Janus Henderson INVESTORS

HORIZON BIOTECHNOLOGY FUND

At a glance

Performance*
The Fund returned 49.37%, the Index returned 33.43% and the Sector returned 33.70%.

Contributors/detractors
Leading positive contributors included Praxis Precision Medicine and Verona Pharma, while positions in Janux Therapeutics and Biohaven detracted.

Outlook
We believe the outlook for the biotech sector is as attractive as ever and continue to favour small- and mid-cap biotech firms with newly launched products or exciting late-stage pipelines.

Portfolio management



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Agustin Mohedas, Ph.D.

Investment environment

- After a lacklustre beginning to 2025, weighed down by policy uncertainty under the Trump administration, proposed drug pricing reforms and tariffs, and elevated long-term US Treasury yields, biotechnology stocks rallied in the second half of 2025. They were driven by elevated deal activity, promising trial results, and improved investor sentiment.
- Three interest-rate cuts by the US Federal Reserve (Fed) supported merger and acquisition (M&A) activity, including several multibillion deals involving fund holdings.
- Positive data read-outs from clinical trials, robust fundraising, and major approvals also helped generate increased investor interest for the sector.

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. Praxis 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.

Respiratory disease specialist Verona Pharma also contributed positively. In the first quarter, Ohtuvayre, an inhaled non-steroidal treatment for chronic obstructive pulmonary disease (COPD), saw 95% sequential sales growth, which was well above expectations. In July, Merck announced it would acquire Verona for $10 billion, leading us to sell our position and use the profits for other ideas.

Janux Therapeutics, a firm focused on developing cancer therapies that harness the immune system with its tumor-activated T cell engagers (TRACTr) platform for solid tumours, detracted. Even though the firm's prostate cancer treatment, JANX007, showed efficacy in managing prostate cancer, the market was disappointed by the limited data and the long timelines to market. We believe markets overreacted and remain optimistic that JANX007 could play an important role in prostate cancer treatment.

Other detractors included Biohaven. During the year, Biohaven reported positive phase 1 data for BHV-1300, an experimental protein degrader to treat immune-related disorders that fell short of expectations. We think investors set their sights too high for this dose-ranging study and are encouraged by BHV-1300's clean safety profile. Biohaven also announced receipt of a Complete Response Letter from the US Food and Drug Administration (FDA), declining approval of its drug candidate Vyglxia for

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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.

spinocerebellar ataxia, an inherited progressive and degenerative disease that mainly affects the cerebellum. While the news prompted Biohaven to restructure operations and research and development (R&D) priorities, the firm remains committed to working with the FDA on Vyglxia. We have confidence in the firm's many pipeline assets, particularly its proprietary degrader technology, which is designed to treat various autoimmune and other diseases.

Manager outlook

Following a prolonged period of underperformance, biotechnology stocks made a dramatic turnaround at the end of 2025, driven by a clarified policy backdrop that allowed the continued cadence of innovation and strong commercial launches to be recognised by the markets. This was further aided by a more positive interest-rate environment and a surge of deal announcements.

The three Fed rate cuts helped fuel a surge in biotech M&A activity, making 2025 the third most active year on record. The sector saw a wave of multibillion US dollar transactions (including multiple fund holdings), and this trend is expected to continue into 2026, as cash-rich pharmaceuticals seek to offset patent expiries and rebuild their pipelines by acquiring emerging biotech firms. And while initial public offering (IPO) activity lagged prior years, it is expected to ramp up in 2026.

For the year, major innovations included approvals for a novel non-opioid pain drug, and therapies to help manage cardiomyopathy, cancer, and autoimmune diseases.

As such, we believe the outlook for the biotech sector is as attractive as ever and continue to favour small- and mid-cap biotech firms with newly launched products or exciting late-stage pipelines. These companies develop most new drugs and many continue to trade at deep discounts in our view. Indeed, 2026 looks full of data read-outs, including large opportunities across cancer and cardiovascular disease and promising new therapies for autoimmunity.

Performance (%)

Returns	Cumulative				Annualised			
	1 Month	3 Month	YTD	1 Year	3 Year	5 Year	10 Year	Since inception (10/12/18)
A2 USD (Net)	0.28	29.88	49.37	49.37	24.99	12.25	—	19.81
Index	-1.86	17.11	33.43	33.43	11.54	4.52	—	9.01
Sector	-2.26	13.83	33.70	33.70	10.47	0.61	—	6.23
A2 USD (Gross)	—	—	—	—	—	15.62	—	23.60
Target	—	—	—	—	—	6.61	—	11.19

Calendar year	2025	2024	2023	2022	2021	2020	2019	2018 from 10 Dec
A2 USD (Net)	49.37	6.06	23.28	-3.78	-5.17	61.32	34.70	-7.50
Index	33.43	-0.57	4.59	-10.12	0.02	26.42	25.11	-6.85
Sector	33.70	-4.20	5.25	-17.17	-7.68	27.50	25.36	-7.02

Performance is on a net of fees basis, with gross income reinvested. Source: at 31/12/25. © 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.

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.

Performance fees may be charged before the Fund's outperformance target is reached.

Performance fees are charged separately as a way of rewarding the investment manager for superior returns or for outperforming specified targets. A Performance Fee is accrued where the NAV outperforms the relevant Hurdle NAV (subject to a High Water Mark). For further explanation of the performance fee calculation methodology please see the relevant prospectus, available at www.janushenderson.com.

Investment objective

The Fund aims to provide capital growth over the long term. Performance target: To outperform the NASDAQ Biotechnology Total Return 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	10 December 2018
Total net assets	1.37bn
Asset class	Equities
Domicile	Luxembourg
Structure	SICAV
Base currency	USD
Index	NASDAQ Biotechnology Total Return Index
Morningstar sector	Sector Equity Biotechnology
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 a Luxembourg SICAV Fund, regulated by the Commission de Surveillance du Secteur Financier (CSSF). 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% of its assets in shares (equities) and equity-related securities of companies, which are biotechnology or biotechnology-related, of any size, including smaller capitalisation companies, in any country. The Fund may also invest in other assets including bonds (including convertible bonds), preference shares, cash and money market instruments. 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 NASDAQ Biotechnology Total Return Index, which is broadly representative of the companies in which it may invest, as this forms the basis of the Fund's performance target and the level above which performance fees may be charged (if applicable). The Investment Manager has discretion to choose 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 Investment Manager looks to identify innovative biotechnology companies addressing high unmet medical needs and trading at a significant discount to their intrinsic value. The portfolio may have a bias towards development stage companies. 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, prescription models and scenario simulations 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 may incur a higher level of transaction costs as a result of investing in less actively traded or less developed markets compared to a fund that invests in more active/developed markets. 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

Source: Janus Henderson Investors, as at 31 December 2025, unless otherwise noted.

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