LYFGENIA™ FDA approval

December 8, 2023

forward-looking statements

These slides and the accompanying oral presentation contain certain statements that are forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, and that involve risks and uncertainties, including, without limitation, statements regarding the Company's plans and expectations for operations, including with respect to the commercial launch of LYFGENIA and the potentially addressable market for LYFEGNIA; closing of the sale of the Company's Priority Review Voucher; our expectations regarding innovative payment demonstration in 2023; and the anticipated growth of the Company's QTC network and timing thereof.

Statements using words such as "expect", "anticipate", "believe", "may", "will" and similar terms are also forward-looking statements. Such statements are subject to numerous risks and uncertainties, including but not limited to, delays and challenges in the Company's commercialization and manufacturing of its products; the internal and external costs required for ongoing and planned activities, and the resulting impact on expense and use of cash, has been, and may in the future be, higher than expected which has caused the Company, and may in the future cause it, to use cash more quickly than expected or change or curtail some of its plans or both; substantial doubt exists regarding the Company's ability to continue as a going concern; the Company's expectations as to expenses, cash usage and cash needs may prove not to be correct for other reasons such as changes in plans or actual events being different than its assumptions; the risk that the efficacy and safety results from the Company's prior and ongoing clinical trials will not continue or be seen in additional patients treated with its product candidates; the risk of insertional oncogenic or other reportable events associated with lentiviral vector, drug product, or myeloablation; the risk that any one or more of the Company's products or product candidates, including Skysona, Zynteglo or Lyfgenia, will not be successfully commercialized, and other risks as may be detailed from time to time in the Company's Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q and other reports filed with the Securities and Exchange Commission.

Except as required by law, the Company undertakes no obligations to make any revisions to the forward-looking statements contained in this presentation or to update them to reflect events or circumstances occurring after the date of this presentation, whether as a result of new information, future developments or otherwise.

agenda

Welcome and opening remarks

Andrew Obenshain, chief executive officer

Clinical data and label highlights

Rich Colvin, MD, PhD, chief medical officer

Commercial launch plans

Tom Klima, chief commercial and operating officer

Closing

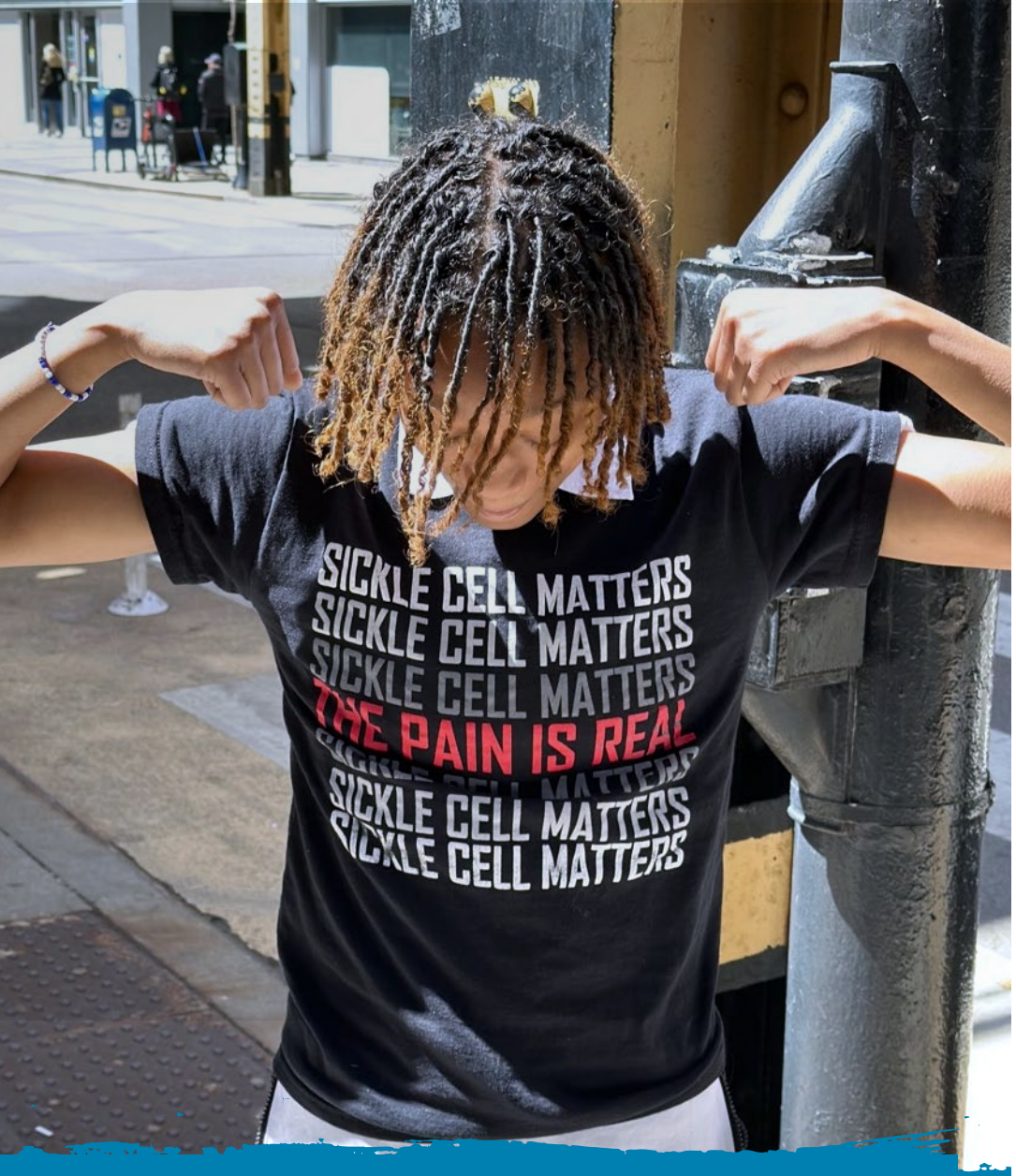
Andrew Obenshain, chief executive officer

Q&A

LYFGENIA: Now FDA Approved

LYFGENIA Clinical Data & Label Highlights

Rich Colvin, MD, PhD, *Chief Medical Officer*



50% to 60% of adults with SCD have end organ damage, with **24%** experiencing damage in multiple organs[1]

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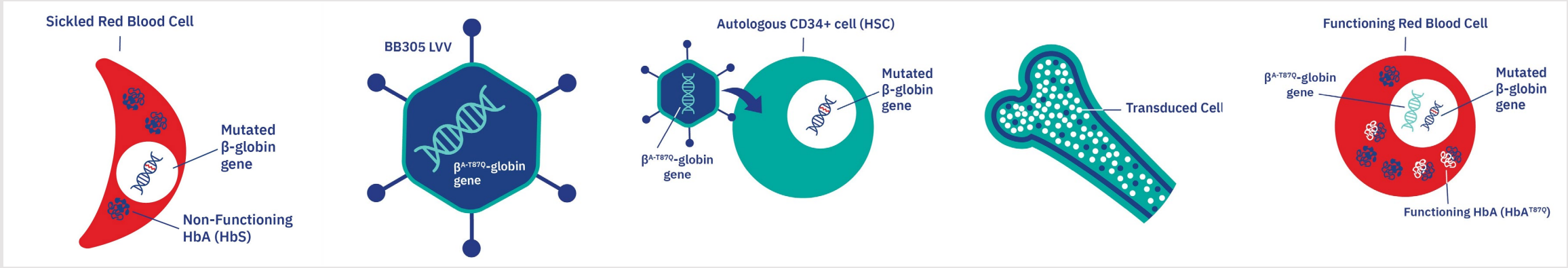
1 in 4 people with SCD have a stroke by **age 45**[2]

Patients average
$4-6M in direct medical costs, despite a median age of death of **only 45** years old[3]

~65% of individuals with SCD report giving up a job due to the disease[4]

1. Chaturvedi S, et al. Am J Hematol. 2018 3; 2. Kato GJ, Piel FB, Reid CD, et al. Sickle cell disease. Nat Rev Dis Primers. 2018;4:18010.
3. Gallagher ME et al, J Med Econ. 2022 Jan-Dec 4. Holdford et al 2021

LYFGENIA is a custom-designed gene therapy that is uniquely traceable



1

A single mutation in the beta-globin gene leads to the production of sickled hemoglobin (HbS) rather than adult hemoglobin (HbA)

2

BB305 LVV is a lentiviral vector that carries a β-globin gene (HbA^{T87Q} globin gene)

3

LYFGENIA is manufactured by transducing autologous CD34+ cells with BB305 LVV

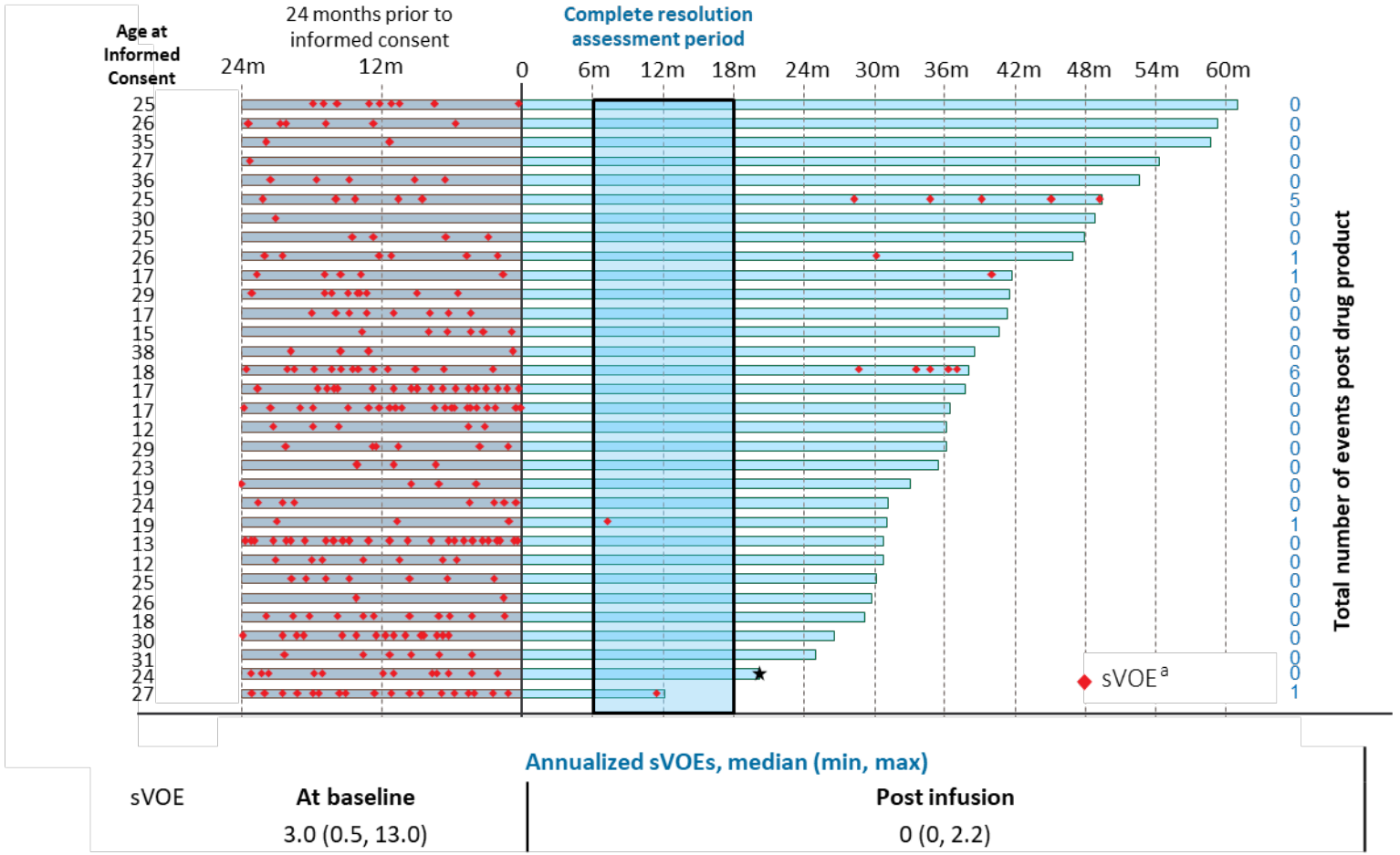
4

Following successful engraftment, red blood cells containing functioning HbA (HbA^{T87Q}) are produced

5

$\beta^{A\text{-}T87Q}$ –globin pairs with α-globin

LYFGENIA supported by the most robust and longest follow-up of any gene therapy program for SCD



★ Death, due to significant baseline SCD-related cardiopulmonary disease; not considered related to lovo-cel.

Data as of Feb 13, 2023

Clinical Data Supporting LYFGENIA

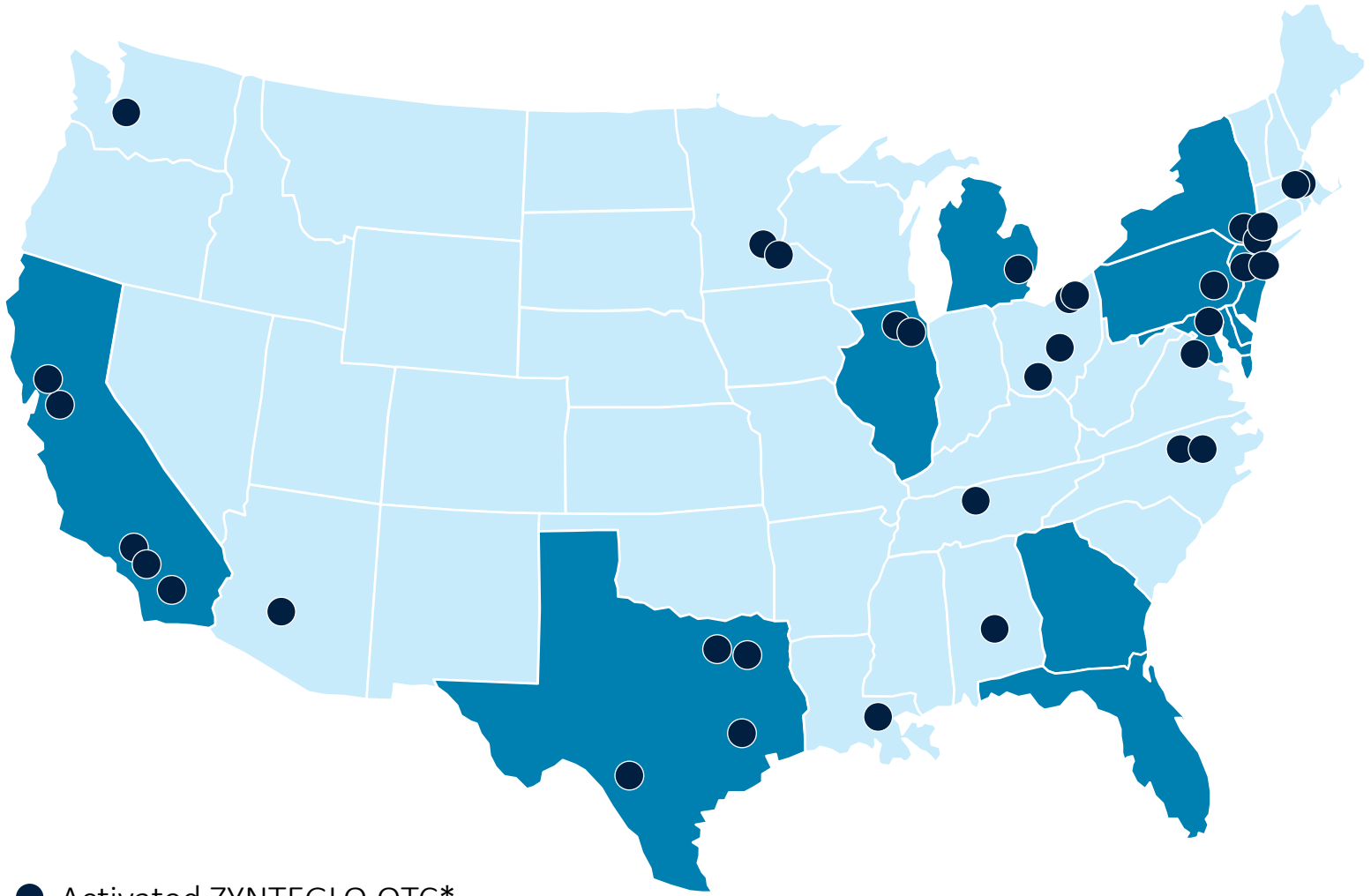
- Label based on efficacy data from 36 patients from HGB-206 Group C (median 38 months follow-up) and safety data from 54 patients*
- February 13, 2023 data cut showing:
  - 32 patients evaluable for VOE endpoints including 8 adolescent patients
  - 94% complete resolution of severe VOEs in the 6-18 months post infusion
  - 88% resolution of VOEs in the 6-18 months post infusion
  - Maintenance of VOE resolution in majority of patients through long-term follow up + stable production of HbA^{T87Q}
  - Majority of AEs attributed to underlying SCD or conditioning with busulfan
  - The label includes a Boxed Warning for hematologic malignancy

*54 patients initiated cell collection in HGB-206 Group A, Group B and Group C. [a] sVOE is defined as a VOE requiring a hospitalization or multiple visits to an emergency department/urgent care over 72 hours and receiving intravenous medications at each visit; all VOEs of priapism requiring any level of medical attention were also considered sVOEs

Commercial Launch Plans

Tom Klima, *Chief Commercial and Operating Officer*

Synergistic network of 35 ZYNTEGLO QTCs preparing to treat SCD patients anticipated in early 2024



- Activated ZYNTEGLO QTC*
- Shading indicates target SCD market

*Activated QTC defined as signed MSA

100% of ZYNTEGLO QTCs have initiated the activation process for LYFGENIA

27 QTCs are ready to receive SCD patient referrals now

Anticipate ZYNTEGLO network will be fully activated for LYFGENIA by **end of Q1 2024**

Anticipate additional **QTC network expansion** in 2024

Access and reimbursement strategy designed to enable timely, equitable access

$3.1M price tied to value

Demonstrated robust and sustained clinical benefit

Lifetime impact of reducing or eliminating VOEs[1]

- Healthcare utilization
- Future earnings
- Life opportunities

Outcomes-based agreement offerings

Meaningful risk sharing

Tied to VOE related hospitalizations

Patients followed for **3 years**

Commercial payer and Medicaid options designed to offer **predictability** and **operational ease**

Encouraging payer interactions

Advanced discussions with largest commercial payers

>15 Medicaid agencies representing **~80%** of individuals with SCD in the US are in discussions[2]

Active engagement with CMMI on innovative payment demonstration (anticipated 2025)

1. Data on file 2. Data based on Prevalence rates of SCD per 1,000 Medicaid Beneficiaries in 2012.

Large patient population with projected demand for gene therapy

>20K individuals with sickle cell disease in the U.S. may be addressed by gene therapy

STRONG DEMAND FOR GENE THERAPY

>70% of patients would consider gene therapy if **recommended by their doctor**[1]

WE KNOW **WHERE** PATIENTS ARE TODAY

95%
of SCD patients[2] are within 200 miles of a planned QTC[3]

60%
of SCD patients[2] are within 50 miles of a planned QTC[3]

88%
of target SCD patients are actively being treated in the healthcare system[4]

1. 70% figure supported by seven years of internal and external market research; 2. Potential addressable population of 20,000; 3. Data on file; 4. Komodo claims data

Experienced commercial gene therapy team well-positioned to launch LYFGENIA™

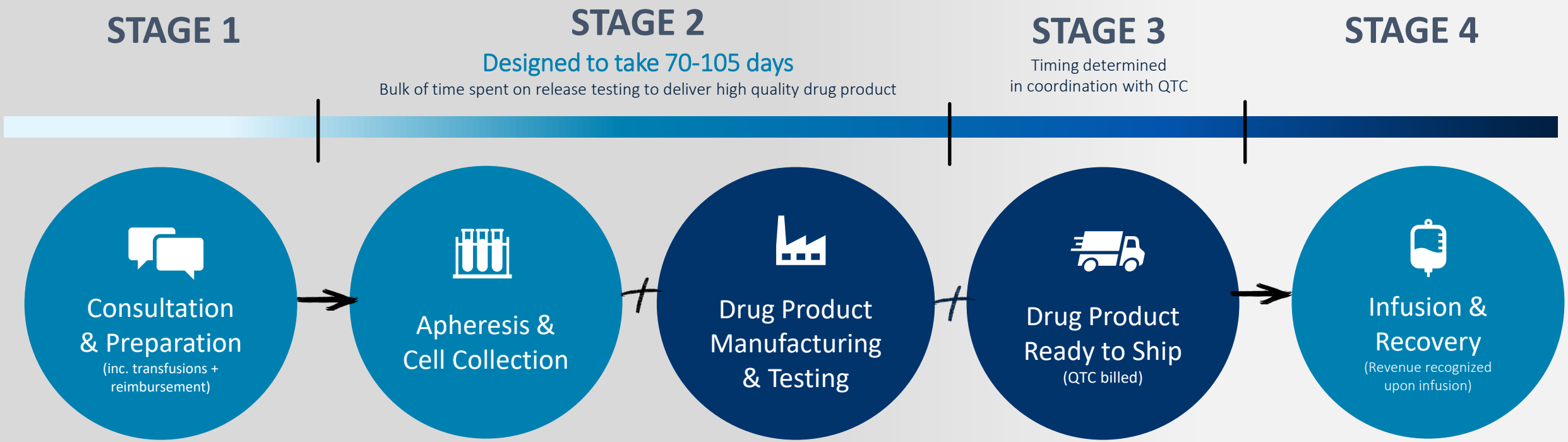
1. A potential multi billion-dollar opportunity with 20,000 addressable patients in the U.S. Strong commercial strategy and projected patient and physician demand

2. 18-month commercial head start leveraging significant ZYNTEGLO launch synergies – anticipate same treating physicians, same treatment centers, same payers

3. Extensive gene therapy expertise including manufacturing experience and an established commercial infrastructure

Delivering a consistent manufacturing process is essential for patients, families and providers

LYFGENIA™ manufacturing process



In clinical trials, patients underwent a median of 2 mobilization cycles[1]

Occurs at QTC Occurs at CMO

QTC: Qualified Treatment Center; CMO: Contract Manufacturing Organization .1. NEngl J Med 2022

Established gene therapy leader poised to unlock shareholder value

Established Clinical Leadership

- 10+ years of gene therapy research
- 180+ patients treated
- 8 clinical trials

Demonstrated Regulatory Success

- Established track record for LVV platform
- 3 FDA approved gene therapies

Commercial Gene Therapy Leader

- 3 commercial launches
- Transplant and cell therapy infrastructure
- Proven reimbursement

Experienced team 100% focused on successfully commercializing gene therapy in the US

bluebirdbio

thank you

to the SCD warriors, caregivers, advocates, healthcare providers, investigators, HCPs, and our bluebird team who made this milestone possible.

Q+A

Andrew Obenshain
chief executive officer

Tom Klima
chief commercial and operating officer

Rich Colvin, MD, PhD
chief medical officer