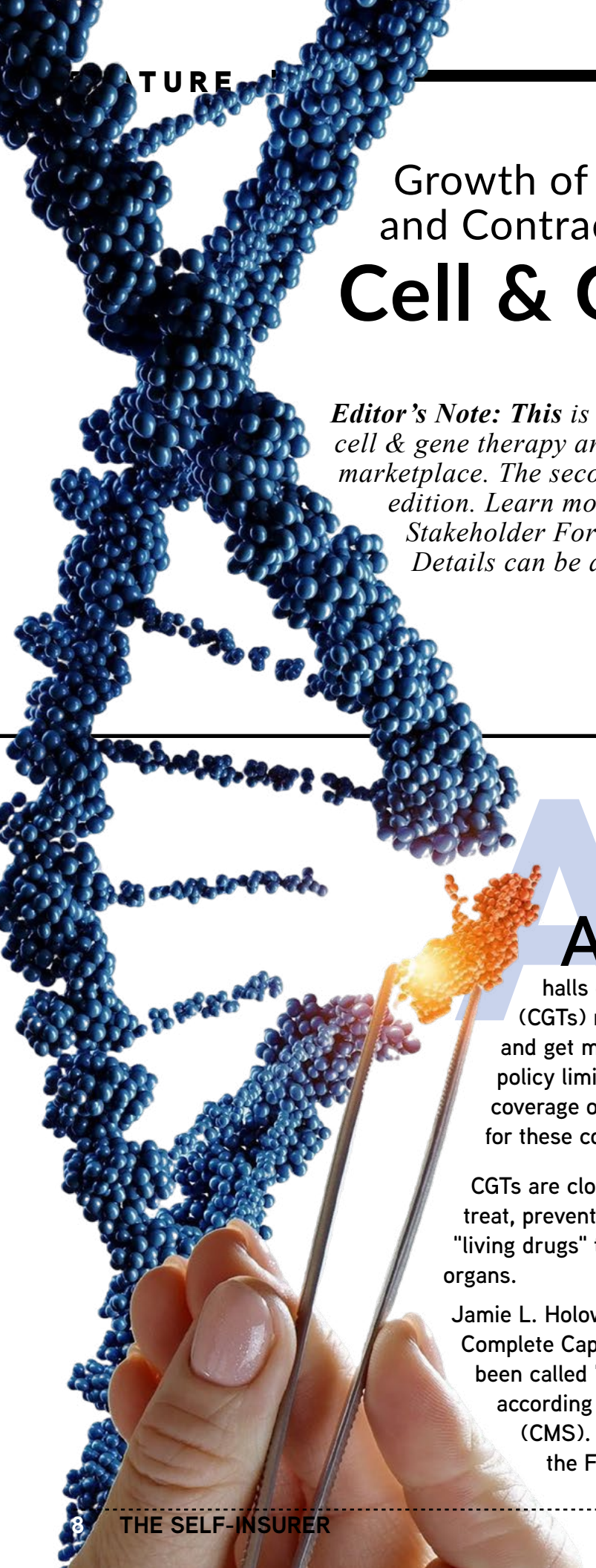


Growth of Value-Based Purchasing and Contracting for

Cell & Gene Therapies

***Editor's Note: This** is the first of a two-part article focused on cell & gene therapy and its implications for the self-insurance marketplace. The second part of the article will appear in the April edition. Learn more about this topic at the SIIA Cell & Gene Stakeholder Forum, scheduled for May 27-28 in Minneapolis. Details can be accessed at www.siia.org*

Written By Laura Carabello

As a political power shift unfolds throughout the halls of Congress, the explosion of cell and gene therapies (CGTs) may be forcing employers to re-think coverage options and get more inventive in their approach to stop-loss coverage, policy limits and exclusions, and payment models. Innovative coverage options are emerging as employee demand accelerates for these costly but potentially lifesaving treatments.

CGTs are closely related and sometimes overlap as both aim to treat, prevent, or potentially cure diseases. They are considered "living drugs" that can heal and replace damaged tissues or diseased organs.

Jamie L. Holowka, B.S., Pharm.D., director of Clinical Strategy, Complete Captive Management Services, explains that CGTs have been called "potentially transformative" and have "great potential," according to the Centers for Medicare & Medicaid Services (CMS). They are not permitted to be described as curative by the Food & Drug Administration (FDA).


Jamie L. Holowka

"Medical science is progressing based on FDA initiatives to focus on rare diseases." she continues.

"CGTs have become a new entry to the market as a competitor to other therapies and treatments. Most of these products are not considered first-line, first choice or the ONLY management option."

Expanding on this concept, Andy Szczotka, Chief Pharmacy Officer, AscellaHealth, a global partner delivering customizable solutions to support the specialty pharmaceutical industry, adds, "CGTs have brought the hope of providing potentially curative and life-changing outcomes for a variety of disease states to patients and physicians," shares "Currently, there have been forty-one (41) CGTs approved by the FDA within the United States, with seven (7) new CGTs approved in 2024. Of these 41 approved CGTs, umbilical cord blood derivatives represent 9 of the 41 approvals to date (≈22%), with CAR-T cell therapies representing the next largest segment, composing 7 of the 41 (≈17%). CGTs used in oncology, hemophilia, and Duchenne muscular dystrophy (DMD) are gaining traction."


Jakki Lynch

While the current CGT pipeline is very robust, there is a mounting concern among plan sponsors that there are now therapies under development that are going to treat more common disease states, like diabetic peripheral neuropathy. Greater challenges lie ahead to ensure affordability and access to these therapies for plan participants.


Andy Szczotka

Jakki Lynch, CCM, CMAS, CCFA, director of Cost Containment, Carbon Stop Loss Solutions, shares this perspective, "The CGT landscape is a significant focus for our health care system as an unprecedented number of treatments for rare and devastating diseases become available for patients. Payers face uncertainty for case volume, clinical effectiveness, and the potential extraordinary costs."

She says payers need affordable solutions and predictable risk since numerous current therapies range in cost from $2M to $4M+, not including administration charges, pharmacy markup and potential inpatient admissions for adverse reactions.

"With the expected growth in future approvals of gene therapies, particularly for a higher number of patients and larger populations, affordability and risk reduction are strategic imperatives," she notes. "Additionally, payers and reinsurers may not experience the projected economic value of these therapies given the mobility risk of members changing plans or plans changing reinsurance carriers."

At Custom Design Benefits, Terri Martin and Alberta Manga, Medical & Risk Management, report no increased demand for CGTs, noting, "In fact, we have only seen two cases in the past four years – requests for Car-T. We are seeing Car-T being approved for coverage in our employer's health plans."

But Dan Winkelman, director, Offering Design Suite, IQVIA, offers a differing perspective, "There has been strong demand for CGTs among health plan members. This can be seen in the breadth of products now available in the U.S. market (36 products) and the growth in the number of patients treated."

For example, he points to seven CAR T-Cell products approved for Hematology cancers (Abecma,

Jeff Auten

Breyanzi, Carvykti, Kymriah, Tecartus, Yescarta, Autolus), noting, "IQVIA U.S. patient models indicate a 30% increase in CAR T-Cell patients treated from 2022 to 2023. This growth is being driven by new indications and early lines of therapy due to the strong efficacy of these products."

Jeff Auten, director of Clinical Consulting (PharmD) at Leaf Health, has found that self-funded plan sponsors continue to be hesitant to cover CGTs, "... even when risk pools are a viable option. Most available risk pools are covering the cost of the gene therapy but administration, hospital stay, and travel expenses are not covered under these pools."

Given the high cost of these therapies, he observes that many self-funded plan sponsors are opting to exclude gene therapies but says the narrative and pressure to cover gene therapies will continue to escalate once more prevalent disease states have a gene therapy option.

"Many gene therapies may not be cost-effective when compared to conventional or current standards of care," continues Auten. "Patients with Sickle Cell Disease (SCD), for example, can incur an average lifetime medical cost up to $2 million with severe cases up to $4-6 million in lifetime medical costs. Considering that current gene therapies for SCD have list prices of $2.2-3.1 million, the cost of these one-time therapies is already totaling the average lifetime medical cost of these patients."

He continues that in the case of a patient with severe SCD, "We may get some cost savings from a gene therapy, but these patients already have significant medical costs even before being considered for this treatment."

Health plan members are increasingly seeking out CGTs to address unmet medical needs and to explore the potential of personalized medicine, reports Jesse Roderick, senior vice president of Accident & Health Claims, QBE North America. He says some of the more requested therapies include Zolgensma (for spinal muscular atrophy), Kymriah (for acute lymphoblastic leukemia), and Luxturna (for inherited retinal disease).

"These therapies are gaining approval for coverage because they can potentially offer long-term, and in some cases, possibly curative benefits for life-threatening conditions," he recounts. "But accessing these therapies is not always straightforward, and several barriers may be encountered, including high upfront costs, uncertain long-term efficacy, and complex regulatory and administrative hurdles. Geographic accessibility also poses a significant challenge, as it can limit access to specialized care that administers these therapies. "

Jesse Roderick

He suggests that the high cost reflects the advanced technology and potential curative benefits these therapies offer, adding, "Often intended as one-time treatments, these costs are also driven up by the small percentage of patients that need access due to the incidence rate of conditions that require such a sophisticated and complex treatment protocol."

These costs significantly impact employer health plans, requiring more action from manufacturing through treatment to reduce the expense.

"Given the significant impact on member health and quality of life, these costs can be viewed as reasonable and justified," he concludes.

CGTs are "living drugs" that can heal and replace damaged tissues or diseased organs. These properties translate into curative therapies for a range of diseases that currently have no cure.

- **Cell therapy**: Involves transplanting cells into a patient to replace or repair damaged cells. Cells can be cultivated or modified outside the body before being injected into the patient.
- **Gene therapy:** Involves transferring genetic material into a carrier or vector, and then into the appropriate cells of the body. Gene therapy can silence a mistake in the gene or replace the faulty gene with a corrected version.
- **CAR T-Cell Therapy:** Involves a way to get immune cells called T cells (a type of white blood cell) to fight cancer by changing them in the lab so they can find and destroy cancer cells. CAR T-cell therapy is also sometimes talked about as a type of cell-based gene therapy because it involves altering the genes inside T cells to help them attack the cancer. While this type of treatment can be very helpful in treating some types of cancer, even when other treatments are no longer working, studies now support their use earlier in a patient's disease, rather than after all other treatment options have been exhausted.

Sources:
2024 Stanford Medicine
2024 American Cancer Society

WHICH CGTS ARE GAINING TRACTION?

With this raft of CGT approvals, it is interesting to gauge some of the therapies are actually gaining adoption.

Oncology

"In oncology, gene therapy aims to control the altered genes or genetic mutations of a cancer to prevent the cancer's growth," explains Szczotka. "Typically, oncology targeted gene therapy is not first-line therapy, but as the availability of multiple lines of oncology therapy grows and extend survival, the use of the later lines of CGTs are continuing to expand and improve survival rates."

Advisers at Lockton observe that traditional cancer surgery, chemotherapy and radiation give patients precious moments but no long-term promise. They say cancer CGTS are changing this by harnessing the power of a patient's own immune system to destroy cancer cells without harming healthy tissue. These therapies work by adding, deleting, or changing the DNA within an individual's existing cells to give those cells a new set of instructions that can help them find and fight cancer.

The Alliance for Cancer Gene Therapy says there is an urgent need to translate the profound success of CAR T therapies for blood cancers into successful therapies for the most complex and deadly cancers – solid tumor cancers. The organization is currently funding breakthrough research to tackle pancreatic cancer, brain cancer, ovarian cancer, sarcomas, lung cancer, and more, and to advance the understanding of solid tumor biology that will lead to curative therapies.

Duchenne muscular dystrophy (DMD)

"With the June 2024 FDA action of providing Elevidys both a traditional approval and an additional accelerated approval for use in DMD, this is one of the leading CGT agents," explains Szczotka.

The eligible population for this gene therapy is expected to soar, asserts the NEWDIGS initiative at Tufts Medical Center. DMD is a rare and serious genetic condition that worsens over time, leading to weakness and wasting away of the body's muscles. The disease occurs due to a defective gene that results in abnormalities in, or absence of, dystrophin, a protein that helps keep the body's muscle cells intact.

One advocacy group that helps patients with DMD reports while about 70% of their DMD cases involve self-insured employers, many payers exclude gene therapies. This organization has been able to get those decisions overturned.

Hemophilia

"Three gene therapies have been approved for the treatment of hemophilia: Roctavian for hemophilia A and Hemgenix and Beqvez for hemophilia B," continues Szczotka. "Traditionally, hemophilia treatment consisted of frequent intravenously administered factor VIII or IX replacement therapies for prophylactic use or on-demand treatment of bleeds to assist with the management of the disease."

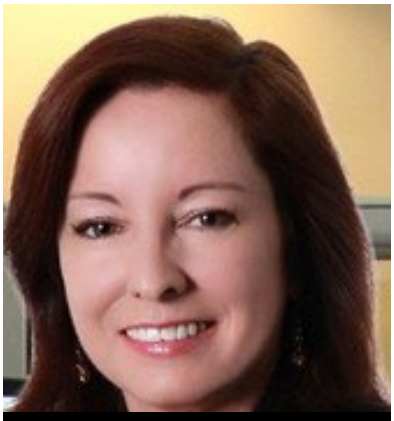
Employers see the value of Hemophilia gene therapies since they provide the potential a one-time administration of therapy to provide potential freedom from prophylactic therapies and the promise of being cost-effective if the patients no longer require prophylactic factor therapy or on-demand factor treatment -- and if they remain covered by the same payer.

Sickle Cell

Consultants at IQVIA forecast that more than 2% or about 2,000 of the patient population with sickle cell disease in the U.S. being treated will benefit from cell-based gene therapy. They report that the reimbursement landscape improved significantly in 2024 for these treatments, with companies reporting that more than half the states have affirmed coverage through a preferred drug list of published coverage criteria, and nearly 50% of Medicaid-insured individuals with sickle cell disease live in a State that has already completed prior authorization approval for use of the therapy in at least one patient.

HIGH COST OF THERAPY: KEY BARRIER TO ADOPTION

Some employers – from small-to-midsize companies -- react to the high price tags of a gene therapy as a bolt of lightning that could upend their entire healthcare spend and potentially threaten health plan financial stability. Some employers may hesitate to shoulder the heavy cost of a one-time treatment for workers who are likely to eventually switch jobs. Manufacturers argue the prices are justified because they offset a lifetime of medical costs patients would otherwise face.



Mary Ann Carlisle

Mary Ann Carlisle, chief revenue officer & COO, ELMCRx Solutions, observes, "Mid-sized PBMs and PBM alternative programs have been talking about these therapies quite a bit for the past six months. Their clients have been asking them about strategies to manage these treatments, not exclude them, but ways to include an oversight component as a way to verify that the care rendered is appropriate."

She points out that these therapies are quite new, so understanding the course of the treatment and outcomes can be a challenge.

"Working with organizations that have experience and provider networks can bring needed expertise into the equation," she says. "Partnering with organizations that provide access to a network of highly specialized caregivers and medical sites seems like a prudent way to approach these treatments."

Lynch explains, "CGT manufacturer pricing is supposed to reflect their potentially unique value—a one-time treatment that provides a durable/curable response without future clinical interventions. The belief is the therapies may yield overall plan savings by curing or improving a chronic disease and reducing the need for other ongoing costly treatments."

She cautions that confirmed long-term data on efficacy and safety is not readily available, especially for the newer therapies with off-target effects – such as malignancies recorded in patients treated with Lyfgenia, a one-time treatment for sickle cell disease. This also includes those therapies approved through an accelerated approval pathway. For example, Elevidys, for Duchenne muscular dystrophy patients, has prompted some payers to exclude coverage of any new FDA-approved drug approved through the accelerated approval pathway for the first 18 months.

Bloomberg recently reported that employer coverage of the treatments is "spotty at best," due to the rarity of the diseases they target and their exorbitant price tags that can exceed $4 million. Editors contend that many employers are dropping coverage and leaving families in a bind.

It is not surprising that the 2024 Large Employer Health Care Strategy Survey conducted by the Business Group on Health shows that 79% of employer respondents are very concerned about the patient and plan affordability of CGTs in the pipeline.

Another industry survey of 185 benefits leaders representing primarily employers, unions/Taft-Hartley plans as well as a swath of health plans and covering an estimated 86.6 million lives, documented that all respondents are concerned about managing these high-ticket items, with 74% of respondents citing affordability to be a moderate or major challenge.

The report shows that higher costs are hitting smaller health plans compared with large employers: 33% of respondents

overall indicate that they use stop-loss insurance to cover these therapies; 41% say they aren't using any form of financial protection; and 17% report they are unsure what financial protections are used, indicating a need for better education.

NEWDIGS, a group at Tufts Medical Center that studies how to pay for new medicines, expresses concerns that companies are excluding gene therapies from their health plans because they worry they will be too expensive. They say that some large employers with low-wage workers are telling employees to seek coverage for high-priced medical treatments from state Medicaid programs. The researchers expect that the number of CGTS will rise to 85 by 2032, costing as much as $40 billion over the next decade. With employer healthcare costs projected to jump as much as 9% in 2025, this group – among others – lay blame on the cost of CGTs.

Bob Gilkin, Senior VP, Trade and Specialty Strategy, AscellaHealth, says, "CGTs provide new treatment options for patients, but come at an extraordinarily high cost. The therapy class is responsible for the world's most expensive drugs, including six therapies that cost more than $3M. However, these treatments can potentially be a life-changing experience for patients. For example, the hemophilia gene therapies may eliminate the need for ongoing therapy in most patients and Zolgensma, for spinal muscular atrophy, has shown sustained efficacy for up to 7½ years post-dose."

Bob Gilkin

He adds that while many therapies offer potential significant clinical benefits, their cost and long-term value in demonstrating a reduction in total healthcare expenditures remains a key concern.

"In addition to conducting their own clinical and cost-effectiveness analyses, payers are looking to third-party organizations such as The Institute for Clinical and Economic Review (ICER), the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), the National Institute for Health Care and Excellence (NICE) and the National Comprehensive Cancer Network (NCCN) for guidance on cost impact and justification," he continues.

ICER, for example, which began as a research program at Harvard Medical School in 2006, today stands as an independent, non-profit, research organization that evaluates the evidence on the clinical and economic value of prescription drugs, medical tests, devices, and health system delivery innovations. ICER engages with leading academic scholars and key stakeholders, including patient groups, clinical experts, life science companies and insurers, to inform their evidence reviews and then publishes their independent results.

Gilkin explains, "The publications provide a well-balanced, clinical, safety and economic analysis to help payers answer if the therapy is cost-justifiable based on the available evidence. Generally, their analyses on CGT therapies often recommend lower prices to meet commonly accepted cost-effectiveness thresholds than what the manufacturer is charging. As an example for CGTs, ICER stated that price benchmarks of $2.9 million for Hemgenix as compared to the actual cost of $3.5 million and a range of $1.1 to $2.1 million for Zolgensma as compared to the actual cost of $2.125 million."

He advises that key hurdles for broader CGTs use include the proven durability of and sustained treatment effects, identifying the most appropriate patient population, elimination of concurrent and/or subsequent treatments, avoidance of long-term complications, regression of the disease state and the availability of alternative or newer therapies.

Terri Martin

"As more long-term clinical data becomes available with these CGTs, these key questions will likely begin to be answered and will assist payers with addressing if these one-time therapies, with potential lifelong impacts from a clinical and quality of life perspectives, are more cost-effective than current conventional therapies," says Gilkin.

Alberta Manga

Martin and Manga also acknowledge that plans are facing significant barriers in providing access to these therapies, adding, "The financial impact for a single hospitalization and treatment is over $1.5 million, which is a significant challenge for many health plans and employers. Even with stop-loss insurance, there is a likelihood of placing the member being treated on a laser and receiving a higher specific deductible. The long-term outcome of cell and gene therapies remains unknown. It has not been found to be a cure."

They concede that the costs are very high, presenting a significant financial burden on many patients and their families.

"One avenue to address the exorbitant costs would be financial assistance from the manufacturing companies for the member being treated," they suggest. "Justifying the cost of therapy remains an unknown -- only time will provide a definitive

answer. The side effects of the CGTs could lead to increased debilitation and additional healthcare cost."


Dan Winkelman

Winkelman agrees that the high cost of these novel therapies, which can range from $100,000 to $3.5M (Hemgenix), is the primary barrier U.S healthcare plans are facing.

"Balancing the initial impact of the high cost of treatment is the potential to cure patients and limit, or even eliminate costly downstream care," he explains. "Another barrier to treatment is the limited number of administration sites associated with these therapies. For example, Roctavian, which is indicated for Hemophilia A and was approved by the FDA in June 2023, is only administered in 15 locations. The funneling of patients to these specialty centers is one of the primary challenges drug manufacturers and healthcare systems face."

Why is gene therapy so expensive?

According to the National Organization for Rare Disorders (NORD), there are key reasons for the high cost of CGTS:

- Complex manufacturing:
  Producing viral vectors, which are used to deliver genetic material into cells, requires specialized equipment and highly trained personnel in cleanroom environments to prevent contamination, significantly increasing production costs.

- Patient-specific treatment:
  Many cell therapies are autologous, meaning they are derived from the patient's own cells, requiring additional processing steps to isolate and manipulate cells before re-administration.

- High research and development costs:
  Clinical trials for gene therapies are often lengthy and expensive due to the need to carefully monitor patients for potential long-term side effects.

- Limited patient population:
  Many gene therapies target rare diseases, meaning the potential market size is smaller, which can inflate the cost per patient to recoup development costs.

- New technology:
  As a relatively new field, the manufacturing techniques for cell and gene therapies are still evolving, leading to higher costs as companies invest in developing optimal production methods.

ADOPTION OF VALUE-BASED CONTRACTS

Ashley Hume, President of ETS and Chair of SIIA CGT Task Force, advises that manufacturers have stepped up to offer value-based contracts (VBCs) for cell and gene therapies (CGTs), which will be more fully explored in Part II of this series.

Ashley Hume

"These arrangements are typically made with ASOs, TPAs, PBMs, or specialty pharmacies—not directly with employers or stop-loss/ reinsurance carriers.," she explains. "This creates a disconnect, as stop-loss and reinsurers remain exposed to the high-cost risk without access to the financial protections VBCs provide. Without direct participation or alternative contracting models, stop-loss and reinsurance markets are left to manage CGT risk using traditional underwriting, limiting their ability to align costs with outcomes. Bridging this gap is critical for sustainable coverage as CGTs continue to expand." ■

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