bluebirdbio®
recode for life™

bluebird bio

Company Presentation

September 2021

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 our research and development programs, 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.

Bringing transformative therapies to people with severe genetic diseases is our mission

Sickle-Cell Disease*

Zero *severe vaso-occlusive events following treatment vs. a median of 3 per year in our HGB-206 study*

Thalassemia*

100% *of patients in our Phase III studies that met the commercial threshold for drug product release achieved transfusion independence*

Cerebral Adrenoleukodystrophy*

Zero *major functional disabilities in the 27 boys who completed our ALD-102 study with up to nearly 7 years of follow-up*

bluebirdbio®

*Real patients pictured, but they have not used our products

The next chapter of bluebird bio begins now

Leadership Team

Experienced team composed of tenured bluebird leaders and recent additions

Products that Matter

Focused on delivering our Core 3 first-in-class transformative gene therapies to patients and their families in need

Commercial Execution

Laser-focused on launching Core 3 products in the U.S.

Post-separation, **bluebird is poised to unlock value** for patients and shareholders

Optimization + Innovation

Strategy in place to optimize existing products and realize next-generation pipeline

Funding + Financial

Increased fiscal discipline; well-funded to execute through significant value-creating milestones

Experienced management team in place

bluebird leaders

Andrew Obenshain
Chief Executive Officer

Richard Colvin
Chief Medical Officer

Jason Cole
Chief Business Officer

Anne-Virginie Eggimann
Chief Regulatory Officer

Melissa Bonner
Head of SGD Research

Kasra Kasraian
SVP, CMC Strategy & Operations

Scott Shoemaker
SVP, SGD Quality

Recent additions

Gina Consylman
Chief Financial Officer

Tom Klima
Chief Commercial Officer

3 first-in-class gene therapies in the U.S.

Treated more patients with longer follow-up than any other company in the field

Approx. 466 patient-years of experience with bluebird's gene therapies

SCD

bb1111

47 patients treated in clinical trials

Up to **3.5** years of patient follow-up

Update on regulatory path by year-end 2021

~20,000 patients living with severe SCD in the U.S.

TDT

beti-cel

63 patients treated in clinical trials

Up to **7** years of patient follow-up

BLA **on track** for 3Q 2021

~1,500 patients living with TDT in the U.S.

CALD

eli-cel

67 patients treated in clinical trials

Up to **nearly 7** years of patient follow-up

BLA **planned by** year-end 2021*

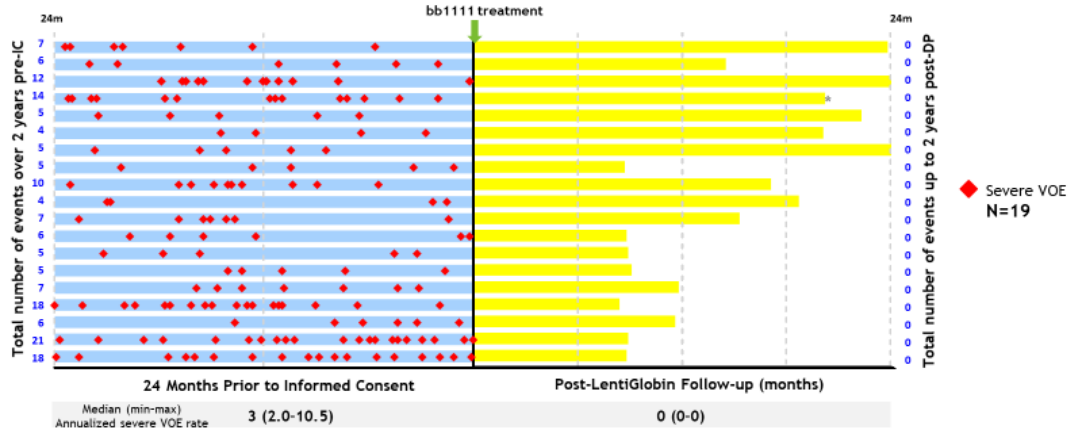
~50 annual patients with CALD in the U.S.

**Pending resolution of clinical hold*

Over a decade of advancing programs through the clinic to deliver life-changing medicines to 150+ patients

LentiGlobin for SCD

SCD: Unparalleled efficacy with complete resolution of severe VOEs post-bb1111 treatment in HGB-206 Group C clinical study



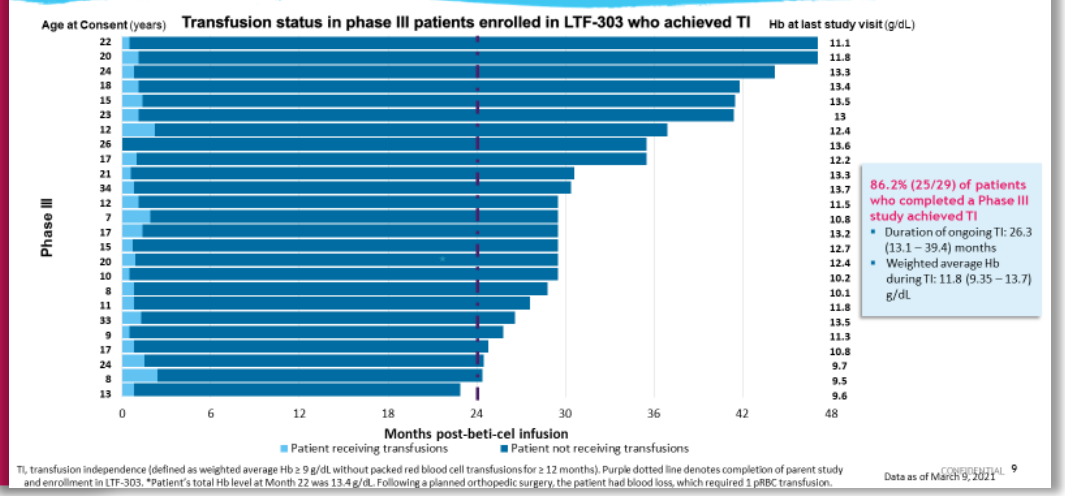
Protocol sVOEs are shown: Patients with ≥ 4 sVOE at baseline before IC and with ≥ 6 months of follow-up post-DP infusion are included. A severe VOE is as an event with no medically determined cause other than a vaso-occlusion, requiring a ≥24-hour hospital or emergency room observation unit visit or at least 2 visits to a day unit or ER over 72 hours with both visits requiring intravenous treatment for the following: acute episodes of pain, acute chest syndrome, acute hepatic sequestration, and acute splenic sequestration; [1]HbA[T87Q] stabilizes within 6 months; [2]One death, unlikely related to LentiGlobin. ≥ 18 months post treatment in a patient with significant baseline SCD-related cardiopulmonary disease. [3]Events recorded as an investigator reported VOE but does not meet the definition of a protocol VOE [4]sVOEs, severe VOEs; VOE, vaso-occlusive event; VOC, vaso-occlusive crises.

Data as of 20 August 2020

CONFIDENTIAL 8

LentiGlobin for TDT

TDT: Phase III patients treated with beti-cel who achieve TI, maintain TI and had median weighted average Hb of 11.8 g/dl with 3+ years of follow-up



86.2% (25/29) of patients who completed a Phase III study achieved TI
- Duration of ongoing TI: 26.3 (13.1 – 39.4) months
- Weighted average Hb during TI: 11.8 (9.35 – 13.7) g/dL

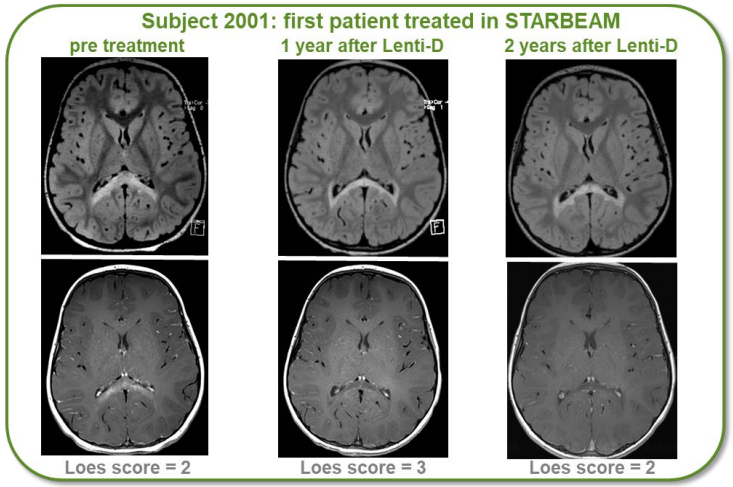
TI, transfusion independence (defined as weighted average Hb ≥ 9 g/dL without packed red blood cell transfusions for ≥ 12 months). Purple dotted line denotes completion of parent study and enrollment in LTF-303. *Patient's total Hb level at Month 22 was 13.4 g/dL. Following a planned orthopedic surgery, the patient had blood loss, which required 1 pRBC transfusion.

Data as of March 9, 2021

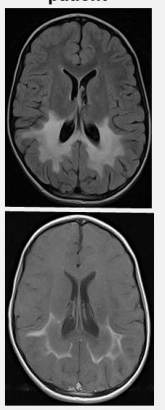
CONFIDENTIAL 9

Lenti-D for CALD

Subject 2001: first patient treated in STARBEAM



Representative untreated patient



Data as of March 31, 2016

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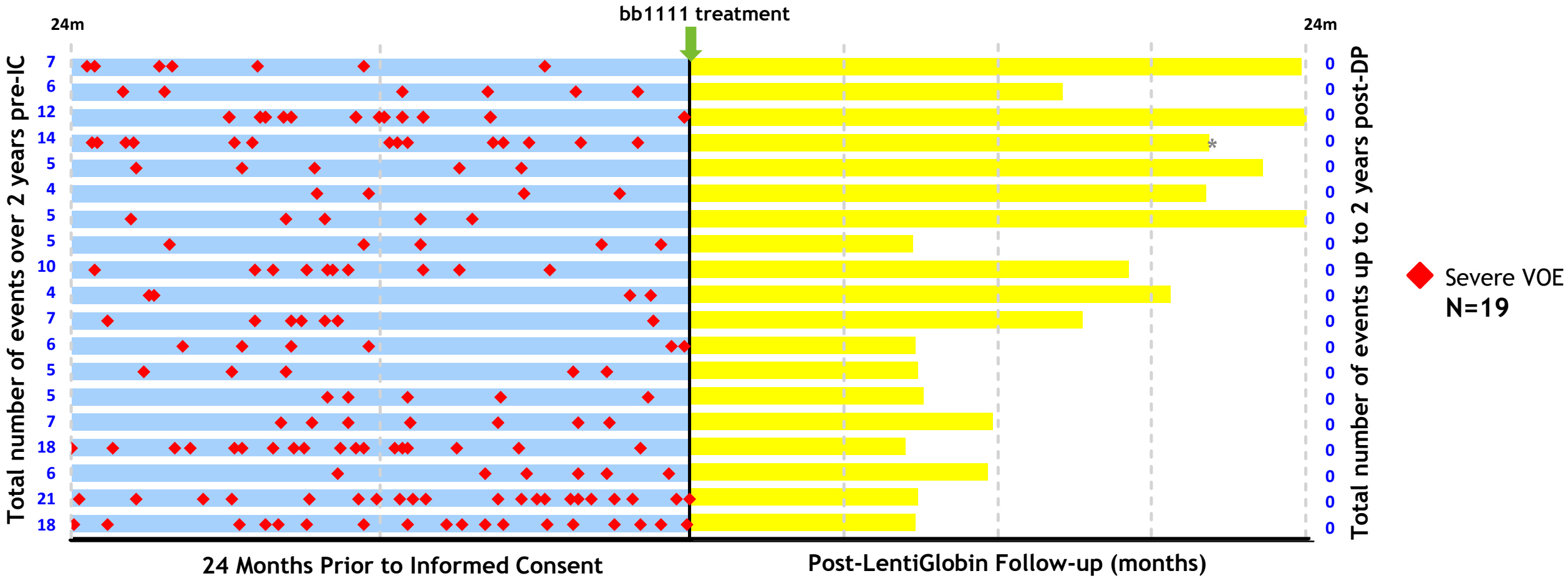
SCD: Unparalleled efficacy with complete resolution of severe VOEs post-bb1111 treatment in HGB-206 Group C clinical study

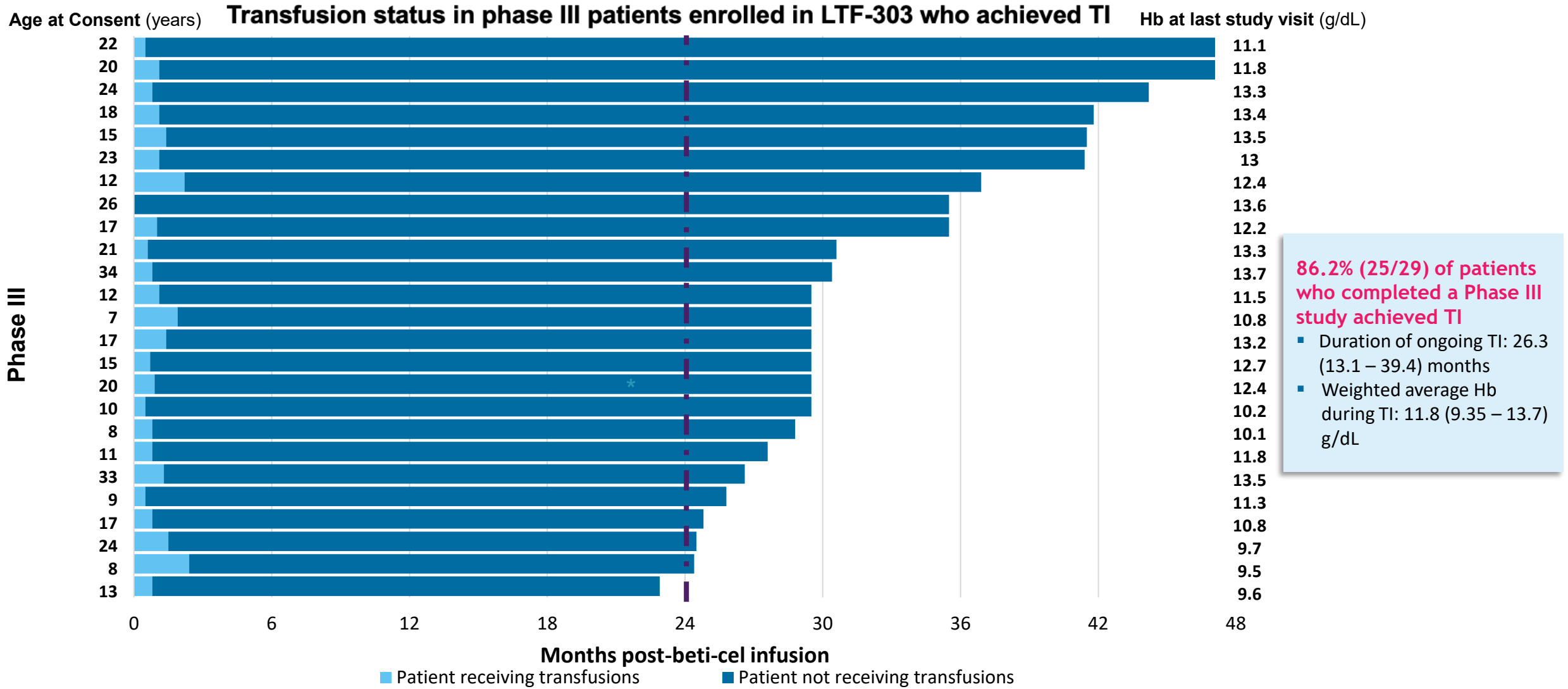


Median (min-max) Annualized severe VOE rate	3 (2.0-10.5)	0 (0-0)

Protocol sVOEs are shown; Patients with ≥ 4 sVOE at baseline before IC and with ≥ 6 months of follow-up post-DP infusion are included. A severe VOE is as an event with no medically determined cause other than a vaso-occlusion, requiring a ≥24-hour hospital or emergency room observation unit visit or at least 2 visits to a day unit or ER over 72 hours with both visits requiring intravenous treatment for the following: acute episodes of pain, acute chest syndrome, acute hepatic sequestration, and acute splenic sequestration; †HbA^{T87Q} stabilizes within 6 months; *One death, unlikely related to LentiGlobin, > 18 months post treatment in a patient with significant baseline SCD-related cardiopulmonary disease.
Note: In the last datacut, one patient had a non-serious VOCexpression at Day 107. This event is recorded as an investigator reported VOE but does not meet the definition of a protocol VOE
DP, drug product; ER, emergency room; IC, informed consent; max, maximum; min, minimum; sVOEs, severe VOEs; VOE, vaso-occlusive event; VOC, vaso-occlusive crises.

Data as of 20 August 2020

TDT: Phase III patients treated with beti-cel who achieve TI, maintain TI and had median weighted average Hb of 11.8 g/dl with 3+ years of follow-up



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Data as of March 9, 2021

CALD: eli-cel (Lenti-D) treatment halts CALD disease progression

Starbeam STUDY

The NEW ENGLAND JOURNAL of MEDICINE

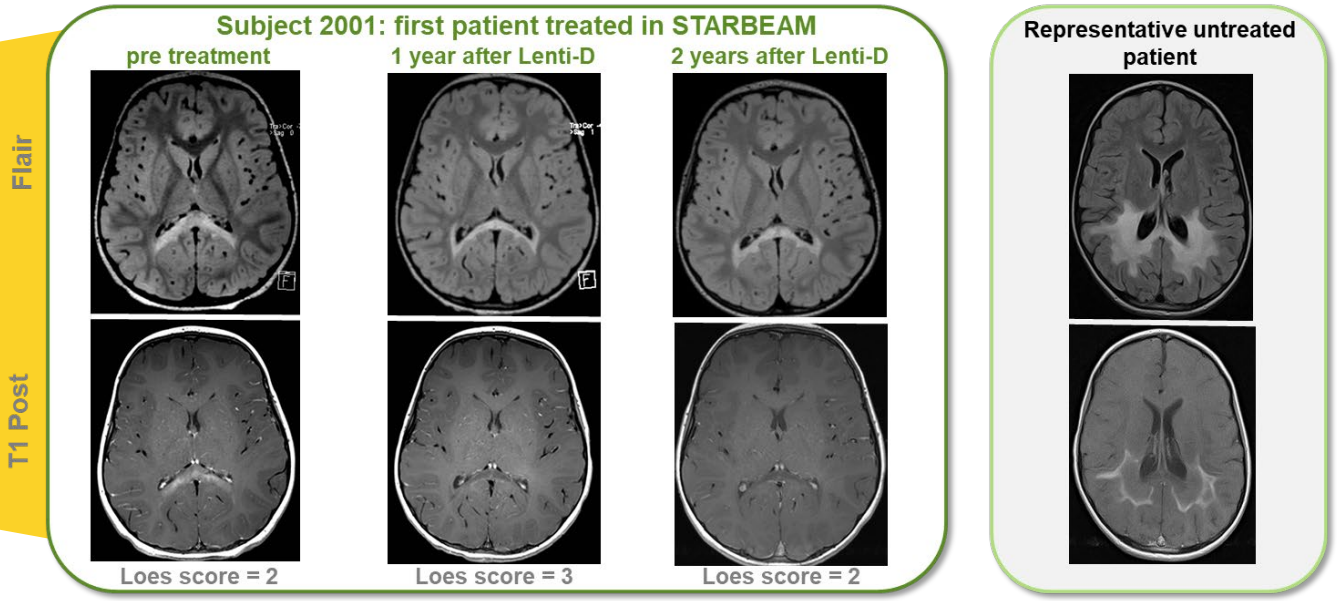
October 4, 2017

ORIGINAL ARTICLE

Hematopoietic Stem-Cell Gene Therapy for Cerebral Adrenoleukodystrophy

Florian Eichler, M.D., Christine Duncan, M.D., Patricia L. Musolino, M.D., Ph.D., Paul J. Orchard, M.D., Satiro De Oliveira, M.D., Adrian J. Thrasher, M.D., Myriam Armant, Ph.D., Colleen Dansereau, M.S.N., R.N., Troy C. Lund, M.D., Weston P. Miller, M.D., Gerald V. Raymond, M.D., Raman Sankar, M.D., Ami J. Shah, M.D., Caroline Sevin, M.D., Ph.D., H. Bobby Gaspar, M.D., Paul Gissen, M.D., Hernan Amartino, M.D., Drago Bratkovic, M.D., Nicholas J.C. Smith, M.D., Asif M. Paker, M.D., Esther Shamir, M.P.H., Tara O'Meara, B.S., David Davidson, M.D., Patrick Aubourg, M.D., and David A. Williams, M.D.

N Engl J Med 2017; 377:1630-1638



Data as of March 31, 2018

ALD-102: all patients who were alive and MFD-free at 24 months follow up (27/30; 90%) continue to be MFD-free with up to 7 years of follow-up

- 32 patients have been treated with eli-cel with a median follow-up time of 38.6 months
- 2 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.

***Program is on clinical hold, pending resolution with FDA**

bluebirdbio®

Data as of October 2020

Confident in U.S. launches; market preparation underway

We have a deep understanding of how to deliver our gene therapies for patients

1. Significant unmet medical need and sizable opportunity
2. Clear path for reimbursement after productive discussions with payers
3. Concentrated qualified treatment center (QTC) network to reach patients in need; excellent partnerships with QTCs
4. Scalable commercial manufacturing, distribution network ready to go, and patient support services to ensure treatment will be available to any patient in need
5. Strong patient community presence with experienced patient advocacy team

In the near term, our focus is on delivering potentially curative therapies to ~22,000 patients in the U.S.

Majority of U.S. opportunity driven by the enormous unmet need in Severe SCD

Addressable patients for bluebird bio gene therapy in the United States

~20,000

Patients living with Severe Sickle Cell Disease (SCD)[1,2]

~1,500

Patients living with Transfusion-dependent ß-Thalassemia (TDT)[3]

~50

Annual patients with Cerebral Adreno-leukodystrophy (CALD)[4,5]

1. *Hassell KL. Population estimates of sickle cell disease in the U.S. Am J Prev Med. 2010;38(4 Suppl):S512 521*
2. *Jul '21 bbb analysis of Komodo patient-level claims data (Apr '20 - Mar '21), IQVIA patient-level claims data (Aug '18 - Jul '19)*
3. *Hulihan, Mary M., et al. State-based surveillance for selected hemoglobinopathies. Genetics in Medicine 17.2 (2015): 125-130.*
4. *Bezman L, et al. Adrenoleukodystrophy: Incidence, new mutation rate, and results of extended family screening. Ann Neurol. 2001;49:512-517*
5. *Moser HW, Mahmood A, Raymond GV. X-linked adrenoleukodystrophy. Nature Clin Pract Neurol. 2007;3(3):140-51*

Significant unmet need for patients living with SCD and TDT

Our therapies will provide a potentially curative option and change lives

SCD

Lakiea, patient living with SCD

SCD has a significant negative impact on quality of life and shortens life expectancy

Despite recent approvals, current options target individual disease domains, but are not potentially curative and significant unmet need remains

- Majority of SCD patients experience 1) chronic daily pain, 2) reduction in their ability to work or attend school and 3) fatigue
- Many patients have had to put personal goals and aspirations on hold to manage SCD; even with medication, patients agree SCD makes it difficult to plan for the future
- Over half report being fearful of the long-term effects of SCD despite current *treatment*

TDT

Laurice, patient living with TDT

Despite advances in iron management, TDT patients suffer from serious complications and organ damage caused by excess iron

While other therapies may reduce transfusion burden for some, it cannot provide the transfusion independence or near-normal Hb levels attainable with GT

- Laurice (pictured) experienced hemoglobin of 6.9 g/dL growing up, congestive heart failure at ages 9 & 25, splenectomy at 10, tonsillectomy at 13, gall bladder removal at 22, severe osteoporosis, chronic pain; she has lost many friends with TDT over the course of her life
- Nearly half of TDT patients are extremely concerned about organ damage that may result from iron chelation therapy

Investing in Reduced Toxicity Conditioning (RTC) and Mobilization because our patients deserve better treatment options

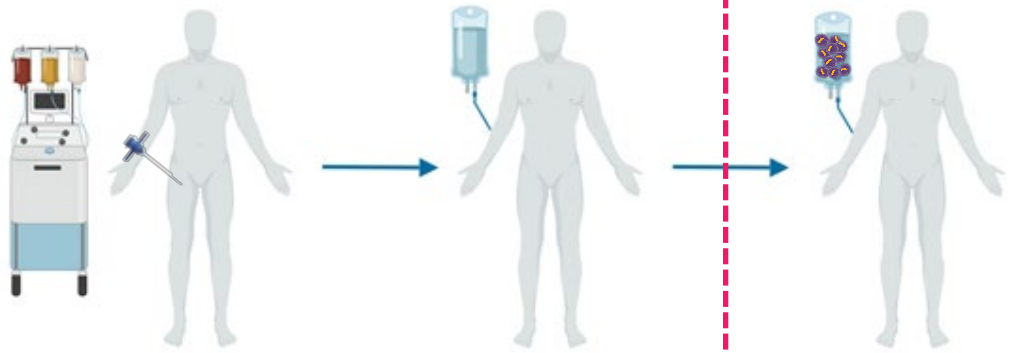
Optimization + Innovation

Current Transplant Process

HSC collection
Bone marrow harvest or mobilization with plerixafor & apheresis

Busulfan myeloablative conditioning

DP infusion



Critical for engraftment of gene-modified cells

LET'S RECODE THE SYSTEM

Not without known risks
(infertility, secondary malignancy, etc.)

Benefits of Future Optimization

Improve patient experience

- *Potential to reduce the severe side effects of myeloablative conditioning*
- *Allow broader patient reach*

Drive our competitive advantage

- *A safer regimen with reduced infertility risk would confer a significant advantage with physicians and patients in a highly competitive GTx landscape*

Accelerate the financial upside

- *Patient and physician preference for RTC is anticipated to significantly increase SCD uptake*

Enable new therapeutic areas (TAs)

- *First company to "solve" RTC may get opportunities beyond SCD and TDT where the risk-benefit for ex-vivo gene therapy is not as clear* today

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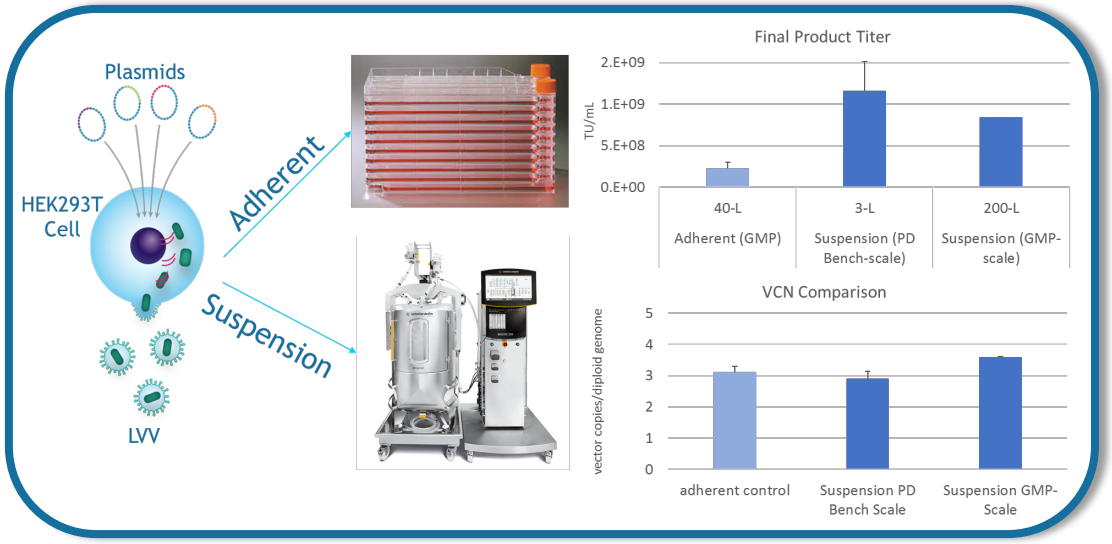
Developing enhanced manufacturing methods to scale and reduce COGS

Optimization + Innovation

Techniques to lower the drug cost burden and create shareholder value over time

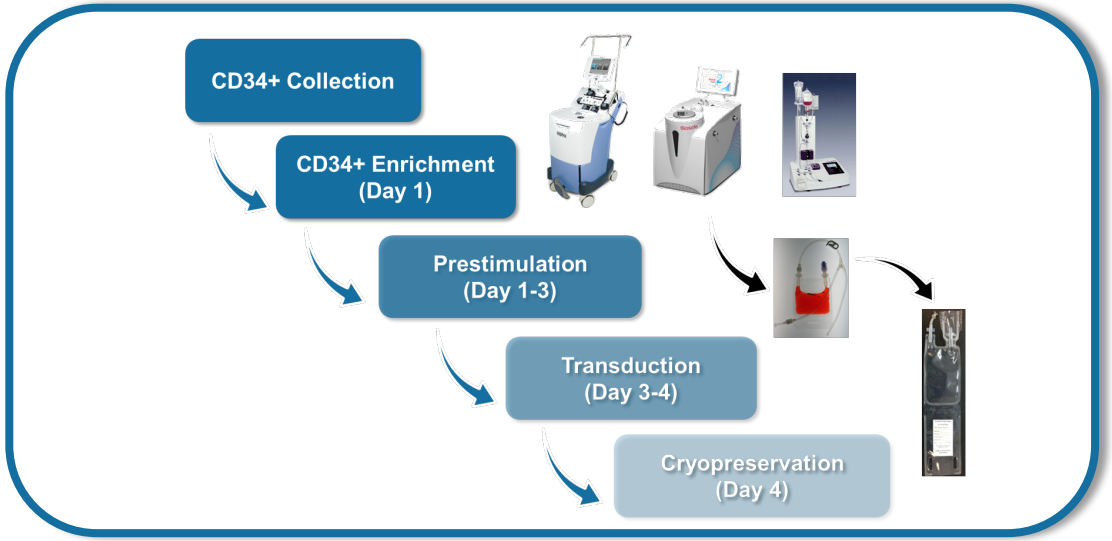
Developed: Suspension lentiviral vector (sLVV)

- Up to 10X yield increase (COGS reduction)
- Gaining clinical experience now
- Will launch SCD (bb1111) with sLVV



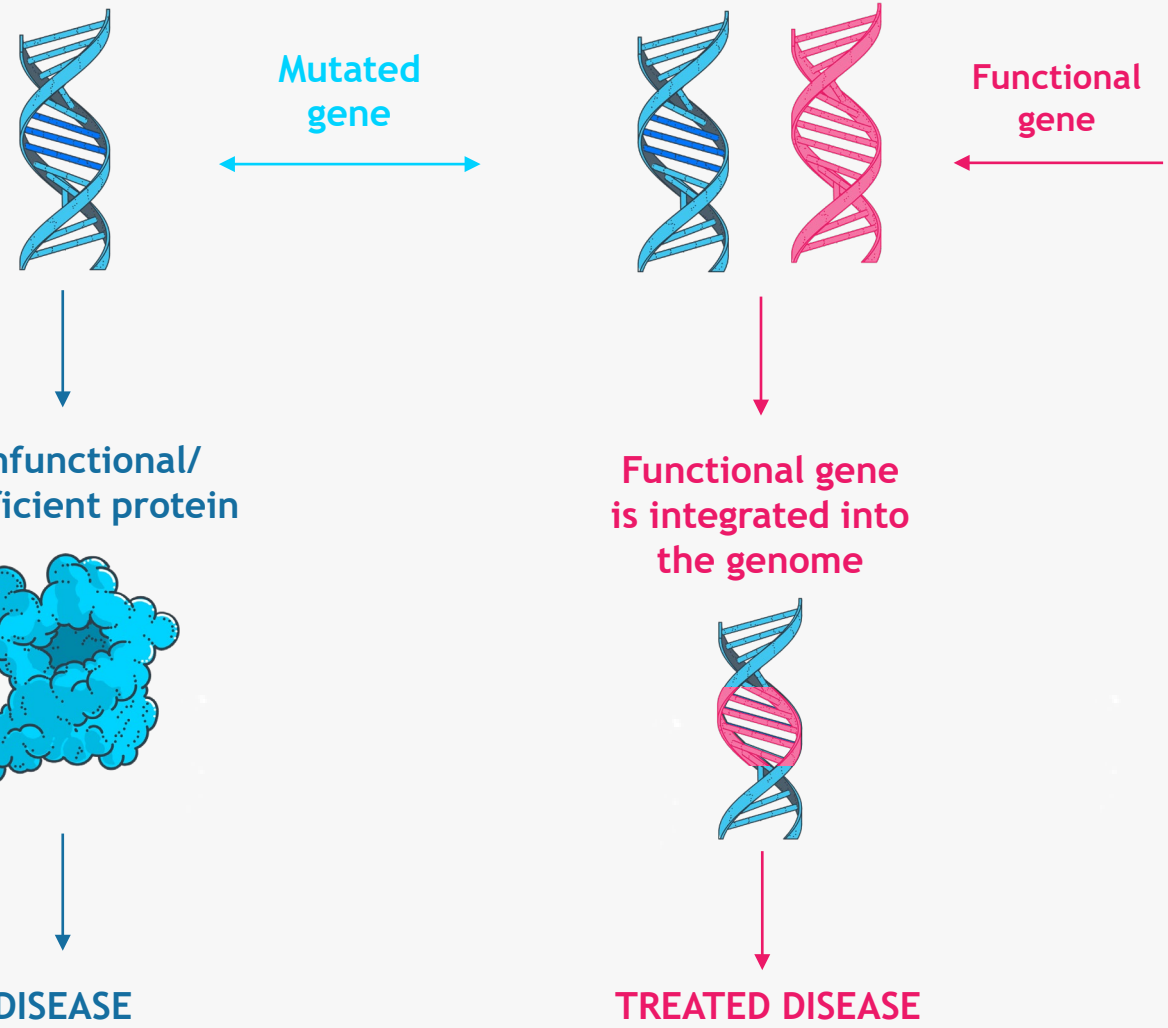
In development: Cryopreservation

- More efficient use of manufacturing slots (COGS reduction)
- Reduce need for additional manufacturing runs for a single patient



Pioneering the gene therapy field

GENE ADDITION: our lentiviral vector (LVV) gene therapy introduces functional copies of a gene to the patient's stem cells to address the underlying genetic cause of disease



Deeply Studied

LVV gene therapy has been deeply studied in more than 300 patients over nearly 15 years.

Custom-designed

Because of the differences in the underlying cause of particular diseases, we custom-design every gene therapy, through the design of the specific LVV used and manufacturing process.

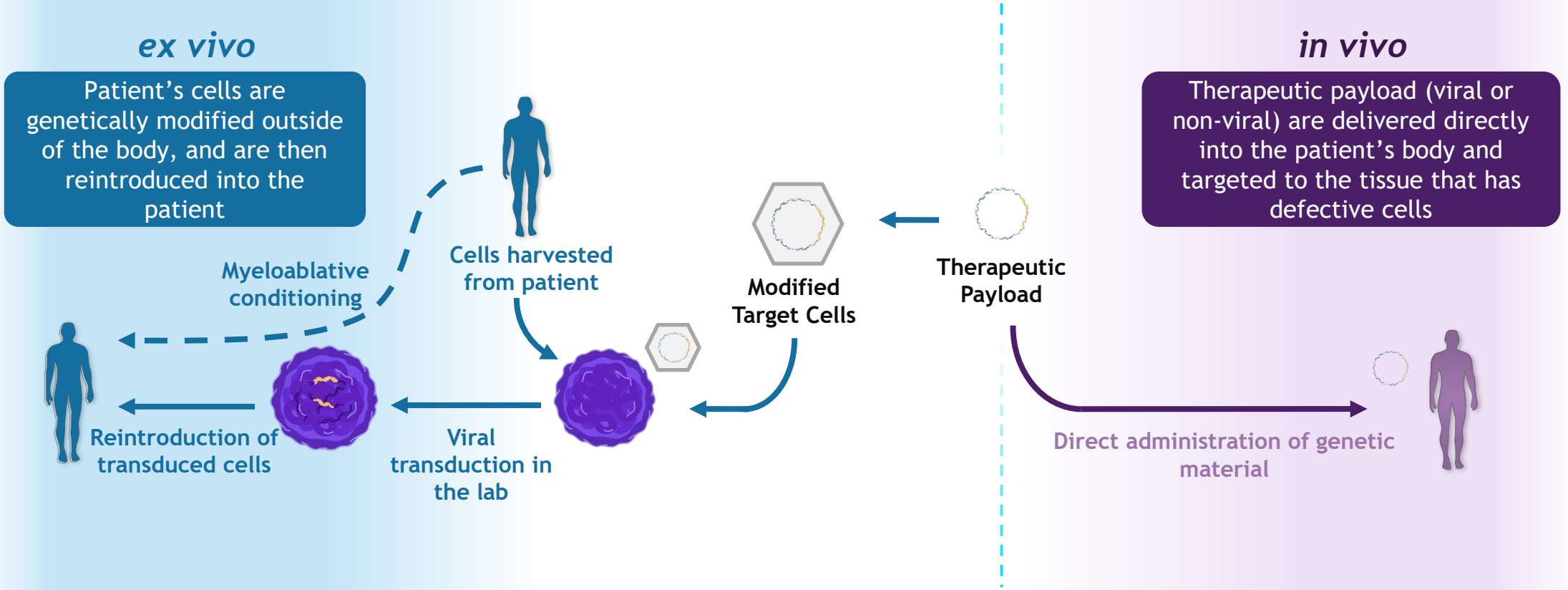
Traceable

Insertion site is traceable for patients receiving our therapies allowing for ongoing monitoring.

Based on advantages we believe LVV has over AAV, we are extending our core LVV platform by investing in direct *in vivo* LVV

LET'S RECODE THE SCIENCE

Gene therapy can be delivered both *ex vivo* and *in vivo*



bluebird is poised to unlock value for patients and shareholders

✓ *Leadership Team*	• Experienced management team in place composed of tenured bluebird leaders and recent additions
✓ *Products that Matter*	• TDT BLA on track for 3Q 2021 • CALD BLA by end of 2021* • SCD regulatory path update by end of year
✓ *Commercial Execution*	• Laser-focused on launching Core 3 products in the U.S. • Market prep underway: Concentrated QTC footprint established, clear path for reimbursement after productive discussions with payers, scalable commercial manufacturing in place
✓ *Optimization + Innovation*	• Focused investments in R&D to optimize existing programs: RTC, enhanced mobilization, sLVV, cryopreservation. Investment in in-vivo LVV research
✓ *Funding + Financial*	• Increased fiscal discipline • Anticipate ~$975m pre-split cash on hand; provides both companies with a meaningful runway • Additional savings through planned orderly wind down of Europe

**Pending resolution of clinical hold*

Simple Vision; Profound Mission

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.