Janus Henderson INVESTORS

HORIZON BIOTECHNOLOGY FUND

At a glance

Performance*
The Fund returned 0.51%, the Index returned 2.88% and the Sector returned −0.35%.

Contributors/detractors
Travere Therapeutics and Bicara Therapeutics were among the main detractors for the month, while BridgeBio Pharma and AstraZeneca were among the contributors.

Outlook
We believe the outlook for the biotech sector remains attractive, and we continue to favour small- and mid-cap biotech stocks with newly launched products or promising late-stage pipelines.

Portfolio management


Andy Acker, CFA


Daniel Lyons, Ph.D., CFA


Agustin Mohedas, Ph.D.

Investment environment

- An investor shift away from what we viewed as more speculative investments during October pushed small-cap biotechnology stocks lower, while larger-cap biotechs rose.
- The US Department of Health and Human Services released draft guidance to help advance personalised gene therapies for rare genetic diseases.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, which could potentially accelerate timelines for companies developing personalised gene-editing and rare-disease therapies.
- Drug approvals in October were highlighted by the approval of bepirovirsen, the first antisense therapy to demonstrate functional cure rates above those achieved with the current standard of care for chronic hepatitis B. Additionally, the first once-monthly subcutaneous injectable version of olanzapine for schizophrenia was approved, with the potential for improved compliance.
- 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 the development of its RNAi therapy targeting Factor XI for thrombosis prevention. Other notable offerings included Iambic Therapeutics, 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

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

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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.

modify the underlying disease biology of IgA Nephropathy (IgAN) beyond its established effects on reducing blood pressure and proteinuria. While investors are closely tracking the launch of Filspari in its second indication, focal segmental glomerulosclerosis (FSGS), debate continues around the durability of Filspari's market share in IgAN as new therapies advance into the market. However, we believe the therapy is likely to remain a core component of the standard of care in IgAN and we see potential for significant growth ahead in FSGS. As a result, we viewed the recent share price weakness as a long-term opportunity.

Bicara Therapeutics, a company developing a treatment to improve tumour penetration in head and neck cancer, detracted. Its share price fell after a competing therapy reported positive phase 3 results, including improved overall survival in the same indication. We remain constructive on Bicara's prospects to offer benefits in this condition as the company releases pivotal data in the coming year.

BridgeBio Pharma was among the top contributors after reporting third-quarter revenue of $353 million, driven by US Attruby sales that exceeded consensus expectations. Attruby, which treats transthyretin amyloid cardiomyopathy (ATTR-CM), is expected by management to reach approximately $4 billion in peak annual sales. We also believe the market may be anticipating three new pipeline launches for Bridge over the coming year.

AstraZeneca also contributed, helped by a strong third-quarter earnings report alongside positive clinical data in oncology. Robust growth in the firm's core franchises, particularly from lung cancer therapy Tagrisso and immunotherapy, drove accelerated revenue growth. During the month, late-stage trial data for sonesitatug vedotin in advanced gastric cancer showed a 53% reduction in the risk of death among third-line and later patients, highlighting the strength of AstraZeneca's pipeline.

Manager outlook

Market performance in biotechnology diverged again in October, with many fundamentally strong biotechnology stocks lagging. However, underlying industry fundamentals remained constructive, in our view. Capital-raising activity was active, reflecting continued investor appetite for differentiated innovation despite higher interest rates and broader market volatility. Strategic partnership and licensing activity also continued as large pharmaceutical companies seek external innovation to strengthen pipelines ahead of significant patent expirations.

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 will be rewarded over the long term. As always, our investment process emphasises finding the next wave of medical breakthroughs with the potential to change the practice of medicine.

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)	0.51	-2.98	10.75	22.36	31.23	14.26	—	19.08
Index	2.88	13.56	28.81	37.17	26.52	8.81	—	11.54
Sector	-0.35	4.75	15.13	20.88	21.59	3.84	—	7.46
A2 USD (Gross)	—	—	—	—	—	17.99	—	23.19
Target	—	—	—	—	—	10.99	—	13.77

Calendar year	YTD at Q3 2026	2025	2024	2023	2022	2021	2020	2019	2018 from 10 Dec
A2 USD (Net)	10.19	49.37	6.06	23.28	-3.78	-5.17	61.32	34.70	-7.50
Index	25.20	33.43	-0.57	4.59	-10.12	0.02	26.42	25.11	-6.85
Sector	15.54	33.69	-4.20	5.25	-17.17	-7.68	27.50	25.36	-7.02

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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.

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	2.20bn
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 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. 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. 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. The sustainability approach applied may exclude potential investments which do not meet certain criteria (e.g. non-financial criteria such as ESG screens). This may cause differences in performance compared to similar products that are permitted to invest in those investments.

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INVESTORS

Source: Janus Henderson Investors, as at 31 October 2026, unless otherwise noted.

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