



2024 State of the Industry Briefing

Achieving a new normal



Tim Hunt, CEO, Alliance for Regenerative Medicine
January 8, 2024 | Biotech Showcase

Today's agenda

Industry Update

Tim Hunt, CEO, Alliance for Regenerative Medicine

Expediting the Development of Cell and Gene Therapy

Peter Marks, M.D., Ph.D., Director, Center for Biologics Evaluation and Research, FDA

A Seminal Moment Arrives for Gene Therapy and Sickle Cell Disease – What's Next?

Gbola Amusa, M.D., CFA, Partner, Chief Scientific Officer, Chardan (*Moderator*)

Samarth Kulkarni, Ph.D., Chairman and CEO, CRISPR Therapeutics

Andrew Obenshain, CEO, bluebird bio



ARM is the Global Voice of the Cell & Gene Therapy Sector

A non-profit advocacy organization representing 400+ members worldwide

OUR FOCUS



Convening the sector



Advancing the field through data and analysis



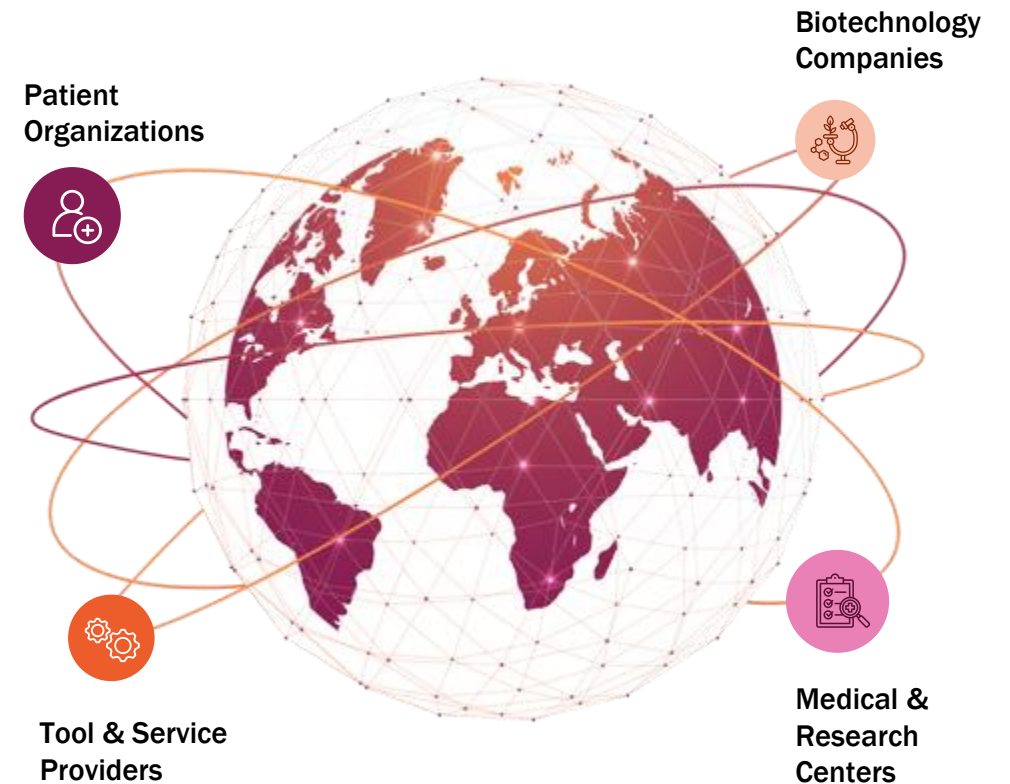
Engaging key stakeholders



Enabling the development of advanced therapies



Modernizing healthcare systems



2023 headlines sometimes highlighted our challenges

Finance and economics | A pricey shot

America will struggle to pay for ultra-expensive gene therapies

BIOTECH

STAT+

FDA investigating whether CAR-T, a treatment for cancer, can also cause lymphoma

BUSINESS & REGULATION | Trends & Forecasts, Business Practice, Advanced Medicine

Weathering the Storm: Cell and Gene's Economic Downturn

HEALTH

Sickle cell disease

Add Topic +

Gene therapy might cure sickle cell, but at a steep cost for patients, society

BIOTECH

Gene therapy is in crisis. For nine hours, the field's leading minds looked for a solution

HEALTH

↗

Jim Wilson warns Philly gene therapy conference of the 'paradox' that hurts investment



The reality is CGT is maturing, achieving a 'new normal'



**Breakthroughs are becoming
the norm**



5x5x5 comes true

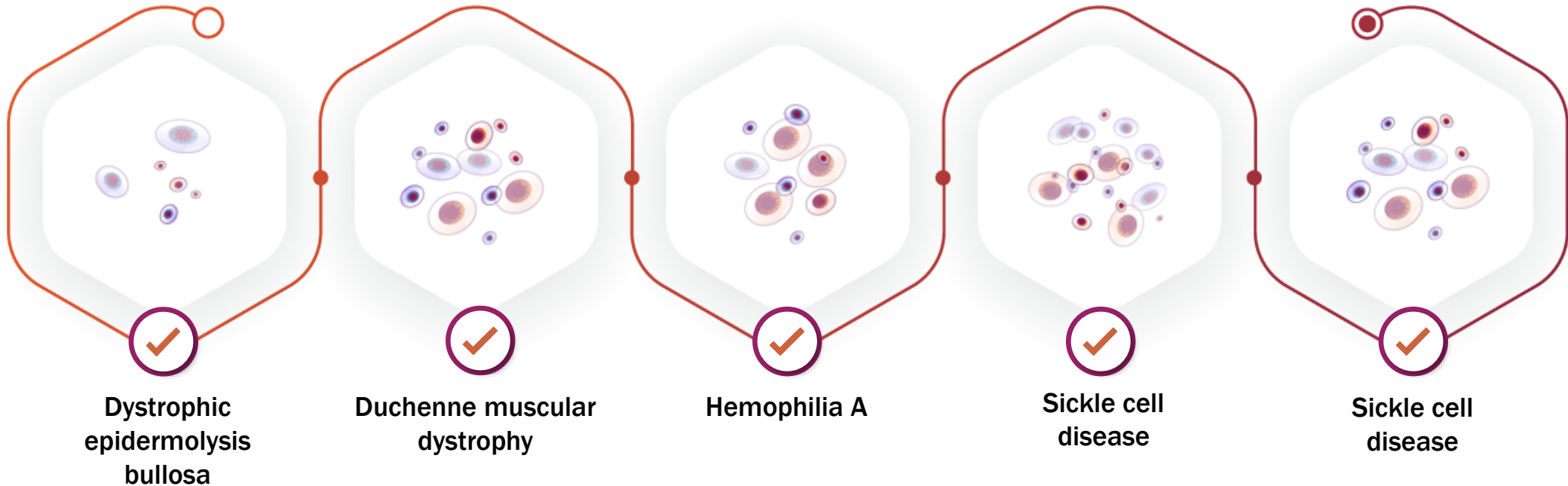
In the **five** years from late 2017 through 2022, the FDA approved **five** gene therapies for rare genetic diseases



Last year, we forecast that it could approve **five** gene therapies for rare genetic diseases in 2023 alone

← 2023 →

And it came true! →



2023: A breakthrough year of approvals in the US

Therapies approved in the United States

Casgevy (Vertex Pharmaceuticals and CRISPR Therapeutics)

Condition: Sickle cell disease

Lantidra (CellTrans Inc.)

Condition: Type 1 diabetes

Omisirge (Gamida Cell)

Condition: Patients undergoing stem cell transplant for blood cancer

Vyjuvek (Krystal Biotech)

Condition: Dystrophic epidermolysis bullosa

Elevidys (Sarepta Therapeutics)

Condition: Duchenne muscular dystrophy

Lyfgenia (bluebird bio)

Condition: Sickle cell disease

Roctavian (BioMarin Pharmaceutical)

Condition: Hemophilia A








Therapies approved in the European Union

Hemgenix (UniQure and CSL Behring)

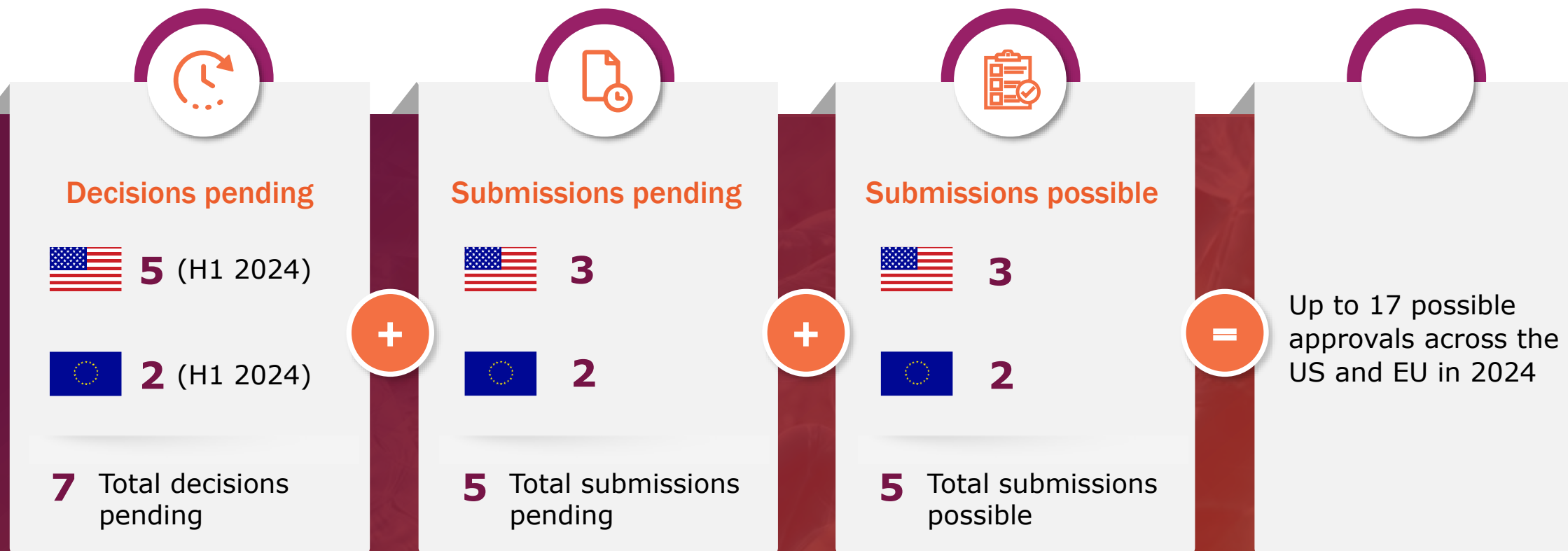
Condition: Hemophilia B



Interim 2023 Data: The sector's foundation is strong

	 2023	 North America	 Asia Pacific	 Europe	Total
 Developers		1,088	859	495	2,526
 Clinical Trials		972	790	358	1,894
 Investment*		\$8.1B	\$2.1B	\$1.2B	\$11.7B

2024 regulatory outlook: Up to 17 possible US & EU approvals



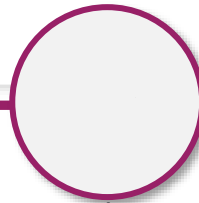
5X5X5 becomes '10 in 2'?
5 more rare genetic disease gene therapy approvals possible in US

Potential 2024 milestones

First-ever approval
of adoptive cell
therapy for solid
tumor (US) and first
US approval of
allogeneic T-cell
therapy



**Additional
therapies** to treat
hemophilia A,
hemophilia B, and
dystrophic
epidermolysis bullosa



In 2019, the FDA
predicted it would
**approve 10-20
therapies per year**
starting in 2025



Tracking to 2025



Value for patients and society



Does this sound familiar?*

“The most expensive drug sold in the United States.”

One patient advocate said she was “appalled” by the price.

“[The price] threatens to put this promising treatment out of reach of many patients, even those who are well-insured.”

Policymakers react to drug prices, calling them “exorbitant...akin to ransom.”



It should... but it's not about gene therapy



When did
this
happen?

1991-1992



Which
company
was it?

Genzyme



What
medicine
was it?

**Ceredase
(Gaucher's
disease)**



How much
was the
price?

**\$300,000+
per year**



Healthcare systems have adapted before, and they are adapting right now... and we will work through these challenges yet again.

**Source: Inside the Orphan Drug Revolution by James A. Geraghty*

ARM's Gene Therapy for Patients & Society (GPS) Framework

01

Target devastating, often deadly diseases



02

Target incredibly expensive diseases



03

Are highly effective



04

Often save healthcare systems money



05

Are affordable... even before taking into account cost offsets



Target devastating, often deadly diseases

The average life expectancy for rare diseases targeted by approved gene therapies is
~40 years – HALF the normal lifespan

Examples

Sickle cell disease:

45 to 55 years

Cerebral adrenoleukodystrophy:

10 years

Duchenne muscular dystrophy:

22 years



Target incredibly expensive diseases

The lifetime cost of the standard of care for most rare diseases targeted by approved gene therapies is several million \$

Examples

Patient with severe Hemophilia A is over **\$21M**

Patient with severe Sickle Cell Disease is **\$4-6M**

Patient with Transfusion-Dependent Thalassemia is **\$5.4 million**



Are highly effective

Orphan gene therapies are 3.5 times more likely to be approved once entering Phase 1 trials than average drugs included in BIO's Global Trends in R&D 2023 Report

Examples

48% higher
success rate in
Phase 1 clinical
trials

65% higher
success rate in
Phase 2 clinical
trials

30% higher
success rate in
Phase 3 clinical
trials



Often save healthcare systems money

The Institute for Clinical and Economic Review (ICER) confirmed the high cost offsets from durable gene therapies in hemophilia, sickle cell, and other rare diseases

Examples

Sickle cell
therapies
~\$2M

Hemophilia B
therapies
~\$3M

TDT therapies
~\$2M



Are clearly affordable... even before taking into account cost offsets

NEWDIGS projects US gene therapy revenue to reach \$7.5B in 2030

Context

0.1% of projected healthcare spending and **1.3%** of projected prescription drug spending in 2030

Comparable to what Medicare paid for **one diabetes drug** in 2022

1.8% of the economic burden of rare diseases in the US in 2019

\$1.6M for a heart transplant (3,500 per year) and **\$1M+** for an allogeneic bone marrow transplant (9,950 per year) in 2020



US Healthcare Systems Are Modernizing



Center for Medicare and Medicaid Innovation's (CMMI) Cell and Gene Therapy Access Model



- The model will establish a voluntary partnership among CMS, state Medicaid agencies and biotech companies to set up and administer outcomes-based agreements (OBAs)
- This will particularly help smaller states without the resources to administer OBAs
- Originally proposed to begin in 2026, the model is now projected to launch in 2025
- This is a welcome effort to modernize how we pay for cell and gene therapies



The FDA is modernizing to prepare for the CGT wave



Established new Office of Therapeutic Products (OTP 'Super Office')



Nicole Verdun, MD, five months into tenure as the new Director of OTP; hired Rachel Anatol, PhD, as Deputy Director in late Dec.



Hiring to keep pace: CBER had met 83% of its FY 2023 goal of 132 new hires as of Sept. 30



Leaning into Accelerated Approval for rare disease gene therapies



START ("Operation Warp Speed for Rare Disease") pilot program: More early communication with companies



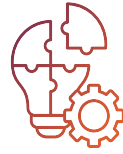
ARM & FDA are collaborating to prepare for the future

Streamlining CGT development and manufacturing



FDA Scientific Exchange on Building Blocks of Platform Technologies: AAV, LNP, iPSCs

Collaborating on complex CMC issues



Addressing potency assay-related challenges through a scientific exchange and white paper; in December the FDA released new potency assay draft guidance

Improving societal readiness for CGTs



Attended the Transformational Therapeutics Leadership Forum, an ARM gathering of sector leaders mapping the future of cell and gene therapy

Horizon scanning for future technologies



Identify emerging technologies in the sector that are most likely to require novel solutions for regulation over the next 3-10 years



Reflections on Sickle Cell Disease



December 8 FDA dual approvals of Casgevy and Lyfgenia: The biggest day in the history of gene therapy



A new technology (CRISPR), a long-overlooked patient population, and the largest patient population to date



Biggest test yet for healthcare system readiness: Up to 20,000 eligible patients, most of whom are covered by Medicaid



Transforming – and often saving – lives



Victoria Gray *The New York Times*

“It meant a new beginning. It is more than I ever dreamed of for everything [the symptoms] to be gone.”

Victoria was the first patient to receive the now-approved CRISPR sickle cell disease treatment.



Tesha Samuels

In 2018, Tesha received an autologous gene therapy transplant. She went from experiencing daily pain and sometimes life-threatening conditions to having minimal or no pain.

The background of the slide features a repeating pattern of concentric circles and dots in a light gray color. The circles are of varying sizes and are scattered across the entire surface. The dots are placed at regular intervals along the circumference of each circle. The overall effect is a subtle, textured background.

Thank you.

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