

# High-Stakes Medicine: Rethinking Policies for the Cost and Value of Cell and Gene Therapies



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# High-Stakes Medicine: Rethinking Policies for the Cost and Value of Cell and Gene Therapies

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# POLICY CONTEXT

Existing policy solutions have not resolved persistent access barriers to life-saving cell and gene therapies (CGTs). Expanding access will require coordinated reforms that better align payment with long-term value while protecting insurers, providers and manufacturers from excessive risk. Near-term solutions should prioritize private-market innovation, including third-party financial intermediation to structure value-based agreements, smooth payments over time, and ensure adequate and timely reimbursement to treatment centers. If market mechanisms prove insufficient, policymakers should consider a public-private model—building on frameworks such as Medicare Part D—that pairs coverage mandates with transparent health technology assessment and structured price-setting tools such as final-offer arbitration. Across all approaches, federal leadership will be needed to standardize longitudinal outcomes tracking, clarify provider reimbursement pathways under Medicare and Medicaid, and create predictable rules that sustain innovation while ensuring clinically eligible patients can access FDA-approved CGTs.

## KEY TAKEAWAYS

- The U.S. system is built around chronic treatments paid over time and thus is poorly structured for one-time therapies whose value accrues over decades.
- Cell and gene therapies (CGTs) create extreme stress on the current reimbursement system by combining very high up-front prices with long, uncertain benefit horizons.
- Existing market solutions address pieces of the problem but fall short of a system-wide solution. Stop-loss insurance, drug mortgages, and value-based agreements can mitigate concerns over payment timing and performance risk, but they don't address the risks of adverse selection, patient churn among insurers, and inadequate provider reimbursements.
- Unlike other predictable high-cost events such as trauma or premature birth, many CGT candidates can often be identified in advance through diagnosis or genetic testing. This limits the effectiveness of stop-loss insurance, since insurers can anticipate claims and price the risk into higher premiums.
- Provider reimbursement is an important but underappreciated access barrier. Hospitals and other providers often incur losses administering CGTs due to inadequate bundled payments (including new technology add-on payments), substantial upfront capital investments, and the opportunity cost of replacing chronic treatment revenue streams.
- We propose a stepwise approach to ensure broad, equal access to CGTs, beginning with the least intrusive option of private-market intermediation. Then, if necessary, progressing to more intensive interventions, including public-private hybrid models and, ultimately, direct public financing.

## SUMMARY

Cell and gene therapies (CGTs) represent a new era of medicine, offering the potential to cure diseases once deemed untreatable. Yet, their promise is constrained by economic and structural barriers within the U.S. healthcare system. The multimillion-dollar up-front cost of many CGTs, coupled with uncertain and potentially heterogeneous long-term health benefits, challenges traditional reimbursement models designed for chronic, recurring treatments. These therapies expose misaligned incentives among payers, providers, manufacturers and patients: Insurers face short time horizons relative to the decades-long benefits of CGTs; manufacturers must cover research and development costs without predictable returns; and hospitals may incur financial losses administering therapies reimbursed below acquisition cost. Existing market-based solutions—such as stop-loss coverage, drug mortgages and value-based agreements—address individual risks but fail to align incentives systemwide or ensure sustainable access. This paper reviews these challenges and proposes a policy framework to guide CGT financing and reimbursement reform. We propose a stepwise approach, beginning with the least intrusive option of private-market intermediation, and then, if necessary, progressing to more intensive interventions, including public-private hybrid models and, ultimately, direct public financing. We evaluate the costs and benefits of all three pathways.

## Introduction

Cell and gene therapies (CGTs) modify a patient's cells or genetic material to treat or cure disease. After decades of research, these therapies are now entering the clinic, offering the prospect of functional cures for some cancers, inherited disorders and other conditions once deemed untreatable. Gene therapies for blood and clotting disorders could add years of life for terminal conditions and relief from lifelong, debilitating flare-ups and hospitalizations.[1, 2] Many CGTs offer the prospect of one-time or short-term treatment that produces long-lasting improvements.

However, CGTs are typically quite expensive, costing hundreds of thousands to millions of dollars to treat a single patient.[3] Most treat rare diseases with very small patient populations and require multiple hospitalizations, including cell removal and immune suppression and custom cellular preparations. One-time therapies with potentially millions of dollars of future value to patients carry seven-figure price tags, reflecting the current drug paradigm of paying drug companies up front when the drug is administered.[4]

As a result, high costs have often presented the primary barrier to access, ahead even of the risks and complexities of treatment.[5] The diffusion of CGTs has lagged behind expectations, even for subpopulations that might realize life-changing benefits, such as people with sickle cell disease (SCD).[6] Medicaid programs face constraints in their ability to finance large outlays for even a small number of qualifying patients.[7, 8] Meanwhile, among commercial insurers, traditional stop-loss insurance mechanisms have proven insufficient to address the challenge. Carriers often underwrite stop-loss insurance policies annually, evaluating spending both in aggregate and for individual patients, even "lasering out" or limiting coverage for some specific patients.[9, 10]

Underuse of CGTs is worrisome on multiple levels, exposing cracks in the drug pricing and reimbursement system as well as misaligned incentives among payers, clinicians, manufacturers and patients. New approaches to CGT financing must, at minimum, better match payments with the actual value realized. Payers and drug recipients cannot bear all the risk of underperforming treatments, but neither can manufacturers be expected to continue innovating if slow uptake and anemic revenue persist.[11] Meanwhile, hospitals and treatment centers could experience reduced revenue from substituting one-time CGTs for ongoing treatment for lifelong conditions. Some hospitals are reimbursed less for CGTs than the actual prices of the therapy, further impeding uptake.[12]

The situation will become even more complicated as CGT technology improves, expanding beyond rare diseases to more prevalent conditions.[13] CAR-T cell therapies now approved to treat leukemias and lymphomas, for example, are being tested against a broader swathe of autoimmune conditions including lupus and refractory rheumatoid arthritis.[14] Next-generation treatments may prove cheaper to manufacture or may be administered in vivo, side-stepping the need for lympho-depleting chemotherapy, but neither possibility is certain.[15, 16]

The immediate task is to establish consensus among key constituencies around a set of policies and practices to finance CGTs as they exist, allocating price and efficacy risks without compromising innovation. This paper summarizes the economic and structural challenges that distinguish CGTs from prior breakthrough therapies, along with existing proposals to solve these issues. Ideally, market mechanisms could be developed to address all these problems, but the unique stresses that CGTs place on existing fissures in the healthcare payment system may require government intervention to resolve. As detailed below, existing policy proposals that solve bilateral issues between

manufacturers and payers often fail to address the complications that hospitals and patients face and vice versa. We propose a phased approach, beginning with private-market solutions and transitioning to public/private or fully public financing mechanisms only if market participants are unable to ensure broad and equitable access.

The American drug pricing system features several well-known points of stress. CGTs seem almost perfectly engineered to place unique, and in some cases unprecedented, pressure on all of these areas.

**Patients value long-term health, but employers and other third-party payers often face short-term horizons.** The one-time administration of a CGT may provide benefits that last many years, but patients or their families may change jobs or insurance coverage much sooner. This leaves payers with, in effect, an uncompensated cost, having paid for the CGT without covering the recipient for sufficient time to realize its benefits. Job transitions and subsequent coverage changes (i.e., patient churn) or a transition to Medicare can create frictions that insurers have objected to in other high-cost treatment contexts, but the financial stakes are much larger for each use of CGT.[17] Median job tenures vary with age, with median tenures in the three- to five-year range for those under age 45.[18] This is not a new problem, but CGTs carry it to a new extreme by coupling high up-front price tags with the possibility of decades spent accruing future health benefits.

Employers and individual insurers may also face incentives to narrow benefits in response to adverse selection. People who qualify for a CGT, or have a family member who qualifies, may seek jobs or specific plans that ensure CGT access. The Affordable Care Act (ACA) of 2010 prohibits insurers from denying coverage or charging higher premiums based on preexisting conditions. Thus, excluding specific therapies may become a tool for limiting adverse selection.

**Third-party payers do not derive value in proportion to their cost outlays.** This too is a well-recognized problem that CGTs carry to new heights.[19] Unlike with drugs for chronic disease, CGT costs are borne entirely before any of their value can be realized.[20] Even if that value were perfectly predictable and aligned with CGT prices, this causes problems for a payer that faces the prospect of a CGT-treated patient switching to another payer, which then "free rides" off the investment of its predecessor. Ongoing rather than one-time treatment makes more financial sense to a payer in this position, even when it makes less clinical or economic sense to the patient. The unpredictability of long-term value exacerbates this problem further. The full cost of the CGT treatment is borne before any information about effectiveness is revealed, possibly putting millions of dollars of value at risk for a single course of treatment.[5] Moreover, even if the expected value of a CGT is well known, the rarity of CGT use coupled with heterogeneity in treatment response drives a wedge between this expected value and the actual value accruing to a particular payer.

**Hospitals and physicians are paid for services, not value.** Hospital and physician reimbursements face the same absence of value-based pricing.[21] Our predominantly volume-based system creates incentives to provide a lifetime of chronic disease management and penalizes the provision of a one-time cure. For example, to administer CGTs, hospitals must typically make up-front and ongoing investments in equipment and personnel for each specific treatment, because many CGTs require an orchestrated set of procedures, which sometimes last from weeks to many months.[22] Existing reimbursement structures often fail to account for these investments, and sometimes fail even to account for the cost of the CGT itself.[23, 24] While CGTs are not the only treatment options disfavored by the complex

economics of provider reimbursement, they once again carry the problem to an extreme. In numerous cases, for example, administering the CGT is a strictly money-losing option for a hospital or treatment center,[25–27] not just a less lucrative option, thus tying CGT access to the willingness of providers to absorb costly financial losses.

For all of these reasons, payers and providers may be inclined to limit access to CGTs absent a requirement to do so or financial protection if they do offer access.[9, 28] These frictions preclude patients from realizing the value of CGTs. In sum, by combining unprecedented up-front costs, the potential for substantial patient benefit, long and uncertain benefit periods, and financial penalties for many administering providers CGTs expose and exacerbate structural limitations in the current healthcare reimbursement ecosystem.

### **What makes cell and gene therapies different?**

CGTs represent a fundamental shift in medicine, offering the potential to correct underlying genetic causes for diseases rather than just treating the symptoms. However, the healthcare system is struggling to manage the unique promise of CGTs in a reimbursement ecosystem built over decades to manage traditional, chronically dosed therapies. The challenges arise from the unique characteristics of CGTs.

**CGTs are associated with unprecedented up-front costs.** CGTs are among the most expensive therapies to be approved by the Food and Drug Administration (FDA). The magnitude of the cost challenge is illustrated by Lyfgenia, a gene therapy to treat SCD that costs \$3 million. This up-front cost can be many times more than the lifetime costs for red blood cell transfusions and pain-management therapy to treat disease flare-ups.[29] To illustrate the scale of the budgetary challenge, consider the example of Maryland, where the SCD population is estimated at over 5,812 individuals.[30] Using the standard assumption that 20% of SCD patients exhibit the severe disease phenotype and are eligible for Lyfgenia,[31] and assuming that just 10% of potential recipients (116 individuals), undergo CGT treatment in a year, the medical costs would consume about 6% of the state's share of annual Medicaid funding.[32] While a variety of other factors have slowed Lyfgenia uptake,<sup>1</sup> the budgetary hurdle will remain, absent changes to the cost model. Similarly, a handful of employees who qualify for CGTs could increase premiums significantly for employers in private markets with experience-rated health insurance or stop-loss reinsurance. Notably, Lyfgenia is not the only or the most expensive gene therapy. In fact, the top five highest-priced drugs in 2024 were gene therapies, ranging from \$3 million to \$4.5 million per one-time treatment.[33]

**CGTs also have the potential to deliver great value.** Compared to prior therapies, CGTs promise extraordinary clinical improvements that will transform patients' lives and benefit society. For example, SCD is a lifelong, inherited blood disease that is associated with unpredictable painful episodes where misshaped blood cells block blood flow, often requiring emergency care or hospitalization. Over time, SCD leads to organ damage and premature death. As recently as 2017, SCD patients faced a median age at death of just 43 years and total lifetime medical costs of \$1.7 million or more.[34] Lyfgenia and another SCD gene therapy, Casgevy, offer the potential for permanent relief from painful SCD episodes, increasing a recipient's ability to work and live normally, and extending life by over two decades on average.[35] A 2023 Institute for

Clinical and Economic Review (ICER) report estimates a value-based price for Lyfgenia and Casgevy of \$1.91 million (assuming quality-adjusted life years (QALYs) valued at \$150,000).[36]

Transfusion-dependent beta-thalassemia (TDT) is another disease that better CGT access could transform. Patients with TDT suffer from little or no production of functional beta-globin chains, leading to chronic anemia,[37] and require lifelong, regular red blood cell transfusions to survive, which can result in iron overload and significant organ damage. Zynteglo, a gene therapy, enables the body to produce functional hemoglobin through insertion of a modified beta-globin gene into the patient's hematopoietic stem cells. Clinical trials have demonstrated that treatment can eliminate or significantly reduce the need for transfusions in most patients, providing the possibility of a one-time disease-modifying treatment that substantially improves upon standard care.[38] In 2022, ICER estimated a value-based price of \$2.73 million for Zynteglo (assuming \$150,000 per QALY).[39]

Beyond monogenic disorders, CAR-T cell therapies first used to treat liquid cancers are showing promise in treating autoimmune conditions like systemic lupus erythematosus (SLE), a progressive condition characterized by chronic inflammation and organ damage. Direct medical costs in severe SLE cases exceed \$50,000 annually, in addition to indirect costs imposed by lost productivity and reduced life expectancy.[40, 41] Early clinical data on SLE-focused cell therapies suggests the potential for durable remission among moderate and severe cases.[42] If these results are validated in later-stage trials, CAR-T therapy could become a viable replacement for chronic immunosuppression and treatment of lupus complications. CAR-T therapy has also shown initial promise in treating inflammatory bowel disease and greatly improved the life of a young woman with multidrug-resistant ulcerative colitis.[43]

**CGTs have long and uncertain benefit periods.** The potential value from CGTs must be considered alongside the high up-front costs, the risk that benefits will not last, and the long waiting period until taxpayers or premium-paying beneficiaries recoup the high up-front investment in the treatment. The recent availability of CGTs means that follow-up periods are short. While a handful of gene therapy recipients in clinical trials have been followed for at least five years after treatment,[44, 45] most individuals have been followed for less than three years. For treatments promising decades of benefit, this leaves a great deal of uncertainty around value. To take the case of SCD, most of the available follow-up data from CGTs is encouraging, with both manufacturers of CGTs reporting response rates above 90%.[46] Vertex, the pharmaceutical company manufacturing Casgevy to treat SCD and TDT, reported relief from vaso-occlusive events for a mean duration of 2.9 years with a maximum of 5.5 years.[47] Competitor Bluebird Bio reported that 95% of recipients were free of severe vaso-occlusive events within 18 months of treatment and that 85% were able to eliminate all forms of vaso-occlusive events.[48, 49] However, fewer than 200 individuals have received one of these two therapies, making it unclear how durable or scalable the benefits will ultimately be.[31]

There is similar uncertainty in the durability of efficacy in CGTs for several fatal and life-shortening developmental conditions. Duchenne muscular dystrophy (DMD) is a progressive muscle-wasting disease in children that leads to a loss of independent walking and eventual respiratory and cardiac failure. Elevidys, a gene therapy developed to combat DMD, received accelerated

1. Note that although our example is hypothetical, in recent filings Bluebird Bio—manufacturer of Lyfgenia—reported supply chain challenges that may limit the ability to achieve 10% uptake even in the absence of access barriers. Other CGTs have faced similar supply chain challenges in the months after FDA approval. <https://www.fiercepharma.com/pharma/vertex-and-crispr-build-out-casgevy-launch-sickle-cell-doctor-warns-supply-bitches-analysts>.

approval in mid-2023.[50] While it fell short of achieving its primary Phase III endpoint,[51] subsequent follow-up studies showed stable disease among recipients and some improvements in other measures of motor function.[52] Most recently, the FDA has narrowed the indication for Elevidys to ambulatory DMD patients who are at least 4 years old and issued a black box warning to highlight the risk of serious liver injury and failure.[53] Similarly, two- to five-year outcome studies of infants receiving gene therapy for spinal muscular atrophy (SMA)—a rare, inherited neuromuscular disorder characterized by the progressive loss of motor neurons in the spinal cord and brainstem—suggest significant functional improvements, although about half of patients experienced a treatment-emergent adverse effect.[54, 53]

Data for use of CAR-T therapies to treat blood cancers, including B-cell lymphomas and multiple myelomas, indicates that a majority of recipients achieve durable long-term remission, far more than with previous therapies.[55] There is longer-term follow-up evidence for CAR-T therapies for these diseases; however, here too, the durability of results varies, with some recipients enjoying multiyear remission, and potentially a functional cure, while others relapse after a few years.[56, 57] Results also vary between pediatric and adult recipients.

The risk for insurers across all these therapies is whether their enrollees ultimately experience long-term functional improvements or disease recurrence. Until there are decades-long studies with wider use of all therapies, this will remain an open question.

**CGTs are sometimes associated with financial penalties for providers.** The high up-front costs and unique delivery methods associated with CGTs pose major reimbursement challenges for hospitals and other providers. Before CGTs can be offered, hospitals often must make substantial investments in specialized infrastructure, equipment and staffing.[26, 58] For example, hospitals may need to retrofit treatment rooms and invest in new equipment and specially trained technicians and physicians. The investment requirements vary based on whether the CGT is administered in vivo (viral-vector or nanoparticle-delivered gene therapies) or ex vivo (therapies that modify cells outside the body and then reinfuse them); however, one study estimated the cost of starting a cell therapy program at over \$1 million.[59] Because these are largely fixed investments, hospitals may require a reliable or even growing volume of CGT therapy patients and improved pricing and reimbursements from manufacturers and payers to justify and sustain the program financially. Thus, at current CGT volumes and with limited to no financial incentives tied to either drug acquisition or payer reimbursement, many hospitals do not have the financial incentives to invest in these therapies.

Beyond the high costs of starting a CGT program, reimbursements for the therapies themselves present serious financial risks for hospitals. Under Medicare, hospitals are typically reimbursed through fixed-rate systems like Medicare Severity Diagnosis Related Groups (MS-DRGs) for inpatient care or Ambulatory Payment Classifications for outpatient services, which often fail to account for the multimillion-dollar price tags of gene therapies.[12, 23, 27] For instance, if a patient with TDT receives Zyntelgo as an inpatient, the hospital may be reimbursed under an MS-DRG that covers typical bone marrow transplant-related admissions, which might reimburse only a fraction of the drug's cost—often well under \$1 million.[60] Not only would the reimbursement fail to capture the drug price, but it would also miss the substantial costs related to cell collection, conditioning chemotherapy, hospitalization and post-treatment monitoring. There is growing interest in shifting appropriate cell therapy patients—particularly those receiving

CAR-T therapies—to outpatient administration, which would enable eligible hospitals to purchase these products under the 340B Drug Pricing Program, where discounted acquisition costs could substantially reduce hospital expenditures. However, to date, approximately 79% of CAR-T infusions are still delivered in the inpatient setting.[61] Further, some states have carve outs for certain CGTs and/or other high-priced therapies in their 340B program.[62]

In addition to the MS-DRG bundled payments, Medicare established a special payment mechanism, the new technology add-on payment (NTAP), to cover the costs of new, innovative and expensive treatments that are not yet reflected in the reimbursement rates. NTAP was designed to protect hospitals and providers from financial loss when providing cutting-edge care like CGTs, but it has historically only covered 50% to 65% of costs in excess of the bundled payment. In the case of CAR-T and other gene therapies, the hospital and/or provider could still be left with a significant financial loss. In 2025, NTAP coverage was increased to 75% specifically to address the high costs of CGTs, but even with these separate pass-through payments or carve outs, the total reimbursement can fall short of covering both the drug cost and the intensive supportive care required. Medicaid reimbursement varies by state, but many programs use similar fixed or bundled payment models that are not designed for high-cost, one-time treatments.[63] As a result, hospitals may face financial losses when administering these therapies, creating disincentives to offer them and potentially limiting patient access. Further, if facilities vary in their ability to leverage the reimbursement system for CGT claims, the financial risks and thus the disincentives to offer CGTs may be particularly great for health systems with less experience administering CGT. Exacerbating these other factors, some therapies present providers with substantial opportunity costs in the form of foregone reimbursement for chronic disease management.[64] Hemophilia is an instructive example, where gene therapy demonstrates long-term cost-effectiveness but nonetheless cuts the revenue hemophilia treatment centers derive from administering clotting factor to patients.[65]

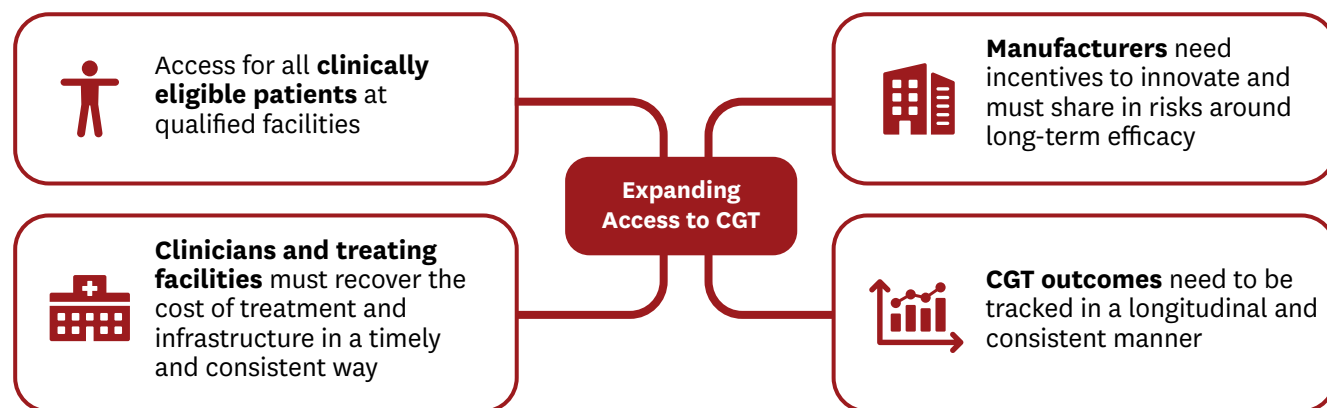
Hospitals may negotiate higher reimbursement with private insurers to cover the fully loaded costs of the therapy, but the reimbursement delays and coverage denials can leave hospitals carrying multimillion dollar costs for weeks or months.[66] The strain of covering these costs can make it difficult for hospitals to meet their other financial obligations in a timely manner.

### **Expanding access to CGTs**

Expanding access to CGTs will require market participants to fashion new structures and practices in parallel, including standardizing approaches to estimating therapeutic value and sharing performance risk, streamlining hospital reimbursement, and equalizing access among private and public payers. We offer the following key principles to which policymakers and marketplace stakeholders should hew when formulating appropriate policy (also shown in Figure 1):

1. Clinically eligible patients need access to CGT treatment at qualified facilities.
2. Manufacturers need incentives to innovate, including some certainty about the price and terms under which FDA-approved CGT therapies can be sold; however, manufacturers must share directly or indirectly in risks surrounding the long-term efficacy of CGTs.
3. Clinicians and treatment facilities administering CGTs must be assured of their ability to recover the cost of treatment infrastructure and administration in a timely and consistent way.

**Figure 1. Key Principles for Policies Aimed at Expanding Access to CGTs**



4. CGT outcomes need to be tracked in a longitudinal and consistent fashion, with results made available in a timely manner to all market participants (while protecting the privacy and identity of CGT recipients).

### **Previously proposed CGT coverage solutions**

To date, most of the market solutions proposed for CGTs have targeted specific challenges rather than addressing the larger interconnected access issues raised by the unprecedented nature of the therapies. The suggestions have involved providing supplemental coverage and developing price structures that begin to share CGT performance risk.[3]

For example, some insurers have begun to offer gene-therapy-specific stop-loss coverage, capping insurers' exposure for any individual's treatment and total CGT-related costs across a covered population. CVS Caremark, for example, offers stop-loss coverage at different premium levels that cap a purchaser's payout per treatment at \$30,000 to \$400,000.[67] While this limits the up-front cost for employers and preserves the price that manufacturers receive, it does little to address the misalignment between fixed prices and uncertain benefits, or the financial costs of CGT administration to providers.

Insurance mechanisms like stop-loss work best for sudden, unpredictable events of finite duration, e.g., a premature birth or trauma surgery. Predictable costs accruing from patients with diagnosed conditions treatable by CGT—hemophilia, SCD, cancer and the like—may compel employers either to accept higher stop-loss premium costs or exclude predictable CGT spending from stop-loss coverage.[68] This tradeoff will become more acute as more CGTs enter the market. As CGT-related payouts grow, some employers could in principle exclude coverage even for unpredictable CGT spending if doing so would lower overall healthcare costs, especially if public payers without genuine stop-loss coverage lead the way in making such exclusions "thinkable." Despite the use of stop-loss insurance, CGT access remains a challenge.

A second set of solutions focuses on spreading out payments and mitigating the risk of therapy failure.[68] A drug mortgage, for example, enables the up-front CGT price to be spread out over multiple years, as happens with a home loan. The annual payment may be set on a level, amortized basis with payouts over a few years, or it may include a higher first-year payment to cover treatment costs followed by a series of preset future amounts. For instance, a drug mortgage for a \$2 million CGT could spread the cost over four years with annual outlays of \$500,000, plus an

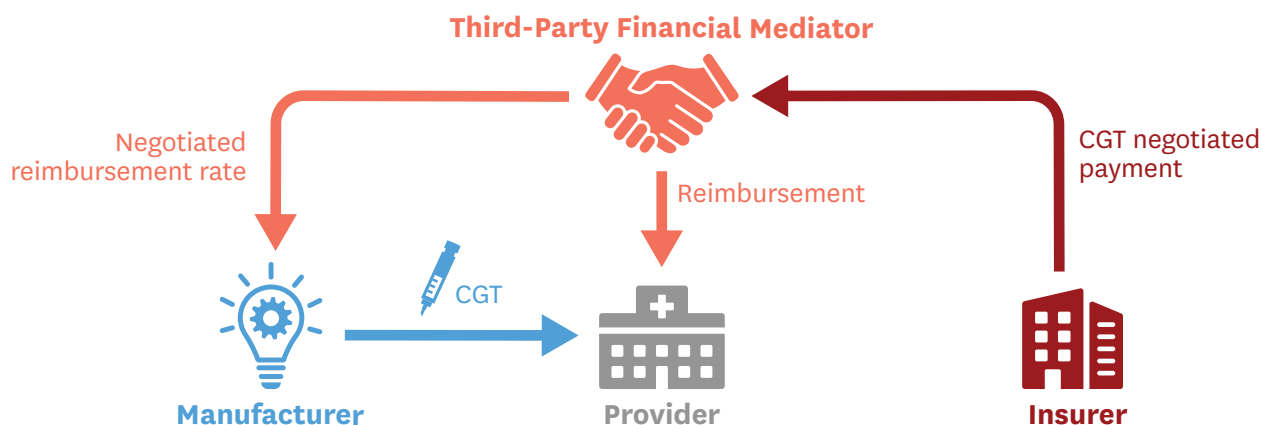
amount to account for time value. Although the mortgage will help smooth out the magnitude of annual payments, it does not address the uncertainty in long-term treatment efficacy, adverse selection or patient insurance churn. Drug mortgages also do nothing to address provider reimbursement gaps.

A value based agreement (VBA), on the other hand, can address the uncertainty in long-term outcomes by linking the total amount paid or retained by a manufacturer to post-treatment clinical outcomes.[69] The two VBA approaches in use are rebates and warranties. In the former case, a manufacturer agrees to repay a portion of the up-front price to an insurer if the treatment ceases to work as hoped. For example, Bluebird Bio offers rebates for its beta-thalassemia and SCD CGTs.[70] Payers may receive up to 80% of the up-front price if a CGT recipient is hospitalized for a serious manifestation of the disease the CGT is expected to solve, for two or three years after treatment.[71] The optimal time horizon depends in part on how quickly treatment nonresponse manifests, which may itself be uncertain when a CGT is newly launched. As a result, longer time horizons will tend to provide better assurance for payers. Similarly, CMS established the Cell and Gene Therapy Access model that allows it to negotiate a VBA featuring outcome-linked rebates with manufacturers of SCD gene therapies on behalf of state Medicaid programs. To date, 33 states as well as D.C. and Puerto Rico have agreed to participate in the model.[72]

Outcomes-linked rebates are paid in the event of some predetermined "treatment failure" event. In a warranty structure, a third-party guarantor (or potentially the manufacturer itself) agrees to pay all such rebates during a specified post-treatment period in exchange for a predetermined premium paid by the manufacturer.[68] For example, BioMarin provides a warranty for Roctavian, its gene therapy for severe hemophilia. Coverage lasts for four years post-treatment, with the maximum potential claim declining on a pro rata basis from 100% repayment in the first year after treatment to 25% in the fourth year.[73]

It is also possible to combine elements of a drug mortgage with a VBA. The mortgage would spread CGT payments out over a few years, with payments after the first year reduced or even zeroed out to the extent that a treatment underperforms agreed-upon clinical benchmarks. Although these solutions mitigate payment timing and performance risks, neither solves the issues of adverse selection, recipients changing coverage soon after treatment initiation, or risk pooling among smaller employers unable to access or afford stop-loss coverage. Moreover, none of these solutions address the financial penalties providers face from CGT administration, a major obstacle to access.

**Figure 2. Financial Mediator for CGT Reimbursement**



### **New public and private approaches to increase CGT access**

Effective reform to expand access to CGTs will require novel strategies that more directly address the key needs and incentives of all the key stakeholders outlined above—patients, insurers, manufacturers and providers. In practice, the new policies could proceed using private financing, public-private financing, or public financing. We propose beginning with the least intrusive option, leveraging private-market intermediation, and escalating to more intensive policy interventions only if these measures prove insufficient. Below, we outline these policy options and discuss the relative merits and trade-offs of each.

**Private coverage.** The status quo approach to financing CGTs in the U.S. remains a market-based structure, where insurers are responsible for all the drug costs and can condition access on price concessions. This private-market price negotiation introduces some level of access risk for patients, but it also avoids the conflict of interest posed by the government setting prices for the goods it buys. To date, the private approach has led to very limited access as discussed in this paper. Importantly, drug payments are not well aligned with value limiting their coverage, and there is insufficient reimbursement of providers limiting their use. Policy approaches that solve these issues while maintaining the predominantly private approach to coverage may offer the easiest “first-line” policy approach, as they would require fewer systematic changes.

One potential private market solution is financial intermediation of CGT reimbursement. A third-party company or group could negotiate a reimbursement amount with the drug manufacturer, featuring an up-front payment, with “success fees” tied to clinical milestones for treated patients. The same third party would also negotiate payments from insurers, set to vary with the realized performance of the therapy, as well as appropriate reimbursements for providers that incentivize administration of the CGT therapies. Insurer payments to the third-party intermediary could be fixed or spread out over time as a form of debt financing. The latter would likely be needed only for smaller payers, Medicaid programs or others that do not already have ready access to debt financing. This third-party company could also help hospitals raise the capital needed for up-front infrastructure investments in CGT delivery. For example, CGT manufacturers may be willing to support hospitals in developing a CGT program, but anti-kickback rules

complicate their ability to fund the hospital directly. A third-party company may be able to facilitate the mutually beneficial support. The financial intermediation approach is depicted in Figure 2.

The private market already has several examples of independent start-ups providing supportive services to insurers that fill gaps in the CGT market that pharmacy benefit managers do not. For example, new companies provide supportive services to insurers for CGT VBAs and warranty contracts.[74] Several companies also support patient navigation and outcomes tracking; however, none of the companies tackle the important issue of provider and hospital compensation. Under our proposal, the third-party intermediary could take the form of a for-profit company or insurer-funded cooperative. A cooperative approach would minimize rents absorbed by the third party, but it may require an explicit exemption from antitrust laws to facilitate collective bargaining over CGT prices with providers. For example, agricultural marketing cooperatives receive a limited exemption under the Capper-Volstead Act of 1922 for certain collective practices that would otherwise violate antitrust laws.

Although the financial intermediation approach addresses the misalignment of prices with value, insufficient provider reimbursement and problems created by public coverage, it does not solve all the status quo barriers to broad CGT access. For example, patient churn and adverse selection will remain challenges. If insurer payments to the third party are spread over time, who will inherit the payments when beneficiaries switch insurance carriers? If payment responsibility shifts to the new insurer, patients treated with a CGT may become marginally harder to insure in the private market. If it stays with the original insurer, that payer would be saddled with “uncompensated cost.” In fact, insurers face these challenges with all drug-coverage decisions, and they can only be solved through broad coverage across all insurers and/or through coverage mandates.

**Publicly subsidized private coverage.** If private-market intermediation fails to expand CGT access to clinically eligible patients, an alternative or next-step approach would follow the Medicare Part D model, offering public subsidies to private insurers in exchange for making FDA-approved CGTs essential medicines that must be covered without utilization restrictions for patients clinically eligible according to the label. This public-private financing method solves several of the challenges associated with CGTs, but it also presents several risks that must be addressed.

First, coverage mandates address adverse selection, but they undermine the market price-negotiation mechanism because they strip third-party payers and pharmacy benefit managers of the ability to threaten coverage limits when negotiating prices against patent-protected manufacturers. Thus, mandating coverage by private insurers without utilization restrictions requires some nonmarket mechanism to set prices. An accurate, predictable and objective health technology assessment (HTA) process would then be needed. Accuracy requires value-assessment methods that appropriately and consistently account for disease severity; generalized risk-adjusted cost-effectiveness (GRACE) would meet this need.[75] A predictable HTA process would enable innovators to forecast returns and respond appropriately to incentives. Objectivity may be harder to achieve, because the government faces a clear conflict of interest when measuring the value of a good it is paying for itself. There may not be a perfect solution to this problem, but basing government assessments on a set of externally conducted studies from manufacturers, payers, academics and other third parties would be a good start, because it would move the underlying analyses outside the relevant government agency.[76]

Assuming that third-party payers are made to share some of the CGT cost in a publicly subsidized model, as in the Part D program, they retain incentives to drive down CGT prices. In this context, a final-offer arbitration model may be an attractive approach, where payers and manufacturers submit proposed value-based prices and the independent arbitrator must choose one or the other.[77, 78] The “either/or” structure of the choice limits the incentive for gamesmanship. If the arbitrator can pick any price, both sides might be tempted to submit prices that are too high or too low in order to move the outcome in their favor, but the binary choice structure penalizes this behavior. The price determination would need to be repeated over time as new evidence emerges, since the expected value of therapy may rise or fall with the accrual of additional data.

Second, providers need predictable and consistent coverage and payment terms, and must be made whole for the costs of CGT therapy and any initial capital investments. This requires a linkage between CGT coverage and provider reimbursement issues that traditionally lie outside the scope of “drug benefit” coverage. For non-Medicare beneficiaries, CGT coverage mandates could stipulate sufficient provider reimbursement levels, perhaps by including provider costs within the scope of a final-offer arbitration model for proposed value-based reimbursement. For Medicare beneficiaries, the process may be more complicated if provider reimbursement reforms must be harmonized with Medicare’s current byzantine, MS-DRG-base payment and reimbursement structure. On the other hand, creating a program *de novo* represents a heavy political and regulatory lift that would further delay access. On balance, the public-private hybrid model addresses some of the challenges in the private-market intermediation model, and it merits consideration by policymakers as a next step.

**Direct public coverage.** Given the number and nature of these challenges, some argue that CGTs should be universally covered for all clinically eligible Americans in a publicly administered health insurance program like Traditional Medicare, without utilization management restrictions.[79] While we agree with the goal of universal access, this particular approach brings several hidden costs that render this a “later-line” option, in case private or hybrid public-private options fail.

Direct publicly administered coverage, as in Traditional Medicare, would necessitate government determinations about prices and clinical eligibility, which would be largely unprecedented in the U.S. for newly launched drugs. An accurate, predictable and objective HTA process would again be needed. Additionally, regardless of how value assessments

are conducted, a public-financing approach must account for changes in value over time, as new evidence accrues about the effectiveness of CGTs. Positive evidence of real-world benefit should trigger success fees or bonus payments to manufacturers, and vice versa. Price adjustment could be tied to individual patient experiences in a VBA structure. Alternatively, patient outcomes could be linked to evidence of value on average, e.g., from a Phase IV study of long-term efficacy. Patient-specific payments could better align prices with value, but they introduce additional administrative complexity.

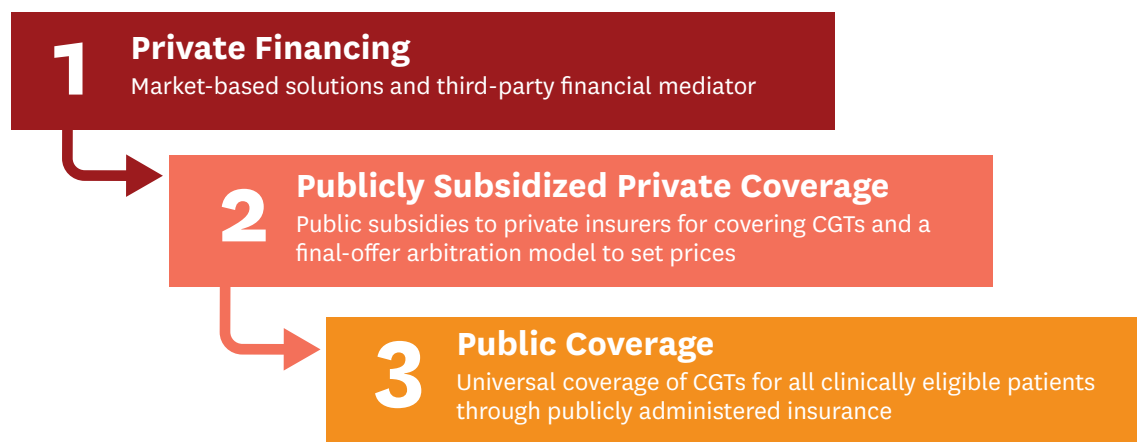
Direct public coverage for CGTs would also require reforms to provider reimbursement. For example, CMS’s Cell and Gene Therapy Access model requires participating states to reimburse treatment hospitals at the actual acquisition cost for the therapies outside of the bundled payment.[72] However, a fully public coverage program that situates CGT access within Medicare could trigger the same problems for Medicare reimbursement reform that arose with the public/private hybrid model requiring a *de novo* program or major revisions the existing structure.

In many non-U.S. markets, healthcare and health insurance are publicly financed such that there is universal coverage for all successfully negotiated drugs. However, the single-payer negotiation process does not always result in an agreement, and in the case of gene therapies we have seen some drugs not covered at all. For example, the manufacturers of Zynteglo—a beta-thalassemia treatment—withdrawed from the European market after failing to come to terms on price.[80] In these instances, patients have no access to the treatments, which underscores the need for an accurate, objective and predictable HTA process that can set a fair value-based price. Just as important, a predictable HTA process aligns manufacturers’ *ex ante* pricing expectations with the actual prices they are likely to be offered, encouraging innovation efforts to focus on CGTs where the measured value results in a financially viable price. Where price negotiations have been successful, the price for CGTs is still an order of magnitude larger than traditional therapies and access can be delayed or denied.[81] Even when using some of the payment strategies discussed in this paper, such as outcomes-based agreements,[82] access to CGTs remains limited in foreign countries.[81, 83]

Regardless of the policy approach pursued—public, private or hybrid—CGT outcomes need to be tracked in a longitudinal and consistent manner to ensure that their long-term safety, durability and effectiveness are fully understood. Such data will help align the price of each therapy with the value it provides and inform providers about patients who are most likely to benefit. The key for any registry or data repository will be to keep treatment results updated and available in a timely fashion such that all market participants—including regulators, payers, providers and manufacturers—have access, while also protecting the privacy and identity of CGT recipients. CMS often requires registry participation as part of its “coverage with evidence development” decisions, and something similar could be considered for CGT coverage.

CGTs present unprecedented risks and opportunities for patients and society. So far, their promise remains largely untapped. We recommend a “stepwise” approach to this problem, as shown in Figure 3, starting with marketplace solutions and progressing to public/private financing in the event that marketplace participants are unsuccessful in achieving broad access. We expect that all participants will learn over time what works and adapt accordingly. The goal continues to be greater access and use, rewards for therapies that provide long-term relief or functional cures, and the right therapy for each patient.

**Figure 3. Stepwise Proposal for Expanding Access to CGTs**



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