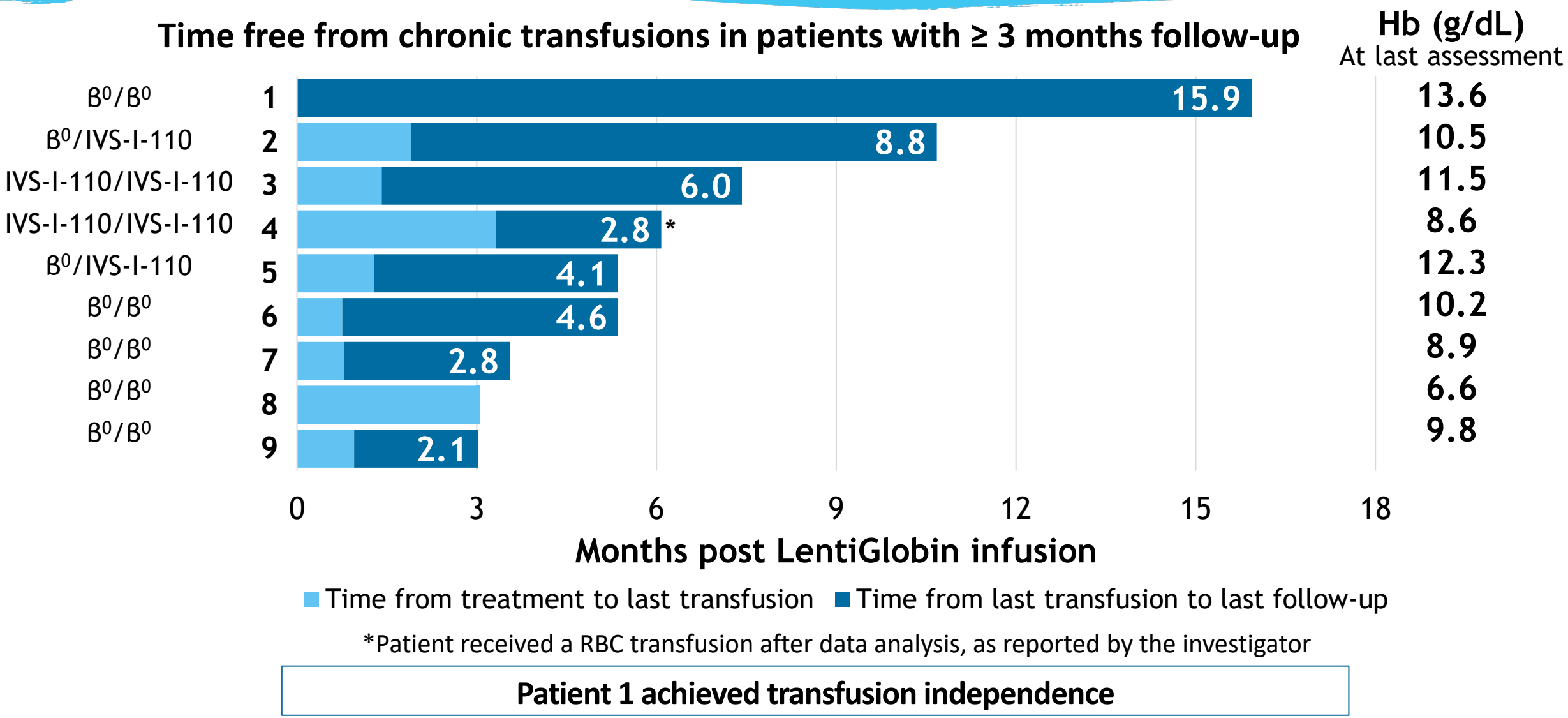


- **4/5 (80%) evaluable patients achieved the primary endpoint of transfusion independence (TI)**
  Weighted average hemoglobin ≥ 9 g/dL without any transfusions for ≥ 12 months
- **Median duration of TI: 13.6 months** (min – max: 12.0 – 18.2 months)
  All responses are ongoing
- **Median weighted average Hb during TI of 12.4 g/dL** (min – max: 11.5 – 12.6 g/dL)

Definitions: Hb, hemoglobin; RBC, red blood cell

Data as of 13 December 2018

HGB-212: Hb of 10.2 – 13.6 g/dL in patients off RBC transfusions for ≥ 3 months (n=5)



*Patient received a RBC transfusion after data analysis, as reported by the investigator

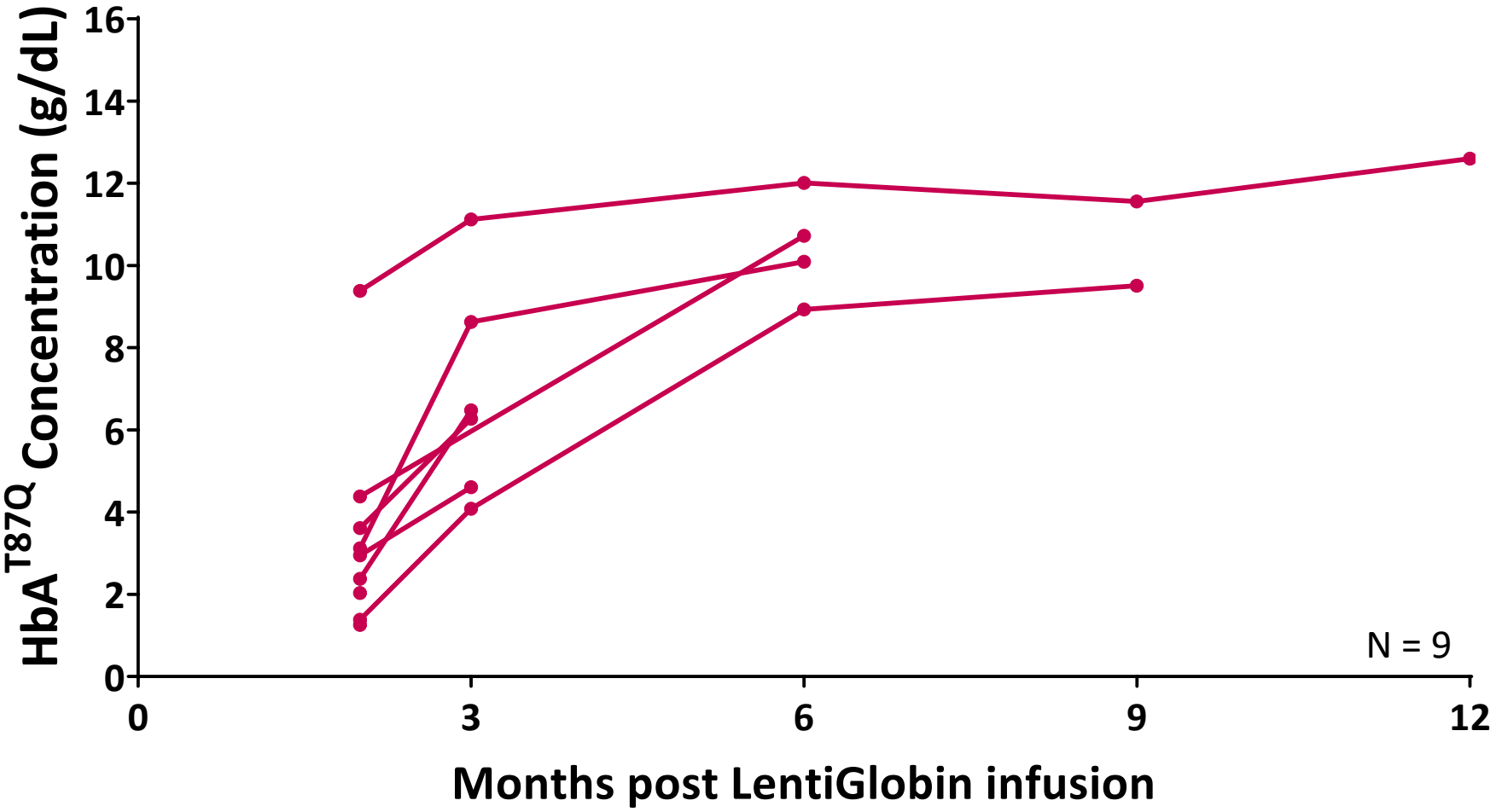
Patient 1 achieved transfusion independence

Definitions: Hb, hemoglobin; RBC, red blood cell

Data as of 12 April 2019

HGB-212: HbA^{T87Q} in patients following treatment with LentiGlobin

All patients at month 6 have HbA^{T87Q} ≥ 8 g/dL (n=4)



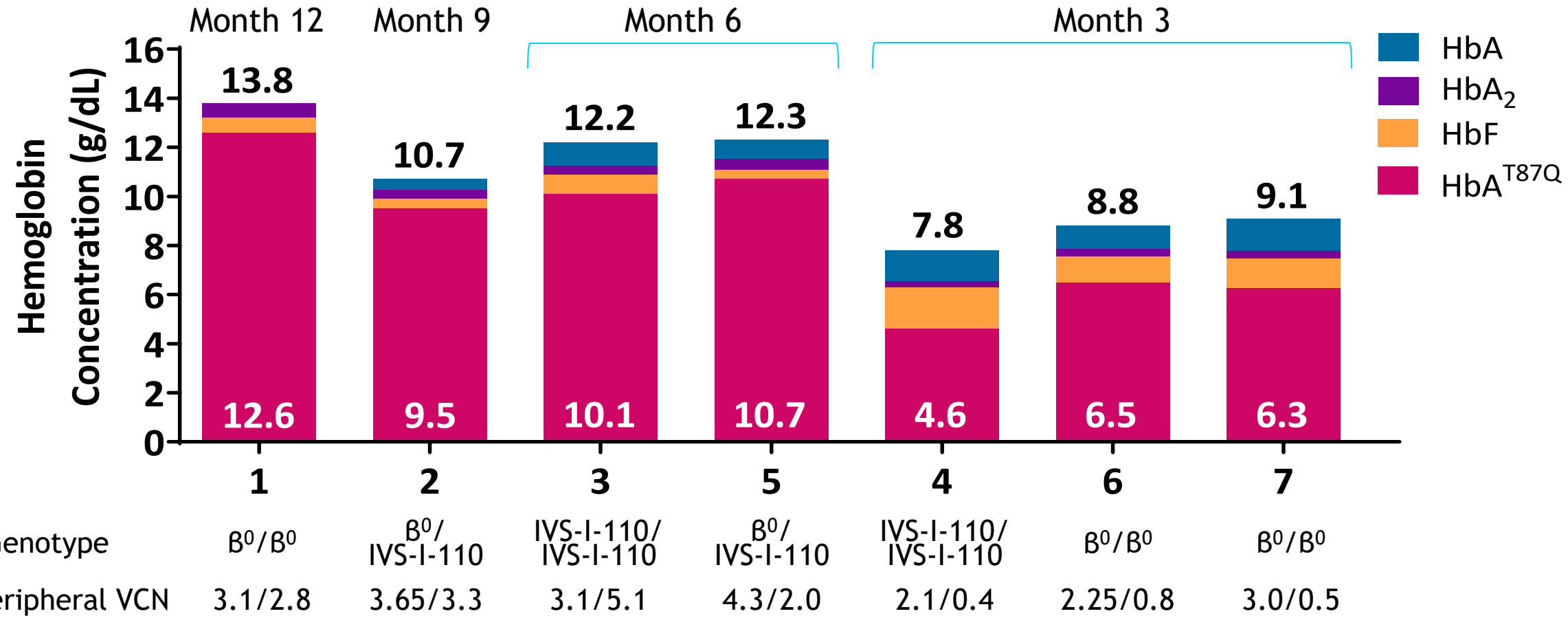
Definition: Hb, hemoglobin

Data as of 12 April 2019

HGB-212: gene therapy-derived HbA^{T87Q} significantly contributes to Hb

59 - 91% of total Hb is HbA^{T87Q}

Hb fractions in patients with ≥ 3 month visit



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

Data as of 12 April 2019

Sickle Cell Disease (SCD)

- Severe blood disorder that causes anemia, frequent pain crises and shortened lifespan
- Global annual birth incidence ~ 300,000 – 400,000
- Mean age of death in the U.S. is 44 years[1]

program overview

- Plan to pursue accelerated development path based on hematological primary endpoint
  - Phase 3 study to begin in 2019
- HGB-206 amended and Group C expanded

[1]Paulukonis et al, California's Sickle Cell Data Collection Cohort, 2005-2015* ASH 2017*

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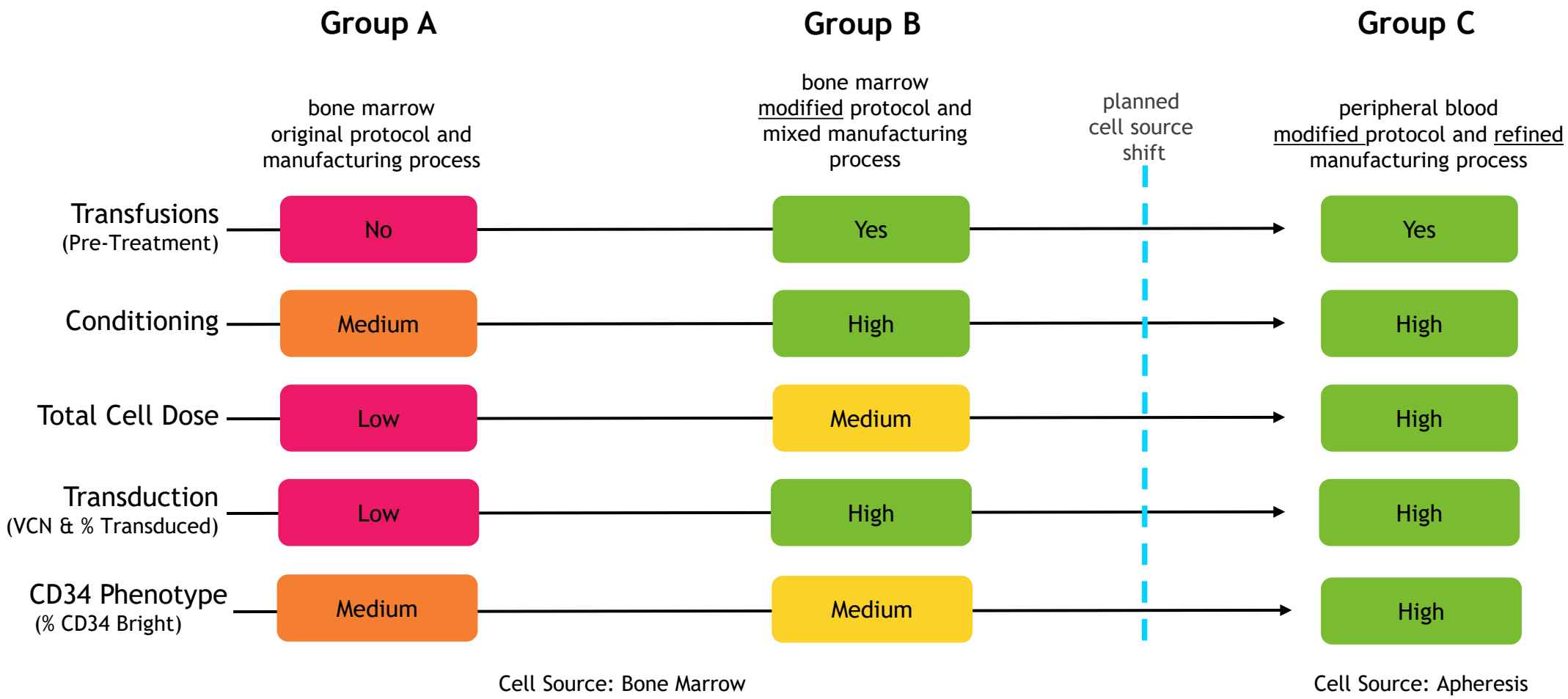
HGB-206: evolution of LentiGlobin in SCD



HGB-206 group C: patient characteristics

N=19 patients who started cell collection

HGB-206

Parameter	Group C N=19
Age at consent, years median (min - max)	26 (18 - 36)
Gender	8F 11 M
Genotype, β^S/β^S	19
SCD History	
Hydroxyurea[#], n	11
VOCs[*], n	15
Annualized no. of events, median (min – max)	4.0 (2.0 - 13.5)
ACS[†], n	2
Annualized no. of events, median (min - max)	1 (1 - 1)
Stroke, n	3
TRJV > 2.5 m/s, n	1

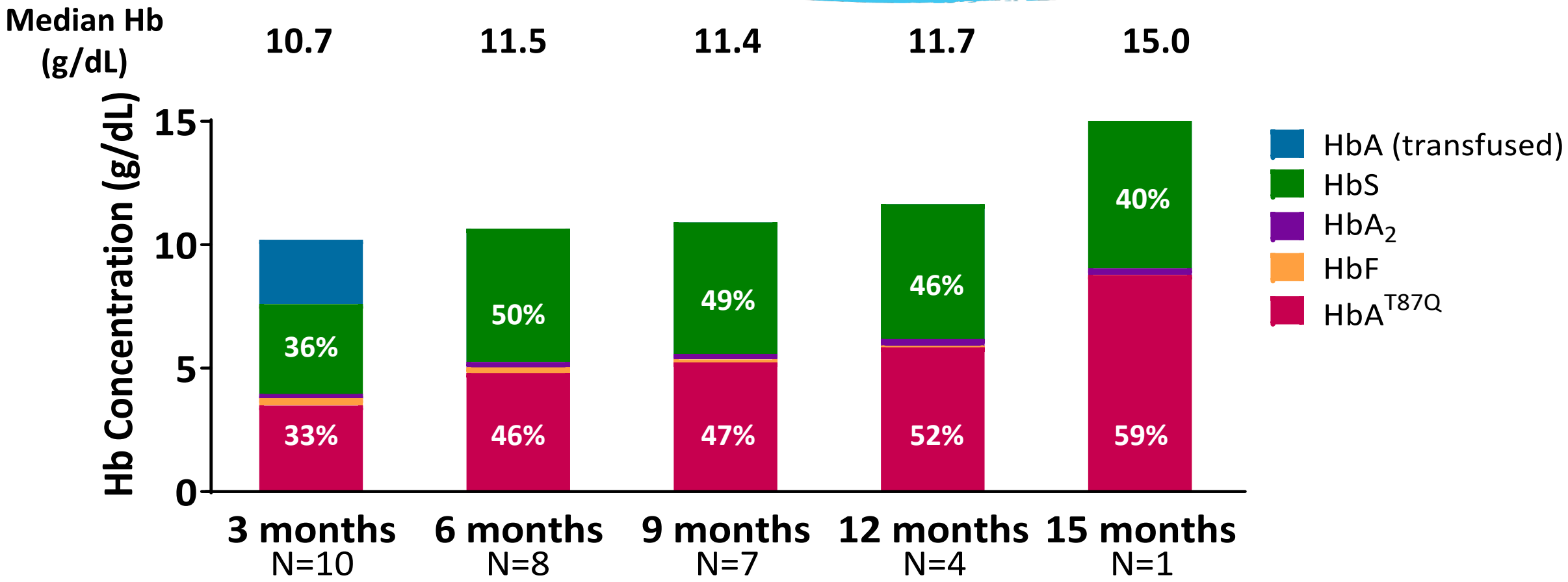
[*]≥ 2 events/year in preceding 2 years; [†]≥ 2 episodes in preceding 2 years, with ≥ 1 episode in the past year or in the year prior to the initiation of regular transfusions; [#]Within 30 days prior to informed consent

Definitions: ACS, acute chest syndrome; F, female; M, male; TRJV, tricuspid regurgitant jet velocity; VOC, vaso-occlusive crisis

Data as of 7 March 2019

HGB-206 group C: median HbS ≤ 50% of total Hb in patients with ≥ 6 months of follow-up post LentiGlobin treatment

HGB-206



Total Hb and HbA^{T87Q} ranged from 10.2 - 15.0 g/dL and 4.5 - 8.8 g/dL, respectively, at last visit in patients with ≥ 6 months of follow-up

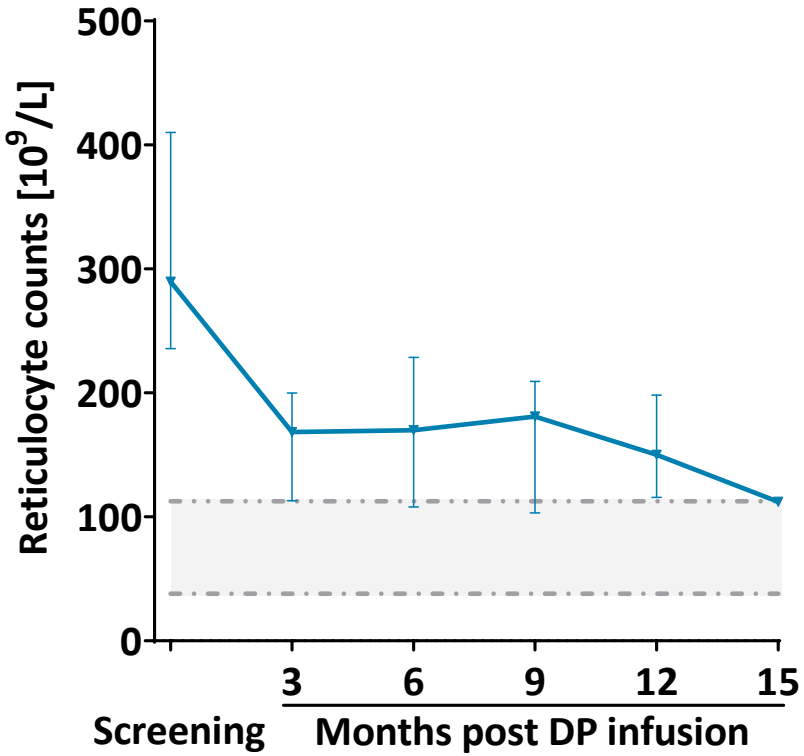
Definitions: % represent median Hb fractions as % of total; Hb, hemoglobin

Data as of 7 March 2019

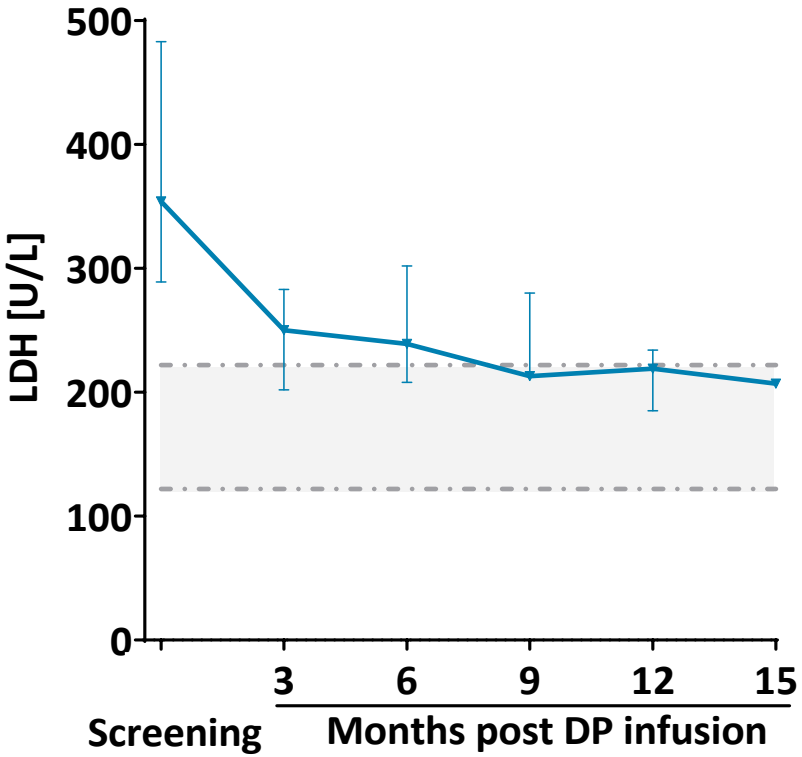
HGB-206 group C: decreased hemolysis following LentiGlobin treatment

HGB-206

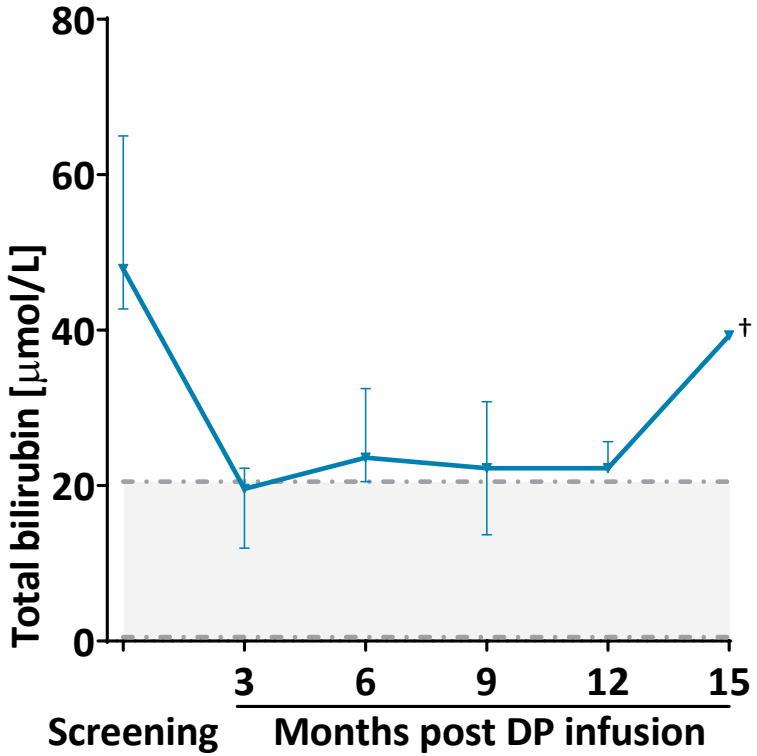
Reticulocyte Counts



Lactate Dehydrogenase



Total Bilirubin



N*	13	10	8	7	5	1
	11	10	7	7	5	1
	13	10	8	7	5	1

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

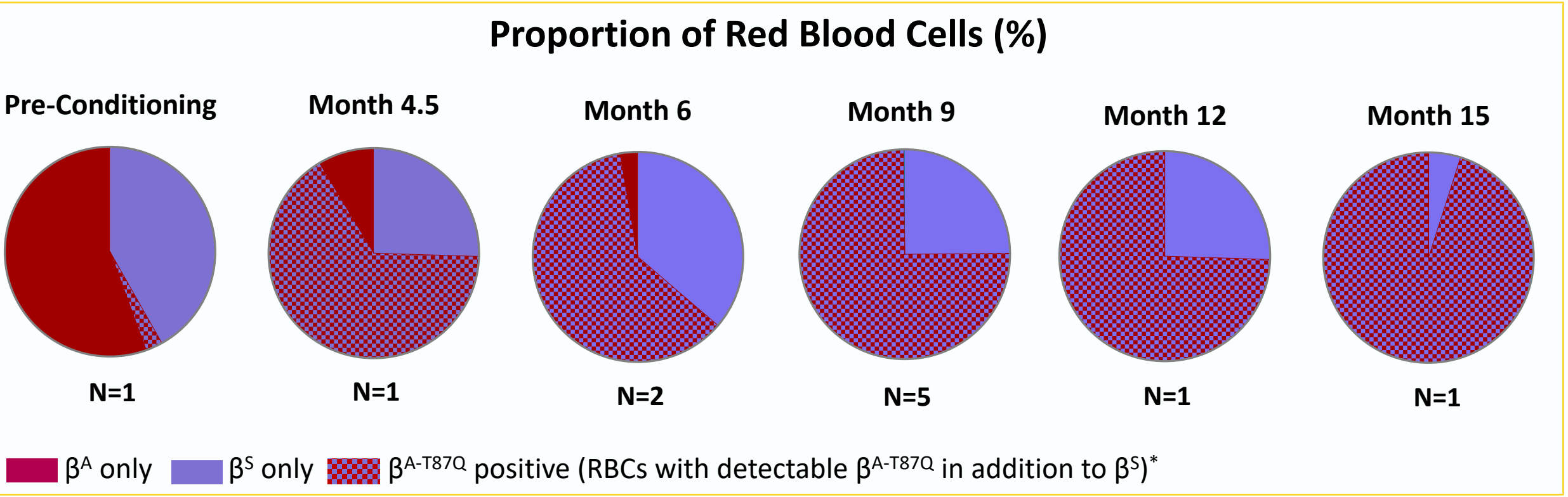
Definition: LDH, lactate dehydrogenase

Data as of 7 March 2019

HGB-206 group C: on average, ≥ 70% of RBCs from patients treated with LentiGlobin contain $\beta^{A\text{-}T87Q}$ by month 9

HGB-206

- Single RBC western blot assay was performed in multiple patient samples

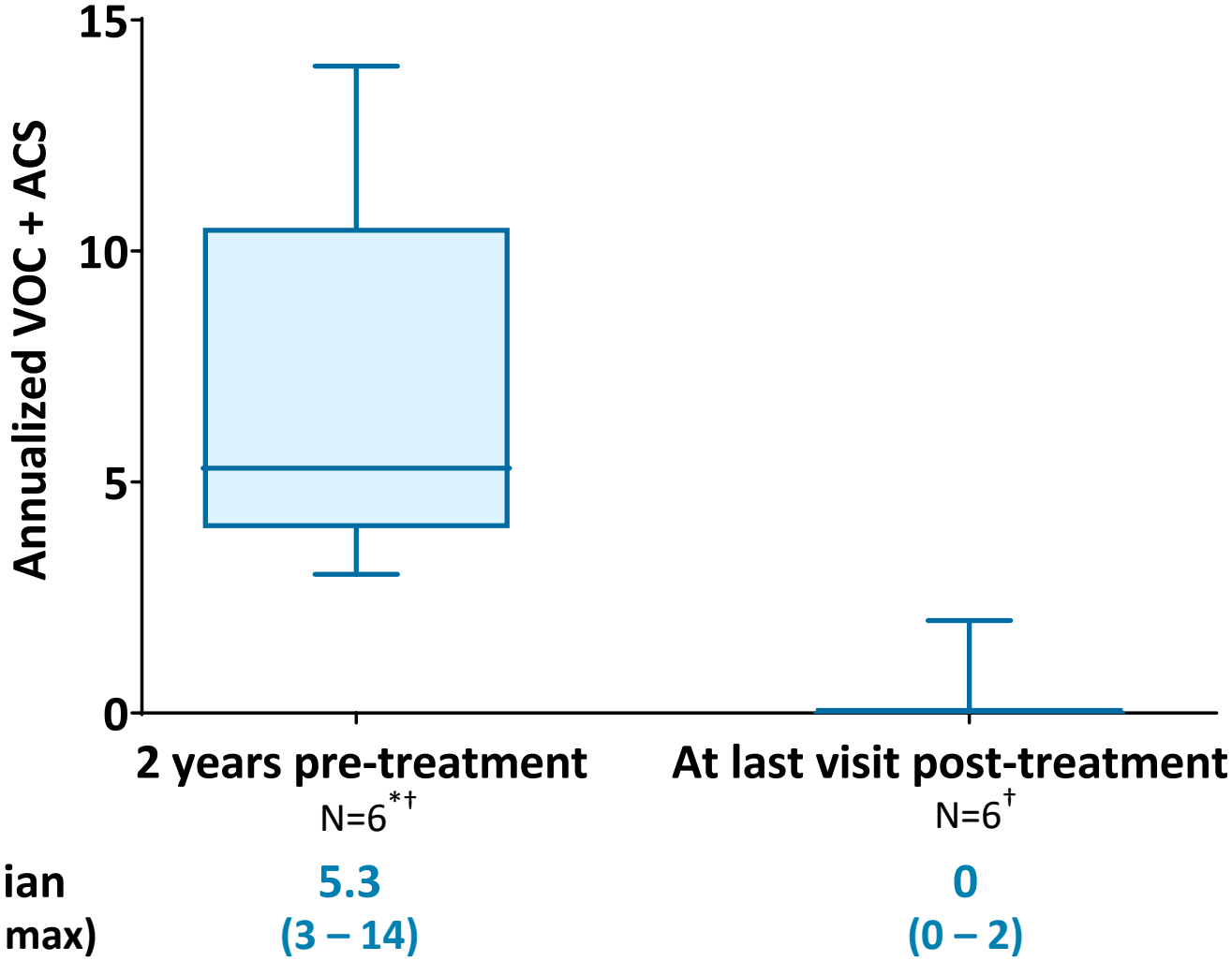


Mean is depicted - if N=1, data show technical replicates; *Pre-conditioning sample does not contain any $\beta^{A\text{-}T87Q}$, signal represents false positives
Definition: RBCs, red blood cells

Data as of 7 March 2019

HGB-206 group C: reduction in annualized rate of VOC plus ACS post treatment

HGB-206



- No ACS or serious VOCs occurred in any Group C patient post-LentiGlobin treatment to date
- 1 non-serious Grade 2 VOC was observed in 1 pt ~3.5 months post DP infusion

Investigator-reported adverse events of VOC or ACS are shown;
*Patients with ≥ 1 VOC/ACS in the 2 years before Informed Consent; †Patients with ~ ≥ 6 months of follow-up post DP infusion

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

Data as of 7 March 2019

HGB-206 group C: safety profile consistent with myeloablative busulfan conditioning

HGB-206

Non-hematologic grade ≥ 3 AEs* Post DP infusion in ≥ 2 patients	N=13 n (%)
Febrile neutropenia	10 (77)
Stomatitis	7 (54)
Abdominal pain upper	2 (15)
Alanine aminotransferase increased	2 (15)
Blood bilirubin increased	2 (15)
Nausea	2 (15)
Serious AEs* Post DP infusion in ≥ 2 patients	N=13 n (%)
Nausea	2 (15)
Vomiting	2 (15)

- Serious AEs post DP infusion were reported in 6 patients
- No DP-related adverse events
- No cases of veno-occlusive liver disease observed to date
- No graft failure or deaths reported
- No vector-mediated RCL detected and no evidence of clonal dominance across LentiGlobin studies†
- No further cases of MDS have been observed across studies of LentiGlobin†▪

*Hematologic AEs commonly observed post-transplant have been excluded;
†As of 20 Sep 2017 (HGB-205); 13 Dec 2018 (HGB-204, HGB-207), and 12 Apr 2019 (HGB-212)
▪One patient in Group A was reported to have MDS at last data update (ASH 2018). There was no evidence of LVV-mediated oncogenesis and the MDS SAE was considered unlikely related to LentiGlobin gene therapy.

Definitions: AE, adverse event; DP, drug product; RCL, replication competent lentivirus

Data as of 7 March 2019

accelerated development plan using novel composite primary endpoint based on hemoglobin

EXPANDED

Updated Primary Endpoint

Up to additional 21 patients

Expanded age range

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

HGB-210

Sickle Cell Disease, history of VOEs over 24 months

Phase 3, single arm, multi-center, global study

- Primary Endpoint: HbA^{T87Q} and Total Hb
- Key Secondary Endpoint:
  - Reduction in severe VOEs

NEW

Planned for 2019

Additional Clinical Investigation in Other Patient Types and Ages Planned

Plans Based on Ongoing Engagement with Regulators

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multiple myeloma

A lethal blood cancer that often infiltrates the bone marrow causing anemia, kidney failure, immune problems and bone fractures

BCMA program overview

- ide-cel (bb2121): Enrollment in KarMMa registration-enabling study complete (N=140)
- Additional studies advancing:
  - KarMMa-2 in 2nd line Phase 2 study open
  - KarMMa-3 in 3rd line+ Phase 3 study open
  - Opportunities for ide-cel in newly diagnosed MM including high risk, transplant ineligible and transplant eligible vs. transplant under evaluation
- bb21217 CRB-402 phase 1 study underway

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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 1	 10 (48) 11 (52)	 6 (27) 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, 2018

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CRB-401 data at ASCO 2018 - heavily pretreated patient population

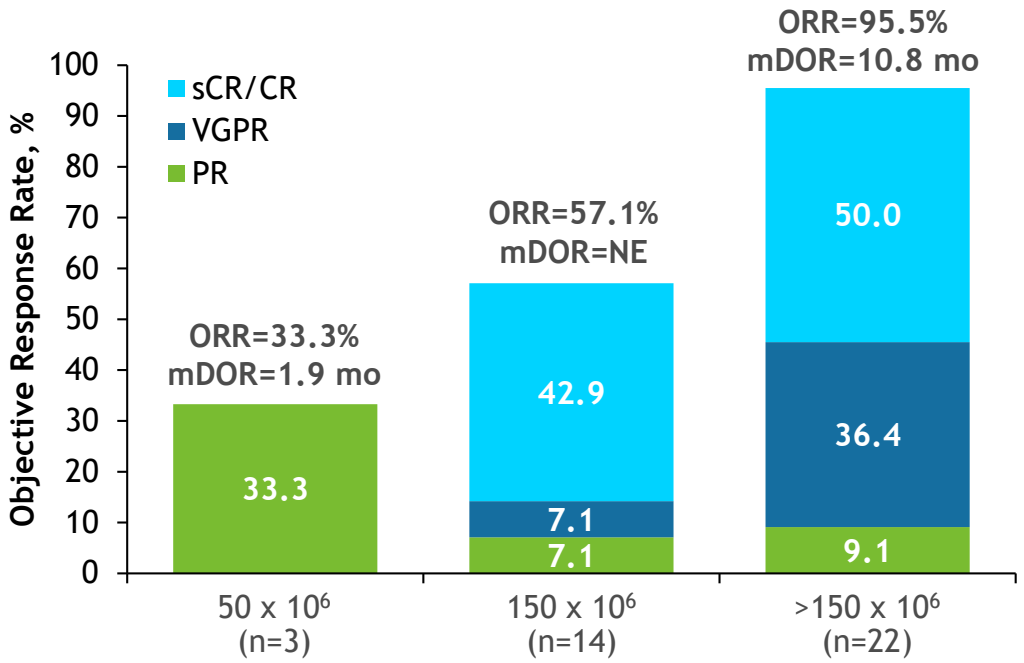
Parameter	Escalation (N=21)	Expansion (N=22)
Median (min, max) prior regimens	7 (3, 14)	8 (3, 23)
Prior autologous SCT, n (%)	21 (100)	19 (86)
0	0	3 (14)
1	15 (71)	14 (64)
>1	6 (29)	5 (23)

	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.

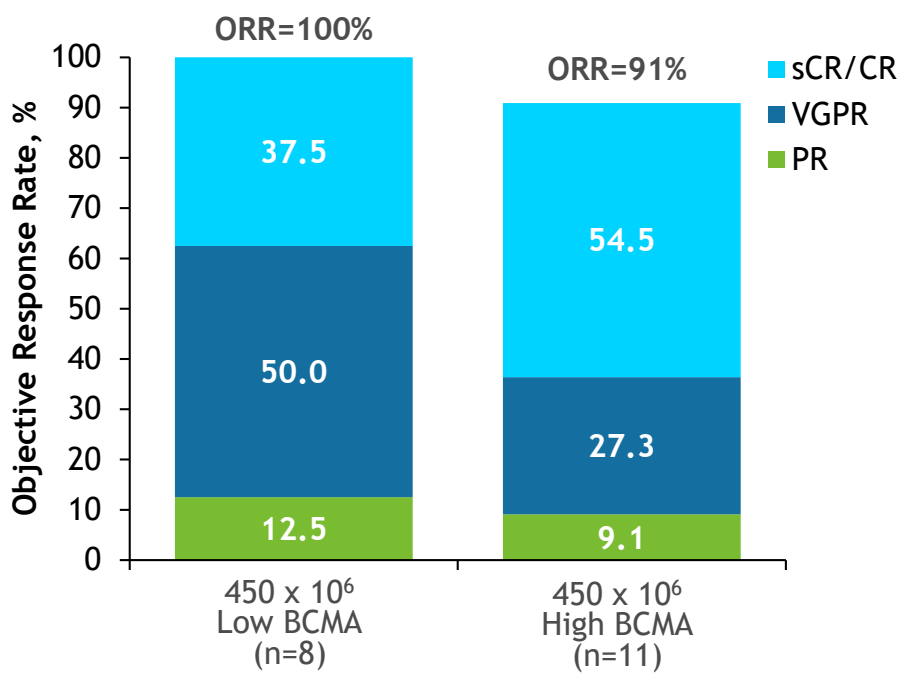
CRB-401 data at ASCO 2018 - tumor response:
dose-related and independent of Myeloma BCMA expression levels

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%.

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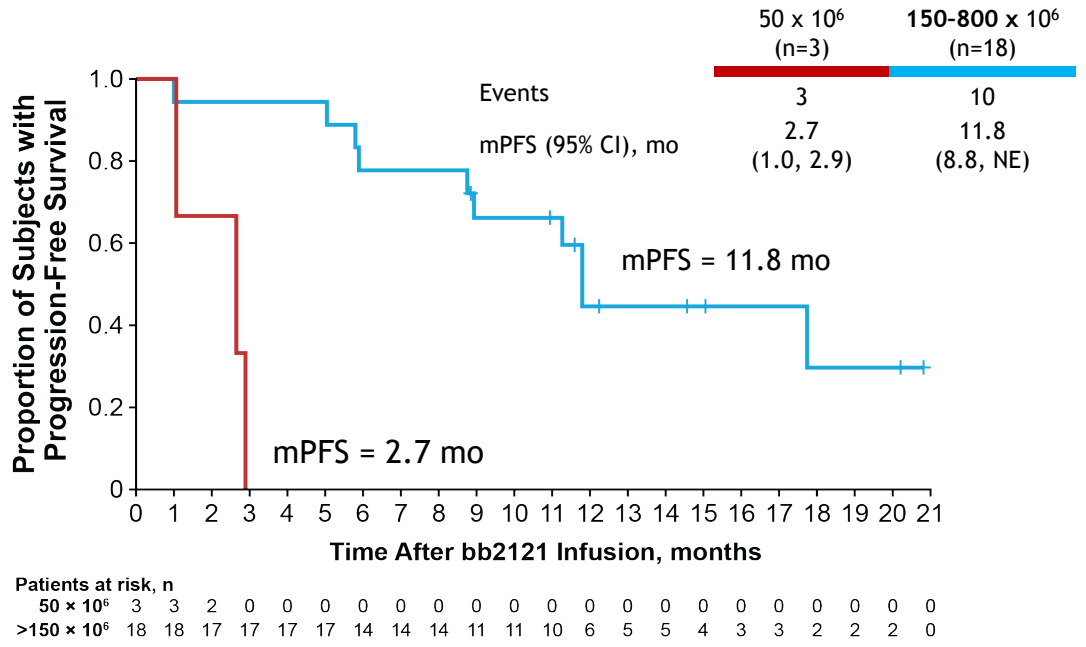
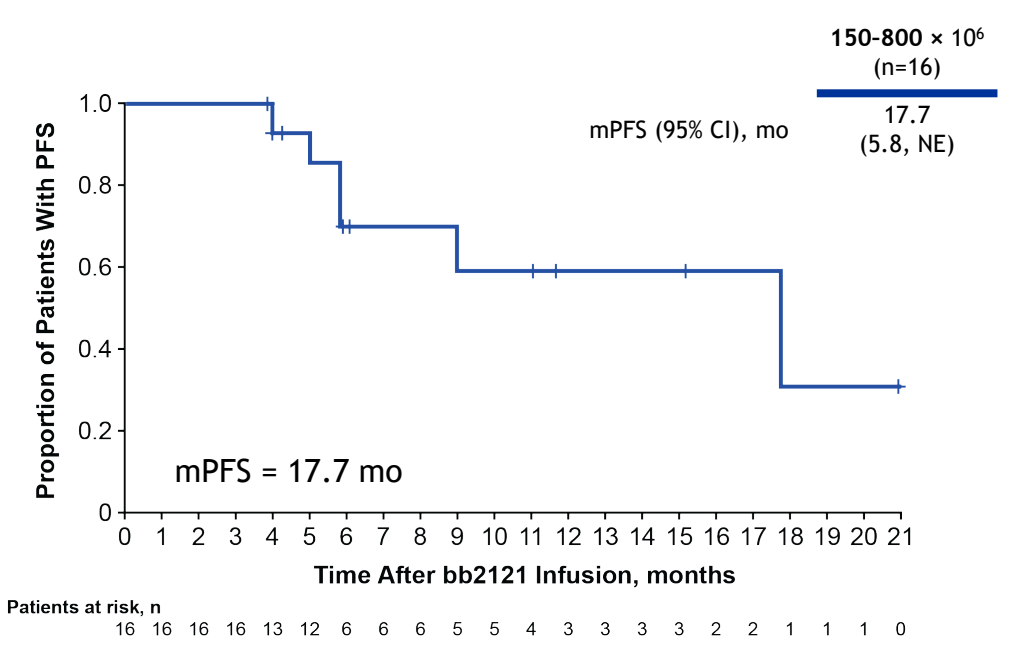
CRB-401 data at ASCO 2018: hitting the mark for progression free survival

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



PFS in MRD-Negative Responders
Escalation and Expansion Cohorts



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

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

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

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CRB-401 data at ASCO 2018 - bb2121 continues to be generally well-tolerated; no new safety signals

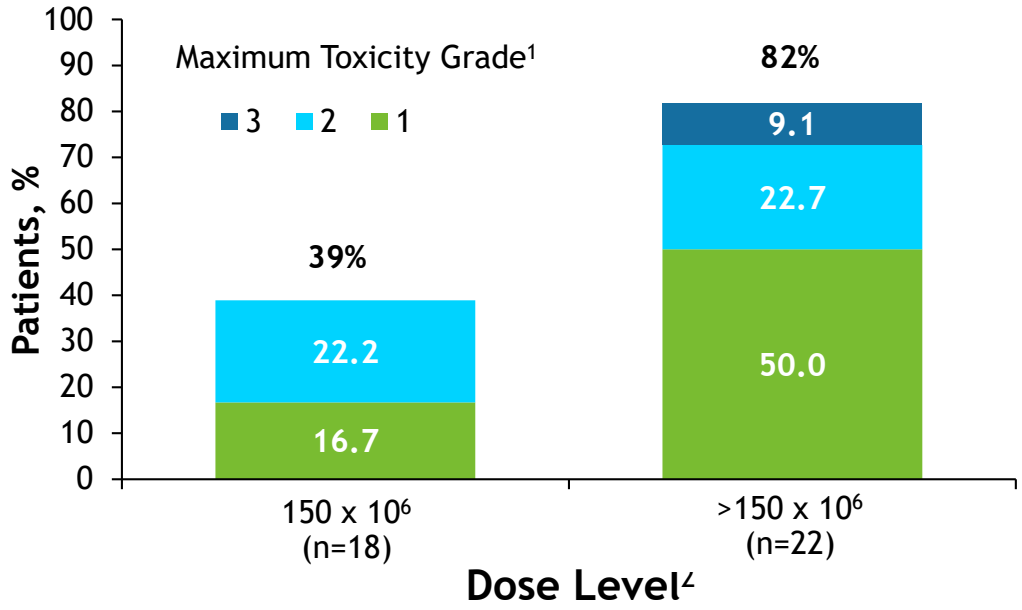
CAR T Treatment-Emergent Adverse Events : All Infused Patients (N=43)

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)

No grade 4 CRS events

No fatal CRS or neurotoxicity events

Cytokine Release Syndrome By Dose Level



Patients with a CRS event, 63%

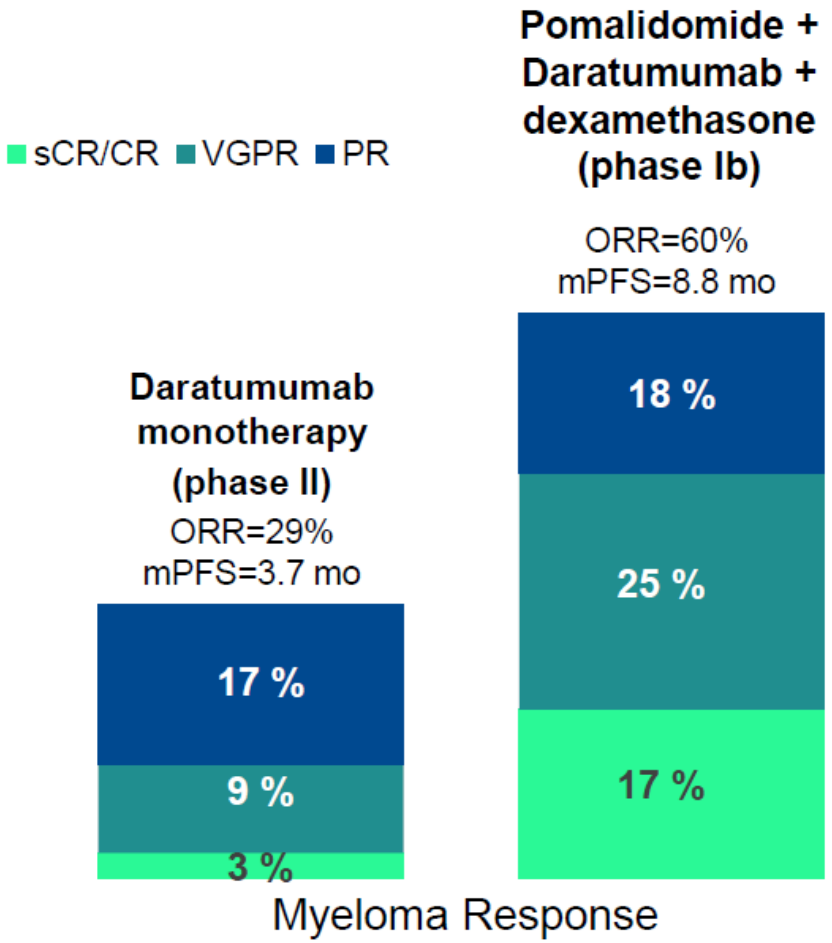
Data cut-off: March 29, 2018. NE, not estimable.[1]CRS uniformly graded per Lee et al., Blood 2014;124:188-195. [2]Events occurring in first 28 d and including dizziness, bradyphrenia, somnolence, confusional state, nystagnmus, insomnia, memory impairment, depressed level of consciousness, neurotoxicity, 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:

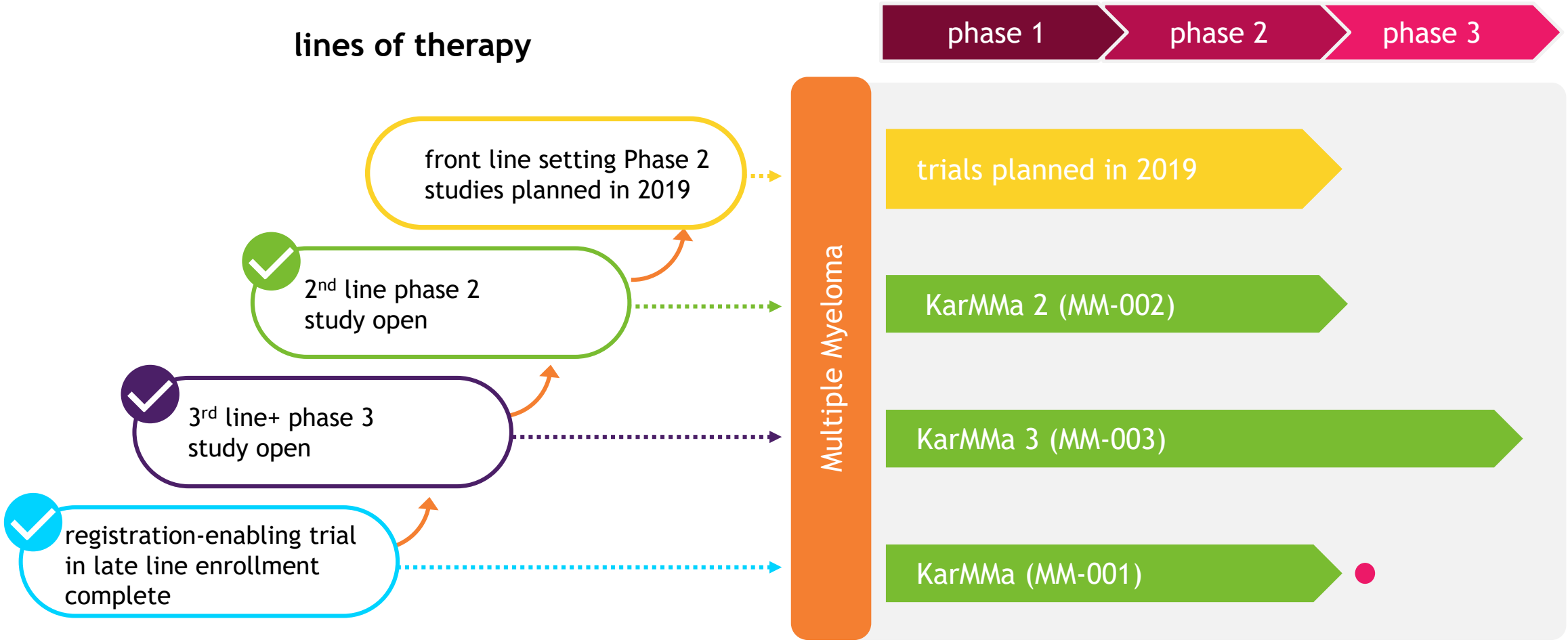
	Dara	PDd	bb2121
Phase	II	I	I
N	106	103	43
Eligibility	≥ 3 prior lines Pom allowed Dara-naive	≥ 2 prior lines Pom-naïve Dara-naive	≥ 3 prior lines Pom allowed Dara allowed
Median prior lines	5	4	7

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



Chari, A. Blood 2017

advancing ide-cel (bb2121) into earlier lines of multiple Myeloma



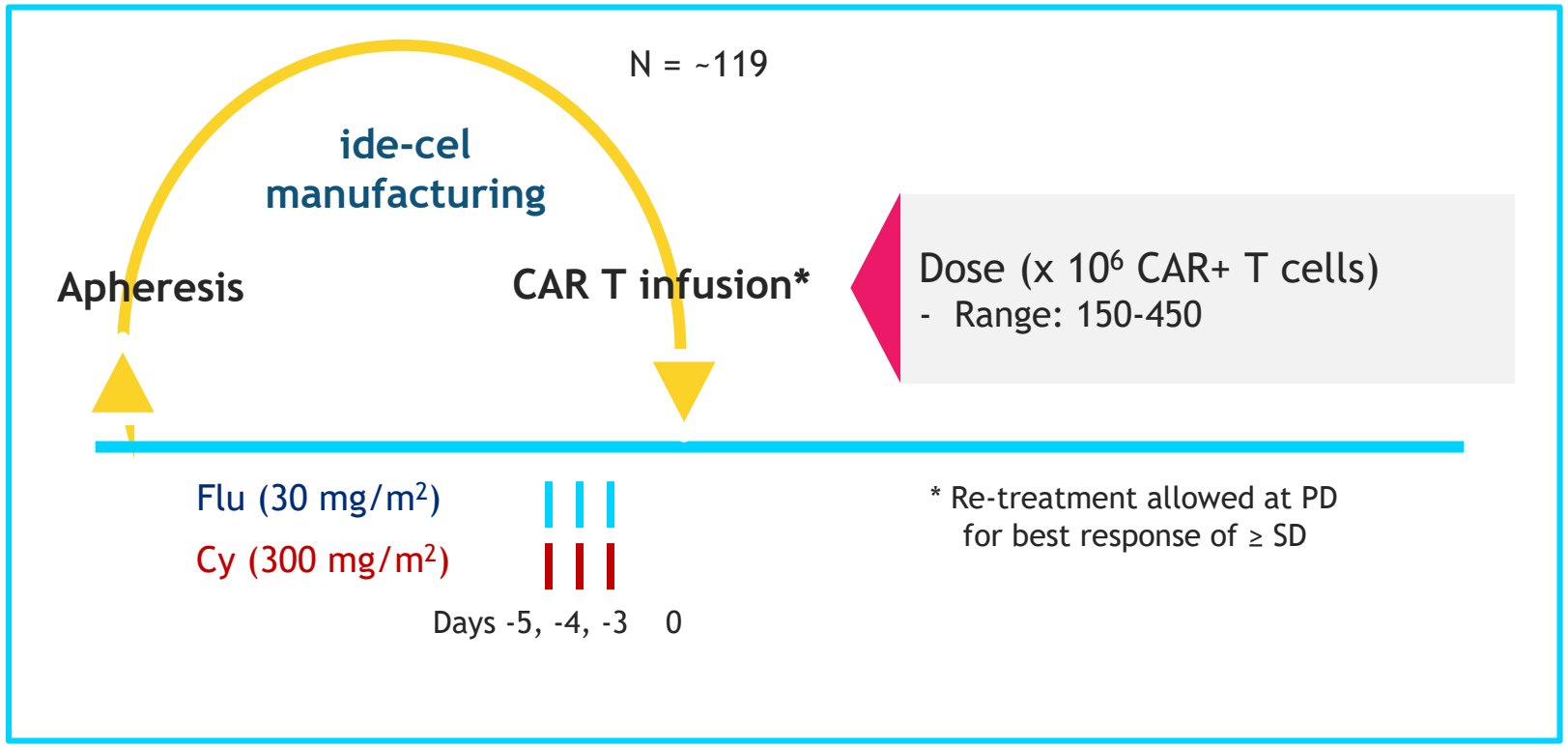
● anticipated approval in 2020

bb2121-MM-001: ide-cel registration-enabling trial (KarMMa)

KarMMa

Relapsed and refractory MM

- ≥3 prior treatment regimens with ≥ 2 consecutive cycles each (unless PD was best response)
- Received prior IMiD®, PI and anti-CD38
- Refractory (per IMWG) to last treatment regimen



Endpoints

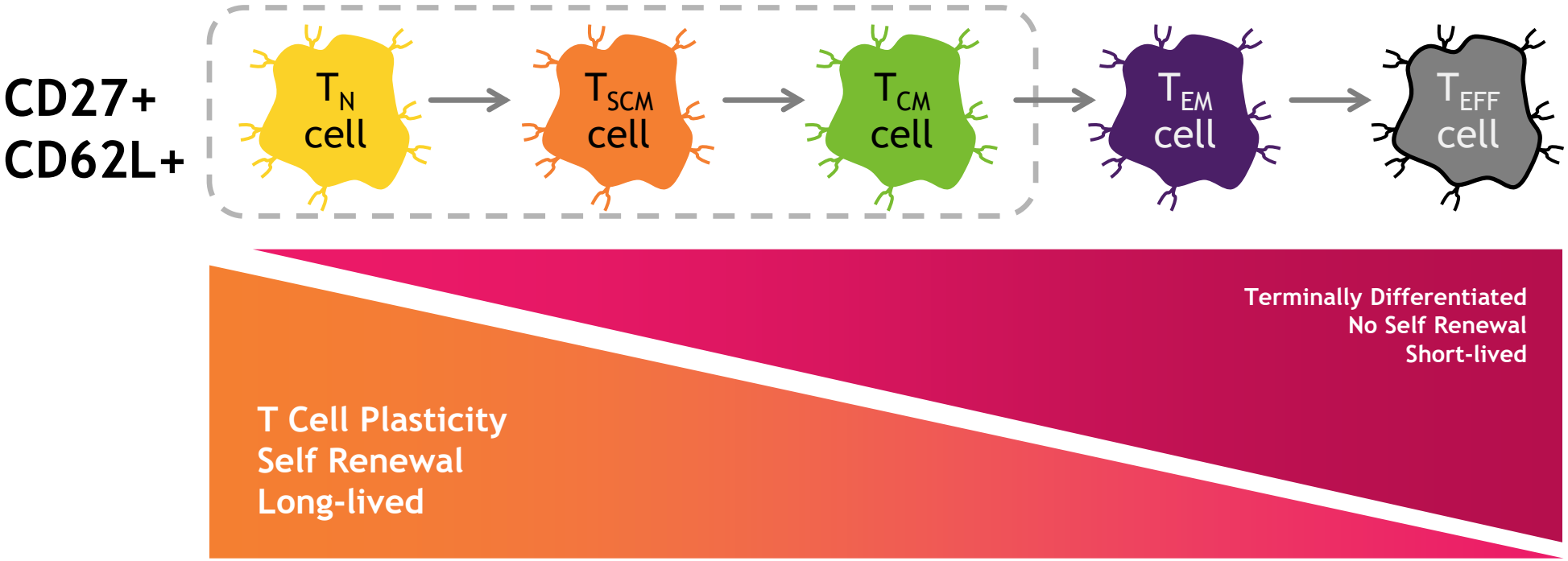
Primary: ORR

Key Secondary: CR, TTR, DOR, PFS, TTP, OS, Safety, bb2121 expansion and persistence, MRD (genomic and flow assays)

Exploratory: BCMA expression/loss, T cell immunophenotype, GEP in BM, HEOR

bb21217: PI3K inhibition during manufacturing drives increase in long-lived, memory-like T Cells

CRB-402

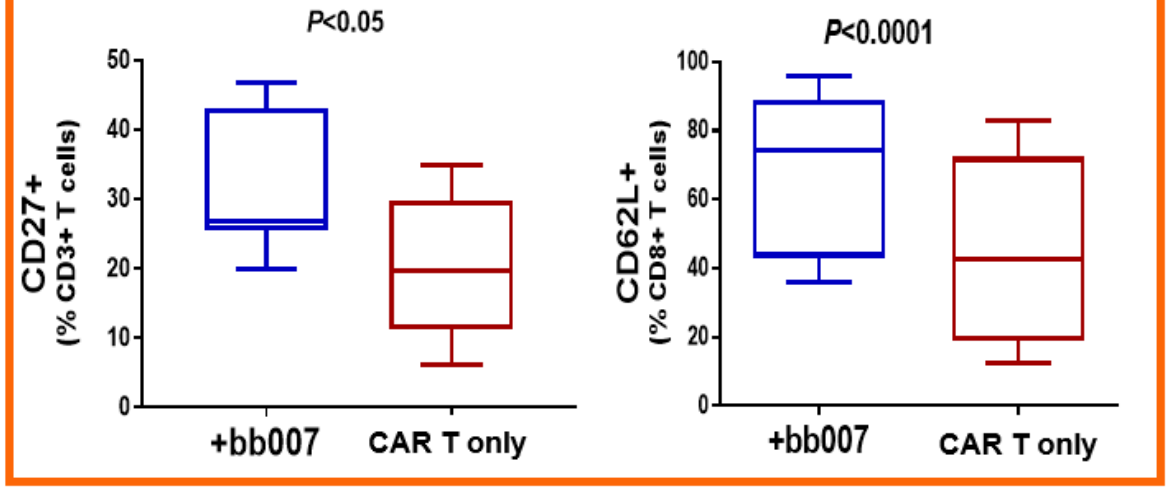


Hypothesis: Increasing long-lived, memory-like T Cell subsets in the drug product may result in enhanced persistence of functional anti-BCMA CAR T cells in vivo

preclinical models: bb21217 is enriched for memory-like T cells exhibits; enhanced persistence of anti-tumor effect

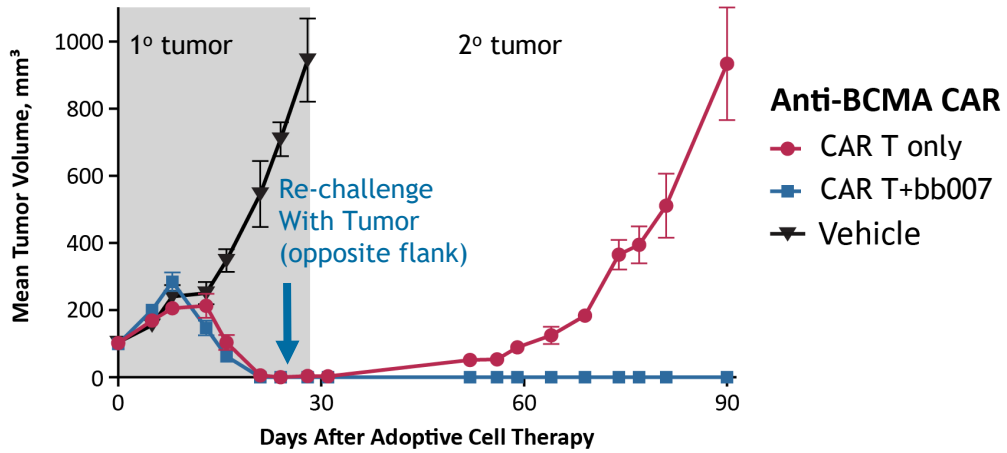
CRB-402

bb007 enriches for memory-like T Cell phenotype



- CD62L and CD27 are markers of memory-like T cells
- bb21217 is significantly enriched for T cells with this memory-like phenotype

bb007 enhances anti-tumor effect in mouse models



- ONLY CAR T cells cultured with PI3K inhibitor bb007 (i.e. bb21217) clear a second tumor challenge
- Data are consistent with improved persistence of functional CAR T cells leading to sustained anti-tumor effect

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CRB-402 Phase 1 Study Design and Status

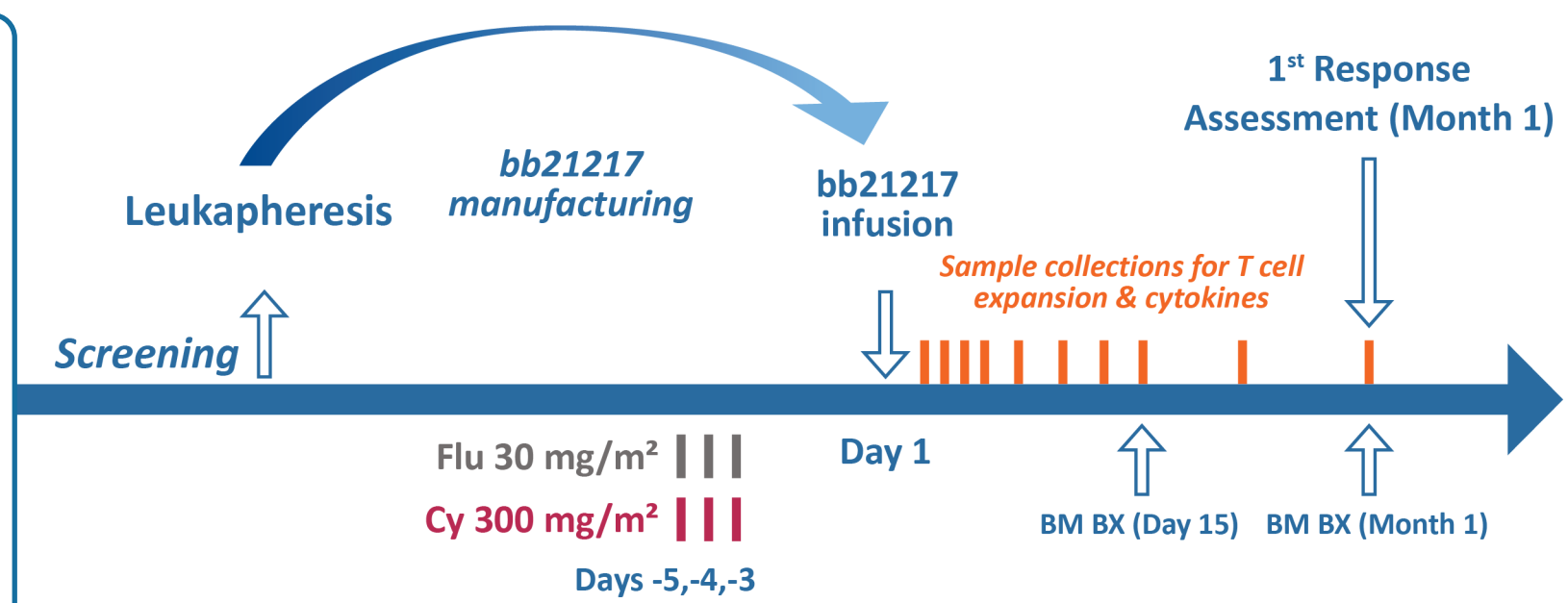
CRB-402

3 + 3 dose escalation[a]

CAR+ T cell dose: 150 × 10^6 → 300 × 10^6 → 450 × 10^6 → 800 × 10^6

N ≈ 50

- R/R MM
- ≥3 prior regimens
  - IMiDs and
  - Proteasome inhibitors
  - Or double-refractory
- ≥50% BCMA expression (dose escalation only)



study status as of Oct 18, 2018

- Collected N=13
- Dosed N=12 (150 × 10^6 dose)
  - HTB[b] n=6
  - LTB[b] n=6
- Median (min, max) follow-up: 26 wk (4, 51)

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

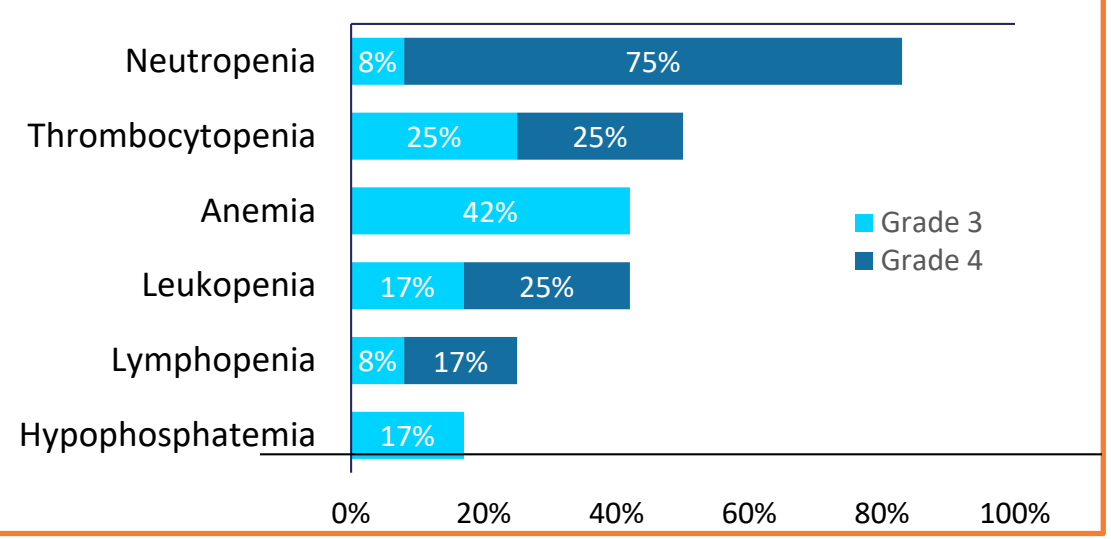
NCT03274219

AE, adverse events; BCMA, B-cell maturation antigen; DLT, dose-limiting toxicity; HTB, high tumor burden; IMiD, immunomodulatory imide drugs; LTB, low tumor burden; MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival; R/R MM, relapsed/refractory multiple myeloma. [a]All patients to date received 150 × 10^6 CAR+ T cells; an intermediate dose of 300 × 10^6 CAR+ T cells will be the next dose level. [b]HTB defined as ≥50% bone marrow plasma cells pre-infusion; LTB <50%. [c]Per International Myeloma Working Group criteria.

early clinical safety and tolerability consistent with CAR T experience

CRB-402

Grade ≥3 AEs in >1 Patient[a]



AEs of Special Interest[a]

Grade, n (%)	1	2	3	4
CRS[b]	4 (33)	3 (25)	1 (8)	-
Neurotoxicity[c]	1 (8)	1 (8)	-	1 (8)

- CRS occurred in 67% of patients
  - Mostly grade 1/2, 1 grade 3, no grade 4
  - Median time to onset of CRS 4.5 days (2,11)
  - Manageable with or without tocilizumab
- 1 patient experienced DLT (grade 4 encephalopathy and grade 3 CRS)
  - Patient had high tumor burden and rapidly accelerating disease at baseline
  - No other DLTs occurred
- 1 grade 3 catheter-related infection; no other severe infections reported to date
- 4 patients experienced 1 or more SAEs
- No deaths on study to date

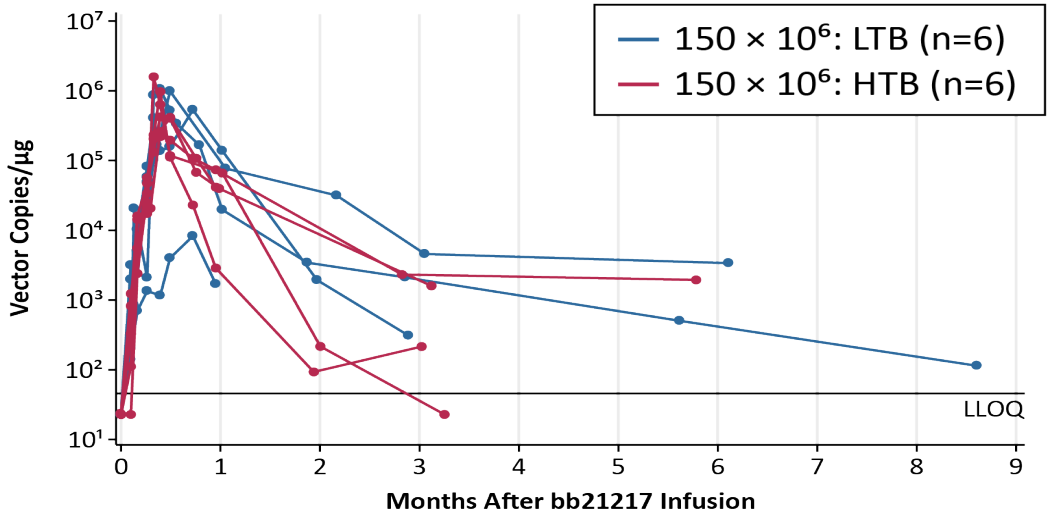
AE, adverse event; DLT, dose-limiting toxicity; SAE, serious adverse event. [a]AEs occurring between bb21217 infusion and disease progression. [b]Cytokine release syndrome (CRS) uniformly graded according to Lee et al., Blood 2014;124:188-195. [c]Events selected as CAR T neurotoxicity on the case report form occurring within 90 days after bb21217 infusion.

Data as of October 18, 2018

clinical data is early but consistent with goal of enhanced persistence

CRB-402

Vector Copy Number Over Time by Baseline Tumor Burden



	Month 1	Month 3	Month 6	Month 9
At risk, n	9	7	3	1
With detectable vector, n (%)	9 (100)	6 (86)[a]	3 (100)	1 (100)

- Robust and reliable bb21217 CAR T cell expansion post-infusion observed at first dose
- Early bb21217 clinical data is consistent with robust functional CAR T cell persistence
  - Enrichment for memory-like CAR T cells observed in preclinical studies, and in patients post-infusion
  - Vector detectable up to 9 months post-infusion, and in 3/3 patients at 6-month time point
  - Sustained sBCMA suppression observed, reflecting ongoing plasma cell aplasia

HTB, high tumor burden; LLOQ, lower limit of quantitation; LTB, low tumor burden.
[a]One patient with undetectable vector received cyclophosphamide on day 15 for grade 4 encephalopathy.

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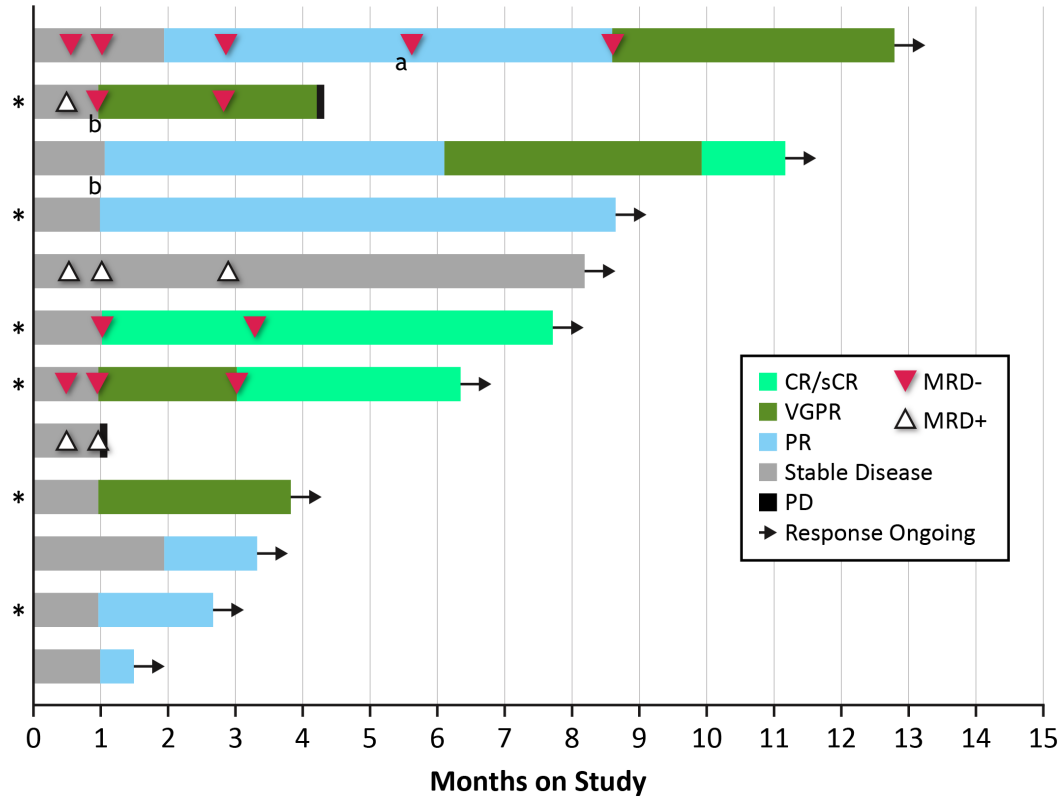
Data as of October 18, 2018

clinical responses observed in 10/12 patients (83%) at first dose level tested (150 x 10^6 CAR+ T cells)

CRB-402

Clinical Responses Over Time



- 10/12 patients (83%) achieved an objective response at the first tested dose (150 × 10^6 CAR+ T cells)
- Deepening responses over time; CR achieved as late as month 10
- 100% MRD negativity in 4/4 responders evaluable for MRD status
- Responses are ongoing in all but 1 responder; the first patient dosed continues response >1 year after treatment

CR, complete response; MRD, minimal residual disease; PR, partial response; VGPR, very good partial response. *Patients with high tumor burden. [a]Progression based exclusively on appearance of new bone lesions. [b]MRD status not available.

High Clinical Response Rate Observed at First Dose Level (150 x 10^6 CAR+ T cells)

CRB-402

Clinical Response	
	bb21217-Treated (N=12)
ORR,[a] n (%) [95% CI]	10 (83.3) [51.6, 97.9]
sCR/CR	3 (25)
≥VGPR	6 (50)
MRD status in bone marrow, n	
MRD-evaluable responders[b]	4
MRD-neg	4[c]
Median time to first response (min, max), [a,d] mo	1 (1, 2)
Median time to best response (min, max), [a,d] mo	1 (1, 10)
Median follow-up duration (min, max), mo	5.9 (1.0, 11.8)

CR, complete response; MRD, minimal residual disease; ORR, objective response rate; PR, partial response; VGPR, very good partial response. *Patients with high tumor burden. [a]Includes unconfirmed responses. [b]Patients with ≥PR and valid MRD assessments. [c]Two MRD-neg. responses at 10^{-6} and 2 at 10^{-5} sensitivity level by Adaptive next-generation sequencing. [d]Among 10 responders with ≥PR.

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

Cerebral Adrenoleukodystrophy

a 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

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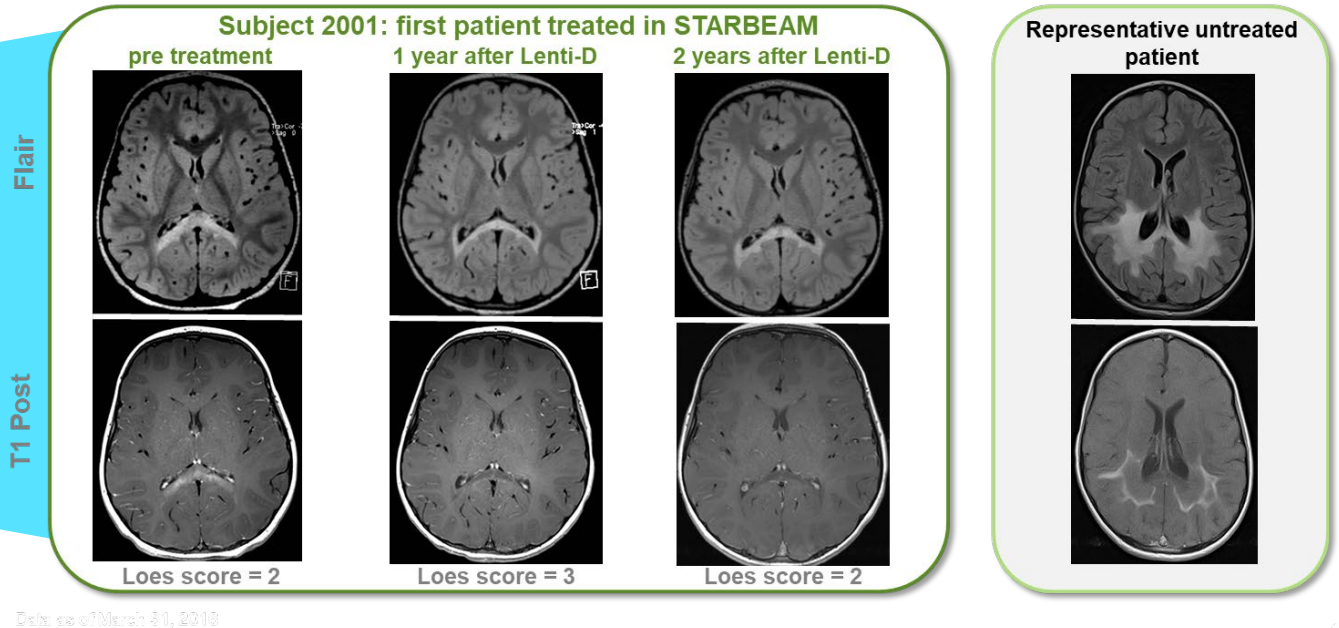
Lenti-D treatment halts CALD disease progression



Data as of March 31, 2018

- **All patients who were alive and MRD-free at 24 months follow up (15/17; 88%) continue to be MFD-free with up to 5 years of follow-up**
  - 32 patients have been treated with Lenti-D with a median follow-up time of 21.2 months
  - 14 patients are still on study with less than 24 months of follow-up and show no evidence of MFDs
  - Three patients did not or will not meet the primary efficacy endpoint; two patients withdrew from the study at investigator discretion, and one experienced rapid disease progression early on-study resulting in MFDs and death.
- **Safety profile consistent with autologous transplantation**
  - No GvHD, no graft rejection
- **Enrollment completed in Starbeam study**
  Phase 3 ALD-104 study currently enrolling

Data as of April 25, 2019

R&D BLUE style: what do we work on?

Core Research Principles

Programs with the Potential to Transform Patient Lives	Diseases with Definitive Endpoints of Clinical Success	Targets with Human Genetic and/or Functional Validation	Disruptive Solutions to the Problems that Need to be Solved
We tackle diseases with a clear unmet medical need based on the magnitude of impact and not necessarily the number of patients	Clinical success should be objective, measurable, un-incremental, and rapid	Biology may be complex but the role of the target in the disease must be definitive	We don't do incremental science. We take on the big problems that, if successful, will disrupt our field

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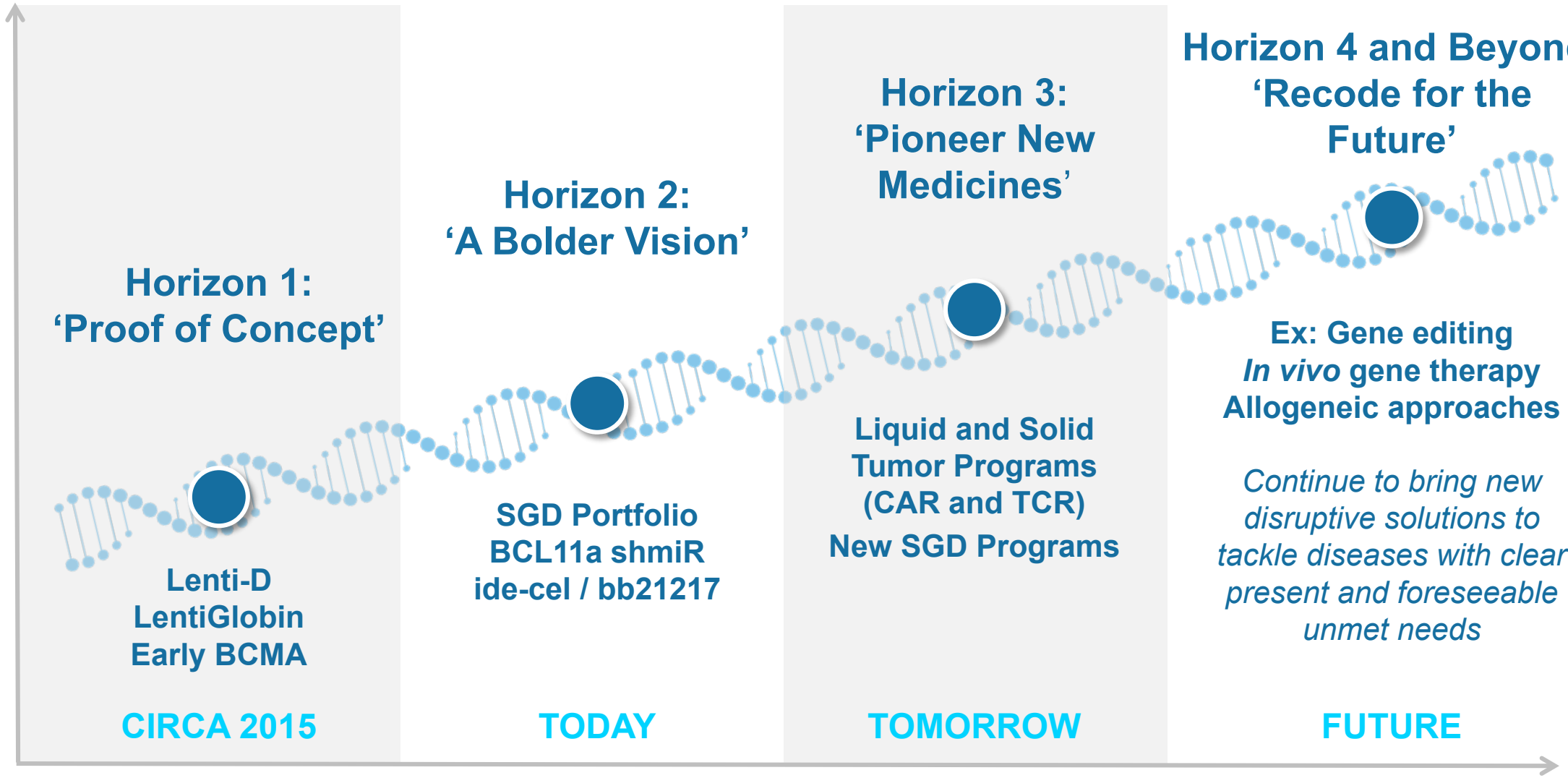
continuous innovation is in our DNA



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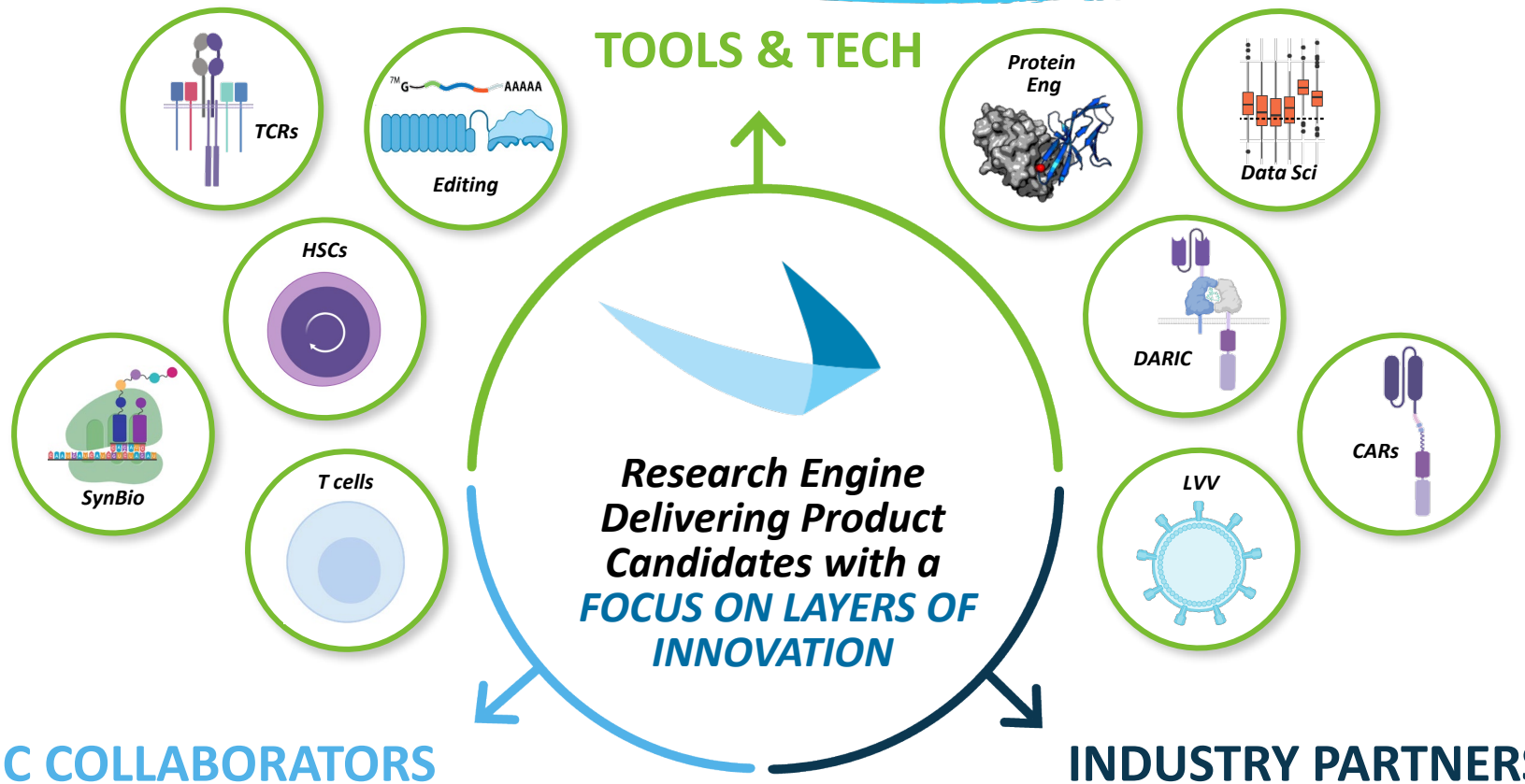
we believe the winning strategy will require: the right tools, leading partnerships, stellar collaborators



ACADEMIC COLLABORATORS

INDUSTRY PARTNERSHIPS

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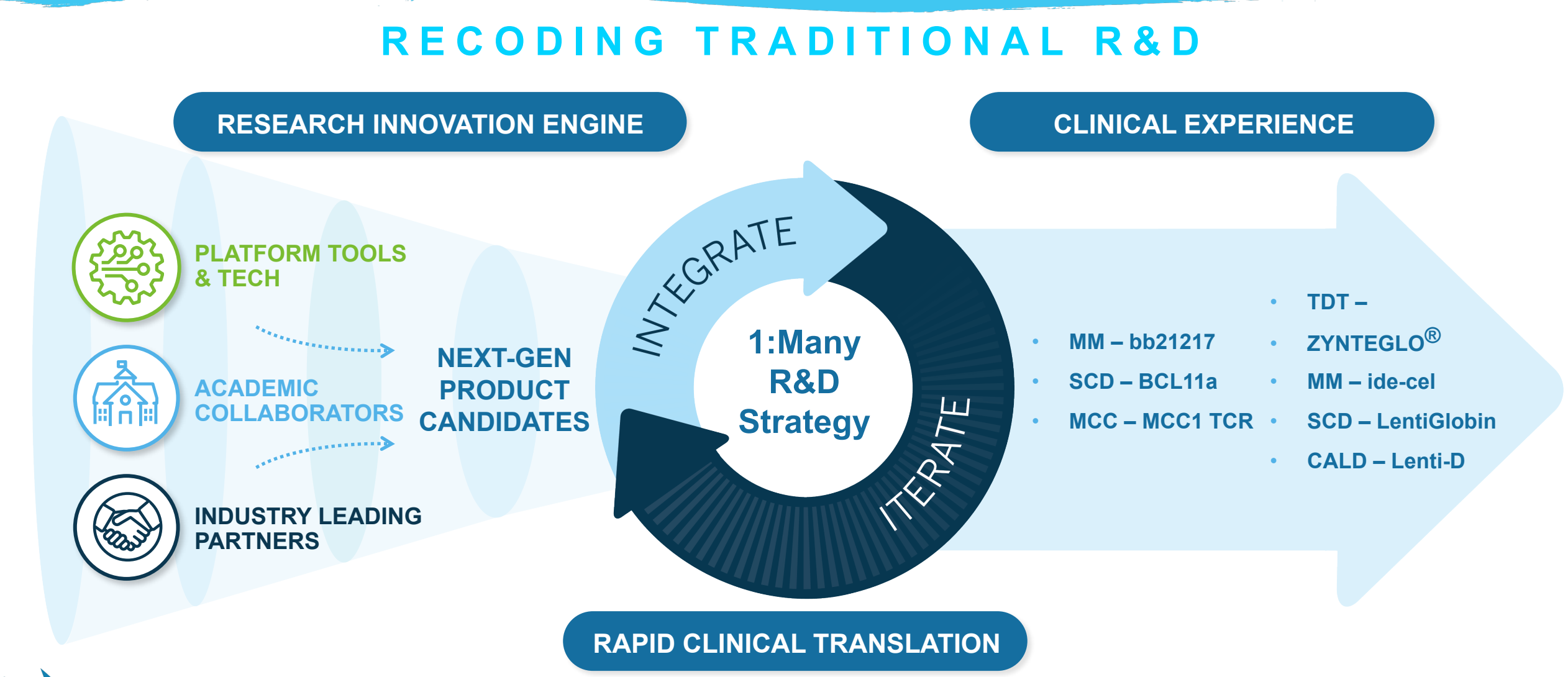
anti-pure play principles - what do we mean?
recoding traditional R & D



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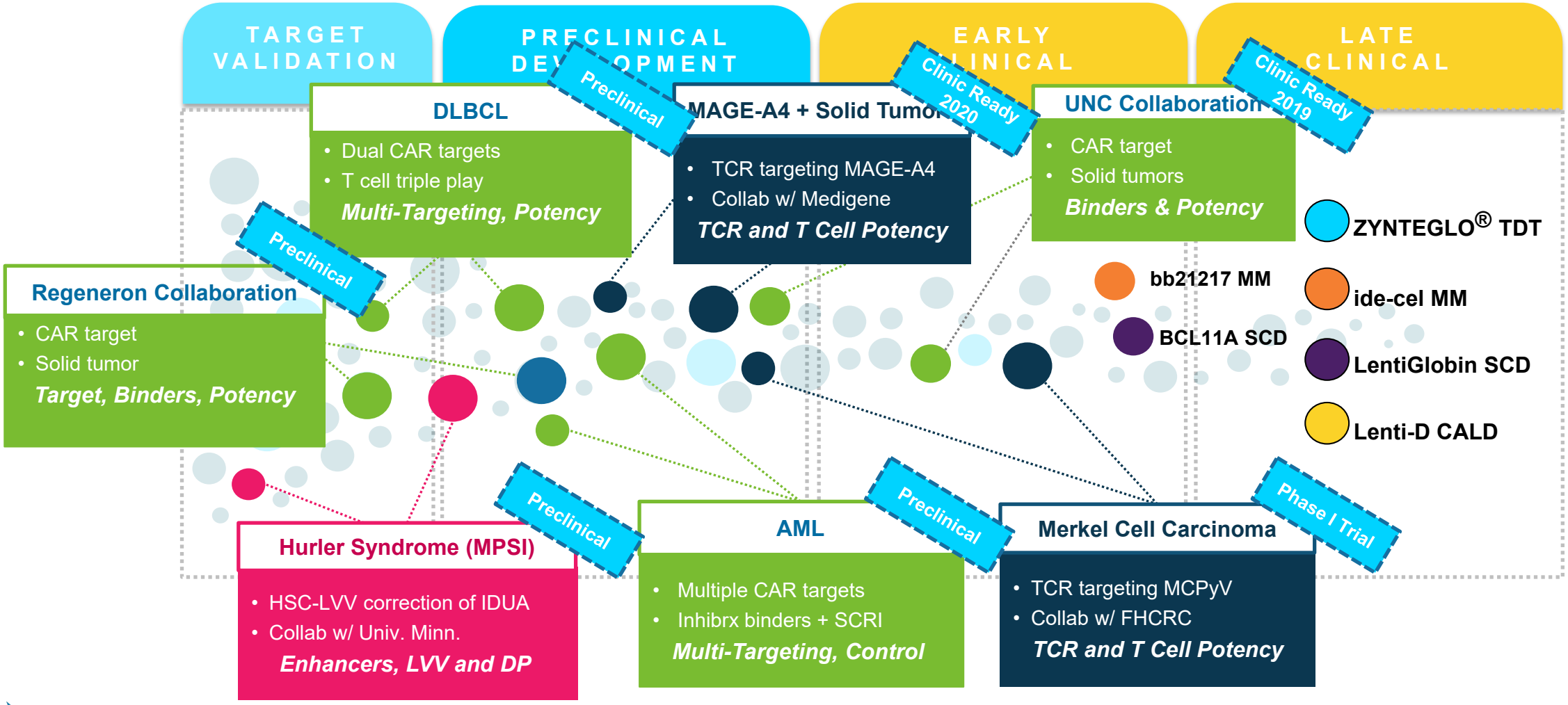
our research strategy in action:
emerging pipeline of nextgen products



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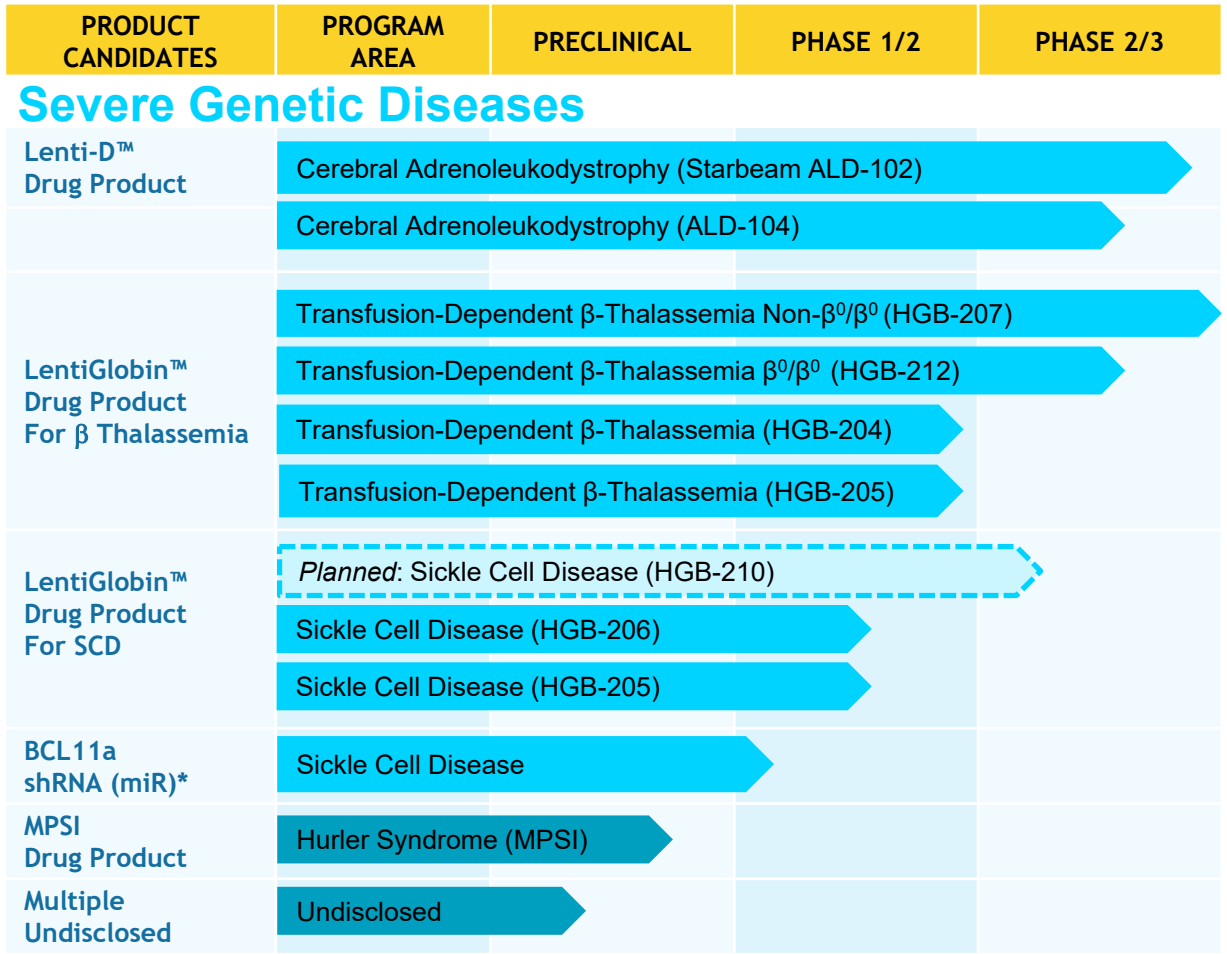
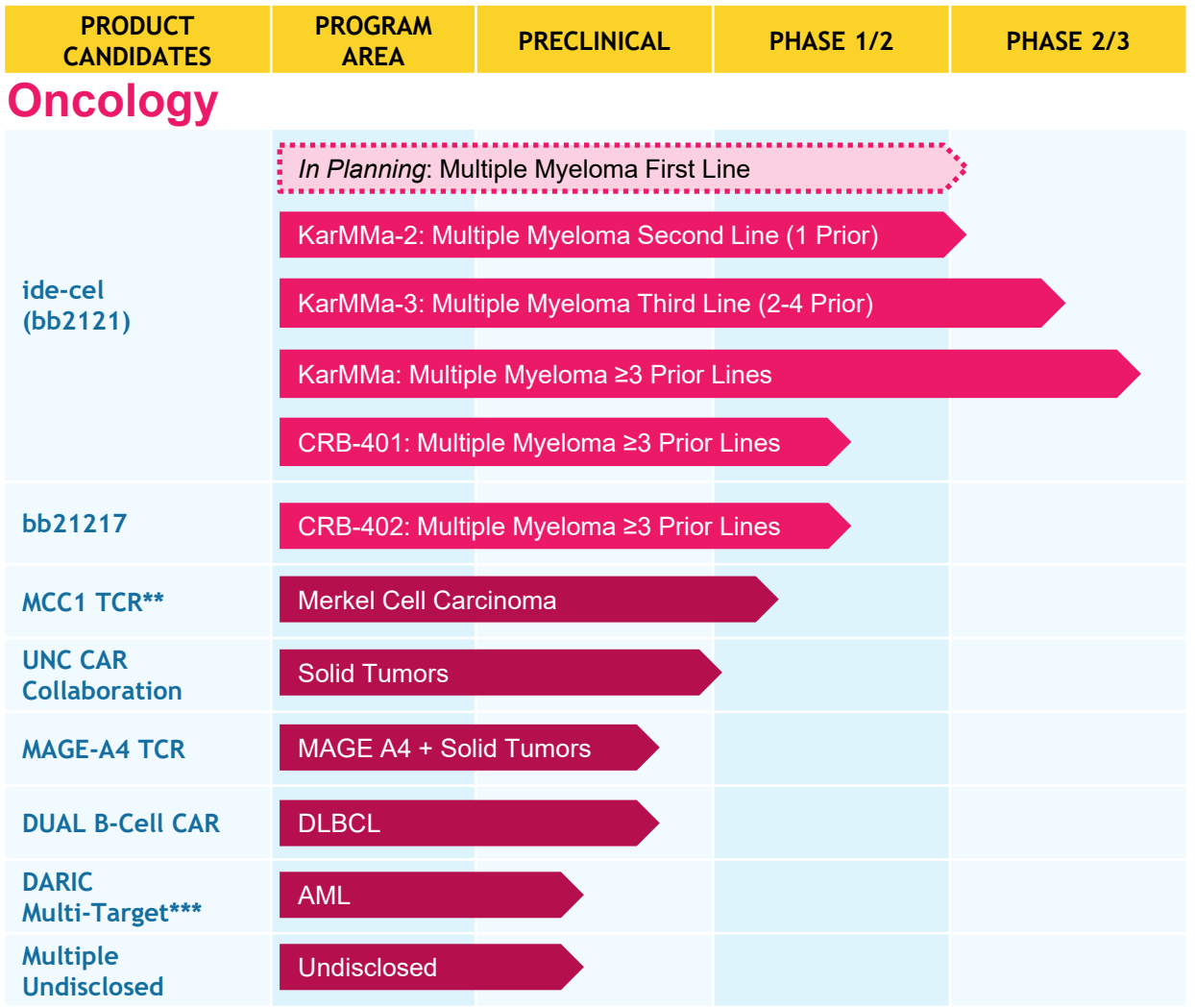
let's recode the science: pipeline overview





*Development is led by Dana-Farber/Boston Children's Cancer and Blood Disorders Center
**Development is led by Fred Hutch Cancer Research Institute
***Development is led by Seattle Children's Research Institute

ide-cel (bb2121) and bb21217 development in collaboration with Celgene

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LET'S RECODE
THE STORY