

Performance Review

- Renewed global growth worries, simmering trade tensions and slumping commodity prices trounced US stocks in the fourth quarter of 2018, leaving few areas immune to the selloff. Health care equities generally held up better than most, but biotechnology and pharmaceutical industry stocks suffered much steeper three-month declines than the sector as a whole.
- For the quarter, the fund's A (acc) USD shares returned -22,16%, and its benchmark, the NASDAQ Biotechnology Index, returned -20,65%.

QUARTERLY KEY PERFORMANCE DRIVERS

	Stocks	Industries
HELPED	argenx (Overweight)	Health Care Equipment (Lack of Exposure)
	Array BioPharma (Overweight)	Health Care Services (Off-Benchmark Exposure)
	Heron Therapeutics (Off-Benchmark Exposure)	Life Sciences Tools and Services (Stock Selection)
HURT	Amgen (Significant Underweight)	Biotechnology (Stock Selection)
	G1 Therapeutics (Overweight)	Pharmaceuticals (Stock Selection, Overweight)
	Alexion Pharmaceuticals (Significant Overweight)	—

- During the quarter, the stocks of small- and mid-capitalization biotech and pharmaceutical firms generally sold off more than nearly any other type of equity investment, and they also posted bigger losses than their large-cap counterparts in both industries. In absolute terms, the fund's biotechnology industry holdings, which averaged about 77% of the portfolio during the period, collectively shed about a fifth of their equity value, as did our 6% exposure to life sciences tools and services companies, while the roughly 13% of the fund dedicated to pharmaceutical industry stocks fell by almost a third.
- Amongst the key detractors from performance relative to the benchmark index, none lost more value than G1 Therapeutics. The firm has been developing trilaciclib, a cell-preserving adjunct to chemotherapy designed to reduce anaemic side-effects and protect neutrophils (white blood cells) that are usually destroyed by chemotherapy. In December, investors reacted negatively to Phase II trial data that did not show quite as high a level of efficacy as expected in terms of preserving how the immune system functions during chemotherapy. Further trials and discussions with the US Food and Drug Administration (FDA) are set to take place in early 2019.
- Amongst the key relative contributors, Netherlands-based biopharmaceutical company argenx, which develops antibody-based therapies for the treatment of severe autoimmune diseases and cancer, said it signed a deal with an affiliate of Johnson & Johnson's Janssen Pharmaceutical Companies unit to develop its Cusatuzumab drug for treatment of certain types of cancer (AML, MDS and other haematological malignancies in particular). The deal, which is potentially worth up to US\$1.6 billion, represents a global collaboration and licensing agreement for Cusatuzumab.

ONE-MONTH KEY PERFORMANCE DRIVERS

	Stocks	Industries
HELPED	argenx (Overweight)	Life Sciences Tools and Services (Stock Selection, Underweight)
	Global Blood Therapeutics (Overweight)	Pharmaceuticals (Stock Selection)
	Heron Therapeutics (Off-Benchmark Exposure)	—
HURT	Alexion Pharmaceuticals (Significant Overweight)	Biotechnology (Stock Selection)
	G1 Therapeutics (Overweight)	—
	Amgen (Significant Underweight)	—

- During the December and the fourth quarter selloff, the fund's modest cash position (ranging from 5% to 6% of total net assets, on average) was actually its number-one contributor to relative performance. Amongst our active investments, Global Blood Therapeutics stock had a strong December result, rallying after news of positive Phase III clinical updates for its lone drug candidate, voxelotor, a haemoglobin-restoration treatment for sickle cell disease. Soon afterwards, the drug was granted an "accelerated approval pathway" designation from the FDA.
- Heron Therapeutics stock had a solid year in 2018 and, though it declined in December, fared better than the benchmark index for the month. Heron has shown pipeline progress in a number of indications lately, including late-stage trials in acute-pain candidate HTX-011. Beyond providing long-acting pain relief, HTX-011 has consistently been shown to significantly reduce the need for opioids following various surgical procedures, which several other experimental pain medications have failed to achieve, prompting the FDA to give HTX-011 a "Breakthrough Therapy" designation.
- Shares of Alexion Pharmaceuticals, which specialises in orphan drugs for rare diseases, slumped in December despite a lack of negative company-specific news, and seemed to have been caught up in the general spike in market volatility, which hit biotech stocks especially hard. For its part, Alexion said in early December that its newest blood disorder treatments appear to be progressing well through clinical testing phases. The company also reported rising sales of Soliris, an approved drug that treats a type of blood disease and neuromuscular condition.

Outlook & Strategy

- Biotechnology firms, particularly those in early stages of research and development, have significant risk associated with specific factors including trial results, regulatory approvals, competitor developments and others. We attempt to address these risks in two ways: (1) through our disciplined, bottom-up research and analytical process; and (2) by using position size as a risk management strategy, investing less in developmental-stage companies with few products and more in commercial-grade companies with multiple products. This helps us in seeking to minimise the downside impact to the overall portfolio of a single binary event such as a trial disappointment or regulatory disapproval.
- Looking ahead, rapid advances in life sciences, a surge in medical breakthroughs, improved efficacy in health care treatments and an increase in FDA drug approvals are revitalising the biotechnology industry, which we believe continues to offer tremendous opportunities to long-term investors. As innovation within the biotechnology and pharmaceuticals industries has reached unprecedented levels, in our view, we are particularly interested in companies working on significant advancements in gene therapy, orphan diseases, immuno-oncology, and targeted approaches for cancer therapy. We are also encouraged by companies that have focused their efforts on new drug discovery platforms and novel compounds.
- According to data from Dealogic, biotechnology IPOs had their second-biggest year on record in 2018 (with 2014 taking the top spot), and we have been investing in several of them along the way. Driven by advances in medical science and an FDA that is increasingly willing to accelerate approval of innovative drugs, biotech companies are tapping public markets at early stages of development these days—some even before they have a drug in a clinical trial. Some 269 biotech companies have gone public since 2013, nearly as many as total biotech IPOs from 1995 through 2007.
- While cutting-edge developments are exciting, we remain disciplined and highly selective in our investment approach, which focuses on high-quality companies that are at the forefront of producing first-in-class, best-in-class and only-in-class drugs and therapies.
- Political pressure on drug-price legislation in the United States has been elevated for a couple years and has yet to wane, but the commercial landscape in health care remains favourable for innovative drugs that deliver value to patients. Beyond the regulatory front, higher rates of drug utilisation and health care spending due to the greying of the global population present a strong long-term demand backdrop for the biotech and pharmaceutical industries.

Fund Details

Inception Date	03/04/2000
Benchmark	NASDAQ Biotechnology Index

Fund Description

The fund aims to achieve capital appreciation by investing principally in equity securities of biotechnology companies and discovery research firms located mainly in the US.

Performance Data

Discrete Annual Performance (%) as at 31/12/2018

	12/17-12/18	12/16-12/17	12/15-12/16	12/14-12/15	12/13-12/14
A (acc) USD	-16,31	16,93	-17,87	4,93	34,70
NASDAQ Biotechnology Index USD	-9,32	21,06	-21,68	11,42	34,32

Performance Net of Management Fees as at 31/12/2018 (Dividends Reinvested) (%)^{1,2}

	1 Mth	3 Mths	YTD	1 Yr	3 Yrs	5 Yrs	10 Yrs	Since Inception (03/04/2000)
A (acc) USD	-11,59	-22,16	-16,31	-16,31	-7,03	2,58	12,96	5,33
NASDAQ Biotechnology Index	-11,25	-20,65	-9,32	-9,32	-4,91	5,17	15,51	5,76

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Years Experience 26

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Years with Firm 2
Years Experience 5

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Years Experience 29

What Are the Key Risks?

The value of shares in the Fund and income received from it can go down as well as up and investors may not get back the full amount invested. Performance may also be affected by currency fluctuations. Currency fluctuations may affect the value of overseas investments. The Fund invests mainly in equity securities of biotechnology companies. Such securities have historically been subject to significant price movements that may occur suddenly due to market, sector or company-specific factors. As a result, the performance of the Fund can fluctuate significantly over relatively short time periods. Other significant risks include: liquidity risk. For full details of all of the risks applicable to this Fund, please refer to the "Risk Considerations" section of the Fund in the current prospectus of Franklin Templeton Investment Funds.

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2. When performance for either the portfolio or its benchmark has been converted, different foreign exchange closing rates may be used between the portfolio and its benchmark.



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