IS INNOVATION WITHOUT AFFORDABILITY INNOVATION?

5 Realities Regarding U.S. Pharmaceutical Innovation and Pricing

Authors:

Joshua Barrett
Associate Director of Research, Center for the Business of Health

Zoey Kernodle
Director, Center for the Business of Health

UNC CENTER for the BUSINESS of HEALTH

cboh.unc.edu

This insights report is intended for general audiences who are seeking background on the complexities involved in pharmacuetical innovation and pricing and investigating problems within the system.

In 2023, the Center for the Business of Health began exploring the topic of pricing within the U.S. healthcare system. As we examined various aspects of pricing, including the influence of consolidation, artificial intelligence, the cost of clinical labor and rising hospital prices, and more, pharmaceutical pricing stood out. Pharmaceutical pricing has been a consistent topic of discussion for several years. The advent of new gene therapies with startling price tags, the massive demand for GLP-1s, and heightened assessments of various types of organizations within the pharmaceutical value chain (notably pharmacy benefit managers), highlighted the need for additional attention in the pharmaceutical space.

In the spring of 2024, we convened leading experts across the pharmaceutical sector under Chatham House Rules(1) to discuss these topics and to take a deep dive into the question: ***"what is the price we pay for pharmaceutical innovation?"***

This white paper condenses the insights we gathered during the day and provides clarity on the current state of pharmaceutical pricing in the United States.

UNC CENTER for the BUSINESS of HEALTH

1. https://www.chathamhouse.org/about-us/chatham-house-rule

TABLE OF CONTENTS

INTRODUCTION

The United States Is the Engine of Global Pharmaceutical Development

- As Figure 1 shows, the United States has led the world in pharmaceutical research and development (R&D) for decades.
  - Innovation traditionally comes from several players: venture capital, academia, the federal government, state governments, and industry.
- After a brief drop during the COVID-19 pandemic, investment in pharmaceuticals may be growing again, especially when it comes to treatments that could cure and treat rare disorders.
  - In 2023, the 20 leading global pharmaceutical companies invested $145 billion(2) in research and development, a 4.5% increase from 2022 .
  - Spending on cell and gene therapies reached $5.9 billion(3) in 2023, up 38% from 2022 .
- But recent changes have brought headwinds that have affected innovation, particularly for small molecules .
  - Innovation is moving from the traditional intersection of biotechnology companies, pharmaceutical firms, and universities to more diverse areas, reflecting increased caution and strategic efforts from large pharmaceutical firms.

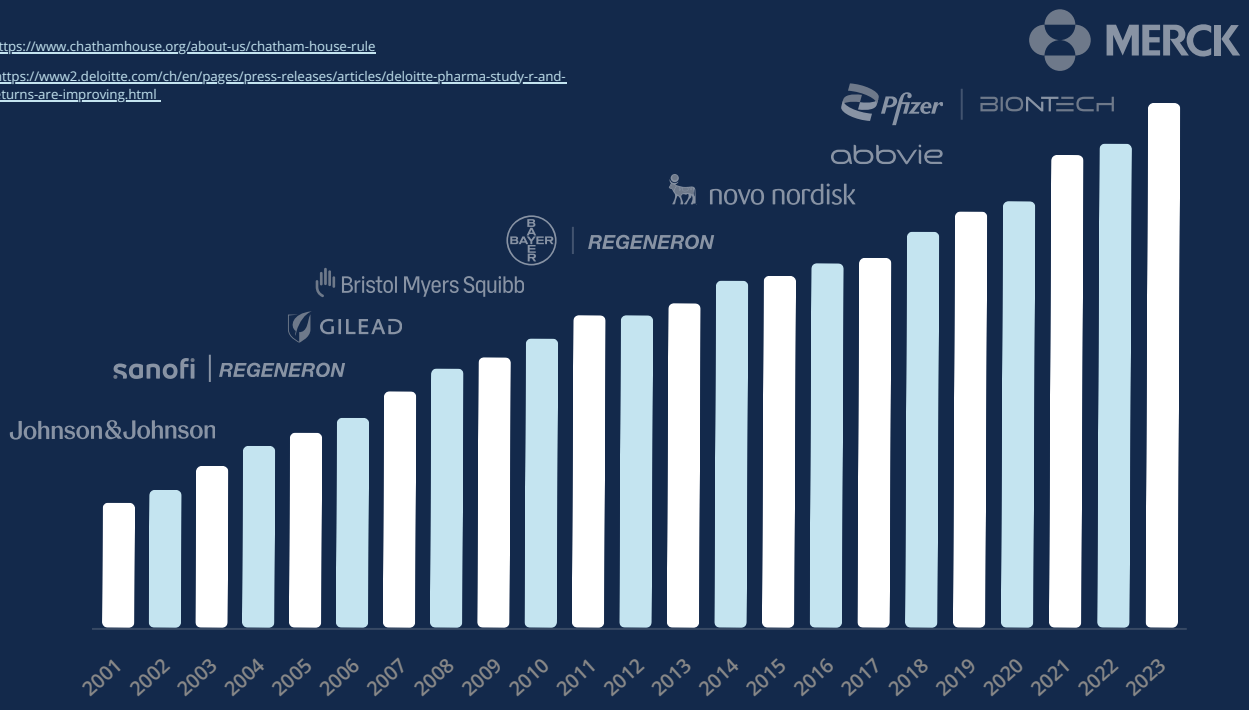
Key Insights

1.6tr USD
Revenue of the worldwide pharmaceutical market in 2023

53.3%
Revenue share of the North American pharmaceutical market in 2023

99.5 bn USD
Pharmaceutical sales in oncologics

Figure 1: Pharmaceutical investment over time - https://www.statista.com/topics/1764/global-pharmaceutical-industry/



2. https://www.chathamhouse.org/about-us/chatham-house-rule

3. https://www2.deloitte.com/ch/en/pages/press-releases/articles/deloitte-pharma-study-r-and-d-returns-are-improving.html

INTRODUCTION

Industry Warning Signs: Will the United States Continue to Lead?

- The distinction between risk — which is quantifiable — and uncertainty — which is unpredictable — is critical since it shapes investment and R&D strategies.
- High rates of pipeline failures are a major concern for pharmaceutical firms, impacting overall investment strategies and risk management
  - These firms have an approximately 4% risk-adjusted return on R&D expenses, a return that is lower than it is for other industries.
  - There is a shift toward controlling early-stage risks, reflecting increased caution and strategic adjustments in investment.
  - Managing the "unknown-unknowns" is a significant challenge, requiring adaptive and resilient strategies to handle unforeseen risks.
- Investors are becoming more selective, focusing on companies with strong scientific foundations and clear pathways to commercialization.
- There is a growing trend of funding early-stage biotech companies, emphasizing the importance of innovative ideas and breakthrough technologies(4).
- Partnerships and collaborations between biotech companies and larger pharmaceutical firms are increasing, aiming to leverage resources and expertise for mutual benefit.
- Venture capital (VC) funding for biotech peaked in 2021 and has trended downward since(5), with VCs focusing on sustaining existing portfolio companies rather than new investments. This shift has led to pipeline cuts and layoffs within these companies.
- The biotech sector is experiencing increased competition for limited venture funding, particularly in early-stage investments. The competition has resulted in an $8 billion shortfall in follow-on capital for Series A companies compared to the previous year(6), forcing many firms to cut back on pipelines and staff.

> “It’s not about the known risk. It’s about the ‘unknown-unknowns’ for pharma innovation, and no one knows what to do with that calculus.”

4. https://www.iconplc.com/insights/blog/2023/05/05/trends-in-the-biotech-funding-environment
5. https://www.iconplc.com/insights/blog/2023/05/05/trends-in-the-biotech-funding-environment
6. https://www.pharmaceutical-technology.com/analyst-comment/biotech-funding-optimism-rises/

INTRODUCTION

Does Innovation Matter If People Cannot Afford It?

Current System Does Not Work for Patients

Despite headwinds, the U.S. pharmaceutical industry is entering an era of rapid innovation that could eradicate diseases or conditions that, each year, cost Americans their lives and livelihoods. These cures could unlock remarkable benefits for society and the world economy. So much is possible, but the current system for determining price does not integrate well with rapid innovation. U.S. patients, payors, and employers struggle to bear the cost of innovation.

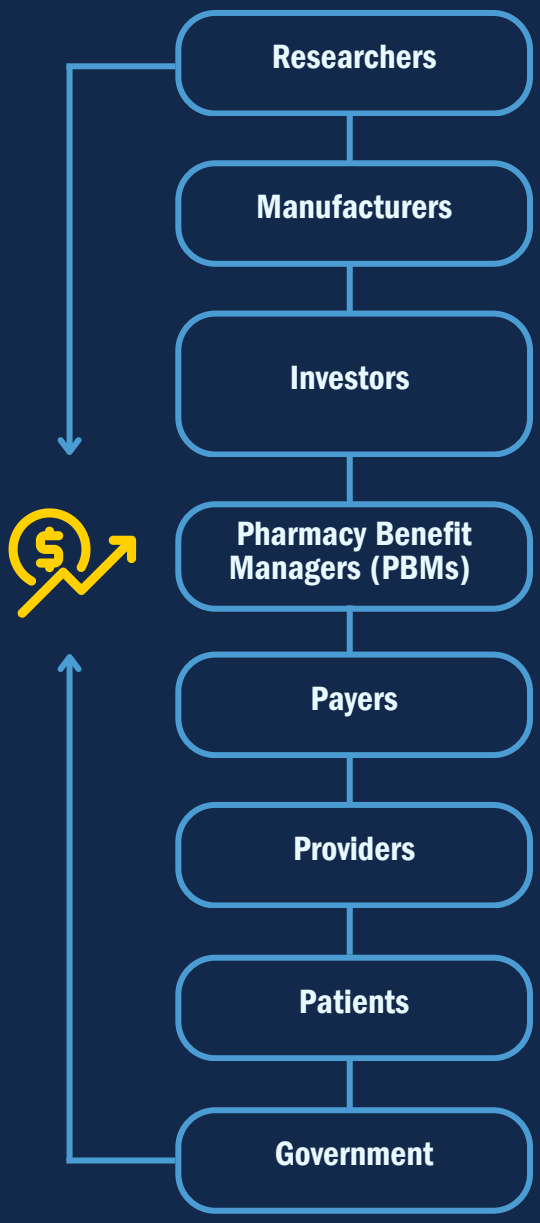
The average cost to develop a drug, from discovery of an active substance to market launch, was $2.3 billion(7) in 2023. Innovators must recoup these costs in order to continue R&D, but the list price of drugs in the United States is a constant source of tension and debate.

As Figure 2 indicates, unlike other countries, pricing in the United States reflects the influence of many stakeholders all with something to say about "cost" versus "price." In addition to these entities, regulators and lawmakers influence the country's market-based system.

Federal policymakers have attempted to control drug prices, most recently with the 2022 Inflation Reduction Act (IRA). The U.S. Departments of Veterans Affairs and Defense also require manufacturers to offer discounted prices for drugs and the 340B Program requires manufacturers to offer discounts on outpatient drugs to certain hospitals, community health centers, and other facilities(8).

Still, regulatory frameworks often struggle to keep pace with industry trends. Academic literature calls this issue the "regulatory disconnection."(9)

Figure 2:



7. https://www2.deloitte.com/ch/en/pages/press-releases/articles/deloitte-pharma-study-r-and-d-returns-are-improving.html
8. https://www.commonwealthfund.org/blog/2016/drug-price-control-how-some-government-programs-do-it
9. https://digitalcommons.wcl.american.edu/cgi/viewcontent.cgi?article=1028&context=aublr

INTRODUCTION

What We Risk By Not Getting Pricing Right.

Gene therapy could one day treat or prevent many of the more than 7,000 genetic disorders(10) that exist, freeing patients from the burden of sometimes severe and lifelong chronic disease management.

Questions about who bears the cost to develop these drugs, the resulting prices, and determined value divide the industry, public, press, and policymakers. Add the fact that employers and payors may not be able to shoulder the burden of one-time curative therapies, and it is apparent there are serious questions about whether the future really is now.

This paper will explore five realities regarding U.S. pharmaceutical innovation and pricing we heard from leading experts in the pharmaceutical sector.

REALTY #1: Determining Value and Prioritizing Patients Is Challenging in the United States

REALTY #2: Drug Pricing Is a Reflection of the U.S.'s Uniquely Complex Healthcare System

REALTY #3: Private Sector Complexity and Policy Shaping Make the System Less Transparent

REALTY #4: Innovation Places a Disproportionate Burden on Payors and Employers

REALTY #5: If There Is a Path Forward, It Will Require More Tranparency and Tradeoffs

10. https://my.clevelandclinic.org/health/diseases/21751-genetic-disorders

CASE STUDY:

Metachromatic Leukodystrophy

- Metachromatic leukodystrophy (MLD) affects 1 in 40 U.S. children annually
- A nerve disorder, MLD strikes toddlers, quickly taking away their ability to speak and walk; children usually die within 5 years of diagnosis(11)
- A new therapy, Lenmeldy, hit the U.S. market in early 2024
- The wholesale cost, $4.25 million, was more than a Brooklyn brownstone or a Miami mansion(12)
- A parent of a child with MLD may say no price is too high for an insurer to bear since Lenmeldy could save their child's life
- That parent's health insurer or employer may argue the $4.25 million cost — if repeated for multiple patients — would bankrupt them
- The European Commission approved Lenmeldy in December 2020; it "has slowly won reimbursement from payors, but in the third quarter of 2023, sales were only $5.6 million(13)
- Lenmeldy begs the question: does innovation matter if no one can afford it?

> "A lot of employers and payors are not set up with their current drug payment plans to afford potential gene therapies with huge price tags. Consider an employer with a $1 million budget faced with a therapy cost of $4 million—even with strong long-term returns based on reduced utilization across the healthcare system or over that patient's lifetime, it doesn't offset the initial cost of treatment for that initial payor."

11. https://www.cnn.com/2024/03/19/health/gene-therapy-orchard-mld/index.html
12. https://www.technologyreview.com/2024/03/20/1089996/there-is-a-new-most-expensive-drug-in-the-world-price-tag-4-25-million/
13. https://www.biopharmadive.com/news/orchard-fda-approval-lenmeldy-gene-therapy-metachromatic-leukodystrophy/710673/

REALITY #1

Determining Value and Prioritizing Patients Is Challenging in the United States

What Is Drug Innovation Anyway?

When it comes to pharmaceutical innovation, stakeholders in the pharmaceutical ecosystem — pharmaceutical companies, payors, pharmacy benefits managers (PBMs), employers, and patients — each have their own unique definitions and priorities.

For pharmaceutical companies, innovation often means the development of a novel therapy for a disease that currently has no treatment, or discovering new indications for an existing drug. For example, Wegovy was originally approved for weight loss, but now has a new indication for reducing heart disease risk. These companies view any progress, whether it is a brand-new drug or a new use for an existing drug, as a significant innovation.

In contrast, payors and employers are primarily focused on the pricing and cost-control aspects of innovation. While they recognize the value of new therapies, their priority is managing the financial impact these innovations have on healthcare costs. They often view innovation through the lens of affordability and cost-effectiveness, questioning whether the high prices of new drugs are justified by the benefits they offer.

Patients, on the other hand, may see innovation as a means to improve their health in ways they had not considered before. For them, innovation represents hope and the potential for improved quality of life. They value therapies that offer new treatment options, especially for conditions that were previously untreatable.

The varying definitions of innovation held by these stakeholders reflect their distinct roles and priorities within the U.S. pharmaceutical ecosystem. These differing perspectives shape the system as it currently operates, influencing how innovation is pursued, evaluated, and funded across the industry.

REALITY #1

Patient Outcomes Do Not Determine Value

Ideally, drugs that can impact many people should be widely accessible. The value of a drug should consider real-world contexts and societal benefits, including considerations of dynamic pricing, productivity, and metrics that are more difficult to measure like the value of hope.

In a free market system, however, patients are not the only beneficiaries of a drug innovation. There are investors, shareholders, and even taxpayers to satisfy. In practice, this scenario means that while patient-centricity is a priority in principle, it is often overshadowed by financial concerns.

As Figure 3 on the next page indicates, drugs are often not priced based on disease incidence rates or access concerns. The graph compares three drugs: the diabetes-turned-weight loss drug Ozempic, the MLD treatment Lenmeldy, and Casgevy. Each of these drugs could change a patient's life forever in signiciant ways, and could reduce per person lifetime healthcare costs and consumption, allowing people to live longer and more economically impactful lives. Still, decisions on price and how each of these drugs should be valued is wildly different.

> "The current pricing structure benefits some stakeholders more than others, often leaving patients as the most disadvantaged."

REALITY #1

	OZEMPIC	LENMELDY	CASGEVY
U.S. List Price	$969 (per month)	$4,250,000	$2,200,000
ICER recommendation *Health-benefit price benchmark (HBPB), a price range matching the clinical benefit a patient is expected to receive*	$6,400 - $7,100 (per year)	$2,300,000 - $3,900,000	$1,350,000 - $2,050,000
Estimated Patient Cost (With Insurance)	~ $25-$300/monthly	Unknown (too few cases)	Unknown (too few cases)
PBM Negotiated Rate	$700/monthly (*Optum PBM negotiated rate)	Unknown	Unknown
Treatment Course	Monthly, Long-term	One-time	One-time
Benefit	Weight-loss, decreased cardiovascular event risk	Reduce risk of severe motor impairment or death for children with MLD	Prevents red blood cells from turning sickle-shaped
Potential U.S. Population	~135,000,000	~ 8,000	~ 100,000

Figure 3: Comparing Ozempic, Lenmeldy, and Casgevy

REALITY #1

> "We would ideally want to make the things that are high value for patients, society, and payers free. Some things are so valuable that we should have no barrier to take them ever."

Do Some Drugs Have Such High Value to Society that They Should Cost the Patient Nothing?

According to the American Cancer Society (ACS), more than 1.9 million new cancer cases were expected to be diagnosed in 2023. The ACS estimated deaths would total nearly 610,000, or 1,670 a day(14). As Figure 4 illustrates, a February 2023 JAMA Oncology study estimated the global economic cost of cancer between 2020 and 2050 to be $25.9 trillion.(15)

Given those numbers, we ask: if a pharmaceutical company announced a cure for cancer, any cancer, tomorrow, how much should patients have to pay?

If the U.S. system only considered patient outcomes when setting price, the answer would be $0.

But no one, including panelists and members of the audience at our symposium, were comfortable saying the price should be nothing. The United States could not remain the world's leading innovator if the price for all drugs were $0.

While the price cannot be zero for a treatment, it also cannot be so high that it prevents payors from affording it and patients from accessing it. The price must be somewhere in the middle, but because the United States does not have generally agreed upon methods to determine public value, deciding fair price is a nearly impossible task.

14. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2023/2023-cancer-facts-and-figures.pdf
15. https://jamanetwork.com/journals/jamaoncology/fullarticle/2801798

1.9M

New Cancer Cases in 2023

610,000

Expected Deaths

$25.9T

Global Economic Cancer Cost

Figure 4: The economic cost of cancer.

REALITY #1

Recent History Shows How Intractable Pricing Questions Are

The Inflation Reduction Act (IRA) of 2022, which requires pharmaceutical firms to pay rebates for certain drugs to Medicare when prices increase faster than inflation, was the U.S. government's most recent major attempt at broad-based pricing reform, and political players are still fighting over it. In June 2024 letter, for example, organizations argued, "Basic economics dictates that imposing price controls on one class of products will simply force manufacturers to stop producing or investing in those products."(16)

In addition to the Medicare rebates, the IRA capped the price of insulin for Medicare Part D users.

The battle over insulin prices had been roiling for years. As Harvard Medical School and Brigham and Women's Hospital researchers explained, in the 20 years before the IRA, pharmaceutical firms increased list prices on insulin every year, resulting "in a century-old drug becoming increasingly unaffordable, even for patients with health insurance."(17)

It took years of political and public pressure for change to occur. What finally helped solve the issue? Stakeholders working together to prioritize patient outcomes. The pharmaceutical firm Eli Lilly proffered a $35 cap to policymakers. The proposal came after a two-year experiment in which the company determined that, "around $35 per month, patients would pay the required amount, and would stay on their medication." (Patients abandoned their prescriptions if costs went much higher.) The $35 is what the IRA adopted.(18)

16. https://e217a245-0934-448f-b4ac-5bb0ce3995ec.usrfiles.com/ugd/e217a2_56ef9a2b6c5546e585f5936719453731.pdf
17. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2806020
18. https://www.statnews.com/2024/06/13/insulin-cost-copay-medicare-biden-trump/

> "The most important price is the price the patient is charged, and unfortunately, we don't like to talk about how we get to that price."

REALITY #2

Drug Pricing Is a Reflection of the U.S.'s Uniquely Complex Healthcare System

The United States Is a Drug Pricing Outlier

In Europe, national health authorities negotiate prices for new drugs with manufacturers.(19) In Japan, the government does not negotiate, simply setting a price for new drugs (and offering patients reimbursement).(20) Australia uses a value-based pricing method. Under that nation's single-payer healthcare system, independent federal committees evaluate the cost effectiveness and utilization data for drugs seeking to be covered under the Pharmaceutical Benefits Scheme (PBS), and recommend a price. If the manufacturer does not agree to this price, the drug is either not approved or approved with access restrictions.(21)

In the United States, drug prices are determined through chaotic interplay between manufacturers, PBMs, payors, providers, and policymakers. Each stakeholder has their own priorities and motives, leading to a system where prices are not only difficult to predict, but also often disconnected from the actual value of the drug. This multi-layered process also can result in access issues for patients.

One panelist referred to this system as "hilariously American," meaning it is complex and sometimes even absurd.

19. https://jamanetwork.com/journals/jama-health-forum/fullarticle/2799713
20. https://healthadvances.com/insights/blog/drug-pricing-in-japan-the-changing-landscape-and-future-prospects
21. https://www.americanprogress.org/article/value-based-pricing-prescription-drugs-benefits-patients-promotes-innovation/

> "What we have is a hilariously American healthcare system."

REALITY #2

> “For patients, it mainly comes down to what insurance card you have in your pocket.”

No Single Stakeholder Believes They “Win” in the Current Pricing System, but Patients Clearly Lose

The U.S. system leads to wide disparities between what Americans pay for drugs, and what their counterparts in other countries pay. A 2022 analysis found:

- U.S. prices were 256% of those in the 32 comparison countries.
- U.S. prices ranged from 170% of prices in Mexico to 779% of prices in Turkey.
- The gap between U.S. and other countries’ prices was larger for brand-name originator drugs.
- U.S. prices were 190% of prices in other countries after adjusting U.S. prices downward to account for rebates and other discounts.(22)
  - For example, Wegovy’s U.S. list price is $1,349/month. In the United Kingdom it is $92/month and in Denmark(23) it is $186/month.

There are pricing disparities domestically too since the prices patients ultimately pay depend on how well employers negotiated with their preferred insurer and how well insurers negotiate with pharmacy benefit managers (PBMs) — who, on occasion, are owned by the same parent company as the insurers who work with them on pricing.

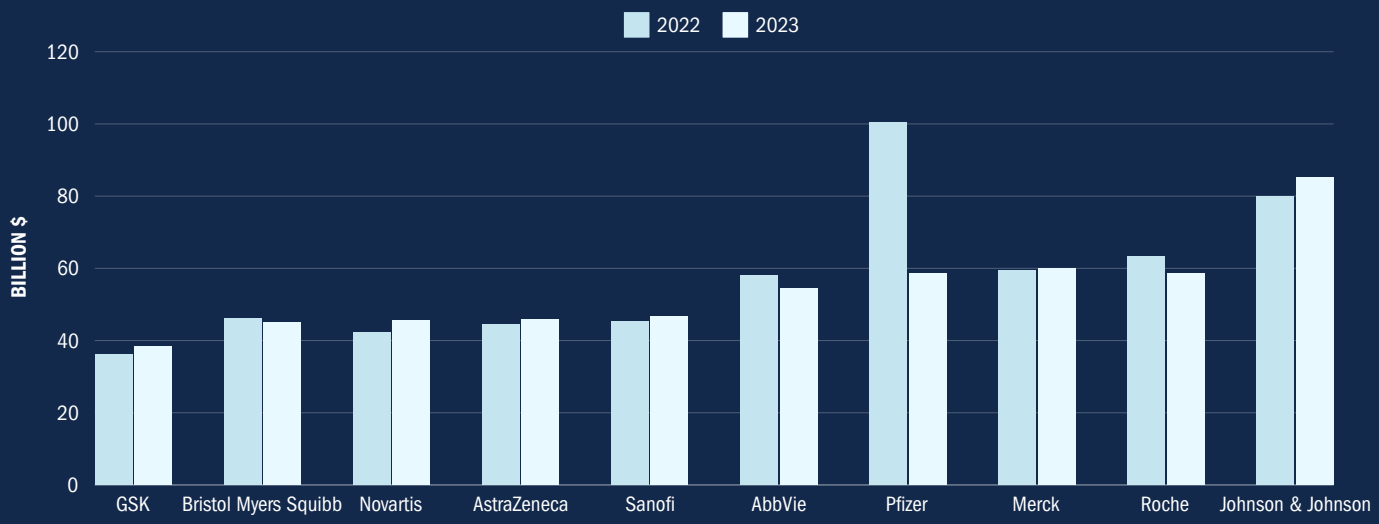
This current system leads to significant inequities since the patient price largely depends on the insurance card they carry in their wallet, and who their employer is or is not. Patients that are insured by a community payor or have coverage through a smaller employer, are more likely to pay more. The more complex the system becomes, the more it benefits those who can navigate it while leaving those who cannot at a disadvantage.

Meanwhile, as Figure 5 on the next page shows, payors, PBMs, and drug manufacturers are raking in huge revenues and gaining market share.

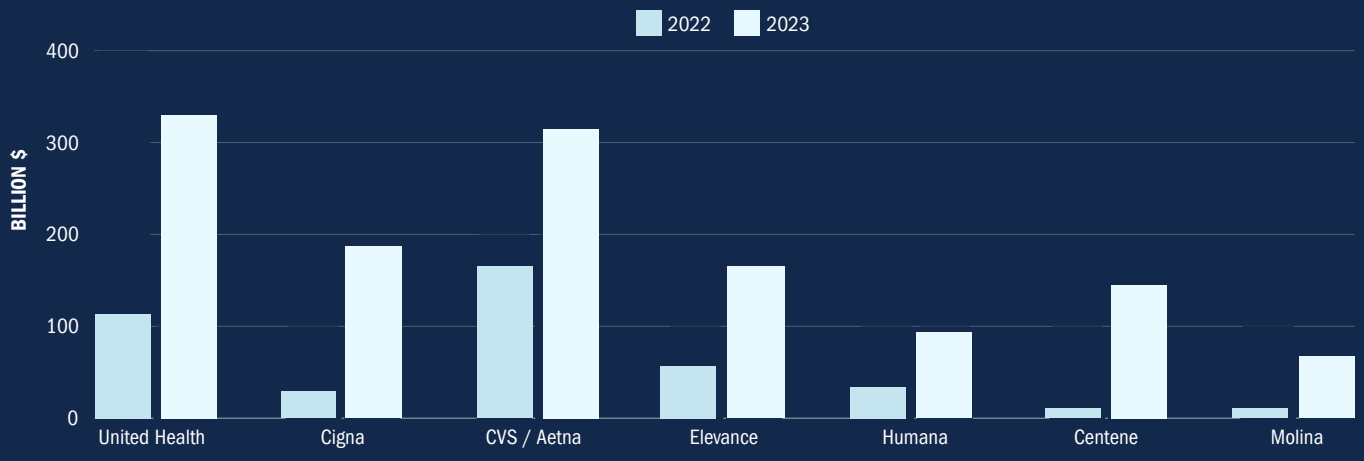
22. https://aspe.hhs.gov/reports/international-prescription-drug-price-comparisons
23. https://www.statnews.com/2024/07/23/wegovy-medicare-medicaid-costs-why-not-buy-manufacturer-novo-nordisk/

REALITY #2

Global Top 10 Companies 2022 and 2023 Profits



Total Insurer 2012 Revenues Compared to Total 2022 Revenues



[Figure 5: Patients lose, but drug makers, payors, and PBMs profit. Potential resources: https://tinyurl.com/d2zcfnwt, https://tinyurl.com/v6fcwkby, https://tinyurl.com/4w5htpke, and https://tinyurl.com/mrs7tth8]

REALITY #3

Maneuvering by Stakeholders Has Increased Complexity

Private Sector Complexity and Policy Shaping Make the System Less Transparent

While patient prices vary significantly due to factors like insurance coverage, employer, and geography, other factors also matters.

Pharmaceutical manufacturers set initial prices, but other players in the value chain influence the process. The maneuvers often include:

- Manufacturer (copay) coupons: issued by the pharmaceutical company for a particular brand name drug; can be used to reduce patient copays.
- Prescription discount cards: a savings card from a third-party company (not an insurance provider or drug manufacturer).
- Prescription discount coupons: issued by PBMs and cannot be used to reduce copay.
- Rebates: PBMs secure rebates from drug manufacturers in return for granting the manufacturers' drugs preferred status on a health plan's formulary.
- Large associations and lobbying bodies that represent various parts of the industry do the work of "policy shaping" on behalf of their corner of the healthcare market.

Each of these factors complicates the pricing discussion, reduces transparency, and makes it difficult to determine the actual patient cost of drugs. Employers, for example, are often unaware of the net price of drugs because they rely on rebate checks. The lack of a "real price" sustains the complex pricing system, exacerbating challenges for all stakeholders.

> "Everyone is addicted to rebates."

REALITY #3

Vertical Integration Raises Prices

In recent years, payors and PBMs have increased their strength against pharmaceutical manufacturers through vertical integration. As an August 2023 study of Medicare Part D found, vertically integrated insurers' market share increased from about 30% to 80% between 2010 and 2018. The study also looked at a large insurer-PBM mergers in 2015 to assess the trade-offs of vertical integration–harms to competition due to input and customer foreclosure on the one hand and improved efficiency on the other. It identified premium increases after the merger for insurers who bought PBM services from rivals, which is consistent with vertically integrated PBMs raising costs through input foreclosure.(24)

> "There is no notion of real price."

As Figure 6 shows, these mergers mean payors and PBMs, along with healthcare providers, often are all part of the same corporation that answers to the same shareholders. What remains is a system where patients are disproportionately affected by high out-of-pocket costs, leading to issues like drug abandonment and the inability to adhere because of the price of a drug.

As part of a two-year long inquiry, in July 2024 the U.S. Federal Trade Commission released a report(25) that detailed how vertical integration and consolidation has enabled the three largest PBMs, CVS Caremark Rx, Express Scripts, and OptumRx, to control nearly 80% of the approximately 6.6 billion prescriptions filled in the country. The report also found pharmacies affiliated with the three largest PBMs took in nearly $1.6 billion in excess revenue over three years on two cancer drugs by reimbursing their own pharmacies at much higher rates than unaffiliated ones. At the time our report went to press, it was expected the FTC would soon announced a lawsuit against those companies.

Figure 6. This visual is reprinted from https://www.drugchannels.net/2024/05/mapping-vertical-integration-of.html

24. https://www.nber.org/papers/w31536
25. https://www.ftc.gov/system/files/ftc_gov/pdf/pharmacy-benefit-managers-staff-report.pdf

REALITY #3

Policymakers Layer on Complexity

As Figure 7 shows, U.S. retail prescription drug spending exploded by 91% between 2000 and 2020. RAND estimates it will continue to rise by 5% each year through at least 2030. U.S.(26) policymakers have been working for years to arrest rising prices, but these efforts can complicate the system even further, leading to additional disparities.

In January 2024, for example, the U.S. Food and Drug Administration (FDA) announced it would allow the state government of Florida to import certain prescription drugs from Canada, saving patients and taxpayers there $183 million a year.(27) Florida is the only state to have won this approval from the FDA, meaning this program will result in wider disparities between the prices Florida residents and residents of other states pay.

Federal lawmakers also have proposed to alter the system for drug patents. While lawmakers have not approved a comprehensive package of reforms, the 2022 Inflation Reduction Act (IRA) contains what some researchers have called implicit (or "cryptic") patent reform.(28) Under the IRA, if a small molecule drug is selected for price negotiation, the period of market exclusivity drops from 13 years to 9.(29) Venture capital firms have argued that, because biologics were exempt from this provision, it creates a disparity in the marketplace that will influence investment.(30)

The increasing threat of government oversight also influences drug prices. Internal documents show that. when setting list prices, one pharmaceutical firm considered how high they could set a price without attracting the ire of lawmakers, and a possible congressional hearing.(31)

278% HIGHER

U.S. vs. Global Drug Prices

91% RISE

U.S. Drug Spending, 2000-2020

$183M SAVED

Florida Drug Imports Annually

Figure 7.

26. https://www.rand.org/pubs/research_reports/RRA788-3.html
27. https://www.flgov.com/2024/01/05/florida-becomes-first-in-the-nation-to-have-canadian-drug-importation-program-approved-by-fda/
28. https://repository.law.umich.edu/cgi/viewcontent.cgi?article=1366&context=law_econ_current
29. https://healthpolicy.usc.edu/research/mitigating-the-inflation-reduction-acts-potential-adverse-impacts-on-the-prescription-drug-market/
30. https://www.biospace.com/article/ipm2024-ira-favors-biologics-over-small-molecule-drugs-and-hurts-innovation-say-industry-analysts
31. https://www.finance.senate.gov/imo/media/doc/3%20The%20Pricing%20of%20Sovaldi%20%28Section%203%29.pdf

REALITY #4

Innovation Places a Disproportionate Burden on Payors and Employers

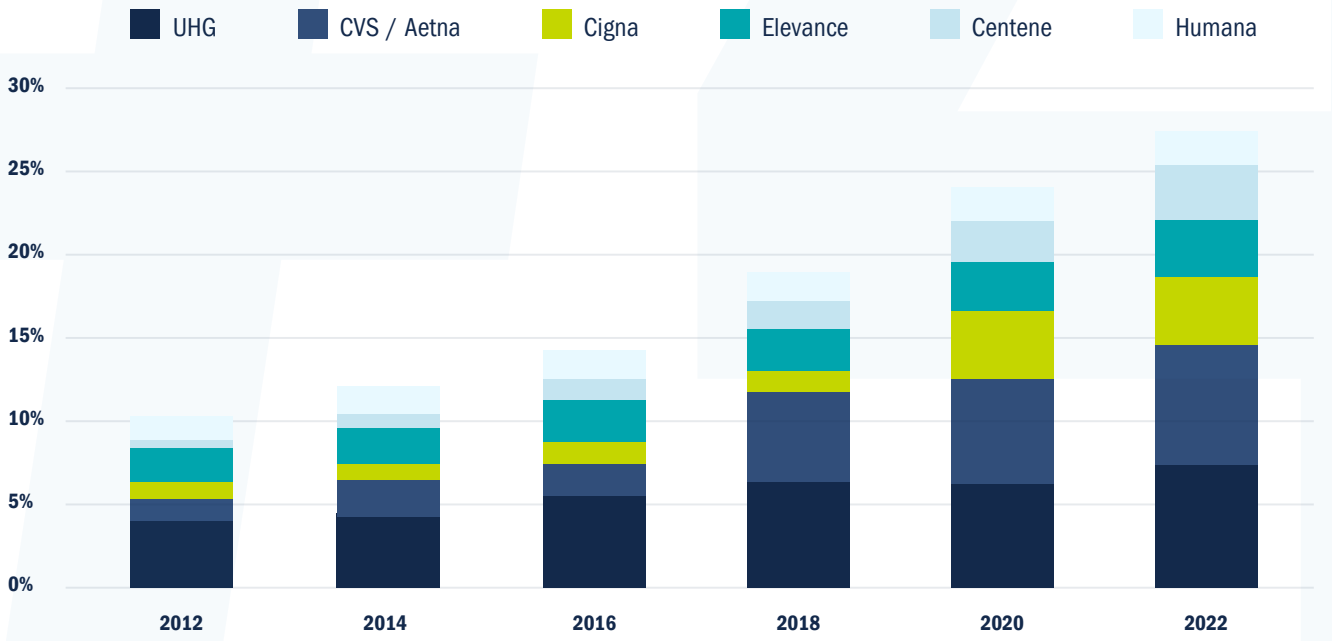
Insurers Still Profit, but Innovation Presents a Dilemma

Hemgenix is a gene therapy treatment for hemophilia that could save the U.S. health care system about $6 million per person treated.(32) As Figure 8 demonstrates, insurers are running huge profits. They should cover Hemgenix … right?

The problem is that the drug comes with a price tag of $3.5 million. An insurer that shoulders the price for this treatment is unlikely to reap the lifetime economic benefits since Americans cycle through multiple insurance plans throughout their lifetimes.

The child covered right now will grow into an adult likely covered by another payor. So, how do you convince a payor to shoulder the burden of a multi-million dollar treatment when that patient may not be their customer within the next year, much less 10?

32. https://www.scientificamerican.com/article/3-5-million-hemophilia-gene-therapy-is-worlds-most-expensive-drug/



REALITY #4

Innovation Could Bankrupt Employers, Especially Small Firms

In the United States, health insurance usually comes with a job. While employees pay a portion of their health insurance premiums, as Figure 9 shows, employers shoulder the largest portion. That is why employer and insurer price negotiations are a delicate dance, with insurers passing on as much risk and cost as they can to companies that insure their employees.

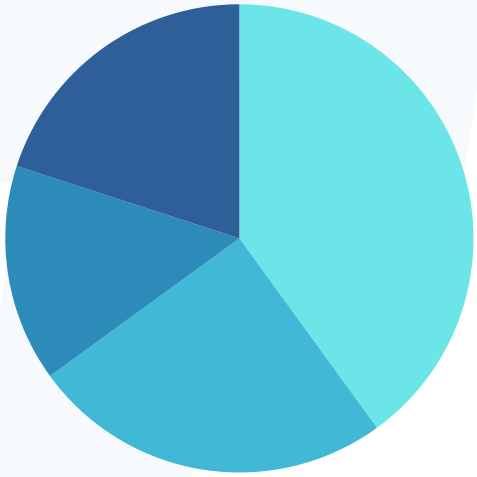
In recent years, insuring workers has become even more expensive for employers. The average annual premium for employer-sponsored health insurance in 2023 was $8,435 for single coverage and $23,968 for family coverage, a 7% increase from 2022. Over the last five years, the average premium for family coverage rose 22%.(33)

The smaller the employer, the more of the bottom line that is subsumed by health insurance premiums. A June 2024 JP Morgan Chase study found that for organizations with annual revenue totaling less than $600,000, insurance premiums were about 12% of payroll expenses. For firms averaging more than $2.4 million in revenue, premiums were about 7% of payroll expenses.(34)

Higher drug prices are one reason for these increases, and employers understand this fact. According to the nonprofit Business Group on Health's (BGH) 2024 Large Employers' Health Care Strategy and Plan Design Survey report, 92% percent of employers are concerned or very concerned about high-cost drugs in the pipeline. BGH said these worries are "well-founded" since employers experienced an increase in the median percentage of healthcare dollars spent on pharmacy, from 21% in 2021 to 24% in 2022.(35)

Figure 9.

Average Breakdown of Employer Healthcare Costs



Insurance Premiums: The largest slice, driven by rising healthcare prices and increased demand for medical services. A focus area for potential savings through better negotiation strategies with providers.

Direct Healthcare Costs: Significant due to chronic disease management and specialized treatments. Opportunities for savings might include wellness programs to reduce the incidence of chronic conditions.

Innovation Costs: Investments in R&D and technology may be costly upfront but are aimed at long-term savings through more effective treatments and preventive care.

Administrative Costs: Although necessary, optimizing administrative processes and adopting automated systems could reduce these expenditures.

33. https://www.kff.org/report-section/ehbs-2023-summary-of-findings/
34. https://www.jpmorganchase.com/institute/all-topics/business-growth-and-entrepreneurship/small-business-health-insurance-burdens
35. https://www.businessgrouphealth.org/resources/2024-large-employer-health-care-strategy-survey-executive-summary

CASE STUDY:

No One Can Afford Glucagon-Like Peptide-1 (GLP-1) Drugs

Glucagon-like peptide-1 drugs, or GLP-1s, were initially developed for diabetes, but gained recognition for their weight loss benefits starting in the 1990s. The popularity surged with Ozempic in 2017, initially marketed for Type 2 diabetes with weight loss as a side effect.

As of May 2024, about 12% of Americans(36) have tried a GLP-1. More than 73% of Americans (37) are considered overweight or obese, so tens of millions more may be taking them soon, presenting a price times volume problem for which lawmakers, payors, and employers are not prepared.

The enormous market for these drugs means that, as a of mid-2024, there were more than 100 GLP-1s in development, many of which have attracted significant venture capital funding. The number of companies offering diabetes and obesity solutions also has increased from 432 in 2023 to more than 700 today, again reflecting the market's rapid expansion. Many of the drugs are similar, so their manufacturers will try to find new approval pathways.

This competition may eventually lower retail prices and improve access. But for now, at an average price of $1,000 a month per patient, who will — or even is able to — pay for these treatments, especially if this is a cost that patients, insurers, and employers have to bear over the entire span of an individual's life?

State governments have admitted they cannot shoulder the burden(38) while some insurers are retracting coverage.(39) Employers use strategies like step therapy, prior authorization, and limiting quantity to manage costs, which can act as barriers to access. Affordable Care Act (ACA) marketplaces are not covering GLP-1s,(40) and before taking a first step to allowing Medicare to cover GLP-1s, a panel of federal lawmakers narrowed the scope of patients who would be eligible for coverage to only those who were qualified as obese. (Originally, the bill, which, as of July 2024 had not been considered by either chamber of Congress, would have allowed coverage for individuals who are overweight.)(41)

It is likely that public and private payors will have to do what that panel of lawmakers did: limit coverage. But patients, who are already eagerly asking their primary care doctors for GLP-1 prescriptions, will fight back. In fact, they already have, using the Americans with Disabilities Act to claim that insurers must pay for drug that help them with their obesity.(42)

> "GLP-1s bring up the question of if payors should pay for lifestyle drugs and is the high cost a responsible investment for what it will do to healthcare expenses and total costs."

36. https://www.kff.org/health-costs/poll-finding/kff-health-tracking-poll-may-2024-the-publics-use-and-views-of-glp-1-drugs/
37. https://www.niddk.nih.gov/health-information/health-statistics/overweight-obesity
38. https://www.nytimes.com/2024/06/25/health/obesity-ozempic-wegovy-west-virginia.html
39. https://www.fiercehealthcare.com/payers/blue-cross-blue-shield-michigan-pulling-back-glp-1-coverage
40. https://www.kff.org/affordable-care-act/press-release/costly-glp-1-drugs-are-rarely-covered-for-weight-loss-by-marketplace-plans
41. https://www.beckerspayer.com/policy-updates/house-committee-considers-limited-medicare-coverage-of-weight-loss-drugs.html
42. https://www.themainewire.com/2024/06/maine-woman-files-sues-insurance-company-that-wont-pay-for-ozempic-claims-obesity-a-disability/

REALITY #5

If There Is a Path Forward, It Will Require More Transparency and Fairer Tradeoffs

Public Policy May Have Limited Impact on Prices

Asking the question, "What is the price we pay for pharmaceutical innovation?" has confounded policymakers for years. Government intervention like Centers for Medicare and Medicaid Services (CMS) regulations, the 340B program, drug importation, and the 2022 Inflation Reduction Act (IRA) benefit some players in the value chain while creating challenges for others. There are always tradeoffs.

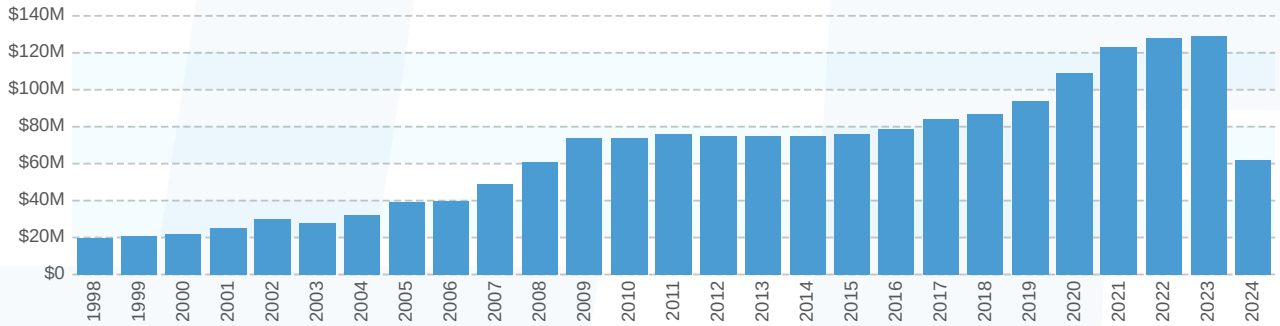
Ultimately, these policies are temporary fixes, and do not address underlying systemic issues, including concerns about equity and access. The IRA, for example, which selects the top 50 gross spending drugs for price negotiations, does not account for net spending or the long-term impact on drug availability and innovation. And while the U.S. House and Senate are examining how to reform the practices of key players like PBMs, it is likely that reform will not make a significant impact on the price of drugs in the United States. (Research also suggests the IRA has potential to delay the launches of new medicines.)

There also is this fact: as Figure 10 shows, stakeholders are increasingly focused on shaping policy in response to legislation like the IRA and the dialogue surrounding PBMs. These firms are actively seeking to shape policy dialogue and regulatory frameworks to better fit their needs — with patient needs too often landing in the periphery.

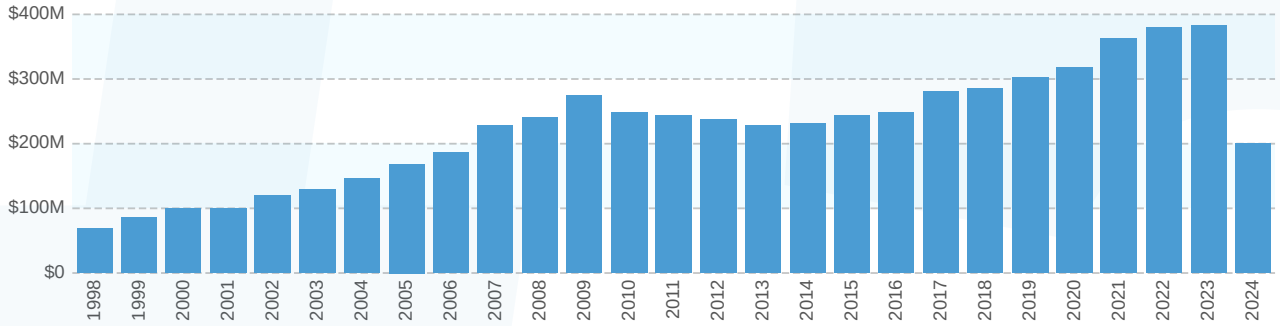
REALITY #5

Annual Lobbying on Health Services/HMOs

Figure 10: Insurers spent almost $130 million on federal lobbying in 2023 and pharmaceutical and health product firms shelled out nearly $385 million.



Annual Lobbying on Pharmaceuticals/Health Products



> “This [gene therapy] is pretty much the science fiction we were all hoping for growing up, and I’m really worried we’re about to screw it up.”

REALITY #5

More Frameworks for Pricing are Needed

The question of whether there is a true 'fair' price for innovative pharmaceutical treatments raises concerns about health benefits-to-pricing ratios, fair access, and sustainable innovation practices.

The Institute for Clinical and Economic Review (ICER) is one entity that attempts to balance each of these elements. It has developed a Value Assessment Framework(43) for assessing what the fair prices of drugs should be. Assessments include a clinical evidence review of all available data, an understanding of the patient perspective, comparative clinical effectiveness research, long-term effectiveness analyses, potential benefits, and other considerations. ICER also considers how much longer a patient would live, the quality of those years (QALY), and how much should be paid for each year of health gain.

Figure 11, found on the following page, provides examples of ICER's work, showing instances where the manufacturer's price largely matched with ICER's assessments, along with innovations for which there was a large gulf between the two. The graphic demonstrates ICER attempts to find the "best" price for all stakeholders.

The pharmaceutical industry has historically used an approach to pricing that asks what the return on investment and cost of capital would be. Public discourse has shifted with the advent of entities like ICER, prompting questions about individual and societal value. To accelerate this shift, the country needs ICER and other entities, including experts in ethics and health equity, who can evaluate price questions through perspectives beyond just economics and business. Practicing clinical leaders who interface with patients everyday should also be represented in these analyses and debates.

43. https://icer.org/our-approach/methods-process/

REALITY #5

Price Benchmarks (Non-Gene Therapy Examples)

Assessment	Drugs	Discount Needed
Pulmonary Arterial Hypertension	Winrevair	85-93%
Alzheimer's Disease	Leqembi	19-66%
Rheumatoid Arthritis	Rinvoq	25-26%
Asthma	Xolair, Nucala, Cinqair, Fasenra, Dupixent	62-80%
Treatment-Resistant Depression	Spravato	25-52%

Assessment	Drugs	Discount Needed
NASH/MASH	Rezdiffra	0%
Cardiovascular Disease	Xarelto	0%
Migraine	Nurtec, Ubrelvy	0%
Obesity	Wegovy	0%
Hemophilia A	Hemlibra	0%

ICER 10

Price Benchmarks (Gene Therapy Examples)

Assessment	Drugs	Discount Needed
Spinal Muscular Atrophy	Zolgensma	0%
CAR-T for Leukemia and Lymphoma	Yescarta and Kymriah	0%
Beta-Thalassemia	Zynteglo/LentiGlobin	1-24%
Metachromatic Leukodystrophy	Lenmeldy	7-46%
Sickle Cell Disease	Casgevy	7-39%
Sickle Cell Disease	Lyfgenia	34-56%

ICER 10

CASE STUDY:

Rapid Deployment of COVID-19 Vaccine Shows What Happens When Stakeholders Collaborate

The complexity of the U.S. healthcare system, with its high costs and poor outcomes, necessitates a focus on solutions that ensure equitable access to high-value treatments for all patients.

There is one instance during which all stakeholders, pharmaceutical firms, investors, policymakers, government, and insurers, all came together to produce treatments that were subsidized at no-cost, effective, and widely available to the American public in a time of need. Stakeholder coordination and transparency during the COVID-19 pandemic demonstrated potential for collaborative success when it comes to drug pricing and rapid innovation.

The result? In early 2021, more than 300 million COVID-19 vaccine doses were given over the span of just 150 days.(44) The vaccines were free to anyone for whom the U.S. Food and Drug Administration had approved their use, and the innovators who developed the drug still added to their bottom lines.(45) Additionally, the United States has donated nearly 700 million COVID vaccine doses to countries across the globe.(46)

Instances like this one, in which all stakeholders collabortated to prioritize public health, should be the norm, but it remains to be seen if pricing and innovation can find balance within the U.S. system.

44. https://www.whitehouse.gov/briefing-room/statements-releases/2021/06/18/fact-sheet-300-million-shots-in-150-days-the-presidents-covid-19-strategy-is-delivering-for-americans/
45. https://www.fiercepharma.com/pharma/top-20-pharma-companies-2022-revenue
46. https://www.state.gov/covid-19-recovery/vaccine-deliveries/

CONCLUSION

Addressing the complexities of drug pricing in the United States requires a transparent and equitable approach that acknowledges the intricacies of a uniquely complex healthcare system.

As stakeholders navigate the competing interests of pharmaceutical companies, payors, and patients, it becomes evident that the desire for comprehensive access, high-quality care, and continuous innovation often conflicts with the realities of cost management. While policies like the Inflation Reduction Act and efforts to reform PBM practices offer partial solutions, they fall short of resolving the systemic issues at play.

To move forward effectively, a framework that balances fairness and transparency is needed, incorporating diverse perspectives beyond mere economics. The challenge is finding a pricing strategy that mitigates the inequity of tradeoffs, where patients often bear the greatest burden. As a more cohesive approach is sought, it is crucial to recognize and address these inherent tradeoffs, ultimately working toward a system that meets the diverse needs of all stakeholders without sacrificing patient access and affordability.