Janus Henderson INVESTORS

GLOBAL LIFE SCIENCES FUND

At a glance

Performance*
The Fund returned 1.56%, the Index returned 2.35% and the Sector returned 1.46%.

Contributors/detractors
Positioning in biotechnology weighed on relative performance, while stock selection in pharmaceuticals aided returns.

Outlook
We believe attractive valuations, mergers and acquisitions (M&As) and accelerating innovation could propel the sector in 2024.

Portfolio management

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Investment environment

- Health care stocks continued their strong start to the year, delivering another month of gains along with the broader market. Ongoing excitement around new GLP-1 weight-loss drugs and a first quarter pick-up in capital markets activity helped power the sector's surge.
- Gains were shared across sub-sectors, with biotechnology and health care services only slightly edging out medical devices and pharmaceuticals.
- Health care providers performed well thanks to rising utilisation by patients, which drove demand for services. However, the demand increased costs for insurers, which also face lower reimbursement rates in Medicare Advantage plans.

Portfolio review

Looking at individual holdings, Ardelyx weighed on relative performance, with the stock pulling back on what appears to be profit-taking following a strong run. In October, the US Food and Drug Administration (FDA) granted expanded approval for tenapanor (brand name Xphozah) for the control of serum phosphate in kidney dialysis patients with an inadequate response to standard of care phosphate binders.

The stock then continued to rise as Ardelyx provided additional visibility into the commercial prospects for tenapanor's original indication, Ibsrela, for irritable bowel syndrome with constipation. Ibsrela recorded $80 million in revenues for its first calendar year in market, and Ardelyx now says it expects sales to peak at more than $1 billion annually. Xphozah (also off to a strong start) could provide additional potential.

Zai Lab was another detractor. The China-based biotech firm was impacted by weakness in the Chinese equity market during the period. Even so, Zai Lab has seen double-digit revenue growth thanks to strong commercial franchises in China, and recently launched Vyvgart, a treatment for adults with generalised myasthenia gravis.

Zai Lab licenses the drug for sale in China, and in December Vyvgart was added to China's National Reimbursement Drug List, dramatically widening the therapy's addressable market in the country. Vyvgart -

*For benchmark and sector, if applicable, refer to Fund details on page 3. For relevant descriptions, risks and the Fund's investment policy statement, refer to Additional fund information on page 4.

which first launched in the US as an intravenous version in late 2021, then as a subcutaneous (under the skin) therapy in mid-2023 - has already achieved over $1 billion annual sales in the US.

Avadel Pharmaceuticals contributed positively to performance. The biotech firm is in the early stages of rolling out narcolepsy drug, Lumryz, which the FDA approved last year. Another company, Jazz Pharmaceuticals, has claimed patent infringement of its drug, Xyrem, which shares the same active ingredient as Lumryz. Jazz sued for a royalty payment of 27%, but was granted the equivalent of less than 1%. Lumryz is viewed as a major improvement over Xyrem, which requires patients to wake for a second dose during the night. Lumryz, on the other hand, is taken once at bedtime, and early signs suggest the drug's launch is off to a strong start.

An underweight to Johnson & Johnson (J&J) also aided performance. The stock declined due to uncertainty around the company's liability from ongoing talcum-powder lawsuits. In addition, during the month J&J's med-tech Abiomed division was hit with a recall for select models of its miniaturised heart pump. This followed other recalls issued in 2023. J&J offers a robust balance sheet and strong free cash flow, but given these headwinds we retain an underweight position in the stock.

Manager outlook

After falling out of favour with investors in 2023, health care stocks have started to rebound thanks to low valuations, innovation, and recent drug launches. Sales of new GLP-1 obesity and diabetes drugs, for example, topped $20 billion globally in 2023 and are expected to continue growing rapidly.

Meanwhile, the FDA approved a record number of novel medicines last year, and these drugs - some with blockbuster potential (sales of $1 billion or more annually) - are now beginning revenue cycles of 10 years or longer. Merger and acquisition (M&A) activity has been another boon, as large biopharmaceutical firms seek to offset patent expirations with promising new technologies, such as antibody-drug conjugates, radiopharmaceuticals and cell therapies. Given discounted valuations and innovation, the deal-making is expected to continue throughout the year.

Not all areas of the sector have been as positive. Managed care companies have lagged given concerns about rising medical costs and regulation, including lower reimbursement rates for Medicare Advantage (MA), the privately administered health plan for the elderly. Furthermore, increased government scrutiny of M&A could put some insurers in the spotlight during the US election. Sales of COVID-19 products also continue to decline, while supply imbalances for tools and services firms caused by the pandemic may take until mid-year to get sorted out.

With these factors in mind, we remain overweight small- and mid-cap biotechs with newly launching products or exciting late-stage pipelines. Many of these stocks trade at a discount following a three-year pullback in biotech - a drawdown we think could be ending now that rate hikes in the US have most likely concluded. While managed care faces near-term headwinds, we believe these companies still have a strong long-term outlook given their ability to reprice services annually and now discounted valuations. They also retain important defensive qualities should economic growth slow amid today's tighter financial conditions.

In the end, though, we think health care's many medical advances and long-term growth trends will be the dominant story in 2024. In our view, these opportunities, along with still-attractive valuations, could help support the sector throughout the year.

Performance (%)

Returns	Cumulative 1 Month	3 Month	YTD	1 Year	Annualised 3 Year	5 Year	10 Year
A2 USD (Net)	1.56	8.07	8.07	15.99	5.68	9.56	9.50
Index	2.35	7.47	7.47	13.32	7.85	10.33	9.18
Sector	1.46	4.28	4.28	7.23	-0.28	5.60	6.23
A2 USD (Gross)	—	—	—	—	—	12.17	12.14
Target	—	—	—	—	—	12.53	11.37

Calendar year	YTD at Q1 2024	2023	2022	2021	2020	2019	2018	2017	2016	2015	2014
A2 USD (Net)	8.07	5.44	-4.35	4.72	23.41	27.06	2.01	20.55	-13.79	5.69	32.75
Index	7.47	3.76	-5.41	19.80	13.52	23.24	2.51	19.80	-6.81	6.60	18.10
Sector	4.27	2.67	-13.91	7.12	20.53	21.80	-3.40	21.68	-9.37	5.90	18.33

Performance is on a net of fees basis, with gross income reinvested. Source: at 31/03/24. **Past performance does not predict future returns.** Performance/performance target related data will display only where relevant to the share class inception date and annualised target time period. **The value of an investment and the income from it can fall as well as rise and you may not get back the amount originally invested.** Source for target returns (where applicable) - Janus Henderson Investors. Please note index returns are net of tax.

Fund charges will impact the value of your investment. In particular, the ongoing charges applicable to each fund will dilute investment performance, particularly over time. For further explanation of charges please visit our Fund Charges page at www.janushenderson.com.

Note that any differences among portfolio securities currencies, share class currencies and costs to be paid or represented in currencies other than your home currency will expose you to currency risk. Costs and returns may increase or decrease as a result of currency and exchange rate fluctuations.

Investment objective

The Fund aims to provide capital growth over the long term. Performance target: To outperform the MSCI World Health Care Index by at least 2% per annum, before the deduction of charges, over any 5 year period.

For the fund’s investment policy, refer to the Additional fund information on page 4.
Past performance does not predict future returns.

Fund details

Inception date	31 March 2000
Total net assets	4.08bn
Asset class	Equities
Domicile	Ireland
Structure	Irish Investment Company
Base currency	USD
Index	MSCI World Health Care Index
Morningstar sector	Sector Equity Healthcare
SFDR category	Article 8

In accordance with the Sustainable Finance Disclosure Regulation, the Fund is classified as Article 8 and promotes, among other characteristics, environmental and/or social characteristics, and invests in companies with good governance practices.

Additional fund information

Tax assumptions and reliefs depend upon an investor's particular circumstances and may be subject to change. Please note the performance target is to be achieved over a specific annualised time period. Refer to the performance target wording within the objective. Availability of share classes shown may be limited by law in certain jurisdictions. Performance records/scenarios are detailed within the fund's specific KIID/KID; fees and charges, and the respective risk rating may vary. Further information can be found in the fund's prospectus and KIID/KID, which must be reviewed before investing. Please consult your local sales representative and/or financial adviser if you have any queries. As of 31 January 2023, Daniel Lyons Ph.D., CFA also manages this fund. This is an Irish Investment Company regulated by the Central Bank of Ireland. A short-term trading fee may be applied upon exiting the fund as per the prospectus. These are the views of the author at the time of publication and may differ from the views of other individuals/teams at Janus Henderson Investors. Any securities, funds, sectors or indices mentioned within this article do not constitute or form part of any offer or solicitation to buy or sell them. The information in this commentary does not qualify as an investment recommendation. Investment into the fund will acquire units/shares of the fund itself and not the underlying assets owned by the fund. The ongoing charge is calculated using the PRIIP methodology. The PRIIP methodology differs to the UCITS ongoing charge methodology, as the PRIIP methodology captures additional recurring charges, including but not limited to: Interest paid on borrowing (e.g. bank interest); Any fees incurred in relation to stock-lending activity (i.e. the fee paid to the lending agent); Any costs associated with holding closed-ended vehicles. Cash balances and exposures are based on settled and unsettled trades as at the reporting date.

Investment policy

The Fund invests at least 80% in shares (also known as equities) of companies, of any size, including smaller capitalisation companies, with a life sciences orientation, in any country. Up to 20% may be invested in developing markets. The Fund may also invest in other assets including cash and money market instruments. The Sub-Investment Adviser may use derivatives (complex financial instruments) to reduce risk, to manage the Fund more efficiently, or to generate additional capital or income for the Fund. The Fund is actively managed with reference to the MSCI World Health Care Index, which is broadly representative of the companies in which it may invest, as this forms the basis of the Fund's performance target. The Sub-Investment Adviser has discretion to choose individual investments for the Fund with weightings different to the index or not in the index, but at times the Fund may hold investments similar to the index.

Investment strategy

The Sub-Investment Adviser looks to identify innovative healthcare companies addressing high unmet medical needs across fields including biotechnology, pharmaceuticals, healthcare services and medical technology. The team understands that success of drug development is binary in nature, creating wide disparities between winners and losers. The investment process leverages proprietary statistical models to analyse the probability of a company's success, focusing on products they believe can overcome the rigours of clinical development. Additional tools, such as physician surveys and prescription models, attempt to more accurately predict commercial viability.

Fund specific risks

When the Fund, or a share/unit class, seeks to mitigate exchange rate movements of a currency relative to the base currency (hedge), the hedging strategy itself may positively or negatively impact the value of the Fund due to differences in short-term interest rates between the currencies. The Fund could lose money if a counterparty with which the Fund trades becomes unwilling or unable to meet its obligations, or as a result of failure or delay in operational processes or the failure of a third party provider. Shares/Units can lose value rapidly, and typically involve higher risks than bonds or money market instruments. The value of your investment may fall as a result. Shares of small and mid-size companies can be more volatile than shares of larger companies, and at times it may be difficult to value or to sell shares at desired times and prices, increasing the risk of losses. If a Fund has a high exposure to a particular country or geographical region it carries a higher level of risk than a Fund which is more broadly diversified. The Fund is focused towards particular industries or investment themes and may be heavily impacted by factors such as changes in government regulation, increased price competition, technological advancements and other adverse events. The Fund may use derivatives to help achieve its investment objective. This can result in leverage (higher levels of debt), which can magnify an investment outcome. Gains or losses to the Fund may therefore be greater than the cost of the derivative. Derivatives also introduce other risks, in particular, that a derivative counterparty may not meet its contractual obligations. If the Fund holds assets in currencies other than the base currency of the Fund, or you invest in a share/unit class of a different currency to the Fund (unless hedged, i.e. mitigated by taking an offsetting position in a related security), the value of your investment may be impacted by changes in exchange rates. Securities within the Fund could become hard to value or to sell at a desired time and price, especially in extreme market conditions when asset prices may be falling, increasing the risk of investment losses.

Source: Janus Henderson Investors, as at 31 March 2024, unless otherwise noted.

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