

Platinum International Health Care Fund



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Portfolio Manager

Performance

(compound p.a.⁺, to 30 September 2021)

	QUARTER	1YR	3YRS	5YRS	SINCE INCEPTION
Platinum Int'l HC Fund*	0%	34%	18%	19%	12%
MSCI AC World HC Index [^]	4%	17%	12%	14%	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.

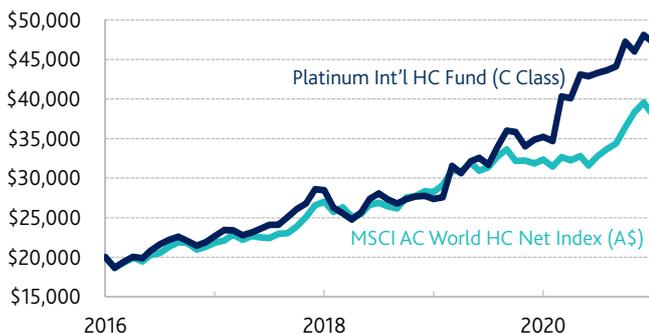
[^] Index returns are those of the MSCI All Country World Health Care Net Index in AUD. Source: Platinum Investment Management Limited, FactSet Research Systems.

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

30 September 2016 to 30 September 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 -0.2% for the quarter and 34.0% for the year.¹

It was a much quieter quarter, with Northern Hemisphere residents taking a well-earned summer holiday, which traditionally means limited medical meetings.

Acquisition announcements in healthcare were limited as well, adding to subdued sentiment, particularly in the biotech sector.

The valuations of many biotechs have gradually declined and a number of companies are increasingly very close, or even below, cash balances. The obsession with catalysts or 'following the herd' often results in stark imbalances in the sector, which offer some very interesting investment opportunities for long-term investors like ourselves.

Oncology is an interesting example of the dichotomy that exists in biotech. During the quarter, a number of our less-known oncology holdings (**Innate Pharma** +101% over the quarter, **Leap Therapeutics** +145%, **Redx Pharma** +39%, **Arcus Biosciences** +27%) released some interesting data, quickly propelling them into the spotlight. This reinforced our belief that investing in biotech requires a lot of patience, persistence, long-term thinking and independent thought (more on that below). It is not about the next fad that everyone talks about, it is more about what is not being talked about, but is scientifically sound.

Our Chinese biotech investments had a difficult quarter (**CStone Pharmaceutical** -37%, **Zai Lab** -40%, **Innovent Biologics** -17%, **Genetron** -31%), not due to pipeline or product setbacks, on the contrary, all are making great progress. Uncertainty about government regulation and pricing pressure has been the culprit, making rational thinking challenging. China is a significant therapeutic market that has made tremendous regulatory progress and is experiencing immense investment in its biotech industry. As a result, while we see long-term opportunities in that market, we expect it will be a bumpy ride.

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.

During the quarter, we trimmed some of our holdings that have performed very well for the year, such as **Ideaya Biosciences** (+103%) and **Alkermes** (+86%). We also added a less-known US biotech that started clinical trials of its SARS-CoV-2 protease inhibitor, as well as a German biotech that specialises in enzyme and organism engineering.

Commentary

Getting carried away by short-term delays or setbacks in biotech can distract the mind from keeping a firm eye on the long term. Roche's 125-year anniversary on 1 October was a reminder that pharma companies have been around for a long time. In fact, Roche is more 'middle-aged' than 'old'. Johnson & Johnson has been in existence for 135 years, US Merck 130 years, Eli Lilly 145 years, Bayer 158 years, Pfizer 171 years, Takeda 240 years, while Merck KGaA is the grand dame at 353 years.

Sure, acquisitions have been part of their growth journey, as have setbacks (mistakes), but over time, these companies have evolved and shaped the future of therapies, as much as the future has shaped them. These companies have learned to adapt and embrace biotechs. As investors in the healthcare sector we are not so dissimilar to these companies. We pay attention to how a particular field or sector evolves over time and focus on what is needed to really make an impact. We learn a lot from the companies we invest in.

So, when it comes to something like immuno-oncology we have learned quickly that it is fascinatingly complex. Sadly, there are many patients who do not achieve a durable response when treated with current approved checkpoint inhibitors (drugs that help your immune system recognise and mount a defence against the tumour). Immuno-oncology is a treatment paradigm that has many layers, but ultimately, it will transform the way cancer is diagnosed and treated. As a consequence, it requires many different approaches, as well as different companies.

Tumours essentially modify (manipulate) their surroundings (called the tumour microenvironment or TME) to suit their needs and most importantly, make sure the immune system does not recognise them properly. The TME is fascinating and unsurprisingly, is the focus of many scientists. Understanding what is happening in the TME is crucial to progressing to the next chapter in immuno-oncology beyond current approved checkpoint inhibitors. Hence, we have (and will be) investing in companies that are razor-focused on this area. It is not an easy space to succeed in and there are many challenges, but during the quarter it was gratifying to see real advances taking place.

Disposition of Assets

REGION	30 SEP 2021	30 JUN 2021	30 SEP 2020
North America	42%	36%	35%
Europe	20%	21%	29%
Australia	10%	10%	12%
Asia	8%	12%	8%
Japan	4%	4%	6%
Other	1%	1%	1%
Cash	15%	16%	10%
Shorts	-1%	-1%	-7%

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

Net Sector Exposures

SECTOR	30 SEP 2021	30 JUN 2021	30 SEP 2020
Biotechnology	54%	53%	49%
Pharmaceuticals	21%	22%	26%
Life Sciences Tools & Services	6%	7%	9%
Chemicals	1%	0%	0%
Electronic Equip Instruments	1%	0%	0%
Machinery	0%	0%	1%
Health Care Technology	0%	0%	-1%
Health Care Equip & Supplies	0%	0%	-1%
Health Care Providers & Serv	0%	0%	1%
Other	1%	0%	-1%
TOTAL NET EXPOSURE	84%	83%	83%

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	4.5%
Takeda Pharmaceutical	Japan	Pharmaceuticals	3.7%
Sanofi SA	France	Pharmaceuticals	3.0%
Bayer AG	Germany	Pharmaceuticals	2.5%
Telix Pharmaceuticals Ltd	Australia	Biotechnology	2.3%
Ideaya Biosciences Inc	US	Biotechnology	2.2%
Centogene NV	Germany	Biotechnology	2.1%
Icosavax Inc	US	Biotechnology	2.1%
Gilead Sciences Inc	US	Biotechnology	1.9%
Coherus Biosciences Inc	US	Biotechnology	1.9%

As at 30 September 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>.

The TME is made up of varying levels of different immune cells - their signalling molecules along with molecules coming from the tumour itself. The goal for drug developers is simple: turn off the immune inhibitory signals coming from the tumour, while strengthening the immune response against the tumour. The latter goal can be achieved in various ways, in the long term resulting in more efficacies in achieving longer-lasting immune cells in the TME.

French biotech **Innate Pharma** has been working for years on harnessing the power of Natural Killer (NK) cells, which are essentially the front-line of defence for our immune system. These cells recognise a foreign body, attack it, release cytokines (small proteins important in cell signalling), that attract the next more-specific layer of the immune system's so-called T cells, who then turn the first response into a long-lasting (adaptive) immune response. A lot of investors have been focusing on genetically engineered NK cell transplants, whereby the NK cells are provided by a donor or derived from induced pluripotent stem cells (iPSCs). The steps required to make the engineered NK cells are cumbersome and require very careful characterisation of the NK cells, particularly when they are derived from iPSCs. In contrast, Innate Pharma focuses on how to leverage the patient's own NK cells, hence no cell transplants are needed. It focuses on the molecules that sit on the surface of NK cells. They orchestrate the signalling. Innate develops biologics that target these molecules, so-called NK cell engagers.

At the ESMO² 2021 Congress, held in September, Innate's Monalizumab, a monoclonal antibody (licensed to AstraZeneca) showed promising data in lung cancer when combined with AstraZeneca's Durvalumab antibody. Besides Monalizumab, Innate is also working on biologics that engage several NK cell surface molecules simultaneously, highlighting the progress of molecular and protein engineering in the field (see Fig. 1 for an illustration).

As investors, while we can see the promise of NK cell transplants, we struggle with valuations of the leading biotechs in this field (e.g. Fate Therapeutics' current valuation of US\$5.6 billion). Whereas we feel that Innate is an expert in NK cells and with a valuation of US\$460 million, represents much better value.

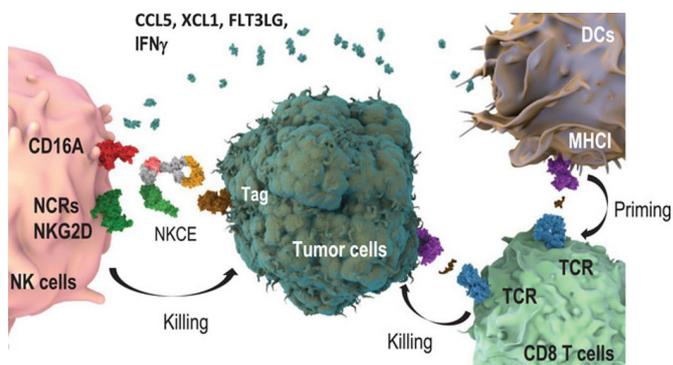
² The European Society for Medical Oncology is the leading professional organisation for medical oncology. It comprises 25,000 members representing oncology professionals from over 160 countries worldwide. ESMO is the society of reference for oncology education and information. Source: ESMO.

Outlook

On the last day of the quarter, US Merck announced it will acquire **Acceleron** (a holding in the Fund) for US\$11.5 billion in cash. Merck will gain access to royalties from Luspatercept (used to treat anaemia) and Sotatercept, a drug in phase 3 trials for pulmonary hypertension. In the coming year, we expect to see more such acquisitions, not only from pharma companies but also in the life science tool space.

Private biotechs continue to flourish, albeit we are getting lost in the many CRISPR enzyme companies that are emerging, but overall, innovation continues unabated. New listings on the stock market continue as well, however, the premiums to cross-over rounds (i.e. the final pre-IPO price) are not as significant as they have been. In addition, new listings no longer show stellar performance either. Within biotech, exuberance and neglect always coexist, allowing us to find good investment opportunities for the long term.

Fig. 1: Innate's Antibody-Based Natural Killer Cell Engager, NKCE



Source: <https://onlinelibrary.wiley.com/doi/10.1002/eji.202048953>

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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