Platinum International Health Sciences Fund

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Overview

- It was a difficult quarter in the Health Sciences space with subdued M&A activity and some disappointing clinical dataset releases. However, we believe that as the regulatory picture becomes clearer in the US, firms will be better able to plan and invest in 2025.
- The Chinese biotech industry is rapidly churning out new molecules. Whilst Chinese firms lack the patient capital required to complete a full development program, they are helping international companies to more quickly gain access to clinical stage assets.

Performance

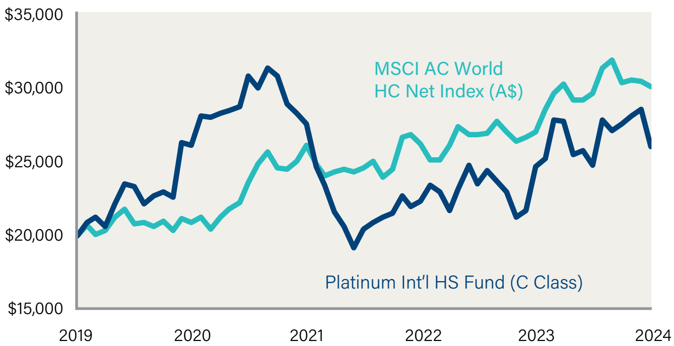
compound p.a.+, to 31 December 2024

	QUARTER	1YR	3YRS	5YRS	SINCE INCEPTION
Platinum Int'l HS Fund*	-5%	6%	-2%	5%	9%
MSCI AC World HC Index^	-1%	11%	5%	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 5. Numerical figures have been subject to rounding.

Value of $20,000 invested over five years

31 December 2019 to 31 December 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.

This quarter was challenging for the healthcare and biotech sectors – and the Fund. In November the US election (which led to the nomination of Robert F. Kennedy as Health Secretary) put a temporary stop to the gradual recovery of the biotech sector. To make matters worse, a number of clinical datasets disappointed. Meanwhile M&A activity remains subdued. As we explain below, licensing deals dominated instead.

The spread between the healthcare index (XLV) and the S&P500 continues to widen. It is now sitting at a 15-year low. The Healthcare weighting in the S&P500 is also the lowest it has been in 24 years and the divergence between the Biotech and Tech indices continued to grow this year. In the biotech subsectors gene editing and gene therapy companies performed the worst. One would think we have cured all diseases! Far from it.

A number of our holdings had to terminate mid-stage clinical trials due to emerging safety issues (e.g. **Bioage** and **Keros**) while other biotech holdings reported disappointing clinical data when testing new drugs for new therapeutic targets (**Anaptys**, **Q32** and **Percheron**). We exited all these investments and will potentially revisit them at a later time.

On positive news, **Syntara**, an Australian biotech, presented encouraging early stage clinical results for its Lysyl oxidase inhibitor (SNT-5505) in myelofibrosis (bone marrow cancer) patients who continue to have symptoms despite current standard of care (SOC). Syntara showed that adding SNT-5505 to SOC results in symptom improvement and reduction in spleen volume, two hallmarks clinicians are interested in. This efficacy continues to improve over time, while the drug's safety profile is encouraging. We believe this data signals that Syntara has a viable drug and hence supported the recent capital raising.

Imricor, an ASX-listed US medical device company aiming to make MRI-guided cardiac ablation a reality is, step-by-step, expanding its partner and hospital network ahead of regulatory approval this year. As with Syntara, we supported Imricor's recent capital raise given the progress the company has made and its current valuation.

Commentary – drug discovery made in China

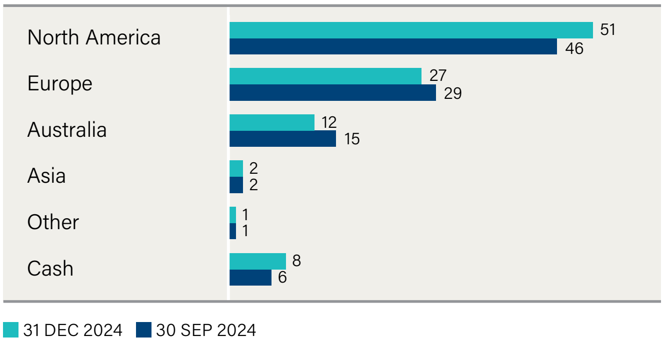
The pace of change in the drug development industry is now akin to the 80s when high throughput screening revolutionised drug discovery. We are in an era where companies cannot simply maintain the status quo given pricing pressure and advances in protein engineering and computer science. Another factor is the maturing of the Chinese biotech industry which is churning out new molecules – particularly antibodies – seemingly overnight.

Today in biotech land many companies work on the same drug target ("crowding") with differentiation (if any) only fully visible during clinical development. Speed to the clinic is vital as is smart clinical development, particularly in areas such as lung cancer and inflammatory disease. We've lost count of how many PD1[1] assets had been in development. Yet it is Keytruda who continues to dominate the immuno oncology (IO) market.

Pharma companies and cashed up biotechs are in some ways spoiled for choice when it comes to licensing opportunities. However, there is a persistent fear of setbacks, a tough commercial outlook and sellers' valuation expectations may be too high. Immune oncology has been particularly difficult and after ten years we continue to wait for another successful checkpoint asset.

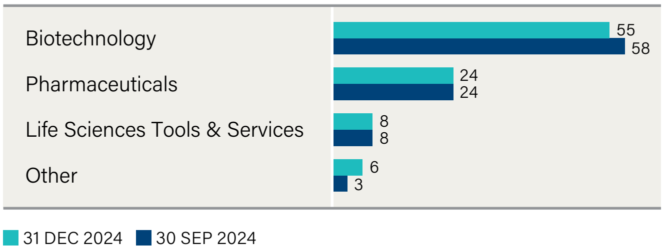
1 Immunotherapeutic agents that are used to treat different tumour types.

Disposition of Assets %



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

Net Sector Exposures %



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

Top 10 Holdings

COMPANY	COUNTRY	INDUSTRY	WEIGHT
Pharmaxis Ltd	Australia	Pharmaceuticals	5.7%
Imricor Medical Systems Inc	US	Health Care Equipment & Supplies	4.3%
Roche Holding AG	US	Pharmaceuticals	3.6%
Oxford Nanopore Technologies	UK	Life Sciences Tools & Services	3.6%
Sanofi SA	US	Pharmaceuticals	3.4%
Roivant Sciences Ltd	US	Biotechnology	3.1%
Centessa Pharmaceuticals PLC	US	Biotechnology	3.1%
Zealand Pharma A/S	Denmark	Biotechnology	2.9%
SpeeDx Pty Ltd	Australia	Biotechnology	2.7%
Johnson & Johnson	US	Pharmaceuticals	2.6%

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

More and more companies are turning to China to license assets. In the space of a week, two of our holdings, **Roche** and **Ideaya**, each licenced a phase 1 DLL3-ADC from Chinese biotechs. Ideaya paid $75m upfront to Hengrui Pharma, while Roche paid Innovent $80m.

Meanwhile **Merck**, in quick succession licensed a preclinical oral GLP1 receptor agonist *and* a PD1/VEGF bispecific from Chinese companies. It spent $700m upfront. This is pocket change for Merck but it means it hedges its bets if the PD1/VEGF bispecific target turns out to be the next great IO therapy.[2]

Companies in China have an army of scientists rapidly engineering molecules for the West at reduced cost. That is not a new concept but what has matured is the scale and clinical data packages that are now available. The challenge that Chinese biotech companies face is a lack of patient investors to provide the capital to complete a full global development program. International pharma is one option for funding. US VC firms are the other. These biotech specialist firms form a US company around Chinese assets, hire well-versed drug developers and form a funding syndicate to accelerate clinical development.

In a nutshell, competition in drug discovery has increased a notch. As anticipated some years ago, China is now providing pipeline assets at a fast rate, often with clinical trial data attached given the speed of starting clinical development. However, it remains to be seen how well these assets are optimised in terms of doses and pharmacokinetics once larger, global clinical trials are done. At this stage China is helping companies to more quickly gain access to clinical stage assets (US company Merck is one example).

For pharma the capital allocation questions becomes even more important given all these licensing opportunities. Take Merck, again, as an example. They have been beavering away in their own labs as well as via myriad partnerships to come up with a Keytruda successor. When Akeso/Summits data became available Merck rapidly pounced and licenced its own PD-1/VEGF. This leads Merck – and others – to the strategic question. "How much capital and focus should be allocated to internal versus external opportunities?"

For US and EU biotechs, ignoring the changing dynamics is not an option. Firstly, speed to the clinic is so important. The underlying quality of the asset and the speed of manufacturing scale-up are crucial as well. And of course, there is the opportunity for new therapeutic targets. The risk profile is higher there – but it is still an important consideration.

2 Earlier this year Ivonescimab, a PD1/VEGF tetravalent bispecific from Chinese biotech Akeso showed better progression free survival as a monotherapy versus Keytruda in first line Chinese lung cancer patients. This is interesting data but confirmation in a global trial in combination with chemo versus Keytruda and chemo alone is required to really challenge Keytruda.

Giving away the pharma?

For Chinese biotechs we wonder what will happen in years to come when some realise they have licensed out their most valuable asset. It is hard to envisage a wave of Western companies acquiring Chinese biotechs.

In our work we are looking at how efficient companies are and how thoughtful their clinical development is. There is lots of work going on using computer science together with wet labs to decipher biology (find new targets) and automate drug synthesis as well as drug testing. If linked to machine learning this should speed up and enhance efficiency. The merger of **Recursion** and **Excscientia** (two of our holdings) was a logical one, albeit the upfront investment required to get everything set up and to build the foundation was very significant.

Absci – another of our holdings – focuses on antibody design, reducing timelines and cost by again combining wetlabs and computer science. AstraZeneca and Merck have partnered with Absci and in the next 18 months we should see clinical data. In further positive news for the company, it recently announced that Advanced Micro Devices is investing USD20 million into Absci to collaborate on AI-driven drug discovery.

Outlook

Post-election, the regulatory environment in the US should become more certain and this will allow companies to plan and deploy capital.

Weight management continues to be of interest and we expect dealmaking in this sector to pick up. This will be accompanied by more debate on pricing and by more segmentation of the market.

There are a number of new product launches we are watching closely. Many private biotech companies are now considering going public.

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.

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