Platinum International Health Care Fund

Bianca Ogden Portfolio Manager

Disposition of Assets

REGION	SEP 2016	JUN 2016	SEP 2015
Europe	41%	42%	36%
North America	39%	32%	25%
Australia	3%	1%	1%
Japan	3%	3%	3%
Asia	0%	0%	3%
Cash	14%	22%	32%
Shorts	<1%	<1%	-1%

Source: Platinum. Refer to note 3, page 4.

Top 10 Holdings

STOCK	COUNTRY	INDUSTRY	WEIGHT
AstraZeneca Plc	UK	Health Equip & Services	4.1%
Sanofi SA	France	Pharmaceuticals	4.0%
Ipsen SA	France	Pharmaceuticals	3.2%
Qiagen NV	Germany	Health Equip & Services	3.1%
Roche Holding AG	Switzerland	Pharmaceuticals	2.9%
Johnson & Johnson	USA	Pharmaceuticals	2.6%
Gilead Sciences Inc	USA	Biotechnology	2.4%
PerkinElmer Inc	USA	Health Equip & Services	2.2%
Foundation Medicine	USA	Health Equip & Services	2.1%
Aerie Pharmaceutical	USA	Pharmaceuticals	2.1%

Source: Platinum. Refer to note 4, page 4.

For further details of the Fund's invested positions, including country and industry breakdowns as well as currency exposures, updated monthly, please visit https://www.platinum.com.au/fund-updates/#MonthlyUpdatesForThePlatinumTrustFunds.

Performance and Changes to the Portfolio

(compound pa, to 30 September 2016)

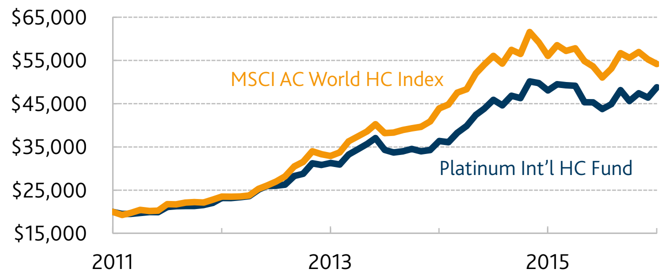
	QUARTER	1YR	3YRS	5YRS	SINCE INCEPTION
Platinum Int'l HC Fund	7%	2%	16%	20%	9%
MSCI AC World HC Index	-3%	-3%	18%	22%	9%

Source: Platinum and MSCI. Refer to note 1, page 4.

Our decision over the past six months to increase our exposure to small and mid cap biotechs, rather than adding more established large cap names, has contributed significantly to our performance. The past three years have seen many new biotech listings which reminded us of the years following the genome excitement in 2000. That was the right time to refresh the portfolio with new seeds and that is exactly what we have done (and continue to do): adding to existing holdings in companies that are making great progress in establishing themselves commercially, while also adding at good valuations new companies with interesting technology and assets that have shown promising results.

Value of $20,000 Invested Over Five Years

30 September 2011 to 30 September 2016



Source: Platinum and MSCI. Refer to note 2, page 4.

These types of companies are the lifeblood of the industry and innovation today is as strong as it has ever been (please see our recent Regional Roadshow presentation – The Future of Healthcare on our website), thus offering great opportunities to get involved over the coming years. Consolidation within the sector is a major theme and we have seen some activity, albeit mostly driven by one company: Allergan. Immuno-oncology remains a focus not only for drug developers, but also for tool companies offering products that help characterise the tumour and its environment in detail. This is a new era for oncology, offering many opportunities beyond the approved PD-1 and PD-L1 inhibitors.[1]

We had data for Bristol-Myers' Opdivo and Merck's Keytruda, two PD-1 inhibitors being tested for front-line treatment of lung cancer (the Fund holds a small position in Merck). Merck is focused on tumours expressing high levels of the biomarker PD-L1, while Bristol-Myers tested its drug on a wider range of expression levels. Keytruda succeeded, whereas Opdivo did not. This is a good example for why precision medicine is paramount. Knowing your "cancer" will be ever more important, and so we have been adding to companies that do just that – providing the tools for analysing tumour micro-environment.

Sanofi continues to struggle and was significantly outbid by Pfizer which was prepared to pay over 30% more for Medivation. Furthermore, Pfizer was happy to pay the full price upfront rather than use a contingent value right to allow for future milestone payments once the pipeline progresses. It clearly showed that there are some deep pockets around and that companies are not afraid to use their cash.

While it is a loss to Sanofi, we do support their more disciplined approach and expect deals in the future. For Sanofi the focus has returned to its Lantus franchise in the US. Here, competitive bidding for formulary positions at pharmacy benefit managers (PBMs) is fierce,[2] and the degree of uncertainty high. The diabetes landscape in the US has changed significantly and commercial acumen is now almost more important than the drug itself. Sanofi's earnings will remain under pressure, but current valuation accounts for that.

Some of our biotech holdings have been particularly strong. Companies with a commercial product along with respectable sales infrastructure are in high demand. Ariad (up 85% for the quarter) and Seattle Genetics (up 34% for the quarter) both fall into that group and for both companies pipeline assets are progressing as well.

We also had a positive data read from the late stage testing for Aerie Pharmaceuticals' glaucoma drops, setting the company for partnership discussions as well as getting ready for product launch. Aerie's stock price jumped 114% over the quarter.

Danish biotech Lundbeck on the other hand reported phase 3 trial failure for its Alzheimer's drug (stock was down 13% for the quarter). While this is disappointing, our investment case for Lundbeck was based on the launch of its schizophrenia and depression drugs along with a focus on changing the company's cost structure. This is happening as planned.

Commentary

While years ago it was enough to have a great drug that gained approval, today this is just the "middle of the game", as Michael Rosenblatt (ex-Chief Medical Officer of Merck) recently said in an interview. Drug development has changed significantly over the past ten years. Companies now not only have to convince physicians that the drug has value, but also have to make sure that payers and patients are on board. To achieve that, commercial thinking has to be applied at the pre-clinical stage. This means input is required from manufacturing and marketing experts as well as reimbursement specialists (and here one has to consider different jurisdictions) and late stage clinical development scientists.

This is a big ask for a small biotech that has to manage a very tight budget. Consequently, we believe that a biotech that has managed to establish itself commercially deserves respect.

Ariad is such a company, and we have held it in the Fund for some time. Along the way we trimmed and added, but overall we believed in the bones of the company. This company has experienced the ups and downs of being a biotech and has come out on the other side. Often these are the companies with stamina.

1 Programmed cell death protein 1, also known as PD-1, is a cell surface receptor that functions as a "brake", down-regulating the immune system. Its ligand or binding partner in crime is PD-L1.

2 PBMs are third party administrators of prescription drug programs in the US. They are primarily responsible for developing and maintaining the formulary (i.e. a list of drugs approved for prescription under health plans administered by that PBM), contracting with pharmacies, negotiating discounts and rebates with drug manufacturers, and processing and paying prescription drug claims.

Not only has Ariad built a US and EU commercial framework, it also had to deal with a temporary suspension of its only marketed product. Today the company is back on track, the "issue" drug back on the market and its pipeline progressing towards approval. It has not been an easy journey and some management changes were necessary, but the company never changed its core scientific focus. Its key scientist has been with the company for over 20 years.

Ariad is based in Cambridge, Massachusetts and focuses on particular enzymes called kinases. These kinases do not function properly in cancer cells, often due to genetic mutations. Many drug developers have worked on these enzymes, but over time these kinases mutate again and become resistant to the drug. This is when Ariad's R&D expertise comes in with its rationally-designed drugs. Ariad makes sure that its drugs hit the right "mutation" spot of the kinase and as a consequence allow for a deeper response.

Ponatinib was Ariad's first drug which gained approval in December 2012 for chronic myeloid leukaemia (CML) patients who are intolerant or resistant to available therapies due to a particular genetic mutation. Ariad had big plans for the drug, looking to expand its indication to treat newly diagnosed CML patients and hoping to show that Ponatinib is better than available therapies for these patients. Clinical trials were set up with the commercial setting in mind, with the drug being compared to the gold standard Gleevec. However, side effects (thrombotic events) derailed those plans and the drug was temporarily withdrawn in the US in October 2013 (but not in the EU). Not only was this a significant setback for a small company, it also demanded a lot of difficult decision-making, extensive documentation and a forward strategy. Patients that were doing well on the drug were devastated and needed to continue taking the drug. Ariad managed all that and the drug returned to the market two months later.

Today, issues relating to the side effects of Ponatinib are well understood and doctors know how to use the drug. It is a powerful drug, even at low dosage. The thrombotic events appear to be more prevalent in patients with a predisposition, thus careful risk assessment of the patient is now standard. Ponatinib does have a future and Ariad's persistence should pay off with the drug moving into the second-line setting (trials are currently underway).

But Ariad is not only about Ponatinib. Its scientists have also worked hard on drug resistance in lung cancer. Brigatinib (an ALK inhibitor) is awaiting approval for ALK+ lung cancer patients who are resistant to available therapy. Brigatinib is also being studied in front-line ALK+ lung cancer treatment as compared to available therapy. Brigatinib is another powerful drug that is showing signs of being able to tackle brain metastasis more efficiently. Finally, there is AP32788 coming through for a different subset of lung cancer patients.

This company is back on its feet and indeed in much better shape. Recently, it sold its EU operations to Incyte who also licensed Ponatinib for EU territories, giving Ariad a royalty stream. This has added to Ariad's balance sheet which helps to put the company in good stead for the Brigatinib launch next year.

Ariad is a US$2.8 billion company with annual sales of about US$210 million and US$25 million in royalties from next year. This purely reflects the sale of Ponatinib in late line treatment of CML patients and some sales in later lines of ALK+ lung cancer therapy. There is a lot more to come and in today's world of companies looking for commercial assets, Ariad will not be unnoticed. While we have trimmed our position given the recent strong share price performance, we remain invested in Ariad as it is a company that has all the ingredients to become a real success.

Outlook

Smaller biotechs have gotten a little bit ahead of themselves in terms of valuation, so we will remain disciplined and trim our positions at times. However, biotechs remain the life blood of the industry and we will continue to add new ideas to the Fund. Allergy is an area we are exploring, as is robotics in surgery.

The pricing debate will continue, but we believe that increased scrutiny on other participants and stakeholders of the system will spread the heat from drug developers.

Notes

1. The investment returns are calculated using the relevant Fund's unit price and represent the combined income and capital return for the specified period. They are net of fees and costs (excluding the buy-sell spread and any investment performance fee payable), are pre-tax, and assume the reinvestment of distributions. The investment returns shown are historical and no warranty can be given for future performance. You should be aware that historical performance is not a reliable indicator of future performance. Due to the volatility in the underlying assets of the Funds and other risk factors associated with investing, investment returns can be negative (particularly in the short-term).

   The inception dates for each Fund are as follows:

   Platinum International Fund: 30 April 1995
   Platinum Unhedged Fund: 28 January 2005
   Platinum Asia Fund: 4 March 2003
   Platinum European Fund: 30 June 1998
   Platinum Japan Fund: 30 June 1998
   Platinum International Brands Fund: 18 May 2000
   Platinum International Health Care Fund: 10 November 2003
   Platinum International Technology Fund: 18 May 2000

   (NB: The gross MSCI Index was used prior to 31 December 1998 as the net MSCI Index did not exist.)

2. The investment returns depicted in this graph are cumulative on A$20,000 invested in the relevant Fund over the specified five year period relative to the relevant benchmark index (in A$) as per below (the "Index"):

   Platinum International Fund - MSCI All Country World Net Index
   Platinum Unhedged Fund - MSCI All Country World Net Index
   Platinum Asia Fund - MSCI All Country Asia ex Japan Net Index
   Platinum European Fund - MSCI All Country Europe Net Index
   Platinum Japan Fund - MSCI Japan Net Index
   Platinum International Brands Fund - MSCI All Country World Net Index
   Platinum International Health Care Fund - MSCI All Country World Health Care Net Index
   Platinum International Technology Fund - MSCI All Country World Information Technology Net Index

   The investment returns are calculated using the relevant Fund's unit price. They are net of fees and costs (excluding the buy-sell spread and any investment performance fee payable), pre-tax and assume the reinvestment of distributions. It should be noted that Platinum does not invest by reference to the weightings of the Index. Underlying assets are chosen through Platinum's individual stock selection process and as a result holdings will vary considerably to the make-up of the Index. The Index is provided as a reference only.

3. Regional exposures (i.e. the positions listed other than "cash" and "shorts") represent any and all physical holdings, long derivatives (stock and index), and fixed income securities.
4. The table shows the relevant Fund's top ten long stock positions. Long derivative exposures are included. However, short derivative exposures are not.

Disclaimer

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