June 2025

GCT
National Strategy
Gene- and Cell-Based Therapies
GeneNovate

Cell and Gene Therapy, society and patients: Believing in the promise …

Miguel Forte, MD PhD
President ISCT
ARM Board and Executive Committee Member
CEO Kiji Tx

Berlin – 27th June 2025

Topics

- Status of biotech …
- Update on C&GT
- The Investor attitude
- Political and Regulatory environment
- Alternative models: business and others…
- One example: autoimmunity
- Ethics
- Take home

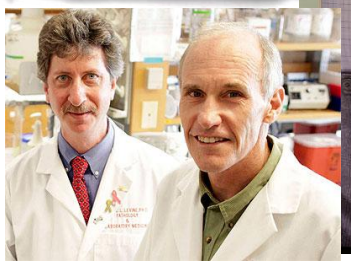
The urgency of bringing value to stakeholders and patients !

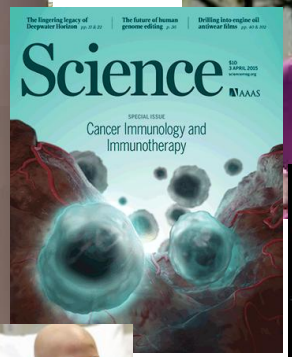
"My dear, here we must run as fast as we can, just to stay in place. And if you wish to go anywhere you must run twice as fast as that."

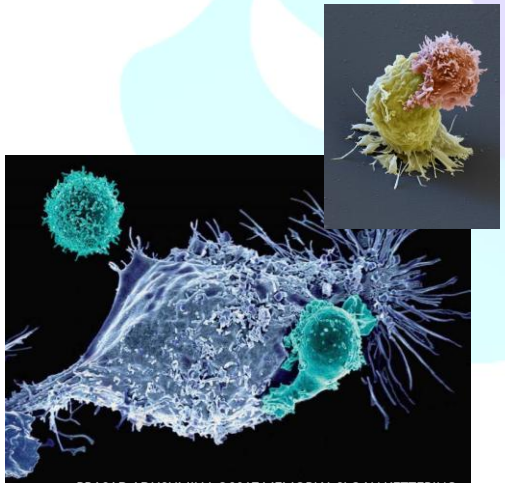
— Lewis Carroll, Alice in Wonderland

C&GT: where are we …

Fantastic value C&GT: long term benefit / cure







Any new development with extraordinary impact and promise …

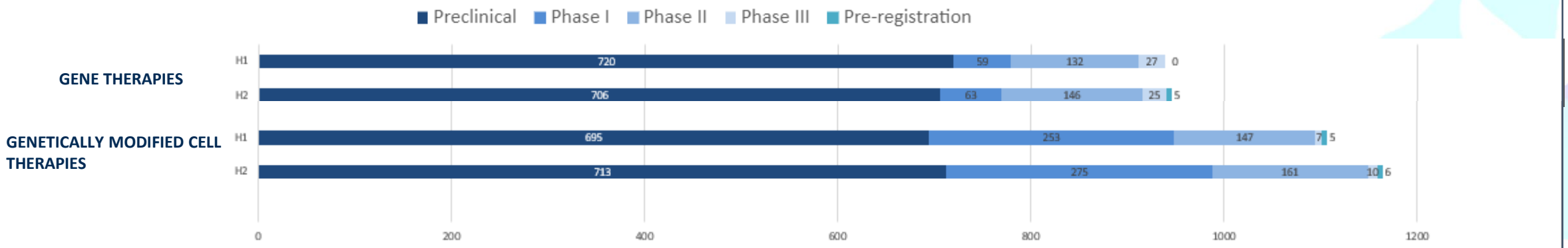
is always overestimated in the short term

and underestimated in the long run…

Global Regulatory CGT Pipeline – EOY 2024

	H2 2024 Report (December 2024)	H1 2024 Report (June 2024)
Global Pipeline	**3063** therapies in pipeline (**+7.5%**)	**2848** therapies in pipeline
	1165 *genetically modified* | ***945*** *gene therapies* | ***953*** *non-genetically modified*	
Approved Products	**106** approved products globally (**+6.0%**) **18 genetically-modified cell therapies** **17 gene therapies**	**100** approved products globally
Products Under Regulatory Review	**91** CGT products are under regulatory review (**+7.1%**) of which **78** products are in Phase III clinical trials (**+1.3%**)	**85** products are Under Regulatory Review of which **77** products are in Phase III Clinical Trials

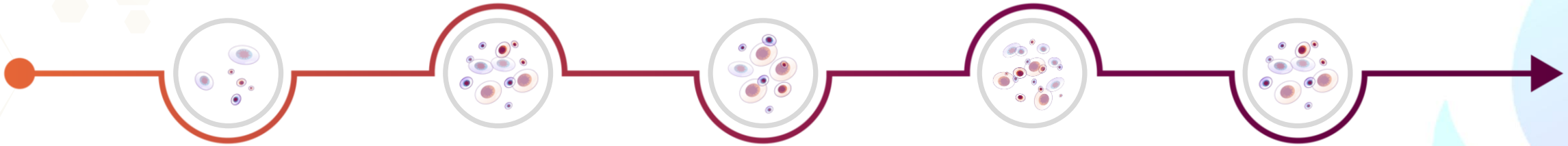
Growing CGT Pipeline with Potential Approvals on Horizon



Source: Pharmaprojects | Citeline, December 2024

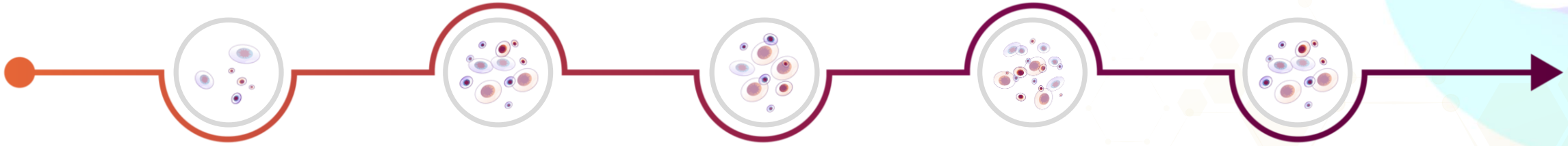
Gene therapy approvals are accelerating

2017 — 5 gene therapies for rare genetic diseases were approved in the US — **2022**



- Inherited retinal disorder
- SMA
- Beta thalassemia
- CALD
- Hemophilia B

2023 — 5 such therapies were approved in 2023 alone



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

2025 Regulatory Outlook

As of May 19, 2025

Approved new therapies

2

1

3 Total new drug approvals

2025 decisions pending

5

4

9 Total decisions pending

2025 regulatory applications pending

1

3

4 Total applications pending

Possible H1 2025 regulatory submissions

1

1 Possible H1 submissions

Possible 2025 approvals

7 - 9

5 - 8

12 - 17 Possible approvals

After only seeing 3 new product approvals from 2023-2024, Europe is poised to see a rebound, with 5-8 approvals possible in 2025

International Society
ISCT
Cell & Gene Therapy®

CELL AND GENE THERAPY GLOBAL REGULATORY REPORT

H2 2024

DATA PARTNER: CITELINE
a norstella company

Developments of note …

- **Decentralized** manufacturing
- **Rapid** manufacturing; Complex CAR design
- **Gene delivery**, the virus vs Lipid Nano Particles (LNP)
- **Gene editing** approaches

- In vivo engineering
- N-of-1

- Antigen specific and antigen boosted **TIL**
- Optimization of cell sourcing (**iPSC**) and targeting/potency (multiple gene engineering)

- Expansion to **new areas** – Autoimmune; Expansion to **new cell types** !

- ***Cell and Gene****: Engineer cells for a purpose: the professionalization of cell as a therapeutic product!*

Challenges to address …

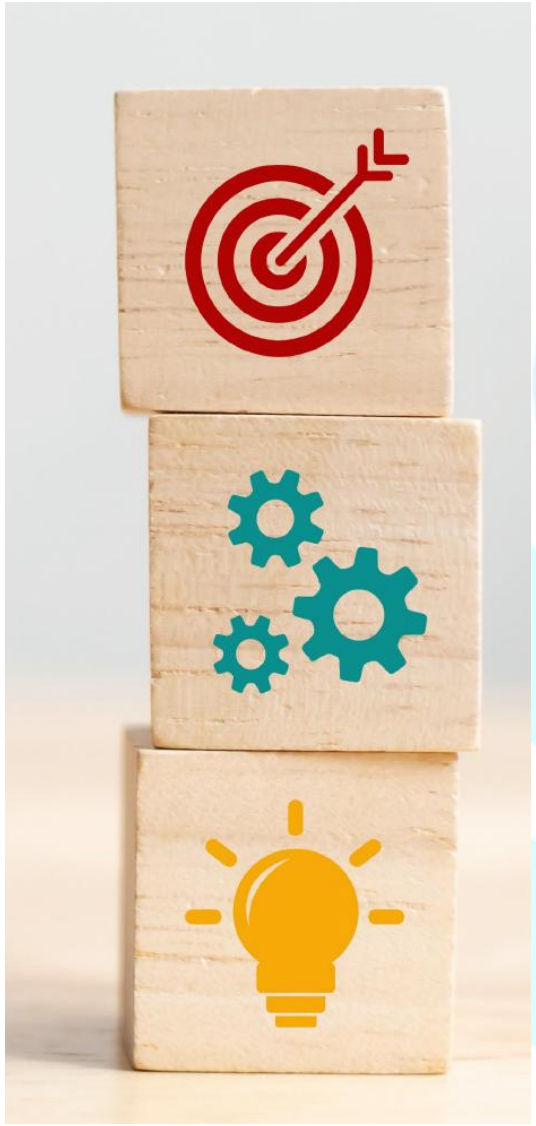
- **Regulatory** approaches and risk assessment: further flexibility
- **Global development and local delivery**
- Technology developments – efficiency and CoG

- Training and talent availability

- **Funding**: Perception on the field and expectation management

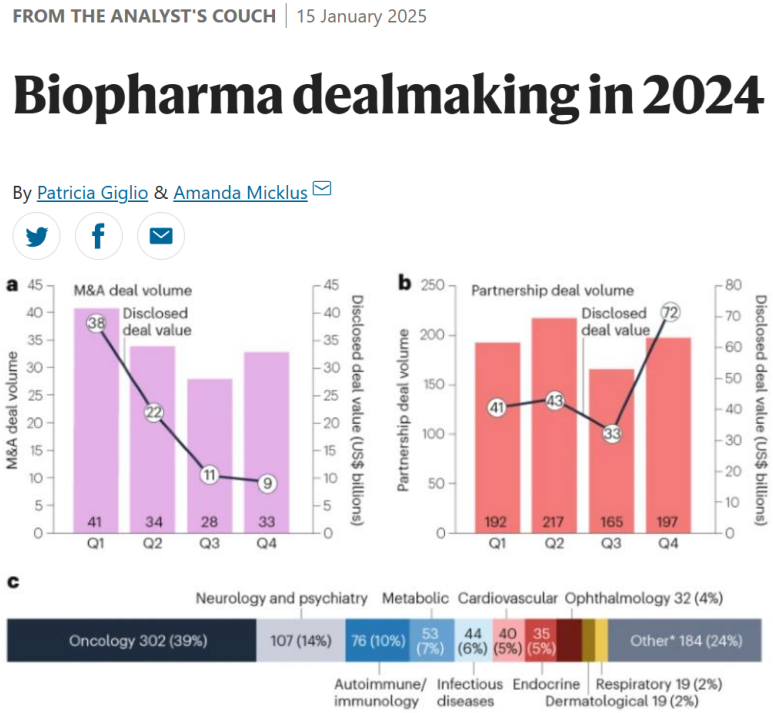
- **Patient access – Local and Global**
- Need for new models

- **Ethics**: Reactively and proactively



Status of the Field:
The weather conditions for Biotech

Status of the biopharmaceutical field



FROM THE ANALYST'S COUCH | 15 January 2025

Biopharma dealmaking in 2024

By Patricia Giglio & Amanda Micklus

3/25/25, 10:05 AM Cell and gene therapies have seen setbacks — but are still promising | STAT

OPINIONS+

Impatient about cell and gene therapy? Progress in biotech is not always linear

The data suggests great cause for optimism

ERIC PIERMONT/AFP via Getty Images

- High level of **uncertainty**

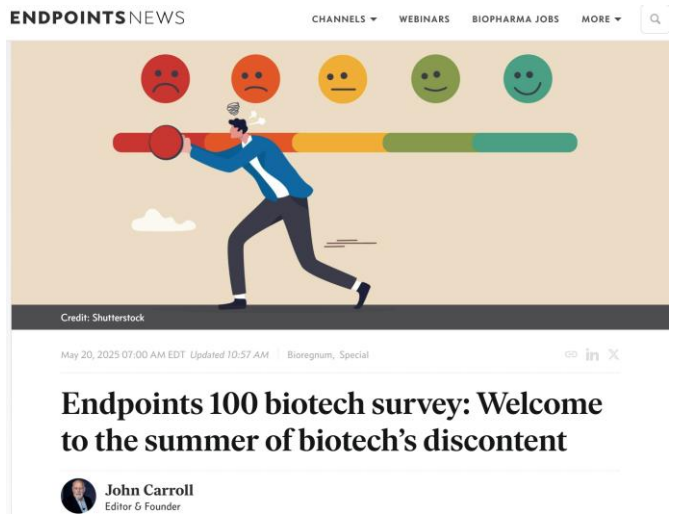
- The **winter of biotech** has continued into 2025
- Deals are taking place but are slower, with lower valuations
- Fewer deals with bigger values

- Investors look for **less risk**: the desire/value of **clinical data**

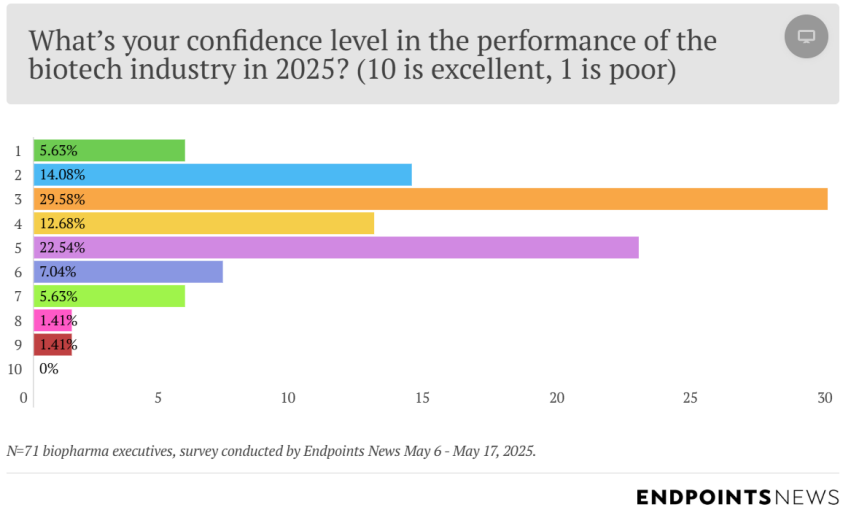
- The **challenges to public funding**

- The search for **alternative geographies** (Asia) **and modalities** (BD; M&A)

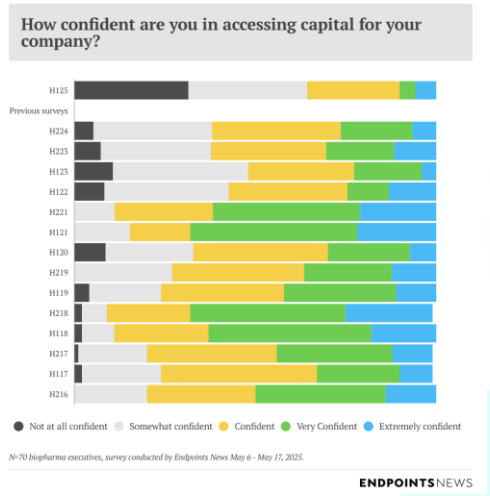
Biotech CEO's sentiment in 2025 !...



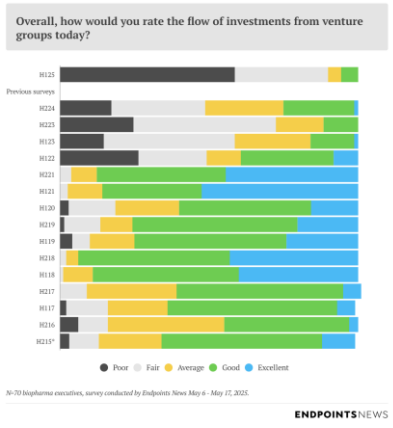
Overall confidence in 2025



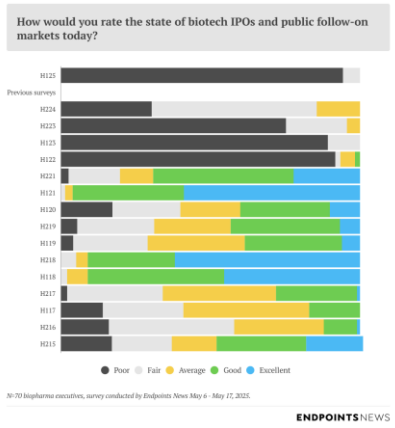
Confidence in raising in 2025



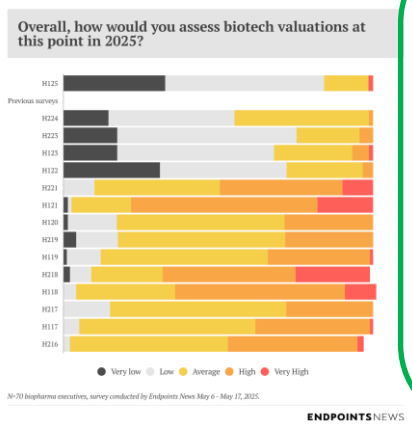
Flow of investment



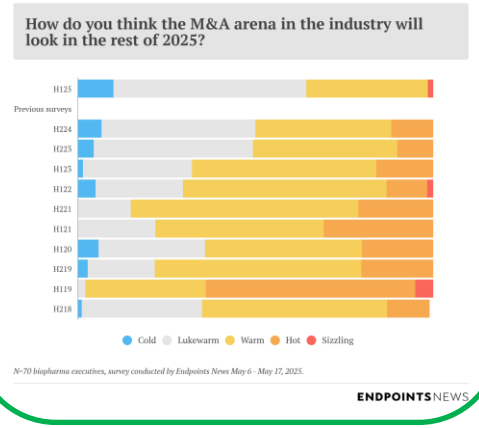
IPO



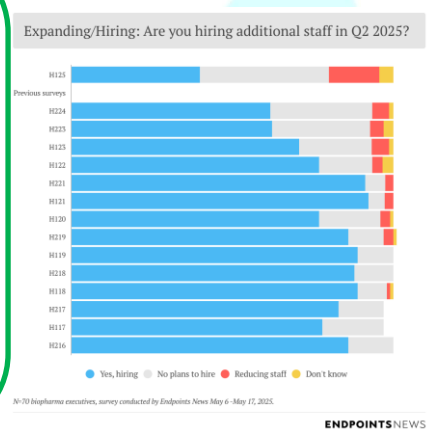
Valuations



M&A



Investment in staff

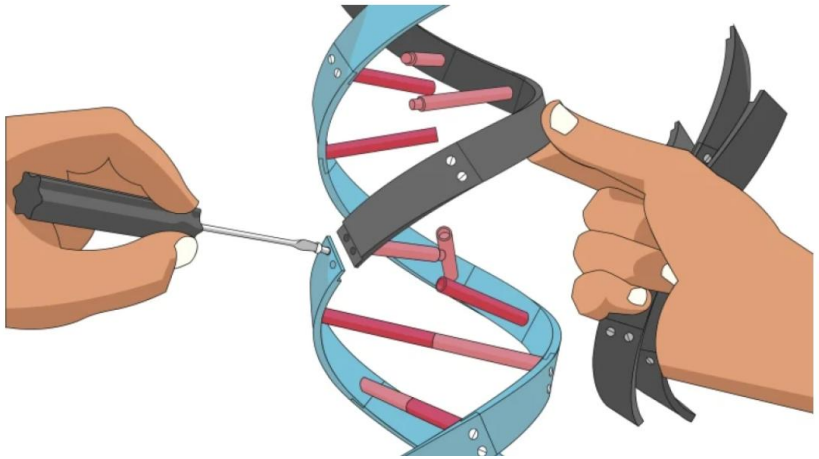


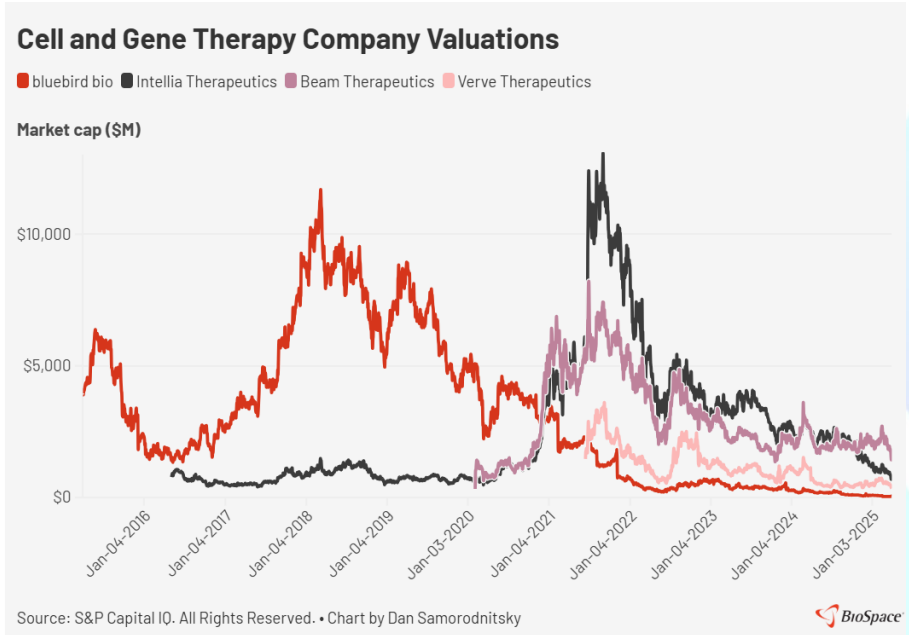
2025 expectations for C&GT - valuations

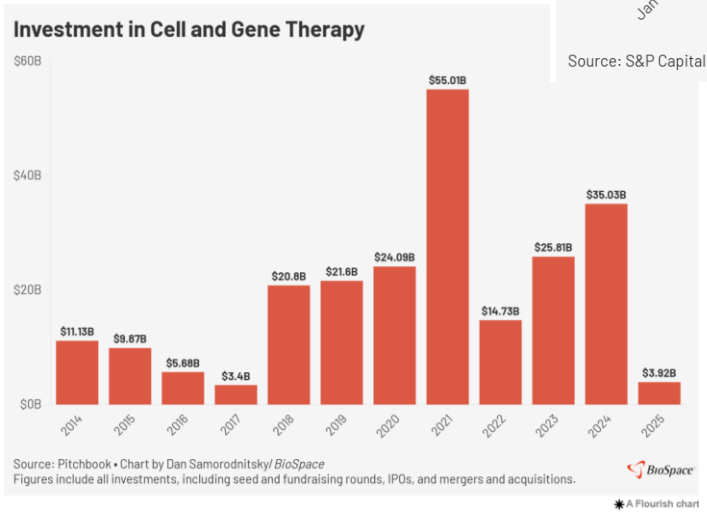
News › Business

As Gene Therapy Endures ‘Cold Winter,’ FDA Leaders Promise Support

June 11, 2025 | 6 min read | Dan Samorodnitsky







BioSpace®

11 June 2025

Challenges for C&GT funding – Reduction of interest in C&GT ?

- **Uncertainty**: Political / Geo-political instability; Public funding at risk

- **Very challenging to raise** despite good science; Low equity prices, down rounds
- Limited valuation of platform approach and pre-clinical assets;
- Company closures, reduction of staff, talent attrition
- Early science still being funded but more selectively

- Generalists abandoning sector, herd mentality
- Specialists looking for clinical stage or rapid return companies, large indications

- **Low appetite for high costs therapies**: cost of development and CoG
- Difficult to identify leads; **Need to have blockbuster products**
- Need to have ROI and adoption plus commercial traction of C&GT products

- Big pharma focused on large indications; Low appetite for small markets

- Alternative geographies; Alternative financing: M&A; BD

- **Critical to launch successfully: Launch is more than efficacy**

C&GT reasons to believe

Challenges for C&GT funding – Reasons to believe

- **Political environment in US; EU and Asia favorable to C&GT** product development: flexibility and focus
- Regulatory and HTA addressing the specificities of C&GT (accelerated; platform)

- Policies to improve competitiveness of biotech through funding; bio-hubs; regulatory agility

- **Clinical success with cure and long-term therapeutic value**
- Developments addressing the **reduction of CoG** and increase in capacity
- Move to **larger and more prevalent indications**

- **Expected commercial success**
- Market expansion to over **50 billion USD by 2030**
- Target of over **10 blockbuster** products by 2030 with 5 already in 2025

- **Success of the field – restore confidence and willingness to invest**
- Lower CoG; adequate launches and patient adoption; return on investment

- BD through licensing and M&A as **funding alternatives: Pharma exits!**

- Opportunity to **train and educate** those inside and outside C&GT field!!!!

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

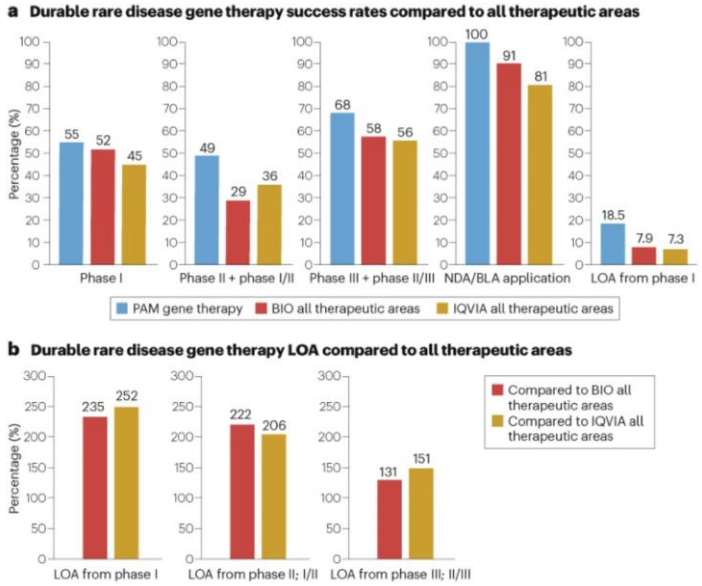
In-vivo CARs enter the scene: Groundbreaking in-vivo CAR-T and CAR-Gene therapy concepts enter clinical trials

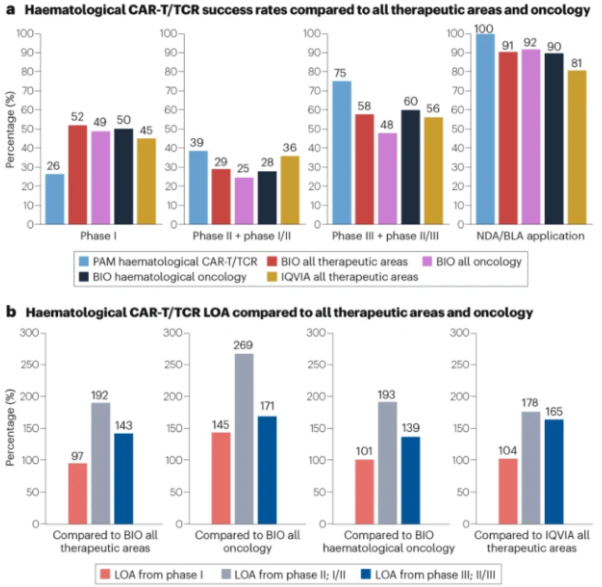
CGTs Are More Likely to be Approved

nature reviews drug discovery

FROM THE ANALYST'S COUCH | 27 February 2025

Clinical development success rates for durable cell and gene therapies





Durable orphan gene therapies

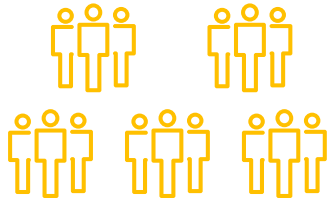
Hematological CAR-T/TCRs

18.5%
overall likelihood of FDA approval once entering Phase 1 clinical trials

2.5 times
more likely to receive FDA approval than all drugs once entering Phase 1 trials (IQVIA)

40%
more likely to receive FDA approval than other oncology drugs (BIO 2011-2020)

Prevalent Disease Breakthroughs Are Coming

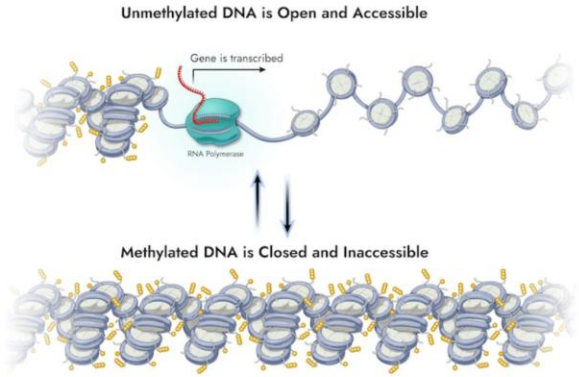
Wet AMD	Parkinson's	Multiple Sclerosis	Type 1 Diabetes	HeFH / Premature CAD
				
5.7 million patients in US, EU and Japan	**10 million** patients worldwide	**1.5 million** patients in US, EU and Japan	**3.8 million** patients in US, EU and select geographies	**3 million*** patients in US and EU
Phase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

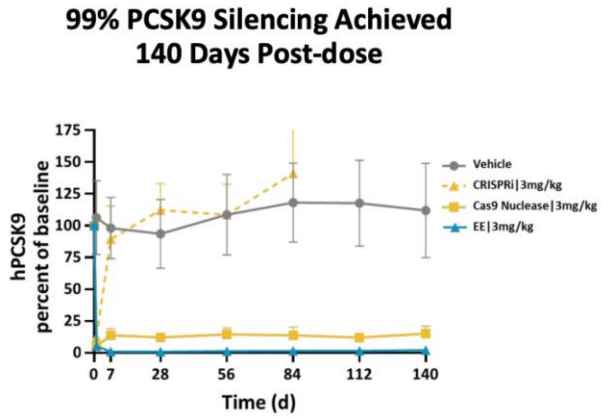
Source: Company estimates from Vertex Pharmaceuticals, Kyverna Therapeutics, REGENXBIO, BlueRock Therapeutics and Verve Therapeutics

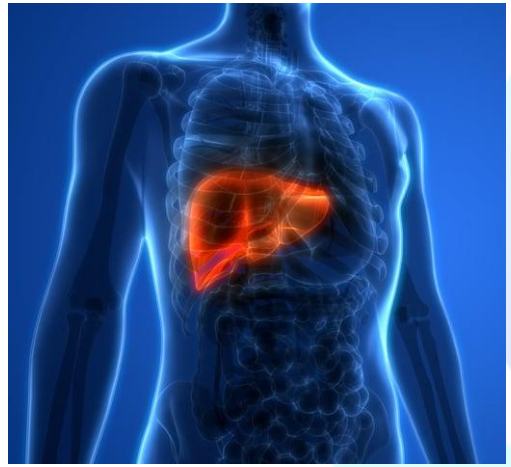
* Patient figure is Heterozygous Familial Hypercholesterolemia (HeFH) only

Epigenetic editing and large population gene therapy!

Editing “above the level of DNA”







https://chromamedicine.com/wp-content/uploads/2023/08/2023_ASGCT-Spotlight-IO.pdf

PCSK9 is a proprotein convertase which is involved in the degradation of LDL receptors in the liver.
Blocking the activity of PCSK9 reduces the degradation of LDL receptors and increases the clearance of LDL-cholesterol.

June 17, 2025 07:15 AM EDT | Deals

Lilly to bolster gene editing pipeline, buying Verve for up to $1.3B

Reynald Castañeda
Deputy Editor

17th June 2025

It appears that Eli Lilly couldn’t wait to get its hands on Verve Therapeutics’ PCSK9 program.

CoG for autologous cell therapies poised to decline

Leerink estimates gross margins improving to ~80% by 2030, driven by:

Product Volume

CAR-T market (NHL+MM) growth

2023: $2.4Bn

↓

2030: $6.8Bn

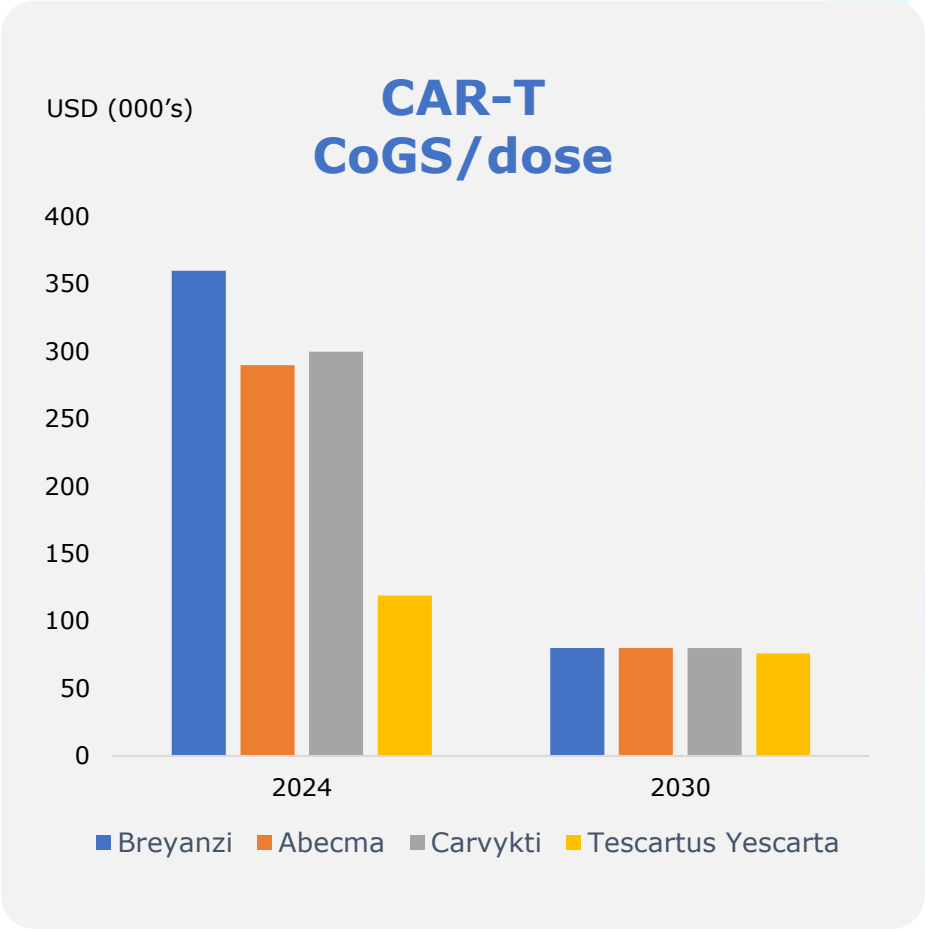
Process Improvement

	2023	2029
OOS Rate:	13%	→ 3%
MFG Time:	30d	→ 12d

Innovation

Automation & Tools

LVV Cost Reduction



Leerink Partners, March 2024

The Promise of In Vivo Gene Therapy

Advantages

- **Direct delivery** of genetic material
- Avoids ex vivo manipulation, reducing complexity
- Potential for widespread tissue targeting (e.g., liver, CNS, etc.

Key Modalities

- **Viral vectors** (AAV, lentivirus, adenovirus) – high transduction efficiency, tissue tropism
- **Non-viral approaches** (LNPs, polymeric nanoparticles, electroporation) – lower immunogenicity

Therapeutic Potential

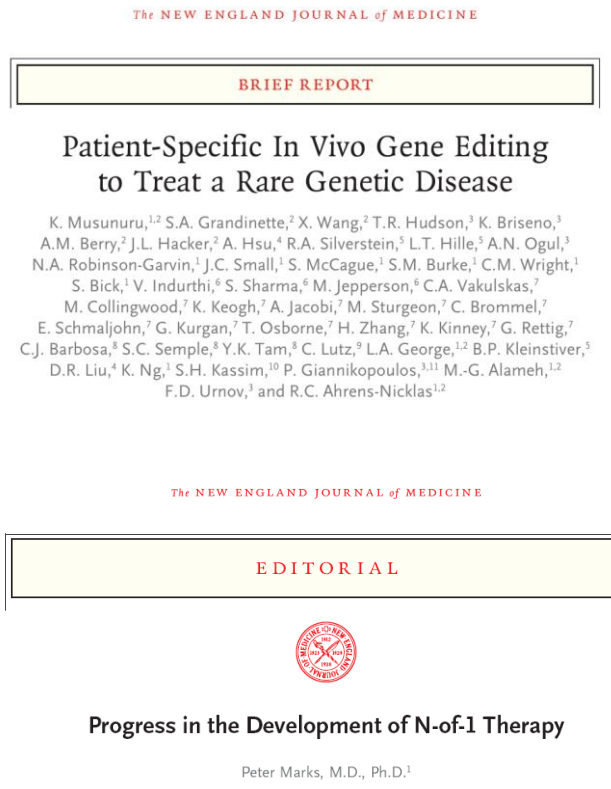
- Monogenic disorders (e.g., hemophilia, muscular dystrophy)
- Neurodegenerative diseases (e.g., SMA, Huntington's)
- Cardiac and metabolic disorders (e.g., Danon)

Challenges to Overcome

- **Immune responses** against vectors (pre-existing antibodies to AAV)
- **Scalability** and manufacturing bottlenecks

Adapted from Caldwell et al., Frontiers in Immunology 2021, 11

The individual gene editing therapy – “N-of-1”



The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Patient-Specific In Vivo Gene Editing to Treat a Rare Genetic Disease

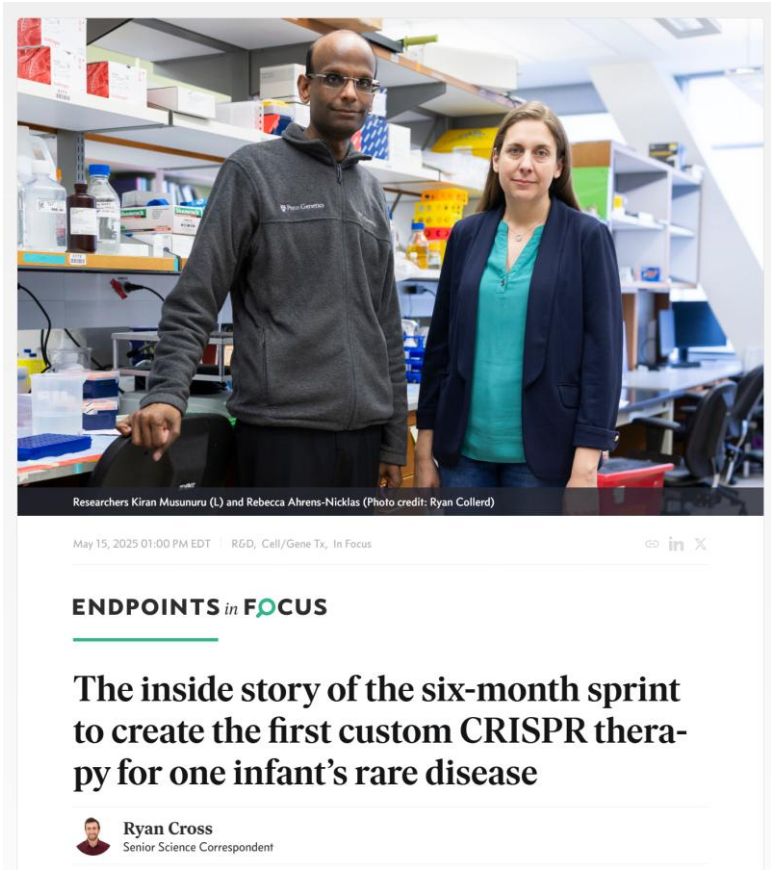
K. Musunuru,[1,2] S.A. Grandinette,[2] X. Wang,[2] T.R. Hudson,[3] K. Briseno,[3] A.M. Berry,[2] J.L. Hacker,[2] A. Hsu,[4] R.A. Silverstein,[5] L.T. Hille,[5] A.N. Ogul,[3] N.A. Robinson-Garvin,[1] J.C. Small,[1] S. McCague,[1] S.M. Burke,[1] C.M. Wright,[1] S. Bick,[1] V. Indurthi,[6] S. Sharma,[6] M. Jepperson,[6] C.A. Vakulskas,[7] M. Collingwood,[7] K. Keogh,[7] A. Jacobi,[7] M. Sturgeon,[7] C. Brommel,[7] E. Schmaljohn,[7] G. Kurgan,[7] T. Osborne,[7] H. Zhang,[7] K. Kinney,[7] G. Rettig,[7] C.J. Barbosa,[8] S.C. Semple,[8] Y.K. Tam,[8] C. Lutz,[9] L.A. George,[1,2] B.P. Kleinstiver,[5] D.R. Liu,[4] K. Ng,[1] S.H. Kassim,[10] P. Giannikopoulos,[3,11] M.-G. Alameh,[1,2] F.D. Urnov,[3] and R.C. Ahrens-Nicklas[1,2]

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

Progress in the Development of N-of-1 Therapy

Peter Marks, M.D., Ph.D.[1]



Researchers Kiran Musunuru (L) and Rebecca Ahrens-Nicklas (Photo credit: Ryan Collerd)

May 15, 2025 01:00 PM EDT | R&D, Cell/Gene Tx, In Focus

ENDPOINTS in FOCUS

The inside story of the six-month sprint to create the first custom CRISPR therapy for one infant’s rare disease

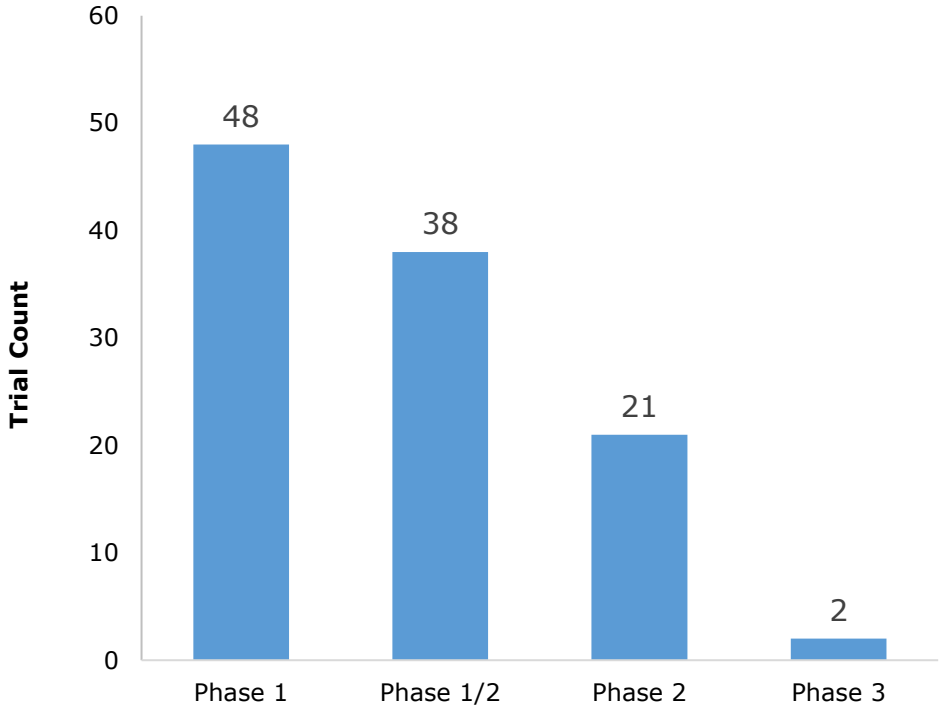
Ryan Cross
Senior Science Correspondent

Baby Kyle Patrick “KJ” Muldoon, Jr., shortly after his birth (left); KJ and his parents soon after receiving treatment, at the Children’s Hospital of Philadelphia (courtesy of the Children’s Hospital of Philadelphia and the Muldoon family)

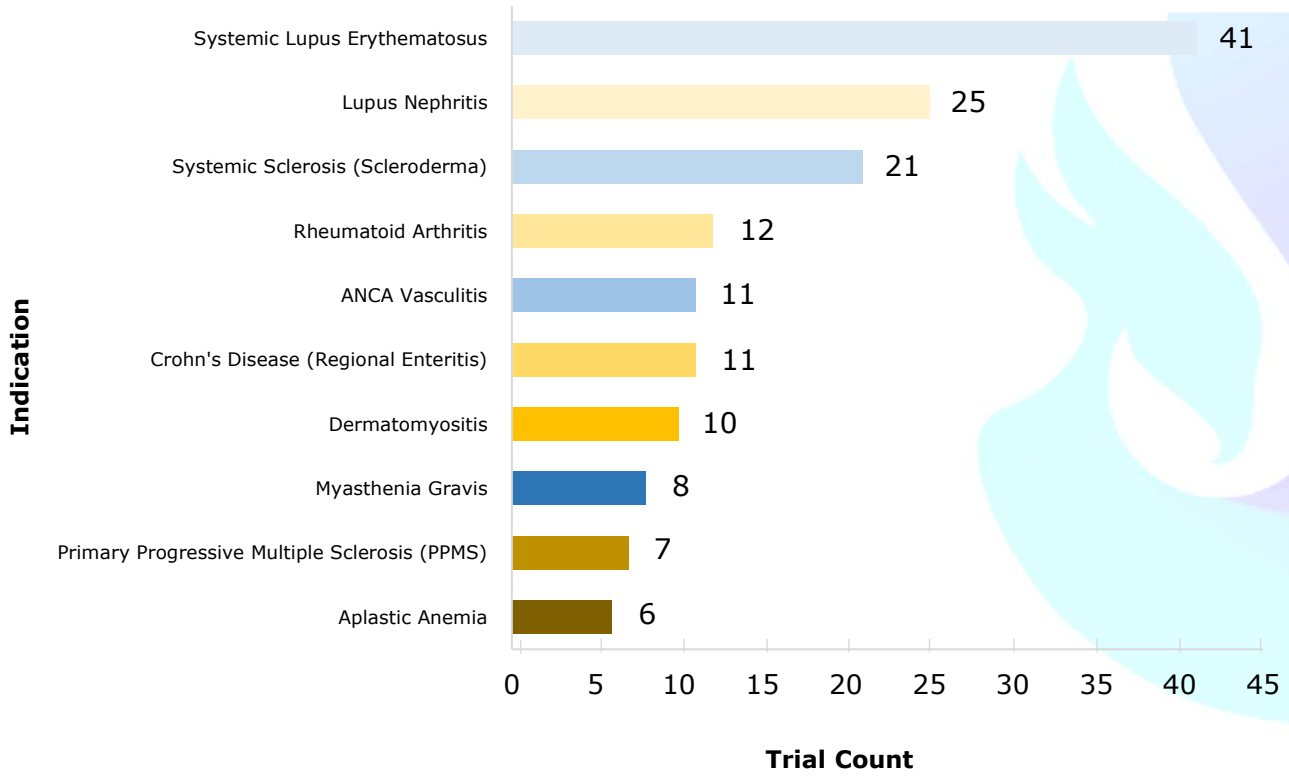
- KJ, born with severe c**arbamoyl-phosphatase synthetase 1 deficiency**
- Treated with a customized **lipid nanoparticle-delivered base-editing** therapy
- Collaborative effort between the Children’s Hospital of Philadelphia, the Innovative Genomics Institute, Berkeley, Danaher, and others
- The first patient to receive a **patient specific gene editing therapy**

Promise in Autoimmune Diseases: 107 Ongoing Trials

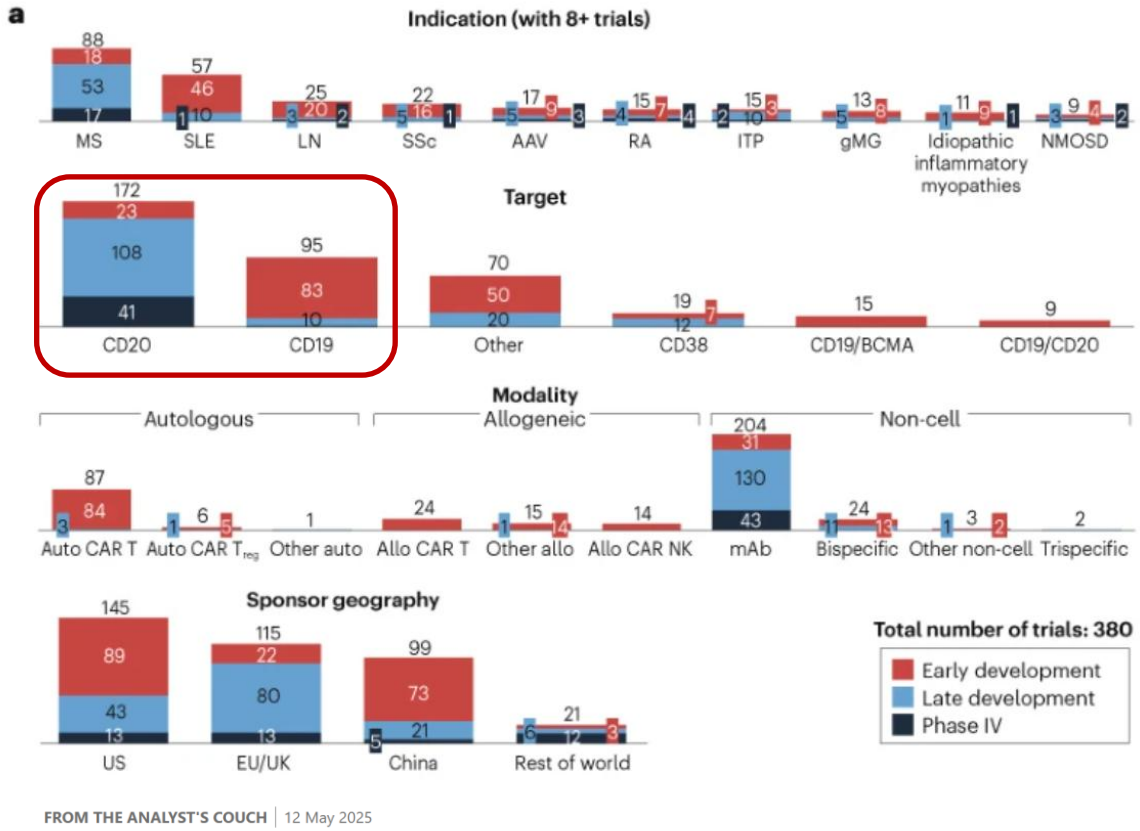
Autoimmune Trials by Phase



Top 10 Most Explored Autoimmune Indications



The race to reset the immune system - Autoimmunity



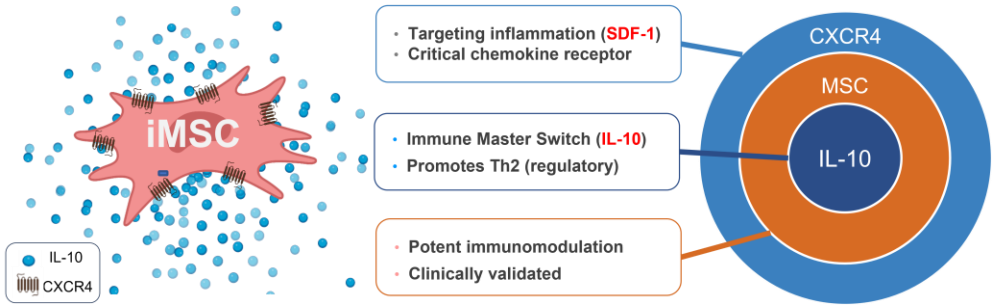
FROM THE ANALYST'S COUCH | 12 May 2025

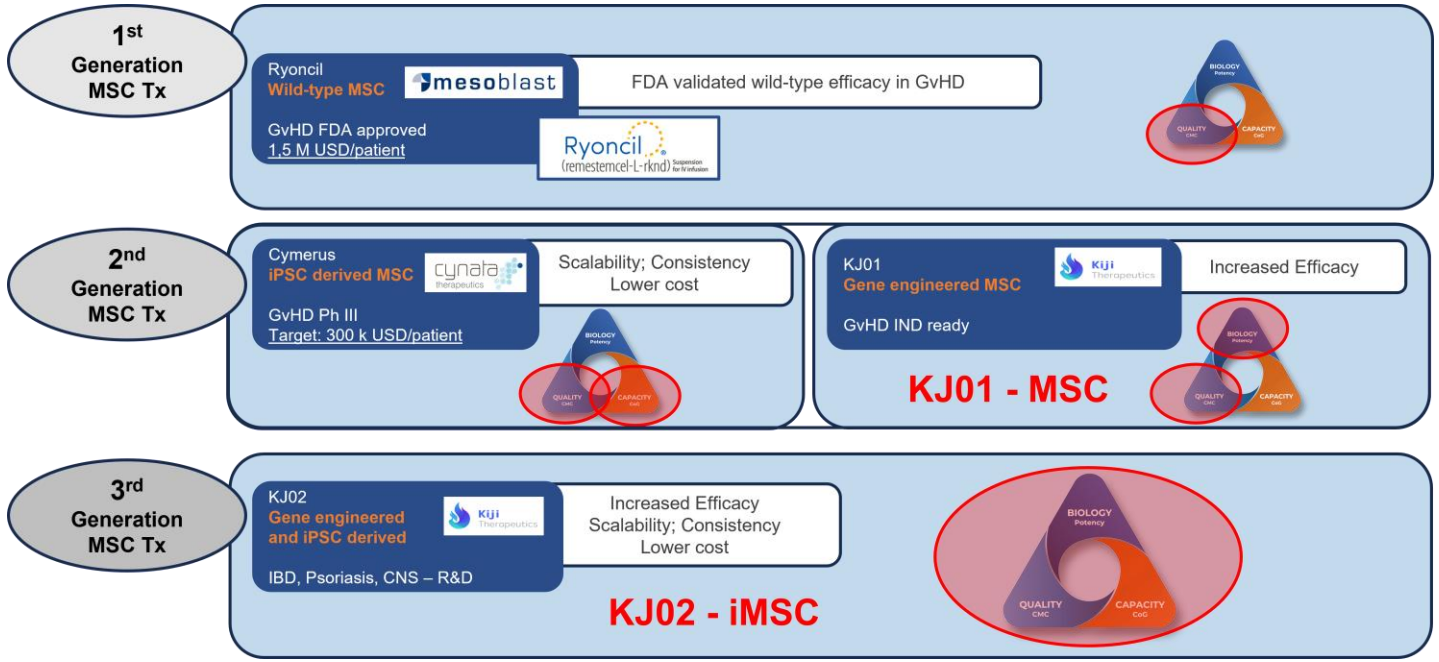
The race to reset autoimmune diseases

By Mayank Bhandari, Jeffrey F. Smith, Emily Capra & Guang Yang

High number of IIS – Public/Private opportunity
Insistence in CAR-T: B Lymphocyte focus
Large unmet medical need; Huge market opportunity

Resetting autoimmune diseases with gene engineered iMSCs - Kiji Therapeutics





- Proprietary multi-gene engineered cell therapy, lentiviral IL10/CXCR4, for improved clinical benefit in autoimmune diseases –

  GvHD, IBD and Psoriasis

- **Resetting the innate immune system** for long term clinical benefit with extensive pre-clinical MoA data in multiple positive animal models

- **Milestones:**
  - Clinical data in GvHD in 2026/27
  - iPSC derived MSC platform in 2027
  - Initiate clinical development for IBD, Psoriasis in 2027/2028

Pipeline

	Technology (Allogeneic; Off-the Shelf)	Indication	Stage				
			Discovery/ Pre-clinical	IND/CTA enabling studies	Clinical		
					IND/CTA	FPFV	Data
KJ01	Donor Ad-MSC (IL10/CXCR4) GMP grade	SR-aGvHD	IND package available		2H25	1H26	1H27
KJ02	iPSC - iMSC (IL10/CXCR4) R&D grade	IBD	IND package in development		1H27	1H27	2028
		Psoriasis	R&D; Pre-clinical		1H27	2H27	2028
		CNS (collaboration R&D / option)	R&D		2H27	1H28	2029

Multiple clinical indications within the next 3 to 4 years;

The market …

Commercial success needed….

Drug	Company	2024 Revenue ($M)	Cost ($)	Modality	Disease
Yescarta	Kite Pharma (a Gilead company)	1,600	424K	Ex-vivo autologous CAR-T (CD19)	Relapsed/Refractory Large B cell lymphoma
Zolgensma	Novartis	952 (Q1-Q3)	2.1M	AAV9-*SMN*	Spinal muscular atrophy (SMA)
Carvykti	Legend Bio, J&J	963	465K	Ex-vivo autologous CAR-T (BCMA)	Relapsed/Refractory Multiple myeloma
Elevidys	Sarapeta Therapeutics	820	3.2M	AAVrh74 -*micro-dystrophin*	Duchenne muscular dystrophy (DMD)
Breyanzi	Juno Therapeutics, (a BMS company)	747	500K	Ex-vivo autologous CAR-T (CD19)	Relapsed/refractory NHL and and CLL
Kymriah	Novartis	443	475K	Ex-vivo autologous CAR-T (CD19)	Relapsed/Refractory ALL in children and young adults, and DLBCL and FL in adults
Tecartus	Kite Pharma (a Gilead company)	403	373K	Ex-vivo autologous CAR-T (CD19)	Relapsed/Refractory Mantle cell lymphoma (MCL) or ALL
Vyjuvek	Krystal Biotech	290	24K/ vial $631K/annually	HSV-1-COL7A1 (topical)	Dystrophic epidermolysis bullosa (DEB)
Abecma	Celgene Corporation (a BMS company)	242	420K	Ex-vivo autologous CAR-T (BCMA)	Relapsed/Refractory Multiple myeloma
Amtagvi	Iovance Biotherapeutics	103.6	515K	TILs	Unresectable or metastatic melanoma

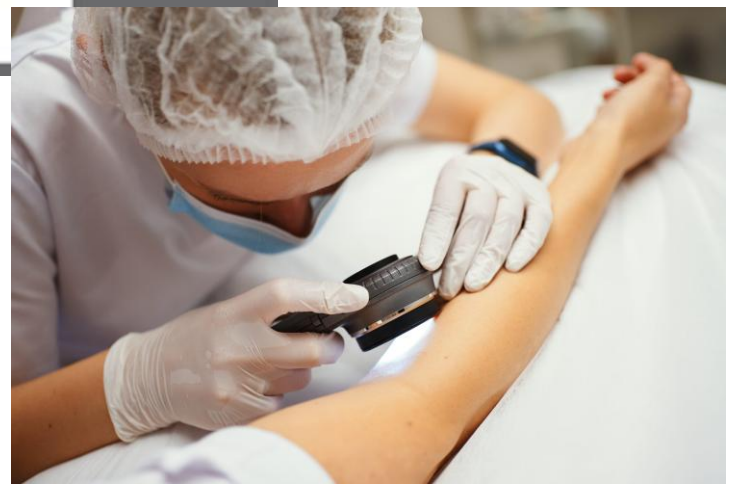
The ZOLGENSMA™ Success Story

- **Approved in over 50 countries**
- Access established in over 45 countries (68% of revenue comes 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 ELEVIDYS™ Success Story

- Approved in **eight countries**
- ELEVIDYS broad coverage is progressing and not a single patient has been permanently denied coverage as of February 2025
- Over 800 patients treated worldwide
- **On track for blockbuster status in 2025**
- Expansion of label in 2024 improves growth prospects; possible additional expansion to toddlers

The VYJUVEK™ Success Story



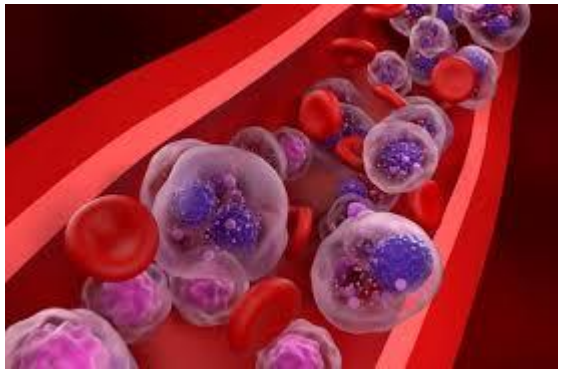
- USA Approval in 2023 (first redosable gene therapy)
- **Robust nationwide coverage in US** and achieved positive policies or coverage decisions from plans covering 97% of commercial and Medicaid lives
- Approved in the EU (2025); seeking approval in Japan
- In 2024, Vyjuvek generated $290 million in revenue
- Reached **gross margin** of 95% in Q4 2024

The YESCARTA™ Success Story

- Approved in **over 30 countries**
- Access established in over 21 countries (58% of revenue came from ex-US in 2024)
- Over 20,000 patients treated worldwide
- **Blockbuster status since 2023 and projected to grow to over $2B in global sales by 2030**
- Captured 92% of US academic ATCs, covering over 97% of the serviceable population. Expanding into the second-line relapsed or refractory DLBCL setting in Europe.

The CARVYKTI™ Success Story

CARVYKTI™
(ciltacabtagene autoleucel) Suspension for IV Infusion



- Approved in over 5 countries
- Only approved CAR-T in MM that has significant use in **outpatient settings** (50%), with 100+ authorized treatment centers
- Over 5,000 patients treated worldwide
- **On track for blockbuster status in 2025 and projected to exceed $6B in peak annual sales**
- 60% of usage comes from 2nd to 4th line setting

The Ryoncil™ Success Story

FDA approved in December 2024

First and only MSC C&GT approved in the US.
Significant milestone in cell therapy

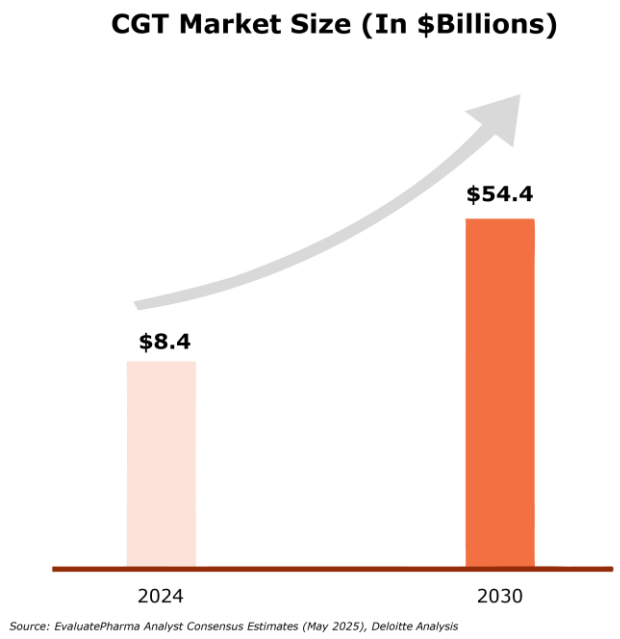
Targeting the unmet medical need og GvHD

Towards good market penetration and willingness to use

Intention for **label-extension to other autoimmune** diseases

Scientific Breakthroughs Become Commercial Successes

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



Source: EvaluatePharma Analyst Consensus Estimates (May 2025), Deloitte Analysis

Commercial Blockbusters

(with estimated >$1B annual worldwide sales)

2018 *Global CGT revenue totals ~500 million*

1 **2021** zolgensma

2 **2022** YESCARTA

5 **2025** CARVYKTI (ciltacabtagene autoleucel) Elevidys Breyanzi (lisocabtagene maraleucel) SUSPENSION FOR IV INFUSION

10 **2030** *Driven by currently launched and late-stage pipeline therapies (analyst Consensus Data)*

Source: EvaluatePharma Analyst Consensus Estimates (May 2025), Deloitte Analysis

Significant C&GT Financings and Partnerships in 2025

Public Financings	Venture Capital	Partnerships (Upfront Payments)
Beam Therapeutics	TUNE Therapeutics	AstraZeneca, EsoBiotec
$500M	$175M	$425m
SOLID Biosciences	Atsena Therapeutics	MeiraGTx
$200M	$150M	$200M
Taysha Gene Therapies	SpliceBio	Nippon Shinyaku, REGENXBIO
$200M	$135M	$110M

Big Biopharma is Committed to Partnering with Emerging Biotech to Accelerate Early Efforts

Since 2020, 20 largest biopharma companies have entered into:[1]

>110 partnerships with CGT-focused biotechs

$5B+ In aggregate up-front cash

$73B+ in aggregate deal value

COLLABORATIONS ALLOW BIOTECHS TO EXPAND OR ACCELERATE THEIR PIPELINES, BROADEN THEIR GEOGRAPHIC REACH, AND/OR ACCESS ENABLING TECHNOLOGIES[2]

- abbvie + Umoja Biopharma — CAR-T cell therapy for oncology
- Lilly + verve Therapeutics — Gene editing for cardiovascular disease
- Bristol Myers Squibb + prime medicine — Gene editing for next-generation cell therapies
- Novartis + VYRIAD — *In vivo* CAR-T cell therapies
- Gilead + Arcellx — Cell therapy for multiple myeloma
- Vertex + ORNA — Gene editing program for SCD and TDT

[1] Data per BioCentury database; [2]deals shown here are representative sample

Politics, regulation and society…

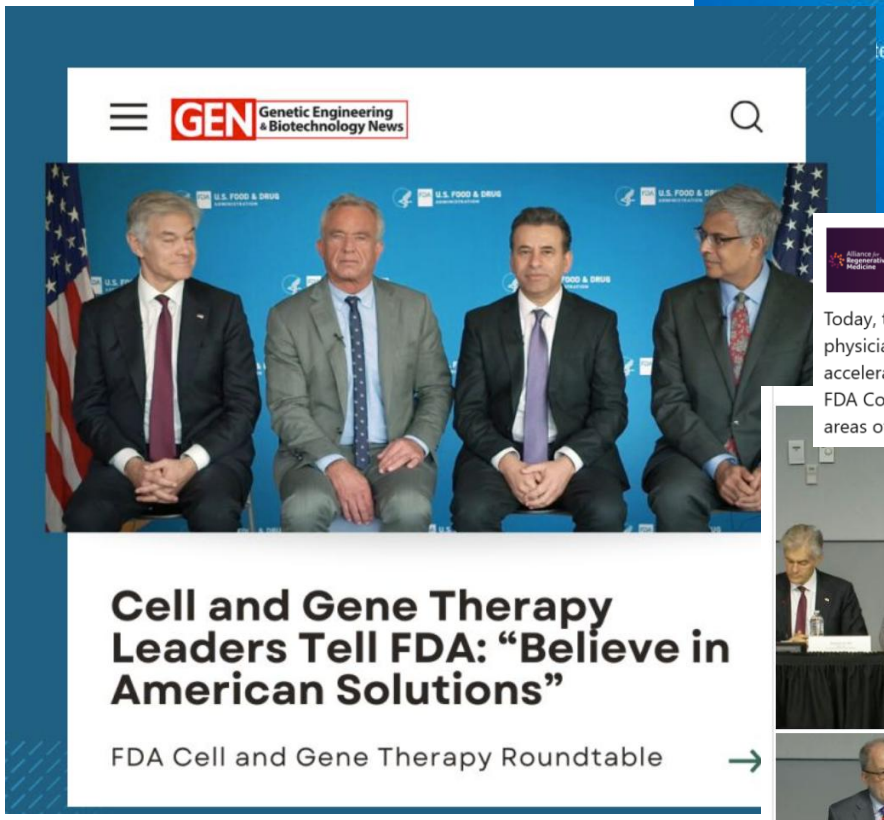
Cell and Gene Therapy Sector Data: Q4 2024

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%

The evolving political landscape in US and EU



Alliance for Regenerative Medicine
29,088 followers
1w • Edited •

Today, the most senior U.S. health agency leaders met with leading scientists and physicians, patient advocates, and company leaders to explore how we can accelerate the development of, and patient access to, cell and gene therapies – what FDA Commissioner Dr. Marty Makary described as "one of the most cutting-edge areas of all clinical medicine."

Alliance for Regenerative Medicine
29,088 followers
6d •

Today, ARM brought together leaders from the advanced therapy sector in Brussels for high-level dialogue with EU Health Commissioner Olivér Várhelyi.

The EU Biotech Act: Europe’s answer to global biotech competition

The EU is preparing a Biotech Act to strengthen Europe’s position in the global life sciences race.

The aims in a nutshell:

- **Cut regulatory red tape**
- **Attract capital**
- **AI/digital first**
- **Compete against US & China.**

Regulatory simplifications

- **Streamlining HTA approval processes**
- Reducing **regulatory fragmentation** for multi-country clinical trials
- Establishing regulatory sandboxes to accelerate market introduction

Creation of an EU Biotech Hub

- Dedicated operational tool to help biotech companies navigate regulations and access support

Integration of AI and supercomputing

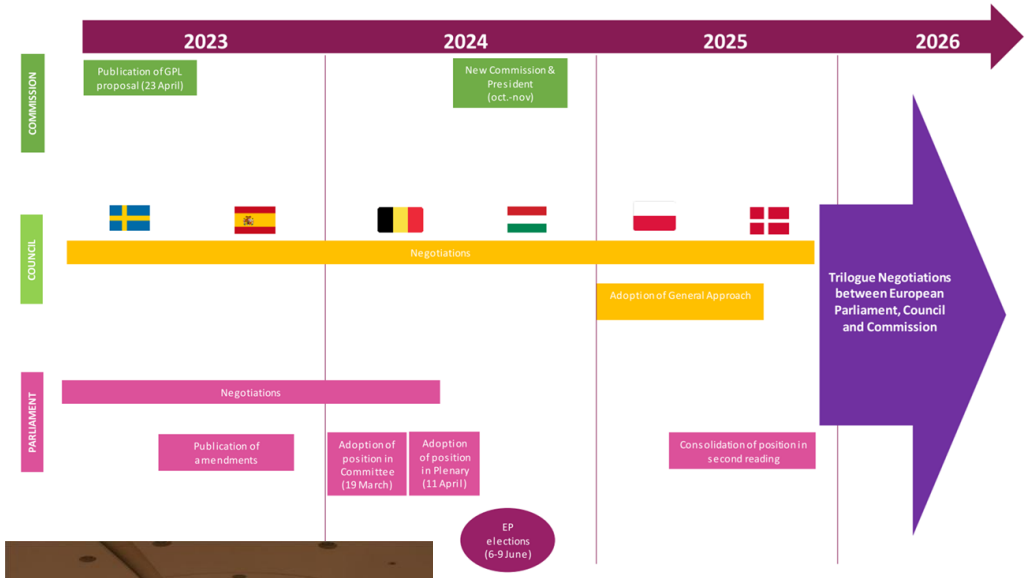
- AI to enhance pharmaceutical advancements and drug discovery
- Quantum technology to improve medical diagnostics and personalized treatments

Investment and funding support

- **Public and private investments** through existing (EU4Health, Horizon Europe, HERA Invest) and potential new programs (European Innovation Council Accelerator, European Investment Bank)

Reform of the EU pharmaceutical legislation

- Removal of **CAT**
  - Concern to lose the knowledge, expertise and the focus
  - Maturity of the system?
- **BWP** not fully representative of EU MS
- Classification of MP and ATMP
  - Article 61 gives the mandate to the Agency to recommend classification - MS disagreement is possible
- **GMO in CT**
  - Centralized assessment of GMO according to Directive 2001/18 on deliberate release by CHMP
- **Hospital Exemption**
  - Article 2 confirms HE
- Additional **master files**
  - Article 26 makes it more flexible
- **SoHO** regulation
  - No significant change (import/export starting materials: potential challenge)



HTAR: a value system under construction

Opportunity:

- Single system; Evolution as the Centralized Regulatory System
- Joint expertise
- Integration with the regulatory process
- Speed

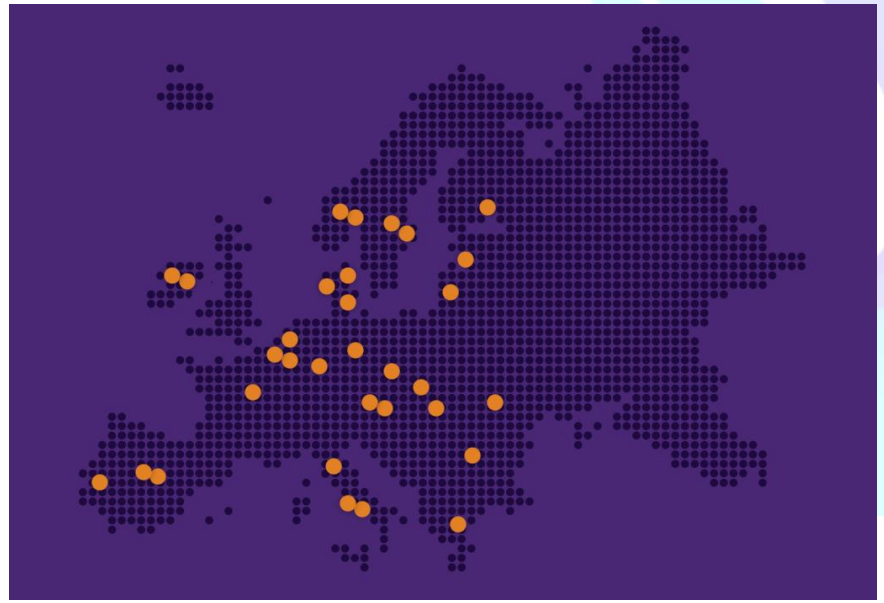
Challenges:

- Growing pains through implementation
- Need to be suited to purpose - Pragmatism
- Methodologies for the JCA
- Transposition to MS actions

Clearly a positive move aligned with EU vision reflecting the challenges of EU implementation

HAG
HEADS OF HTA AGENCIES GROUP

32 different **HTA Bodies** all over Europe



Europe: stakeholder collaboration: Public/Private

- **Increase EU competitiveness**

- Research and development
- **Company creation** – Academia; Public Institutions

- **Flexible funding**: small faster vs large slower: **The Public as LPs and the hubs as VCs**
- Public / Private partnerships: IIS and Private Sponsors

- Clinical development; **Clinical trials**
- **Faster, adaptable and flexible regulatory, including HTA**

- Patient associations; NGO and non-for-profit; Academic and Professional organizations

- **Commercial success**: Patient access; Commercialization alternatives; return on investment

Ethics

Ethics: Tackling the field issues proactively

C&GT, Ethics and society

- Cell and Gene therapy value and pricing – innovation, access and sustainability
- Industrialization for global access
- Low patient numbers and orphan/rare diseases versus large indications
- The frontiers of technology and innovation

- **Evidence; Cost; Value; Access; Global view**

Guardrails of HHGE: Heritable Human Genome Editing

COMMENT

Don't edit the human germ line

Heritable human genetic modifications pose serious risks, and the therapeutic benefits are tenuous, warn **Edward Lanphier**, **Fyodor Urnov** and colleagues.

Contents lists available at ScienceDirect

Editorial

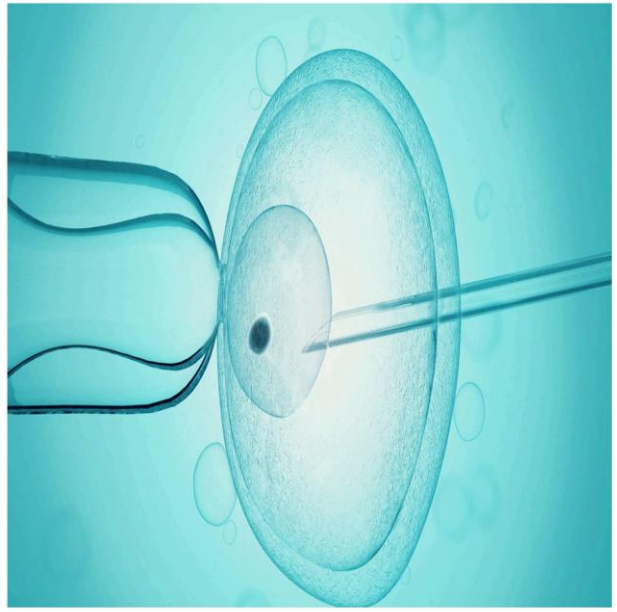
CYTOTHERAPY

journal homepage: www.isct-cytotherapy.org

International Society ISCT Cell & Gene Therapy®

International Call for a 10-Year Moratorium on Heritable Human Genome Editing

A multi-stakeholder initiative to ensure safe and responsible use of genetic technologies May 2025



Alliance for Regenerative Medicine

ASGCT American Society of Gene + Cell Therapy

International Society ISCT Cell & Gene Therapy®

The danger of over-DE-regulation

Montana Set to Become a "Wild West" Hub for Experimental Medical Treatments and Therapies

May 22, 2025

Cytotherapy 24 (2022) 686–690

Contents lists available at ScienceDirect

CYTOTHERAPY

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International Society ISCT Cell & Gene Therapy®

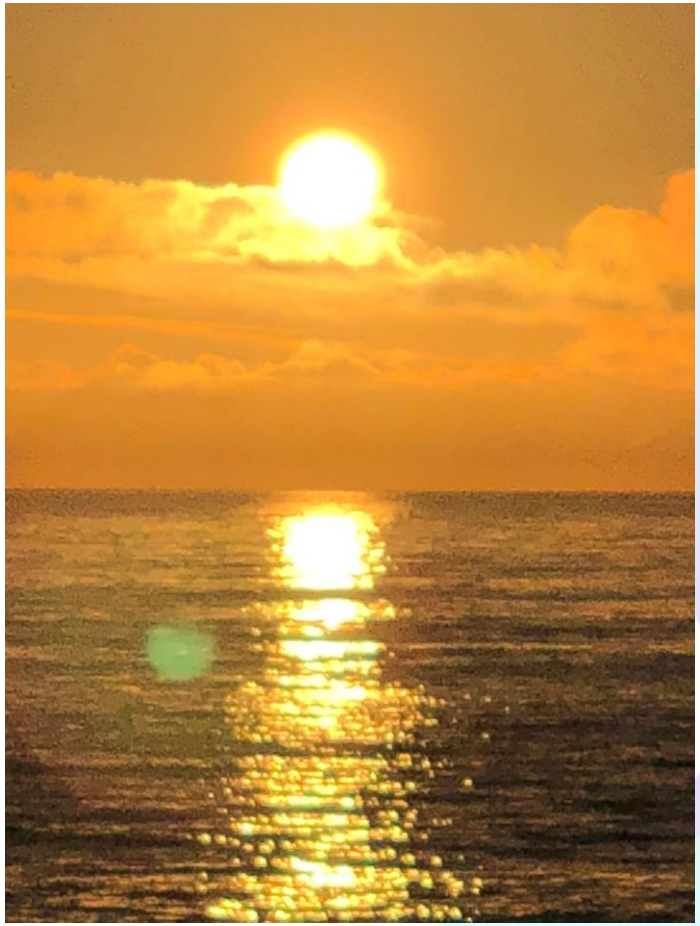
ELSEVIER

ISCT Committee Paper

Patient access to and ethical considerations of the application of the European Union hospital exemption rule for advanced therapy medicinal products

Natividad Cuende[1,*], Rachele Ciccocioppo[2,*,**], Miguel Forte[3,4], Jacques Galipeau[5], Laertis Ikonomou[6], Bruce L. Levine[7], Alok Srivastava[8,9], Patricia J. Zettler[10,11,12]

Alternative business models



The need for new models / approaches

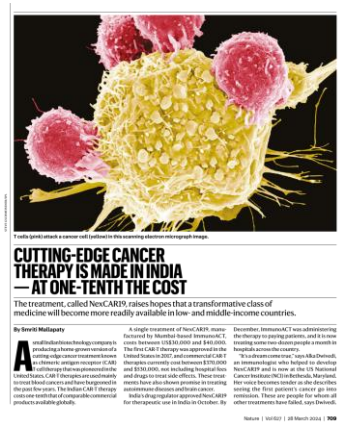
Models for Academic and Institutional R&D
Translational models – Company creation
Funding; Public and Private
Private / Public partnership

Regulatory approach
Models for clinical development
Models for HTA assessment

Approach to launch – Efficacy is not all; the market needs to be educated – product launch
Models for payment

Regional models for **global access**
ATMP and **Hospital Exemption**

Make sure not to alienate the out of CGT fields;
Comply with the real world. Not special just sometimes different



CUTTING-EDGE CANCER THERAPY IS MADE IN INDIA — AT ONE-TENTH THE COST

The treatment, called NexCAR19, raises hopes that a transformative class of medicine will become more readily available in low- and middle-income countries.

NEWS | 06 October 2023

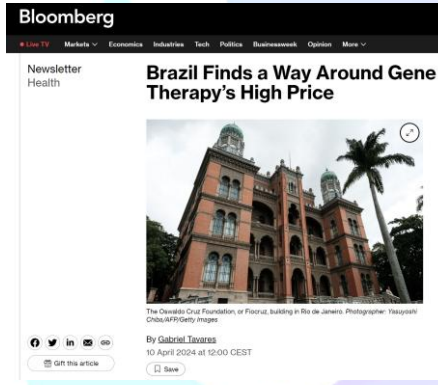
Rescue of an orphan drug points to a new model for therapies for rare diseases

In a world-first, the Italian research charity Telethon will manufacture and distribute a gene therapy for an inherited immunodeficiency that was dropped by the industry.

By Maria Cristina Valsecchi

Several gene therapy or stem cell products have been dropped by commercial manufacturers because of high production costs. Credit: RF/Andrew Brookes/Getty Images

Telethon Foundation has decided to take over the licence to produce and distribute Strimvelis, a gene therapy product that is the only available cure for a rare condition called ADA-SCID, and that the biopharma company Orchard Therapeutics had discontinued in 2022. It's the first time in the world that a non-profit organisation takes on such a role.



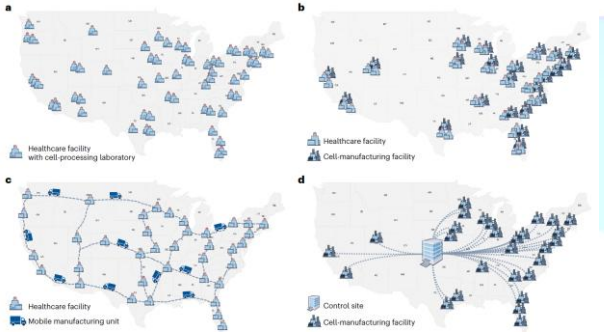
Bloomberg

Newsletter
Health

Brazil Finds a Way Around Gene Therapy's High Price

The Oswaldo Cruz Foundation, or Fiocruz, building in Rio de Janeiro. Photographer: Yasuyoshi Chiba/AFP/Getty Images

By Gabriel Tavares
10 April 2024 at 12:00 CEST



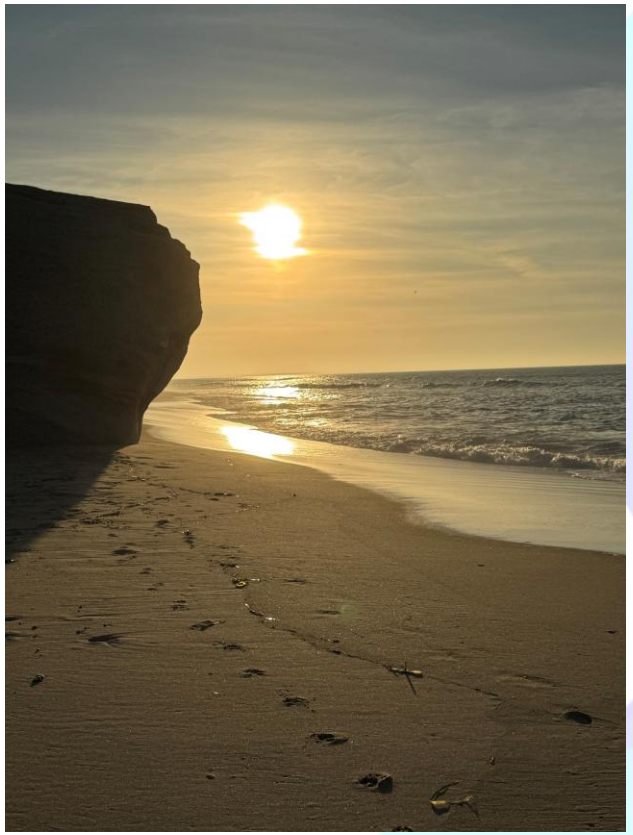
a
Healthcare facility
with cell-processing laboratory

b
Healthcare facility
Cell-manufacturing facility

c
Healthcare facility
Mobile manufacturing unit

d
Control site
Cell-manufacturing facility

Take home message !



Europe, ATMPs, innovation, competition, patient access

C&GT, Ethics and society

- **Evidence** supporting C&GT products benefit; Challenges with unproven C&GT products
- **Value**, cost and payment; **Manufacturing**
- **Global patient access**
- **Gene therapy**; Germ line editing

Global access

- **Workforce development**: R&D, production, assessment, administration
- Global and **point of care** manufacturing
- Financing, HTA, fair price,
- Alternative models: Public – Private partnerships; **Patient access**

R^2D^2

Risk square/ Decision square

Winter to or Summer for C&GT

- The value for patients; Patient access; Manage and deliver to stakeholder expectations
- **Foster innovation; develop alternative models for funding and collaborations**

- **Resilience and optimism**

Transforming – and often saving -- lives

Jimi Olaghere

After receiving a gene therapy treatment for his sickle cell disease, Jimi reports that he **no longer requires regular care for his condition** other than clinical follow-up.

Emily Whitehead

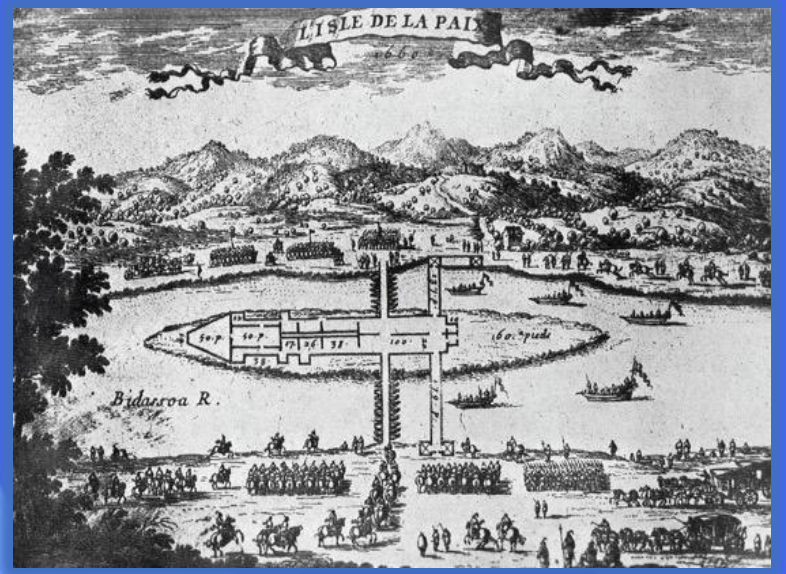
Diagnosed with acute lymphoblastic leukemia at age 5. Emily was the first pediatric patient globally to receive a CAR-T cell therapy. **Over 13 years later, she is still cancer-free**.

Weston Cook

Weston was diagnosed with Spinal Muscular Atrophy type 1, which kills many patients by age 2. Weston received gene therapy, which gave him **a shot at a normal life.**

KJ

KJ was born with a rare disease that put his life at risk. Thanks to a collaborative effort between CHOP, Danaher, and many others, he became the first patient to receive a **custom gene editing therapy and is now growing well and thriving**.



International Society ISCT Cell & Gene Therapy

Alliance for Regenerative Medicine

Kiji Therapeutics

UNIVERSIDADE DE LISBOA

m4Tx

StemBond Technologies

Swarm

Thank you!

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