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

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

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

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’

01 Breakthroughs are becoming the norm

02 Value for patients and society

03 US healthcare systems are modernizing
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

Dystrophic epidermolysis bullosa
Duchenne muscular dystrophy
Hemophilia A
Sickle cell disease
Sickle cell disease

2023

And it came true!
## 2023: A breakthrough year of approvals in the US

### Therapies approved in the United States

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Company</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casgevy</td>
<td>Vertex Pharmaceuticals and CRISPR Therapeutics</td>
<td>Sickle cell disease</td>
</tr>
<tr>
<td>Lantidra</td>
<td>CellTrans Inc.</td>
<td>Type 1 diabetes</td>
</tr>
<tr>
<td>Omisirge</td>
<td>Gamida Cell</td>
<td>Patients undergoing stem cell transplant for blood cancer</td>
</tr>
<tr>
<td>Vyjuvek</td>
<td>Krystal Biotech</td>
<td>Dystrophic epidermolysis bullosa</td>
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<tr>
<td>Elevidys</td>
<td>Sarepta Therapeutics</td>
<td>Duchenne muscular dystrophy</td>
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<tr>
<td>Lyfgenia</td>
<td>bluebird bio</td>
<td>Sickle cell disease</td>
</tr>
<tr>
<td>Roctavian</td>
<td>BioMarin Pharmaceutical</td>
<td>Hemophilia A</td>
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</tbody>
</table>

### Therapies approved in the European Union

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Company</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemgenix</td>
<td>UniQure and CSL Behring</td>
<td>Hemophilia B</td>
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Interim 2023 Data: The sector’s foundation is strong

<table>
<thead>
<tr>
<th></th>
<th>North America</th>
<th>Asia Pacific</th>
<th>Europe</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developers</td>
<td>1,088</td>
<td>859</td>
<td>495</td>
<td>2,526</td>
</tr>
<tr>
<td>Clinical Trials</td>
<td>972</td>
<td>790</td>
<td>358</td>
<td>1,894</td>
</tr>
<tr>
<td>Investment*</td>
<td>$8.1B</td>
<td>$2.1B</td>
<td>$1.2B</td>
<td>$11.7B</td>
</tr>
</tbody>
</table>

*Reflective of full-year 2023 data
2024 regulatory outlook: Up to 17 possible US & EU approvals

Decisions pending
- US: 5 (H1 2024)
- EU: 2 (H1 2024)
Total decisions pending: 7

Submissions pending
- US: 3
- EU: 2
Total submissions pending: 5

Submissions possible
- US: 3
- EU: 2
Total submissions possible: 5

Up to 17 possible approvals across the US and EU in 2024

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.”

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

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

Policymakers react to drug prices, calling them “exorbitant...akin to ransom.”
It should... but it’s not about gene therapy

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 adrenoleuko-dystrophy: 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

- **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

Collaborating on complex CMC issues

Improving societal readiness for CGTs

Horizon scanning for future technologies

- FDA Scientific Exchange on Building Blocks of Platform Technologies: AAV, LNP, iPSCs
- Addressing potency assay-related challenges through a scientific exchange and white paper; in December the FDA released new potency assay draft guidance
- Attended the Transformational Therapeutics Leadership Forum, an ARM gathering of sector leaders mapping the future of cell and gene therapy
- 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

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.

Victoria Gray

“\textit{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.
Thank you.
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