Genomics Medicine 101

THBI
Legislative Briefing and Reception
January 2023

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UT Southwestern
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Cell and Gene Therapy: Emerging Transformative Paradigms for Treatment of Human Disease

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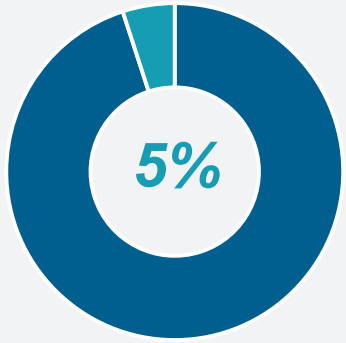
Any stated opinions are Dr. Gray's own, and not necessarily representing UTSW.

The **HUMAN GENOME** has approximately **20,000** genes

More than **6,000** diseases are caused by genetic mutations

Many are **RARE** diseases affecting 30 million Americans *(1 of 10)*

ONLY **5 percent** of these diseases have **APPROVED** therapies



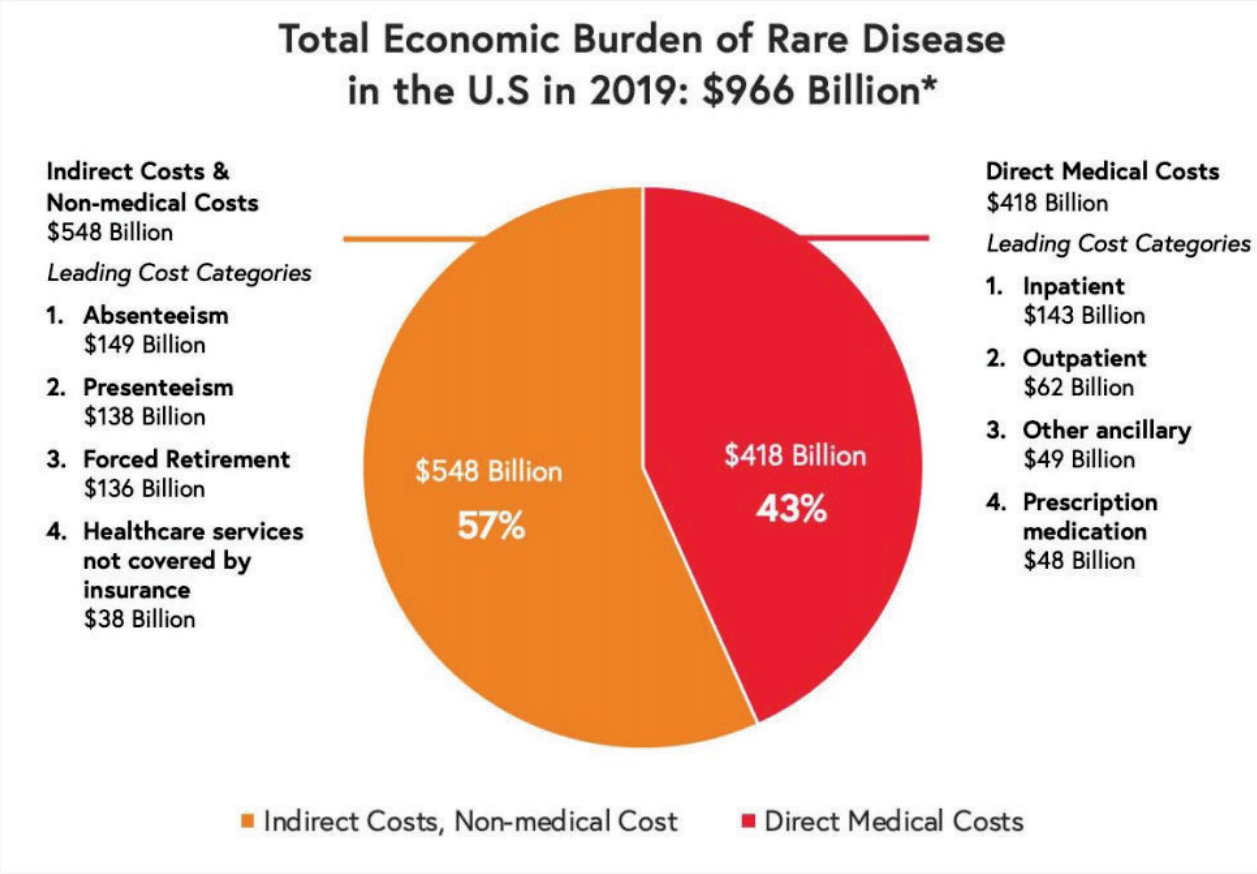
CBS NEWS NEWS SHOWS VIDEO CBSN MORE

FDA approves gene therapy for rare form of blindness

FORTUNE

The Way We Treat Cancer Will Be Revolutionized as Gene Therapy Comes to the U.S.

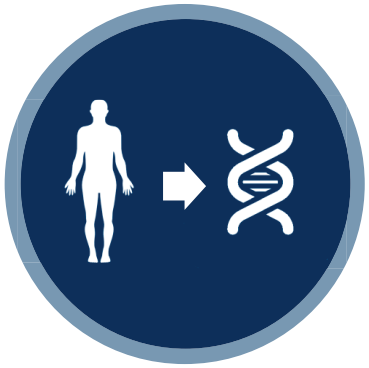
“Rare” Genetic Disease – a large but hidden problem



Source: EveryLife Foundation, published Feb 25, 2021

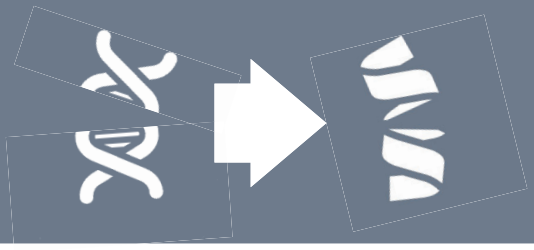
Broken Genes Lead to Broken Proteins

Humans are made of cells that contain our **genes**



Genes are instructions for **proteins**

Proteins help **cells** function in a healthy manner



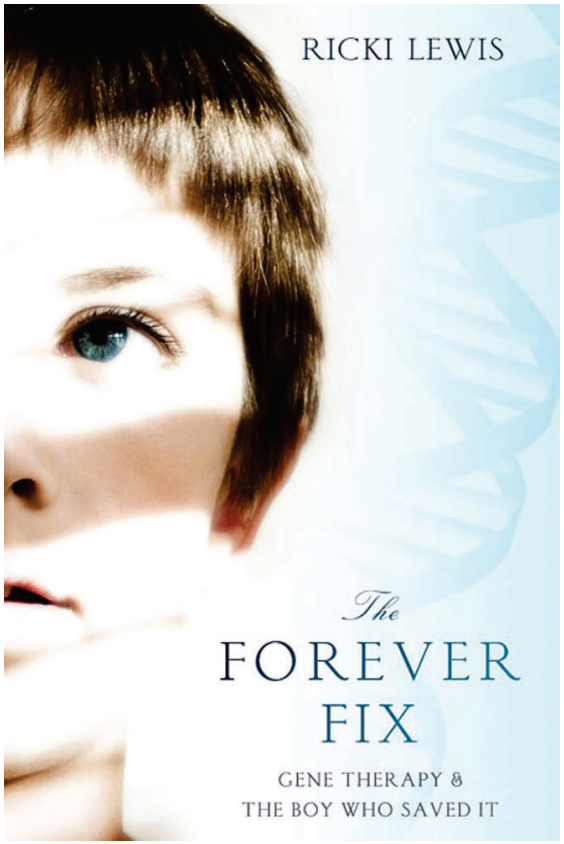
Abnormalities in genes can result in proteins that do not function properly

Gene Therapy vs *Cell Therapy*

- ✓ **Gene and cell therapy technologies work differently**
- ✓ **Both treat, prevent, and possibly cure disease**
- ✓ **Both are changing the way we fight disease, especially for patients with rare diseases and conditions**

Gene Therapy

Cell Therapy

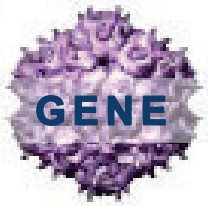


The promise of **gene therapy** is to fix a genetic disease at the source.

If you fix the DNA, you've solved the problem permanently.

How Does Gene Therapy Work?

Identify the causal defective gene



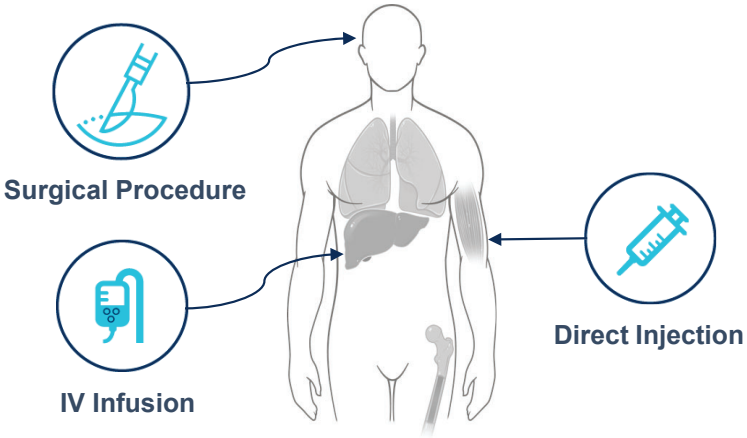
Package a ***working*** copy of the gene into a carrier like an engineered virus

Deliver the working copy of the gene back into the patient

Gene Therapy: Treating Patients

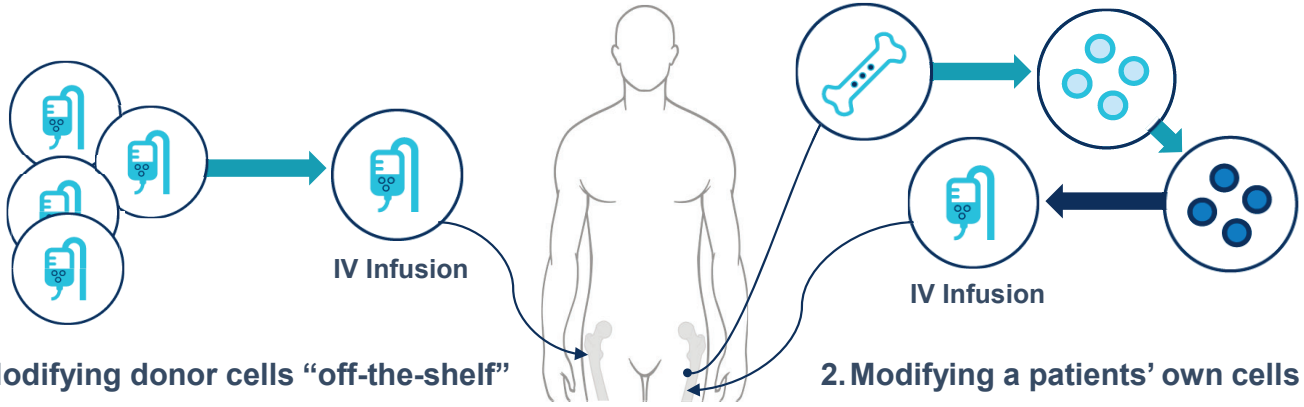
In Vivo Approaches

- Intervene inside the body
- Genome modifications within target cells after individuals receive a genomic medicine
- e.g., surgery, injection

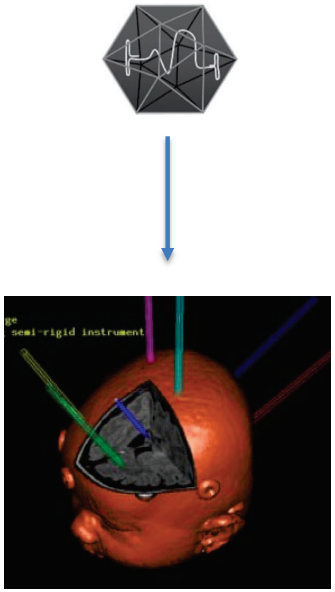


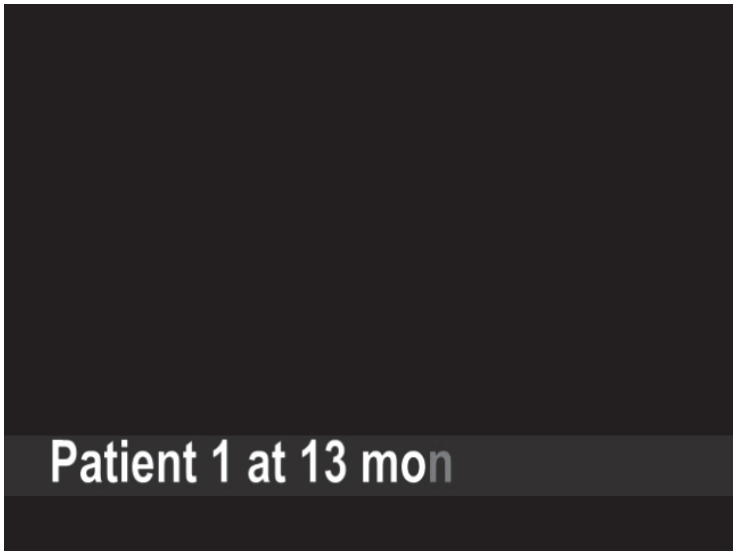
Ex Vivo Approaches

Outside the body,
create cell medicines by:



AAV Gene Therapy for AADC Deficiency





Sci Transl Med. 2012 May 16;4(134):134ra61.

Gene therapy for aromatic L-amino acid decarboxylase deficiency.

Hwu WL, Muramatsu S, Tseng SH, Tzen KY, Lee NC, Chien YH, Snyder RO, Byrne BJ, Tai CH, Wu RM.

Krabbe Disease

Affects ~1:200,000 children

Symptoms start at ~6 months

Typically fatal by 1-3 years old.

Jim and Jill Kelly with their son Hunter in 2004. Hunter, who had Krabbe disease, died in 2005 at age 8.

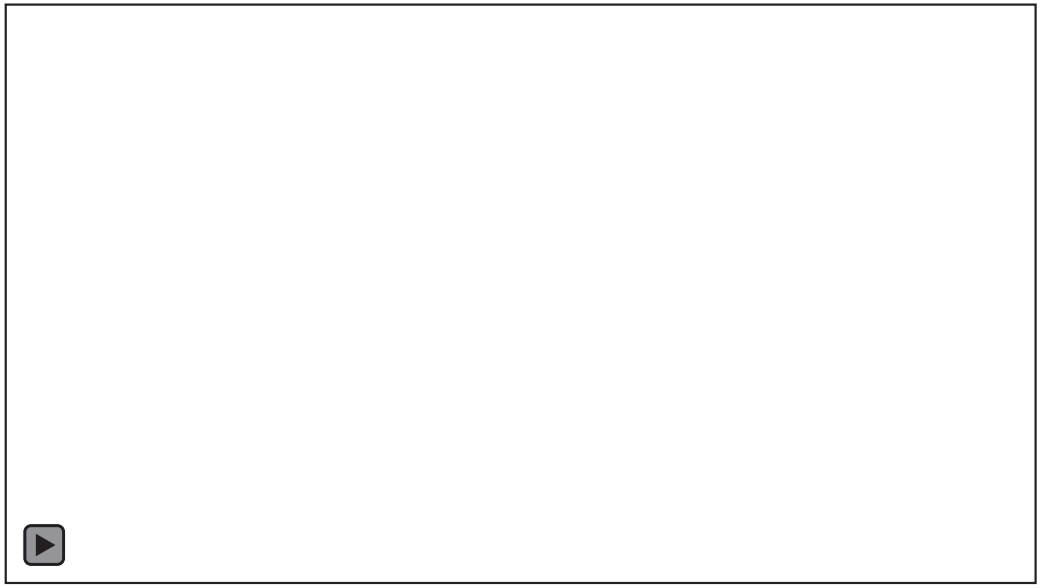
Don Heupel/AP

https://www.npr.org/sections/health-shots/2013/12/18/255226663/screening-newborns-for-disease-can-leave-families-in-limbo

Treatment of Dogs With Krabbe Disease

"Placebo" – 10 weeks old

Treated – 70 weeks old

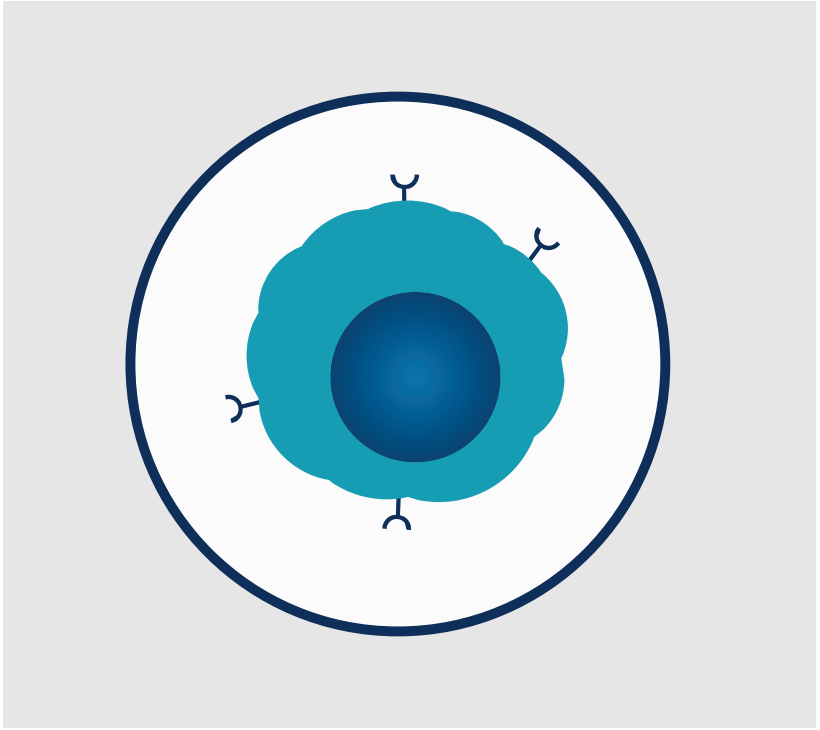


Bradbury et al, Journal of Clin Inv, 2020

Cell Therapy

- Cell therapy refers to the use of whole cells to treat disease
- Includes **replacing** or **repairing** tissue and /or cells damaged by disease, or **attacking** cancer cells
- Hematopoietic stem cell transplantation (bone marrow transplant) is the most frequently used cell therapy and is used to treat a variety of blood cancers and hematologic conditions.
- Potential applications*:
  - Treating cancers
  - Treat autoimmune disease
  - Rebuilding damaged cartilage in joints
  - Repairing spinal cord injuries
  - Improving weakened immune systems
  - Treating neurological disorders

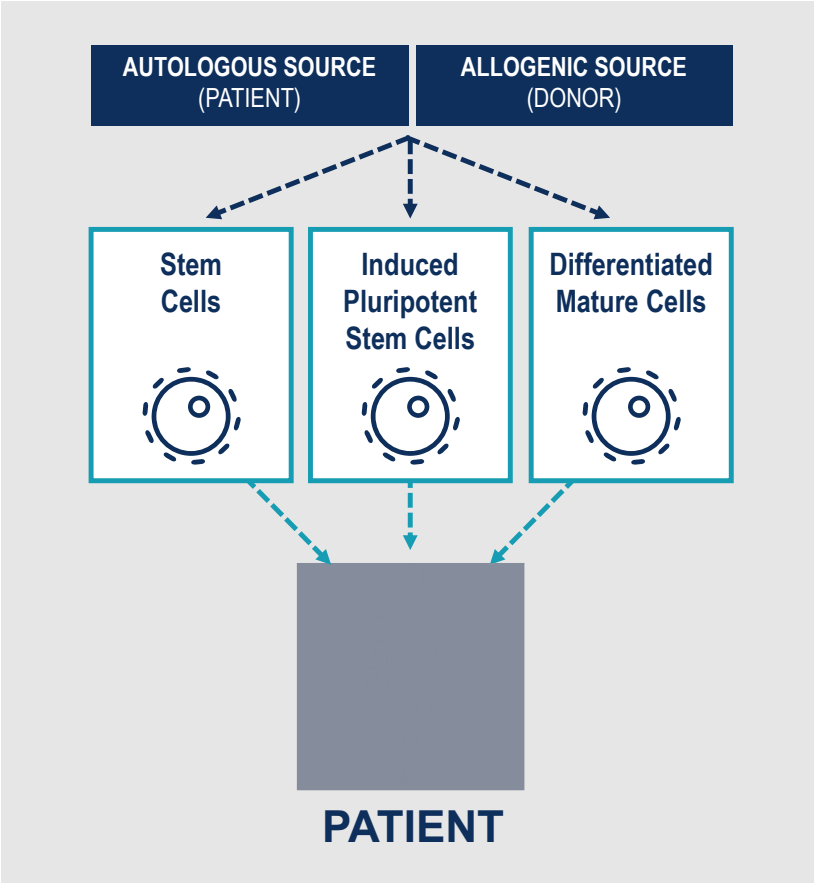
* ***Facts About Cellular Therapy*, AABB at www.aabb.org**



Cell Therapy Technology

Cells can be Derived from:

- **Stem Cells** (e.g., bone marrow)
- **Reprogrammed mature cells** (e.g., iPSCs / adult stem cells)
- **Differentiated mature cells** (e.g., lab stem cells)



Regulating Genomic Medicine

- Regulation of gene & cell therapies are governed by the U.S. Department of Health & Human Services HHS (FDA & NIH)
- FDA treats all genome edited cells as medical products
- Federal law prohibits the FDA from reviewing INDs using human germline cells and prohibits the NIH from funding research in germline cells
- FDA prohibits the conduct of clinical trials using germline editing

Regulating Gene & Cell Therapy Products

- FDA has an established regulatory framework to regulate cell and gene therapy products
- FDA has recently developed new regulatory programs to help expedite review of cell and gene therapy products:
  - INTERACT
  - RMAT
- Cell and gene therapy products must fulfill the same evidentiary standards to prove safety and efficacy as any other FDA-approved drug

Sources:
FDA. *Human Gene Therapy for Rare Diseases: Draft Guidance for Industry*. July 2018.
FDA. *Testing of Retroviral Vector-Based Human Gene Therapy Products for Replication Competent Retrovirus During Product Manufacture and Patient Follow-up; Draft Guidance for Industry*. July 2018
FDA. *Long Term Follow-up After Administration of Human Gene Therapy Products; Draft Guidance for Industry*. July 2018.

EvaluatePharma Study on Largest Genetic Medicine Pipeline & Companies by 2024

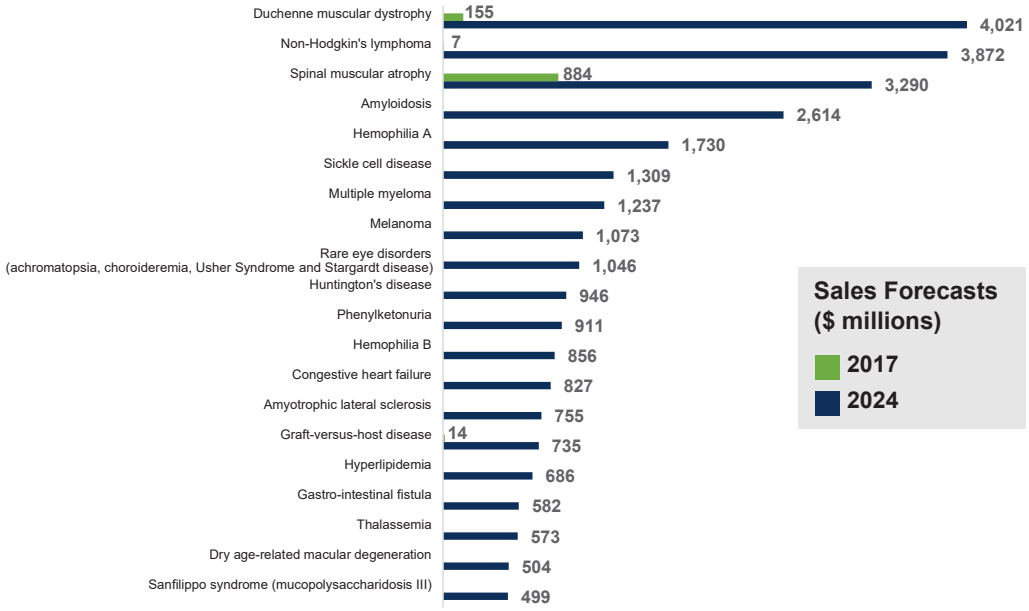


Fig 2. Top 20 indications, based on 2024 forecasted sales.

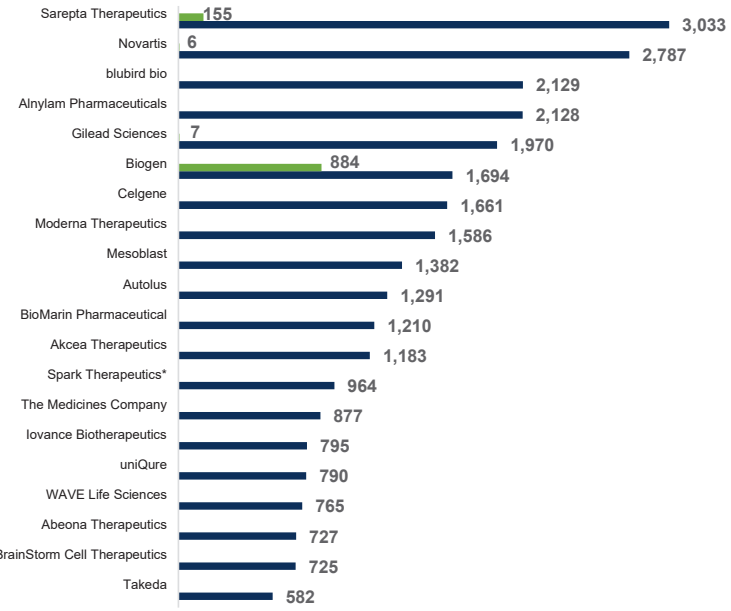


Fig 3. Top 20 companies in the field of cell, gene and nucleic acid therapies, based on 2024 sales forecasts.
*Acquisition by Roche announced in February 2019. Source: EvaluatePharma, March 2019.

Source: https://biopharmadealmakers.nature.com/users/9880-biopharma-dealmakers/posts/51056-next-generation-therapeutics-cell-and-gene-therapy-gathers-pace

Thank You