BIOTECH: HEALTHCARE'S INNOVATIVE UNDERBELLY

13/11/2024 | MARK DENHAM

***Mark Denham**, fund manager of the Carmignac Portfolio Grande Europe Fund, explains the fund's large healthcare weighting and the differentiating value that its biotech exposure brings to the portfolio.*

Compare the sector allocations of the Carmignac Portfolio Grande Europe Fund with any of its peers and one stark difference stands out: healthcare. All of our competitors hold approximately 20% in the sector; we, on the other hand, have closer to 40%[1] . While these competitors inevitably own index heavyweight Novo Nordisk (Novo) – rightly so, as do we; it is an exceptional business – our healthcare reach goes that bit further.

UNCORRELATED BIOTECH: THREE-YEAR CORRELATION[2]

#	MSCI Europe Pharma	MSCI Europe Healthcare	Stoxx 600
MSCI Europe Biotech	0.49	0.56	0.35

We have always seen healthcare as an amalgamation of sub sectors, incorporating core or traditional pharma, B2B suppliers, biotech and medtech. Where we stand out among our peers is this deeper healthcare exposure; indeed, as at the end of September 2024, some 8% of the fund is held in the biotech sphere. With a low correlation to pharma and the broader healthcare sector, and an even lower correlation versus the Stoxx 600; biotech exposure can be a true differentiator.

Many of our peers shy away from this section of the market due to the – often perceived – potential risks related, along with the required expertise needed to truly understand and evaluate biotech companies. The result? A number of underappreciated opportunities. Now, these are few and far between – and that's where our exhaustive screening and qualitative research comes in – but there are in our view, undoubtedly pockets of remarkable innovation and value.

Our biotech focus tends to fall on those companies with technology platforms, that are not reliant upon one particular drug – the boom or bust model – but instead, like companies such as Zealand Pharma, Argenx and BioNtech, have technologies that mean they will be potentially developing new drugs every year. The huge advantage of a technology platform in the biotech arena is being able to engineer antibody fragments to treat illnesses; this skillset enables the 'multiple-shot' potential.

BIOTECH EXPOSURE: CARMIGNAC PORTFOLIO GRANDE EUROPE FUND

- Exposure: a maximum of 8% of the fund;
- Diversified exposure: held across three or four names;
- Liquid exposure: Any holding must be >€1bn market capitalisation.

Since Mark Denham took over the fund in 2016, the fund's biotech exposure has produced an excess alpha contribution of c.20% versus its benchmark, the STOXX 600[1].

Outside of the innovation sleeve (dominated by biotech recently) all fund holdings are demonstrable high-quality businesses with proven financials and growth; this framework of the fund manager has been unchanged for 20 years.

THE GLP1AYBOOK

Glucagon-like peptide-1s (GLP1s) have had incredible success over the course of the past 10 years. A class of drugs that is designed to mimic the hormones released by the stomach when food is consumed, the first GLP1 was approved by the US Food and Drug Administration in 2005. However, success in two particular fields – the treatment of diabetes and obesity – has really launched them into public consciousness in the last decade. Both diabetes and obesity provide a sizeable externality cost to society and are arguably presenting as urgent a challenge as climate change itself; the potential effects of GLP1s are seismic.

Most notable has been the success of Ozempic, a Novo drug used to treat type 2 diabetes; the once-weekly injectable, which helps sufferers manage their blood levels, now has an estimated low-teens percentage penetration of the volume of drugs prescribed to treat type 2 diabetes in the US. This number is expected to rise to a whopping 25 or 30% in the coming decade. And, of course, Ozempic is sold worldwide, too.

Novo enjoys some 55% market share in GLP1s, but there is huge scope for competition and further innovation from the biotech space. Indeed, one of the fund's holdings, Zealand, has historically been involved with the development of peptide drugs, to treat gastrointestinal illnesses, and has now repurposed itself towards addressing obesity.

The Danish drug maker has three or four products in development, at various stages of creation and with different mechanisms of action. These are largely targeting the same market as the likes of Novo's Wegovy – from the same molecule as Ozempic – but another of Zealand's pipeline drugs would be complementary in the sense that it has a very different mode of action so could be taken in conjunction with Ozempic in the treatment of diabetes; the drugs are known as amylin analogues. Meanwhile, Zealand's leading obesity drug, Survodutide, is a direct competitor to those of Novo and Eli Lilly in the diabetes space. The impact of GLP1s, and the headlines success of Ozempic and Wegovy, in particular, has seen forecasts predicting sales of obesity treatments will breach the US$100bn mark by 2030[3].

Eli Lilly and Novo dominate the GLP1 space but there are a number of companies, such as Zealand – which is expected to grow EPS by 40% in the next 12 months – that have strong and promising pipelines in these areas, and who, in Zealand's case, are boosted by a recent capital raise that enables further investment in its obesity programme. Indeed, that possibility casts something of a shadow over the mid-term prospects for Novo and Eli Lilly. The market could easily become a far more complex and diverse landscape than today's picture suggests.

UNTAPPED POTENTIAL

The Dutch biotechnology business Argenx is another perfect case study for why we invest in biotech, and the best example of our long-term focus on this part of the healthcare market.

We first met Argenx in 2017 and at the time the company satisfied our liquidity threshold, had a technology platform, and had already developed a version of an antibody to treat a range of neurological conditions. It was using one molecule to develop drugs to address a number of these conditions, so had, as we like to put it 'many shots on goal', and its leading drug in development was being developed to target myasthenia gravis, which is a rare long-term condition that causes muscle weakness in the eyes, face and throat, helping to disrupt the process by which the body's immune system attacks neurological function.

Over the past seven years, the drug has gone through various stages of clinical development, with a value uplift at each stage; Vyvgart has now been on the market in the US for the past two years, and latterly worldwide, showing strong growth. And because the molecule had a number of shots on goal, it has also had approval for a drug treating a second neurological condition – CIDP, a neurological disorder that causes progressive weakness and reduced sensation in the arms and legs – which came to market in the last couple of months, and led to an uplift in the share price, with a further ramp up in sales over the coming years now expected. Meanwhile, it has a series of related, relatively niche auto-immune and neurological products in development.

Argenx also has a number of other molecules it is working on in different areas, each with a number of drugs in earlier stages of development, providing further scope for diversification. The success of the likes of Vyvgart also means that the company is fundamentally de-risked compared to many of its peers, as it has sales and therefore cash coming in, providing a virtuous circle. Importantly, the company is also playing the key role of creating novel drugs to address thus far unmet medical needs in rare illnesses.

Such has been its success, Argenx *could* be profitable next year, depending on how much it wants to reinvest. We tend to label those companies within the biotech sleeve as being at an innovative stage of development, where they are not profitable, so when Argenx reaches profitability, it will exit the biotech sleeve and be recategorised as a high-quality compounder.

Bought as a relative ‘unknown’ in 2017, the company is now established, well known and profitable (should it wish to be!), and its share price has risen some 820% since we first invested seven years ago.

M&A REBOUND

Within the broader healthcare sector, sub sectors such as life sciences, pharma services, biotech and devices have seen a notable jump in merger and acquisition activity this year; the first half of 2024 saw a 26% uplift in deal values versus the same period a year earlier.[4]

In turn, 2023 had seen a 79% uplift on aggregate biotech deal value versus 2022, breaking through the US$150bn mark, its highest annual figure since 2019. Deal size has continued to trend upwards since 2020.[5]

WAITING OUT THE COVID NOISE

The biotech sector dominated the global headlines for a brief period in the early 2020s amid the Covid-19 vaccine rush, but we sat out that particular dance.

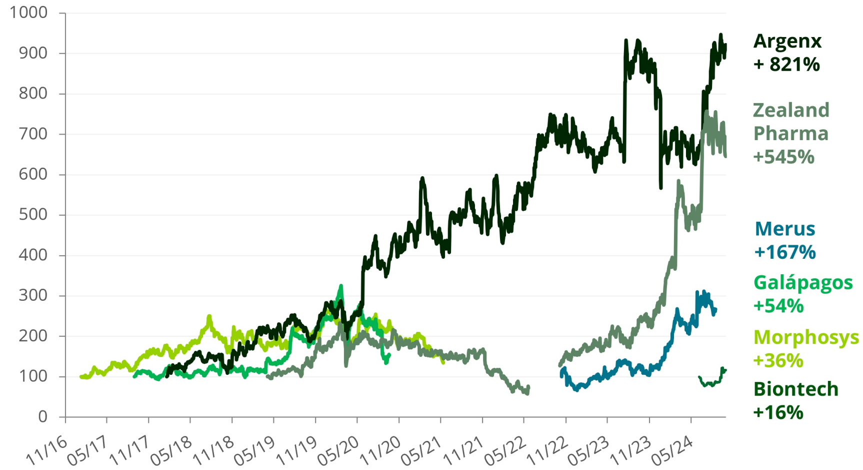
We avoided Moderna and BioNTech despite hugely speculative share-prices moves, as we felt the nature of the pandemic meant it wasn’t likely to usher in a long-term high level of demand for such vaccines. We wanted to avoid getting sucked into a bubble, which played out with the move in the BioNTech share price (up to US$450 at one stage, but now down to US$100).

Now that the Covid hype has dissipated – the drugs sell but in a smaller quantity, albeit still to the tune of some US$3bn each year for BioNTech – it gives us the chance to look at companies like BioNTech, the other strings to its bow, and the projects to which it is applying its technology. Indeed, we initiated our first investment in BioNTech in the summer of 2024 on the back of its pipeline of cancer drugs.

The company has 32 projects in development for a range of illnesses, mainly cancer, using its innovative mRNA technology, of which by the end of 2024, 10 are expected to be at advanced phase. Meanwhile, BioNTech’s previous vaccine success means it can fund projects internally using the large cash reserves built up from Covid vaccine sales – it currently has US$17bn on its balance sheet.

Which returns us to the virtuous circle, which, in biotech, is truly the golden bullet.

THE ULTIMATE DIFFERENTIATOR



For Illustrative purposes only. Past performance is not necessarily indicative of future performance. Portfolio composition may vary over time. All prices in local currency.

Source: Carmignac, Bloomberg, 30/09/2024.

The Carmignac Portfolio Grande Europe Fund has benefited notably over the past decade from its targeted biotech exposure. With a low correlation to traditional healthcare and pharma, and the broader market, coupled with low correlations between biotech companies and their larger pharma peers, biotech exposure has proven to be a tangible differentiator.

The fund has enjoyed significant excess alpha from its exposures to 'quality growth', innovative, and well diversified biotech companies. What's more, it enjoys early access to tomorrow's potentially world-class pharmaceutical companies.

PERFORMANCE OF OUR BIOTECH INVESTMENT[6]

[1] Carmignac, as at 30 September 2024.

[2] Bloomberg, as at 30 September 2024.

[3]

https://www.biopharmatrend.com/post/907-obesity-rd-the-making-of-a-100-billion-market/#:~:text=Looking%20to%20the%20%24100%

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[4] https://www.bcg.com/publications/2024/m-and-a-market-insights-series-h1-2024.

[5] https://www.iqvia.com/blogs/2024/01/biopharma-m-and-a-outlook-for-2024.

[6] The Biotech theme exposure is capped at ca 8% as a result of the European strategy's investment process, so as to contain the risk of this sub-sector at a portfolio level. Biotech investments performance calculated over the effective holding period for Carmignac Portfolio Grande Europe.

CARMIGNAC PORTFOLIO GRANDE EUROPE A EUR ACC

(ISIN: LU0099161993)

SFDR - Fund Classification** :

Article 9

LOWEST RISK HIGHEST RISK

1	2	3	4*	5	6	7

Recommended minimum investment horizon 5 YEARS

MAIN RISKS OF THE FUND

EQUITY: The Fund may be affected by stock price variations, the scale of which is dependent on external factors, stock trading volumes or market capitalization. **CURRENCY**: Currency risk is linked to exposure to a currency other than the Fund's valuation currency, either through direct investment or the use of forward financial instruments. **DISCRETIONARY MANAGEMENT**: Anticipations of financial market changes made by the Management Company have a direct effect on the Fund's performance, which depends on the stocks selected.

The Fund presents a risk of loss of capital.

*Risk Scale from the KID (Key Information Document). Risk 1 does not mean a risk-free investment. This indicator may change over time. **The Sustainable Finance Disclosure Regulation (SFDR) 2019/2088 is a European regulation that requires asset managers to classify their funds as either 'Article 8' funds, which promote environmental and social characteristics, 'Article 9' funds, which make sustainable investments with measurable objectives, or 'Article 6' funds, which do not necessarily have a sustainability objective. For more information please refer to https://eur-lex.europa.eu/eli/reg/2019/2088/oj.

FEES

Entry costs : 4,00% of the amount you pay in when entering this investment. This is the most you will be charged. Carmignac Gestion doesn't charge any entry fee. The person selling you the product will inform you of the actual charge.

Exit costs : We do not charge an exit fee for this product.

Management fees and other administrative or operating costs : 1,80% of the value of your investment per year. This estimate is based on actual costs over the past year.

Performance fees : 20,00% when the share class overperforms the Reference indicator during the performance period. It will be payable also in case the share class has overperformed the reference indicator but had a negative performance. Underperformance is clawed back for 5 years. The actual amount will vary depending on how well your investment performs. The aggregated cost estimation above includes the average over the last 5 years, or since the product creation if it is less than 5 years.

Transaction Cost : 0,41% of the value of your investment per year. This is an estimate of the costs incurred when we buy and sell the investments underlying the product. The actual amount varies depending on the quantity we buy and sell.

PERFORMANCE (ISIN: LU0099161993)

Calendar Year Performance (as %)	2015	2016	2017	2018	2019
Carmignac Portfolio Grande Europe	**-1.4 %**	**+5.1 %**	**+10.4 %**	**-9.6 %**	**+34.8 %**
Indicateur de référence	+9.6 %	+1.7 %	+10.6 %	-10.8 %	+26.8 %

Calendar Year Performance (as %)	2020	2021	2022	2023	2024
Carmignac Portfolio Grande Europe	**+14.5 %**	**+21.7 %**	**-21.1 %**	**+14.8 %**	**+11.3 %**
Indicateur de référence	-2.0 %	+24.9 %	-10.6 %	+15.8 %	+8.8 %

Annualised Performance	3 Years	5 Years	10 Years
Carmignac Portfolio Grande Europe	**+0.3 %**	**+7.0 %**	**+6.9 %**
Indicateur de référence	+4.0 %	+6.6 %	+6.8 %

Source: Carmignac at Dec 31, 2024.
Past performance is not necessarily indicative of future performance. Performances are net of fees (excluding possible entrance fees charged by the distributor).