bluebird bio

May 2022

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

bluebird bio: setting the industry standard for gene therapy

>500 patient-years

of experience with bluebird bio's gene therapies

170+ patients

studied across
8 clinical trials

10+ years

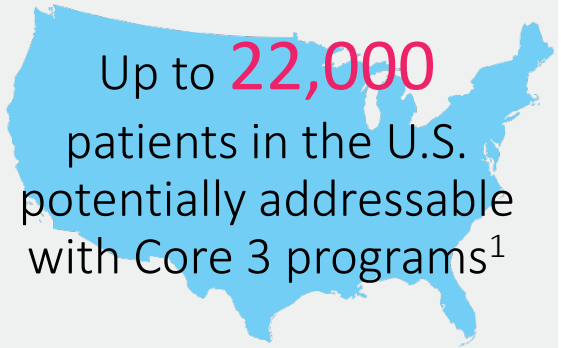
since inception

Target 3 U.S. approvals

by the end of 2023

200+

drug product lots manufactured across Core 3 programs



1X

potentially curative treatment

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

three near-term opportunities to bring transformative LVV gene therapy to patients

Anticipate first to market for hemoglobinopathies

beti-cel for beta-thalassemia

- FDA Advisory Committee Meeting June 9-10, 2022
- PDUFA date August 19, 2022
- Commercial launch planned for beginning of Q4, pending FDA decision

lovo-cel for sickle cell disease

- Plan to complete manufacturing of commercial drug product validation lots by mid-2022
- Expect completion of vector and drug product analytical comparability by Q4 2022
- BLA submission planned for Q1 2023

eli-cel for cerebral adrenoleukodystrophy

- FDA Advisory Committee Meeting June 9-10, 2022
- PDUFA date September 16, 2022
- Potential therapy availability Q4 2022

as a leader in LVV gene therapy, bluebird bio is pioneering the evolution of the field

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

deeply studied

- >170 patients treated
- >8 years of follow up
- 500+ patient years of experience across our LVV clinical studies

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traceable

- Ability to identify and track inserted gene after delivery to a patient
- Unique aspect improves understanding of safety and efficacy for our therapies

beti-cel for beta-thalassemia

Upcoming anticipated milestones

- FDA Advisory Committee Meeting June 9-10, 2022
- PDUFA date August 19, 2022
- Commercial launch planned for beginning of Q4, pending FDA decision

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

β-THALASSEMIA

Transfusion-Dependent Patients Require Time-Consuming, Highly Specialized Care for Life

~1,500 potentially **addressable patients** in the US

Average patient receives a **blood transfusion** every 2-5 weeks[1] – for life

Up to 170 hours a year
spent managing transfusions

Transfusions Only Temporarily Relieve Symptoms, and *Typically Lead to Health Complications Due To Iron Overload*

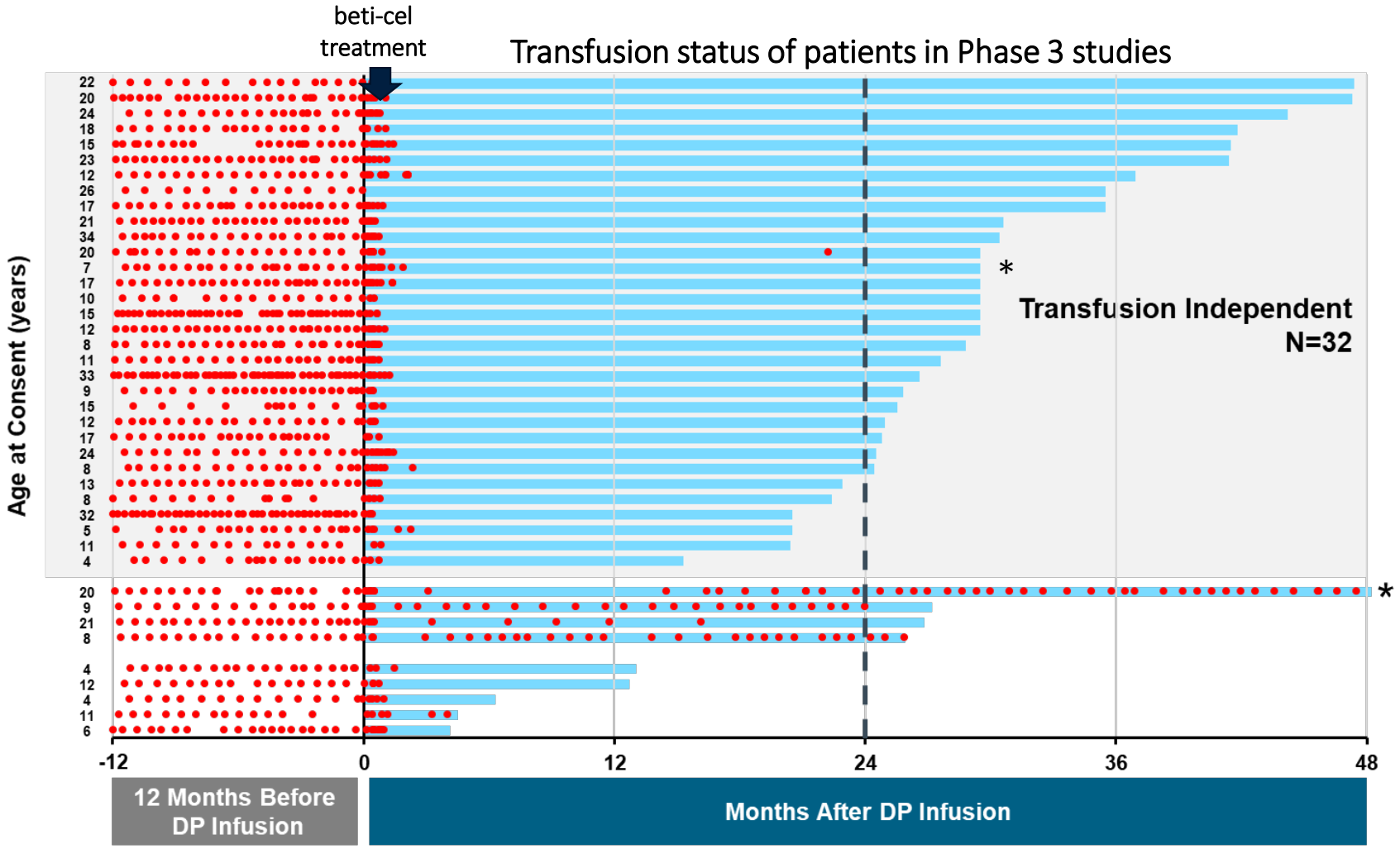
- 5X the mortality rate of the general population[3]
- Average age of death in the U.S. over the last decade is 37[4]
- 80% have at least one disease-related complication[5]

High Economic Burden Associated with a Lifetime of Chronic Care

- $6.4 million average lifetime medical care cost per patient[8]
- 23X higher average total health care cost per patient per year vs. general population[4]
- 688 hours – over 86 workdays spent managing disease a year[6]

[1] Cappellini et al. 2021 [2] TIF Guidelines [3] Jobanputra et al Br J Haematol 2020./Galanello and Origa. Orphannet J Rare Dis 2010
[4] Chieco and Butler 2022 [5] Jobanputra et al Br J Haematol 2020./Galanello and Origa. Orphannet J Rare Dis 2010 [6] Bonifazi et al 2017 [7] Vekeman 2016 & Porter 2011 [8] Weiss et al 2019; Shal et al 2021 [9] Paramore et al 2021

beti-cel: largest β-thalassemia gene therapy data set in the industry presented at ASH 2021 and published in NEJM



beti-cel LTF-303

- 90% of patients achieved transfusion independence (TI) and production of normal or near-normal hemoglobin levels
- 41.5 months of median post-infusion follow-up
- All 46 patients who achieved TI maintained it through last follow-up in LTF-303, demonstrating long-term durability
- Zero deaths or vector-derived replication-competent lentivirus, and no events of insertional oncogenesis or malignancy in LTF-303.
- Majority of AEs and SAEs were unrelated to beti-cel and consistent with the known side effects of HSC collection and busulfan conditioning regimen.

*Patient received acute transfusion for serious blood loss due to orthopedic surgery.

Data as of August 18, 2021

three key factors expected to underpin a successful beti-cel launch

Access & reimbursement

- Focused on rapid access and quality coverage across all payer segments
  - ~70% of β-thalassemia patients are commercially insured
- Value of one-time time therapy with anticipated life-long effect is recognized
- To date, received positive response from 90% of targeted payers

Targeted qualified treatment center (QTC) footprint

- Positioned for rapid adoption
  - Targeting centers with significant experience in novel cell and gene therapies and HSCT
- Focused on high prevalence states with centers actively treating β-thalassemia patients today
- Anticipate first patients scheduled by early Q4 2022

Robust patient services at launch

- *mybluebirdsupport* patient support services designed to mitigate nonclinical barriers to gene therapy
- Designed to foster a positive patient and provider experience
- Informed by insights from previous cell and gene therapy launches

lovo-cel for sickle cell disease

Upcoming anticipated milestones

- Plan to complete manufacturing of commercial drug product validation lots by mid-2022
- Expect completion of vector and drug product analytical comparability by Q4 2022
- Planned BLA submission Q1 2023

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

SICKLE CELL DISEASE

Sickle cell disease is a serious, progressive and debilitating genetic disease caused by a single mutation in the β-globin gene

1 in 365 Black or African American babies is born with sickle cell disease[1]

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

Disease unpredictability and health disparities create significant challenges for patients living with SCD

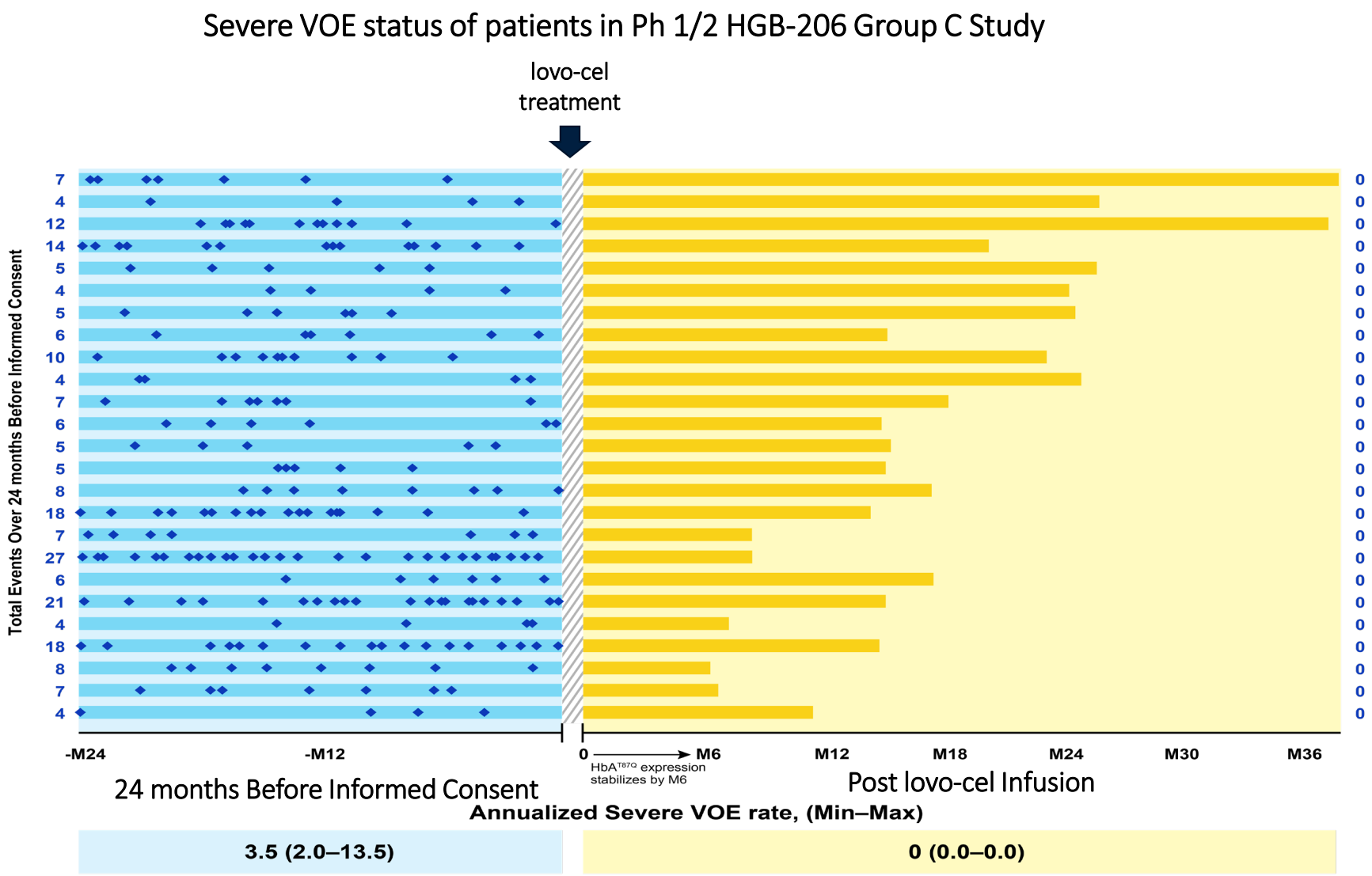
- Approximately 80 percent of hospital stays for patients with SCD began in the emergency department[2]
- 50% of patients are discharged prematurely while still experiencing severe pain[3]
- 25% experience a stroke by age 45; organ failure and organ damage are common[3]
- Median age of death remains in the 40s[3]

Life with sickle cell disease can be associated with considerable costs and impact on daily life

- Up to $180,000 in annual direct medical costs depending on frequency of events[4]
- Up to $9M in lifetime direct medical costs[4]
- 75% report missing more than a month of work on average during the previous year[5]

1. CDC.
2. Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), National Inpatient Sample (NIS), 2016
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.
5. Holdford D, Vendetti N, Sop DM, Johnson S, Smith WR. Indirect Economic Burden of Sickle Cell Disease. Value Health. 2021 Aug;24(8):1095-1101. doi: 10.1016/j.jval.2021.02.014. PMID: 34372974.

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

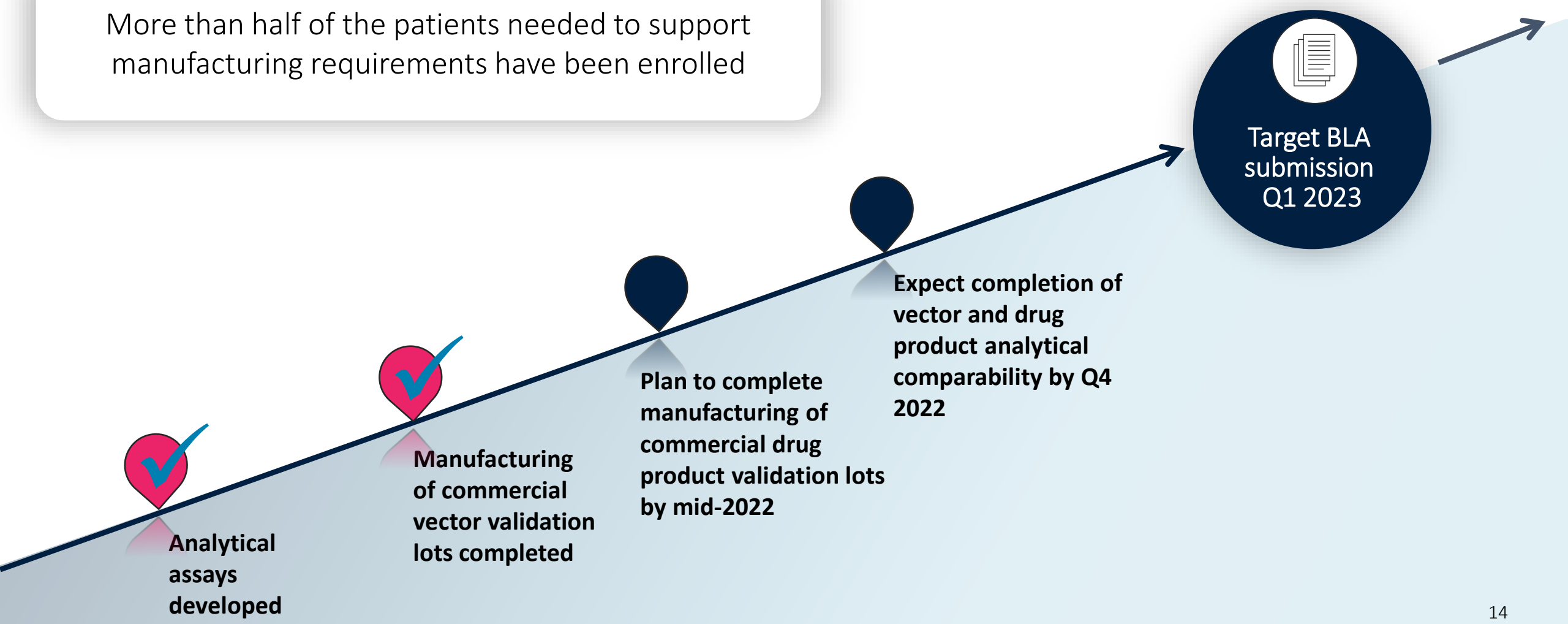
Complete resolution of severe VOEs thru 36 months

- 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

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

More than half of the patients needed to support manufacturing requirements have been enrolled



eli-cel for cerebral adrenoleukodystrophy (CALD)

CALD is a rare neurodegenerative disease primarily affecting young children that can lead to progressive, irreversible loss of neurologic function and death

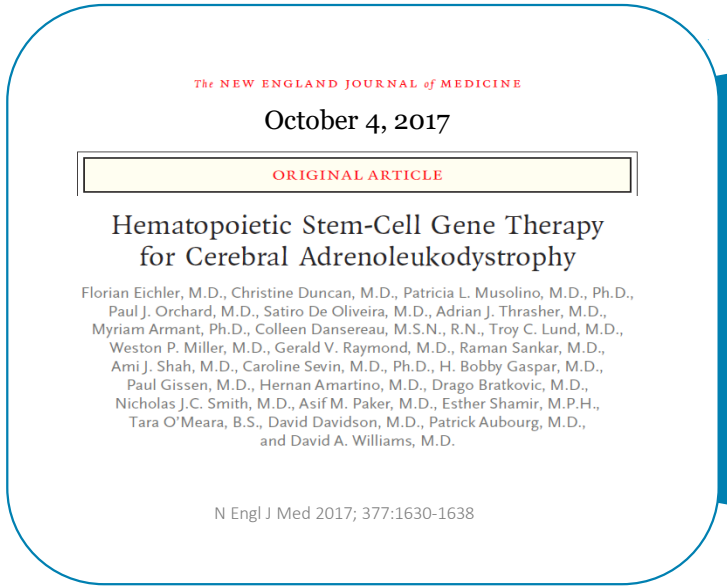
~40 patients are diagnosed with CALD in the U.S. each year

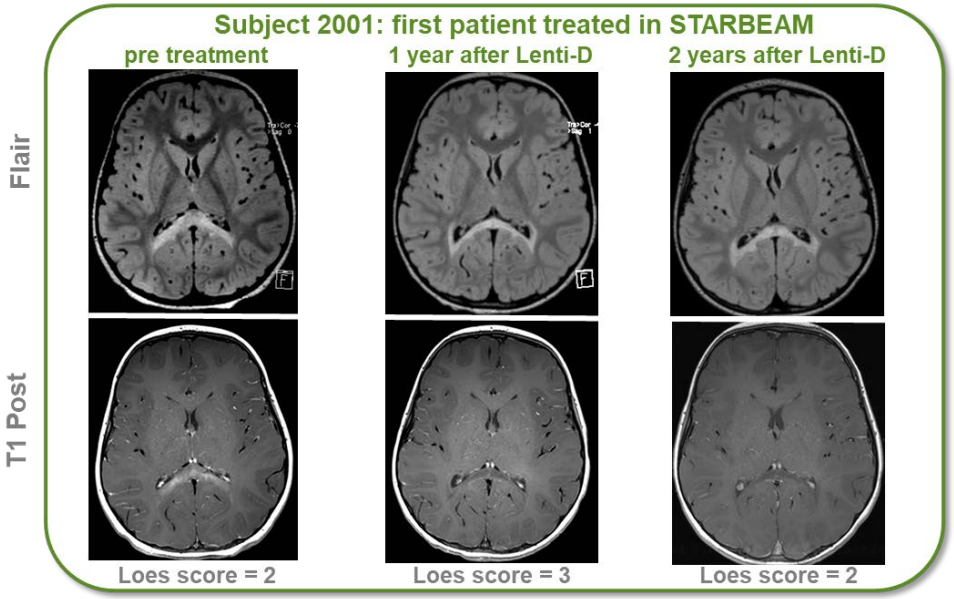
Upcoming anticipated milestones

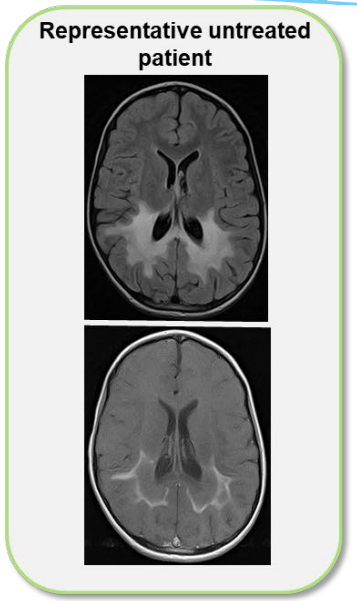
- FDA Advisory Committee Meeting
  June 9-10, 2022
- PDUFA date September 16, 2022
- Potential therapy availability in Q4 2022

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

eli-cel treatment has the potential to halt CALD disease progression







Data as of March 31, 2018

EFFICACY

90.6% (29/32) major functional disabilities (MFD)-free survival at 24 months (ALD-102)

67 patients treated in clinical trials

Up to nearly 7 years of follow-up

SAFETY

Based on the overall benefit/risk profile, eli-cel will be a meaningful treatment option for patients with early CALD who do not have a matched sibling donor

3 cases of MDS reported; 2 were likely mediated by Lenti-D LVV insertion and 1 is under investigation

The eli-cel clinical hold remains in place

strengthened financial position extends expected cash runway through pivotal upcoming milestones in the first half of 2023

Restructuring to deliver **up to $160 million** in cost savings over the next two years

35-40% reduction in operating costs anticipated by year-end 2022

March 31, 2022 unaudited restricted cash, cash and cash equivalents and marketable securities of **$312 million***

Savings realized expected to reduce the Company's cash burn in 2022 to **less than $340 million**

Continuing to evaluate financing options, including **public or private equity financings** and **monetizing priority review vouchers** that may be issued upon potential approval of beti-cel or eli-cel

*Cash balance includes restricted cash of ~$45 million

2022 will be the most catalyst rich year in bluebird's history

Beta-thalassemia

- *Ad Comm*
  JUNE 9-10, 2022
- *FDA PDUFA date*
  AUGUST 19, 2022
- *Potential commercial launch*
  BEGINNING OF Q4 2022

Cerebral Adrenoleukodystrophy

- *Ad Comm*
  JUNE 9-10, 2022
- *FDA PDUFA date*
  SEPTEMBER 16, 2022
- *Potential therapy availability*
  Q4 2022

Sickle Cell Disease

- *Plan to complete manufacturing of commercial drug product validation lots by*
  MID-2022
- *Expect completion of vector and drug product analytical comparability by*
  Q4 2022
- *BLA submission*
  Q1 2023

thank you