Platinum International Health Care Fund

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Performance

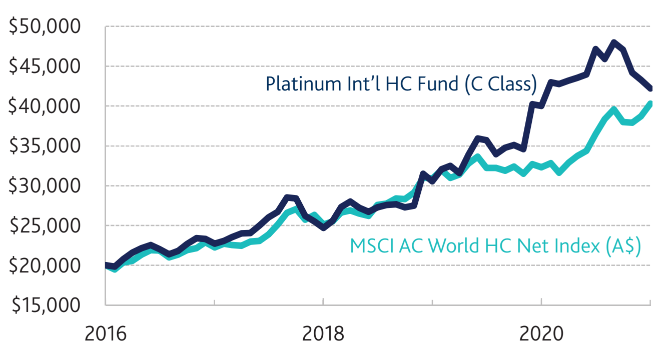
(compound p.a.⁺, to 31 December 2021)

	QUARTER	1YR	3YRS	5YRS	SINCE INCEPTION
Platinum Int'l HC Fund*	-10%	5%	20%	16%	11%
MSCI AC World HC Index^	6%	25%	17%	15%	10%

⁺ Excludes quarterly returns.
* C Class – standard fee option. Inception date: 10 November 2003.
After fees and costs, before tax, and assuming reinvestment of distributions.
^ Index returns are those of the MSCI All Country World Health Care Net Index in AUD. Source: Platinum Investment Management Limited, FactSet Research Systems.
Historical performance is not a reliable indicator of future performance. See note 1, page 4. Numerical figures have been subject to rounding.

Value of $20,000 Invested Over Five Years

31 December 2016 to 31 December 2021



After fees and costs, before tax, and assuming reinvestment of distributions. Historical performance is not a reliable indicator of future performance. Source: Platinum Investment Management Limited, FactSet Research Systems. See notes 1 & 2, page 4.

The Fund (C Class) returned -10.4% for the quarter and 5.5% for the year.[1]

While 2020 was a good year for investors in biotech, 2021 was a rather different story.

The MSCI All Country World Healthcare Index, which has very limited exposure to mid- and small-sized biotech stocks, had a strong year. In stark contrast, the XBI, an index of US biotech stocks,[2] experienced the largest, most prolonged drawdown in five years (see Fig. 1). Even more stark is the spread between the XBI and the S&P 500 Index and the XLV, an index of US healthcare stocks,[3] with performance of the latter driven by a concentrated group of companies, such as Pfizer (vaccine/antiviral therapy) and Eli Lilly (Alzheimer's disease/diabetes). Fig. 2 (on the following page) illustrates how wide the performance gap between the pharma and biotech sector was in 2021.

Many of our biotech holdings have been caught up in the decline. We had trimmed a number of our biotech stocks earlier in the year for valuation reasons following strong performance, but the overall dynamic in biotech continued to

1 References to returns and performance contributions (excluding individual stock returns) in this Platinum International Health Care Fund report are in AUD terms, unless otherwise specified. Individual stock returns are quoted in local currency terms and sourced from FactSet Research Systems, unless otherwise specified.

2 SPDR S&P Biotech ETF (XBI) tracks an equal-weighted index of US biotechnology stocks.

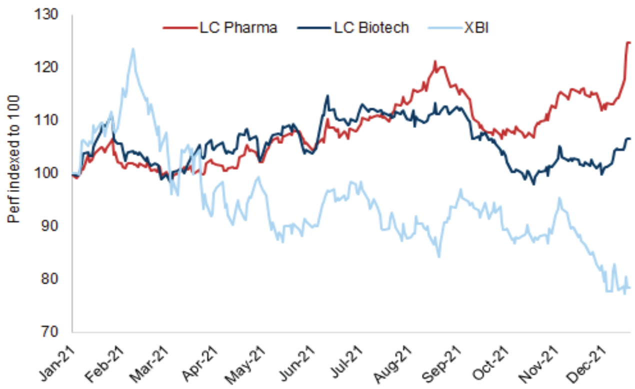
3 Health Care Select Sector SPDR Fund (XLV) tracks health care stocks from within the S&P 500 Index, weighted by market cap.

Fig. 1: 2021 - Biggest Drawdown in US Biotech in Five Years

Drawdown Period	Number of trading days	XBI	XBI vs S&P 500	XBI vs XLV
Jul 2015-Feb 2016	144	-49%	-35%	-32%
Apr-May 2016	14	-14%	-13%	-11%
Jun 2016	17	-17%	-12%	-11%
Sep-Oct 2016	30	-23%	-18%	-13%
Nov-Dec 2016	27	-13%	-17%	-11%
Mar-Apr 2018	19	-14%	-8%	-6%
Sep-Dec 2018	78	-35%	-16%	-22%
Apr-Sep 2019	123	-20%	-22%	-17%
Feb-Mar 2020	18	-33%	-3%	-11%
Jul-Sep 2020	35	-14%	-16%	-12%
Average	51	-23%	-16%	-15%
Median	29	-19%	-16%	-12%
Feb-Dec 2021	**218**	**-37%**	**-56%**	**-57%**

Source: Goldman Sachs, USD.

Fig. 2: 2021 – A Very Different Path for Pharma vs. Biotech



Source: Goldman Sachs, large cap, USD.

deteriorate. Chinese healthcare was also in the doldrums, due to a potential regulatory issue, which provided an excuse to sell Chinese biotech stocks. Our holdings were dragged lower on the sentiment shift, despite gaining product approvals or making very solid business progress.

Centogene (-52% over the quarter), a rare disease diagnostic company was a key detractor due to concerns about its balance sheet. We believe these will be resolved in the near future. **Genetron** (-56%), a Chinese diagnostic company, lost significant value during the quarter as investors reduced exposure to Chinese ADR listings. **Esperion Therapeutics** (-59%) sold off heavily after it raised money along with dilutive warrants. The launch of Esperion's cholesterol-lowering pill continues to be challenging and outcome data in the next 12 months will be key. **Albireo Pharma** (-25%), a company that develops treatments for rare diseases, recently received approval for odevixibat, a treatment for pruritus (chronic itchy skin due to higher levels of bile salt accumulating under the skin) in patients with progressive familial intrahepatic cholestasis, a disorder that causes progressive liver disease. Unfortunately, new product launches have been out of favour. Post quarter end, Albireo reported that the product launch had exceeded expectations.

On the bright side, **Telix Pharmaceuticals** (+29%), an Australian biotech who received its first cancer imaging product approval during the quarter, has been a great investment for us. Similarly, US oncology biotech company **Merus** (+45%) continued to progress its pipeline, resulting in share price appreciation. **Prometheus Biosciences** (+67%) rallied strongly on gaining interest in its therapeutic candidate that targets certain inflammatory diseases.

We have been adding to various tool companies, along with biotechs that have recently launched new drugs for rare diseases. In the coming decade, we believe there will be significant progress in diagnosing and treating

Disposition of Assets

REGION	31 DEC 2021	30 SEP 2021	31 DEC 2020
North America	43%	42%	35%
Europe	23%	20%	23%
Australia	12%	10%	11%
Asia	8%	8%	10%
Japan	4%	4%	6%
Other	1%	1%	1%
Cash	10%	15%	13%
Shorts	-4%	-1%	-3%

See note 3, page 4. Numerical figures have been subject to rounding.
Source: Platinum Investment Management Limited.

Net Sector Exposures

SECTOR	31 DEC 2021	30 SEP 2021	31 DEC 2020
Biotechnology	54%	54%	49%
Pharmaceuticals	24%	21%	26%
Life Sciences Tools & Services	7%	6%	7%
Health Care Equip & Supplies	-3%	0%	1%
Health Care Providers & Serv	0%	0%	1%
Other	5%	3%	1%
TOTAL NET EXPOSURE	86%	84%	84%

See note 4, page 4. Numerical figures have been subject to rounding.
Source: Platinum Investment Management Limited.

Top 10 Holdings

COMPANY	COUNTRY	INDUSTRY	WEIGHT
SpeeDx Pty Ltd	Australia	Biotechnology	4.7%
Takeda Pharmaceutical	Japan	Pharmaceuticals	3.7%
Sanofi SA	France	Pharmaceuticals	3.4%
Telix Pharmaceuticals Ltd	Australia	Biotechnology	3.2%
Bayer AG	Germany	Pharmaceuticals	2.6%
Exscientia Ltd	UK	Biotechnology	2.2%
Quanterix Corp	US	Life Sciences Tools	2.1%
Pardes Biosciences	US	Financials	2.0%
Gilead Sciences Inc	US	Biotechnology	2.0%
Zai Lab Ltd	China	Biotechnology	1.9%

As at 31 December 2021. See note 5, page 4.
Source: Platinum Investment Management Limited.

For further details of the Fund's invested positions, including country and industry breakdowns and currency exposures, updated monthly, please visit https://www.platinum.com.au/our-products/pihcf.

neurodegenerative diseases. Similarly, we believe the way drugs will be discovered and developed will also change, and hence we continue to invest in the next-generation drug developers.[4]

Commentary

Significant shifts happen periodically in healthcare. Initially, scepticism reigns, but over time, data trumps and momentum starts to build. In 1990, **Roche** invested in US biotech **Genentech**. At the time, biotech was a young industry with many of Roche's peers sceptical about large molecules targeting smaller disease indication. Manufacturing of these biologics was difficult, requiring significant investment versus very profitable small molecule pills (the standard at the time). Fast forward to today and biologics are omnipresent. For Roche, partnering with Genentech was a future-defining deal that culminated in the full acquisition of Genentech in 2009. It turned Roche into the oncology company it is today and added scientific foresight to the organisation. We are invested in Roche and pay close attention to its hiring and deal activity - regardless of how large or small. Often these corporate actions signal early industry trends.

In 2020, Roche hired Aviv Regev as head of Genentech Research and Early Development (gRED). Prior to Roche, Aviv Regev worked as a computational and systems biologist and was a Professor of Biology at the Broad Institute (of MIT and Harvard). She is not your typical drug hunter, chemist or protein engineer; for her, it is all about molecular circuitry, computation and mathematics. She recently said that "Advances in human biology, massively parallel high-resolution methods, modalities, and computation and mathematics are on track to change the nature of drug discovery."[5]

We fully agree and hence have invested in companies (such as Exscientia, Recursion and Roivant), that combine tech and biotech, as well as computers and wet labs. During the quarter, Roche further confirmed its ambition in deciphering the biological system as a priority by forming a broad alliance with Recursion, a US biotech founded in 2013. Recursion characterises cells (normal and diseased) at industrial scale and uses computers to pinpoint minute differences. Recursion essentially does what Aviv Regev refers to as "massively parallel high-resolution methods", conducting about one million experiments a week. Combining Recursion's capability with Roche's drug development expertise is a deal not to ignore. The scale of the deal is significant, potentially including up to 40 programs (US$150 million upfront, plus US$300 million per program over time), with neurosciences a focus. Genentech gave Roche oncology, could Recursion be a pillar for Roche's next chapter in neurosciences?

In neuroscience, we are years behind oncology in deciphering the molecular pathology of disease, hence Recursion's 'operating system' fits into unravelling new targets. While we are excited about this alliance, the market reaction has been subdued. There remains scepticism that the machine-learning approach will increase R&D efficiency, however, it improves with more experiments and additional data, and that is exactly what this alliance should achieve (and more), as Roche adds the therapeutics modalities, along with drug development experience to the mix.

Outlook

There are a myriad of reasons that contributed to the biotech conundrum in the second half of 2021, the simplest one being the fact that exuberance in the previous year was unlikely to continue. The economic environment also plays a role, but of most interest to us, is the dynamic that has developed in the biotech universe itself. Money has been plentiful for the past decade, particularly over the past five years. The shift by many healthcare-dedicated funds towards investing in private companies at all levels of maturity (founding, seed to crossover) has been unprecedented. The number of new companies being founded in gene editing is simply mind-boggling and we are seeing 'target' crowding, where many companies work on the same drug target with differentiation hard to come by.

Today, private biotech valuations are in stark contrast to their listed peers, they are booming and securing access in an investment round is akin to a pageant event, particularly in the US. In many ways, we are seeing a lack of buoyant public biotech investing as a consequence. Combine this with a flood of new biotech listings that fail to find ongoing investor support outside of equity raises and you get a trading dynamic that is disconnected from the fundamentals of a company. Topping it all off has been rather subdued M&A activity. Where to from here? Large life science tool companies, diagnostic companies and pharma all have solid balance sheets, and history has shown that they will go shopping. It is also clear that therapeutic innovation has not ceased. New laboratory tools are coming to the market, along with automation and machine learning that will facilitate the next chapter of innovation. Consequently, the fundamental reason why we invest in biotech has not changed: to invest in companies that increase our longevity and improve our quality of life.

4 For a more in-depth explanation of our thoughts on the future of the healthcare sector see: https://www.platinum.com.au/Insights-Tools/The-Journal/Biotech-Driving-Another-Decade-of-Change-in-Health

5 Source: *Nature*, March 2021.

Notes

Unless otherwise specified, all references to "Platinum" in this report are references to Platinum Investment Management Limited (ABN 25 063 565 006, AFSL 221935).

Some numerical figures in this publication have been subject to rounding adjustments. References to individual stock or index performance are in local currency terms, unless otherwise specified.

1. Fund returns are calculated by Platinum using the net asset value unit price (i.e. excluding the buy/sell spread) of the stated unit class and represent the combined income and capital returns over the specified period. Fund returns are net of fees and costs, pre-tax, and assume the reinvestment of distributions. The MSCI index returns are in AUD, are inclusive of net official dividends, but do not reflect fees or expenses. MSCI index returns are sourced from FactSet Research Systems. Platinum does not invest by reference to the weightings of the specified MSCI index. As a result, the Fund's holdings may vary considerably to the make-up of the specified MSCI index. MSCI index returns are provided as a reference only. The investment returns shown are historical and no warranty is given for future performance. Historical performance is not a reliable indicator of future performance. Due to the volatility in the Fund's underlying assets and other risk factors associated with investing, investment returns can be negative, particularly in the short term.
2. The investment returns depicted in the graph are cumulative on A$20,000 invested in C Class (standard fee option) of the Fund over the specified period relative to the specified MSCI index in AUD.
3. The geographic disposition of assets (i.e. other than "cash" and "shorts") shows the Fund's exposures to the relevant countries/regions through its long securities positions and long securities/index derivative positions, as a percentage of its portfolio market value. With effect from 31 May 2020, country classifications for securities were updated to reflect Bloomberg's "country of risk" designations and the changes were backdated to prior periods. "Shorts" show the Fund's exposure to its short securities positions and short securities/index derivative positions, as a percentage of its portfolio market value. "Cash" in this table includes cash at bank, cash payables and receivables and cash exposures through derivative transactions.
4. The table shows the Fund's net exposures to the relevant sectors through its long and short securities positions and long and short securities/index derivative positions, as a percentage of its portfolio market value. Index positions (whether through ETFs or derivatives) are only included under the relevant sector if they are sector specific, otherwise they are included under "Other".
5. The table shows the Fund's top ten positions as a percentage of its portfolio market value taking into account its long securities positions and long securities derivative positions.

Disclaimers

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