Health Innovation Quarterly Update

31 March 2024

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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.
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Potential for Profit and Loss

All investment strategies have the potential for profit and loss.

Stock Examples

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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

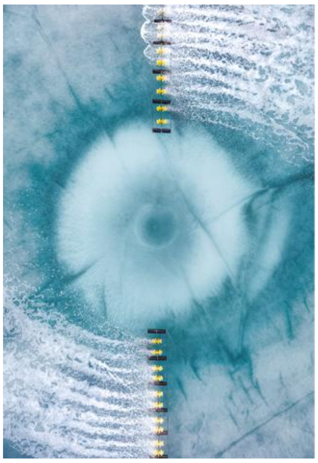
Key Statistics	
Number of Holdings	37
Typical Number of Holdings	25-50
Active Share	100%*
Rolling One Year Turnover	9%

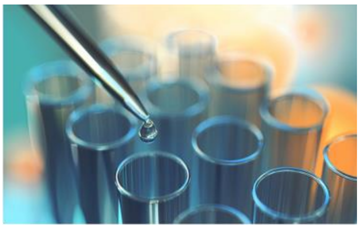
*Relative to MSCI ACWI Index. Source: Baillie Gifford & Co, MSCI.

The extreme headwinds faced by innovative healthcare companies continue to abate

Turnover has ticked up as we seek to capitalise on recent market dislocations

Accelerating innovation and attractive valuations are providing plentiful opportunity





Baillie Gifford Key Facts

Assets under management and advice	US$290.9bn
Number of clients	655
Number of employees	1817
Number of investment professionals	393

'Healing is a matter of time, but it is also a matter of opportunity'. Hippocrates

As the spectre of rapidly rising rates that has weighed so heavily on long-duration equities over recent years continues to lift, we are increasingly witnessing signs of healing within the innovative healthcare space. This is providing significant opportunities to us as long-term investors.

For example, we are seeing an acceleration in biological innovation, evidenced by a strong rise in new drug approvals in 2023, with the US Food and Drug Administration approving nearly 50% more new drugs than in 2022, and a revival in the number of clinical trials initiated.

Furthermore, as macroeconomic headwinds abate, there are positive indications that the funding environment for healthcare companies is recovering. This is particularly important for the healthcare ecosystem as it enables companies to progress clinical trials, invest in their pipelines, and further their research and development. Biopharmaceutical initial public offerings (IPOs) are already up 105% (annualised) in 2024 versus last year, and the capital raised so far in 2024 by the sector is almost 50% higher than the same period in 2023. The pace of equity follow-ons has also recovered meaningfully, with levels now back at pre-pandemic levels. Within our own portfolio too, we have seen a number of holdings take advantage of the improved backdrop to raise capital in the first quarter to fund their pipelines, including Denali, Alector, Sartorius and Sana. This will enable them to capitalise on the innovative treatments and technologies that they are developing.

Antifragile: things that gain from disorder. Nassim Taleb

Nassim Taleb's concept of anti-fragility resonates strongly with our own experience of investing in innovative healthcare companies. Antifragile refers to how certain entities can thrive amidst disorder, with the investment implication being that those companies that can weather adversity emerge stronger.

2022 and 2023 were undoubtedly two years of significant disorder for healthcare companies. Last year alone, the healthcare sector underperformed the broader global equity market by 20 per cent and our own portfolio also experienced a sharp drawdown in returns.

However, we believe that this disorder is now masking a large bifurcation between companies that have succumbed to the disorder, and those that have used it to cement their competitive advantages and strengthen their resiliency.

Within the portfolio, as we look to the year ahead, there are a number of holdings which have not only emerged in a stronger position but have sizable catalysts for growth over the months ahead.

For example, 2023 was an excellent year for Dexcom, the continuous glucose monitoring (CGM) company, where it expanded its patient population to 2.3 million, launched its next-generation G7 device, and sold the Dexcom ONE in multiple new markets. In 2024, Dexcom has already gained approval from the FDA for Stelo, its over-the-counter CGM for those who do not need insulin therapy. This clearance is an important step that will materially expand its addressable market to encompass the 25 million people in the US living with type 2 diabetes.

Elsewhere, Vir has used its healthy cash balance to bolster its pipeline and stimulate further value creation for patients and investors. Vir is an immunology company with a focus on infectious diseases. It has already successfully proven the capabilities of its technology platform with its antibody-based treatment being administered to millions of patients during the pandemic. But it is also working on some of the major unmet needs in infectious diseases, including, Hepatitis, HIV, and RSV. This year, it has important readouts from its Hepatitis D and Hepatitis B programmes. As it progresses these trials, Vir has proactively reached out to our Health Systems Specialist, Maria Souza, to "find intelligence and connect us to the right people" to support its Hepatitis D market-shaping plan. Our intention is that it can benefit from our "connective tissue" within the healthcare ecosystem, which links entrepreneurs, investors, scientists, healthcare professionals and NGOs to improve our portfolio holdings' chances of success.

We are also expecting key readouts for Moderna in 2024, which will further prove the company's capabilities beyond its COVID-19 vaccine. We expect news on the approval of its RSV vaccine in the first half of the year, and multiple Phase 3 readouts later in 2024, including for its CMV, and combination flu and covid vaccines.

Ongoing monitoring and patience

Some companies will likely require ongoing patience and additional scrutiny. For example, WuXi Biologics, the Chinese contract research and development organisation, has recently been caught in the crosshairs of geopolitical tensions between the US and China. Several US lawmakers are trying to advance a bill that will restrict WuXi's activities in the US. However, historically bills like this have had a low chance of being signed into law and we believe that the bear case scenario is now reflected in WuXi's stock price. Despite these concerns, the company continues to execute well and is investing in its overseas facilities to diversify its footprint. The bill's potential impact will take time to become evident and we will continue to monitor the situation closely.

We also believe that Alnylam, the gene-silencing pioneer, merits additional patience. It recently announced changes to its pivotal HELIOS-B trial, lengthening the trial by three months and splitting the patient population. Changes to clinical trials at this late stage are unusual and the market reacted badly to the news. However, the management team believe these changes will better highlight the superior efficacy of its drug. We await the results announcement in June and while this trial is important for Alnylam, it is just one in a broad and potentially lucrative pipeline for the company.

Exploiting market disorder

We can characterise the market of the past two years as one which has rewarded execution and punished missteps with the same vigour. As we enter an environment that is driven more by stock selection than market sentiment, it is creating interesting opportunities for us as long-term, fundamental-driven stock pickers. This has been evidenced by an uptick in transaction activity over the past quarter, as the team have taken advantage of valuation disconnects to purchase a number of new names for the portfolio.

For example, this quarter we initiated positions in BioNTech and Twist, both of which have fallen by around 70% from their peaks. BioNTech is most known for its COVID-19 vaccine, however, it has used the substantial cash generated from that to progress its oncology pipeline, and now has one of the broadest and deepest pipelines in this area, that spans multiple technology modalities, a necessity in tackling the complexity and heterogeneity of cancers. Twist, on the other hand, is one of the core companies at the centre of the synthetic biology movement - the practice of programming biological systems to create therapies, diagnostics, energy, and materials. The DNA "writing" market is at a much earlier stage than the DNA sequencing market, but Twist has built an enviable position as the provider of choice, and we believe it has an exceptional growth trajectory ahead.

The recent success of the new generation of anti-obesity drugs has caused significant share price weakness in a number of medical companies treating adjacent areas, as the market seems to have oversimplified the relationship between weight and chronic disease. This was the case with Inspire Medical and Insulet, which develop devices for sleep apnoea and diabetes delivery respectively. The market's preoccupation with GLP-1s caused the share prices of both companies to decline by almost 30%, providing an attractive entry point to two companies which we have long admired.

We have not, however, been complacent that all companies will display the requisite degree of anti-fragility that we require within the Health Innovation portfolio. A combination of management missteps and an inability to navigate the changing economic environment, has meant that Masimo, Teladoc, and Novocure have emerged as less resilient businesses and we have therefore taken the decision to sell them from the portfolio.

Outlook

Innovation across healthcare continues to advance strongly. Whether it be the increase in drug developer Research and development (R&D) budgets, new drugs approved, or clinical trial starts, these metrics demonstrate the health of the industry and provide a strong backdrop for its long-term prospects. Advancing technologies continue to bring a more data-driven era of personalised medicine closer. In the short term, industry revenues and profits are finally picking back up, improving market confidence, and resetting growth expectations higher.

We believe recent market uncertainty continues to mask the true potential of the companies in the portfolio. Valuations are extremely supportive, with the portfolio now trading at the lowest price to sales, and near the lowest price to earnings since its inception in 2018. This is despite the continued strong fundamentals of our holdings, which are growing their revenues and earnings at a rate that is at least double that of the index, while still investing for their futures, and therefore increasing their chances of long-term success.

As the companies' drug pipelines continue to advance, and their devices and services evidence a differentiated value proposition to patients and customers, we believe that they are well placed to emerge from the recent market disorder in robust health and full of opportunity.

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

GBP	Composite Net (%)	Benchmark (%)	Difference (%)
3 Months	2.8	9.3	-6.5
1 Year	-13.2	21.2	-34.4
3 Year	-14.5	10.7	-25.2
5 Year	2.3	12.1	-9.9
Since Inception	4.2	12.0	-7.7

USD	Composite Net (%)	Benchmark (%)	Difference (%)
3 Months	1.8	8.3	-6.5
1 Year	-11.3	23.8	-35.1
3 Year	-17.0	7.5	-24.4
5 Year	1.6	11.5	-9.8
Since Inception	4.0	11.7	-7.7

EUR	Composite Net (%)	Benchmark (%)	Difference (%)
3 Months	4.2	10.8	-6.6
1 Year	-10.8	24.5	-35.3
3 Year	-14.6	10.5	-25.1
5 Year	2.4	12.3	-9.9
Since Inception	5.0	12.7	-7.8

CAD	Composite Net (%)	Benchmark (%)	Difference (%)
3 Months	4.5	11.2	-6.7
1 Year	-11.3	23.8	-35.1
3 Year	-14.9	10.1	-25.1
5 Year	1.9	11.7	-9.8
Since Inception	4.6	12.4	-7.7

AUD	Composite Net (%)	Benchmark (%)	Difference (%)
3 Months	6.5	13.3	-6.8
1 Year	-9.0	27.1	-36.1
3 Year	-12.6	13.2	-25.7
5 Year	3.4	13.4	-10.0
Since Inception	5.6	13.5	-7.8

Annualised periods ended 31 March 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

GBP	31/03/19-31/03/20	31/03/20-31/03/21	31/03/21-31/03/22	31/03/22-31/03/23	31/03/23-31/03/24
Composite Net (%)	9.3	63.8	-21.4	-8.4	-13.2
Benchmark (%)	-6.2	39.6	12.9	-0.9	21.2

USD	31/03/19-31/03/20	31/03/20-31/03/21	31/03/21-31/03/22	31/03/22-31/03/23	31/03/23-31/03/24
Composite Net (%)	4.0	82.3	-25.0	-14.0	-11.3
Benchmark (%)	-10.8	55.3	7.7	-7.0	23.8

EUR	31/03/19-31/03/20	31/03/20-31/03/21	31/03/21-31/03/22	31/03/22-31/03/23	31/03/23-31/03/24
Composite Net (%)	6.5	70.2	-20.7	-11.9	-10.8
Benchmark (%)	-8.7	45.0	13.8	-4.7	24.5

CAD	31/03/19-31/03/20	31/03/20-31/03/21	31/03/21-31/03/22	31/03/22-31/03/23	31/03/23-31/03/24
Composite Net (%)	10.8	61.0	-25.4	-6.8	-11.3
Benchmark (%)	-4.9	37.1	7.1	0.8	23.8

AUD	31/03/19-31/03/20	31/03/20-31/03/21	31/03/21-31/03/22	31/03/22-31/03/23	31/03/23-31/03/24
Composite Net (%)	20.7	46.5	-23.9	-3.6	-9.0
Benchmark (%)	3.6	24.8	9.3	4.3	27.1

Benchmark is MSCI ACWI Index.
Source: Revolution, MSCI.
The Health Innovation composite is more concentrated than the MSCI ACWI Index.

Stock Level Attribution

Top and Bottom Ten Contributors to Relative Performance

Quarter to 31 March 2024

Stock Name	Contribution (%)
ShockWave Medical	3.2
Apple	0.8
Edwards Lifesciences	0.7
Tesla Inc	0.4
Alk-Abello	0.3
Veeva Systems	0.3
Ascendis Pharma	0.2
Dexcom	0.2
Sana Biotechnology	0.2
Staar Surgical	0.2
10X Genomics	-1.8
Alnylam Pharmaceuticals	-1.7
Wuxi Biologics	-1.6
NVIDIA	-1.2
Genmab	-0.8
Ionis Pharmaceuticals	-0.8
M3	-0.6
Exact Sciences	-0.5
Teladoc	-0.4
Zai Lab	-0.4

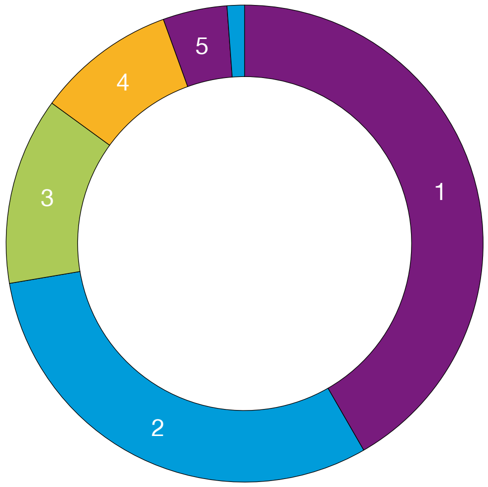
One Year to 31 March 2024

Stock Name	Contribution (%)
ShockWave Medical	1.6
Apple	0.7
Ascendis Pharma	0.4
Tesla Inc	0.3
Recursion Pharmaceuticals	0.3
Dexcom	0.2
Tencent	0.2
Sana Biotechnology	0.2
Pfizer	0.2
Nestle	0.1
Wuxi Biologics	-3.5
Moderna	-3.4
Genmab	-2.9
Alnylam Pharmaceuticals	-2.8
Illumina	-2.7
M3	-2.4
10X Genomics	-2.1
NVIDIA	-1.9
Novocure	-1.7
Masimo	-1.3

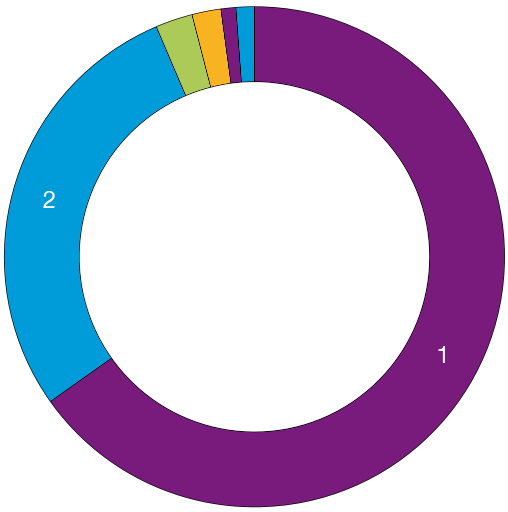
Source: Revolution, MSCI. Health Innovation composite relative to MSCI ACWI Index.
The holdings identified do not represent all of the securities purchased, sold or held during the measurement period. Past performance does not guarantee future returns. A full list showing all holdings' contributions to the portfolio's performance and a description on how the attribution is calculated is available on request. Some stocks may not have been held for the whole period. All attribution figures are calculated gross of fees, relative to the index from stock level up, based on closing prices. As attribution is shown relative to the benchmark, not all stocks shown are held in the portfolio.

Top Ten Largest Holdings

Stock Name	Description of Business	% of Portfolio
ShockWave Medical	Medical devices manufacturer	8.0
Moderna	Biotechnology developing mRNA-based therapeutics	6.9
Dexcom	Continuous glucose monitoring technology for diabetes management	5.9
argenx	Antibody based drug development	5.7
Genmab	Antibody based drug development	5.7
Edwards Lifesciences	Services to treat late-stage cardivascular disease	5.3
Sartorius Group	Biopharmaceutical and laboratory equipment supplier	4.6
Ambu	Danish developer, producer and marketer of life saving equipment	4.5
ALK-Abello	Health care	4.4
Exact Sciences	Non-invasive molecular tests for early cancer detection	4.3
Total		55.3



Industry Weights		(%)
1	Biotechnology	41.7
2	Health Care Equipment & Supplies	30.6
3	Life Sciences Tools & Services	12.7
4	Health Care Technology	9.4
5	Pharmaceuticals	4.4
6	Cash	1.2



Regional Weights		(%)
1	North America	65.2
2	Europe (ex UK)	28.4
3	Developed Asia Pacific	2.4
4	Emerging Markets	1.9
5	UK	1.0
6	Cash	1.2

Figures may not sum due to rounding.

Voting Activity

Votes Cast in Favour		Votes Cast Against		Votes Abstained/Withheld	
Companies	3	Companies	1	Companies	None
Resolutions	35	Resolutions	1	Resolutions	None

Company Engagement

Engagement Type	Company
Environmental	Twist Bioscience Corporation
Governance	ALK-Abello A/S, Exscientia, Genmab A/S, Sartorius Aktiengesellschaft, WuXi Biologics (Cayman) Inc.

Company	Engagement Report
Exscientia	Objective: Because of the recent upheaval within Exscientia's boardroom, as shareholders, it was imperative to assess the board's response to these challenges and evaluate their commitment to fostering better stewardship within the company. Discussion: After the CEO's dismissal due to misconduct and the chair's resignation, Exscientia is focusing on maintaining unity and transparency to rebuild trust internally and externally. The company is shifting from an ad-hoc approach to a more systematic and focused strategy for governance discipline. Exscientia's board has devised a stepwise plan for recovery, emphasising the implementation of best practices and soliciting input from all levels of the organisation. Regular town hall meetings/listening sessions were initiated to foster a culture of inclusivity and candour. A process to identify the new CEO is also underway. The board is open and straight about the fact that Exscientia now needs to continue focusing on science and accelerate its timeline when possible. Outcome: The recent actions of the board and its new priorities reflect Exscientia's efforts to navigate through the challenges, stabilise the company, and maintain shareholder confidence by promoting transparency, accountability and sound governance principles. It will be essential for Exscientia's board to continue demonstrating good stewardship in the face of adversity and seeing the company execute its strategy and grow.
WuXi Biologics	Objective: Unprecedented price volatility has affected Wuxi Biologics' share price. Much of this is due to geopolitical tensions, but part of the volatility can be attributed to management communication. We spoke to CEO Chris Chen twice to understand his communication skills and how he managed this volatility. Discussion: Wuxi Biologics had been anomalously bullish while the rest of the biotech industry struggled - having maintained their targets for the year and been persistently positive, they issued an unexpected profit warning in early December and noted that targets for adding new projects would be missed. In January, Wuxi Biologics' optimism recovered - full-year project targets had been met (despite the warning), and guidance for 2024 project numbers was revised upwards. We were concerned by the lack of consistency of these messages - and why management appeared to have such limited visibility over company performance. Chris Chen accepted that guidance had not been perfect and the company should have communicated weakness earlier - he said that management was guilty of over-optimism - it had always set challenging goals and met them in the past. He also noted that a pick up in projects in December had been unexpected - and that there is a short lead time on early-stage projects, so they did not have visibility over the turnaround when the announcement was made. After this, Wuxi Biologics has been a target of the US Biosecure Act, leading to substantial share price volatility. This appears to be being managed reasonably - the company has sensible strategies to deal with what will be a period marred by geopolitical tensions - it has held town halls to communicate with staff clearly and to try to improve morale - and is focusing on ensuring work continues as usual. It is hoped that a long-term focus on client satisfaction and project delivery will be more important than the current tensions in the US and China. Outcome: We were pleased that Chris Chen acknowledged the company's communication shortcomings and hope that a lesson has been learned. It is reassuring that Wuxi Biologics are managing current volatility with a reassuringly long-term client-centric mindset.

New Purchases

Stock Name	Transaction Rationale
BioNTech	We decided to take a position in BioNTech, a leading oncology-focused biotechnology company. We believe the combination of deep cancer expertise from the founders' decades of experience, its strong balance sheet of over $16bn in cash, and its access to new technologies, through internal development and partnerships, materially increases the company's chance of success. The market's focus on its declining COVID-19 vaccine revenues has left its valuation depressed, undervaluing the breadth and depth of its drug pipeline. We took the opportunity to add it to the portfolio.
Inspire Medical Systems	Inspire offers a revolutionary way of addressing obstructive sleep apnoea (OSA). Its implant stimulates a nerve to push the tongue forward and clear the throat. It is used as an alternative to pressurised masks worn while sleeping, which can have low compliance rates. With only 50k devices implanted today and an estimated 6m severe OSA patients alone in the US, there is potential to grow the number of procedures at over 20% per year for the next 10 years. Inspire has made clear progress in unlocking this market by evidencing the implant's effectiveness, making the procedure easier, improving awareness and establishing reimbursement, and it is now working to unlock surgeon capacity to boost procedure numbers further. Its stock price has halved since June due to the perceived impact of the obesity drugs despite these having no effect in treating OSA due to tongue collapse, which Inspire's devices treat. This has provided an attractive entry point to take a position in the company.
Insulet	We took a new position in Insulet which has developed the only fully disposable and automated insulin delivery pump on the market. Its easy-to-use, compact tubeless pump connects to a continuous glucose monitoring device to administer insulin in a more efficient way than alternatives. This has led it to take share rapidly against competitors. We believe that Insulet can expand its share in type 1 diabetes patients, but its largest opportunity will be its increased adoption by the 2.8m insulin-intensive type 2 diabetes suffers in the US where pumps are less than 5% penetrated. Our base case has the company growing its revenues at over 20% per year over the next five years, as well as expanding margins as it scales. Its stock price remains depressed due to fears that obesity drugs will limit its addressable market. This presented an attractive valuation opportunity to take an initial holding.
Twist Bioscience	Twist Bioscience manufactures DNA which is used in a number of applications such as in drug development, synthetic biology and clinical diagnostics. It makes synthetic DNA at a lower cost, at a higher throughput and with fewer errors than competitors. Its engineering-led approach can produce replicable success across various markets. Firstly, Twist has the potential to take share in the synthetic biology market through customer acquisition and new products and by the accelerated adoption of its sequencing products in the rapidly expanding diagnostics market. This can drive Twist's revenue growth higher, which combined with its recent capacity expansion, will lead to improved profitability over the next five years. Beyond this, the company also has compelling outlier potential in nascent markets such as in energy storage or its optimised antibodies for drug development.

Complete Sales

Stock Name	Transaction Rationale
Masimo	We sold the holding in Masimo, a developer of non-invasive patient monitoring devices. This was after already reducing the holding earlier in the month to fund a new purchase in Inspire Medical. Masimo's core business of monitoring infrastructure for hospitals is high quality, but its sales had slowed due to budget tightening across its customer base. More concerning was the severe hit in demand for its premium audio business which it acquired in 2022. We have monitored the progress of this acquisition since its completion and have concluded that it has worsened the quality of the business overall. We have therefore reallocated the proceeds of the sale to companies where we have more conviction.
Novocure	We decided to sell the position in Novocure. The company's Tumour Treating Field (TTF) devices emit electric fields which can stop and reverse the progression of cancer. After disappointing results in phase three trials in lung and ovarian cancer last year, we have less conviction that its TTF technology can become a backbone of cancer treatments in the future as the oncology field continues to change rapidly. With the next key trial results not expected for some time, we decided to reallocate the proceeds to a higher conviction new idea.
Teladoc	We sold the holding in Teladoc, the virtual healthcare company, due to its worsening growth prospects and a lack of faith in its management team. The pandemic propelled Teladoc to be the dominant telemedicine provider in the US and entrenched relationships with health insurers and employers. However, the company has not been able to leverage its platform across primary and chronic care to demonstrate value in the way we would have hoped. The cross-selling of its services has disappointed, and alongside slowing growth for its BetterHelp mental health app, undermined our confidence that the management team have the skills to navigate the complex needs of its customer base in the face of increasing competition.

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