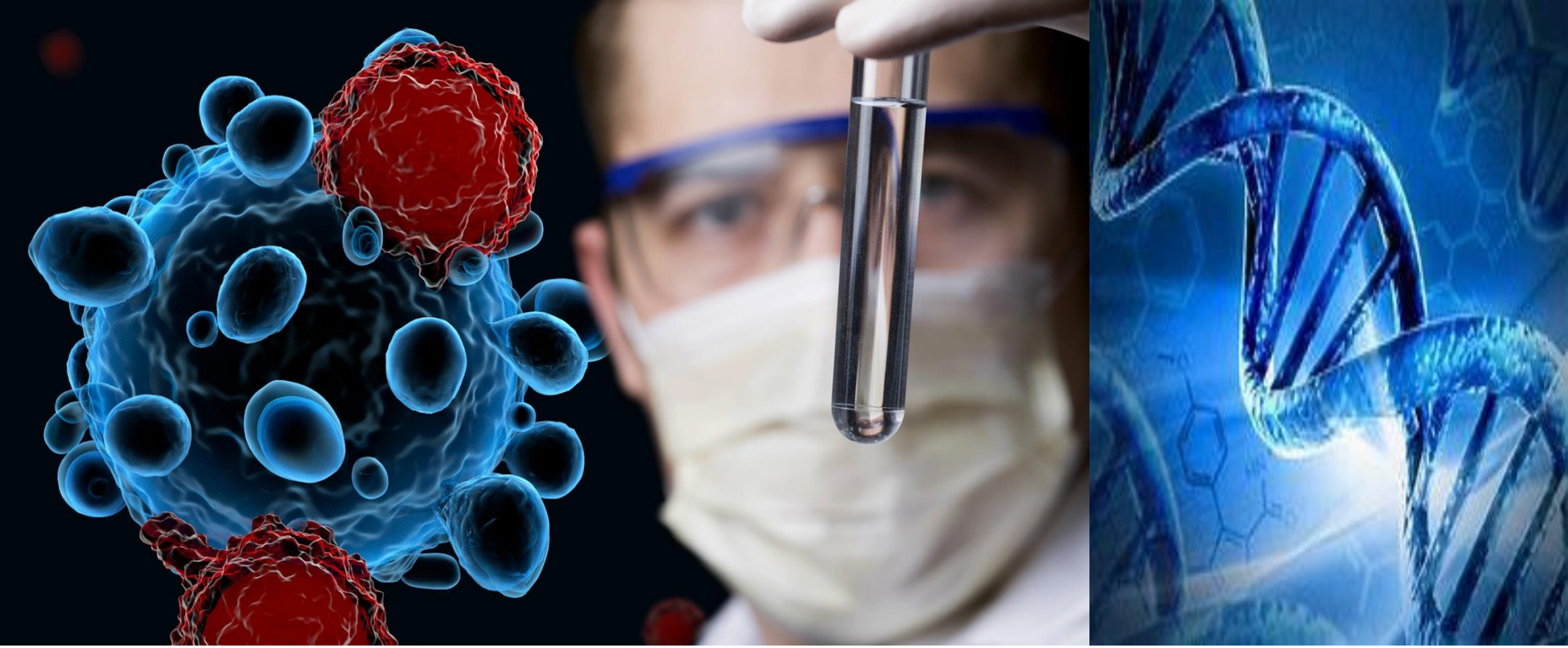

Cell and Gene Therapy:

A Fuller Picture of the Benefits, Risks, and Assumptions for Sickle Cell Disease Therapies

Amy Earhart-Connell, RN and Wendy Windsor, ASA

SEAC/ACSW November 16, 2023

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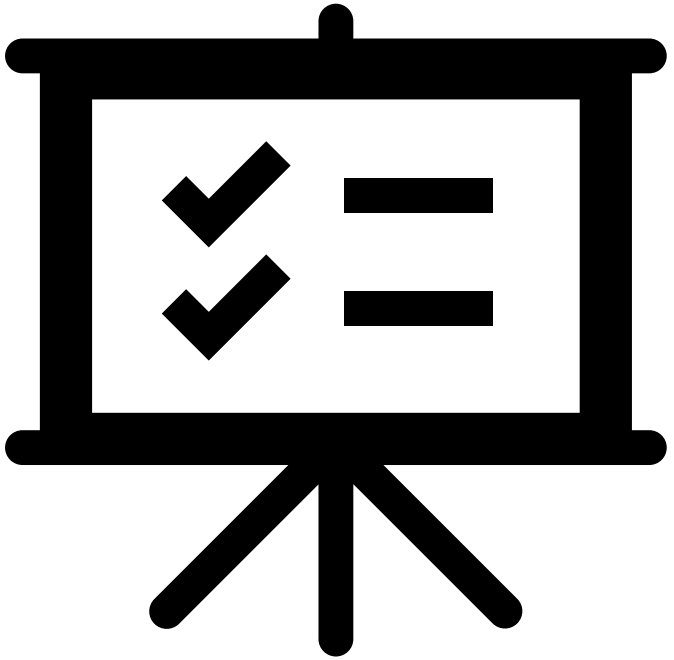
Objectives

- Cell and Gene Therapy (C&GT) Background
- Deep dive into Sickle Cell Disease
  - Disease description and complications
  - Costs to both patients and payers
- C&GT Benefits vs Costs (both financial and clinical)
- Assumption Drivers
- Payment/Risk Mitigation Options



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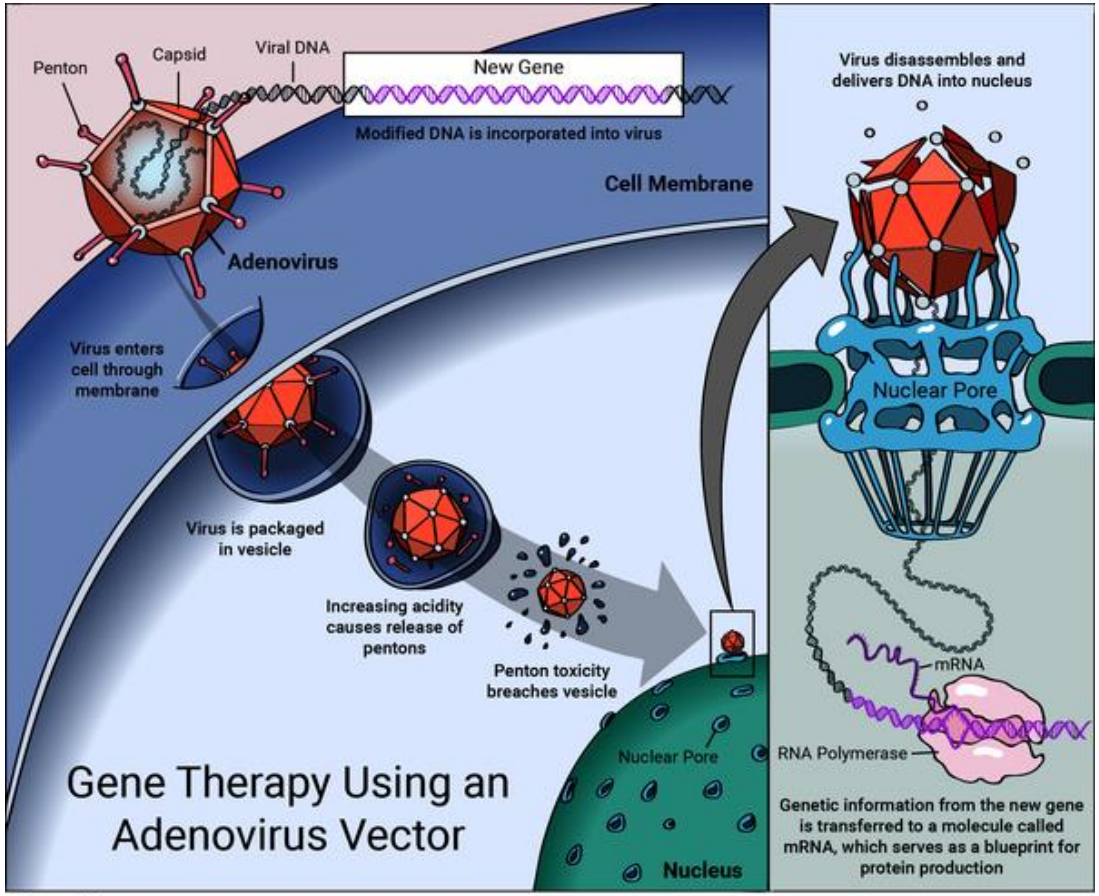
What are Cell & Gene Therapies?



- **Gene therapy** involves altering one's genes in effort to treat or stop disease either inside the body (in vivo) or outside of the body (ex vivo).
- **Cell therapy** is the injecting, engrafting, or implanted use of viable cells into a patient in order to receive a medicinal effect

Sources: https://medlineplus.gov/genetics/understanding/therapy/procedures/
Gene therapy - Mayo Clinic

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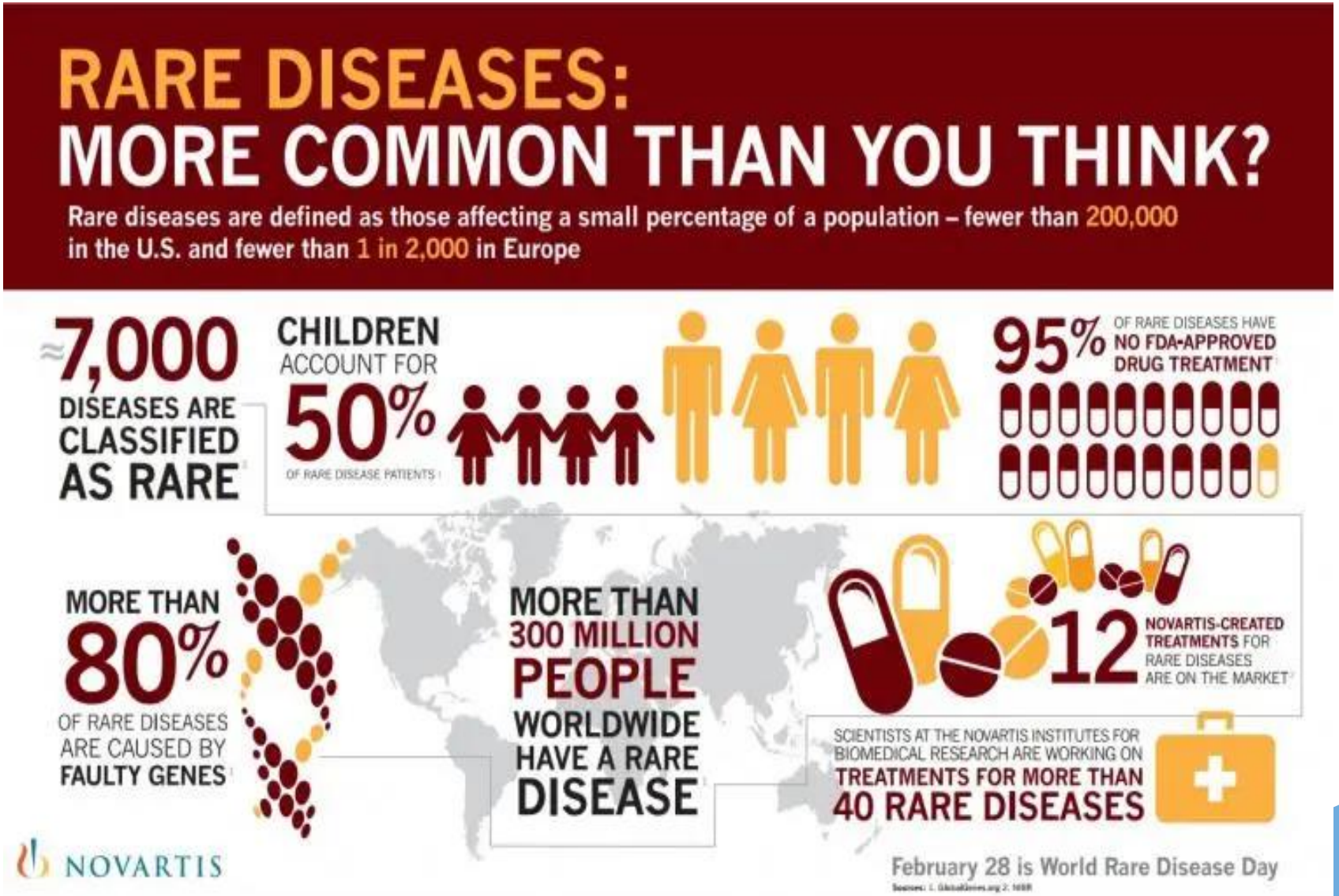
Why do we need these therapies?



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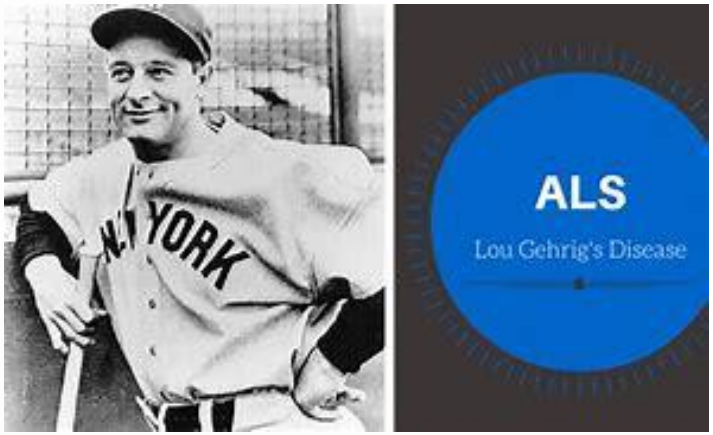
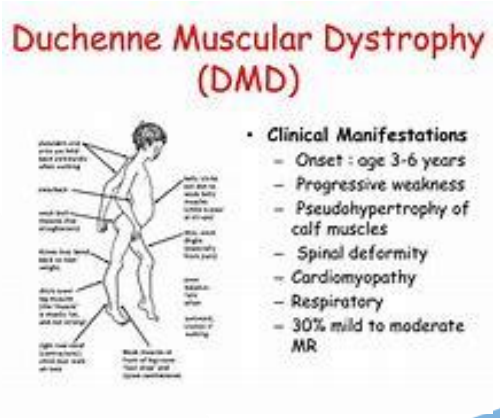
Well Known Rare and Orphan Diseases

- **Earliest gene and cell therapies targeted blood cancers and are rapidly moving to inherited blood disorders and other inherited diseases.**





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Gene Therapy Pipeline

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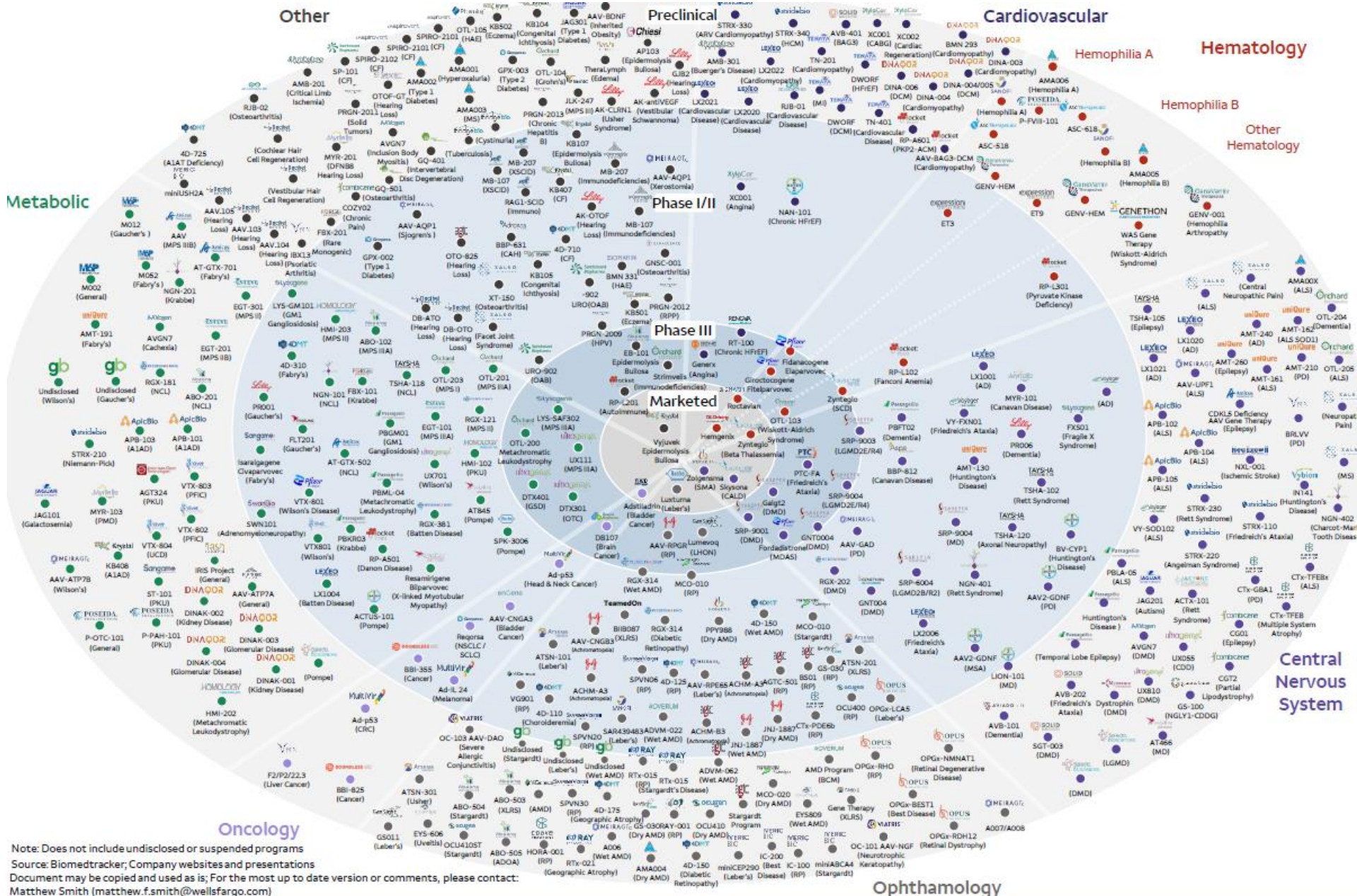

Note: Does not include undisclosed or suspended programs

Source: Biomedtracker; Company websites and presentations

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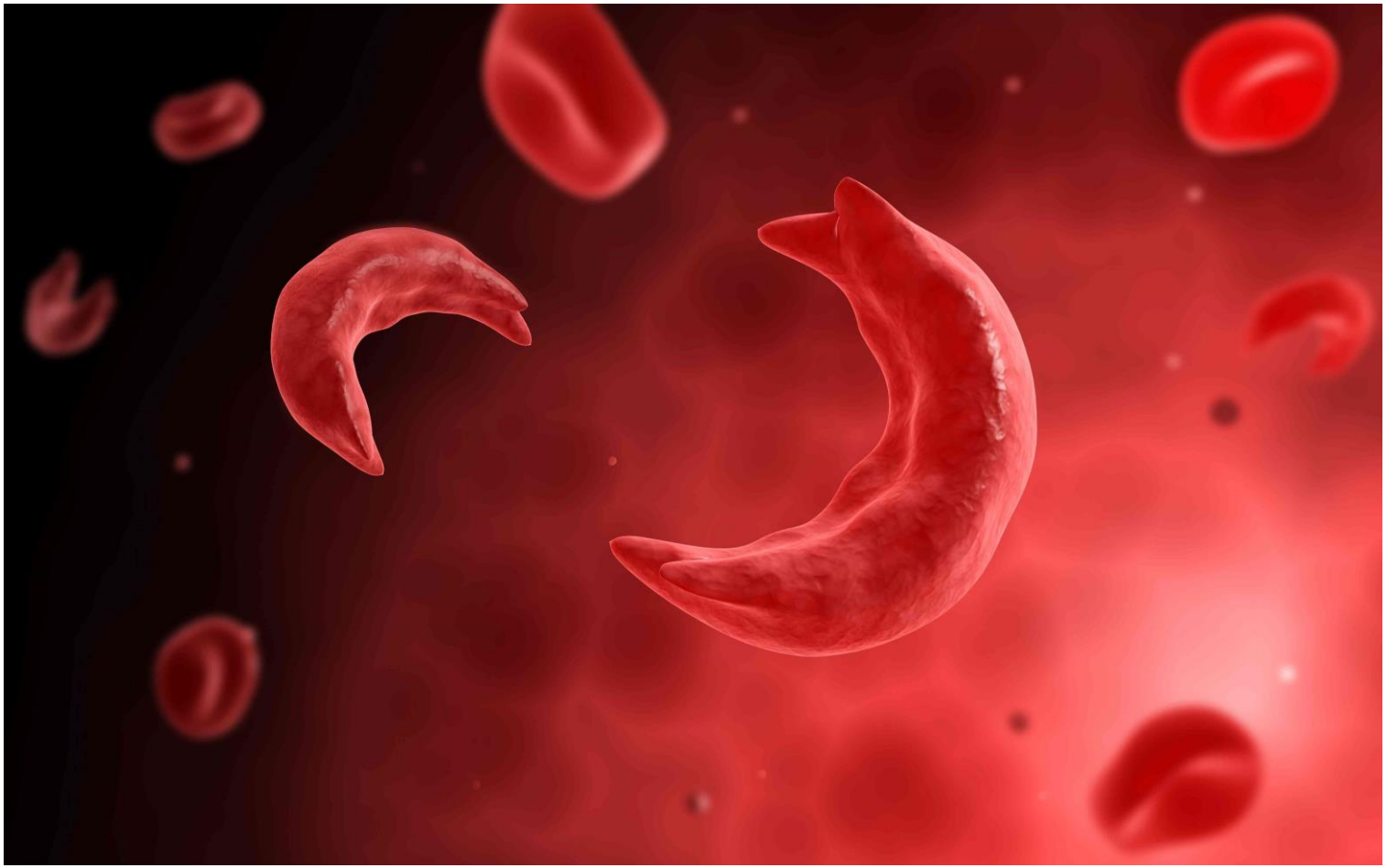
Matthew Smith (matthew.f.smith@wellsfargo.com)

Deep Dive into Sickle Cell Disease



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What is Sickle Cell Disease?

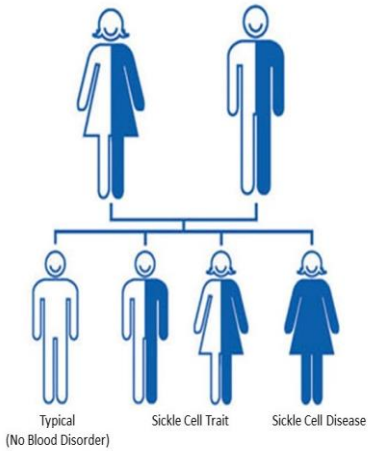
Where?
- 100k affected in the U.S.

Who?
- Most common in people of African and Mediterranean descent

When?
- Passed down genetically by both mother and father to their child

What?
- Caused by an abnormal type of hemoglobin called Hemoglobin S

How?
- Red blood cells that are normally shaped like a disk take on a sickle or crescent shape and become fragile



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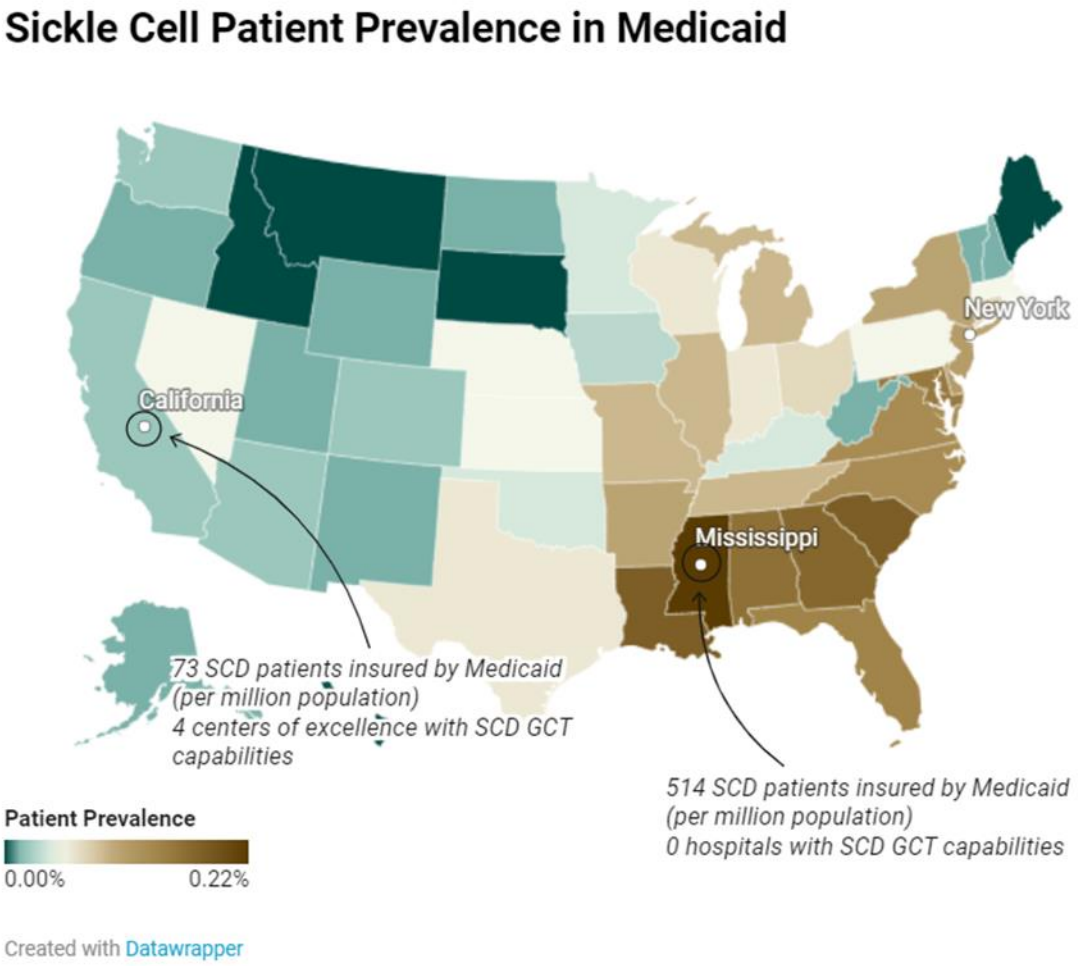
Geographical Considerations



Source: Quantile Health

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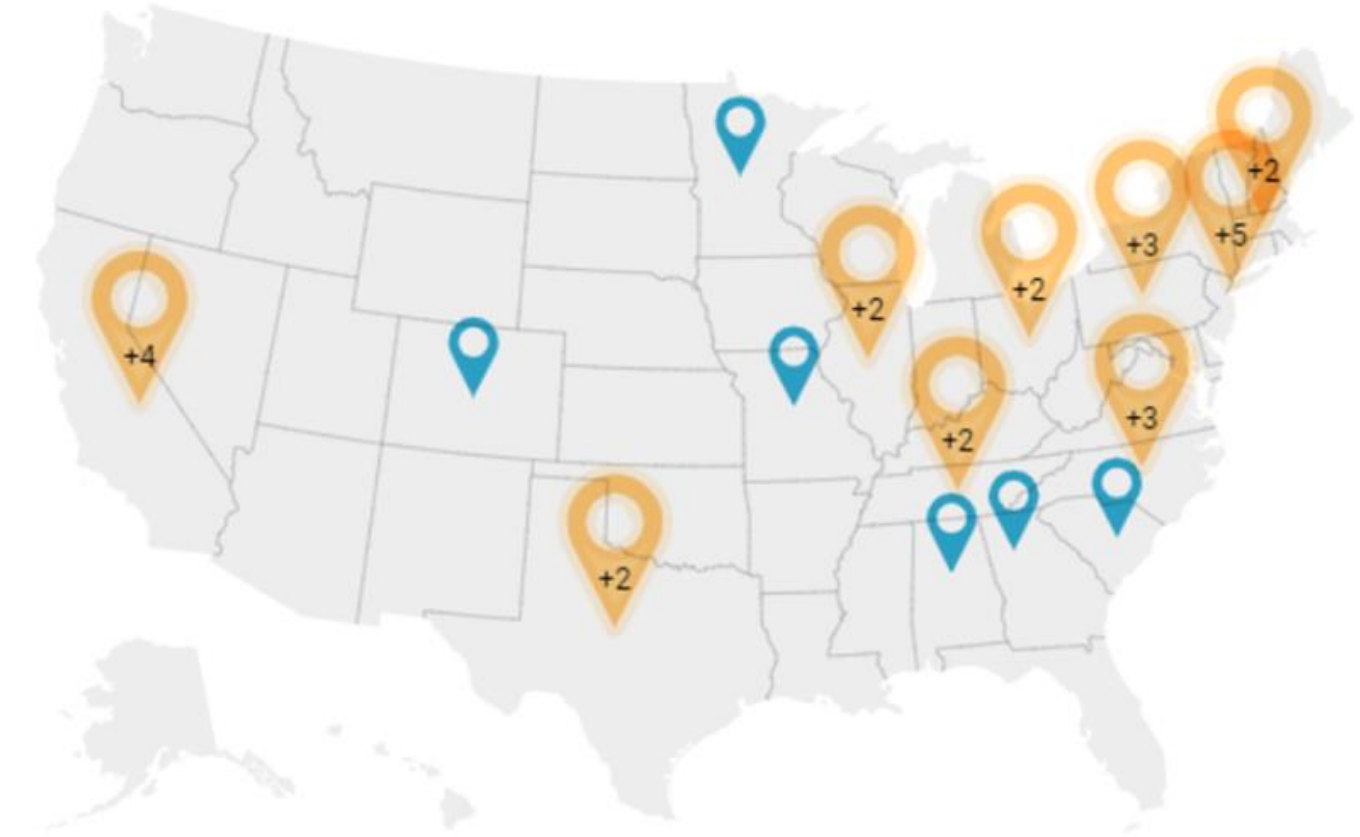
Centers of Excellence Involved in GCT Trials for SCD By State



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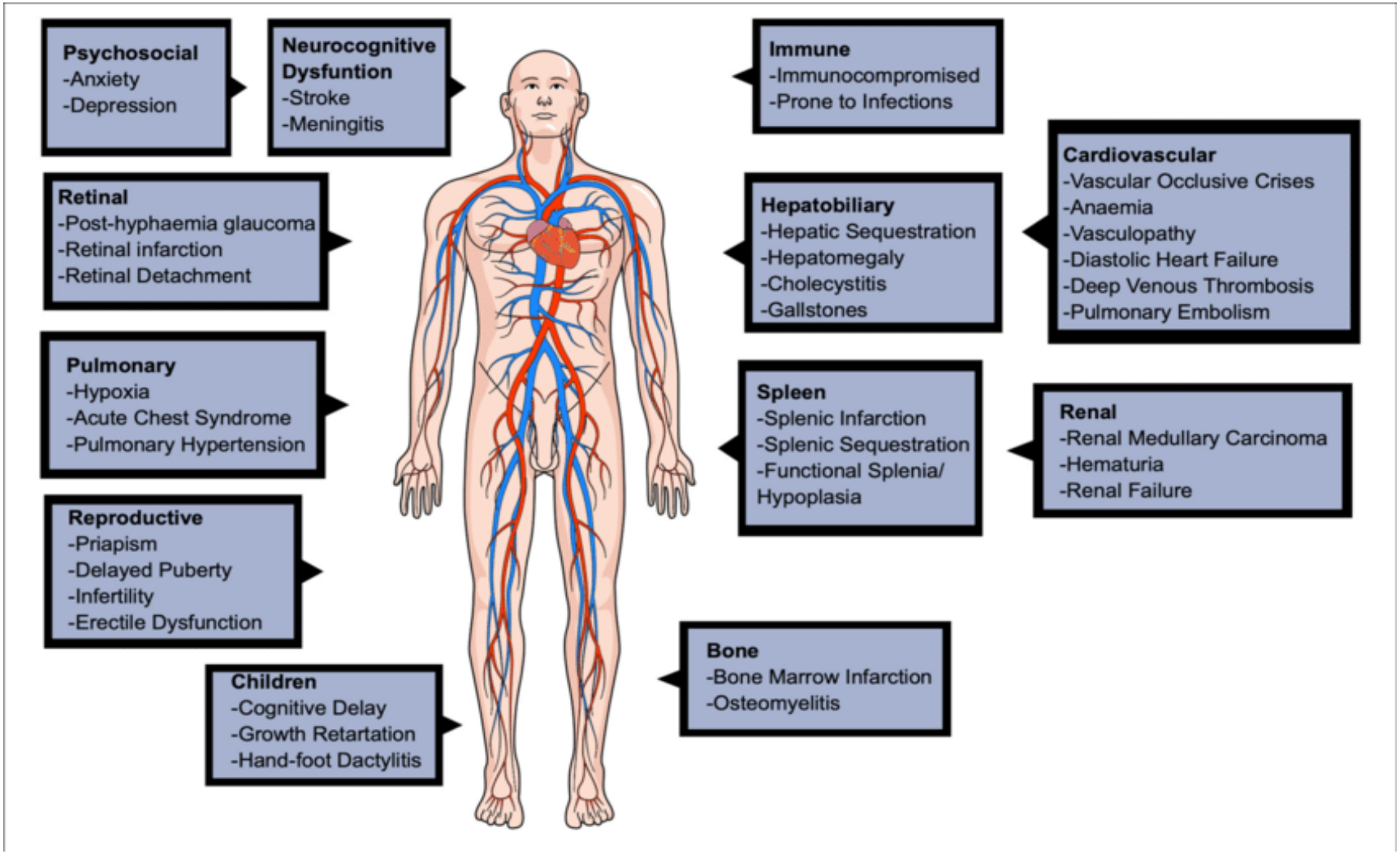
Multiple complications exacerbate costs



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What's the cost to patients and payors?

- Roughly **$75,000 annual** medical cost for SCD patients with multiple pain crises (3+ vaso-occlusive crises/year).[1]
- Annual cost burden could be approximately 5-10% of their income.[2]
- About **$44K of out-of-pocket expenses** to patients in a lifetime
- Around **$15K per individual per year** due to **absenteeism and presenteeism** due to pain events..[3]

[1]"Medical Resource Use and Costs of Treating Sickle Cell-related Vaso-occlusive Crisis Episodes: A Retrospective Claims Study". Shah N, Bhor M, Xie L, Paulose J, Yuce H. JHEOR. 2020;7(1):52-60. doi:10.36469/jheor.2020.12852.

[2] The Cost of Living with Sickle Cell Disease - Hematology.org

[3] "Indirect Economic Burden of Sickle Cell Disease", David Holdford, PhD, et al

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Current available Treatments for Sickle Cell Disease- Palliative in Nature

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- Stem Cell Transplant ~$800k/yr without complications
- Crizanlizumab (Inj) ~$85k-$113k/yr
- Blood Transfusions ~$3.7K per transfusion (w/o complications)
- Pain Reliving Medications

- Voxelotor (Oral Med) $127k/yr
- L-Glutamine oral powder (Endari) ~$20k per year
- Hydroxyurea (oral) $1k-$1.2K/Yr

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New Therapies: What to Expect?

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Exa-Cel

- Vertex/CRISPR
- First US marketed CRISPR therapy if/once approved
- Ex-Vivo therapy utilizing Cas9 gene editing

Lovo-Cel

- Bluebird Bio
- Ex-Vivo therapy using a lentiviral vector encoding a modified beta-globin gene into an autologous transplanted hematopoietic stem cell to produce anti-sickling hemoglobin

Timing:	• **Dec 8, 2023 & Dec 20, 2023**
Target Population:	• Anticipating ~**42,500 potential candidates** aged 12 and older
Target Price:	• **$1.4M-$3.0M for drug cost alone**

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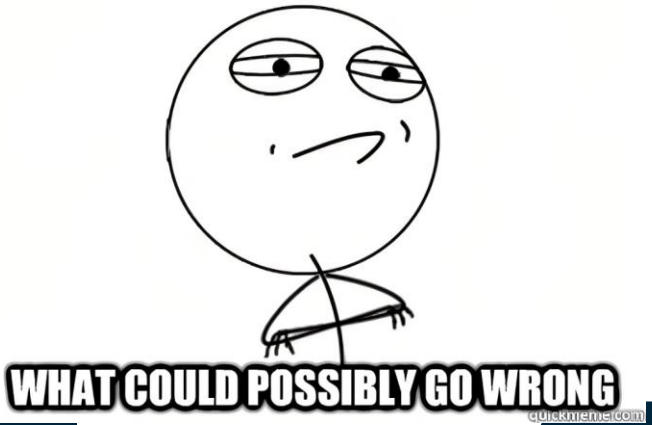
Life after Gene Therapy—Other Potential Costs

Development of certain types of cancers

Unwanted immune system reactions*



Targeting the wrong cells

Unknown long-term effects

* "Is Recent Gene Therapy Setback for Duchenne Muscular Dystrophy (DMD) Déjà vu All Over Again?" October 12, 2023, Ricki Lewis, PhD, PLOS BLOGS, DNA Science

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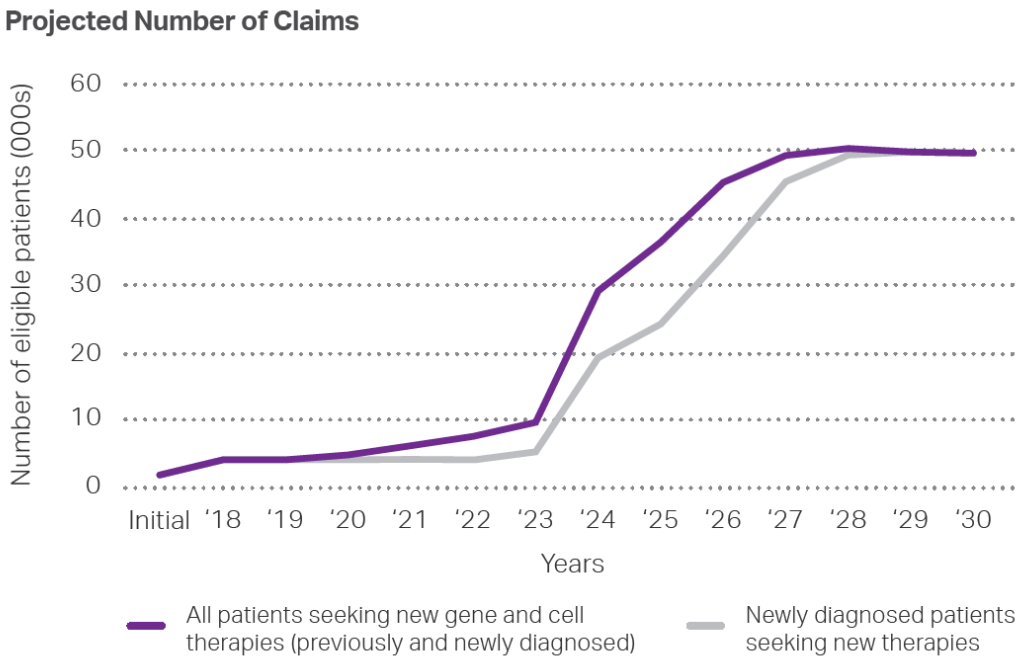
What are Actuaries Doing About It, Generally?



Graph: Medimpact

Predicting the risk

- Examining claims ICD-10 codes of current in-force for potential candidates for drugs
- Using population incidence/prevalence to estimate risk to block of business
- Watching pipeline for changes to approval dates, withdrawals, or usage indications

Quantifying the risk

- Modeling PMPM/PEPM cost loads based on expected total costs and drug utilization
- Challenges in predictability/utilization, lack of historical data, clinical knowledge required to determine appropriateness of treatment

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The Great Unknowns—Higher Uptake Rate?

Relatively wide range of age eligibility with minimal exclusionary criteria

"Dying" for quality of life

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The Great Unknowns—Low Uptake Rate?

- Socioeconomic factors in obtaining the treatment
- Stigma around the Lentiviral vector
- Lack of trust in the medical field
- Lifestyle changes

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Actuarial Challenges in Quantification

Frequency

- Starting point: Use population incidence/prevalence to estimate risk
  - This could vary significantly by type of medical coverage (Commercial, Medicare, Medicaid) as well as geography
  - For example, 1/3 of sickle cell patients are in the commercial population, the other 2/3 in Medicaid programs
- ICD-10 codes for claimants (Sickle-cell disorders: D57-) can give indication within specific population of who may be eligible
- Specific clinical criteria needs to be met; having the disease is usually not enough to qualify for the therapy
- Watch pipeline closely for changes in approval dates, FDA rejections, or changes in clinical indications

The biggest unknown of all: human behavior

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Actuarial Challenges in Quantification

Severity

- Two components: the drug cost itself and the administrative costs
  - In vivo: “go in, get a shot.”
  - Ex vivo: “cells are extracted, modified, and reinserted.” Much more expensive due to higher admin costs/inpatient stays
- Other considerations: discounts (340B rebates), hospital billing practices, complications, cost offsets (i.e., a hemophiliac no longer needing expensive factor drug), patient travel, time off from work
- Cost of drug is often not known until day of approval, sometimes even later

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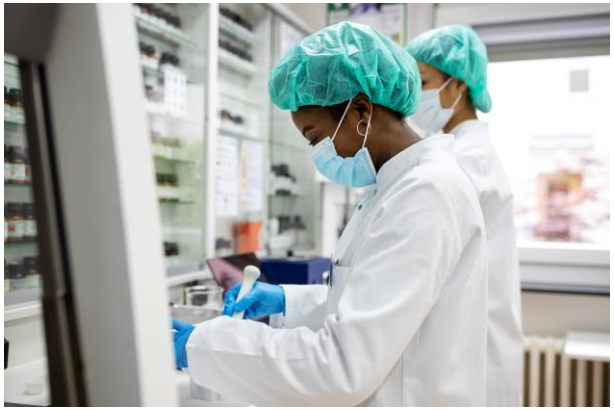
As we think about cost impacts….

- One problem is, with the disease, we know the outcome; with the therapies we don't know all the consequences.
- These therapies have risks, both clinically and financially.
- These risks and opportunities will continue to increase as more and more therapies evolve from blood cancers to inherited diseases to solid tumors.
- Cultural and historical forces can affect uptake takes
- Ultimately, the purpose of these therapies is curative.



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How do we manage this risk?

Let’s get down to business

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Current Solutions in the Market

Payer reinsurance/stop-loss/carve-out

- Carve out of financial responsibility or risk for specified cell and/or gene therapies
- Available as stand-alone products or incorporated into existing specific/aggregate/ASD coverage
- No performance guarantees

Contract negotiation & data management services

- Act as third parties to negotiate contracts for cell and gene therapies, and provide data/outcomes tracking services
- Contracts may include performance guarantees, but the service company themselves do not assume financial risk

Provider contract negotiation

- Oriented towards providers and patient care pathways
- Multiple services offered, including COE network creation and contracting, data analytics and cost containment
- Performance guarantees are oriented towards clinical services and outcomes rather than financial guarantees

Financial and pharma company warranty services

- Include payment plans, with or without performance guarantees, and warranties for purchase by pharmaceutical companies that can provide protection to payers for suboptimal product performance

Sources: https://newdigs.mit.edu/sites/default/files/FoCUS-WP-CGT-Market-Solutions.pdf;

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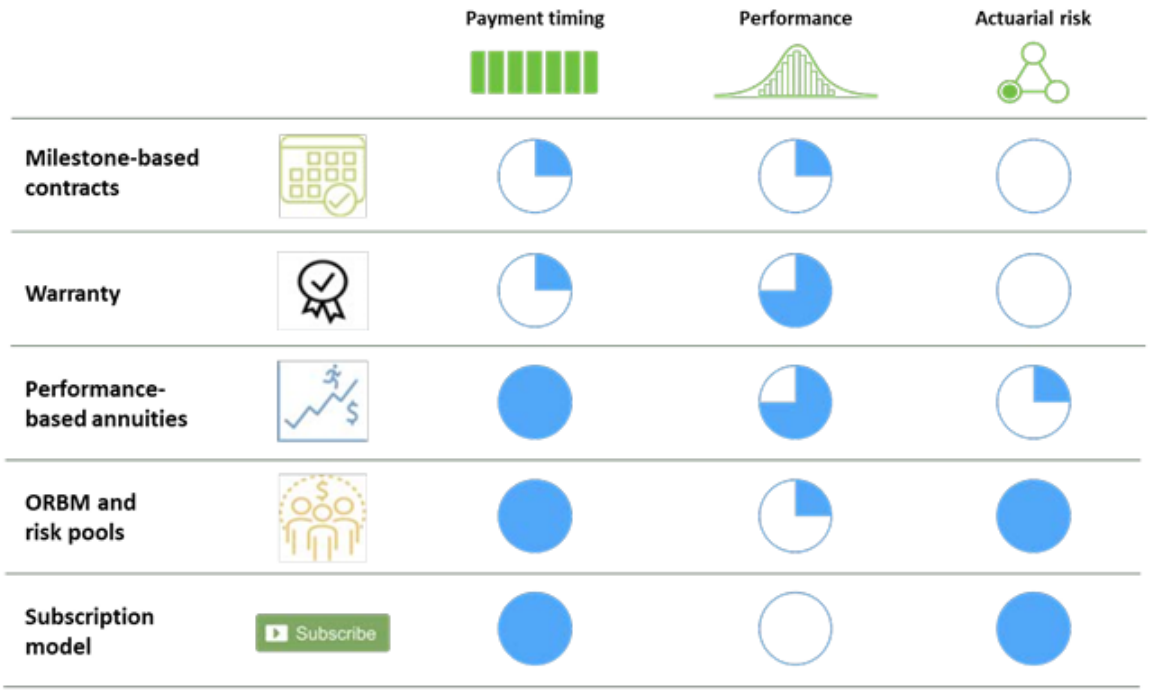
What Comes Next?

Figure 1. FoCUS precision financing solutions and their ability to address key challenges associated with cell and gene therapies

Blue circles represent the proportion of the associated challenge (payment timing, performance, actuarial risk) addressed by the precision financing solution. A full blue circle indicates the challenge is fully addressed; an empty circle indicates the solution has not addressed the challenge.



No single solution checks all the boxes

Source: https://newdigs.tuftsmedicalcenter.org/wp-content/uploads/2022/06/FoCUS-WP-CGT-Market-Solutions.pdf

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Thank you!

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