Janus Henderson INVESTORS

HORIZON BIOTECHNOLOGY FUND

At a glance

Performance*
The Fund returned −7.72%, the Index returned −0.10% and the Sector returned −2.34%.

Contributors/detractors
Dyne Therapeutics and Praxis Precision Medicines were the main detractors for the month, while Kodiak Sciences and an underweight position in Amgen contributed.

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

Portfolio management

Andy Acker, CFA

Daniel Lyons, Ph.D., CFA

Agustin Mohedas, Ph.D.

Investment environment

- Biotechnology stocks paused in September, as a broader market sell-off and renewed “higher-for-longer” interest rate expectations weighed on investor sentiment. Performance within the biotechnology space diverged markedly as investors gravitated toward artificial intelligence (AI)-related names, pressuring many of the sector's most widely owned stocks while driving gains in heavily shorted companies.
- Following a period of uncertainty, regulatory visibility improved as permanent leaders were appointed to CDER and CBER, while US Food and Drug Administration (FDA) Commissioner nominee Dr. Heidi Overton continued to progress through the confirmation process.
- In an encouraging step for drug developers, the FDA launched an initiative intended to streamline and accelerate early clinical trials for new medicines. The program reflects a broader policy effort to keep more research activity in the US, which could help reduce development timelines and improve patient access to innovative therapies.
- Regulatory activity included several notable FDA approvals for fund holdings, including Mirum Pharmaceuticals' Atebrioz for fibrodysplasia ossificans progressiva (FOP), an ultra-rare disorder in which soft tissue progressively transforms into bone. Also approved was Scholar Rock's Isembyld for spinal muscular atrophy, marking the first muscle-targeted therapy approved for the disease.
- While September activity slowed, 2026 remains expected to be a record year for biotech initial public offerings (IPOs), reflecting continued investor interest in innovative healthcare companies and improving capital markets conditions. ADARx Pharmaceuticals became the first RNA interference (RNAi) biotech to complete a US IPO in more than a decade, and inflammation-focused Electra Therapeutics also completed its public debut.

Portfolio review

Dyne Therapeutics detracted from performance during the month following disappointing Phase 3 results from a competing myotonic dystrophy type 1 (DM1) therapy, weighing on sentiment for Dyne. DM1 is the most common form of muscular dystrophy with adult onset. While the news was not company-specific, the outcome prompted investors to reassess the broader DM1 treatment landscape. We remain optimistic about Dyne’s clinical

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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.

pipeline and market prospects, including its potential in Duchenne muscular dystrophy.

Praxis Precision Medicines, a developer of therapies for central nervous system disorders, also detracted. The stock was emblematic of a broader pullback 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 high unmet medical need.

Contributors included Kodiak Sciences. The firm announced results from its phase 3 trial for a six-month dosing regimen for wet age-related macular degeneration (AMD), that demonstrated efficacy comparable to current therapies with substantially less frequent treatment. Wet AMD affects approximately 1.5 million Americans and leads to rapid vision loss in people over age 50.

An underweight allocation to Amgen also contributed to performance. Its shares declined during September after a competitor's cholesterol treatment trial failed to demonstrate a meaningful reduction in major cardiovascular events despite significantly lowering levels of the genetically inherited risk factor Lp(a). The disappointing results weighed on sentiment for Amgen, which also has an Lp(a)-lowering agent in pivotal trials.

Manager outlook

Investor enthusiasm for AI-enabled drug discovery fuelled a narrow rally in select biotechnology companies, driving valuations to extreme levels in our view, while many fundamentally strong companies underperformed. We believe this divergence was driven more by market sentiment and positioning than intrinsic value.

While biotechnology stocks broadly declined during the month, underlying industry fundamentals remained constructive. 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)	-7.72	-6.29	10.19	43.11	25.53	14.33	—	19.23
Index	-0.10	8.50	25.20	46.62	22.52	7.78	—	11.27
Sector	-2.34	2.87	15.62	31.60	18.56	3.70	—	7.60
A2 USD (Gross)	—	—	—	—	—	17.90	—	23.23
Target	—	—	—	—	—	9.94	—	13.49

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	15.62	33.69	-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 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.

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	2.08bn
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). Ongoing charge represents the ongoing costs to the fund, which includes the AMC and other charges for services such as keeping a register of investors, calculating the price of the fund's units or shares and keeping the fund's assets safe. 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.

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Source: Janus Henderson Investors, as at 30 September 2026, unless otherwise noted.

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