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4 April 2018

**Australia**  
**Healthcare**

## Pharma M&A increasing – who’s next in Oz?

### Positive catalysts for ongoing M&A activity in the pharma sector

We believe there are a number of positive catalysts for ongoing pharma/biotech M&A activity in the near term. These include: 1) increasing cost of pharma R&D associated with fewer new drug successes per dollar of R&D spent; and 2) recent US tax reform, leading to increased CY18 cash for big pharma. If history is any guide, then some of these increased cash balances will be used for pharma/biotech M&A. We have looked at Australian pharma/biotech companies that have the potential to operate globally should their technology be proven or if already proven, be transferred to additional geographies. These companies include: Clinuvel; Ellex; Medical Developments; Mesoblast; Nanosonics, Osprey; Pro Medicus and Telix.

### Increase in 2018 NPAT from US tax reform of at least US\$4.1bn

We believe there are a number of positive catalysts for ongoing M&A activity in the pharma sector in the near term. These include: 1) increasing cost of pharma R&D associated with fewer new drug successes per dollar of R&D spent; and 2) recent US tax reform, leading to increased CY18 cash for big pharma. We calculate an implied increase in 2018 NPAT from US tax reform of ~US\$4.1bn for the largest 11 listed pharma companies that have given 2018 tax guidance.

### Some of the increased cash will likely be used for pharma/biotech M&A

Globally, we have seen a number of acquisitions in CY18. Announced pharmaceutical and healthcare transactions have already reached about US\$156bn in CY18, according to data compiled by Bloomberg.

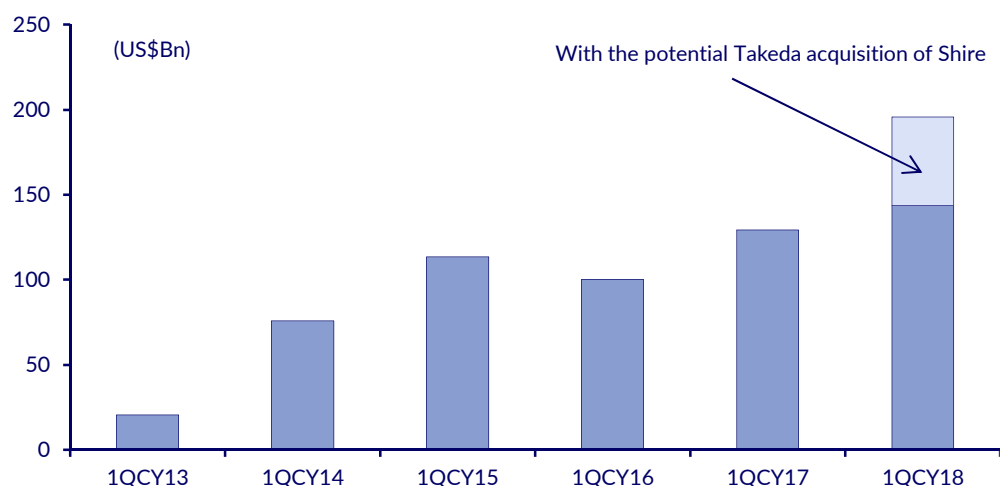
### A number of potential M&A candidates in Australia, in our view

We looked at Australian healthcare/biotech companies that have: 1) the potential to operate globally should their technology be proven to work, or 2) if already proven, be transferred to additional geographies. These include: Clinuvel; Ellex; Medical Developments; Mesoblast; Nanosonics, Osprey; Pro Medicus and Telix.

### We believe investors should be aware of the potential for further M&A

Given the reasons outlined above, more than at any time probably over the past decade, we flag the potential for further M&A in the Australian healthcare and pharmaceutical space.

Value of global healthcare transactions (1QCY13 to 1QCY18)



Source: CLSA, Bloomberg

## Pharma M&A activity increasing - who could be next in Australia?

There are a number of positive catalysts for ongoing M&A activity

Australian healthcare/biotechnology companies

Costs for pharmaceutical R&D have significantly increased over the past few decades

R&D spend in US\$m per new molecular entity (NME)

### Summary

We believe there are a number of positive catalysts for ongoing M&A activity in the pharmaceutical sector in the near term. These include: 1) increasing cost of pharma R&D, associated with fewer new drug successes per dollar of R&D spent; and 2) recent US tax reform, leading to increased CY18 cash for big pharma. We calculate an implied increase in 2018 NPAT from tax reform of ~US\$4.1bn for the largest 11 listed pharmaceutical companies that have given 2018 tax guidance.

If history is any guide, then some of the increased cash will be used for pharma/biotech M&A. Globally, we have seen a number of acquisitions in CY18. Announced pharmaceutical and healthcare transactions have already reached about US\$156bn in CY18, according to data compiled by Bloomberg.

We have looked at Australian healthcare/biotechnology companies with the potential to have global platforms, should their technology be proven to work, or, if proven, by transferred to other geographies, in our view. These companies include: Clinuvel (CUV AU); Ellex Medical (ELX AU); Medical Developments International (MVP AU); Mesoblast (MSB AU); Nanosonics (NAN AU); Osprey Medical (OSP AU); Pro Medicus (PME AU) and Telix (TLX AU).

### Positive catalysts for ongoing M&A activity in the pharma sector

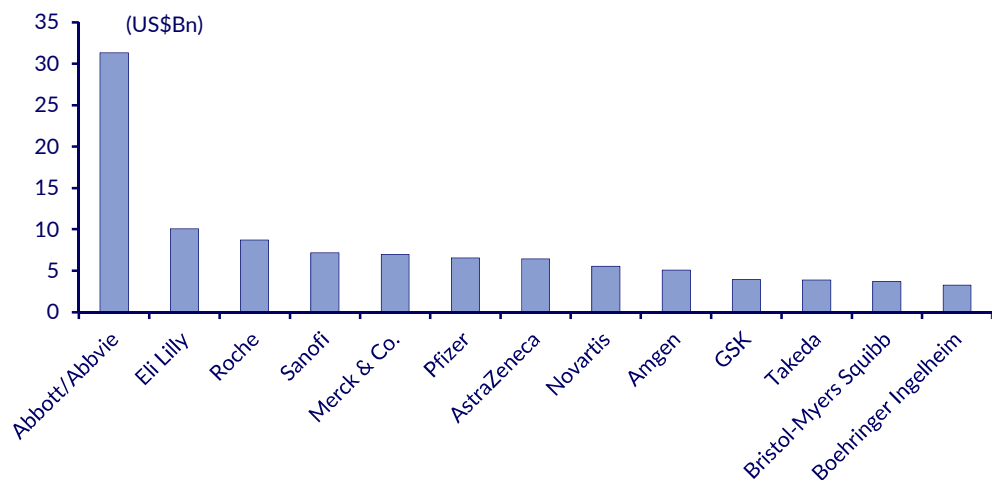
We believe there are a number of positive catalysts for ongoing M&A activity in the pharmaceutical sector in the near term. We outline these below.

#### Rising R&D cost associated with fewer new drug successes per dollar spent

The cost of pharmaceutical R&D has significantly increased over the past few decades, with an annual inflation-adjusted increase of 8.6% for the period of 1950-2009, according to Munos et al.

Figure 1

R&D spend in US\$m per new molecular entity (2006-2014)



Source: PubMed

In addition, the costs per new molecular entity (NME) were US\$250m before the 1990s; the average out-of-the-pocket costs per NME have subsequently been calculated to be US\$403m (2000s) and US\$873m (2010), respectively, according

High price per NME

A single corporate tax rate of 21% from CY18

G20 corporate tax rates

Deemed repatriation of overseas profits at a rate of 15.5% for cash and equivalents

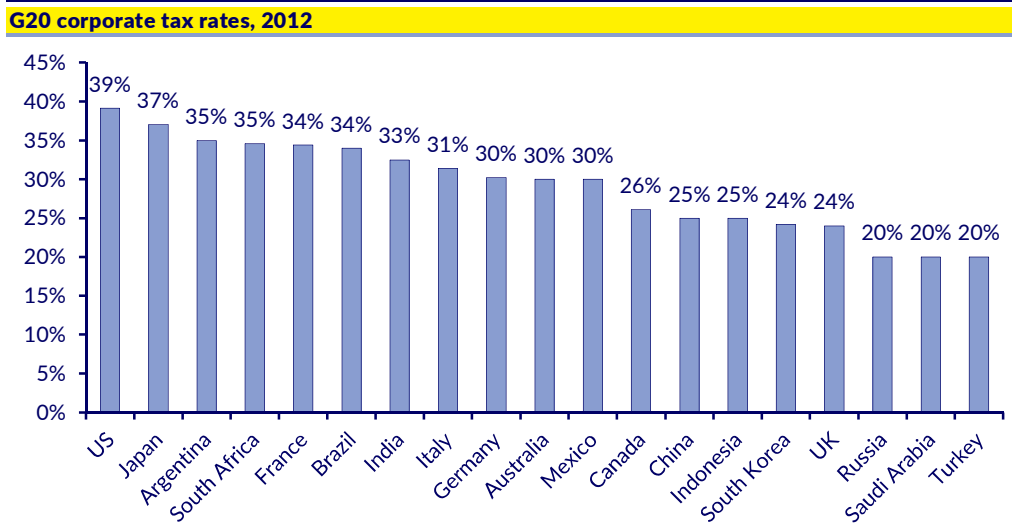
to PubMed. Furthermore, according to Schuhmacher et al, from 2006 to 2014 the average R&D expenditure per NME approved by the US FDA was ~US\$7.8bn for the largest global pharmaceutical companies.

Notwithstanding that the US is ~60% of the global pharmaceutical market, this high price per NME also places pressure on the sustainability of the global pharmaceutical companies' R&D models, in our view. Hence, these companies may increasingly be looking for acquired growth.

**US tax reforms**

US President Trump signed the *Tax Cuts and Jobs Act* into law on 22 December 2017. The US Senate passed the bill on 20 December by a party-line vote of 51 to 48. The House of Representatives passed the bill on 21 December by a vote of 224 to 201. Amongst other aspects, the law created a single corporate tax rate of 21% in CY18. The top US corporate tax rate was previously 35%.

Figure 2



Source: CLSA, US Congressional Budget Office

Combined with the average state and local taxes, the US statutory rate under the new law is 26.5%, according to the US-based Tax Foundation. Supporters of the corporate tax rate cut argue that it will reduce incentives for corporate inversions, in which companies shift their tax base to low- or no-tax jurisdictions, often through mergers with foreign firms.

In addition, the law enacted a deemed repatriation of overseas profits at a rate of 15.5% for cash and other liquid assets and 8% for illiquid assets. The law introduced a territorial tax system, under which only domestic earnings are subject to tax. Companies with over US\$500m in annual gross receipts are subject to the base erosion anti-abuse tax (BEAT), which is designed to counteract base erosion and profit shifting, a tax-planning strategy that involves moving taxable profits made in one country to another with low or no taxes. BEAT is calculated by subtracting a company's regular corporate tax liability from 10% of its taxable income, ignoring base-eroding payments. Tax credits can offset up to 80% of BEAT liabilities.

Increase in available cash

Implied cumulative increase in 2018 NPAT from tax reform of ~US\$4.1bn

We believe there will be a great deal of cash freed up by US tax reform

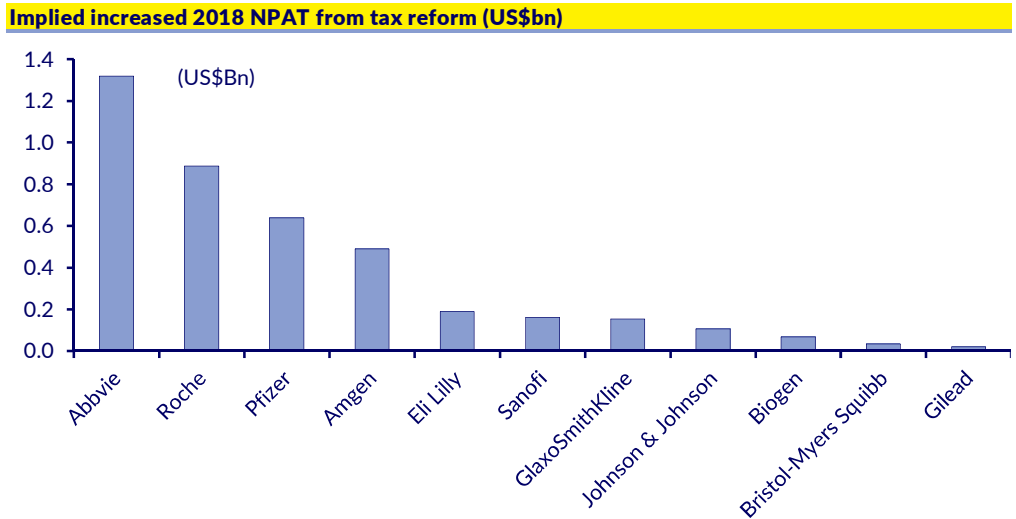
GlaxoSmithKline bought out Novartis in their consumer health joint venture for US\$13bn

Sanofi will acquire Bioverativ for an equity value of approximately US\$11.6bn

**Implications for global pharmaceutical companies**

Owing to: 1) the lower corporate tax rate of 21%; and 2) a repatriation of overseas profits taxed at 8% to 15.5%, we calculate an implied increase in 2018 NPAT from tax reform of ~US\$4.1bn for the largest 11 listed pharmaceutical companies that have given 2018 tax guidance. This is seen in the following figure and is likely to translate into an increase in available cash for these companies.

Figure 3



Source: Bloomberg, Company data, CLSA

There will also likely be an increase in 2018 NPAT for smaller pharmaceutical companies. Hence, we believe there will be a great deal of cash freed up by US tax reform for global pharmaceutical companies.

**If history is any guide, then some of the increased cash will be used for pharmaceutical M&A**

Globally, we have seen a number of acquisitions in CY18. Announced pharmaceutical and healthcare transactions have already reached about US\$156bn in 1HCY18, according to data compiled by Bloomberg. Some of the more notable larger pharmaceutical deals announced in 1HCY18 include:

- ❑ **GlaxoSmithKline:** UK drug maker GlaxoSmithKline bought out Novartis in their consumer health joint venture for US\$13bn;
- ❑ **Celgene:** US biotech Celgene acquired Juno Therapeutics for US\$9bn, and agreed to buy Impact Biomedicines for ~US\$1.1bn.
- ❑ **Sanofi:** Sanofi (SAN) and Bioverativ (BIVV, Bioverativ is the haemophilia spin out of Biogen), entered into a definitive agreement in January 2018 under which Sanofi will acquire Bioverativ for an equity value of approximately US\$11.6bn. In addition, in January 2018, SAN announced that it will acquire Ablynx for an equity value of ~US\$4.8bn.

Announced healthcare transactions have already reached about US\$156bn

Japan-based Takeda has confirmed its interest in potentially acquiring Shire

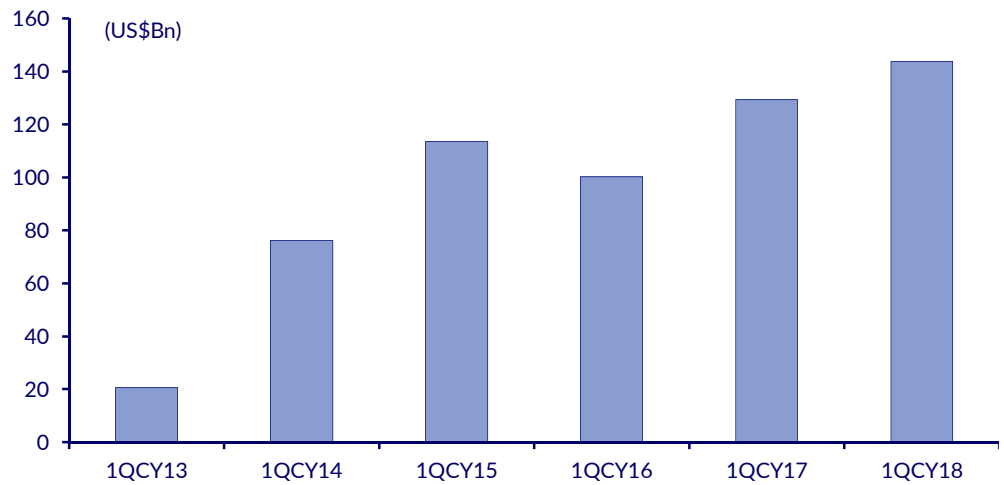
Australia has seen a number of inbound healthcare deals

Varian will acquire Sirtex

PEP will acquire LifeHealthcare

Figure 4

**Value of announced global healthcare transactions (1QCY13 to 1QCY18)**



Source: CLSA, Bloomberg

- ❑ **Astellas:** In January 2018, Astellas Pharma announced that it had completed the acquisition of Mitobridge. Astellas paid US\$225m. In addition, Mitobridge shareholders will be eligible for additional payments from Astellas that total a further US\$225m depending on the progress of various programmes in clinical development.
- ❑ **Takeda:** Japan-based Takeda has confirmed its interest in potentially acquiring Shire. Press reports suggest a price of ~US\$52bn, which implies a takeover multiple for Shire of 7.8x CY18 EV/Ebitda and 11.1x CY18 PE (based on Bloomberg consensus estimates).
- ❑ **Procter & Gamble:** CNBC recently reported that Procter & Gamble was potentially interested in acquiring Pfizer's consumer health business. Pfizer put this division up for sale in October 2017.

**Australia has seen a number of inbound healthcare deals**

In Australia, in 1QCY18 Sirtex, Viralytics, LifeHealthcare and RHS have announced they will be acquired:

- ❑ **Sirtex:** In January 2018, SRX announced that it entered into a binding Scheme Implementation Deed with Varian under which Varian will acquire Sirtex by way of a Scheme of Arrangement for A\$28 per share in cash. This valued SRX at ~A\$1.59bn (~US\$1.2bn).
- ❑ **Merck:** In February 2018, Merck announced that it will acquire Viralytics. This valued Viralytics at ~A\$502m (US\$394m).
- ❑ **LifeHealthcare Group:** In February 2018, LHC announced that it had entered into a binding Scheme Implementation Deed with Pacific Equity Partners, under which PEP will acquire LifeHealthcare by way of a Scheme of Arrangement for A\$3.75 per share in cash. The Scheme Consideration implied a fully diluted market capitalisation for LifeHealthcare of A\$179m and an enterprise value of ~A\$211m.

Fewer highly leveraged acquisitions

The median enterprise value/Ebitda multiple for buyouts of more than US\$250m was 10.5x in 4QCY17

Clinuvel is a biopharmaceutical company focused on developing drugs for the treatment of a range of severe skin disorders

- ❑ **RHS:** In February 2018, single cell genomics company RHS Ltd announced a takeover offer from PerkinElmer at A\$0.28 per share, valuing the bid at ~A\$25m.

#### **That said, what is the potential impact of an increase in interest rates?**

We believe it is likely we will see fewer highly leveraged acquisitions, including those by private equity players. The new US tax law limits interest deductibility to 30% of Ebitda until 2021 and restricts it further to 30% of Ebit thereafter.

In the US in 4QCY17, the median enterprise value/Ebitda multiple for buyouts of more than US\$250m was 10.5x. At 10.5x EV/Ebitda and with a debt-to-enterprise value of 50%, an interest rate greater than 5.7% would lead to interest expenses above 30% of Ebitda, which we believe would be a limiting factor. In a rising interest rate environment, this may cause private equity firms and their banks to rethink leveraged buyout financing structures.

Following its 20-21 March 2018 meeting, the US Federal Reserve's median interest rate projection for 2018 is 2.1%, indicating another two interest rate increases this year. The committee then expects three interest rate rises in 2019 with the federal funds rate at 2.9% by end 2019, and two interest rate rises expected in 2020 seeing rates at 3.4% by end 2020.

#### **Which Australian healthcare or biotechnology company could be next to be bid for?**

We have looked at Australian healthcare/biotech companies that have: 1) the potential to operate globally should their technology be proven to work, or 2) if already proven, have the potential for their technology to be transferred to other geographies. Note that we have not looked at healthcare services providers although these could be taken out by a global player that wants scale. We have identified those companies that we think:

- ❑ have the potential to have a global platform;
- ❑ have a better chance that their technology will work, in our view; and
- ❑ do not have an especially large market capitalisation.

These companies include (in alphabetical order):

- ❑ **Clinuvel (CUV):** Clinuvel is a biopharmaceutical company focused on developing drugs for the treatment of a range of severe skin disorders. CUV's lead compound is Scenesse (afamelanotide), a drug targeting Erythropoietic Protoporphyrin (EPP). Scenesse is a photoprotective drug; it acts by increasing the levels of melanin in the skin and shields against UV radiation (UVR) and sunlight. Scenesse is delivered via a subcutaneous dissolving implant approximately the size of a grain of rice. Erythropoietic Protoporphyrin is a rare genetic disease characterised by severe phototoxicity of skin. CUV completed Phase II and III trials in the US and Europe. Trial results showed Scenesse could reduce the severity of EPP symptoms. The drug has marketing authorisation under exceptional circumstances from the European Medicines Agency for the prevention of phototoxicity in adults with the orphan disease Erythropoietic Protoporphyrin (EPP).

ImpediMed is a company engaged in the development of bio-impedance devices

Mesoblast is a company engaged in the development of biologic products for regenerative medicine

- ❑ **Ellex Medical (ELX):** Ellex Medical Lasers is a company that engages in the development, manufacture and sale of lasers and diagnostic equipment for the treatment of eye diseases. Ellex sells ophthalmic lasers and devices that treat glaucoma, retinal disease primarily caused by diabetes, secondary cataract and vitreous opacities, as well as age-related macular degeneration. ELX sells its branded products in Japan, Australia, USA, Germany and France.
- ❑ **ImpediMed (IPD):** ImpediMed is a company engaged in the development of bio-impedance devices with a focus on medical applications for use in a variety of healthcare segments. Currently, IPD operates in two segments, which are Medical and Test & Measurement. The Medical segment is a supplier of non-invasive medical devices to two under-served markets aiding in the subclinical assessment of individuals at risk of secondary lymphoedema and the monitoring of body composition and hydration. Currently, IPD offers products under brand names such as L-Dex U400, SFB7 for Body Composition, DF50 and ImpediVET. The Test & Measurement segment is a supplier of power precision testing and measuring equipment.
- ❑ **Medical Developments International (MVP):** Medical Developments operates in three segments, being Pharmaceuticals (sale of Pentrox); Medical Devices (sale of particularly the Space Chamber and Breathy-Alert Peak-Flow meter); and Veterinary Products. MVP is the manufacturer of active molecule and inhaler analgesic from its locations in Springvale, Victoria, Australia and develops new markets and applications for Pentrox. Pentrox is a non-narcotic inhalational analgesic that is self-administered by conscious haemodynamically stable patients via the hand-held Pentrox Inhaler to provide emergency pain relief. The division sells Pentrox primarily within Australia and New Zealand, Japan, some parts of Europe, the Middle East and North America. MVP also has the Asthma Space Chamber, which universally fits all asthma and COPD medication devices.
- ❑ **Mesoblast (MSB):** Mesoblast is a company engaging in the development of biologic products for regenerative medicine. The key focus is on research and development of adult Mesenchymal Precursor Cells (MPCs), Mesenchymal Stem Cells (MSCs), Dental Pulp cells and Adipose cells. Its intellectual property covers a range of applications in key markets including the United States, Europe, Japan and China. MSB's allogeneic medicine products focus on repair of damaged tissue and modulation of inflammatory responses in conditions with significant unmet medical needs. The product candidates use its MPC or MSC platform technologies to focus on a number areas: systemic diseases of inflammation and immunity; orthopaedic diseases of the spine; cardiovascular diseases; and oncology conditions.
- ❑ **Nanosonics (NAN AU):** Nanosonics is involved in the manufacturing and distribution of the Trophon EPR ultrasound probe disinfectant and its associated consumables and accessories. It is also involved in research, development and commercialisation of infection control and decontamination products and related technologies. NAN is headquartered in Sydney, Australia with offices in the USA (Nanosonics Inc) and Europe (Nanosonics Europe GmbH). NAN commercialises Trophon EPR as its first fully automated system for disinfecting ultrasound probes.

Osprey is a medical device company focused on protecting patients from the harmful effects of X-ray dye

Telix's principal activity is molecularly targeted radiation (MTR) products

- **Osprey Medical (OSP):** Osprey is a medical device company focused on protecting patients from the harmful effects of X-ray dye (contrast) used during commonly performed angiographic imaging procedures. The company currently has two products – the Avert system and DyeVert system. The Avert System reduces and monitors the amount of contrast dye used in commonly performed heart and peripheral vascular procedures. The DyeVert System is a self-adjusting product that reduces the amount of contrast dye used in commonly performed heart and peripheral procedures. DyeVert interfaces with standard syringe-manifold systems. Both the Avert and the DyeVert aid the physician in achieving the current medical guidelines established for minimising dye volume in patients at risk for kidney injury.
- **Pro Medicus (PME):** Pro Medicus is an imaging IT provider. The company provides a range of radiology IT software and services to hospitals, imaging centres and healthcare groups worldwide. The company offers a suite of radiology information system (RIS), picture archiving and communication system (PACS) and e-health solutions constituting a comprehensive end-to-end offering in radiology. Pro Medicus offers software applications and services designed to aid the management of medical practices. The software includes medical accounting, clinical reporting, appointments/scheduling and marketing/management information modules and can be integrated with third-party applications.
- **Telix (TLX):** Telix's principal activity is molecularly targeted radiation (MTR) products. MTR products emit radiation that can be detected with imaging systems (PET/SPECT). Telix is developing a pipeline of molecularly targeted radiation therapies to image and treat cancer. MTR therapy has a radionuclide, or an atom with an unstable nucleus which, to become more stable, emits ionizing radiation energy in the form of rays or high-speed particles. This energy is attached to a targeting agent such as a small molecule or antibody. This targeting agent specifically binds to tumours and delivers a radioactive payload in a highly selective way, killing cancer cells, shrinking tumours and halting their growth. MTR therapies are very selective and are typically well tolerated by patients.

### **Investors should be aware of the potential for further M&A**

Given the reasons outlined above, more than at any time probably over the past decade, we flag the potential for further M&A in the Australian healthcare and pharmaceutical space.



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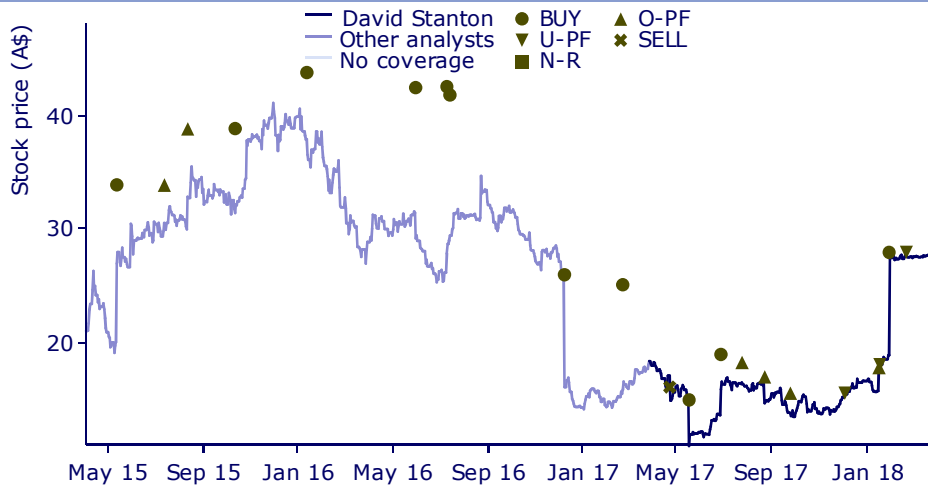
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Amgen (N-R)  
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Biogen Idec (N-R)  
Bioerativ (N-R)  
Bloomberg (N-R)  
Boehringer Ingelheim (N-R)  
Bristol-Myers (N-R)  
Celgene Corp (N-R)  
Clinuvel Pharma (N-R)  
Eli Lilly (N-R)  
Ellex Medical (N-R)  
Gilead Sciences (N-R)  
GSK (N-R)  
GSK Consumer Healthcare (N-R)  
Impact Biomedicines (N-R)  
Impedimed (N-R)  
Johnson & Johnson (N-R)  
Juno Therapeutics (N-R)  
LifeHealthcare Group (N-R)  
Medical Developments International (N-R)  
Merck (N-R)  
Mesoblast (N-R)  
Mitobridge (N-R)  
Nanosonics Europe (N-R)  
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Osprey Medical (N-R)  
P&G (N-R)  
Pacific Equity Partners (N-R)  
PerkinElmer (N-R)  
Pfizer (N-R)  
Pro Medicus (N-R)  
RHS Ltd (N-R)  
Roche (N-R)  
Sanofi (N-R)  
Shire PLC (N-R)  
Sirtex Medical (SRX AU - A\$27.79 - U-PF)  
Takeda Pharma (4502 JP - ¥5,285 - BUY)  
Telix (N-R)  
Varian (N-R)  
Viralytics (N-R)

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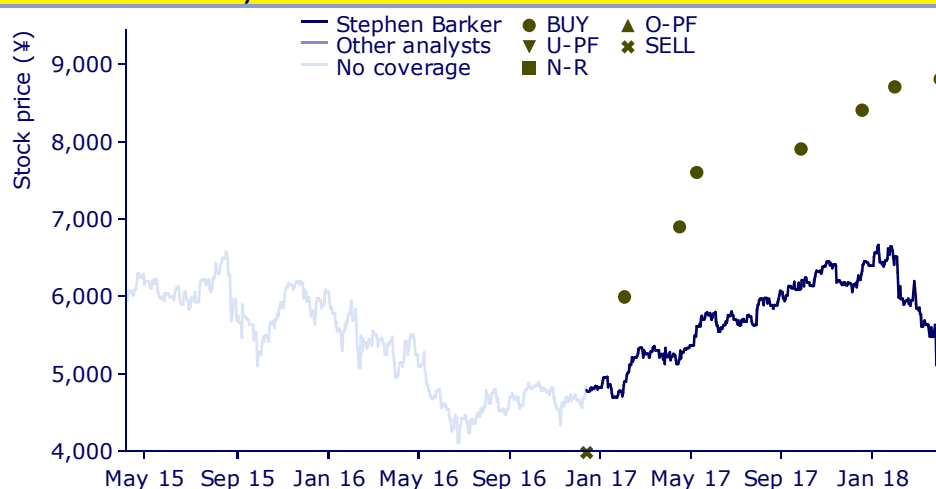
**Recommendation history of Sirtex Medical Ltd SRX AU**



Date	Rec	Target	Date	Rec	Target
21 Feb 2018	U-PF	28.00	22 Feb 2017	BUY	25.10
30 Jan 2018	BUY	28.00	09 Dec 2016	BUY	26.00
18 Jan 2018	U-PF	18.00	15 Jul 2016	BUY	42.00
17 Jan 2018	O-PF	17.75	11 Jul 2016	BUY	42.75
04 Dec 2017	U-PF	15.45	01 Jun 2016	BUY	42.65
25 Sep 2017	O-PF	15.45	13 Jan 2016	BUY	44.00
23 Aug 2017	O-PF	16.90	13 Oct 2015	BUY	39.00
25 Jul 2017	O-PF	18.20	13 Aug 2015	O-PF	39.00
28 Jun 2017	BUY	18.90	14 Jul 2015	O-PF	34.00
18 May 2017	BUY	14.85	14 May 2015	BUY	34.00
23 Apr 2017	SELL	16.00			

Source: CLSA

## Recommendation history of Takeda Pharmaceutical Co Ltd 4502 JP



Date	Rec	Target	Date	Rec	Target
03 Apr 2018	BUY	8,800.00	11 May 2017	BUY	7,600.00
01 Feb 2018	BUY	8,700.00	18 Apr 2017	BUY	6,900.00
19 Dec 2017	BUY	8,400.00	03 Feb 2017	BUY	6,000.00
28 Sep 2017	BUY	7,900.00	14 Dec 2016	SELL	4,000.00

Source: CLSA

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