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Medical Topics: Gene Therapy

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Agenda

- Terminology
- Crash course in the science
- Existing FDA-approved gene therapies
- Underwriting implications

Terms related to high value therapies

Regenerative Medicine. Regenerative medicine seeks to rejuvenate the body's natural ability to heal, replace faulty cells with healthy donor cells, or regenerate function by delivering specific types of cells to diseased tissues/organs.[1]

Gene Therapy. A mechanism for correcting a defective gene.

Cell Therapy. Transplantation of human cells to replace or repair damaged tissue.

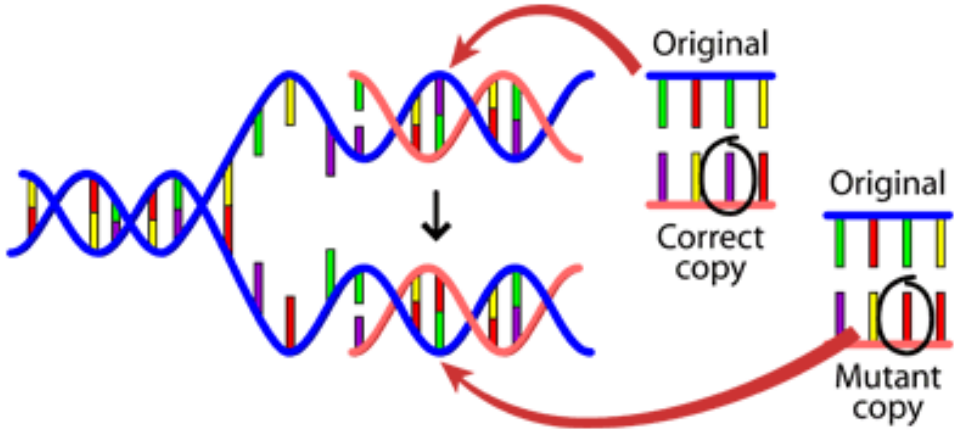
CAR T-Cells. Chimeric antigen receptor T-cell technology. An engineered cell line (versus the use of genetic material in gene therapy) is used to introduce a properly functioning gene in order to deliver the intended therapeutic effect.[2]

1 Mayo Clinic. Center for regenerative medicine. http://www.mayo.edu/research/centers-programs/center-regenerative-medicine/patient-care/about-regenerative-medicine
2 Alliance Regenerative Medicine. Rare Diseases and Regenerative Medicine. https://alliancerm.org/disease/rare-disease-and-regenerative-medicine

Introduction to gene therapies

Crash course in genes and disease

DNA replicates in every cell division.



Sometimes mistakes are made. The body has a tool that fixes errors, but it is not 100% perfect.

If the error is not fixed, cellular dysfunction is introduced. The resulting disease or problem depends on where the error is in the gene and on which chromosome the gene sits. (e.g. cancer, type 1 diabetes, etc.)

U.S. National Library of Medicine. Genetics Home Reference. https://ghr.nlm.nih.gov
University of Utah Genetic Science Learning Center. learn.genetics.Utah.edu

What is gene therapy?

Gene therapy is treatment at the **source** of the problem, whereas many current medications treat the symptoms or slow the progression of the disease.

- Gene therapy inserts a corrected copy of the defective gene or the corrected gene segment into the appropriate cells to get the resulting protein to do what it was originally intended to do.

- The corrected gene is transported to the appropriate cells via a vector (i.e. delivery mechanism/vehicle).
  - Removal of blood or bone marrow to separate out stem cells to which the gene is added.
  - Injection into the blood stream

- Common vectors
  - Viruses (most common)
  - Plasmids
  - Virosomes

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Who benefits most from gene therapy?

- Individuals with a single gene mutation

- Individuals with rare diseases, because an estimated 80% of rare diseases are genetic in nature.[1]
  - A disease in considered rare if there are fewer than 200,000 Americans diagnosed (approximately 0.06% of the U.S. population)[2]
  - There are over 7,000 rare diseases, which affect nearly one in 10 Americans.[3]

Many rare diseases lack adequate treatments. For patients diagnosed with rare genetic diseases, gene therapies may offer a life-changing treatment option, and in some cases, a cure.

1 De Vreuh, R. (March 12, 2013). Background Paper 6.19: Rare Diseases. World Health Organization.
2 U.S. Food and Drug Administration (July 18, 2013). Orphan Drug Act.
3 Office of Rare Disease Research (August 11, 2016). FAQs About Rare Diseases. National Institutes of Health.

Are risks with gene therapy real or hypothetical?

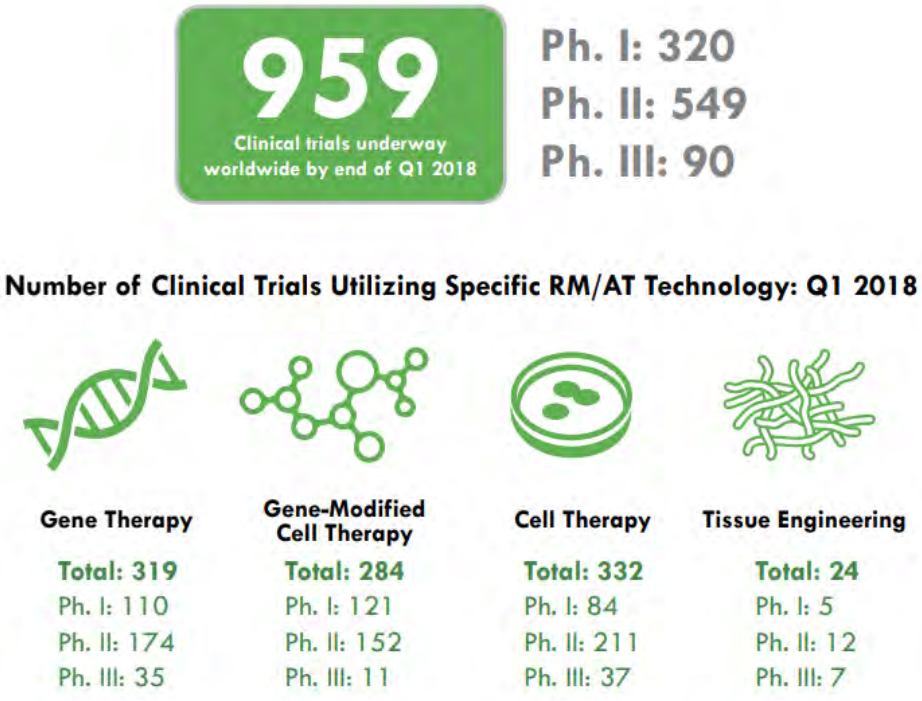
Risks associated with gene therapies are very real

- Organ failure or death due to immune reaction
- Virus could recover ability to cause infection
- New illness or cancer if inserted into the wrong gene or chromosome
- Numerous unknown changes if mutations in the new gene occur
- Short term, rather than long term improvements
- No response from the therapy

https://www.wired.com/2013/08/the-fall-and-rise-of-gene-therapy-2/

American Society of Gene and Cell Therapy http://www.asgct.org/general-public/educational-resources/faqs#faq2

Regenerative Medicine Clinical Trials (Globally)



According to the Q1 2018 ARM quarterly report:

- 54% of the companies investigating regenerative medicines are located in the U.S.
- 53% of current clinical trials are in oncology
- 10% are cardiovascular disorders
- 6% are diseases of the central nervous system

*Source: Q1 2018 Alliance Regenerative Medicine Quarterly Data Report. https://alliancerm.org/wp-content/uploads/2018/05/ARM_Q1_2018_Web_Version.pdf

The number of people who may be candidates for treatment will expand

KEY

Condition
$Launch price, ~ Indicated #

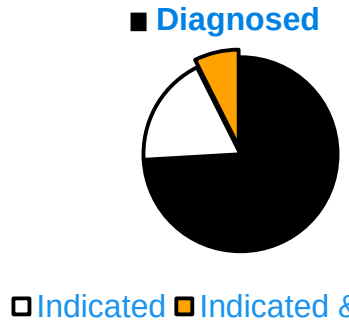
Condition
~ Diagnosed #

US approved gene or cell therapies

- Spinraza $750k, ~9k
- Kymriah $475k, ~4k
- Yescarta $373k, ~10k
- Luxturna $850k, ~1.5k

Pipeline conditions: gene therapy*

- Cystic Fibrosis ~30k
- CCALD ~13k
- Beta thalassemia ~1k
- Leber's ~6k
- Hemophilia A ~16k
- Glioblastoma ~24k
- SMA ~8.5k
- Hemophilia B ~4k

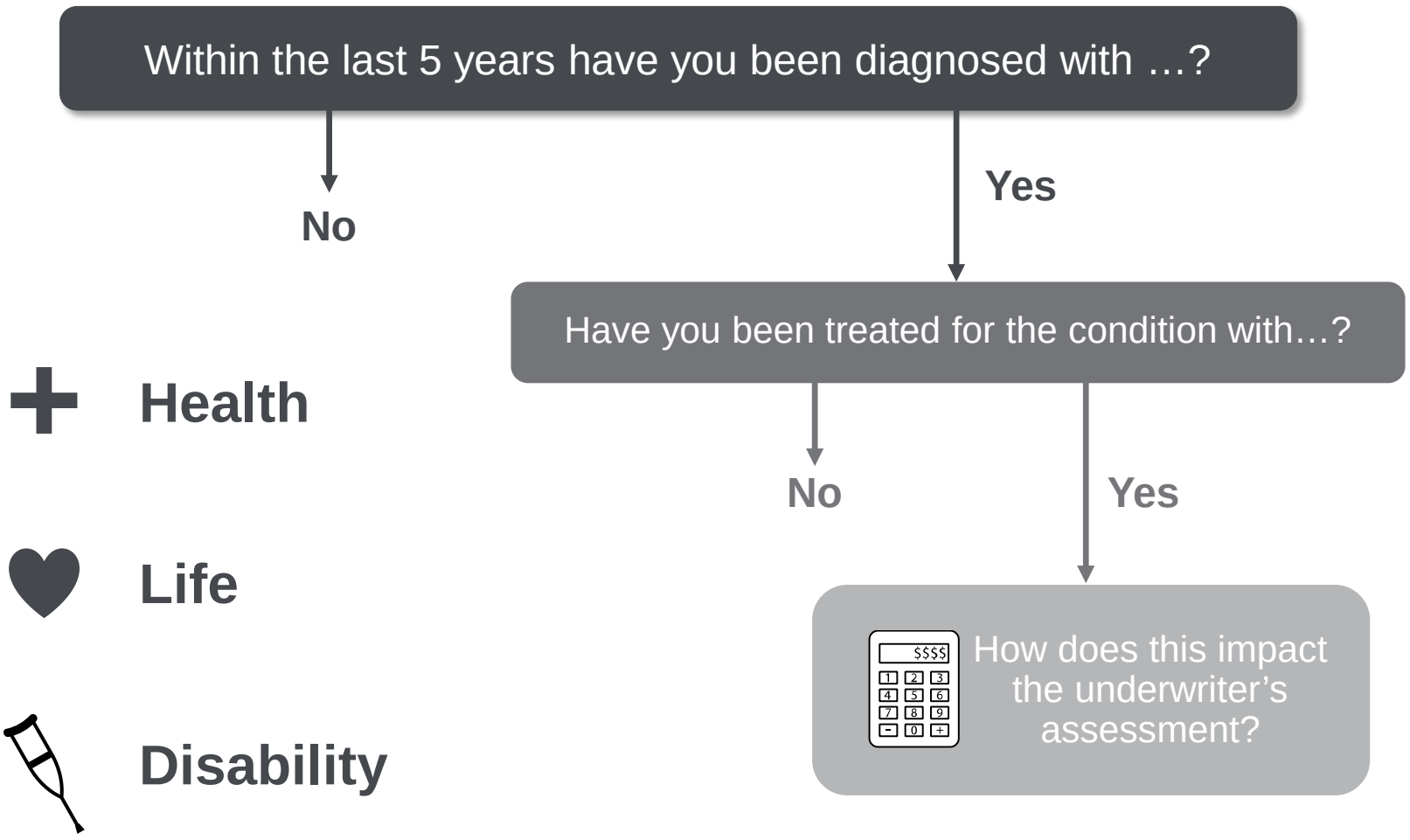


Not all of the diagnosed patients are indicated for treatment. A minimum clinical threshold (i.e. lower level of disease progression) or approval for second- or third-line therapies is a common limitation

*Not exhaustive. Source: Based on 2018 pipeline report. Medical Marketing and Media.

Underwriting Implications

Potential sources of implications



Sources for tracking high value therapies

Gene Therapy Resources

Background Information

- **NIH, Genetics Home Reference:** https://ghr.nlm.nih.gov/
- **University of Utah Genetic Science Learning Center:** http://learn.genetics.utah.edu/

Regulatory

- **FDA**: https://www.fda.gov/biologicsbloodvaccines/cellulargenetherapyproducts/

Publications & Ongoing Research

- **American Society of Gene and Cell Therapy:** http://www.asgct.org/
- **ClinicalTrials.gov:** https://www.clinicaltrials.gov/
- **Gene Therapy Net**: http://www.genetherapynet.com/