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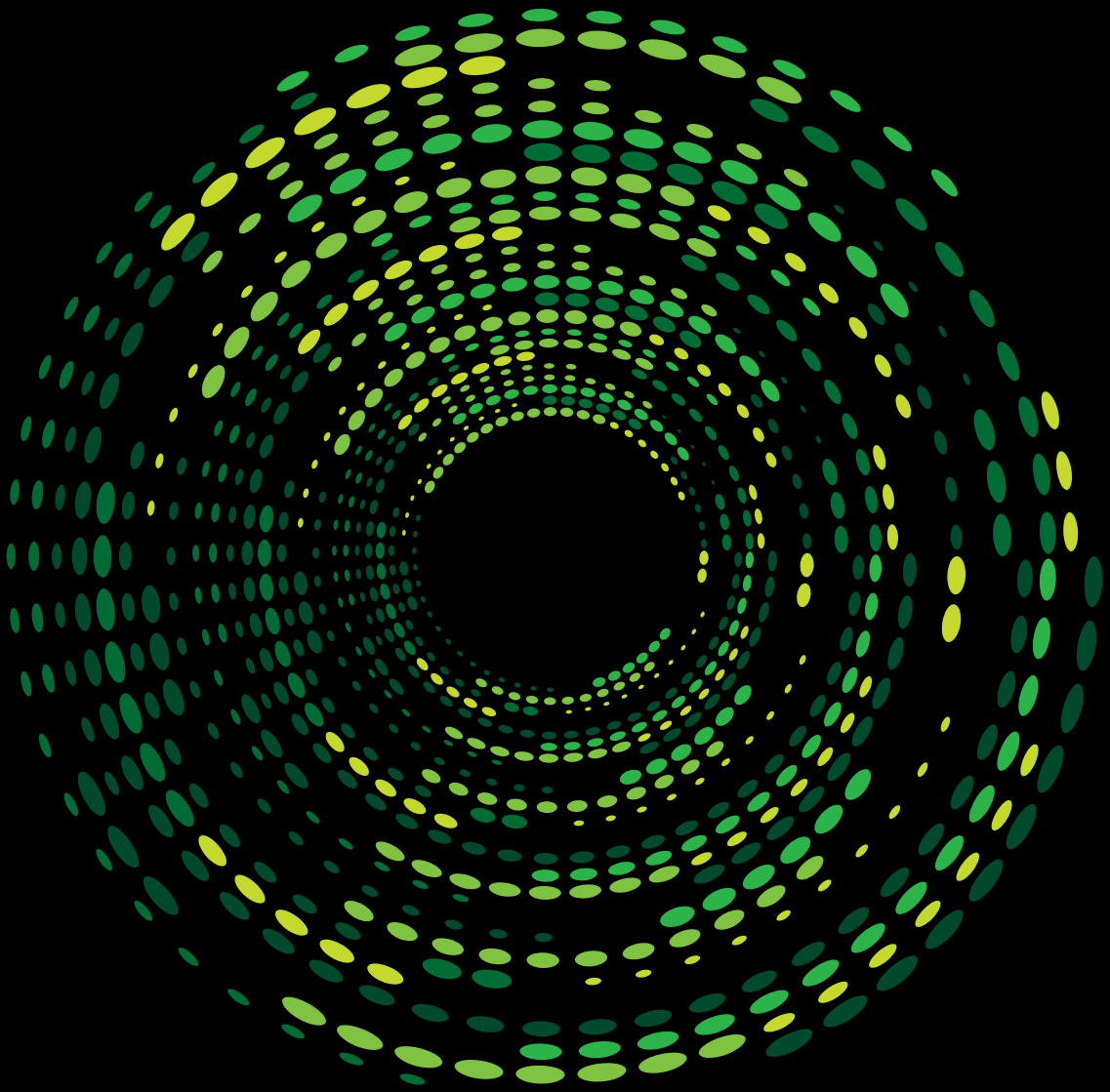


Commercializing Cures

Challenges and implications for biopharmaceutical companies

Introduction

The traditional biopharma business model is being disrupted by biopharma companies ushering potentially curative treatments to market. However, these companies will need to navigate an outdated reimbursement model and challenge traditional commercialization approaches to succeed in the market.

In the US market, even the most cost-effective cures can face significant challenges from the health insurers that must bear the upfront treatment costs. Due to the nature of the commercial insurance market, a health plan that pays for an expensive therapy might never reap the long-term benefits of a member's improved health. Consider recently developed drugs that cure chronic Hepatitis C. Due to the short-term budget impact, these drugs faced intense pricing scrutiny and payer pushback when they were introduced.[1,2] In response, the drug manufacturers had to offer substantial discounts to private payers.

In the context of cures for rare diseases, high prices are often needed to recoup substantial research and development (R&D) investments. Case in point: uniQure NV recently removed the world's first commercially available gene therapy, Glybera,[3,4] from the market. Despite its ability to cure a rare blood disorder, the therapy was unable to achieve commercial success due to a $1 million price tag and a tiny pool of potential patients.

What is a "Cure"?

A cure is more than something that eliminates or provides relief from a disease. For the purpose of this paper, we use the following definition of a cure:

- There must be a **drug product** involved in the treatment of the condition (e.g., as opposed to an exclusively surgical procedure)
- The drug will serve to **stop progression, reverse, or eliminate a disease** (as opposed to a treatment that manages a disease and associated symptoms but does not eliminate the underlying medical condition)
- After a one-time course of therapy with the drug, there should be **no need for follow-up therapy** relating specifically to the disease or condition targeted by the cure

Four key commercialization challenges for curative therapies

This paper describes four key challenges manufacturers might face when commercializing curative therapies. Two of these challenges are broadly applicable to all types of cures. The other two are specific to gene and cell therapies, which are expected to play an increasingly important role in delivering curative treatments to the market.* We also examine how bringing curative therapies to market differs from strategies for more traditional biopharma drugs.

Challenge #1: Sticker shock, budget impact, and outdated payment models

Curative therapies represent immense value to patients. In many cases, they might also generate value for the health care system, and to society in general, due to avoided costs, better outcomes, and an improved quality of life for the patient. However, even cures with demonstrable cost effectiveness can face challenges if it takes too long for health plans to recoup their costs. Potential barriers to commercial success include:

High short-term costs: The price tag attached to some curative treatments could create public relations issues. ***Case in point:*** Sovaldi, Gilead Sciences, Inc.'s cure for Hepatitis C., offered a strong economic value story based on avoided long-term costs (e.g., liver cancer, transplant). However, outrage over the $1,000-per-pill cost of the treatment fuelled significant negative press coverage, led to congressional hearings, and gave payers leverage to push back on the price.[1,2] Future curative treatments could be even more expensive, and could face similar barriers. For example, new CAR-T therapies are projected to have prices as much as $700K that could be justified by cost effectiveness analysis.[5]

Budget strain: Curative treatments could strain payer budgets in the short term as the new therapy becomes available to previously untreated and chronically treated patients. This could be particularly challenging for diseases with large prevalent populations. Ineffective treatment options for Hepatitis C, for example, left a large patient population with unmet needs. While treatment costs were relatively low compared to other specialty drugs, the curative treatments for Hepatitis C, introduced by Gilead and AbbVie, Inc., created a significant and unplanned budget impact on payers as patients sought treatment.[1,2] This challenge will likely be repeated as new—and expensive—curative treatments become available. For example, gene therapies that can halt the progression of Alzheimer's disease are in pre-clinical research and early-stage clinical trials.

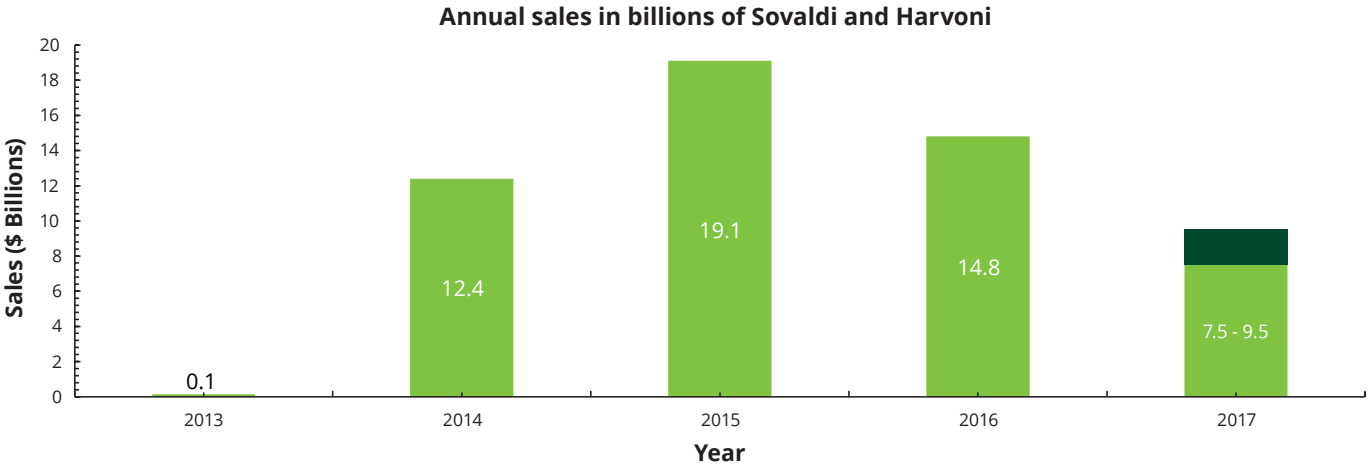
Outdated payment models: The existing payment model for pharmaceutical treatments—where cost is incurred when treatment is administered—does not generally work well for cures that generate value through long-term avoided costs. Given that patients tend to switch insurance carriers every few years, payers might never reap cost savings from costly curative treatments. As more cures reach the market, pressure to design and experiment with alternative funding models (e.g., performance-based annuity payments, value-based contracts) will likely increase. ***Case in point:*** Spark Therapeutics, Inc. is on track to launch voretigene neparvovec—the first approved gene therapy in the United States, which could cure an inherited form of blindness with a single treatment. Analysts estimate treatment could cost $500,000 per eye. The company is said to be considering an amortized payment plan in which a health plan could make a down payment followed by annual instalments if the therapy succeeds.[6]

* As of November 2016, there were more than 150 life sciences companies originating trials in gene and cell therapies. It is premature to assume that all of these will be curative, but it is conceivable that a significant share will be.

Challenge #2: Atypical demand and impact on capability requirements

A typical biopharma forecast model might assume strong growth from launch to peak sales after five years on the market. This would usually be followed by modest but steady growth through loss of exclusivity (LOE). Curative therapies, by contrast, might initially have large pools of eligible patients. However, most sales could be in the rearview mirror after five years. Sales of Gilead's two Hepatitis C products, Sovaldi and Harvoni, fell substantially between 2015 and 2017 (Figure 1).[7,8]

Figure 1



*Notes: Sovaldi Launch December 2013, Harvoni Launch October 2014; 2017 sales value based on Gilead's projection

Challenge #3: Complex administration and management

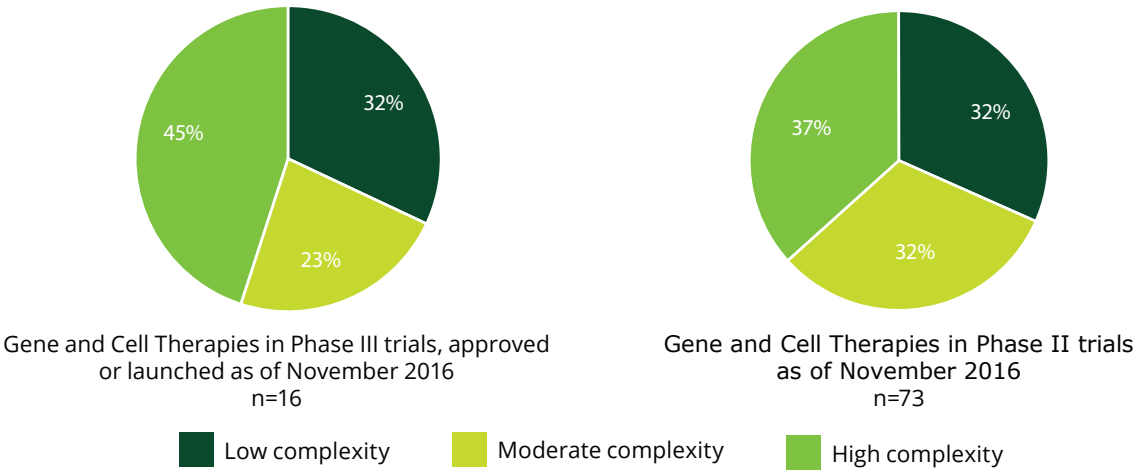
Gene and cell-based therapies will likely represent an important segment of future curative treatments, but these entail additional commercialization challenges that extend beyond cost and payment models.

One challenge stems from complex administration protocols and clinical-care requirements. Higher complexity therapies might be more difficult to commercialize because they can require highly specialized resources and constrained medical capacity both to deliver the therapies and to manage their side effects post-administration. Such therapies also could require further medical education to ensure high quality of delivery. A potentially smaller universe of centers administering treatment, combined with a greater need for health care provider (HCP) education, suggests that the traditional biopharma field sales model may need to be adapted.

Consider this: CAR-T treatment is a process in which a patient's own T cells are extracted, cryopreserved, transported, and modified. Patients undergo preparation for the infusion (e.g., chemotherapy), and after the infusion they must be monitored closely for side effects. A common side effect of this treatment is cytokine release syndrome (CRS), which can be life threatening and complex to treat. Similarly, a treatment in development to cure Parkinson's disease requires intracranial administration, using an MRI to guide the injection. As a result, CAR-T, and similarly complex treatments, will require providers to have sophisticated capabilities. In addition, manufacturers will likely need to work within a more elaborate ecosystem of stakeholders that are involved in the treatment process.

To provide some perspective on this challenge, we have analyzed the overall gene and cell therapy pipeline (not limited to cures) to assess the complexity associated with how these treatments are administered. This analysis finds that, as of November 2016, about 40 percent of gene and cell therapies in phase II and close to half of those in Phase III have highly complex methods of administration (Figure 2).[9]

Figure 2



Challenge #4: High cost and complexity to manufacture and distribute

Complex cures are challenging and costly to manufacture[10,11] due to the lack of commercial scale of the technologies involved in producing them. Careful planning is required to determine which centers will be positioned to deliver these therapies, how this aligns with the manufacturing footprint, and how patients are to be scheduled for therapy to maximize the manufacturing capacity. Likewise, some patients will have to travel long distances to receive the therapy, which adds complexity and risks in the supply chain.

Highly personalized treatments, such as CAR-T, could be produced in large, centralized facilities, which could exacerbate logistical challenges (e.g., transport, handling). Given this, CAR-T cell manufacturing is projected to cost between $25,000 and $35,000 per patient, even after maximum process efficiencies have been exploited.[12] This does not factor in the cost of cryopreserving the cells, nor does it include all of the other costs associated with CAR-T treatment (e.g., pre-infusion treatment, administration and follow-up care).

First-generation personalized cancer vaccine therapies for prostate cancer illustrate the potential consequences of not adequately addressing these manufacturing challenges. At launch, these products were unable to meet robust initial demand because manufacturing capacity was still coming online.[13] They also were reported to have initial cost of goods sold (COGS) over 75 percent.[14] Though investments to automate and cut costs were able to bring COGS down over time, this undermined their commercial viability.

Given the potential demand pattern for curative therapies, it will be critical to ensure that capacity can economically meet peak demand. This requires understanding the geographic nature of demand and its implications for the supply chain and manufacturing footprint, capacity planning and financial risk management.

Implications for commercialization of cures

So far, success has been elusive

Few cures have come to the market—particularly highly complex ones—and there is little precedent to help understand how to commercialize them successfully. As previously mentioned, UniQure's Glybera was the first commercially-approved gene therapy.[15] A lack of demand, however, recently prompted the company to stop commercializing the product.[4] It was developed to cure lipoprotein lipase deficiency, a very rare disease. But administrative complexities—combined with reimbursement challenges for a therapy with an estimated $1 million price tag—limited its access to only one patient in its first years.[16]

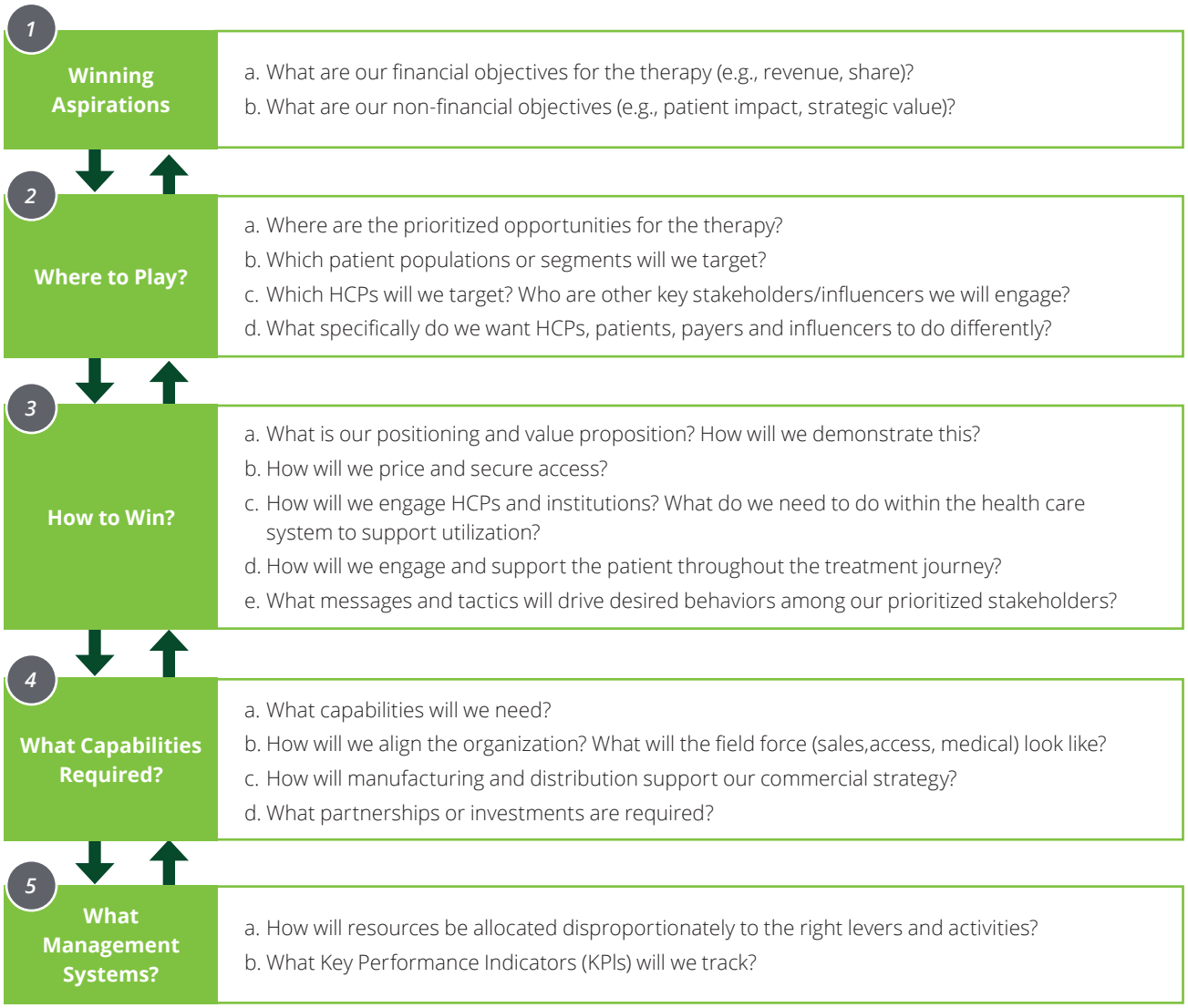
The four major challenges identified demonstrate the need for biopharmaceutical executives to adapt their strategic toolkits. Key areas of difference versus traditional pharmaceutical launches include:

- The nature of the business opportunity and how to drive uptake
- The realities of gaining coverage, reimbursement, and the financing of cures
- The capabilities required to go to market and manufacture/supply the products

Key choices for commercialization teams:

As commercialization teams prepare to bring curative treatments to market, they will need to consider how the challenges above impact the strategic choices they will make for launch. These choices are illustrated in Figure 3, based on Deloitte's Strategic Choice Cascade framework.[17]

Figure 3



The table below highlights some of the choices that are most important for the commercialization of cures.

Key Choices	Strategic Imperatives & Actions
Which patient populations or segments will we target?	Define prioritization and sequencing of patient targets that maximizes the commercial opportunity
	Critical actions for success: • For conditions with sizeable prevalent populations, there will likely be urgency to drive rapid and broad uptake to capitalize on the commercial opportunity before the pool of patients is depleted by competitors • For incidence-driven conditions, it might be more important to tightly control customer/patient experience (arguing for slower ramp to peak), or to define a narrow initial target population (e.g., where value proposition is strongest to support pricing) that is expanded over time
Which stakeholders will we target? **How will we engage HCPs and institutions?**	Engage health care ecosystem to drive demand and enable treatment
	Critical actions for success: • Understand the provider landscape for the disease and determine the network of treatment centers with required capabilities to deliver the therapy (for high-complexity cures) – Consider how treatment might align with provider business models and incentives (both financial and strategic) • Map referral patterns and key stakeholders involved in the treatment pathway. Define how to create a link between the community specialists that will refer patients for treatment, and the centers that will take the patients and deliver treatment • Understand potential drivers and barriers of uptake for each key stakeholder along the treatment process such as: – Provider capacity limitations – Provider education needs around complex treatment protocols and adverse event management – Impact of treatment on provider economics – Patient logistics and costs associated with treatment • Identify the customer model that is required to serve the market successfully, both driving demand generation and building referral pathways, as well as around the delivery of the therapy and post-therapy – Seek to innovate around the type of solutions and pain points that are addressed along the patient journey, and identify opportunities to deliver a differentiated customer experience

Key Choices	Strategic Imperatives & Actions
What is our value proposition? **How will we price and secure access?**	Build the access foundation that will ensure appropriate coverage and reimbursement for a cure
	Critical actions for success: • Focus on understanding the burden of disease and drivers of clinical and economic value for the therapy. This data foundation is critical to drive discussions about the therapy's value proposition • Seek to maximize the strength of the value proposition through the development cycle, privileging potential label options that provide the strongest value proposition and differentiation from the standard of care. • Engage payers and other stakeholders in a dialogue around this value, and identify data needed to demonstrate it • Evaluate opportunities to use or pilot alternative payment models that align payment with value (e.g., outcomes-based contracts or payment plans that allow payers to amortize the cost of cures) • Develop a long-term registry/real-world evidence strategy that is consistent with the collection of outcomes data and supports the implementation of novel payment mechanisms[18]
What capabilities are required?	Create a virtual, lean organization that is able to rapidly scale capacity for the therapy, especially for high-prevalence/low-incidence indications
	Customer engagement & field force: • Leverage digital technologies to more efficiently engage patients, caregivers and HCPs across the treatment journey • For complex therapies, give careful thought to the field resource mix, including whether a traditional sales force is needed, the relative mix versus medical field roles, and whether new roles need to be defined to support adoption • Consider the "rent vs. own" tradeoffs for commercial capabilities (including sales force) given the expected demand pattern **Supply chain and manufacturing:** • Create a manufacturing and scheduling system that maximizes assets • Assess the opportunity to identify and feed new patient pools into the treatment system in order to help drive capacity utilization • Assess how the network of sites of care, and their capacity, will match the manufacturing capacity installed, and the supply chain constraints related to those • Review the build vs. outsource decisions for the manufacturing assets, and potential role of partnerships, given the need for flexibility and the uncertainties on the demand for the product

Conclusion

Advances in the understanding of disease biology—combined with the development of new treatment modalities, including gene therapy—are paving the way for biopharma manufacturers to develop cures for diseases and conditions that were previously only managed. The payment model needed to finance the development of these innovations, however, has generally not kept pace with the biopharma industry. Developing and manufacturing cures and treatments for complex diseases can be a daunting and costly process, due to a lack of commercial scale and the potenially novel technologies involved in producing them.

This paradigm shift—from managing a disease to curing it—involves a distinct set of challenges related to pricing and market access, biopharma resourcing models, and (for complex treatments) the health care delivery system and manufacturing/supply chain.

In the world of curative treatments, cautionary tales continue to outnumber success stories. Before this narrative can change, biopharma companies might need to reimagine their organizations and lead payment-model innovation that rewards effective and cost-efficient cures.

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