ACTION BRIEF

Employer Strategies that Drive Health, Equity and Value

National Alliance of Healthcare Purchaser Coalitions

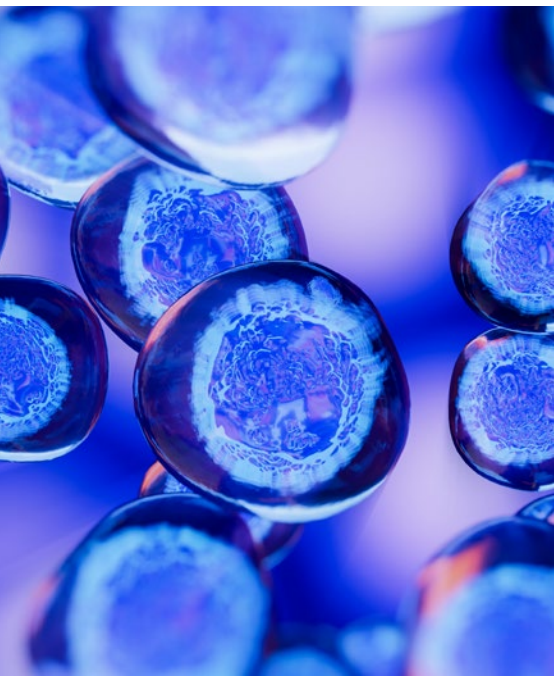
NCBCH NC BUSINESS COALITION ON HEALTH

UNDERSTANDING CELL AND GENE THERAPY AND ITS IMPACT ON THE WORKFORCE

Cell and gene therapies (CGTs) carry life-preserving and life-saving benefits, profoundly affecting those in need and their families.

The successes and growth in CGT are extraordinary:

- Gene therapies for hemophilia A and B have been approved.
- Two gene therapies are now available for treatment of sickle cell anemia.
- Immunotherapy has effectively treated mice with multiple sclerosis (MS), with human trials not far behind.



Note: A companion *Action Brief*: "An Employer Roadmap to Addressing Cell and Gene Therapy," discusses population risk, coverage and payment options, care delivery approaches, and targeted employee communications.

- A gene therapy promising to cure HIV has been fast-tracked by the FDA.
- FDA-approved CGT therapies address muscular dystrophy, multiple myeloma and some bladder cancers, lymphomas and prostate cancers, among others.

After early successes, CGT is rapidly expanding, with nearly 4,000 gene, cell and RNA therapies in the pipeline. Below is an employer Q&A to help explain CGT growth, consequences, and potential.

Q: WHAT IS CGT?

Specific definitions can become complicated. Here are some common definitions.

- **Gene therapy** is a medical approach to treating or preventing disease by transferring genetic material (DNA or RNA) into cells, thus altering the patient's gene expression. Genome editing is a type of gene therapy using technologies such as CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) to make targeted changes to the DNA sequence of a gene.
- **Cell therapy** is placing new, healthy cells into the body, replacing diseased or damaged ones to modulate cell function or to eliminate disease-causing or dysfunctional cells. Immunotherapy is a cell therapy cancer treatment that boosts the immune system to find and destroy cancer cells. CAR-T is a form of cell therapy using T cells from patients, altering them and placing them back into the patient.

Some treatments are one-time injections to replace damaged cells or stop damaged cells from functioning. Other treatments require extracting patient cells, modifying them through genetic engineering, and then re-injecting the genetically altered cells. Treatments include gene addition, gene editing, RNA therapy, and cell therapy. Treatments often are one-time and potentially curative.

Q: WHAT IS THE DISEASE FOCUS OF CGT?

Most gene therapy research is currently focused on treating patients with serious or life-threatening rare blood disorders

and cancers. However, development is accelerating exponentially due to AI, better targeting of specific pathogenic variants and cancers, and expanded manufacturing capabilities.

Diseases with CGT alternative treatments expected in 2024:

Beta thalassemia – An inherited blood disorder requiring frequent, lifelong blood transfusions.

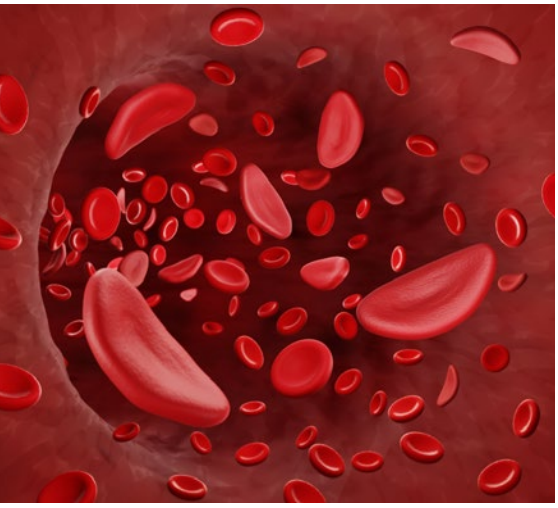
Chronic lymphocytic leukemia – A common type of leukemia in adults that is typically treatable but not curable.

Hemophilia B – A rare bleeding disorder in which affected individuals have insufficient levels of a blood protein necessary for clotting and are at risk for life-threatening bleeding episodes.

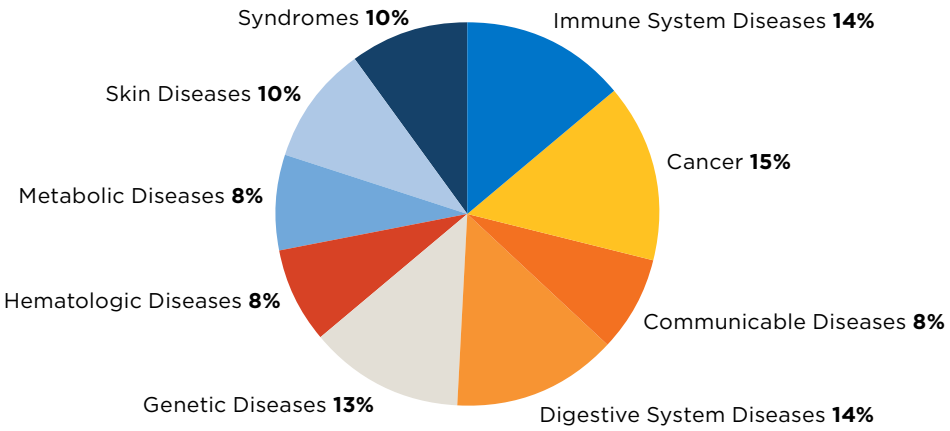
Multiple Myeloma – Cancer of the bone marrow, which occurs when stem cells in the bone marrow mutate and grow abnormally, crowding out healthy cells and preventing them from functioning normally.

Sickle cell disease – A common group of inherited red blood cell disorders with a range of serious health complications.

The USFDA currently lists 34 approved CGTs. Cost per treatment range from: bladder cancer ($160,000–$260,000); sickle cell disease ($2.2 million); hemophilia B ($3.5 million); retinal dystrophy ($425,000 per eye); and large B cell lymphoma ($425,000).



Recent CGT Focus Has Expanded to Many Diseases



Q. HOW FAST IS CELL AND GENE THERAPY GROWING?

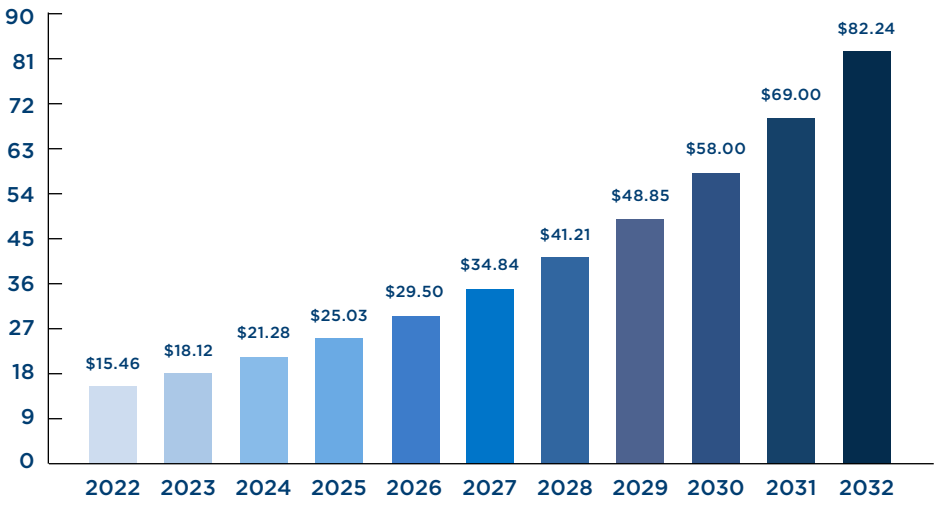
In 2020, about 12,000 US-based patients were treated with gene or stem cell or gene therapy. The number is expected to reach 340,000 by 2030. The FDA is evaluating about 900 CGTs and expects to approve about 10 new therapies each year. Current CGT therapies are estimated to reach approximately $35 billion a year in the US by 2027, roughly doubling today's levels. From an employer perspective, there is an increasing chance an employee or covered plan member will benefit from this science.

Q. WHAT IS THE MANUFACTURING PROCESS FOR CELL AND GENE THERAPIES?

The manufacturing process for cell and gene therapies is complicated and exacting. In cell therapy, healthy cells are manufactured and used to replace diseased cells or attack and destroy diseased cells, either within the patient or outside the patient and then injected into the patient.

In the case of gene therapy, cells are modified either within the patient's body or they are extracted, modified outside the patient's body and injected back into

Exponential Growth Predicted for CGT



Source: Precedence Research, Cell and Gene Therapy Market Size, 2022-2032 (USD Billion)

the patient. Sometimes disease-causing genes are replaced with healthy copies. Other times scientists inactivate disease-causing genes through gene editing.

Gene therapy works by altering genetic code to recover functions of critical proteins. The process is further complicated because the altered or new genes need to be carried into the body by a carrier called a vector, or they usually don't function. Vectors include retroviruses and adenoviruses. Nanoparticles are another vector, less likely to cause immune reactions.

These processes involve working with a patient's unique cells, genes and disease, applying expensive and complex technologies, and also complying with regulatory challenges.

Q. WHY ARE THESE TREATMENTS EXPENSIVE?

Developing new cell and gene therapies involves complex clinical applications that can span decades and cost billions of dollars. Clinical trials are expensive as well because they require processes that are adapted to each patient's genome and disease particulars.

The cost is amplified because only slightly more than 1 in 10 therapeutic development programs complete phases 2 and 3 and reach the FDA for approval.

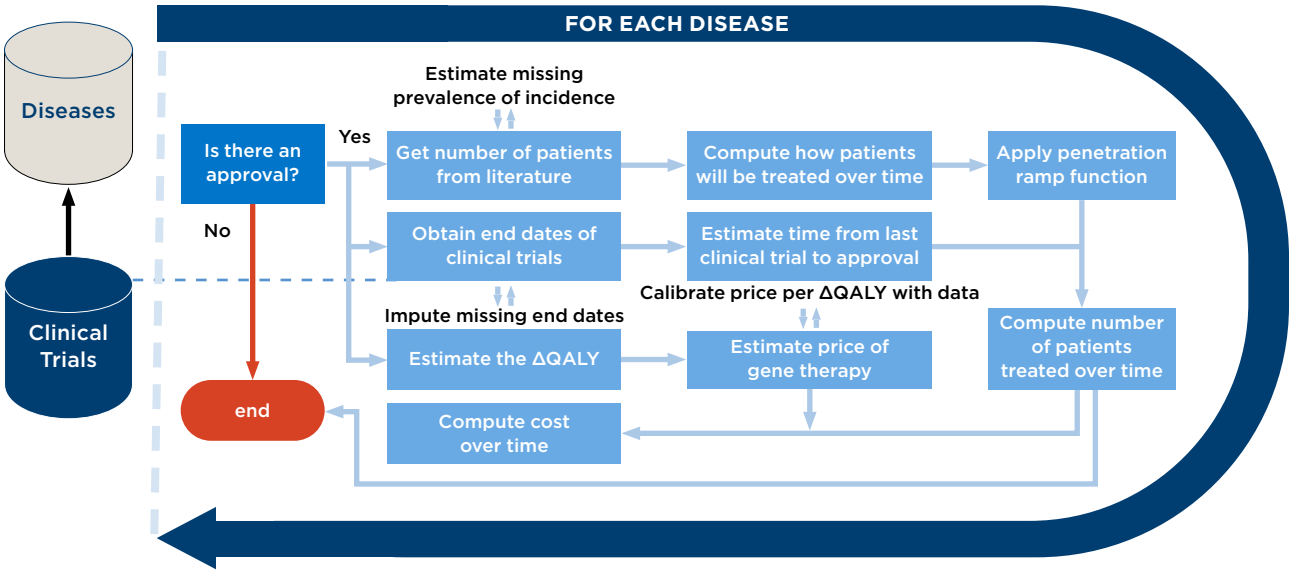
This simulation below from Nature shows the complexity of extracting data from clinical trials of cell and gene therapies to calculate the likelihood of a successful trial.

While CGT costs are high, the Nature article points out that the clinical benefits include providing significant gains in longevity or symptom relief over conventional treatments and addressing often unmet needs in the treatment of rare diseases. Most treatments are one-time and eliminate ongoing and often accelerating costs for traditional medical care.

Q. WHAT IS THE TYPICAL PATIENT JOURNEY WHEN RECEIVING CGT TREATMENT?

Patient journeys for CGT therapies often have two parts: Exhausting all pathways for traditional treatments and then, if qualified, experiencing the CGT treatment.

Once determined to be a candidate for CGT, the patient begins a complex journey. Unlike with traditional medicine, a CGT patient becomes part of the supply chain by contributing their unique cells and genes. Treatment may be through injecting modified cells or



Source: The Estimated Annual Financial Impact of Gene Therapy in the United States, November 3, 2024

infusions that use the patient's body as its own laboratory. Communication and collaboration are required between the patient, the physician, and the CGT manufacturer.

In some cases, the patient will need extended inpatient hospital stays and potentially multiple additional visits to a cell or gene therapy center. If these resources are not local, patients must undergo travel and expenses. The individual nature of these treatments requires case management and, often, behavioral health services.

Q. WHAT ARE THE COST IMPLICATIONS TO EMPLOYERS?

Cell and gene therapies have high upfront costs but have the potential to reduce healthcare spending over time by addressing the underlying causes of disease, reducing the severity of disease, and reducing healthcare utilization.

Until a few years ago, CGTs were limited and their cost to employers (estimated at $5 billion in 2020) were manageable through stop-loss and reinsurance markets. The growth of CGTs will require employers and funding partners to explore flexible ways to address costs. This can be a complicated calculus because often the CGT treatments are curative, avoiding long-term costs typical of traditional non-curative treatments (see sidebar).

Cost implications and employer funding mechanisms are discussed in more detail in the National Alliance *Action Brief*, "An Employer Roadmap to Addressing Cell and Gene Therapies."

Q. WHAT OTHER ISSUES BESIDES COST SHOULD BE CONSIDERED?

CGT raises additional issues beyond financing the treatment. Immediate issues are the control and confidentiality of results of genetic testing and possible discrimination against those found to have genetic diseases by withholding available treatment.

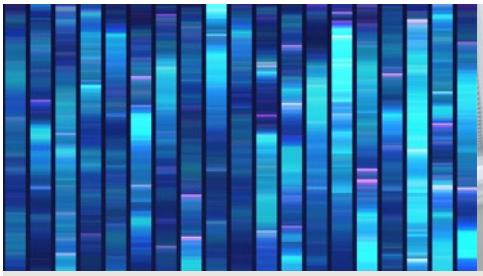
LEARN TO NAVIGATE COVERAGE COMPLEXITIES TO MAKE WELL-INFORMED DECISIONS

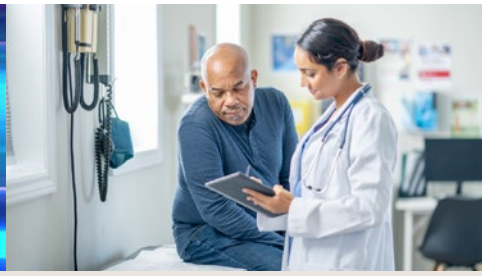
The business case for covering CGT for employees and families includes making complex and often difficult decisions and health policy around appropriateness, equity, and risk/benefit calculations. A coverage decision for any of the new therapies would create a vulnerability for significantly high-cost claims. A second National Alliance *Action Brief* (link coming soon!) considers how to engage partners to fulfill CGT coverage policies, how to manage costs, and how to communicate with affected employees. This *Action Brief* introduces the issues involved in developing CGT coverage policy.

APPROPRIATENESS

Employers responsible for setting health policy must grapple with the difficult assessment of the CGTs as appropriate alternatives over traditional treatment. The following questions help inform this policy:

1. Does the gene therapy have a one-time administration?
2. Is the therapy curative?
3. How will treatment and clinical results be monitored and reported?
4. What are the healthcare cost savings over time, compared to traditional treatment?
5. Are alternative new and better therapies for the same disease in the immediate pipeline?
6. How many candidates for this specific treatment exist in the covered population?
7. What is the financial liability of this coverage, and how will it be met?





TWO CASE STUDIES

Cell and Gene Therapy vs. Traditional Medicine Costs

Many studies compare the cost of one-time CGT to traditional treatment. One complex analysis assessed the cost of gene therapy for severe hemophilia B compared to factor replacement therapies. In 92% of the simulations, CGT was more affordable. CGT avoided traditional treatment costs and complications, predicted hospitalizations and a decreased quality of life.

In another study in 2021, a group of researchers conducted a complicated financial analysis to determine if a one-time CGT treatment of sickle cell disease was a better investment compared to lifetime costs using traditional interventions.

Another important factor is quality of life (QOL), which is not part of an ROI calculation. Living with sickle cell disease requires ongoing frequent blood transfusions; severe pain bouts in the arms, joints, back or chest; fatigue and a shortened life expectancy. QOL is much greater when a person is "cured" by CGT rather than when the person endures a lifetime of pain under the traditional standard of care.

CGT, because it is a one-time upfront cost, was cost effective if the patient either was treated early or lived a long life.

The conclusion: "Large upfront costs of a single administration cure are offset by significant downstream gains in health for patients treated early in life."

Answers to these questions address how treatment options are assessed, whether treatments are covered, to what extent and whether there are limits, what kinds of assessments are required to qualify for the treatment, how clinical outcomes are measured and tracked, and the employee's financial obligations.

EQUITABLE ACCESS

The costs (including employee copays or coinsurance) may lead to disparities in access. Individuals with limited financial resources may be unable to afford treatments, especially for costs not covered by insurance. Payment plans and discounts, yet to be determined, may reduce financial disparities.

While the private sector explores its own models for equitable access to CGT, the federal government has begun testing initiatives to further enable equitable access. A new HHS funding model is targeting equitable access to CGT treatment for sickle cell disease by 2025 among populations dependent on Medicaid. The funding model could be expanded to other types of CGTs in the future.

RISK/BENEFITS

In some cases, the assessment of population risk for CGT is straightforward. Claims identify an employee who may benefit. The cost of treatment is known, and a cost/benefit analysis can be completed.

An obvious vulnerability for employers is when certain employees have diseases known to be treatable by CGT, but this information is not yet appearing in claims data.

In the meantime, employers, providers and insurers are exploring coverage and funding models. See the **National Alliance *Action Brief*: Cell and Gene Therapies: Getting Ahead of the Medical Costs.**

ACKNOWLEDGMENT

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Resources accessed for this *Action Brief*

- Cell and Gene Therapies, An Overview for Employers and Related Stakeholders, Janssen Biotech, Inc. 2023
- Precision Medicine White Paper, Janssen, July 2021

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