bluebird bio
Company Presentation

May 2023

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.

bluebirdbio®

pursuing curative gene therapies ...

TO GIVE PATIENTS AND THEIR FAMILIES MORE BLUEBIRD DAYS

Demonstrating gene therapy expertise across clinical, regulatory and commercial

Clinical Leadership

180+ patients
treated with bluebird therapies across 8 clinical trials

Over 10+ years
of gene therapy research

Regulatory Success

Industry leader with 2 FDA approved gene therapies and seeking 3rd in 2023

Established track record for LVV technology, with 5 regulatory submissions

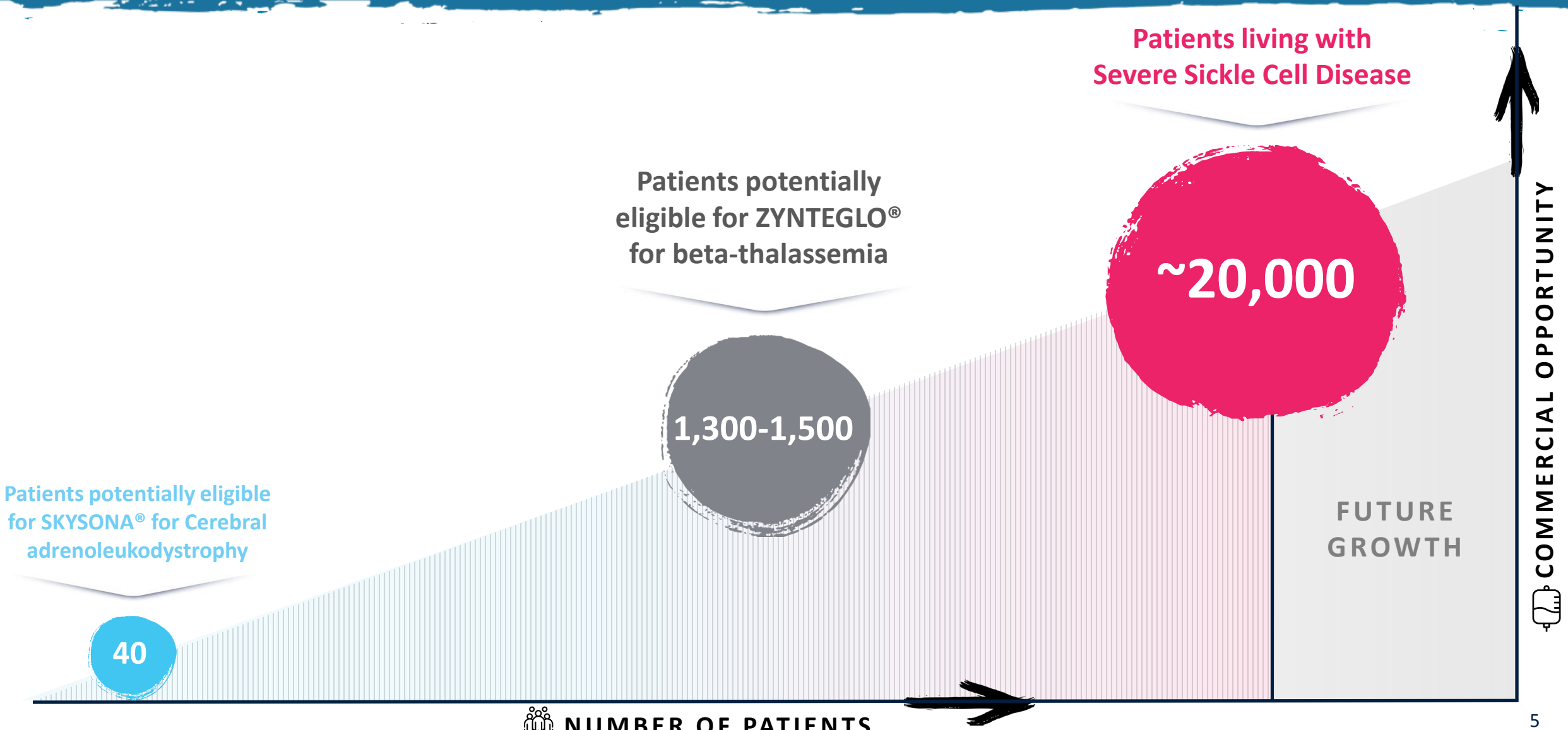
Commercial Impact

2 ongoing US launches,
all with wholly-owned global rights

~22,000 patients
potentially addressable with our 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

Momentum building with near-term commercial launches; opportunity to deliver significant value for patients and shareholders



Inherited hemoglobin disorders

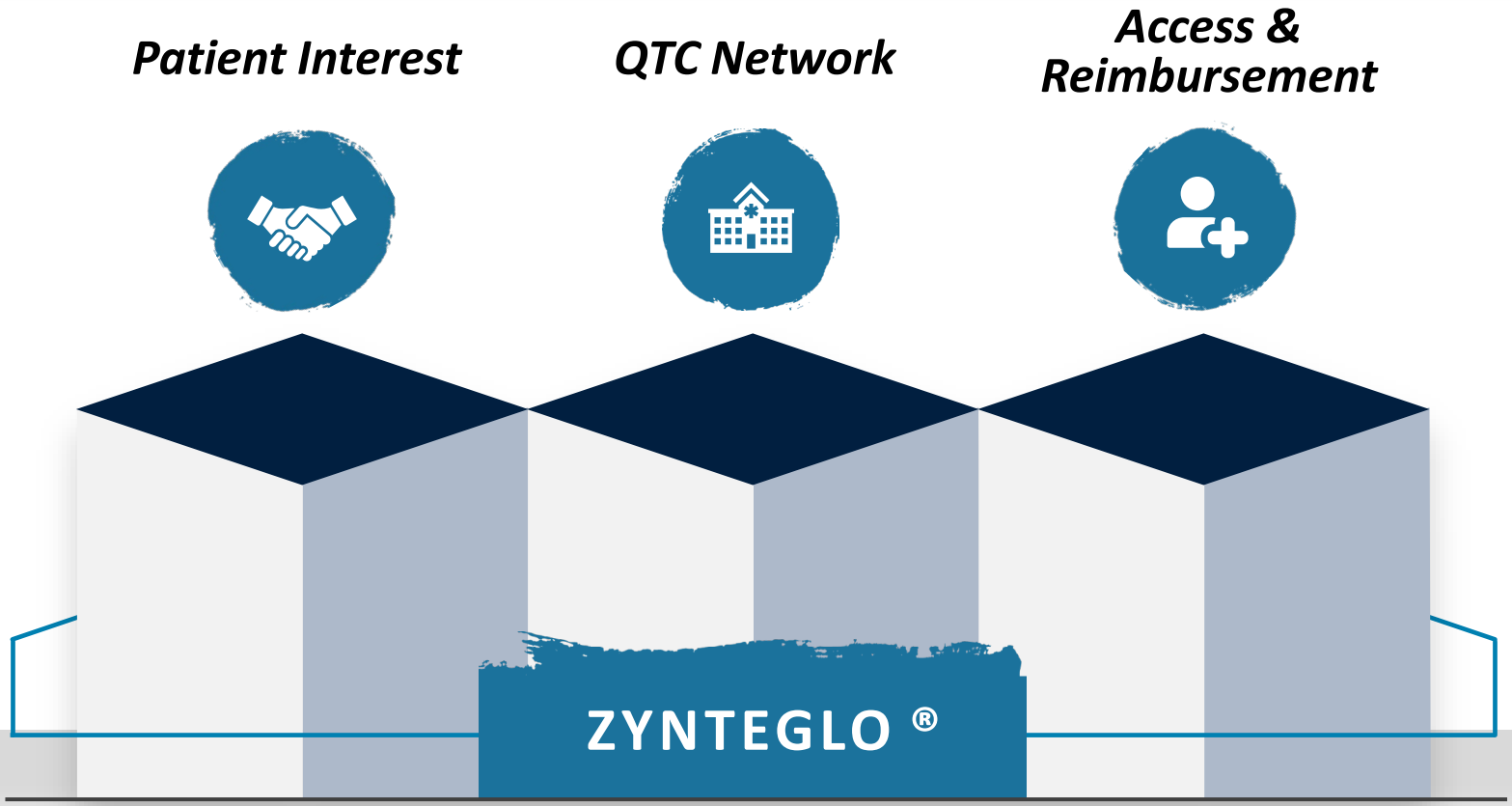
bluebirdbio®

Launching now

zynteglo®
(betibeglogene autotemcel)
suspension for IV infusion

ZYNTEGLO commercial launch off to a strong start

Launch built on three key pillars



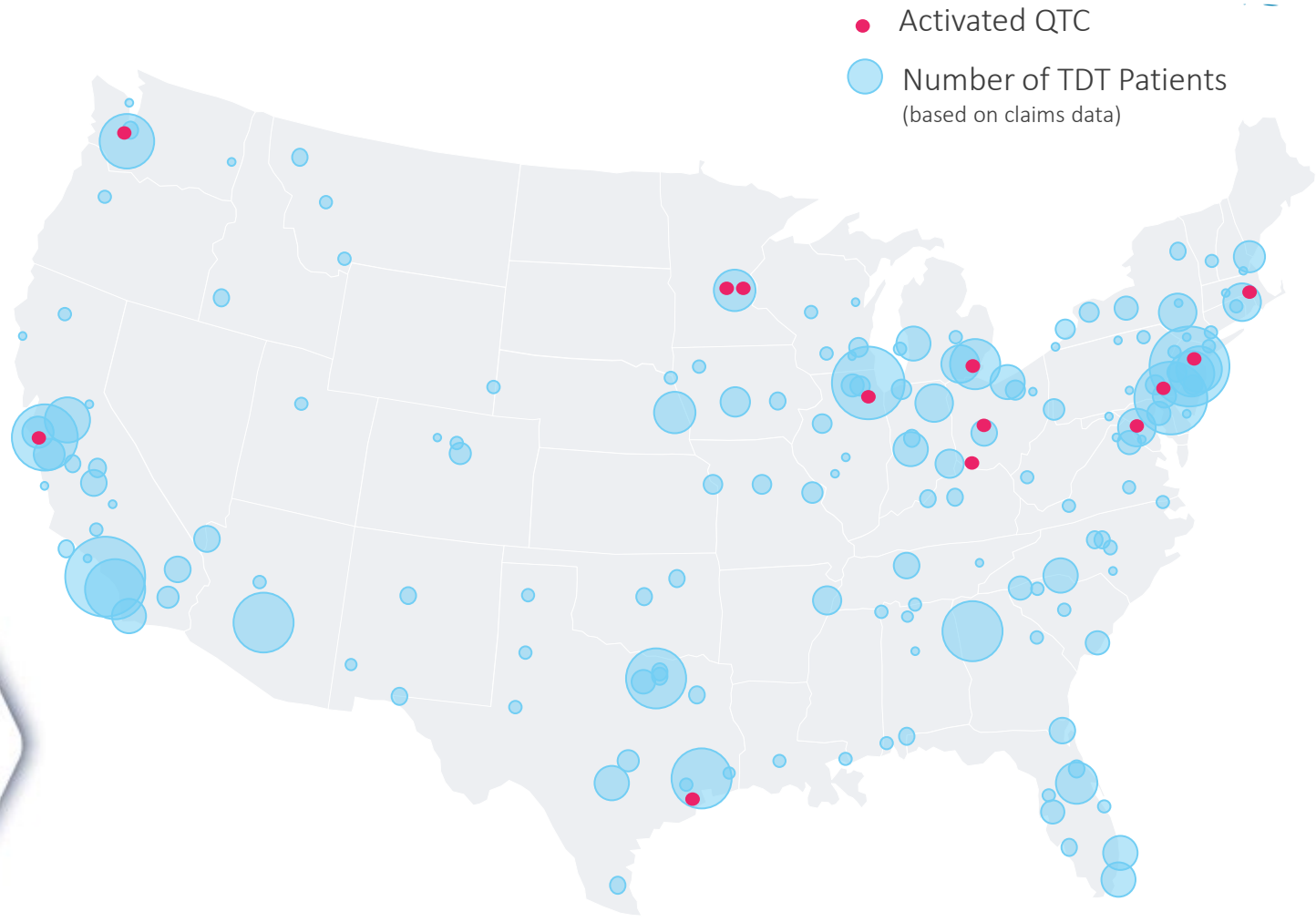
Fit-for-purpose Qualified Treatment Center (QTC) network being activated in waves

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

- QTCs in on-boarding or MSA negotiation stage
- Anticipated expansion to ~40-50 QTCs by YE 2023 to maximize opportunity for ZYNTEGLO and in anticipation of lovo-cel launch



*Graphic is illustrative and subject to change as final QTC network is determined; Activated QTC defined as Qualified Treatment Center with a signed MSA; Activated QTCs as of May 8, 2023

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:

- Estimated 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

Early indications show value of ZYNTEGLO is recognized

Patients are achieving access

>190M

lives covered by a favorable coverage policy

2 weeks

on average for prior authorization approvals for drug product

ZERO

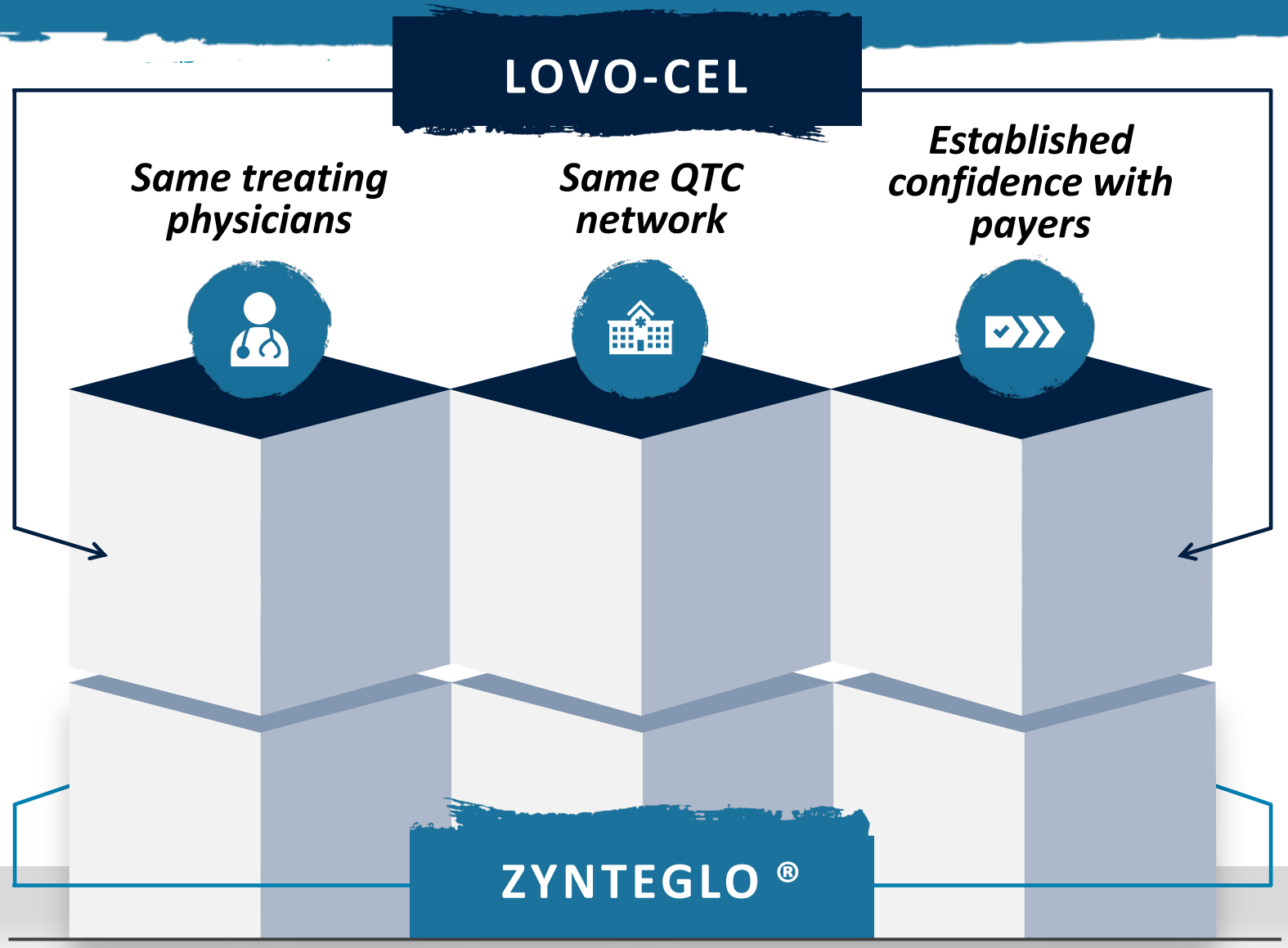
ultimate denials to date

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

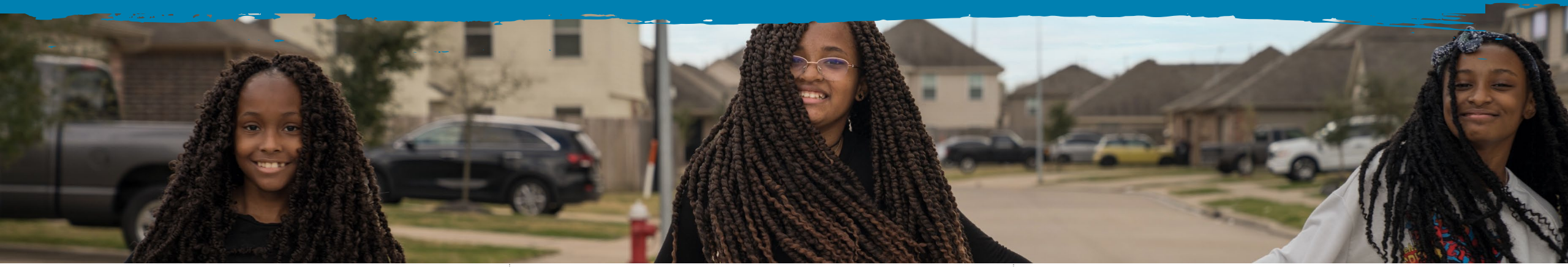
Bulk of time spent on release testing to deliver high quality drug product

QTC: Qualified Treatment Center; CMO: Contract Manufacturing Organization

ZYNTEGLO expected to enable seamless transition to commercializing lovo-cel for sickle cell disease



Opportunity to address a critical unmet need for >20,000 individuals living with severe sickle cell disease 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

- VOEs are the hallmark of SCD, but the disease is more than just pain
- 1 in 4 patients have a stroke by age 45[3]
- Widespread risk of organ damage or organ failure[3]
- 75% report difficulty completing daily tasks[4]

MEANINGFUL OPPORTUNITY

- Patients average $4.0 million in direct medical costs, despite a median age of death of only 45[5]
- Approximately 65% report giving up a job due to SCD[4]
- Estimates of foregone income over a lifetime up to $1.3 million[6]
- Nearly 1/3 report experiencing discrimination in a healthcare setting[7]

[1] CDC [2] Data on file[3] Mortality Rates and Age at Death from Sickle Cell Disease: U.S., 1979–2005 [3] Kato GJ, Piel FB, Reid CD, et al. Sickle cell disease. Nat Rev Dis Primers. 2018;4:18010. [4] Holdford et al 2021 [5] Gallagher ME et al, J Med Econ. 2022 Jan-Dec [6] Graf 2022 [7] Harvard Chan, RWJF Poll 2017

lovo-cel BLA submitted in April 2023

Most robust and longest follow up of any gene therapy program for SCD

BLA includes:

- ✓HGB-206 Group C as primary basis of effectiveness 36 patients with a median 32 months of follow-up and 2 patients in the HGB-210 study with 18 months of follow-up
- ✓Pivotal study HGB-206; largest gene therapy study in SCD to date with clinically meaningful primary endpoint
- ✓Safety data from 50 patients treated across the entire lovo-cel program with six patients with ≥ six years of follow-up

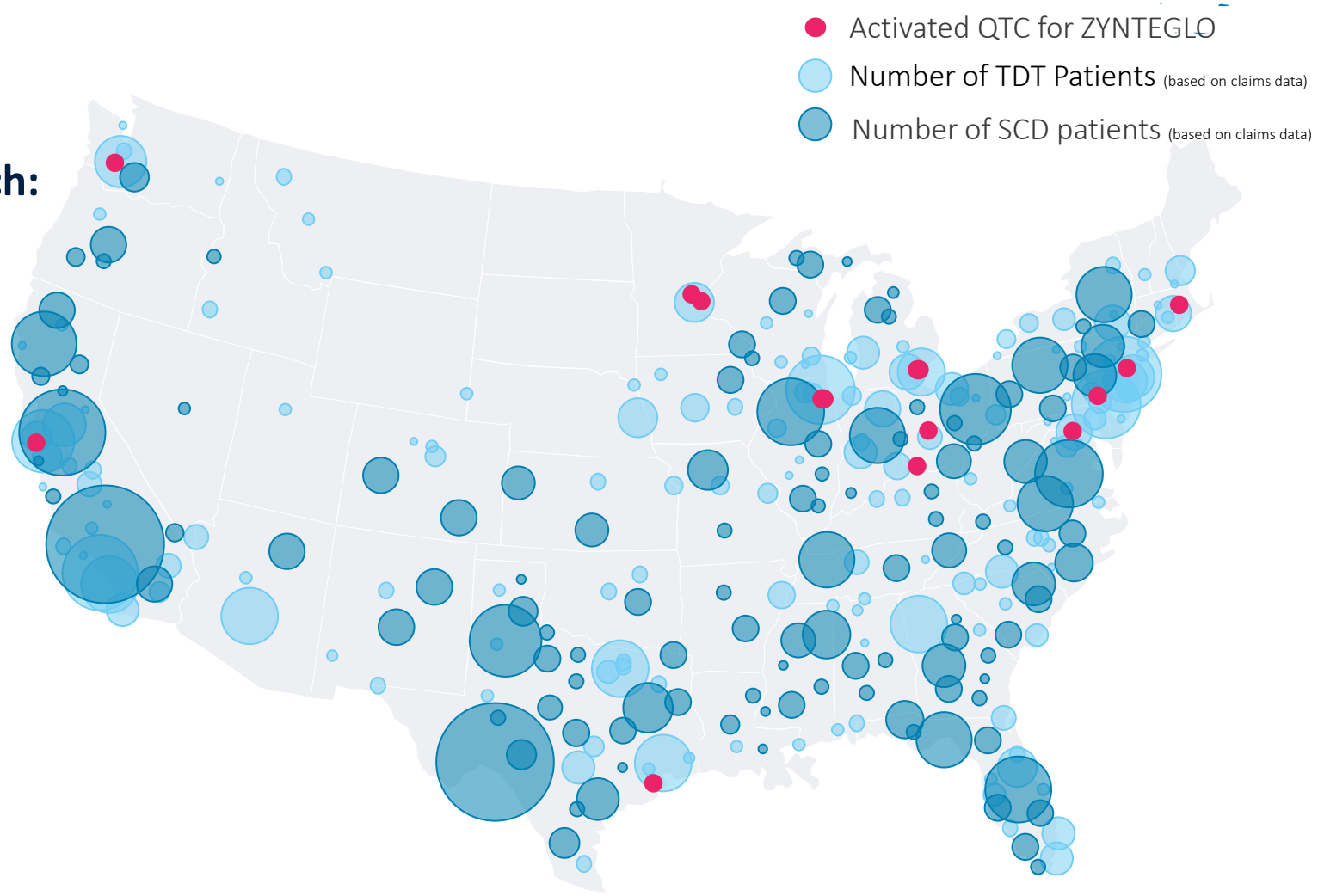
Anticipate BLA acceptance in Q2 2023

BLA: Biologics License Application

Planned 2023 network expansion ensures QTCs are in place and ready to treat appropriate SCD patients upon FDA approval of lovo-cel

Significant synergies in QTC network at launch:

- Expansion to ~40-50 QTCs by YE 2023 maximizes opportunity to rapidly reach patients
- Established contract allows for simplified activation process
- Estimated 65% of SCD patients within 50 miles of a planned QTC; (95% within 200 miles); anticipate continued expansion in 2024



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SKYSONA®

bluebirdbio®

Launching now

skysona™
(elivaldogene autotemcel)

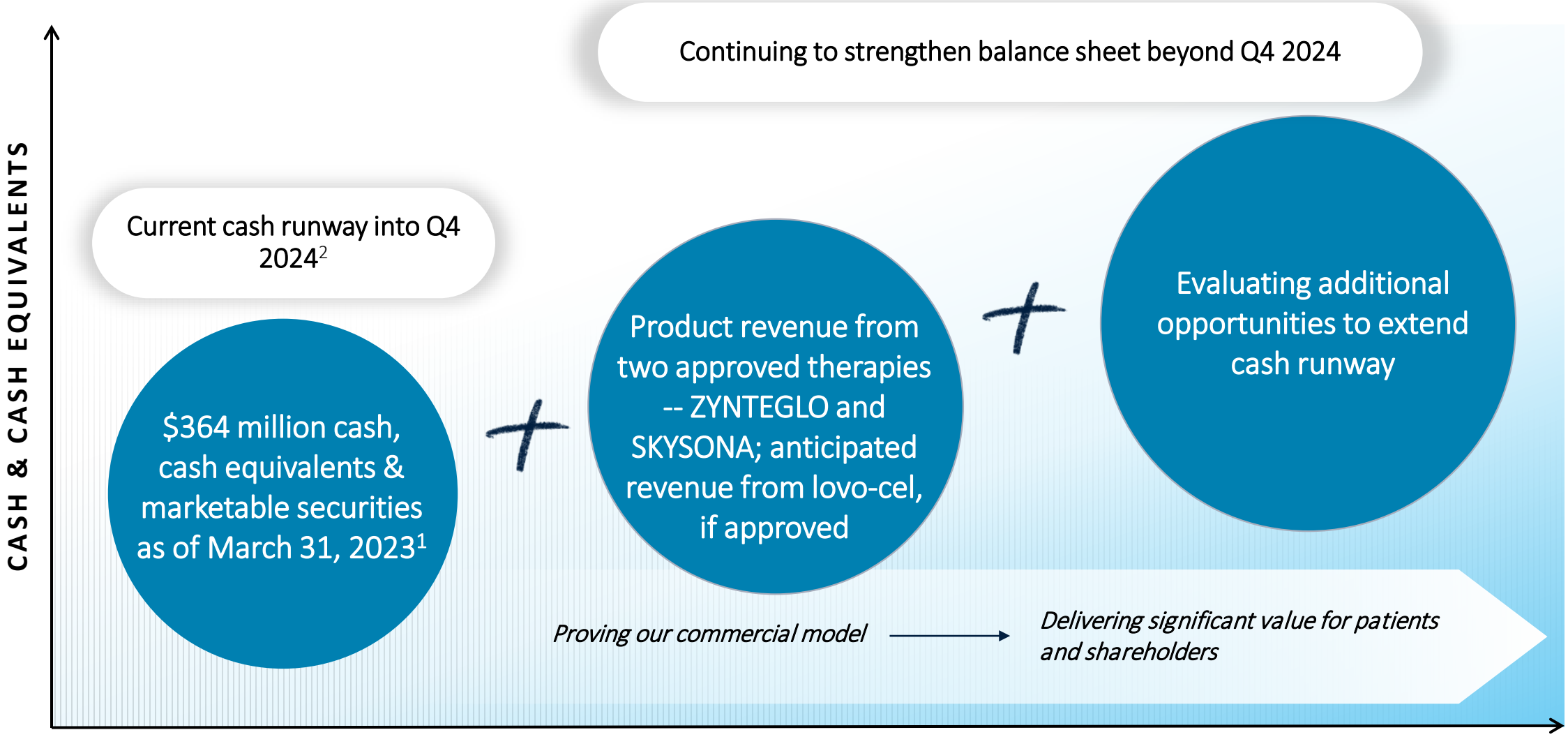
- First commercial infusion has been completed; in total cell collection completed for three patients for SKYSONA
- Three activated QTCs
- Zero ultimate denials to date; payers recognize value and urgency to treat
- Anticipate 5-10 patient starts in 2023

Early, active cerebral adrenoleukodystrophy refers to asymptomatic or mildly symptomatic (neurologic function score, NFS ≤ 1) boys who have gadolinium enhancement on brain magnetic resonance imaging (MRI) and Loes scores of 0.5-9. SKYSONA was granted accelerated approval based on 24-month Major Functional Disability (MFD)-free survival observed in clinical studies. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).*Real patients pictured, but they have not used our therapies. QTC: Qualified Treatment Center

Closing

bluebirdbio®

Strong financial position – cash burn and runway horizon



1. Contains $45m in restricted cash.; 2. Cash Runway is calculated using the current cash balance / net burn rate (cash from revenue less cash paid for expenses)

Upcoming milestones

First to market gene therapy for inherited hemoglobin disorders in the U.S.

SKYSONA® for cerebral adrenoleukodystrophy

- Anticipate 5-10 patient starts in 2023
- Continued launch expansion throughout 2023

ZYNTEGLO® for beta-thalassemia

- First commercial revenue expected in Q2 2023
- Continued launch expansion throughout 2023
- 40-50 QTCs by end of 2023

lovo-cel for sickle cell disease

- Anticipate BLA acceptance in Q2 2023
- Commercial launch expected early 2024

Proving our commercial model → *Significant value driver* →

bluebird bio: Setting the standard and proving the gene therapy commercial model

Demonstrating gene therapy expertise across clinical, regulatory and commercial

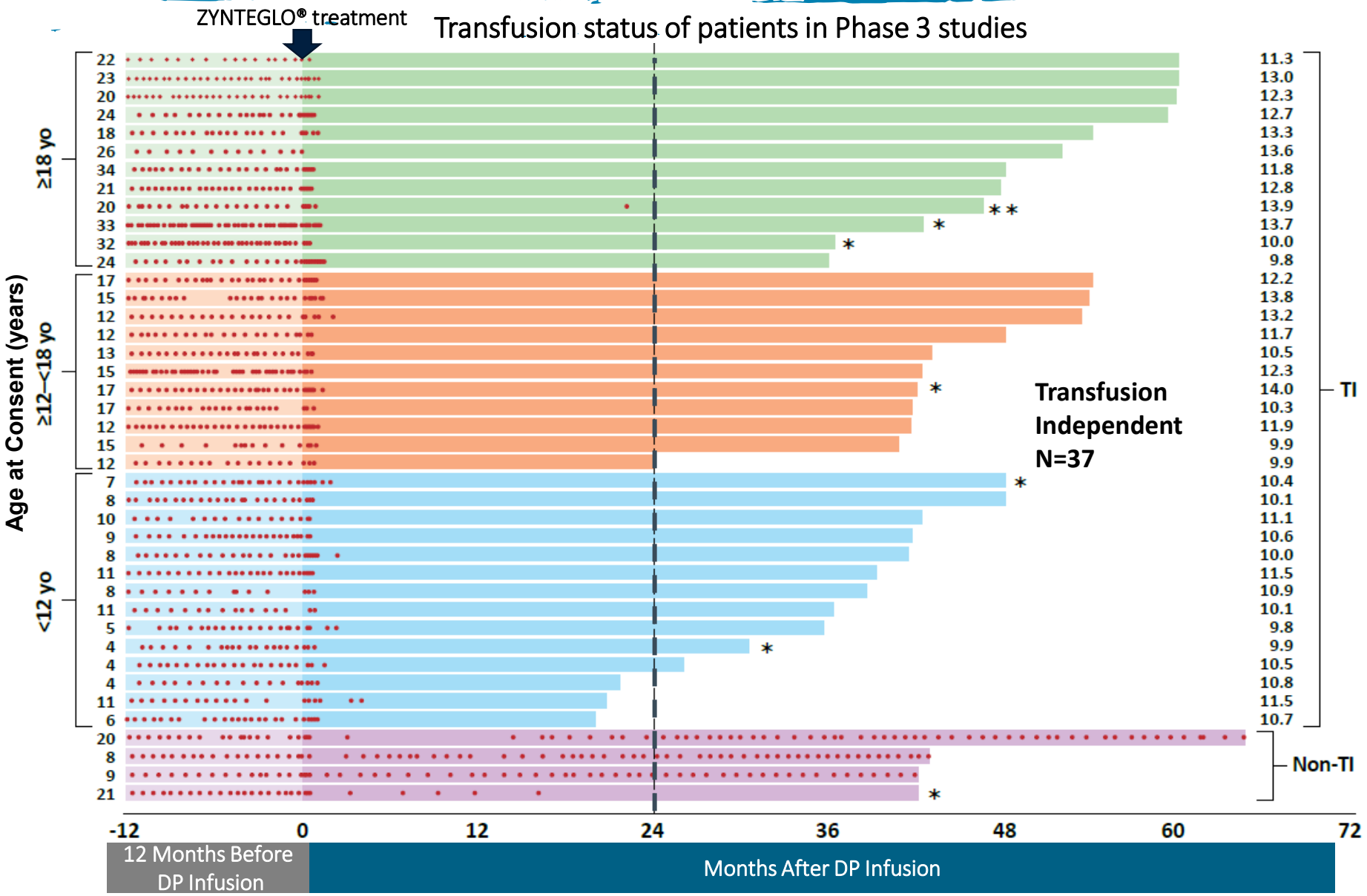
Momentum building with **near-term commercial launches**

Opportunity to deliver significant **value for patients and shareholders**

thank you


Q + A

ZYNTEGLO® approval is underscored by impressive clinical study data



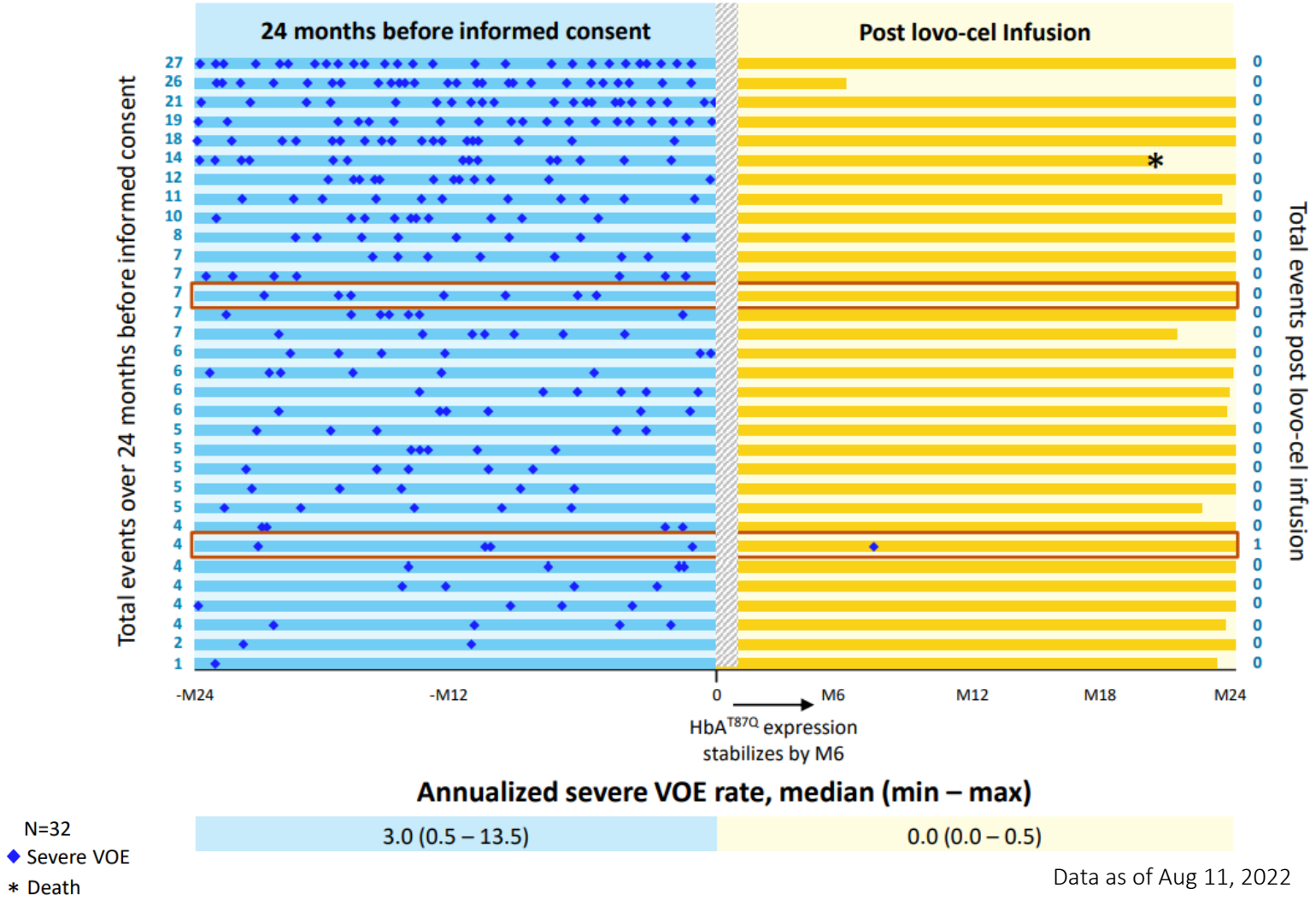
In Phase 3 studies presented at ASH 2022:

- 90% of patients achieved transfusion independence (TI) and normal or near-normal hemoglobin levels
- All patients who achieved TI remained transfusion free as of last follow-up
- Durable results with longest follow-up out to 5 years
- Results were consistent across ages and genotypes
- Majority of AEs and SAEs were consistent with myeloablative conditioning

**After a planned orthopedic surgery, the patient had blood loss, which required 1 packed red blood cell transfusion

Data as of July 2022

lovo-cel: most advanced sickle cell disease gene therapy development program in the industry



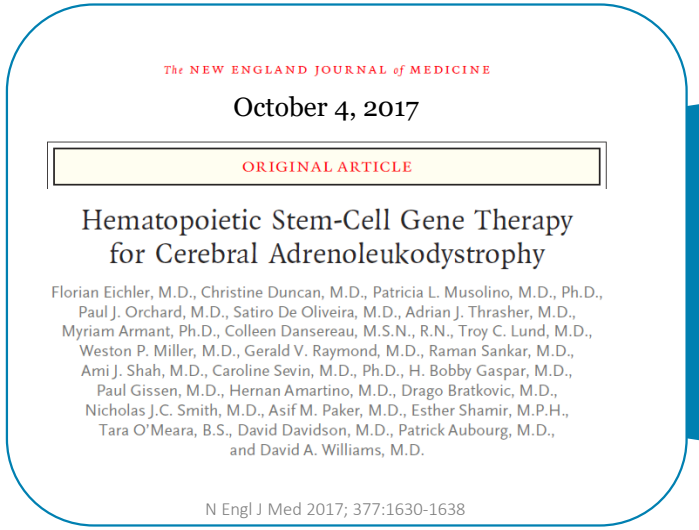
Data as of Aug 11, 2022

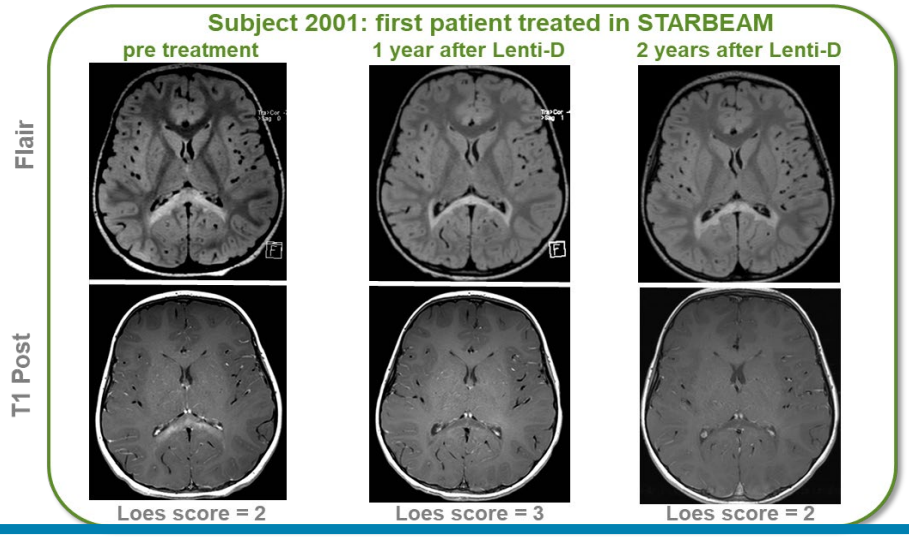
Update on Pivotal Cohort (HGB 206 Group C) Presented at ASH 2022

- **96%** experienced complete resolution of severe VOEs through 24 months of follow-up (ASH 2022)
- As of August 2022, 50 patients had been treated with lovo-cel, with up to **7 years** of follow-up (median: 37.7 months)*
- **Safety data remained consistent** with the known side effects of autologous hematopoietic stem cell collection, myeloablative single-agent busulfan conditioning and underlying SCD
- As previously reported, patient with significant baseline SCD-related cardiopulmonary disease died >18 months post-infusion (considered unlikely to be related to lovo-cel).
- Updated data cut, including long-term follow-up submitted in BLA package

*50 patients treated includes patients from HGB-205, HGB-206 Group A, Group B and Group C and HGB-210

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





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 were 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

Other risks include serious infections, prolonged cytopenias, delayed platelet engraftment, risk of neutrophil engraftment failure, and hypersensitivity reactions.

Under accelerated approval, bluebird has agreed to provide confirmatory data to the FDA

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