

Exploring the Truth of Reimbursement Challenges for Cell and Gene Therapies

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Introduction

Trinity has worked with over a third of companies with cell and gene therapies (CGTs) on market or in Phase 3 clinical trials. Our work has supported business development, launch planning, evidence generation (HEOR, etc.), market access, pricing, and other critical commercial activities to support the development and launch of these therapies.¹ As such, we have seen CGTs morph from a small niche into possibly the most exciting market in pharma. 2019 is poised to be an inflection point for these transformational therapies, changing the way we care for patients and disrupting the pharmaceutical & biotech industry. Despite this potential, however, there remains a lot of misconceptions about the unique challenges facing CGTs in terms of reimbursement, notably:

- Payment requirements (i.e., large lump-sum costs, Medicaid best price)
- Coding requirements (i.e., to ensure that providers are adequately reimbursed)
- High price requirements and payer/stakeholder pushback
- Patient affordability (e.g., given the potential high out-of-pocket exposure for patients)
- Portability and outcome tracking requirements (i.e., to address patient turnover across plans)

In our experience, most of these issues, while important, are manageable by US (and to some extent EU-5 and Japan) payers, and payers are welcoming of these new paradigms in patient treatment. However, as the CGT market is poised to dramatically expand in the coming years, both in terms of the number of products and the patient population volume they target, it is not clear how sustainable the current reimbursement model is and what changes may take place or need to take place. To unravel this, we conducted both primary payer research and economic analyses. This paper provides an overview of our findings and their implications.

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Trinity has worked with 30 unique companies with gene and/or cell therapies on market or in Phase 3 clinical trials



Methods

Trinity conducted qualitative research via telephone interviews with 10 medical directors from national and large regional commercial health insurance plans in the US (see *Table 1*). Interviewed respondents had been medical directors responsible for developing and managing reimbursement and access decisions at organizations covering over one million lives for at least the last three years. During our sixty-minute interviews, we discussed payer’s current coverage of CGTs, challenges associated with reimbursing these therapies, the viability of currently proposed solutions (e.g., annuity- and outcomes-based reimbursement models), and imagined market solutions needed to facilitate the uptake of CGTs.

Table 1: Interviewed Medical Directors

Total Number of Plans Represented	Total Years Experience	Total Number of Unique Lives Covered	Breakdown of Insurance Coverage			
			Commercial / Employer-Sponsored Lives	Medicare	Managed Medicaid	Health Insurance Exchanges
8	121	63.1 million	52%	33%	14%	1%

Additionally, we conducted a high-level economic analysis to understand how the confluence of expected increases in CGT prices, treated patient volume, and number of CGT therapies on the market may trigger payers to overhaul how they handle CGTs as the increasing financial impact on their plans’ overall pharmacy budget becomes unsustainable. To conduct these analysis, total US pharmaceutical spend was calibrated at \$500B.², and we used trigger points for payer intervention of 5-10% of total payer spend for a new CGT asset, and 20% for the class as a whole.

Findings

Through our research we found:

- A. Given current trends in the CGT market (e.g., number of CGTs, prices, target populations), the current reimbursement model is rapidly becoming unsustainable
- B. Misunderstanding of payers’ needs and situation leading to misguided focus of manufacturers entering this space
- C. Revolution in reimbursement model is needed if CGT market expansion is significant

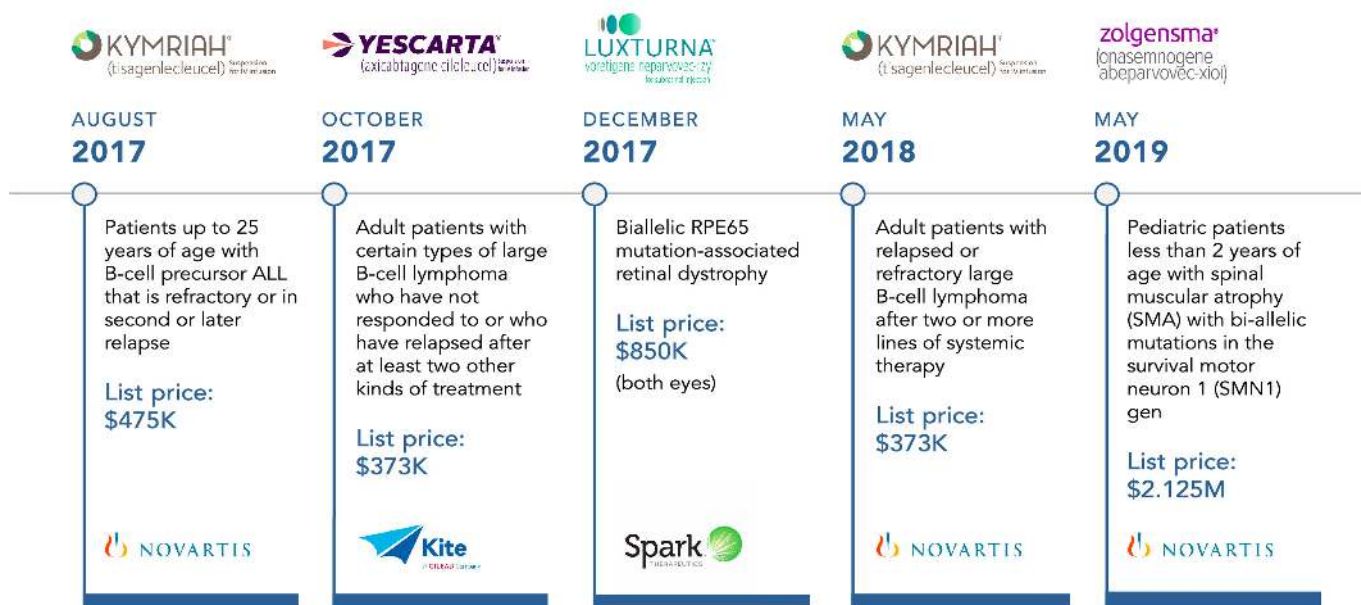
² “Medicine Use and Spending in the U.S.”, IQVIA (May 2019)



A. Unsustainability of Current Model

CGTs are now a primary focus of biopharma R&D investment, and the majority of the largest global biopharma companies are actively developing such products. The scientific promise and clinical abilities of these products are well appreciated by payers. Interviewed medical directors have differing opinions on the effectiveness of today's launched CGTs (Kymriah, Yescarta, and Luxturna; Zolgensma approved but has not launched, see *Figure 1*), but universally recognize that these medicines will soon offer cures to diseases with high unmet need.³ CGTs' unique value profile does not, however, fit into the current US insurance model as payers remain unequipped to pay for these therapies and expressed uncertainty about how they will be funded in the future.

Figure 1: Timeline of US CGT Approvals



"Cell and gene therapies are potentially very exciting. They are the next big wave of treatments with the potential to treat all sorts of conditions and revolutionize medicines. Anything from CF to sickle cell and even immunologic diseases could be treated by these."⁴

³ "FDA approval brings first gene therapy to the United States", FDA (Aug. 2017)

"FDA approves novel gene therapy to treat patients with a rare form of inherited vision loss", FDA (Dec. 2017)

"Spark's price for Luxturna blindness gene therapy too high: ICER", B. Berkrot (Jan. 2018)

"With Approval of CAR T-Cell Therapy Comes the Next Challenge: Payer Coverage", M. Caffrey (Feb. 2018)

"FDA Expands Tisagenlecleucel Approval to Include Relapsed or Refractory Large B-Cell Lymphoma", The ASCO Post (May 2018),

"A cutting-edge new cancer treatment has two different price tags, and it could be the future of how we pay for drugs", L. Ramsey (May 2018)

"FDA approves CAR-T cell therapy to treat adults with certain types of large B-cell lymphoma", FDA (Oct. 2018)

"Novartis slaps \$2M-plus price tag on newly approved gene therapy Zolgensma—and cost watchdogs approve", C. Helfand (May 2019)

⁴ US medical director, interviews conducted in March and April 2019

CGTs offer long-term benefits to patients that can significantly decrease lifetime medical spend, yet health insurance plans have no guarantee that they will realize these cost-savings. With ~20% annual turnover of commercially insured patients, there is a high risk that after a payer authorizes access to a CGT, the patient may move to another plan before the plan is able to realize any cost savings. Additionally, payments are currently not tied to clinical results – one medical director noted covering a CAR-T for a patient that passed away months later. Although the very small qualifying population allows insurers to manage coverage for now, the busy pipeline looms ahead.

“The biggest challenge is the cost. You hope that you don’t have members that are going to need [cell or gene therapies], and if you do, you hope that they’re few and far between.”⁵

The Alliance of Regenerative Medicine (ARM) reports that over 700 CGTs are currently being developed, including nearly 50 therapies in Phase III trials.⁶The wholesale acquisition cost (WAC) of each of the three CGTs launched to date by the FDA have remained under \$1M, but Novartis’s recently approved gene therapy for the treatment of spinal muscular atrophy (SMA) has passed that threshold as Novartis announced a \$2.125 million WAC in late May. Zynteglo (bluebird bio), approved by the EMA and seeking FDA approval for the treatment of transfusion dependant beta thalassemia in late-2019, will likely be priced above \$1M as well. This appears to be only the beginning; manufacturers and payers are already considering prices in excess of \$10M per patient.

“Prices could be \$10 million. It doesn't matter because we pay whatever they charge... The price is the price is the price.”⁵

The American health insurance industry is not prepared to finance such high-cost therapies. Today, in addition to increases in insurance premiums, in order to afford these therapies, plans frequently rely on stop-loss insurance – additional insurance purchased to protect against catastrophic or unpredictable losses. Such reinsurance is utilized by many payers, but rates increase with utilization and reinsurance plans will be unable to maintain profits and remain viable while benefiting insurance plans. These are not long-term solutions and do not help in de-risking patients changing insurance plans and taking their cost-savings with them. The high potential of these therapies makes reimbursement hurdles impossible for payers to continue to ignore.

⁵
US medical director, interviews conducted in March and April 2019

⁶
“ARM 2018 Annual Report”, ARM (Jan. 2018)



“Premium rates for everyone gets raised so everybody pays for it. And pharma has no skin in the game. It’s like Chinese water torture. You don’t see direct effects, but premiums keep going up.”⁷

B. Misunderstanding of payers' need and situation

A number of the first manufacturer entrants in the CGT space have promoted the use of creative, novel contracting agreements for CGTs, and many others, including policy advisors and consultants have jumped on the bandwagon. However, in our experience, interest in such innovative arrangements does not exist beyond national payers (i.e., United, Anthem, Aetna, Cigna, Humana), and even among these payers interest is limited for CGTs. For example, no payers within our sample had – or were building – functional capabilities to enact such contracting agreements with manufacturers. Annuity- and outcomes-based payment models have generated much attention, yet the majority of payers preferred to pay a single lump sum due to the small treated patient populations and low resulting impact to a plan’s budget that would not currently reduce medical spend nor justify the development of a complex alternative payment model.

Throughout our research, annualized payment models garnered little enthusiasm: nine of ten interviewed medical directors flatly rejected this option. Payers realize that annualized models will not discount CGTs’ costs and thus won’t impact their bottom line. Additionally, medical directors are not interested in paying for a patient’s therapy after they have died or otherwise left the plan. This contracting would require universal coverage decisions and unrealistic coordination between plans that would include the sharing of sensitive information with direct competitors.

“Annualized payments is not valuable. It would help our cashflow, but not our financial position.”⁷

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US medical director, interviews conducted in March and April 2019



In the future, outcomes contracts could become economically justifiable, but the additional administrative complexity of managing numerous, complex contracts for rare disease therapies is beyond plans' current infrastructure. Payers have implemented such contracts for larger indications, but for orphan diseases treatable by today's CGTs health plans lack the framework to measure or quantify outcomes and 'value' themselves. Medical directors note that they manage insufficient patients treated with these therapies to compare real-world outcomes to clinical trial data, which is often already limited due to small trial size needed for approval. This due diligence may not even be practical; medical directors tend to believe that evaluating a cell or gene therapy's value would cost more than such an evaluation could potentially save. The payers sampled would rather maintain standard reimbursement models rather than to develop and monitor complex contracts for therapies with a low utilization. As more CGTs gain approval, including those for broader patient populations, it will become acutely necessary to have a framework to evaluate them.

"I would anticipate there would be some push towards the value based arena. But for gene therapy, what is the timeframe that you can measure outcomes over? Patients change health plans, and gene therapies are going to have decades-long effects. Structuring the value based thing is incredibly complex."⁸

"'Value' is the favorite term of proponents of these therapies, but how do you define value. From a payer's perspective it's not about value but how much does something cost. What value is available to a payer when they are going to spend exorbitant amount of money?"⁸

"The value is that a kid that would die is going to live. How do you quantify that?"⁸

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US medical director, interviews conducted in March and April 2019

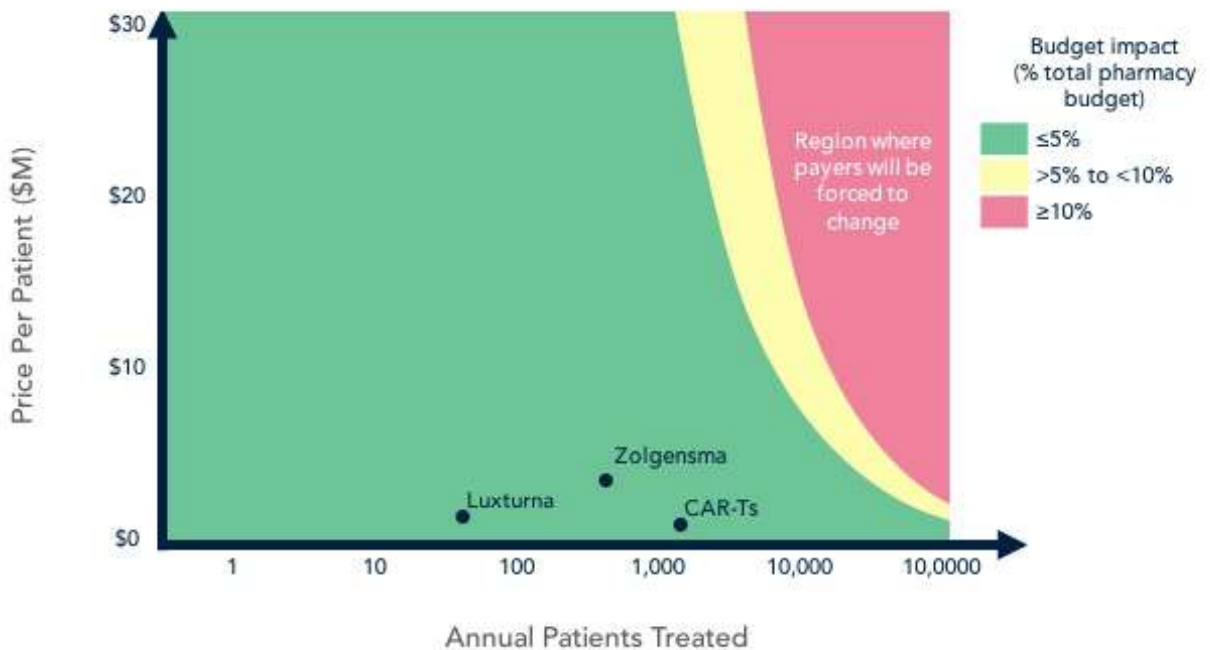


Furthermore, despite their magnitude, drugs' list prices do not account for facility costs that – in the case of Yescarta and Kymriah – can cost as much as the drugs themselves. To bill such novel procedures, clear coding needs to be established so that standard payments are established and lengthy negotiations can be avoided. Ancillary costs remain headwinds slowing the uptake of CGTs.

C. Necessary changes to reimbursement model if CGT market expansion is significant

The confluence of increasing price, patient volume, and number of CGTs on the market will soon push payers and other stakeholders to seek radical changes in the funding of CGTs. The high level economic analysis (Figure 2)⁹ suggests that new CGTs targeting diseases such as beta thalassemia, hemophilia, and sickle cell anemia with addressable patient prevalences in excess of 1,000 are likely to trigger potentially dramatic changes in the reimbursement model for CGTs as CGTs could soon impact payer's budgets by 5-10% (Figure 3)¹⁰.

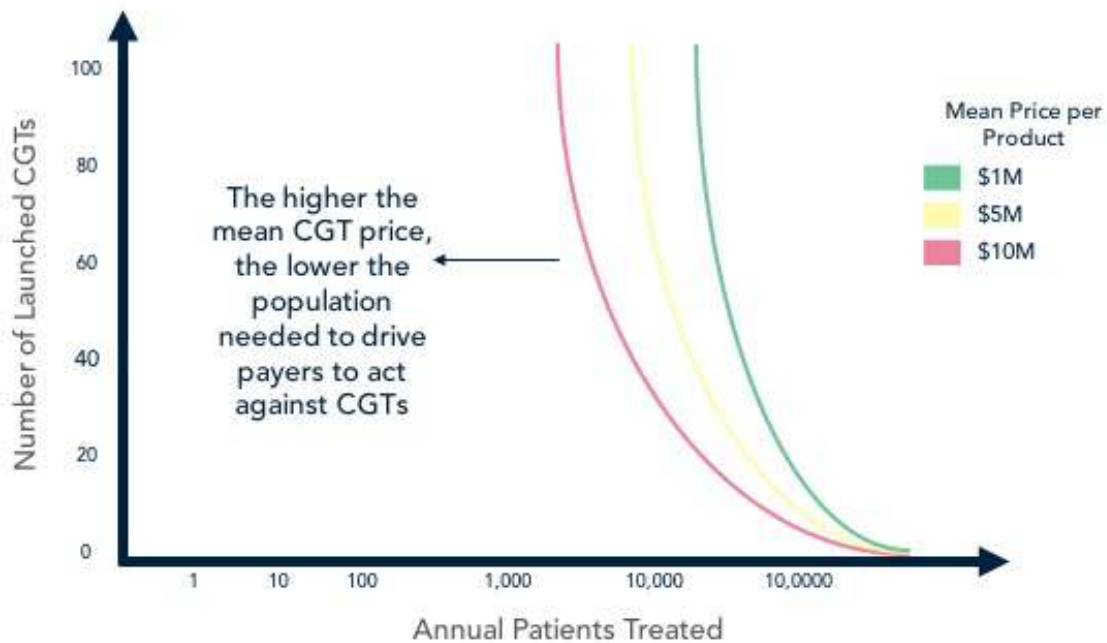
Figure 2: When will a new CGT's price per patient volume be too much for US payers?



⁹ "Prevalence, incidence and carrier frequency of 5q-linked spinal muscular atrophy – a literature review", Verhaart et al. (May 2017)
 "FDA ADVISORY COMMITTEE BRIEFING DOCUMENT: Spark Therapeutics, Inc LUXTURNA", FDA (Oct. 2017)
 "One Year Later: Lessons Learned In CAR-T", B. Koski (Aug. 2018)
 "Medicine Use and Spending in the U.S.", IQVIA (May 2019)
 Primary market research with N=10 US medical directors



Figure 3: When will CGTs' mean price impact US payers' behavior?



Payers concede that novel funding mechanisms (e.g., public or industry funding), changes in reinsurance, and/or legislative involvement will be necessary for the full growth potential of CGTs to be realized. Unkeen to make the first move towards guaranteed coverage, payers are looking towards manufacturers, trade organizations, and the federal government to initiate necessary changes.

¹⁰ "Medicine Use and Spending in the U.S.", IQVIA (May 2019)

Primary market research with N=10 US medical directors



Discussion

The health insurance system will soon need to solve the imminent issue of paying for CGTs, but the solution remains evasive, and several uncertainties add to this dilemma including: the future volume of patients receiving these products, the political landscape and any resulting legislative action, and the expected public outcry that would accompany restricted access to therapies. There are several ways payers imagined that these products could potentially be funded in the future – including public or private funds, and/or legislative change to allow payments to follow patients as they move plans. Many imagined corrective mechanisms would include a high risk pool that is funded over and above normal health expenditure. This funding could come from public or private sources including taxes, increased premiums for high risk members, employers, manufacturers, or health plans themselves. However, no private entity is likely to initiate the first move, so any real solution to manage these therapies will originate in legislative action. Interviewed medical directors imagined that a change will not occur with a divided Congress; there was no consensus if a Democratic or Republican controlled government would be more likely to initiate change. Other medical directors imagined legislative action that would force payments to follow patients as they move between plans. Without forced cooperation, plans will likely not contract with one another and continue to not realize potential long-term cost-savings of curative treatments. Payments following patients would make annualized- and outcomes-based contracting more practical. This mechanism would however require standard approval criteria and access to CGTs across plans to ensure payments would be made by all plans and to avoid adverse selection as patients could leave plans with high premiums and CGT coverage for lower cost plans without coverage. Other payers believe that manufacturers or centers of excellence administering CGTs should be forced to publish real world evidence so that outcomes- based contracts can be established without additionally burdening health plans.

In order to maintain reimbursement of CGTs, medical directors acknowledge that something should change, but continue to decline initiating that change. Medicaid plans operate on the tightest budgets and cannot raise premiums; private plans look towards these plans to initiate change.



Conclusion

We are fast approaching an inflection point at which many CGTs will gain approval and offer clinical benefits for areas of high unmet need. While this development is largely positive for patients with once believed to be incurable diseases, the insurance market will need to be restructured to facilitate the arrival of these therapies. Although payers are not inclined to initiate meaningful and necessary reform, they realize that financing needs to be generated to manage costs and that the uncertainty surrounding reimbursement of ancillary costs for providers needs to be addressed. Therefore, the necessary industry adjustment will need to be developed publicly. Manufacturers will need to engage in public discourse with other key stakeholders to find new solutions that ensure patients can access the transformational benefit of CGTs.

