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EHA Data Review & ZYNTEGLO® Approval Webcast

June 14, 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.

WE **RECODE** FOR LIFE

Our ambition is to recode science, systems and the status quo, so **lives can be lived fully.**

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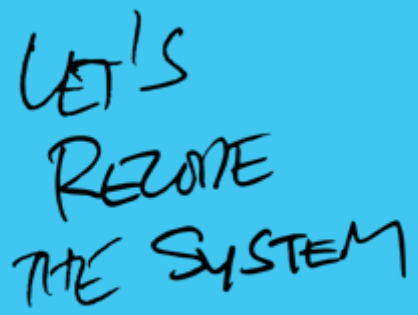

Today's Agenda

SCD Data: HGB-206 Group C	Dave Davidson, MD *chief medical officer*
TDT Data: Northstar (HGB 204), Northstar-2 (HGB-207) and Northstar-3 (HGB-212)	Dave Davidson, MD *chief medical officer*
ZYNTEGLO® Launch Update	Nick Leschly *chief bluebird &* Alison Finger *chief commercial officer*
Q&A	

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Sickle Cell Disease (SCD)

HGB-206 Group C

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Living with Sickle Cell Disease

Sickle Cell Disease

- 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]

Bridgett's Experience

- Diagnosed at 17
- Had over 140 gallstones before diagnosis
- First transfusion at 19, received over 300 transfusions
- Chronic pain
- Constantly concerned about what may trigger the next crisis

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

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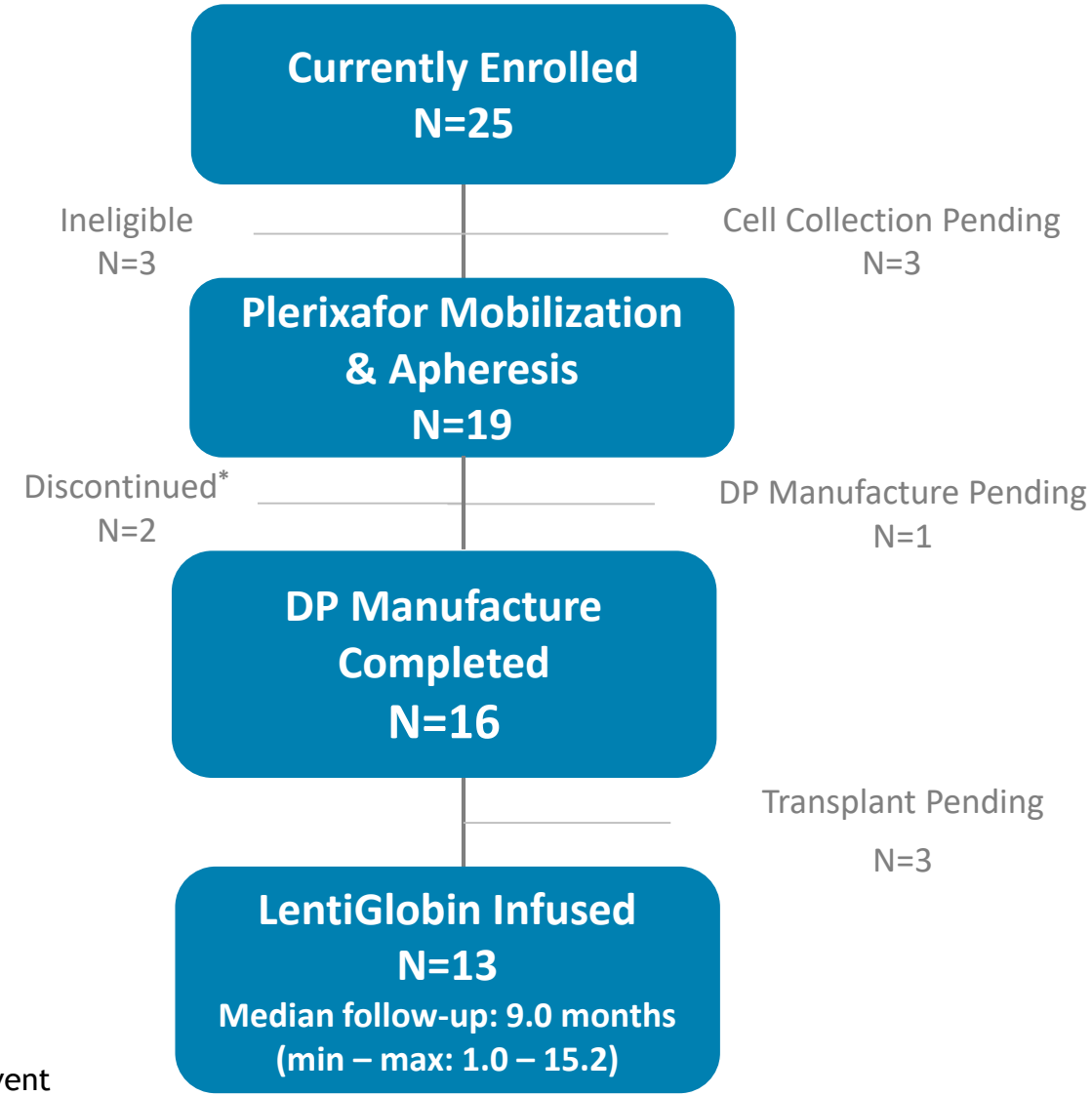
HGB-206 Group C: Disposition

Currently enrolling



*1 withdrew consent, 1 discontinued due to adverse event

Definitions: HSCs, hematopoietic stem cells

Data as of 7 March 2019

HGB-206 Group C: Patient characteristics

N=19 patients who started cell collection

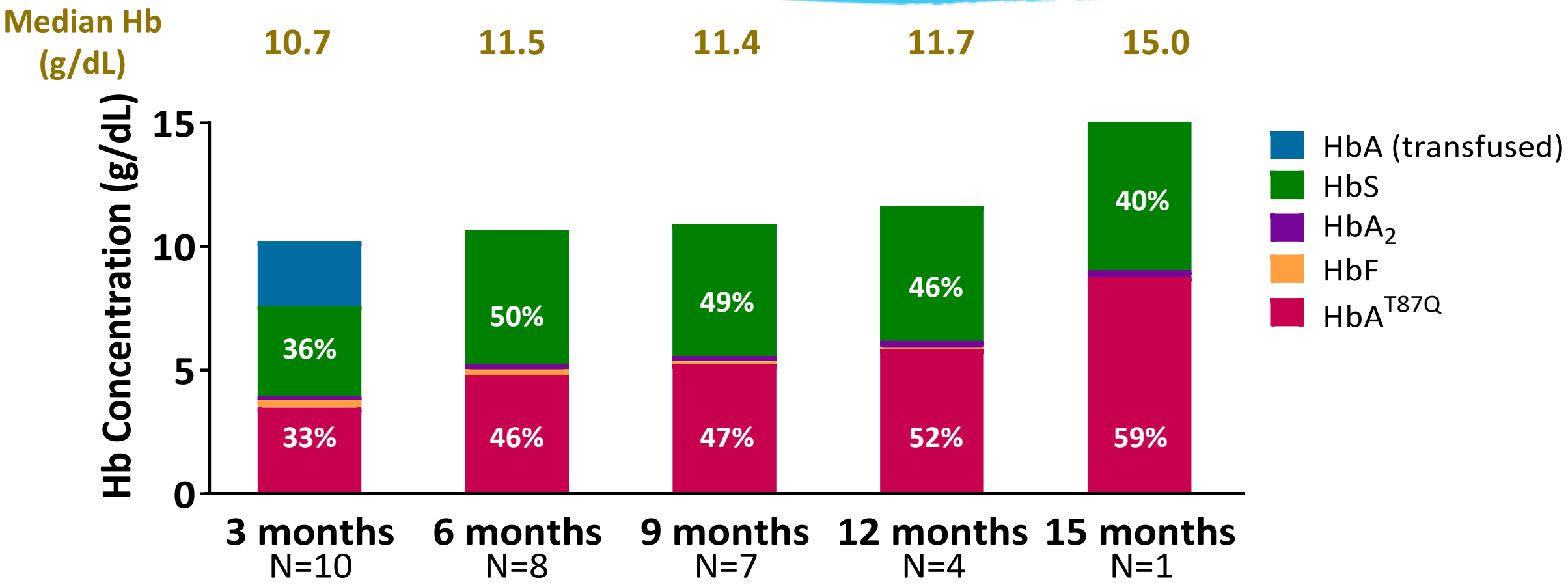
Parameter	Group C N=19
Age at consent, years median (min – max)	**26** (18 – 36)
Gender	**8F 11 M**
Genotype, β^S/β^S	**19**
SCD History	
Hydroxyurea[#], n	**11**
VOCs[*], n Annualized no. of events, median (min – max)	**15** **4.0** (2.0 – 13.5)
ACS[†], n Annualized no. of events, median (min – max)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



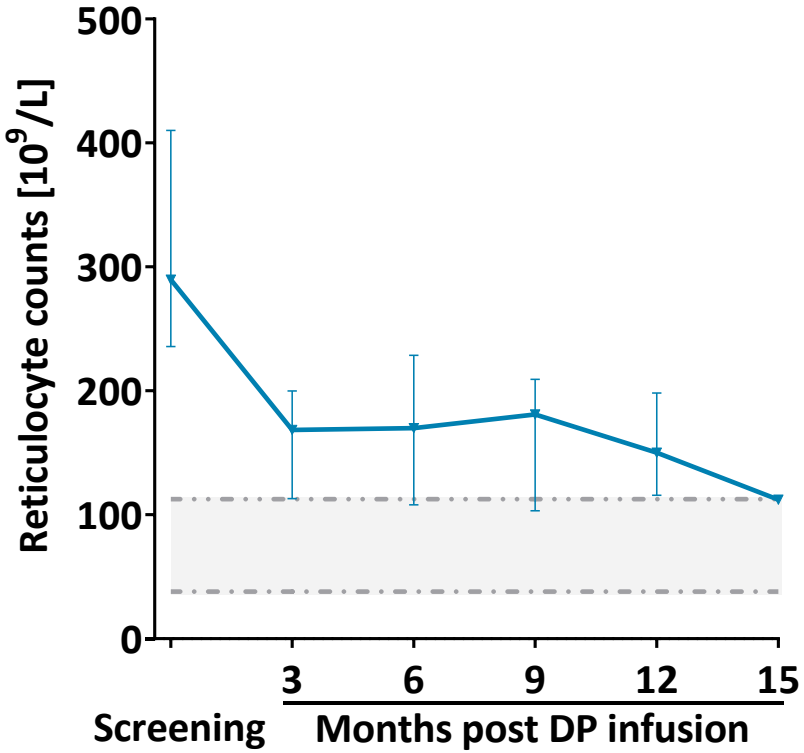
Total Hb and HbA^{T87Q} ranged from 10.2 - 15.0 g/dL and 4.5 - 8.8 g/dL, respectively, at last visit in patients with ≥ 6 months of follow-up

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

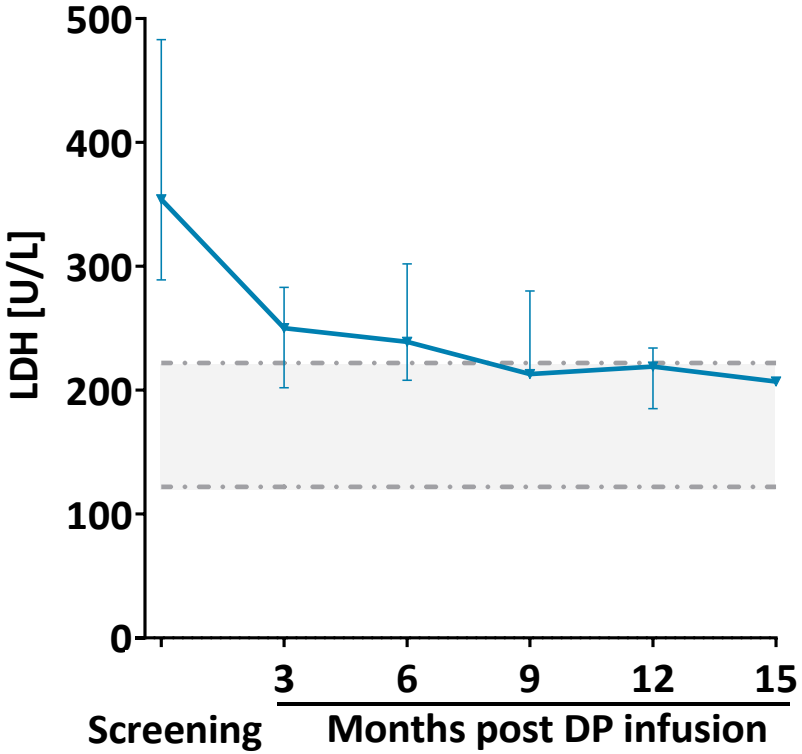
Data as of 7 March 2019

HGB-206 Group C: Decreased hemolysis following LentiGlobin treatment

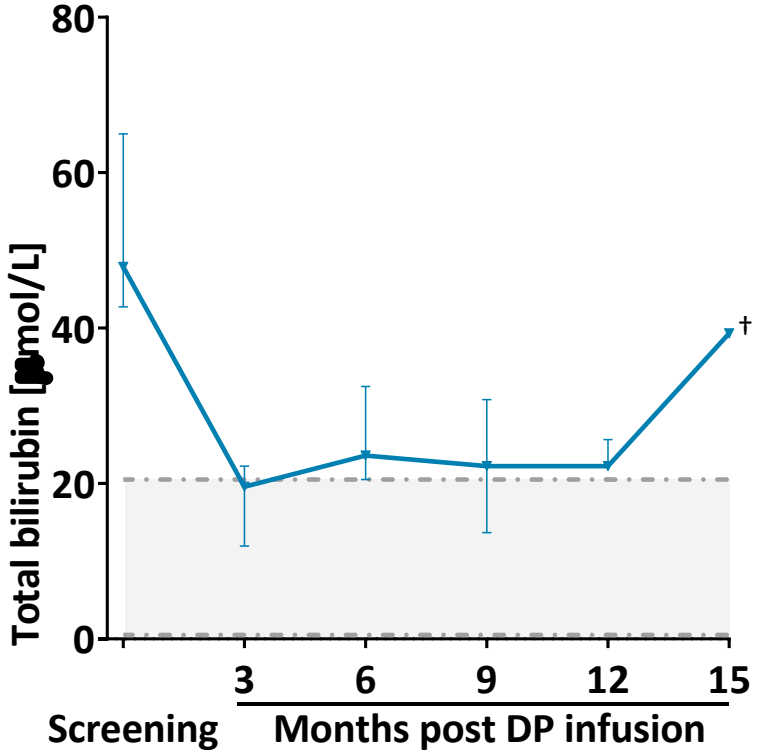
Reticulocyte Counts



Lactate Dehydrogenase



Total Bilirubin



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

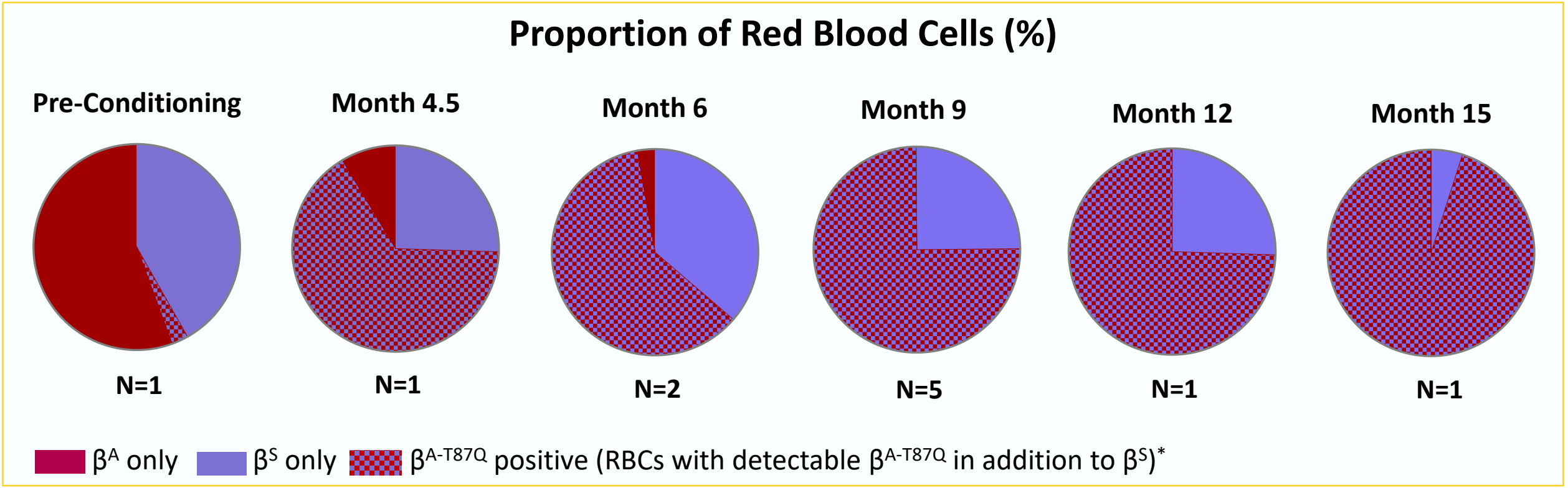
Median (Q1, Q3) depicted; Dot-dash lines denote lower and upper limits of normal values; *Shows number of patients for whom data are available; † Total bilirubin at last follow-up remains > 2-fold lower than at screening

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

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

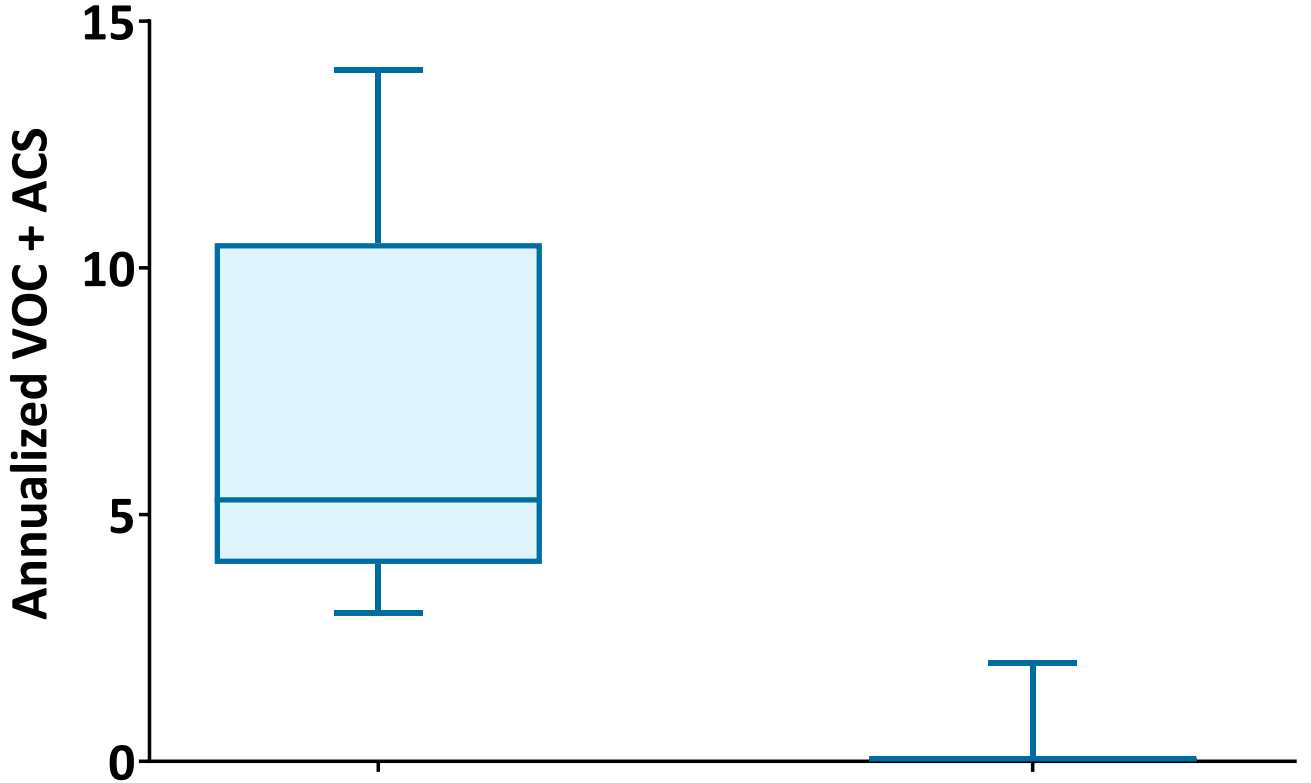


Mean is depicted - if N=1, data show technical replicates; *Pre-conditioning sample does not contain any $\beta^{A\text{-}T87Q}$, signal represents false positives

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



	2 years pre-treatment	At last visit post-treatment
	N=6*†	N=6†
Median (min – max)	**5.3 (3 – 14)**	**0 (0 – 2)**

- 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

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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Transfusion-Dependent β-thalassemia (TDT)

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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

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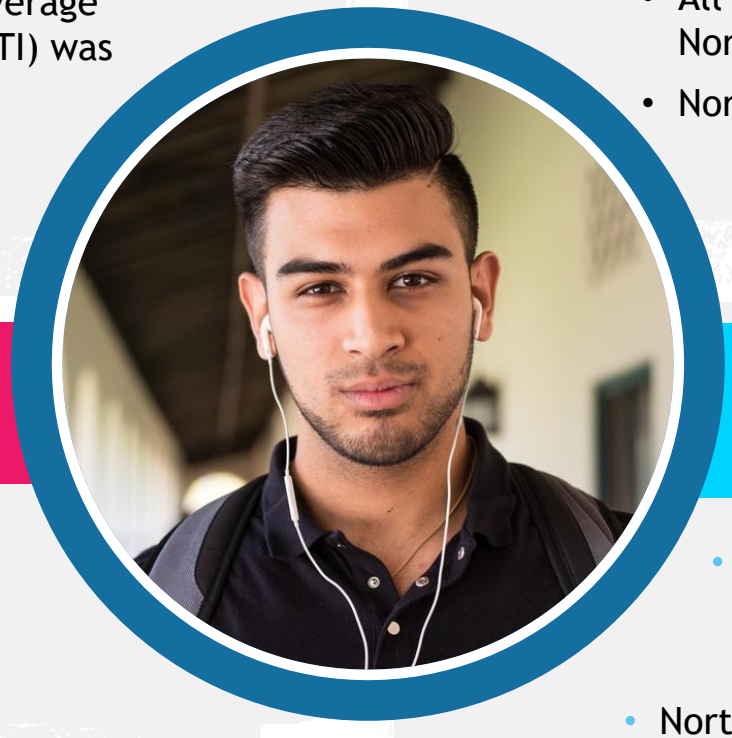
ZYNTEGLO® is the first and only one-time therapy for TDT now approved in the EU for people with TDT and non-β^0/β^0 genotypes

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

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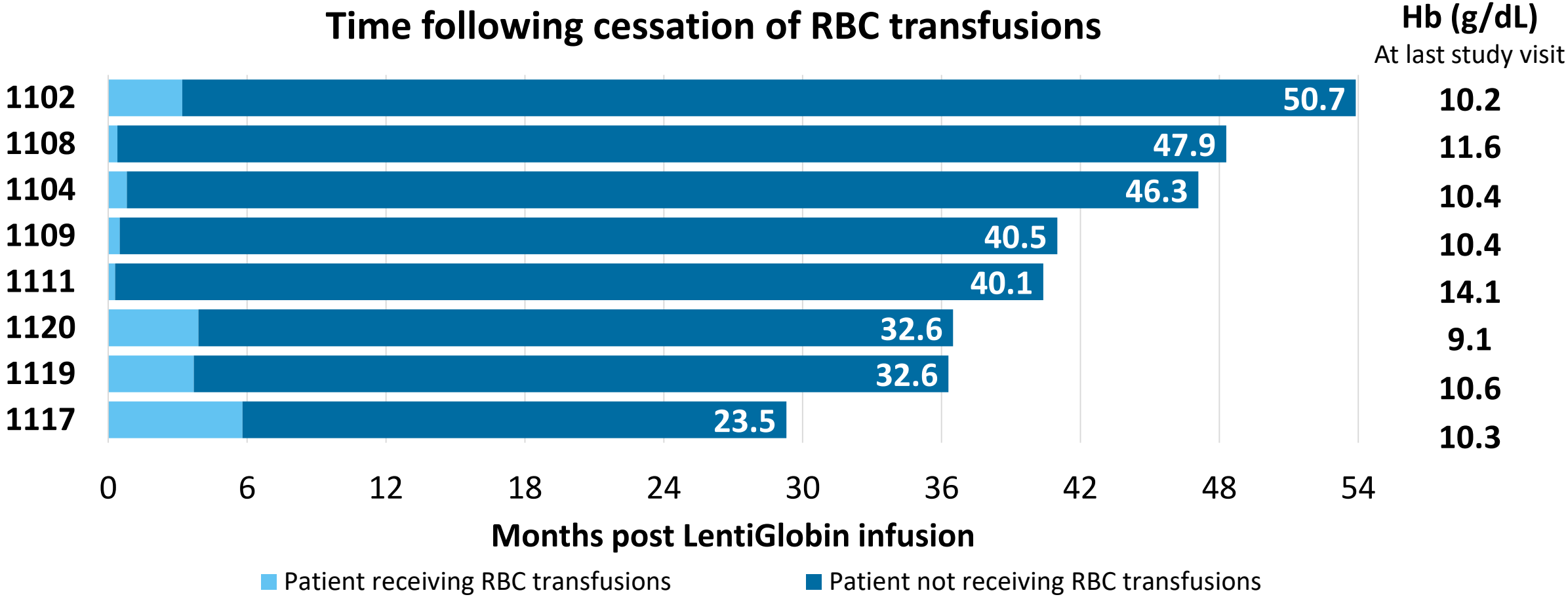
HGB-204: 8/10 patients with non-β^0/β^0 genotypes achieved transfusion independence

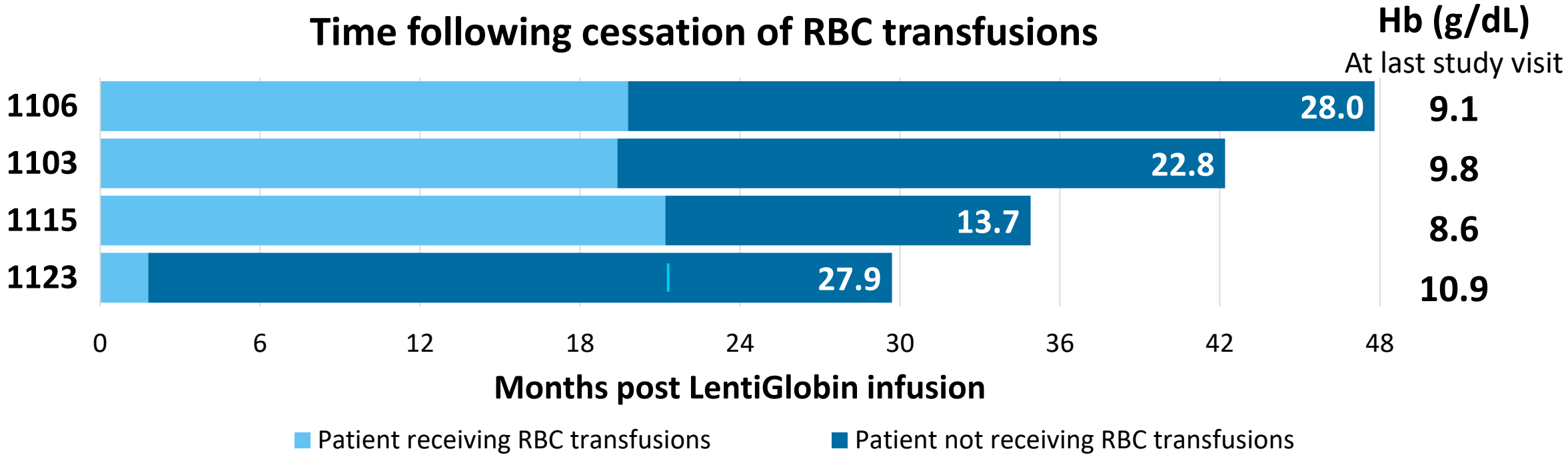


Median duration of TI: 38.0 months (min – max: 21.2 – 45.3 months); responses are ongoing
Median weighted average Hb during TI: 10.3 g/dL (min – max: 9.3 – 13.2 g/dL)

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

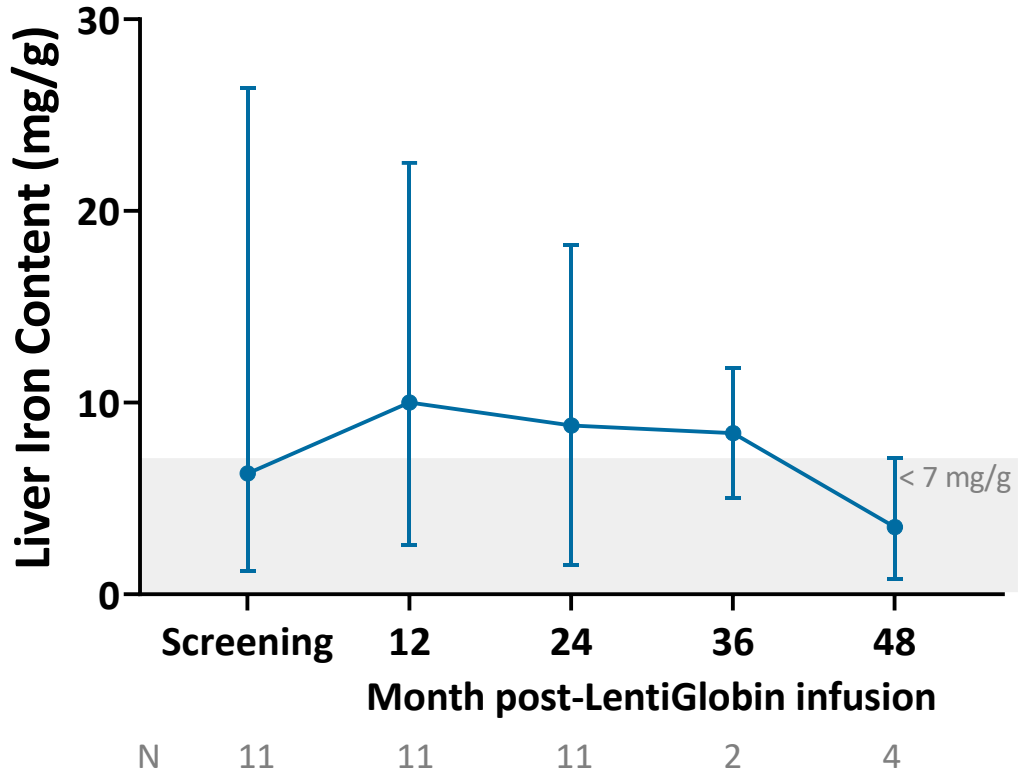
Median weighted average Hb during TI: 9.9 g/dL (min – max: 9.5 – 10.1 g/dL)

| 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)

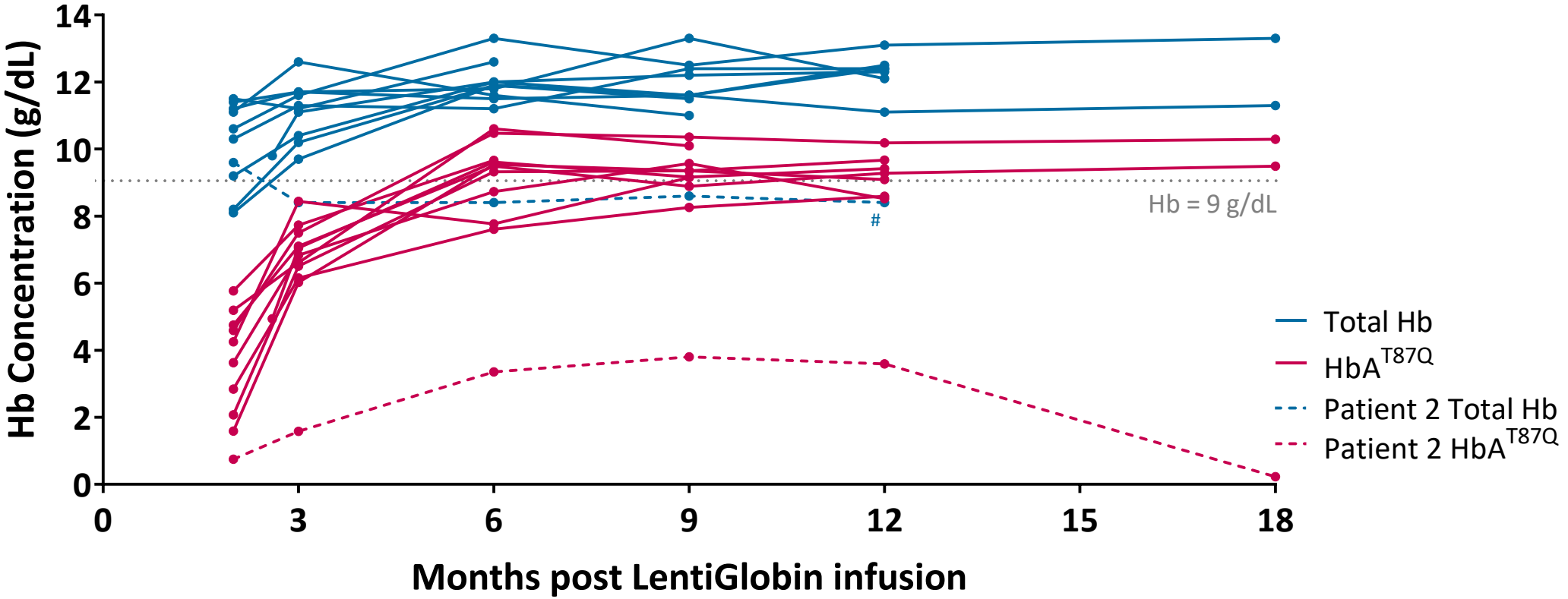
Medians (min, max) depicted
Definitions: LIC, liver iron concentration; M, month

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

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

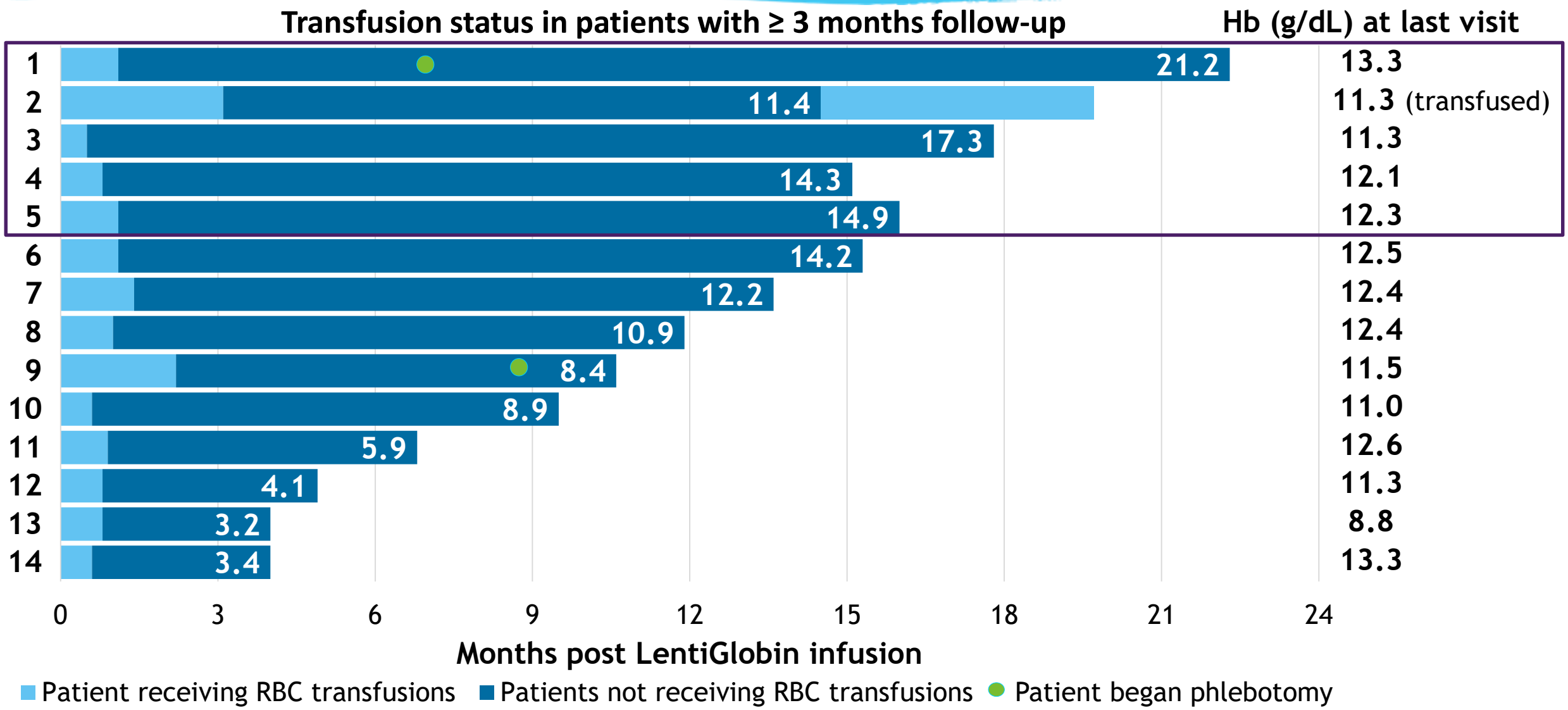
	M6 (n=10)	M9 (n=9)	M12 (n=7)	M18 (n=2)
Total Hb	11.9	11.6	12.4	12.3
HbA^{T87Q}	9.5	9.4	9.3	9.9



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

Data as of 13 December 2018

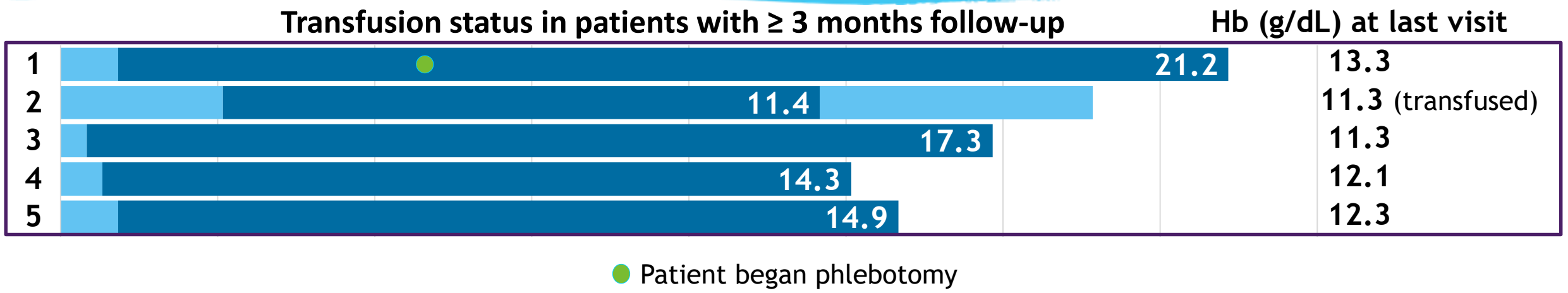
HGB-207: 8.8 – 13.3 g/dL total Hb in patients who have stopped RBC transfusions for ≥ 3 months (n=13)



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

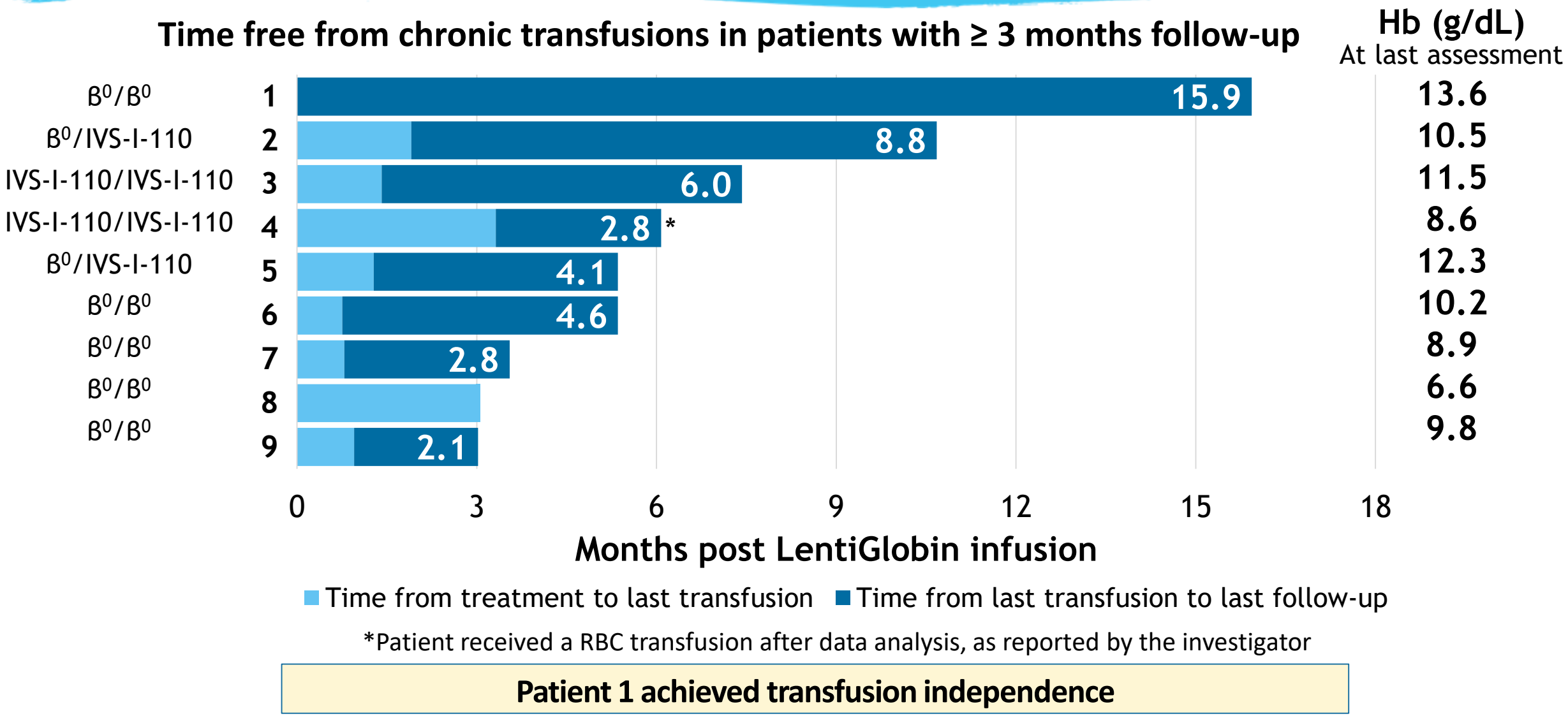


- **4/5 (80%) evaluable patients achieved the primary endpoint of transfusion independence (TI)**
  Weighted average hemoglobin ≥ 9 g/dL without any transfusions for ≥ 12 months
- **Median duration of TI: 13.6 months** (min – max: 12.0 – 18.2 months)
  All responses are ongoing
- **Median weighted average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

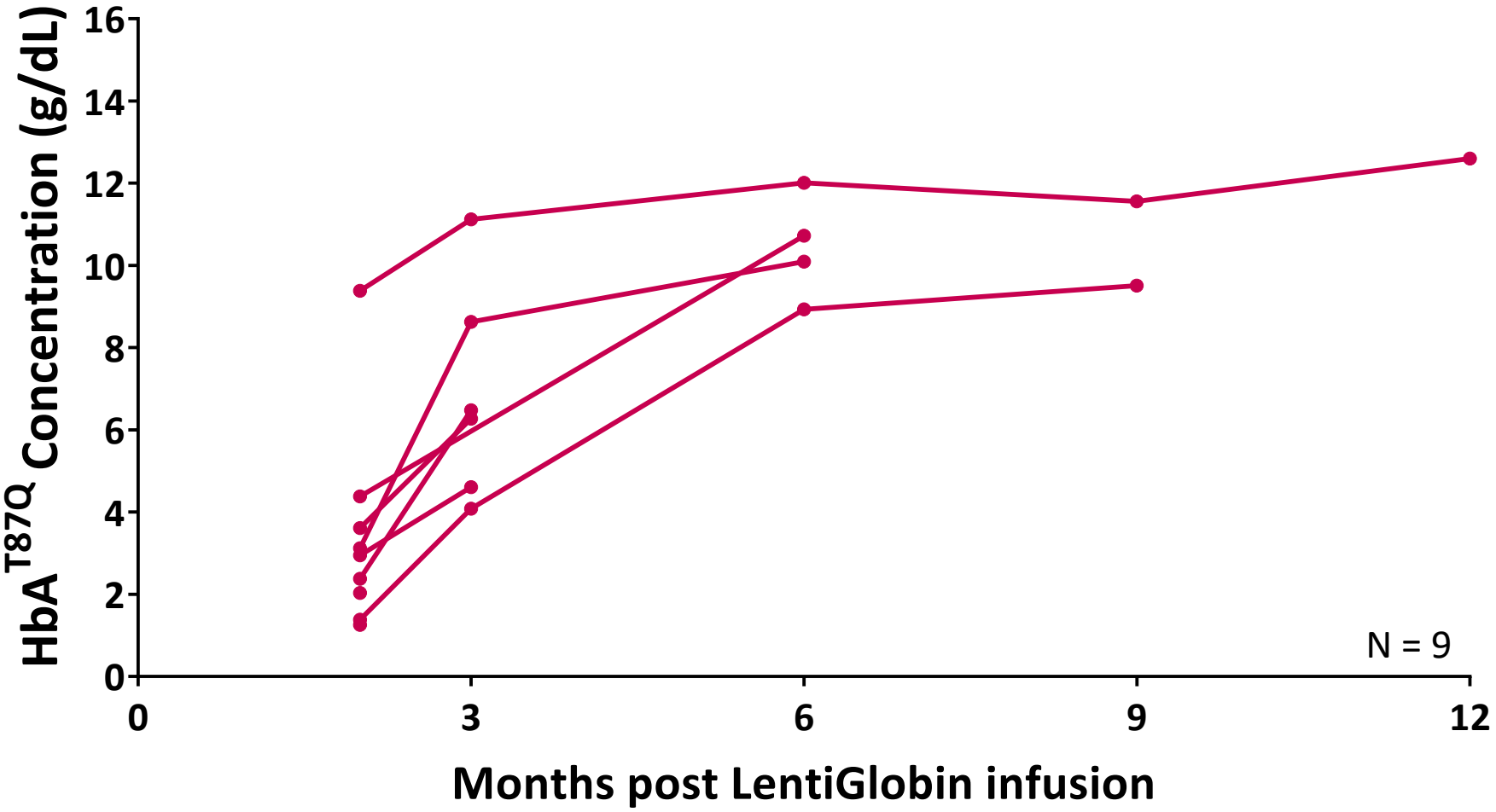
Patient 1 achieved transfusion independence

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)

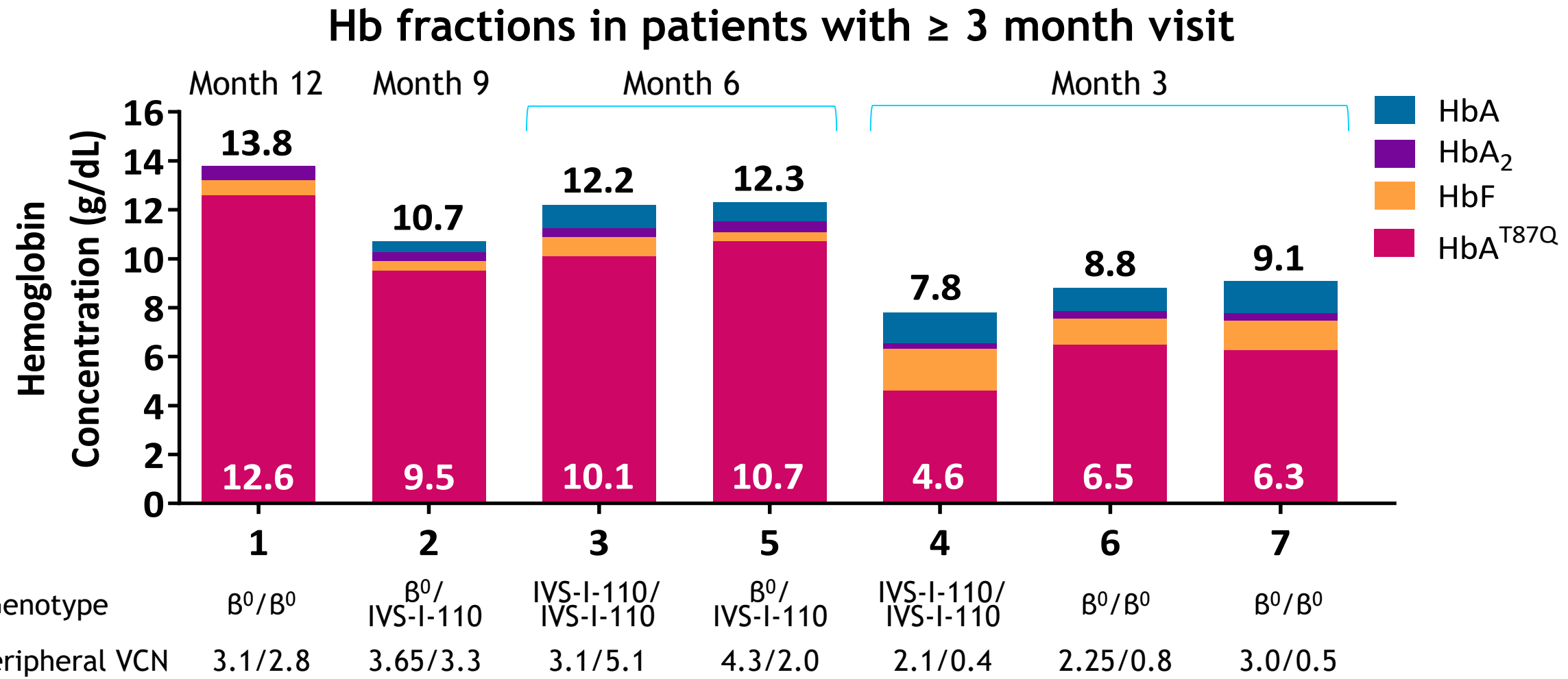


Definition: Hb, hemoglobin

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}



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

Data as of 12 April 2019

Clinical data supports patient and physician desired outcomes in TDT & SCD

HGB-206
Phase 1

- ✓ *In patients who were at least 6 months post-treatment, median level of abnormal sickle hemoglobin (HbS) was reduced to ≤ 50% of total Hb*
- ✓ *At up to 15 months post-treatment there were no reports of serious vaso-occlusive crisis or acute chest syndrome in Group C*

NORTHSTAR STUDY
Phase 1/2

- ✓ *Up to 3.8 years of transfusion independence in Phase 1/2 (HGB-204) study in patients with TDT who do not have a β^0/β^0 genotype*

NORTHSTAR-2 STUDY
Phase 3

- ✓ *80% of evaluable patients achieved transfusion independence in ongoing (HGB-207) study of patients with TDT who do not have a β^0/β^0 genotype*
- ✓ *13/14 were free from transfusions for at least 3 months with total Hb from 8.8-13.3 g/dL at the time of the last study visit*

NORTHSTAR-3 STUDY
Phase 3

- ✓ *Total hemoglobin levels of 10.2 - 13.6 g/dL in patients who have β^0/β^0 genotype or IVS-I-110 mutation and were free of transfusions for at least three months in ongoing Phase 3 (HGB-212) study*

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Commercial launch update

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."**

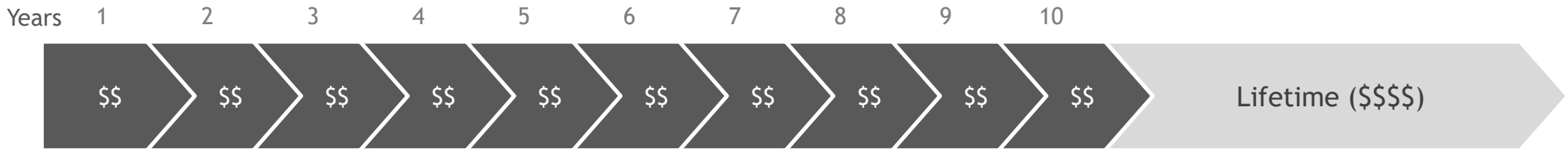
Michael Sherman, M.D.
Harvard Pilgrim Chief Medical Officer

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-time 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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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:

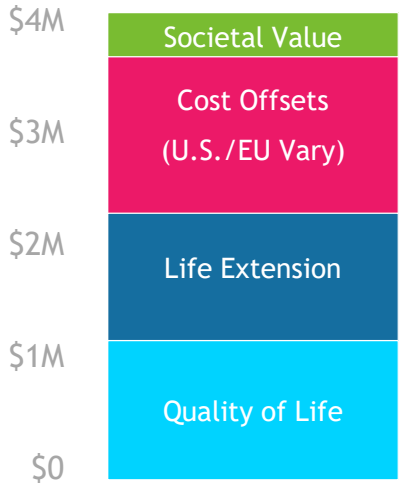
- Hemoglobin of 6.9 g/dL growing up [normal range for females: 12.1-15.1 g/dL][1]
- Congestive heart failure at 9 and 25
- Splenectomy at 10, tonsillectomy at 13, gall bladder removal at 22
- Severe osteoporosis
- Chronic pain
- Under care of PCP, cardiologist, hematologist, endocrinologist, and a pain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

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

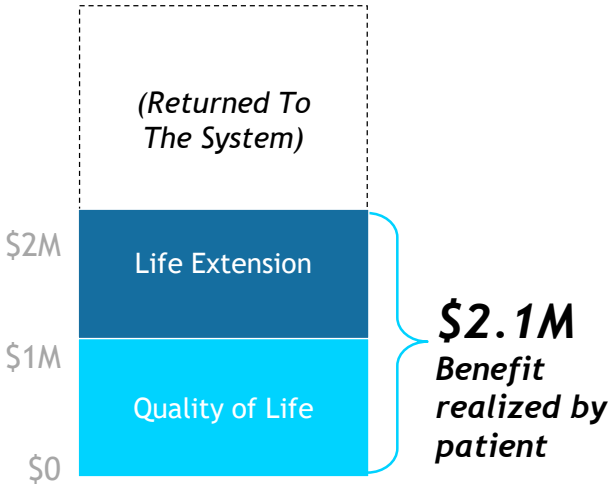
What has (and has not) gone into assessing the value of ZYNTEGLO®?

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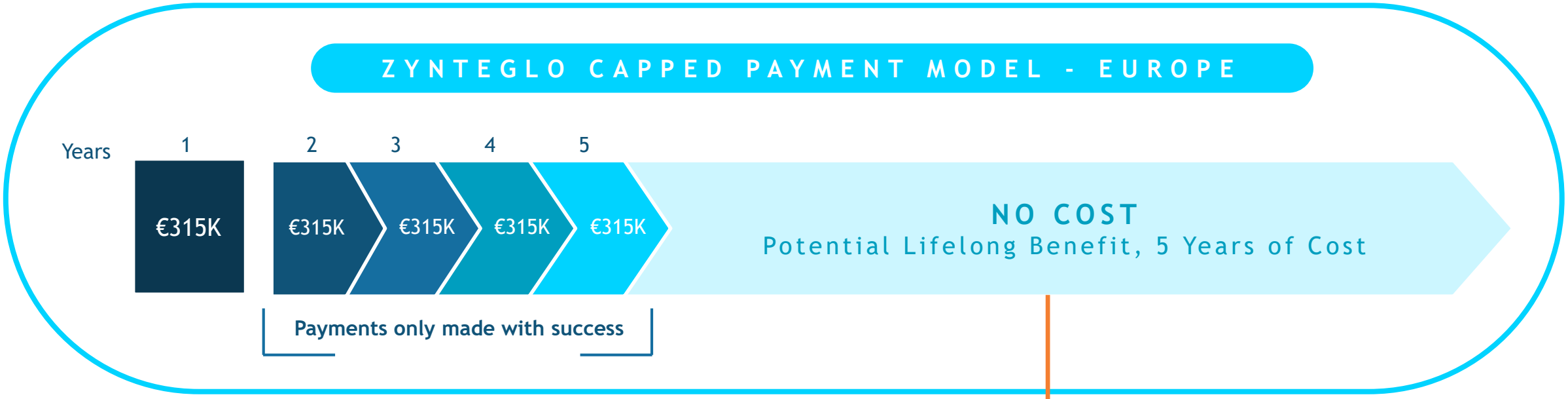
*We have quantified the impact on patient quality of life, survival, treatment cost and society using established health economic modeling techniques.

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

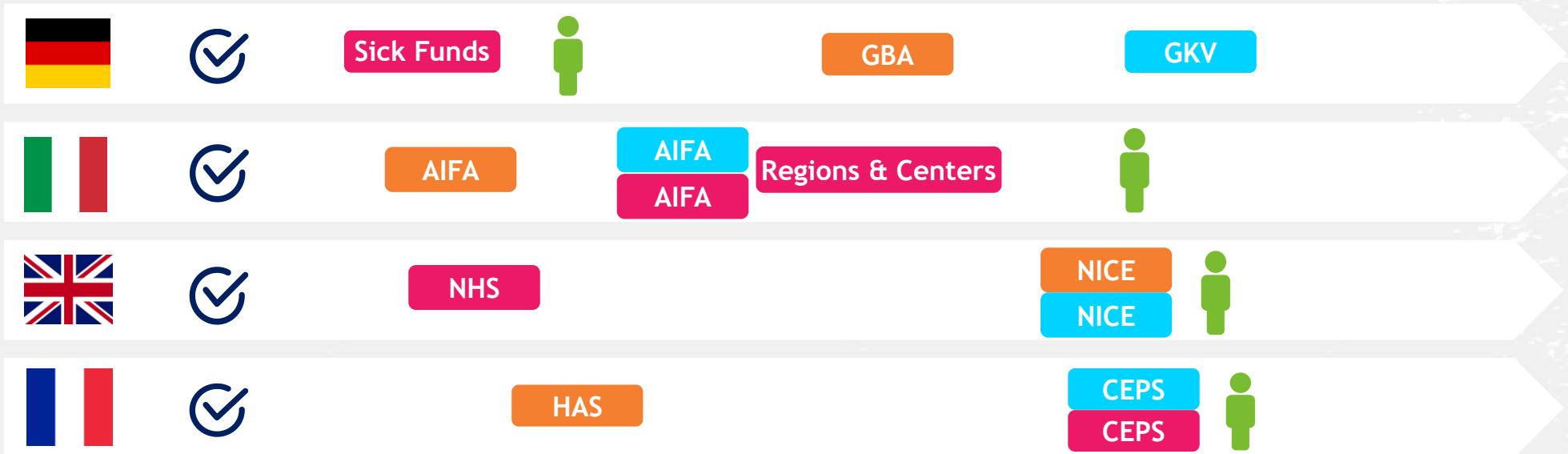
What are next steps and how is launch readiness progressing?

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



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

Q & A

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