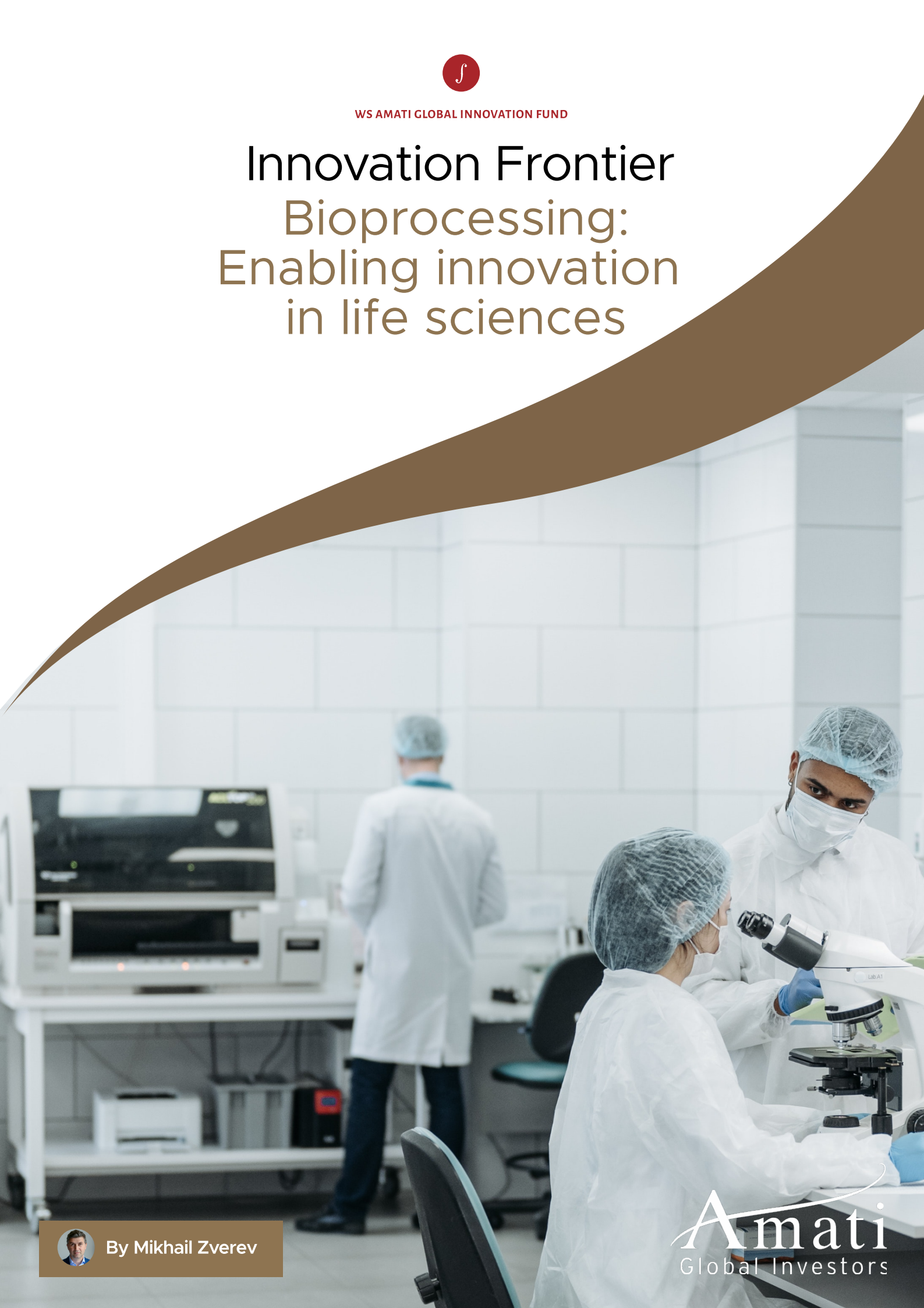
WS AMATI GLOBAL INNOVATION FUND

Innovation Frontier

Bioprocessing: Enabling innovation in life sciences



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Bioprocessing: Enabling innovation in life sciences

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The life sciences, pharma and biotech industries are driven by innovation and technical progress.

Even to an outside observer, recent press headlines indicate thriving innovation in this space: game changing obesity treatments (Wegovy / Ozempic drugs by Novo Nordisk), promising breakthroughs for Alzheimer treatment (Donanemab drug, currently in final stages of clinical trials by Eli Lilly), or less well-publicised but equally dramatic breakthroughs in cancer treatment, such as curing the previously incurable leukaemia of a teenage patient in the Great Ormond Street Hospital (CAR-T cell therapy).

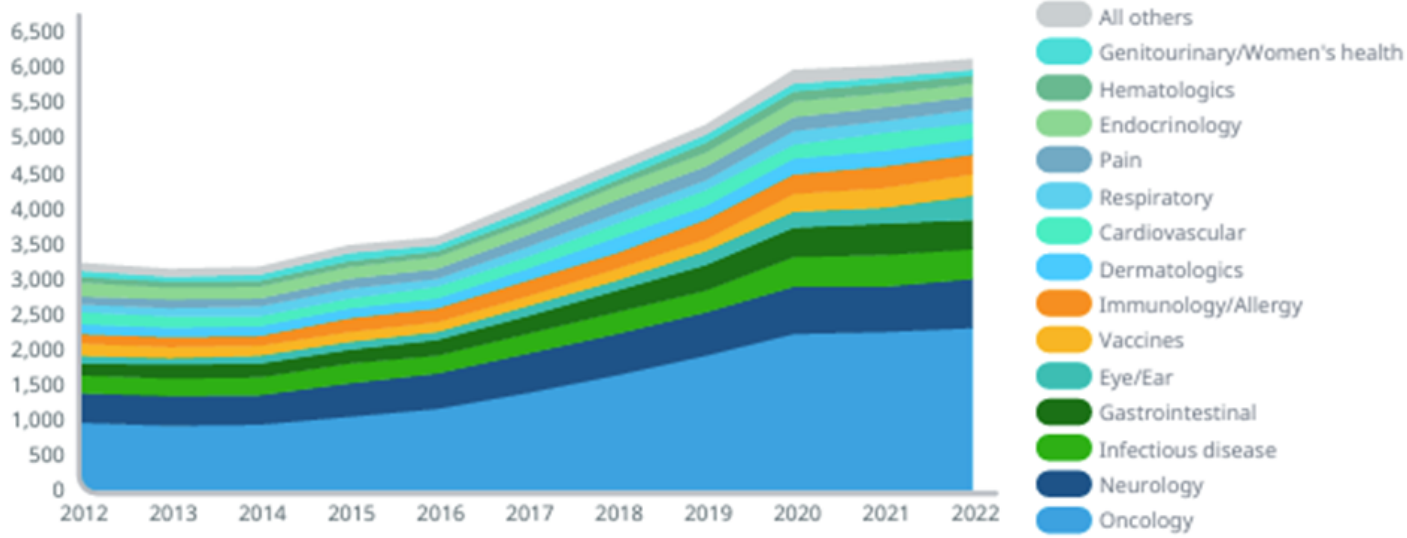
This is a dramatic change since just over a decade ago. In 2008 / 2009 the pharma industry was in the doldrums. Perceived to be under threat from more price controls in the lucrative US market, it was also viewed by some as running out of innovation. In fact, the MSCI ACWI Pharma and Biotech index was trading at 10x forward P/E ratio, with some major pharma companies on single digit P/Es, suggesting that investors expected no growth from the industry going forward.

As we now know, this was an overly pessimistic assessment. The emergence and growth of so-called biologic drugs, large and complex organic molecules, as well as completely new ways of treating disease, such as cell and gene therapies, replaced chemically synthesised "small molecules" and reinvigorated the innovation in the sector. It looks like we're still early in this process.

According to industry data, there were 6,147 products in active development from Phase I to regulatory submission, up 49% from 2017 and even more so compared to the dark days of the early 2010s.

Biologics have already gained substantial commercial traction, accounting for 20% of total pharma sales in 2022 and growing at twice the annual growth rate of traditional small molecules. This is set to continue. For example, in oncology, the largest area of innovation measured by research pipeline product count, small molecules are now in the minority, compared to biologics or next generation treatments such as cell and gene therapies.

Exhibit 8: Number of pipeline products Phase I to regulatory submission by therapeutic drug class, 2012–2022



Source: IQVIA Pipeline Intelligence, December 2022; IQVIA Institute, Jan 2023

Fundamental scientific breakthroughs from the past decade and before, new biochemical pathways, novel compounds, new modes of action are being commercialised into new therapies.

The COVID-19 pandemic illustrated this. The unprecedented pace of analysis and vaccine development became in many ways a showcase for the innovation and progress in life sciences, albeit in an emergency situation.

All this has justified more R&D spending and investment in the space - there simply is more to go after.

That fundamental merit and the sense of urgency and opportunity during the pandemic catalysed strong investor interest in healthcare and turbo-charged the capital flows into the sector. Total healthcare funding, from IPOs to venture capital rounds, in both 2020 and 2021 was more than twice the level of 2019, and more than three times the level of 2016.

Zero interest rate policies, which reduced the cost of capital and increased investor risk appetite, played a role as well.

This has now reversed – with 2022 total funding falling back to pre-pandemic levels.

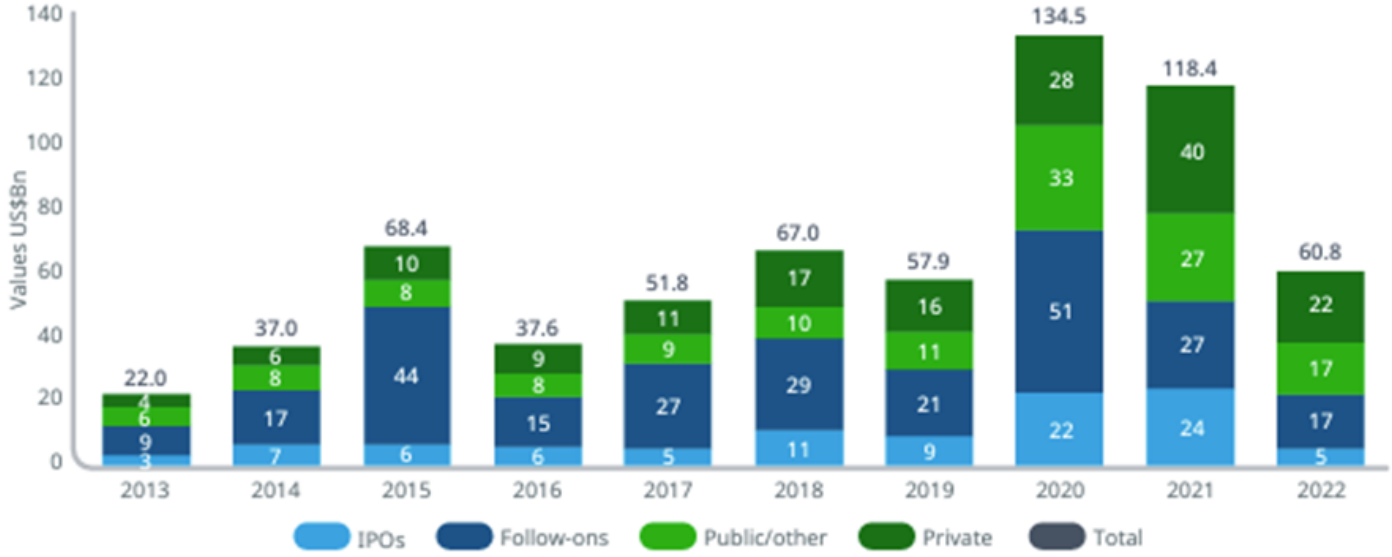
While it's tempting to see this as another manifestation of zero interest rate induced bubble, the underlying fundamental merits of this investment remain. In fact, R&D spending by traditional large pharma companies has reached new record levels, even as funding of smaller biotechs collapsed. The number of therapies in all stages of clinical research also remain at a record level. These new molecules are still worth pursuing, even if capital markets are no longer as generous in their funding and valuations.

A key enabler of this innovation is the bioprocessing industry. Manufacturing biologic drugs or cell and gene therapies is a very different process from the chemical synthesis behind the small molecule drugs. These processes often involve cultivating and modifying living organisms such as bacteria or viruses or even mammalian cells (particular type of Chinese Hamster cells, known as CHO cells, are a firm favourite). These cells and organisms produce, or "express" the compounds that are the active ingredients behind the innovative new drugs. The technical challenge of growing, modifying, nurturing and harvesting these biological systems is formidable, creating high barriers to entry, and very few players have mastered it. In fact, 4 companies – Danaher, Sartorius, Merck and ThermoFisher – dominate the business of producing equipment and consumables involved in bioprocessing. It is a good business – long term revenue growth is in double digits, margins are high, and recurring revenues constitute 70-80% of the total in the relevant business lines.

Increasingly the complexity of the process means that the actual manufacturing is conducted by an outsourced partner – so called Contract Development and Manufacturing Organizations (CDMOs). Again, it's a concentrated industry, with the top 4 players controlling more than 50% of global capacity. Biologic CDMOs also show double digit revenue growth, further benefiting by increasing propensity to outsource biomanufacturing.

Customer relationships in the industry are "sticky" – once the drug is being manufactured in a particular venue, with a particular set of tools and processes, the risks of moving it to a new set-up are too high. This results in multi-year contractual relationships and great revenue visibility.

Exhibit 1: Biopharma funding levels US$Bn, 2013–2022



Source: BioWorld, January 2023

In short, biomanufacturing is a great industry, with a multi-year growth runway. However, these positives are currently obscured by three major headwinds.

First, COVID related business (such as manufacturing vaccines) is rapidly diminishing. Secondly, that reversal of the biotech funding boom did impact R&D spending by the smaller, riskier end of the market – impacting both equipment companies and CDMOs. Finally, the supply chain disruption that affected most industries during the post-COVID recovery had impacted biologic drugs as well. Pharma companies and their suppliers had built safety stocks, which now that supply crunch has eased are no longer needed. As a result, we have seen a slew of profit warnings and guidance downgrades. For some suppliers these amounted to 40% consensus EPS forecast cuts for this year. Both share price and earnings momentum scores are negative. Companies are hopeful that the de-stocking phase is close to the end, but investors are reluctant to get involved before this is clear-cut.

In our view, long term structural growth obscured by transitory and finite headwinds tends to create opportunities for longer term investors who have conviction in the strength of secular technological change. This is such a case.

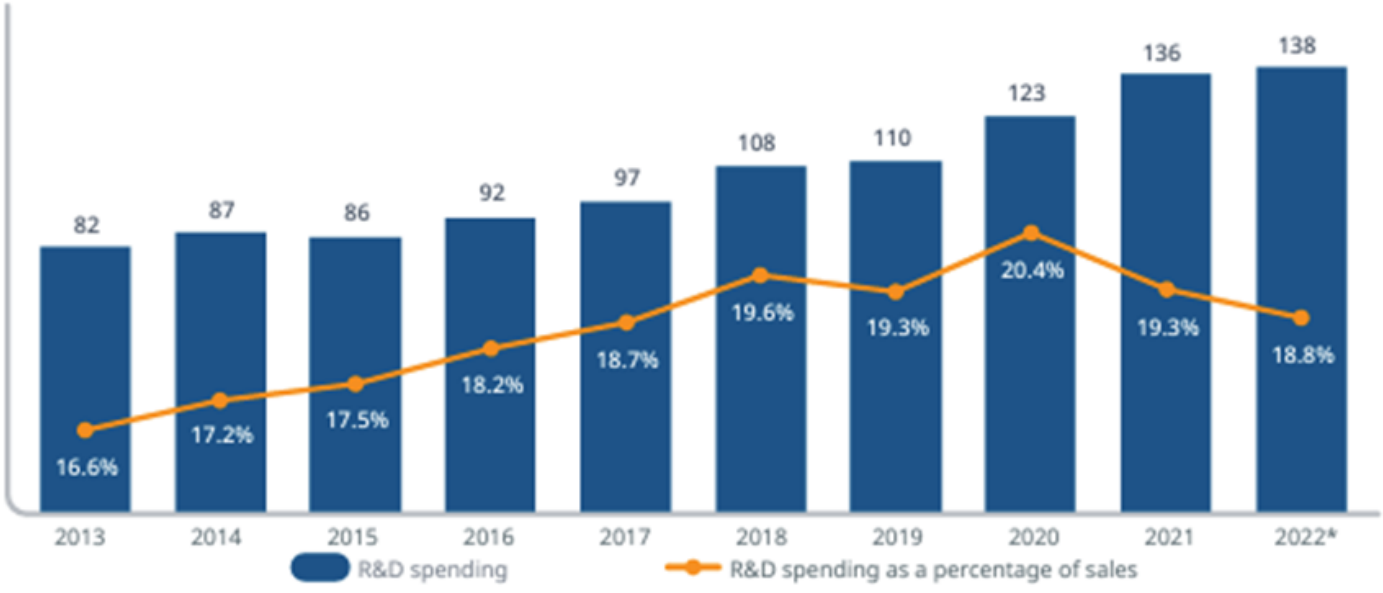
Not only the pipeline of new biologic therapies is fuller than ever, but the underlying demand for manufacturing capacity required to support it continues to increase.

The best-selling biologic drug up until this point is AbbVie's Humira, treating auto-immune diseases such as rheumatoid arthritis. Humira's global sales were over $20bn in 2022. Yet the estimated volume of Donanemab, that promising Alzheimier treatment by Eli Lilly, will require 15x more manufacturing capacity in volume terms than Humira requires today. This is why global CDMOs are aggressively expanding capacity, despite temporary stumbles in demand trends.

In our view, investing in innovation requires a careful balancing of understanding the technical complexity and picking business models that offer compelling risk/reward for an investor.

Within that, our portfolio holding is Danaher. Their bioprocessing assets are best in class, but that is combined with a high quality business model. Their balance sheet and cash generation are the strongest in the sector, and they have history of profitability and superior management execution that attained almost iconic status in more optimistic times. When the merits and secular growth of bioprocessing become clearer, we believe Danaher stands to benefit from both fundamental growth and recovery in investor interest.

Exhibit 6: Large pharma R&D spending and spending as a percentage of sales 2013–2022*, US$Bn



Source: Company financial statements; IQVIA Institute, Jan 2023

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This factsheet does not provide you with all the facts you need to make an informed decision about investing in the fund. Before investing you should read the Prospectus, the Key Investor Information Document (KIID) and the Supplementary Information Document (SID). The Prospectus sets out the main risks associated with the fund, the KIID shows you how costs and charges might affect your investment, and the SID details your cancellation rights. If you are in any doubt as to how to proceed you should consult an authorised financial intermediary.

Fund documentation can be requested from Waystone or Amati using the contact details above, and is available to download from our website.

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