

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of The Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): January 11, 2016

bluebird bio, Inc.

(Exact name of registrant as specified in its charter)

DELAWARE

(State or other jurisdiction of
incorporation)

001-35966

(Commission File Number)

13-3680878

(I.R.S. Employer
Identification No.)

**150 Second Street
Cambridge, MA**

(Address of principal executive offices)

02141

(Zip Code)

Registrant's telephone number, including area code **(339) 499-9300**

Not Applicable

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
 - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
 - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
 - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
-

Item 7.01 Regulation FD Disclosure

The Company will be conducting meetings with investors attending the 34th Annual J.P. Morgan Healthcare Conference in San Francisco beginning on January 11, 2016. As part of these meetings, the Company will deliver the slide presentation attached to this report as Exhibit 99.1, which is incorporated herein by reference.

The information responsive to Item 7.01 of this Form 8-K, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	Investor presentation provided by bluebird bio, Inc. on January 11, 2016

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: January 11, 2016

bluebird bio, Inc.

By: /s/ Jason F. Cole

Jason Cole

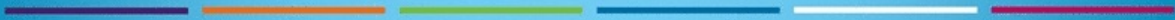
Senior Vice President, General Counsel

EXHIBIT INDEX

<u>Exhibit No.</u>	<u>Description</u>
99.1	Investor presentation provided by bluebird bio, Inc. on December 6, 2015



bluebirdbio®



Making Hope a Reality

Transforming the Lives of Patients
with Severe Genetic and Rare Diseases

Nasdaq : BLUE

Forward Looking Statement

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 the initiation, timing, progress and results of our preclinical and clinical studies and our research and development programs, our ability to advance product candidates into, and successfully complete, clinical studies, and the timing or likelihood of regulatory filings and approvals 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.

Nasdaq: BLUE

bluebird bio: Why We Do What We Do



Ethan



Aidan



Cameron

Our Vision – Make Hope a Reality

Seeking to transform the lives of patients with severe genetic and rare diseases through the development of innovative gene therapy products.



Our Strategic Intent

Severe Genetic Diseases

Hematopoietic Stem Cells (HSCs)

Immunotherapy

T Cells



- *Lentiviral Gene Delivery – Pure, Potent, Reproducible, Scalable*
 - *Global Manufacturing Platform – Virus and Drug Product*
 - *Genome Editing Platform – MegaTALs*

2015 Established Strong Fundamentals

Completed **enrollment** target of key **CALD** trial

Treated first ever **SCD patient** with gene therapy

Defined an **accelerated** U.S. and EU **β -thalassemia** regulatory path

Closed several enabling **oncology** deals and filed IND

Further built team from **research to commercial**

Raised **\$477M** to extend runway through 2018

GREAT MOMENTUM HEADING INTO 2016

2016 Priorities



Ecosystem Explosion

Competition Great For All (Especially Patients)

Gene Therapy (20+)



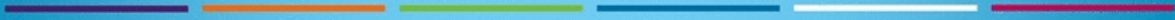
CAR/TCR/T Cell (25+)



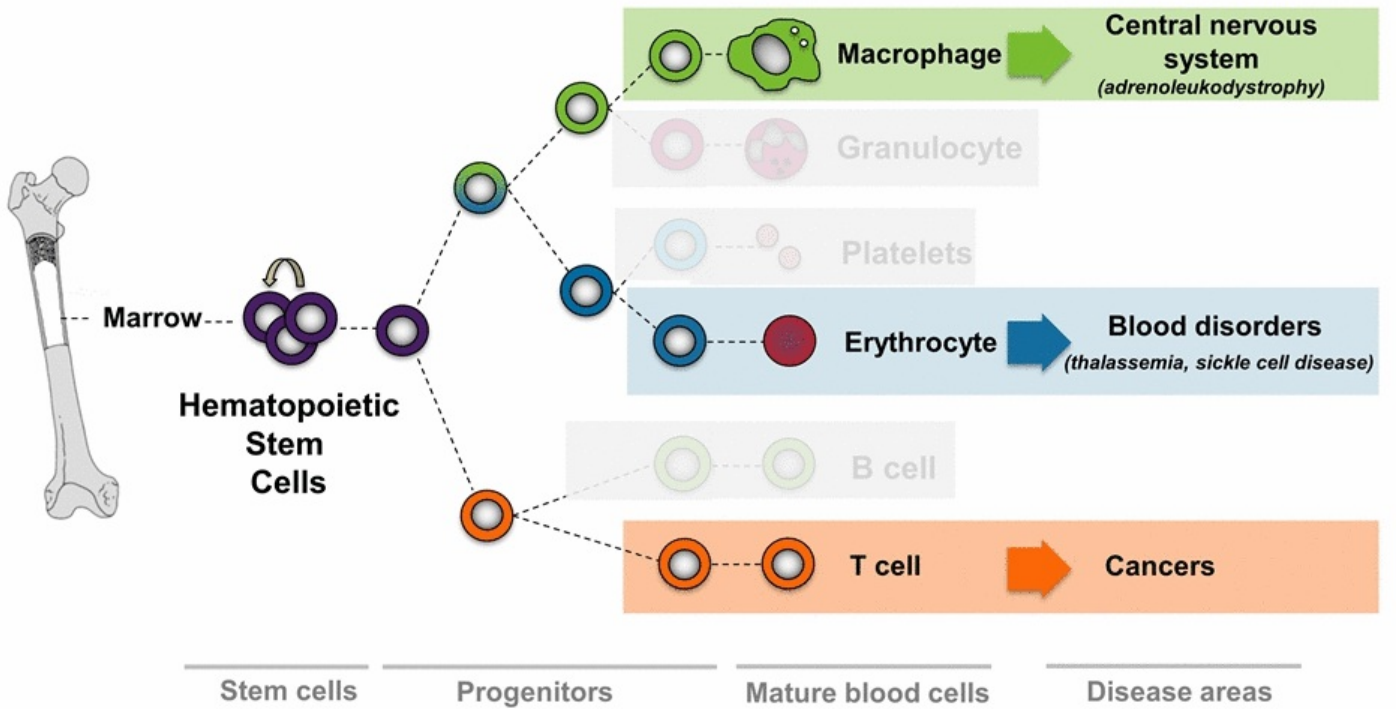
Gene Editing (8+)



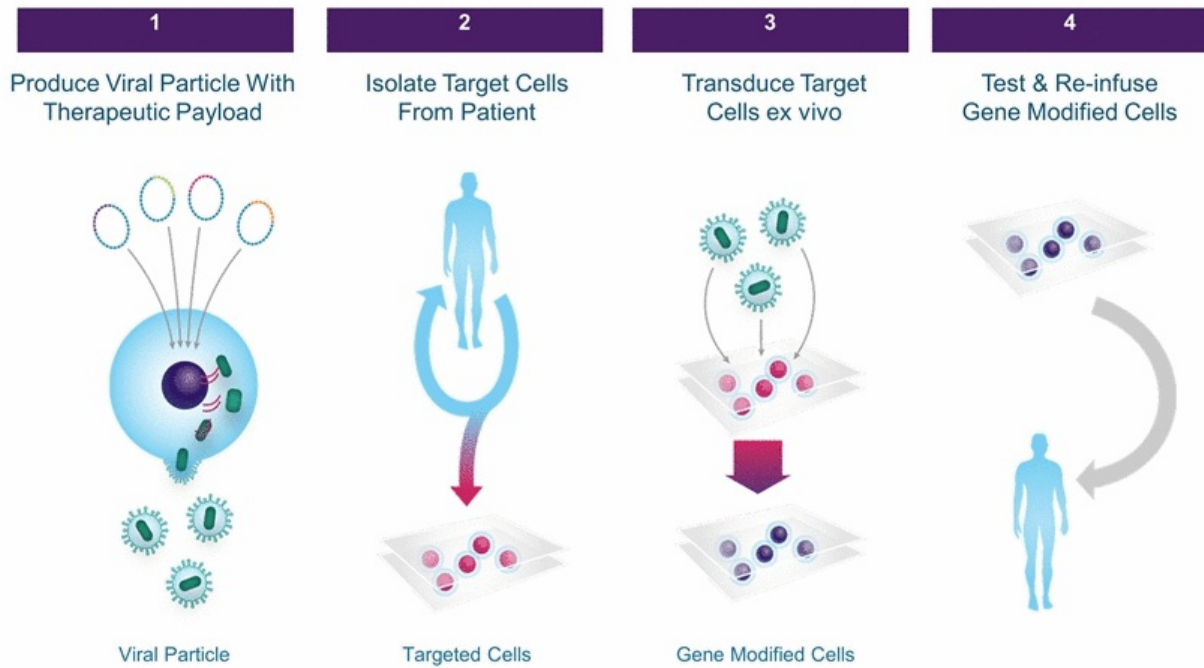
Gene Therapy Platform Capabilities Drive Pipeline



bluebird Lentiviral Stem Cell Platform



How Our Gene Therapy Approach Works

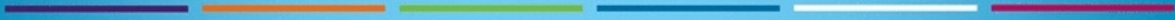


bluebird Pipeline Overview

Product Candidates	Program Area	Preclinical	Phase 1/2	Phase 2/3	Rights/Partner
	CNS Diseases				
Lenti-D™	Cerebral ALD				Worldwide
	Rare Hemoglobinopathies				
LentiGlobin®	Beta-thalassemia Major*				Worldwide
	Severe Sickle Cell Disease				Worldwide
	Oncology				
bb2121 BCMA	Multiple Myeloma				Celgene
Next Gen BCMA	Multiple Myeloma				Celgene
Five Prime Target	Undisclosed				Worldwide
HPV-16 E6 TCR	HPV-associated Cancers				Kite Pharma
Viromed Target	Undisclosed				Worldwide excluding Korea
Other Programs	Undisclosed				Worldwide
	Research				
Early Pipeline	Undisclosed + Gene Editing				Worldwide

* The current clinical trials for LentiGlobin are Phase 1/2 studies that may provide the basis for early conditional approval in some jurisdictions

Clinical Programs



β -thalassemia Major: Disease Overview

DISEASE

Monogenic,
severe anemia

Loss of or reduced
 β -globin production

Poor quality of life and
shortened lifespan

CURRENT TREATMENTS

Frequent/chronic transfusions lead
to iron overload & organ failure

Ongoing iron chelation,
frequently suboptimal

Allogeneic transplant, while
potentially curative, rarely used

- ▶ Difficulty finding a suitable match
- ▶ Morbidity/mortality with graft rejection, graft versus host disease and immunosuppression

EPIDEMIOLOGY

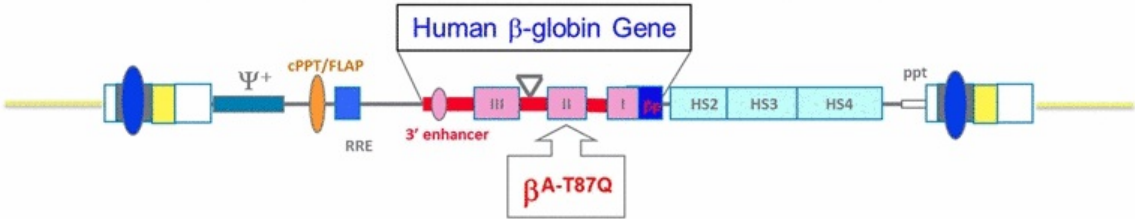
Global prevalence ~288K;
incidence ~60K

U.S./EU prevalence
(treated) ~15K;
incidence ~1.5K

- ▶ 60-80% severe/major

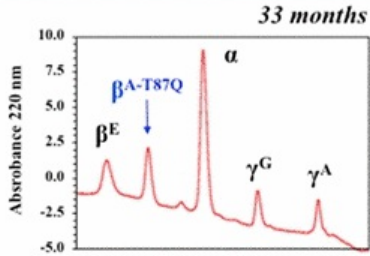
Affects people of
Mediterranean, Middle
Eastern, South Asian
and SE Asian descent

LentiGlobin: Innovative Vector Design

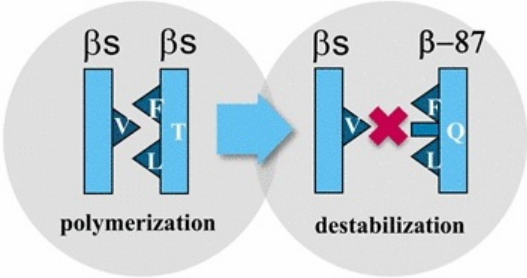


Philippe Leboulch

IN-VIVO BIOMARKER



ANTI-SICKLING PROPERTIES



β -thalassemia Ongoing Clinical Trials *Basis to Seek Conditional Approval in EU*

NORTHSTAR STUDY (β -thalassemia major)

(HGB-204) Phase 1/2, multi-center, global study

- N=18 subjects (up to 3 adolescents added)
- Centralized transduction for drug product manufacturing
- Positive data presented at ASH 2014 and 2015

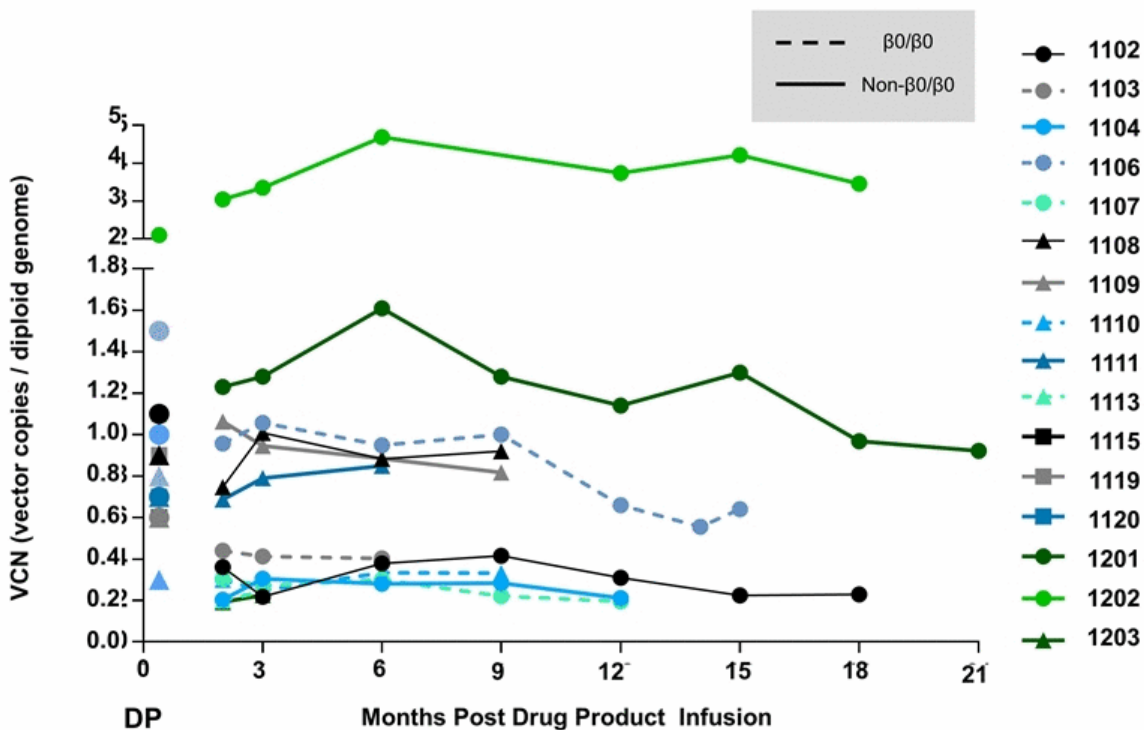
HGB-205

(β -thalassemia major & severe sickle cell disease)

Phase 1/2, single-center study in France

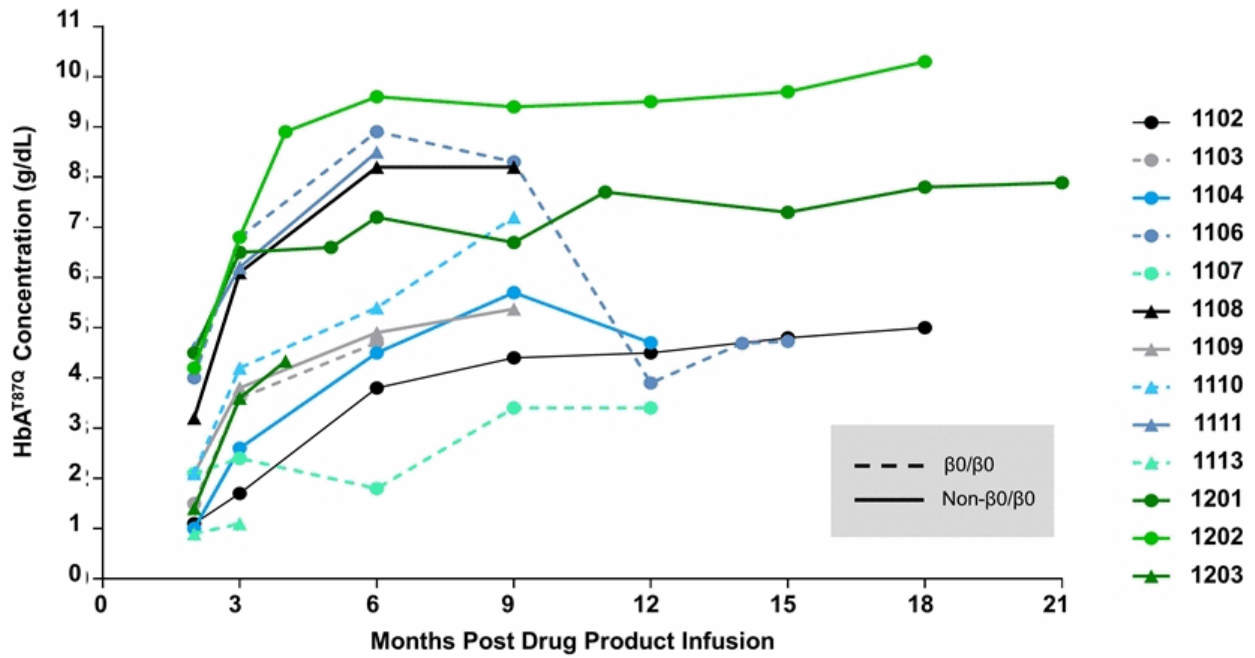
- N=7 subjects (~3-5 β -thalassemia)
- Positive data presented at ASH 2014 and 2015 and EHA 2015
- First patient with SCD ever treated with gene therapy in 2014

Drug Product VCN and VCN in Peripheral Blood Leukocytes After Infusion



Data presented at ASH 2015; as of October 28, 2015. DP VCN for all treated subjects. PBL VCN given for subjects with ≥ 2 months follow-up

Updated Data Continue to Show High Levels of HbA^{T87Q} Production After Infusion

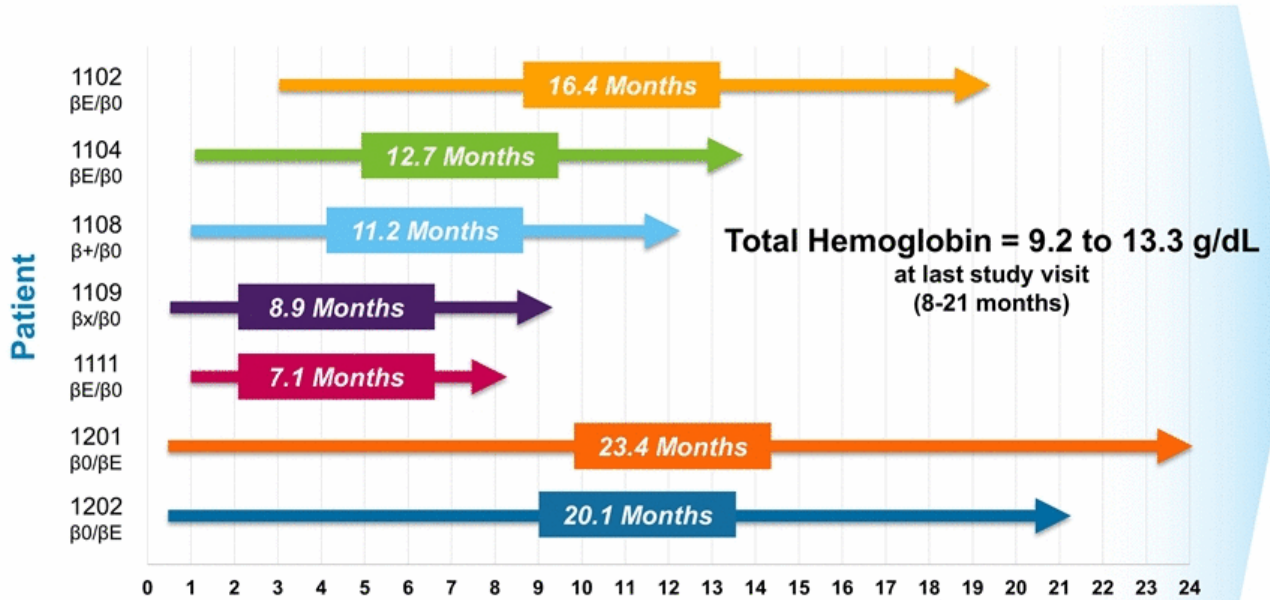


Median HbA ^{T87Q} g/dL	3.8	5.4	6.7	4.4	6.1	7.8
	N=13	N=11	N=9	N=5	N=4	N=3

Data presented at ASH 2015; as of October 28, 2015. Only includes subjects with ≥3 months of follow-up

Updated Data Show Rapid and Sustained Transfusion Independence in Patients with non- β^0/β^0 Genotypes

Months Transfusion-Free*



Subjects with non- β^0/β^0 genotypes stop transfusions shortly after DP infusion with RBC independence extending up to 23.4 months

*Data presented at ASH 2015; as of October 28, 2015 for patients in HGB-204 and November 10, 2015 for patients in HGB-205

Updated Data Show 33% to 100% Reduction in Transfusions in Subjects with β_0/β_0 Genotype

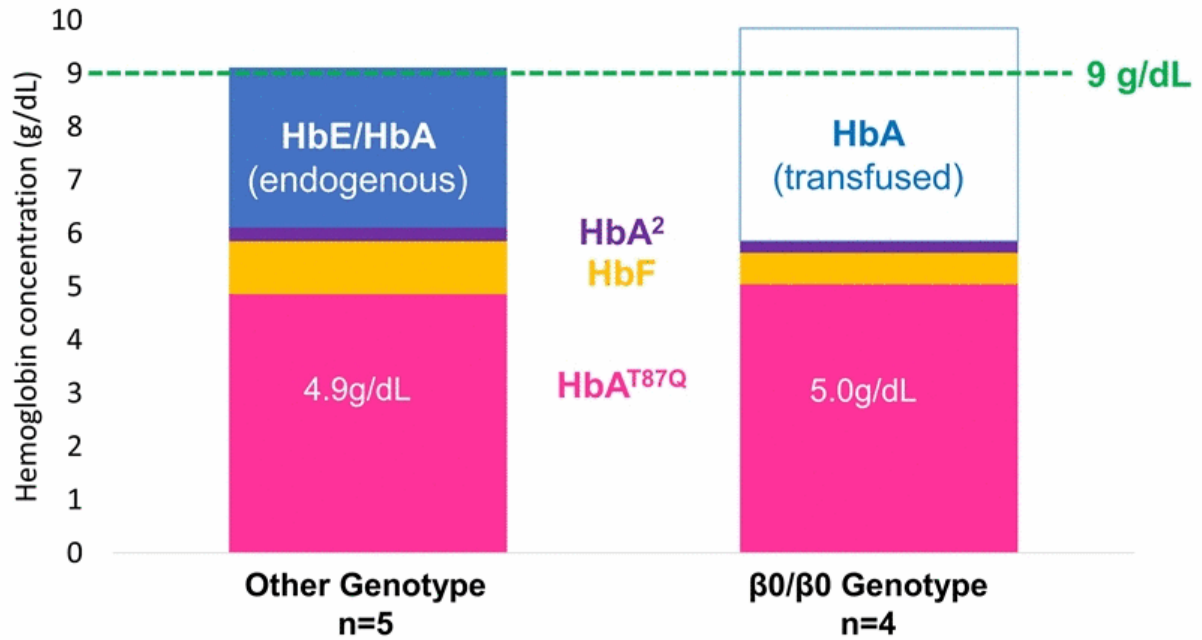


*3-month average number and number of pRBC transfusions over 12 months prior to infusion

Data presented at ASH 2015; as of October 28, 2015. Subjects with ≥ 6 m follow-up, shown to latest 3m interval, as of data cut-off. Subjects 1113 & 1115 had <6 m follow-up.

Hemoglobin Levels by Genotype in Northstar Study

Median Hemoglobin Concentrations at 6 Months



Difference in transfusion independence between genotypes explained by endogenous non-HbA^{T87Q} hemoglobin production

Data presented at ASH 2015

Evolving Clinical and Regulatory Plans

- Initial U.S. regulatory strategy will focus on non- $\beta 0/\beta 0$ patients
- HGB-207 and likely HGB-208 to enroll only non- $\beta 0/\beta 0$ patients
- Collecting more data on $\beta 0/\beta 0$ patients to finalize development path in this genotype, including EU regulatory strategy



Sickle Cell Disease (SCD): Disease Overview

DISEASE

Monogenic, severe anemia

Polymerization of β -globin chains deforms/sickles red blood cells

Poor quality of life

Pain crises, stroke, splenomegaly

Shortened lifespan

CURRENT TREATMENTS

Non curative treatments

- ▶ Hydroxyurea
- ▶ Blood transfusions
- ▶ Pain management

Allogeneic Transplant

- ▶ Match uncommon
- ▶ High morbidity / mortality

EPIDEMIOLOGY

U.S./EU prevalence ~150K

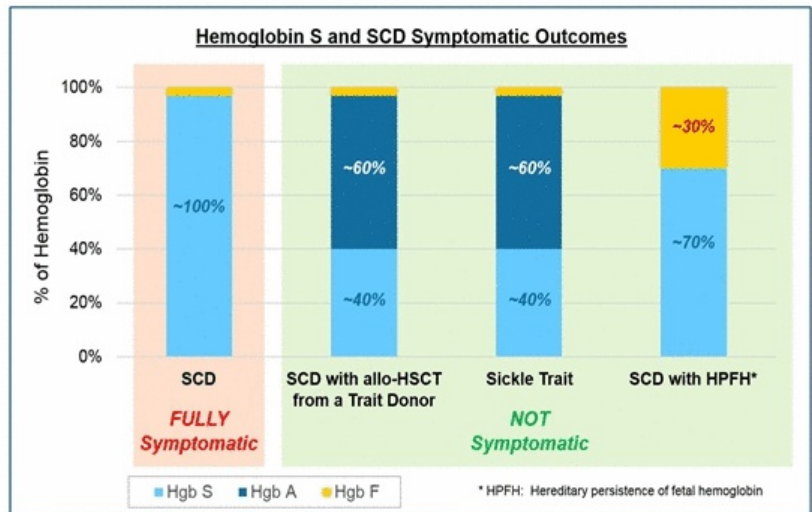
U.S./EU incidence ~3K

Global prevalence ~25M

Global incidence ~300K

Why LentiGlobin May Treat Sickle Cell Disease

- LentiGlobin incorporates anti-sickling amino acid found in fetal hemoglobin
- Patients with SCD and hereditary persistence of fetal hemoglobin are typically asymptomatic with sickle globin levels as high as 70%
- Patients with sickle trait are not symptomatic
- Patients with SCD who undergo allo transplant are functionally cured with donor chimerism as low as 15-20%



These data argue that as little as 3g/dL (~30%) of therapeutic globin and gene marking as low as 20% could potentially achieve a disease-modifying effect

HGB-206: Ongoing Trial in Severe Sickle Cell Disease

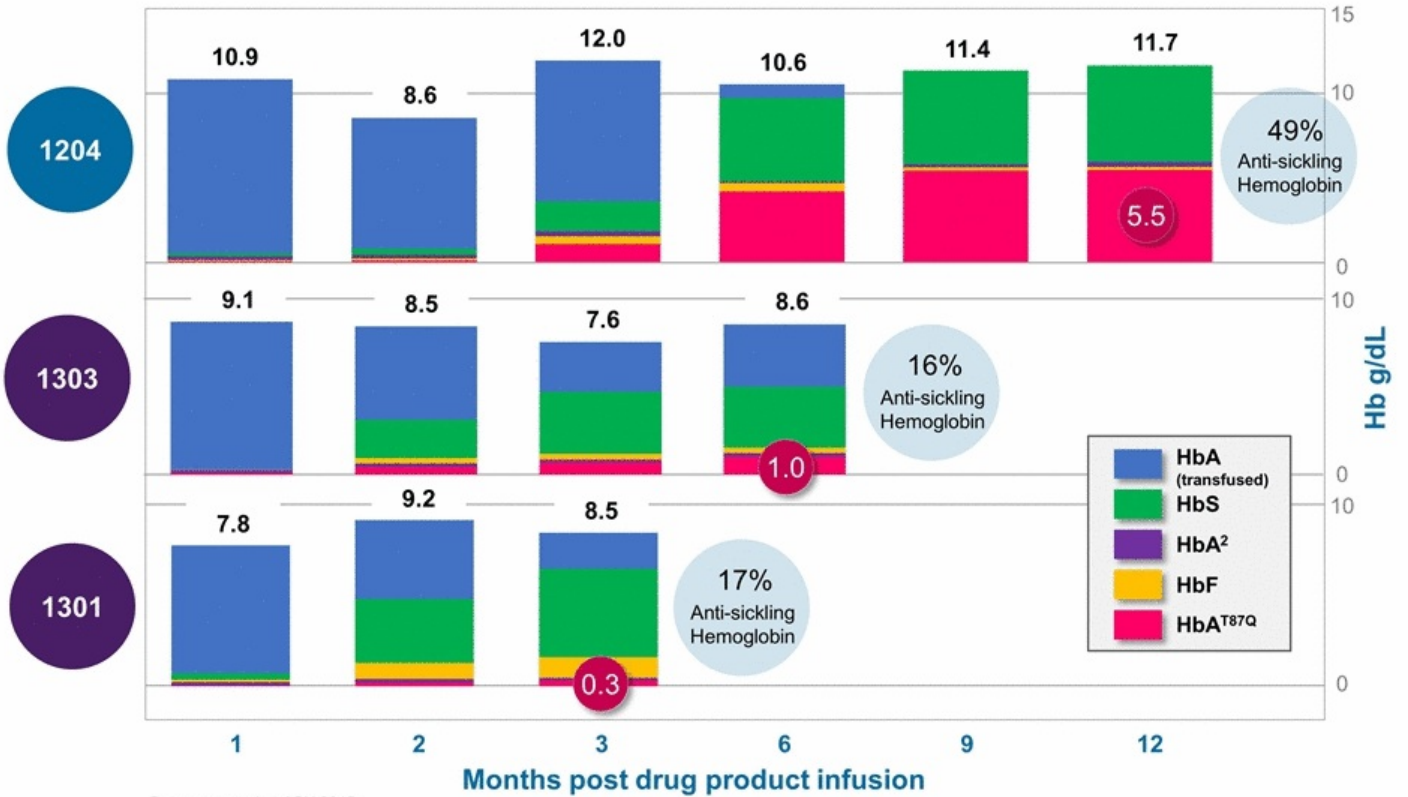
HGB-206

(Severe sickle cell disease)

Open label, multi-center, U.S. based study

- Increased enrollment target from 8 subjects to 20 subjects to provide additional data and flexibility for regulatory strategy
- As of November 17, 2015, 11 subjects enrolled; bone marrow harvest completed for four subjects and in progress for five subjects
- Primary endpoint = Safety of gene therapy among patients with severe SCD
- Secondary endpoints = clinical events, including vaso-occlusive crises or acute chest syndrome

HbA^{T87Q} Production and Globin Change after Infusion



Data presented at ASH 2015

Cerebral Adrenoleukodystrophy (CALD): Disease Overview

DISEASE

Ultra-orphan, X-linked, monogenic, neurological disorder

Mutated gene results in toxic buildup of very long chain fatty acids

Leads to cerebral inflammation & demyelination

CURRENT TREATMENTS

Untreated cerebral ALD leads to dismal outcomes (vegetative state and death)

Allogeneic stem cell transplant standard for CALD (if possible)

EPIDEMIOLOGY

CALD most severe form of ALD

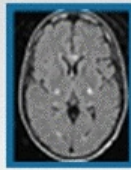
ALD incidence: 1 in 20,000 (live births)

Cerebral disease

- ▶ CCALD accounts for 30-40% of ALD
- ▶ AMN accounts for 40-45% of ALD with 40% cerebral
- ▶ ACALD accounts for 25% of ALD

Starbeam Study for Cerebral Adenoleukodystrophy: Interim Clinical Data Expected in 2016

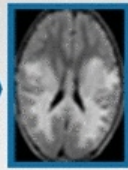
Natural
Course of
Disease



12
months



18
months



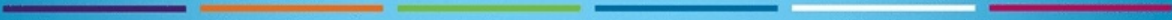
24
months



Open label, single arm,
multi-center, global
study (n=18)

Abstract Submitted for
April 2016 AAN Meeting

Research Platform

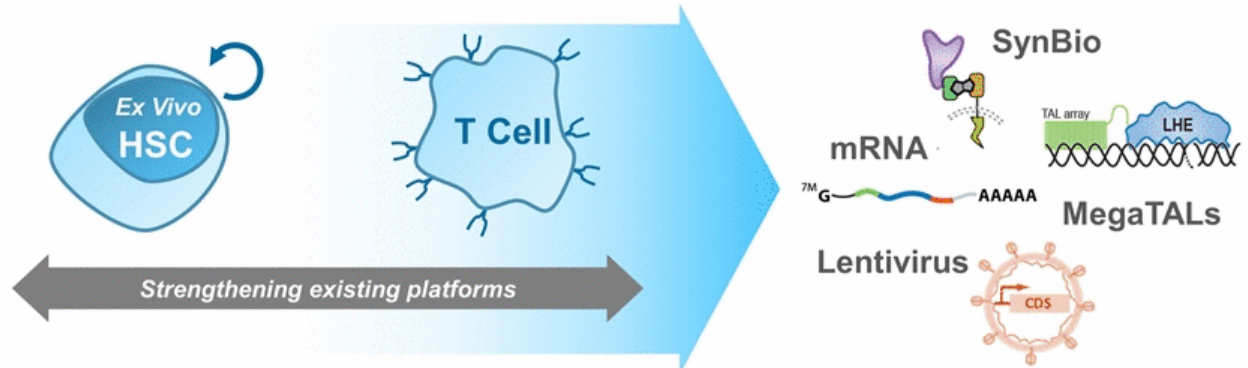


Research Platform and Strategy

HSC Platform

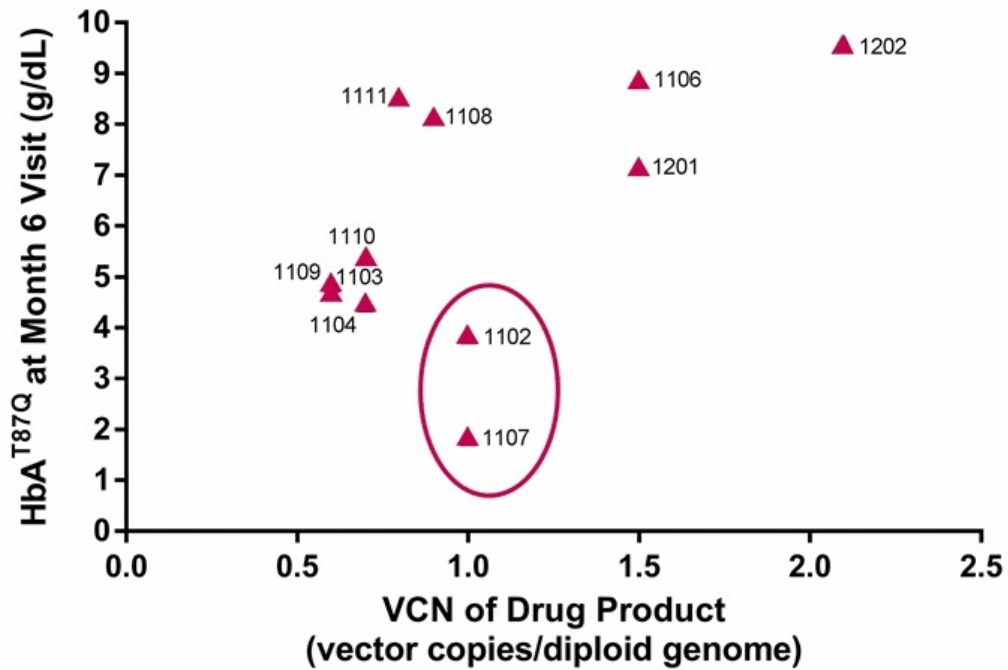
T Cell Platform

Future Pipeline



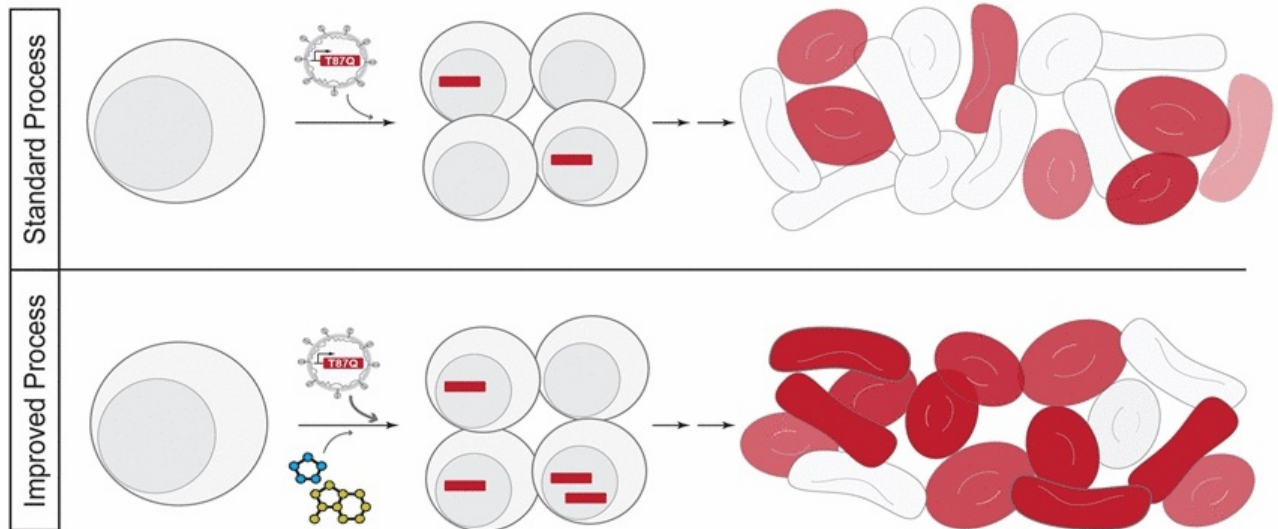
- Powerful research platform with multiple tools and technologies to:
 - Enhance the therapeutic potential of current clinical programs
 - Apply combinations of bluebird's tools/technologies to potentially create "best in class" therapeutic products
 - Drive early innovative science via select academic collaborations
- Goal is to build a product candidate engine to file INDs and feed future pipeline

Hypothesis: Improving VCN in the LentiGlobin Drug Product Should Increase T87Q Levels and Further Improve Clinical Benefit



Improving VCN in the LentiGlobin Drug Product

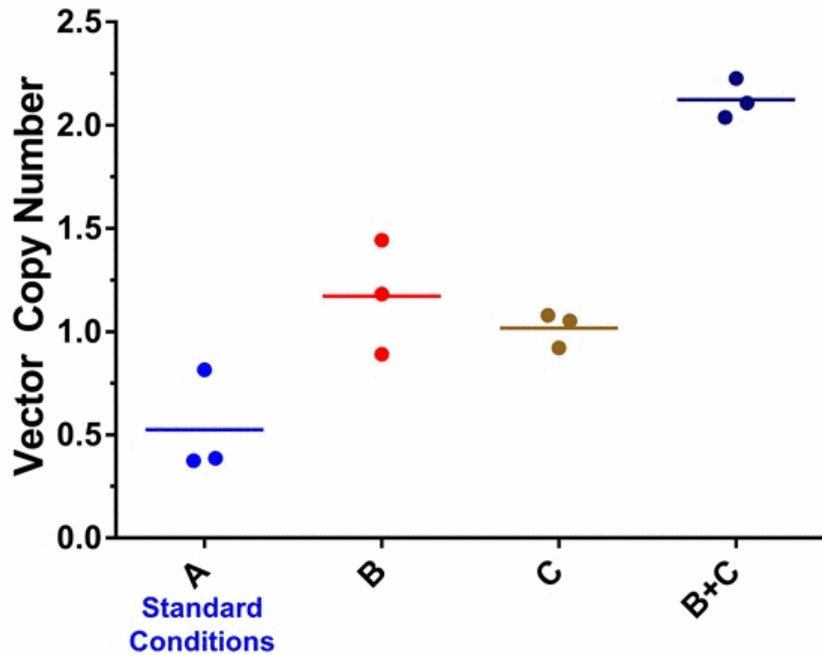
Identifying Compounds that Improve Transduction



Goal: Increased VCN via increased transduction efficiency (% HSCs transduced)

Improving VCN in the Drug Product

Selected Compounds from Screening Results

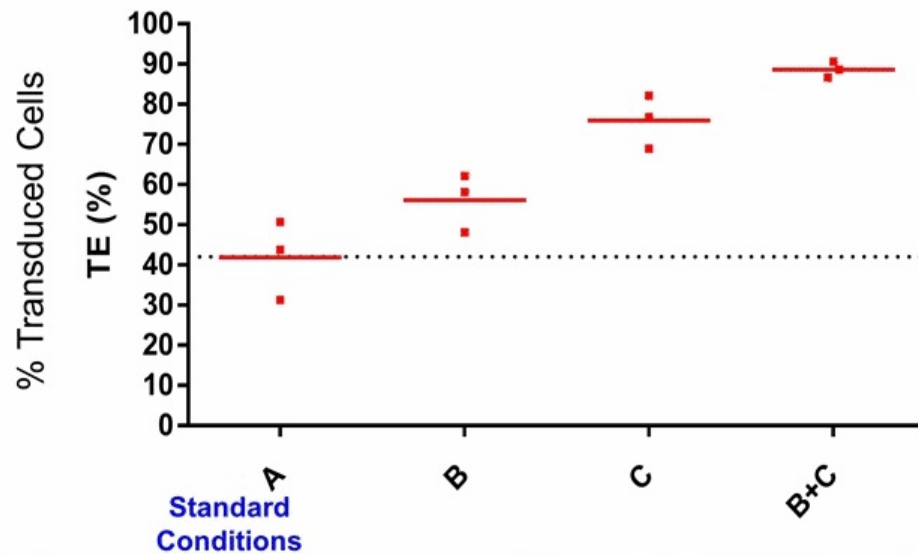


- Experiment performed with pre-characterized “hard to transduce” donor HSCs
- Similar fold improvement in VCN obtained across a wide range of donors, lentiviral vectors and LVV lots
- Process is well tolerated

*preliminary research findings

Improving VCN in the LentiGlobin Drug Product

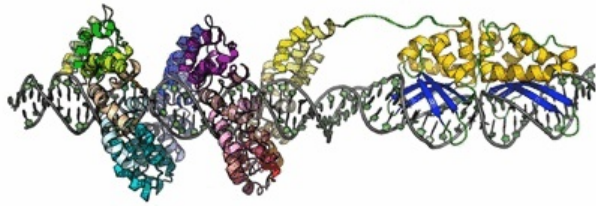
Markedly Increased % Corrected HSCs



*Single-cell PCR assay demonstrates marked increase in transduction efficiency
Up to ~90% of the cells transduced using most optimized conditions*

*preliminary research findings

bluebird Gene Editing Approach MegaTAL Technology



Expertise in homing endonucleases (HE) and MegaTALs

- Robust nuclease discovery platform, proprietary database, broad IP

Multiple advantages of HE and MegaTALs

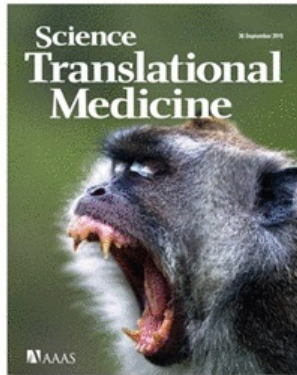
- Naturally occurring proteins
- Highly specific and efficient
- Compact size

Broad range of therapeutic applications

- Complementary to existing programs

MegaTAL Enabled Targeted Gene Addition

Precision Offers Promise of Enhanced Efficacy and Safety



RESEARCH ARTICLE

GENOME EDITING

Efficient modification of *CCR5* in primary human hematopoietic cells using a megaTAL nuclease and AAV donor template

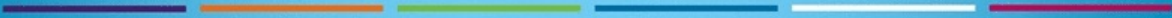
Blythe D. Sather,^{1*} Guillermo S. Romano Ibarra,^{1*} Karen Sommer,¹ Gabrielle Curinga,¹ Malika Hale,¹ Iram F. Khan,¹ Swati Singh,¹ Yumei Song,¹ Kamila Gwiazda,¹ Jaya Sahni,¹ Jordan Jarjour,² Alexander Astrakhan,² Thor A. Wagner,^{3,4} Andrew M. Scharenberg,^{1,4,5†} David J. Rawlings^{1,4,5†}



Seattle Children's[®]
HOSPITAL · RESEARCH · FOUNDATION

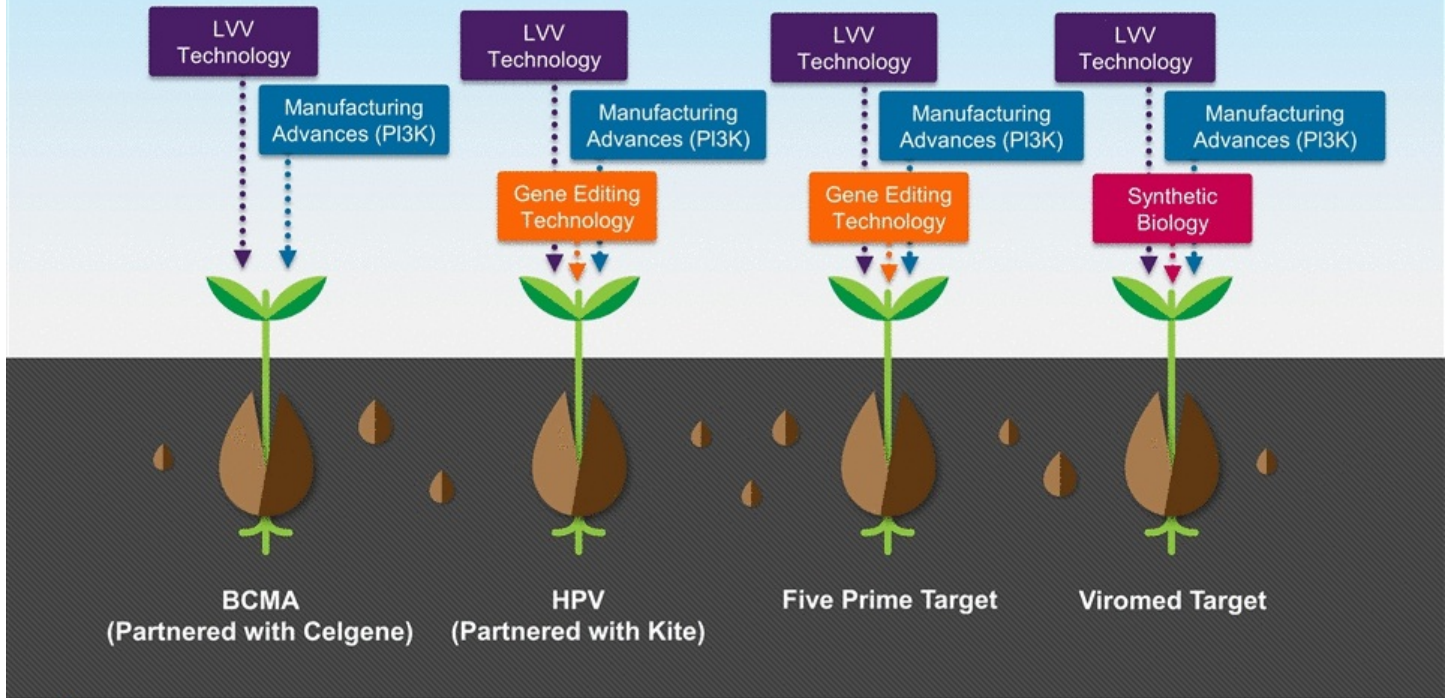
Demonstrates power of megaTAL and AAV platforms – supports NextGen HSC and Cancer Immunotherapy Programs

Immuno-Oncology



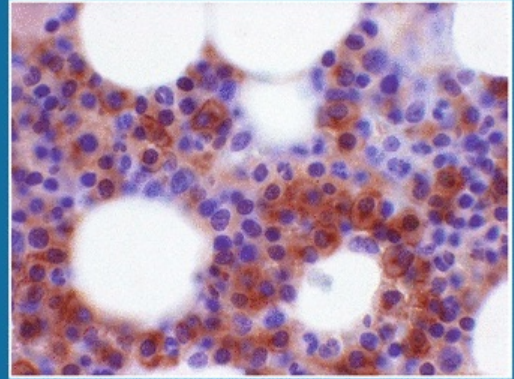
Differentiated Oncology Approach

Deliver differentiated, best-in-class, genetically modified cellular products to patients suffering from cancer.



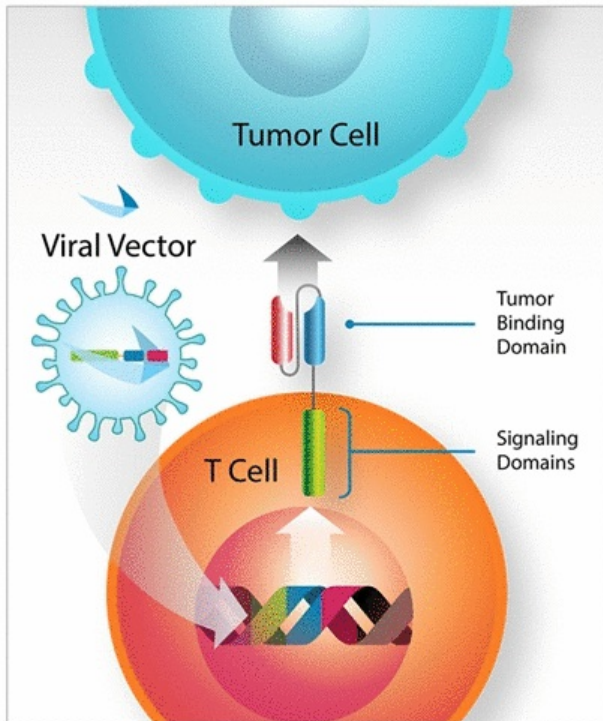
BCMA: A Promising Target in Multiple Myeloma

- B cell maturation antigen (BCMA) is a member of the TNF receptor superfamily.
- BCMA binds B cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL). BCMA is expressed by plasma cells and some mature B cells.
- Mice deficient in BCMA are healthy and have normal numbers of B cells, but reduced survival of plasma cells.
- BCMA RNA is near universally detected in multiple myeloma (MM) cells, and BCMA protein is detected on the surface of malignant plasma cells from patients with MM.



Multiple myeloma cells expressing BCMA
(brown color is BCMA protein)

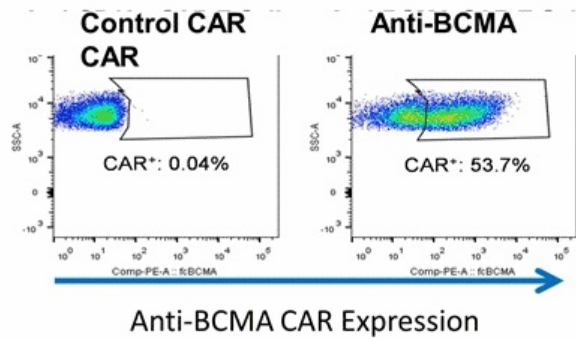
Anti-BCMA CAR – bb2121



bb2121 Vector Design

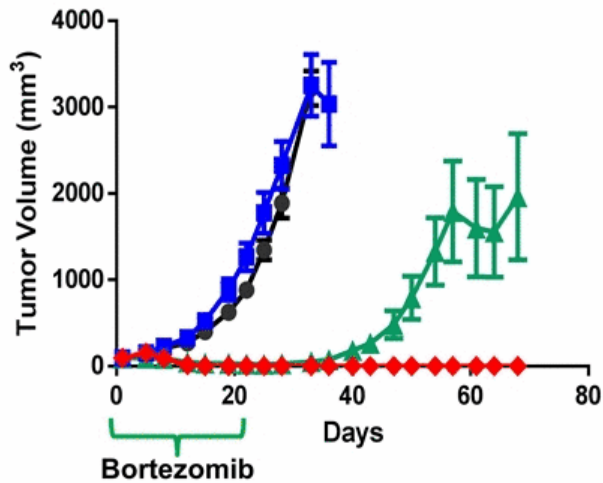


bb2121 CAR Expression

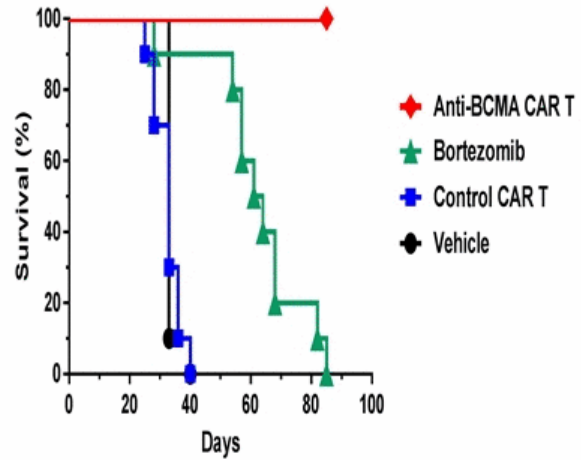


A Single Treatment with bb2121 CAR T Cells Clears Animals of MM and Results in 100% Survival

Tumor treatment

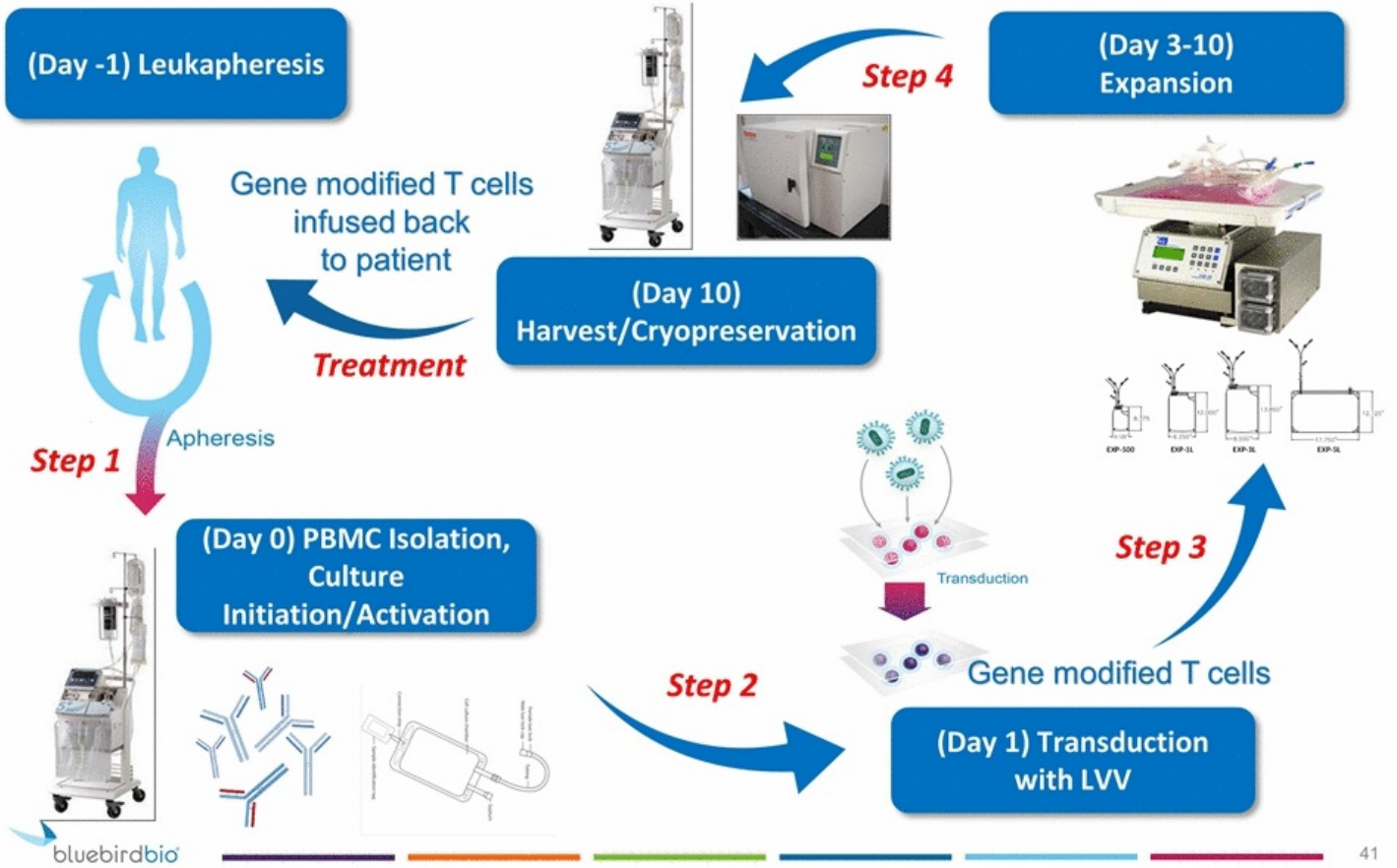


Survival



◆ Anti-BCMA CAR T
 ▲ Bortezomib
 ■ Control CAR T
 ● Vehicle

An Efficient CAR T Drug Product Manufacturing Process



Promising Clinical Proof-of-Concept for bb2121 in NCI Anti-BCMA Latebreaker

- NCI-sponsored Phase 1 first-in-human study of anti-BCMA CAR T therapy in heavily pre-treated patients with multiple myeloma
- Presenter and PI Jim Kochenderfer will serve as a PI for bluebird Phase 1 study of bb2121
- bb2121 on track to enter the clinic in early 2016
- Findings include:
 - As of November 11, patients with advanced multiple myeloma and a median of seven prior therapies have been treated with anti-BCMA CAR T cells at one of four dose levels
 - One patient at highest dose level achieved a stringent complete response within one month since infusion
 - One patient at highest dose level achieved a partial response with myeloma undetectable in bone marrow plasma cells within one month since infusion
 - Patients treated at highest dose levels experienced cytokine release syndrome; toxicity and side effects were mild at lower dose levels

bluebird bio's First Oncology Clinical Trial

CRB-401 (Refractory Multiple Myeloma)

U.S.-based, 6-10 clinical sites – including NCI

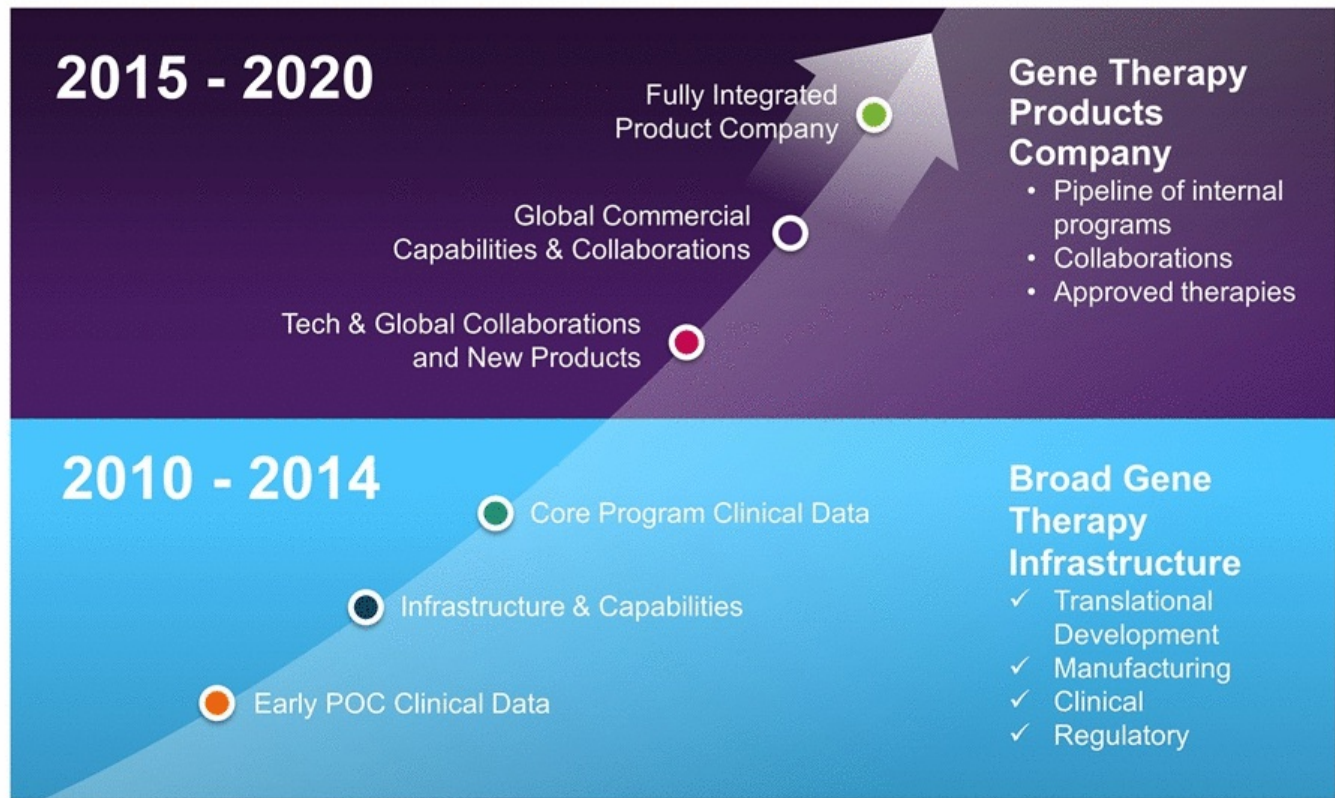
- N = 40 patients, standard 3+3 Design based on CAR+ T cells doses
- Primary endpoint = Determine the maximally tolerated dose and recommended phase 2 dose (RP2D)
- Subjects must have received 3 prior regimens including a proteasome inhibitor (bortezomib, carfilzomib) and immunomodulatory agent (lenalidomide, pomalidomide)
- Following screening, enrolled subjects will undergo a leukapheresis procedure to collect autologous mononuclear cells for manufacturing of bb2121.
- Following manufacture of the drug product, subjects will receive one cycle of lymphodepletion prior to bb2121 infusion

Deepening Pipeline

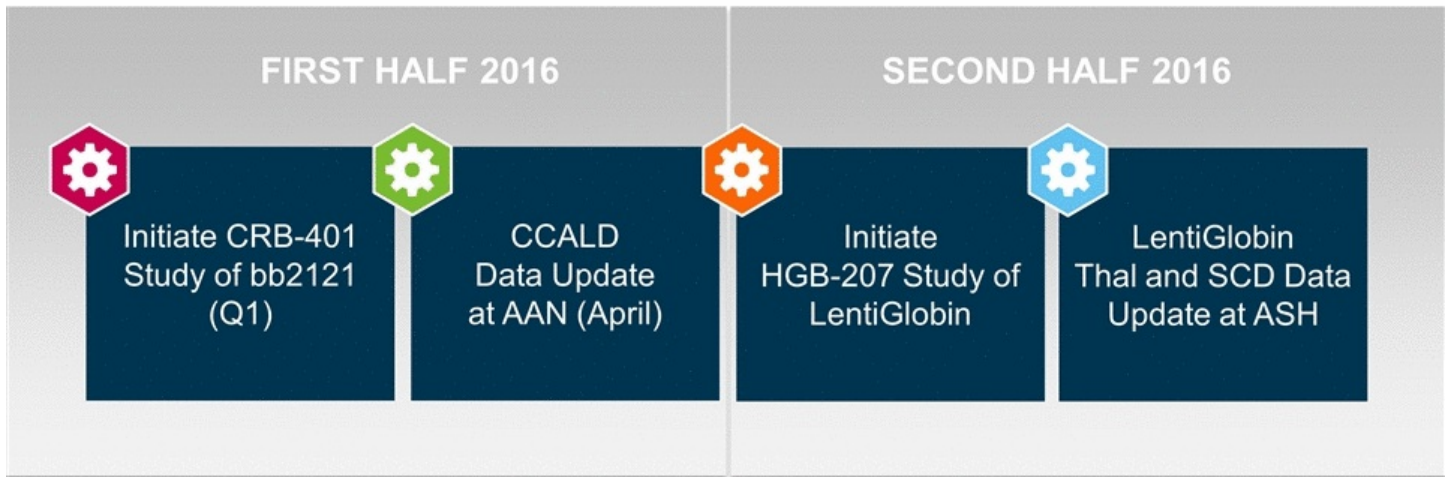
Product Candidates	Program Area	Preclinical	Phase 1/2	Phase 2/3	Rights/Partner	
Lenti-D™	CNS Diseases					
	Cerebral ALD				Worldwide	
LentiGlobin®	Rare Hemoglobinopathies					
	Beta-thalassemia Major*				Worldwide	
	Severe Sickle Cell Disease				Worldwide	
Oncology	bb2121 BCMA	Multiple Myeloma			Celgene	
		Next Gen BCMA	Multiple Myeloma		Celgene	
	Five Prime Target	Undisclosed			Worldwide	
	HPV-16 E6 TCR	HPV-associated Cancers			Kite Pharma	
	Viomed Target	Undisclosed			Worldwide excluding Korea	
	Other Programs	Undisclosed			Worldwide	
	Research	Early Pipeline	Undisclosed + Gene Editing			Worldwide

* The current clinical trials for LentiGlobin are Phase 1/2 studies that may provide the basis for early conditional approval in some jurisdictions

bluebird bio 2020: The Gene Therapy Products Company



Anticipated Significant 2016 Milestones



Cash Runway Through 2018



bluebirdbio®

Making Hope a Reality

Transforming the Lives of Patients
with Severe Genetic and Rare Diseases

Nasdaq : BLUE
