Janus Henderson INVESTORS

GLOBAL LIFE SCIENCES FUND

At a glance

Performance*
The Fund returned 6.76%, the Index returned 9.86% and the Sector returned 5.61%.

Contributors/detractors
Stock selection in the biotechnology sector detracted most from performance, as small-cap biotech stocks declined following a strong rally earlier in the year.

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



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Investment environment

- As investors shifted away from more speculative investments during October, this benefited large-cap pharmaceutical and healthcare services stocks, while small-cap biotechnology stocks fell.
- Managed care stocks generally reported stronger-than-expected quarterly results, as investors focused on signs of stabilisation in medical-cost trends and the outlook for reimbursement and Medicaid-related headwinds in 2027. Drugmakers and medtech firms also reported broadly positive earnings results.
- The Department of Health and Human Services released draft guidance to help advance personalised gene therapies for rare genetic diseases. Patient-specific therapy variants that meet established safety and efficacy parameters may be added to an existing biologics license application without requiring new clinical trials, potentially accelerating development timelines for companies developing personalised gene-editing and rare-disease therapies.
- Drug approvals in October included new treatments across oncology, infectious disease, ophthalmology, and central nervous system disorders. Highlights included the approval of talazoparib plus enzalutamide for patients with mutation-positive metastatic prostate cancers, and bepirovirsen, the first approved antisense to demonstrate functional cure rates above those achieved with the current standard of care for chronic hepatitis B. Additional approvals included treatments for eye redness, herpes virus infections in immunocompromised patients, and a once-monthly injectable treatment for schizophrenia.
- Biopharma dealmaking remained active in October, with Alcon agreeing to acquire Neurotech Pharmaceuticals, adding its cell therapy platform and the only US Food and Drug Administration (FDA)-approved treatment for MacTel (Macular Telangiectasia Type 2), a rare, progressive retinal disease. Viatris announced a $1.65 billion acquisition of Pacira BioSciences to strengthen its non-opioid pain portfolio, while Japan-based Shionogi announced a $2 billion all-cash acquisition of IntraBio centred on the commercialisation of its treatment for rare neurodegenerative disorders.
- Initial public offering (IPO) activity picked up in October, highlighting renewed investor interest in innovative biotech platforms. This included Lycia Therapeutics, which develops protein-degrading therapies, and City Therapeutics, which also went public to support development of its RNAi therapy targeting Factor XI for thrombosis prevention. Other notable offerings included Iambic Therapeutics, which

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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.

is focused on accelerating its AI-driven oncology pipeline; TREX Bio, which is leveraging its platform to discover therapies that modulate regulatory T cells involved in inflammation; and Retension Pharmaceuticals, which is developing treatments for uncontrolled hypertension.

Portfolio review

Biotechnology holdings were the primary detractors from performance in October, as investors took profits. Shares of Travere Pharmaceuticals fell even as the company presented new biomarker data at ASN Kidney Week suggesting that the firm's treatment Filspari may modify the underlying disease biology of IgA Nephropathy, in addition to its established effects on reducing blood pressure and proteinuria.

Shares of Madrigal Pharmaceuticals also fell, despite no company-specific developments. The company markets Rezdiffra, the first FDA-approved treatment for metabolic dysfunction-associated steatohepatitis (MASH), a serious liver disease with high unmet medical need.

Conversely, the position in Glaukos Corp contributed to performance, as the ophthalmic company reported better-than-expected third-quarter results and raised its 2026 net sales guidance (forecasts). The company also announced that patients treated with its Epioxa eye disease therapy maintained improvements in vision and corneal shape three years after a single treatment for keratoconus, a disease that can progressively distort vision.

The underweight position in Merck & Co also benefited relative performance. Its share price fell following the release of phase 3 data for the company's personalised melanoma vaccine being developed with Moderna. While the study showed a meaningful reduction in the risk of recurrence or death when added to Keytruda, the results fell short of investors' elevated expectations, prompting profit-taking despite the trial's positive outcome.

Manager outlook

Performance across healthcare stocks remained bifurcated in October. Investors favoured large-cap pharmaceutical and healthcare services companies, while many fundamentally strong biotechnology stocks lagged.

Looking ahead, we believe fundamentals remain favourable across several healthcare subsectors. Healthcare services companies have been benefiting from improving visibility into medical cost trends and reimbursement dynamics, supporting expectations for earnings growth and margin stability. Meanwhile, biotechnology financing activity remained robust, supporting innovation and development across the sector, and life science tools companies appear positioned to benefit from continued pharmaceutical research and development (R&D) investment and gradually improving demand trends.

Looking ahead, we remain optimistic about the sector, which was trading at a price-to-earnings (P/E) ratio below its long-term average relative to the S&P 500 Index at the time of writing. We believe strong launches could support multiple companies in progressing towards profitability, and 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 could be rewarded over the long term. In the portfolio, we favour early commercial-stage companies with breakthrough products alongside late-stage development companies we believe are clinically de-risked. Overall, we believe the backdrop remains constructive and that healthcare valuations could 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)	6.76	5.98	13.26	23.37	17.62	7.03	11.28
Index	9.86	11.90	15.61	24.01	14.02	6.41	10.68
Sector	5.61	8.01	9.30	14.53	12.69	2.04	7.56
A2 USD (Gross)	—	—	—	—	—	9.59	13.95
Target	—	—	—	—	—	8.54	12.89

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	6.10bn
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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