

NEW DIGS

# FoCUS

Financing and Reimbursement  
of Cures in the US

WHITE PAPER



## Designing financial solutions to ensure affordable access to cures An overview of the MIT FoCUS project

23 August 2018

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**EXECUTIVE SUMMARY**

The reimbursement of emerging durable/potentially curative cell and gene therapies is likely to be a challenge for the US healthcare market. Considering the pricing of cell- and gene-based therapies approved thus far, the acute cost of the numerous pipeline products likely to launch soon may be substantial for payers. This cost, in addition to the lack of long-term clinical durability data, could mean that payers will be reluctant to fund these types of therapies, which could have serious negative consequences for patients.

The value of these treatments accrues over a patient’s lifetime after a single administration event with an acute cost which is counter to how most drugs are delivered and the norm of the US healthcare system of prescription ‘pay as you go’. The combination of high development costs for these drugs, the limited populations in the case of rare diseases and the single dose create an issue. With growing numbers of cell- and gene-based therapies expected to be approved, there is an urgent need for new financing and reimbursement models that can ensure appropriate patient access to needed treatments, remain affordable for payers, and sustain investment in innovation.

The Financing and Reimbursement of Cures in the U.S. (FoCUS) project was launched by MIT’s NEWDIGS Initiative<sup>i</sup> with the objective of further elucidating the challenges and financial impact created by durable/potentially curative therapies and providing implementable financial models to manage the cost burden on the US healthcare system. Numerous healthcare stakeholders, including public and private payers, providers, patient advocates, clinicians, regulators, developers and financiers, are currently involved with FoCUS.

Since 2016, the FoCUS group has been developing precision financing solutions to mitigate the impact of cell- and gene-based treatments in a situation-dependent fashion. The group started by examining factors that may influence solution choice, such as the nature of the therapeutic area, the potential impact of a curative treatment on the current standard of care and the relevance of different payer segments. Potential financing mechanisms were pressure tested in case studies based on real-world scenarios.

The results of the process have been precision financing tools with unique properties that make them more or less appropriate for use in different situations. The tools and guidance on tool selection are being combined into a toolkit to support strategic decision making for stakeholders. The aim of this white paper is to describe the development of the tools and the resulting toolkit, including two examples showing how these tools have been applied to cell- and gene-based therapies.

## BACKGROUND

### Emergence of gene therapies into healthcare markets

The development of transformative cell- and gene-based therapies over the past decade has raised the possibility that rare diseases with severe unmet need that are currently considered chronic or fatal may be significantly slowed down or cured after a single course of treatment (1). These therapies represent a foreseeable reimbursement challenge to current healthcare systems: the upfront cost is acute, but the patient benefits are accrued over time. If these benefits minus the costs are the basis of value, then this accrual is of significant value in a single administration event. Durability could extend for years or even a lifetime.

Drug pricing and reimbursement for new medicines has traditionally been based on models that are pay as you go—the assumption being that patients will require ongoing treatment for a disease until another event, such as disease progression, adverse incident or death, occurs. These models do not consider the potential long-term curative benefits of gene therapy, where the value and delivery of a treatment are so noticeably separated. While there remains the potential for significant savings through the reduction in medium- to long-term costs of patient care, the cost of recently approved cell- and gene-based therapies has been substantial thus far (2-4).

Uniqure's Glybera (alipogene tiparvovec), a potential cure for familial lipoprotein lipase deficiency (LPLD) approved by the European Medicines Agency in 2012, was the first gene therapy approved in the EU. However, the therapy had very limited uptake due to the rarity of the disease and the cost—an estimated €1.4 million per patient based on a single treatment—which led to the therapy being withdrawn from the EU market in 2017. The treatment was used commercially only once in 2015, in Germany, for a discounted price (4, 5). Strimvelis, owned by GlaxoSmithKline, was approved in the EU in April 2016 and is considered a gene-therapy cure for ADA-SCID, a severe combined immune deficiency that is usually fatal. Strimvelis costs around \$665,000 per patient, but GSK has agreed to a money-back guarantee, as the therapy is administered in infancy and thus far lacks long-term results (4). In 2017, tisagenlecleucel (Kymriah) became the first FDA-approved CAR-T cell therapy for children and young adults with relapsed or refractory B-cell ALL (6). The approval was based on 83% of patients achieving complete remission in a single-arm phase II trial. Kymriah is currently priced at \$475,000 per patient in the US and may be reimbursed by the Centers for Medicare & Medicaid Services (CMS) as part of an outcomes-based pricing scheme, where payment will only be for patients who respond to Kymriah by the end of the first month after treatment (6).

Upfront reimbursement in cell- and gene-based therapies may prove risky for payers. In many cases, the long-term

clinical durability of a treatment may be unknown, despite promising initial results. Efficacy is shown on regulatory approval, but follow up effectiveness studies are lagging. This uncertainty around clinical outcomes means that the long-term budget impact and potential cost offsets of gene therapies are difficult to assess (7). With growing numbers of cell- and gene-based therapies expected to be approved soon, there is an urgent need for new financing and reimbursement models that can ensure patient access to needed treatments; affordability for public and private payers; and sustain investment in innovation by developers.

## INTRODUCTION TO THE FOCUS PROJECT

The Financing and Reimbursement of Cures in the U.S. (FoCUS) project was launched in 2016 by the Massachusetts Institute of Technology's NEW Drug Development ParadIGMs (NEWDIGS) Initiative. The objective of the FoCUS project is to deliver an understanding of the challenges and financial impact created by durable/potentially curable cell- and gene-based therapies and provide implementable financial solutions to manage the cost burden on the US healthcare system. The solutions aim to ensure as broad as possible access to patients who would benefit, while balancing the needs of other stakeholders appropriately.

FoCUS is multi stakeholder in nature, with public and private payers, providers, patient advocates, clinicians, regulators, developers and financiers involved with the development of the project, to ensure an appropriate balance between industry and public needs. Targeted disease area work groups (TAGs), comprising individuals representing these different stakeholders, were established in two key areas of interest, gene therapies (non-oncology) and durable oncology treatments.

The FoCUS project has developed a process that has been used to understand appropriate financing mechanisms for specific situations. This process has evolved into a toolkit that currently comprises four components:

- Cure characterization framework
- Stakeholder considerations
- Financing tools
- Decision framework

The initial goal of each TAG was to identify a real-world situation that could be used to understand the influence of situation-specific factors on the choice of preferred financing tools. As part of the Design Lab process, each case study was discussed in detail and key pain points for stakeholders were identified. Potential solutions to these issues were discussed, and learnings about the relationships between situational factors and solutions led to a focus on an integrated

understanding of the cure characteristics and stakeholder considerations. Long-term aims include piloting financing innovations for specific classes of biomedical breakthroughs. Detailing the process the FoCUS group has gone through and how this provides a framework for our toolkit is the aim of this white paper.

## OVERVIEW OF THE FOCUS PROJECT TOOLKIT

### Cure characterization framework

An initial step in the FoCUS project was the development of the cure characterization framework, which aims to refine the impact of a therapy entering the US healthcare market by defining key components of a product and its therapy area. The framework recognizes the differences in the types of cell and gene therapies emerging, which have distinct mechanisms of action, delivery methods, and potential durability.

Key elements of this framework include describing the current epidemiology; burden; and standard of care or treatment of the disease, as well as the cell- or gene-based therapy's characteristics and clinical value. Clinical value can be broadly defined as the ability of the cell- or gene-based therapy to address the current unmet needs of the condition in the incident and prevalent patient population. In some cases, particularly for very rare, fatal genetic conditions with no available treatment, any therapy that provides a quality extension of a patient's life will be an immense and perhaps even unquantifiable benefit (e.g., Strimvelis). Alternatively, cell-based therapies for more common (although still rare) conditions, such as Kymriah for B-cell ALL, may offer a significantly improved durable response over currently approved treatments. However, it is important to note that the FoCUS project objectives are to create precision financing solutions for these new therapies, not to determine value or price.

Characterizing the epidemiology of the disease includes estimates of the incidence and prevalence and estimates of patient backlog should a new treatment be approved. This may mean examining more carefully disease subtypes, the ability and the need to treat (i.e., disease severity), and factors that may influence likelihood of successful treatment. The number of eligible patients, which is a subset of the overall epidemiology of a disease, will impact a payers' ability to provide reimbursement, as many patients requiring treatment in a short period of time could cause financial strain, called the surge effect. The age of the generally affected patient population will also impact which payers are likely to be most involved in reimbursement models.

The patient populations addressed by therapies vary from a handful of patients to thousands, as determined by the scientifically eligible sub-population, annual eligible

incidence, and patient backlog. Durable therapies often target a particular molecular mechanism, clinical classification and/or age cohort, especially for the first regulatory approval. This may significantly reduce the number of patients treated. Paradoxically, a smaller number of patients may increase actuarial financial risk because of greater difficulty in predicting/estimating whether they will be in a particular payer's beneficiary population (8).

Some conditions, if not addressed, result in patient death within a short period of time. These conditions may have only incident populations eligible for treatment, i.e., only relatively newly diagnosed patients. For other conditions, potential target populations may be dominated by longer lived patients managing their condition. Such conditions could result in a potential surge of patient utilization at the time of launch and then lower "steady-state" demand afterwards for only new incident cases after the treatment bolus for backlog patients.

Describing the burden of disease in a patient traditionally includes biomedical aspects, such as measuring the impact of a disease in terms of population morbidity and mortality, and economic consequences, which can include indirect costs such as loss of labor and productivity, and direct costs, which can include inpatient and outpatient medical expenses, among others. For very rare diseases, much of these data will not be openly available, but it can potentially contribute to an understanding of which financial approaches would be most appropriate for a stakeholder or payer. For example, ongoing direct and indirect costs over the lifetime of a patient with a chronic illness may be substantially offset by a one-off treatment course that provides a durable effect (or cure). Alongside burden, examining the current standard of care or treatment pathway is essential to appreciate the multiple effects a new treatment may have on stakeholders, including patients, providers, payers and developers. The most obvious example is of a cure providing a significant improvement in terms of clinical burden for patients, but an increased economic burden through loss of revenue for providers. Payers may remain neutral overall but have a timing issue.

The characteristics of a cell- or gene-based therapy are also fully profiled as part of the cure characterization framework. Durability is considered the length of time the curative effect persists; greater or lesser expected durability dictates whether a short-term or longer-term financing mechanism would be a more appropriate tool. However, in many cases, the durability of a gene therapy at market launch might be unknown. Nearly all approved durable or potentially curative therapies will enter clinical practice with significant uncertainties regarding their durability and performance because the supporting clinical trials were limited to efficacy endpoints with durations of not more than 3 years at launch (7). The relationship between standard clinical endpoints in

therapy areas—for example response rates in oncology—and long-term survival will likely be unknown.

Describing the incremental degree of cure, or an estimate of product’s ability to fulfil current unmet need, as defined by patients, clinicians, regulators and payers, is useful. A curative gene therapy may be completely restorative for a high mortality and morbidity condition with no current treatment alternatives. Where alternative treatments exist, the curative therapy may halt progression but not repair existing damage or the side effects of prior treatments. In lower impact situations, a gene therapy may provide only incremental health impact due to a combination of low inherent morbidity and mortality of the condition, comparable alternative therapies, or low average effectiveness of the curative therapy itself due to high patient response variability. A low-impact cure may remain a viable option for some patients but may be reimbursed differently. Financially for payers, the greater the incremental degree of cure, the more likely that a cost bolus will be created from the confluence of high pricing, a highly prevalent patient population, and rapid adoption.

Figure 1 distinguishes a durable therapy from a non-durable one. Included are two examples, Cerezyme and insulin, which are both replacement products to show good examples of high impact/efficacy products which are NOT durable therapies. While generally effective when used appropriately, these products do not have persistent “curative” benefit beyond treatment. The top right quadrant shows durable/curative therapies that begin to unpack some of the key differentiating features that impact financing solutions such as size of population, uncertainty of efficacy (vertical

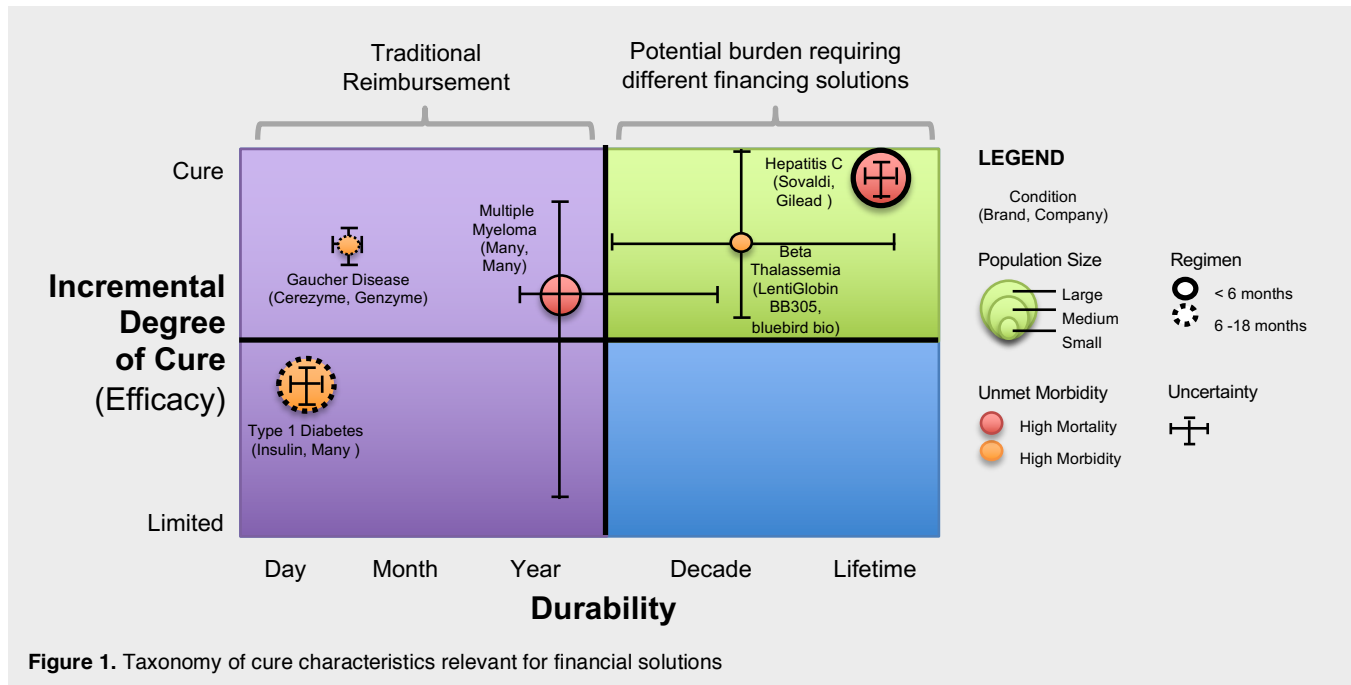
error bars), uncertainty of duration (horizontal error bars), severity of disease (color), etc. The diagram does not yet include the technology type and dosing regimen characteristics.

**Gene therapy archetypes**

Once the FoCUS project began, it became apparent that estimating the scale of the drug development pipeline for these types of therapies would be a crucial component of the cure characterization framework. A project workteam was formed and used citeline’s® Pharmaprojects® database to stochastically predict the future launch activity of products currently under development. Researchers estimated that 39 (+/- 4) gene therapies will be approved by the end of 2022 from the 2017 pipeline of 932 development candidates, including those already approved (9). This would amount to at least 30-40,000 patients per year at the peak but it is very sensitive to whether certain larger indications are included. For example, if there is an expansion into solid tumors, or gene therapies that are pertinent to indications such as cardiovascular disease or Alzheimers’, then the number of patients treated per year could reach the hundreds of thousands. This research alone provides proof of concept that upfront reimbursement for these products means that the total costs could exceed what the healthcare system can manage, and precision financing approaches are required.

The product approvals were divided into four cell and gene therapy archetypes:

1. **Novel breakthroughs:** Treatments for a small disease population (ultra-orphans) with a high unmet need and no alternative therapies, but some



medical standard of care (e.g., Beta-thalassemia) in most, but not all cases.

2. **Orphan disrupters:** Treatments for orphan disease with a population of patients (<200,000 cases per year) that currently have an established treatment pathway (10). Treatment is expected to disrupt the management of the disease as well as current standard-of-care treatments (e.g., hemophilia gene therapies) for a large portion of patients that meet qualification standards. The current SOC will provide financial cost-offsets for durable/curative therapies but do result in different payment timing issues (acute upfront costs with accrued benefits as opposed to pay-as-you-go models).
3. **Oncology products:** Treatments (such as CAR-Ts) for oncology indications with a high incidence and low prevalence.
4. **Quantum leap:** Indications with very large incident and prevalent populations, representing a significant burden in therapeutic areas, such as cardiology, metabolic disorders, neurology and rheumatology.

Within each treatment group, both cures and durable responses can exist. The durability assumption for oncology products was defined as 12- 18 months; for gene therapies, durability was assumed to be at least several years and up to a lifetime. Patient demographics can be a determining factor regarding which payer segments are involved in decisions on financing and reimbursement.

### **Therapy characteristics to further consider**

The distinct characteristics of therapies alter the mix of financing challenges and appropriate solutions. This section describes the key characteristics of the treatment environment that necessitate precision financing solutions. These include differences in the size of the target population, the nature of clinical benefit, therapeutic modality, durability, delivery setting, and degree of cost offsets (7).

- **Size of the target population.**
- **Nature of clinical benefit:** For the eligible population, durable (curative) therapies will vary in their clinical benefit relative to existing standards of care across multiple dimensions, including:
  - **The nature of their expected benefit:** Could range from a “cure” that eliminates all symptoms and modifies all condition processes, to modest reversal or slowdown of selected disease processes over a shorter period of time.
  - **Likelihood and severity of adverse events.**
- **Heterogeneity of patient response:** Disease/treatment combinations differ regarding heterogeneity of response. There will be non-responders, partial responders, and complete responders and they may vary by therapy and may be treated differently from a reimbursement perspective.
- **The clinical benefit compared with alternative treatment options.**
- **Therapeutic modality:** Some durable therapies are oral small molecule medicines such as anti-infectives or injectables such as vaccines. Others employ viral vector delivery of genetic material *in vivo* while still others are similar to advanced transplantation with cellular harvest, *ex vivo* transfection and expansion, followed by cellular re-introduction. Beyond the cost of each modality, therapeutic modality affects the payer benefit classification, provider reimbursement mechanisms, and patient financial participation, which in turn affects the financial challenges these therapies generate.
- **Durability of effect:** Efficacy duration will vary among patients for a single therapy and across therapies in general. Some may experience a lifetime of benefit, but many patients may not. In addition, the full duration of effect for a particular treatment will not be known at the time of initial regulatory approval and launch, due to the urgent need in some cases of getting the treatment to the patients.
  - **Uncertainty based on limited clinical trial data at launch:** Being that most, if not all, of the “cures” coming down the pipeline have limited longitudinal data, it is not known whether the benefits of these “cures” will last for a lifetime or just a few years.
- **Delivery settings:** Durable (curative) treatments vary in where the therapy is administered. Products may be administered within the inpatient or outpatient setting and at a limited number of centers of excellence or a broader set of facilities. Some therapies may require extended hospitalization stays or intensive follow-up, while others may warrant only periodic clinic follow-up. These characteristics not only affect the stakeholders requiring financial solutions but also impact ecosystem-related operational enablers such as appropriate provider networks, certifications, care coordination, product distribution and data monitoring processes to ensure patients have access or financial solutions can be administered or both.

- Offsetting costs and mismatched benefits:** Durable therapies will vary in their net financial impact to the healthcare system, to society and to patients and their caregivers. Some therapies may reduce other healthcare treatment and service spending while also generating higher patient benefit. Other therapies for conditions that generate relatively low costs due to rapid death or absence of treatments for chronic morbidity reduction may increase overall healthcare spending while generating patient benefits. Those benefits may reduce other social program costs and create additional economic benefits. In addition, the timing of financial impact may vary; some treatments could result in immediate healthcare savings, while others could save money over time. These differences in net financial impacts over time generate financial challenges including mismatches among those who pay and those who benefit.

### Considerations for stakeholder segments

There are a number of challenges in ensuring cell and gene therapies are accessible to those in need. Among the most pertinent financial challenges are payment timing/affordability, therapeutic performance risk, and actuarial risk. It is expected that stakeholders across the healthcare system will experience these challenges differently. Proposed financial solutions can be tailored to best meet stakeholder needs, creating ‘precision financing’.

### Patients

Generally, for these treatments the patient will experience a high financial burden due to out-of-pocket costs from co-pays, deductibles, possible loss of income due to treatment, and in some cases travel to care sites. The age of the patient will determine whether and how the income earning members of the household are also affected. However, for some diseases, the costs will be offset by savings from normal treatment regimes (i.e. hemophilia Factor VIII). In some cases, there may be limited providers who are authorized to deliver a particular therapy within the patient’s regional area, which can result in patients seeking out new providers or travelling across state borders in order to access treatment. There is also the potential for payers to restrict access when alternatives are available, even if the alternatives are chronic treatments.

### Providers

Providers, for treatments in some disease areas, may face challenges with redefining their service offering and operations while also facing new financial risks. Services may need to be redefined as cell and gene-based therapies bring new treatment paradigms with them or cause old services to become less common over time (e.g. hemophilia treatment centers (HTCs) will no longer be routinely providing Factor

VIII replacement therapy to all patients but will need to become knowledgeable about giving the one-time therapy). Operation models where there is a reliance on profits from buy and bill processes to defray the cost of providing other services to the patient will need to be modified in the face of a potential loss of that revenue when therapies are transacted directly between the payer and the developer. The high costs of the therapies make it unlikely that payers will be amenable to extending the practice of paying a fixed percentage markup to providers in order to provide them with these operating revenues. Another operational concern is the amount of time it takes for new billing codes to be provided and how providers will be able seek reimbursement during that period. In addition, providers may bear some financial risk, such as gearing up for accreditation in order to deliver new therapies.

### Payers

The challenges for payers vary depending on their size, financial strength and ability to absorb risk and at what level. The demographics of the payer pool and their legal/regulatory restrictions will also impact reimbursement options; for example, Medicare is unlikely to be impacted by treatments for newborns as most patients are over the age of 50. Another consideration is that Medicaid payers will need to follow state regulations, which vary substantially from state to state, and so may not be able to take advantage of ideas like performance-based annuities in the same way as commercial insurers. Payers will want to ensure performance and mitigate payment timing issues. As a group, some payers are very aware and proactive in their coverage decisions regarding cell and gene therapies, whilst others are still in the learning stages (11).

Payer segmentation is one element that drives preferences for financing mechanisms. By defining the likely payers for a treatment, the financial tools available for reimbursement become more apparent. Initially identified payer segments included four broad groups: self-insured employers, commercial health insurers and managed care organizations, Medicare, and Medicaid (12). These groupings can be further differentiated into a multitude of subtypes. A more detailed discussion of payer segmentation can be found in FoCUS Research Brief 2018F202.v014.

### Developers

Payment timing is one of the key considerations for developers. Similar to payers, the varying sizes and financial capacities of developers, in addition to administrative capabilities and preferences, can have different effects on the issues at hand. For example, smaller developers may need outside assistance from financial institutions due to the delay in receiving annuity-based revenues or to guarantee payment of rebates in the case of milestone-based performance

contracts; whereas, larger firms may treat this as an internal issue.

**Financing solutions**

Potential financial solutions by stakeholder were discussed, such as consumer loans for patients, annuities and performance-based payments for providers, risk pools and milestone-based contracts for payers, as well as factoring/hedging for developers. Taken together, the solutions cover a wide-range of possibilities for consideration, not all of which are viable for their target populations.

**Financing solutions for patients**

The key financing challenge for patients is out-of-pocket costs, co-pays and income loss. Few financing solutions can address these concerns: consumer loans or consumer annuities are not ideal given the ethical and legal challenges of both deciding treatment eligibility based on patient demographics or credit history, as well as determining collection methods for treated patients defaulting on agreed-to payments. Compulsory life insurance or insurance against other loss of income could be designed with terminal values in case of unrelated death. However, if a patient changed jobs or insurance plans, this could negate contracts. Other options include ordinary finance tools (personal loans, mortgages, credit cards) or charity. Generally, financing solutions do not specifically target patient challenges, since so much of patient and caregiver financial challenges are based upon indirect or non-medical costs. The implications of financial solutions, such as annuities and milestone-based rebates require further study as to whether they would result in multiple hits to the patient. There is discussion as to whether the patient co-pay would apply only at the time of treatment or be broken down into multiple payments that coincide with the annuity payment. Such an idea is complicated by the annual maximum out of pocket costs calculations. In the case of rebates (failure to meet milestones or performance metrics), current paradigms do not include the patient as a participant.

**Financing solutions for providers**

Most provider-oriented financing solutions are payer financing solutions that also involve providers; such as solutions based on annuities, particularly with performance-based payments. There is a model that sees providers continuing to obtain the therapy directly from the developer, under buy and bill, but without a markup or at a very low percentage one. Assuming a gene therapy is reimbursed under this type of system, providers might face delayed payments for *ex vivo* gene therapy and stem cell transplantation due to delayed payment for the gene therapy *per se*. A key challenge for providers may involve separating therapeutic costs from procedural costs. An additional option for providers is not specifically financing based, but to participate in a new management entity, an orphan

reinsurance and benefit manager (ORBM), which would act as a financier and provide asymmetric payments to providers (13). This entity would operate under the current business model of sharing financial risk with hospital buying groups and developers, while earning a fee for service.

**Financing solutions for payers**

Financing tools for payers were initially aggregated into three categories based on the issues that they address: payment timing; risk allocation and performance reward. Shown below are how each potential financial solution fits into the matrix of solving for one of these issues (Table 1).

Payment Timing	Risk Allocation	Performance
Annuities (Convert 1 payment to stream)	Reinsurance	Rebates • Up front
Factoring (Convert stream to 1 payment)	Risk Pools • Among firms • Public • Public private	• After: population • After: individual  Shared Savings
Balloon (Delay payment)	Securitization (Tranche the risk)	Formulary / UM Preference*
	Care Carve-Out	Bonus • Outcomes • Adherence

**Table 1.** Possible financing tools to utilize in the FoCUS project

Of these, tools being considered by the project to solve specific payer needs include the following, performance-based annuities, milestone-based contracts and risk pools. Payer tools will continue to be refined as the FoCUS project moves forward and additional financing schemes become apparent.

- **Milestone-based contracts** occur when a payer provides compensation at the time of delivery to the developer of a therapy with an understanding that should specific patient recovery milestones not be met, a rebate for that payment would be forthcoming.
- **Annuity with performance-based components** would spread costs over a fixed time and share risk between payers and developers. In this case, payments would be made as pre-agreed performance metrics are met
- **Multi-payer risk pools** would have payers combining together to provide coverage for the orphan and ultra-orphan diseases. This could be done as state-sponsored Medicaid pools, or via commercial elements such as has been proposed by the ORBM discussed earlier.

In addition to the financing tools, tracking and metrics are considered to be essential administrative needs that must be



met in order to manage these financial approaches. Tracking of patient outcomes to ensure either agreed performance metrics or milestones have been reached may include utilizing real world evidence (RWE). If a patient moves from one payer to another after receiving a high cost therapy, a tracking mechanism to follow the patient needs to be in place. It is thought that data from claims, medical records, registries, PROs, and monitors/wearables could be used to provide real world evidence. The availability of this data will help inform decisions on appropriate payer financing tools.

**Financing solutions for developers**

Financing solutions for developers were initially linked to annuities and/or performance-based risk-sharing. These are significant changes from existing payment models (i.e., simple up-front payments) and could mean developers face delayed payments or, depending on the durability of their product’s benefit, reduced or no payments. It is possible that performance-based agreements could prove a deterrent to further investment in curative gene therapies. Relatively simple factoring and/or hedging instruments have been proposed as a solution to manage risk for developers. In addition, there are financial services that will buy a package of accounts receivable, thus solving cash-flow burdens, but lessening compensation.

**Bringing it all together: Financing Decision Framework**

For each treatment, the FoCUS process involves understanding the cure characteristics, demographics of affected populations and payer segment(s) to allow for systematic consideration of the most appropriate financing tools to apply to a treatment (Figure 2). Payer segments will consider each of the issues shown here. What is their appetite for actuarial risk? Is their covered lives pool large enough to make the payment of a high cost therapy affordable for them as an insurer? Will there be savings from cost offsets of chronic treatments the patient will no longer need? Will the payment be direct to the developer or is there a provider in

the payment structure? If the provider, what might the terms be for buy and bill? Or should we reimburse the services and purchase the therapy directly from the developer? From a timing perspective, will the payment be all upfront with rebates for non-performance or can the payments be spread out over time through the use of an annuity? Who is bearing the performance risk? Note that the appropriate financing tool may differ by payer type when considering the financial impacts of the same therapy.

**INITIAL PRESSURE TESTING OF FINANCIAL TOOLS**

**Case study: CAR-T therapy**

A key aspect of the FoCUS project is the pressure testing of financial tools by teams; this process allows for refinements in the toolkit informed by modelling and simulation where appropriate. Using the pressure testing process, a synthetic case study of a CAR-T treatment was created and analyzed by the Oncology TAG. It is likely that the largest number of cell and gene therapy approvals will be oncology products. After defining the product’s impact through the cure characterization framework, four financial system scenarios (FSS) were proposed: business as usual, a milestone-based contract, performance-based annuity, and risk pooling. Further analysis by the FoCUS team established the following:

- Business as usual.
- Milestone-based contracts extending to 12- or 18 months represented the most feasible primary financial tool for oncology treatments. This type of FSS addressed basic performance risk.
- Multi-year performance-based annuities would be useful if the therapy valuation included longer-term durability, for which payers desired a warranty. This type of FSS would extend over 3–5 years with either rebates or contingent payments to address performance risk and payment timing/affordability issues.

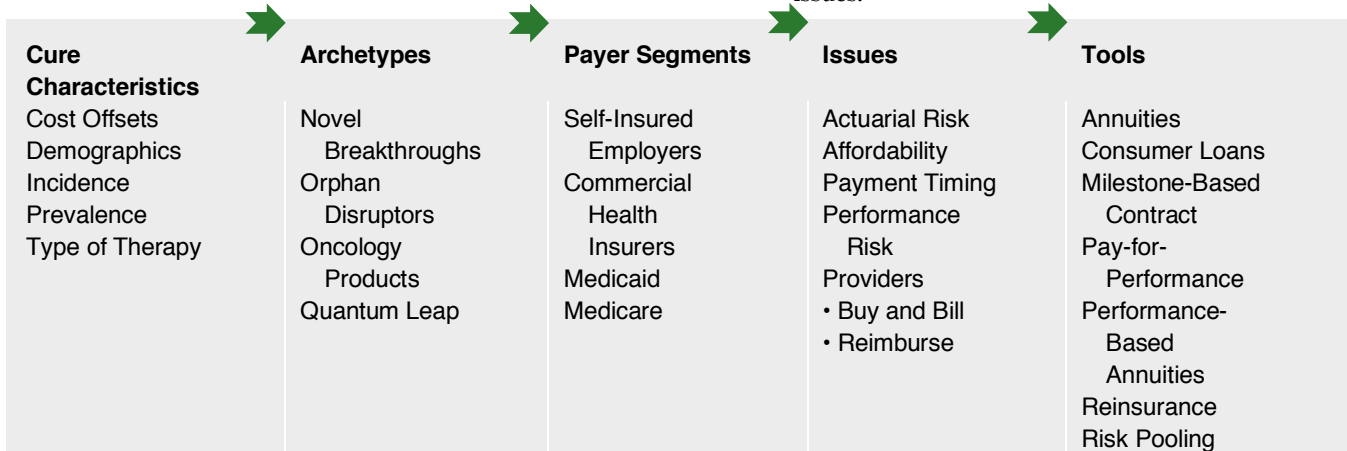


Figure 2. Flow chart for the decision framework

- Although implementing pooling can help address actuarial risk, it was considered too complex to initiate on a small scale, particularly given the expectation that reinsurance and stop-loss providers could likely change their products over time to include CAR-T treatments.

The Oncology TAG is continuing to work through these proposed FSS with an aim to deliver more precise solutions that include mock contracts and a potential model for building centers of excellence to deliver CAR-T therapies.

### Case study: Gene therapy for hemophilia A

An effective gene therapy for hemophilia A would represent an orphan disrupter archetype—a “cure” for a chronic condition, with high potential cost offsets. Patients with hemophilia A are currently treated with factor replacement products, which are generally effective, safe and expensive. In the US, most patients (90%) are treated at Hemophilia Treatment Centers (HTCs), which provide comprehensive support for hemophilia and other blood disorders. A cure for hemophilia A comes with high potential cost offsets based on avoiding FVIII therapy and administration costs.

Based on this scenario, four FSS were reviewed as part of the pressure testing process: proceed with the current financing mechanisms (the “business as usual” approach); a 1-year milestone-based payment; a 5-year performance-based annuity; and risk pools with performance-based contracts. The ‘business as usual’ solution and a 1-year milestone-based payment were deemed the most feasible, with the performance-based annuity also being an option if patient mobility, patient data collection and policy issues could be overcome. The dedicated risk pooling FSS was deemed unlikely.

Further pressure testing of 1-year milestone-based contracts and 3–5-year performance-based annuities for gene therapies of blood disorders more broadly is currently ongoing, with a full analysis of results expected to be published in 2018.

### CONCLUSIONS

Gene therapies have the potential to transform patients’ lives. Like other medical treatments, some patients may not respond, while others may experience an initial response that does not prove durable. Some conditions may be so complex that complete molecular or cellular therapeutic success may only resolve a portion of the etiology and symptoms.

Thus far, research results have shown that there is no single, system-changing, gene therapy product likely to launch in the next few years. As such, stakeholders may not yet be motivated to move away from product-by-product, individual payer negotiated financial arrangements. However, the combined portfolio of gene therapies likely to emerge over

the next several years may dictate a shift towards innovative reimbursement methods that can accommodate the acute cost of these therapies.

The FoCUS project is examining issues that relate to the launch of cell and gene therapies. Case studies have helped identify key issues and have led to discussions of financial solutions that might help mitigate these issues for stakeholders. Preferred financial solutions vary depending on specific case factors, including cure characteristics, treatment archetypes and the nature of the most relevant payers (“precision financing”). Most solutions relate to issues that arise between payers, developers and sometimes providers, with the need for performance-related payments at times that are relevant to risk resolution being common. Relatively few financing solutions arose specifically to address out-of-pocket costs or lost income for patients and caregivers.

Updates on the FoCUS project financing solutions and further research initiatives to support these solutions are published as Research Briefs on the FoCUS project website: <https://newdigs.mit.edu>.

### Upcoming

Challenges that have emerged and will continue to be evaluated by the FoCUS team, with the aim of delivering precise financial approaches to meet the needs of stakeholders include:

- Treatment outcomes tracking: For any performance-based contract to be implemented, a consistent and reliable means of tracking treatment outcomes must be established
- Patient mobility: Patients moving between insurance policies and providers create a challenge to implementing multi-year, performance-based contracts
- Medicaid/Medicare: There are policy hurdles that need to be overcome to include federally and state funded payers in performance-based agreements or risk pools
- Reinsurance/stop-loss insurance: The timing of this type of insurance and terms of coverage does not easily translate into use alongside performance-based agreements
- Actuarial risk: the assessment of risk to payers (especially smaller ones) in this arena requires more study and needs careful consideration.

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<sup>i</sup> See <http://newdigs.mit.edu> for further details