COMMENTARY

Janus Henderson Horizon Biotechnology Fund

August 2023

Marketing communication - For professional investors only
Past performance does not predict future returns

Fund Managers Names

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Investment environment

Biotechnology stocks declined over the month, though outperformed the broader health care sector. An up-and-down pattern for biotech continued, as higher interest rates create headwinds for speculative early-stage companies, while more established firms with platforms de-risked by compelling clinical data seem to have little trouble attracting investor interest or attention from pharmaceutical companies as potential acquisition targets. In keeping with the pattern, smaller biotech stocks again trailed larger caps for the month.

Portfolio review

The fund outperformed its benchmark, the Nasdaq Biotechnology Total Return Index.

Looking at individual stocks, Benitec Biopharma was our top positive contributor, as we participated in a public offering of the company's stock at a highly attractive price. Two weeks before the offering, the company received its first US Food and Drug Administration (FDA) nod to proceed with clinical trials of its proprietary “Silence and Replace” platform for the treatment of oculo-pharyngeal muscular dystrophy (OPMD), a rare adult-onset disorder that causes weakness in the upper eyelids and throat. The platform combines RNA interference (RNAi) with gene therapy to simultaneously facilitate the silencing of disease-causing genes and their replacement with healthy ones through the same adenovirus vector. At present, the expected lifespan of patients with OPMD is close to normal if managed well. However, the only treatment is palliative, such as surgery to correct droopy eyelids, or careful management of food intake to prevent choking and malnutrition. By contrast, Benitec's approach aims to correct the underlying condition (and potentially other genetic disorders as well) at its very source.

Also contributing to relative performance was Sarepta Therapeutics, whose Elevidys was recently approved as the first gene therapy for the treatment of Duchenne muscular dystrophy (DMD). Earlier this summer, investors were disappointed when the FDA issued the drug a less-than-ringing endorsement. Although the agency granted accelerated approval, it limited usage to four- and five-year-olds pending results of a confirmatory trial due for completion this fall. We have remained optimistic about what we see as a potentially game-changing approach to the devastating muscle-wasting disease. We are also encouraged by another late-stage DMD drug from Sarepta using an exon-skipping approach, which could prove complementary to the one-and-done gene therapy. With the date for the confirmatory data approaching, more investors have joined us in focusing on the firm's upside.

Other stocks detracted from relative performance, including the underweight position to Regeneron. The firm's blockbuster eye drug Eylea is approaching loss of exclusivity. Regeneron had sought to protect the franchise on two fronts: by seeking FDA approval of a new higher-dose version of Eylea and by suing rival Mylan for patent infringement. In August, both strategies appeared to gain traction. For one, the FDA approved the high-dose version of Eylea, despite some concerns a manufacturing issue could lead to a delay. Second, in the Mylan court case, testimony seemed to bode well for Regeneron's bid to shore up patent protection of regular-strength Eylea, potentially as far out as 2031. (A ruling is expected in September.) Meanwhile, sales of another Regeneron powerhouse, the eczema and asthma drug Dupixent, surged 33% to $2.8 billion in the second quarter, taking some of the immediate pressure off the Eylea outlook.

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New Horizon Health also detracted from returns. The China-based producer of early detection cancer-testing kits became the subject of a short seller's report alleging inflated shipment data. The company responded quickly, insisting the report seriously distorted the facts. It also held a conference call to review a detailed accounting of the company's financials, which helped pare the share price slide. Part of the issue may be the company's unorthodox methods for recognising revenue. Its ColoClear testing kit has rung up explosive sales growth due to its high sensitivity to advanced adenoma colorectal cancer. But the company only books revenue for the product - which is primarily sold through Chinese hospitals and testing clinics - after customers complete and send in their sample and the lab logs the test report. This has led to discrepancies between shipment and revenue recognition volumes. For its part, the company has made a persuasive case that the pattern is more a feature than bug, and at any rate leaves the firm with ample cash for future development, including for a promising cervical cancer testing kit now in clinical trials.

Source: Janus Henderson Investors, as at 31 August 2023

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Fund information (Investment policy is on the next page)

Index	NASDAQ Biotechnology Total Return Index
Morningstar sector	Europe OE Equity Biotechnology
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.

Performance in (USD)

Performance %	A2 (Net)	Index	Sector	A2 (Gross)	Target (Gross)
1 month	0.1	-0.2	-2.9	-	-
YTD	12.4	-1.8	-2.1	-	-
1 year	37.1	7.4	1.4	-	-
3 years (annualised)	10.3	-0.4	-5.8	-	-
5 years (annualised)	-	-	-	-	-
Since inception 10 Dec 2018 (annualised)	16.6	5.7	2.3	-	-

Source: at 31 Aug 2023. © 2023 Morningstar. All rights reserved, performance is with gross income reinvested. Performance/performance target related data will display only where relevant to the share class inception date and annualised target time period.

Calendar year returns %	A2 (Net)	Index	Sector
2023 to 30 Jun 2023	10.6	-2.8	-1.0
2022	-3.8	-10.1	-17.2
2021	-5.2	0.0	-7.7
2020	61.3	26.4	27.5
2019	34.7	25.1	25.4
2018 from 10 Dec 2018	-7.5	-6.9	-7.0
2017	-	-	-
2016	-	-	-
2015	-	-	-
2014	-	-	-
2013	-	-	-

Source: at 30 Jun 2023. © 2023 Morningstar. All rights reserved, performance is with gross income reinvested. Discrete performance data may change due to final dividend information being received after quarter end.

Investment into the fund will acquire units/shares of the fund itself and not the underlying assets owned by the fund.

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.

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 http://www.janushenderson.com.

Source for target returns (where applicable) – Janus Henderson. Please note the performance target is to be achieved over a specific annualised time period. Refer to the performance target wording within the objective. With effect from 1 January 2023, the Key Investor Information document (KIID) changed to the Key Information Document (KID), except in the UK where investors should continue to refer to the KIID. 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 if you have any further queries.

From 31 January 2023 Agustin Mohedas also manages this fund.

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Past performance does not predict future returns. 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.

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 http://www.janushenderson.com.

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What are the risks specific to this fund?

- 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.
- 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.
- 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.
- 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. These transaction costs are in addition to the Fund's Ongoing Charges.

General risks

- Past performance does not predict future returns.
- 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.
- Tax assumptions and reliefs depend upon an investor's particular circumstances and may be subject to change.

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.

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For further information on the Luxembourg-domiciled Janus Henderson fund range please contact your local sales office or visit our website: www.janushenderson.com.

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