

Health Innovation Quarterly Update

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30 September 2024



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Historical performance results for investment indexes and/or categories, generally do not reflect the deduction of transaction

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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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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  | 24%   |

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



### Baillie Gifford Key Facts

|                                    |             |
|------------------------------------|-------------|
| Assets under management and advice | US\$293.0bn |
| Number of clients                  | 633         |
| Number of employees                | 1708        |
| Number of investment professionals | 376         |

Companies in the portfolio are making operational progress, although we do continue to see significant stock-level volatility. While the portfolio delivered a positive absolute return during the quarter, it lagged the rise in the index due to several company-level developments. For example, high expectations weighed heavily on two of the strategy's equipment providers, Dexcom and Edwards Lifesciences, while a readjustment in the strategic plan at Moderna negatively affected its valuation.

In a 'prove it' market environment, the companies seeing earnings growth accelerate the fastest are being rewarded. ALK-Abello, the immunotherapy tablet developer, is one example. Strong demand for its tablets in Europe and operating leverage coming through as it scales are manifesting in impressive profit growth. With many allergy sufferers unaware of the company's treatments, we believe that the runway for growth extends far into the future.

Doximity, the online networking platform for doctors, and Veeva, the software provider for the pharmaceutical industry, have also delivered improved operating margins and EBITDA growth. Both were negatively affected as pharmaceutical customers pulled back their marketing and software spend. Their continuing recovery is a sign of resilience in customer budgets, but also their ability to provide value and increase their market share, even in more challenging times.

### Progress unveiled and rewarded

It is not just profit strength that influences healthcare company stock prices; they are also driven by companies achieving key milestones and validating their investments. Exact Sciences and BioNTech, two holdings in the portfolio, have recently made significant strides forward on both counts.

For the former, competition in its core colorectal cancer testing market and slowing growth had weighed on its stock price over the last year. That sentiment seemed to shift this quarter after it announced early-stage results for its own blood-based colorectal cancer test which looks far superior to its competitor, Guardant Health. If the trial results hold for a larger population, it will allow Exact Sciences to continue to grow into the estimated 60m-strong unscreened patient population in the US. Its minimal residual disease (MRD) test, which is used to check for the remnants

of cancer after treatment, could also be launched next year, opening a new revenue stream for the company.

For German biotech BioNTech, the story is similar. Having played a vital role in getting the global economy back up and running with its mRNA COVID-19 vaccine, weak vaccine uptake of late has led the market to believe it is a one-off pandemic beneficiary. This is part of the reason we were able to buy shares in the company at an over 70% discount from its peak in 2021. Contrary to the market's view, the interesting element of the BioNTech investment case is its oncology, not infectious disease expertise. It has invested a significant proportion of its COVID-19 vaccine revenues to develop one of the most interesting cancer pipelines in the field, using mRNA, antibodies, cell therapies, and even small molecules.

The company made significant progress during the quarter after it announced phase 1/2 results of its antibody drug, BNT327, in lung cancer. This drug delivered a rare efficacy win over the world's most profitable cancer drug, Keytruda. Considering Keytruda generates \$25bn annually across numerous cancer types, a successful phase 3 trial could mean this drug has real 'blockbuster' potential. As this is just one drug in a pipeline of over 20, we could see a series of positive catalysts as BioNTech's pipeline is validated.

### High expectations require flawless execution

In contrast, we saw the share price of Dexcom, the manufacturer of continuous glucose monitoring systems (CGMs) for diabetics, fall sharply following an announcement of slower-than-expected growth and a reset of expectations for the rest of the year. Dexcom's headache was related to disappointing execution following a recent reorganisation of its sales force, weaker international sales, and a softening of US revenue per customer. These missteps are somewhat out of character for a company such as Dexcom which has displayed impressive fundamental growth since we have held it in the portfolio. We believe that there is a significant opportunity for CGMs and we remain optimistic about the potential of Dexcom's new over-the-counter Stelo product. We are engaging with management to build conviction in their ability to overcome the current challenges and unlock the tremendous growth opportunity ahead.

Edwards Lifesciences, which provides a range of heart valve implants, also detracted from performance during the period. The company is a world leader in tissue replacement heart valves, such as its transcatheter aortic valve replacement (TAVR) product which can be implanted without the need for open heart surgery. Its recent results showed lower growth for TAVR than anticipated. Management commented that this slower growth could be the result of hospitals being under staffing pressure as they scale their structural heart teams to perform the exact type of procedures that Edwards also provides implants for. We believe the market reaction is overdone and continue to have conviction in the opportunity for Edwards from here, not least as it is due to report pivotal data at the end of the year which will look to expand TAVR into asymptomatic severe aortic stenosis.

Moderna's stock price declined during the period following weak COVID-19 vaccine sales and a slow RSV vaccine launch. The company has since announced that it will lower its R&D spend and focus its pipeline, while pushing out profitability until 2027. We met with the CEO, Stephane Bancel, in September to discuss the commercial missteps in more detail and will continue to engage with the company. Regardless of how exciting its technology platform is, its commercial engine must function well to achieve its potential. We are eager to see clear signs of an improvement.

### Notable transactions

After extensive research, our conviction in Novo Nordisk, the obesity drug developer, has increased to a level to take a holding. We believe the obesity market has the potential to be a \$350bn opportunity over the next 10 years, with Novo Nordisk set to take a sizeable share. The insatiable demand in the self-pay market for Novo Nordisk's drugs is unprecedented in the history of chronic diseases and is set to continue. We believe its strong clinical evidence and manufacturing capacity will result in a growing stream of cash flows that it can use to advance its obesity pipeline, which is already the strongest in the industry. This includes developing drugs with improved efficacy, those that can be taken orally or with new mechanisms of action.

We sold Sage Therapeutics after a series of clinical setbacks limited its addressable market and reduced its chance of success. The initial investment case was that Sage's drugs' novel

mechanisms of action had the potential to transform the treatment of depression and other brain disorders. However, despite the approval of its drug Zurzuvae for postpartum depression, recent trial failures in other areas have lowered our confidence that its novel science could translate into commercial results.

## 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        | -1.8                     | 0.2                  | -2.0                  |
| 1 Year          | -1.4                     | 10.5                 | -11.9                 |
| 3 Year          | -19.5                    | 6.5                  | -25.9                 |
| 5 Year          | 0.8                      | 9.9                  | -9.1                  |
| Since Inception | 2.9                      | 9.9                  | -7.0                  |
| <b>USD</b>      | <b>Composite Net (%)</b> | <b>Benchmark (%)</b> | <b>Difference (%)</b> |
| 3 Months        | 4.2                      | 6.3                  | -2.1                  |
| 1 Year          | 8.3                      | 21.4                 | -13.1                 |
| 3 Year          | -19.6                    | 6.3                  | -25.9                 |
| 5 Year          | 2.5                      | 11.8                 | -9.3                  |
| Since Inception | 3.8                      | 10.8                 | -7.1                  |
| <b>EUR</b>      | <b>Composite Net (%)</b> | <b>Benchmark (%)</b> | <b>Difference (%)</b> |
| 3 Months        | 0.1                      | 2.1                  | -2.0                  |
| 1 Year          | 2.8                      | 15.2                 | -12.4                 |
| 3 Year          | -18.6                    | 7.6                  | -26.2                 |
| 5 Year          | 2.0                      | 11.3                 | -9.2                  |
| Since Inception | 4.0                      | 11.1                 | -7.1                  |
| <b>CAD</b>      | <b>Composite Net (%)</b> | <b>Benchmark (%)</b> | <b>Difference (%)</b> |
| 3 Months        | 2.9                      | 5.0                  | -2.1                  |
| 1 Year          | 8.3                      | 21.3                 | -13.0                 |
| 3 Year          | -17.9                    | 8.6                  | -26.4                 |
| 5 Year          | 2.9                      | 12.3                 | -9.3                  |
| Since Inception | 4.3                      | 11.4                 | -7.1                  |
| <b>AUD</b>      | <b>Composite Net (%)</b> | <b>Benchmark (%)</b> | <b>Difference (%)</b> |
| 3 Months        | 0.3                      | 2.3                  | -2.0                  |
| 1 Year          | 0.8                      | 12.9                 | -12.1                 |
| 3 Year          | -18.5                    | 7.7                  | -26.2                 |
| 5 Year          | 2.0                      | 11.2                 | -9.2                  |
| Since Inception | 4.2                      | 11.2                 | -7.1                  |

Annualised periods ended 30 September 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 Health Care Index.

Source: Revolution, MSCI.

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

## Discrete Performance

| <b>GBP</b>        | <b>30/09/19-<br/>30/09/20</b> | <b>30/09/20-<br/>30/09/21</b> | <b>30/09/21-<br/>30/09/22</b> | <b>30/09/22-<br/>30/09/23</b> | <b>30/09/23-<br/>30/09/24</b> |
|-------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Composite Net (%) | 59.0                          | 25.3                          | -34.1                         | -19.6                         | -1.4                          |
| Benchmark (%)     | 16.5                          | 14.3                          | 7.4                           | 1.7                           | 10.5                          |
| <b>USD</b>        | <b>30/09/19-<br/>30/09/20</b> | <b>30/09/20-<br/>30/09/21</b> | <b>30/09/21-<br/>30/09/22</b> | <b>30/09/22-<br/>30/09/23</b> | <b>30/09/23-<br/>30/09/24</b> |
| Composite Net (%) | 66.8                          | 30.7                          | -45.5                         | -12.0                         | 8.3                           |
| Benchmark (%)     | 22.2                          | 19.2                          | -11.1                         | 11.2                          | 21.4                          |
| <b>EUR</b>        | <b>30/09/19-<br/>30/09/20</b> | <b>30/09/20-<br/>30/09/21</b> | <b>30/09/21-<br/>30/09/22</b> | <b>30/09/22-<br/>30/09/23</b> | <b>30/09/23-<br/>30/09/24</b> |
| Composite Net (%) | 55.0                          | 32.3                          | -35.5                         | -18.6                         | 2.8                           |
| Benchmark (%)     | 13.6                          | 20.6                          | 5.2                           | 2.9                           | 15.2                          |
| <b>CAD</b>        | <b>30/09/19-<br/>30/09/20</b> | <b>30/09/20-<br/>30/09/21</b> | <b>30/09/21-<br/>30/09/22</b> | <b>30/09/22-<br/>30/09/23</b> | <b>30/09/23-<br/>30/09/24</b> |
| Composite Net (%) | 68.2                          | 24.0                          | -40.9                         | -13.5                         | 8.3                           |
| Benchmark (%)     | 23.3                          | 13.0                          | -3.6                          | 9.4                           | 21.3                          |
| <b>AUD</b>        | <b>30/09/19-<br/>30/09/20</b> | <b>30/09/20-<br/>30/09/21</b> | <b>30/09/21-<br/>30/09/22</b> | <b>30/09/22-<br/>30/09/23</b> | <b>30/09/23-<br/>30/09/24</b> |
| Composite Net (%) | 56.9                          | 29.7                          | -38.7                         | -12.4                         | 0.8                           |
| Benchmark (%)     | 15.0                          | 18.2                          | -0.1                          | 10.8                          | 12.9                          |

Benchmark is MSCI ACWI Health Care Index.

Source: Revolution, MSCI.

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



## Stock Level Attribution

## Top and Bottom Ten Contributors to Relative Performance

## Quarter to 30 September 2024

| Stock Name            | Contribution (%) |
|-----------------------|------------------|
| Exact Sciences        | 1.3              |
| argenx                | 1.2              |
| Doximity              | 1.1              |
| ResMed                | 0.6              |
| Wuxi Biologics Cayman | 0.5              |
| Sartorius Pref.       | 0.5              |
| BioNTech              | 0.5              |
| Illumina              | 0.5              |
| Alk-Abello            | 0.4              |
| Microsoft             | 0.4              |
| Moderna               | -3.3             |
| Dexcom                | -2.2             |
| Edwards Lifesciences  | -1.7             |
| Staar Surgical        | -0.5             |
| Novo Nordisk          | -0.5             |
| Genmab                | -0.4             |
| Zealand Pharma        | -0.4             |
| Ionis Pharmaceuticals | -0.3             |
| Twist Bioscience      | -0.2             |
| Ambu                  | -0.2             |

## One Year to 30 September 2024

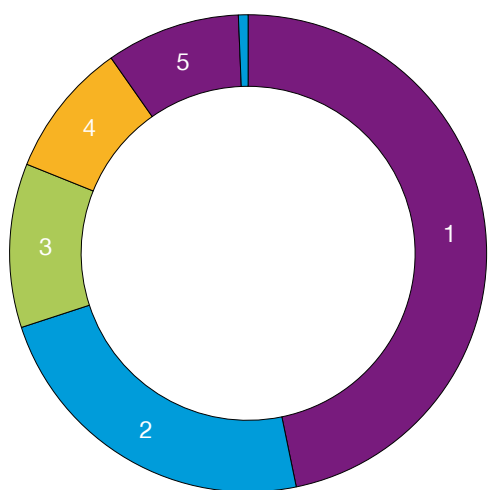
| Stock Name              | Contribution (%) |
|-------------------------|------------------|
| ShockWave Medical       | 2.5              |
| Alk-Abello              | 2.2              |
| Ambu                    | 1.7              |
| Alnylam Pharmaceuticals | 1.3              |
| Doximity                | 1.2              |
| Insulet                 | 0.7              |
| ResMed                  | 0.6              |
| Masimo                  | 0.4              |
| Ascendis Pharma ADR     | 0.4              |
| BioNTech                | 0.3              |
| Genmab                  | -3.7             |
| Wuxi Biologics Cayman   | -3.3             |
| Moderna                 | -3.3             |
| Dexcom                  | -2.3             |
| M3                      | -2.2             |
| 10X Genomics            | -2.1             |
| NVIDIA                  | -2.0             |
| Sartorius Pref.         | -1.9             |
| Edwards Lifesciences    | -1.3             |
| argenx                  | -1.2             |

Source: Revolution, MSCI. Health Innovation composite relative to MSCI ACWI Health Care Index.

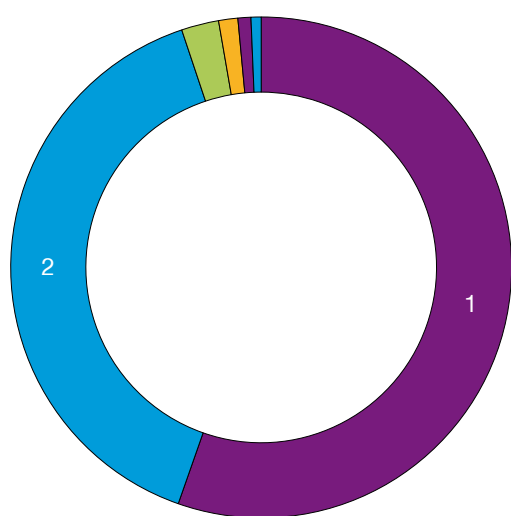
The holdings identified do not represent all of the securities purchased, sold or held during the measurement period. Past performance does not guarantee future returns. A full list showing all holdings' contributions to the portfolio's performance and a description on how the attribution is calculated 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 |
|-------------------------|------------------------------------------------------------------|----------------|
| argenx                  | Antibody based drug development                                  | 7.6            |
| Alnylam Pharmaceuticals | Drug developer focussed on harnessing gene silencing technology  | 7.1            |
| ALK-Abello              | Health care                                                      | 5.6            |
| Ambu                    | Danish developer, producer and marketer of life saving equipment | 5.1            |
| Genmab                  | Antibody based drug development                                  | 4.4            |
| Insulet Corporation     | Medical device company                                           | 4.3            |
| Exact Sciences          | Non-invasive molecular tests for early cancer detection          | 4.1            |
| ResMed                  | Develops and manufactures medical equipment                      | 3.9            |
| Moderna                 | Biotechnology developing mRNA-based therapeutics                 | 3.7            |
| Doximity                | Online healthcare resource and interactive platform developer    | 3.6            |
| <b>Total</b>            |                                                                  | <b>49.6</b>    |



| Industry Weights                   | (%)  |
|------------------------------------|------|
| 1 Biotechnology                    | 46.8 |
| 2 Health Care Equipment & Supplies | 23.2 |
| 3 Life Sciences Tools & Services   | 11.1 |
| 4 Health Care Technology           | 9.2  |
| 5 Pharmaceuticals                  | 9.1  |
| 6 Cash                             | 0.7  |



| Regional Weights         | (%)  |
|--------------------------|------|
| 1 North America          | 55.4 |
| 2 Europe (ex UK)         | 39.5 |
| 3 Emerging Markets       | 2.4  |
| 4 Developed Asia Pacific | 1.2  |
| 5 UK                     | 0.8  |
| 6 Cash                   | 0.7  |

Figures may not sum due to rounding.

Voting Activity

| Votes Cast in Favour |   | Votes Cast Against |      | Votes Abstained/Withheld |      |
|----------------------|---|--------------------|------|--------------------------|------|
| Companies            | 1 | Companies          | None | Companies                | None |
| Resolutions          | 4 | Resolutions        | None | Resolutions              | None |

Company Engagement

| Engagement Type | Company                                                                                                                                                                                                |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Environmental   | Twist Bioscience Corporation                                                                                                                                                                           |
| Social          | DexCom, Inc.                                                                                                                                                                                           |
| Governance      | BioNTech SE, DexCom, Inc., Exscientia plc, Health Catalyst, Inc., Illumina, Inc., M3, Inc., Moderna, Inc., Recursion Pharmaceuticals, Inc., Sartorius Aktiengesellschaft, Twist Bioscience Corporation |
| Strategy        | DexCom, Inc., Illumina, Inc., Moderna, Inc., Sartorius Aktiengesellschaft                                                                                                                              |

| Company | Engagement Report                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Dexcom  | <p>Objective: To gather the chief executive officer and chief financial officer's perspectives on Dexcom's revised full-year revenue guidance and evaluate the strategic measures the company is implementing. We aimed to determine whether the current challenges are temporary or indicative of deeper structural issues within the competitive landscape and growth opportunities.</p> <p>Discussion: Dexcom's unexpected downgrade in full-year guidance resulted in a 40 per cent drawdown in share price in August 2024. According to the management team, several factors were responsible: the lack of visibility in sales, particularly in the Durable Medical Equipment (DME) distribution channel which has a data lag of four to six weeks; the strategic pivot towards the Pharmacy channel, which inadvertently strained relationships with DME partners; and a salesforce reorganisation. Dexcom's proactive measures to tackle these challenges include a commitment to channel agnosticism, co-branding initiatives with DME partners, and a realignment of their salesforce to better serve specialists, endocrinologists and primary care physicians.</p> <p>Outcome: We will continue to monitor and engage with the company as we still have questions about whether this is a transitory situation or a structural shift due to short-term execution issues, growing competition, or both.</p> |

## New Purchases

| Stock Name   | Transaction Rationale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Novo Nordisk | Novo Nordisk is a Danish pharmaceutical company and one of the leaders in metabolic diseases. We took a position as we believe the obesity market has blue sky potential to be a \$350bn opportunity over the next 10 years, with Novo Nordisk set to take a sizeable share. The insatiable demand in the self-pay market for Novo's drugs is unprecedented in the history of chronic diseases and set to continue. Its five-year head start on competitors, strong clinical evidence, and manufacturing capacity will result in a growing stream of cash flows that it can use to advance its obesity pipeline, which is already the strongest in the industry. This includes developing drugs with improved efficacy, those that can be taken orally, or with new mechanisms of action, further expanding the market. |
| RxSight      | RxSight is the US developer of customisable implantable lenses for patients after cataract surgery. Its lenses are unique among competitors in that they can be adjusted through a UV light machine after surgery to ensure perfect vision. With 20 million cataract procedures globally and 7 million in the US alone, we believe RxSight lenses' superior clinical utility can lead it to capture over 50% of the US premium lens market from just over 10% today. Additionally, its lenses are easy to implant and adjust and provide appealing procedure economics for surgeons which can propel its growth. We think the company's valuation leaves significant room for upside due to both the rate and duration of its growth over the next five years.                                                          |

## Complete Sales

| Stock Name         | Transaction Rationale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|--------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Relay Therapeutics | We invested in Relay in 2020 as we felt its cutting edge tools and computational models could provide novel insight into the motion of proteins, leading to the design of safer, more potent drugs. It has made some progress, advancing two programs for specific gene mutations found in a broad range of cancer tumour types. However, this progress has been slower than we had hoped, with the pivoting of one program delaying trial patient recruitment and increasing its capital requirements. A tougher capital-raising environment has narrowed its focus and increases the importance of these lead programs. After visiting the company last month, our conviction in its success has weakened in a highly competitive oncology space and we decided to sell the position. |
| Sage Therapeutics  | We sold Sage Therapeutics after a series of clinical setbacks limited its addressable market and reduced its chance of success. The initial investment case was that the novel mechanisms of action of Sage's drugs had the potential to transform the treatment of depression and other brain disorders. However, despite the approval of their drug Zurzurvae for postpartum depression, trial failures in major depressive disorder, neurological tremors, and Parkinson's disease lowered our confidence that their novel science could translate into commercial results, especially considering the lack of objective biomarkers in these disorders.                                                                                                                              |



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