bluebird bio

November 2022 Company Presentation

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 expectations regarding our programs and therapies, including but not limited to the timing or likelihood of regulatory filings and approvals, our commercialization plans, and addressable market 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.

Pursuing Curative gene therapies …

To give patients and their families more bluebird days

bluebirdbio®

bluebird bio: Setting the industry standard for gene therapy

Gene Therapy Leadership

180+ patients
treated with bluebird therapies across 8 clinical trials

>500 patient-years
of experience with bluebird bio's gene therapies

Validated Platform

Unanimous vote
at recent FDA advisory committees for ZYNTEGLO and SKYSONA that their benefits outweigh risks

>20 articles
published on LVV science and the value of gene therapy

Commercial Focus

3 approvals
expected by the end of 2023, all with wholly-owned global rights

22,000 patients
potentially addressable with our Core 3 programs in the U.S.[1]

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

Realizing significant value for patients and shareholders with three near-term opportunities

First to market gene therapy for hemoglobinopathies in the U.S.

SKYSONA® for cerebral adrenoleukodystrophy

- ☑ FDA Advisory Committee Meeting June 9-10, 2022
  - *Committee unanimously endorsed eli-cel (15-0) for treatment of early active CALD*
- ☑ FDA approved on September 16, 2022
- ❑ Commercial readiness in Q4 2022

ZYNTEGLO® for beta-thalassemia

- ☑ FDA Advisory Committee Meeting June 9-10, 2022
  - *Committee unanimously supported beti-cel (13-0) for beta-thal requiring regular red blood cell transfusions*
- ☑ FDA approved on August 17, 2022
- ❑ Commercial launch and first cell collection in Q4 2022

lovo-cel for sickle cell disease

- ☑ Aligned with FDA on path to BLA
- ☑ Completed manufacturing of commercial drug product validation lots
- ❑ Expect completion of vector and drug product analytical comparability by Q4 2022
- ❑ BLA submission planned for Q1 2023

Proving our commercial model → *Significant value driver*

Established technology addresses the underlying cause of disease by adding a functional copy of a gene

custom designed

- Each genetic disease has a different underlying cause
- Specific LVV and manufacturing process custom-designed to address the respective disease they are aiming to treat
- Therapeutic benefit is expected to be life-long

deeply studied

- >180 patients treated
- >8 years of follow up
- 500+ patient years of experience across our LVV clinical studies

traceable

- Ability to identify and track inserted gene after delivery to a patient
- Unique aspect improves understanding of safety and efficacy for our therapies
- Insertion site analysis is a robust and sensitive tool

In clinical studies for 3 lead therapies, vector-related safety profiles differ

SKYSONA® for cerebral adrenoleukodystrophy

ZYNTEGLO® for beta-thalassemia

lovo-cel for sickle cell disease

Lenti-D LVV

LVV-mediated insertional oncogenesis observed

67 patients treated

3 malignancies

All **3** Lenti-D LVV mediated insertional oncogenesis

BB305 LVV

No LVV-mediated insertional oncogenesis has been observed

63 patients treated

0 malignancy

0 insertional oncogenesis

50 patients treated

2 malignancies

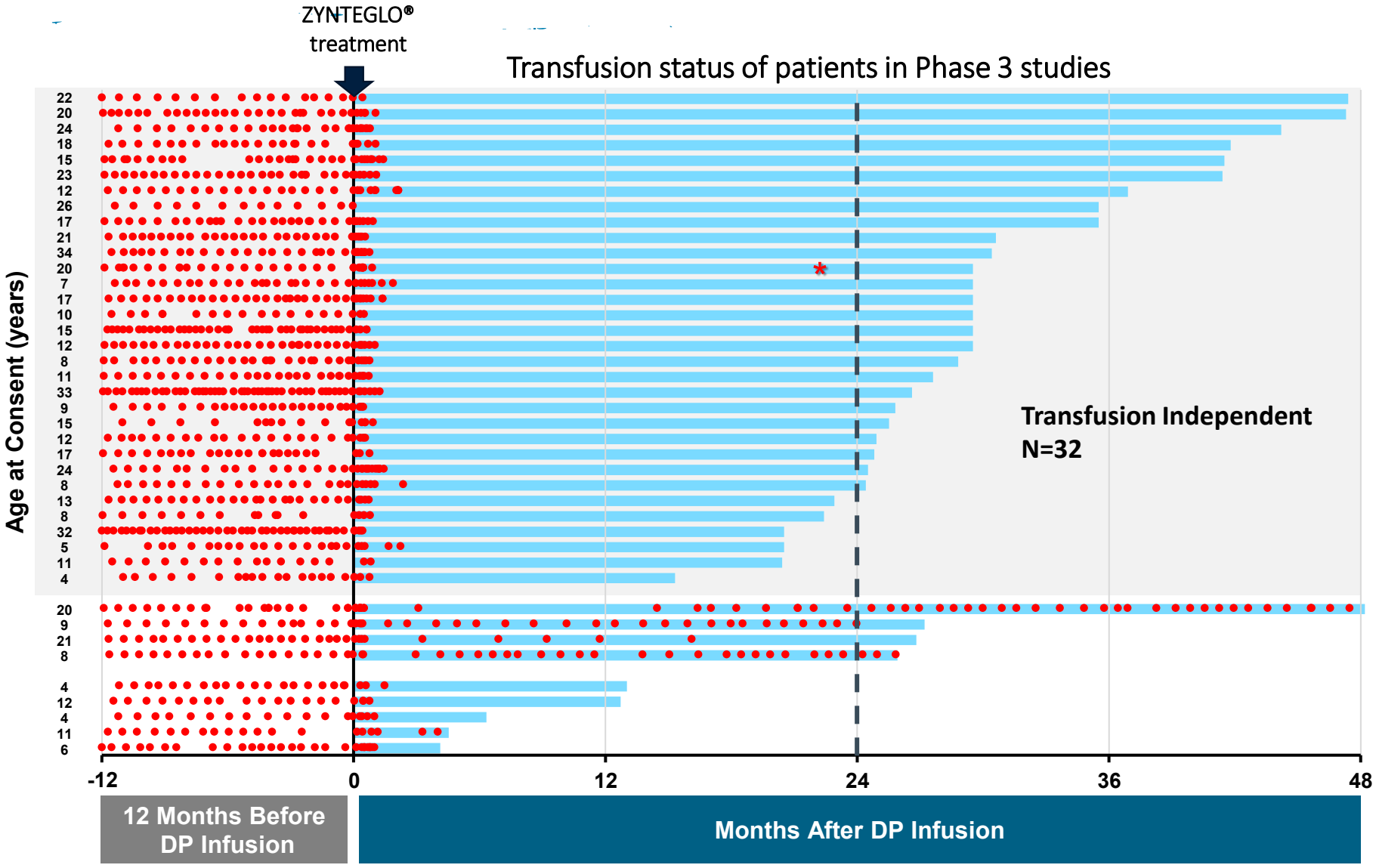
0 insertional oncogenesis

Data as of June 13, 2022

ZYNTEGLO®: Now FDA Approved

zynteglo®
(betibeglogene autotemcel)
suspension for IV infusion

ZYNTEGLO® approval is underscored by impressive clinical study data



In Phase 3 studies:

- 89% of patients achieved transfusion independence (TI) and normal or near-normal hemoglobin levels
- All patients who achieved TI have remained transfusion free
- Durable results with longest follow-up out to 4 years
- Majority of AEs and SAEs were consistent with myeloablative conditioning

*Patient received acute transfusion for serious blood loss due to orthopedic surgery. DP: Drug Product

Data as of March 2021

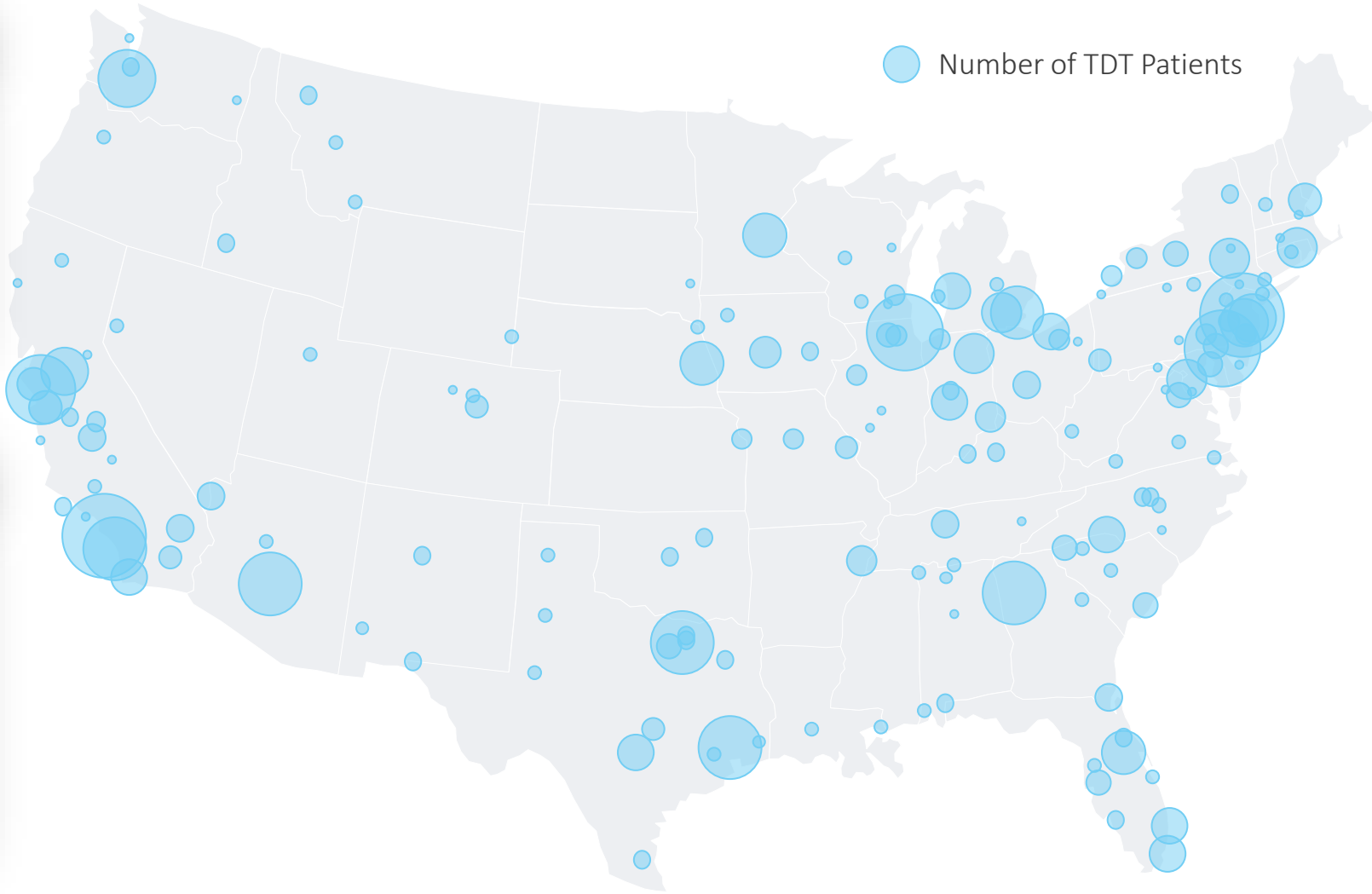
Fit-for-purpose Qualified Treatment Center (QTC) network being activated in waves

Targeted QTC selection

- Focused on high prevalence states
- Centers actively treating beta-thalassemia today
- Deep experience with commercial cell and gene therapies

QTC growth aligned with demand

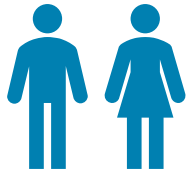
- Wave 1 QTCs fully activated
- Anticipate 1st apheresis in Q4 2022
- Expect low double digits QTCs by year end 2022
- Expansion to ~40-50 QTCs by YE 2023 in anticipation of SCD launch



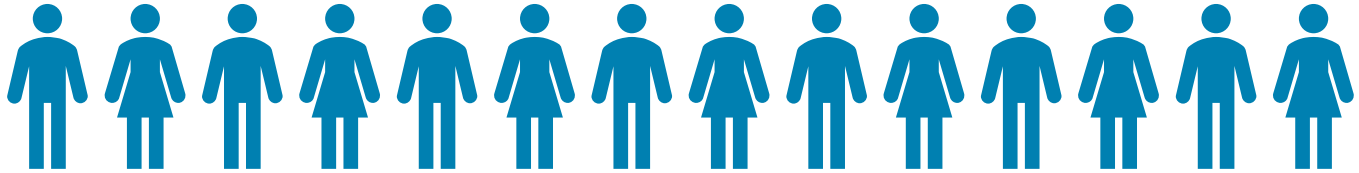
QTC: Qualified Treatment Center

Planned QTC network supports significant U.S. patient opportunity

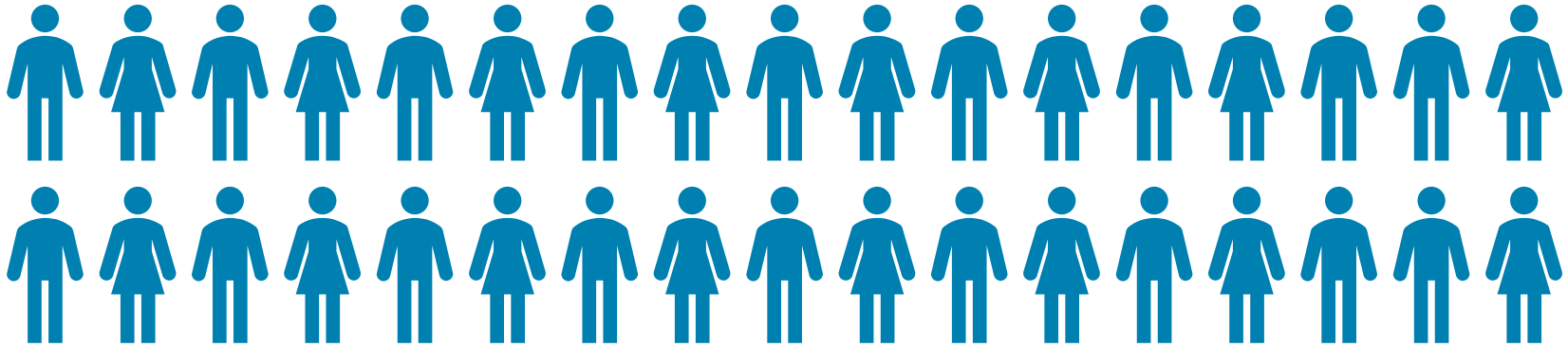
~50 potentially eligible patients currently seen at Wave 1 QTCs



~350 patients eligible with QTC expansion



More than 850 patients potentially eligible for ZYNTEGLO®



55 – 60% of the ~1,500 patients with transfusion dependent beta-thalassemia in the US may be eligible for gene therapy

QTC: Qualified Treatment Center

Confident in timely, quality access and reimbursement with upfront payment at $2.8M price

Price tied to recognized value

- Beta-thalassemia requiring regular RBC transfusions is associated with:
  - $6.4 million average lifetime medical care cost per patient[1]
  - 23X higher average total health care cost per patient per year vs. general population[2]
  - Blood transfusions every 2-5 weeks for life[3]

Simple and innovative payment strategy

- bluebird is offering payers:
  - One-time upfront payment
  - Outcomes-based agreement with up to 80% rebate if patient does not reach transfusion independence within 2 years
  - Clinically-relevant outcome, easily tracked in claims data

Encouraging payer interactions

- All target payers have responded favorably to approach:
  - 70-75% of patients with beta-thalassemia have commercial insurance
  - Engaging with state Medicaid agencies representing ~80% of publicly-insured beta-thalassemia patients

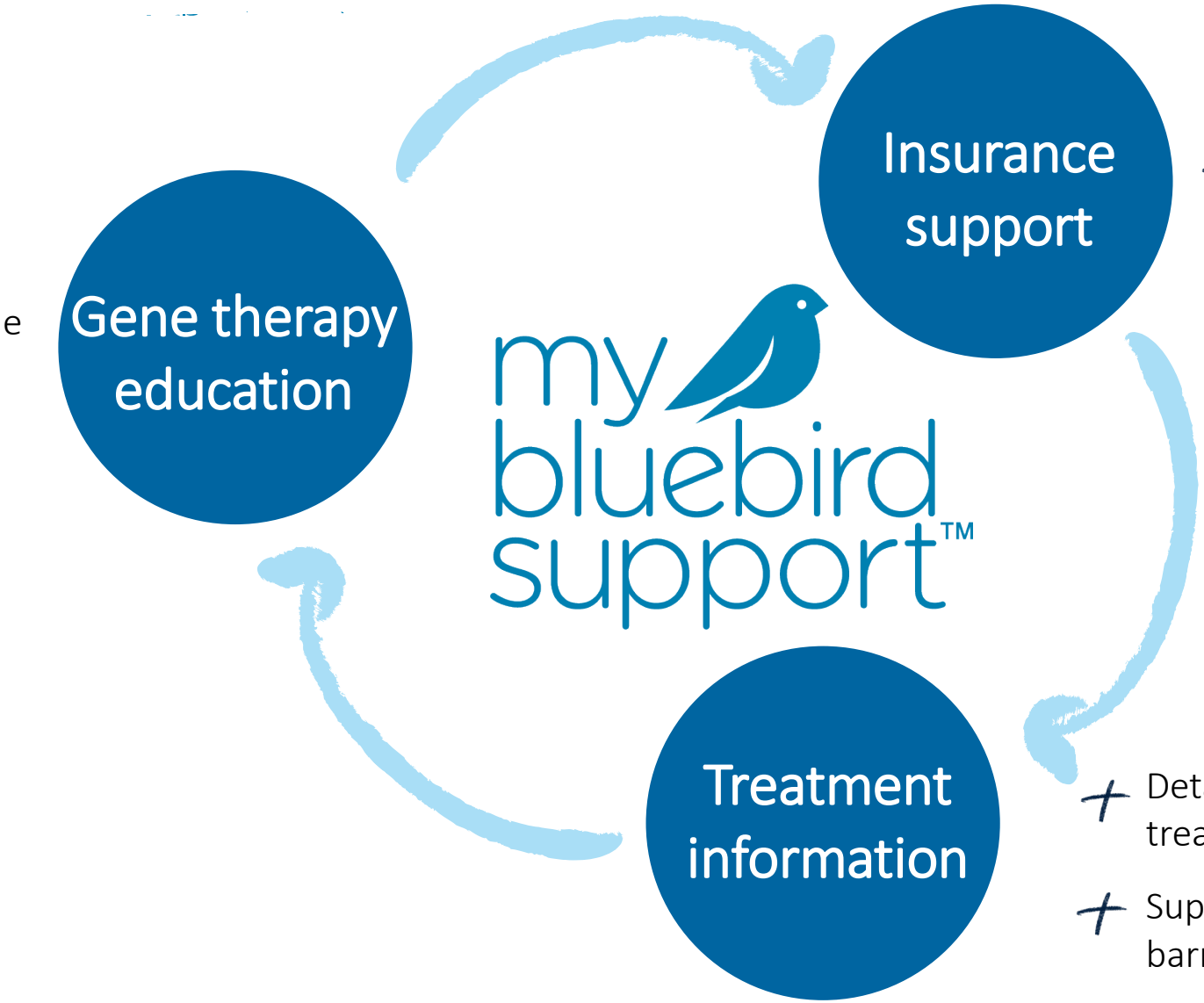
[1] Date on file [2] Weiss et al. 2019 [3]TIF Guidelines

ZYNTEGLO® manufacturing allows for flexible scheduling and is designed to deliver high quality drug product

Bulk of time spent on release testing to deliver high quality drug product

QTC: Qualified Treatment Center; CMO: Contract Manufacturing Organization

my bluebird support helps patients navigate every step of the treatment journey



- Benefits verification
- Assisting with potential sources of support for eligible and underinsured patients

- Information about the treatment process
- Locations of QTCs

- Detailed information on treatment journey
- Support in addressing non-clinical barriers to treatment access

lovo-cel for sickle cell disease

lovo-cel is being studied as a potentially curative option for patients with sickle cell disease

Upcoming anticipated milestones

- ☑ Aligned with FDA on path to BLA
- ☑ Completed manufacturing of commercial drug product validation lots
- ❑ Expect completion of vector and drug product analytical comparability studies by Q4 2022
- ❑ BLA submission planned for Q1 2023

>20,000 SCD patients in the US may be addressed by gene therapy

In active communication with the FDA to resolve the partial clinical hold and resume enrollment and treatment of patients under the age of 18

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

If approved, lovo-cel will address a critical unmet need for >20,000 potentially eligible patients in the US

Large Patient Population

- 1 in 365 Black or African American babies is born with sickle cell disease[1]
- **>20,000 SCD patients** in the US may be addressed by gene therapy[2]

Significant Unmet Need

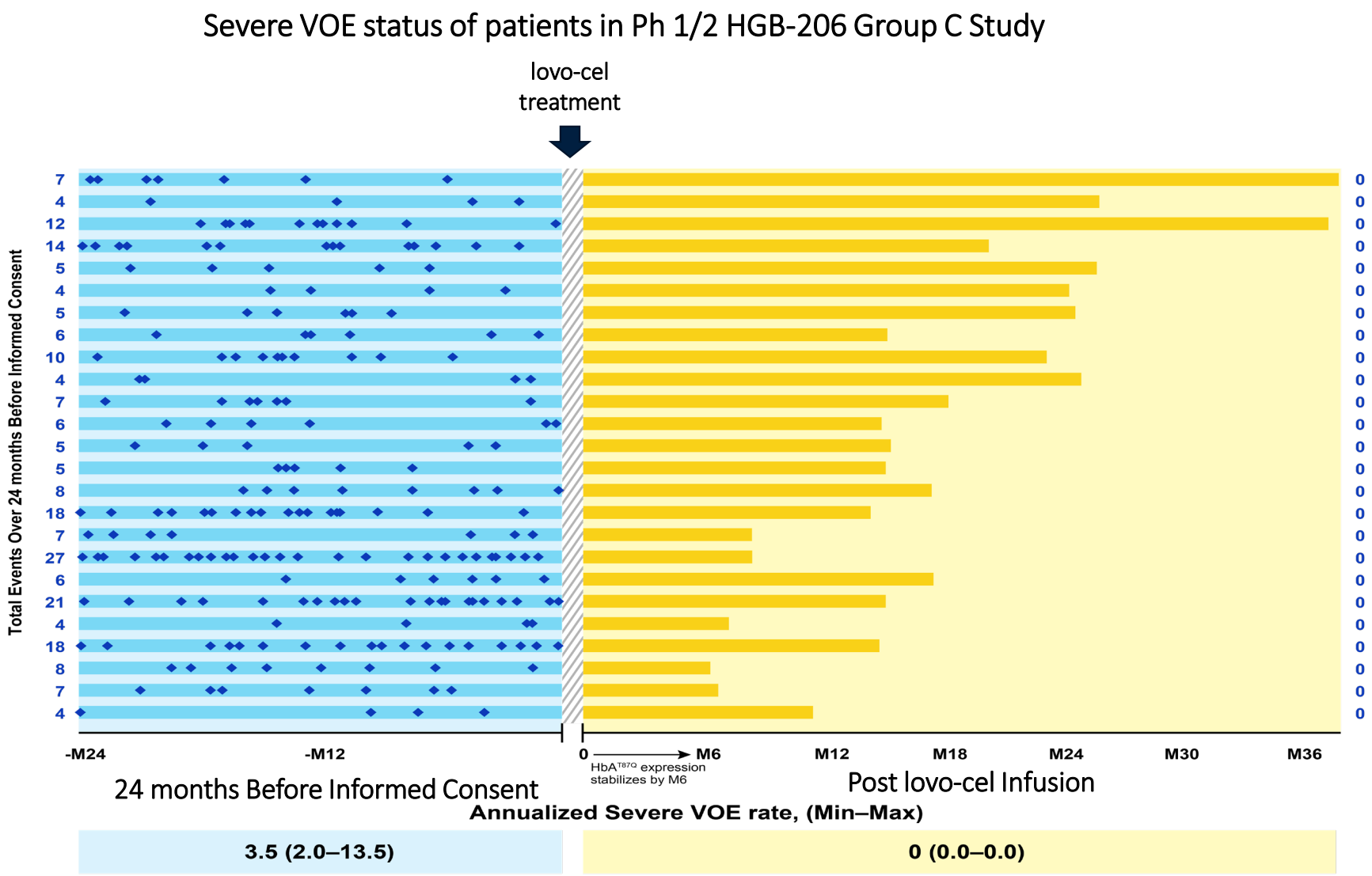
- Limited uptake of disease-modifying therapies to date
- Median **age of death remains in the 40s** despite treatment[3]
- Up to $9M in lifetime direct medical costs[4]

Competitive Advantage

- **Largest clinical dataset** of any gene therapy
- Deep commitment to and engagement with the SCD community

[1] CDC [2] See references on slide 3 [3] Ballas SK, Lusardi M. Hospital readmission for adult acute sickle cell painful episodes: frequency, etiology, and prognostic significance. Am J Hematol. 2005;79(1):17-25 [4] Paramore et al. 2018 ASH poster.

lovo-cel: largest sickle cell disease gene therapy data set in the industry presented at ASH 2021 and published in NEJM



lovo-cel HGB-206

Complete resolution of severe VOEs thru 36 months

- 35 Group C patients had up to 37.6 months of follow-up; **longest follow-up** for any gene therapy in development for SCD
- All evaluable patients (n=25) continued to experience **complete resolution of severe VOEs** through up to 36 months of follow-up
- Patients achieved **near normal levels** of key hemolysis markers and sustained improvements in patient-reported QoL
- **Safety data remain consistent** with the known side effects of autologous hematopoietic stem cell collection, myeloablative single-agent busulfan conditioning and underlying SCD

Data as of 17 February 2021

*In active communication with the FDA to resolve the partial clinical hold and resume enrollment and treatment of patients under the age of 18

Clarified path to BLA submission

Aligned on robust clinical data package with FDA

BLA will include:

- ✓ At least 50 patients treated with up to 7 years of follow-up
- ✓ HGB-206 Group C as primary basis of effectiveness with approximately 30 patients with ≥ 18 mo. of follow up.
- ✓ Pivotal study HGB-206; largest gene therapy study in SCD to date w/ clinically meaningful primary endpoint

All patients evaluable for primary endpoint have been treated

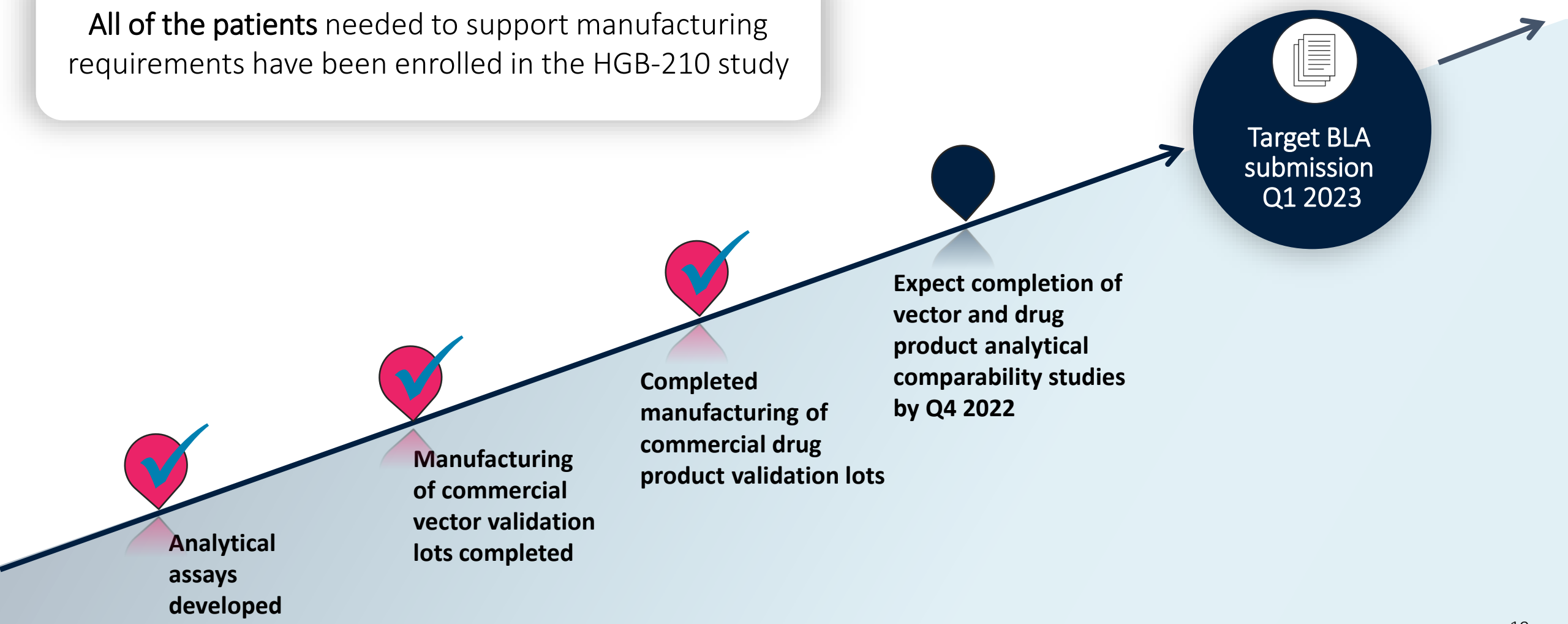
Clarified and confirmed detailed CMC path to BLA

- ✓ Aligned with FDA on reg-CMC road map to BLA submission
- ✓ Aligned with FDA on scientifically-justified analytical comparability requirements
- ✓ Conducting Phase 3 HGB-210 with drug product (DP) manufacturing in commercial facility

Based on this progress, lovo-cel BLA submission expected in Q1 2023

Plan to launch lovo-cel with scalable process to meet commercial demand

All of the patients needed to support manufacturing requirements have been enrolled in the HGB-210 study



SKYSONA®: Now FDA Approved

skysona™
(elivaldogene autotemcel)

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

The approval of SKYSONA® was based on data from bluebird bio's Phase 2/3 study ALD-102 and Phase 3 ALD-104 study

The NEW ENGLAND JOURNAL of MEDICINE

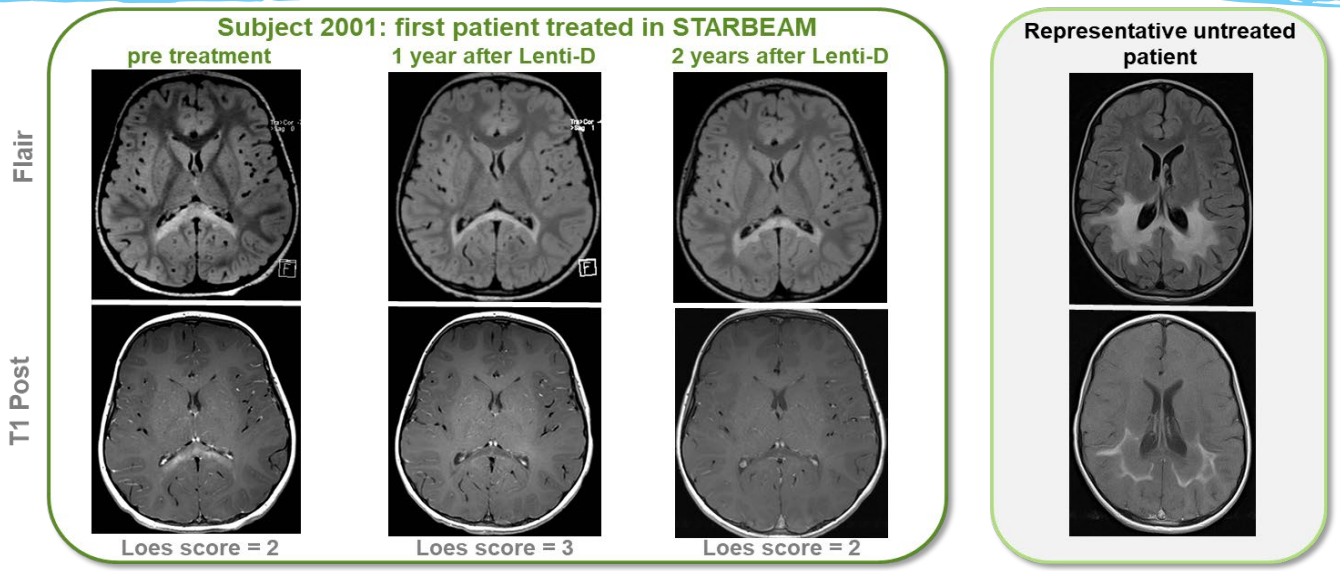
October 4, 2017

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



EFFICACY

Accelerated approval was based on a post hoc analysis of 24-month improvement in major functional disability (MFD) free survival

SKYSONA treated patients (n = 11) had an estimated 72% likelihood of MFD-free survival at 24 months compared to untreated patients in a natural history study (n = 7) who had only an estimated 43% likelihood of MFD-free survival

A total of 67 patients treated in clinical trials

SAFETY

The label includes a Boxed Warning on SKYSONA for hematologic malignancy; as previously reported 3 boys treated in our clinical trials developed MDS which is believed to be caused by insertion of the Lenti-D vector

Under Accelerated Approval, bluebird has agreed to provide confirmatory data to the FDA

The FDA lifted the clinical hold put in place in August 2021

MDS: myelodysplastic syndrome

Strengthened path to financial sustainability

Cash runway into Q2 23

Cash on hand of $141 million* as of 9/30/2022

Anticipated release of **$40 million** of restricted cash in Q4 2022

Targeting Q4 2022 cash burn of **$75-80 million**

Opportunity to extend cash runway

Non-dilutive capital

ZYNTEGLO® and SKYSONA® **PRVs in hand** – plan to monetize promptly and maximize value

Access to **$75 million** ATM; $55 million in net proceeds realized as of 9/30/2022

Evaluating public or private **equity and debt financings**

Product revenue expected beginning in Q1 2023

*Cash balance includes restricted cash of ~$45 million

FDA approvals of ZYNTEGLO and SKYSONA set the stage for lovo-cel BLA submission in Q1 2023

ZYNTEGLO® now FDA approved for patients with beta-thalassemia who require regular RBC transfusions

SKYSONA® now FDA approved for early, active cerebral adrenoleukodystrophy (CALD)

lovo-cel for SCD BLA submission anticipated in Q1 2023

- *Proving our commercial model*
- *Building our infrastructure today*
- *Delivering significant value for patients and shareholders*

Pursuing Curative gene therapies ...

To give patients and their families more bluebird days

thank you