bluebirdbio®
recode for life™

Recode Activated

Q1 2020 Company Presentation

LET'S RECODE THE STORY

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.

Must Beat the Odds.

Period.

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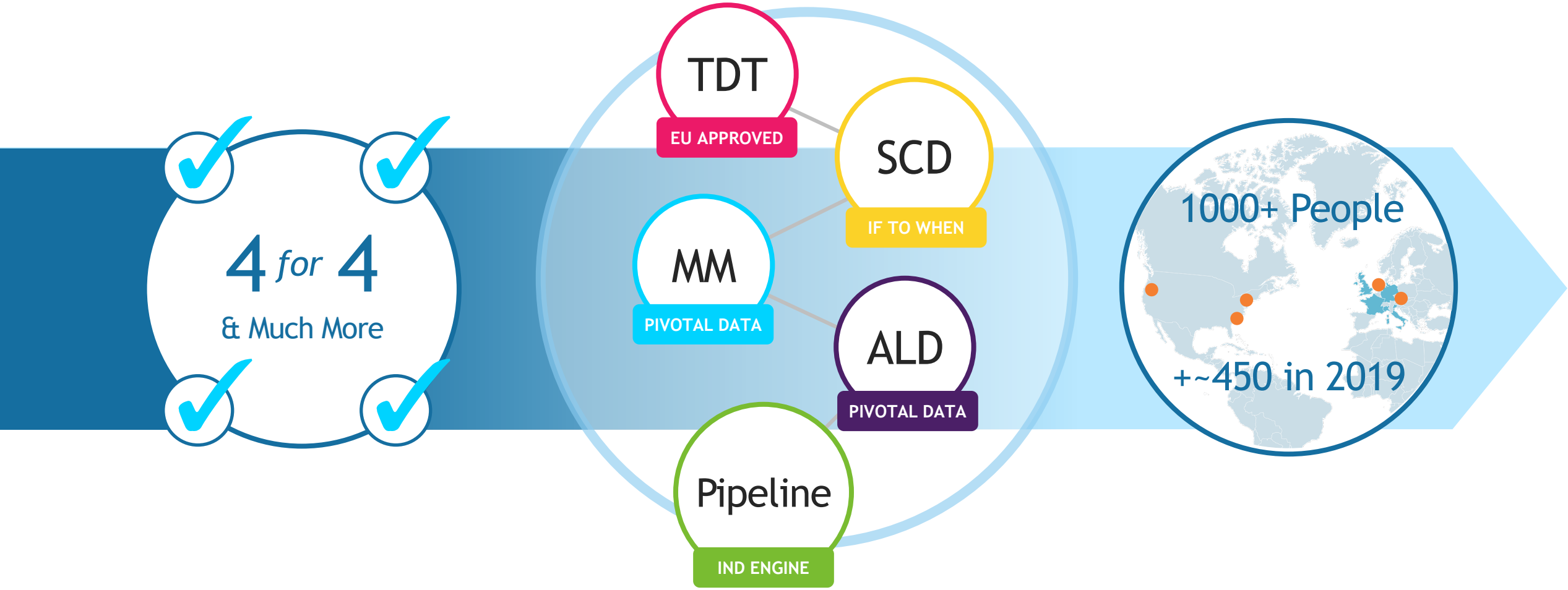
2019 - A Foundational Year



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A Bold Vision in 2019 - Becoming a Reality in 2020

Launched with label expansions

Launched

Launched/Submitted

Launched and moving towards earlier line approvals

1: Many translational engine delivering

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Planned 2020 Milestones – Distilling to Practice

	FIRST HALF 2020	BY SECOND HALF 2020
Regulatory Submissions	• Ide-cel (bb2121) MM U.S. BLA submission	• Lenti-D CALD EU MAA and U.S. BLA Submissions • LentiGlobin for TDT U.S. BLA Submission Completion
Clinical Updates	• Ide-cel (bb2121) KarMMa data* • LentiGlobin SCD Phase 3 HGB-210 study start	• Ide-cel CRB-401 data • Lenti-D ALD-102 data update • Zynteglo Phase 3 (HGB-207 and HGB-212) data • LentiGlobin SCD HGB-206 data and regulatory update • LentiGlobin SCD Phase 3 HGB-211 study start
Commercial & Foundation Building	• ZYNTEGLO first commercial patients treated • ZYNTEGLO QTC and Sick Fund contracts in place	• ZYNTEGLO Access and Reimbursement in additional EU countries established • Ide-cel U.S. launch ready • 1-2 New INDs

CASH RUNWAY INTO SECOND HALF 2021

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our platform

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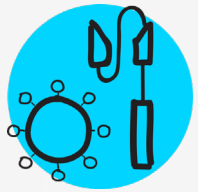
our gene and cell therapy technology platforms

GENE ADDITION

- Each person inherits features in the form of genes, which are made up of a molecule called DNA.
- Genetic disease is caused by mutations (or changes) in one or more genes, which are responsible for carrying genetic information to the body's cells.
- Based on our lentiviral vector platform, bluebird's investigational gene therapy seeks to introduce functional copies of a gene to the patient's own stem cells to address the underlying genetic cause of disease.



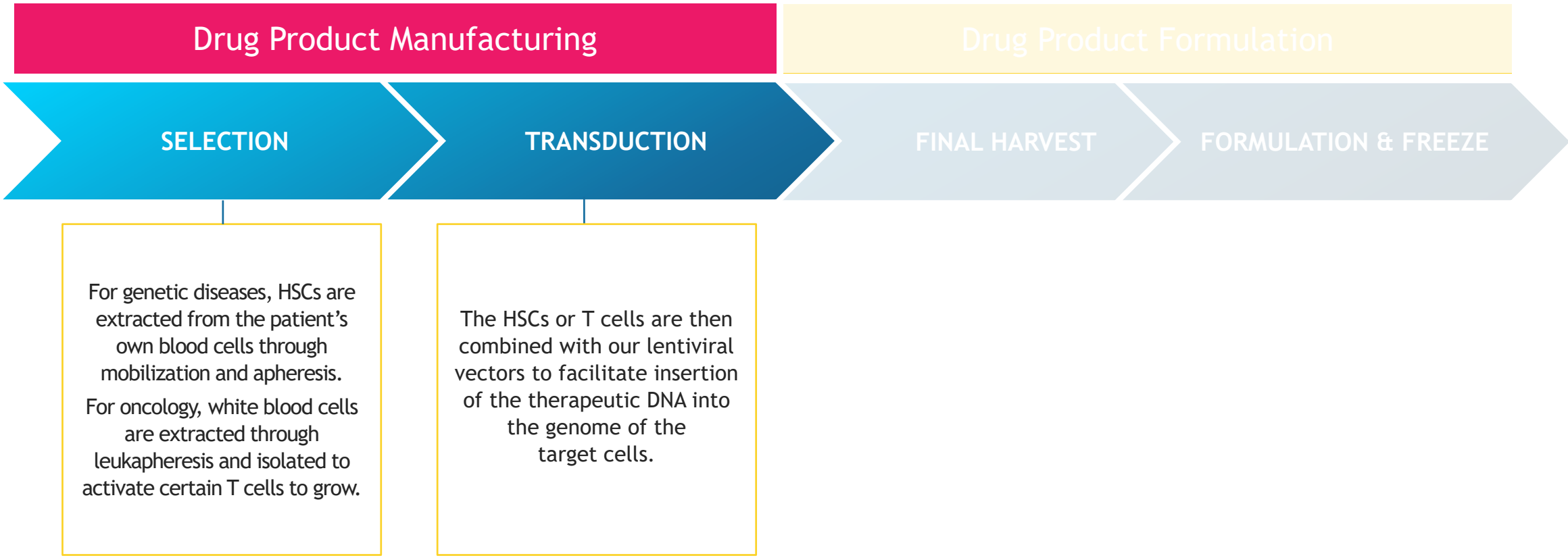
CELL THERAPY

- The body has natural defenses against cancer, and it may be possible to reprogram the immune system to destroy tumor cells.
- Our investigational CAR T approach uses our lentiviral vector platform to modify T cells to help them recognize and attack tumor cells.
- This approach has shown promising results in a variety of blood cancers, and we hope that soon it will be able to be used to address solid tumors as well.

GENE EDITING

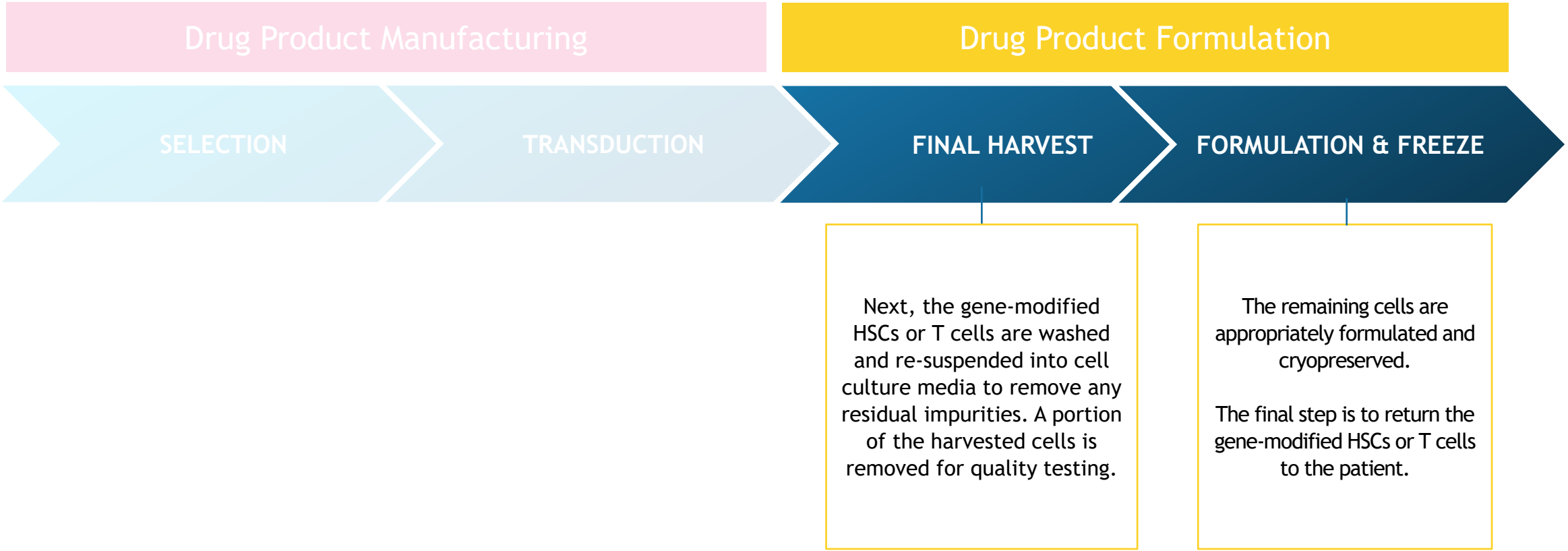
- Gene editing presents the unique ability to disable or correct ("edit") cells to address a variety of diseases at the genetic level.
- We are utilizing our investigational and proprietary homing endonucleases and megaTAL gene editing technology in a variety of potential applications and disease areas, including for oncology and hematology.
- Homing endonucleases and megaTALs are novel enzymes that provide a highly specific and efficient way to modify DNA sequences to edit or insert genetic components to potentially treat a variety of diseases.

gene-modified hematopoietic stem cells (HSCs) and T Cells: our investigational drug products

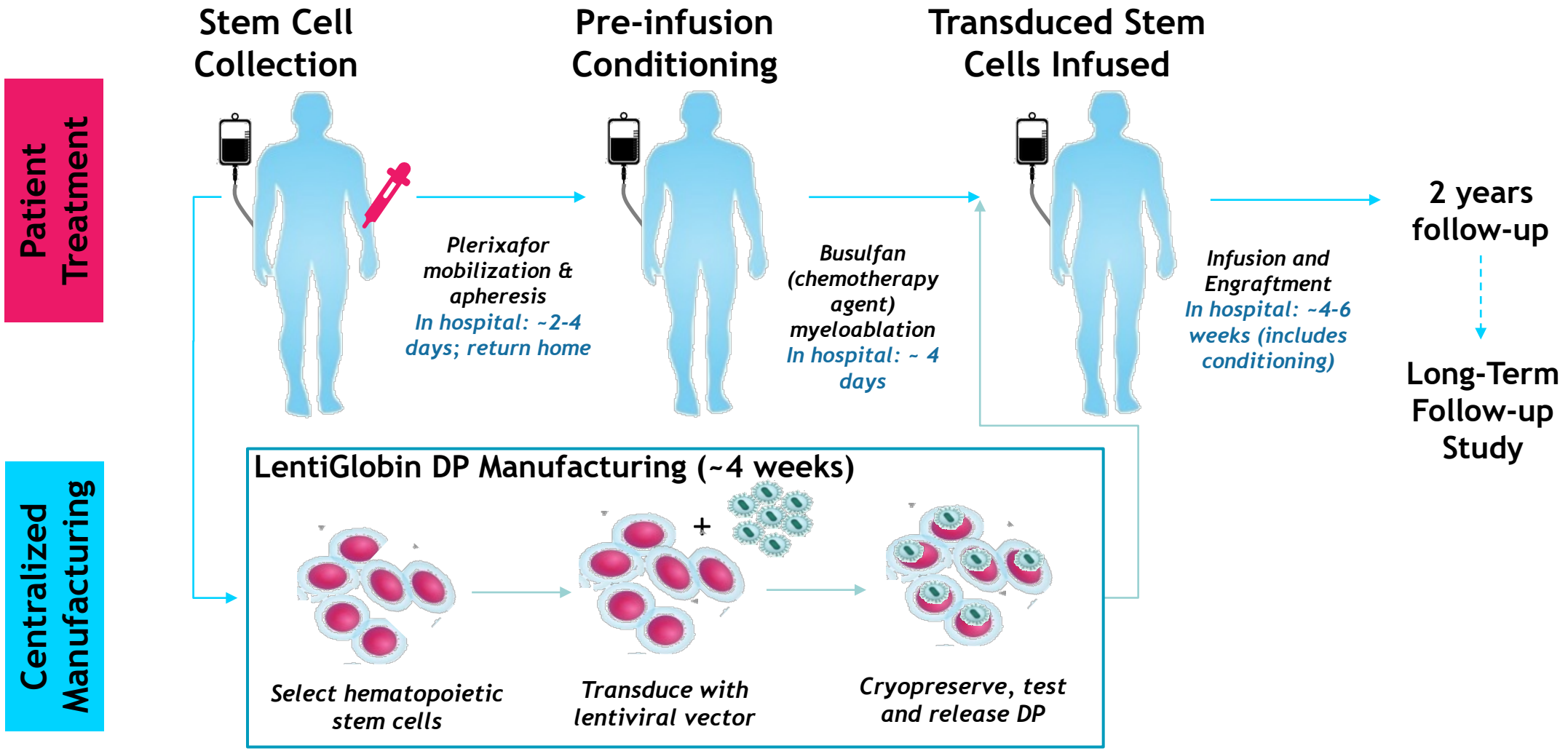


creating the investigational gene-modified HSCs and T Cells

The ultimate product of our manufacturing processes is the patient's own gene-modified HSCs and T cells, which we refer to as investigational **drug products.**

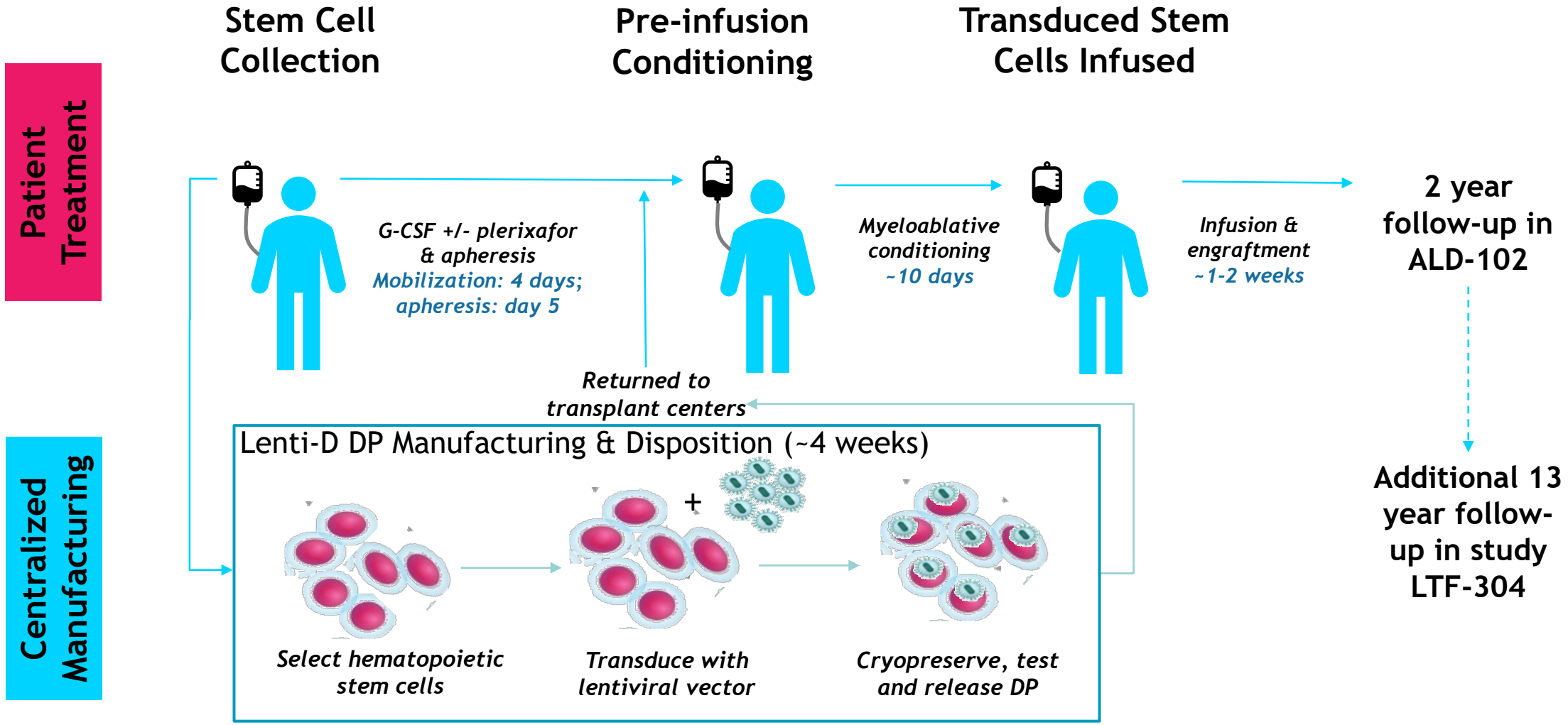


overview of investigational treatment process: hemoglobinopathies



DP, drug product; Treatment timeframes will vary by patient, ranges are approximately 6-10 weeks and include patient treatment and centralized manufacturing

overview of investigational treatment process: cerebral adrenoleukodystrophy



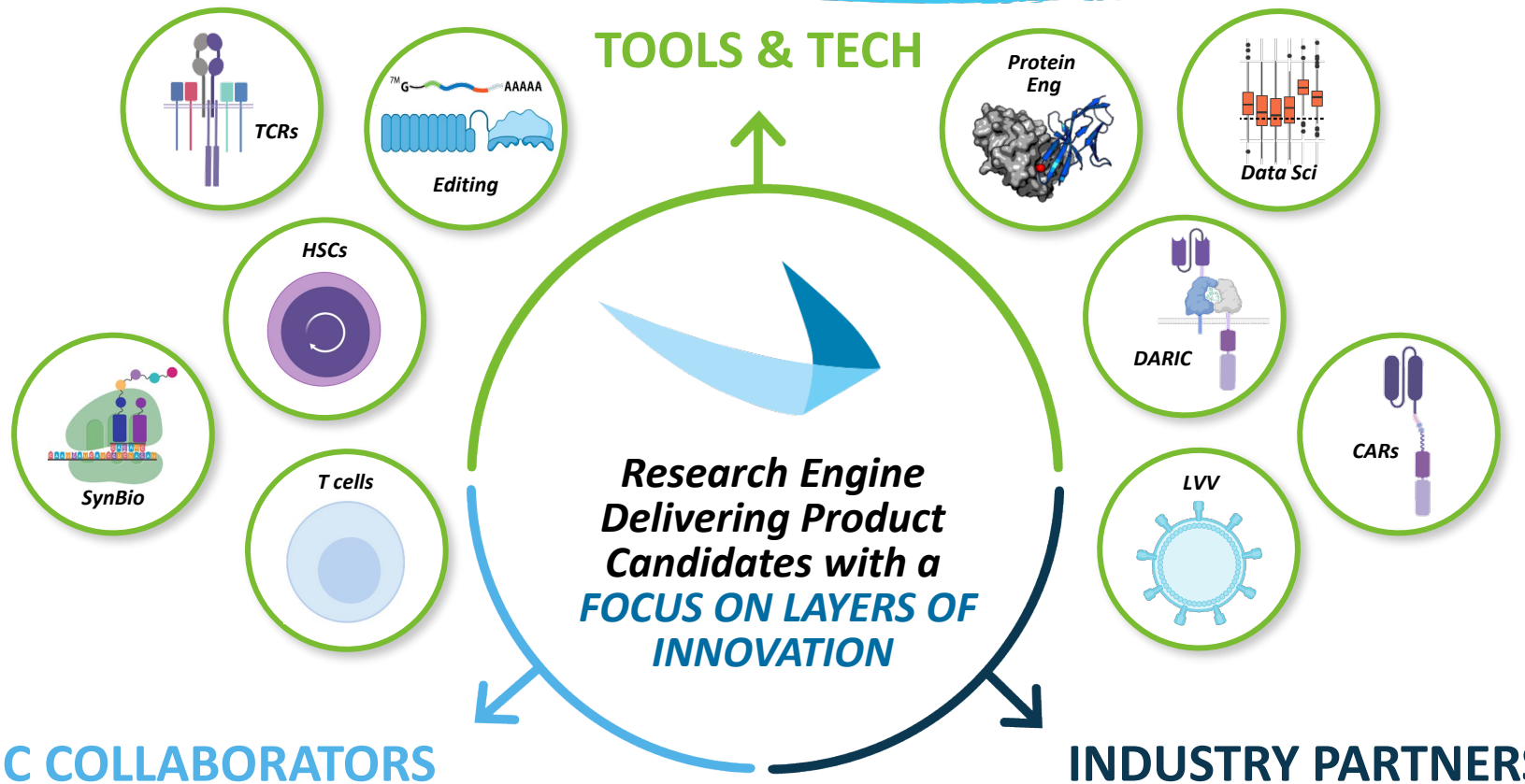
DP, drug product; Treatment timeframes will vary by patient/institution, and ranges include patient treatment and centralized manufacturing

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

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



ACADEMIC COLLABORATORS

INDUSTRY PARTNERSHIPS

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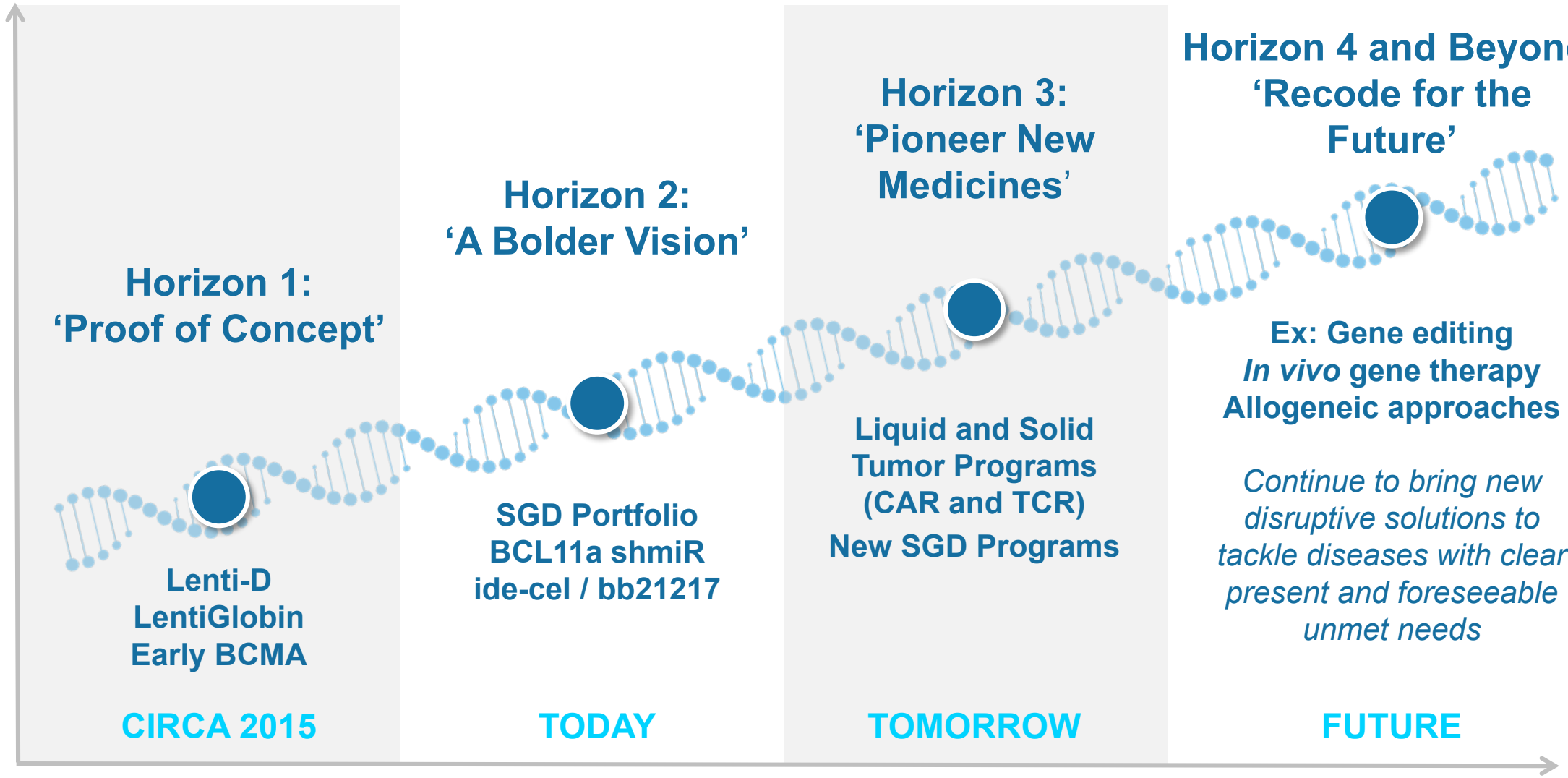
continuous innovation is in our DNA



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Intense & Steep Innovation Curve – R&D With a Soul

RESEARCH INNOVATION ENGINE

- PLATFORM TOOLS & TECH
- ACADEMIC COLLABORATORS
- INDUSTRY LEADING PARTNERS

→ NEXT GEN PRODUCT CANDIDATES

CLINICAL EXPERIENCE

- MM – bb21217
- SCD – BCL11a
- MCC – MCC1 TCR

- ZYNTEGLO™ for β-thalassemia
- ide-cel for MM
- LentiGlobin for SCD
- Lenti-D for CALD

ASK & ANSWER ENGINE

apceth BIOPHARMA · Boston Children's Hospital Until every child is well™ · Bristol-Myers Squibb · gritstone ONCOLOGY · INHIBRX · FortySeven · FRED HUTCH CURES START HERE® · Hitachi Chemical Working On Wonders · Lonza · medigene · University of Minnesota · novo nordisk® · REGENERON · Seattle Children's HOSPITAL • RESEARCH • FOUNDATION · TC BIOPHARM

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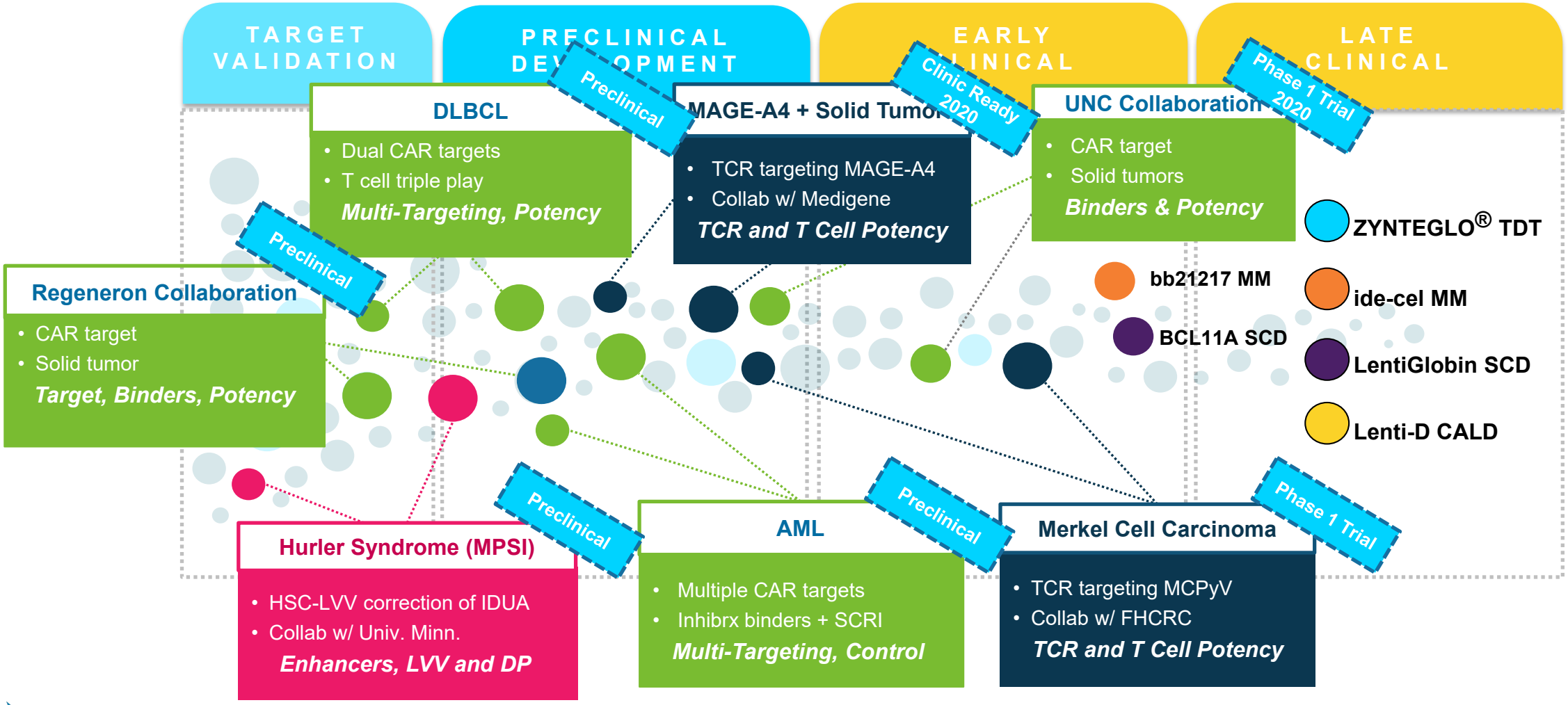
our research strategy in action:
emerging pipeline of nextgen products



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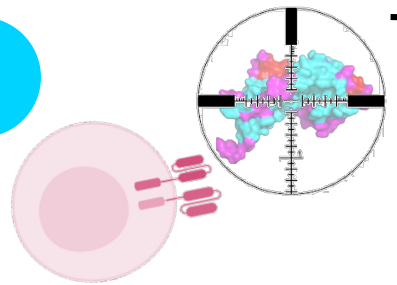
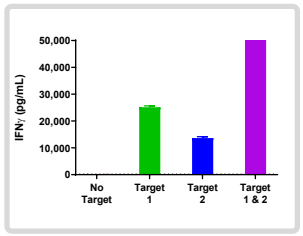
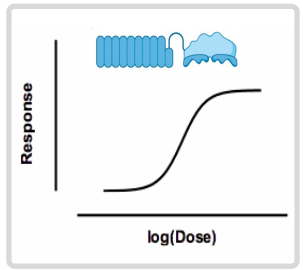
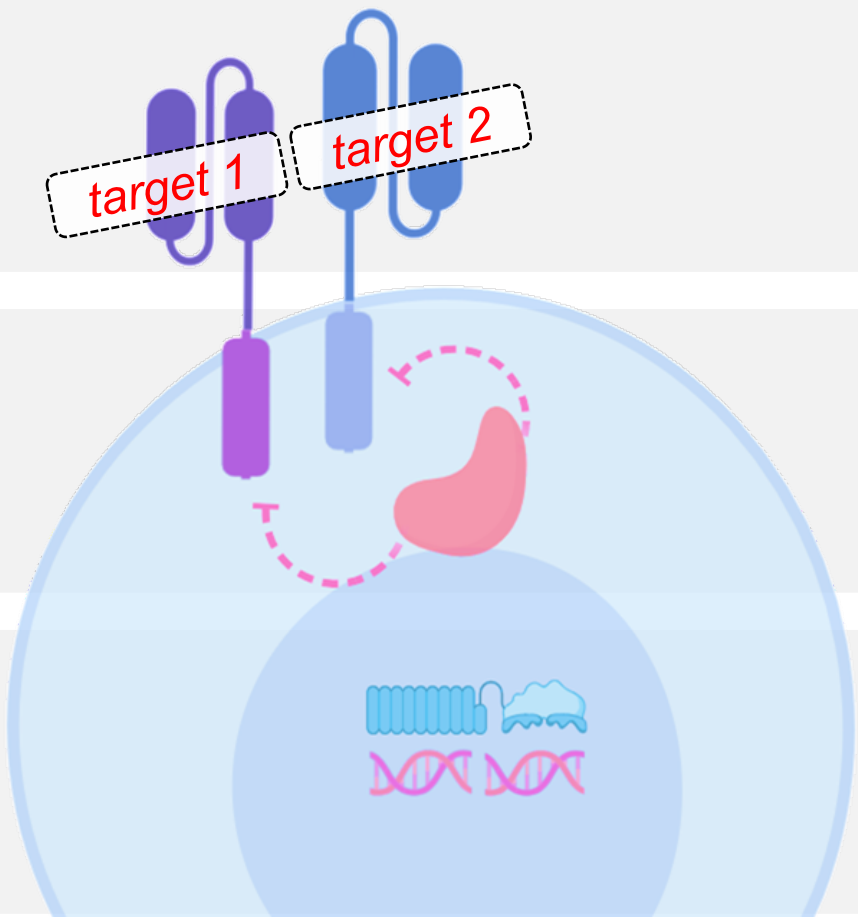
Diffuse Large B-Cell Lymphoma -Triple Threat Approach

	LAYER	PURPOSE
1	*dual-CAR targeting*	prevent escape
2	*signal extension*	enhance T cell activation
3	*signal amplification*	improve T cell persistence









EACH LAYER INFORMS 1:MANY PLATFORM

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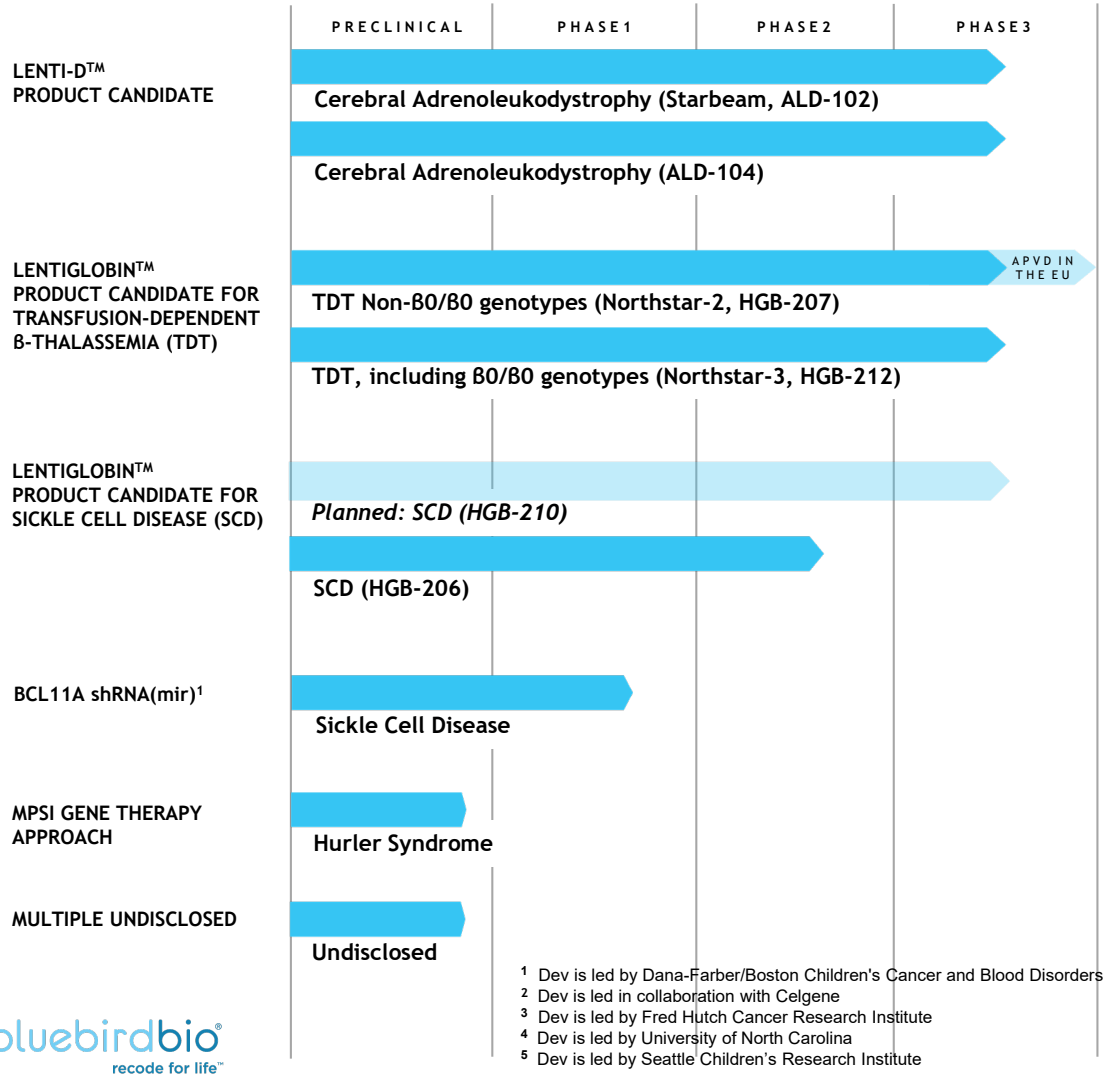
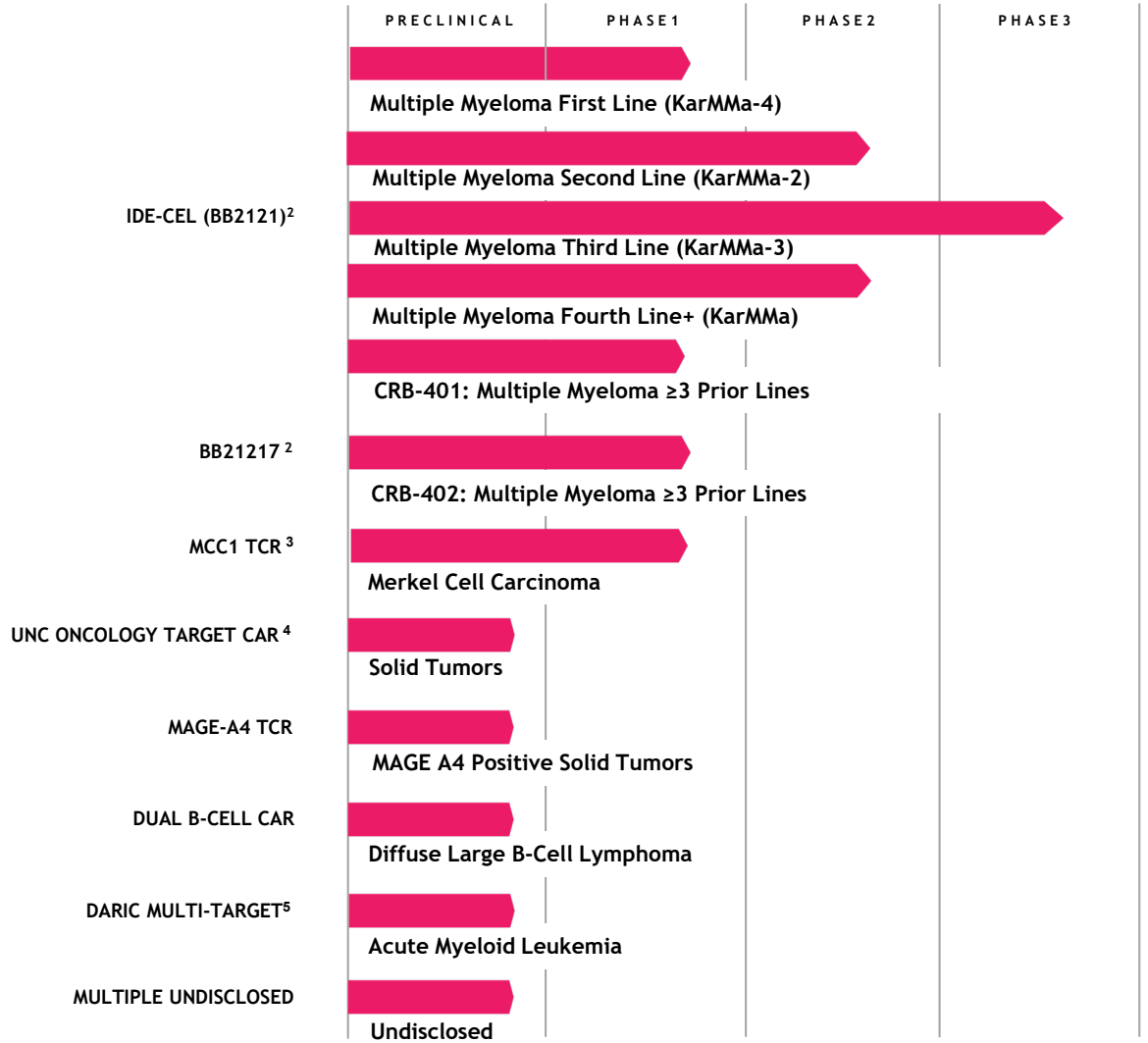
Engine Starting to Deliver

Severe Genetic Diseases



Oncology



1 Dev is led by Dana-Farber/Boston Children's Cancer and Blood Disorders Center
2 Dev is led in collaboration with Celgene
3 Dev is led by Fred Hutch Cancer Research Institute
4 Dev is led by University of North Carolina
5 Dev is led by Seattle Children's Research Institute

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access and value

Access & Value – As An Ecosystem We Can ALL Do Better

Poor Behaviors Persist

- EPS & Q2Q Driven Mindset
  - Because-You-Can Pricing
  - Unexplainable Price Increases
  - Excessive Innovator Rewards - Top 10 Medicines Anticipated ~$1.4 TRILLION in Revenue Through 2024*
- Defending the Status Quo
  - Biosimilar Resistance and Patent Extensions

Good Behaviors Gaining

- Transparent Engagement Across Stakeholders
- Limiting/Eliminating Price Increases
- Resolving Patient Co-Pay and Access
- New Ideas Taking Hold (And Expected)
  - Prevalence Based Revenue Capping
  - At-Risk / Outcomes Based Payments
  - EQRx Newco – "Me Too @ Lower Cost"

Source: EvaluatePharma

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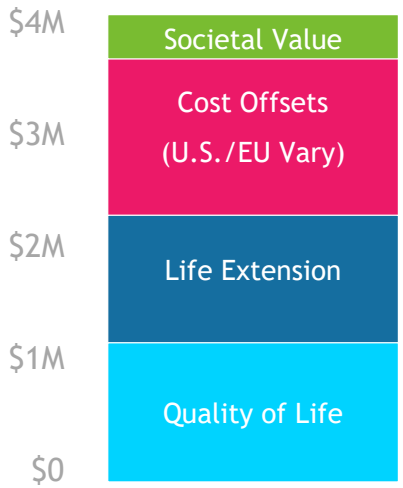
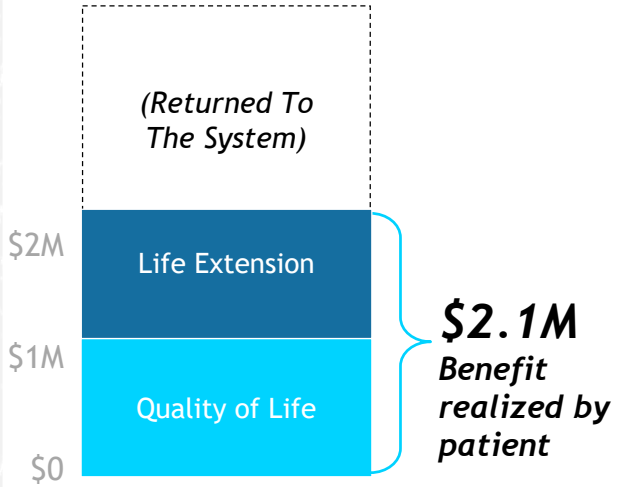
What has (and has not) gone into assessing the value of ZYNTEGLO®?

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

Traditional
All Inclusive Calculation



ZYNTEGLO
Intrinsic 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.

bluebird Value Principles and Ideal Payment Model

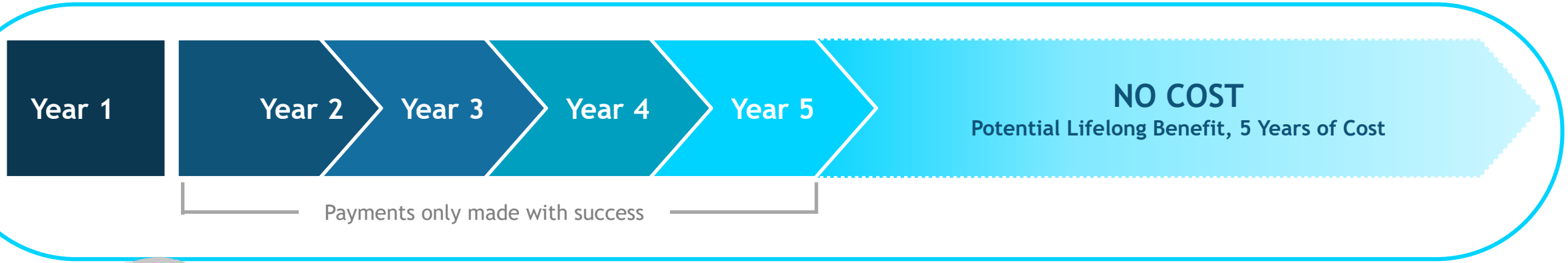
Fair Value Recognition
QoL + Life Extension

Share Risk
Up to 80% at Risk

Consider Patient Affordability
Over ~5 years

System Affordability
XXX Lifetime Cost Capped

BE RESPONSIBLE, FUND INNOVATION AND DON'T DO STUPID STUFF



zynteglo®

- ✓ Estimated cost effective value $3-4 million, ~$2M based on life extension and quality of life (excluding cost offsets)
- ✓ Lifetime cost if successful: $1.76* million (€315K/year, capped at 5 years)

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*Based on exchange rate of 1 Euro = $1.11 USD on January 7, 2020

Lenti-D for CALD

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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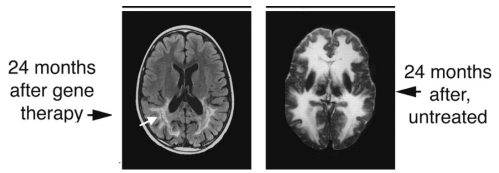
Cerebral Adrenoleukodystrophy - From Tragedy to Hope

2009

Science
AAAS



RECODE

Enhanced Construct
&
Manufacturing

EPNS: 2019

- ✓ 15/17 patients alive and MFD-free at 24 months follow up and continue to be MFD-free with up to 5 years of follow-up
- ✓ 32 total patients treated

Data as of April 25, 2019

2020

- **2H 2020 anticipated regulatory submission**
- **Newborn screening active in 14 US states; several pilot programs in EU**

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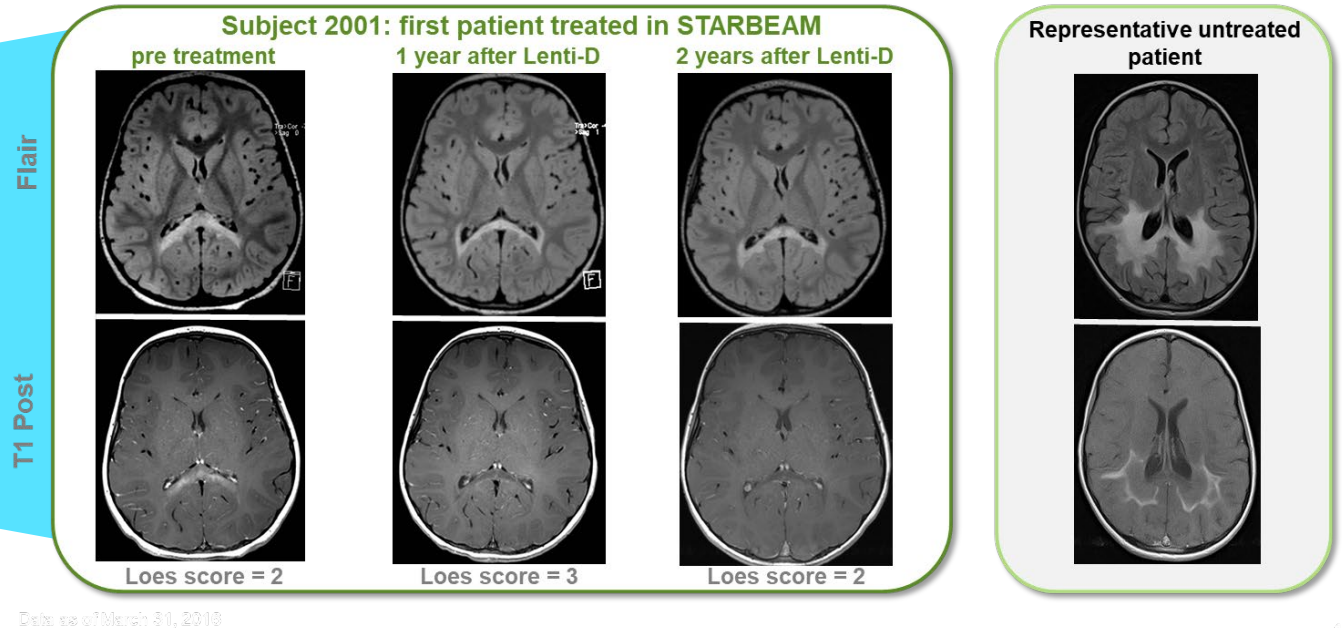
Science 2009

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

LentiGlobin for TDT

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

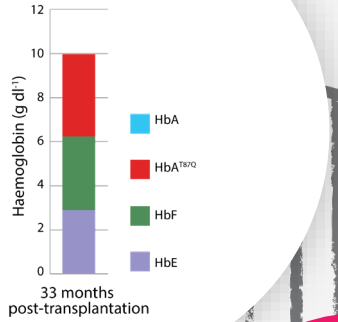
- EU approval granted June 2019
- Studies ongoing:
  - Northstar-2 (HGB-207)
  - Northstar-3 (HGB-212)
  - Long-term follow-up: LTF-303

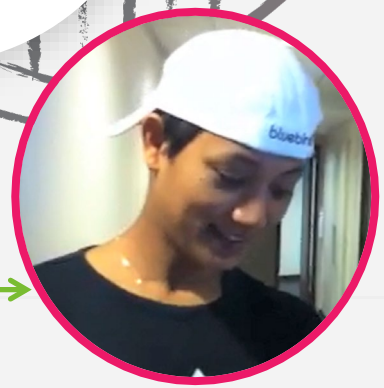
[1]Biffi A. Gene Therapy as a Curative Option for beta-Thalassemia. *N Engl J Med.* 2018;378(16):1551-1552.
[2]SayaniFA, Kwiatkowski JL. Increasing prevalence of thalassemia in America: implications for primary care. Ann Med. 2015;47(7):592-604.
[3]Centers for Disease Control and Prevention. Living with 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.

Transfusion-Dependent ß-Thalassemia – Reimagined Future

2010

nature





RECODE

Vector Potency &

Manufacturing

Enhancement

ASH 2019

- 90% of evaluable patients with a non-ß0/ß0 genotype achieved TI, with median average total Hb levels of 12.2 g/dL in Phase 3 Northstar-2 (HGB-207) study

Data as of June 12, 2019

zynteglo®

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

✓ **EU Approved 2019**

✓ **US rolling BLA initiated 2019**

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Nature 2010

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

NORTHSTAR STUDY	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	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
NORTHSTAR-2 STUDY	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
NORTHSTAR-3 STUDY	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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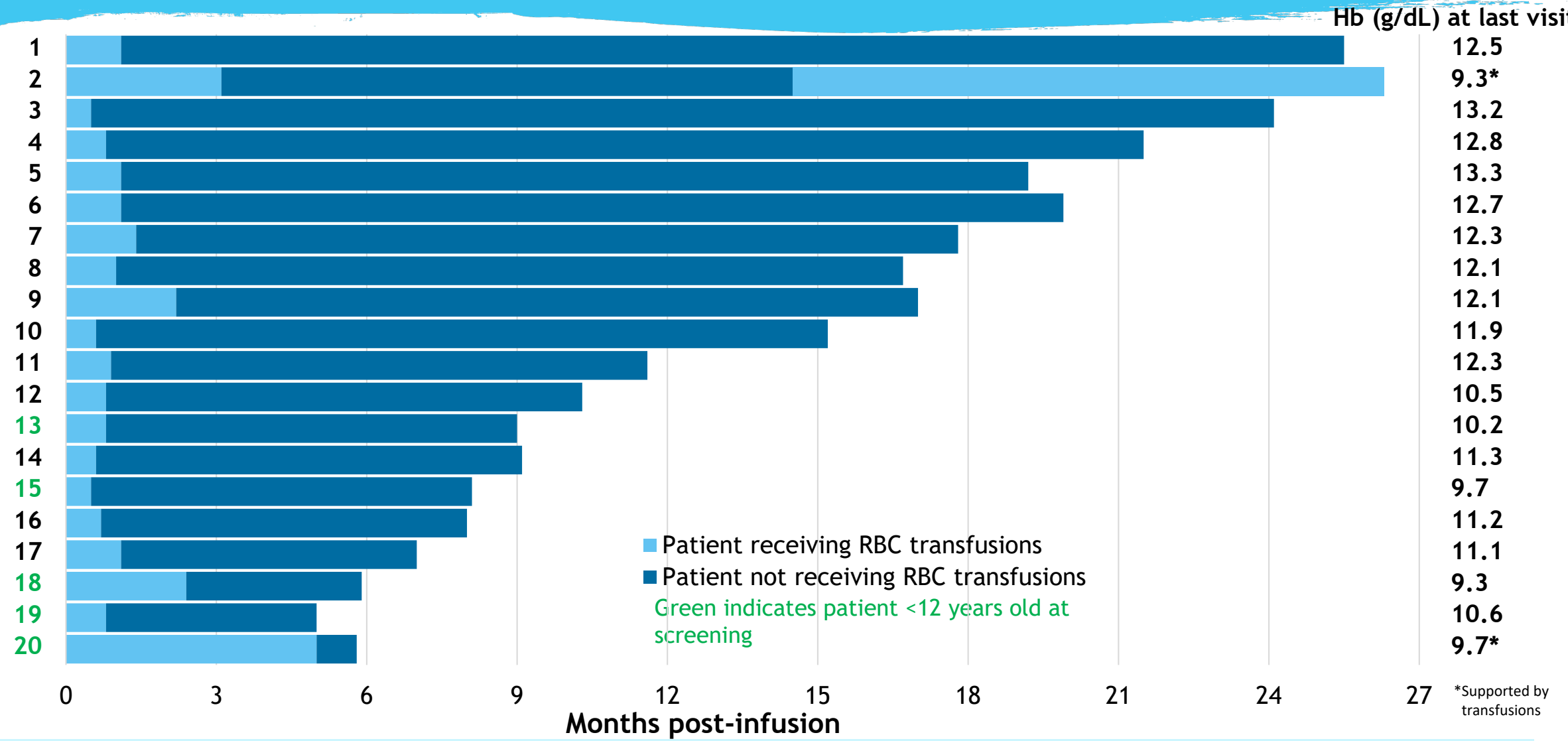
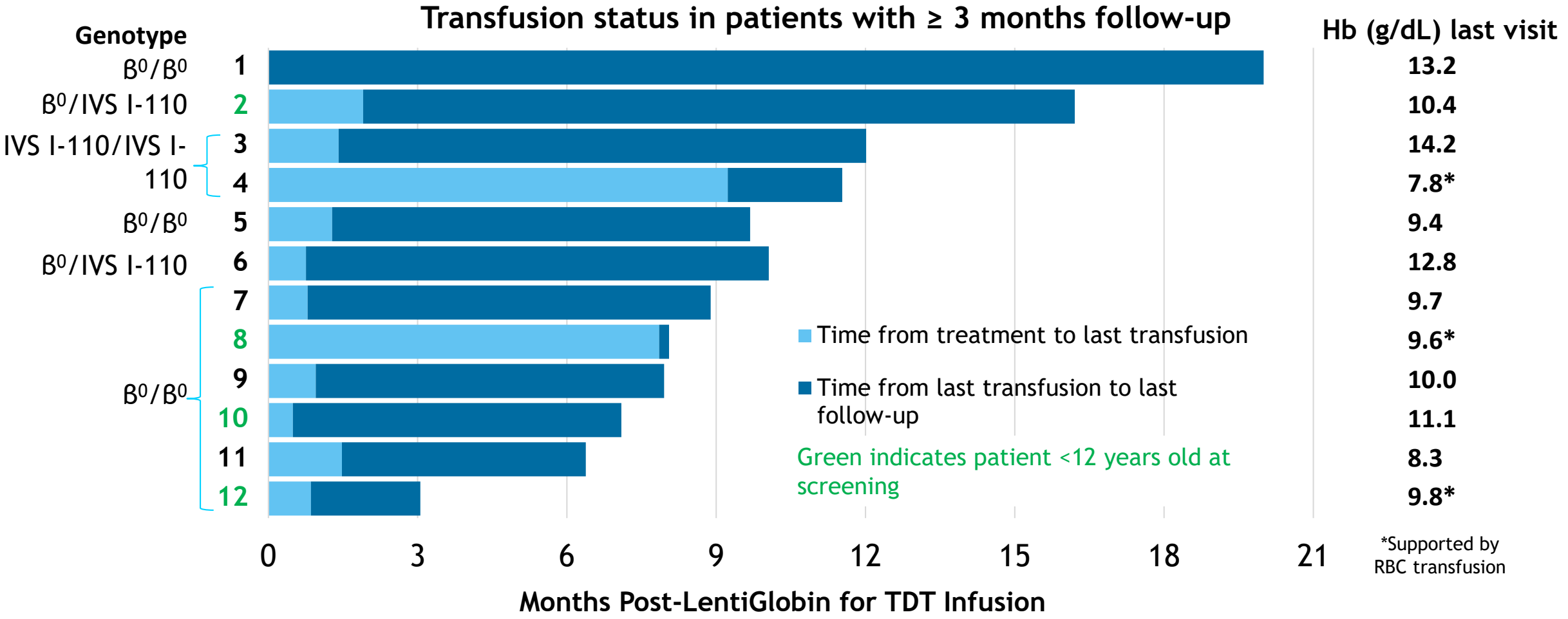
HGB-207: 90% (18/20) of patients with > 3 months follow-up are off pRBC transfusions



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

Data as of 12 June 2019

HGB-212: 9/11 patients with ≥ 6 months follow-up have been off transfusions for ≥ 3 months

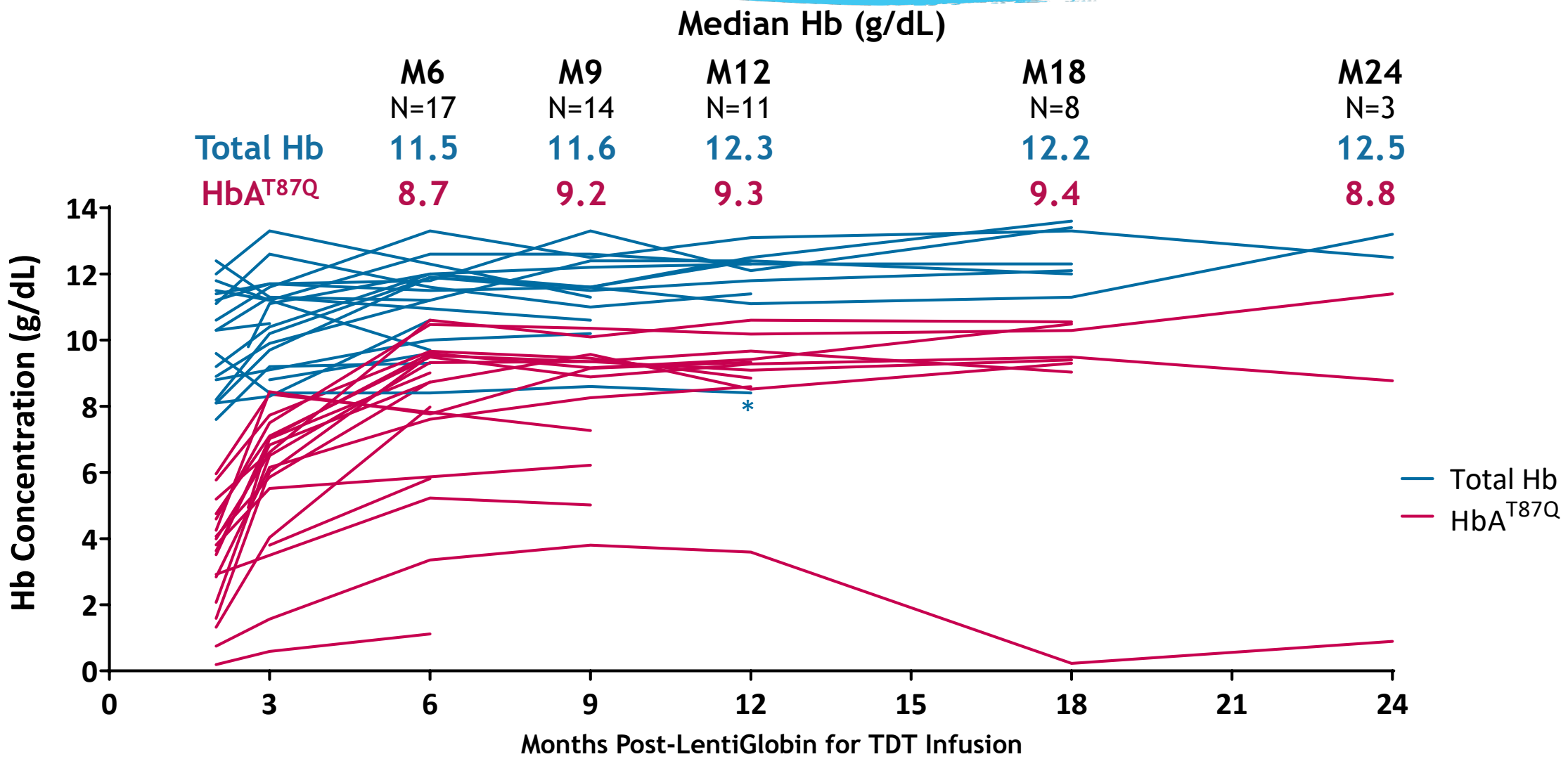


Patients 1 and 2 achieved and maintained transfusion independence Weighted average Hb ≥ 9 g/dL without RBC transfusions for ≥ 12 months

Hb, hemoglobin; RBC, red blood cell

Data as of 30 September 2019

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

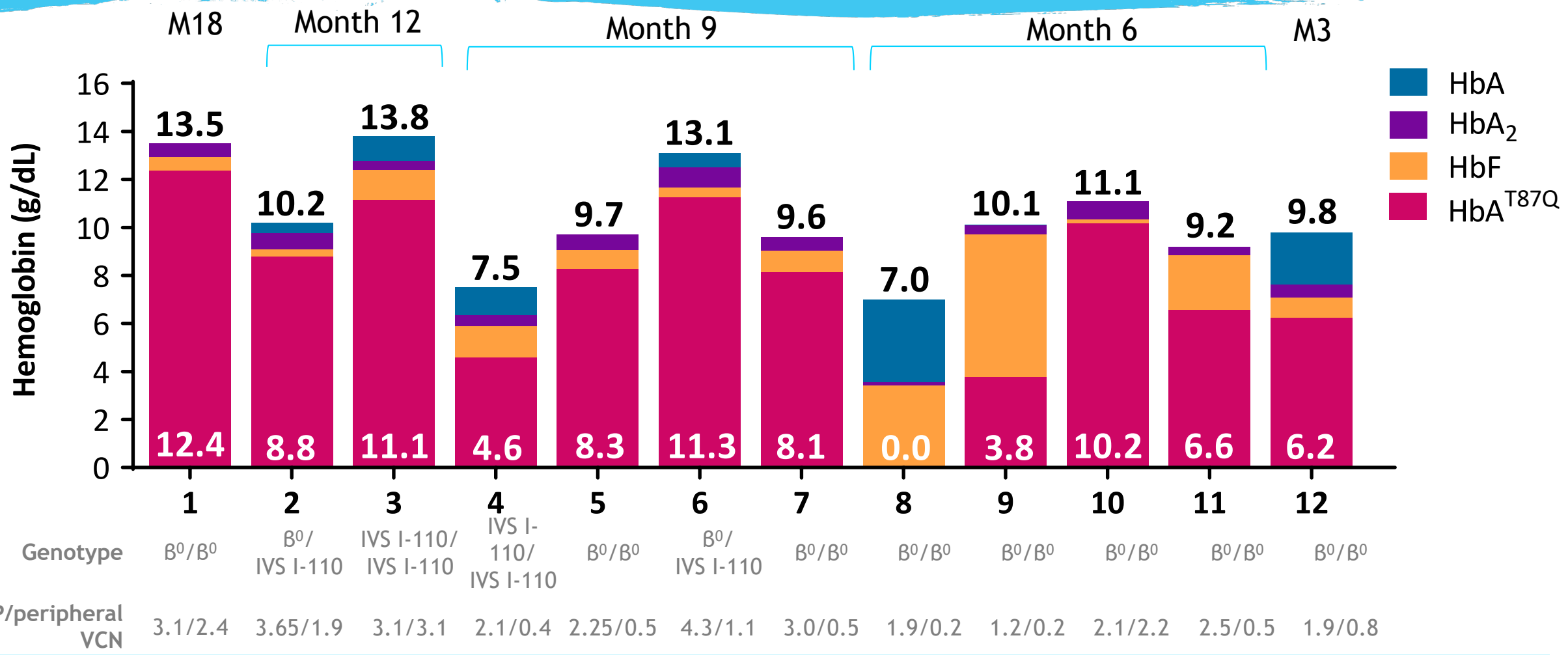


HGB-207 utilized a range of manufacturing process conditions as the commercial manufacturing process was defined

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

Data as of 12 June 2019

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

Data as of 30 September 2019

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

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

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

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

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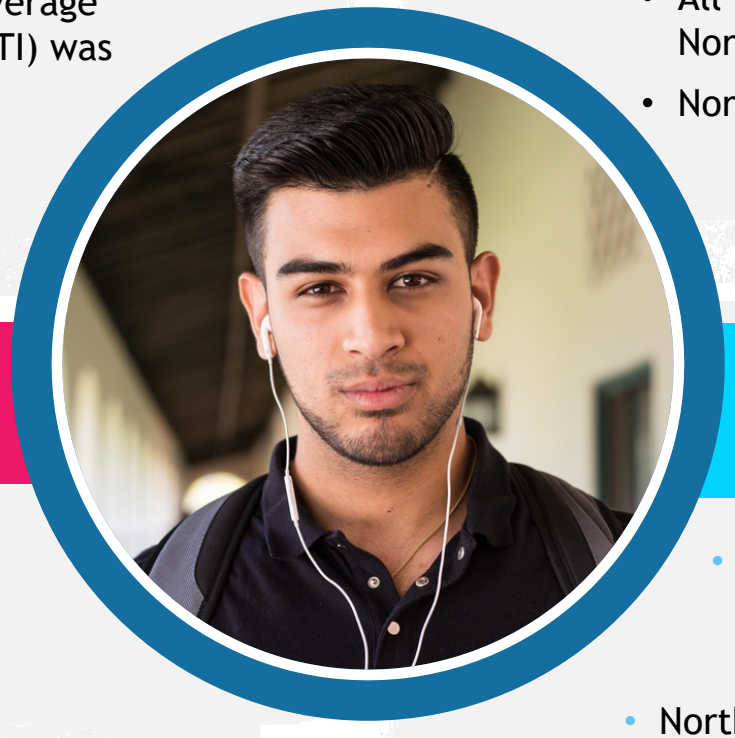
ZYNTEGLO® is the first and only one-time therapy for TDT now approved in the EU for people with TDT and non-β^0/β^0 genotypes

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

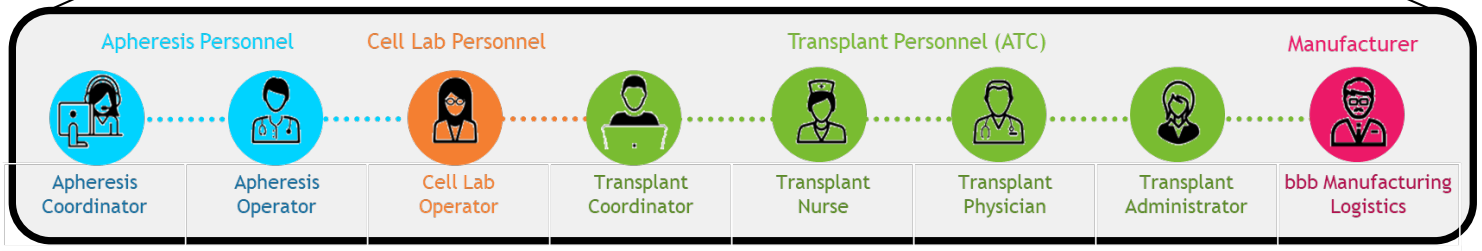
Path To Patients – Making It Happen In The Real World

SUSPENSION

Treating Patients At Scale

COMMERCIAL QUALIFIED TREATMENT CENTERS (QTCs) & DRUG PRODUCT

Delivering For Commercial



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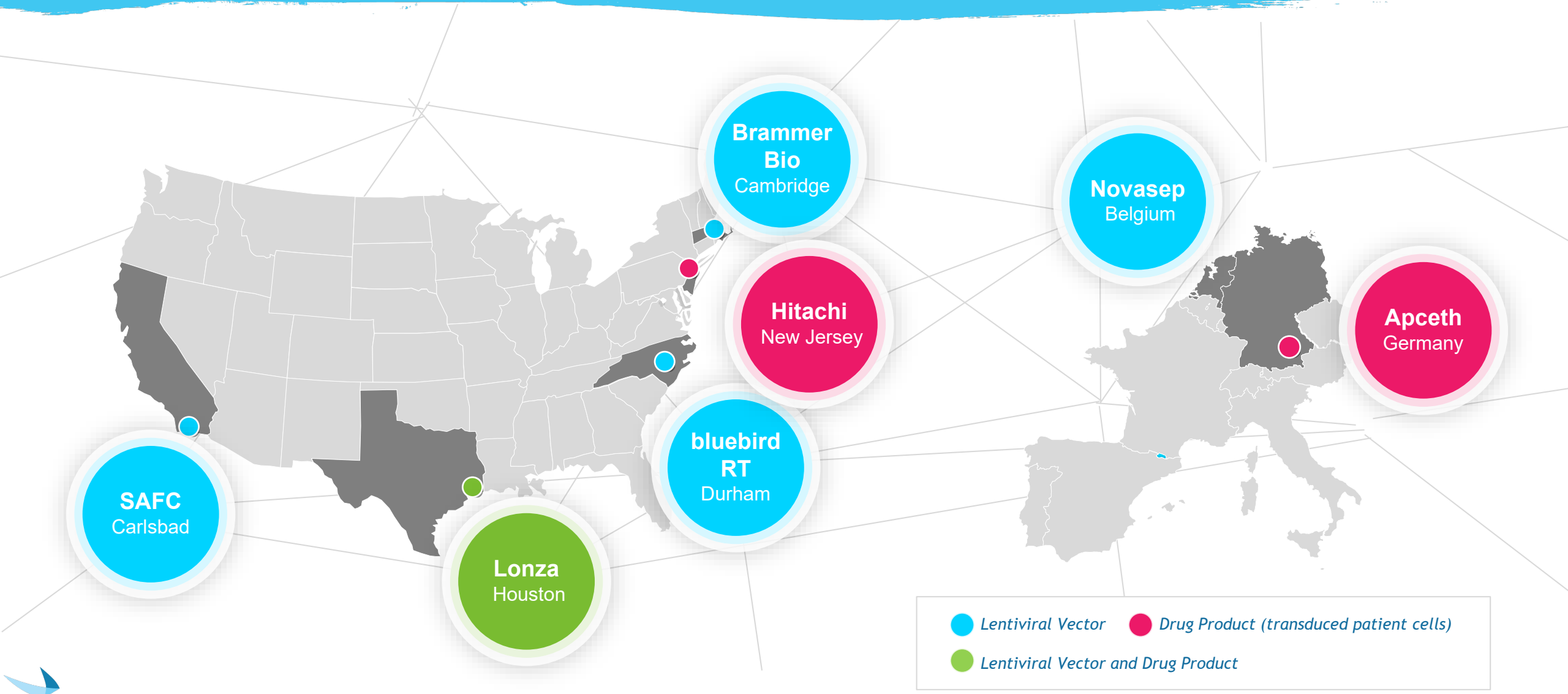
Manufacturing Network Strategy - Product Supply Through Both Internal Capacity & Contract Partners



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Establishing Promising Access & Value Foundation

EU Launch Readiness

- ✓ First ever at-risk value-based agreement signed with multiple Sick Funds in Germany (~50-70% of patients in Germany covered)
- ✓ Team in place in Zug, UK, France, Italy, Germany, and Nordic Markets
- ✓ Qualified Treatment Centers and manufacturing ready in Germany

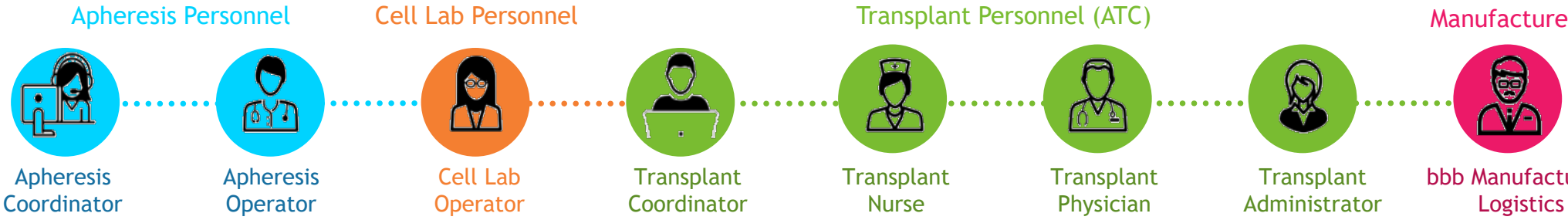
U.S. Launch Readiness

- ✓ Team in place for U.S. commercialization
- ○ Payers (Commercial) – Actively engaging to enable access & value-based payment over time at launch
- ○ Policy (State & Federal) - Focused on enabling value-based payment over time in commercial and for Medicaid markets to drive access
- ○ Distribution – Establishing customized distribution model to serve QTC & payer needs

Market and Patient Engagement

- ✓ Disease Education and outreach in place
- ✓ Patient Advocacy education and initiative support

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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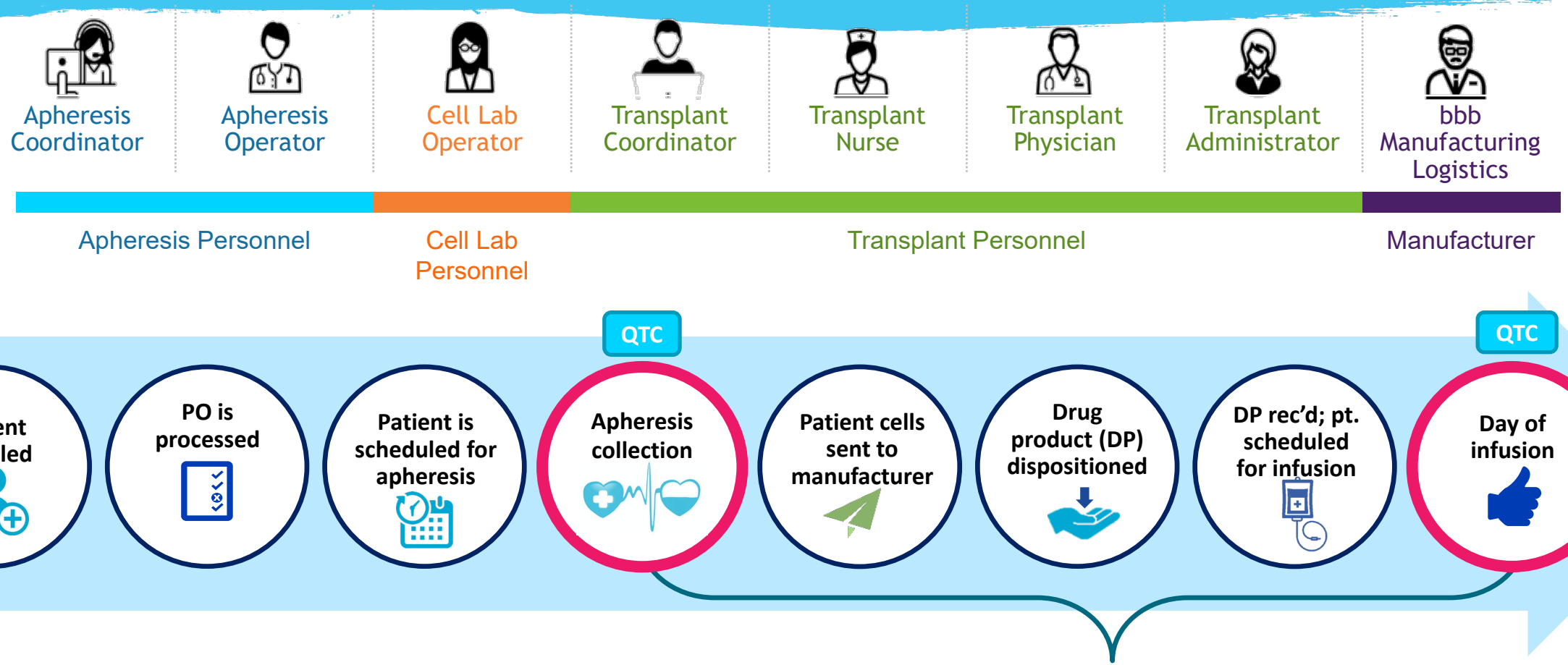
The Patient Journey is an Organizing Framework for bluebird QTC Support



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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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

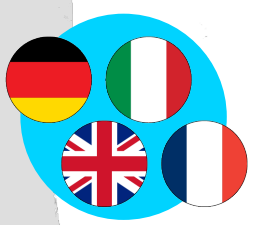
BLUE style commercial success factors

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



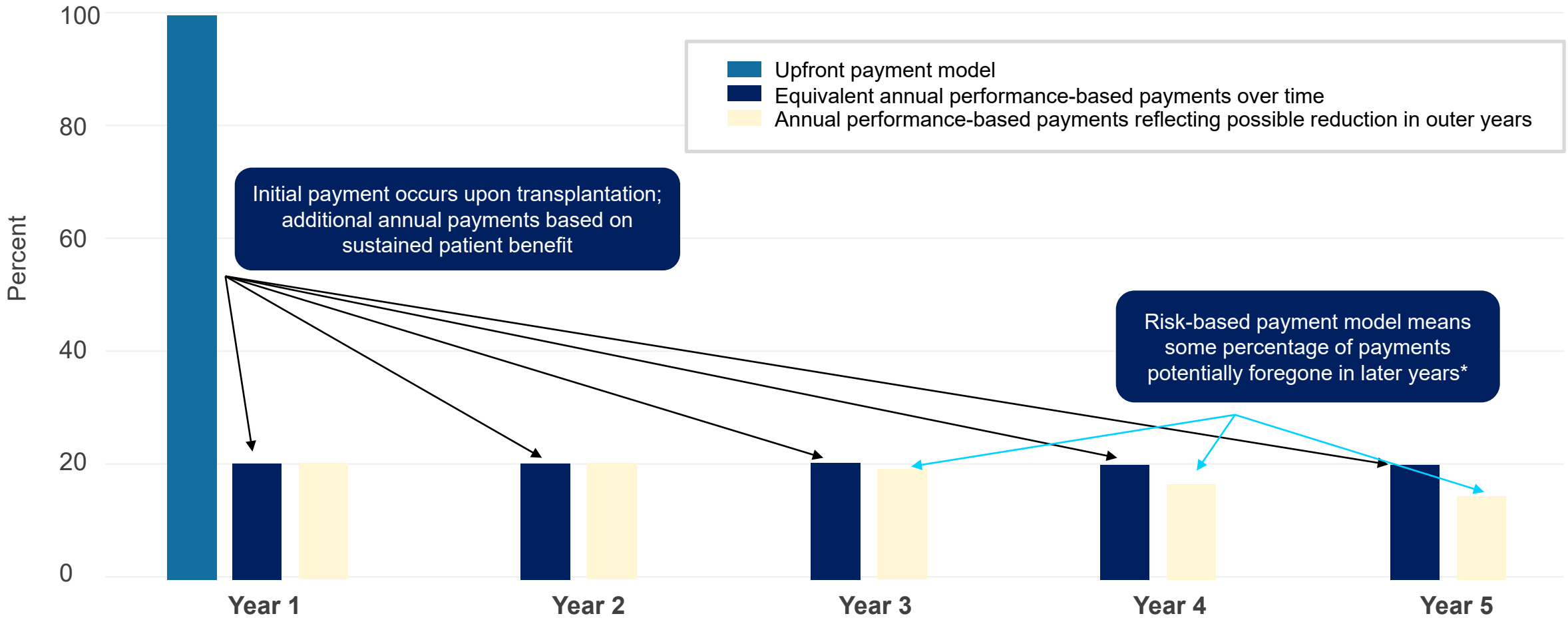
Pricing approval by country

Commercial patient infusions

Learnings and local market insights to inform continuous innovation

Recoding the Payment Model

Payment Modeling Scenarios



*Illustrative reduction in payments

LentiGlobin for SCD

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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

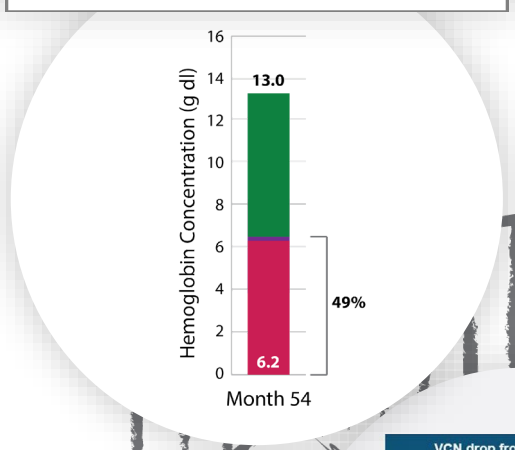
- Plan to pursue an accelerated development path based on hematological primary endpoint
- Phase 3 HGB-210 study to be open and enrolling patients by early 2020
- HGB-206 target enrollment achieved

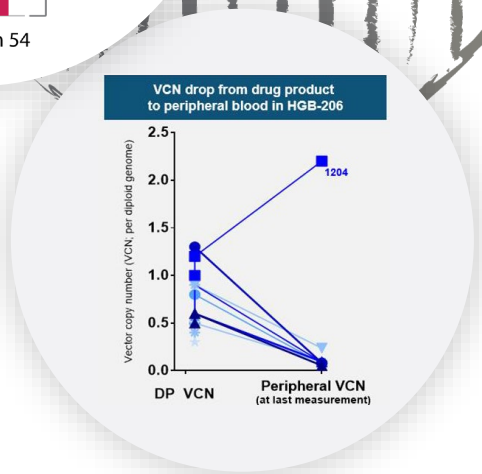
[1]Kato GJ, Piel FB, Reid CD, et al. Sickle cell disease. *Nat Rev Dis Primers*. 2018;4:18010.
[2]Piel FB, Patil AP, Howes RE, et al. Global epidemiology of sickle haemoglobin in neonates: a contemporary geostatistical model-based map and population estimates. *Lancet*. 2013;381(9861):142-151.
[3]Hassell 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*

Sickle Cell Disease – Daring to Dream

2017

The NEW ENGLAND JOURNAL of MEDICINE





RECODE

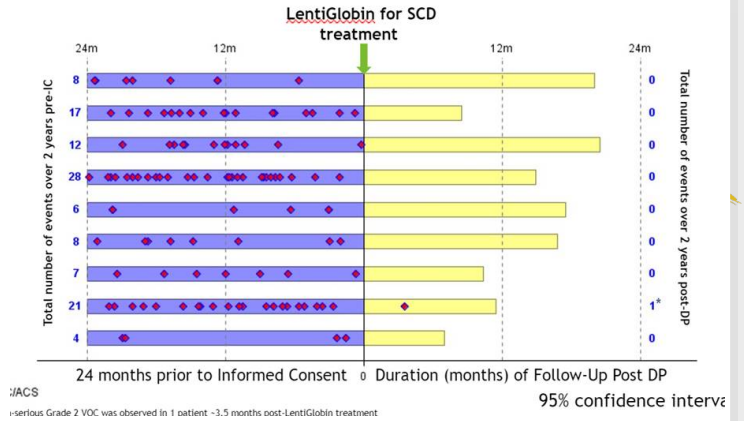
Pre-Tx Transfusions

More Thorough Conditioning

Higher Cell Dose

Higher VCN

ASH 2019



99% reduction in annualized rate of VOC + ACS*

- **Accelerated development underway**

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New England Journal of Medicine 2017

*HGB-206 Group C patients with history of VOCs and ACS who had ≥ 6 months of follow-up; data as of August 26, 2019

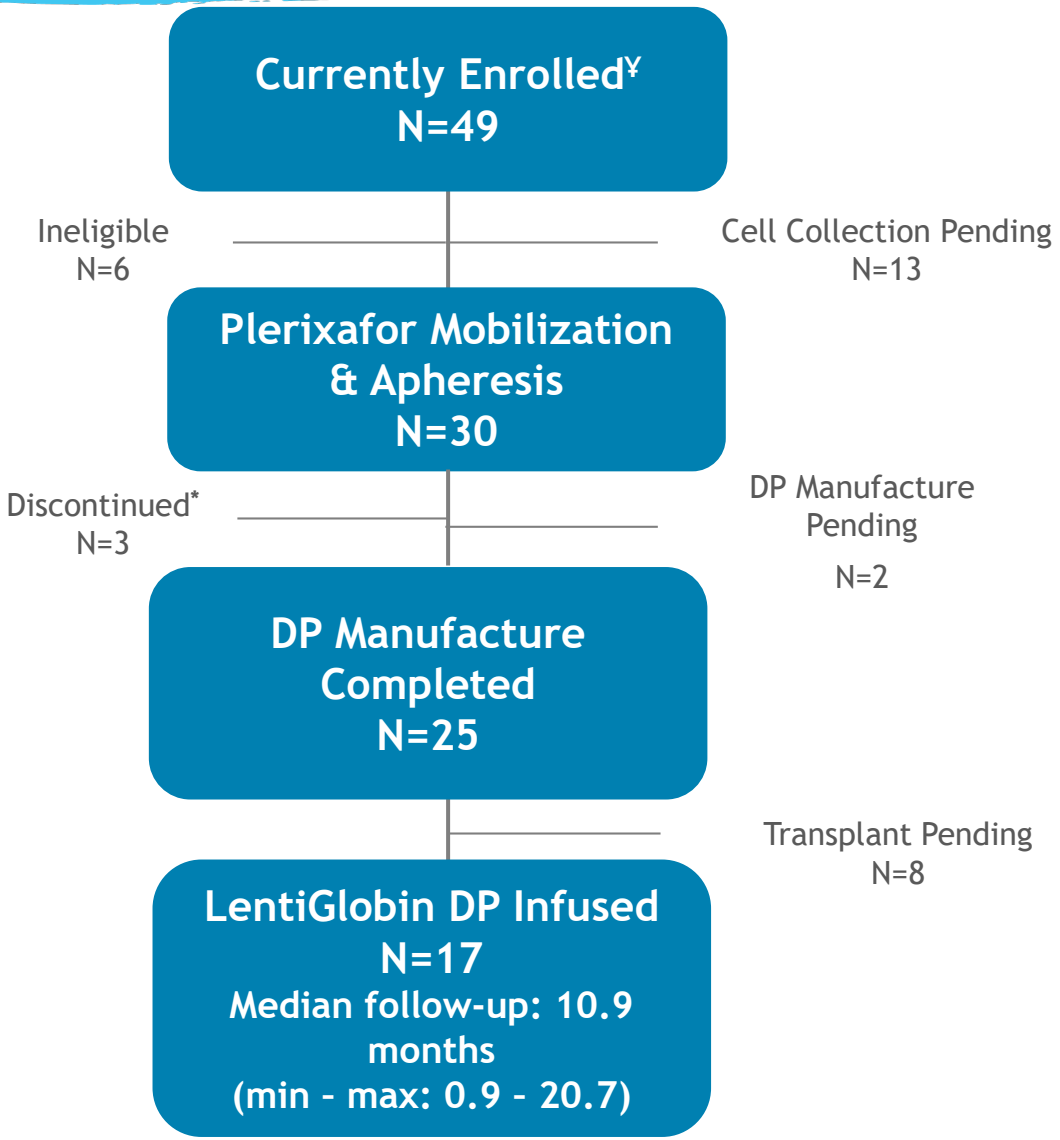
Expanding development program to evaluate LentiGlobin across SCD patient types and ages

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

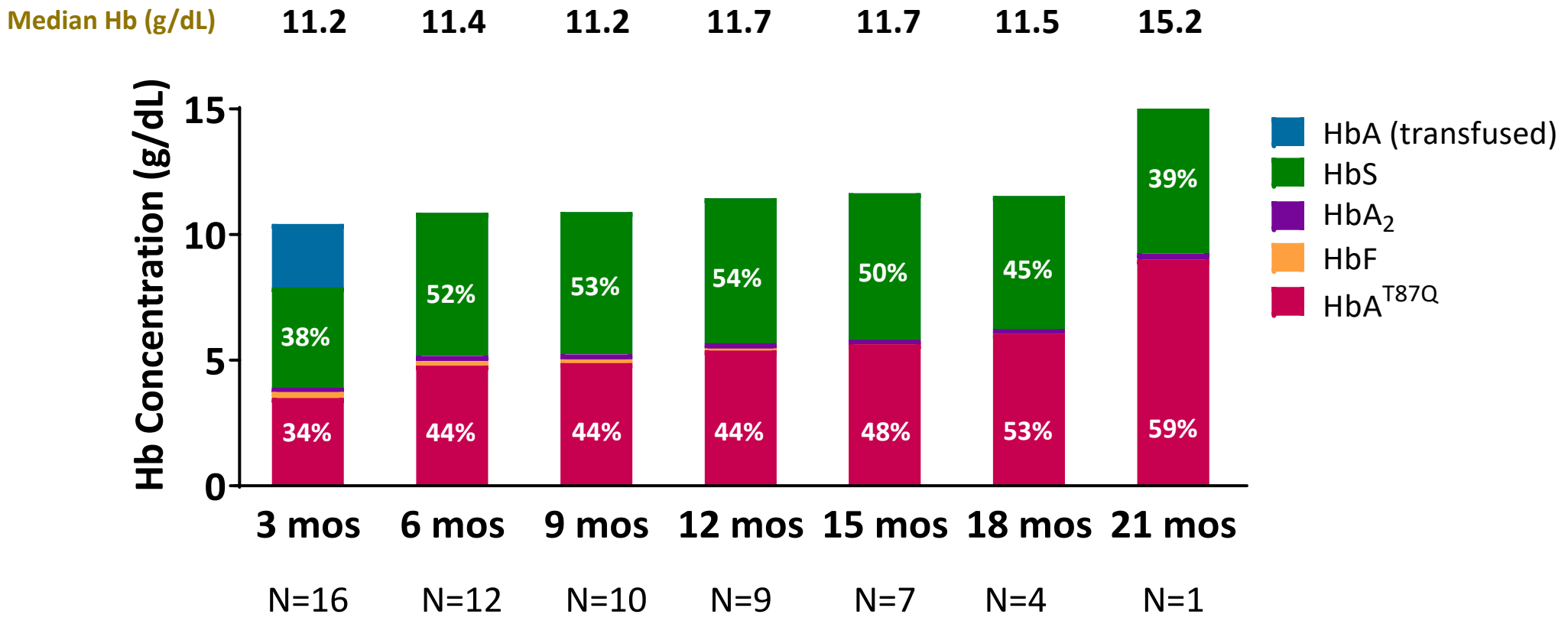


¥ Currently active, not recruiting

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

Data as of 26 August 2019

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)

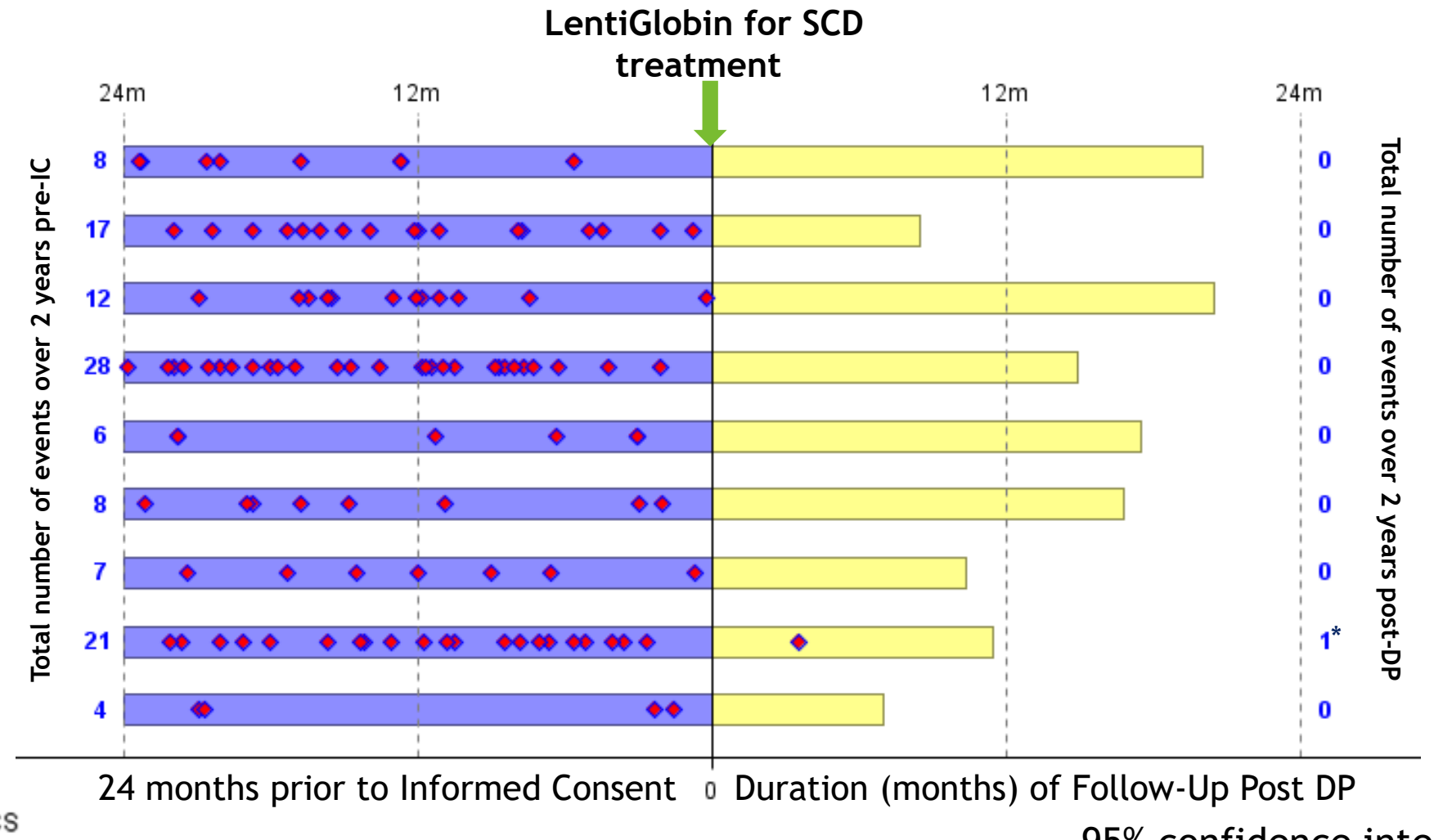


- Median HbS ≤ 60% at ≥ 6 months post-LentiGlobin for SCD treatment
- Total Hb and HbA^{T87Q} ranged from 9.3 – 15.2 g/dL and 2.7 – 9.0 g/dL, respectively, at last visit in patients with ≥ 6 months of follow-up

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

Data as of 26 August 2019

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



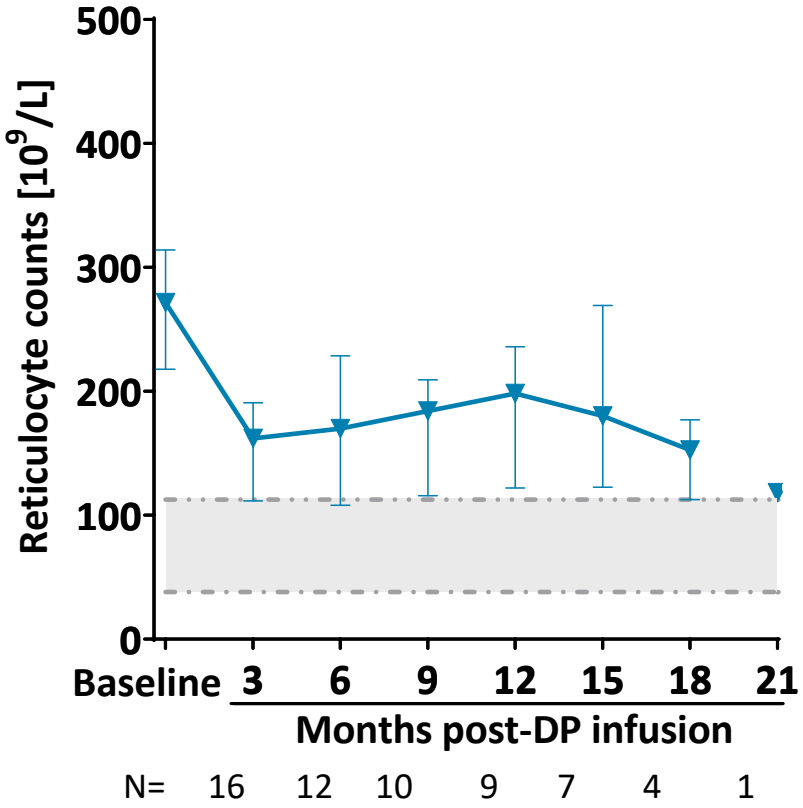
95% confidence interval: 92.5-100%

*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

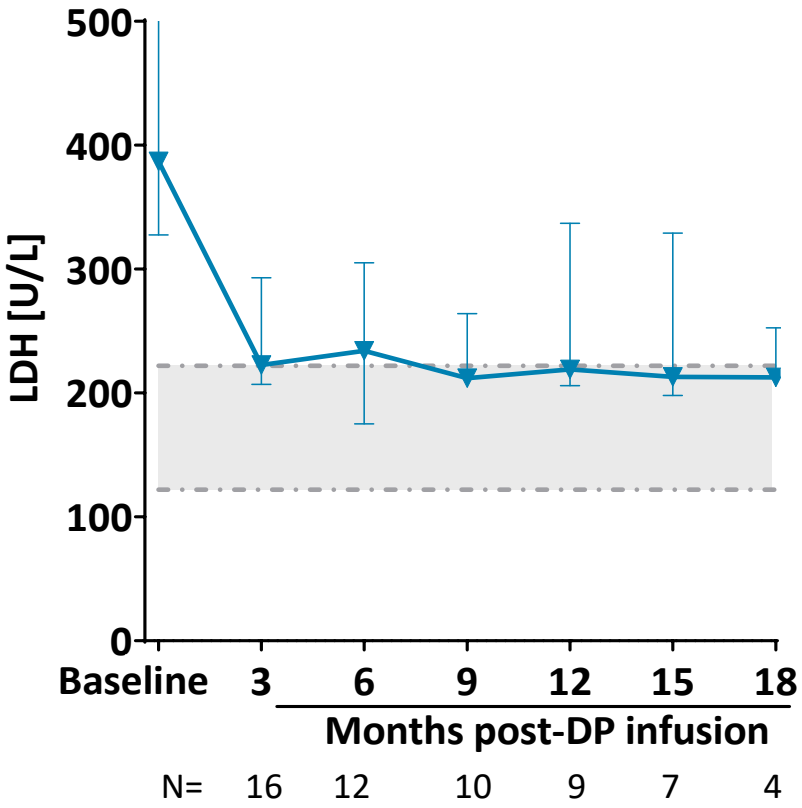
Data as of 26 August 2019

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

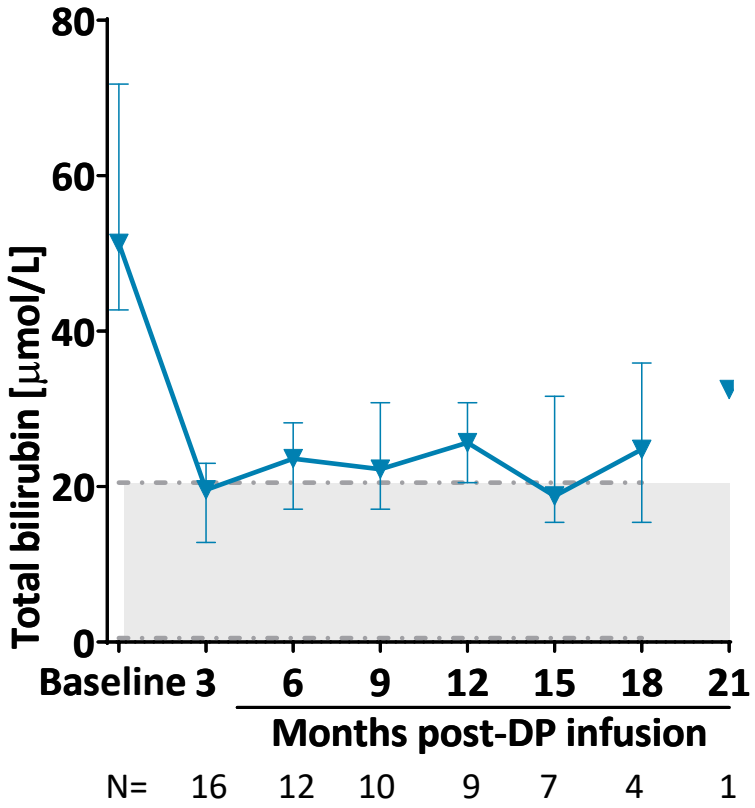
Reticulocyte Counts



Lactate Dehydrogenase



Total Bilirubin



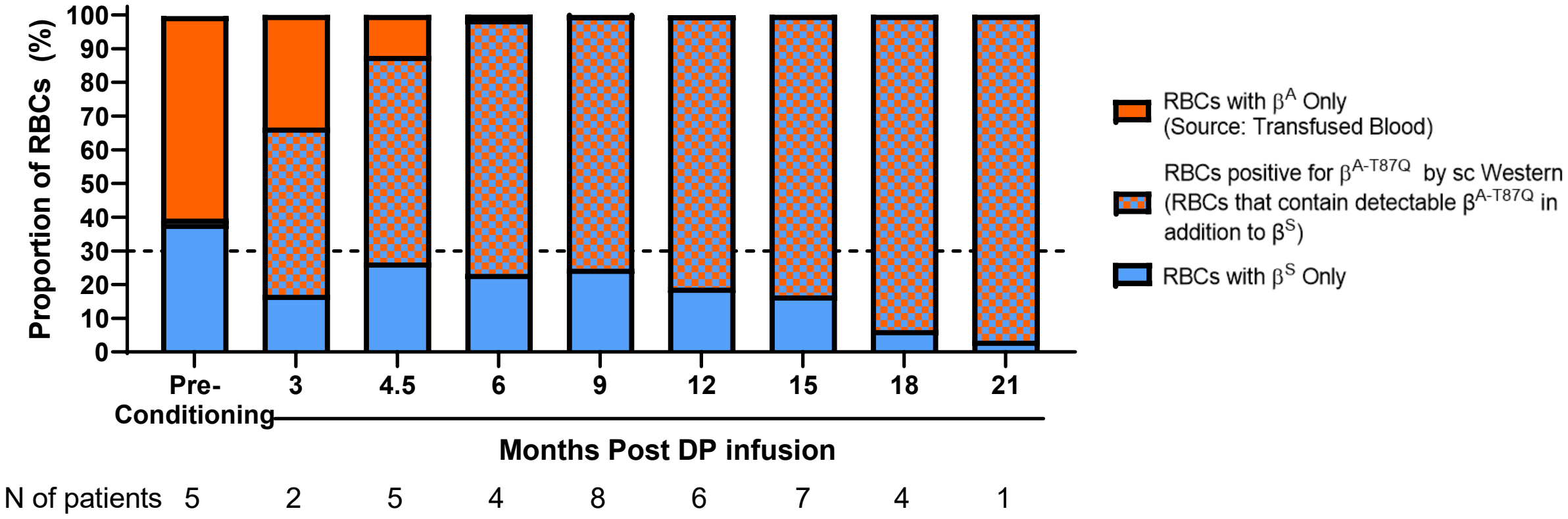
Median (Q1, Q3) depicted; Dot-dash lines denote lower and upper limits of normal values; *Number of patients with data available; †Total bilirubin at last follow-up remains > 2-fold lower than at screening

DP, drug product; LDH, lactate dehydrogenase

Data as of 26 August 2019

HGB-206: On average, ≥ 70% of RBCs from patients treated with LentiGlobin for SCD contain $\beta^{A\text{-}T87Q}$ by month 6

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



Mean is depicted - if N=1, data show technical replicates; *Pre-conditioning sample does not contain any $\beta^{A\text{-}T87Q}$, signal is due to error rate of multiples

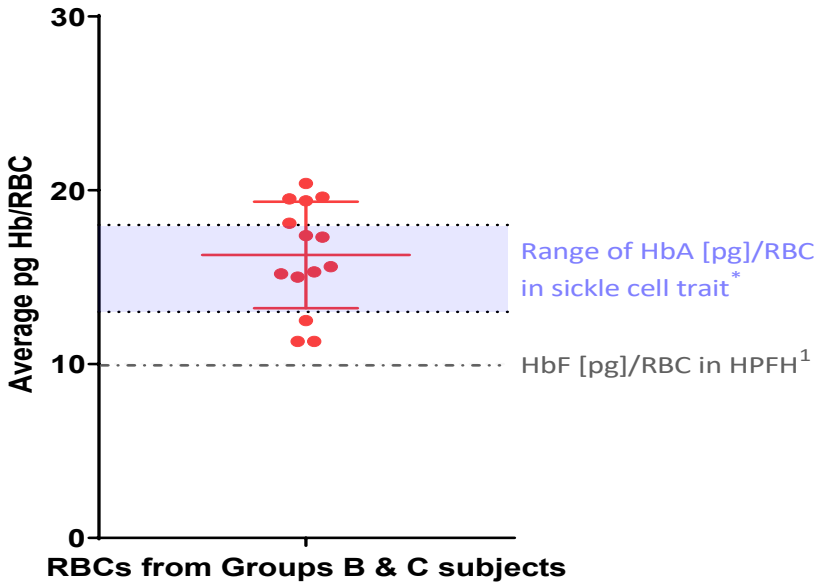
DP, drug product; RBCs, red blood cells; sc, single cell

Data as of 26 August 2019

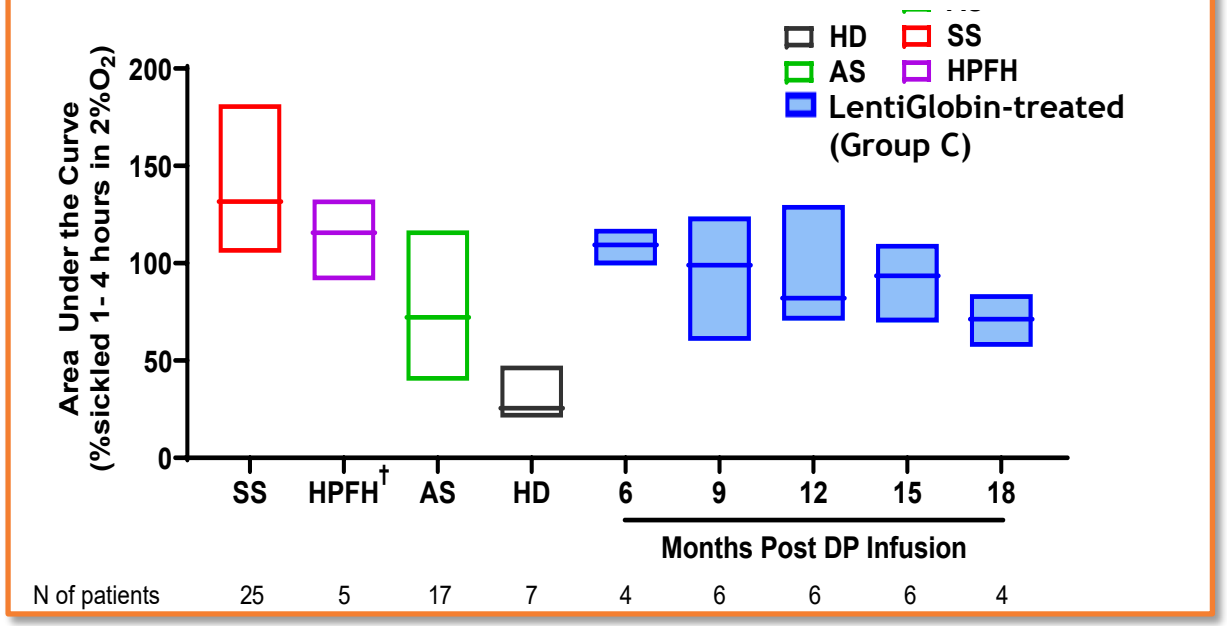
HGB-206: Exploratory assays: high concentrations of $\beta^{A\text{-}T87Q}$ achieved at the cellular level result in reduced propensity to sickle

Propensity to sickle decreases over time post-gene therapy with LentiGlobin for SCD; Group C similar to trait

HbA^{T87Q} pg/RBC comparable to HbA pg/RBC in trait & HbF pg/RBC in HPFH



% sickling for LentiGlobin-treated patients with ≥ 6M follow-up Group C only



Average pg Hb/RBC = (% HbA^{T87Q} of total Hb/% RBCs containing $\beta^{A\text{-}T87Q}$) x MCH

*Calculated using 50% HbA/RBC for the lower end of the range and 60% HbA/RBC for the upper end of the range **Group C only; †HbF contribution to total Hb in these samples ranged from 28% - 42%

1. Steinberg MH et al., Blood. 2014;123(4):481-5.

DP, drug product; Hb, hemoglobin; HPFH, hereditary persistence of fetal hemoglobin; MCH, mean corpuscular hemoglobin; RBC, red blood cells AS, sickle cell trait; HD, healthy donor; SS, sickle mutation on both *HBB* alleles

Data as of 26 August 2019

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

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

Starting 1H:2020

Additional Clinical Investigation in Other Patient Types and Ages Planned

Plans Based on Ongoing Engagement with Regulators

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Multiple Myeloma

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

Multiple Myeloma – Changing What's Possible

Standard of Care*

- ~4 months PFS
- ~30% ORR
- ~3% CR

RECODE

BCMA Target &

Next-Gen CAR

2019 - KarMMa topline

- ✓ Positive Pivotal Data
- ✓ Met primary and secondary endpoints
- ✓ Deep and durable responses across dose levels

2020

- 1H 2020 anticipated U.S. BLA submission
- Ongoing studies in 3L, 2L and 1L (Newly Diagnosed)

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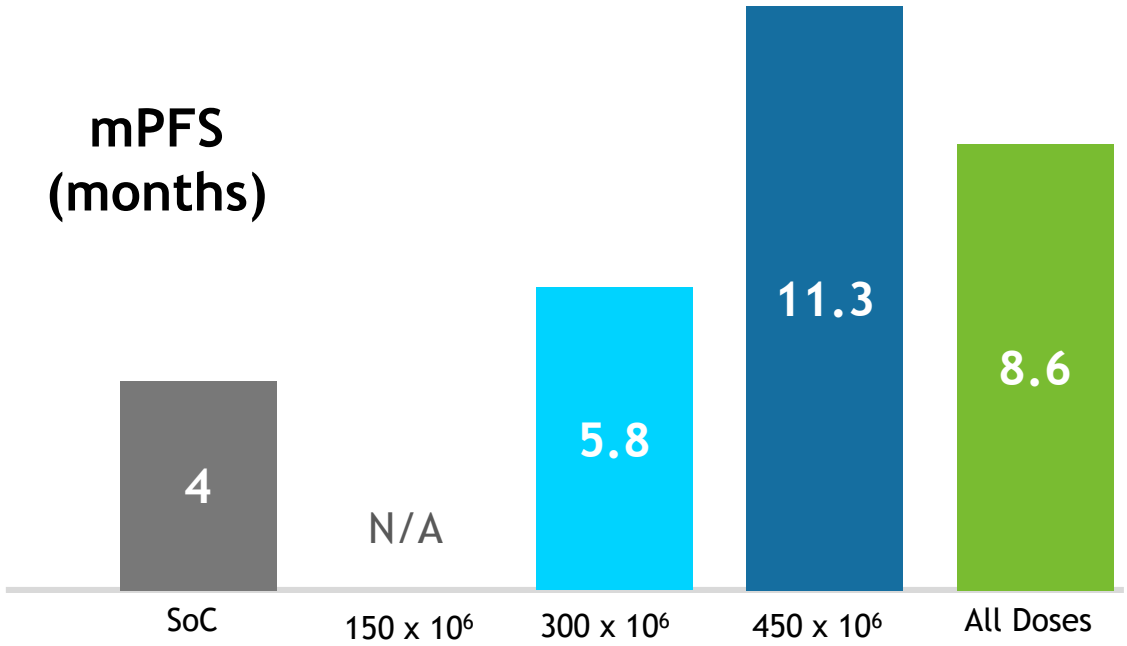
*Lonial et al, Lancet 2016 (Dara); Siegel et al, Blood 2012 (Kyprolis); Hajek et al, Leukemia 2017 (Kyprolis); Chari et al, NEJM 2019 (Selinexor); Richardson et al, Blood 2014 (PomDex)

ide-cel (bb2121) - Positive Pivotal Data



	150 x 10^6 CAR+ T cells (N=4)	300 x 10^6 CAR+ T cells (N=70)	450 x 10^6 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

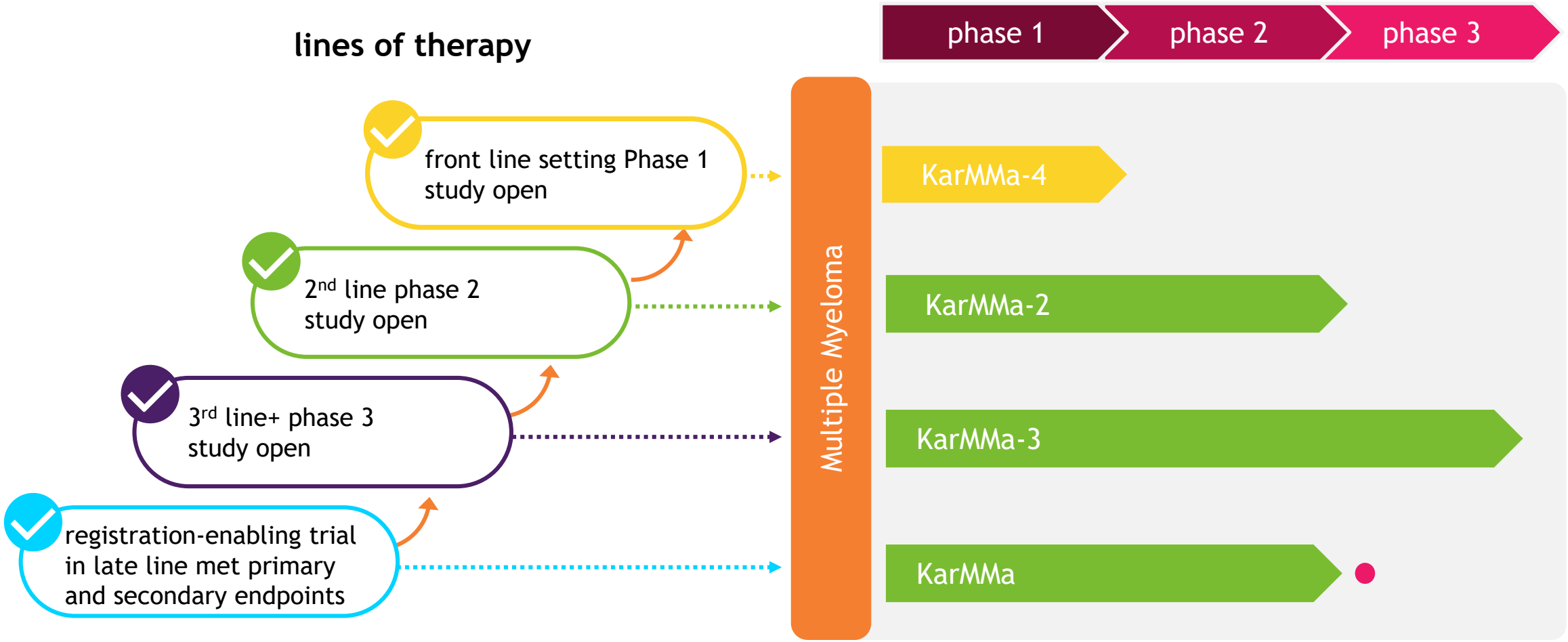
- mPFS of >11mo at the 450 x 10^6 dose
- Durability is consistent across doses

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

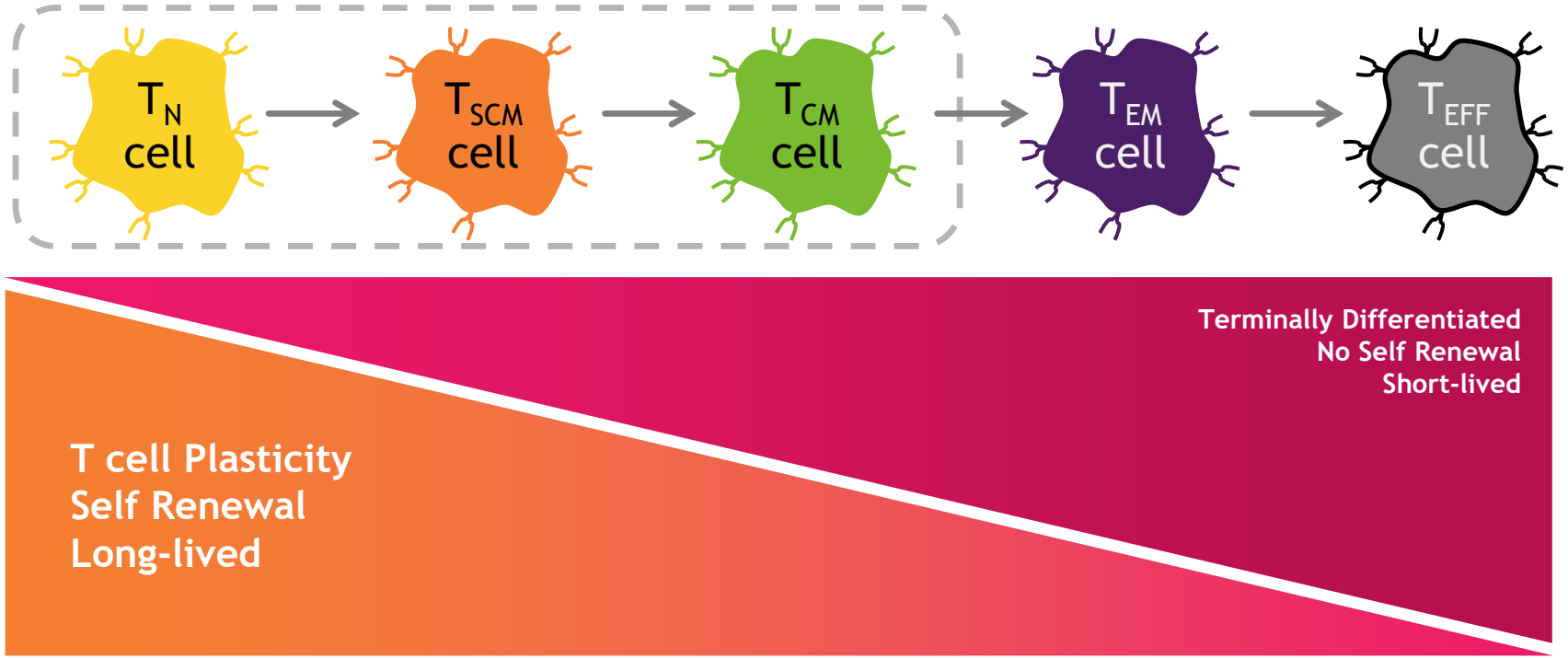
iiNT: investigator identified neurotoxicity
Ide-cel is being developed in collaboration with Bristol-Myers Squibb

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



● Planned 1H:2020 regulatory submission

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*

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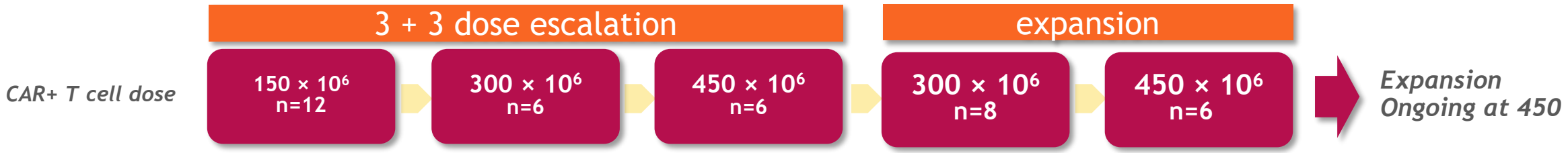
CRB-402: Phase 1 dose-escalation study in heavily pretreated and refractory patient population continues to enroll



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.

Data as of 4 September 2019

CRB-402: 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	12 (32)
1	24 (63)
2	2 (5)
ISS stage[a], n (%)	
I	11 (29)
II	7 (18)
III	10 (26)
Unavailable	10 (26)
High-risk cytogenetics, n (%)	
del(17p), t(4;14), t(14;16)	13 (34)
Unknown	1 (3)

Characteristic		bb21217-Treated (N=38)	
Median (min, max) no. prior regimens[b]		6 (3, 17)	
Prior autologous SCT, n (%)			
0		7 (18)	
1		22 (58)	
>1		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

CRB-402: 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)

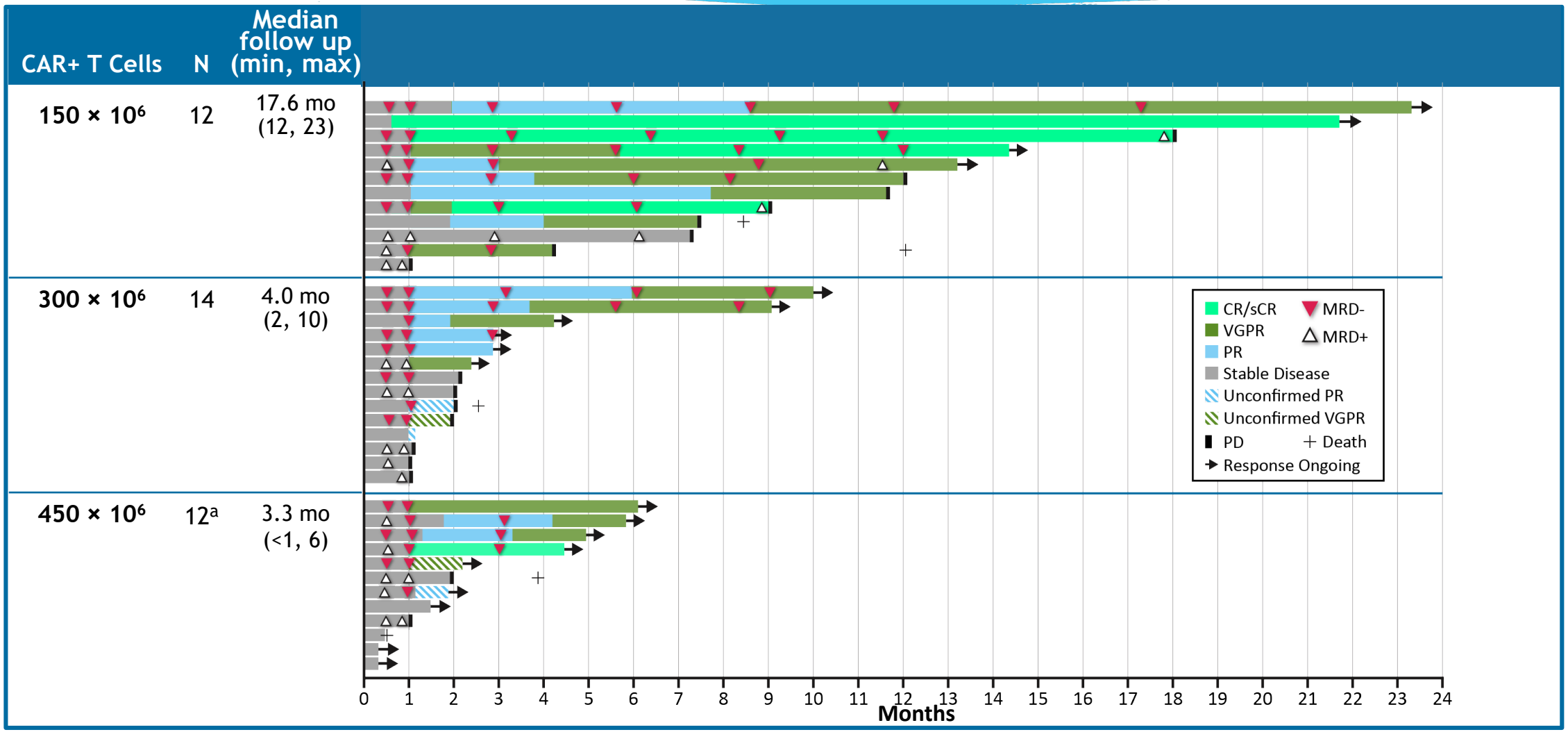
	N	Grade, n (%) 1	2	3	4	5	Total all grades
CRS							
150 × 10^6	12	4 (33)	3 (25)	1 (8)	0	0	8 (67)
300 × 10^6	14	4 (29)	3 (21)	0	0	0	7 (50)
450 × 10^6	12	4 (33)	5 (42)	0	0	1 (8)	10 (83)
Neurotoxicity							
150 × 10^6	12	1 (8)	1 (8)	0	1 (8)	0	3 (25)
300 × 10^6	14	1 (7)	2 (14)	1 (7)	0	0	4 (29)
450 × 10^6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

CRB-402: 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.

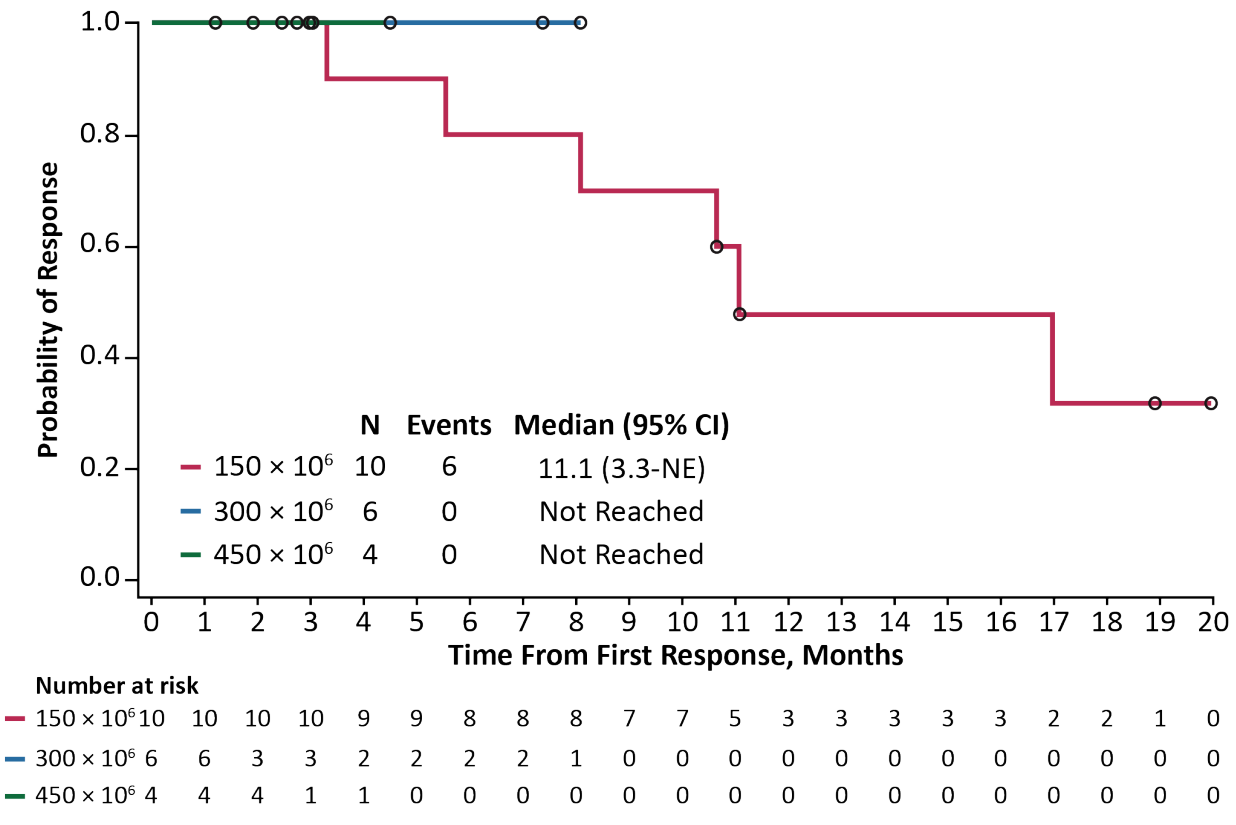
[a] One patient ongoing at the time of the data extraction missed their 2-month visit and another was in VGPR but is reported as a PR owing to a missed assessment.

Data as of 4 September 2019

CRB-402: Confirmed responses across dose cohorts

CAR+ T Cells:	150 × 10^6 (n=12)	300 × 10^6 (n=14)	450 × 10^6 (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]

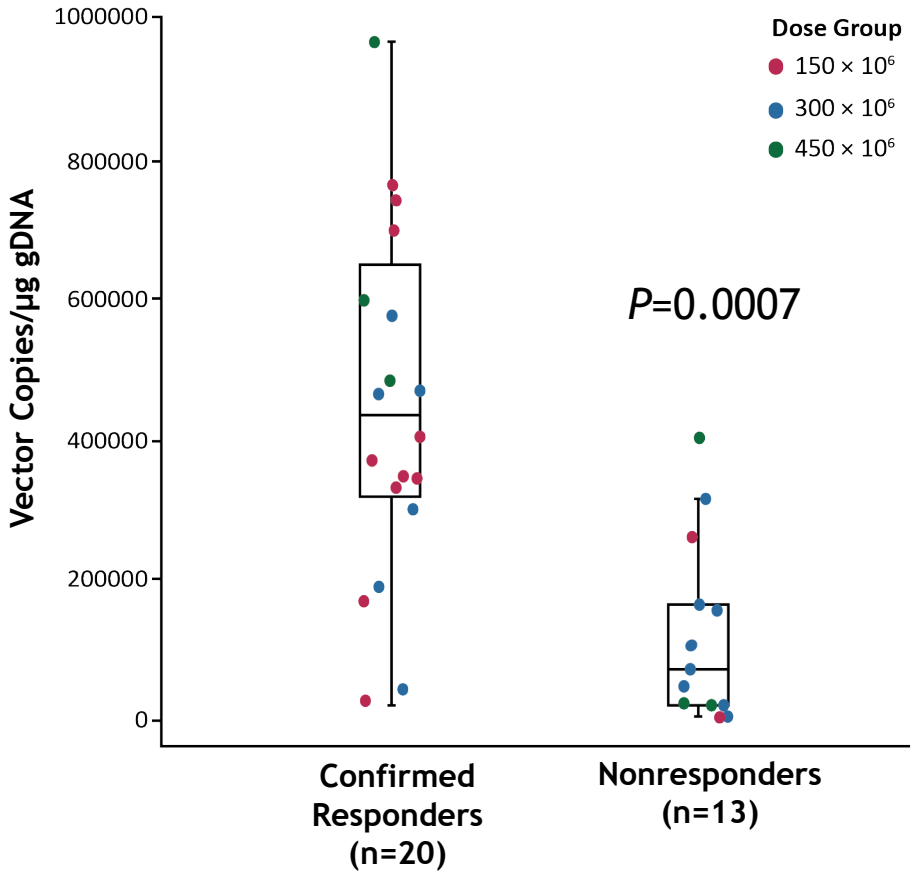


DOR, duration of response; MRD, minimal residual disease; NE, not estimable; PD, progressive disease; PR, partial response; sCR/CR, stringent complete response/complete response; VGPR, very good partial response.
[a]Patients with ≥2 months of follow up or PD/death within 2 months. Response confirmed 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. 150x10^6 dose 6 neg at 10^{-6} and 1 neg at 10^{-5}, 300x10^6 dose 4 neg at 10^{-6} and 1 at 10^{-5}, 450x10^6 2 neg at 10^{-6} and 2 at 10^{-5}.

Data as of 4 September 2019

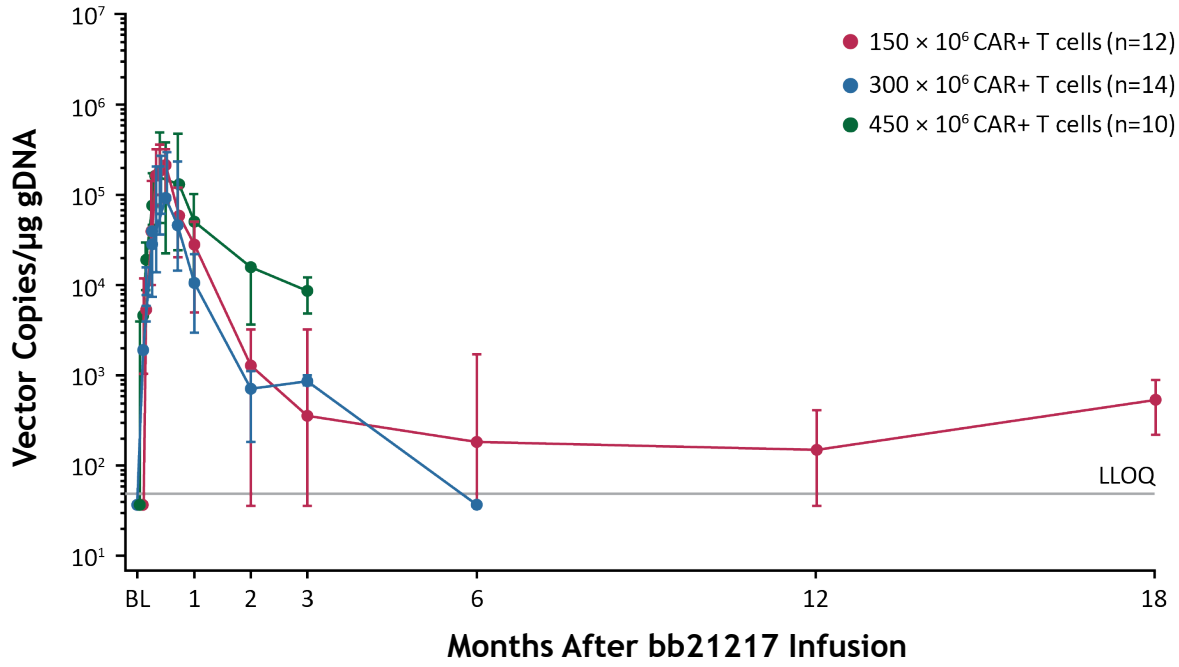
CRB-402: Confirmed responders show increased CAR T cell expansion and durable persistence

peak VCN by response



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

median VCN over time by dose



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

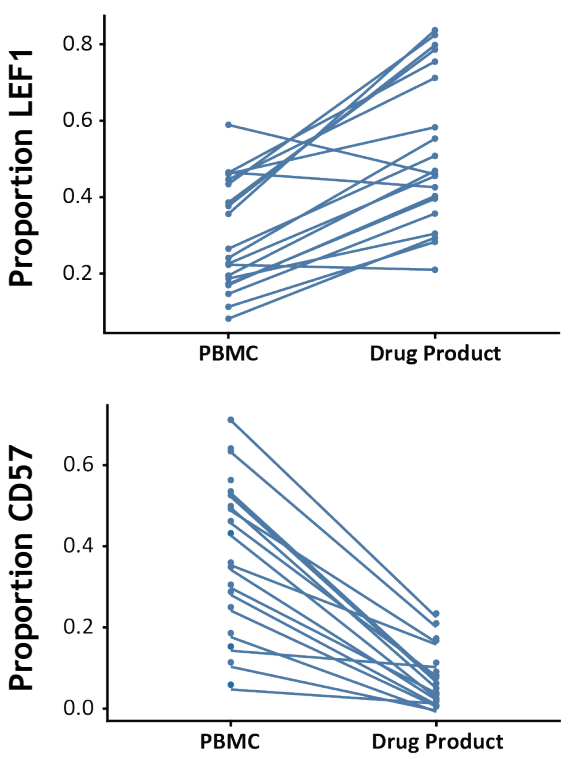
BL, baseline; gDNA, genomic DNA; IQR, interquartile range; LLOQ, lower limit of quantification; VCN, vector copy number.
[a] includes detectable but not measurable. [b] includes VCN data for patients until PD,includes 1 patient who received subsequent chemotherapy before progression. Error bars for median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

Data as of 4 September 2019

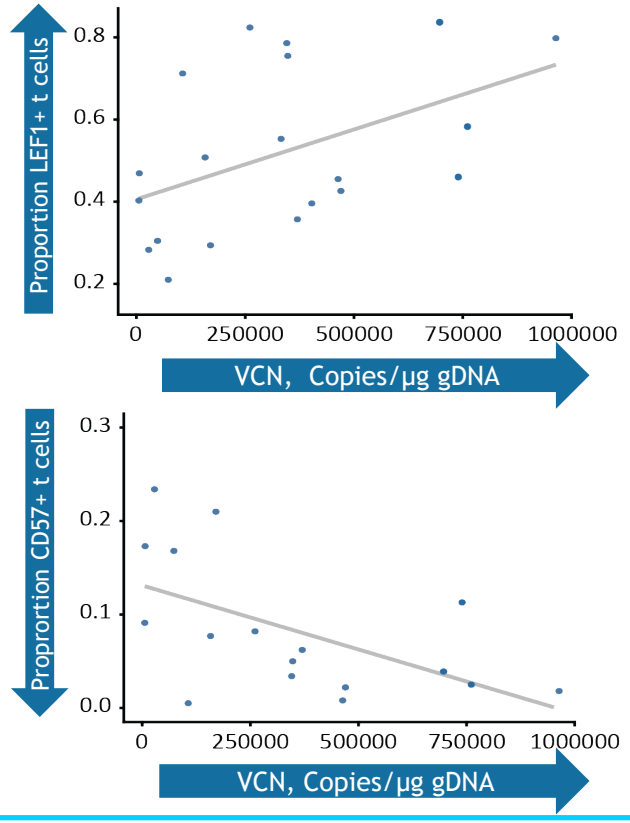
CRB-402: Enrichment for memory-like T cells is associated with robust CAR T expansion and lack of progression by month 6

- 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

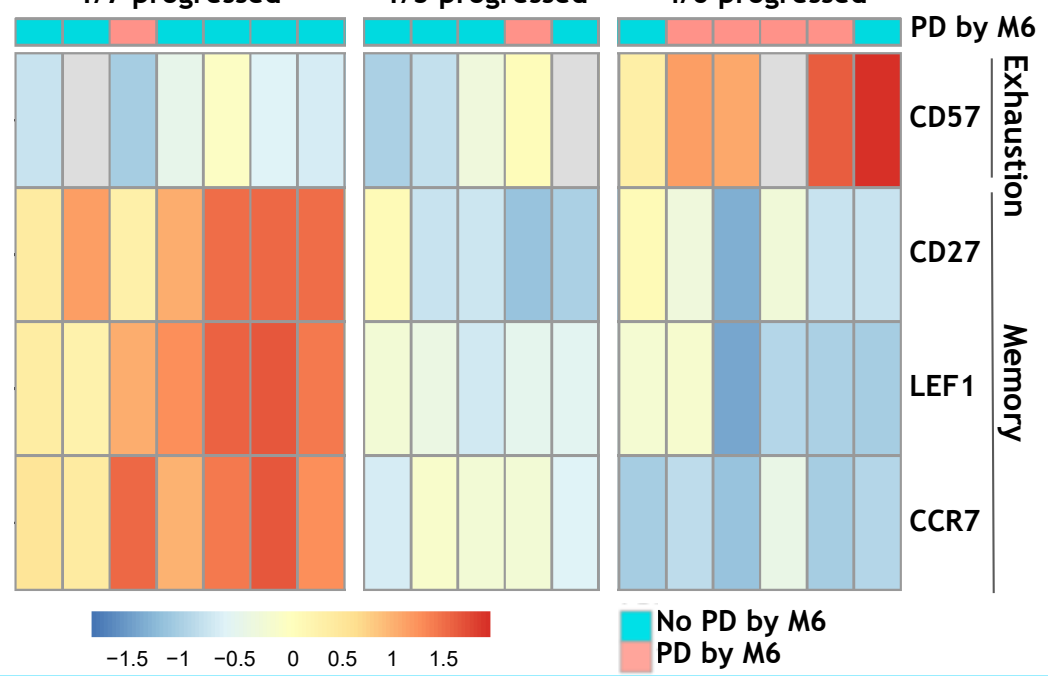
bb21217 drug product enriched for memory-like T cells



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]



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.

Data as of 4 September 2019

CRB-402: 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

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