3Q19 Global & International Equity

FUND COMMENTARY

Global Life Sciences Fund

Market Environment

- Health care stocks underperformed the broad equity market during the quarter due to uncertainty about trade, drug pricing reform and the 2020 U.S. election.
- In September, for example, House Speaker Nancy Pelosi introduced a bill that would allow the government to negotiate the price of up to 250 name-brand drugs.
- At the same time, signs that presidential candidate Sen. Elizabeth Warren is gaining in the polls raised worries about the possibility of a single-payer health plan being introduced in the U.S.
- Finally, a risk-off environment negatively impacted higher-growth/higher-risk areas such as small-cap biotech stocks.

Performance Summary

The Fund underperformed its primary benchmark, the MSCI World Health Care Index℠, and its secondary benchmark, the S&P 500® Index, for the quarter ending September 30, 2019. Stock selection in biotechnology was the largest detractor from relative performance, as our positioning in small-cap biotech stocks – which we believe are driving the sub-sector's best innovation – worked against us. However, stock selection in health care facilities aided relative performance.

For detailed performance information, please visit janushenderson.com/performance.

Portfolio Discussion

Both politics and market volatility were headwinds for health care during the quarter. But idiosyncratic events, such as clinical trial updates, also drove stocks. Often, these events are misunderstood by the market, creating near-term volatility.

Such was the case with Sarepta Therapeutics, our top detractor. During the quarter, the biotech announced a delay in phase 3 trials for its gene therapy for Duchenne muscular dystrophy (DMD). The company also suffered a delay in regulatory approval for another medicine that serves a small subset of DMD patients. Despite these developments, we continue to like Sarepta. Its gene therapy looks promising, and we think the clinical trial delay could help the firm to fine-tune its manufacturing process and optimize trial results.

Insmed was another detractor. During the quarter, investors worried that new patient growth for lead drug, Arikayce, was slowing. In addition, Insmed reported that a first-line study for the drug would be significantly delayed. (Arikayce is currently approved as a second-line therapy, meaning it is administered only after other treatments fail.) While disappointed by the timing setback, we believe patient uptake will continue to exceed Street estimates, based on doctor surveys. We also expect the drug to receive approval outside the U.S. in the near term, which should further boost sales.

At the same time, many companies experienced positive catalysts during the quarter. AstraZeneca, one of our top contributors, reported consensus-beating results, underscoring the strength of the pharma giant's current product cycle. The firm also

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delivered a string of positive news, including six positive data readouts from late-stage clinical trials and three regulatory approvals. In addition, three medicines were put on track to receive expedited regulatory approval. We believe the results showcase AstraZeneca's research-and-development productivity, which should drive future growth.

Bristol-Myers Squibb was another top contributor. The company announced it would sell its Otezla franchise for more than $13 billion, a higher-than-expected price. The sale, which was required by regulators as part of a planned acquisition of Celgene, now provides more cash for stock buybacks and improves the odds of the merger being completed. The firm also reported positive data for its combination immuno-oncology drug (Opdivo/Yervoy) and benefited from a market rotation late in the quarter toward equities trading at low multiples, which included Bristol-Myers' stock.

Top Contributors	Ending Weight (%)	Contribution (%)
AstraZeneca PLC	3.26	0.29
Bristol-Myers Squibb Co	2.65	0.28
Edwards Lifesciences Corp	1.49	0.23
Globus Medical Inc	1.14	0.18
Neurocrine Biosciences Inc	2.14	0.17

Top Detractors	Ending Weight (%)	Contribution (%)
Sarepta Therapeutics Inc	0.77	-0.65
Silk Road Medical Inc	1.39	-0.53
Insmed Inc	1.18	-0.49
ICU Medical Inc	0.90	-0.47
Anthem Inc	2.35	-0.38

The holdings identified in this table, in compliance with Janus Henderson policy, do not represent all of the securities purchased, held or sold during the period. To obtain a list showing every holding as a percentage of the portfolio at the end of the most recent publicly available disclosure period, contact 800.668.0434 or visit janushenderson.com/info.

Manager Outlook

With more than a year until the 2020 election, we think political uncertainty will remain an overhang for health care in the near term. We have experienced periods like this before (including the last presidential election), and believe the best solution is to take a balanced approach. To that end, we have built up positions in medical device companies that we believe should help offset near-term volatility. These firms largely sit outside the political quagmire and are driving advances in robotic-assisted surgery, continuous glucose monitors for diabetes and other areas that we believe are in the early innings of a long growth cycle. For similar reasons, we also favor companies that manufacture cash-pay products, such as contact lenses, and animal health.

At the same time, we remain encouraged by the rapid advances being made across a number of therapeutic areas and rising demand for health care globally. By sticking to a disciplined investment strategy – looking for stocks that trade at a discount to our estimate of a company's intrinsic value and analyzing both the clinical and commercial opportunities of a product or service – we aim to cut through near-term volatility and be well positioned to capture these growth opportunities over the long term.

Portfolio Management

Andy Acker, CFA

For more information, please visit **janushenderson.com.**

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Please consider the charges, risks, expenses and investment objectives carefully before investing. For a prospectus or, if available, a summary prospectus containing this and other information, please call Janus Henderson at 800.668.0434 or download the file from janushenderson.com/info. Read it carefully before you invest or send money.

Past performance is no guarantee of future results. Call 800.668.0434 or visit janushenderson.com/performance for current month-end performance.

Discussion is based on the performance of Class I Shares.

As of 9/30/19 the top ten portfolio holdings of Janus Henderson Global Life Sciences Fund are: Merck & Co Inc (4.59%), Novartis AG (ADR) (4.31%), Abbott Laboratories (3.67%), AstraZeneca PLC (3.25%), Thermo Fisher Scientific Inc (3.08%), UnitedHealth Group Inc (2.86%), Bristol-Myers Squibb Co (2.64%), Takeda Pharmaceutical Co Ltd (2.63%), Sanofi (2.53%) and Boston Scientific Corp (2.43%). There are no assurances that any portfolio currently holds these securities or other securities mentioned.

The opinions are as of 9/30/19 and are subject to change without notice. Janus Henderson may have a business relationship with certain entities discussed. The comments should not be construed as a recommendation of individual holdings or market sectors, but as an illustration of broader themes.

Security contribution to performance is measured by using an algorithm that multiplies the daily performance of each security with the previous day's ending weight in the portfolio and is gross of advisory fees. Fixed income securities and certain equity securities, such as private placements and some share classes of equity securities, are excluded.

Investing involves risk, including the possible loss of principal and fluctuation of value.

Foreign securities are subject to additional risks including currency fluctuations, political and economic uncertainty, increased volatility, lower liquidity and differing financial and information reporting standards, all of which are magnified in emerging markets.

Concentrated investments in a single sector, industry or region will be more susceptible to factors affecting that group and may be more volatile than less concentrated investments or the market as a whole.

Initial Public Offerings (IPOs) are highly speculative investments and may be subject to lower liquidity and greater volatility. Special risks associated with IPOs include limited operating history, unseasoned trading, high turnover and non-repeatable performance.

MSCI World Health Care Index℠ reflects the performance of health care stocks from global developed markets.

S&P 500® Index reflects U.S. large-cap equity performance and represents broad U.S. equity market performance.

Index performance does not reflect the expenses of managing a portfolio as an index is unmanaged and not available for direct investment.

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