January 26, 2019

PharmExec.com
COMMERCIAL INSIGHTS FOR THE C-SUITE

Precision Financing of Durable, Potentially Curative Therapies

Jan 27, 2019

By Jane Barlow, Russell Teagarden, Mark Trusheim

Gene therapy financial challenges

Gene therapies and cellular treatments create multiple financial challenges for US healthcare payers beyond price. The work of the multi-stakeholder Financing and reimbursement of Cures in the US (FoCUS) consortium suggests that payer type affects the manner and severity of these challenges, which in turn makes a single financial solution unlikely. Rather, FoCUS participants suggest that US payers require a precision financing toolset customizable for each payer's needs, for each durable therapy's characteristics and in the context of the growing portfolio of such treatments.

Durable and potentially curative gene therapies and cellular treatments are being developed for conditions ranging from blindness to blood disorders, such as hemophilia and sickle cell disease, to cancer. They may provide years of benefit from a short treatment such as single injection of a viral vector vehicle or a process over several months to harvest, transform and re-infuse a patient's cells. While a boon for patients, this could prove a financial bane for payers. Usually patients take, and payers reimburse, medications over time which matches years of benefits with years of payments. Gene therapies condense all those payments into a single, much larger, upfront payment at the time of treatment. The MIT NEWDIGS (New Drug Development ParadIGMS) Consortium launched the FoCUS Project in 2016 to design and pilot alternative financing approaches to address the three financial challenges these new durable, potentially curative, therapies exacerbate:

1. **Payment timing** transformation from chronic drug payments to larger single period payment creating a mismatch of payment and benefits received.
2. **Performance uncertainty** regarding the efficacy level and durability of the therapeutic benefit.
3. **Actuarial uncertainty** concerning the unpredictable number of patients to receive the treatment, especially since many of these new therapies treat rarer, even orphan, conditions.

The payer type, the size of the target patient population and patient backlog can have an impact on the ability of a specific precision financing approach to address these challenges. US healthcare payers are diverse. Some are privately funded and some publicly. Some are national while others are regional. Some self-insured employers cover fewer than 1,000 people. Traditional health plans may cover hundreds of thousands to millions while Federal Medicare fee-for-service beneficiaries number about 40 million. Additional issues impacting this assessment, and discussed throughout the Design Labs[i], include stop loss and reinsurance options, and patient mobility challenges generated when a patient switches payers after receiving a treatment that has high upfront cost with the accrual of benefits over time. FoCUS participants recognize the importance of these issues and note that they will be discussed further in a separate publication.

FoCUS hosted a series of Design Labs from 2016 through 2018 to elucidate and pressure test potential solutions to financial challenges across a range of conditions with candidate gene therapies in development such as AAV delivered hemophilia therapies, AAV and Lentiviral delivered gene therapies for ultra-orphan childhood genetic conditions and cellular CAR-T therapies for hematological cancers. These therapies, while potentially transformative from a clinical perspective, could face patient access barriers without new financial models. Multiple other groups—including those sponsored by the Duke Margolis Center for Health Policy, NEHI, American Society for Gene and Cell Therapy—and the Centers for Medicare and Medicaid Services are also exploring aspects of this broad set of issues.[1],[2],[3],[4],[5] FoCUS has been unique in concentrating on the financial challenges AFTER the price has been negotiated, distinguishing the challenges facing each participating stakeholder (from patient to payer, provider to developer and policy maker), and designing solutions that satisfy the core needs of each stakeholder while navigating the many policy and operational challenges.

Two precision financing models

The FoCUS group has emphasized two alternative financing models that payers, developers and providers can implement directly:

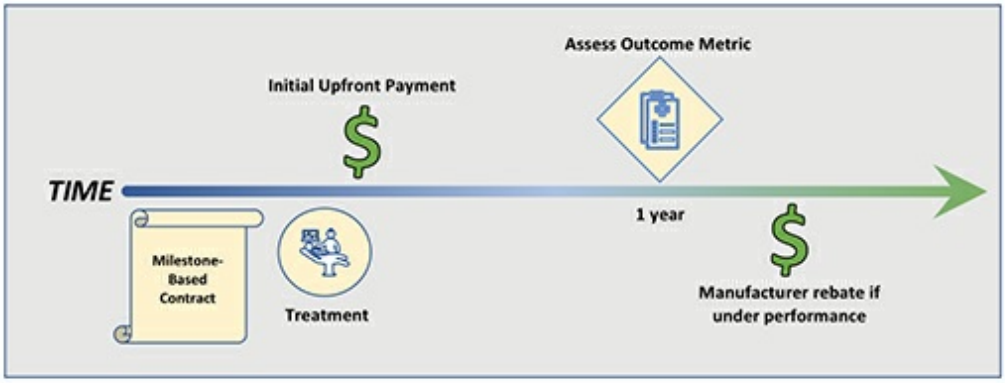
- One-year, milestone-based contracts which are simpler to implement and mitigate short-term performance uncertainty.
- Multi-year performance-based annuities which address longer-term performance risk, payment timing and, to some extent, actuarial risk.

FoCUS designed a third precision financing solution, the Orphan Reinsurer and Benefit Manager (ORBM), which carves-out small population gene therapies to an intermediary which combines aspects of contracting, care management and reinsurance with a patient tracking infrastructure to implement performance-based agreements. Here, we emphasize the milestone-based contract and performance-based annuity solutions. For a deeper description of the ORBM concept see the ORBM Research Brief and article.

The one-year milestone-based contract

The One-Year, Milestone-Based solution (Figure 1) addresses the short-term performance risk uncertainty associated with a durable / potentially curative therapy. As the name implies, it does not materially address the multi-year benefit accrual to upfront payment timing mismatch. Neither does it address therapeutic durability risk past the first year nor the actuarial risks of patient backlog surge or rare event cost smoothing. It is, however, the simplest performance-based approach to implement and does provide risk sharing for therapies such as CAR-T cellular therapy for cancer which has significant immediate manufacturing and 30-day cellular infusion success risk and substantial one-year morbidity risk.

Figure 1: Activity Flow – One-Year, Milestone-Based Performance Contract



This model begins with a performance contract in which an up-front payment of 100% of the agreed price of the product occurs between the relevant parties at time of patient treatment. This could be a transaction between a provider (hospital or physician office) and the developer or between the payer and a developer, specialty pharmacy or wholesaler depending on the care setting and the medicine distribution model. The developer then offers outcomes-based performance rebates to the payer in the event of therapy under-performance. Achievement of the agreed upon outcomes triggers no rebate.

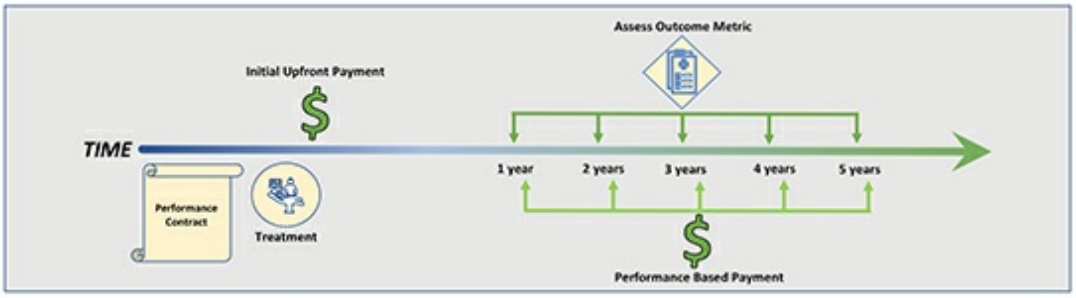
The multi-year performance-based annuity

The mismatch between the upfront cost of a durable/potentially curative therapy and the multi-year benefits from that therapy underlies many of the financial challenges these therapies generate compared to traditional medicines for chronic conditions that are taken repeatedly over time. The solution of performance-based annuities directly, albeit imperfectly, addresses that mismatch by spreading the payments over time, along with providing a hedge against the uncertainty of a therapy's efficacy over time. It also provides some actuarial risk mitigation by spreading the upfront cost over time, if the payments are structured as contingent payments rather than non-performance rebates.

The performance-based annuity solution contains a core transaction between the payer and developer. In this example, an up-front payment of some portion of the product cost is made,

as well as a commitment to further value exchanges with the developer every year (for five years in the Figure 2 example), triggered by outcomes measures. Those future value exchanges are structured as deferred payments to the developer from the payer and only paid if the outcome threshold is achieved. Agreed-upon sources of data and methods for calculating this outcome must also be set up at the time of contracting.

Figure 2: Performance-based Annuity: Payer to Developer Structure



Implementation hurdles

Both precision financing solutions face operational and regulatory challenges. Tracking patient outcomes is difficult: providers may not collect the needed outcome in regular practice, patients may change doctors, states or plans and patient privacy laws may hinder sharing the outcomes once collected. Initial arrangements such as that among Spark Therapeutics, and Harvard Pilgrim with a 30 month outcomes-based rebate for LUXTURNA™, a gene therapy for blindness, demonstrate that these hurdles can be mitigated to the satisfaction of the contracting participants.[6] The FDA guidance that require developers to follow all their gene therapy product recipients for 5 to 15 years is helping to align all stakeholders to obtain the needed information.

Payer segmentation driven by funding source and regulatory framework

Payers in the U.S. represent a multitude of organizations and individuals, further composed of constituents with pluralities in purposes, processes, and preferences. Therefore, FoCUS seeks solutions—not just *a* solution— that will resonate with the precision needed to address specific types of payers in the U.S.

Despite this diversity, payers may be grouped into segments that aggregate commonalities among how they may experience the durable therapy financial challenges as well as the applicable tools for creating precision financing solutions to address them. The source of the funds for paying the medical costs and the regulatory framework proved a critical selection criteria for the financing tools. The methodology is described in Supplemental Materials.

As summarized in Table 1, payers were segmented into four categories – Risk bearing employers, Insurers and Managed Care Organizations (MCOs), Medicare and government stewarded health systems, and Medicaid with over 20 sub-types in total.

1. **Risk bearing employers** provide health benefits to retain employees, fund those benefits directly from their operating budgets and via ERISA or federal regulation are enabled to pay those costs directly as they are incurred. This includes state and federal employee plans.
2. **Insurers/MCOs** are funded via premiums and are regulated as health insurers.
3. **Medicare and government stewarded health systems** are funded by the government, usually the Federal government, to provide health care to designated populations such as the elderly, veterans (Veterans Health Administration), native Americans (Indian Health Service), the incarcerated, and the disabled. The government often directly manages the provider networks or may contract with MCOs to do so.
4. **Medicaid**, which also includes the CHIP program, serves low income people. The programs are jointly funded by the US federal and state governments. Each state manages its programs under specific Medicaid and CHIP statutory and regulatory authority with some states contracting with MCOs to operate 'managed Medicaid' systems.

Pharmacy benefit managers (PBMs), specialty pharmacies, compounding pharmacies, hospital pharmacies and drug wholesalers have been excluded, even though they often perform critical functions beyond distribution such as contracting, utilization management and quality assurance. They generally do not assume specialty drug cost risk and therefore were not included as payers for durable gene and cell therapies. Similarly, hospital and consumer pharmacies are excluded, as are the advisory groups such as actuarial and benefits management firms.

The membership of each segment, its position in the financial flow, the financial challenges durable therapies present to the segment and the fit of the precision financing approaches are now described in greater detail.

Table 1: Payer Segment Summary

Risk Bearing Employers	Insurers / MCOs	Medicare & Gov't Stewarded	Medicaid
Self-insured employers	Commercial group plans	Fee-for-Service	State Administered Medicaid
Federal employee health plan	Individual market plans	Medicare Advantage	Medicaid Managed Care Organization (MCO)
Department of Defense	Provider-based plans	Part D prescription program	Children's Health Insurance Program (CHIP)
State and local government employee health plans	Affordable Care Act marketplace plans	Medicare disability	
Union / retirement health systems	National Insurers (for profit & non-profit)	Indian Health Service (tribal 638 programs and clinics)	
	Regional & single state insurers (for profit & non-profit)	Federal Bureau of Prisons healthcare	
	Workers Compensation insurance (NA)	State correctional health care systems	
	Medical cost sharing plans/ministries	Veterans Health Administration	

Risk-bearing employers

Employer-sponsored health care coverage began in a significant way in the early 1940s after the War Labor Board in 1943 made it allowable for public and private organizations to carve out contributions to health insurance and pensions from the wage freezes in place at the time.[7] In recent years, many employers moved from covering employee health care through insurers to become self-insured, i.e., paying health care bills directly. Now self-insured employer plans account for approximately 60% of private employer covered employees in the U.S.[8]

In addition to self-insured private employers, FoCUS participants also include federal, state and local government employee plans plus union administered plans (United Auto Workers) and retirement systems in this segment. These plans all utilize healthcare benefits to recruit, retain and reward employees. Government and union plans, however, may be subject to laws and regulations, and to political and social pressures that constrain them more than other self-insured organizations. They are similar enough to self-insured businesses, however, that FoCUS participants could expect that they would react the same way to some financing mechanisms.

Self-insured employers and these related organizations do not generally have the scale to directly contract provider networks, negotiate drug prices, or adjudicate billing and payment. They rely on third party administrators (TPAs) or administrative service organizations (ASO) which are often divisions of commercial health plans or stand-alone entities such as PBMs. Self-insured employers and related organizations thus share potential constraints in the financing methods they can use to those that their TPAs and ASOs can adjudicate for them.

Most private self-insured employers use stop loss insurance to limit their exposure to the actuarial risk of unexpected high cost events such as premature births and organ transplants. Such arrangements would also mitigate durable therapy costs, assuming their coverage is not excluded by the stop-loss insurer or by direction of the employer.

Risk bearing employers using stop loss policies are reasonably insulated in the short term from the actuarial risk of unexpected, often rare, high cost events triggering gene therapies. In the medium and longer term, stop loss premiums may rise as more therapies are approved, but the stop loss mechanism for pooling the risk and expense of high cost events is well established.

By reducing the immediate financial cost and perhaps only partially passing through rebates, stop loss insurance and TPAs reduce the incentives for risk bearing employers to mitigate product performance uncertainty and payment timings. Shorter-term milestone-based contracts appear the better fit for those employers that want further risk reduction. Performance-based annuities might also prove attractive if the employer can capture significant rebates through the TPA and not jeopardize stop loss first period payouts. Large

employers currently benefiting from PBM and TPA negotiated pharmacy rebates, including high cost biologic therapies for cancer, immunology and neurodegenerative disorders suggest that precision financing might complement stop loss coverage.

Healthcare insurers and managed care organizations

This payer segment comprises the commercial business lines of healthcare insurers and managed care organizations (MCOs) that provide fully insured healthcare products to groups (e.g., employer-sponsored insurance) and to individuals (e.g., private insurance or Affordable Care Act marketplace plans). This segment is distinguished by its funding source of charging fixed premiums to cover a specified scope of health care products and services, with the payers at risk for any costs that exceed revenue from premiums.

FoCUS participants also put into this segment health care provider organizations that take some form of financial risk for health care costs, and as such have been referred to as provider-based, provider-led, or provider-sponsored health plans. The ownership of the full healthcare related costs of patients could make certain financing options involving value-based outcomes more preferable than they do to insurers or providers independently. Compared to risk-bearing employers these payers more directly negotiate healthcare provision and contracting activities with the bearing of the financial risk arising from those activities and the variability of healthcare events.

Health insurers and MCOs vary significantly in size. Some plans may manage as few as 10,000 lives while some national carriers may have tens of millions of members. The actuarial risk of incurring a high cost durable therapy case similarly varies from quite unlikely to nearly certain. To smooth this risk, smaller health insurers (or larger insurers for select geographies or at higher limits) may use reinsurers who provide much the same service as stop loss insurers for employers but in a manner consistent with insurance regulations.

Health insurers and MCOs already possess many of the capabilities required for implementing milestone-based contracts and performance-based annuities to address the durability and efficacy uncertainties of gene and cellular therapies. Patient Mobility (member turnover) presents a hurdle for implementing longer-term performance-based annuities for these payers. Imperfect solutions exist such as termination payments, but further innovation is needed.

This payer segment has the most flexibility to implement precision financing as illustrated by the Harvard Pilgrim Health Care and Spark Therapeutics milestone-based contract type agreement announced for LUXTURNA™, a gene therapy for a rare blindness disorder.[9]

Medicare and government stewarded programs

Medicare represents a societal commitment to provide access to a minimum core set of health care products and services for older people and people with certain disabilities. It was born of and operates by the will and ways of the federal government. In its form as an indemnity plan (fee for service), Medicare takes the risk for beneficiary costs, and manages its own risk, all according to governing laws and regulations, and sometimes in reaction to

political pressures and social sentiments.[10] Other government stewarded programs are also placed in this category including Indian Health Service programs for Native American and Alaskan populations including the tribal 638 programs and clinics; the Federal Bureau of Prisons healthcare system; state correctional health care systems and the Veterans Health Administration. These additional programs also serve targeted populations in which the government pays the providers on a fee-for-service or direct contracted basis, albeit with differing payment levels, covered services and detailed regulations than Medicare.

FoCUS participants also placed the health care insurer and MCO organizations that serve the Medicare Advantage program and Medicare Part D into this segment. These organizations provide the same health care coverage as the fee for service Medicare benefit. While they serve the same population as the fee for service program, their population can be in flux as they move to other Medicare Advantage providers or return to the fee for service program.

Due to its large covered population, Medicare fee-for-service faces low actuarial risk (variability) from durable therapies. Those same patient numbers considerably increase the absolute performance-based risk Medicare faces. Medicare and other government stewarded programs could therefore benefit from milestone-based contracts and performance-based annuity approaches. It is not clear that the Federal government with its advantageous borrowing rate and large total spending needs additional financial tools to spread payments over time.

In contrast, Medicare Advantage plans face many of the same needs and would benefit from the same tools as insurers and MCOs above, although as noted they may face other constraints from the Medicare regulation.

Medicaid

Medicaid, like Medicare, represents a societal obligation to provide access to some level of health care for a subset of the U.S. population–those with low income–and is publicly funded. But, it is quite different than Medicare. The Medicaid beneficiary population enters and exits the program on a frequent basis based on income-based eligibility criteria.[11] States jointly fund and individually operate their Medicaid programs with significant coverage and eligibility differences. With balanced budget requirements, limited borrowing capacities and no dedicated state revenue stream, states can struggle to fund their Medicaid programs. This limits their funding flexibility when challenged with unexpected and significant durable therapy costs.

Most states delegate their Medicaid programming to MCOs but often retain full or partial risk for high cost patients or drugs. Managed Medicaid MCOs must operate under the same rules as their corresponding state agencies. The MCOs receive fixed funding from the states not driven by their own medical cost estimations, their beneficiary population churns at a frequent rate, and the population faces multiple additional hurdles to health management for good health outcomes. Managed Medicaid MCOs like other MCOs can access reinsurance to

manage actuarial risk. Due to high Medicaid turnover and time limited MCO vendor contracts, shorter milestone-based contracts appear a better fit for Managed Medicaid than performance-based annuities.

Precision financing innovation required

Durable, potentially curative, gene and cellular therapies increase payer financial challenges. They exacerbate actuarial risk facing payers; concentrate years of patient benefit value, and so therapy cost, into a single upfront payment; and contain significant uncertainty regarding the durability and effectiveness for any single patient.

Each US payer segment, from Medicaid and Medicare to commercial insurers and risk bearing employers, experiences these financial challenges to different extents, and possesses varying abilities to mitigate them due to each payer segment's regulatory environment, number of covered lives, and funding sources.

Table 2 summarizes the FoCUS matching of precision financing solution to payer segment described in the sections above. The best approach also requires a consideration of the specific therapy characteristics and the epidemiology of the medical condition it treats.

Table 2: Financial Solutions Suggested for Each Payer Segment

Precision Financing Solution	Payer Segment			
	Risk Bearing Employer	Insurers / MCOs	Medicare & Gov't Stewarded	Medicaid
Milestone-based contract	✓	✓	✓	✓✓
Performance-based Annuity		✓✓	✓	
ORBM	If Stop Loss excludes	For small plans	Possible	

Operational hurdles such as patient tracking, coding, data collection, analysis and auditing, favor those organizations with scale and expertise. Risk-bearing employers and smaller payers (public or private) may prefer to leverage third parties such as their TPAs, PBMs, MCOs or an ORBM if that business model emerges.

Regulatory and legal hurdles in the Medicare and Medicaid context must be addressed as soon as possible given the long lead-time in doing so and the exacerbated risk these challenges pose to implementing precision financings in federal healthcare programs.

After two years of collaborative work, the FoCUS group of payers, providers, patients and developers (among others), has designed a set of precision financing solutions that can be customized to meet the financial challenges of each stakeholder in the context of each durable therapy and the patients it targets. Gene and cell therapies are exciting scientific and clinical innovations. Ensuring that patients can access them also requires financial innovation.

Supplemental material: segmentation methodology

FoCUS participants used an iterative, multi-stakeholder modified Delphi approach that included input from four FoCUS Design Labs from October 2016 through April 2018, as outlined in the FoCUS Research Brief published in February 2018.[12] In addition, FoCUS participants convened multiple meetings of a subset of stakeholders from the payer, developer, academic and advisor communities. The participants drew upon their experience of payer organizations, interests, decision making processes, regulatory setting and demonstrated behaviors as well as overview statistics of membership numbers. The participants also drew upon the emerging frameworks of the types of durable and curative therapies, a financial eco-system diagram illustrating the layers of financial risk bearers and intermediaries, as well as the early inventories of potential financing tools and emerging alternative financial solutions.

From this set of inputs, the multi-stakeholder group built a consensus of segments. These segments balanced the following characteristics: payer business model, view on healthcare coverage, duration of time members spend with plan, applicability of statutory regulations, internal ability to conduct billing and coding, utilization of reinsurance/stop loss, and impact of political pressure.

FoCUS participants note that this method is not exact: there are outliers in each category and constituent types of one segment may fit better under another segment, highlighted during the analysis.

About the authors

Jane Barlow is Senior Advisor to FoCUS Project (Jane Barlow & Associates, LLC); Russell Teagarden is Research Affiliate and Senior Advisor to FoCUS Project (Massachusetts Institute of Technology); and Mark Trusheim is Strategic Director, NEWDIGS and Visiting Scientist, Sloan School of Management, Massachusetts Institute of Technology.

[i] Design Labs are multi-stakeholder workshops run under Chatham House Rule using NEWDIGS case study methodology to understand complex, system-wide issues, and propose/pressure test solutions

[1] Centers for Medicare & Medicaid Services. Feedback on New Direction Request for Information (RFI) Released, CMS Innovation Center's Market-Driven Reforms to Focus on Patient-Centered Care. Press release April 23, 2018. Available at https://www.cms.gov/newsroom/press-releases/feedback-new-direction-request-information-rfi-released-cms-innovation-centers-market-driven-reforms. Accessed December 27, 2018.

[2] Jacobsen, G.,Damico, A., Neuman, T., Gold, M. Enrollment Market Update. *Henry J. Kaiser Family Foundation.* June 6, 2017. Available at https://www.kff.org/medicare/issue-brief/medicare-advantage-2017-spotlight-enrollment-market-update/.

[3] Duke Margolis Center for Health Policy. Overcoming the Legal and Regulatory Hurdles to Value-Based Payment Arrangements for Medical Products. December 2017. Available at https://healthpolicy.duke.edu/publications/overcoming-legal-and-regulatory-hurdles-value-based-payment-medical-products. Accessed December 27, 2018.

[4] Network for Excellence in Health Innovation (NEHI) Advancing Value-Based Contracts for Biopharmaceuticals. https://www.valuebasedcontracting.net/. Accessed December 27, 2018.

[5] Value of Gene and Cell Therapy. American Society for Gene and Cell Therapy. https://www.asgct.org/advocacy/pillars-of-advocacy/value-of-gene-and-cell-therapy. Accessed December 27, 2018.

[6] Spark Therapeutics. Spark Therapeutics Announces First-of-their-kind Programs to Improve Patient Access to LUXTURNA™ (voretigene neparvovec-rzyl), a One-time Gene Therapy Treatment. Press release January 3, 2018. Available at http://ir.sparktx.com/news-releases/news-release-details/spark-therapeutics-announces-first-their-kind-programs-improve. Accessed December 27, 2018.

[7] U.S. Health Policy Gateway. (n.d.). Employer tax exclusion. Retrieved from http://ushealthpolicygateway.com/vi-key-health-policy-issues-financing-and-delivery/health-financing/tax-expenditures/employer-tax-exclusion/. Accessed December 27, 2018.

[8] Claxton, G., Rae, M., Long, M., Damico, A., Foster, G., & Whitmore, H. (2017). Employer health benefits: 2017 annual survey. *Henry J. Kaiser Family Foundation and Health Research & Educational Trust.* Retrieved from http://files.kff.org/attachment/Report-Employer-Health-Benefits-Annual-Survey-2017. Accessed December 27, 2018.

[9] Spark Therapeutics. Spark Therapeutics Announces First-of-their-kind Programs to Improve Patient Access to LUXTURNA™ (voretigene neparvovec-rzyl), a One-time Gene Therapy Treatment. Press release January 3, 2018. Available at http://ir.sparktx.com/news-releases/news-release-details/spark-therapeutics-announces-first-their-kind-programs-improve. Accessed December 27, 2018.

[10] The official U.S. government site for Medicare. (n.d.). What's Medicare?. Retrieved from https://www.medicare.gov/sign-up-change-plans/decide-how-to-get-medicare/whats-medicare/what-is-medicare.html. Accessed December 27, 2018.

[11] Medicaid: Keeping America healthy. (n.d.). Program history. Retrieved from https://www.medicaid.gov/about-us/program-history/index.html. Accessed December 27, 2018.

[12] MIT NEWDIGS FoCUS Project. Research brief: payer segmentation. 2018. Retrieved from http://newdigs.mit.edu/sites/default/files/FoCUS%20Research%20Brief_2018F202-014.pdf. Accessed December 27, 2018.