

Platinum International Health Care Fund



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Portfolio Manager

Performance

(compound p.a.⁺, to 31 December 2020)

	QUARTER	1YR	3YRS	5YRS	SINCE INCEPTION
Platinum Int'l HC Fund*	14%	31%	21%	15%	11%
MSCI AC World HC Index [^]	0%	5%	13%	9%	9%

⁺ 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 2015 to 31 December 2020



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 13.9% for the quarter and 30.8% for the year.¹

In years to come, documentaries will remind us of the 2020 pandemic. It will be remembered as a year when economies came to a halt, working from home became normal and acronyms like PCR and mRNA made it into the popular press. In less than a year, BioNTech/Pfizer and Moderna have accomplished what most thought was impossible - developing a vaccine from scratch. As the CEO of Novartis, Vas Narasimhan said, "we are witnessing an RNA revolution". We believe vaccines are just the start of this revolution, with more to come.

This achievement has unsurprisingly sparked broad interest in genomics biotech companies, while interest in the slower growing pharmaceutical and mature biotech companies has waned. Today, the valuation gap between the S&P 500 Index and these 'old guard' drug developers is at historical levels. This is not due to these companies sitting idle. To the contrary, many are retooling. **Bayer**, for instance, acquired gene therapy biotech **Asklepios BioPharmaceutical** (AskBio) during the quarter and is building out its cell and gene therapy division, while at the same time increasing its exposure to the synthetic biology field (via Leaps by Bayer²).

Many holdings contributed to the Fund's performance this quarter. While the COVID-19 vaccine makers **CureVac** (+74% over the quarter), **Moderna** (+48%) and **BioNTech** (+18%) performed well, many other investments also made great progress, which is particularly exciting. Since the launch of the Fund in 2003, we have been stern believers in personalised medicine and the impact that genomic advances will have on drug development, diagnostics and healthcare. We have witnessed a rapidly expanding playbook in molecular biology deciphering the inner workings of cells.

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

2 Leaps by Bayer aims to conquer the top 10 challenges faced by humanity. Since 2015, Leaps by Bayer has invested over \$US800 million in ventures that tackle fundamental breakthrough and shift core paradigms in the health and agriculture industries. For further details visit: <https://leaps.bayer.com/approach#10leaps>

Given the cash inflow for many diagnostic companies due to testing of the SARS-CoV-2 virus, we expect consolidation in the tool space. **Horizon Discovery** (+94%), a company we have been invested in for some time, has been industrialising so-called CRISPR screens, which use gene editing technologies to understand signalling pathways and produce customised cell lines. During the quarter, **PerkinElmer** (+14%), another holding in the Fund and a company that had a windfall from SARS-CoV-2 testing, acquired Horizon Discovery to expand its product offering.

Pacific Biosciences of California (+163%), a company we highlighted in our September 2020 quarterly report,³ continued its stellar performance, buoyed by the signing up of new customers and the market's increasing realisation of the potential of long-read genetic sequencing, particularly for personalised medicines and treatment of rare diseases. Similarly, **NanoString Technologies** (+50%) continued to broaden its product offering to allow scientists to spatially analyse the genomic and molecular structure of a cell. Again, it is all about gaining a much more comprehensive understanding of what is happening inside a cell.

On the therapeutic front, **Five Prime Therapeutics** (+262%) announced that bemarituzumab (a potential first-in-class therapeutic antibody) in combination with chemotherapy helped patients with gastric and gastroesophageal junction cancer to live longer. Two of our biotech holdings received US approval for their first-ever product. US biotech **BioCryst** (+117%) received approval of ORLADEYO™, an oral treatment for hereditary angioedema (whereby an allergic reaction triggers a swelling of the area beneath the skin). US biotech **Myovant Sciences** (+97%) obtained marketing authorisation for Orgovyx, an oral treatment for advanced prostate cancer. Myovant also entered an alliance with Pfizer during the quarter to accelerate commercialisation of Orgovyx. A very fitting partnership given Pfizer's prostate cancer drug Xtandi and the fact that Myovant's previous CEO Lynn Seely was behind the development of Xtandi at Medivation (Medivation was acquired by Pfizer in 2016).⁴

Gene editing has seen a flurry of data this quarter. **Intellia Therapeutics** (+175%) started its first clinical trial, directly administering the gene editing system 'NTLA-2001' for hereditary transthyretin amyloidosis (hTTR), a disease where the protein transthyretin (TTR) misfolds and forms deposits that affect the nerves, heart, kidneys and eyes. NTLA-2001 comprises two parts: the guide ribonucleic acid (RNA) that is specific for the diseased gene and a messenger RNA (mRNA)

³ https://www.platinum.com.au/PlatinumSite/media/Reports/pihfqtr_0920.pdf

⁴ Myovant announced the appointment of David Marek as the new CEO on 4 January 2021.

Disposition of Assets

REGION	31 DEC 2020	30 SEP 2020	31 DEC 2019
North America	35%	35%	36%
Europe	23%	29%	28%
Australia	12%	13%	13%
Asia	10%	8%	5%
Japan	6%	6%	7%
Cash	13%	10%	11%
Shorts	-3%	-7%	-2%

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

Net Sector Exposures

SECTOR	31 DEC 2020	30 SEP 2020	31 DEC 2019
Biotechnology	49%	49%	48%
Pharmaceuticals	26%	26%	30%
Life Sciences Tools & Services	7%	9%	9%
Health Care Providers & Serv	1%	1%	1%
Health Care Technology	0%	-1%	0%
Health Care Equip & Supplies	1%	-1%	1%
Industrials	1%	1%	0%
Other	0%	-1%	0%
TOTAL NET EXPOSURE	84%	83%	88%

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

Top 10 Holdings

COMPANY	COUNTRY	INDUSTRY	WEIGHT
Takeda Pharma Co	Japan	Pharmaceuticals	3.8%
SpeeDx Pty Ltd	Australia	Biotechnology	3.6%
Sanofi SA	France	Pharmaceuticals	3.3%
Bayer AG	Germany	Pharmaceuticals	2.9%
Telix Pharmaceutical	Australia	Biotechnology	2.8%
Kazia Therapeutics	Australia	Biotechnology	2.1%
Zai Lab Ltd ADR	China	Biotechnology	2.0%
Almirall SA	Spain	Pharmaceuticals	1.9%
Quanterix Corp	US	Life Sciences Tools	1.8%
CStone Pharma	China	Biotechnology	1.8%

As at 31 December 2020. 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>.

that encodes for the Cas9 enzyme (a protein that plays a vital role in the immunological defence of certain bacteria against DNA viruses and plasmids). The guide RNA and mRNA are both delivered inside lipid nanoparticles, similar to how the SARS-CoV-2 vaccines are delivered. The aim of NTLA-2001 is to knock out the target gene. This is a milestone for gene editing as well as mRNA. Intellia also showed that in non-human primates its gene editing system is able to insert the SERPINA1 gene into liver cells and hence allow for the production of human alpha-1 antitrypsin (AAT). Mutations in SERPINA1 can cause AAT deficiency, which can cause serious lung or heart disease.

Our pharmaceutical holdings detracted from performance, while we also had setbacks at **Assembly Biosciences** (-63%), **Galapagos** (-34%) and **Ovid Therapeutics** (-60%).

During the quarter, we trimmed our mRNA vaccine holdings following strong share price performance, initiated positions in a number of new biotech holdings and added to biotechs that have struggled to launch new therapeutics during the COVID-19 pandemic.

Commentary

The fast development of an mRNA vaccine has drawn people into the world of biotech and genomics. 'Plug and play' is used to describe this exciting therapeutic platform, but don't be fooled, drug development is not like developing an app. Biology is one of the most sophisticated systems there is and cracking the 'code' only represents one layer of this system, there are many more. It is indeed exciting to see computational biology making great strides and machine learning being applied to predicting the structure of proteins. However, proteins are not static, they continually turn and change shape. To make a drug against a target, scientists must determine which conformation is worthwhile attacking. The SARS-CoV-2 spike protein, for example, has two distinct conformations, an 'up' mode and a 'down' mode, whereby 'up' allows it to attach to its target receptor, while in 'down' mode, no interaction with the target receptor can happen. This is important information when developing a drug or vaccine, as targeting the 'up' conformation or preventing the 'down' mode from flipping into an 'up' mode will be effective.

The good news is, there are companies that focus on protein dynamics and technology will help us get ahead. Understanding the interactions within a cell as well as the chatter between cells is absolutely crucial, hence advances in the tools and computational biology sector are vitally important.

We are seeing the industrialisation of the drug discovery process, robotic wet labs being put together, automation on the rise, and an increase in data science. The line between biotech and tech is becoming increasingly blurred. Investor presentations today contain 'techie' language like code and foundry, with RNA the software and CRISPR a new hardware. At times, software as a service (SaaS) makes an appearance as well. Genetic, cell and protein engineering have come a long way to make all the innovation possible and generate ever-more sophisticated drugs. These days, antibody drug conjugates are being made that carry a mask. The mask will only come off when a certain enzyme is present in the cell microenvironment, hence extending the therapeutic window.

Induced pluripotent stem cells (iPSCs) are progressing through clinical trials. For example, recently modified natural killer cells that are derived from iPSCs have shown promising results in haematological cancer. While biotechs tout about their progress, pharma companies are quietly retooling. As mentioned above, Bayer is putting together a very interesting cell and gene therapy division, having acquired BlueRock Therapeutics (iPSCs neurology, cardiology, immunology) in 2019 and AskBio in 2020. These therapy approaches focus largely on manufacturing and remind us of the plasma business in the early days, however, the opportunities are much vaster.

We monitor all the above, digest and decipher to make sure, as investors, we are part of the journey for years to come.

Outlook

The COVID-19 vaccination phase has now started, so over the coming months we should see new drug launches that had been impacted by the pandemic improve gradually. On other fronts, Alzheimer's disease will likely be in focus, as Biogen continues its rollercoaster ride to get its aducanumab drug approved by the US Food and Drug Administration (FDA). During the December quarter, there were several acquisitions in the liquid biopsy space with companies positioning for the future. While cell and gene therapies, given their high cost, will have to prove that they are indeed curative. We will likely see more demand for biomarkers to make sense of the myriad of oncology drugs that are in development. Biomarkers will also gain importance in targeted neurology and we will likely continue to see manufacturing evolve from a volume business to a more customised approach, with smaller volumes but many different products. There is no doubt that the next decade will be an exciting period in biotech.

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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