



A more perfect union

Recombinant DNA

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A more perfect union

Scientific progress often begins by combining what had previously remained separate. In the case of recombinant DNA, that meant joining genetic material from different organisms to produce something new. The discovery of rDNA in the 1970s enabled therapies that would transform medicine and launch the biotechnology industry. It was a literal form of union—one that expanded what science could do, even as it raised questions about what it should do.

From the outset, those risks were not theoretical. Early pioneers, led by Paul Berg, recognized that recombinant DNA could produce unintended and potentially dangerous outcomes. Rather than advance unchecked, the scientific community called for a pause. The 1975 Asilomar Conference did not eliminate uncertainty, but it established a framework to manage it—defining containment standards and acceptable lines of inquiry before large-scale experimentation resumed.

The commercial implications followed quickly. Genentech's development of humanized insulin, and later monoclonal antibody therapies, expanded treatment options and drew significant investment into biotechnology. But as the field scaled, so

too did the complexity of its risks, extending beyond laboratory safety to questions of access, intellectual property, and the pace of clinical adoption. Technologies that followed—gene editing, cell therapies, RNA-based vaccines—continue to build on rDNA while raising similar questions in new forms.

Recombinant DNA illustrates that progress is not simply a function of discovery, but of how that discovery is governed. The same act of combining genetic material that made new therapies possible also introduced risks that required collective restraint. As new applications emerge, the precedent set at Asilomar remains relevant—not as a finished solution, but as an example of how a scientific community acted before the full implications were clear. Similar questions are now emerging around artificial intelligence, where capability is advancing faster than the systems designed to oversee it.

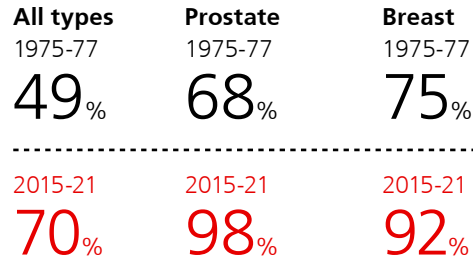
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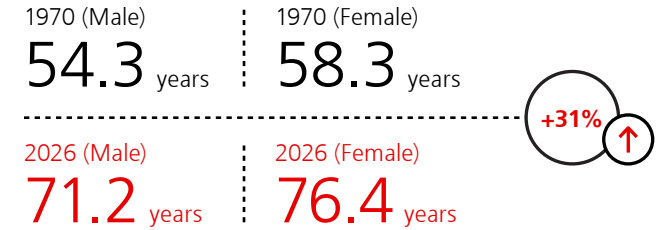
Infographic

Since its discovery in 1972, advances in rDNA have driven the development of breakthrough treatments, from human insulin to targeted cancer therapies, improving survival rates and dramatically enhancing quality of life. Over time, these advances transformed treatment from limited, resource-constrained approaches into scalable, highly effective therapies capable of reaching millions of patients worldwide. As the biotechnology industry evolved, rDNA became the foundation for a wave of therapies that has continued to extend and improve millions of lives worldwide.

Cancer survival rate



Global average life expectancy



Development of rDNA

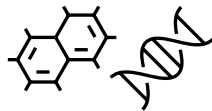
Before rDNA



After rDNA

Unlimited

Human insulin from bacteria/yeast acting as "mini factories"



Life years gained from rDNA therapy

Breast cancer

Drug: Herceptin (trastuzumab)

3.85 Life years



Ovarian cancer

Drug: Lynparza (olaparib)

2.77 Life years

DNA mapping (2003)

Time

13 years

Cost

3bn USD

Completion

92%

DNA mapping (2026)

Time

24-48 hours

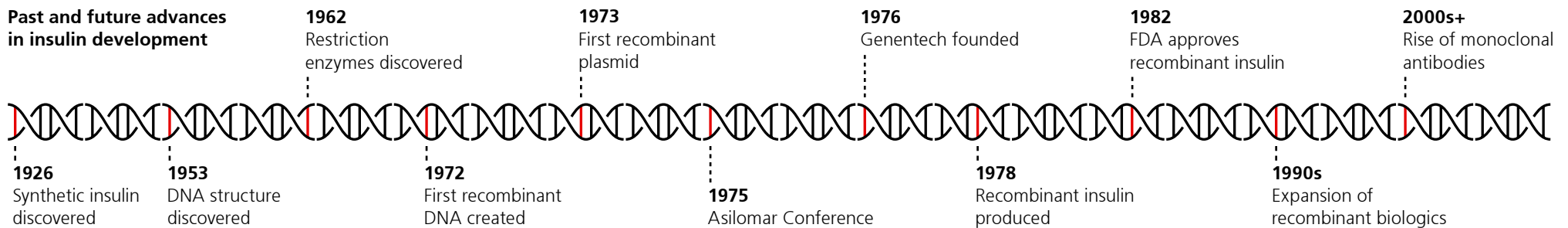
Cost

200-500 USD

Completion

100%

Past and future advances in insulin development



Sources: American Cancer Society, International Journal of Gynecological Cancer, Bulletin of Cancer, ScienceDirect, US Food and Drug Administration, American Council on Science and Health, Science History Institute, Worldometer, Eurofins Scientific



The history lesson

1980—the start of a new decade—one that would spark unprecedented innovation in the life sciences industry, yet also include a year ominously envisioned by George Orwell four decades earlier, bringing for some a sense of foreboding. In reality, however, 1980 brought both prominent recognition and commercial advancement for the burgeoning biotechnology industry. That year, Stanford University biochemistry professor Paul Berg shared the Nobel Prize in Chemistry for his groundbreaking 1972 discovery of recombinant DNA (rDNA). In the same year, Genentech became the first biotechnology company to list its shares publicly on the Nasdaq exchange. During that single year, and remarkably on a single October day, the scientific community celebrated the discovery of rDNA, while the broader investment world began to appreciate the commercial impact rDNA would soon have on the emerging biotechnology industry. Although George Orwell's 1984 cast a shadow of dystopian foreboding over the decade, the reality was one of scientific optimism, as the advent of rDNA technology opened new possibilities for human health and progress.

As in almost all instances of scientific innovation, multiple creative and hard-working individuals contributed to discovery, building on both prior and contemporary research efforts. In

1980 the Nobel Committee recognized Paul Berg's Stanford lab as the first to combine genetic material from different organisms into an rDNA-derived molecule. Over the following eight years, rDNA technology advanced into commercial application, giving rise to the modern biotechnology industry with Genentech's initial public offering (IPO).

Paul Berg's work with rDNA set the stage for additional scientific application, as well as some initial controversy and debate. In 1973, professor Herbert Boyer from the University of California, San Francisco (UCSF) and professor Stanley Cohen of Stanford University jointly advanced rDNA into broader application. Comparing their teams' separate research efforts, and limitations, professors Boyer and Cohen designed an experiment that would effectively stitch together genetical material from two distinct genetic sources, creating a hybrid organism with recombined (recombinant) genetic material. That new organism's engineered genetic code would then be inserted into a bacterium, multiplying as the bacterium reproduced itself, rapidly copying the new recombined genetic material. Professors Boyer and Cohen, in essence, harnessed Professor Berg's rDNA framework to create a cellular mass production process for engineered genetic material.

Before Paul Berg's rDNA discovery advanced into the initial commercialization phase, Dr. Berg and other leading scientists recognized the potential risks associated with widespread rDNA development and experimentation. He issued a public statement to the scientific community outlining the need for regulation of rDNA research to manage these risks and

recommended a moratorium on future development until the industry and government could establish protocols and boundaries for future research and commercial application.

Following Dr. Berg's open letter, scientific leaders convened at the Asilomar Conference in 1975 to discuss the path forward for rDNA technology. The conference produced guidelines that lifted the rDNA research moratorium while establishing biosafety protocols, including containment standards specifying which types of experiments required specific levels of physical isolation, and which bacterial strains could be used to avoid the emergence and survival of a dangerous engineered organism outside the laboratory. With safety protocols established at Asilomar and the research moratorium lifted, commercial development and further scientific advancement proceeded, a remarkable example of the scientific community's self-regulation of groundbreaking technology that would become a powerful economic growth and wealth creation engine in subsequent decades.

In 1976, Dr. Boyer joined Robert Swanson to formally commercialize the rDNA process into therapeutic drug development. Robert Swanson had previously worked for Kleiner Perkins Caufield and Byers, a leading Silicon Valley venture capital firm. Swanson and Boyer formed the company Genentech and raised venture capital funding, with Swanson serving as its chief executive.

Once formed and capitalized, Genentech used rDNA technology to develop human insulin. Insulin is a hormone

produced by the human pancreas that regulates blood sugar. Diabetics lack sufficient insulin production to effectively regulate their blood sugar, and this inability can lead to significant health consequences, including death.



rDNA technology enabled development of effective humanized insulin in much larger quantities.

At the time of Genentech's formation, diabetic patients relied on insulin derived from other mammals, mainly pigs, to regulate their blood sugar. Porcine pancreases were harvested and processed to produce insulin, but the production was time-consuming and expensive, and had very limited capacity. In addition, the porcine-derived insulin was foreign to the human immune system, often triggering immune responses and limiting its effectiveness. With supply constraints, high costs, and the limited effectiveness of non-human insulin, rDNA technology enabled development of effective humanized insulin in much larger quantities than had been possible with porcine-derived insulin. Once engineered using rDNA and inserted into a host cell, humanized insulin multiplied within the host cell line, which was then harvested at scale.

As Genentech advanced its humanized insulin through the clinical development process, it continued to fund its operations through additional private venture capital. As development advanced and Genentech's capital needs grew, the company turned to the public equity market. Genentech listed shares in an initial public offering (IPO) on 14 October, 1980—coincidentally, the same day the Nobel Committee announced Paul Berg would share that year's Nobel Prize in Chemistry.

While it is unclear whether investors that day understood the significance of this timing, they clearly saw the potential of rDNA technology through the lens of Genentech's IPO. The company offered one million common shares at an initial price of USD 39 per share. By the end of the day, Genentech shares—then trading under the Nasdaq ticker GENE—had risen as high as USD 89 and closed at USD 73, yielding a USD 500 million market capitalization for a company formed only four years earlier with modest seed capital.

The Genentech IPO was one of the most successful in history up to that point, with an intraday market capitalization increase that surpassed other notable IPOs of the year, including Nike in December, and trailing only Apple's IPO later that same year (see Fig. 1). The scale of profits made on that first trading day alerted investors to the significant potential of biotechnology and of the core rDNA technology that drove Genentech's research and product development. With revenue and profit still many years away and highly uncertain at that stage, investors

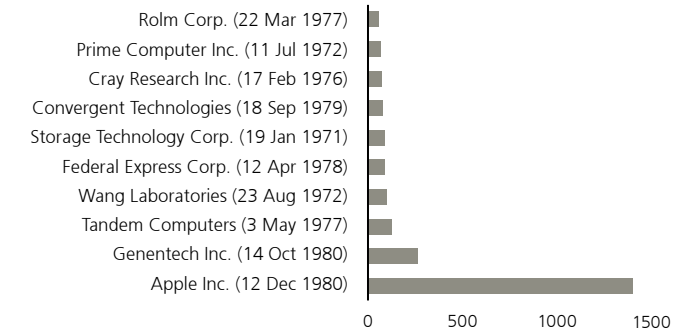
demonstrated a strong appetite for risk and the growth opportunities presented by Genetech and the broader biotechnology sector.

As a young company with limited commercialization capabilities and neither sales force nor production infrastructure, Genentech licensed its humanized insulin program to an established pharmaceutical company, Eli Lilly (LLY). Lilly and other pharmaceutical companies had been producing drugs for many decades, mostly using traditional medicinal chemistry, an effective but far less targeted approach to drug development. With the licensing of Genetech's insulin program and rDNA technology, Lilly would begin its multi-decade investment into biotechnology. Lilly helped steer the humanized insulin product through clinical development and the regulatory approval processes, while also scaling production capacity.

In 1982, the US Food and Drug Administration (FDA) approved Lilly's Humulin, the first humanized insulin product available to diabetic patients. Recombinant DNA enabled insulin production using primarily human DNA, which generated a much weaker immune response compared to non-human DNA and provided a more effective treatment for regulating blood sugar levels. Recombinant DNA also allowed for faster production of insulin, significantly increasing capacity. Humulin was a safer, more effective, and scalable insulin therapy that enabled many more diabetic patients to receive effective treatment.

Humulin generated significant sales for Lilly, with Genentech receiving royalties from those sales. By 1990, Humulin sales had grown to an estimated USD 750mn. In 1995, Lilly developed Humalog, a rapid-acting form of humanized insulin. By 2000, combined sales of Humulin and Humalog reached nearly USD 2 billion. Since the FDA's approval of Humulin in 1982, Lilly has generated over USD 90bn of combined humanized insulin sales (see Fig. 2). Genentech used royalties received from LLY's insulin sales to advance additional research programs.

Figure 1
Genentech's IPO marked biotech's arrival in public markets
US IPOs from 1970-80: Day-1 market capitalization gain, in USD millions

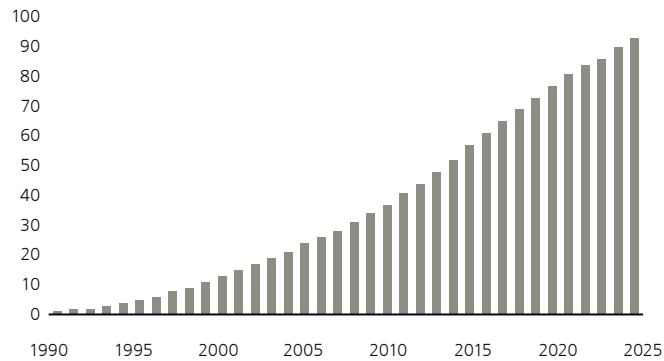


Source: SEC disclosures, Edgar, UBS as of 26 May 2025

By 2025, annual insulin sales from the top three global suppliers, Lilly, Novo Nordisk (Novo), and Sanofi, exceeded USD 13bn. Today, an estimated 150 million people use insulin worldwide. Recombinant DNA enabled the mass production of humanized insulin. Without rDNA, millions of diabetic patients would have gone without access to these life-preserving medicines.

Venture capital investment in the emerging US biotech sector increased from approximately USD 30mn in 1980, the year

Figure 2
Humanized insulin became one of biotech's first commercial successes
Eli Lilly's cumulative Humulin/Humalog sales, in USD billions

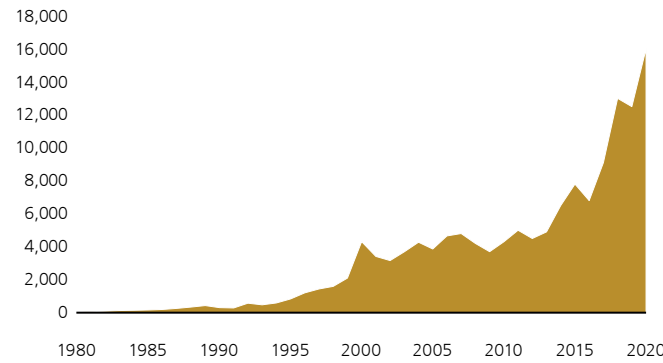


Source: Eli Lilly SEC documents, UBS as of 26 May 2026

Genentech went public, to over USD 300mn in 1990 and reached USD 1.2bn by 1996 (see Fig. 3). Recombinant DNA technology advancements continued to fuel that investment appetite and generated substantial investment returns as the industry developed additional rDNA-enabled therapies.

Additional biotech IPOs followed the surge in venture capital investment. Amgen went public in 1983, followed by Chiron later that year. In 1983, 10 US biotechnology companies went public, raising over USD 300mn in those IPOs. By 1987,

Figure 3
Venture capital helped propel the early biotech industry
US biotech venture capital investment from 1980-2020, in USD millions

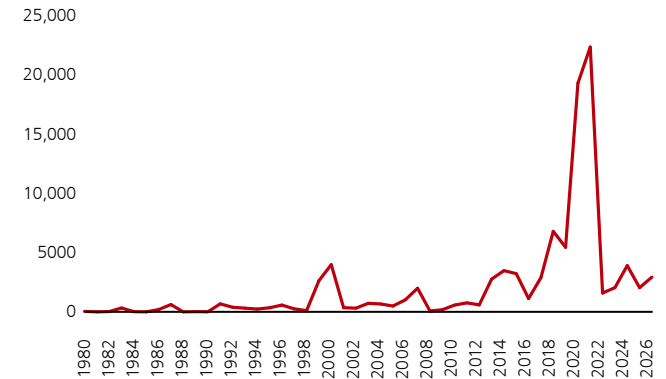


Source: NSF Science & Engineering Indicators; PwC/NVCA MoneyTree Report; McKinsey Life Sciences Research, UBS as of 26 May 2026

biotechnology companies had raised USD 1.2bn in annual IPO funding. As with any growth sector, biotech funding expanded, and periodically contracted, within broader investment cycles. At the most recent peak in 2021, the biotech sector raised USD 22bn that year from US IPOs, with 125 biotech companies undertaking IPOs that year (see Fig. 4).

With the early success of rDNA-enabled products and continued investment into biotech, the application and innovation of rDNA expanded. Biotech companies increasingly focused

Figure 4
Biotech IPO funding grew with the industry's expansion
Annual biotech IPO capital, in USD millions



Source: Bloomberg, UBS as of 26 May 2026

on monoclonal antibody (mAb) therapies to address disease. Prior scientific research demonstrated how monoclonal antibodies had the potential to more precisely target various diseases, theoretically enabling more effective therapies. By the mid-1970s, scientists had already developed mAb capabilities, but these were limited by the need to use DNA derived from mice (murine DNA). When introduced to humans, murine DNA often caused immune responses, limiting effectiveness and causing significant side effects.



By 1987, biotechnology companies had raised USD 1.2bn in annual IPO funding.

Recombinant DNA made chimerization possible, a process that combines human DNA with lower levels of murine DNA to neutralize a biological disease target while limiting the immune response. In 1994, the FDA approved the first chimeric antibody drug abciximab, brand name ReoPro, developed by Centocor to help prevent blood clotting after

cardiovascular surgery. The suffix “imab” became a portmanteau for a chimeric monoclonal antibody. Centocor would later develop the drug infliximab, brand name Remicade, which became a blockbuster treatment for rheumatoid arthritis and eventually led to Johnson & Johnson’s (JNJ) acquisition of Centocor in 1999 for USD 4.4bn. Remicade generated peak annual sales of USD 7.0bn for JNJ and cumulative sales of USD 95bn by 2025.

Genentech continued its rDNA innovation with its own mAb research and development investments. In 1997, the FDA approved rituximab, brand name Rituxan, to treat B-cell lymphoma, a form of lymphatic cancer. Rituxan would become one of the most successful cancer treatments, generating peak annual sales of more than USD 7bn, and cumulative sales of more than USD 100bn by 2025.

Rituxan would also anchor Genentech’s broader oncology research and development program, which over time would lead to additional breakthroughs in cancer treatment. Genentech evolved its application of rDNA to mAb targets by engineering drugs that were even more humanized, with 90% human DNA. In 1998, the FDA approved trastuzumab, brand name Herceptin, for the treatment of HER2-positive breast cancer. The suffix “umab” captured

the more humanized nature of a specific mAb. Herceptin would also generate peak sales of USD 7.0bn and cumulative sales of more than USD 95bn by 2025.

Genentech then advanced its research into fully humanized mAbs. In 2004 the FDA approved bevacizumab, brand name Avastin, which targets various solid tumors. Avastin works by starving tumors of growth factor and became Genentech’s most successful drug, generating peak annual sales of over USD 7bn and cumulative sales of USD 107bn through 2025.

The success of Genentech’s cancer research—Rituxan, Herceptin, and Avastin—led Swiss pharmaceutical company Roche to acquire Genentech for USD 44bn in 2008. Roche had held a significant investment in Genentech for over a decade, and the clinical and commercial success of Genentech’s mAb drug development were key factors in Roche’s consolidation of Genentech.

Roche’s acquisition of Genentech ended one of the groundbreaking biotechnology innovation stories. But the pioneering innovation unleashed by Genentech and its commercialization of rDNA technology led to widescale drug development, including recent advancements across multiple therapeutic areas.



A modern view

The development of purer and more effective humanized mAbs consistently led to the most successful and wide-selling biotechnology drugs. Abbvie's adalimumab, brand name Humira, reached peak annual sales of USD 21bn in 2022, making it the industry's top-selling drug. Humira treats multiple autoimmune conditions, including rheumatoid arthritis, psoriasis, and Crohn's disease. Humira has generated cumulative sales of over USD 240bn and continues to generate more than USD 5bn in annualized sales today, even after its patents have expired.

Merck's cancer drug pembrolizumab, brand name Keytruda, has since succeeded Humira as the industry's top-selling drug. Merck launched Keytruda in 2014 as one of the first immuno-oncology drugs that effectively harnesses the body's immune system to fight solid tumors. Keytruda generated 2025 sales in excess of USD 31bn and has generated cumulative sales of nearly 200bn since its launch (see Fig. 5).

Beyond oncology, the impact from rDNA is evident throughout the biopharmaceutical industry. The current GLP-1 drugs used to treat obesity and diabetes were developed by the same companies that successfully developed and marketed the first humanized insulin products—Novo Nordisk and Eli Lilly.

Novo Nordisk used its leadership position in the diabetes market to advance from humanized insulin into GLP-1 therapies, first for diabetes with liraglutide and later with semaglutide (brand name Ozempic), and then into obesity with semaglutide (brand name Wegovy). In 2025, Novo generated USD 34bn from its GLP-1 drug sales.

Eli Lilly followed a similar path, building on its insulin franchise to also expand into GLP-1 therapies. In 2025, Lilly generated over USD 36bn in GLP-1 sales, with its drug tirzepatide, brand names Mounjaro in diabetes and Zepbound in obesity. Over the next few years, GLP-1 obesity drugs will likely become the best-selling branded drugs in history.

The therapies that followed recombinant DNA's discovery have generated well over USD 1 trillion of revenue. More importantly, hundreds of millions of human lives have been helped and extended by the therapies enabled through rDNA's discovery and commercial application.

In 2023, the global biopharmaceutical industry spent approximately USD 265bn on research and development of drug candidates. Fig. 6 shows the breakdown by scientific approach. Monoclonal antibodies (33%), Cell & Gene Therapy (12%), RNA-based therapies (7%), and Biologics/Proteins (15%) are all enabled by rDNA. Recombinant DNA enabled approximately two-thirds, or just under USD 180bn, of recent annual R&D spending.

The industry's R&D spending also reflects the impact of recently developed drugs and vaccines. Ribonucleic Acid (RNA)-based therapies include both of the leading COVID-19 vaccines. Cell therapies now include chimeric antigen receptor T-cell (CAR-T) therapies for leukemia. Gene therapies

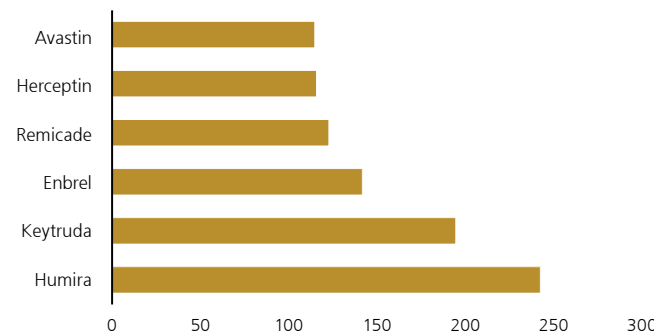
encompass gene-editing approaches enabled by clustered regularly interspaced short palindromic repeats (CRISPR) as well as gene replacement treatments that offer potential cures to myriad genetic diseases. These recent drug development pathways, including the Nobel Prize-winning science behind CRISPR, all trace back to rDNA's discovery and commercialization in the 1970s.

The application of recombinant DNA has extended human lifespans by making possible effective therapies for many of the leading causes of death—heart disease, cancer and, more recently, upstream conditions such as metabolic disease—as well as less common rare diseases. Further advances that build on rDNA have the potential to deliver even more effective treatments and cures for many

conditions that continue to plague humanity. While we are only five decades into the transformative therapeutic era triggered by rDNA's discovery and rapid application, this innovation cycle likely remains in a relatively early stage, with continued advances and benefits yet to come.

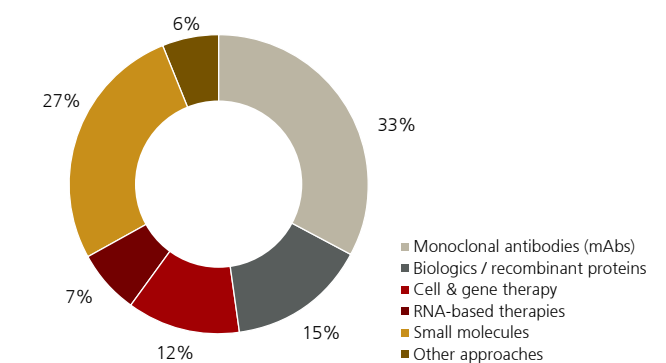
Recombinant DNA's discovery launched the biotechnology industry. From that discovery—along with subsequent advancement, self-regulation, investment, risk taking, and innate human curiosity—biotechnology has emerged as one of the most impactful industries in human history, improving the quality and length of countless human lives. George Orwell's 1984 imagined a future defined by control and limitation, but the story of biotechnology has unfolded as one of ingenuity, collaboration, and optimism.

Figure 5
Biotech's leading therapies became major commercial successes
Select cumulative monoclonal antibody drug sales through 2025, in USD billions



Source: SEC disclosures, EDGAR, Bloomberg, UBS as of 26 May 2026

Figure 6
Two-thirds of R&D spending on biopharma traces its roots to rDNA
R&D spend share by approach, in %



Note: Figures are approximate and estimated as of 2023
Source: Industry R&D pipeline and reported spending data, UBS as of 26 May 2026

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