bluebird bio J.P. Morgan Presentation

January 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 manufacturing and commercialization plans, and addressable market for approved products or product candidates, the timing of our first revenue, our preliminary unaudited cash position as of December 31, 2022, and our cash runway 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

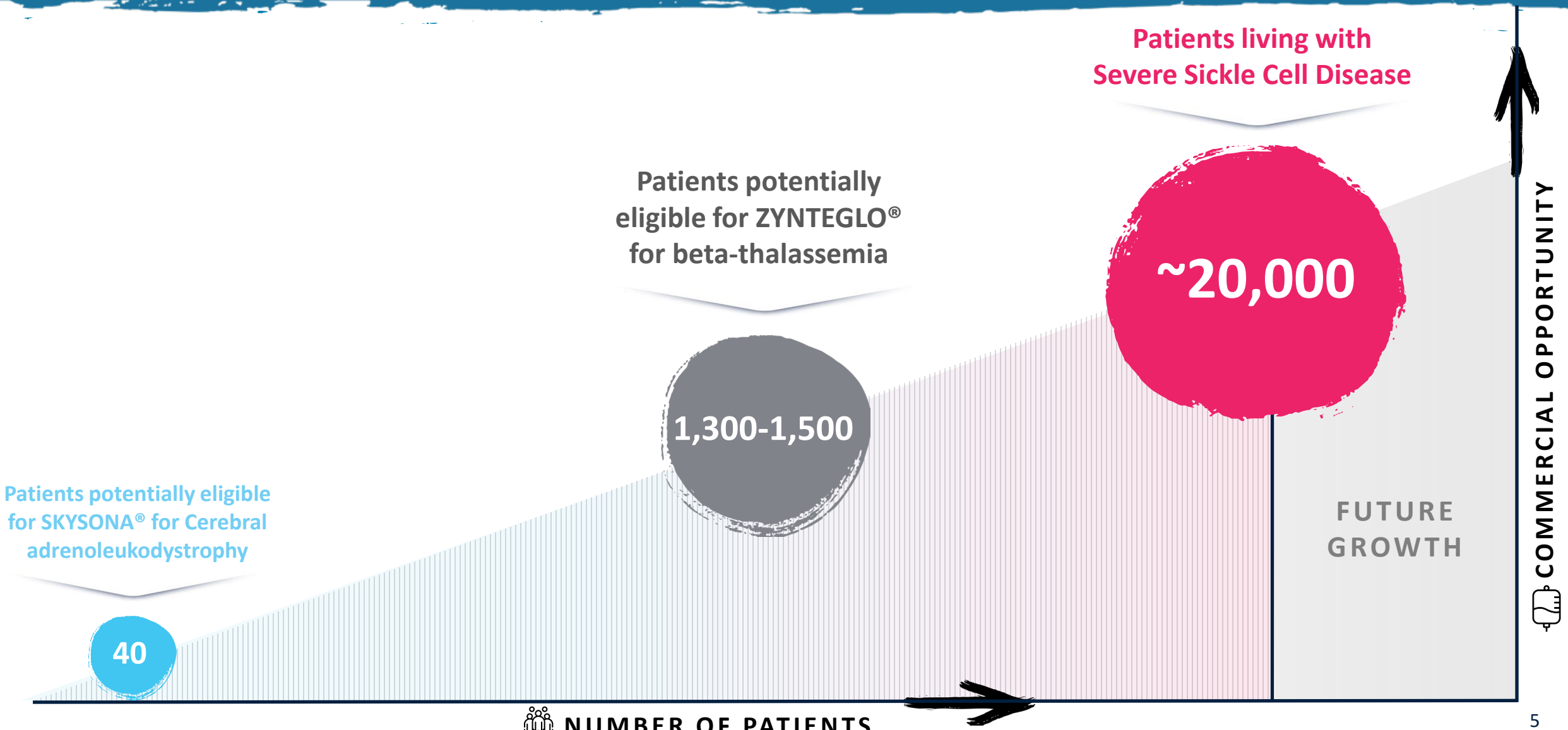
Commercial Impact

2 ongoing US launches,
revenue expected in Q1 2023, 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

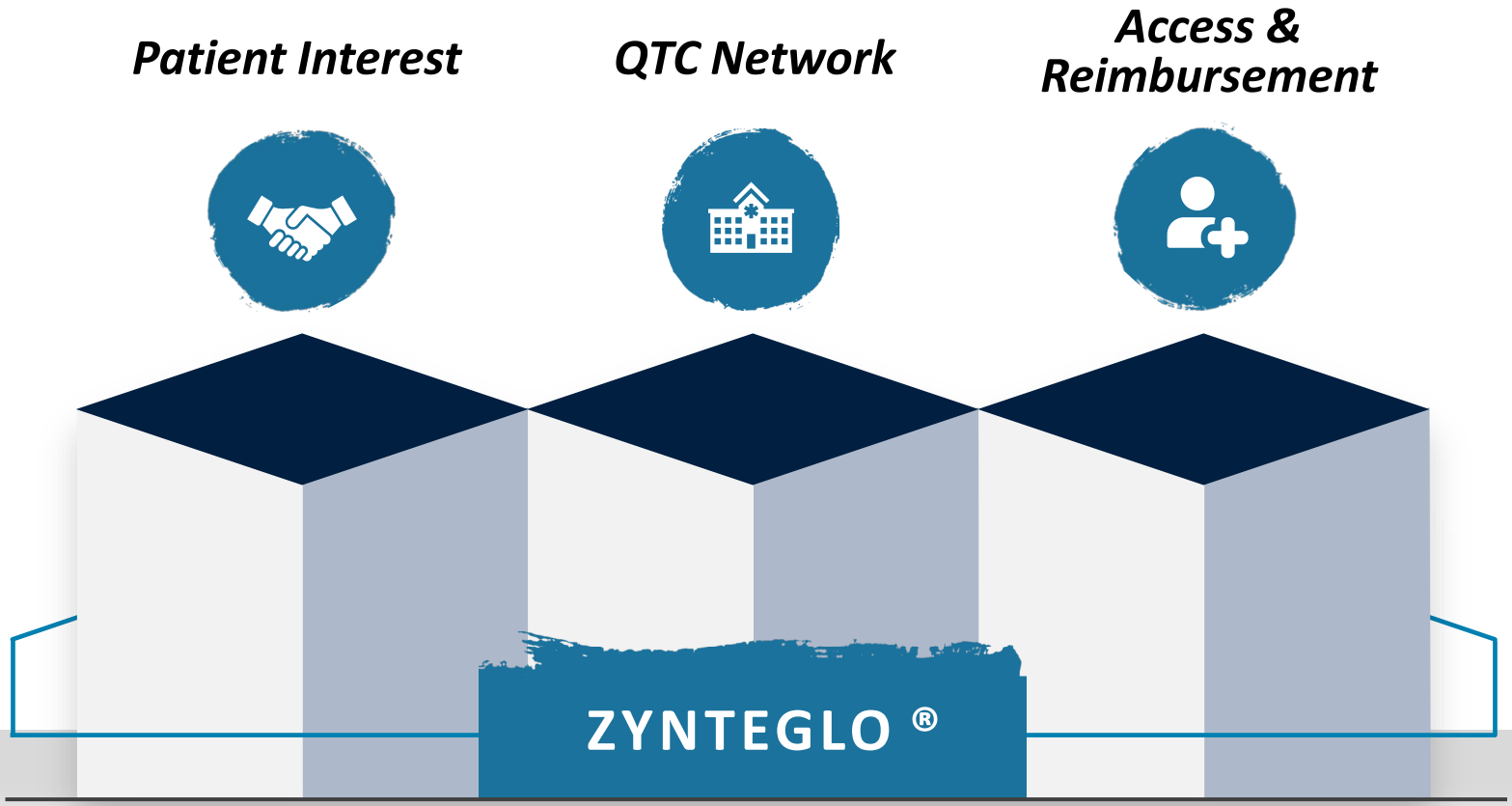
bluebirdbio®

Launching now

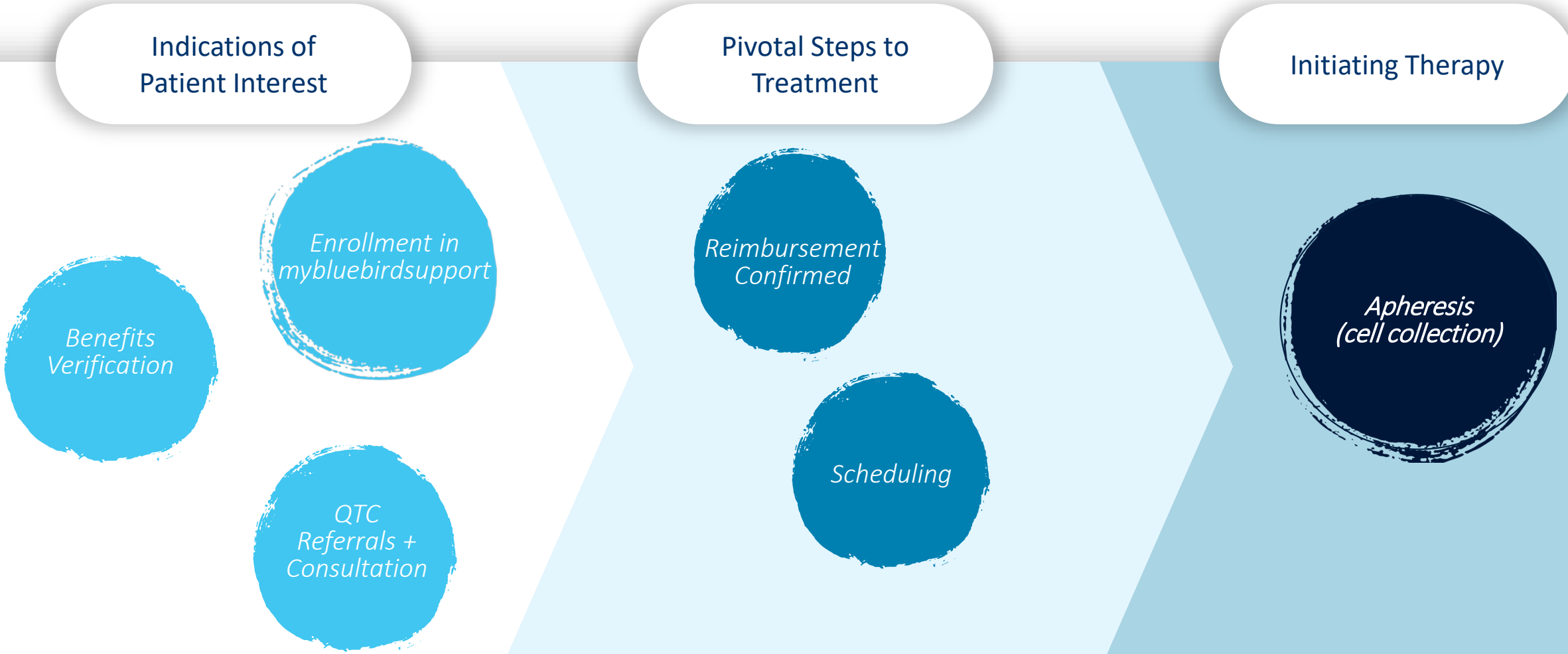
zynteglo®
(betibeglogene autotemcel)
suspension for IV infusion

ZYNTEGLO commercial launch off to a strong start

Launch built on three key pillars



Path to treatment is multi-faceted



Clear signs of early patient uptake approximately four months into launch

Indications of Patient Interest

~40

*Patients initiated benefits verification**

Pivotal Steps to Treatment

2 WEEKS

*Average time to prior authorization approval***

Q1 2023

Multiple cell collections scheduled

Initiating Therapy

1ST

Apheresis Completed

*Estimate based on mybluebirdsupport data and metrics provided by QTCs
**Estimate based on QTC reports

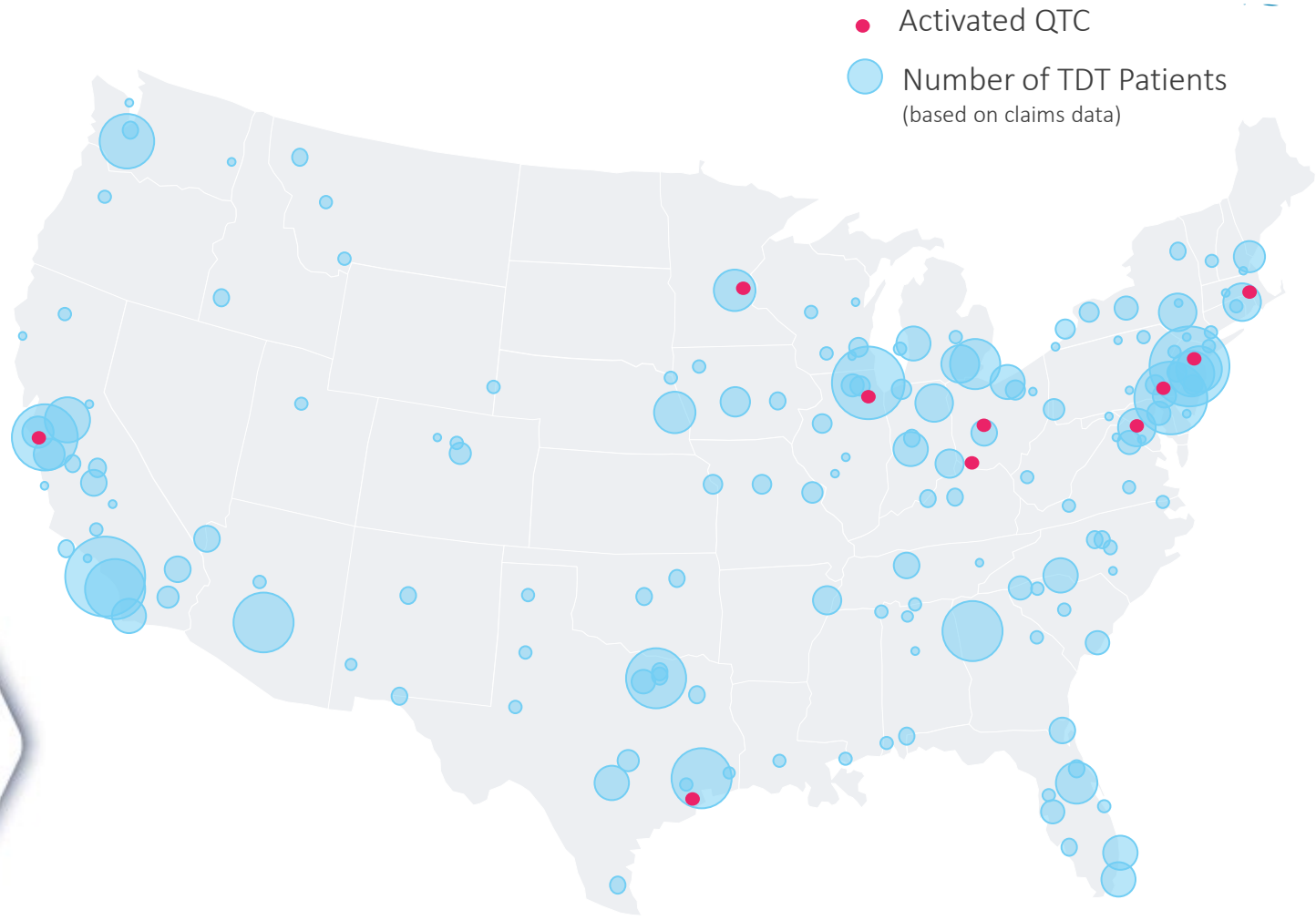
Fit-for-purpose Qualified Treatment Center (QTC) network being activated in waves

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

- 10 QTCs activated
- >15 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

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

~4 months since FDA approval:

~190M

lives covered by a favorable coverage policy

THREE

of the largest PBMs have signed outcomes-based agreements

ZERO

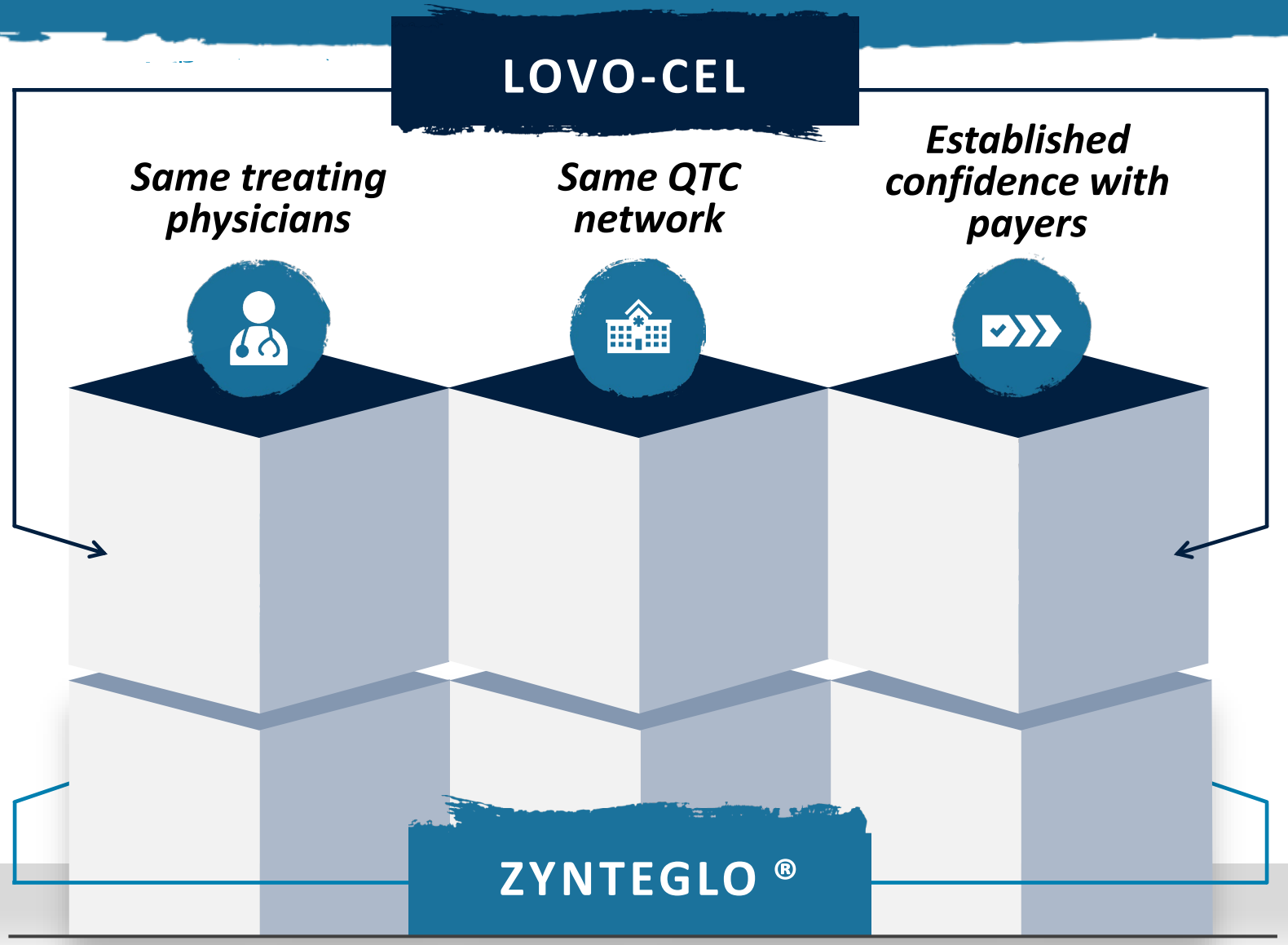
ultimate denials

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

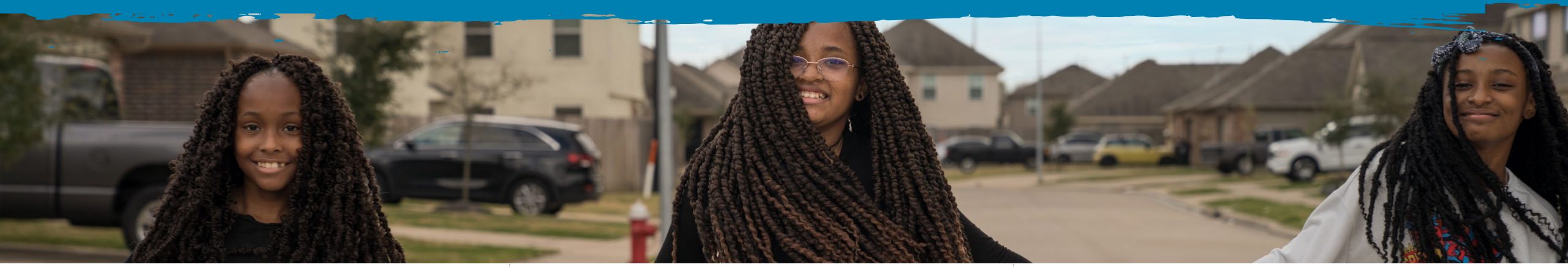
Bulk of time spent on release testing to deliver high quality drug product

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]

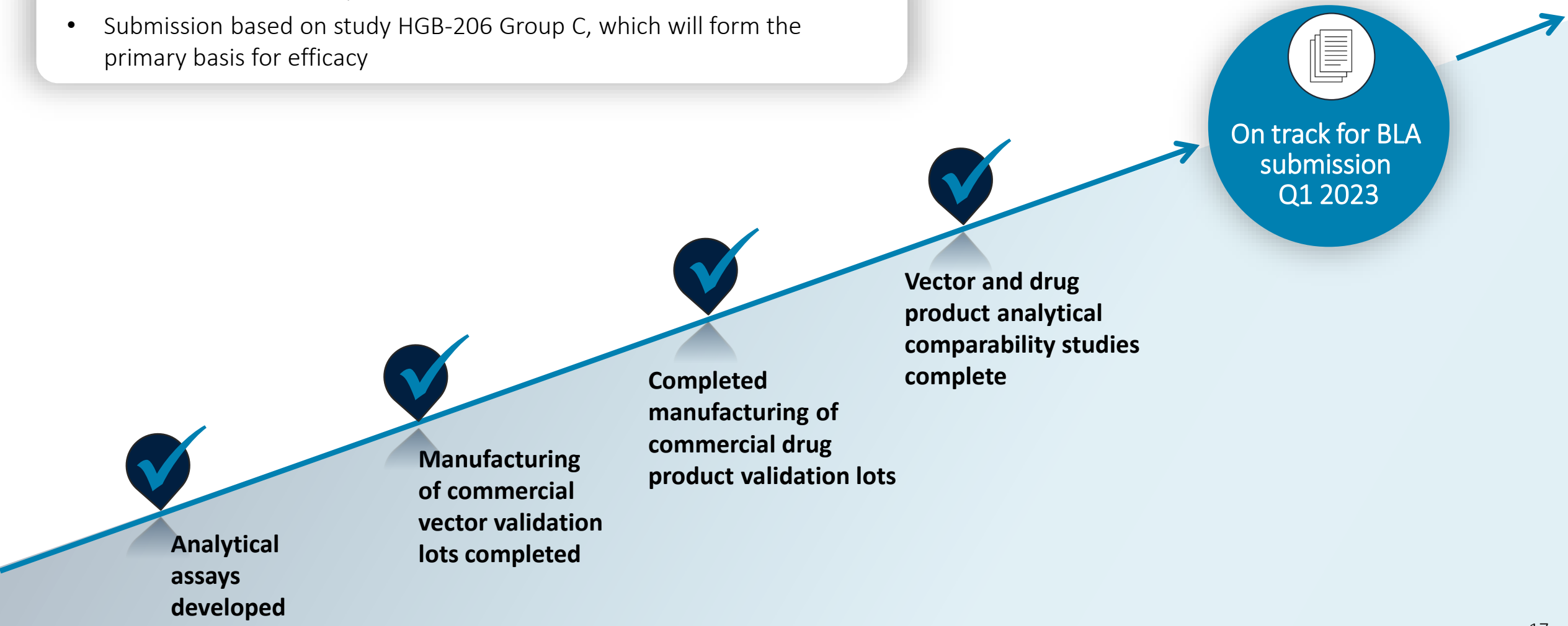
MEANINGFUL OPPORTUNITY

- 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 submission on track for Q1 2023; comparability studies complete

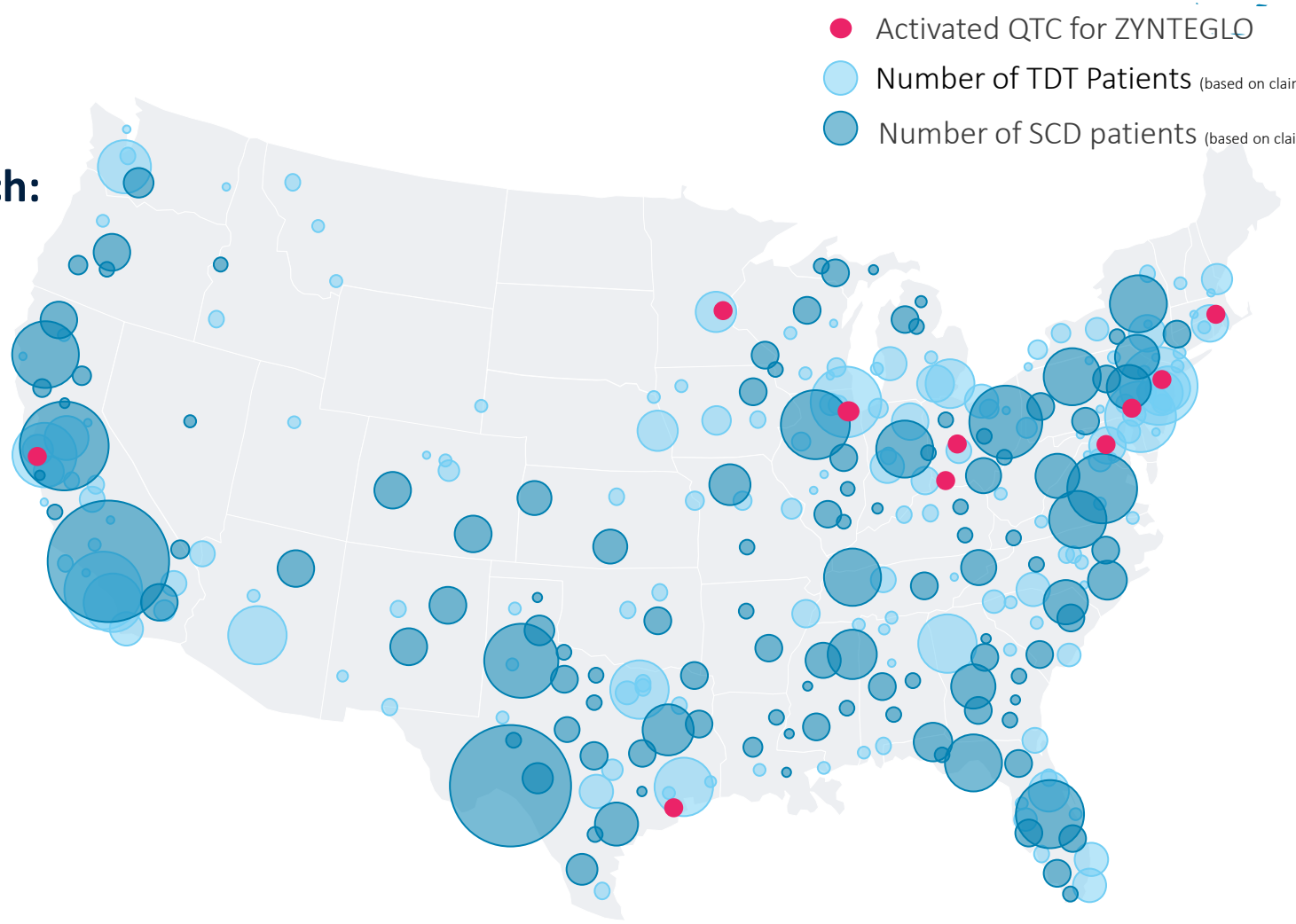
- Plan to submit BLA for patients 12 and older
- Submission based on study HGB-206 Group C, which will form the primary basis for efficacy



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



*Graphic is illustrative and subject to change as final QTC network is determined; Activated QTC defined as Qualified Treatment Center with a signed MSA

SKYSONA

bluebirdbio®

SKYSONA®: FDA Approved

skysona™
(elivaldogene autotemcel)

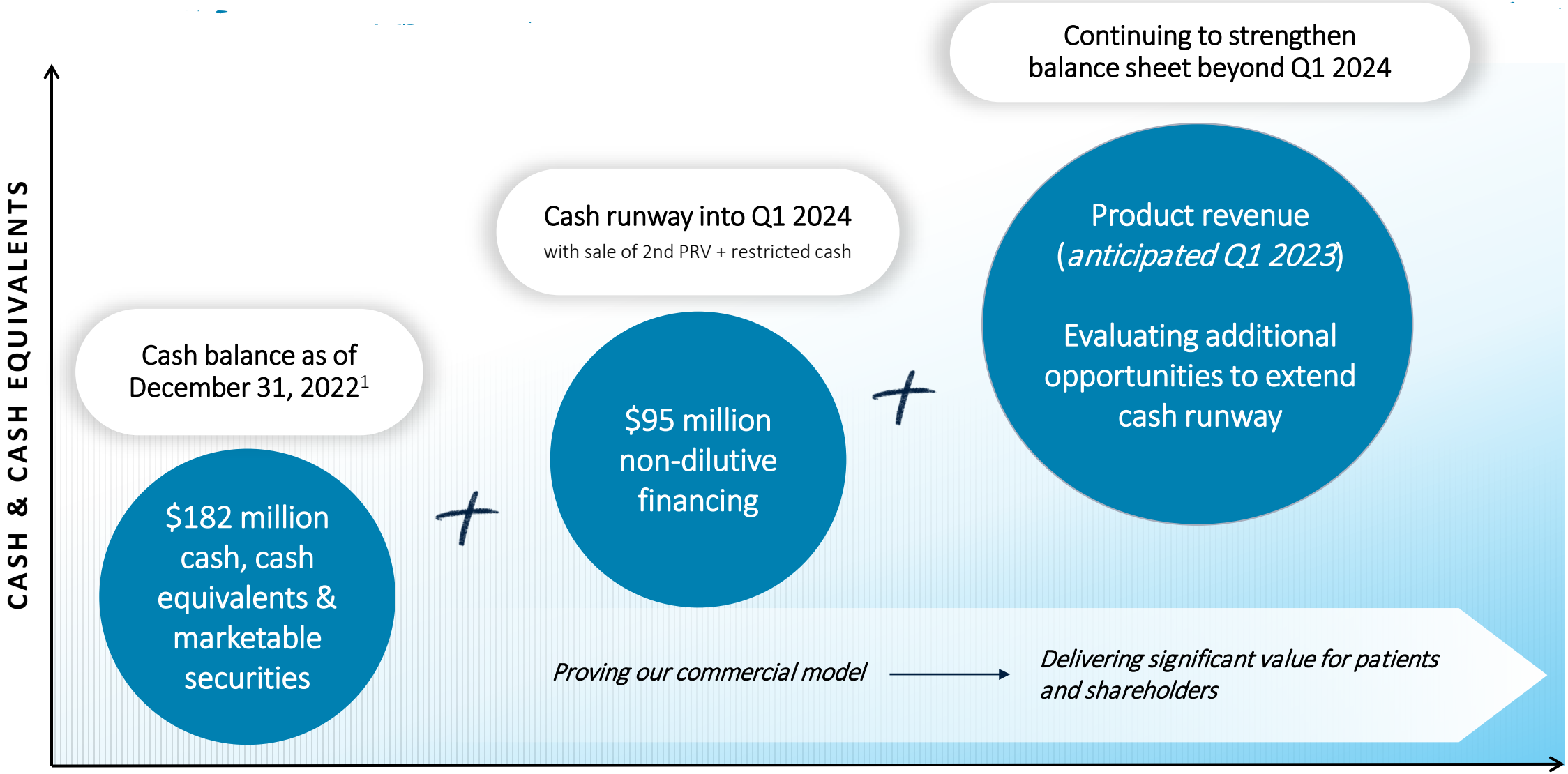
- First apheresis scheduled for January 2023
- Two activated QTCs; three additional planned
- Zero ultimate denials; payers recognize value and urgency to treat
- Anticipate 5-10 patient starts in 2023

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. Excludes $45m in restricted cash. The cash, cash equivalents and marketable securities information above is based on preliminary unaudited information and management estimates for the year ended December 31, 2022, is not a comprehensive statement of the Company's financial results as of and for the fiscal year ended December 31, 2022 and is subject to completion of the Company's financial closing procedures. The Company's independent registered public accounting firm has not conducted an audit or review of and does not express an opinion or any other form of assurance with respect to, this preliminary estimate.; 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

- First cell collection scheduled for January 2023
- Continued launch expansion throughout 2023

ZYNTEGLO® for beta-thalassemia

- First commercial revenue expected in Q1 2023
- Continued launch expansion throughout 2023
- 40-50 QTCs by end of 2023

lovo-cel for sickle cell disease

- BLA submission planned for Q1 2023
- Potential FDA approval expected by end of 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

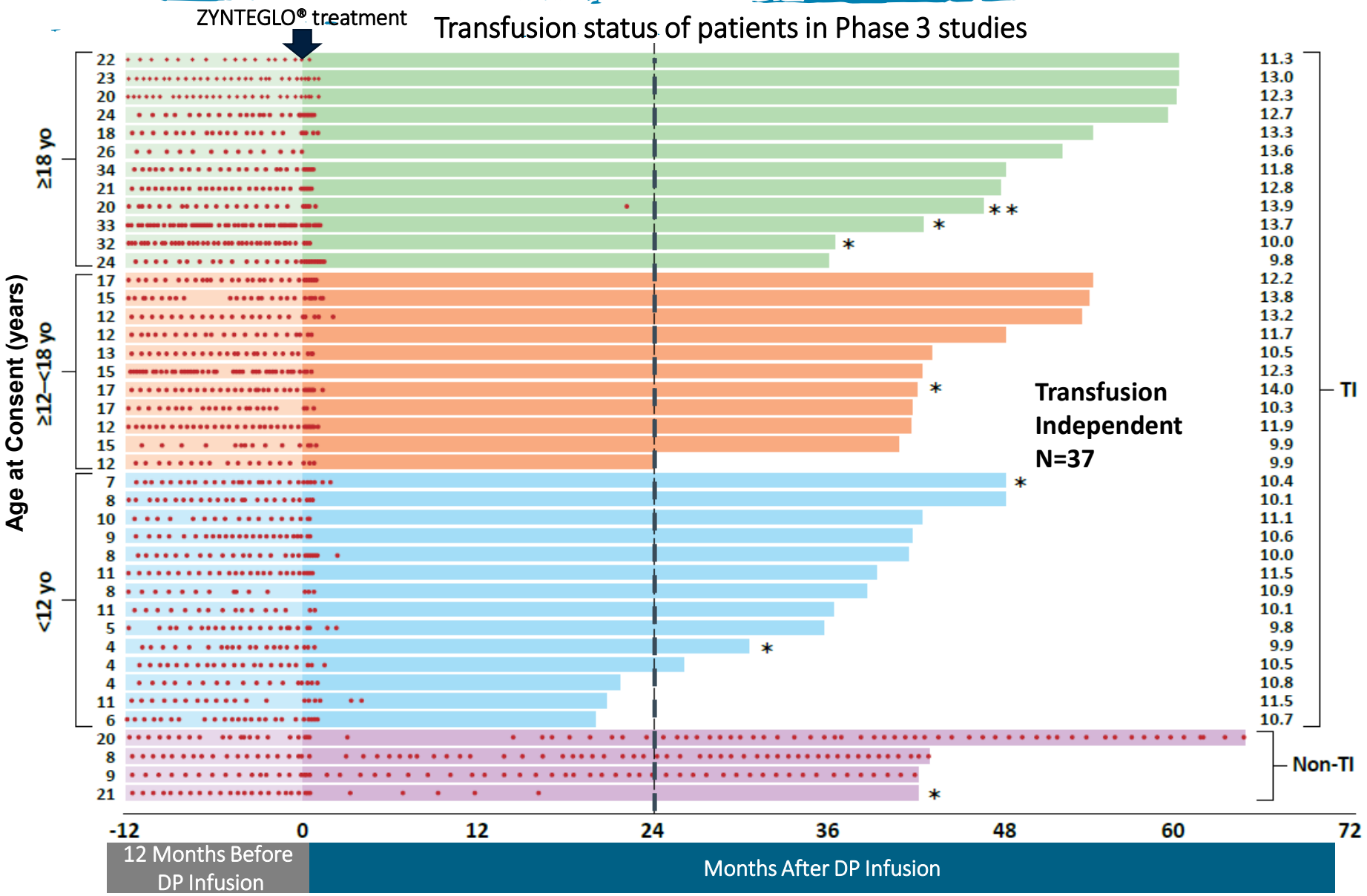
Demonstrating gene therapy expertise across clinical, regulatory and commercial

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

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

thank you

ZYNTEGLO® approval is underscored by impressive clinical study data



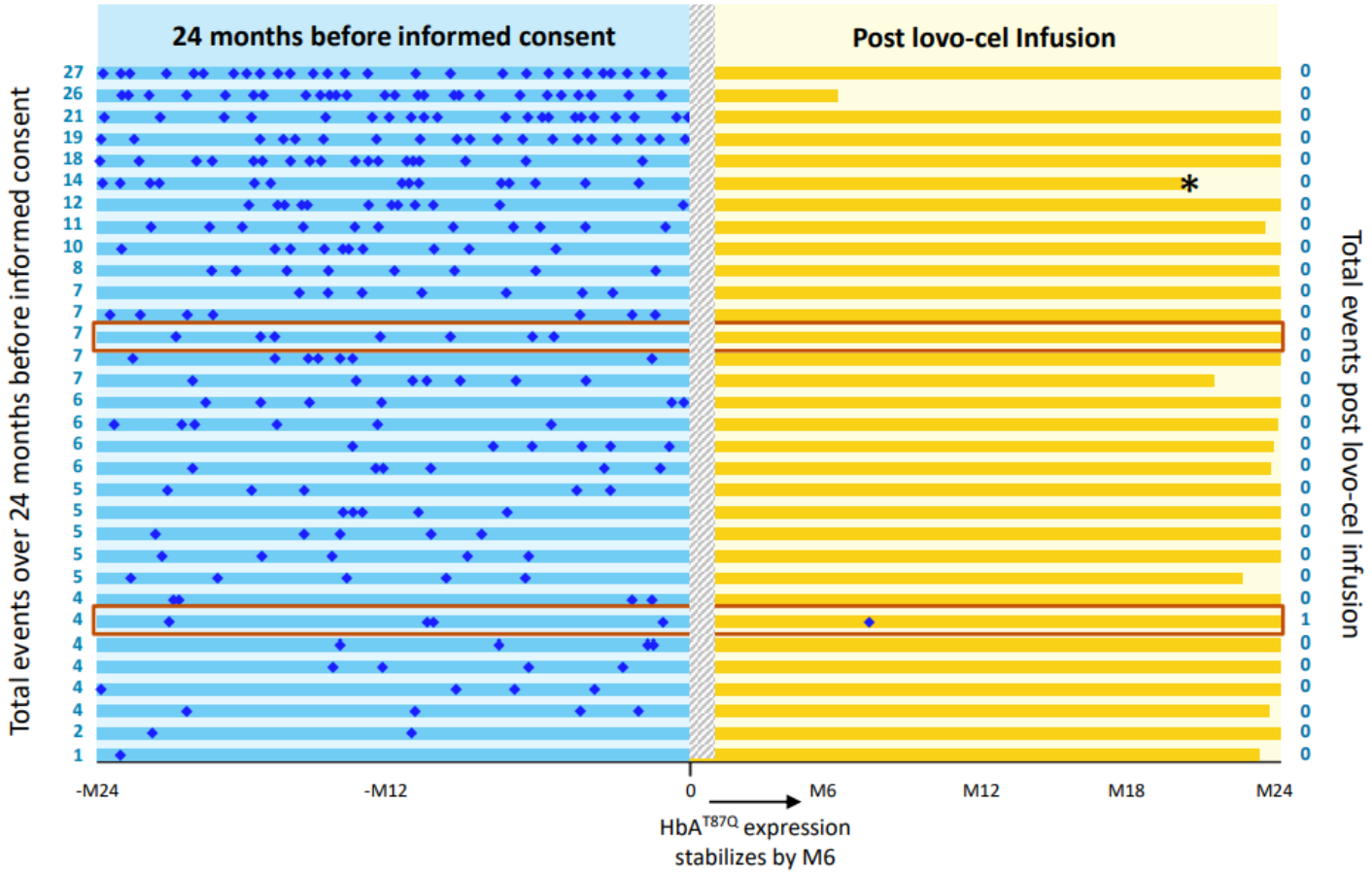
In Phase 3 studies presented at ASH 2022:

- 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

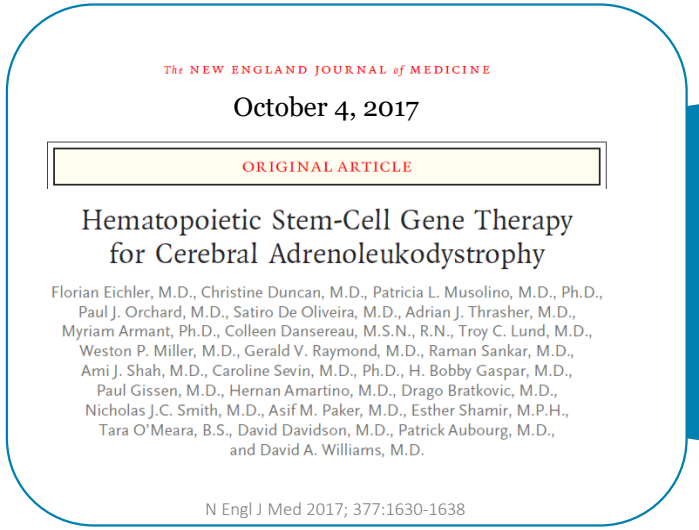


Update on Pivotal Cohort (HGB 206 Group C) Presented at ASH 2022

- **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, being prepared for BLA submission anticipated in **Q1 2023**

Data as of Aug 11, 2022

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

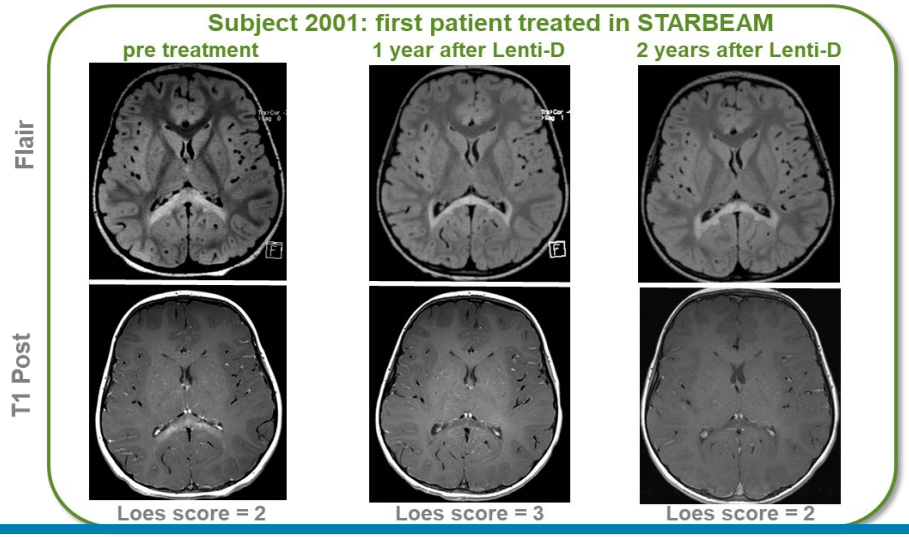
October 4, 2017

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 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

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). MDS: myelodysplastic syndrome