



Evaluate Pharma®

WORLD PREVIEW 2021 Outlook to 2026...

14TH EDITION – JULY 2021

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FOREWORD

The Evaluate Pharma 2021 World Preview marks the second year that this report has been produced within the framework of the Covid-19 pandemic. Much has changed in the last 12 months. Vaccines have been developed and deployed, treatments now exist to help those hospitalised with Covid-19 and in many developed countries society is beginning to open up again.

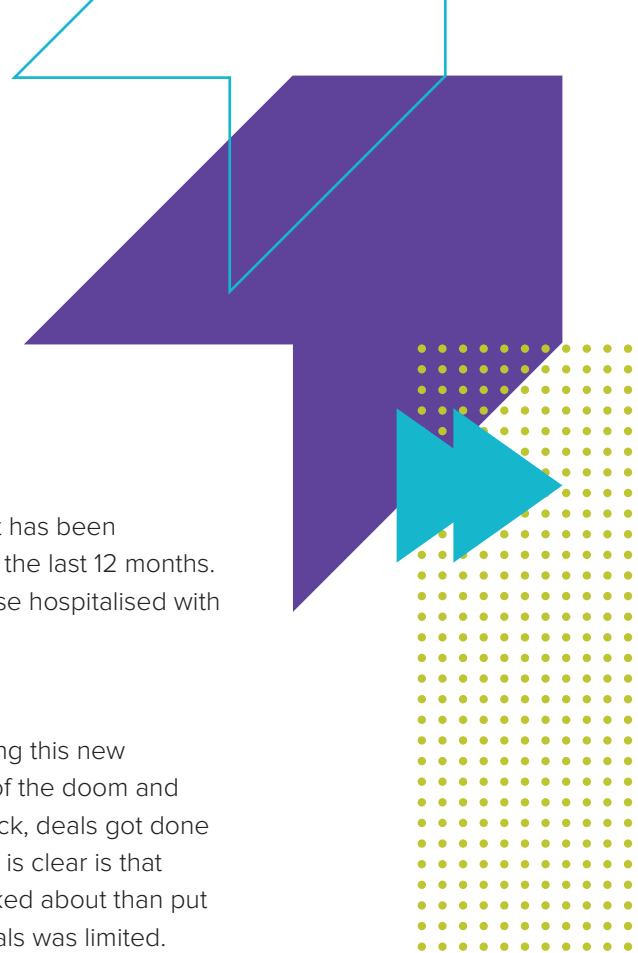
This year the World Preview focuses on how biopharma companies are navigating this new landscape, and the potential lasting effects of the pandemic. Fortunately, much of the doom and gloom forecast in 2020 failed to materialise. Stalled clinical trials got back on track, deals got done and the FDA continued to approve drugs at similar rates to previous years. What is clear is that many existing biopharma trends have accelerated. Digital health, often more talked about than put into action, moved centre stage as face-to-face access to healthcare professionals was limited. This included a shift to remote clinical trials, helping developers to remain on track with their R&D programmes.

The report also examines the rise of China. Pharma's eastern giant is starting to make forays into the west, and substantial investment is fuelling a move away from 'me-too' products towards innovative R&D. The country's growing international confidence will have been boosted by its vaccine diplomacy, which has seen it supply low-cost jabs to low and middle-income countries.

A longer-term consideration is whether China will compete with Western pharma groups over price. Concern over rising drug charges are one of the biggest themes of this year's report. The increasing noise around affordability and the 'financial toxicity' of some treatments has moved pricing further up patients' agendas, and the political agenda. While the threat of pricing reform has been a much-debated topic in US over the past few years, there now appears to be more impetus to take material action.

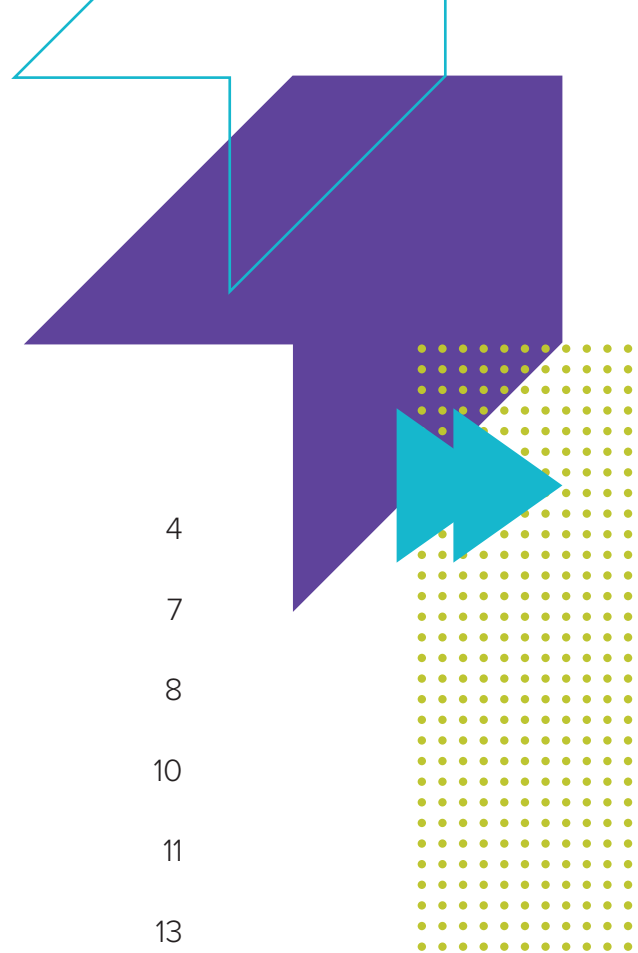
Evaluate's report forecasts continued strong growth in prescription drug sales over the next five years, to just over \$1tr in 2026. It also predicts that AbbVie will overtake Roche to become the biggest pharma company by sales that year. Sellside analysts, on whose estimates these figures are based, do not appear to believe that pricing reform will materially impact the industry any time soon. A more cautious outlook might well be warranted, however. The report clearly shows that in the midst of the economic turbulence caused by the pandemic, pharma provided a safe haven for investors. The amounts invested in fledgling biopharma companies breached previous records and investors showed huge appetite for developers debuting on the stock market.

The 2021 World Preview paints a positive picture of an industry whose relevance has been made readily apparent by demand for pandemic therapies, and beyond.



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Fast-forwarding Pharma – and its Pressures



► The World Preview 2021 was written by Melanie Senior

The money and attention focused on biopharma reflects the sector's strategic importance, but also adds urgency to questions around drug pricing, R&D efficiency and focus.

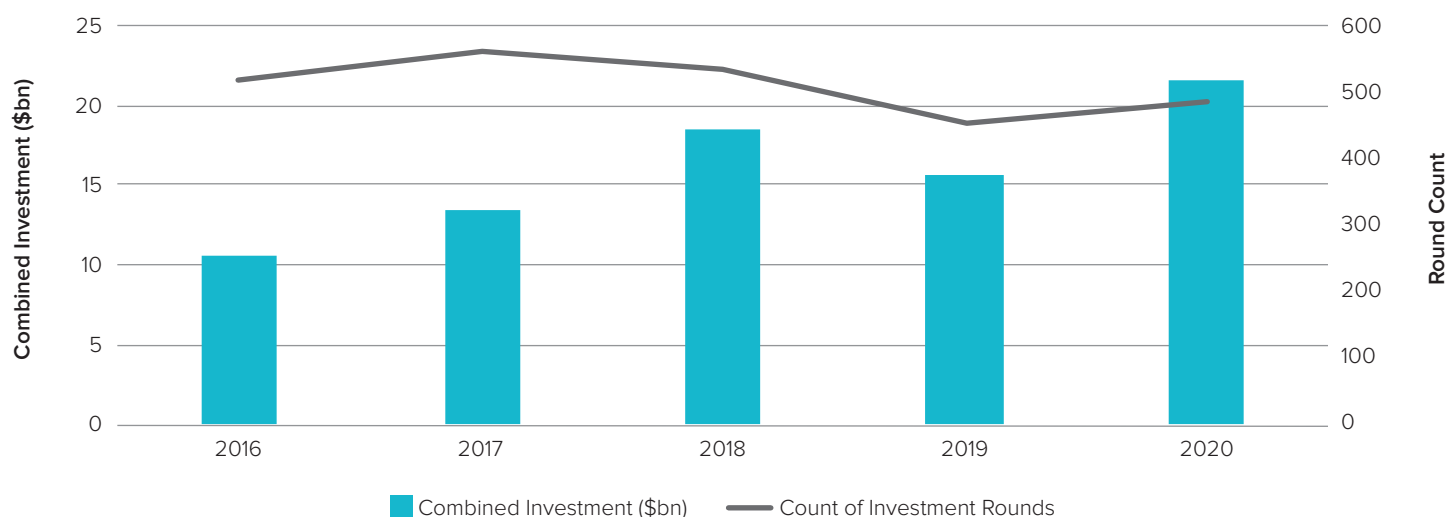
The pandemic compressed years into months, underscoring the industry's strength and creativity, but also exacerbating concerns over drug pricing and health system sustainability.

As the world cowered under Covid-19, the biopharma industry's prominence, relevance and reputation rose. Scientists became heroes. Healthcare concerns trumped economic ones; public and private investment flooded in at record-breaking levels. Vaccines emerged at speed, mobilising and validating both old and new technologies. The pandemic also fast-forwarded several trends already under way: the rise of digital solutions, including virtual (or remote) clinical trials, online healthcare provision and telemedicine, and an expanding biotech investor base. It also flipped vaccines and anti-infectives from underdogs to stars of the show.

Good practices emerged from the crisis. The UK-wide Recovery study and the World Health Organization's 12,000-patient international Solidarity trial of potential Covid-19 medicines delivered policy-changing results within months, showing how rapid and streamlined large trials can be. Data-sharing and collaboration expanded, including among competitors. Regulators were responsive and flexible, supporting adaptive trial designs and ushering in treatments and vaccines as fast as possible. After initial disruption, many biopharma research teams settled into shift work, using technology and data more widely and efficiently than before.

As industry mobilised to produce vaccines, investors piled in. Existing specialists doubled down, while new investors switched out of stricken sectors into one whose strategic importance has never been greater. The Nasdaq Biotech Index gained over 30% in 2020 to reach an all-time high at the start of 2021. Preclinical companies listed, raising hundreds of millions of dollars. Venture financing also hit new records, with private start-ups raising almost \$22bn in 2020, 39% more than the previous year.

Annual Venture Capital Investments into the Biopharma Sector





Amid the rising tide were several stand-out winners, most obviously vaccine pioneers Moderna – now worth over \$90bn, over 10 times its pre-pandemic value – and BioNTech and its partner Pfizer, which expect to sell \$26bn worth of vaccine in 2021. Even AstraZeneca, selling at cost a vaccine that faced

production delays and side-effect concerns, is worth 25% more now than it was pre-pandemic. Companies with vaccine businesses that failed to hit the Covid-19 jackpot, including Sanofi, GlaxoSmithKline and Merck & Co, have seen share price falls over the period.

Share Price YE 2019 – H1 2021

	YE 2019	YE 2020	H1 2021	% Change
Moderna	19.05	104.47	234.98	1,133%
BioNTech	31.19	81.52	184.46	491%
Sanofi	83.27	75.8	88.36	6%
AstraZeneca	49.01	49.99	59.9	22%
Pfizer*	38.91	36.81	39.16	1%
Merck & Co	91.03	81.8	77.77	-15%
GlaxoSmithKline	17.79	13.42	14.19	-20%

*Period includes performance after Upjohn spin off

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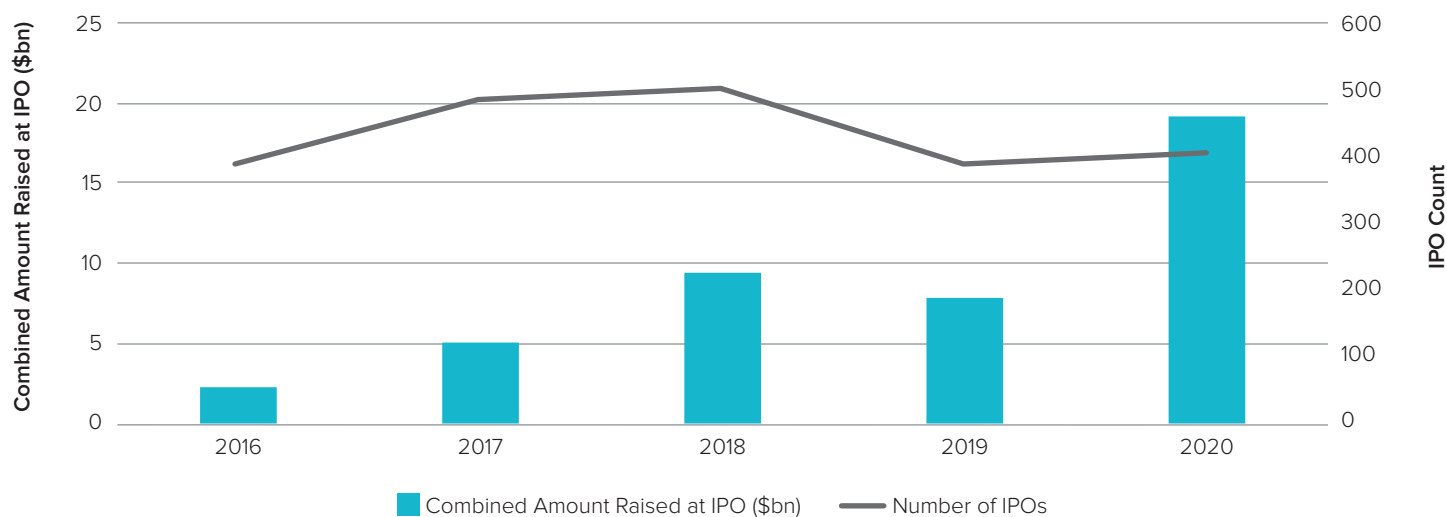
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While there have been winners and losers has the pandemic fundamentally re-shaped the biopharma industry's trajectory? Probably not. Biotech funding and valuations, already buoyant through 2018-19, may endure a while longer as investors'

excess cash chases inflation-protected growth. IPOs in 2021 so far are outpacing even last year's high. But, even if the sector graduates to a new baseline funding level, cycles will return, as surely as R&D programmes will fail.

Five Years of Biopharma Flotations



Meanwhile, worldwide prescription sales continue upward, forecast to top \$1tr by 2026 (See Figure 1). The 10 best-selling drugs that year, most of them biologics, will together sell \$127bn. Oncology will continue to dominate, though AbbVie's new immunology duo of Rinvoq and Skyrizi will keep the group at the top of the sales ranking. Pfizer and Moderna's

Covid-19 vaccines will add a new flavour of blockbuster – each pulling in an expected \$50bn in combined sales by 2026 – but these revenues will quickly tail off. That said, Novavax's protein-based candidate could sell \$5bn in 2026, particularly from low and middle-income countries (See Figure 11).

Pharma's Image Makeover?



As vaccine batches began shipping, talk was of a reputation repaired. Pharmaceutical companies no longer languished with tobacco at the bottom of the rankings, and pharma CEOs were making the front pages of mainstream newspapers. They dutifully put \$1 billion into an AMR Action Fund to develop new anti-infective medicines (See Box 2).

But the shine is already coming off pharma's image. The threat of drug pricing reform quickly re-emerged with US President Biden's inauguration in early 2021; in June it burst into full view when the FDA controversially approved Biogen's \$56,000-per-year Alzheimer's drug Aduhelm. That single event may have ripped away the sector's reputational gains. Uneven vaccine

distribution across the globe has not helped, though most of the blame for this has fallen on politicians.

So, far from being excused from its past ills, this newly visible sector faces increased scrutiny. As government stimulus packages in the West begin to dry up public payers, insurers and the public are already asking more urgently how much they can afford to pay for healthcare. The resulting actions – from insurers, health technology assessment bodies and employers, if not from law-makers – could wipe away much of the collaborative spirit seen during the crisis. It might also temper valuations.

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Pricing Pressure Builds



Drug pricing reform bills have been swirling around Washington for years, but never quite seem to settle. Ex-president Trump's loudly touted 'most favoured nation' rule, which sought to tie US prices of some hospital-administered drugs to those in other countries, faltered in the law courts. Yet lower US drug prices is one of the few things Biden and Trump agree on. Biden is calling for Medicare-negotiated drug prices and lowering the Medicare eligibility age to 60. But with only a narrow majority in Congress and almost certain industry

lobbying, he is limited to a verbal wish-list, rather than concrete policy. Smaller legislative and regulatory measures may slip through, but experts say he is unlikely to get any major reforms into law, at least before the mid-term elections.

Still, the devastating economic impact of the pandemic, plus Aduhelm's approval, have lit up other, non-legislative price-lowering levers.

The impact of Aduhelm

As millions of Americans lost employer-sponsored health insurance, the pressure piled onto government-funded health programmes such as Medicaid for low-income families and Medicare for the elderly. With drug costs already front-of-mind, Aduhelm's approval lit the torchlight. Medicare will be hit hardest, since most Alzheimer's patients are over 65. Yet this drug, approved with a broad label for a condition that affects about six million Americans and with no competition, is unlike any product that the Center for Medicare & Medicaid Services has had to cover. The budget impact could be more than double that already spent on all other physician-administered drugs. Patients need expensive brain scans, and it's not yet clear who will pay for those scans. Coverage policy, when it emerges, could necessarily limit treatment usage - and private insurers are likely to follow suit. Yet even with restricted coverage, the drug will likely push up insurance premiums and out-of-pocket drug costs.

Hence the outrage. A coalition of employers and healthcare purchasers wrote to lawmakers urging comprehensive prescription drug pricing reform. The group wants the US government to negotiate prices in these monopolistic situations, where market forces are absent. However, few if any of the drug reform bills currently on the table would have solved the Aduhelm dilemma. For example, its price can't be linked to those in other countries as no such drug exists elsewhere.

Aduhelm's approval and pricing have also added urgency to calls for a more formal US health technology assessment body. The non-profit Institute for Clinical and Economic Review (ICER) already assesses new drugs and determines 'value-based' price ranges but has no legal mandate. ICER's value-based price for Aduhelm was \$3,000-8,400 per year, which Biogen clearly ignored.

But, Aduhelm aside, ICER prices are increasingly referenced in pricing negotiations. There have been high-profile examples

of sponsors sticking to the ICER price – Novartis's Entresto, for instance – or eventually bowing to it, in the case of the PCSK9 inhibitors. If the US government does decide to introduce a more formal drug pricing and health technology assessment body, ICER is a good place to start.

Meanwhile, insurers continue to use their coverage levers more aggressively – though ICER has also begun to rule on insurers' coverage policies. State legislators in the US have also become more active. Over a dozen have set up 'drug



affordability boards’, which limit prices and price increases. In Colorado, manufacturers must provide the list price of any drug they present to prescribers, along with the prices of at least three other medicines in the same therapy category, if they exist. Several states also require advance warning of planned drug price increases above certain thresholds.

Lower-cost biosimilars are beginning to have an impact in the US. At least half a dozen copies of AbbVie’s top-selling product Humira are lined up for the 2023 final patent expiry, and the FDA’s 2020 [decision](#) to make biosimilar insulins interchangeable with their branded counterparts will continue to provide downward price pressure. Some insurers are also providing cash incentives to patients who switch to cheaper biosimilars.

Meanwhile, the UK drugs regulator [MHRA is proposing](#) that biosimilar developers skip comparative efficacy trials and in vivo animal studies – potentially leading to cheaper biosimilar development and faster approvals.

Industry itself is starting to acknowledge the drug pricing time bomb, too. ‘Financial toxicity’ – referring to the access-limiting prices of some cancer drugs – [was a theme at this year’s ASCO conference](#), where the latest cancer drug developments are aired. PhRMA, the US industry association, recently expressed support for drug firms reimbursing Medicare for some pricey drugs that private purchasers can buy more cheaply.

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A Martinangelo, Sr Director, Competitive Intelligence & Prospection, Novartis

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The emerging Chinese biotech sector may also help push down US prices. This, too, had begun pre-pandemic, but the crisis heightened Chinese biopharma's global prominence, in part because the country came out earlier from lockdown than the US and Europe. The focus of many Chinese biopharma companies is evolving from “me-too” or generic drugs, to “me-better” and even first-in-class drugs. Validated immuno-oncology targets are a popular focus; there is room to create molecules and combinations that can be differentiated on efficacy, toxicity, indication or position in the treatment pathway.

Price is an additional competitive advantage. Chinese companies combine the latest technologies with a single-minded focus on R&D efficiency and speed – drilled in from their roots in copycat drugs. Several Chinese biotechs' straplines include words like “affordable” or “accessible”.

As China's healthcare market opens up to innovative drugs, medicines like PD-L1 inhibitors for cancer are making it onto the country's national drug reimbursement list (NRDL). The three winners in the latest edition of the NDRL – all domestic companies – offered 70-80% discounts, reaching prices less than 25% of those in the US.

Such pricing will not sustain an innovative pipeline for long. That is why a growing number of China's biotechs are seeking to launch in the US too, where even a 10-20% price cut could grab market share. They enjoy several tailwinds: an FDA increasingly open to Chinese clinical data, harmonising regulatory and clinical development standards, and increasingly discount-hungry US payers.

Hence Western-Chinese partnerships are multiplying and R&D-stage licensing deals involved Chinese firms are up. Chinese developers are also creating a new category of affordable, non-biosimilar drugs: Shanghai Junshi Biosciences in February

2021 licensed US and Canadian rights to its China-marketed PD-1 antibody toripalimab to US company Coherus for \$150 million up front, with another \$380 million on the line.

With its focus on R&D efficiency and speed, Chinese biotech could help urge the rest of the sector in a more sustainable direction. Granted, Chinese companies are for now working mostly on well-established targets, and with tools developed in the West. But as the sector matures, they could bring novelties other than greater affordability. In some sub-sectors, like next-generation CAR-T cells, Chinese scientists already have an advantage thanks to the technology's classification as a medical device, which accelerates approvals.

Non-Chinese biotechs are also working on more efficient R&D. EQRx wants to shake up the current US system by partnering with payers, slashing marketing costs and introducing a new purchasing platform for more affordable drugs. With 2020's largest A round and a further half-a-billion dollars from a January 2021 financing, EQRx has already in-licensed at least two Chinese assets. In June 2021 it tied up with AI-powered Exscientia to accelerate small molecule discovery. Exscientia is among a growing cohort of biotechs seeking to find or design new medicines in a more systematic, data-supported fashion.

Other firms are focused on making newer therapeutic modalities, such as gene and cell therapies, more cheaply and easily. This activity could streamline drug development and even support price moderation over the next 5-10 years.

There are now several forces picking at the thicket of interested parties and misaligned incentives within the US healthcare system. These will continue into and beyond 2026. A radical shift – like US price controls – is unlikely, but alternative pressures will combine to temper unsustainable and unjustified prices.

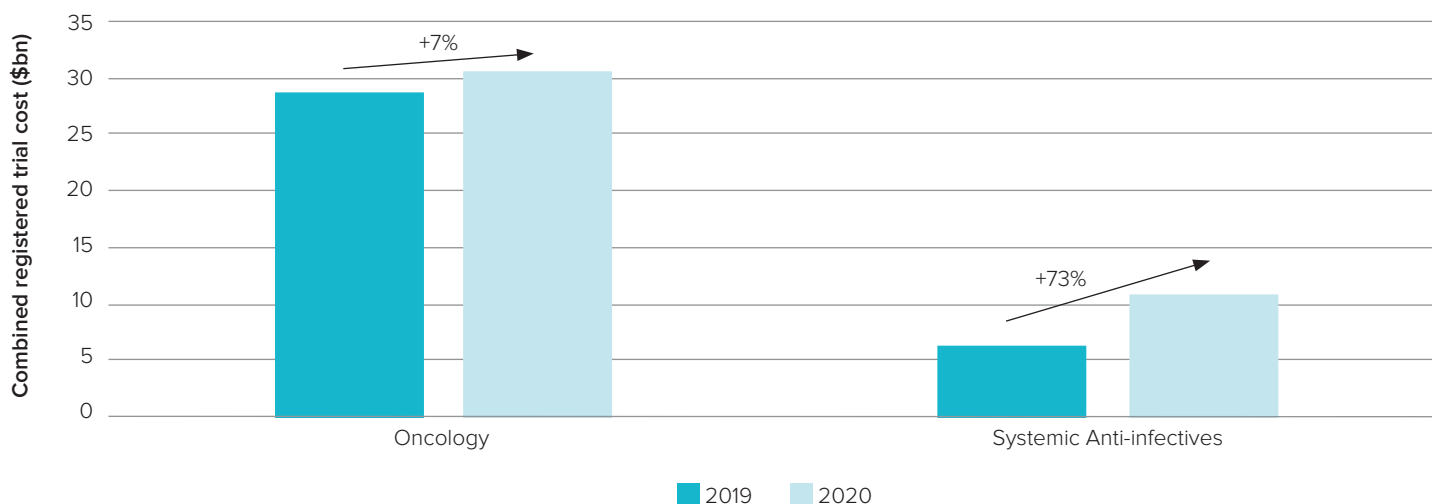
Cancer Stays on Top



The pandemic has not – and will not – end oncology’s dominance. Cancer has absorbed the lion’s share of R&D money for years and continued to do so even as a rapidly replicating virus shook the world economy and squeezed out

trillions of dollars of government support. Major therapeutic advances have been made across many cancers; there was even discussion at ASCO 2021 around whether the word ‘cure’ is being discussed in ever more settings.

Combined Registered Clinical Trial Costs



Regulatory and pricing tailwinds, plus a next generation of immuno-oncology targets such as LAG-3 and TIGIT, provide continued momentum. Since the FDA’s Accelerated Approval Pathway was introduced informally in 1992, two thirds of the beneficiary drugs have been cancer therapies. These medicines command high prices as they often represent one of few, or no, treatment alternatives for patients in need. Cancer’s clear genetic signatures and its speed of progression provide opportunities and obligations to extend lives, even by just a few months. This is often not possible for, say, an acute severe infection.

These dynamics will continue. Questions have surfaced around some of the FDA’s expedited approval routes but slowing access to cancer treatments is not on the agenda. Cancer drug developers are now seeking the next cohort of checkpoint inhibitors to enhance or replace the current ones –despite its success, market leader Keytruda is ineffective in many tumour types.

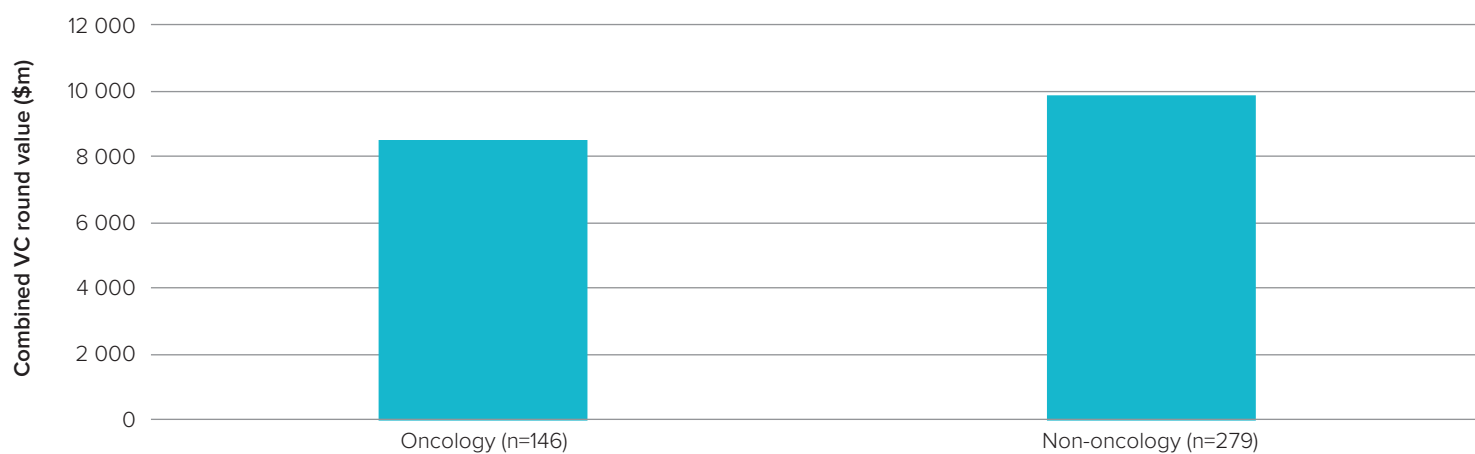
As the PD-L1 inhibitor sub-segment becomes more crowded, prices should eventually lower – even if the decline is slowed by a scramble for treatment combinations. Similarly, complex new modalities like CAR-T cell therapies will in theory become more accessible, and cheaper, as off-the-shelf versions materialise.

Faced with questions around oncology’s dominance, industry execs often argue that the technologies and discoveries uncovered in cancer research will spread to other areas. Genomic advances and new tools are pushing more personalised, molecularly defined approaches into immunology, neuroscience and beyond. The growth of platforms like mRNA and newer modalities such as engineered genes and cells, whose applications span multiple therapy areas, should in theory accelerate the shift.

For now, though, a re-balancing away from oncology is not obvious in sales or investment figures, despite the near-term uptick in interest in vaccines and anti-infectives.



2020 Venture Capital Spend by Investee Focus



Still, eight of today's 10 most valuable R&D projects, measured by NPV, are in disease areas other than oncology (See Figure 9). Reassuringly perhaps, numbers one and three – Eli Lilly's tirzepatide and donanemab – address diabetes and Alzheimer's disease respectively, corresponding to society's

other urgent public health threats. There were twice as many deaths in the US from heart disease than from Covid-19 in 2020; the virus also hit those with chronic conditions like obesity more severely than others.



One thing the pandemic has done is catapult anti-infectives and vaccines from sleepy and under-invested to exciting and important. Anti-microbial resistance and pandemic preparedness made it onto the G7 agenda, and a recent US 21st Century Cures Act 2.0 [discussion draft](#) includes sections

on pandemic preparedness and better incentives for AMR drug development. Political leaders are now acclimated to the dangers of pandemics – which clearly was not the case two years ago.

Tackling Anti-microbial Resistance – For Real, This Time

England's then-Chief Medical Officer Dame Sally Davies warned of the “catastrophic effect” of drug-resistant bugs back in 2013. Six years later, she catapulted the issue onto the world stage, warning the United Nations that drastic action was needed. Reports and a bit of funding emerged. But still not enough.

If this pandemic does not trigger meaningful investment in anti-infectives and drugs that address AMR, then it is hard to imagine what will. The [AMR Action Fund](#) was launched in 2020 by 20 or so pharma companies plus the World Health Organization, Wellcome Trust, European Investment Bank. It's offering up to \$1 billion to help develop 2-4 new anti-infectives over a decade.

It is a good start...

Government money and legislation is what will really move the needle in anti-infectives R&D. The UK NHS has since 2019 been piloting a subscription model for anti-infectives, whereby sponsors of an effective drug receive an annual payment over 10 years, regardless of how much the medicine is used. The US must follow suit with sufficiently high payments to offer an attractive monetary incentive.

Encouragingly, the PASTEUR (Pioneering Antimicrobial Subscriptions to End Up surging Resistance) Act was re-introduced into Congress in mid-June and later made it [into a draft 21st Century Cures Act 2.0](#). The proposed contract sizes range from \$750 million to \$3 billion – tiny in comparison with the trillions spent on Covid-19, but potentially a nice blockbuster for the sponsor.

Vaccines are also in fashion. Few would have expected annual sales of an infectious disease vaccine to surpass peak revenues of the world's top-selling drug, Humira, which last year had sales of \$20bn. Those big numbers won't last, but there should still be over \$10 billion's worth of Covid-19 vaccine sales in 2026 (See Figure 11). Prevention has not been a priority for drug makers. But they need to know that it is a key consideration for public and private payers, who will spend money on preventing transmissible respiratory diseases in particular – as well as continuing to embrace digital solutions to encourage healthier lifestyles.

The rapid, remarkable efforts to develop Covid-19 vaccines helped hone existing technologies and production methods, and introduce new ones, most notably messenger RNA – the

technology behind Pfizer/BioNTech and Moderna's vaccines. This – and the lucrative contracts that resulted for some of those that succeeded – has spawned new vaccine start-ups. Larger players with existing vaccines businesses – even those that have so far failed in Covid-19, like Merck & Co, GlaxoSmithKline or Sanofi – have confirmed their commitment.

The vaccine giants are also investing in mRNA, trying to bring some of the Covid-19 magic to seasonal flu, RSV or other respiratory viruses. Glaxo tied up with Germany's CureVac in February 2021 and is sticking with its partner on a second-generation jab, despite disappointing phase 3 results in June 2021 from CureVac's first vaccine. Sanofi extended a 2018 deal with Translate Bio and now has a Covid-19 and a flu candidate in trials.

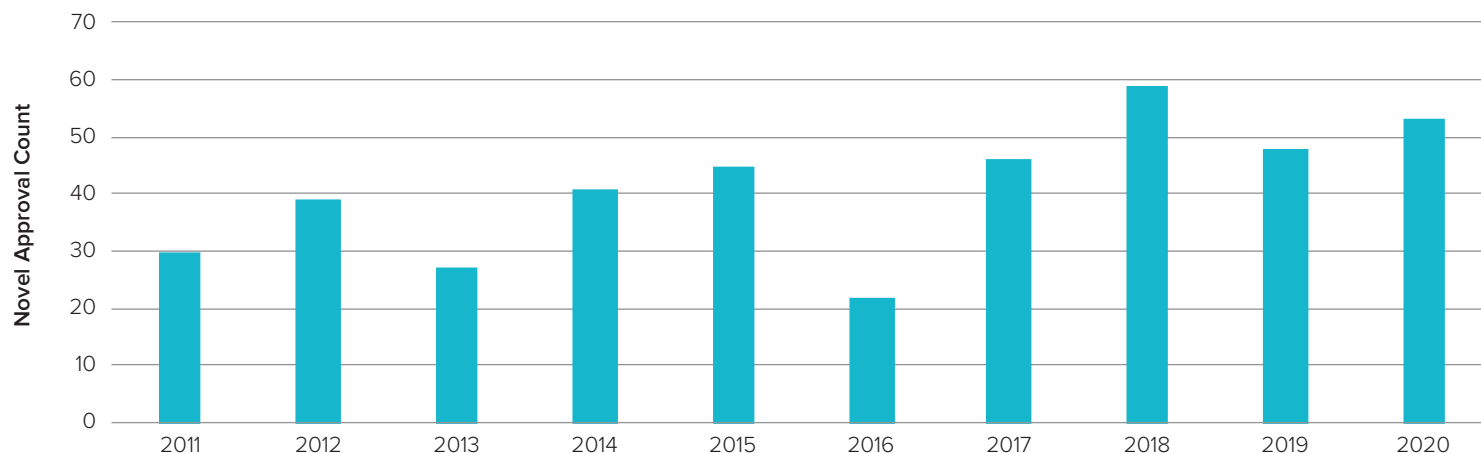
Is the FDA Becoming a Pushover?



Regulators were agile and responsive during the pandemic – another pre-Covid-19 trend that was accelerated. The FDA issued Emergency Use Authorisations for Gilead’s Veklury and three Covid-19 vaccines, and launched the Coronavirus

Treatment Acceleration Program to streamline trial reviews and advice to accelerate access to effective medicines. Yet even without the Veklury EUA, 2020 marked the second-highest new drug approval tally in last decade.

Novel CDER Approvals (NDA+BLA)



Nearly 60% of those were for orphan conditions or rare disease treatments. Almost 70% were in one of the several expedited categories and 92% of drugs were approved on the first appraisal cycle.

Have things swung too far in favour of expedited access? Few would argue with the pandemic measures, though there are calls on the agency to slow down the transition of vaccine EUAs into full approvals. Accelerated Approval in particular is drawing criticism – including from cost-watchdog ICER, which questions whether the pathway strikes the right balance between enabling rapid access and upholding safety and efficacy. Aduhelm’s accelerated approval based on an unvalidated surrogate endpoint made those questions louder, and three expert committee members resigned over the decision.

Looser regulators contribute to pricing pressures by allowing more drugs onto the market earlier – including expensive

oncology drugs. It also fuels upstream asset price inflation, boosting deal values – including IPOs. All of this drives criticism that the agency is in industry’s pocket. European policymakers are also discussing whether the 10-year orphan drug exclusivity period is over-compensating industry.

The FDA is awaiting the appointment of a permanent commissioner. Some experts expect a more hawkish candidate than the acting incumbent Janet Woodcock – a change that could change industry dynamics and investor confidence.

The picture is more nuanced than ‘strict versus light touch’, however. Regulators have multiple new forces and opportunities to contend with – from real-world data, computer model-informed drug development and the ongoing march of digital technologies. The FDA will have to remain flexible – yet also perhaps more clearly mark out the limits of that flexibility.

Moderating M&A



The US Federal Trade Commission does appear likely to sharpen up its focus on companies, though. With the recent appointment of the big tech critic [Lena Kahn](#) at its helm, the FTC is expected to clamp down on M&A that may result in price hikes, price fixing or other anti-competitive practices. The FTC is coordinating its pharmaceutical M&A scrutiny with counterparts in Europe, the UK and Canada. Illumina's \$8 billion purchase of cancer screening company Grail has attracted US and European regulatory scrutiny – and that of the [US lawcourts](#).

M&A of all sizes is a major driver of sector investment and

valuations. It continued strongly through the pandemic: \$132 billion worth of deals were signed in 2020, still dominated by cancer and rare diseases. The largest included AstraZeneca-Alexion (\$39bn), Gilead-Immunomedics (\$21 billion) and BMS-MyoKardia (\$13.1 billion). Mega deals like BMS-Celgene in 2019 and the big pharma mergers of yesteryear are now rare, so are unlikely to be hit by changes at the FTC. But bolt-on deals may not escape scrutiny either, if they lead to dominance of a given disease segment. Hence some expect the new antitrust focus to have a greater impact on the pharma sector than any pricing moves.

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Onwards and upwards to 2026, but not so fast



The newly prominent biopharma sector will continue to do well after Covid-19; healthcare has never seemed more central. But as any celebrity knows, with greater fame and funding comes greater scrutiny. Policymakers, regulators and the public will be watching more closely how companies behave and may be less tolerant of error.

They will be seeking an industry that is more price-sensitive, more transparent, more diverse and more ESG-friendly, where patient-centricity is more than a buzzword. Infectious diseases and vaccines should have gained and maintained higher priority.

There may be bumps in the road. Once the trillions of dollars of stimulus funds designed to cushion economies and money markets are shut off, the full brunt of this crisis will be felt. Biopharma will not be directly in the firing line, but increased hardship among the general public will squeeze out-of-pocket

payments and tighten payers' purses.

Full-blown US drug pricing reform looks unlikely. But Chinese competition, biosimilars, state legislators and an emerging set of companies focused on affordability mean the pressure will not let up. Meanwhile a tougher FDA could slow approvals, and tougher regulators could curb M&A. Each would take the steam out of the biopharma financing boom.

That may be no bad thing. SkYROCKETING asset and company valuations in discovery and early development – witness Sana Biotech's \$700m series A VC round followed by a \$676m IPO this year – fuel even higher downstream prices since no investor wants a down-round. The inevitable clinical failures then hurt even more, and even more publicly. That shakes confidence and may reverse the cycle, as any seasoned biotech follower knows.

For a deeper dive into the numbers...

Now that we have explored the key themes shaping the biopharma landscape, let's take a more detailed look at the data behind our insights and analyses.

As you will see, Evaluate Pharma's consensus forecasts predict that worldwide prescription sales will continue to sweep upward between 2021 and 2026, growing at an annualised rate of 6.4%. AbbVie is set to replace Roche as the highest ranking company by worldwide prescription drug sales in 2026, thanks to swift growth in the next-generation immunology products Rinvoq and Skyrizi.

Bristol Myers Squibb is anticipated to see the sharpest decline in rankings from 2020 to 2026, despite Opdivo being on course to become the second best-selling drug in 2026. This is principally due to the loss of Revlimid patents in 2022.

Merck & Co's Keytruda is expected to overtake Humira and become the top-selling product by 2026, with global sales of \$27bn and a 11% CAGR.

Finally, in the Covid-19 vaccine market, Pfizer and Moderna's vaccines are each projected to pull in more than \$50bn in combined sales by 2026. However, these revenues will tail off, with Novavax's NVX-CoV2373 forecast to be the only vaccine with growing sales to 2026.

Highlights

- Worldwide prescription drug sales to grow at +6.4% CAGR between 2021 and 2026.
- AbbVie to lead worldwide prescription sales in 2026, with \$59.3bn.
- Keytruda to be the top-selling product in 2026 with global sales of \$27bn and a 11% CAGR.
- Oncology prevails as the largest therapy area in 2026, accounting for 22% of prescription drug sales that year.
- Worldwide pharma R&D spend to grow at an annualised rate of 4.2% to \$254bn in 2026, with Roche as the biggest investor at \$14bn.
- The highest valued R&D project, ranked by NPV, is Eli Lilly's tirzepatide, at close to \$22bn.
- Patent expiries will put \$226bn in worldwide prescription drug sales at risk between 2021 and 2026.
- Novavax's NVX-CoV2373 is the only Covid-19 vaccine predicted to grow sales to 2026, provided production scales up.



Worldwide prescription drug sales are forecast to grow at an annualised rate of 6.4% between 2021 and 2026, according to Evaluate Pharma's consensus forecasts. These numbers are based on sellside estimates and will include forecasts for R&D projects that are not guaranteed to make it to market, or live up to expectations.

Pressure on drug prices in the world's richest nations is also unlikely to abate, and the subject remains high on the political agenda in the important US market. As such, any acceleration in the growth of top-line prescription drug sales beyond historical norms seems unlikely to materialise.

Orphan indications and rare diseases remain a big focus for developers. As a result, Evaluate Pharma predicts that orphan sales will double between 2020 and 2026, to reach \$268bn.

Figure 1: Worldwide Total Prescription Drug Sales (2012-2026)

Source: Evaluate Pharma® (May 2021)

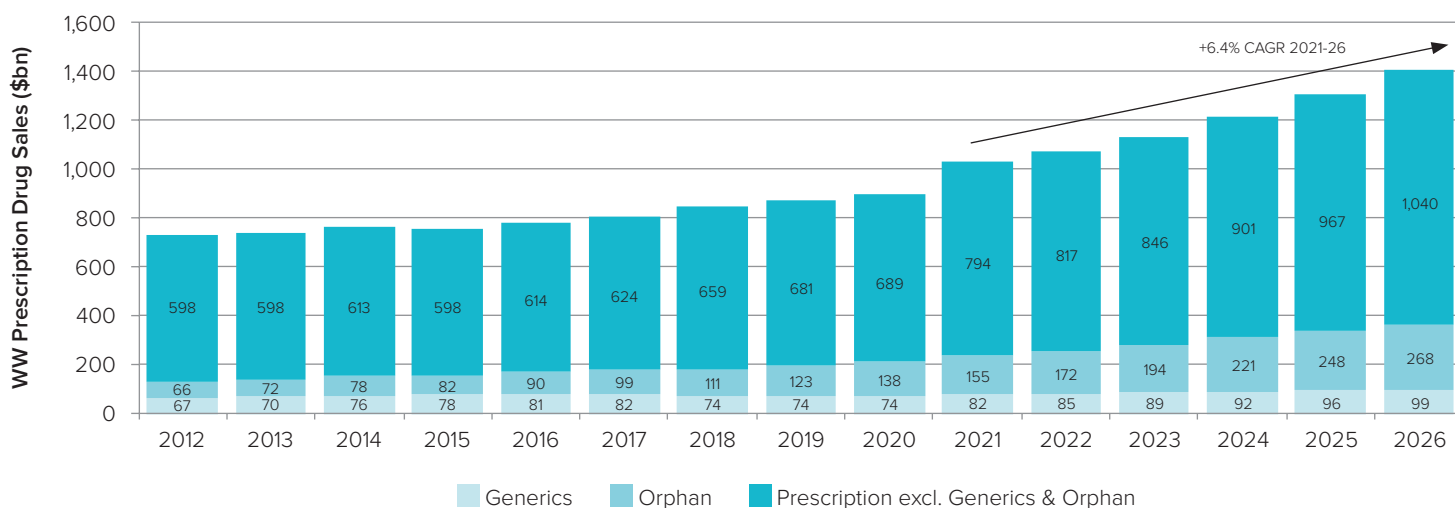


Table 1: Worldwide Prescription Drug Sales (2012-2026)

Source: Evaluate Pharma® (May 2021)

	WW Prescription Sales (\$bn)														
Year	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Prescription	731	740	767	759	785	806	845	877	901	1,031	1,075	1,128	1,213	1,311	1,408
Growth per Year		+1.2%	+3.7%	-1.0%	+3.4%	+2.6%	+4.9%	+3.8%	+2.8%	+14.3%	+4.3%	+5.0%	+7.5%	+8.0%	+7.4%
Change vs. May 2020 (\$bn)	-	-	-	-	-	-	-	-	-10	63	36	16	12	9	7
Generics	67	70	76	78	81	82	74	74	74	82	85	89	92	96	99
Generics as % of Prescription	9.1%	9.4%	9.9%	10.3%	10.3%	10.2%	8.8%	8.4%	8.3%	8.0%	7.9%	7.9%	7.6%	7.3%	7.1%
Prescription excl. Generics	664	670	691	681	704	723	771	803	827	949	989	1,040	1,121	1,215	1,309
Growth per Year		+0.9%	+3.2%	-1.5%	+3.4%	+2.7%	+6.5%	+4.2%	+3.0%	+14.7%	+4.3%	+5.1%	+7.8%	+8.4%	+7.7%
Orphan	66	72	78	82	90	99	111	123	138	155	172	194	221	248	268
Prescription excl. Generics & Orphan	598	598	613	598	614	624	659	681	689	794	817	846	901	967	1,040

Prescription incl. Generics CAGR 21-26 +6.4%

Note: Sales to 2020 based on company reported sales data. Sales forecasts to 2026 based on a consensus of leading equity analysts' estimates for company product sales and segmental sales.

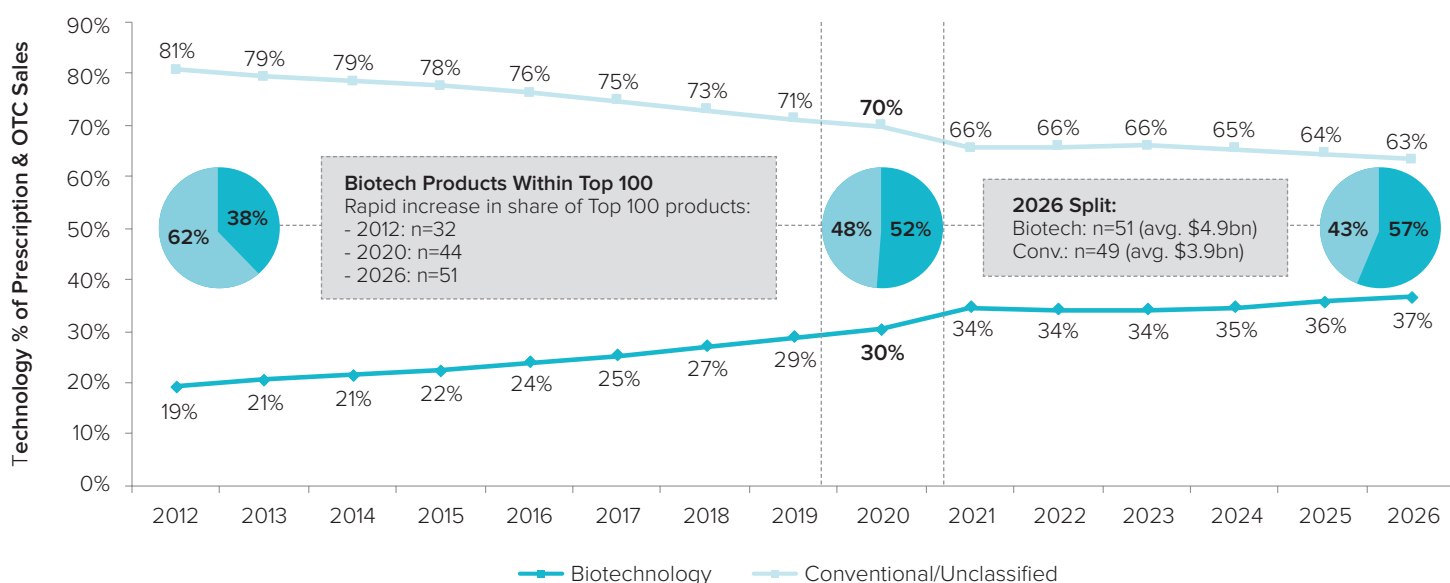


The importance of drugs based on biotechnology will continue to grow: biotech products will account for 37% of total prescription and OTC sales in 2026, up from 30% in 2020.

By 2026, biotechnology will account for more than half the 100 top selling medicines; according to Evaluate Pharma's projections 51 will be biotech-based. These products will generate 57% of the sales from this cohort, speaking to the higher price that biotech assets tend to command.

Figure 2: Worldwide Prescription Drug & OTC Pharmaceutical Sales: Biotech vs. Conventional Technology

Source: Evaluate Pharma® (May 2021)



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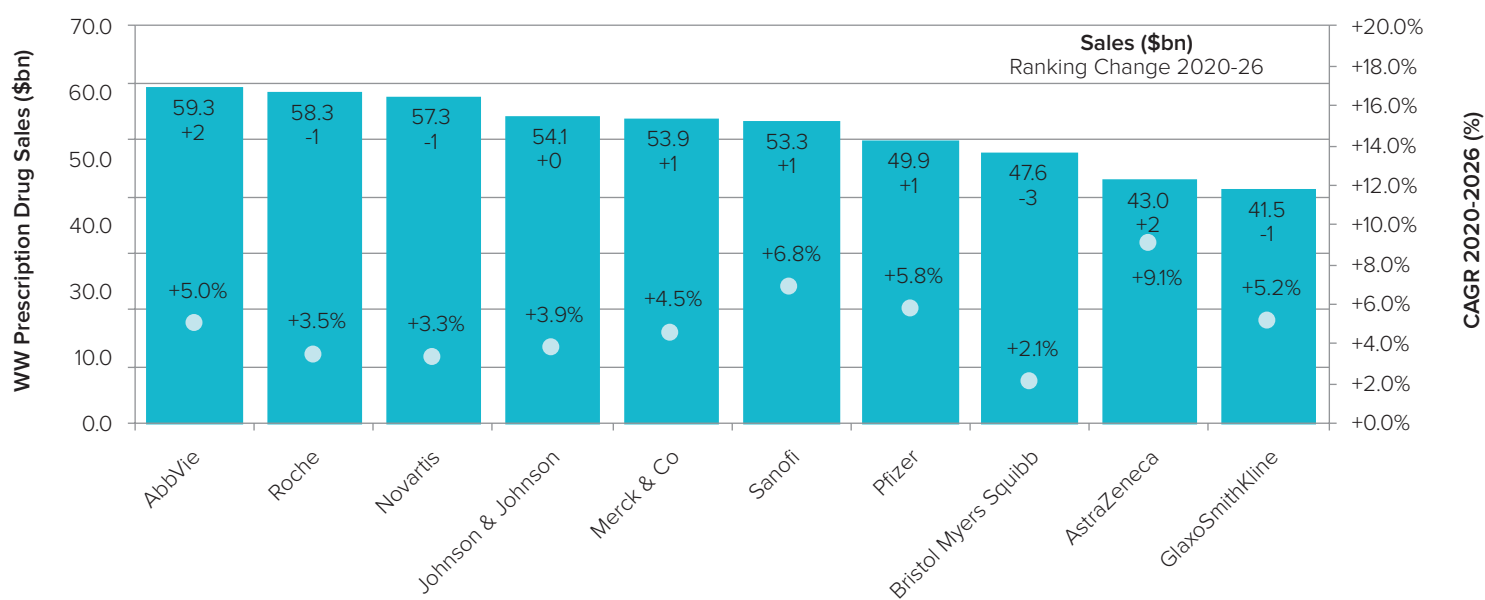


AbbVie will be the top company by worldwide prescription drug sales in 2026, according to Evaluate Pharma's consensus forecasts. The company will unseat Roche from the top spot thanks to rapid growth in the next-generation immunology products Rinvoq and Skyrizi, which are seen making up for Humira's loss of exclusivity in the US in January 2023.

Bristol Myers Squibb is set to see the steepest fall in rankings from 2020 to 2026, largely due to loss of Revlimid patents in 2022. This is despite Opdivo, the company's anti-PD-1 checkpoint inhibitor, being on track to become the second best-selling drug in 2026. Merck & Co's competing MAb, Keytruda, is forecast to unseat Humira as the biggest selling product in 2023.

Figure 3: Worldwide Prescription Drug Sales in 2026: Top 10 Companies

Source: Evaluate Pharma® (May 2021)

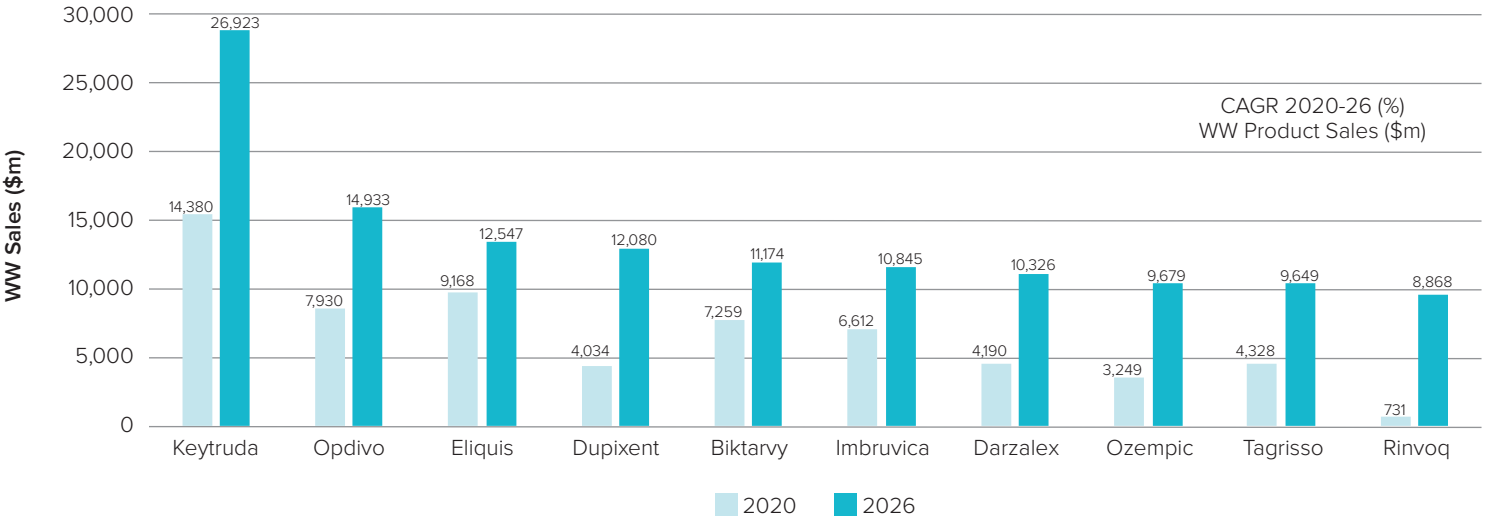




Rinvoq is projected to become the 10th best-selling drug in 2026, climbing from 38th place in last year's rankings. The Jak inhibitor is currently approved for rheumatoid arthritis, and needs to secure additional approvals in diseases including atopic dermatitis and ulcerative colitis to meet these expectations.

Figure 4: Top 10 Selling Products WW in 2026

Source: Evaluate Pharma® (May 2021)



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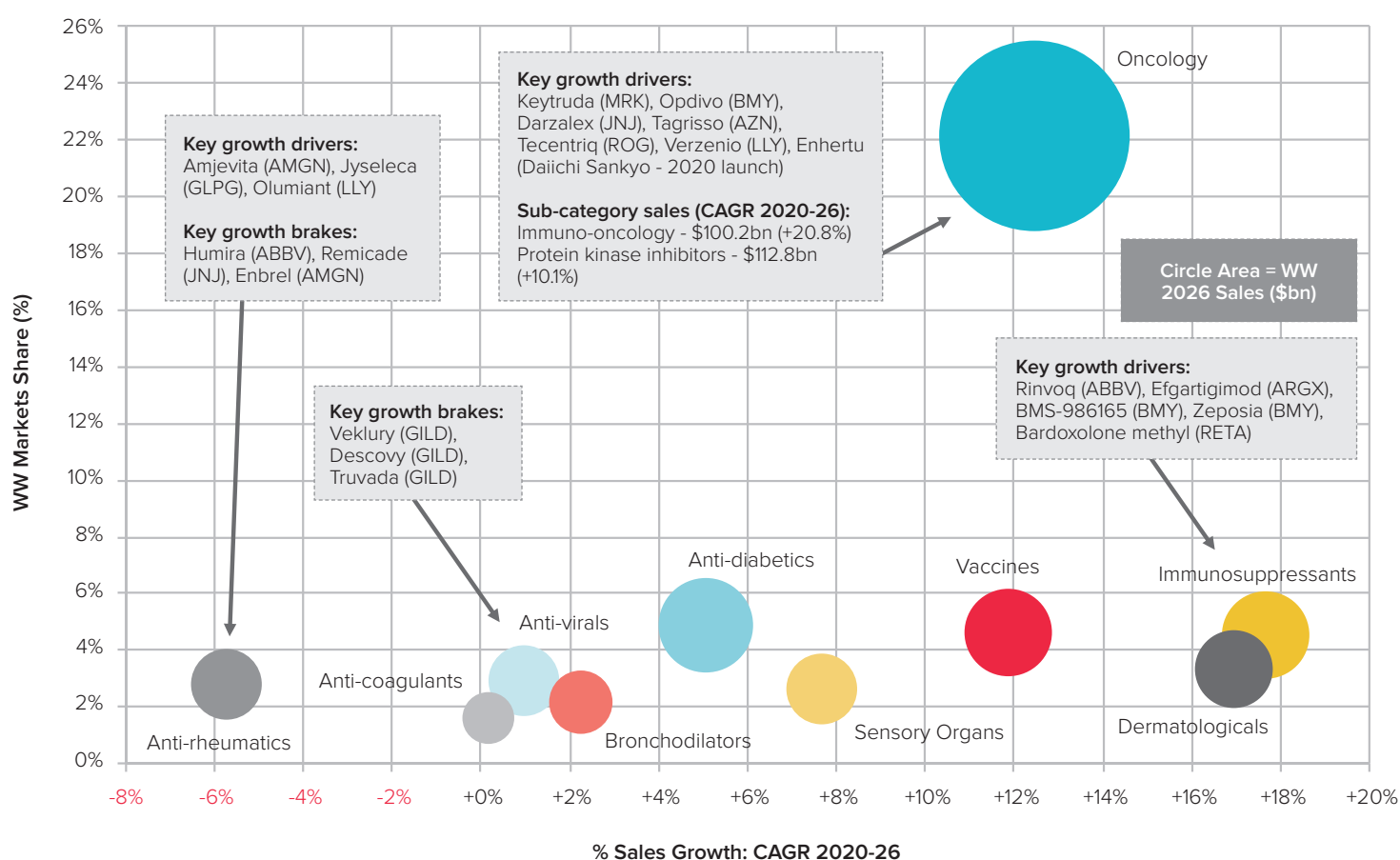


Oncology is set to remain the largest therapy area in 2026, accounting for 22% of prescription drug sales that year. According to Evaluate Pharma's projections, this amounts to cancer drug sales of \$319bn in 2026. The booming immuno-oncology subcategory is a major driver of oncology sales, led by the PD-1 inhibitors Keytruda and Opdivo.

The anti-rheumatics sector is expected to decline at an annualised rate of -5.7% from 2020 to 2026. The decrease can be attributed to the entry of biosimilar versions of Enbrel, Remicade and Humira. Worldwide sales of Humira are expected to drop by around \$14.5bn by 2026.

Figure 5: Top 10 Therapy Areas in 2026, Market Share & Sales Growth

Source: Evaluate Pharma® (May 2021)



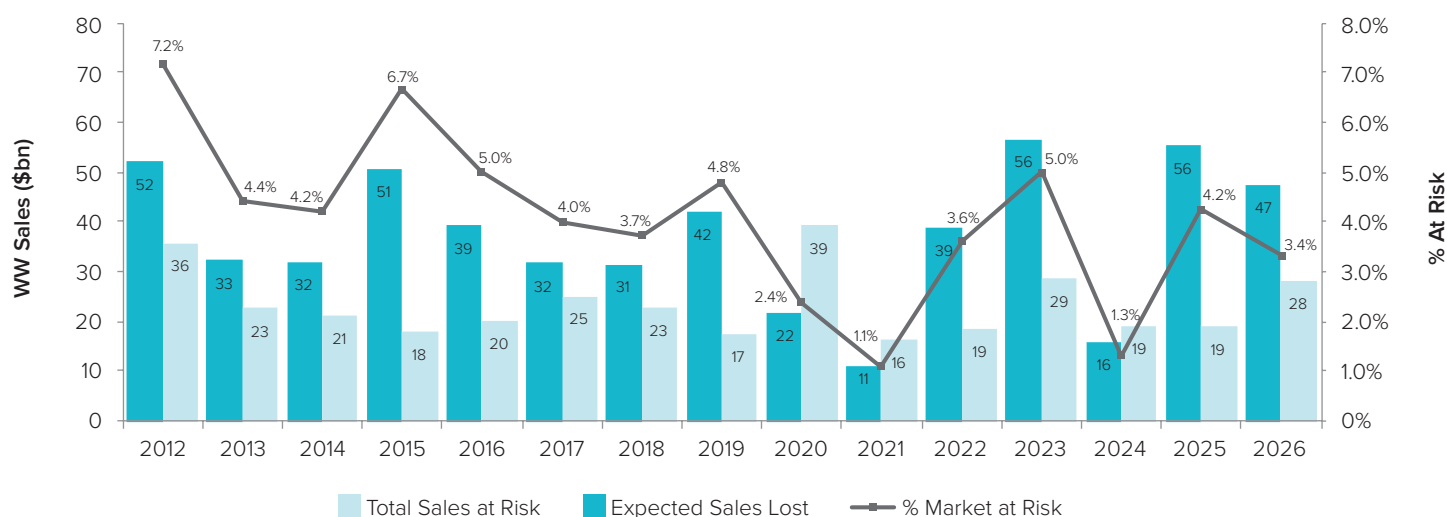


Two major patent cliffs are approaching for biopharma. First in 2023, when Humira loses exclusivity in the US, which is expected to cause an \$8bn drop in the drug's sales that year. Blockbusters from two Japanese majors will also be hit: Takeda's ADHD drug, Vyvanse, and Sumitomo Dainippon's antipsychotic Latuda will also succumb to generics.

In 2025 big sellers set to lose exclusivity include Bristol Myers's Pomalyst, Pfizer's Xeljanz and Boehringer Ingelheim's Ofev.

Figure 6: Worldwide Sales at Risk from Patent Expiration (2012-2026)

Source: Evaluate Pharma® (May 2021)



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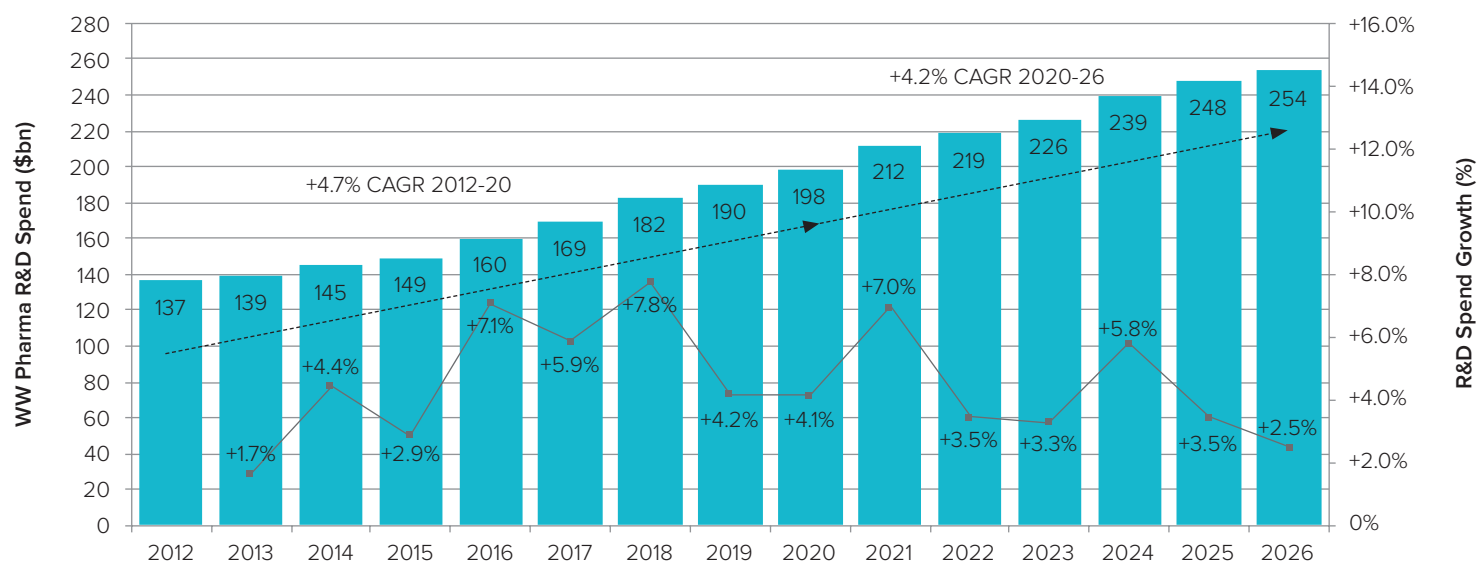


Evaluate Pharma® finds that worldwide pharmaceutical R&D spend is forecast to grow at an annualised rate of 4.2% between 2020 and 2026 to reach \$254bn, slightly slower than the historical CAGR of 4.7% between 2012 and 2020.

While biopharma is striving to improve R&D efficiencies, there are reasons why industry-wide spending on drug development could expand in the coming years. The financing climate has been strong for some time, granting smaller developers access to funds and facilitating a significant expansion of research endeavours beyond the big pharma group.

Figure 7: Worldwide Total Pharmaceutical R&D Spend in 2012-2026

Source: Evaluate Pharma® (May 2021)

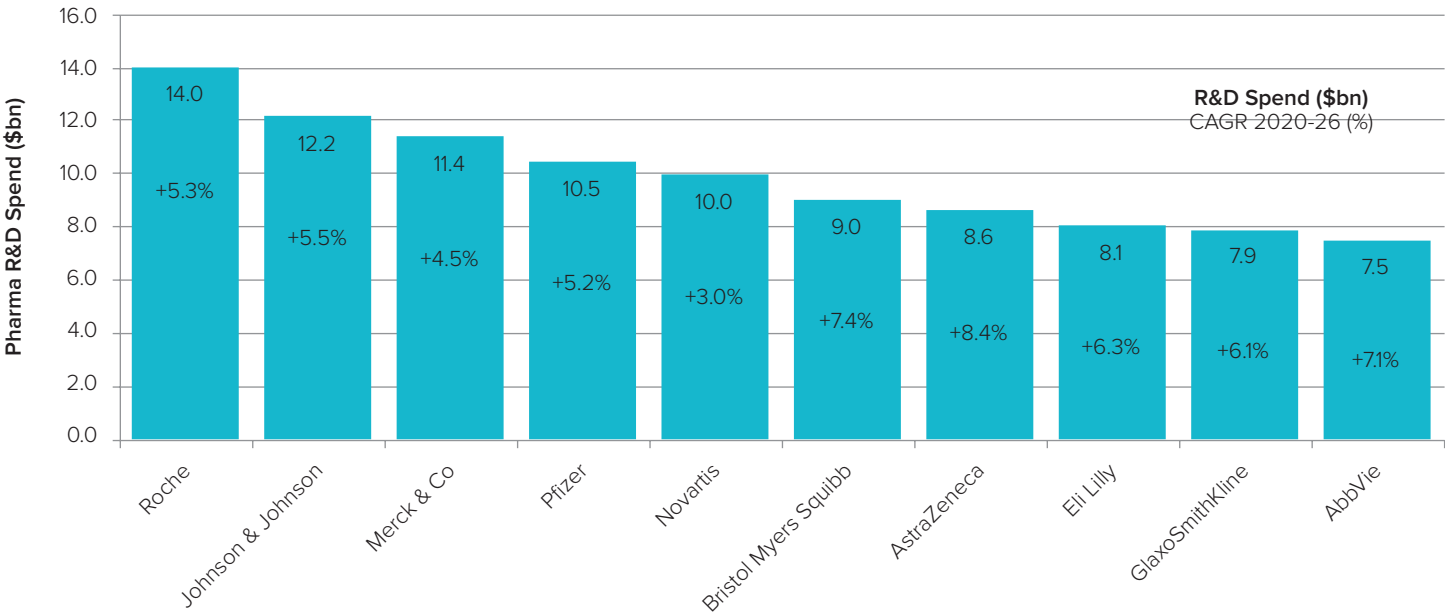




On a company level, Roche is projected to be the biggest investor in pharmaceutical R&D in 2026, considerably outspending its competitors with an outlay of \$14bn. AstraZeneca and Bristol Myers Squibb are expected to undertake the biggest R&D budget expansions over the 2020 to 2026 period.

Figure 8: Pharmaceutical R&D in 2026: Top 10 Companies

Source: Evaluate Pharma® (May 2021)



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Of the pharma majors, Lilly has traditionally invested the largest amount in R&D as a proportion of sales; the company now has two experimental medicines featuring in the 10 most valuable R&D projects. Tirzepatide employs a novel mechanism and is being investigated primarily for diabetes, while donanemab is a beta amyloid antibody in trials for Alzheimer's disease, which Lilly plans to file for approval later in 2021.

Bristol Myers Squibb's Tyk2 inhibitor deucravacitinib, another novel mechanism in the immunology space, also has substantial expectations behind it. This project is being tested in a wide range of autoimmune settings.

Oncology and immunology are well represented among the most valuable R&D projects. Leading the cancer projects in value is Daiichi Sankyo's antibody-drug conjugate DS-1062, which is being developed in lung cancer in collaboration with AstraZeneca. Novavax's Covid-19 vaccine, NVX-CoV2373, is also seen as potentially very valuable, despite being a late comer to the first wave of pandemic vaccines.

Table 2: Top 10 Most Valuable R&D Projects (Ranked by Net Present Value)

Source: Evaluate Omnium® (May 2021)

Rank	Product	Company	Phase (Current)	Mechanism of Action	WW Product Sales (\$m) 2026		Today's NPV (\$m)
1	Tirzepatide	Eli Lilly	Phase III	Gastric inhibitory polypeptide (GIP) receptor agonist; Glucagon-like peptide 1 (GLP-1) receptor agonist	4,802		22,108
2	NVX-CoV2373	Novavax	Phase III	Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) immunoglobulin stimulant	7,122	New Entry	12,732
3	Donanemab	Eli Lilly	Phase III	Beta amyloid N3 protein antibody	1,900	New Entry	12,381
4	BMS-986165	Bristol Myers Squibb	Phase III	Tyrosine kinase 2 (TYK2) inhibitor	2,395		9,661
5	Efgartigimod	argenx	Filed	Neonatal Fc receptor (FcRn) antibody	2,928	New Entry	9,505
6	Bardoxolone Methyl	Reata Pharmaceuticals	Filed	Nuclear factor erythroid 2-related factor (Nrf2) stimulant	2,333	New Entry	6,333
7	DS-1062	Daiichi Sankyo	Phase III	Topoisomerase I inhibitor; Tumour-associated calcium signal transducer 2 (TROP2) antibody	1,212	New Entry	6,140
8	Tiragolumab	Roche	Phase III	T-cell immunoreceptor with Ig & ITIM domains (TIGIT) receptor antibody	1,150	New Entry	5,951
9	SAR442168	Sanofi	Phase III	Bruton's tyrosine kinase (BTK) inhibitor	656	New Entry	5,484
10	Bimekizumab	UCB	Filed	Interleukin-17A (IL-17A) antibody; Interleukin-17F (IL-17F) antibody	1,951	New Entry	5,238
Top 10					26,449		95,532
Other					187,329		547,561
Total					213,778		643,093 +1%
NPV of R&D Pipeline May 2020:							634,866

Note: Today's NPV (\$m) relates to the Net Present Value of the product as of the June 2nd, 2021, based on the Evaluate Omnium® NPV Analyzer.

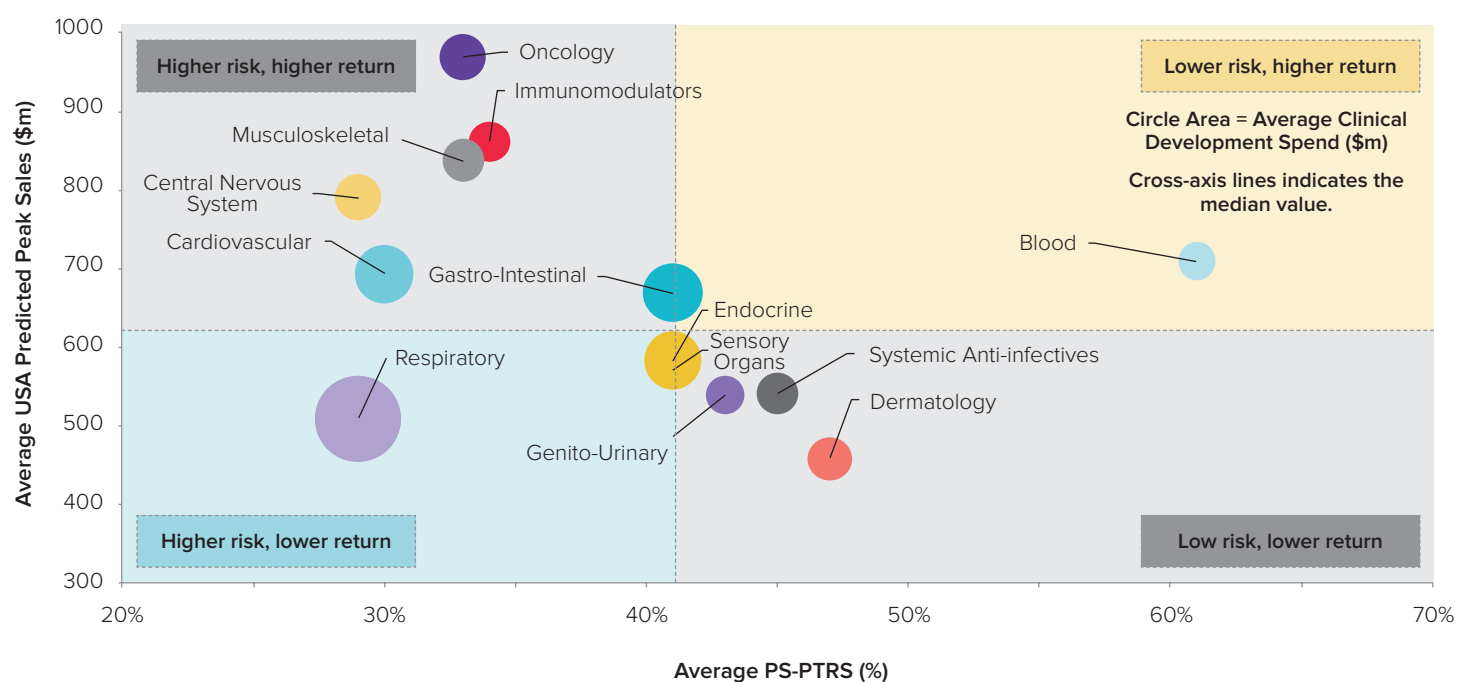


Evaluate Omnium calculates that, of the phase III assets currently in the pipeline, oncology boasts 131 new molecular entities in development in the US. These carry a relatively high risk profile, with an average PS-PTRS of 33%, but also have a high return profile, with average US peak sales of nearly \$969m.

Dermatology projects sit in an opposite position, with a higher average PS-PTRS but much lower return; this is the only therapy area with average US peak sales below \$500m.

Figure 10: PTRS vs. Predicted Peak Sales by Therapy Area of Current US Pipeline Phase III Assets

Source: Evaluate Omnium® (May 2021)



Inclusion criteria: Analysis refers to products which are in phase III of US clinical development. Only NMEs with no prior global approval are included.

Methodology: 'Clinical Development Spend' by Therapeutic Category is calculated using Evaluate Omnium's proprietary R&D Cost model and represents the sum of the costs of all commercial clinical trials currently listed on ClinicalTrials.gov for the included products - clinical development spend is typically 50% of total R&D expenditure.

'Average PTRS' is calculated using the average of Evaluate Omnium's proprietary product-specific probability of technical and regulatory success (PS-PTRS) for the lead indication of each product within the specified therapy area.

'Average USA Predicted Peak Sales' is sourced from Evaluate Omnium on June 2nd, 2021 and is calculated based on Evaluate's proprietary machine learning model.



Pfizer's early dominance in the Covid-19 vaccine market has come from its ability to manufacture at scale. Pfizer and its German partner BioNTech gained emergency use authorisation for Comirnaty in the US only a week ahead of Moderna, but Pfizer has produced almost double the number of shots since the start of 2021.

Pfizer's leading position among Covid-19 vaccine makers is predicted to wane from 2021, however its mRNA-based product is expected to achieve sales of over \$51bn in the next five years, according to Evaluate Pharma. More than half of that is likely to be booked in 2021.

Sales of Moderna's vaccine are also forecast to decline from 2021. Demand is likely to ebb in the main markets of Europe and the US as more people become fully vaccinated, and newer entrants are used as booster jabs. Moderna's mRNA Covid-19 vaccine is also predicted to have combined sales of over \$50bn by 2026.

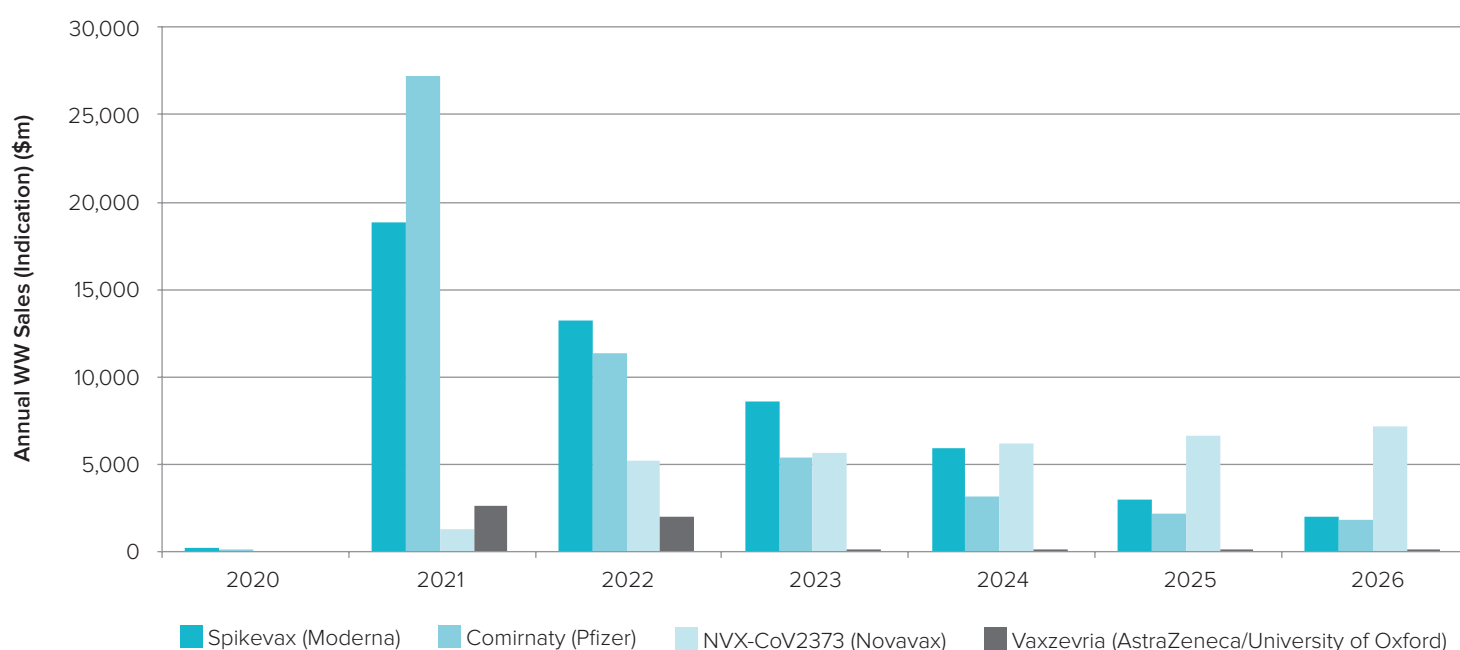
AstraZeneca and Oxford University's Covid-19 vaccine is forecast to see the most rapid and severe revenue dip, with sales dropping by over \$2.5bn between 2021 and 2026.

In contrast, Novavax's NVX-CoV2373 is the only vaccine for which Evaluate Pharma's consensus forecasts predict growing sales to 2026. The recombinant protein vaccine only reported phase III data in June and is not expected to launch in the US before the third quarter of 2021.

Novavax is expected to meet demand from middle and lower income countries across the globe, thanks to its vaccine's relatively low manufacturing cost, convenient refrigerator storage, strong efficacy and expected low cost. However, the company will have to find ways to scale up production for NVX-CoV2373 to meet current forecasts.

Figure 11: WW Consensus Forecast Sales: Covid-19 Prophylaxis

Source: Evaluate Pharma® (May 2021)





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