Janus Henderson INVESTORS

GLOBAL LIFE SCIENCES FUND

At a glance

Performance*
The Fund returned 22.66%, the Index returned 14.83% and the Sector returned 16.75%.

Contributors/detractors
Security selection and an overweight position to biotechnology were the leading positive contributors to fund performance, followed by stock selection in pharmaceuticals.

Outlook
Looking at 2026, we remain optimistic about the sector, which has still been trading at a price-to-earnings ratio below the long-term average versus the S&P 500 Index.

Portfolio management



Andy Acker, CFA



Daniel Lyons, Ph.D., CFA

Investment environment

- Healthcare stocks rose during the year but underperformed the broader markets.
- The year began with the threat of tariffs and policy uncertainty, driven by the election of Donald Trump and his nomination of Robert F Kennedy Jr to head the Department of Health and Human Services. Kennedy's nomination was followed by other controversial appointments to federal health agencies, along with funding cutbacks and staff reductions.
- Proposals for drug pricing reform and pharmaceutical tariffs further weighed on biotechnology and pharmaceutical stocks, while planned cuts for Medicaid, the government-provided insurance program in the US, were a headwind for health insurers.
- However, the sector rallied towards the end of the year, with pharmaceuticals leading performance, closely followed by biotechnology. Optimism was lifted by the early October deal between Pfizer and the US administration to focus discounts in limited channels like Medicaid for a few legacy drugs, and to avoid tariffs through commitments to invest in US manufacturing. This was followed by arrangements with several other key drug companies that were also well received.
- Following three successive interest-rate cuts by the US Federal Reserve (Fed) and upcoming patent cliffs faced by large pharmaceutical firms, deal activity was robust and included several multi-billion-dollar acquisitions. Drug approvals also continued at a high pace, including the first non-opioid painkiller in more than 20 years, the first treatment for Prader-Willi syndrome (a devastating condition in which children suffer from insatiable hunger), and the first alternative to GLP-1 injections, a once-daily oral version of semaglutide to manage obesity.

Portfolio review

Leading positive contributors included Praxis Precision Medicine, a developer of targeted therapies for central nervous system disorders. Following highly successful phase 3 results for its experimental drug, ulixacaltamide, for patients with essential tremor, Praxis received Breakthrough Therapy Designation and plans to submit a New Drug Application for the treatment in early 2026. Essential tremors are the most common type of tremor, impacting an estimated seven million US patients, and there are no approved therapies.

BridgeBio also contributed positively. The firm’s newly launched drug, Attruby, has seen strong sales growth, delivering revenues of $37 million in its first quarter on the market - roughly triple consensus expectations. The drug treats ATTR cardiomyopathy, a progressive disease where

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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.

misfolded TTR proteins accumulate in the heart, leading to heart failure. Attruby is one of only two oral options on the market and has a differentiated profile, contributing to its rapid uptake.

Sarepta Therapeutics was the largest detractor. During the period, the firm announced weak first-quarter results and reduced its 2025 product revenue guidance (forecasts). This followed the unfortunate death of a patient on Elevidys, its gene therapy for Duchenne muscular dystrophy. Shares of Sarepta and other gene and cell therapy developers also came under pressure following the appointment of Vinay Prasad as director of the US Food and Drug Administration (FDA) which regulates them. Prasad is a well-known critic of his predecessor's speedy approval of Elevidys. Given the headwinds, we exited the position.

Vaxcyte was another detractor. The company is developing novel 24- and 31-valent vaccines designed to prevent more strains of invasive pneumococcal disease than current offerings. In late March, Vaxcyte reported positive phase 2 results for VAX-24, but the shares sold off due to policy uncertainty created by the appointment of Robert F Kennedy Jr (a vaccine sceptic) to head the Department of Health and Human Services. It remains to be seen how Mr. Kennedy might impact vaccine access in the US, but public and political backlash could be severe if policies go too far. Meanwhile, clinical data suggests Vaxcyte's pipeline could be best in class for the emerging $10 billion pneumococcal vaccine market.

Manager outlook

The uncertainty surrounding drug cost changes, tariffs, and evolving leadership across key federal agencies that pulled healthcare stocks lower in the first half of 2025 have largely been alleviated. This has been replaced by merger and acquisition (M&A) excitement, clinical progress and innovations, as well as further drug pricing transparency.

Deal activity, which included several multibillion US dollar transactions involving fund holdings, is expected to continue into the new year, as cash-rich pharmaceutical companies seek to strengthen their pipelines by acquiring emerging biotech firms. Pharmaceutical companies continue to need innovation from the biotech sector to help offset looming patent cliffs.

Potential headwinds include uncertainty related to leadership changes within key healthcare agencies, a situation we are closely monitoring. On a positive note, sales of several new drug launches last year exceeded expectations, highlighting the continued support of the US healthcare system for novel therapies. Furthermore, the Commissioner's National Priority Voucher Program could significantly accelerate the review and approval of drugs that address high unmet medical needs.

Looking ahead to 2026, we remain optimistic about the sector, which at the time of writing was still trading at a price-to-earnings (P/E) ratio that is below the long-term average relative to the S&P 500 Index. The rapid pace of data releases is expected to continue, with the potential for large new opportunities across oncology, cardiovascular, and neurological diseases, as well as in specialised areas such as myotonic dystrophy and achondroplasia.

Within the portfolio, we continue to favour early commercial-stage companies with breakthrough products and late-stage development companies that we believe are clinically de-risked. We also favour medical device companies with exposure to markets still in the early stages of growth. Areas such as electrophysiology, left atrial appendage closure, and continuous glucose monitoring address large, chronic conditions through minimally invasive, technology-driven solutions. We also see opportunities within managed care, as these companies trade at a discount to both historical averages and the market, despite expected rate increases. Greater policy and regulatory clarity could help the sector trade more on its impressive innovation, which is at the core of our investment process.

Performance (%)

Returns	Cumulative				Annualised		
	1 Month	3 Month	YTD	1 Year	3 Year	5 Year	10 Year
A2 USD (Net)	-0.28	18.29	22.66	22.66	9.57	5.68	8.16
Index	-0.79	10.60	14.83	14.83	6.41	6.43	8.13
Sector	-1.45	8.41	16.75	16.75	5.88	1.82	5.52
A2 USD (Gross)	—	—	—	—	—	8.19	10.75
Target	—	—	—	—	—	8.56	10.30

Calendar year	2025	2024	2023	2022	2021	2020	2019	2018	2017	2016
A2 USD (Net)	22.66	1.72	5.44	-4.35	4.72	23.41	27.06	2.01	20.55	-13.79
Index	14.83	1.13	3.76	-5.41	19.80	13.52	23.24	2.51	19.80	-6.81
Sector	16.75	-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	4.61bn
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/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. 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 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. 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.

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Janus Henderson
INVESTORS

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