McKinsey & Company

Helix

Rewiring the DNA for the next wave of impact in biopharma

September 2022

Contents

1 Stepping back to leap further

A look back: The biopharma industry has been shaped by five fundamental forces that are now signaling a critical turning point

While multiple factors have influenced the growth and structure of the industry, we believe five have been the most impactful:

1. Evolving patient needs

2. Regulatory frameworks for drug approval and IP protection

3. Breakthroughs in scientific understanding and technology

4. Market access and pricing environment

5. Capital availability and sources of innovation

In this brief introduction, we describe how these forces have shaped the industry and draw lessons from those events.

Exhibit 1 charts examples of how each force has affected the shape and direction of the industry over the years:

1. **Evolving patient needs:** Therapeutic innovations and improvements in healthcare have shifted patients' mortality and morbidity burdens from infectious diseases to chronic lifestyle diseases, and most recently to cancer, immunology and age-related disorders, with the industry shifting rapidly to address these patient needs as they emerge. Patient advocacy has raised awareness and mobilized the industry to meet underserved needs, such as treatments for rare diseases.

Exhibit 1

A brief history of the five forces shaping the biopharma industry

	Pre-1980s	1980 – 1995
Evolving patient needs 	Early focus on infectious diseases and symptomatic needs **1923:** Discoveries of insulin **1928:** Discovery of penicillin **1977:** Tagamet, the first blockbuster, is released to treat heartburn	Innovation addresses population level diseases while Food and Drug Administration (FDA) is urged to focus more on rare diseases **1980s:** Patient Advocacy Groups like ACT UP form to increase access to rare disease therapies **1984:** First statin for high cholesterol, Lovastatin, is released **1987:** First SSRI for depression, Fluoxetine, approved by the FDA
Regulatory frameworks 	Foundations of regulatory framework begin being laid **1938:** The Federal Food, Drug and Cosmetic Act requires manufacturers to show that drugs are safe before bringing them to market **1962:** Kefauver-Harris Amendment passes after thalidomide disaster, mandates "proof of efficacy" through well controlled studies, mainly RCTs before new drug approvals	Regulation begins to promote medicine for rare diseases **1983:** Orphan drug act is approved **1984:** Hatch-Waxmen act is passed, creating a new regulatory pathway for generic medicines while also providing a period of data exclusivity for innovators and restoring patent life lost during federal approval
Breakthroughs in science understanding & technology 	New technology lays foundation for future of medicine **1796:** Basis for vaccination is discovered in smallpox **1881:** Louis Pasteur created the first vaccine for anthrax **1972:** Invention of recombinant technology lays the foundation for biologics therapy and basic mechanism for research	The golden age of small molecules **1982:** Humulin, first commercial recombinant insulin, is launched **1995:** GPCR drugs reach more than 25% of compounds by 1995
Market access and pricing environment 	Access begins being codified into international standards **1946:** World Health Organization includes right to health in constitution **1978:** WHO releases Model List of Essential Medicines	The rise of Pharmacy Benefit Managers (PBMs) creating new access pressures for pharmacos **1995:** PBMs become a significant player in the ecosystem as drug prices rise, managing 60M patients in 1989 to 100M by 1995, and thus create pathways for low cost therapy
Capital availability and sources of innovation 	Industry grows from apothecaries and pharmacies; many of today's top 15 companies go public in first half of 20th century **1688:** Merck formed from an apothecary in Germany **1849:** Pfizer founded in the USA as a chemical business **1863:** Bayer, initially a dye and chemical company, discovers medical uses for products	Venture capital funds the first generation of biotechs **1980:** Emergence of biotech companies (e.g., Amgen, Biogen, Genentech, Genzyme, and Regeneron)

Source: PharmaProjects, EvaluatePharma, WHO, American Chemical Society, CDC, Cambridge.org, NY Times, LA Times, EMA, Diabetes.org, GAVI, WHO, Yahoo Finance, Congress.gov, FDA, Press search, Academic literature, Company websites

1995 – 2010

First wave of orphan approvals with 100+ coming from the FDA, while population level disease medicine remain popular

1995: Pulmozyme, first drug specifically for Cystic Fibrosis, is released to the market

2010: 4 out of the top 5 revenue generating drugs are for population-level diseases (Lipitor, Advair, Plavix, Avastin)

Rise of regulatory organizations around the world

1995: European Medical Agency founded

1998: China's State Drug Administration is established

The first wave of biologics arrive in monoclonal antibodies and recombinant proteins

1997: Antibody Rituxan, is launched

2003: Human Genome Project is completed which helps unlock the next wave of therapeutics targeting genetic diseases

Global organizations form to improve vaccine access

2000: The GAVI vaccination alliance is formed to improve vaccine access in low-income countries

2010: Access to generic drugs increases as global sales reach ~$60B

Biotech boom continues as these companies become large producers of various compounds

2005: Nearly two thirds of all compounds are being developed by companies outside of the top 15

2010 – 2020

Oncology research rises in the US, EU, and China

2013: China is conducting nearly twice as many oncology clinical trials as any other therapeutic areas

2020: 2 out of the top 3 revenue generating drugs are oncology focused (Keytruda, Revlimid)

FDA creates avenues to accelerate approvals with potentially substantive jumps in outcomes

2012: Congress approves the FDA Safety and Innovation Act that allows the FDA to expedite breakthrough therapies

2017: China joins ICH

2018: FDA drug approvals with biomarkers reached more than 50%

Industry introduces medicines that act as functional cure for diseases including immuno-oncology assets that represent one of the biggest single-step changes in cancer care

2017: Immuno-oncology asset, Kymriah released to treat B-cell Acute Lymphoblastic Leukemia with 86% success rate

2019: Harvoni is released to treat Hepatitis C with a 94% success rate

World organizations continue to expand access

2015: WHO adds ground-breaking treatments for various diseases, including hepatitis C, to its Model List of Essential Medicines

External funds spur the next phase of innovation

2021: IPO funds grow more than 3X from 2019 to 2021, reaching ~24B, while VC funds double in the same time period, reaching $38B

Industry raises ~$65B from biopharma IPO funds and ~$130B from VC funds over the course of the decade

2020 – Present

Pandemic brings the industry front and center

2021: Industry innovates against the COVID pandemic by developing a vaccine within a year of the beginning of the pandemic and delivering 10B+ doses globally

Legislative focus on real world evidence (RWE) and equity in clinical trials

2016: 21st Century Cures Act increases focus on RWE

2021: Diverse Trials Act is introduced in congress

New wave of technologies and modalities allow the creation of innovative vaccines

2020s: Industry combats COVID-19 pandemic with the development of new technology (e.g., mRNA, AV vaccines). Next frontier of innovative modalities appear (e.g., Silencing RNA)

COVID highlights the importance of access

2020s: COVID vaccine access across the world becomes a top priority

China's biotechs begin to mature

2021: Valuations of Chinese biotech companies reach $380B, up from $3B in 2016 with innovative therapies produced by multiple companies (e.g., BeiGene, Hutchmed, Legend)

2. **Regulatory frameworks:** A handful of landmark regulatory changes fundamentally shaped how the industry operates. Clearer approval criteria, for example, paved the way for innovations, and the gold standard of randomized control trials (RCTs) laid the groundwork for safer and more efficacious therapeutics. Broad IP protection has allowed the industry to make substantial investments to bring new therapeutics to market, while creating a pathway for scaling impact through generics and biosimilars. Other regulations such as breakthrough designations, "accelerated approval" mechanisms, and special treatment for orphan and rare diseases, have given companies incentives to invest in areas of great need.

3. **Breakthroughs in scientific understanding and technology:** Advances have occurred in three main areas: 1) understanding the biological basis of disease, such as with receptor biology and immuno-oncology; 2) new modalities such as monoclonal antibodies and CAR-T that expand the universe of targets and diseases that can be addressed; and 3) fundamental technology and tools that support drug development and manufacturing, from recombinant DNA and PCR to whole-genome sequencing and high-titer cell culture production.

   The discovery of penicillin ushered the age of anti-infectives; research in underlying disease mechanisms and modulation of a small family of receptor targets fundamentally shaped the direction of cardio-metabolic treatment. Large molecule science—proteins and mAB—ushered in entirely new ways of treating many diseases, particularly cancer. The genomic revolution that began after 2000 created a new world of personalized therapies linked to specific gene mutations.

4. **Market access and pricing environment:** The biopharma industry aims to help as many people as possible live longer, healthier lives, but innovation has long been influenced by access and pricing regimens. Historically, the industry benefited from relatively open access for new products—even late followers in a given therapeutic class had a real chance of success. As standards of care improved, generics became available, and innovation outpaced the health system's capacity to pay, biopharma companies faced more restricted access and constrained pricing. In response, many pursued innovation in oncology, rare diseases and other areas and geographies, especially the United States, where access and pricing are more favorable. Meanwhile, public health organizations such as GAVI, CEPI and WHO have helped steer the industry towards global priorities and created COVAX and other mechanisms to improve access in developing regions.

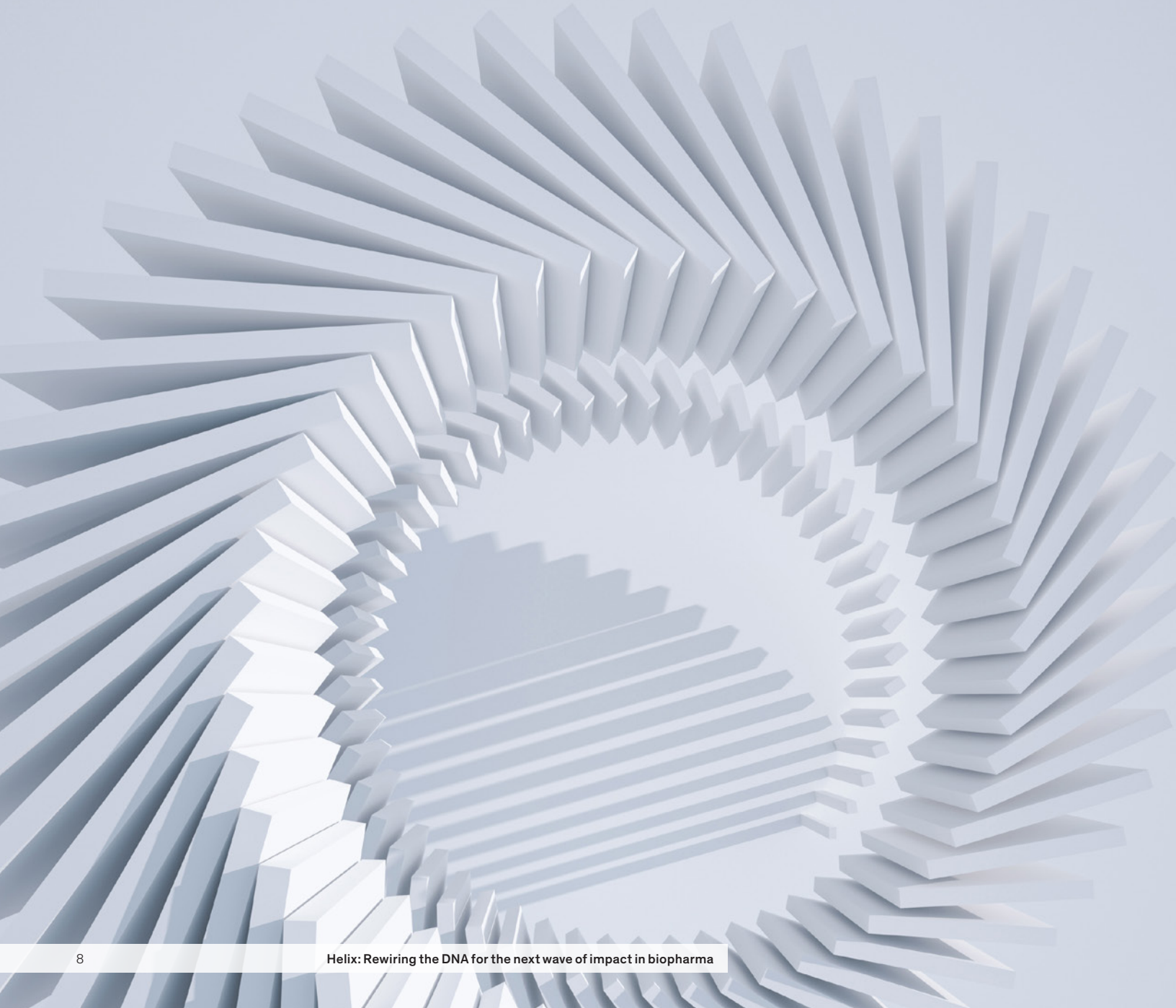
5. **Capital availability and sources of innovation:** Despite waves of consolidations and M&A, the industry's fundamental structure and concentration have remained constant, with few changes in the list of top 15 companies and only a gradual decline in concentration of revenue pools in those companies. The sources of innovation that feed the industry has substantially changed, however. The availability of private and public capital has expanded the number of

biotech companies pursuing drug discovery—over 2000[1] public companies are active in drug discovery and development, representing about 80 percent of the innovation pipeline.[2] More of these companies are being founded outside the US, EU5, and Japan, with China emerging as an important source of innovation for the industry and many other regions stepping up investments. Top pharmacos have also used their legacy cash flows to augment organic innovation pipelines through in-licensing and acquisition—internally originated therapies account for only about 55 percent of the pipelines of the top 15 companies by revenue.[3]

That's the look back. The push, pull, and interaction of these forces have continually changed the environment where the industry operates, creating new opportunities and complexities. The industry has continually adapted to deliver holistic impact for patients, healthcare providers, investors, and society at large. In the following sections, we showcase recent examples of industry impact while calling out potential gaps, setting the stage for key questions for leaders in biopharma as they aspire to build on and expand their impact in the decades ahead.

[1] CAPIQ.
[2] Pharmaprojects | Informa, 2022; McKinsey analysis of innovation pipeline.
[3] Ibid.

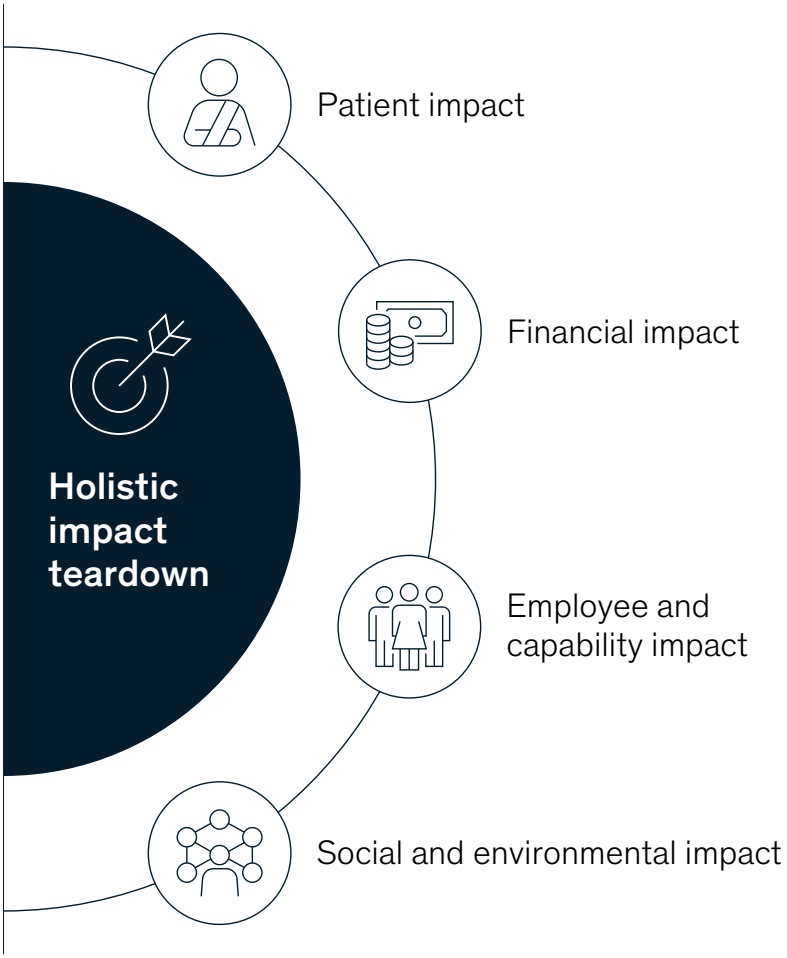
2 Taking stock of biopharma's impact over the past decade: A holistic impact teardown



The biopharma's industry impact is often assessed primarily through a narrow financial lens by industry observers and even the management teams of the companies themselves. For a more balanced perspective, we consider the industry's impact across multiple dimensions: patient, financial, employee & capability, and social & environmental (Exhibit 2). There is a lot to be proud of across these dimensions—at the same time, we see areas where ambition for impact could be raised even further.

Exhibit 2

We assessed the industry's impact through a holistic lens.



Patient impact

500+

NMEs approved in the last 10 years in the US

Source: FDA (CDER and CBER)

The pursuit of patient impact is the reason the biopharma industry exists, and why so many talented people around the world make their careers there. They have much to be proud of.

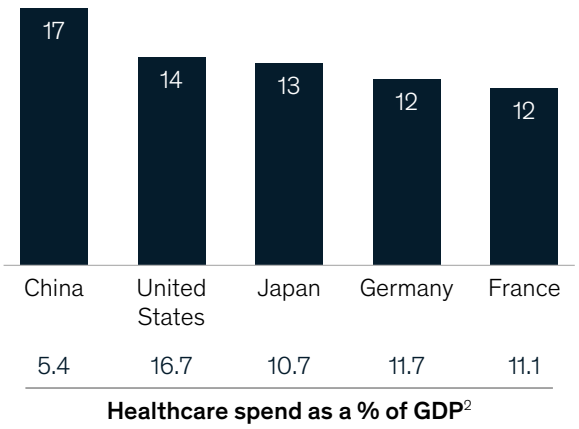
In the past 10 years, immunotherapies have become the mainstay of treatment for many cancers, most cases of hepatitis C have become curable, and multiple sclerosis now has disease-modifying treatments.[4] Vaccines can now dramatically reduce the risk of shingles. These are just a few examples of the transformative impact of biopharma innovation. In the last decade, more than 500 new molecular entities have been approved by the FDA and other global bodies to treat a wide range of diseases, many of which had poor or no standards of care.[5] Over half of these approved molecules were first in their class, evidence that the industry is consistently bringing new science to market.

The industry has delivered these innovations without increasing its relative share of healthcare spend, which has been stable at about 14 percent over the past ten years (Exhibit 3), while overall healthcare spend has gone up at about 4 percent a year.[6]

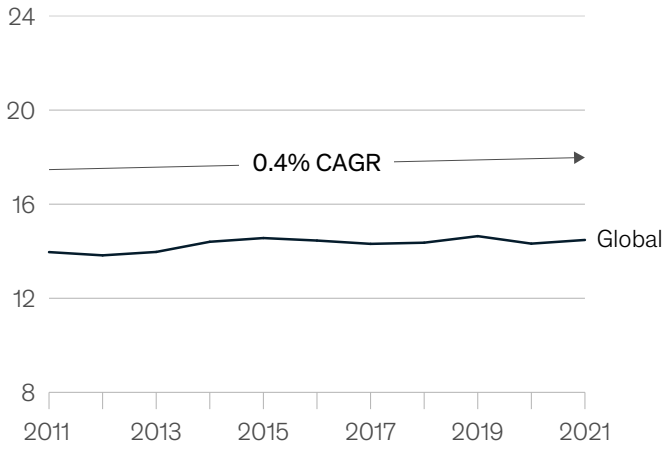
Exhibit 3

Pharma's share of global healthcare spend has remained consistent overall but varies widely by country.

Pharma spend as a percentage of healthcare spend, by country, 2021,[1] % spend



Pharma spend as a percentage of healthcare spend, globally,[1] % spend



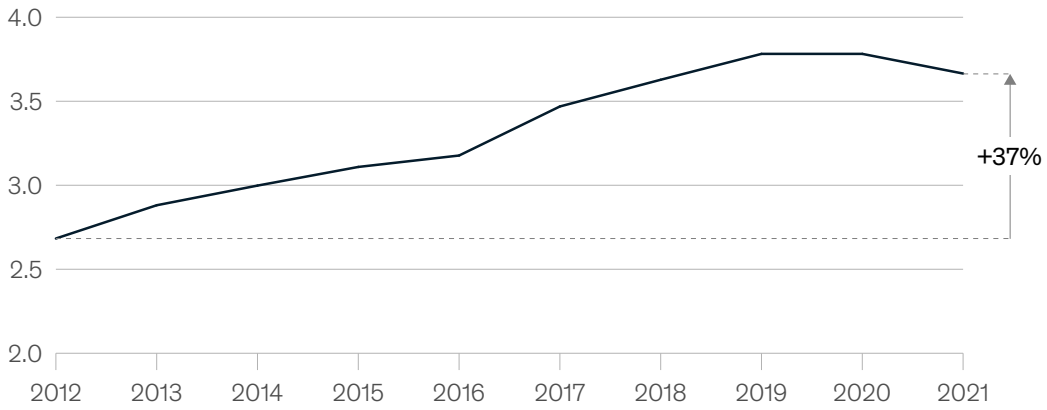
[1]At invoice price levels for pharma and healthcare.
[2]2019 data.
Source: OECD, Fitch Solution, IHME, World Bank, WHO, CMS, AAM

[4] CDER and CBER.
[5] Ibid.
[6] OECD, Fitch Solution, IHME, World Bank, WHO, CMS, AAM.

Exhibit 4

Globally, pharmaceutical daily doses increased by nearly 37% since 2012.

Defined daily doses globally by year, trillions of doses



89%
of Rx filled are generics

Source: OECD, Fitch Solution, IHME, World Bank, WHO, CMS, AAM

The genericization of blockbusters has created headroom for innovative new therapies today and expanded the impact of innovations. As top-selling drugs such as statins, antipsychotics, and antidepressants went generic, the number of US patients benefiting from those therapies increased by approximately 50 percent, from about 40 million in 2010 to about 60 million in 2020.[7] This growth is not limited to developed markets. Globally, the number of medication doses taken annually increased by nearly 40 percent from 2012 to 2021[8] for a total of "daily defined doses" of about 3.7 trillion, or an average of over one pill per day for every person in the world (Exhibit 4). This may be one reason why life expectancy from birth in the least developed countries has risen remarkably fast since 2000, from under 56 years to more than 65.[9]

We see opportunities for the industry to raise its aspiration for impact on patients and healthcare systems. Innovations increasingly focus on diseases with relatively small patient populations, leaving significant needs unmet in chronic diseases that afflict large numbers of people. Cardiovascular disease, for example, has a disability-adjusted life year impact twice as big as cancer and affects 3.5 times more patients; public health risks are on the rise, including antibiotic resistance—a particularly concerning example.[10] In our research reported in April 2022, we found that musculoskeletal diseases and mental health also drive high unmet needs but are under-researched. About 25–30 percent of this burden could be addressed with existing therapies, but the remainder will require biopharma companies to develop new innovations.

Access remains a challenge in many lower-income and developing markets; some innovative drugs are not launched due to minimum global price thresholds, gaps in healthcare infrastructure, or because patients in a specific healthcare system cannot afford them. Even affordable low-

[7] McKinsey analysis of blockbuster drugs, IMS Health, National Sales Perspectives, 2010, PHAST volume data, DailyMed dosage data (The information attributed to Source Healthcare Analytics herein is provided as is, and Source Healthcare Analytics makes no representation and/or warranty of any kind, including but not limited to, the accuracy and/or completeness of such information), HCP interviews on treatment duration, EvaluatePharma® May 2022, Evaluate Ltd.
[8] IQVIA's The Global Use of Medicine 2022, OECD, Fitch Solution, IHME, World Bank, WHO, CMS, AAM.
[9] World Bank data, 2000–2022.
[10] IHME, Pharmaprojects | Informa, 2022, EvaluatePharma® May 2022, Evaluate Ltd.

cost generics are underutilized due to limited healthcare infrastructure in developing markets. Without action, disparities in access will get wider, since most of the roughly two billion people born the next ten years will live in developing markets.[11]

We also see opportunities for the industry to play a bigger role in translating innovations into outcomes that matter for patients, health systems, and overall society. Too many therapies do not deliver optimal impact because of gaps in the care continuum, and persistent health inequities—manifesting as unmet patient needs, limited access to treatment, and broadly underserved communities—undermining the industry's potential.

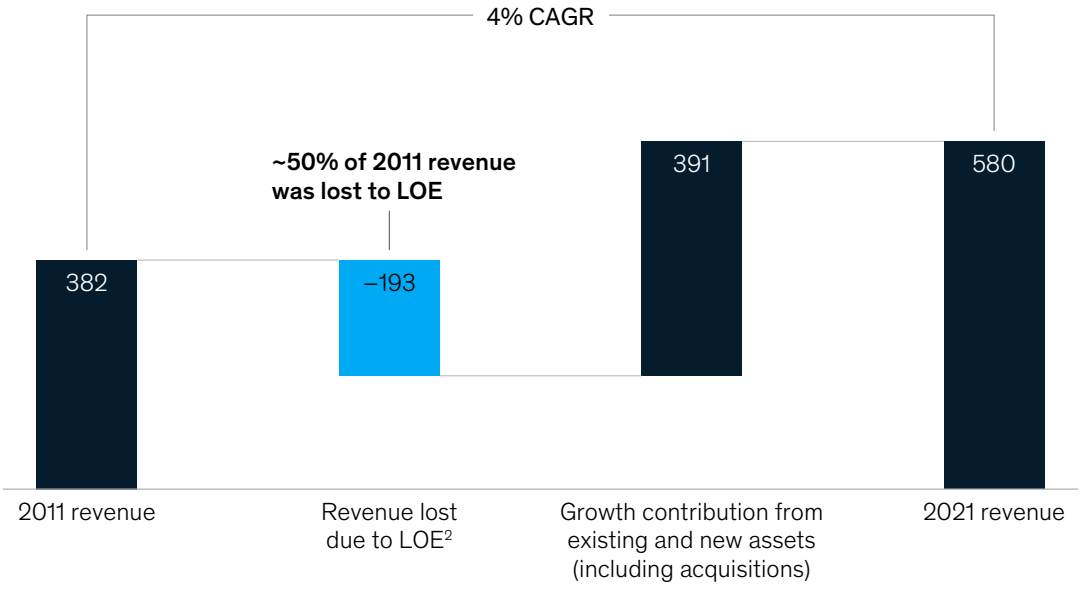
Financial impact

At an aggregate level, the biopharma industry has delivered steady operational results over the past decade. Revenues have grown at about 4 percent per year, essentially in line with the growth in global healthcare spending, topping $1 trillion in 2021 (Exhibit 5).[12] (All financial figures in US dollars.) Of course, growth varies drastically from market to market. Revenues grew faster than average in the US and much faster in emerging markets, such as China, Saudi Arabia, and

Exhibit 5

The industry has generated steady growth despite exclusivity losses.

Revenue growth of 15 largest pharmaceutical companies by revenue from 2011 to 2021, $ billions[1]



[1]Top 15 by 2021 revenue.
[2]Assumed to be an LOE if revenue loss was greater than 60% from peak sales.
Source: EvaluatePharma® May 2022, Evaluate Ltd.

[11] John Gramlich, "For World Population Day, a look at the countries with the biggest projected gains—and losses—by 2100," Pew Research Center, July 10, 2019.
[12] EvaluatePharma® May 2022, Evaluate Ltd., IQVIA's The Global Use of Medicine 2022.

Vietnam, but were slower than average in EU5 markets.[13] Moreover, growth in the low single digits masks the challenge of replacing revenue lost due to patent expiry—a unique attribute of the biopharma industry—but overall, the industry has remained profitable over the last ten years.

To illustrate this point, losses of exclusivity cost the 15 largest biopharma companies $193 billion in revenue, approximately 50 percent, from 2011–2021, but they still averaged 4 percent annual growth, adding $198 billion to the top line through organic innovation and business development.[14] These companies also maintained high and relatively stable profitability—typically 30–40 percent EBITDA margins—despite increasing R&D spending as a percent of sales.[15]

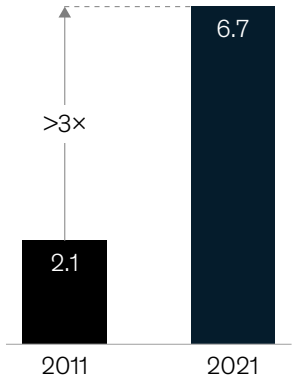
The industry has also maintained a relatively capital-efficient model, cumulatively returning about $1.25 trillion in cash flows to shareholders in the form of dividends and buybacks, on top of significant investments in acquisition and in-licensing.[16]

Shareholders have benefitted. The market capitalization of the global biopharma industry has grown from about $2.1 trillion to $6.7 trillion in the last ten years, an average of 13 percent annually (Exhibit 6).[17] The market caps of the 42 largest public biopharma companies grew from

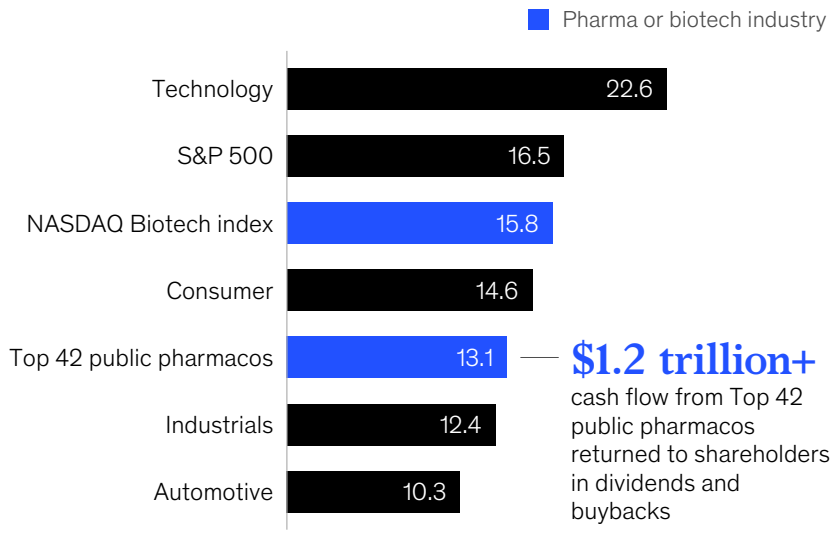
Exhibit 6

The industry market cap has more than tripled in a decade, and the largest pharmacos have delivered competitive shareholder returns.

Market capitalization of global pharma and biotech industry, $ trillion (n = 2,722)



10-year annualized TSR,[1] Dec 2011–Dec 2021, %



[1]Excludes companies listed during the 10-year TSR window (eg, AbbVie).
Source: S&P Capital IQ, CPAnalytics, McKinsey analysis

[13] IQVIA, Global use of medicines 2022.
[14] CPAnalytics, EvaluatePharma® May 2022, Evaluate Ltd.
[15] McKinsey analysis of company annual reports/form 10k.
[16] CAPIQ; McKinsey analysis of 42 largest public pharma companies.
[17] Ibid.

$1.7 trillion in 2011 to $3.8 trillion in 2021, while their share of the overall industry market cap declined from approximately 80 to 60 percent.[18]

This growth, though impressive, ranks in the middle across industries—half that of technology but ahead of industrials, automotive, and travel. Meanwhile, the market cap of the rest of the industry grew from $400 million to $2.9 trillion, a compound annual rate of more than 20 percent. Much of this growth is from new companies, with about 200 IPOs in US and 63 in China in the last three years alone. Today, more than 2,700 biopharma companies are publicly listed.[19]

The 42 largest public biopharma companies delivered total shareholder returns of 13.1 percent over the past decade, while smaller biotechs (as measured by NASDAQ Biotech Index) delivered 15.8 percent. While these returns are below the overall S&P500 returns of 16.5 percent, which are heavily influenced by tech leaders, they are in line with other well-performing industries.[20]

Employee and capability impact

The industry has been a stable employer, with headcount holding steady. The 10 largest companies have held headcount nearly stable over the past 3 years, employing about 750,000 people in 2021. This implies a significant increase in productivity per employee, provided that contingent worker counts have not increased significantly as part of a "shadow workforce."[21]

However, there is significant change beneath the surface. Evolving portfolios and changes in customer needs force companies to continually reinvent their talent base. Many have overhauled their therapeutic area expertise in medical and commercial, brought in new expertise in manufacturing and R&D, and embedded new disciplines such as data science and data engineering. The geographic makeup of the employee base is also changing, with massive

<1%

Growth in top 10 pharma employee count (2011–21)

[18] Ibid.
[19] Ibid.
[20] Ibid.
[21] McKinsey analysis of company annual reports/form 10k.

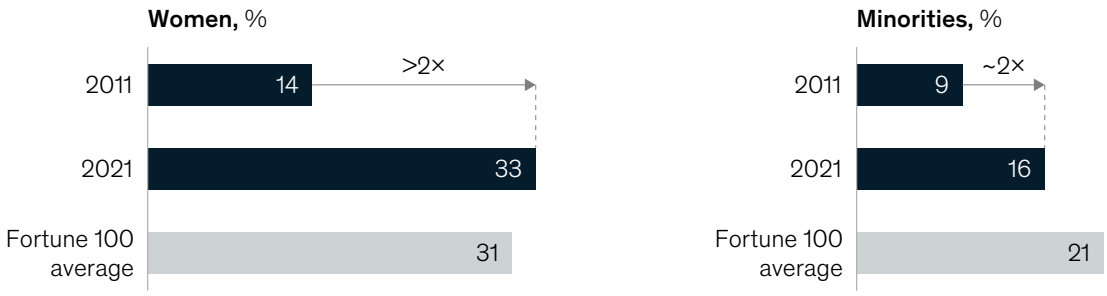
growth in mainland China, where AstraZeneca, for example, now employs more than 14,000 colleagues. The industry has also catalyzed massive second-order employment growth across the broader ecosystem, such as with CDMOs, CROs, and patient services providers.

The industry is making slow but steady progress in diversity and inclusion. Women now hold on average a third of positions on biopharma boards and direct reports to the CEO, up from 14 percent in 2011 (Exhibit 7).[22] China has moved to a leadership position in female representation, with the number of women leading the 25 largest biopharma businesses jumping from two in 2011 to 13 in 2021—or over 50 percent.[23]

Exhibit 7

Pharmacos have doubled female and minority board representation but lag Fortune 100 benchmarks for minorities.

Top-20 pharma board representation



Source: McKinsey analysis of company websites and annual reports

Minority representation is rising at a slower pace. At the board level in the 20 largest companies, for example, it improved from 9 to just 16 percent. However, minority representation on boards across the industry is 5 percentage points lower than the 21-percent S&P500 average in 2021.[24]

To compete with high-tech and other sectors for essential skills in high demand, the industry will need to become a magnet for global talent, reaffirming its noble purpose globally in ways that resonate with Generations Z and Alpha.

A major and ongoing effort will be required, since "Big Pharma" is often the subject of negative media coverage and is regularly ranked as one of the least desirable industries to work in. Across LinkedIn, Fortune, and Forbes, no more than three biopharma companies have ranked among the top 50 places to work in any year since 2012. In a 2019 survey, Gallup ranked biopharma

[22] McKinsey analysis of company annual reports/form 10k.
[23] Ibid.
[24] Ibid.

last among 25 sectors, with 58 percent of US citizens viewing biopharma negatively and only 27 percent seeing it positively.

COVID-19 raised the profile of the industry, of course: Pfizer jumped to the #4 spot on Fortune's 2022 list of "most admired companies in the world," behind only big tech companies. It remains to be seen whether this new sheen can be sustained and rub off on other companies. Becoming a talent magnet will also require making progress in diversity and inclusion, particularly in key functional areas like R&D, commercial, and operations leadership.

Biopharma can also raise its aspirations in building next-generation tech capabilities. With some exceptions, the industry has made timid progress in increasing its digital capabilities, trailing other industries on the digital transformation curve. As even more disruptive new technologies emerge, the industry's ability to acquire the necessary capabilities and transform its culture will be put to the test.

Social and environmental impact

The industry, including its generics arm, has played an important role helping more people around the world live longer, healthier lives. From 1960 to 2000, life expectancy in G7 countries increased by about 2.5 years each decade.[25]

While the availability of innovative therapies is far from being the sole driver of improvements in life expectancy, returns appear to be diminishing. The rate of improvement, at least in life expectancy, has slowed across most major markets. From 2010 to 2020, it improved only marginally in the US, from 78.5 years in 2010 to 78.9, and in France from 81.3 to 82.7, while China enjoyed a bigger bump, from a lower base, from 74.3 to 77 years. Improvements have been somewhat faster in low- to middle-income countries as access continues to expand: since 1990, life expectancy in those nations has increased by about 2.9 years each decade.[26]

Pharma companies are also investing heavily in improving disease awareness and early diagnosis, training HCPs, and building healthcare capacity and access to heavily subsidized medications across a broad range of therapeutic areas and geographies.

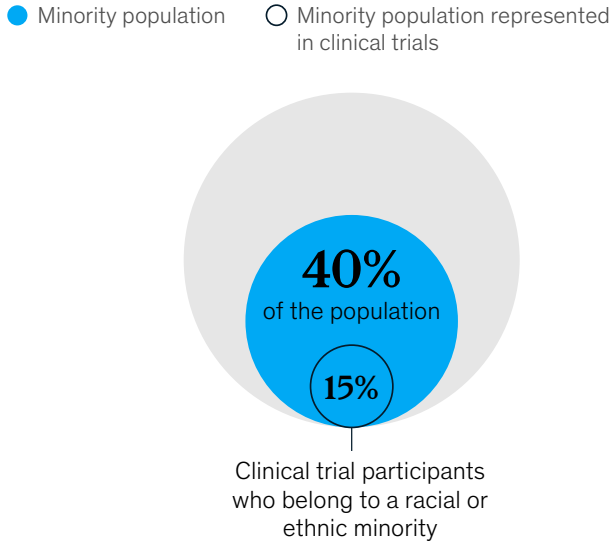
Yet they still have much more ground to cover in access and innovation.

According to Access to Medicine, "many leading pharmaceutical companies have made progress in improving access to medicine. Yet the fact remains that billions of people still cannot access the medicines that they need, and essential healthcare services are out of reach for half the world's population."

[25] Jason D. Buxbaum, Michael E. Chernew, et alia, "Contributions of Public Health, Pharmaceuticals, and Other Medical Care to US Life Expectancy Changes, 1990–2015," Health Affairs, Sept. 2020.
[26] United Nations – World Population Prospects, https://population.un.org/wpp/.

Exhibit 8

Minority representation in clinical trials does not reflect patient populations.



Source: NCI, June 2020

The industry's innovation and clinical methods do not yet reflect all populations. Only 10–20 percent of clinical trial participants in the US belong to a racial or ethnic minority, for example, despite representing about 40 percent of the population (Exhibit 8).

Medicines may have inherent limitations if they are developed based on data collected mostly from patients of European descent—as an example, patients of European descent are represented over six times more in trials compared to their share of the population.[27] Much of the cancer research by leading Western biopharma multinationals does not prioritize cancer types more prevalent in Asian populations. For example, three to five times more trials are underway for prostate and colorectal cancer, which are more common in the US, than liver or gastric cancer, which are more common in China.[28] The industry invests only about 1 percent of R&D funding on female-specific conditions beyond oncology.[29]

Access to innovations depends significantly on a country's ability and willingness to pay—emerging markets with low ability to pay still experience much slower product rollouts. Polio took 29 years longer to be eradicated in Africa than in the West, for example, despite the widespread availability of inexpensive vaccines. As of December 2021, just 28 percent of people in lower- and middle-income countries and only 7 percent in African countries had received COVID-19 vaccines, compared to 60 percent in high-income countries.[30] Even within European developed markets, availability of innovative drugs is often curtailed by local access conditions that severely restrict access to innovative therapies (vs. the US market benchmark).

Although the industry is not regarded as carbon-intensive, it ranks poorly on major environmental indices. RobecoSAM ranks biopharma and biotech below semiconductors, personal products, med tech, and apparel. According to MSCI, top issues include water withdrawal, waste, and energy use.[31] Nearly 40 of the top 50 pharmacos have set decarbonization targets, but only ten have committed to net zero by 2050.[32]

Since 2017, ESG ratings have declined for the top 15 biopharma companies. Though the industry continues to act in many ways on health equity and environmental reform, perceptions of the industry on ESG have not changed.[33] The industry clearly can and must step up its game.

[27] Fatumo et al. *A roadmap to increase diversity in genomic studies*. Nature Medicine. 2020.
[28] "The Burden of Cancer in Asia," Pfizer Facts and EvaluatePharma® May 2022, Evaluate Ltd.
[29] "Unlocking opportunities in women's healthcare," McKinsey, February 14, 2022.
[30] Paul Adepoju, "As COVID-19 vaccines arrive in Africa, Omicron is reducing supply and increasing demand," Nature Medicine, Dec. 13, 2021.
[31] RobescoSAM.
[32] Science-based targets, Company websites, MSCI global index.
[33] S&P Global.

3 Post-pandemic leap: Nine questions to shape impact

Building on the industry's momentum over the last 10 years, biopharma is poised to make a leap forward in impact over the next decade. This will require setting a bold aspiration for impact in the future and successfully navigating the multitude of interacting forces transforming the healthcare ecosystem.

We believe senior leaders in biopharma will need to answer nine critical questions, detailed below, to shape their companies and the industry over the next ten years. None of these questions has a single right answer, but leaders will have to make choices, based on robust discussions in the boardroom, to make the jump.

Nine questions to consider as industry takes its post-pandemic leap.

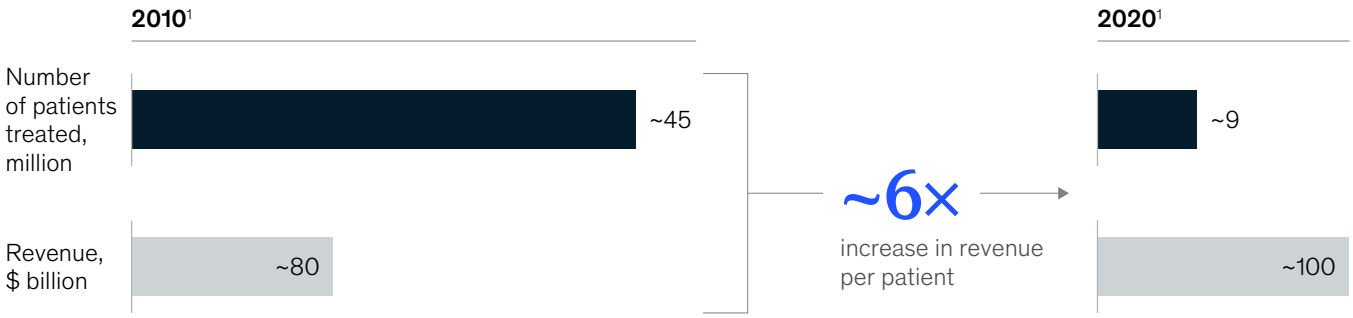
1 How can biopharma companies meet broader patient needs rather than overemphasizing already crowded areas with the greatest economic returns?

The industry has a strong track record of R&D investments, which have topped $1 trillion in the last decade.[34] These investments have produced a steady stream of innovative products, including the launch of more than 500 new molecular entities, over half of which were "first-in-class" products, as noted.[35]

Increasingly, this spend is focused on launching products focused on smaller patient populations. Orphan/accelerated approvals, often for narrow indications, have grown substantially—accelerated approvals now account for about half of all drug approvals.[36] Over the past five years, approvals for primary care indications have fallen by roughly 10 percent relative to 2010-2015, while therapies for specialty care have increased by about 10 percent.[37] The focus on oncology has intensified, driven partly by the emergence of immuno-oncology, with eight of the 20 top-selling drugs in this therapeutic area (TA). From a patient perspective, the number of US patients on the top 20 blockbusters, excluding vaccines, declined by 80 percent between 2010 and 2020, while revenue from those assets increased 25 percent to roughly $100 billion.[38] This implies a ~6× increase in revenue per patient for the top 20 drugs in the US (Exhibit 9).

Exhibit 9

From 2010 to 2020, the number of US patients on top 20 blockbuster drugs fell by ~80%, but revenue increased by ~25%.



[1]Excluding vaccines (ie, Prevnar).
Source: McKinsey analysis of blockbuster drugs; IMS Health, National Sales Perspectives, 2010; CMS's ASP Drug Pricing; PHAST volume data; DailyMed dosage data, HCP interviews on treatment duration; EvaluatePharma® May 2022, Evaluate Ltd.

[34] EvaluatePharma® May 2022, Evaluate Ltd.
[35] McKinsey analysis of new molecular entities.
[36] FDA.gov.
[37] FDA [CDER New drug approvals review for 2015–2021], Pubmed [2011–2015], EvaluatePharma® May 2022, Evaluate Ltd.
[38] McKinsey analysis of blockbuster drugs; IMS Health, National Sales Perspectives, 2010; CMS's ASP Drug Pricing; PHAST volume data; DailyMed dosage data (The information attributed to Source Healthcare Analytics herein is provided as is, and Source Healthcare Analytics makes no representation and/or warranty of any kind, including but not limited to, the accuracy and/or completeness of such information), HCP interviews on treatment duration; EvaluatePharma® May 2022, Evaluate Ltd.

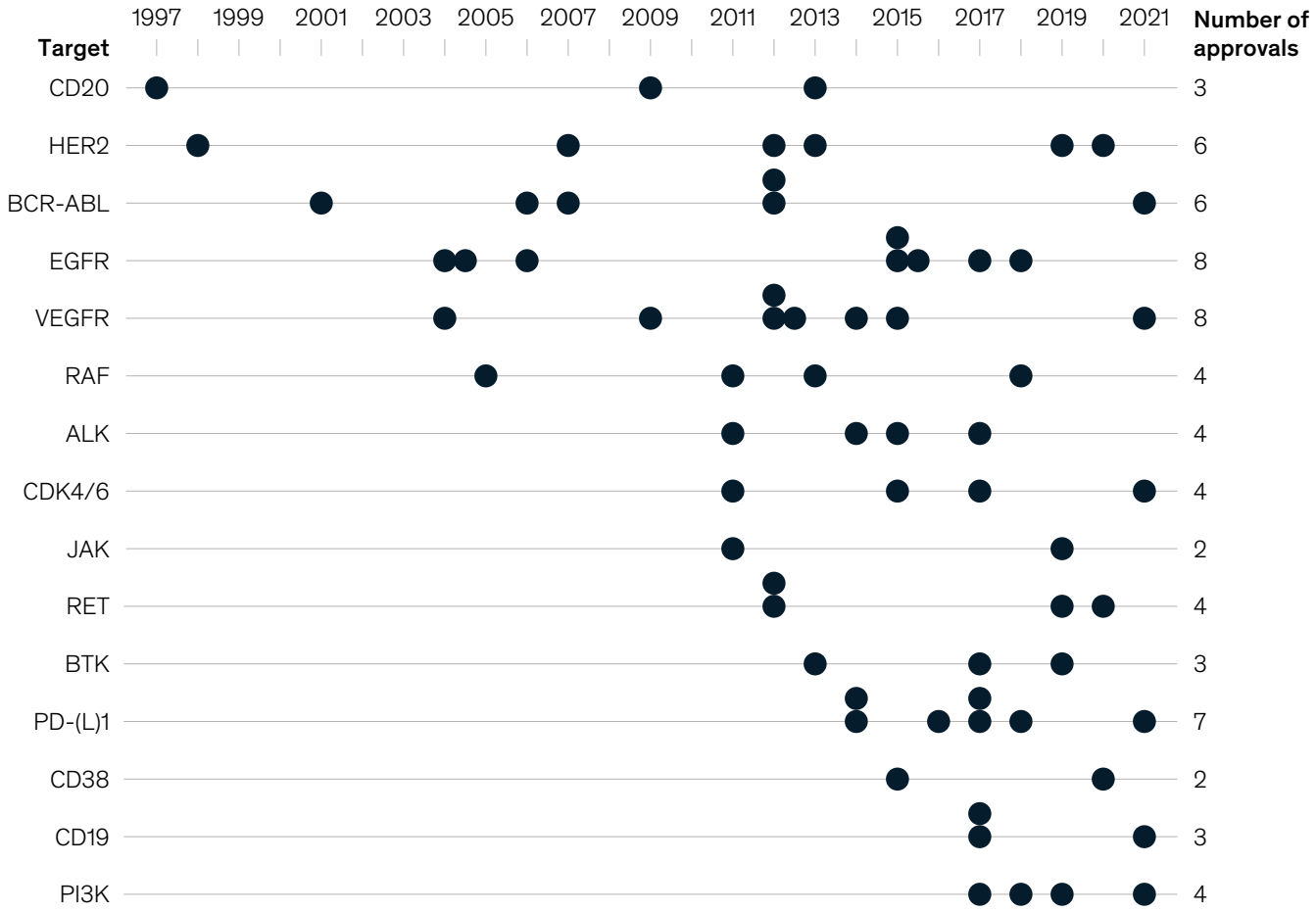
In many ways, the focus on oncology and rare diseases is a rational response to forces that have shaped the market. Regulators have provided accelerated pathways to incentivize drug development for orphan and other diseases with poor standards of care, including many oncology indications. Sharp increases in the cost of trials required to demonstrate improvement over a standard of care have steered companies away from pursuing innovations in large population chronic therapies. And payors in the US have historically imposed fewer price controls in oncology, rare diseases and some other areas, driven by a combination of regulations and public and political sentiment.

Biopharma leaders need to determine whether this strategy will remain successful over the next decade; no one wants to see another quintupling of drug revenue per patient in the US for the largest drugs over the next ten years. Meanwhile, smaller indications are becoming increasingly crowded, reducing the upside for any individual company. The pace of oncology launches has increased dramatically, for example. In the late 1990s and early 2000s, the gaps between first

Exhibit 10

In recent years, competition has increased across major oncology targets.

Approvals by year for select targets



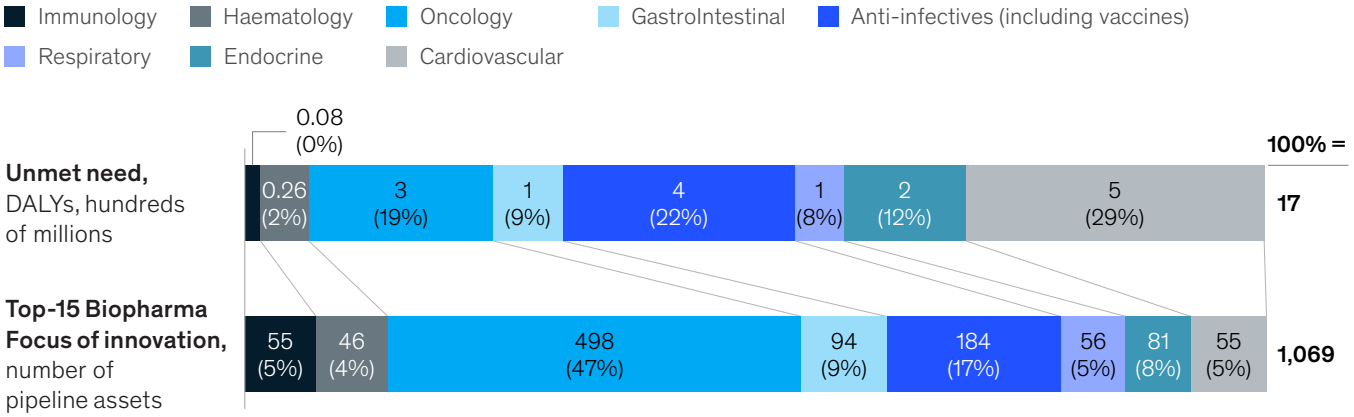
Source: FDA, EvaluatePharma® May 2022, Evaluate Ltd.

movers and subsequent launches in oncology targets such as CD-20, HER2, and BCR-ABL were five to eight years (Exhibit 10). In contrast, seven major PD(L)-1 drugs have entered the market since the first approvals in 2014.[39]

From the perspective of population health, there are substantial unmet needs in large disease areas, and few corresponding assets are in the pipeline (Exhibit 11). One extreme example is next-generation anti-infectives, where demand increases every year as drug resistance grows. By 2050, antibiotic-resistant bacteria may cause over 10 million deaths,[40] more than cancer, most in developing regions where access is already inequitable. The industry has created no novel antibiotic class since the 1980s and has not focused major research efforts in this critical arena.

Exhibit 11

Innovation efforts do not fully align with global patient needs.



Sources: WHO, EvaluatePharma, PharmaProjects

Key questions for leaders in biopharma

- Does your portfolio match your broader stated mission and purpose?
- What would it take to tackle the pressing unmet needs in the market – both internally (e.g., operating model, portfolio prioritization) and externally (e.g., reimbursement, regulatory pathways)?
- How can you apply breakthroughs in disease understanding and innovative modalities to address health challenges facing broader patient needs?
- What changes in the business model, such as more innovative approaches to pricing and access, will be necessary to profitably address broader patient needs?

[39] McKinsey analysis of drugs to market; Pharmaprojects | Informa, 2022.
[40] "New report calls for urgent action to avert antimicrobial resistance crisis," WHO news release, April 29, 2019.

2 Will biopharma companies transform R&D to deliver breakthrough medicines faster at lower cost? Or will they be stuck with rising development costs and lower asset NPVs?

Scientific innovation and breakthrough medicines have been core to the value delivered by the industry. The scale, intensity, diversity, and sophistication of innovation continues to grow. In 1995, about 1,200 assets were in the global industry pipeline, more than 90 percent of them small molecules. By 2021, more than 5,600 assets were in the pipeline, plus about 9,500 known preclinical assets. About 20 percent of these therapies were in new modalities such as cell and gene therapy and mRNA,[41] opening new targets and bringing fresh hope to patients. Over the same period, proliferation of new modalities has opened up the possibilities of what is druggable and also offered the possibility of cure in some disease areas. We have transformed from an industry with innovation concentrated in 2–3 modalities to one that is pursuing innovative therapies across 10+ modalities (Exhibit 12).

At an aggregate industry level, however, the fundamental returns on R&D have not improved. Major scientific advances have yielded more assets in the clinic but not raised the probability of success, which has remained flat over the past ten years, at about 11 percent for bringing a medicine from Phase I to market. This is despite the promise of novel R&D operating models and new tools/technologies intended to accelerate innovation and reduce cost (e.g., adaptive trial designs, advent of gene sequencing, in-silico drug discovery and development, real-world evidence, and “plug and play” platforms). The costs of developing an NME have also risen. Recent

While many industries experience the productivity gains (the “Moore’s law” effect), the cost to bring a biopharma asset to market continues to rise.

[41] Pharmaprojects | Informa, 2022; McKinsey analysis of treatment modalities.

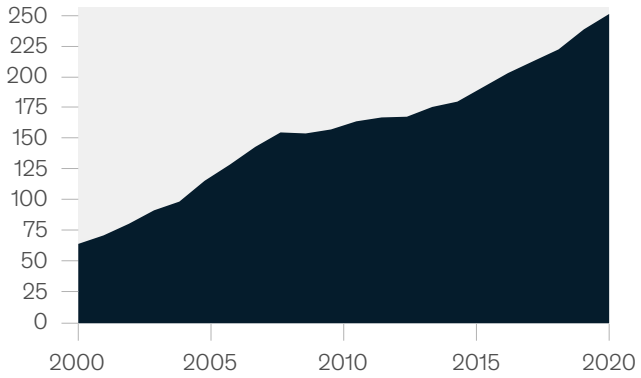
estimates of capitalized NME costs range from slightly over $1 billion to more than $2 billion, much higher than in prior decades.[42]

Not only does the industry as a whole have a sustained productivity challenge, but a further examination of the industry pipeline reveals that the 70 percent of breakthrough innovations were generated outside of large biopharma—a share that is likely to be sustained given investments in the biotech sector. Half of the top 20 blockbusters launched by large biopharma between 2011–2021 were sourced externally, and they correspond to 60 percent of the cumulative industry peak year sales.

Exhibit 12

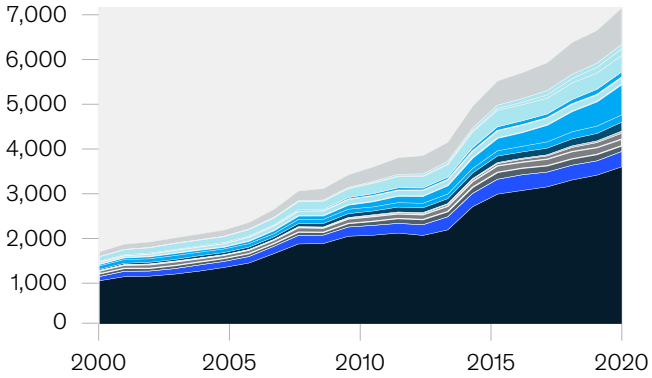
R&D spend has increased as the pipeline has become more diverse.

Pharma R&D spend, $ billion per year



~$2 trillion
in cumulative R&D spend

Size of global pipeline by therapeutic modality,
number of assets in Ph. I to III



- Antibodies (including engineered multifunctionals)
- Proteins & (synthetic peptides)
- Cell therapy & gene therapy
- Oligonucleotide therapies
- Viral therapies (excluding gene)
- Other biologics, natural products, microbiome modulators
- Other vaccines (including oncology)
- Anti-infective vaccines
- Small molecules

Source: Evaluate Pharma; PharmaProjects

[42] Schlander, M., Hernandez-Villafuerte, K., Cheng, CY. et al. "How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment," PharmacoEconomics, Aug. 9. 2021; and DiMasia, Grabowski and Hansen, "Innovation in the pharmaceutical industry: New estimates of R&D costs," Journal of Health Economics, May 2016.

As a consequence, investors will continue to put pressure on big biopharma to deliver biotech-like R&D productivity, while harnessing the power of their large scale R&D engines. We expect material transformations to the R&D operating models of large companies as they create "strategic innovation distance" through:

1. Deepening disease and modality understanding (leveraging functional genomics and RWE) to design winning innovative therapeutics with sharp target product profiles that address significant unmet needs.

2. Harnessing advances in AI and machine learning in in-silico drug discovery and operational automation to deliver step-change improvements in innovation effectiveness and productivity.

3. Capitalizing on the external innovation ecosystem—not just to source pipeline assets but increasingly to collaborate with external players, such as biotechs, academia, health systems, and databanks, to shape the next generation of medicines that can transform the lives of patients.

Key questions for leaders in biopharma

— What is your "North Star" for the R&D organization, including aspirations for success rates and speed to market?

— How can you fundamentally re-think and optimize the end-to-end innovation process, from discovery to approval?

— How can you experiment and rapidly scale new technologies like AI, ML, and Quantum Computing?

— How can you embed continuous improvement, agility, and capability building across the R&D organization?

3 How can companies escape "pilot purgatory" to fully harness the power of digital and analytics and start viewing investments in digital and analytics through an R&D lens?

Most life-sciences executives agree that long-term value creation lies in innovation-led growth, with digital and analytics as "core" as molecular innovation and disease understanding. And most companies have made significant investments to harness that value, undertaking projects and pilots that give glimpses of the exciting rewards ahead.

Despite the talk, promises, and potential, pharma's digital maturity still lags that of most other industries outside the public sector (Exhibit 13). Even highly regulated industries such as banking have used D&A to transform how they operate and engage with customers. Many C-suite leaders in pharma talk about D&A with internal audiences and their boards but lack the conviction to drive D&A at scale. Without an existential threat of disruption, most line leaders are incentivized to meet short-term P&L goals rather than pursue new capabilities that present real and perceived delivery risks.

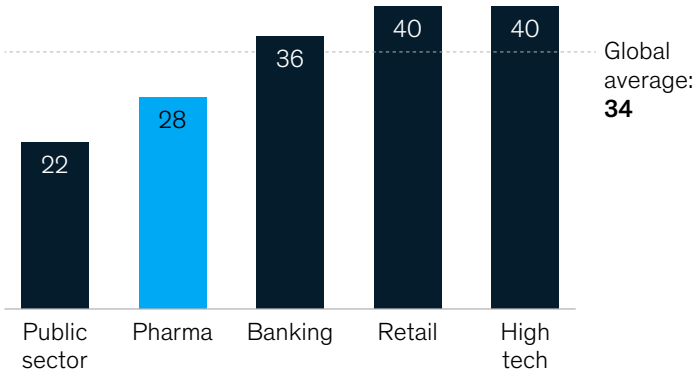
Pharma has not yet needed to make a massive digital leap, thanks to high margins, low competitive low competitive intensity in digital offerings, and little consumer demand for digital engagement at scale. But the question is when, not if, digital disruption will roil the industry.

Digital advances will continue at a breakneck pace, creating new transformational opportunities faster than the pharma industry can capture them. While other industries are on their next digital S-curve, pharma is still struggling to climb its first.

Exhibit 13

Pharma is early in digital maturity.

Digital maturity index—McKinsey Digital Quotient, Points (out of 100)



Source: Self-reported digital quotient score, 2019

We see three imperatives for maximizing the value for pharma shareholders and patients through digital and analytics:

Shifting from "digitizing" to "truly digital"

The vision of a digitally transformed life-sciences company—where people, data, technology, and partner organizations work together in a virtuous cycle of innovation and value creation—remains tantalizingly out of reach.

Most digital investments in pharma are designed to make incremental improvements in discreet processes, such as engaging healthcare providers, processing invoices and rebates, or selecting clinical trial sites. While these use cases can create value, they will have only limited structural impact.

A decade ago, no top 20 pharma company had a chief digital or technology officer. Today, nearly every large pharmaco has one who reports directly to the CEO.

The evolution of the most digitally successful pharmacos during the pandemic has set the stage for the broader industry transformation. Moderna, for example, aims to be the first "digital biotech," using processes designed with modern, digitized approaches from the ground up. This is an example of a company that believes it can break away from the pack in the next three to five years, thanks to the structural advantages of getting to scale faster than peers and quickly anticipating and adopting technological advances.

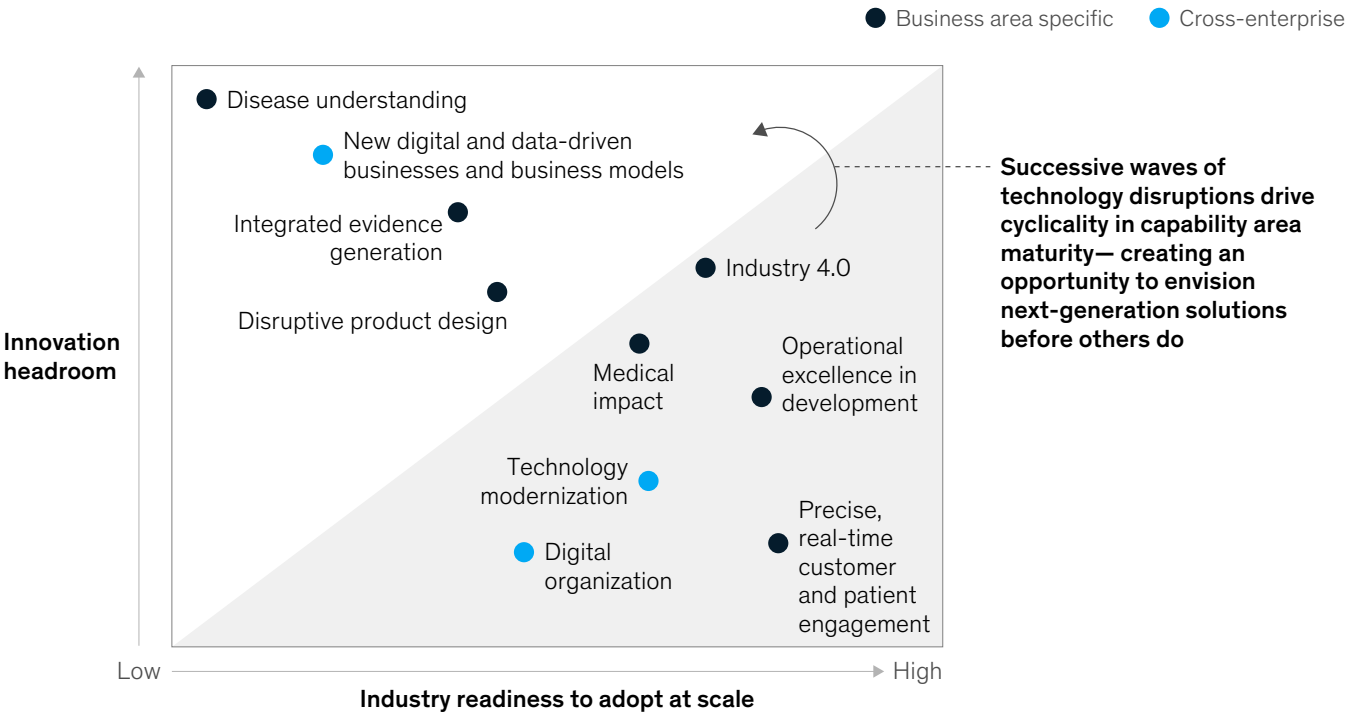
Winning in the next wave of digital impact areas at-scale

Most digital successes in the pharma industry have been in mature impact areas such as precision customer engagement, next best action in commercial, and clinical trial site selection. In these areas, the uses and value of D&A are clear, and the primary competitive advantages arise from scale rather than innovation.

Digital's role in high-impact areas like disease understanding is still taking shape (Exhibit 14). Some early-stage startups and established technology players, including BenevolentAI and Exscientia, are experimenting with technologies like multimodal AI to enable understanding of biological systems and accelerate target identification and molecular design. Researchers at MIT recently used a machine learning algorithm to discover a novel antibiotic; Insitro, an AI-powered drug discovery company, raised more than $400 million to develop its machine learning platform.[43]

Exhibit 14

Innovation headroom and adoption readiness by D&A capability area.



[43] "Insitro raises $400M for machine learning-powered drug discovery efforts," Fierce Biotech, March 15, 2021.

No individual pharmaco is likely to succeed across all next-generation impact areas—companies will need to make trade-offs in their pursuits.

Embracing new technologies before they reach maturity

Technological innovation will continue to accelerate. The next waves of disruptive technology, including blockchain, quantum computing, machine learning, Web 3.0, and 5G, all have the potential to create opportunities across the value chain (Exhibit 15).

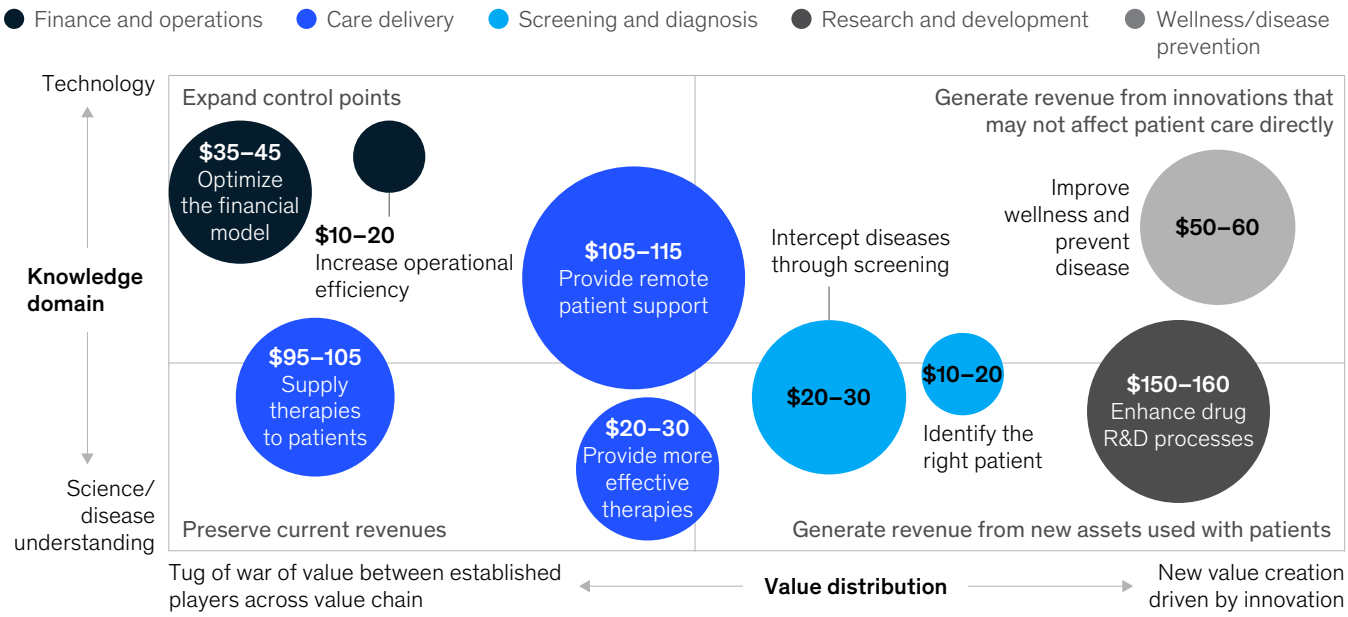
Molecular identification in the pharma industry remains slow. Companies continue to process molecules with non-quantum tools in computer-assisted drug discovery (CADD) where basic calculations predict the behavior of medium-size molecules with corresponding protein targets. Even with today's most advanced hardware, finding a promising new molecule could take a lifetime—or several lifetimes.

Quantum computing could transform R&D and even redefine our basic understanding of biology by making calculations exponentially faster. Algorithms that required protracted lengths of time to run would execute orders of magnitude faster (e.g., equations that support typical computational biology problems such as Bayesian methods could handle to the power of two more data in the same timeframe).[44]

Exhibit 15

Established players and new entrants have significant opportunities across the value chain.

Global Market Size 2024, $ billion



Source: Global Market Insights, TechNavio, BIS Research, BCC Research, Grand View Research, Fior Markets, McKinsey Pharma/Healthcare Systems & Services Practice Research

[44] Joan Koka, "The AI-driven initiative that's hastening the discovery of drugs to treat COVID-19," Argonne National Laboratory, Feb. 9, 2021.

Exponentially faster computing power could drastically change the R&D process by redefining our basic understanding of biology and biological pathways. Researchers might assess and test potential drugs in silico in greatly compressed time scales with significantly better accuracy, enabling the "drugification" of previously undruggable molecules—even "holy grail" drug targets like RAS, the most frequently mutated gene family in cancers, could become tenable. The industry has already experienced some success in drug discovery with the use of AI, given its enhanced capability to simulate interactions between a drug and its target during development over pure physics-based computations.[45] Notably, AI simulations were used in the development of Paxlovid to simulate its efficacy in blocking SARS-CoV-2's 3CL protease in the wake of new viral variants.[46]

Although true quantum computing is still out of reach, pilot experiments suggest that it has potential, especially among hybrid algorithms and approaches, such as Variational Quantum Eigensolver or Variational Circuit Learning.[47] That said, despite industry-wide collaborations and initiatives, quantum computing drug development strategies have yet to be developed.[48]

Key questions for leaders in biopharma

- How do you shift mindsets to support massive enterprise-wide scaling and transformation, vs. "bright stars on a dark night" of impact?
- What would an R&D-like mindset look like for digital, where there is comfort for experimentation, an engine to support scaling, and a longer timeframe for demonstrating value (5–10 years)?
- How will you compete for talent against the tech juggernauts and other industries? Can you offer a more compelling value proposition as a legacy organization with a well-established culture and operating model?
- How will you create the right culture and attract the right talent to supercharge innovation?

[45] Ibid.
[46] Oliver Peckham, "Supercomputer Simulations Show How Paxlovid, Pfizer's Covid Antiviral, Works," Feb. 3, 2022 HPC Wire.
[47] Maritza Hernandez, Guo Liang Gan et alia, "A Quantum-Inspired Method for Three-Dimensional Ligand-Based Virtual Screening," Journal of Chemical Information and Modeling, Oct. 18, 2019; Sam Lemonick, "Largest molecular quantum computation performed," C&EN, Aug, 27, 2020.
[48] Rick Mullin, "Let's talk about quantum computing in drug discovery," C&EN, Sept 13, 2020.

4 What changes in strategy and operating model are required to realize the global opportunity? Will companies continue to depend on select large markets like the US?

Like many other industries, biopharma has been on a long road to globalization, driven by demographic trends, rising disease burdens, economic growth, and growing healthcare spending around the world. On many dimensions, the industry is succeeding in its push towards globalization and meeting global patient needs.

Despite this push for global expansion, the industry increasingly relies on a narrow set of large markets to drive performance. Four countries in particular—China, Germany, Japan, and the US—account for the vast majority of revenues (i.e., greater than 65%) and are the strategic focus of senior management for most pharmacos.

China specifically has emerged as a significant market for many pharmacos over the last decade, growing at more than double the rate compared to developed countries. China now accounts on average for 6 to 7 percent of revenue for the global top 15 pharmacos, with a few companies above 10 percent.[49] But while the industry has experienced strong growth in China, several other industries have even deeper penetration. China now accounts for about 30 percent of global revenues for the 15 largest luxury and automotive multinationals based in the US and Europe, for example.[50]

Globalization is not limited to European and US companies expanding their commercial footprints. Most of the largest pharmacos now maintain some R&D footprint in Asia, reflecting China's growing significance in clinical operations. China itself has become a source of innovation, evidenced by the emergence of BeiGene, HutchMed, I-MAB, Legend and other companies. In the last two years, Chinese originators have signed more than 60 deals to commercialize their therapies abroad.[51]

China, Germany, Japan, and the US account for over 2/3 of total revenues and are the strategic focus of senior management for most Pharmacos.

[49] McKinsey analysis of company annual reports/form 10k.
[50] Ibid.
[51] GBI; press release; company annual report 2020; company interim report 2021 H1 McKinsey analysis of company reports.

How is China set to impact the global biopharma industry?

In an upcoming article, "Vision 2028—How China will impact the biopharma industry," we examine the state of the industry in China and potential growth scenarios.

The state of play: China's innovation ecosystem is poised for global impact
To understand where China stands today, we considered it through three-lenses: enablers, value chain capabilities, and innovation. While the country cannot yet innovate toe-to-toe with the US or Europe, its enablers are propelling rapid ecosystem evolution, including pro-innovation regulatory reform, vast increases in public and private investment, and vibrant cross-border transactions, such as partnerships and in- and out-licensing deals.

China's links and contributions in the value chain are getting stronger in specific areas. With improving clinical development capabilities, it has tripled the number of innovative assets under clinical development in the last five years—and become a high-quality, cost-competitive manufacturing hub for small molecules, with CROs and CDMOs serving global customers with competitive solutions. The country's affordable innovation could yield breakthroughs if meeting global standards—the first wave of assets from China-originated biotechs are now reaching the commercial stage in China, with new modalities and technologies coming online.

Three scenarios for China's impact on the global biopharma industry
We foresee three possible scenarios unfolding by 2028, which we call Stunted, Momentum, and Transformative. Each encompasses a range of inputs and outcomes, adjusted to reflect the geopolitical and regulatory uncertainties that will shape the sector's development:

— In a Stunted scenario, which we see as somewhat less likely, geopolitical discord hampers regulatory integration, potentially tipping the current progressive trajectory into reverse. China effectively decouples from the global ecosystem and returns to its limited role outside its frontiers, delivering global impact in just a few areas such as the provision of active pharmaceutical ingredients.

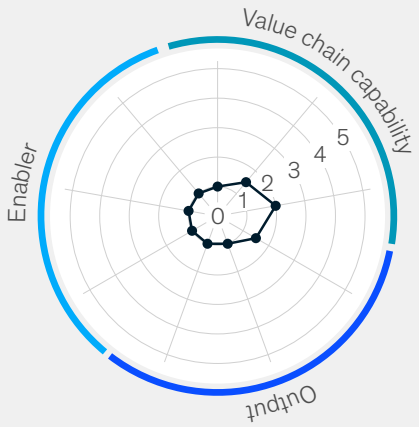
— In a Momentum scenario, which we believe is most likely, sectoral momentum continues, and China integrates further into the global biopharma value chain. As some aspects of the ecosystem develop more rapidly, China penetrates more deeply and has more impact in areas such as contract research organizations (CROs) and contract development and manufacturing organizations (CDMOs). In this scenario, China's progress in research and discovery remains subdued, yielding few genuinely groundbreaking innovations in this time horizon.

— A Transformational scenario is the most intriguing: landmark shifts in industry structure—such as China's full integration into the global innovation and regulatory ecosystem, full-blown competitive value chain capabilities, and emergence as a global powerhouse for innovation—would have major implications for global patient access to innovative therapies. In our view, this scenario's highly disruptive nature makes it the least likely, but the implications are so far-reaching that they cannot be ignored.

Exhibit

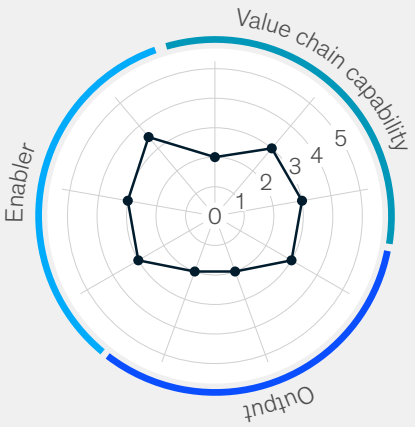
China's impact on global biopharma by 2028—3 potential scenarios.

Stunted impact



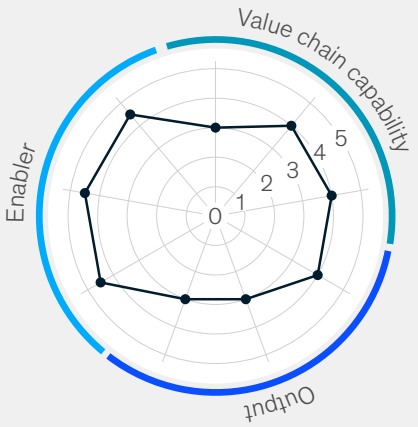
- Global integration stalls or goes in reverse
- Funding dries up, capabilities are stunted, role remains limited to sourcing of selected services (eg, API)
- Limited global footprint among China-originated biopharma companies
- Affordable innovation does not take off beyond China
- Limited/no notable China-originated BIC/FIC reach global markets

Momentum scenario



- Global integration continues at pace, with some gaps
- Expanded capabilities, some world-leading, established in selected areas to supply global needs
- More than five China-originated biopharma companies have built scaled global operations, with sizable ex-China revenue
- Leverage of China as a core platform in value chain by other industry participants
- Affordable innovation adopted in selected global markets (eg, SEA); several breakthrough innovations reach global key markets with blockbuster potential

Transformational impact



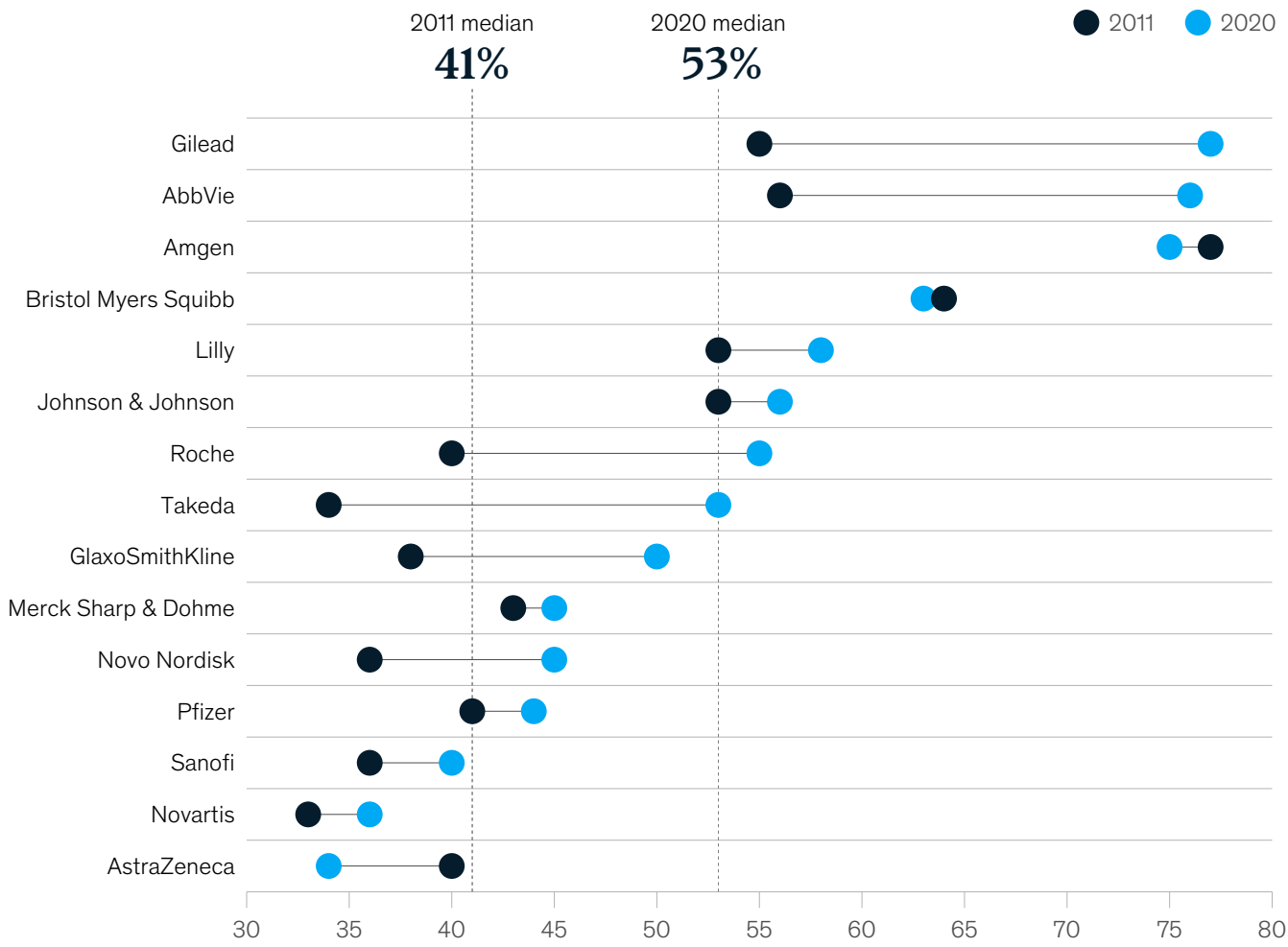
- Full integration within global innovation ecosystem
- Full-blown capabilities and services addressing global needs across modalities at scale
- Emergence of numerous next-generation global pharma leader/shaper(s) of Chinese origin
- Leverage of China as a central platform for transformative impact by other industry participants
- Affordable innovation impacts global pharma access system; China establishes itself as a global innovation hub with steady flow of high-quality breakthrough innovations, substantiated by scientific merits, creating global impact at scale

Within this trend of increasing reliance on a few core markets, the US stands out for growth and profitability (Exhibit 16). For 12 of the 15 leading public pharmacos, the share of revenues from the US has grown over the decade—with the average share increasing from 41 to 53 percent.[52] A company's concentration in the US market clearly correlates with profitability (Exhibit 17).

Exhibit 16

Twelve of the top 15 pharma companies grew their US share of revenue.

US share of worldwide revenue, %

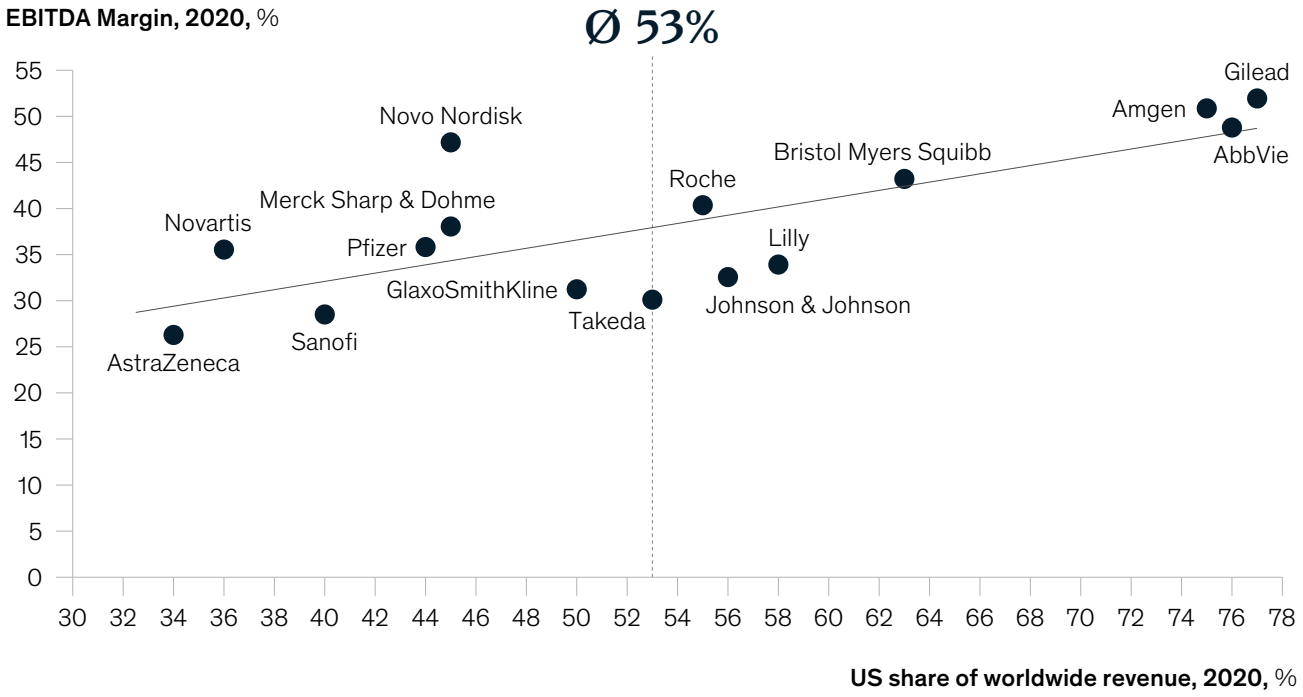


Source: McKinsey analysis of company annual reports/form 10k; EvaluatePharma® May 2022, Evaluate Ltd.; CPAnalytics

[52] McKinsey analysis of company annual reports/form 10k; EvaluatePharma® May 2022, Evaluate Ltd.; CPAnalytics.

Exhibit 17

US share of worldwide revenue has a positive correlation with EBITDA margin.



Source: McKinsey analysis of company annual reports/form 10k; EvaluatePharma® May 2022, Evaluate Ltd.; CPAnalytics

Key questions for leaders in biopharma

- Are you comfortable with steady drift to an even more US-focused business, or prepared to alter course and be truly global again?
- How flexible are your operating model and guardrails to serve an increasingly heterogeneous set of markets? What is the right balance between a uniform operating model built for simplicity and speed versus a more complex model that can adapt to any market?
- Do you have a clear plan to react to pricing disruptions in the US, which drives the majority of growth and operating profits?
- Do you have a clear view on potential geopolitical scenarios and regulatory changes that could significantly impact your business?

5 How can biopharma companies rely more on ecosystem partners, create more flexible and resilient operating models, and overcome their preference for owning capabilities and capacity outright?

Biopharmaceutical success requires operating in (and in many cases, building) a broader ecosystem. Historically, large biopharma companies have relied on a relatively vertical integrated model with a preference for owning most capabilities across the value chain and outsourcing only in selected areas. The main exception is steadily increasingly insourcing of innovation from smaller biotech companies, funded by plowing back legacy cashflows from existing products. Smaller biotech companies have relied on a network of ecosystem service providers including discovery players, CROs, CDMOs, and commercial service providers, and partnerships with large biopharma for late-stage development and commercialization.

As we look ahead, the broader biopharma ecosystem is poised for significant changes given underlying dynamics and trends in key areas.

Other industries have similar evolutions from captive to ecosystem-centric models.

The computer industry, for example, was highly vertical in the late 1970s and early 1980s: IBM, HP, and DEC produced nearly all elements of their systems, including hardware. As the personal computer revolution began, IBM outsourced two major components—processors from Intel and the operating system from Microsoft.

Component manufacturers began to drive innovation, with product cycle times a fraction of what a company like IBM could achieve.

We see similar evolutions in automotive, where complex components such as transmissions and infotainment are now the province of external innovators, and in consumer electronics where Apple focuses on design and software while Foxconn supports manufacturing.

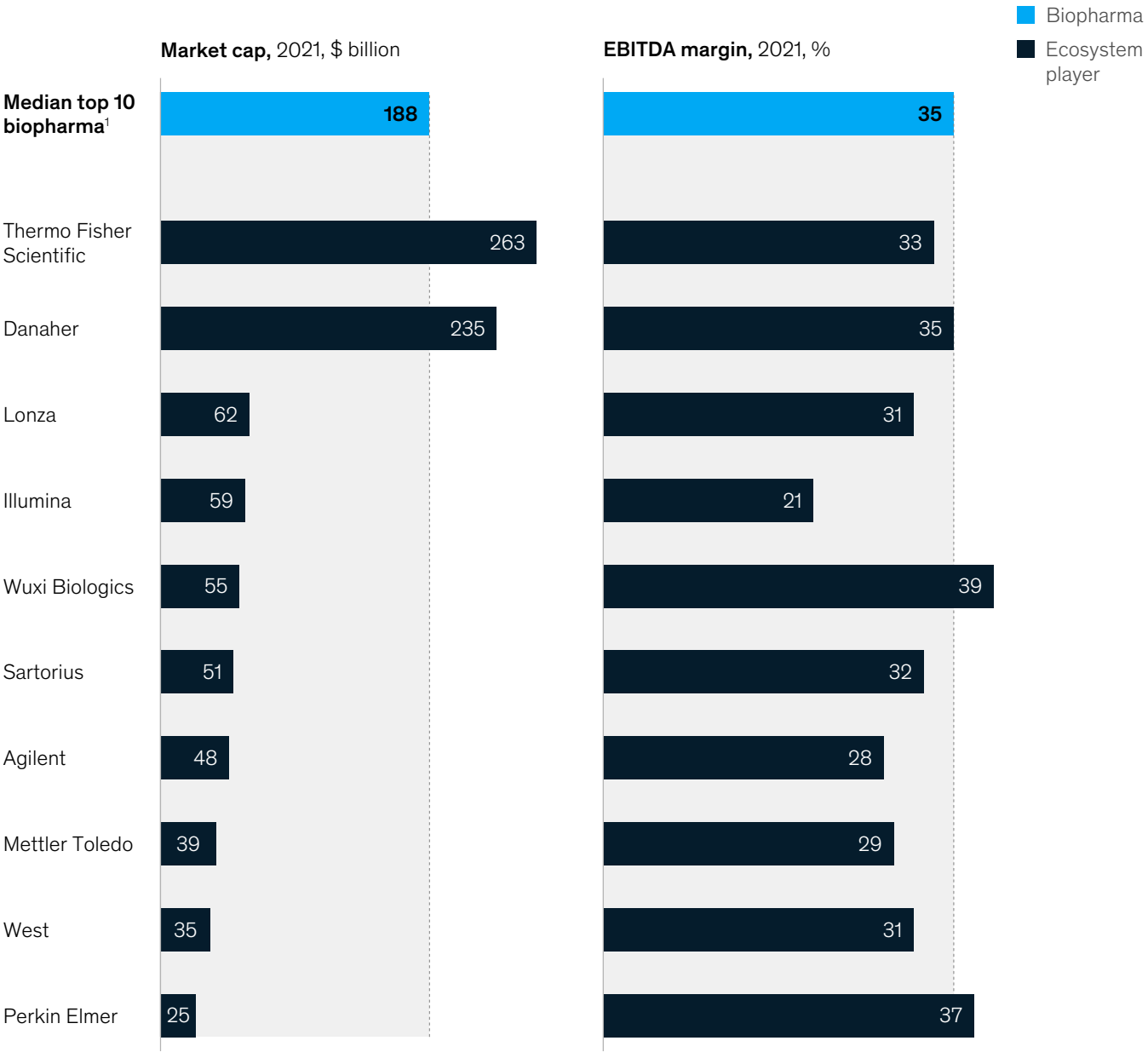
The traditional scale advantages of large biopharma are becoming less valuable. Scale advantages in development mean less for assets targeted at small populations—the exception being multi-indication blockbusters. The importance of large sales forces is also slowly declining, driven by changing health system policies and physician preferences. Manufacturing network scale and capital requirements are often significantly lower for many of the new modalities.

Meanwhile, the ecosystem of service providers is maturing in size and capability. The CDMO and CRO markets both grew revenues by more than 8 percent per year over the last five years, and now deliver about $200 billion in revenue annually.[53] Similarly, the 14-percent annual growth of service sector enterprise value over the last five years has far outpaced that of the biopharma sector at just 6 percent, showing evidence of the markets' confidence in these strategic partnerships. Market capitalization of leaders in this space has grown significantly. ThermoFisher and Danaher have market caps that exceed the median top 10 pharmacos—with "pharma-like" margins (Exhibit 18).[54] China has significantly scaled and improved its CRO and CDMO capabilities to meet global standards with the aim of serving global markets. Roughly half the market capitalization of the life science industry in China comes from CDMO and CRO companies. Companies like Catalent, ThermoFisher, and Lonza have invested tens of billions[55]
of dollars in acquisitions to create a broader, end-to-end offering for customers.

[53] Frost & Sullivan, 2017, market research & market research.
[54] Transparency Market Research (2020), Grand View Research (2021), Global Industry Analysts (2021), Mordor (2020), Industry Standard Research (2021), Markets and Markets (2021), Frost & Sullivan (2020, 2021), Koncept Analytics (2021), TechNavio (2021), Bourne Partners (2020), CP Analytics, team analysis.
[55] Press releases.

Exhibit 18

The market cap and margins of the largest ecosystem players are now comparable with those of biopharma.



[1]Includes: Novartis, Sanofi, Roche, Pfizer, GlaxoSmithKline, Bristol Myers Squibb, Abbvie, AstraZeneca, Merck, Takeda.
Source: McKinsey analysis of company annual reports/form 10k; CapIQ

These and other moves reflect the reality that the pace of technological advances across the value chain will make it harder for large biopharma companies to continue to own vertically integrated capabilities. As modalities and platforms proliferate, it will be increasingly difficult to build leading capabilities internally, from discovery platforms to manufacturing plants, across a wide variety of technologies. And as asset lifecycles get shorter, companies will need to become more flexible to rapidly adjust manufacturing capacity and commercial resourcing, underscoring the need to tap all the resources of the ecosystem rather than invest fortunes in organic builds.

Key questions for leaders in biopharma

- How can the ecosystem allow companies to focus on areas of competitive advantage while allowing them to focus less on other activities?
- How does the calculus change for small biotechs in deciding whether to develop on their own or partner with or sell to a large pharmaco?
- How can the ecosystem help you become more flexible in the face of proliferating modalities and technologies and build greater resiliency into your value chain?
- How will partnership models evolve in the new ecosystem? Will we continue to work with CDMOs/CROs/CSOs as vendors or will we create bespoke products together, co-creating IP, and co-investing in infrastructure (similar to how Foxconn partners with its customers to invest in new technologies)?

6 How can the industry play a larger role in driving patient outcomes and realize the full potential of innovative therapies?

Pharma's traditional method of creating value is developing new compositions of matter and charging for each dose. While few would argue that the industry's intent is to deliver outcomes, most of its interventions beyond delivering drugs have addressed pain points in physician and patient journeys, such as injection training, reimbursement support, and symptom tracking.

While the biopharma industry has traditionally been content to own treatment efficacy, "the pill" is only a small variable of the overall outcomes equation. Outcomes are influenced by physicians, payors, patients and other stakeholders with varying incentives, engagement, expertise and understanding. Add the complexity of each patient's needs and significant differences in how medicine is practiced around the world—and even from doctor to doctor—and this challenge is even greater. We see significant opportunities to improve: in a 2020 report, we estimated that 40 percent of the global disease burden could be addressed with existing interventions.[56]

Biopharma focuses on delivering efficacious medicines but many other factors impact patient outcomes

Driven by pharma

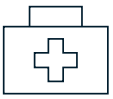
- Efficacy of therapy ("the pill")

Driven by patient

- Patient lifestyle choices and therapy adherence

Driven by physician knowledge and guidelines

- Right diagnosis
- Right treatment selections and right delivery



Driven by patient, payors, and HCP

- Capturing data on success of treatment
- Integrating data to refine treatment decisions

Digital health interventions will be a key to improving disease state outcomes. Tech players, established and nascent, are developing offerings across the value equation—increasing adherence, tracking and guiding lifestyle choices, and monitoring improvements and declines in patient conditions. While tech companies have experienced some notable failures, they continue to invest heavily in innovation—some of which will cause significant disruptions in the years ahead. Digital interventions to improve care delivery, for example, could save $140–270 billion each year in the US alone, according to McKinsey estimates. While these digital interventions often times were treated as novelties or a distraction, increasing consumer engagement with digital health tools combined with the emergence of telehealth and remote care creates new avenues to embed these offerings in the core of health care delivery.

Digital health companies take a fundamentally different approach to the market compared with biopharma. While the pharma development model extensively tests and proves the efficacy of products before filing and going to market, tech companies often release health solutions as "lifestyle offerings" to collect real-world data to support a regulatory filing. This allows them to come to market quickly and iterate rapidly with much lower cost and risk. A gap remains, however, in payors' willingness to cover the costs of digital

[56] "Prioritizing health: A prescription for prosperity," Jul, 8, 2020, McKinsey.com.

health solutions without clinical evidence. Payment models may need to shift for the success of tech-enabled health solutions—and signs of those shifts are becoming apparent. Virta, for example, provides a non-pharmaceutical treatment for type-2 diabetes that includes personalized behavioral and nutrition therapy alongside remote monitoring. The company has announced outcome-based pricing and is reimbursed by insurers.[57] Virta has demonstrated the efficacy of its program in clinical trials; further disruptions may be needed to enable business models that support digital products without such trials. Biopharma may have a unique opportunity to partner with tech players. We see complementary strengths on both sides, as the industry has the infrastructure and experience to develop strong bodies of RCT-grade evidence that could lead to registration and reimbursement.

As new offerings provide more patient and health system impact, they could also build the industry's resiliency to thrive in the face of rapidly evolving healthcare payment models. Beyond pharma, healthcare is moving to outcomes-based payments in the US, with the number of lives in fully-capitated contracts expected to double over the next 5 years.[58] Growing use of real-world evidence could also reveal areas where clinical trial data does not translate to real-world outcomes. Data generated during highly controlled clinical trials benefit from near-ideal patient selection, treatment paradigms and adherence, for example. The real world looks vastly

40%

of the global disease burden could be addressed with existing interventions.

[57] Jonah Comstock, "Virta Health announces risk-based pricing for controversial diabetes management platform," MobilHealthNews, Nov. 14, 2018 and Paige Minemyer, "Humana to offer Virta Health's diabetes care platform for self-funded employer plans," Fierce Healthcare, Nov. 9, 2022.
[58] McKinsey EPT (Enrollment projection tool), Truven commercial claims data and external reports/expert interviews.

different, and stakeholders are taking notice. Already, 44 percent of Cochrane Reviews conclude that "the evidence is insufficient for clinical practice" because clinical trials represent only small, homogeneous populations and are not generalizable to most of the study population.

Over time, playing a broader role in the care ecosystem might be a necessity, not a choice. If the industry structure evolves in the direction of outcome-based care and some companies take more proactive and broader service-oriented stances, will it influence the expectations of other players and set new norms for the industry? Will companies shape the industry structure or wait to be shaped by it?

Key questions for leaders in biopharma

- What is your aspiration? Will your company be only a provider of medication, or provide demonstrably better patient outcomes, and influence them beyond providing medication?
- Which distinctive insights and capabilities, such as disease understanding, proprietary data from clinical trials, or commercial reach, give your company a right to play in the broader provision of care beyond the "pill"?
- What offerings can you and should you build internally, and which should your create through acquisition or partnership? What investments do you need to place now even without an immediate need to play a broader role?
- What disruptive threats could fundamentally change your business, such as algorithms to drive treatment selection?

7 What bold actions can the industry take to fully leverage its capabilities and resources and be at the forefront of meeting rising standards in ESG?

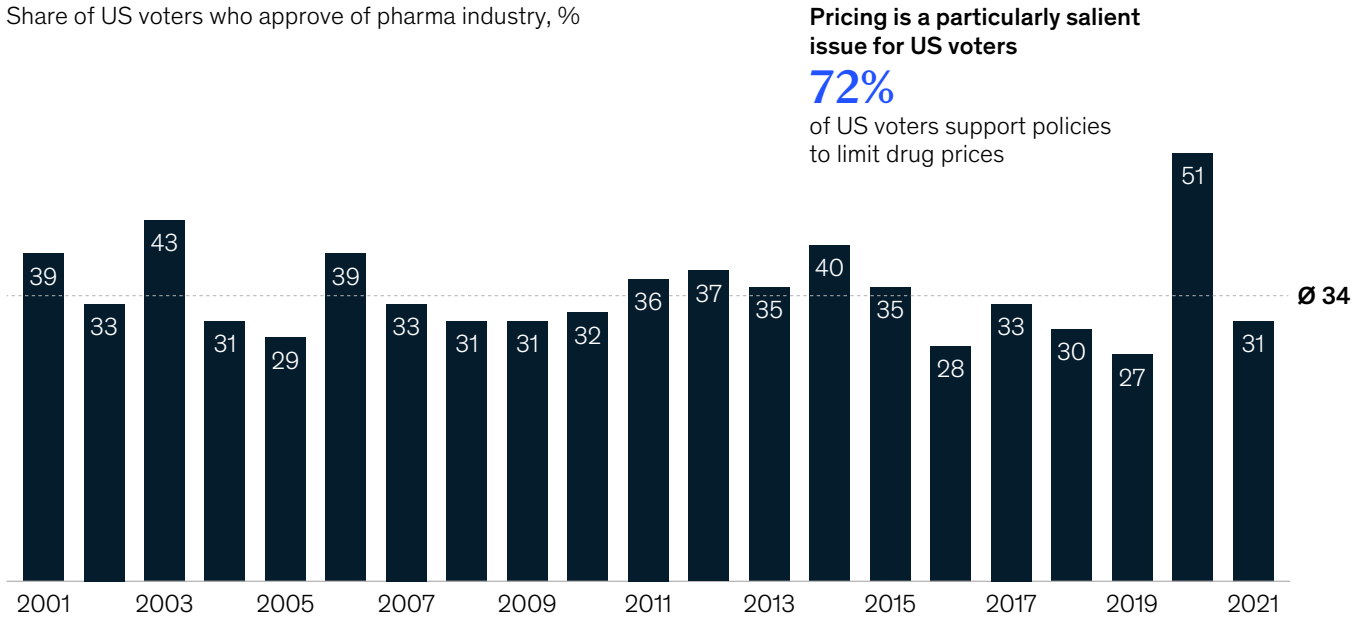
The industry has made significant progress in environmental, social and governance (ESG) imperatives. On health equity, 19 of the top 20 pharmacos are now transparent on patents, supply and availability; all 20 have set goals on access to medicine, and the number of drug assets directed against WHO-priority diseases has risen by more than 50 percent.[59] The industry has also responded to the growing global sentiment that multinationals must help achieve environmental goals: nearly 40 of the top 50 pharmacos have set decarbonization targets.[60]

Most significantly, the industry made a phenomenal contribution to human health and thereby to society during the pandemic. As a consequence, in 2020, for the first time in decades, a majority of Americans said they had a favorable view of the industry, with similar reputational gains in countries around the world (Exhibit 19).[61]

Exhibit 19

ESG: The public perception of the industry remains low, despite a fleeting increase in 2020.

Public perceptions of pharma have reverted to the mean following an increase in approval during COVID-19.



Source: Gallup

[59] Access to Medicine Index, 2022.
[60] Science-based targets; Company websites, MSCI.
[61] "2020 Global Pharma Study," Group Caliber, Sept. 15, 2020.

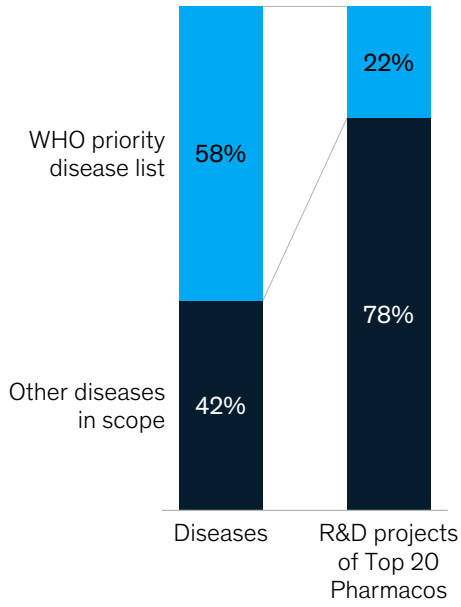
However, the perception of the industry among Americans dropped back down to pre-pandemic levels in 2021 and investors, regulators, employees and the public continue to expect biopharma companies to set and deliver on bold ESG agendas. This will require material, timely investment, often in collaboration with other partners or actors where ESG outcomes and benefits are by no means guaranteed. In this context, biopharma leaders are reflecting on what ESG leadership means for their company and how to deliver measurable ESG impact at pace.

We see opportunities for the biopharma industry to lead in social advances—the S in ESG. As noted, the industry is uniquely positioned to deliver global societal benefit by improving human health, but too many pipelines today are designed to serve patients in the richest nations. Measured in terms of publications, the industry invests eight times more in research into diseases concentrated in high-income countries, for example (Exhibit 20). As companies design target product profiles, they should consider whom the medications are for and to whom they will be accessible.

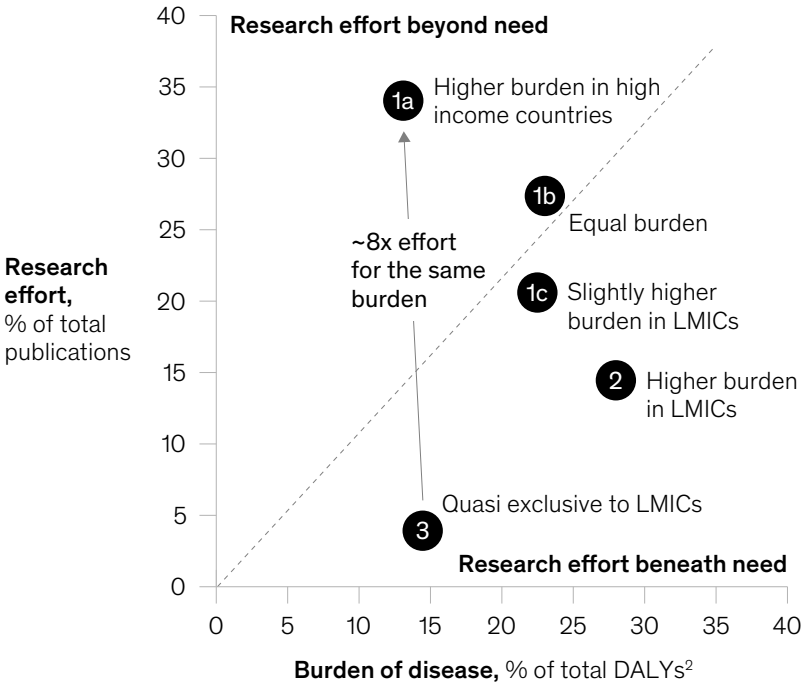
Exhibit 20

Innovation will be required to tackle the world's biggest disease burdens.

WHO priority disease[1,2] vs. Pharma R&D projects, share of diseases and R&D projects in priority list



Research effort vs. Burden of Disease, by disease type according to WHO classification



Smart partnerships can help drive innovation to realize break-throughs for remaining disease burden

[1]A medicine, vaccine, diagnostic or other product that does not exist but is urgently needed by people living in low- and middle-income countries.
[2]Priority products listed on Policy Cures Research G-FINDER neglected diseases, products and technologies (2017), Policy Cures G-FINDER reproductive health areas, products and technologies (2014); WHO R&D Blueprint (2017), Initiative for Vaccine Research gaps (2017), priority pathogens list for R&D of new antibiotics (2017).
Source: Access to Medicine Index 2018; Yegros, et al, 2019 Exploring Why Global Health Needs Are Unmet by Research Efforts, http://dx.doi.org/10.2139/ssrn.3459230

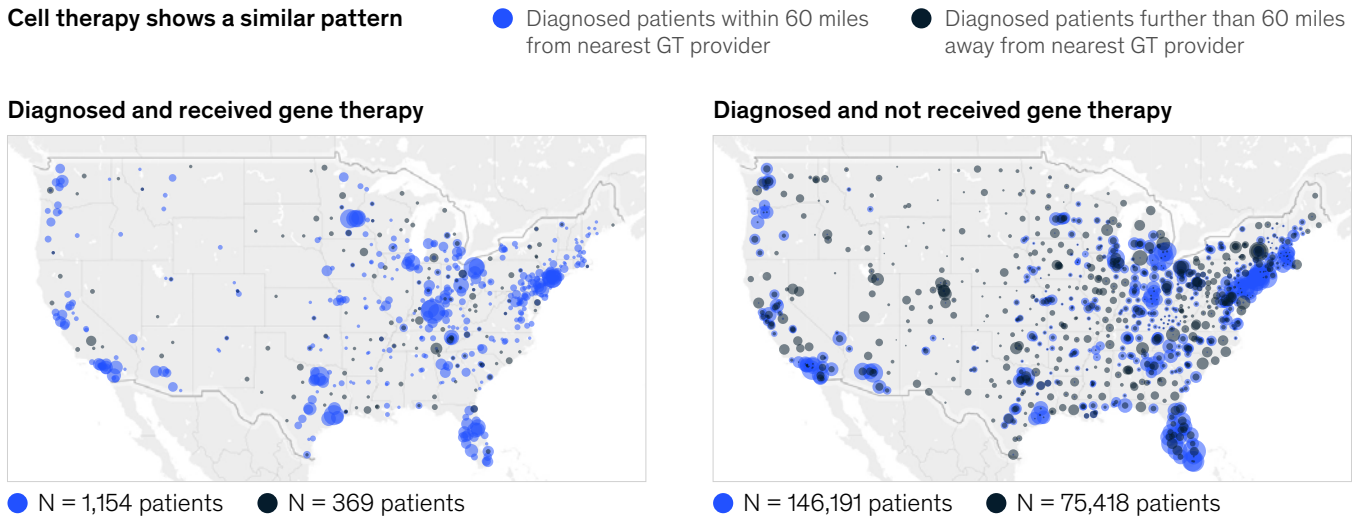
Stakeholders will also increasingly expect pharmaceutical companies to go beyond pricing considerations and actively shape how healthcare is delivered to ensure all patients receive medicines when they need them. This challenge extends to developed markets: even in the US, patients who live farther from gene therapy providers, for example, have a much lower probability of receiving gene therapy (Exhibit 21).

Improvements will likely require a broad range of interventions depending on a company's portfolio but increasingly include rethinking pricing, innovation, and operational partnerships with local healthcare systems and/or national NGOs and supranational collaborations to bring the best innovations in care to every patient everywhere.

While the industry establishes leadership in the social aspects of ESG, it will also need to meet rising obligations in environmental and governance aspects. And in an increasingly ecosystem-driven industry, improvements will require close partnerships with suppliers. For example, about 90 percent of the industry's greenhouse gas emissions are from up- and downstream sources, also known as scope 3,[62] that are out of the industry's direct control (Exhibit 22).

Exhibit 21

Holistic impact: In the US, the likelihood of patients receiving gene therapy is strongly tied to their proximity to a GT provider.



4.4× Patients within 60 miles of an HCP or facility offering GT are 4.4× more likely to receive GT

Source: Snowflake data, Source: compile.com. 1) Data includes only 2017-2020. 2) Invalid patient IDs are and duplicate claims are removed 3) Only relevant ICD10 and J-Codes are considered

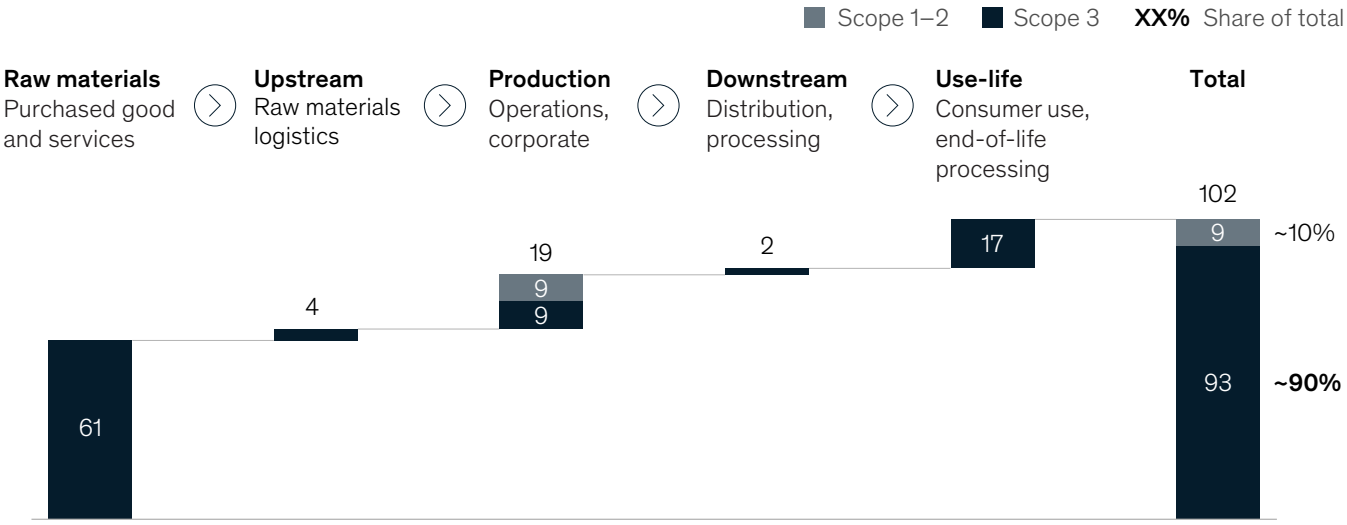
[62] CDP self-reported.

To significantly reduce emissions, industry leaders will need to examine their supply chain partners' emissions closely and might need to share the costs of improvements. The industry can also expand on its diversity and inclusion efforts to include those of its suppliers, building more representative workplaces along the end-to-end production process.

Exhibit 22

To reduce GHG emissions, pharma will need to address supply chains, which generate 90% of emissions.

GHG emissions from top players[1] (representing 40% of revenue), millions of metric tons



[1]Includes: BMS, GSK, J&J, Merck, Novartis, Pfizer, Roche, Sanofi
Source: CDP self reported

Key questions for leaders in biopharma

- Where will you lead in ESG, with the understanding that you will need to make real investments and set clear priorities?
- How can the industry shape its own ESG narrative outside the narrative of industries with much larger carbon footprints?
- How can you embed "ESG thinking" across the organization and connect it to the mission?
- How can you help mobilize suppliers, distributors and other partners to support ESG objectives?

8 What actions must companies take to build on their record of value creation? What bold moves will be required to deliver attractive returns in an evolving marketplace?

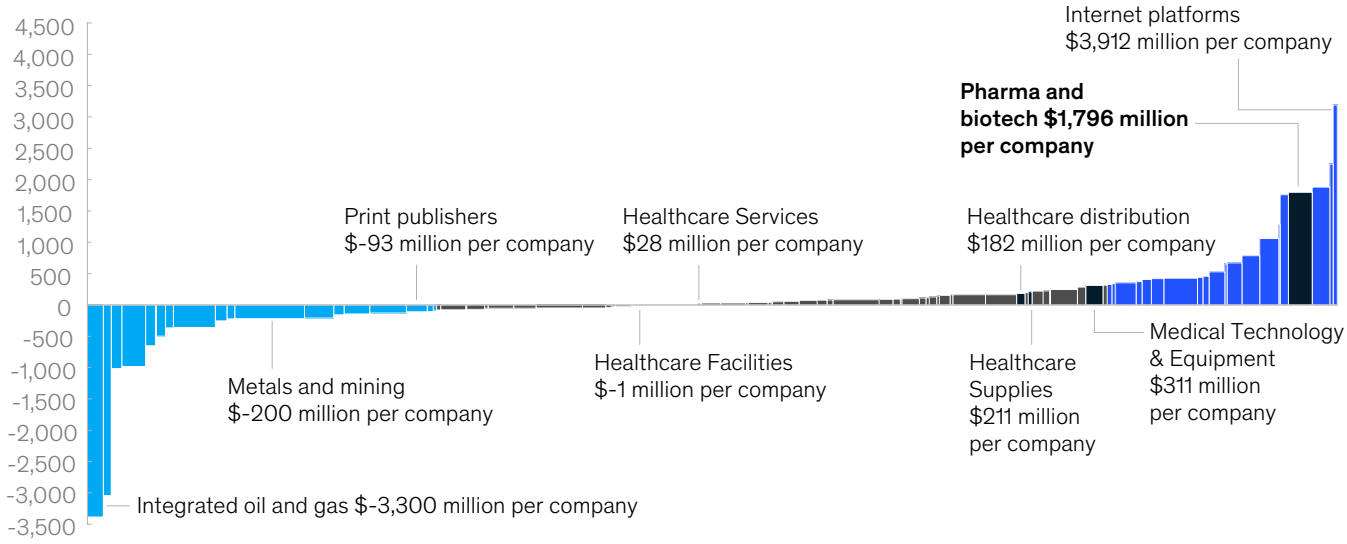
The biopharma industry has a strong record of shareholder value creation over the past decade. Biopharma is the leading sector for average economic profit generated per company (Exhibit 23), and one of the top three industries in total return to shareholders.[63]

While the largest public pharmacos have lagged the S&P500 over the last two years in total returns to shareholders (TRS)—12.6 percent vs. 23.4 percent for the S&P500—the record of biopharma over a ten-year horizon is favorable, with TRS similar to the S&P 500: 13.1 percent vs. 16.5 percent for the S&P 500. Tech was the only sector that substantially outperformed biopharma, driven by few large players with outsized returns.[64]

Exhibit 23

Pharmaceuticals garner more economic profit than most other industries.

Average economic profit of companies by industry,
2015–19, $ million, N = 2,689[1] companies, 95 industries



[1]Largest companies globally where sufficient data is available; incl. financial institutions; excl. private companies and real estate & REITS.
Source: S&CF Insights, Corporate Performance Analytics, S&P Global

[63] S&P Capital IQ.
[64] S&P Capital IQ: Top 50 public companies by revenue (top-42).

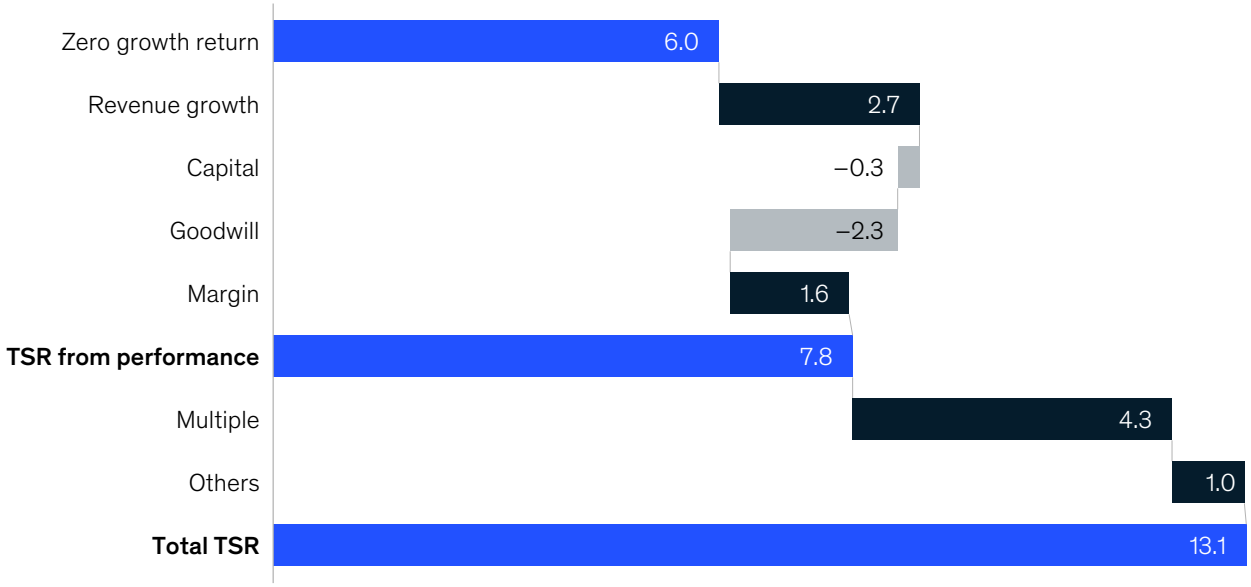
Over the past decade, three key elements have driven shareholder value created by the biopharma industry (Exhibit 24): sustained low- and mid-single-digit revenue growth (a 2.6-percent average from 2011–2021 and about 4 percent in recent years); steadily improving margins, with an EBITDA improvement from 42.2 to 45.4 percent; and price-to-earnings ratios rising from 15 in 2011 to 26 in 2021.[65] The industry has been distributing more free cash flow to shareholders—about 30 percent of revenues are being returned to shareholders in the form of dividends, share repurchases, or debt repayments.

The industry may not be able to maintain and build on this record of success by pulling levers incrementally for several reasons. First, revenue growth is likely to continue to hover around 3 percent—and even that may be difficult to sustain as today's top selling drugs go off patent. In fact, drugs accounting for 40–80 percent of revenue for top pharmacos are likely to lose exclusivity this decade.[66]

Exhibit 24

Value creation has been driven by revenue growth, margin improvement, and higher multiples.

10-year TSR decomposition for 42 largest public pharma companies,[1]
Dec 2011–Dec 2021, annualized TSR %



Note: Figures may not sum precisely, because of rounding.
[1]By 2021 revenue; excluding companies listed during the 10-year TSR window (eg, AbbVie).
Source: S&P Capital IQ, McKinsey analysis of TSR

[65] CAPIQ.
[66] Bernstein Analysis.

Will the recent downturn in biotech valuations impact innovation in the long run?

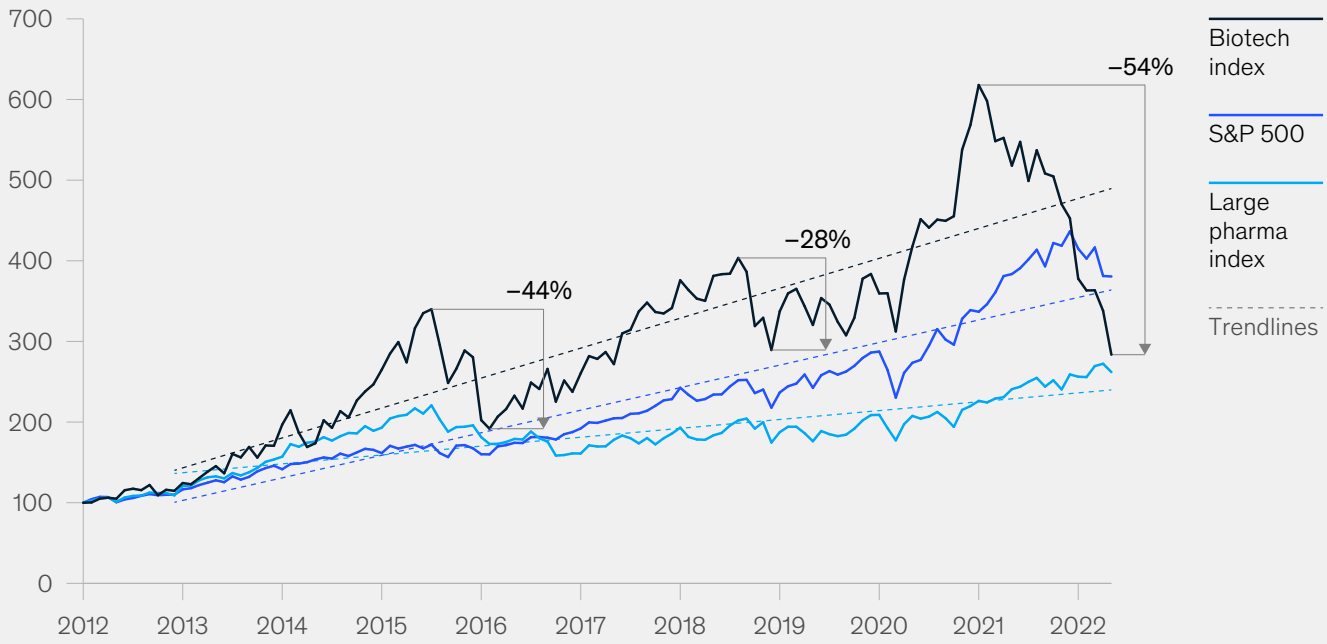
Many observers have noted the recent collapse in biotech valuations—XBI, one commonly tracked industry index, has plummeted by 54 percent since January 2021 (exhibit). This sharp drop has been limited to biotech, however, and over the last ten years, the industry has experienced "boom-bust" cycles, recovering well from downturns (exhibit). There is also a trend towards higher returns over the long run in exchange for greater volatility. So while the bar for true breakthroughs may now be higher, investors seem likely to continue to value biotech innovation in the long run. Indeed, venture funding in biotech has remained steady in recent quarters despite the recent downturn in public valuations, with the exception of Q1 2021, an outlier.[1]

Exhibit

Biotech valuations have fallen sharply since January 2021, but the industry has recovered from past declines.

Biotech, pharma, and S&P index performances over time,[1] Dec 2011–May 2022

Index value, 12/31/2011 = 100



[1]Indices used: SPDR S&P Biotech ETF (XBI), VanEck Pharmaceutical ETF (PPH), SPDR S&P 500 ETF Trust (SPY).
Source: S&P Capital IQ

[1] Jacob Plieth and Edwin Elmhirst, "In 2021 it paid to stay private when the chips were down," Jan 5, 2022, Evaluate Vantage.

~30%

of biopharma revenues were returned to stakeholders through dividends, share buybacks, and debt repayment from 2018–2021

Meanwhile, operating margin growth from the current 34 percent to 37–39 percent over the next three to five years is already baked into valuations; incremental growth beyond this may be difficult, and the prospect of pricing reform could put downward pressure on margins. It may also be difficult to increase payouts to shareholders given the need to fill pipelines either with M&A or additional R&D.

Leading companies in the industry have amassed unprecedented amounts of cash. A recent estimate from SVB Leerink suggests that 18 large-cap biopharma firms will have over $500 billion in cash by the end of 2022, with a theoretical ability to do nearly $1.7 trillion worth of deals if they leverage assets to borrow additional capital.[67] Biotech indices have declined by about 30 percent over the past year, presenting potentially unique buying opportunities. A major driver of value creation over the next decade may be how well companies deploy their capital now.

Senior leaders should consider their companies' stances on capital and resource management as well as shareholder returns. Incrementally improvements are unlikely to generate attractive shareholder returns. Previously, we showed that companies who reallocate capital to value-creating areas generate about double the returns of companies who are slow to reallocate capital.[68]

Key questions for leaders in biopharma

- How can you move to more aggressive and proactive portfolio management, including M&A and divestitures, to build a portfolio more fit for the future?
- How do you redesign the enterprise operating models to drive a major reset on cost—such as transforming the commercial model, which has remained at about 50 percent of non-R&D operational costs—and invest the freed-up cash in R&D and M&A?
- How do you build confidence in the long-term pipeline that translates into a multiple expansion by accelerating the transformation of R&D? Can you convince investors that your R&D engines have real platform value beyond individual on-market or late-stage drugs?
- Can you make at least one or two big, bold bets, such as building a new business, entering an adjacency, or committing to one major choice in a TA or platform, and provide enough resources for a multi-year commitment that could transform your company's future?

[67] Angus Liu, "Get ready for M&A: Large biopharma companies will have $1.7T in dealmaking firepower next year, analyst says," Dec. 1, 2021.
[68] "How nimble resource allocation can double your company's value," Aug, 30, 2016, McKinsey.com.

9 What changes must biopharma companies make in their organizational and operating models? How must they evolve value propositions to attract talent?

The biopharma industry employs more than 800,000 people in the US.[69] Historically, it has attracted talent with mostly stable, high-paying jobs: the industry's average annual salary in the US, about $127,000, was more than double the private sector average in 2017,[70] in part because employees in the industry are over three times more productive than the average in other industries.[71] Employment in the largest biopharma companies has remained relatively stable,[72] thanks to productivity gains and more outsourcing of clinical operations, manufacturing and some other functions.

While biopharma companies have introduced new capabilities and piloted to flexible models such as agile in select areas, the industry's basic operating model has remained largely unchanged for several decades. But functional hierarchies with franchise- and geography-based cells, and high productivity per employee, mask challenges in the fundamental operating model and capabilities. We expect three disruptions in pharma's organizational fabric in the near future:

1. *Increased need for speed.* If companies want to keep doing one thing they learned in the pandemic, it is making decisions and executing at speed. Those who have reduced the complexity of governance and decision making, de-matrixed their organizations and empowered lower-level managers to make decisions are poised to outperform their peers.

2. *Need for a more compelling employee value proposition.* Across industries, people's relationships to work are changing—many want more autonomy and professional development opportunities, for example, along with a stronger sense of purpose. While pharma has the noble mission of helping people live longer, healthier lives, it does not always provide the opportunities for rapid personal and professional development that some other industries may offer. As biotechs increasingly commercialize products, they are attracting more top talent with the promise of faster professional growth and less bureaucracy. Indeed, rankings of the best places to work[73] suggest that large pharma companies have been losing ground to biotech—and that the biopharma industry as a whole is struggling to acquire and retain the talent it needs.[74]

3. *Need for new capabilities.* Digitization and automation are changing the nature of competition in the industry and thus the labor market. As more routine and repetitive activities are automated, workers from manufacturing to finance may be displaced, and people with new capabilities will be required, such as in advanced analytics to optimize R&D productivity, agile content to drive omnichannel engagement with physicians, and compliant patient journey approaches to deliver seamless experiences. Today, however, roles in this area represent only about 3–4 percent of the biopharma employee base.[75] Since the industry will not be able to fill all of the additional roles by hiring, it will have to launch significant reskilling programs.

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[69] PhRMA 2019 Report on the Economic Impact of the US Biopharmaceutical Industry.
[70] Ibid.
[71] Ibid.
[72] Statista (pulling from company annual reports).
[73] "Top 10 Life Sciences Companies with 'Most Interesting and Meaningful' Work," BioSpace, Oct. 9, 2019.
[74] "2022 forecast: Talent war in life sciences, salary inflation in C-suite builds to 'negative feedback loop,'" Fierce Biotech, Dec. 22, 2021.
[75] Company annual reports; LinkedIn search of people's job descriptions containing "digital."

A common misconception is that speed and flexibility are the necessary trade-offs of scale. That is often true in today's matrixed organizations, but what if companies were organized in fundamentally different ways? Companies at significant scale may be able stay nimble by organizing around value creation and reconfiguring teams more quickly as opportunities shift.

To make such major changes, they will need to change backbone processes, technologies, mindsets and fundamental ways of working. Most biopharma companies have shied away from transformations like these, given the challenges and investments required. They could learn from incumbents in other industries, from insurance to retailing, that have continued to thrive despite the emergence of fast-moving digital natives and other attackers flush with talent and capital.

In terms of purpose and mission, biopharma starts from a privileged position, and it can now draw from broader pools of talent who can work remotely. The industry's opportunities in digital and analytics are vast, from finding molecules to running trials, making sales calls and improving patient compliance. First movers will gain important and lasting advantages.

Key questions for leaders in biopharma

- How can you move faster? Can you rethink how work gets done and who does it?
- Does your talent strategy truly enable the corporate strategy? Are you doubling down on digital and analytics skills?
- How should you configure the enterprise to thrive in an ecosystem with more porous borders, a heavier reliance on partnerships and so on?
- How can you connect your purpose to your talent value proposition in more meaningful and compelling ways?

Major industry uncertainties

Few people anticipated some of the key forces that shaped the industry over the last decade: the democratization of R&D, the emergence of life sciences as a fast-growing subsector, the concentration of investment in a narrower set of diseases, or the swift arrival of China on the global stage.

Few people can guess what the industry structure will look like in 2030; a range of distinct scenarios could play out. That said, the answers to six questions will help determine which scenario unfolds:

1. Could regulatory pathways truly transform?

Biopharma will always be heavily influenced by regulatory guidelines and frameworks. But following a decade with little major change, regulation could evolve on several axes:

— Will the US FDA remain the global pathway of reference to bring innovative drugs to market, or might an alternative emerge with global influence, such as the EMA?

— Will the US regulatory pathway allow for a much larger number of new molecules to be approved, breaking through a half-century plateau?

— Will regulators become more willing to rely on real-world data for decision making, building on early promises and overcoming limitations observed to date?

2. Will drug discovery experience a renaissance?

Several major trends appear to be converging that could transform drug discovery, including new technologies and progress in disease understanding. Trends to follow include:

— Discovery efforts moving toward earlier stages of disease understanding, including a systematic push by big biopharma to license programs at earlier stages of development.

— The acceleration of in-silico trials and discovery, leading to the emergence of an ecosystem of AI-based drug discovery companies. Indeed, about $4.5 billion in venture capital was invested in machine-learning-enabled drug discovery between 2019 and 2021.[76]

— Quantum computing, which could begin to fulfill its promise towards the second half of the decade.

[76] McKinsey analysis of Pitchbook data.

— A broadening of the industry pipeline with the re-emergence of therapeutic areas with significant unmet medical needs, including anti-infectives, central nervous system treatments, and a rebalancing towards small molecules.

— A greater emphasis on the use of RWE, including a shift to using RWE to support NDAs/BLAs.

3. Will the global biopharma industry become global again?

Decades-long trends have created a paradox. An industry with the noble purpose of helping people live longer, healthier lives around the world has become largely US-centric. The world's 15 largest biopharma companies make approximately 53 percent of revenues[77] and an even higher share of their profits in the US. Some changes could disrupt this industry structure:

— The US pricing umbrella could come under sufficient pressure to recalibrate pricing corridors across key global markets and lead to different commercial and launch decisions.

— New entrants, such as EQRx,[78] could gain traction with their business models, offering "new medicines at radically lower prices." The democratization of technology and the evolution of the biopharma value chain could allow more small participants to enter the industry, become full-fledged biopharma leaders and challenge the status quo.

— Big biopharma might once again embrace a broader geographic footprint, rebalancing its dependency on the US market, and providing much larger populations with more timely access to innovative drugs. Clearer geographic segmentation could emerge, with more autonomous operating models covering the US and a few developed markets rather than simply China and the rest of the world.

4. Will the tech industry disrupt biopharma?

The empowerment of patients, a profound underlying trend, can only accelerate as more technology players enter the fray. Big biopharma's role in that picture will be determined by answers to the following questions:

— After years of investment, will global tech giants crack the code of healthcare and take leading roles, transforming how patients make decisions and access healthcare?

— What is pharma's 'right to play' in patient and population management? Can the industry build distinctive offerings from its depth of disease understanding and trial data?

— What new profit pools will be created, and how will existing value pools evolve?

[77] McKinsey analysis of company annual reports/form 10k.
[78] EQRx.com.

5. Will China reshape the global value chain?

As China emerges as an integral part of the global biopharma ecosystem, this is the time to consider scenarios that could play out:

— Stunted impact: Sharp regulatory and geopolitical challenges could limit China's global influence and impact on the industry.

— Momentum impact: China could have outsized influence in specific parts of the value chain, such as CRO and/or CDMO.

— Transformational impact: China could help speed and lower the costs of discovery, leading to a rise in affordable innovation on a broad scale.

6. Will the industry structure remain relatively stable or experience a shakeup?

Biopharma companies must remain nimble in the face of potential industry structural changes. Some points worth considering:

— Will smaller biotech continue to take their assets independently? Or recede as a consequence of recent commercial setbacks?

— Will the current biotech valuation correction (see sidebar) reaffirm big pharma's role as effective owner of the development and commercial links in the value chain?

— Will life sciences companies continue to outperform biopharma firms in value creation, leading to a redistribution of value pools?

In separate articles, we will dive deeply into some of these uncertainties to help inform the dialogue on where the global biopharma industry is headed.

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Acknowledgments

We wish to thank the following individuals for their contribution to this work: Anchal Aggarwal, Nalin Balooni, Michael Balz, Axel Baur, Roy Berggren, Cameron Combs, Sara Cordero, Martin Dewhurst, Ajay Dhankar, Matthias Evers, Edd Fleming, Reinout Goedvolk, Prakshi Gupta, Jake Henry, Barbara Jeffrey, Brahma Kumar, Austin Lessin, Chris Llewellyn, Peter Pfeiffer, David Quigley, Abhishek Saxena, Cary Shoda, Navjot Singh, Sven Smit, Nicole Szlezak, Shail Thaker, Howard Tomb, Brian Trench, Rodney Zemmel, Austin Zimmet.

September 2022

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Printed in the United States of America.

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