COMMENTARY

Janus Henderson Global Life Sciences Fund

August 2023

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

Fund Manager Name

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Investment environment

Health care stocks finished the month in negative territory but outperformed the broader equity market as 'Big Tech' gave up some gains in the face of higher Treasury yields. Pharmaceuticals performed the best, fuelled by upbeat data from a clinical trial about the cardiovascular benefits of Wegovy, a new class of weight-loss drug known as a GLP-1 receptor agonist (originally developed to treat diabetes). The results raised pressure on health systems and employers in the US to reimburse for Wegovy and other GLP-1s under development. Conversely, health care equipment stocks declined as investors considered how the new weight-loss medicines might limit demand for some diabetes devices and obesity-related products.

Portfolio review

For August, the fund (class A2 US dollar shares) returned -1.5%, underperforming the MSCI World Health Care Index℠ benchmark which returned -0.8%. Positioning in pharmaceuticals weighed on relative returns while stock selection in and an underweight position to health care equipment firms contributed positively to performance.

Despite having significant positions, our underweights to Eli Lilly and Novo Nordisk were the biggest individual detractors. Novo Nordisk's SELECT trial was a market mover for both stocks because of how it changes the paradigm for how physicians and insurers view the companies' new weight-loss medications. The study showed that Novo Nordisk's Wegovy reduced the incidence of heart attack and stroke in obesity patients by 20% - three to five percentage points more than analysts had predicted. The company's stock, which had been losing some momentum to Eli Lilly's (whose Mounjaro has been shown to produce even greater weight loss) immediately surged.

Eli Lilly's stock also saw a bounce. The halo effect from its rival's study added to better-than-expected sales for Mounjaro. The diabetes medication is not even approved yet by the Food and Drug Administration (FDA) for weight loss (expected later this year) but has already seen a boost in revenue from off-label usage. In addition, Eli Lilly benefited from enthusiasm over its growing pipeline of next-generation weight-loss drugs (including a promising triple hormone version) and Alzheimer's candidate, donanemab, which was recently submitted for FDA approval. We added to our positions in both Novo and Eli Lilly but lagged the stocks' growing weights in the benchmark.

Sarepta Therapeutics also contributed positively to performance. Earlier this year, investors were disappointed when the FDA issued a less-than-ringing endorsement of Elevidys, the company's gene therapy treatment for Duchenne muscular dystrophy. Although the FDA granted accelerated approval, it limited usage to four and five year-olds pending results of a confirmatory trial. We have remained optimistic about what we see as a potentially game-changing approach to the devastating muscle-wasting disease. With the confirmatory data approaching, investors seem to be refocusing on the firm's potential.

Akero Therapeutics was another positive contributor. The biotech firm is developing efruxifermin (EFX) for non-alcoholic steatohepatitis (NASH), a fatty liver disease that affects over 10 million adults in the US and is a leading cause of liver failure. Late last year, investors grew optimistic about data from a phase 2 study showing that EFX significantly improved liver fibrosis (tissue scarring) and NASH resolution in patients. Akero's shares have been up and down since as EFX vies for position in what has proven to be a crowded and challenging. But in June, the company released even more encouraging data from a mid-phase study evaluating EFX in combination with GLP-1 therapies like Novo Nordisk's Ozempic (the diabetes-focused version of Wegovy). While Akero's NASH treatment is unlikely to be first to market, it is shaping up as potentially the most effective therapy in development.

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Manager outlook

Optimism around artificial intelligence (AI) and a slower pace of interest rate hikes have led some tech-heavy equity indices to outperform so far this year. Health care has lagged by comparison. But we believe the risk of recession will continue into 2024, as higher rates and tighter lending standards work through the economy. Against this backdrop, we think health care's defensive characteristics could help lift the sector relative to peers, especially as many health care stocks now trade significantly below the market average.

Meanwhile, innovation continues to be robust. More than 80 new drugs are up for review by the FDA this year, with dozens already receiving approval. Many therapies target large disease categories with high, unmet medical needs, including Leqembi, the first drug to show clear evidence of slowing cognitive decline in Alzheimer's patients. These and other newly approved drugs could represent the start of major product cycles, driving revenue growth for a decade or more.

With our excitement about industry innovation and our concerns for a slowing economy, we continue to take a barbell approach, seeking to balance the sector's defensive qualities with potential new growth opportunities. To that end, we favour large-cap biopharma and managed care firms, which can generate strong free cash flow and we believe can hold up well in a recession. We also maintain an overweight position to small- and mid-cap biotechs with newly launching products or exciting late-stage development opportunities, which we believe offer growth potential with reduced clinical risk.

As we have seen recently, some of these biotechs have been acquisition targets. In fact, 13 deals of $1 billion or more have been announced so far this year, putting 2023 on track for the highest number of any year in the past decade. In our view, these acquisitions will likely continue given looming patent expirations for large-cap biopharma and the added pressure of drug price negotiations from the Inflation Reduction Act. We believe this could drive companies to pursue even more deals - potentially favouring our overweight to small- and mid-cap biotech firms.

Source: Janus Henderson Investors, as at 31 August 2023

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Fund information (Investment policy is on the next page)

Index	MSCI World Health Care Index
Morningstar sector	Europe OE Sector Equity Healthcare
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.

Performance in (USD)

Performance %	A2 (Net)	Index	Sector	A2 (Gross)	Target (Gross)
1 month	-1.5	-0.8	-3.0	-	-
YTD	1.9	1.3	0.3	-	-
1 year	12.1	10.1	4.9	-	-
3 years (annualised)	4.7	6.5	0.0	-	-
5 years (annualised)	6.8	8.2	3.6	9.3	10.4
10 years (annualised)	10.6	10.1	7.4	13.3	12.3

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	2.5	0.8	1.6
2022	-4.3	-5.4	-13.9
2021	4.7	19.8	7.1
2020	23.4	13.5	20.5
2019	27.1	23.2	21.8
2018	2.0	2.5	-3.4
2017	20.5	19.8	21.7
2016	-13.8	-6.8	-9.4
2015	5.7	6.6	5.9
2014	32.7	18.1	18.3
2013	52.5	36.3	35.1

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.

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.

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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.

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% in shares (also known as equities) of companies, of any size, 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 investment manager 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 investment manager 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.

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

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Important information

ESG integration is the practice of incorporating material environmental, social and governance (ESG) information or insights in a non-binding manner alongside traditional measures into the investment decision process to improve long term financial outcomes of portfolios. This product does not pursue a sustainable investment strategy or have a sustainable investment objective or otherwise take ESG factors into account in a binding manner. ESG related research is one of many factors considered within the investment process and in this material we seek to show why it is financially relevant.

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