



Novel Financing Approaches are Needed to Capitalize on Life-Saving Gene Therapies*

Thanks to rapid advances in biomedical research, several gene therapies have recently been approved for use in the U.S. Unlike pharmaceutical drugs that help control diseases, gene therapies can provide cures. Despite the substantial one-time upfront costs of gene therapy (potentially exceeding \$1 million per patient), policymakers and healthcare payers must realize the potential long-run benefits these treatments offer. This ConsumerGram shows that, compared to traditional treatments for several debilitating genetic diseases, gene therapies can be very sound investments. Consumers, as well as the overall economy, stand to benefit greatly from the development of gene therapies, but only if they are accessible to patients. Policymakers and payers must develop new value-based approaches to funding these life-saving cures.

What is Gene Therapy?

Healthcare costs are out of control and the present system is not sustainable. Expenditures are approaching 20 percent of GDP with no end in sight.¹ To constrain costs, our healthcare system needs to emphasize keeping people healthy and increasing patients' quality of life. New medical innovations, gene replacement and cell therapies, have the potential to do both.

Gene therapy is a medical intervention that treats, cures, or prevents disease by changing a person's genes, the blueprints that govern how our bodies function. Up

* Dr. Joseph Fuhr, Jr. is a Senior Fellow with the American Consumer Institute and Professor Emeritus from Widener University, Liam Sigaud is a Manager of Economic Policy with The American Consumer Institute, and Steve Pociask is President with The American Consumer Institute. For further information, follow us on Twitter @ConsumerPal or visit www.TheAmericanConsumer.Org.

¹ Centers for Medicare and Medicaid Services, "Historical: National Health Expenditure Data," 2018, <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NationalHealthAccountsHistorical.html>.

to 4,000 diseases (including some types of cancer, cystic fibrosis, and neurodegenerative diseases like Parkinson's and Alzheimer's) are rooted in genetic mutations that prevent proteins from being synthesized properly in our cells.² By repairing or replacing these defective genes, gene therapies can restore normal functioning and address debilitating diseases at their source. As such, gene therapy holds incredible promise for the millions of Americans who suffer from chronic hereditary diseases that previously meant, at best, a lifetime of expensive and imperfect treatments and a reduced quality of life.

Research on gene therapy is progressing rapidly, and the last few years have brought important breakthroughs. The Food and Drug Administration (FDA) approved three gene therapies for use in the United States in 2017, and biotech and pharmaceutical companies are working aggressively to develop new therapies.³ FDA Commissioner Dr. Scott Gottlieb predicted in June 2018 that 40 additional gene therapies would be approved in the next four years; and in January 2019 he projected that by 2025, “the FDA will be approving 10 to 20 cell and gene therapy products a year based on an assessment of the current pipeline and the clinical success rates of these products.”⁴

According to Dr. Michael White of Washington University’s Center for Genome Studies, “The United States federal database of clinical trials lists more than 300 ongoing gene therapy trials, and another 800 that are currently enrolling patients. The diseases covered by these trials range from rare genetic diseases to congestive heart failure, cancer, and HIV.”⁵

To be sure, gene therapy is unlikely to be a panacea. Direct cause-and-effect relationships from genetic mutations to diseases are relatively rare, and scientists are still working to target therapies more effectively and avoid possible adverse side-effects. Still, about 25-30 million Americans (nearly 10 percent of the population) have a rare medical condition, the majority of which are thought to be related to a genetic defect.⁶ This number does not capture the millions of people with more common genetic disorders who could also benefit from gene therapy.

² National Human Genome Research Institute, “Genetic Information and the Workplace,” 1998, <https://www.genome.gov/10001732/genetic-information-and-the-workplace-report/>.

³ Mark Terry, “Gottlieb at BIO 2018: 40 Gene Therapy Approvals by 2022,” *BioSpace*, June 7, 2018, <https://www.biospace.com/article/gottlieb-at-bio-2018-40-gene-therapy-approvals-by-2022/>.

⁴ “Statement from FDA Commissioner Scott Gottlieb, M.D. and Peter Marks, M.D., Ph.D., Director of the Center for Biologics Evaluation and Research on new policies to advance development of safe and effective cell and gene therapies,” U.S. Food and Drug Administration, January 15, 2019, <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm629493.htm>.

⁵ Michael White, “Why Gene Therapy Is No Longer a Pipe Dream,” *Pacific Standard*, 2018, <https://psmag.com/social-justice/gene-therapy-no-longer-pipe-dream>.

⁶ U.S. Department of Health and Human Services, “FAQs About Rare Diseases,” 2017, <https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases>.

A Game-Changer Compared to Traditional Pharmaceutical Treatments

Tens of millions of Americans live with genetic diseases, most of which are managed with pharmaceutical drugs. Traditional pharmaceuticals use small molecules or biologics to mitigate the symptoms of a disease and can fall short of providing complete relief. Over the years, pharmaceuticals have done enormous good, improving the quality of life of countless patients. In some cases, however, pharmaceutical treatments are very expensive, even if government programs absorb much of the costs. They often require patients to take a cocktail of several drugs over several years or even their entire lifetime. On top of that, some pharmaceuticals can produce unwanted side effects.

Gene therapies are fundamentally different. By fixing the underlying causes of genetic diseases, gene therapies offer the opportunity to fully cure disorders instead of merely alleviating their symptoms. An added advantage is that instead of needing to follow a never-ending pharmaceutical regime, patients undergoing gene therapy often only need a single dose with little follow-up care required.

Economics, Efficiency, and R&D

The goal of economics is to allocate limited resources, given virtually unlimited wants, in the most efficient manner. Economists speak of allocative and dynamic efficiencies. To achieve allocative efficiency, the price of a good or service must reflect the marginal costs of production (opportunity costs). Dynamic efficiency has to do with the incentive for firms to innovate. Often, these two efficiencies are in conflict. If allocative efficiency is prioritized, firms may have difficulty getting an adequate return on risk-adjusted investment because R&D costs will not be recovered. Consider the effects of marginal cost pricing on software which can be downloaded at virtually no expense. Such a pricing strategy would severely undercut any incentive for companies to develop software, which would be a loss to consumers. Similarly, marginal cost pricing in the pharmaceutical market would result in many drugs that are very beneficial to society not being developed. Simply put, firms need the economic incentive of profit to innovate.

There is a tradeoff between competition with lower prices and innovation. Policymakers need to balance these goals. Without the prospect of receiving a return on investment, firms will be unwilling to take the risk of developing new gene therapies. Also, given that most gene therapies, like orphan drugs, will involve relatively few patients, prices will need to be relatively high to obtain a suitable return on investment. The economic rationale for patent laws and other exclusivity protections is to give innovators the chance to get a return on their investment. Many of these therapies can result in considerable benefits to patients and society but failing to incentivize sufficient R&D will discourage innovation in an entire pipeline of potential cures, depriving everyone of these benefits.

High Costs of Innovation

A major reason for the high costs of the American healthcare system is the tremendous cost of innovation. For example, the R&D costs for an originator biologic have been estimated to be between \$1.3 billion and \$2.6 billion.⁷ Taking failures into account, the costs could be as much as \$5 billion each. Merck estimates that 75% of its R&D is spent on failures.⁸ Only 5 percent to 10 percent of drugs that reach clinical trials get FDA approval.⁹ Only 30 percent of those are commercial successes.¹⁰ Over the last 18 years, there have been 75 unsuccessful efforts and only 3 new successful drugs for brain cancer.¹¹ Gene therapy, while still nascent, will face similar, if not higher, risk in terms of failure and the costs of R&D.

The amount of pharmaceutical innovation in the United States is closely linked to the cost payers face. One study estimated that “in the long run, a 10% decline in drug prices would be likely to cause at least a 5% to 6% decline in two measures of pharmaceutical innovation.”¹²

Despite the high cost of medical innovation, many diseases would not be treatable were it not for these investments, hurting patients and making our society and economy worse off. The development of gene therapies is a costly enterprise, and most patients seeking a cure will not be able to afford these treatments unless financing mechanisms change. Even those with insurance are unlikely to afford the co-pays.

The Costs of Gene Therapy

Despite their promise, gene therapies present healthcare stakeholders with difficult challenges. Most importantly, gene therapies are very costly and are likely to pose major affordability and access hurdles for patients, as well as public and private healthcare payers that already face pressures to constrain costs.

⁷ Erwin A. Blackstone and Joseph P. Fuhr, Jr., “Biologics and Biosimilars: The Possibility of Encouraging Innovation and Competition,” *The SciTech Lawyer*, Spring 2015, <https://pdfs.semanticscholar.org/bf63/c072c5019dbb294f85c8f865adbcc0bd698a.pdf>.

⁸ Erwin A. Blackstone and Joseph P. Fuhr Jr., “The Future of Competition in the Biologics Market,” *Temple Journal of Science, Technology, and Environmental Law*, Summer 2012, pp. 1-30.

⁹ Erwin A. Blackstone and Joseph P. Fuhr Jr., “Biosimilars and Biologics; The Prospect for Competition” in Laszlo Endrenyi, et al, eds., *Development of Biosimilar Drug Products*, Taylor & Francis, 2017, pp.414-438.

¹⁰ J. Loo, Standard and Poor’s Industry Survey: Biotechnology, S&P Capital IQ, McGraw Hill Financial, March 2015.

¹¹ J. Loo, Standard and Poor’s Industry Survey: Biotechnology, S&P Capital IQ, McGraw Hill Financial, August 2016.

¹² Frank R. Lichtenberg, “The Benefits of Pharmaceutical Innovation: Health, Longevity, and Savings,” Montreal Economic Institute, 2016, https://www.iedm.org/files/cahier0216_en_0.pdf.

The initial pricing of gene therapies in Europe and the United States suggests that per-patient costs could be as high as \$1 to \$2 million. Even though there are signs that costs may be declining, it's easy to see how the cumulative budget impact of these treatments on our health system could be substantial.¹³

However, sticker-shock should not deter policymakers and payers from using gene therapy as a viable intervention for certain diseases. Despite high up-front costs, gene therapies can generate significant savings by replacing expensive long-term pharmaceutical treatments, reducing hospitalizations, shrinking the number of medical procedures, preventing additional health deterioration, and improving quality of life.¹⁴ No assessment of gene therapy's affordability to the health system would be complete without considering these opportunities for long-term cost reductions.

Pricing a new treatment involves complex calculations that account for its clinical and quality of life effects, as well as the broader economic impact on our healthcare system and society. When making tough decisions about which treatments to finance, policymakers and payers must consider the upfront price of new therapies in the proper context, realizing their long-term value.

Promising Examples

When the avoided costs of conventional, chronic treatments are considered, gene therapies should often pay for themselves over time, as the following examples demonstrate.

Hemophilia, a genetic disorder that weakens the body's clotting capabilities and can cause severe bleeding from even minor cuts, is a good example of how gene therapy can slash long-term health costs. Every year, 400 infants are born with hemophilia.¹⁵ Until recently, they faced a life of chronic pain, astronomical medical expenses, and restrictions on their ability to play sports and engage in other physical activities.

¹³ Emily Mullin, "Tracking the Cost of Gene Therapy," *MIT Technology Review*, 2017, <https://www.technologyreview.com/s/609197/tracking-the-cost-of-gene-therapy/>.

¹⁴ Grace Hampson, Adrian Towse, Steven D. Pearson, William B. Dreitlein, and Chris Henshall, "Gene therapy: evidence, value and affordability in the U.S. health care system," *Journal of Comparative Effectiveness Research*, 2017. Vol. 7, No. 1, <https://www.futuremedicine.com/doi/full/10.2217/cer-2017-0068>.

¹⁵ Meg Tirrell, "A grandpa's hope for hemophilia cure leads him to gene therapy clinical trial," *CNBC*, 2018, <https://www.cnbc.com/2018/11/16/biomarins-hemophilia-gene-therapy-offers-patients-a-hope-for-a-cure.html>.

Currently, the annual cost of hospitalizations and surgeries to treat hemophilia can reach \$1 million.¹⁶ Clotting protein replacement therapy can add hundreds of thousands of dollars per year to a patient's medical bill.

Recent research indicates that hemophilia may soon be curable through just one infusion of gene therapy. Early trials have already yielded promising results.¹⁷ One participant in a clinical trial in 2018, James Addie, had struggled with complications from hemophilia for decades; the illness caused progressive joint damage, ultimately leading to the replacement of his left knee and both hips, and an HIV infection from being exposed to contaminated blood used for treatment. After gene therapy, Addie's blood clotting quickly returned to normal levels and stabilized.

When they become widely available in a few years, the one-time gene therapy treatments for hemophilia are expected to cost a million or more – still potentially less than a single year of treatment using existing methods.¹⁸ Over the life of a patient, the potential savings from replacing conventional treatments with gene therapy could reach tens of millions of dollars. Moreover, quality of life would be significantly enhanced.

Spinal muscular atrophy (SMA) is another example of how gene therapy can deliver substantial long-term savings and better health outcomes. SMA is a neurodegenerative disease that impairs muscle movement and limits a person's ability to breathe, swallow, or walk. SMA afflicts about 1 in 6,000 infants and claims the lives of more young children than any other genetic disorder.¹⁹

Currently, little can be done to slow the disease's progression. The only treatment that exists costs \$750,000 for the first year and \$375,000 per year thereafter and requires several invasive injections every year.²⁰

A gene therapy for SMA is expected to become FDA-approved in 2019 and promises to reduce the lifetime burden of this devastating illness for both families and healthcare payers. While this new therapy has yet to be priced, independent analysts estimate a \$4 million price tag would be justified, given its unprecedented ability to improve the

¹⁶ Gina Kolata, "They Thought Hemophilia Was a 'Lifelong Thing.' They May Be Wrong," *The New York Times*, 2018, <https://www.nytimes.com/2018/08/13/health/hemophilia-gene-therapy.html>.

¹⁷ Meg Tirrell, "A grandpa's hope for hemophilia cure leads him to gene therapy clinical trial," *CNBC*, 2018, <https://www.cnbc.com/2018/11/16/biomarins-hemophilia-gene-therapy-offers-patients-a-hope-for-a-cure.html>.

¹⁸ Mackenzie Bean, "Hemophilia therapy could be first drug with \$1M price tag: 3 things to know," *Becker's Hospital Review*, 2018, <https://www.beckershospitalreview.com/supply-chain/hemophilia-therapy-could-be-first-drug-with-1m-price-tag-3-things-to-know.html>.

¹⁹ Gwendolyn Strong Foundation, "What Is Spinal Muscular Atrophy (SMA)?" downloaded January 28, 2019, https://thegsf.org/press/detail/what_is_spinal_muscular_atrophy_sma/.

²⁰ Aimee Picchi, "The cost of Biogen's new drug: \$750,000 per patient," *CBS News*, 2016, <https://www.cbsnews.com/news/the-cost-of-biogens-new-drug-spinraza-750000-per-patient/>.

quality and length of life.²¹ While there is no certainty that the manufacturers will price this treatment so high, the \$4 million one-time expense provides an example where, over the lifetime of the patient, these treatments could cost less than the current conventional treatments. The table below provides a general illustration of the cost payback that gene therapy can provide over current treatments.

Years to Payback: Two Gene Replacement Therapies Compared to Current Treatment

	Current Annual Treatment Costs (Thousands of Dollars)	Onetime Gene Therapy Cure (Thousands of Dollars)	Number of Years to Reach Financial Payback
Severe Hemophilia	\$690 ²²	\$1,000 ²³	1.45 Years
Spinal Muscular Atrophy	\$750 Year-1 ²⁴ \$375 After Year-1	\$4,000 ²⁵	<10 Years

It’s important to note that the annual costs of current treatments presented in the table reflect only the price of direct medical interventions – factor replacement for hemophilia, for instance – and fail to capture other costs associated with

²¹ John LaMattina, “Novartis’ \$4 Million Gene Therapy -- Real Price or A Negotiation Ploy?” *Forbes*, 2018, <https://www.forbes.com/sites/johnlamattina/2018/11/13/novartis-4-million-gene-therapy-real-price-or-a-negotiation-ploy/#22b3d56c58fc>.

²² Adult patient treatment cost run between \$580,00 to \$800,00, according to Leerink Partners, for an average of \$690,000 - see Mackenzie Bean, “Hemophilia Therapy Could Be First Drug with \$1 Million Price Tag,” *Becker’s Hospital Review*, May 8, 2018, <https://www.beckershospitalreview.com/supply-chain/hemophilia-therapy-could-be-first-drug-with-1m-price-tag-3-things-to-know.html>. This figure is low considering that shots and surgeries can be as high as \$1 million per year each. For an example, see Gina Kolata, “They Thought Hemophilia Was a ‘Lifelong Thing.’ They May Be Wrong,” *New York Times*, August 13, 2018, <https://www.nytimes.com/2018/08/13/health/hemophilia-gene-therapy.html>.

²³ Mackenzie Bean, “Hemophilia Therapy Could Be First Drug with \$1 Million Price Tag,” *Becker’s Hospital Review*, May 8, 2018, <https://www.beckershospitalreview.com/supply-chain/hemophilia-therapy-could-be-first-drug-with-1m-price-tag-3-things-to-know.html>. Another study estimated the cost to be \$850,000 but raised the cost to be \$1 million, assuming a 90% effectiveness and including costs for complications. See Nicoleta Machin, Margaret V. Ragni and Kenneth J. Smith, Gene Therapy in Hemophilia A: A Cost-Effectiveness Analysis, *Blood Advances*, Vol. 2(14), July 24, 2018, pp. 1792-1798, <http://www.bloodadvances.org/content/2/14/1792>. We will use this higher cost estimate for gene therapy.

²⁴ Aimee Picchi, “The Cost of Biogen’s New Drug: \$750,000 Per Patient,” *CBS News*, December 29, 2016, <https://www.cbsnews.com/news/the-cost-of-biogens-new-drug-spinraza-750000-per-patient/>.

²⁵ There is no estimated price, but one article claims that a \$4 million price tag would be justified, see John LaMattina, “Norvartis’ \$4 Million Gene Therapy - Real Price or a Negotiated Ploy?” *Forbes*, November 13, 2018, <https://www.forbes.com/sites/johnlamattina/2018/11/13/novartis-4-million-gene-therapy-real-price-or-a-negotiation-ploy/#64d372aa58fc>.

traditional treatment, including the cost of more frequent hospitalization, increased hospital readmissions, shortened longevity, reduced quality of life, paid caregiving and unpaid caregiving by family members, problems with drug adherence, lost income, reduced productivity and other labor market difficulties, as well as costs shared and covered by Medicare, health insurance providers and others. As a result, when compared to gene replacement therapy, the current treatment figures in the table should be viewed as incomplete and low estimates.

There are other examples where gene therapy costs may yield lower long-term costs. For example, a rare form of blindness, Best Disease, could be cured with gene therapy, but at a cost of around \$850,000.²⁶ In addition, a novel gene therapy for children and young adults with lymphoblastic leukemia costs about \$475,000 for a one-time treatment for children and \$373,000 for adults.²⁷ By contrast, one study put the cost of conventional treatments – stem cell transplants – at \$683,099 for the first year and substantial costs in the following years.²⁸ In short, curing a disease, rather than treating it, can save insurers and taxpayers money in the long-run, even if the initial investment is significant, and provide an immense improvement to longevity and quality of life. In addition, drug costs normally increase over time thus understating the cost savings from gene therapy.

Novel Financing Methods Are Needed to Make Gene Therapies Widely Available

Payers, policymakers, and manufacturers must recognize that existing mechanisms to finance medical treatments and manage affordability may be inadequate to cope with the growing number of gene therapies being introduced. To overcome this hurdle, stakeholders should collaborate on policies that create pricing and financing structures that maximize consumer access to these technologies while incentivizing further research and innovation.

Under the present healthcare system, insurance companies are often reluctant to pay for therapies that have high upfront costs and whose benefits are spread over a lifetime. One reason for this is that patients often change insurance companies (a phenomenon known as “churning”), meaning that one insurance company may incur

²⁶ Mackenzie Bean, “Hemophilia therapy could be first drug with \$1M price tag: 3 things to know,” *Becker's Hospital Review*, 2018. Available at: <https://www.beckershospitalreview.com/supply-chain/hemophilia-therapy-could-be-first-drug-with-1m-price-tag-3-things-to-know.html>.

²⁷ Michelle Andrews, “Staggering Prices Slow Insurers’ Coverage Of CAR-T Cancer Therapy,” *Kaiser Health News*, 2018, <https://khn.org/news/staggering-prices-slow-insurers-coverage-of-car-t-cancer-therapy/>.

²⁸ Richard T. Maziarz, Annie Guérin, Geneviève Gauthier, Julie Heroux, Maryia Zhdanova, Eric Q. Wu, Simu K. Thomas, and Lei Chen, “Five-year direct costs of acute lymphoblastic leukemia pediatric patients undergoing allogeneic stem cell transplant,” *International Journal of Hematologic Oncology*, 2016. Vol. 5, No. 2, <https://www.futuremedicine.com/doi/abs/10.2217/ijh-2016-0001?src=recsys&journalCode=ijh>.

the upfront costs of the therapy while another insurance company may receive the benefits of lower patient costs. As a result, some insurance companies can “free ride” on the system by not offering to pay for the drugs, while still reaping the benefits as patients switch insurers. Long-term financing of partial payments to drug companies has been proposed so that when a patient changes insurance companies, the new insurer pays some of the drug costs. Such an arrangement introduces new challenges, like the fact that insurers and employers may be encouraged to discriminate against those with high levels of pre-existing debt.

Other promising financing options are being discussed.²⁹ Outcome-based payments and risk-sharing agreements, where payers are absolved of financial responsibility if a therapy fails to produce the expected clinical outcome, have been used successfully in France and Spain to manage the costs of some drugs, and Medicare already uses such agreements to cover the lymphoblastic leukemia gene therapy referenced above.³⁰ In the past, some drug companies have objected to value-based pricing because of a lack of patient adherence to a prescribed regime of traditional pharmaceutical drugs. Unlike the drug market, one of the advantages of administering a one-time cure via gene therapy is that it avoids many of these adherence issues, making these therapies prime candidates for value-based pricing. Value-based pricing should come from the perspective of the patient and society and take into account the net benefit of the gene therapy over the patient’s lifetime.

One possibility would be for insurers to use reinsurance and capital markets to diversify the risk and spread the cost of gene replacement therapy, thereby protecting them from catastrophic losses. A second option could include a universal service fund as a percentage of revenue of each insurance company to aid underinsured patients. In either case, ongoing, but smaller, payments would spread the upfront medical costs of gene replacement therapy, much like an amortized payment. Longer term, the result would enable cost savings and improved patient outcomes without the “sticker shock” associated with this innovative therapy.

Conclusion

For decades, gene therapy was a pipedream for scientists around the world. Now, that vision is becoming reality for an ever-growing number of debilitating and deadly diseases. These treatments have the potential to transform the lives of patients and give them a better quality of life.

²⁹ Grace Hampson, Adrian Towse, Steven D. Pearson, William B. Dreitlein, and Chris Henshall, “Gene therapy: evidence, value and affordability in the U.S. health care system,” *Journal of Comparative Effectiveness Research*, 2017. Vol. 7, No. 1, <https://www.futuremedicine.com/doi/full/10.2217/cer-2017-0068>.

³⁰ Jacob Bell, “Medicare to pay hundreds of thousands for CAR-T therapies,” *BioPharma Dive*, 2018, <https://www.biopharmadive.com/news/medicare-to-pay-hundreds-of-thousands-for-car-t-therapies/520806/>.

In the long-run, gene therapy also promises to reduce overall health costs. To accommodate their up-front costs, stakeholders should collaborate to develop novel, value-based financing mechanisms that expand access to these technologies and encourage continued innovation in this area.

Additional Reading

Erwin A. Blackstone, and Joseph P. Fuhr, Jr., “Biologics and Biosimilars: The Possibility of Encouraging Innovation and Competition,” *The SciTech Lawyer*, Spring 2015, pp. 4-7.

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N. Machin, M. V. Ragni, and K. Smith, “Gene therapy in hemophilia A: a cost-effectiveness analysis,” *Blood Advances*, July 2008, Volume 2, Number 14.