

Health Innovation Quarterly Update

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30 June 2024



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**Calton Square, 1 Greenside Row, Edinburgh EH1 3AN  
Telephone +44 (0)131 275 2000 [bailliegifford.com](http://bailliegifford.com)**

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Historical performance results for investment indexes and/or categories, generally do not reflect the deduction of transaction costs and/or custodial charges or the deduction of an investment management fee, the incurrence of which would have the effect of decreasing historical performance results. It should not be assumed that recommendations/ transactions made in the future will be profitable or will equal performance of the securities mentioned.

## **Potential for Profit and Loss**

All investment strategies have the potential for profit and loss.

## **Stock Examples**

Any stock examples, or images, used in this paper are not intended to represent recommendations to buy or sell, neither is it implied that they will prove profitable in the future. It is not known whether they will feature in any future portfolio produced by us. Any individual examples will represent only a small part of the overall portfolio and are inserted purely to help illustrate our investment style. A full list of portfolio holdings is available on request.

The commentary relates to the above mentioned strategy and not all stocks mentioned may be held in the portfolio.

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Product Overview

The strategy aims to produce capital growth over the long term. The investment policy is to invest mainly in global equities selected from companies involved in the healthcare industry and which are innovative in their focus. The strategy will not be restricted to equity securities in the healthcare sector as defined by any particular index. Investment will be concentrated by the number of stocks held but diversified across a range of healthcare themes.

Risk Analysis

Key Statistics

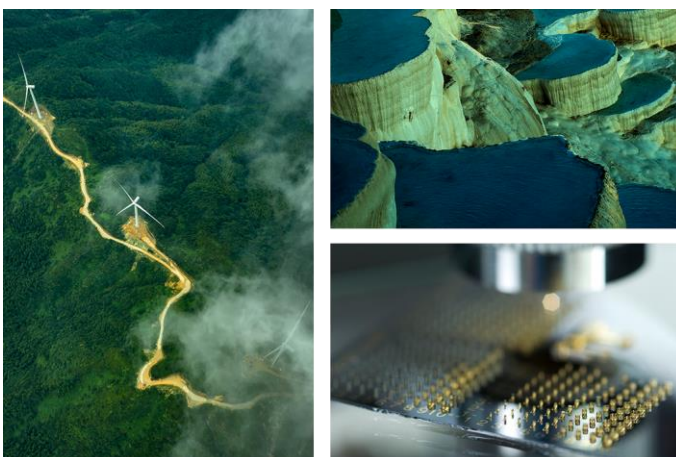
Number of Holdings	39
Typical Number of Holdings	25-50
Active Share	99%*
Rolling One Year Turnover	21%

\*Relative to MSCI ACWI Index. Source: Baillie Gifford & Co, MSCI.

Holdings have weathered significant adversity and are now emerging in strengthened positions

Robust fundamentals are laying solid foundations to power future growth

Accelerating innovation and attractive valuations continue to provide plentiful opportunity



Baillie Gifford Key Facts

Assets under management and advice	US\$283.7bn
Number of clients	649
Number of employees	1738
Number of investment professionals	372

*“Medicine is the restoration of discordant elements; sickness is the discord of the elements infused into the living body” – Leonardo da Vinci*

The continuing backdrop of higher interest rates, post-COVID adjustments, and budget constraints has presented an extremely challenging infusion for the types of innovative healthcare companies that we hold in Health Innovation.

As we progress through 2024, while performance is still muted and lagging behind that of the benchmark, it is reassuring that such headwinds have not concomitated a sickness within the broader portfolio. Indeed, the majority of companies in the portfolio continue to deliver solid operational progress and indications are that fundamental growth is accelerating across the portfolio. For example, forward earnings growth is now at its highest level since the portfolio's inception. We have also seen a significant step up in free cash flows, with holdings such as Alnylam and Exact Sciences recently becoming free cash flow positive as they scale up their operations. Finally, overall cash positions are very strong, with earlier-stage companies, such as Denali, raising capital to validate its platform, and placing the portfolio in a strong position to navigate a higher for longer interest rate environment.

### Obesity beyond Ozempic

That being said, while the overall portfolio remains in good health, it is ineluctable that not owning the major obesity drug manufacturers, Eli Lilly and Novo Nordisk, has proved to be a headwind for recent portfolio performance. While Eli Lilly and Novo Nordisk's valuations sit at their highest levels in their respective histories, we are now also witnessing the highest revenue forecasts for drugs associated with the obesity industry. We, therefore, continue to monitor these companies closely and to challenge ourselves about their future upside potential.

Obesity is extremely prevalent, with over one billion people worldwide suffering from the disease. Given demographics, lifestyle choices, and the 200+ diseases associated with it, treating obesity is likely to continue to be an important growth area within the healthcare sector. It is now estimated that it could become the biggest drug market globally over the course of the next decade.

As this market grows, evolves, and matures, we believe that it will become increasingly fragmented, with more companies entering the market, bringing different drugs with new mechanisms of action to tackle the condition. The rate of change will have several second-order impacts beyond the drug developers themselves, creating opportunities and risks. As such, this is an important area of research for the team, and we categorise the opportunity into five categories of active research:

1. Enablers: the picks and shovels for GLP-1s, for example, those companies that are producing delivery products, including syringes and vials, used by GLP-1s
2. Alternatives and complements to GLP-1s
3. Reversing side effects: there are multiple side effects associated with GLP-1's and there are a range of companies with pipeline drugs that could eventually reverse these
4. Maintenance treatments: compliance with GLP-1s is low. We are exploring companies that could be used alongside GLP-1s to improve adherence
5. GLP-1 drug developers: we continue to monitor and research the GLP-1 drug developers themselves.

This quarter, we initiated two new positions related to the obesity industry. The first, Zealand Pharma, can be categorised as an alternative or complement to the GLP-1s. Zealand Pharma is a Danish biotech company that has a long history of making drugs for diabetes, obesity, and other metabolic diseases. We believe it has a strong potential to take share in this expanding market.

Zealand is developing an entirely new mechanism of action to target obesity compared to the other GLP-1 drugs on the market. Zealand's amylin drug, petrelintide, is in a different family of hormones from GLP-1s. Broadly speaking, its main function in the body is to increase satiety, which, unlike GLP-1s, work by suppressing appetite. Zealand's drug has shown in early human studies that it can potentially generate a similar magnitude of weight loss compared to other GLP-1 drugs on the market, but with fewer side effects, such as lean muscle loss, nausea, and vomiting. If successful, Zealand's drug could be used as a standalone therapy, or as a combination therapy for obese patients. Furthermore, recent trial success

suggests that the drugs could be better tolerated by patients than GLP-1s, which could provide for strong commercial success given estimates that 30% of GLP-1 users stop taking the drugs within a month of starting.

We also initiated a position in Schott Pharma, a German manufacturer of syringes, cartridges, and vials for drug delivery and containment. Its products are low-cost but mission-critical in drug administration. Schott is one of just a handful of suppliers in an industry experiencing enhanced demand due to the increase in biologic drugs, such as messenger RNA vaccines and obesity drugs. Schott is the only company that has announced significant long-term contracts with the GLP-1 players, and we believe it can capitalise on this drug class' evolution over the next decade.

### Navigating discord

Beyond the market's voracious appetite for obesity, some elements have infused a greater degree of discord into a number of our holdings, and they have been notable detractors to recent performance.

For example, Sartorius Group, the lab equipment manufacturer, weighed on performance following a mixed set of quarterly results. On the negative side, revenues missed consensus as the company reported weak orders from Chinese, and to a lesser extent, European, customers. A Chinese clampdown on drug pricing has been one of the contributing factors to its muted biopharma market, however, Sartorius noted the restrictions are already partially lifted, indicating optimism for a Chinese recovery. On the positive side, orders, particularly within its consumables segment, grew over the period and there seems to be less of a drag from destocking. As a reminder, customers have been clearing out their inventories following the pandemic, but Sartorius now believes this process is 'very far advanced' and should be complete by the end of 2024, leading to a return to the long-term mid-double-digit growth rates the structural rise of biologic drugs is driving.

Elsewhere, 10x Genomics and Exact Sciences have faced difficulties growing their businesses against industry demand challenges and increasing competition. We have, therefore, seen

disappointing performance from both over recent quarters.

While we continue to admire all three for their innovative products or approaches, we are monitoring them closely given the high bar for inclusion in the portfolio.

### The medicine of innovation

In contrast, several holdings have demonstrated significant progress in recent months, providing further validation of their differentiated platforms and materially expanding their addressable markets.

For example, Alnylam, a clinical-stage biotech, released positive results from its phase 3 trial of vutrisiran, its treatment for patients with ATTR amyloidosis with cardiomyopathy (a progressive and deadly form of heart disease). The trial showed that vutrisiran reduced the risk of death, heart-related hospital visits, and hospitalisations by 28%, compared to placebo in patients. This positions vutrisiran as a potential first RNA silencing therapy for this condition, targeting a market currently led by Pfizer. Alnylam plans to proceed with global regulatory submissions later this year. If approved, it is expected to generate between \$2-4bn in annual sales (a considerable increase on Alnylam's current \$1.5bn annual sales).

Moderna also continues to make significant progress, with two notable developments in recent months. First, its respiratory syncytial virus (RSV) was approved by the Food and Drug Administration (FDA) for use in adults over 60 in the US. Moderna will launch its vaccine later this year. The second development was Moderna's encouraging three-year follow-up data on its phase II individualised neoantigen therapy (INT) for the treatment of stage III/IV melanoma, a form of skin cancer. In addition, the vaccine continues to show favourable safety data, which increases the chance of the company applying for accelerated approval, which may allow an earlier launch of the product while running a confirmatory clinical trial. These types of developments are evidencing our long-held thesis that Moderna is moving from a 'covid' story to a maturing diversified mRNA therapeutics platform.

Finally, we have injected a further dose of innovation into the portfolio this quarter, with the purchase of Vertex, a larger-cap US biopharma company. We admire Vertex's serial approach to innovation, whereby it aims to out-innovate the

competition in each new disease area it enters. Vertex has played an important role in developing treatments for cystic fibrosis (CF), a genetic disease that results in excessive mucus in the lung and often leads to serious infections. Prior to effective treatments, many CF patients did not reach adulthood. Today, life expectancy for CF patients is over 70 years, with some patients living into their 80s. CF treatments provide a profitable revenue stream for Vertex, which generated \$10 billion in sales and \$4 billion in operating profit in 2023. This profit stream helps to fund research and Vertex's expansion into new disease areas, including sickle cell disease, diabetes, renal diseases, and pain.

**Outlook**

In the face of the discord sown by higher interest rates, post-COVID adjustments, and budget constraints, the portfolio has not succumbed to sickness but demonstrated significant resilience, adaptability, and innovation. The solid operational progress and accelerating fundamental growth across the portfolio, exemplified by recent milestones achieved by Alnylam and Moderna, highlight the transformative power of innovation and the potential that lies in addressing unmet medical needs through pioneering science and technology. As we look forward to the latter half of 2024, we remain very enthused about the pace of innovation that we are still seeing in our portfolio companies and the scale of the opportunities ahead of them.

## Performance Objective

To outperform any sensible global index (default MSCI ACWI) by +3% gross of fees annualised, over a five year investment horizon.. The performance objective is aspirational and is not guaranteed. We don't use it to compile the portfolio and returns will vary. A single performance objective may not be appropriate across all vehicles and jurisdictions. We may not meet our investment objectives if, for example, our growth investment style is out of favour, or we misjudge the long-term earnings growth of our holdings.

## Periodic Performance

<b>GBP</b>	<b>Composite Net (%)</b>	<b>Benchmark (%)</b>	<b>Difference (%)</b>
3 Months	-3.6	2.9	-6.5
1 Year	-12.6	20.6	-33.2
3 Year	-19.7	9.1	-28.9
5 Year	1.1	11.4	-10.3
Since Inception	3.4	12.0	-8.6
<b>USD</b>	<b>Composite Net (%)</b>	<b>Benchmark (%)</b>	<b>Difference (%)</b>
3 Months	-3.5	3.0	-6.6
1 Year	-13.0	19.9	-33.0
3 Year	-22.1	5.9	-28.0
5 Year	1.0	11.3	-10.3
Since Inception	3.2	11.8	-8.6
<b>EUR</b>	<b>Composite Net (%)</b>	<b>Benchmark (%)</b>	<b>Difference (%)</b>
3 Months	-2.8	3.8	-6.6
1 Year	-11.5	22.1	-33.6
3 Year	-19.4	9.6	-29.0
5 Year	2.2	12.6	-10.4
Since Inception	4.2	12.9	-8.7
<b>CAD</b>	<b>Composite Net (%)</b>	<b>Benchmark (%)</b>	<b>Difference (%)</b>
3 Months	-2.5	4.2	-6.6
1 Year	-10.1	24.0	-34.1
3 Year	-19.4	9.5	-29.0
5 Year	1.9	12.3	-10.4
Since Inception	3.9	12.6	-8.6
<b>AUD</b>	<b>Composite Net (%)</b>	<b>Benchmark (%)</b>	<b>Difference (%)</b>
3 Months	-5.8	0.6	-6.4
1 Year	-13.3	19.5	-32.9
3 Year	-19.0	10.1	-29.1
5 Year	2.0	12.4	-10.4
Since Inception	4.3	12.9	-8.7

Annualised periods ended 30 June 2024. 3 Month & 1 Year figures are not annualised.

Inception date: 31 October 2018

Figures may not sum due to rounding.

Benchmark is MSCI ACWI Index.

Source: Revolution, MSCI.

The Health Innovation composite is more concentrated than the MSCI ACWI Index.



## Discrete Performance

<b>GBP</b>	<b>30/06/19- 30/06/20</b>	<b>30/06/20- 30/06/21</b>	<b>30/06/21- 30/06/22</b>	<b>30/06/22- 30/06/23</b>	<b>30/06/23- 30/06/24</b>
Composite Net (%)	44.6	41.5	-41.2	0.5	-12.6
Benchmark (%)	5.7	25.1	-3.7	11.9	20.6
<b>USD</b>	<b>30/06/19- 30/06/20</b>	<b>30/06/20- 30/06/21</b>	<b>30/06/21- 30/06/22</b>	<b>30/06/22- 30/06/23</b>	<b>30/06/23- 30/06/24</b>
Composite Net (%)	40.4	58.2	-48.3	5.2	-13.0
Benchmark (%)	2.6	39.9	-15.4	17.1	19.9
<b>EUR</b>	<b>30/06/19- 30/06/20</b>	<b>30/06/20- 30/06/21</b>	<b>30/06/21- 30/06/22</b>	<b>30/06/22- 30/06/23</b>	<b>30/06/23- 30/06/24</b>
Composite Net (%)	42.3	49.8	-41.4	0.8	-11.5
Benchmark (%)	4.1	32.5	-4.0	12.2	22.1
<b>CAD</b>	<b>30/06/19- 30/06/20</b>	<b>30/06/20- 30/06/21</b>	<b>30/06/21- 30/06/22</b>	<b>30/06/22- 30/06/23</b>	<b>30/06/23- 30/06/24</b>
Composite Net (%)	46.3	43.8	-46.1	7.9	-10.1
Benchmark (%)	7.0	27.2	-11.8	20.2	24.0
<b>AUD</b>	<b>30/06/19- 30/06/20</b>	<b>30/06/20- 30/06/21</b>	<b>30/06/21- 30/06/22</b>	<b>30/06/22- 30/06/23</b>	<b>30/06/23- 30/06/24</b>
Composite Net (%)	43.1	45.1	-43.6	8.7	-13.3
Benchmark (%)	4.6	28.3	-7.6	21.0	19.5

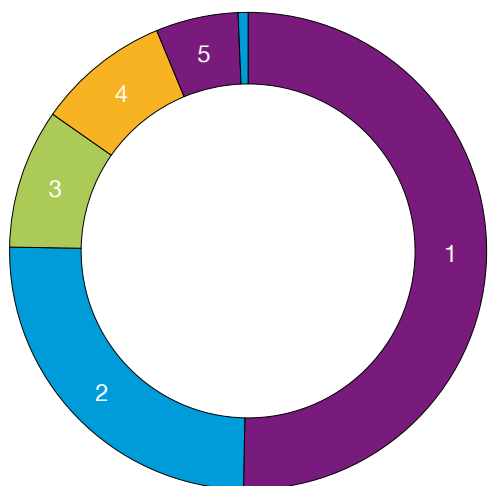
Benchmark is MSCI ACWI Index.

Source: Revolution, MSCI.

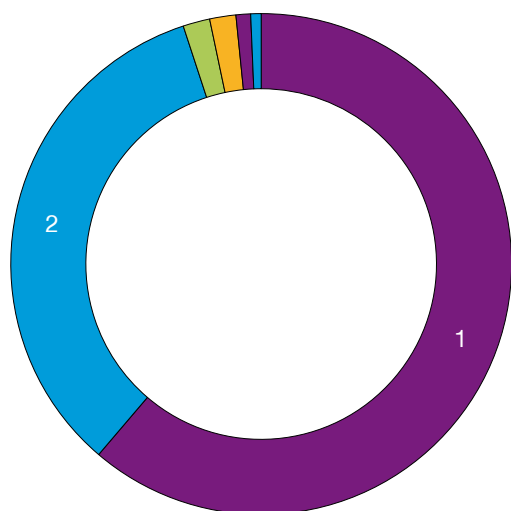
The Health Innovation composite is more concentrated than the MSCI ACWI Index.

Top Ten Largest Holdings

Stock Name	Description of Business	% of Portfolio
Alnylam Pharmaceuticals	Drug developer focussed on harnessing gene silencing technology	7.1
Moderna	Biotechnology developing mRNA-based therapeutics	7.0
argenx	Antibody based drug development	6.5
ALK-Abello	Health care	5.6
Ambu	Danish developer, producer and marketer of life saving equipment	5.3
Dexcom	Continuous glucose monitoring technology for diabetes management	5.0
Edwards Lifesciences	Services to treat late-stage cardiovascular disease	4.9
Genmab	Antibody based drug development	4.9
Ionis Pharmaceuticals	RNA targeted drugs	4.0
Insulet Corporation	Medical device company	3.6
<b>Total</b>		<b>53.8</b>



Industry Weights	(%)
1 Biotechnology	50.3
2 Health Care Equipment & Supplies	24.9
3 Life Sciences Tools & Services	9.5
4 Health Care Technology	9.0
5 Pharmaceuticals	5.6
6 Cash	0.7



Regional Weights	(%)
1 North America	61.2
2 Europe (ex UK)	33.7
3 Developed Asia Pacific	1.7
4 Emerging Markets	1.7
5 UK	0.9
6 Cash	0.7

Figures may not sum due to rounding.

Voting Activity

Votes Cast in Favour		Votes Cast Against		Votes Abstained/Withheld	
Companies	29	Companies	5	Companies	2
Resolutions	211	Resolutions	7	Resolutions	4

Company Engagement

Engagement Type	Company
Environmental	Vir Biotechnology, Inc.
Governance	10x Genomics, Inc., Alnylam Pharmaceuticals, Inc., Denali Therapeutics Inc., Edwards Lifesciences Corporation, Illumina, Inc., Lyell Immunopharma, Inc., Moderna, Inc., STAAR Surgical Company, Sage Therapeutics, Inc., Vir Biotechnology, Inc., WuXi Biologics (Cayman) Inc., Zai Lab Limited
Strategy	10x Genomics, Inc., Denali Therapeutics Inc., Sartorius Aktiengesellschaft, WuXi Biologics (Cayman) Inc.

Company	Engagement Report
Alnylam Pharmaceuticals, Inc.	<p><b>Objective:</b> This was a post-results call with chief executive officer (CEO) Yvonne Greenstreet. Given ambitious plans to target more prevalent diseases, we wanted to understand how the organisation managed growth.</p> <p><b>Discussion:</b> Greenstreet explained that the first era at Alnylam had focused on rare diseases to validate the company's RNAi technology. Greenstreet became CEO in 2022 and is now focusing on taking RNAi into larger disease opportunities and looking at RNAi targets outside the liver. Having focused on rarer diseases, she now needs to build up the company's capabilities while maintaining the strengths that have brought Alnylam to its current position. The company is now investing in developing its commercial footprint while continuing to invest in research and the pipeline. Alnylam is an ambitious company - and we were comforted that it looks for areas where it has a differential advantage and then pursues those spaces "hard and fast." As the company grows, we also noted the challenges this can present to culture: Greenstreet is determined to stay focused and nimble, even as the company moves into more common diseases.</p> <p><b>Outcome:</b> There is a good deal of ambition at Alnylam, and it is exciting to hear about its drive to remain at the forefront of RNAi treatments. However, it is also good to hear that it is determined to keep its culture, even as it targets more prevalent diseases.</p>
Denali Therapeutics Inc.	<p><b>Objective:</b> We met with biotech company Denali in May to discuss its strategic advance in neurodegenerative disease treatments. Discussions with chief executive officer Ryan Watts and chief operating and financial officer Alex Schuth centred on understanding Denali's drug pipeline development and financial strategies to support long-term growth, particularly its innovative blood-brain barrier (BBB) technology platform.</p> <p><b>Discussion:</b> Denali's executives provided significant updates on its drug pipeline, highlighting the Enzyme Transport Vehicle (ETV) franchise and the anticipated accelerated approval of DNL-310 for Hunter Syndrome. This approval is expected to pave the way for other programmes within the ETV franchise, leveraging biomarkers for accelerated approval for similar diseases. The OTV (Oligonucleotide Transport Vehicle) franchise was emphasised as 'the crown jewel', potentially addressing significant diseases like Alzheimer's, Parkinson's and ALS/MND by delivering gene-silencing medicines across the BBB. Management's strategy to maintain as much independence as possible with the OTV franchise was discussed. This was partly behind the decision to strengthen the balance sheet and secure a cash runway until 2028 via a \$500m primary offering with Baker Brothers Advisors and other investors.</p> <p><b>Outcome:</b> Denali is at a pivotal point, shifting from a pre-commercial to a commercial biotech company with the potential first drug approval from its BBB technology platform on the horizon. The ETV franchise, particularly DNL-310, represents a significant revenue opportunity and a new standard of care for Hunter Syndrome. The OTV franchise stands out for its potential to unlock treatments for major neurodegenerative diseases. Denali's strategic fundraising aims to sustain its independence and fuel long-term growth, positioning the company for a promising future in neurodegenerative disease treatment.</p>

Company	Engagement Report
Moderna, Inc.	<p>Objective: Ahead of Moderna's 2024 AGM, we had a call with the company's chief legal officer and her team to better understand the board's approach to refreshment and executive compensation. We have been advocating for compensation alignment, long-termism, and board refreshment for several years, and we again were able to ask about the board's plans in these areas.</p> <p>Discussion: While there have been recent rotations between board committees, Moderna informed us that we can expect board refreshment within the next 12 months. Following an external board review, it is looking for pharmaceutical expertise and is interested in experience in responsible AI and government affairs. We agreed that more expertise in these areas will be essential for the company's ambitions in the next five years. Again, we expect to see further improvement and long-termism in executive compensation in the next plan. Finally, we discussed Moderna's approach to equal pay, ESG, and its work with suppliers to reduce their emissions. We questioned its approach to climate risk, on which it has done a company-wide assessment in 2023.</p> <p>Outcome: We continue to support Moderna's long-term shareholders and look forward to any announcement of new board directors. On the call, we queried whether Moderna would consider a more differentiated and simplified approach to its compensation plan. We plan to discuss this again before the company sets future plans.</p>

## New Purchases

Stock Name	Transaction Rationale
SCHOTT Pharma	Schott Pharma is a German manufacturer of syringes, cartridges and vials for drug delivery and containment. Its products are low cost but mission critical in drug administration. It is one of just a handful of suppliers in an industry experiencing enhanced demand due to the increase in biologic drugs, such as messenger RNA vaccines, or obesity drugs. We believe the company can capitalise on this drug class evolution over the next decade while improving its unit economics through product mix changes.
Vertex Pharmaceuticals	We purchased drug developer Vertex for the portfolio as we believe the company is set to reap the benefits of its research and development efforts over the last ten years and launch drugs across multiple disease areas. Vertex's distinctive culture and business model is focused on serial innovation and the domination of the disease areas they enter. It has achieved this in cystic fibrosis, with the cash generated fuelling drug launches in pain, sickle cell disease, and potentially type 1 diabetes. Vertex offers significant upside potential combined with a resilient core drug franchise.
Zealand Pharma	As the obesity market matures and evolves over the next decade, we believe that the Danish biotech Zealand Pharma, has a chance of taking share in a large and expanding market. The company's edge in peptide synthesis, its improving commercial acumen, and its strengthening balance sheet position it favourably. It has a number of drugs in development, but its peptide drug Amylin, which could generate weight loss comparable to Novo Nordisk and Eli Lilly's drugs with less severe side effects, could dominate the company's sales in the next ten years if it navigates clinical trials successfully.
Zealand Pharma	We have taken a new holding in Danish Biotechnology company Zealand Pharma for the portfolio. As the obesity market matures and evolves over the next decade, we believe that Zealand has an excellent opportunity to take a share in this large and expanding market. The company's edge in peptide synthesis, its improving commercial acumen, and its strengthening balance sheet, position it favourably. It has a number of drugs in development, but we believe its peptide drug petrelintide to be the most valuable, having recently shown weight loss comparable to Novo Nordisk and Eli Lilly's 'GLP1s' in early clinical trials, but with less severe side effects. With supportive and meaningful data for what could be an exceedingly valuable asset, as well as a broader and promising pipeline beyond that, we believe that the balance between risk and potential reward is compelling.

## Complete Sales

Stock Name	Transaction Rationale
GRAIL	We decided to exit our holding in Grail because it is a subscale holding resulting from the spin-off from Illumina. Grail is still at an early stage of business development, and we do not yet have enough conviction in the company's path to commercialisation.

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