

Platinum International Health Sciences Fund



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Portfolio Manager

Overview

- This quarter our holdings **Zealand Pharma** (up over 80%) and **Wave Life Sciences** (up 22%) reported progress with their next generation obesity assets. Their share prices responded positively.
- We added **Apogee** – a US biotech – to the portfolio last year. This company aims to reduce the injection burden for anti-inflammatory antibodies by extending the half-life of its antibodies. Both the early pre-clinical data and the team behind the company were appealing to us, hence we invested at the IPO. This quarter Apogee announced positive human data confirming 3-6 months dosing. Performance has been exceptional (it rose over 130% in the past quarter) and we trimmed our holding.
- Looking forward, the second quarter of the year will feature more medical meetings for the Platinum Health Sciences team and we will carefully watch some obesity outcome trials.
- We're in a much more positive funding environment today. We expect the move towards alliances, partnerships and M&A to continue as large companies look for nimbler partners to help them innovate.

Performance

compound p.a.⁺, to 31 March 2024

	QUARTER	1YR	3YRS	5YRS	SINCE INCEPTION
Platinum Int'l HS Fund*	12%	27%	-1%	9%	10%
MSCI AC World HC Index [^]	12%	16%	12%	12%	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.

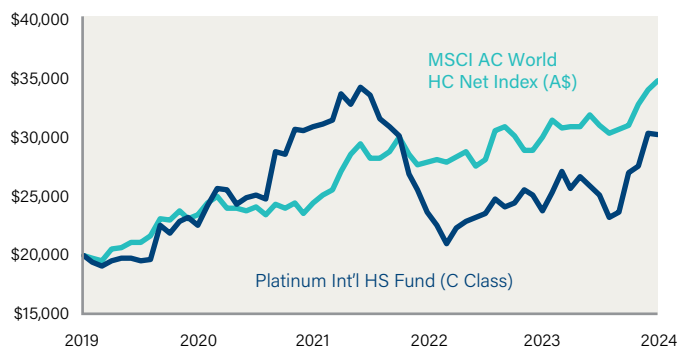
[^] Index returns are those of the MSCI All Country World Health Care Net Index in AUD. Source: Platinum Investment Management Limited, FactSet Research Systems.

Historical performance is not a reliable indicator of future performance.

See note 1, page 5. Numerical figures have been subject to rounding.

Value of \$20,000 invested over five years

31 March 2019 to 31 March 2024



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 5.

During the quarter, publicly listed biotech companies raised significant capital via follow on offerings, IPOs and so called PIPEs (private investment in public equity), which are akin to private syndicated capital raises but for a listed company. Over \$18 billion was raised – a stellar number. Similarly, private US biotech companies enjoyed a healthy funding environment (raising over \$3 billion) therefore allowing companies to mature prior to listing. This is in stark contrast to a year ago when the Silicon Valley Bank collapse forced many biotechs to restructure and reassess their business models.

For biomanufacturing and tool companies, the US Government's desire to reduce the dependency on China and other countries (via the Biosecure Act) is causing uncertainty. It remains to be seen how this situation evolves but company executives may need to diversify their manufacturing base and are considering all outcomes.

Obesity and radioligand therapeutics remain a key focal point. As we anticipated, the obesity/metabolic disease treatment landscape is evolving with new entrants and combination therapies emerging. In the radiotherapy space consolidation continues with pharma companies looking to add modality technologies.

Movement in our portfolio

This quarter Novartis acquired **Morphosys** – a holding in the Fund. Morphosys is a German biotech founded in 1992 on the basis of its phage display technology. The company was one of the key antibody partners in the early days of biotech. It did have to pivot however, given antibody design became mainstream. Morphosys acquired Constellation Pharma in 2021 gaining pelabresib, a BET inhibitor for myelofibrosis. This drug, now close to approval, attracted us to re-invest last year and this quarter sealed the deal with Novartis.

Our holding **Inhibrx** is also being acquired. This is an interesting deal structure as Sanofi is acquiring the lead therapy, an AAT-Fc fusion protein¹ for the treatment of AATD (alpha-1 antitrypsin deficiency²), while spinning out the Inhibrx oncology portfolio into a new company. Sanofi will hold an 8% stake in the new entity. Our main investment objective was the AAT-Fc fusion protein given its superior efficacy and dosing schedule compared to the current standard of care.

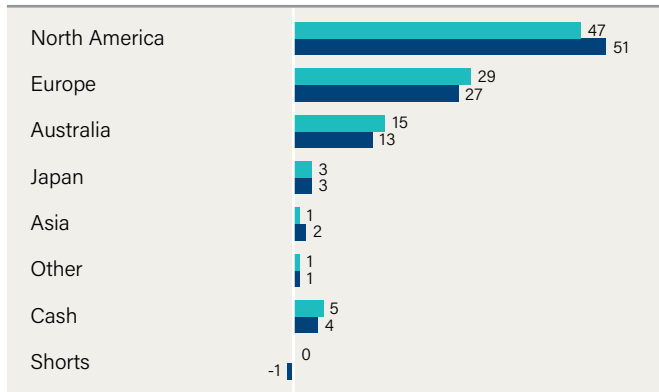
This quarter our holdings, **Zealand Pharma** (up over 80%) and **Wave Life Sciences** (up 22%) reported progress with their next generation obesity assets. Zealand Pharma, with its partner Boehringer Ingelheim, announced positive results for survoteide (a Glucagon/GLP-1 dual receptor agonist) in patients with liver disease due to MASH.³ This is an important dataset as it suggests the drug can differentiate itself from other first generation obesity drugs. Zealand Pharma is also garnering a lot more attention given its proprietary pipeline in metabolic disease and particularly Petrelintide, an amylin analog. We have trimmed our position this quarter given strong performance. The obesity field is evolving with next generation mechanisms emerging, including a focus on muscle mass as well as cardiovascular effects.

1 AAT-Fc fusion protein: Alpha-1-antitrypsin is a serine protease inhibitor that due to mutations is dysfunctional in AATD. Inhibrx recombinant AAT is fused to a human immunoglobulin (Ig) Fc fragment.

2 AAT deficiency: genetic disorder caused by mutations in the SERPINA1 gene leading to early onset emphysema and can also cause liver disease.

3 MASH: Metabolic dysfunction-associated steatohepatitis.

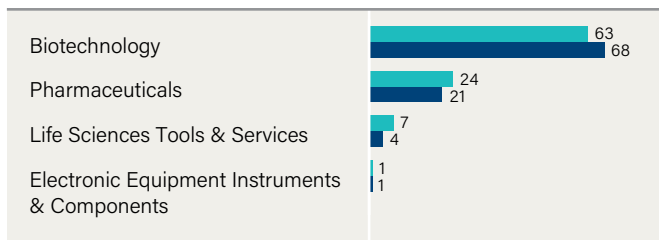
Disposition of Assets %



■ 31 MAR 2024 ■ 31 DEC 2023

See note 3, page 5. Numerical figures have been subject to rounding.
Source: Platinum Investment Management Limited.

Net Sector Exposures %



■ 31 MAR 2024 ■ 31 DEC 2023

See note 4, page 5. Numerical figures have been subject to rounding.
Source: Platinum Investment Management Limited.

Top 10 Holdings

COMPANY	COUNTRY	INDUSTRY	WEIGHT
SpeeDx Pty Ltd	Australia	Biotechnology	6.9%
Zealand Pharma A/S	Denmark	Biotechnology	3.8%
Apogee Therapeutics Inc	US	Biotechnology	3.6%
Exscientia Plc	UK	Biotechnology	3.2%
Sanofi SA	US	Pharmaceuticals	2.7%
Takeda Pharmaceutical Co	Japan	Pharmaceuticals	2.7%
Bicycle Therapeutics PLC	UK	Biotechnology	2.7%
Roche Holding AG	US	Pharmaceuticals	2.6%
Telix Pharmaceuticals Ltd	Australia	Biotechnology	2.6%
UCB SA	Belgium	Pharmaceuticals	2.5%

As at 31 March 2024. See note 5, page 5.
Source: Platinum Investment Management Limited.

Wave Life Sciences, a genomic medicine company we have owned for some time due to their expertise in antisense and RNAi technologies, has announced its clinical small interfering RNA (siRNA) targeting the Inhibin betaE (INHBE) protein. INHBE is a promising target given its genetic validation. People with a loss of function mutation in INHBE have reduced abdominal obesity and a lower risk of type 2 diabetes and coronary artery disease. The aim of an INHBE siRNA is to achieve healthy weight loss but be muscle sparing while at the same time allow for 1-2x a year dosing.

Apogee is a US biotech we added to the portfolio last year. This company has set out to reduce the injection burden for anti-inflammatory antibodies by extending the half-life of its antibodies. Both the early pre-clinical data and the team behind the company were appealing to us, hence we invested at the IPO. This quarter Apogee has announced positive human data confirming 3-6 months dosing. Performance has been exceptional (it rose over 130% in the past quarter) and we trimmed our holding.

Kidney disease is an area seeing progress, and IgAN (IgA nephropathy) is getting a lot of attention. **Vera Therapeutics**, one of our holdings, reported strong data for atacicept that showed disease modifying efficacy, stabilising a key marker for kidney function (eGFR). Given strong performance following the data we trimmed our holding.

UCB, our Belgium biotech holding, performed well (up over 40%) following the successful launch of bimekizumab in the US. We have long been believers in this product given its deep and fast effect in psoriasis as well as psoriatic arthritis.

Our Oxford based biotechs disappointed. **Oxford Nanopore** (down 40%) reduced guidance for its sequencing products, while **Exscientia** fired its CEO/Founder due to inappropriate behavior. We were pleased Exscientia dealt with the issue decisively. We feel the company has a deep bench and the business will be able to move on. We added to our position.

During the quarter we increased our weighting in **Roche** as we believe the company will be able to build a metabolic disease franchise.

Commentary – top guns in biotech?

In February we travelled to San Diego to visit biotech companies and join an investor bus trip – akin to a school excursion for adults talking science and biotech. Engaging with other investors adds valuable perspective. The mood was upbeat given the sector's healthy fundraising environment and the fact that corporate deals are getting done at solid valuations.

San Diego is a thriving biotech hub similar to Boston – but with a lot more space. For a Top Gun fan it has fighter jets flying above and at times interrupting meetings! Pharma companies like the area as it has strong academic research and well-known Institutes. Two recent Fund holdings that have been acquired at healthy premia – **Prometheus Biosciences** and **Rayzebio** – are from San Diego.

We visited private and public companies covering obesity, rare disease, oncology and kidney disease as well as different therapeutic modalities (RNAi, small molecules, radiotherapies, ADCs). Visiting private companies is essential for keeping abreast with the industry and gathering competitive intelligence.

Many private companies are at the forefront of next generation therapeutics and must be included in any due diligence. **Recludix** is an example. This company is of interest to us given its expertise in protein-protein interaction, its chemistry expertise and the fact that Recludix negotiated a deal with Sanofi whereby Sanofi parted with \$125 million upfront for a preclinical asset. This company should be on anyone's radar when looking at inflammatory diseases. Its expertise in targeting the Src homology 2 (SH2) domain of signaling proteins is rare to find. The SH2 domain of a protein is crucial in mediating signals from the outside to the inside of a cell. It has long been classified as an undruggable target given many proteins share this domain and inhibitors need to be very specific.

Through assay development and new chemical approaches Recludix has identified potent SH2 inhibitors for STAT (Signal Transducer and Activator of Transcription) proteins. STATs are key molecules in the inflammatory process and hence ideal targets. Early preclinical data so far indicates that Recludix has molecules that are highly competitive – and pretty unique. We have seen large deals by pharma to access similar types of molecules that are less exciting.

Outlook

The Biosecure Act will remain a focus over the coming months, as will the upcoming elections. IPOs in the space remain mixed but are important to watch carefully. The second quarter of the year will feature more medical meetings for the Platinum Health Sciences team and we will see more obesity outcome trials read out. As always we expect alliances, partnerships and M&A to continue in this space given the need for large companies to embrace innovation.

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. Country classifications for securities reflect Bloomberg's "country of risk" designations. "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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