Janus Henderson INVESTORS

GLOBAL LIFE SCIENCES EQUITY FUND

At a glance

Performance*
The Fund returned −0.07%, the Index returned 3.33% and the Peer Group returned 4.31%.

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

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

Portfolio management



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Investment environment

- The healthcare sector advanced 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 being Revolution Medicines' highly anticipated pancreatic cancer treatment, which may offer 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 major benefit given these injections are administered directly into the eye. Wet AMD affects approximately 1.5 million Americans 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 therapeutic areas. Notable transactions spanned

Marketing communication
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*For benchmark/usage and peer group, 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.

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 program 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 forecast 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 achieved 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 modeling and coronary plaque analysis. Its 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 fuelled a narrow rally in select companies, driving valuations to levels we considered extreme, while many fundamentally strong biotech companies underperformed. We believe this divergence was 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 have been 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 positioned to benefit from stronger biotech financing activity, healthy pharmaceutical research and development (R&D) spending and gradually improving demand trends.

Capital-raising activity has also remained 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 trades 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 may create meaningful opportunities across oncology, cardiovascular and neurological diseases.

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	Since inception (14/09/23)
I Acc (Net)	-1.67	-0.07	9.37	32.62	11.23	—	—	10.47
Index	0.26	3.33	6.99	18.54	6.46	—	—	5.82
Peer Group	0.62	4.31	10.04	24.48	8.08	—	—	7.13

12 month rolling	Sep 2025-Sep 2026	Sep 2024-Sep 2025	Sep 2023-Sep 2024	Sep 2022-Sep 2023	Sep 2021-Sep 2022
I Acc (Net)	32.62	-8.68	13.63	—	—
Index	18.54	-7.86	10.48	—	—
Peer Group	24.48	-7.37	9.49	—	—

Performance is on a net of fees basis, with gross income reinvested. Source: at 30/09/26. © 2026 Morningstar, Inc. All rights reserved. The information contained herein: (1) is proprietary to Morningstar and/or its content providers; (2) may not be copied or distributed; and (3) is not warranted to be accurate, complete, or timely. Neither Morningstar nor its content providers are responsible for any damages or losses arising from any use of this information. **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. This is a representative share class for the fund, other share classes are available and may be more suitable for your investment needs.

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 (5 years or more). Performance target: To outperform the MSCI World Health Care Index by 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	14 September 2023
Total net assets	70.57m
Asset class	Equities
Domicile	United Kingdom
Structure	OEIC
Base currency	GBP
Index	MSCI World Health Care Index
Peer group	IA Healthcare

For benchmark/usage description, refer to Additional fund information on page 4.

Additional fund information

Tax assumptions and reliefs depend upon an investor's particular circumstances and may be subject to change. Availability of share classes shown may be limited by law in certain jurisdictions. Performance records are detailed on the specific KIID, fees and charges may vary and further information can be found in the fund's prospectus and KIID which must be reviewed before investing. Please consult your local sales representative if you have any further queries. 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. Cash balances and exposures are based on settled and unsettled trades as at the reporting date.
The Fund is actively managed with reference to the MSCI World Health Care Index, as this forms the basis of the Fund's performance target.
The Investment Association (IA) groups funds with similar geographic and/or investment remit into sectors. The fund's ranking within the sector (as calculated by a number of data providers) can be a useful performance comparison against other funds with similar aims.

Investment policy

The Fund invests at least 80% of its assets in a portfolio of shares (also known as equities) of companies that have a "Life Sciences" orientation. The Fund may invest in companies of any size, including smaller capitalization companies, in any country. The Fund may also invest in Collective Investment Schemes, money market instruments, and cash. The Investment Manager may use derivatives (complex financial instruments), with the aim of making investment gains in line with the Fund's objective, to reduce risk or to manage the Fund more efficiently. The Fund is actively managed with reference to the MSCI World Health Care Index, as this forms the basis of the Fund's performance target. The Investment Manager has discretion to choose investments for the Fund with weightings different to the index or not in the index. As an additional means of assessing the performance of the Fund, the IA Healthcare sector average, which is based on a peer group of broadly similar funds, may also provide a useful comparator.

Investment strategy

The Investment Manager seeks to identify innovative companies addressing high unmet medical needs across fields including biotechnology, pharmaceuticals, healthcare services and medical technology. The investment process makes use of 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. 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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Source: Janus Henderson Investors, as at 30 September 2026, unless otherwise noted.

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