NCPO

2015 National Conference of Pharmaceutical Organizations

January 8-10, 2015 | St. Regis Bahia Resort, Puerto Rico

Promise for Healthcare: New Directions in Pharmaceutical Research

bluebirdbio™

Faraz Ali
Vice President, Global Commercial Development and External Affairs
January 10, 2015

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.

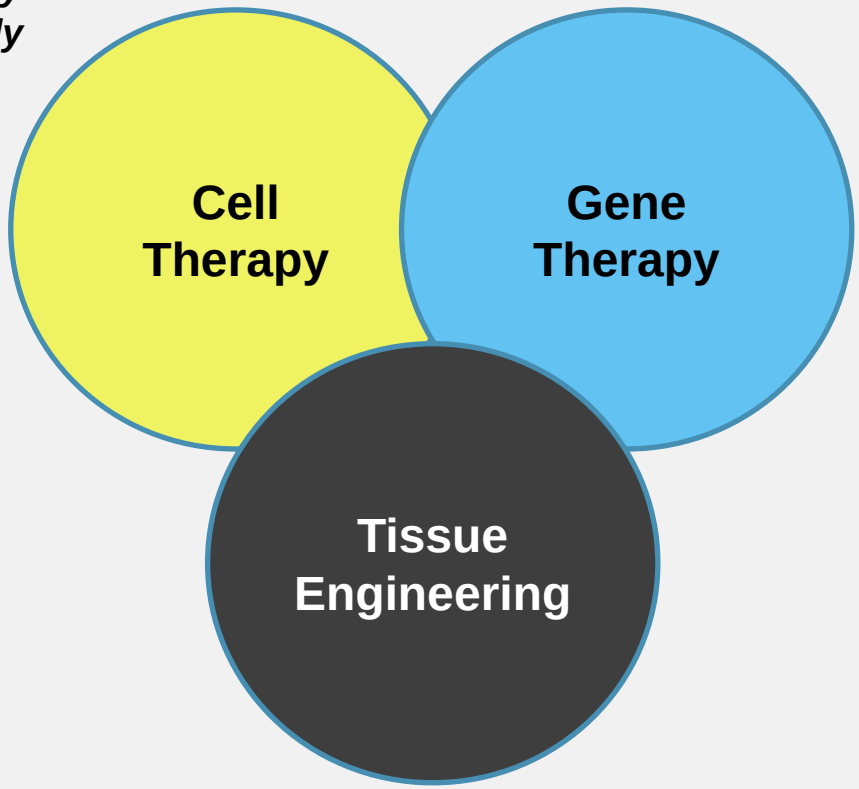
Agenda

1. Regenerative Medicine Overview
2. bluebird bio Overview
3. Potential Implications for Biopharmaceutical Industry
4. Questions and Discussion

The Coming Wave of Regenerative Medicine

What is “Regenerative Medicine”?

Using cells therapeutically to repair function to bodily tissue or organs.



Inserting or editing genes in patients cells or tissues to treat diseases that are linked to defective or mutated genes needing either correction or improved regulation.

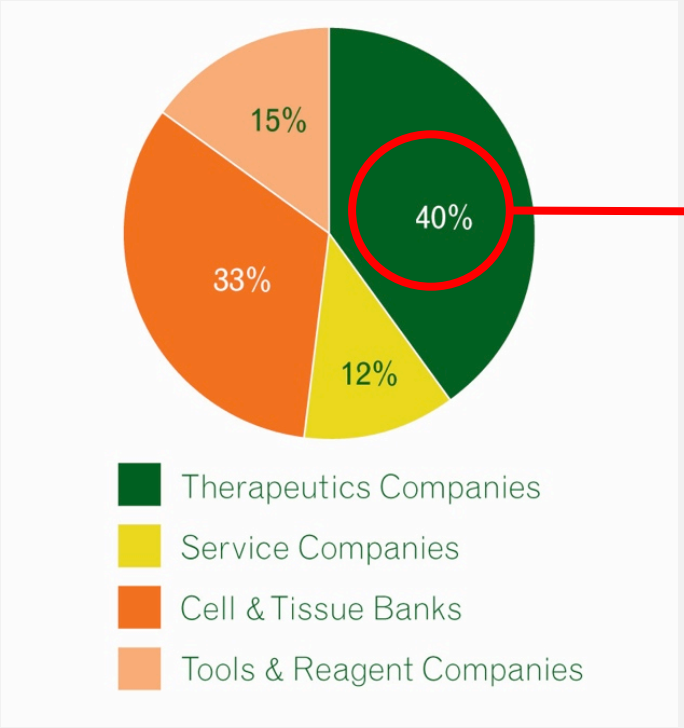
Creating new organs, and tissues to replace or repair existing organ function

Source: ARM 2013 Annual Report

Regenerative Medicine Industry Overview

The Regenerative Medicine (RM) industry comprises service and manufacturing companies, tools and non-therapeutic products, cell, gene and tissue based therapies, regenerative compounds, devices and biopharmaceuticals.

Regenerative Medicine Industry Sectors

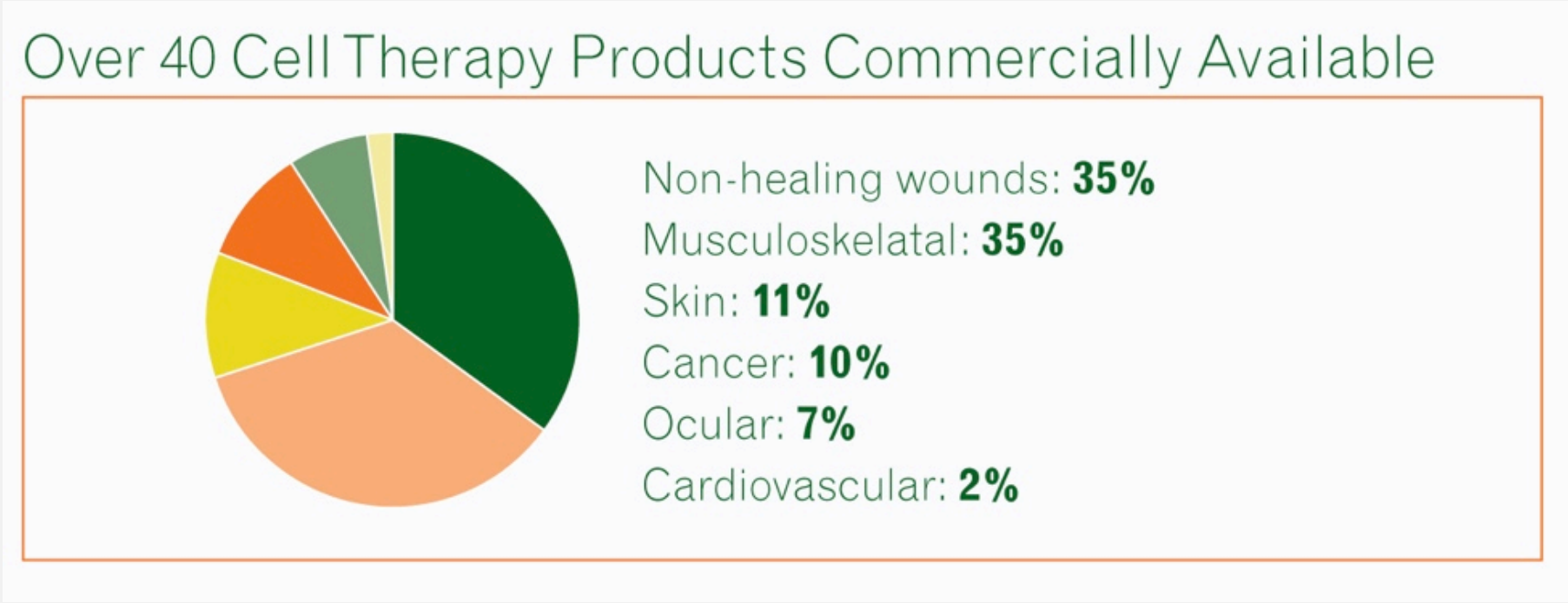


Source: ARM 2013 Annual Report

- Cell therapy companies 60%
- Tissue engineering companies 27%
- Gene therapy companies 8%
- Small mol/biologics companies 5%

Cell Therapies and Tissue Engineering

Most early commercial experience is with cell therapies and tissue engineering products



Source: ARM 2013 Annual Report

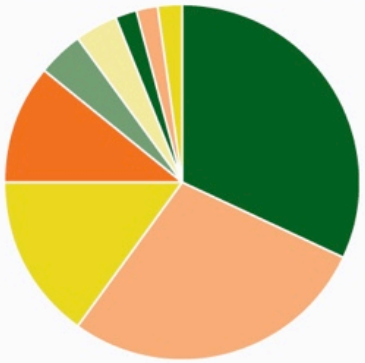
Cell Therapies and Tissue Engineering Drug Development

Healthy pipeline of cell therapy and tissue engineering drug products

Ongoing Industry-Sponsored Cell Therapy Trials by Phase

54 Late-Stage	209 Mid-Stage	63 Early-Stage
43 companies	*114 companies*	*49 companies*

Currently in Late-Stage Industry-Sponsored Cell Therapy Trials (Phase 2/3, 3, pivotal)

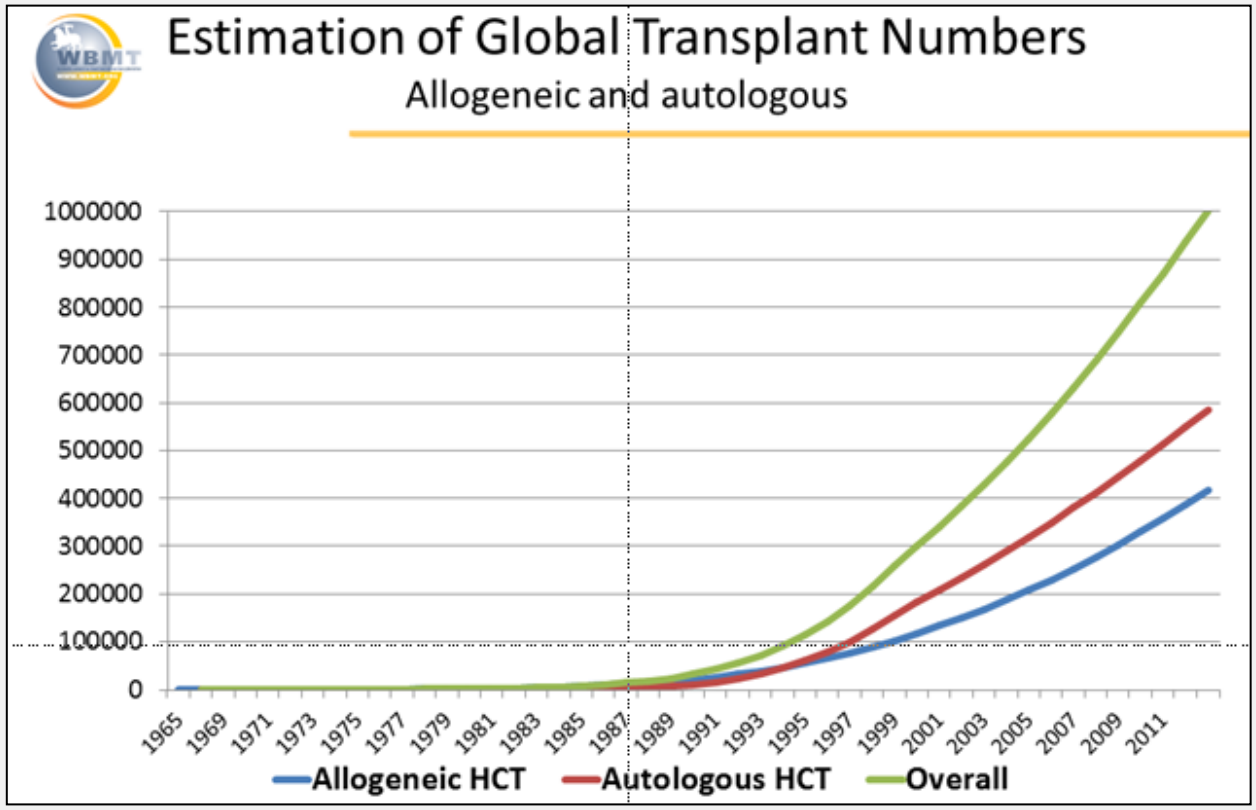


Cancer: **32%**
Musculoskeletal: **28%**
Non-healing wounds: **15%**
Cardiovascular: **11%**
AutoImmune: **4%**
Ocular: **4%**
Stoke: **2%**
Skin: **2%**
Other **2%**

Source: ARM 2013 Annual Report

Cell Therapies and Tissue Engineering Drug Development

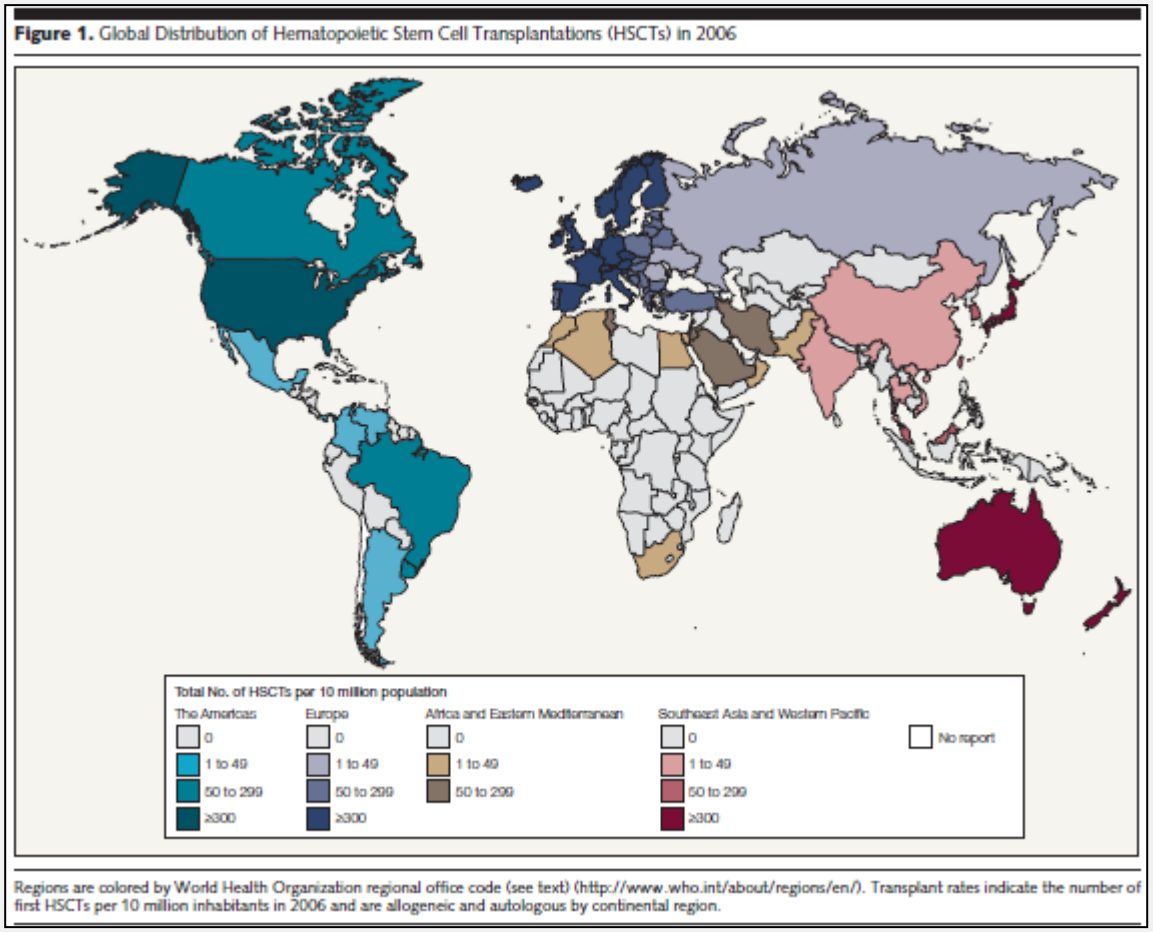
Growth of “curative” hematopoietic stem cell transplantation (HSCT) procedures



- Recent estimates that 1MM patients have been treated globally (recent volume ~50K/year)
- 70 indications, but volume primarily driven by oncology

Cell Therapies and Tissue Engineering Drug Development

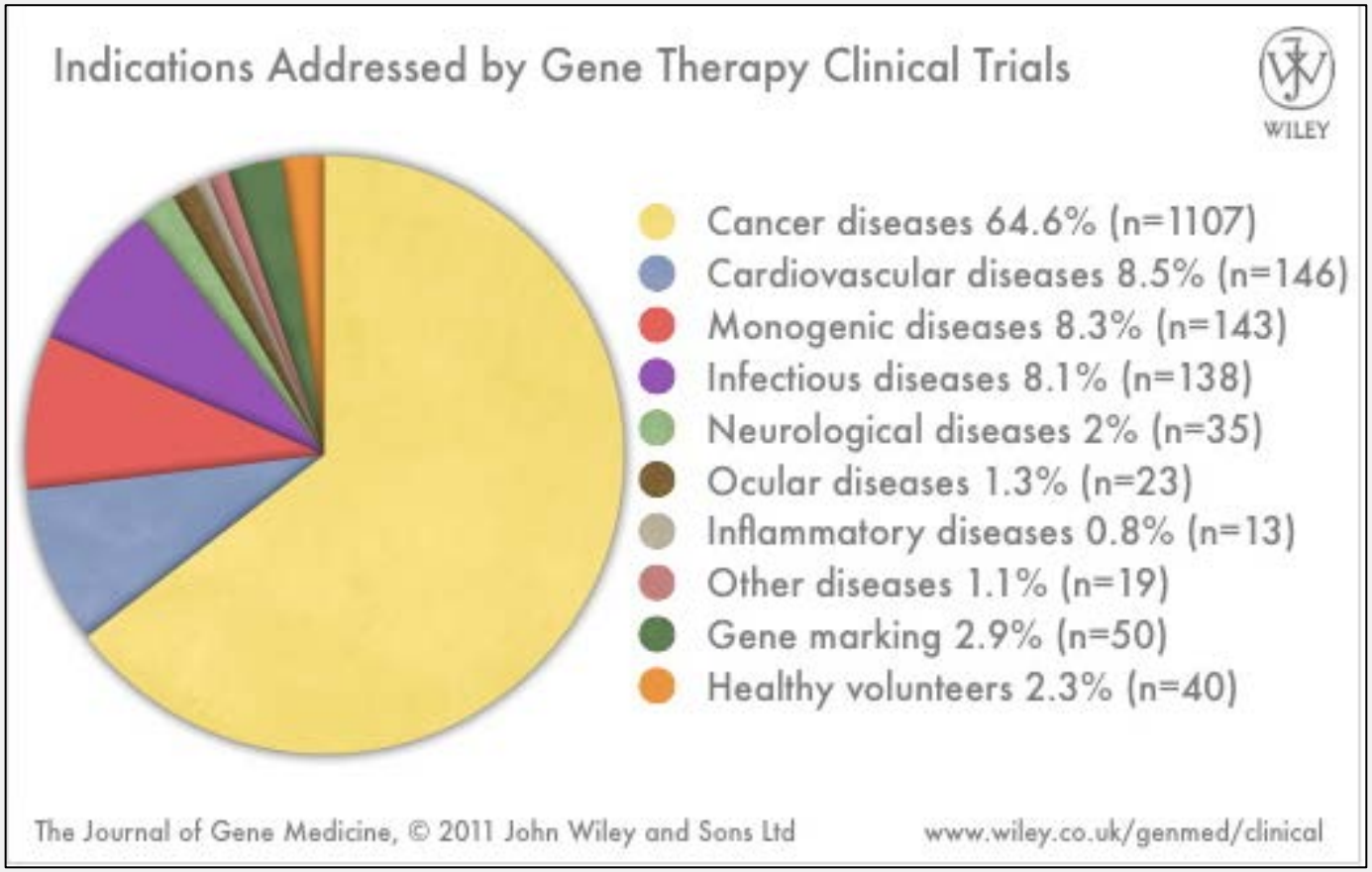
Global adoption of “curative” hematopoietic stem cell transplantation (HSCT) procedures



- 177 centers total in US
- Surprisingly high adoption developing world, despite resource limitations
- Growing emphasis on enabling more, e.g. via establishment of national and international marrow and cord blood registries

Gene Therapy Drug Development

2000+ gene therapy clinical studies conducted to date



The Promise of Regenerative Medicine

Results illustrate this is no longer the stuff science fiction

*Clinical Data Maturing**

Lenti

ALD N=5

Science 2009

Hematopoietic Stem Cell Gene Therapy with a Lentiviral Vector in X-Linked Adrenoleukodystrophy

Lenti

B-Thal N=7

nature September 2010

Transfusion independence and *HMGA2* activation after gene therapy of human β-thalassaemia

AAV

Hem B N=14

The NEW ENGLAND JOURNAL of MEDICINE

Adenovirus-Associated Virus Vector–Mediated Gene Transfer in Hemophilia B

Lenti

MLD N=9

Science 2013

Therapeutic Benefit in Metachromatic Leukodystrophy by Lentiviral Hematopoietic Stem Cell Gene Therapy

Lenti

WAS N=12

Science 2013

Lentiviral Hematopoietic Stem Cell Gene Therapy in Patients with Wiskott-Aldrich Syndrome

Lenti

ALL&CLL N=>100

The NEW ENGLAND JOURNAL of MEDICINE

Chimeric Antigen Receptor–Modified T Cells in Chronic Lymphoid Leukemia

* Patient numbers reflect aggregate patients treated by indication as of ESGCT 2013

The Promise of Regenerative Medicine

Results attracting attention from media

The New York Times

"All the News That's Fit to Print"

NEW YORK, MONDAY, DECEMBER 30, 2012

In Girl's Last Hope, Altered Cells Beat Leukemia

sky NEWS

Search Sky News

Home UK World US Business Politics Technology Entertainment Strange News Weather More Watch Live

sky

Believe in better

Gene Therapy Breakthrough Could 'Cure' Blindness

Doctors who injected a genetically-modified virus into the eyes of blind patients discover it significantly improves their sight.

07:33, UK, Thursday 16 January 2014

WGNtv.com CHICAGO'S VERY OWN

NEWS MORNING NEWS MIDDAY NEWS SPORTS SHOWS WATCH LIVE WEATHER

Gene replacement could replace need for life-long blood transfusions

POSTED 8:21 PM, DECEMBER 30, 2014, BY KATHARIN CZINK AND DINA BAIR, *UPDATED AT 09:47PM, DECEMBER 30, 2014*

Bloomberg

News Quick Markets Personal Finance Tech U.S. Politics Sustainability

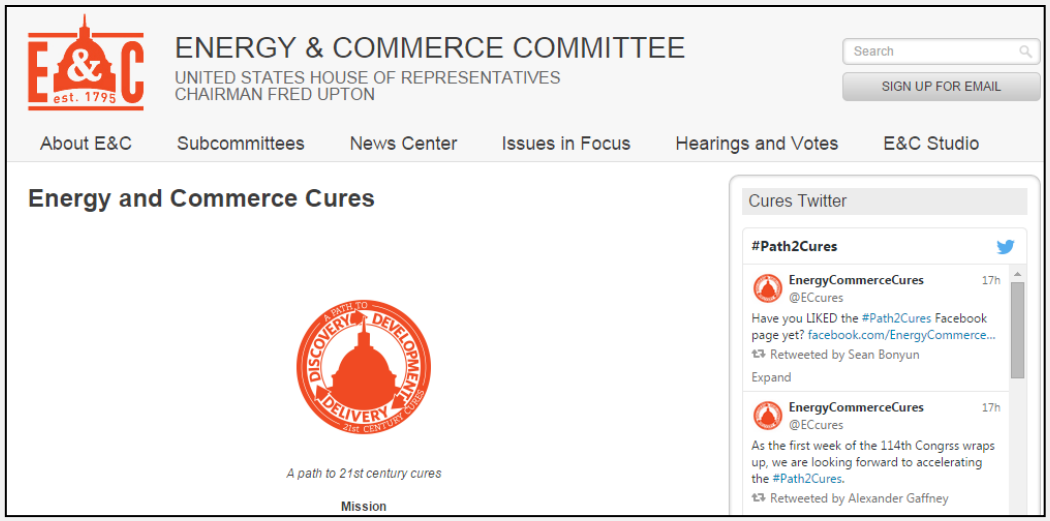
[redacted]

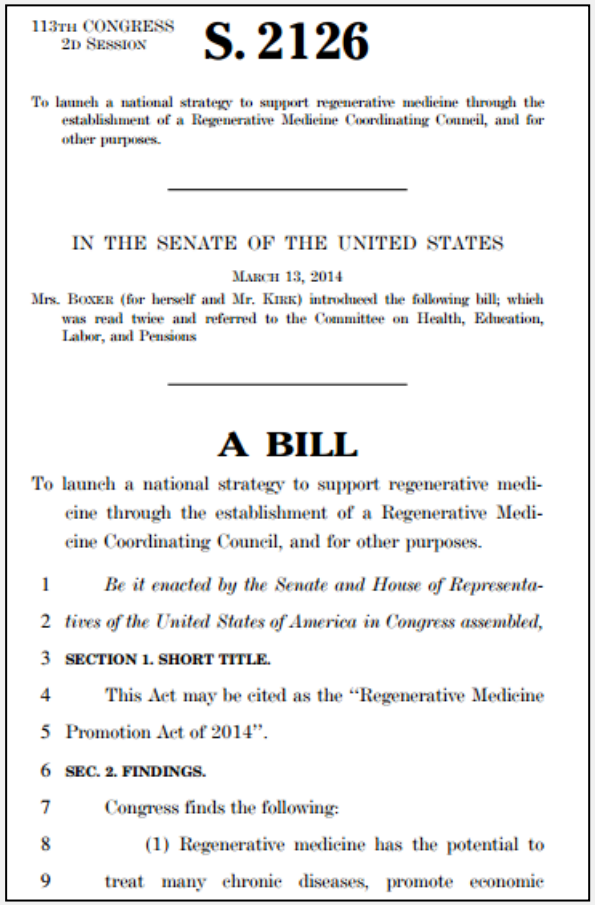
Can You Really Reverse Hearing Loss? Drugmakers Try Gene Therapy

Save + By Simeon Bennett | Jan 7, 2015 7:00 PM ET | 12 Comments Email Print

The Promise of Regenerative Medicine

Results attracting attention from policy makers





113TH CONGRESS
2D SESSION

S. 2126

To launch a national strategy to support regenerative medicine through the establishment of a Regenerative Medicine Coordinating Council, and for other purposes.

IN THE SENATE OF THE UNITED STATES

MARCH 13, 2014

Mrs. BOXER (for herself and Mr. KIRK) introduced the following bill; which was read twice and referred to the Committee on Health, Education, Labor, and Pensions

---

A BILL

To launch a national strategy to support regenerative medicine through the establishment of a Regenerative Medicine Coordinating Council, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "Regenerative Medicine Promotion Act of 2014".

SEC. 2. FINDINGS.

Congress finds the following:

(1) Regenerative medicine has the potential to treat many chronic diseases, promote economic

The Promise of Regenerative Medicine

Results attracting investor attention

Introduction to bluebird bio

Why We Do What We Do

Ethan

Aidan

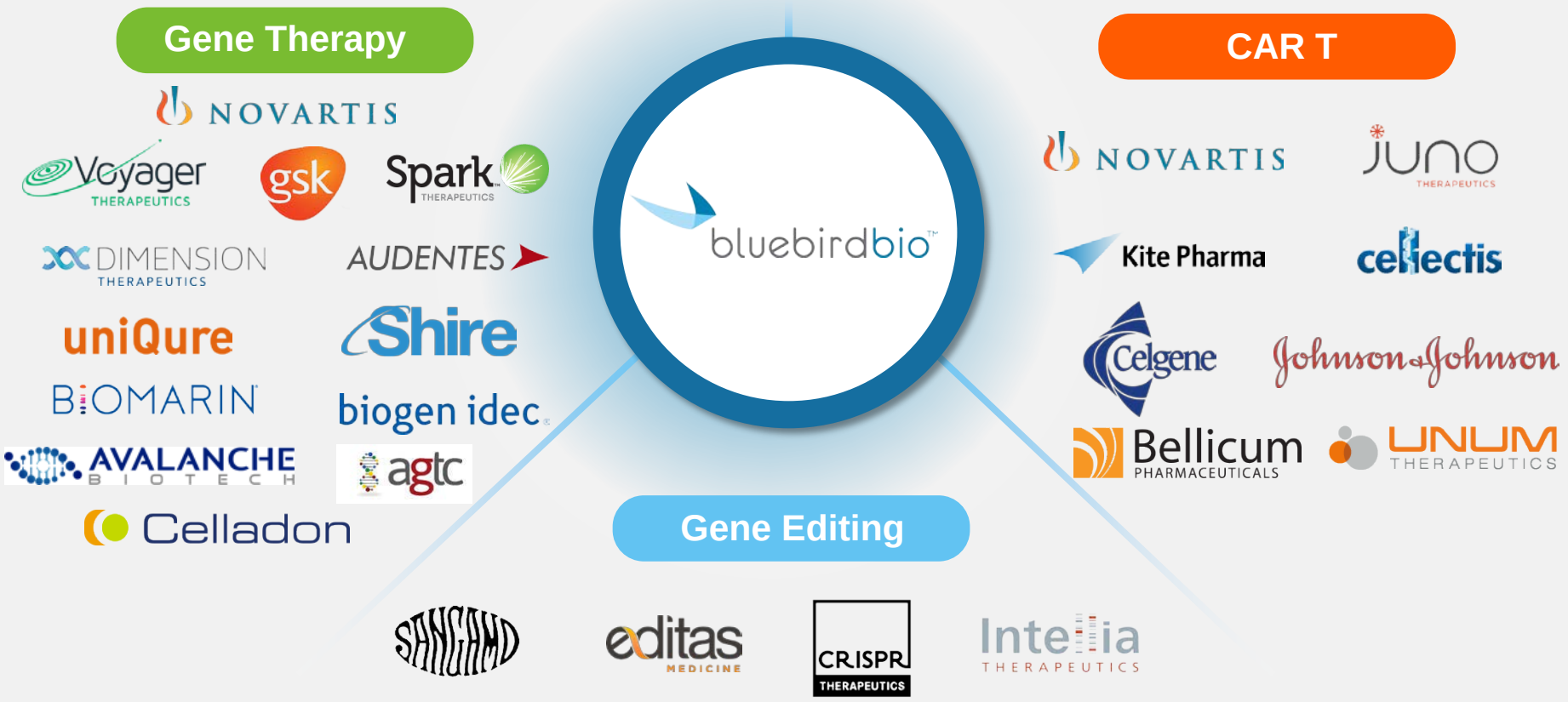
Cameron

Our Vision – Make Hope a Reality

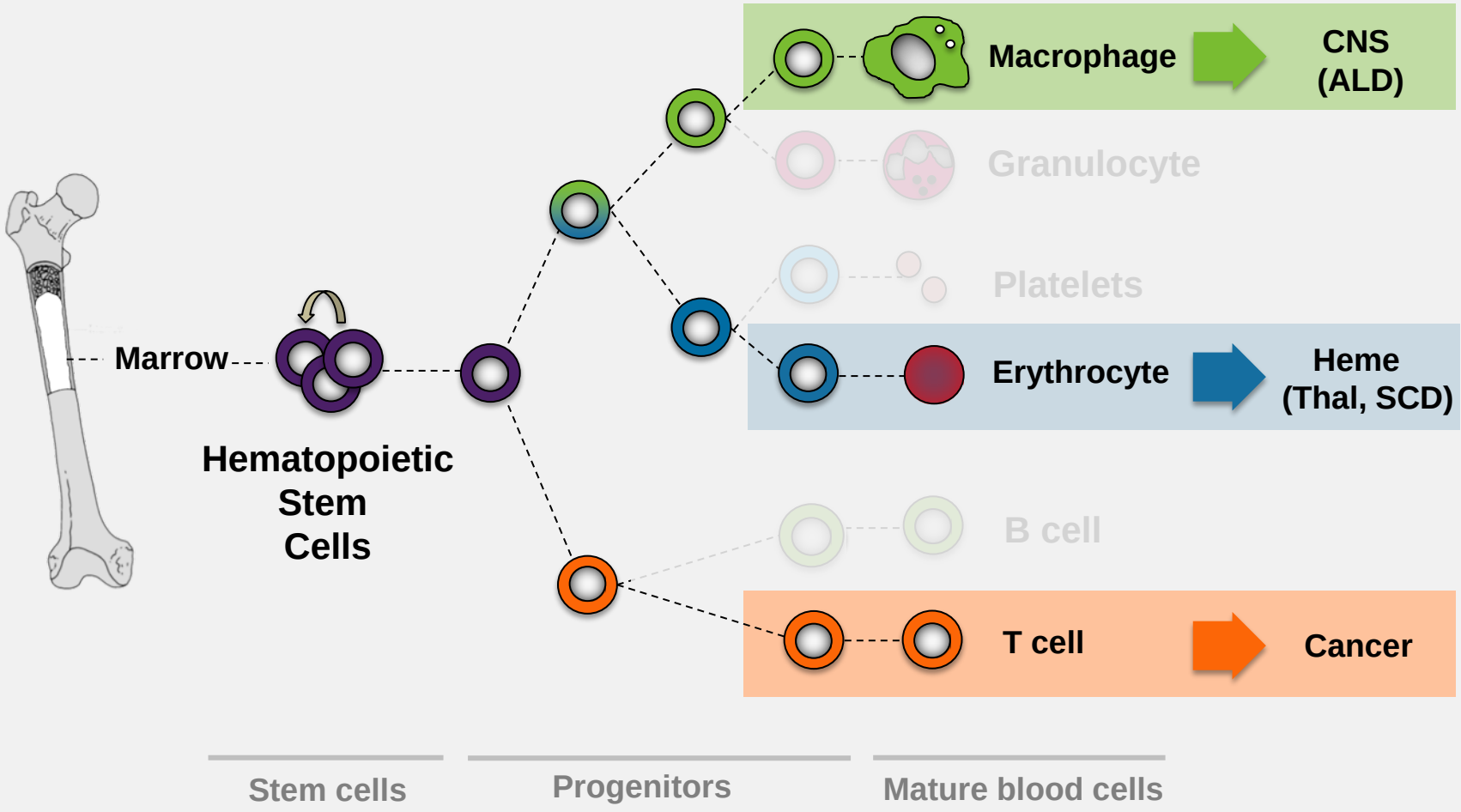
Seeking to transform the lives of patients with severe genetic and orphan diseases through the development of innovative gene therapy products.

Leading Gene Therapy For The Long-Term

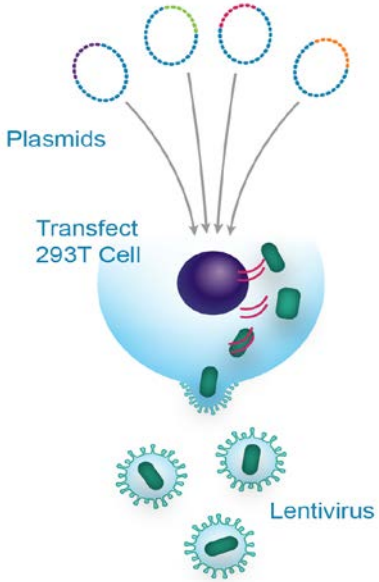
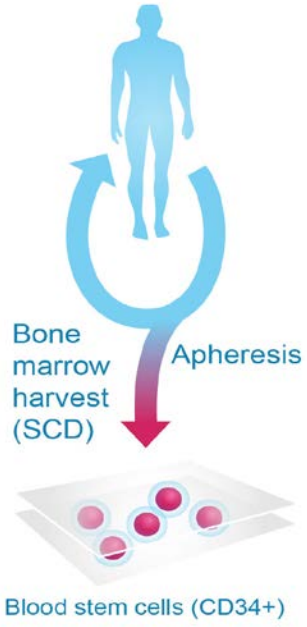
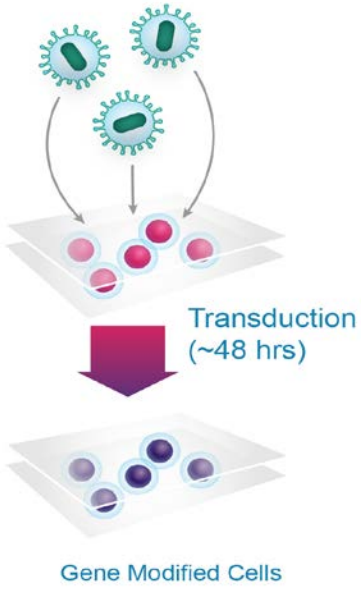
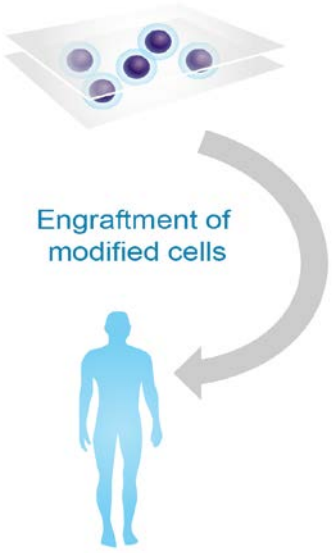
Integrated Product Platforms with Broad Therapeutic Potential



Lentiviral Stem Cell Platform



How Our Gene Therapy Approach Works

1	2	3	4
Produce Virus With Therapeutic Payload	Isolate Target Cells From Patient	Transduce Target Cells *ex vivo*	Test & Re-infuse Gene Modified Cells
			
	2 Weeks	<1 Week	4-6 Weeks (when ready)

Investments in Product Enhancements

- Improved process
- Selective vector changes

Results

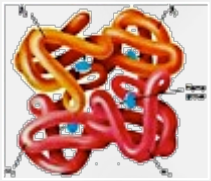
- ✓ 25-30-fold reduction in non-infectious viral particles
- ✓ 3x vector copy number increase

bluebird bio Pipeline

Products	Program Area	Preclinical	Phase 1/2	Phase 2/3	Rights	Milestones
	CNS Diseases					
Lenti-D	Childhood Cerebral ALD – Starbeam Study*				Worldwide	Complete enrollment
	Hematologic Diseases					
LentiGlobin™	β-thalassemia/SCD (France) – HGB-205 Study**				Worldwide	Complete enrollment & present data
	β-thalassemia (U.S./Thailand/Australia) – Northstar Study**					Complete enrollment, present data & define regulatory path
	Sickle Cell Disease (U.S.) – HGB-206 Study					Enroll patients & present data
	Oncology					
CAR T Cells	Hematologic/Solid Tumors				Global Celgene Collaboration	Initiate clinical study in early 2016
	Research					
Early Pipeline	Undisclosed + Gene Editing				Worldwide	Advance preclinical pipeline

* The Phase 2/3 Starbeam Study is our first clinical study of our current Lenti-D viral vector and product candidate
** The Phase 1/2 HGB-205 and Northstar Studies are our first clinical studies of our current LentiGlobin viral vector and product candidate

β-thalassemia Major: Disease Overview



Disease

- β-thalassemia major (e.g. transfusion-dependent)
- Monogenic, severe anemia
- Loss of or reduced β-globin production
- Poor quality of life and shortened lifespan

Current Treatments

- Frequent, chronic transfusions leading to iron overload and organ failure
- Ongoing iron chelation, frequently suboptimal
- Allogeneic transplant can be curative (rarely used)
  - Finding a suitable match
  - Morbidity/mortality with graft rejection, graft versus host disease and immunosuppression

Epidemiology

- Global prevalence ~288K; incidence ~60K
- US/EU prevalence (treated) ~15K; incidence ~1.5K
  - 60-80% severe/major
- Affects people of Mediterranean, Middle Eastern, South Asian and SE Asian descent

β-thalassemia: Clinical Trial Summary
Second Generation BB305 Vector

NORTHSTAR STUDY

(HGB-204)

Phase 1/2, multi-center, global study

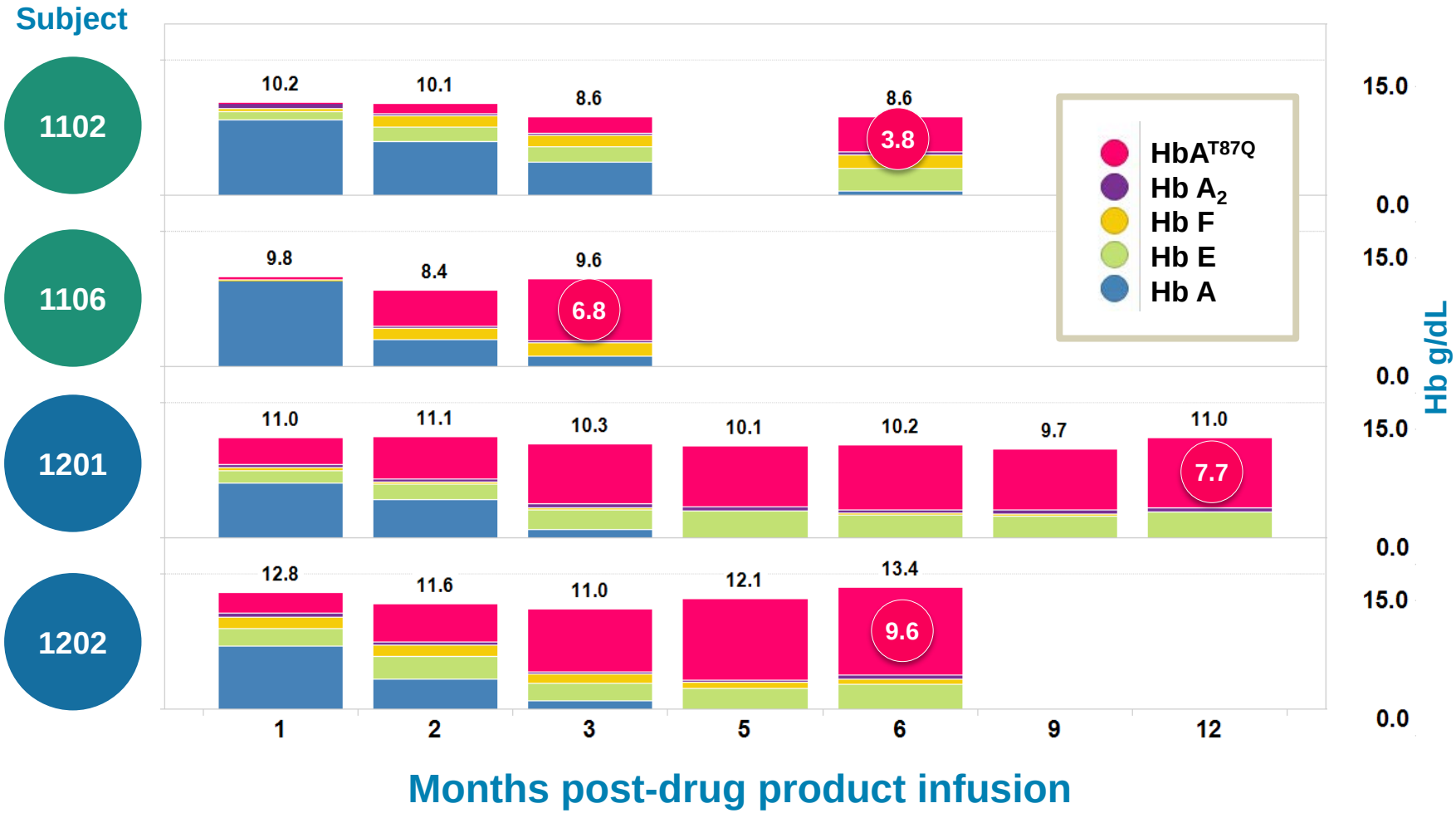
- N=15 patients
- Centralized transduction for drug product manufacturing
- Positive data presented at ASH 2014 annual meeting
- Enrollment completion expected in 2015

HGB-205

Phase 1/2, single-center, French study

- N=7 patients
- Positive data presented at ASH 2014 annual meeting
- First SCD patient ever treated with gene therapy in 2014
- Enrollment completion expected in 2015

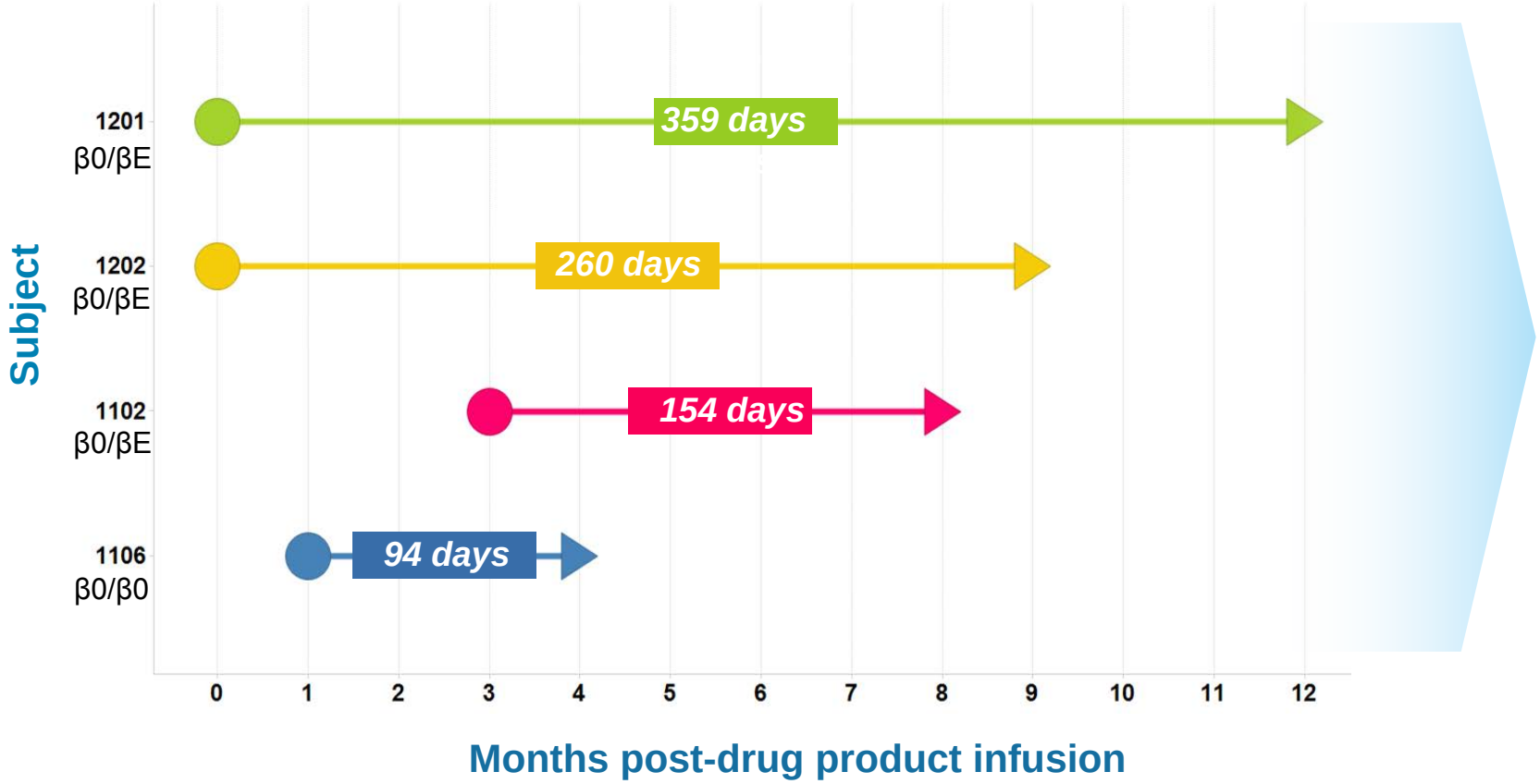
Consistently Robust βA-T87Q-globin Levels



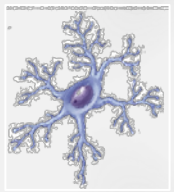
All Subjects with at Least 3 Months of Follow-up are Transfusion-Free, Regardless of Genotype

Days Transfusion-Free

as of December 1, 2014



Childhood Cerebral Adrenoleukodystrophy (CCALD): Disease Overview



Disease

- Ultra-orphan, X-linked, monogenic, neurological disorder
- Mutated ABCD1 peroxisomal transporter results in toxic buildup of very long chain fatty acids (VLCFA)
- Leads to cerebral inflammation & demyelination

Current Treatments

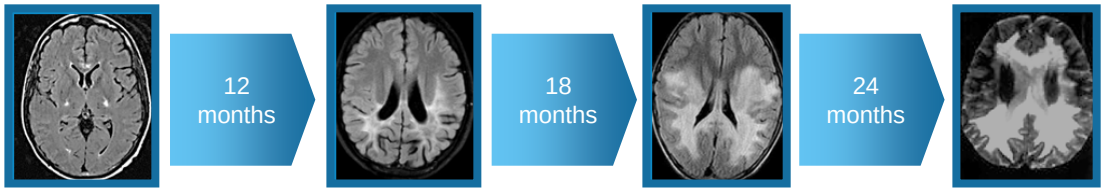
- Untreated cerebral ALD leads to dismal outcomes (vegetative state and death)
- Allogeneic stem cell transplant standard for CCALD (if possible)

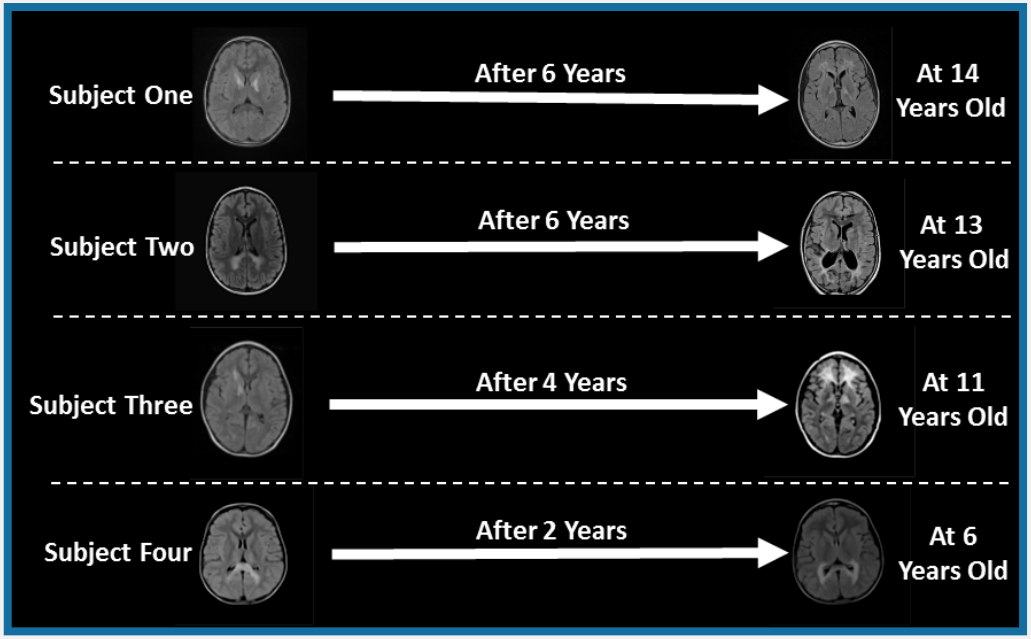
Epidemiology

- CCALD 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 5% of ALD

Promising Clinical Data – CCALD (TG04.06.01) Study

Natural Course of Disease



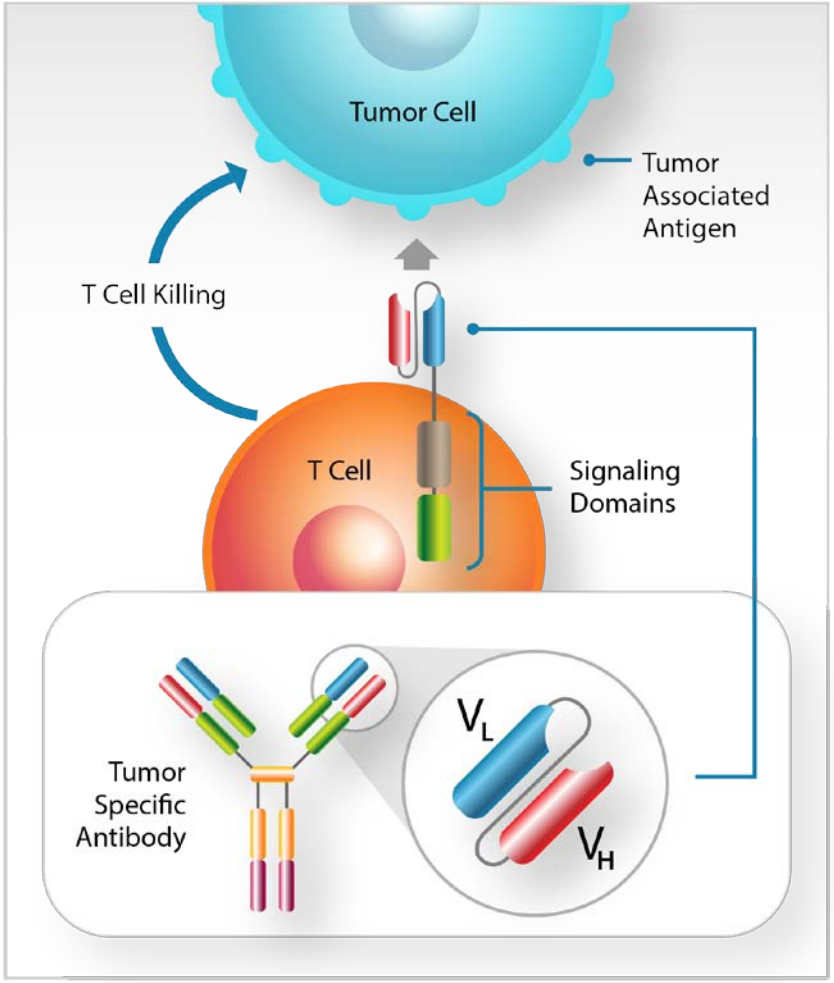


*NFS – Neurological Function Score
**Gad – gadolinium enhancement

- NFS* / Loes stable in all subjects, as of last follow up
- Gad** resolved in 3 out of 4 subjects
- Efficacy results comparable to allogeneic transplant
- No gene therapy-related adverse events

Chimeric antigen receptor (CAR) T Cell Overview

- For years, the standard of care for treating cancer has been surgery, chemotherapy and radiation
- CAR T cell therapy represents a promising emerging approach to treating a variety of cancers
  - Clear clinical POC with CD19 antigen
- Uses patient's own genetically modified T cells to selectively target and destroy cancer cells
- Provides potentially curative option after other treatment approaches have failed



bluebird's CAR T Program

Collaboration Highlights

- ✓ Signed in 2013 with goal of entering clinic in 3 years
- ✓ $75M upfront payment; 3 years (extensions possible for up to an additional 3 years)
- ✓ bluebird right to 50/50 co-develop, co-promote and profit share in the US
- ✓ bluebird is responsible through Phase 1
- Anticipate entering clinic by early 2016

Our Strategic Intent

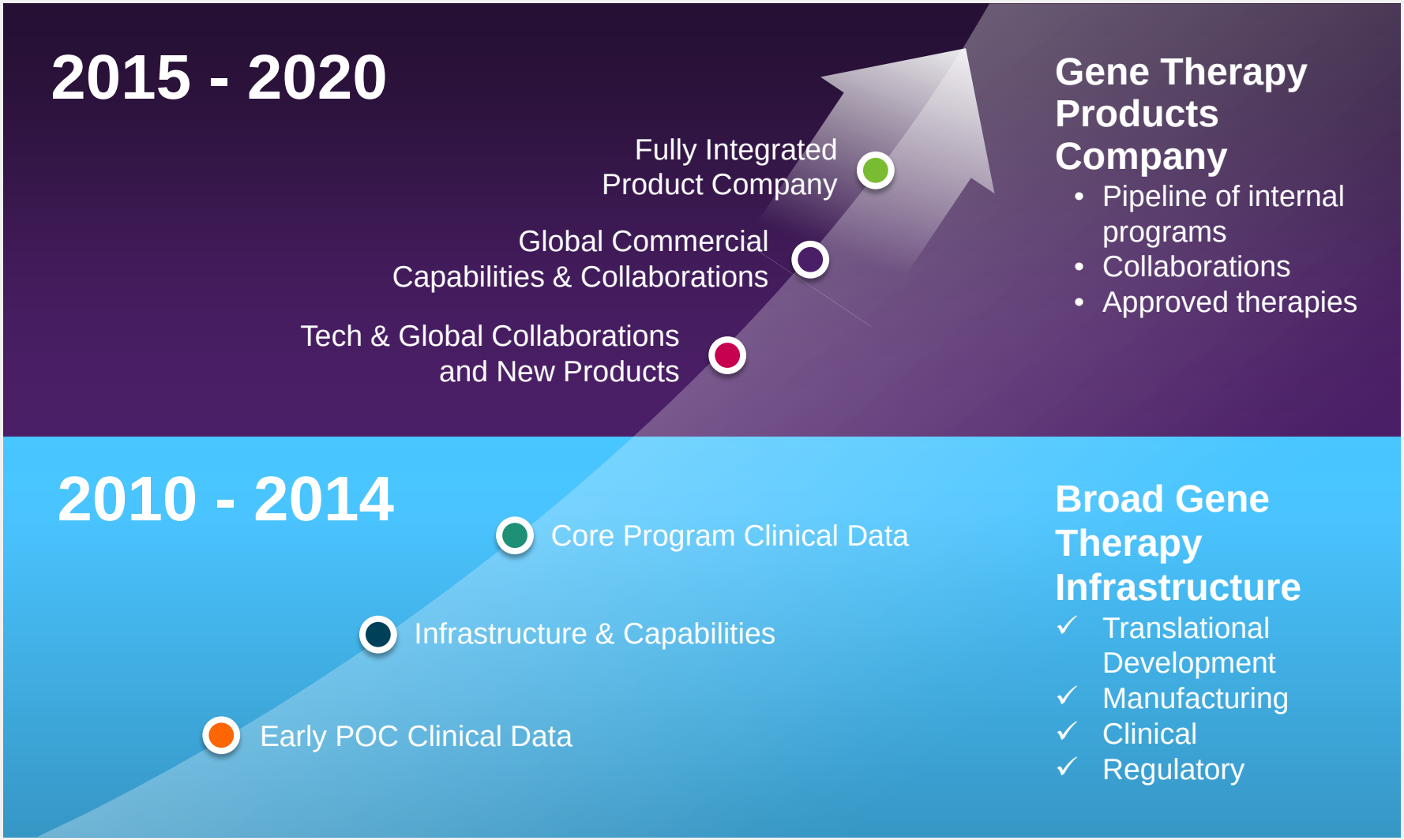
Severe Genetic Diseases
Hematopoietic Stem Cells (HSCs)

Immunotherapy
T Cells

- ***Lentiviral Gene Delivery –*** *High Quality and Large Scale*
- ***Cellular Transduction Capabilities –*** *Global*
- ***Gene Editing –*** *MegaTALs/Homing Endonucleases*

- **Deliver** transformative data in the clinic on a **global** scale
- Advance **SGD** and **immunotherapy** products through late stage clinical trials
- Leverage, integrate and grow **core technologies** to **build a pipeline and collaborations** for the long-term
- **Engage** with **regulatory** authorities and **payers** to chart the course for one-time transformative therapies

bluebird bio 2020: The Gene Therapy Products Company



Implications

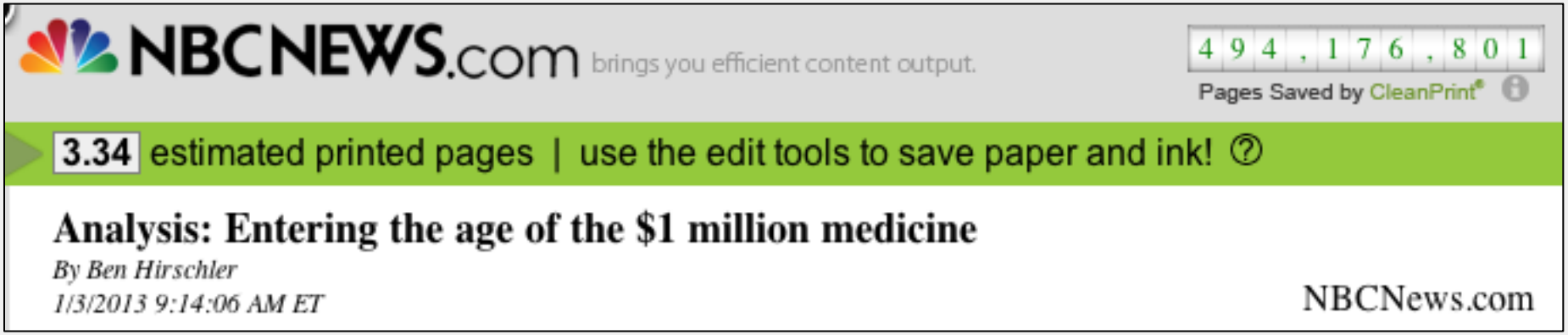
"Curative" Therapies Represent a Potentially Dramatic Paradigm Shift

Typical Chronic Therapies		Gene Therapy
• Address disease symptoms	→	• Potentially "curative"
• One size fits all	→	• Patient's own cells → ultimate "personalized medicine"

• Daily/Weekly/bi-weekly/monthly tx
  • Adherence issues
  • Quality of life impact
	→	• One-time tx with durable response
		  • Adherence irrelevant
		  • Patient convenience

• Significant additional costs to healthcare system over patient lifetime	→	• Potential savings to healthcare system over patient lifetime
• Adjustments can be made over time to optimize tx (e.g. dose, formulation) • Possible to discontinue or switch to alternative if failure to respond	→	• Irreversible treatment that cannot be adjusted or removed once done

Media Response to the Promise of Curative Therapies


NBCNEWS.com brings you efficient content output.

494,176,801
Pages Saved by CleanPrint®

3.34 estimated printed pages | use the edit tools to save paper and ink!

Analysis: Entering the age of the $1 million medicine

By Ben Hirschler
1/3/2013 9:14:06 AM ET

NBCNews.com

"The Western world's first drug to fix faulty genes promises to transform the lives of patients with an ultra-rare disease that clogs their blood with fat. The only snag is the price."

"In the case of gene therapy, extreme pricing may be unavoidable, since a single dose could last a lifetime, giving any drug manufacturer just one shot at recouping its investment."

"It's unsustainable."

"There are signs payers are pushing back."

"Scrutiny of the sky-high prices charged for this wave of new drugs is growing."

Media Response to the Promise of Curative Therapies


THE WALL STREET JOURNAL.

BUSINESS

Senate Committee Is Investigating Pricing of Hepatitis C Drug

Gilead Charges $84,000 for a Standard 12-Week Regimen of Sovaldi


The Washington Post

Wonkblog

The drug that's forcing America's most important – and uncomfortable – health-care debate


Forbes

PHARMA & HEALTHCARE 4/28/2014 @ 8:00AM | 19,613 views

At $1,000 A Pill, Hepatitis C Drug Sovaldi Rattles Medicaid Programs

Need to Better Communicate VALUE

The potential savings from regenerative medicine treatments for the United States in terms of reducing the direct costs associated with chronic diseases have been estimated at approximately $250 billion per year.

Cardiovascular Disease
- 100 million U.S. people afflicted
- $316 billion – U.S. aggregate direct costs

Diabetes
- 25 million U.S. people afflicted
- $175 billion – U.S. aggregate direct costs

Stroke
- 795 thousand U.S. people afflicted each year
- $73 billion – U.S. aggregate direct costs

Alzheimer's Disease
- 35.6 million U.S. people living with the disease
- $200 billion – U.S. aggregate direct costs

Age-related Macular Degeneration
- 1.8 million U.S. people afflicted
- $255 billion – global direct costs

Parkinson's Disease
- 1 million + U.S. people afflicted
- $23 billion – U.S. aggregate direct costs

Spinal Cord Injury
- 275 thousand U.S. people afflicted
- $40.5 billion – U.S. aggregate direct costs

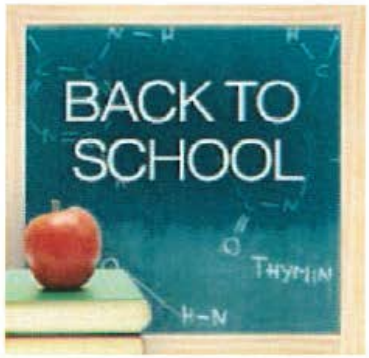
Peripheral Arterial Disease (PAD)
- 10 million U.S. people afflicted
- $4.4 billion – U.S. aggregate direct costs

Source: ARM Annual Report

Need to Better Communicate VALUE

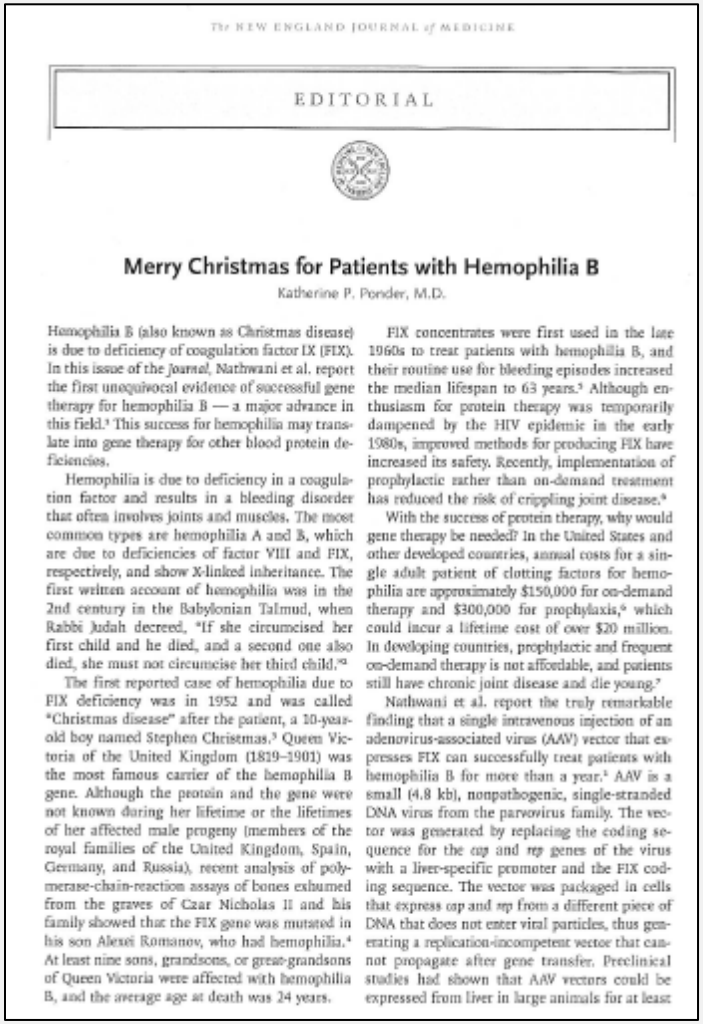
BioCentury™

STRATEGY



APPROACHES THAT SET PRICES BASED ON THE PROMISE OF OUTCOMES REMOVE THE COSTS OF R&D AND MANUFACTURING FROM THE EQUATION, AND FOCUS ALL STAKEHOLDERS ON VALUE.

Regenerative Medicine Illustrates How Biopharma is Prepared to Disrupt Itself



The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

Merry Christmas for Patients with Hemophilia B

Katherine P. Ponder, M.D.

Hemophilia B (also known as Christmas disease) is due to deficiency of coagulation factor IX (FIX). In this issue of the *Journal*, Nathwani et al. report the first unequivocal evidence of successful gene therapy for hemophilia B — a major advance in this field.[1] This success for hemophilia may translate into gene therapy for other blood protein deficiencies.

Hemophilia is due to deficiency in a coagulation factor and results in a bleeding disorder that often involves joints and muscles. The most common types are hemophilia A and B, which are due to deficiencies of factor VIII and FIX, respectively, and show X-linked inheritance. The first written account of hemophilia was in the 2nd century in the Babylonian Talmud, when Rabbi Judah decreed, "If she circumcised her first child and he died, and a second one also died, she must not circumcise her third child."[2]

The first reported case of hemophilia due to FIX deficiency was in 1952 and was called "Christmas disease" after the patient, a 10-year-old boy named Stephen Christmas.[3] Queen Victoria of the United Kingdom (1819–1901) was the most famous carrier of the hemophilia B gene. Although the protein and the gene were not known during her lifetime or the lifetimes of her affected male progeny (members of the royal families of the United Kingdom, Spain, Germany, and Russia), recent analysis of polymerase-chain-reaction assays of bones exhumed from the graves of Czar Nicholas II and his family showed that the FIX gene was mutated in his son Alexei Romanov, who had hemophilia.[4] At least nine sons, grandsons, or great-grandsons of Queen Victoria were affected with hemophilia B, and the average age at death was 24 years.

FIX concentrates were first used in the late 1960s to treat patients with hemophilia B, and their routine use for bleeding episodes increased the median lifespan to 63 years.[5] Although enthusiasm for protein therapy was temporarily dampened by the HIV epidemic in the early 1980s, improved methods for producing FIX have increased its safety. Recently, implementation of prophylactic rather than on-demand treatment has reduced the risk of crippling joint disease.[6]

With the success of protein therapy, why would gene therapy be needed? In the United States and other developed countries, annual costs for a single adult patient of clotting factors for hemophilia are approximately $150,000 for on-demand therapy and $300,000 for prophylaxis,[6] which could incur a lifetime cost of over $20 million. In developing countries, prophylactic and frequent on-demand therapy is not affordable, and patients still have chronic joint disease and die young.[7]

Nathwani et al. report the truly remarkable finding that a single intravenous injection of an adenovirus-associated virus (AAV) vector that expresses FIX can successfully treat patients with hemophilia B for more than a year.[1] AAV is a small (4.8 kb), nonpathogenic, single-stranded DNA virus from the parvovirus family. The vector was generated by replacing the coding sequence for the *cap* and *rep* genes of the virus with a liver-specific promoter and the FIX coding sequence. The vector was packaged in cells that express *cap* and *rep* from a different piece of DNA that does not enter viral particles, thus generating a replication-incompetent vector that cannot propagate after gene transfer. Preclinical studies had shown that AAV vectors could be expressed from liver in large animals for at least

Source: Ponder, *NEJM*, 2011

"With the success of protein therapy, why would gene therapy be needed?

In the United States and other developed countries, annual costs for a single adult patient of clotting factors for hemophilia are approximately $150,000 for on-demand therapy and $300,000 for prophylaxis, which could incur a lifetime cost of over $20MM.

This technology may soon translate into applications for other disorders."

Sickle Cell Disease (SCD): Gene Therapy Value Proposition vs Standard of Care

- SCD lifetime cost of care estimated by one KOL to be $8.75MM
- Annual costs for care escalate dramatically as patient ages and disease progresses
- Research with physicians and payers illustrates dissatisfaction with current treatment options

TABLE III. Fees for Life Care Plan for a Patient with Sickle Cell Anemia Based on An Assumption of 50 Year Life Expectancy

Period	Annual Fees	Total Fees/Period
1. Age 0 – 5 years	$35,488	$177,439.00
2. Age 6 – 10 years	$56,576	$282,879.00
3. Age 11 – 18 years	$111,749	$893,990.00
4. Age 19 – 50 years	$231,050	$7,393,600.00
Total for life		$8,747,908.00

Source: Ballas, *AJH*, 2009

Satisfaction With Current Treatments

Treatments	Payer Ratings (Low – High)	Comments
Bone marrow transplant (allogeneic)		• Good efficacy but high safety risks and high cost • Only available as treatment option for limited patients
Hydroxyurea		• Unsatisfied with efficacy & safety • Low cost perceived as strength

Source: bluebird bio research on file

"Unless a cure becomes available this disease will continue to be expensive and chronic."

β-Thalassemia Major:
Gene Therapy Value Proposition vs Standard of Care

Clinical Benefits

- Transfusion independence
- Effects on iron overload, chelation and phlebotomy use
- Safety

+

Health-Related Quality of Life Benefits

- Patient-reported outcomes: sense of physical / mental well-being, pain, independent functioning, etc.

+

Healthcare System Costs / Resources Benefits

- Averted future costs associated with currently available treatment options (esp lifelong treatment with red blood cell transfusions and iron chelation therapy

+

Societal Benefits

- Improvements in work productivity, school attendance, etc. e.g. due to reduced absenteeism

Payers willing to reward innovation, but expect industry to do a better job quantifying and communicating different sources of value generated

Potential Implications for Industry

1. Pricing and Reimbursement
2. Deployment and Distribution
3. Global Opportunities
4. Your Organizations?

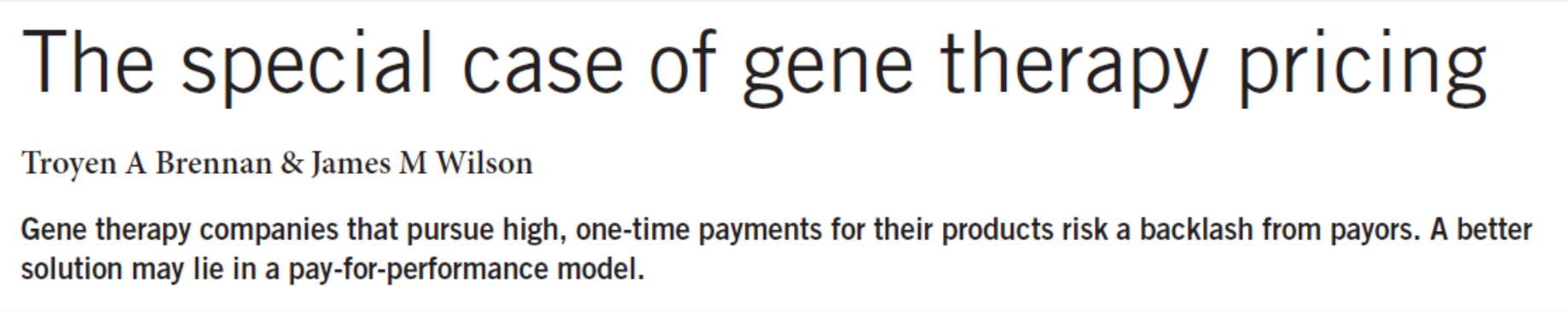
Potential Implications for Pricing and Reimbursement


AEI RESEARCH

Establishing new payment provisions for the high cost of curing disease

By Scott Gottlieb, MD, and Tanisha Carino

July 2014

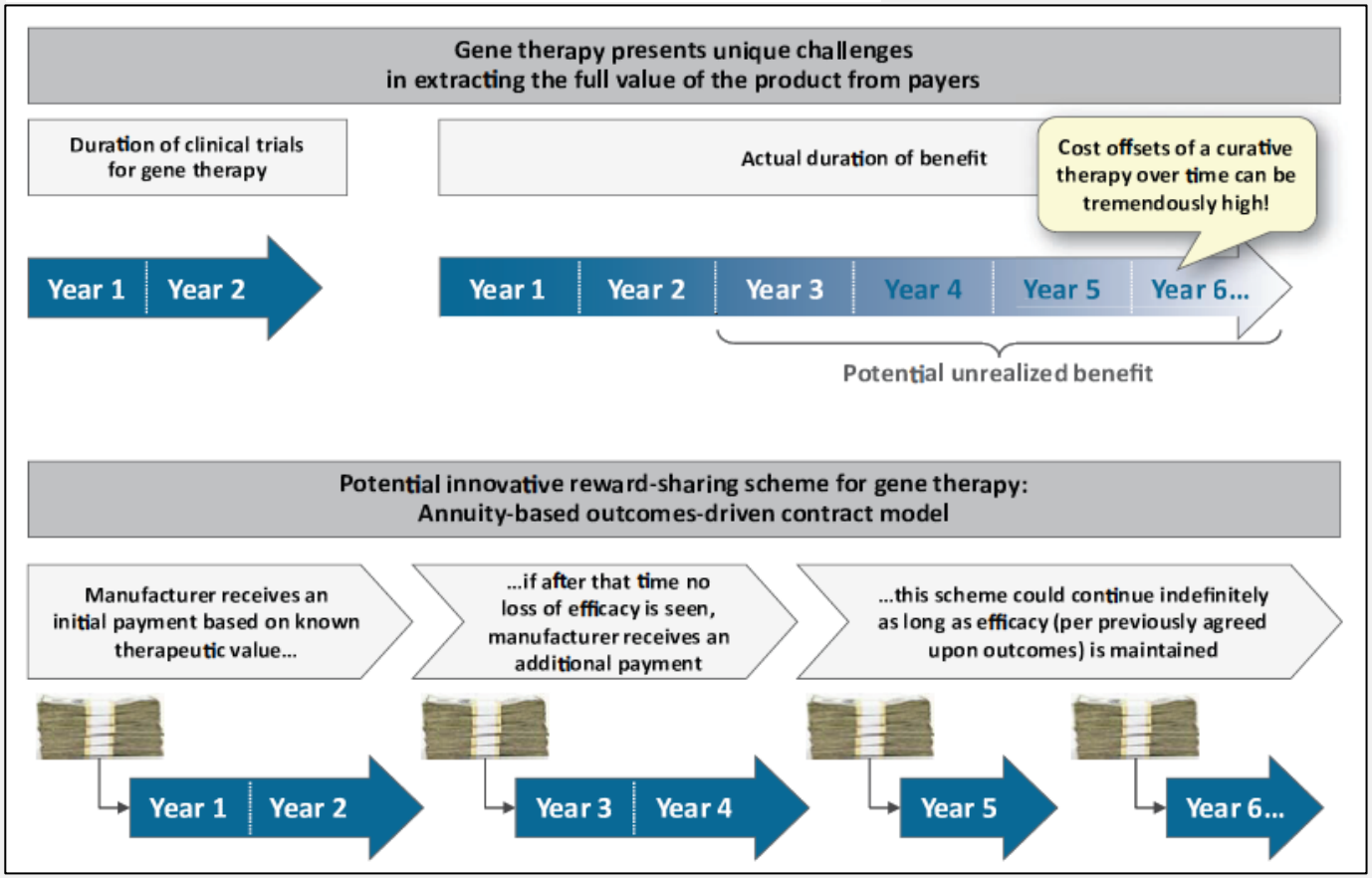

The special case of gene therapy pricing

Troyen A Brennan & James M Wilson

Gene therapy companies that pursue high, one-time payments for their products risk a backlash from payors. A better solution may lie in a pay-for-performance model.

Potential Implications for Pricing and Reimbursement

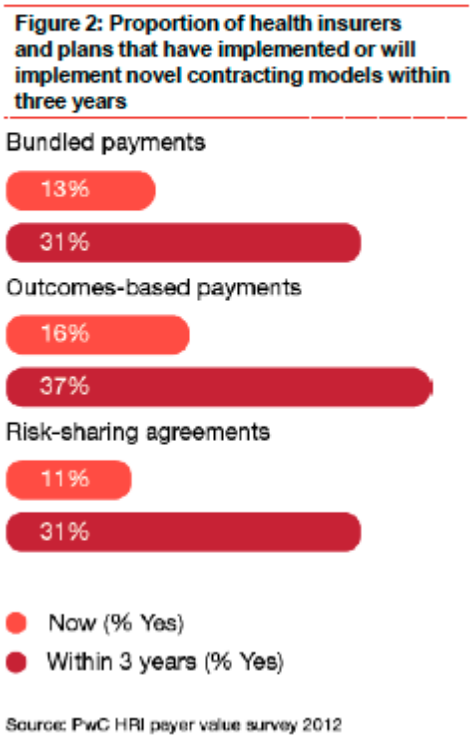
From risk-sharing to reward-sharing:
How gene therapy can revolutionize medicine and payer-manufacturer relations



Source: Simon Kucher & Partners

Potential Implications for Pricing and Reimbursement

16% of payers currently have outcomes-based contracting arrangements with pharmaceutical companies and one-third expect to support them within three years

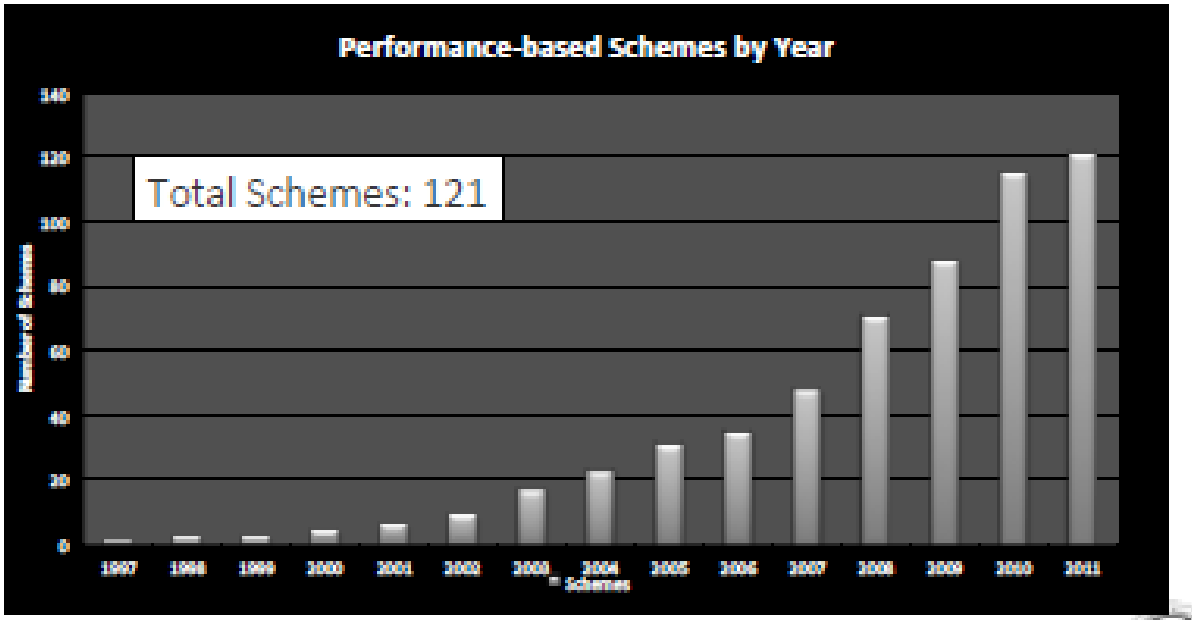


Source: PriceWaterhouseCoopers, 2012

Potential Implications for Pricing and Reimbursement

UNIVERSITY of WASHINGTON

Performance-based schemes by year

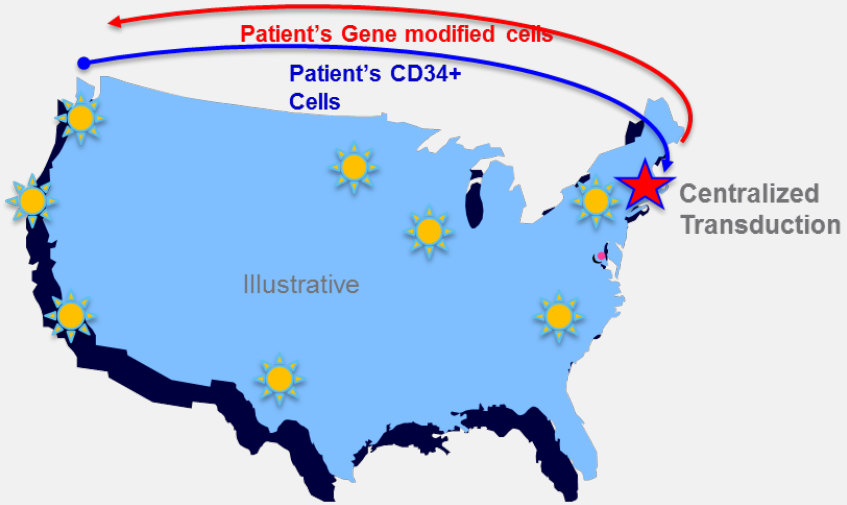


Source: ISPOR 2012

Potential Implications for Distribution

The Foundation for Accreditation of Cellular Therapy (FACT) establishes standards for the collection, transport, and use of cells. Accredited centers adhere to requirements for staffing, record-keeping, quality management, and procedures for storing and shipping cell products.					
Current Procedures and Precedents	▪ Transplant centers – Harvest cells for sibling donors and local adult donors – Existing SOPs conform to FACT requirements	▪ Hospitals – Ship cells from unrelated donors – Submit cord blood to banks ▪ Cord blood banks – Ship frozen cells worldwide	▪ FDA guidance – CMC for gene therapies ▪ Academic hospitals – Validated cell manipulation facilities for HCT – Must use GTP and/or GMP procedures	▪ FDA guidance – Potency testing for cell and gene therapies – Validation of rapid sterility testing ▪ Cord blood banks – Cell release criteria under FDA guidance	▪ Transplant centers receive frozen cord blood and fresh BM – Bedside viability test and gram stain prior to HCT – Cells are handled under GCP / GTP

Potential Implications for Distribution



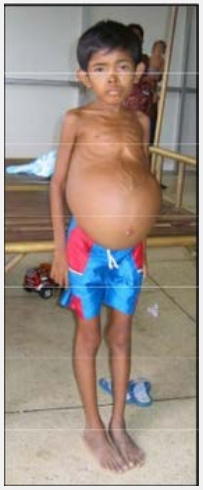
Centralized Transduction Facility in the US

Local Clinical Treatment for:

- CD34+ cell harvest
- Myeloablation
- Transplant
- Follow-up

Global Launch w/ Regional Transduction Centers

Developing World Interest in Curative Therapies



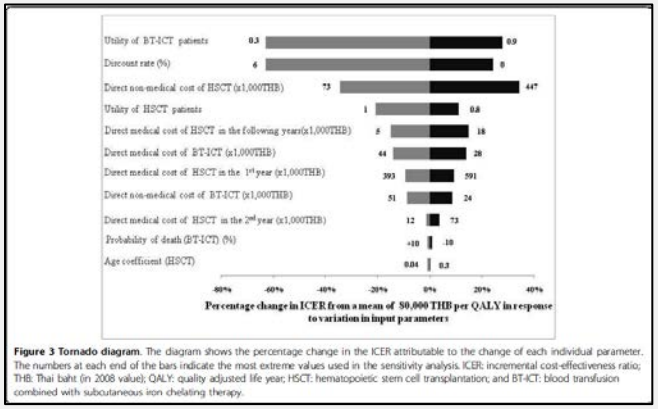


Figure 3 Tornado diagram. The diagram shows the percentage change in the ICER attributable to the change of each individual parameter. The numbers at each end of the bars indicate the most extreme values used in the sensitivity analysis. ICER: incremental cost-effectiveness ratio; THB: Thai baht (in 2008 value); QALY: quality adjusted life year; HSCT: hematopoietic stem cell transplantation; and BT-ICT: blood transfusion combined with subcutaneous iron chelating therapy.

Source: Leelahavarong, *BMC Health Services Research*, 2010

- **Thailand has one of the largest β-Thalassemia populations**
  - ~100K prevalent cases and ~4K incident cases per year
  - Standard of care is lifelong blood transfusion + iron chelation
- **70% patients interested in curative allo HSCT**
  - But only ~30% find a match (< 20% find a sibling match)
  - Historically not reimbursed by Thai MOH
- **Detailed health economic assessment commissioned by Thai govt in 2010**
  - Provided compelling evidence for cost effectiveness of allo HSCT over SOC
  - National coverage for allo HSCT will be initiated as a direct result of analysis
  - Thai govt and KOLs expressing interest in expanding access to curative potential of gene therapy

Potential Implications for Your Organization?

Conclusions

- **Regenerative medicine represents a wave of innovation with incredible clinical promise and unique value proposition**
- **Regenerative medicine therapies may introduce paradigm shifts in multiple dimensions that are exciting and challenging**
- **There is a lot of value to be created and captured in the process, and the biopharmaceutical industry needs to do a better job of quantifying and communicating this value**
- **Biopharmaceutical industry needs to think proactively about these changes and need to engage early with stakeholders, including policy makers, payers, media, etc.**

Questions and Discussion