Janus Henderson INVESTORS

GLOBAL LIFE SCIENCES FUND

At a glance

Performance*
The Fund returned −1.28%, the Index returned 3.33% and the Sector returned 3.23%.

Contributors/detractors
Stock selection in biotechnology detracted as investors favoured what we consider to be more speculative companies with higher valuations. An overweight position in the sector modestly contributed.

Outlook
Despite recent volatility, we see a positive backdrop with attractive valuations. We believe the sector's levels of innovation will continue to result in positive clinical data and strong product launches.

Portfolio management



Andy Acker, CFA



Daniel Lyons, Ph.D., CFA

Investment environment

- The healthcare sector rose during the period, driven by strong performance in biotechnology and devices and medical technology stocks. Performance in the biotech sector was driven by a narrow, momentum-fuelled rally concentrated in a small group of stocks perceived to benefit from artificial intelligence (AI)-related tailwinds. Life science tools companies were supported by similar themes.
- During the quarter, stability appeared to return to the US Food and Drug Administration (FDA) with the nomination of Dr Heidi Overton to supervise the agency. Additionally, the interim directors of both the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) were appointed as permanent leaders.
- FDA approvals continued steadily throughout the quarter. The most notable was Revolution Medicines' highly anticipated pancreatic cancer treatment, offering patients the chance to avoid toxic chemotherapy while nearly doubling overall survival expectations compared with standard treatment.
- Approvals spanned a broad range of therapeutic areas. Notably, portfolio holding Protagonist Therapeutics received approval for a hepcidin mimetic therapy targeting a rare blood cancer. Other novel treatments approved during the period target ADHD, cholesterol management, narcolepsy, multiple myeloma, wet age-related macular degeneration (AMD) and IgA nephropathy (Berger disease). Beyond pharmaceuticals, approvals included Johnson & Johnson's Ottava surgical robot and Abbott Laboratories' first continuous glucose and ketone monitoring system for people with diabetes.
- Clinical trial activity remained robust during the quarter, highlighted by positive Phase 3 results for Lilly's obesity therapy retatrutide, Moderna and Merck's personalised melanoma vaccine, and several oncology programs that further advanced next-generation targeted and immunotherapy treatments. Additionally, Kodiak Sciences announced results from its Phase 3 trial for a novel regimen for wet AMD that demonstrated efficacy comparable to current therapies, with the potential for only twice-yearly dosing for many patients – a substantial gain over competitors and a major benefit given these injections are administered directly into the eye. Wet AMD affects approximately 1.5 million US citizens and can lead to rapid vision loss in people over age 50.
- Acquisition and partnership activity remained robust as large pharmaceutical companies continued to strengthen their pipelines and expand into new

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*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.

therapeutic areas. Notable transactions spanned autoimmune disease, rare disease, neuroscience, oncology, and precision medicine, including acquisitions by Eli Lilly, Vertex Pharmaceuticals, and argenx SE, underscoring continued demand for differentiated clinical assets.

Portfolio review

Praxis Precision Medicines, a developer of therapies for central nervous system disorders, detracted from relative performance. The stock was emblematic of a broader fall among companies that had generated strong first-half returns on the back of clinical progress, as specialist investors reduced exposure amid a rally in heavily shorted stocks. We remain constructive on the firm's outlook, supported by the potential for clinical data from its epilepsy programme in the fourth quarter and the anticipated 2027 approval of its novel therapy for essential tremor, a condition that affects over seven million people in the US and represents a significant unmet medical need.

Rare-disease specialist Mirum Pharmaceuticals also detracted. While the firm reported net sales above forecasts and raised its full-year product sales outlook, its shares were pressured by news of a delayed FDA timeline for Mirum's treatment for primary sclerosing cholangitis, a chronic liver disease. However, late in the quarter Mirum received regulatory approval for its treatment for an ultra-rare bone disease that turns soft tissues into bone.

Crinetics Pharmaceuticals was a top contributor to relative performance. During the quarter, Vertex Pharmaceuticals announced plans to acquire the company in a transaction valued at approximately $10 billion. The deal highlighted the value of Crinetics' commercial franchise, led by Palsonify, the first once-daily oral treatment for the rare hormonal disorder acromegaly, as well as its late-stage pipeline for rare endocrine disorders.

Medical technology company HeartFlow also contributed. The company specialises in AI-powered, non-invasive cardiac diagnostics, including 3D modelling and coronary plaque analysis. Revenue growth accelerated during the quarter, marking its fastest pace in eight quarters. Growth was driven by strong adoption of the company's plaque assessment products, including its flagship coronary CT angiography offering, which provides a detailed visualisation of arterial plaque. Management also expects continued adoption of its recently launched risk stratification tool, which could further expand the platform's clinical utility and market opportunity.

Manager outlook

Investor enthusiasm for AI-enabled drug discovery has fuelled a narrow rally in select companies, driving their valuations to what we consider very high levels, while many fundamentally strong biotech companies have underperformed. We believe this divergence has been driven more by market sentiment and positioning than intrinsic value.

Despite this backdrop, we believe fundamentals remain favourable across several healthcare subsectors. Managed care companies are seeing improving visibility into reimbursement rates, and the trajectory of medical cost trends supports confidence in longer-term margin recovery. Meanwhile, life science tools appear poised to benefit from stronger biotech financing activity, healthy pharmaceutical research and development (R&D) spending, and gradually improving demand trends.

Capital-raising activity also remains robust. Even in a higher interest rate environment, biotechnology companies remain a critical source of innovation for pharmaceutical companies as they prepare for significant patent expirations over the coming years.

Looking ahead, we remain optimistic about the healthcare sector, which, at the time of writing, was trading at a price-to-earnings (P/E) ratio below its long-term average relative to the S&P 500 Index. We expect a steady cadence of clinical data releases could create opportunities across oncology, cardiovascular and neurological diseases, as well as specialised areas such as myotonic dystrophy and achondroplasia.

While the current environment has created a temporary headwind for the portfolio, we remain confident that disciplined stock selection, valuation awareness, and a focus on differentiated clinical innovation may be rewarded over the long term. Within the portfolio, we favour early commercial-stage companies with breakthrough products, several of which are approaching profitability, alongside late-stage development companies we believe are clinically de-risked. Overall, we believe the backdrop remains constructive and that healthcare valuations may increasingly reflect the sector's underlying innovation over time.

Performance (%)

Returns	Cumulative				Annualised		
	1 Month	3 Month	YTD	1 Year	3 Year	5 Year	10 Year
A2 USD (Net)	-4.22	-1.28	6.09	25.49	12.58	6.55	9.41
Index	-1.79	3.33	5.23	16.38	8.96	5.29	8.86
Sector	-2.05	3.23	3.49	12.21	8.64	1.33	6.18
A2 USD (Gross)	—	—	—	—	—	9.10	12.04
Target	—	—	—	—	—	7.40	11.04

Calendar year	YTD at Q3 2026	2025	2024	2023	2022	2021	2020	2019	2018	2017	2016
A2 USD (Net)	6.09	22.66	1.72	5.44	-4.35	4.72	23.41	27.06	2.01	20.55	-13.79
Index	5.23	14.83	1.13	3.76	-5.41	19.80	13.52	23.24	2.51	19.80	-6.81
Sector	3.49	16.77	-0.97	2.67	-13.91	7.12	20.53	21.80	-3.40	21.68	-9.37

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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	5.66bn
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. 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

Shares 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. High exposure to a particular country or geographical region carries a higher level of risk than a more broadly diversified portfolio. 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. 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. seeks to mitigate exchange rate movements between the share/unit class currency and the base currency of the Fund), the value of your investment may be impacted by changes in exchange rates. Derivatives may be used to help achieve the investment objective. This can result in leverage (higher levels of debt), which can magnify an investment outcome. Gains or losses 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. 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. Securities 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. Losses could be incurred if a counterparty became 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.

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Janus Henderson
INVESTORS

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