President's Report

Jonathan Thomas, PhD, JD
CIRM President/CEO

ICOC/ARS Meeting
January 30, 2025

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Agenda

1. ARM's State of the Industry Review at the JP Morgan Conference

2. Recap of the Citizens Financial Accountability Oversight Committee (CFAOC) Meeting

ARM's State of the Industry Review at the JP Morgan Conference

CELL GENE

STATE *of the* INDUSTRY BRIEFING

The Sector Evolves Toward a Bright Future

Alliance *for* Regenerative Medicine

Tim Hunt, CEO, Alliance for Regenerative Medicine

January 13, 2025 | Biotech Showcase

What We'll Cover Today

History as a Guide

01

Addressing Questions About CGT Commercialization

02

The Incredibly Bright Future of CGT

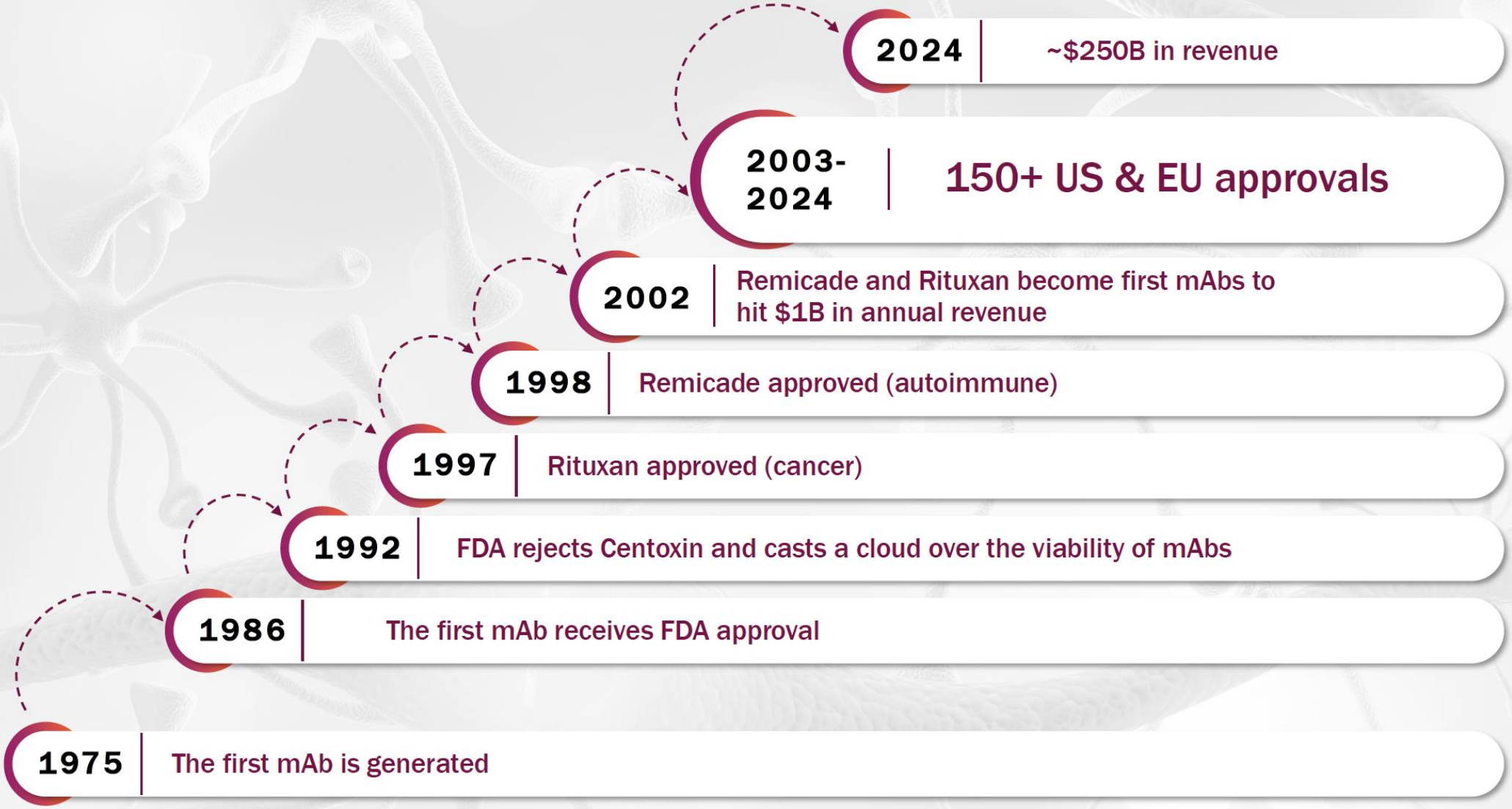
03

Opportunities in the New Administration

04

History as a Guide

The (Long) Journey of Monoclonal Antibodies



The Similar (Non-linear) Journey of CGTs in the US

1972
Theodore Friedmann first conceptualizes gene therapy

2017
FDA approves LUXTURNA, KYMRIAH, and YESCARTA

2018
FDA approves ZOLGENSMA

2019
FDA Commissioner Scott Gottlieb predicts 10-20 approvals a year by 2025

2021
ZOLGENSMA becomes a blockbuster product

2022
YESCARTA becomes a blockbuster product

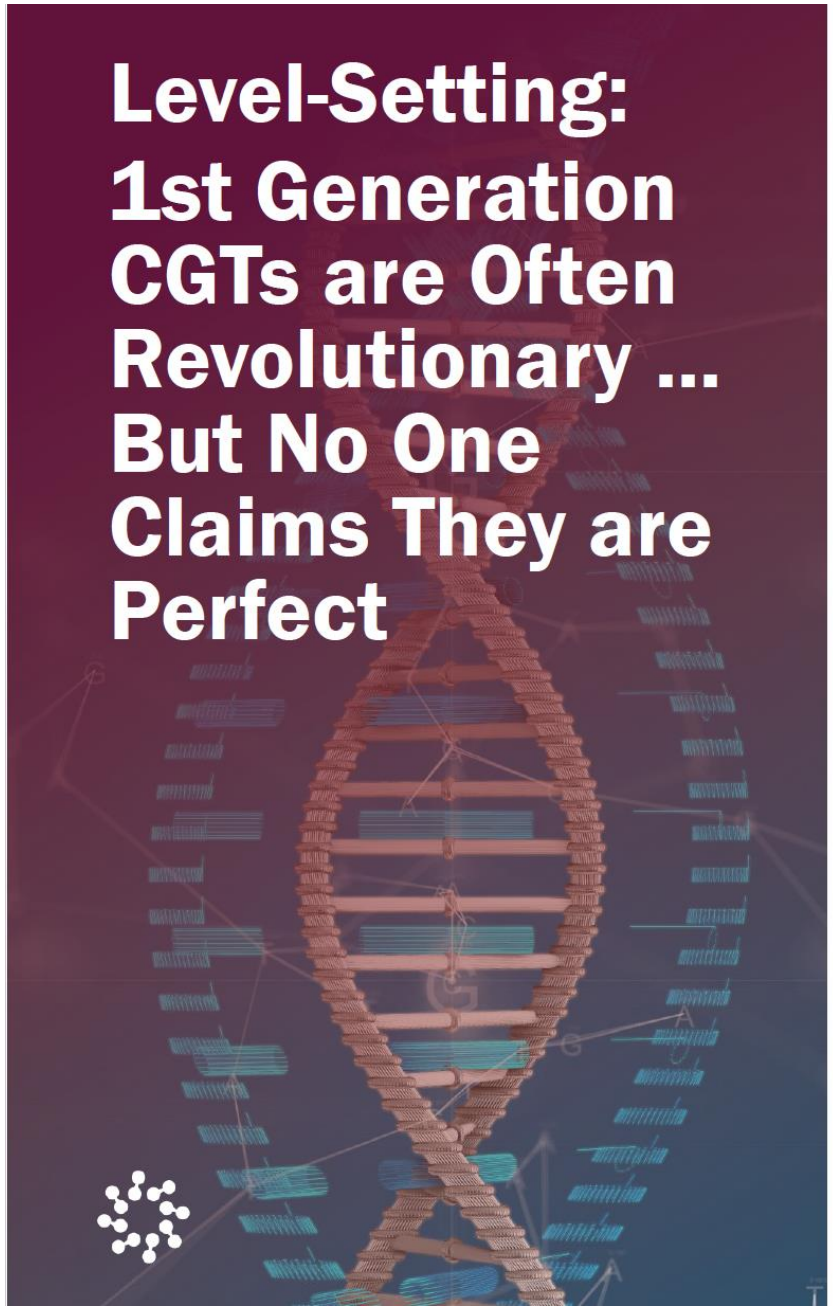
2023
FDA approves 5 gene therapies for rare genetic diseases

2024
FDA approves a record 9 CGTs, including first 2 adoptive cell therapies for solid tumors

2025
The FDA's 2019 prediction is within reach

Addressing the Questions We Hear About CGT Commercialization

Level-Setting: 1st Generation CGTs are Often Revolutionary … But No One Claims They are Perfect



01

Some therapies face challenges related to efficacy, safety, and durability of response, and require complex treatment regimens

02

While significant progress is being made, the cost of goods for manufacturing and administration remains high for many products

03

Some therapies confront commercial hurdles including competition, real-world patient dynamics, and/or very small patient populations

A Revolutionary Impact for Jimi Olaghere

Sickle Cell Warrior and CASGEVY™ Recipient

- Lived through decades of countless pain crises and emergency room visits
- Received CASGEVY™ in 2020
- Four years later, Jimi climbed the summit of Mt. Kilimanjaro

Alliance for Regenerative Medicine

Question 1:

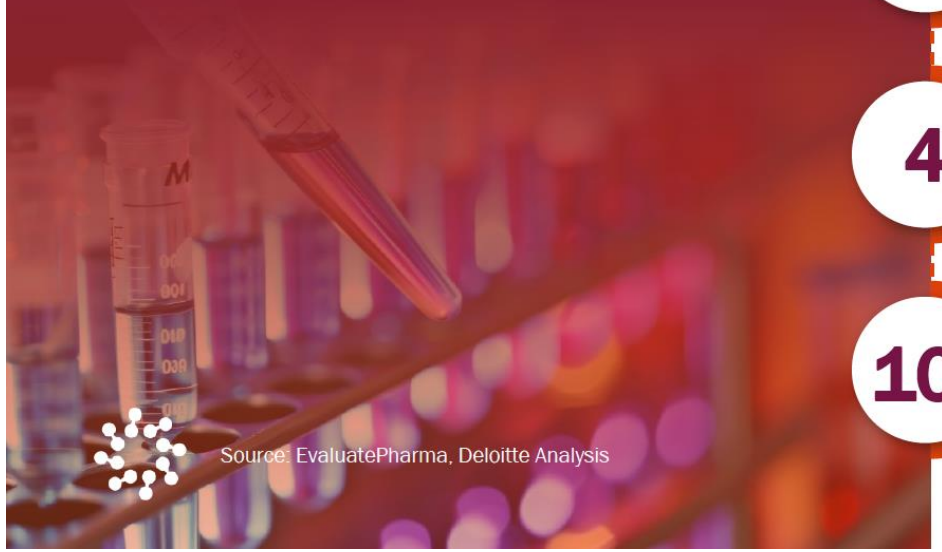
Do CGTs Represent Compelling Commercial Opportunities?

Analysis in partnership with:

Deloitte.

Scientific Breakthroughs Become Commercial Successes

From 2 blockbusters in the last 6 years (2018-2024) to 10+ by 2030



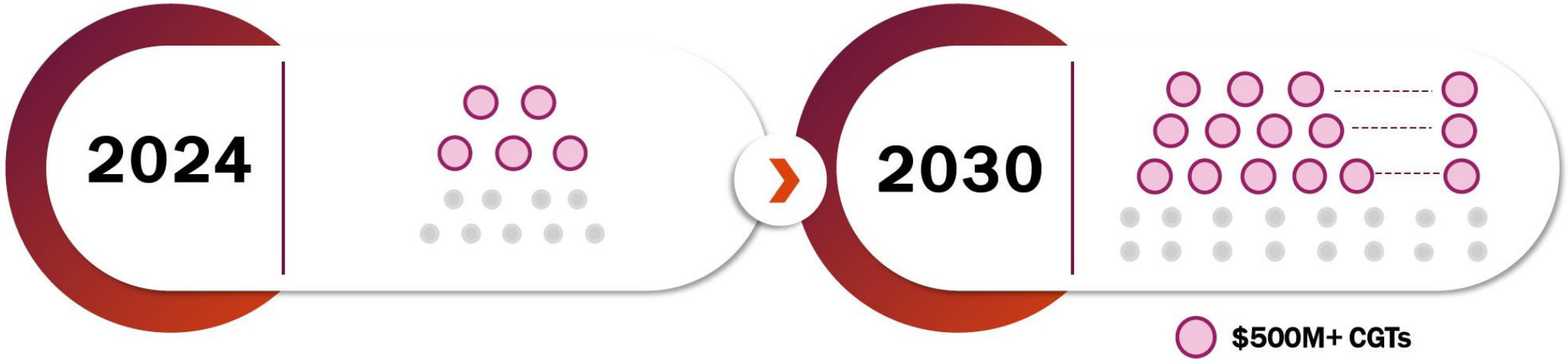
Source: EvaluatePharma, Deloitte Analysis

Commercial Blockbusters
(with estimated >$1B worldwide sales)

	2018	*Global CGT revenue totals $450 million*
1	2021	zolgensma
2	2022	YESCARTA
4	2025	CARVYKTI (ciltacabtagene autoleucel) Elevidys
10+	2030	*Driven by currently launched and late-stage pipeline therapies (Analyst Consensus Data)*

Success Beyond Blockbusters

From 5 CGTs today with $500M+ in annual worldwide revenue, to 30+ CGTs in 2030*



Source: EvaluatePharma (Analyst Consensus Data), Deloitte Analysis

*Includes currently launched and late-stage pipeline therapies

Promising Markets With Blockbuster Potential

Severe Sickle Cell Disease

25,000
patients in the US and EU

VERTEX
CRISPR THERAPEUTICS
bluebirdbio
Beam THERAPEUTICS

Duchenne Muscular Dystrophy

39,000
patients in the US and EU

SAREPTA THERAPEUTICS
Roche
REGENXBIO
SOLID BIOSCIENCES

Dystrophic Epidermolysis Bullosa

9,000
patients globally

Krystal
Abeona THERAPEUTICS
Castle Creek Biosciences

Danon Disease

15,000 – 30,000
patients in the US and EU

rocket pharma

Question 2:

Are Large-Cap Biopharma Companies Investing in CGTs?

Big Biopharma Buys In

13 of 15 largest biopharma companies by market cap are investing in the development and/or commercialization of CGT

01 Lilly — Market cap = $716 billion

02 novo nordisk — Market cap = $384 billion

03 J&J — Market cap = $344 billion

04 abbvie — Market cap = $309 billion

05 MERCK — Market cap = $252 billion

06 Roche — Market cap = $234 billion

07 AstraZeneca — Market cap = $210 billion

08 NOVARTIS — Market cap = $199 billion

09 Pfizer — Market cap = $152 billion

10 AMGEN — Market cap = $141 billion

11 SANOFI — Market cap = $123 billion

12 Bristol Myers Squibb — Market cap = $114 billion

13 GILEAD — Market cap = $110 billion

14 VERTEX — Market cap = $106 billion

15 CSL — Market cap = $85 billion

Figures updated as of January 10, 2025

Large-Cap Biopharma Can Drive Commercial Success via Partnerships and Acquisitions

- NOVARTIS avexis ✓
  Gene therapy for SMA Type 1
- VERTEX CRISPR THERAPEUTICS ✓
  CRISPR gene editing therapy for SCD and TDT
- Roche SAREPTA THERAPEUTICS ✓
  Gene therapy for Duchenne muscular dystrophy
- abbvie REGENXBIO
  Gene therapy for Wet AMD
- Bristol Myers Squibb CELLARES
  Expanding manufacturing capacity to commercialize CAR-T for B-cell lymphoma
- astellas AVIADOBIO
  Gene therapy for frontotemporal dementia
- Roche POSEIDA THERAPEUTICS
  Non-viral cell therapies for cancer, autoimmune, and rare diseases

✓ = Approved in the US or EU

Question 3:

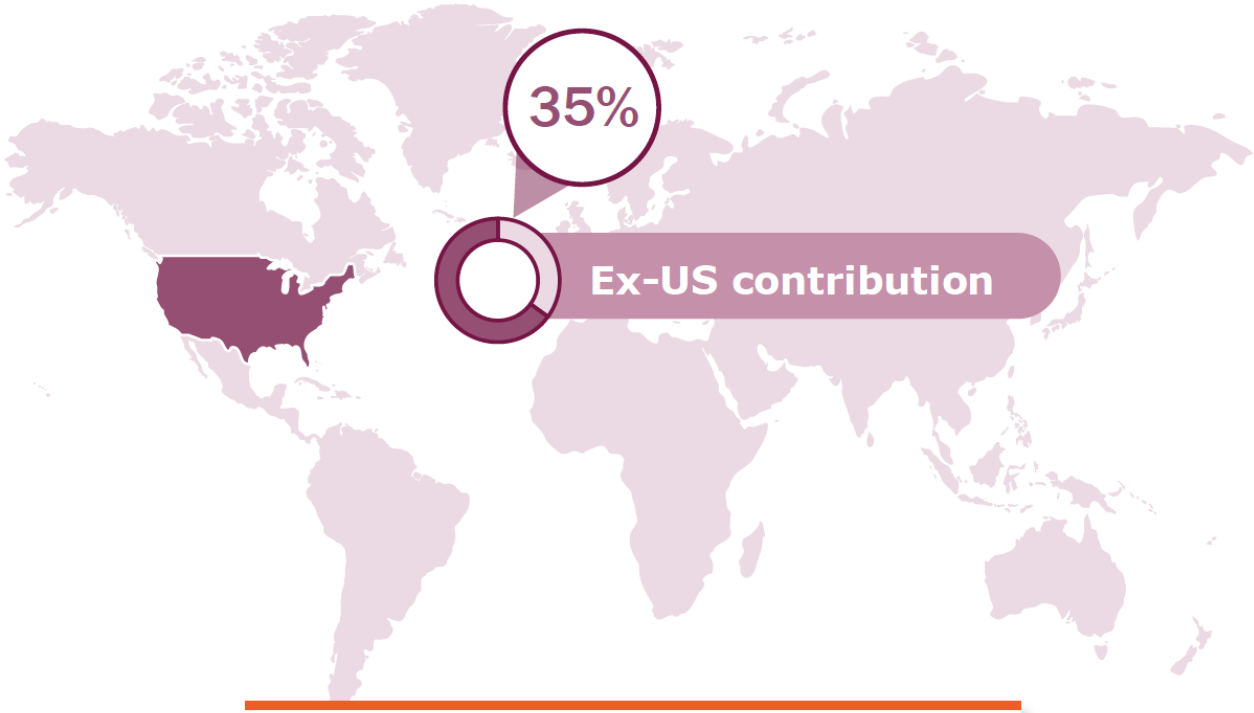
Is CGT Just a US Business?

Analysis in partnership with:

Deloitte.

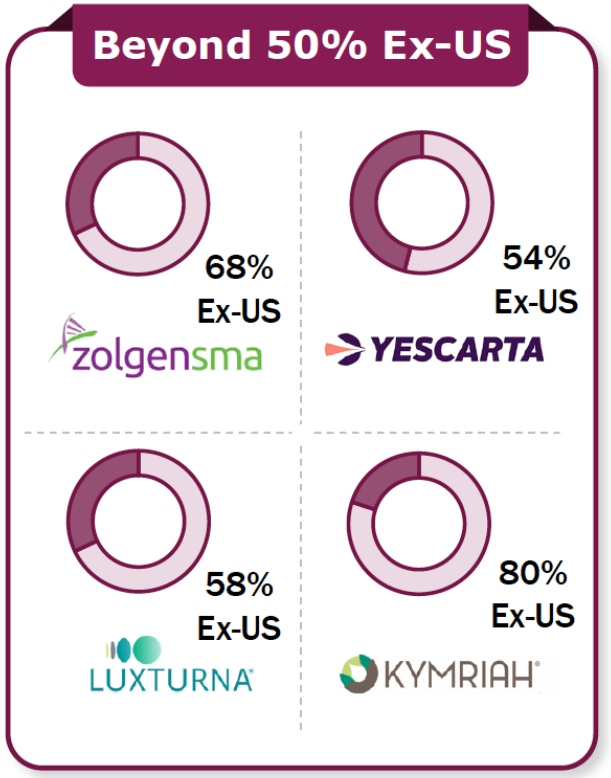
Significant Commercial Opportunities Outside the U.S.

Global CGT revenue in 2024



Going global gives more options to optimize commercialization

Beyond 50% Ex-US



Source: EvaluatePharma, Deloitte Analysis

The ZOLGENSMA™ Success Story

- Approved in over 50 countries
- Access established in over 45 countries (68% of revenue come from ex-US)
- Over 4,000 young children treated worldwide; recent phase III data supports use in children up to age 18
- Blockbuster status since 2021 and projected to grow to $2B by 2028
- Establishing access capabilities early is critical for commercialization

The Incredibly Bright Future of Cell and Gene Therapy

The US Continues to Lead, but the Sector is Globalizing Fast

Interim 2024 Data

2024	Developers (Snapshot value)	Clinical Trials (Snapshot value)	Investment (2024 Total)
North America	1,230	981	$11.8B
Asia Pacific	1,029	879	$1.5B
Europe	581	384	$2.0B
Total (y/y growth)	2,936* ↑6%	1,975* ↑3%	$15.2B* ↑30%

GlobalData.

*Totals refer to unique quantities and include data from other regions not shown

2024 Saw Significant Financings and Acquisitions

Public Financings	Venture Capital	Acquisitions
insmed	ArsenalBio	Roche, POSEIDA THERAPEUTICS
$650M	$325M	$1.5B
kyverna	capstan therapeutics	NOVARTIS, KATE THERAPEUTICS A NOVARTIS COMPANY
$300M+	$175M	$1.1B
immatics	OBSIDIAN THERAPEUTICS	MilliporeSigma, mirus bio
$150M	$160M	$600M

Prevalent Disease Breakthroughs Are Coming

Wet AMD	Parkinson's	Multiple Sclerosis	Type 1 Diabetes
			
5.7 million patients in US, EU and Japan	**10 million** patients worldwide	**1.5 million** patients in US, EU and Japan	**3.8 million** patients in US, EU and select geographies
Phase 3 REGENXBIO, abbvie	**Phase 3** BlueRock Therapeutics, Bayer	**Phase 2** kyverna	**Phase 1/2** VERTEX, Sana Biotechnology

Source: Company estimates from Vertex Pharmaceuticals, Kyverna Therapeutics, REGENXBIO, and BlueRock Therapeutics

Top Pipeline Trends Driving CGT Advancement

Progress in Solid Tumor

Strong early-stage pipeline: 657 active trials

Prevalence: Account for 90% of new adult cancer cases globally (GCO)

2024 Milestones: first FDA approvals for cell therapies to treat solid tumors

CAR-T Advances

Earlier treatment options: CAR-Ts for MM advance as earlier lines of treatment; CAR-T in testing to be 1st line treatment for first time

Autoimmune promise: Several trials advancing in early/mid-stage clinical trials

Milestones for In-Vivo

CRISPR in late-stages: Second-ever in-vivo CRISPR gene editing therapy enters phase III trials

In-vivo CARs enter the scene: Groundbreaking in-vivo CAR-T and CAR-Gene therapy concepts enter clinical trials

Opportunities in the New Administration

Administrations Bring Headwinds & Tailwinds

Headwinds

Immigration ban challenged biotech workforce

Attempt to tie the prices of Medicare Part B drugs to those paid in foreign countries (Most Favored Nation rule)

Passage of IRA and related price controls

High inflation and rising interest rates placed downward pressure on biotech capital markets

Aggressive FTC posture toward biopharma M&A

Tailwinds

Appointment of Dr. Scott Gottlieb as first FDA commissioner (2017-2019)

Proposed CMS rule to promote outcomes-based arrangements in commercial market and Medicaid (Multiple 'best prices')

Cancer moonshot initiative to spur biotech capacity

CMMI Cell and Gene Therapy Access Model is a meaningful step toward modernizing Medicaid payment for CGT

Trump Administration 2.0 Presents Real Opportunities

Developments that may support CGT sector

01 Strong alignment with aspects of 'Make America Healthy Again' philosophy by addressing root cause of disease and reducing need for 'chronic' care

02 Continuation of strong modernization efforts at CBER/OTP, including regulatory flexibility, use of Accelerated Approvals, and efforts around platforms for gene editing

03 Continuation of CMMI CGT Access Model - both companies with approved SCD therapies have chosen to participate; states now have option of joining

04 Strengthening US biomanufacturing capacity/onshoring ('America First' agenda)

05 New leadership at Federal Trade Commission & more supportive regulatory environment for M&A and CGT sector consolidation

Key Takeaways from Today

History Provides a Guide

CGTs are following a well-established (non-linear) path toward greater adoption

Blockbusters Beckon

CGT is becoming a global business & more blockbusters are expected in the next 5 years

Science Breaks Through

CGTs are advancing into new diseases with more advanced approaches

Systems Modernize

CMMI CGT Access Model and other policy opportunities are on the horizon

Recap of the Citizens Financial Accountability Oversight Committee (CFAOC) Meeting