July 1, 2013

Breakthrough status: Aust biotechs could apply

US FDA 'breakthrough status' could be potentially valuable for ACL, CUV, MSB, PRR or SPL

The FDA has granted 'breakthrough status' this year on 15 potential drugs, mostly for cancer and rare diseases

The US Food and Drug Administration already has numerous ways it can speed up the market authorisation of new medicines, ranging from 'accelerated approvals' to 'priority reviews' to its fast-track program. Even so, sometimes the existing mechanisms for speeding drugs to market, which typically require data from the traditional three phases of drug development, still take considerable amounts of time. The so-called 'breakthrough therapy' designation introduction may be a signal that the FDA will approve exceptional drugs more quickly with this new regulatory pathway. Ultimately, a breakthrough drug may be approved by the FDA without completing all three phases of clinical trials typically required before an approval decision.

Breakthrough designation could be potentially valuable

Breakthrough therapy designation is intended to expedite the development and review of drugs for serious or life-threatening conditions. The criteria for breakthrough therapy designation require preliminary clinical evidence that demonstrates the drug may have substantial improvement on at least one clinically significant endpoint over available therapy.

Breakthrough status increasingly granted – companies under our coverage could apply

We believe that a number of Australian companies under our coverage could potentially eventually apply for breakthrough status. These companies include Alchemia, Clinuvel Pharmaceuticals, Mesoblast, Prima Biomed and Starpharma. Breakthrough status would potentially: 1) convey the FDA's belief that the potential drug has excellent, albeit early clinical trial results compared to drugs already on the market; and 2) addresses an unmet clinical need; which may 3) lead to earlier entry into the US market, the largest pharmaceutical market. We will be watching for potential breakthrough status applications by the companies under our coverage.

Fig. 1: Stocks for action

Company	Code	Rating	Price (A$)	Price target A$	Up/downside (%)
Alchemia	ACL.AX	Buy	0.32	0.47	46.9
Clinuvel Pharmaceutic	CUV.AX	Buy	1.81	3.14	73.5
Mesoblast	MSB.AX	Buy	5.3	7.78	46.8
Prima BioMed	PRR.AX	Buy	0.07	0.21	200.0
Starpharma Holdings	SPL.AX	Buy	0.82	1.69	106.1

Source: Nomura estimates

Anchor themes

The Australian healthcare sector looks attractive, in our view, given its positive fundamentals, including high barriers to entry and an ageing population, which should lead to sustained demand growth over the longer term.

Nomura vs consensus

Our analysis indicates that an economic recovery (particularly in the US) should lead to sector outperformance.

Research analysts

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See Appendix A-1 for analyst certification, important disclosures and the status of non-US analysts.

US FDA 'breakthrough status' could be potentially valuable for ACL, CUV, MSB, PRR or SPL

The FDA has granted 'breakthrough status' this year on 15 potential drugs, mostly for cancer and rare diseases. Breakthrough designation could be potentially valuable. Breakthrough status is increasingly being granted. We believe some companies under our coverage may apply.

Breakthrough therapy designation is intended to expedite the development and review of drugs for serious or life-threatening conditions. The criteria for breakthrough therapy designation require preliminary clinical evidence that demonstrates the drug may have substantial improvement on at least one clinically significant endpoint over available therapy.

In this note, we:

- Outline what 'breakthrough status' means;
- Describe other drugs that have gained breakthrough status; and
- Highlight what it means for some of the biotech companies under our coverage.

1. What is 'breakthrough status'?

The Food and Drug Administration Safety and Innovation Act (FDASIA) (signed into law on July 9, 2012) includes a provision that allows sponsors to request that their drug be designated as a Breakthrough Therapy. FDA is in the process of developing guidance related to this designation.

A breakthrough therapy designation conveys all of the fast-track program features as well as more intensive FDA guidance on an efficient drug-development program. The FDA also has an organizational commitment to involve senior management in such guidance. FDASIA requires the following actions, as appropriate:

The FDA has granted 'breakthrough status' this year on 15 potential drugs, mostly for cancer and rare diseases

- holding meetings with the sponsor and the review team throughout the development of the drug;
- providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable;
- taking steps to ensure that the design of the clinical trials is as efficient as practicable, when scientifically appropriate, such as by minimizing the number of patients exposed to a potentially less efficacious treatment;
- assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the cross-discipline members of the review team (i.e., clinical, pharmacology-toxicology, chemistry, manufacturing and control (CMC), compliance) for coordinated internal interactions and communications with the sponsor through the review division's Regulatory Health Project Manager; and
- involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review.

How is this different from other approaches to expedited approval?

There are a number of different methods that the FDA can use to expedite drug approval. This is shown in the following table.

Fig. 2: FDA approaches to expedited approval

	Fast track	Accelerated approval	Priority review	Breakthrough therapy
Eligibility	A drug that treats a serious condition and for which nonclinical or clinical data demonstrate the potential to address an unmet clincial need	A drug that treats a serious condition, provides meaningful therapeutic benefit over available therapies and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit	A drug that offers major advances in treatment over existing therapies or provides a treatment where no adequate therapy exists	A drug that treats a serious condition and for which evidence indicates that the drug may demonstrate substantial improvement over available therapies
Designation	Can be requested at any time; the FDA has 60 days to respond	No formal process	Requested at time of new drug or biologic application submission; FDA has 45 days to respond	Can be requested at any time after investigational new drug application; FDA has 60 days to respond
Clinical development	Earlier and more frequent communication	Conditional approval granted using surrogate endpoint(s) from Phase 2 to interim Phase 3 data; confirmatory trials with hard clinical endpoints required	Standard	Abbreviated or condensed development, with earlier and more frequent communication and delegation of senior reviewers and cross-disciplinary review team
Review process	Option for rolling data submission; standard review after last data submitted	Data submitted in one package: standard 10 month review	Data submitted in one package: review time shortened to 6 months	Data submitted as they are accumulated; review time submitted
Year established	1988	1992	1992	2012

Source: UD FDA

2. How many drugs have been granted breakthrough status?

As of 28 June 2013, there have been 23 drugs granted breakthrough status in the US, (from October 1, 2012).

Fig. 3: US FDA breakthrough requests granted

FY13 CDER Breakthrough requests	Oct 1 2013 to June 28, 2013
Total requests received	61
Total requestes granted	23
Total requests denied	15

Source: US CDER, Nomura research

Potential drugs that have been granted breakthrough status include:

- **Drisapersen**: GlaxoSmithKline (GSK LN, unrated) has been granted the FDA's breakthrough therapy designation for drisapersen, a late-stage treatment for Duchenne muscular dystrophy (DMD), after regulators reviewed Phase II data;
- **LDK378**: this is Novartis (NOVN SIX, unrated) experimental lung cancer drug, which gained breakthrough therapy designation. Novartis plans to file for approval the drug, now in mid-stage clinical trials, in early 2014. Clinical development began in 2011;
- **Kalydeco and VX-809**: Vertex's (VRTX US, unrated) Kalydeco and VX-809 have recently been granted breakthrough status for cystic fibrosis; and
- **Ibrutinib**: this is an experimental lymphoma drug ibrutinib from Pharmacyclics (PCYC US, unrated) and its partner Johnson & Johnson (JNJ US, unrated).

3. What does it mean for the companies under our coverage?

We believe that a number of Australian companies under our coverage could eventually apply for breakthrough status for some of the drugs they are developing. These companies include Alchemia, Clinuvel Pharmaceuticals, Mesoblast, Prima Biomed and Starpharma.

Breakthrough status would potentially: 1) convey the FDA’s belief that the potential drug has excellent, albeit early clinical trial results compared to drugs already on the market;

and 2) addresses an unmet clinical need; which may 3) lead to earlier entry into the US market, the largest pharmaceutical market. Hence, we believe breakthrough status would be valuable. We will be watching for potential breakthrough status applications by the companies under our coverage. We highlight the parts of the above companies' portfolio that may qualify for breakthrough status.

A. Alchemia

The HA-irinotecan trial is fully recruited. Should it be positive, breakthrough status would likely lead to expedited regulatory approval

ACL is developing potential anticancer products. The lead product from this HyACT platform is HA-irinotecan. ACL's HA-irinotecan preferentially targets the cell surface receptor CD44. CD44 is thought to be a marker of cancer stem cells (CSC), so targeting this may target CSCs. Recently, research has focused on the theory that many cancers are driven by transformed CSCs (i.e. early-stage cancer cells).

What is irinotecan?

Irinotecan is a semisynthetic camptothecin derivative that works by inhibiting the topoisomerase 1 enzyme, which is involved in cancer cell replication. Irinotecan is a standard therapy for patients with metastatic disease who have failed 5-Fluorouracil (5-FU)-based therapy. Single-agent irinotecan can be given according to a variety of schedules, including 350 mg/m2 every 3 weeks, which demonstrates similar efficacy to other alternatives.

What is HA-irinotecan?

In an attempt to increase the benefit associated with irinotecan-based treatment and/or to reduce the dose-limiting toxicity often associated with this therapy, irinotecan has been formulated with the naturally ubiquitous polysaccharide, hyaluronan (HA), resulting in ACL's proprietary product (HA-irinotecan). This process is called HyACT. This product utilises the physiochemical and biologic properties of HA as a macromolecular carrier of drugs to solid tumours. After intravenous administration, the HA-drug combination enters the tumour and aggregates, thereby forming a vascular microembolism within the tumour where the intra-tumoural drug depot persists, increasing drug accumulation and retention. The increased intra-tumoural drug concentration enables the increased internalization of the anti-cancer agent via a CD44-mediated mechanism, ultimately enhancing efficacy. A secondary effect is the diversion of the drug from healthy tissue, leading to a reduction in some commonly observed treatment toxicities.

What is CD44?

In many cancers of epithelial origin there is an up-regulation of CD44, a receptor that binds hyaluronic acid (hyaluronan or HA). In other cancers, HA in the tumour matrix is over-expressed. Both CD44 on cancer cells and HA in the matrix have been targets for anti-cancer therapy. Even though CD44 is expressed in normal epithelial cells and HA is part of the matrix of normal tissues, selective targeting to cancer is possible. This is because macromolecular carriers predominantly connect and deliver their payload into the tumour and not normal tissue; thus CD44-HA targeted carriers administered intravenously localize preferentially into tumours.

Completes recruiting for HA-Irinotecan trial

ACL has recruited the 390th patient to its pivotal Phase III clinical trial of HA-Irinotecan. 390 patients have been recruited at 76 sites since the study began. The study's primary objective is to demonstrate that HA-Irinotecan is superior against irinotecan alone in metastatic colorectal cancer patients, as indicated by an increase in Progression-Free Survival (PFS) of six weeks or more. The primary endpoint of this double-blind trial will be reached when 350 patients have experienced disease progression.

Patients on the trial receiving treatment for longer than expected – potentially positive sign …

However, statistical review and modelling on the available blinded data suggests that on average, patients on this trial are continuing treatment for longer than anticipated, before their disease progresses. This means that the primary endpoint is likely to be met in 1HCY14.

Fig. 4: Clinical trials of antibody anti-CD44 conjugates

Antibody	Drug	Injection Method	Cancer Type	Effect
U36	Re-186	Single intravenous	Head and Neck Squamous Cell Carcinoma	Stable disease in 5 of 9 patients, mild myelotoxicity
BIWA 4	Tc-99m	Single intravenous	Head and Neck Squamous Cell Carcinoma	Tumor targeting
BIWA 4	Re-186	Dose escalation	Head and Neck Squamous Cell Carcinoma	Stable disease in 3 of 6 patients, limiting myelotoxicity
BIWA 4	Re-186	Single intravenous	Early Stage Breast Cancer	Moderate tumor identification, no correlation with CD44v6 expression
BIWA 4	Mertansine	Dose escalation	Head and Neck Squamous Cell Carcinoma	Moderate disease stabilization, skin toxicity
BIWA 4	Mertansine	Dose escalation	Head and Neck Squamous Cell Carcinoma	Low interpatient pharmacokinetic variability, skin toxicity
BIWA 4	Mertansine	Dose escalation	CD44v6 Positive Metastatic Breast Cancer	Stable disease in 12 of 24 patients, dose limiting toxicity

Source: PubMed, Nomura research

In summary, several intrinsic characteristics of HA highlighted its potential as a drug-delivery vehicle:

- The nature of HA makes it a vehicle for the delivery of smaller molecules;
- There is up-regulation and activation of the HA receptor CD44 on malignant cancer tissue. An active CD44 within the tumoural environment mediates HA internalization; and
- HA is non-immunogenic and considered by regulatory bodies as a biologically inert compound.

Hence, there is a potential opportunity to target the HA tumour matrix to provide a sustained drug source within the tumour. There have been a number of Targeted Drugs and Drug Carriers trials using HA.

Fig. 5: Targeted drugs and drug carriers in vitro

Carrier	Drug	Cancer targeted	Effect
LMW-HA	Paclitaxel	mammary, colon, ovarian	Cytotoxicity, CD44 specific uptake
HMW-HA	Butyrate	mammary, liver, non-small cell lung	Inhibited proliferation, CD44 specific uptake
HMW-HA	Paclitaxel	bladder, ovarian	Cytotoxicity
HMW-HA	Paclitaxel	ovarian	Cytotoxicity
HMW-HA	Carborane	colorectal, mammary, ovarian, transitional cell	CD44 specific uptake
LMW-HA, HMW-HA	siRNA	colon	CD44 specific uptake, gene silencing
HMW-HA Fe2O3 Particle	Peptide	alveolar squamous	Peptide internalization
HPMA Polymer, LMW-HA	Doxorubicin	mammary, colon, ovarian	Cytotoxicity, CD44 specific uptake
Liposome HA Oligos	Doxorubicin	melanoma	Cytotoxicity, CD44 specific uptake
HMW-HA PLGA Particle	Doxorubicin	breast	Cytotoxicity, CD44 specific uptake

Source: PubMed, Nomura research

B. Clinuvel Pharmaceuticals

CUV aims to show that its lead compound, afamelanotide, has efficacy against several sun-related diseases. CUV could seek breakthrough status for EPP and Vitiligo in the US, in our view. Afamelanotide is a synthetic analogue of a hormone called alpha-melanocyte-stimulating hormone, or alpha-MSH. This hormone is released when ultraviolet (UV) radiation from the sun penetrates the upper layers of skin and causes damage, stimulating melanin production in the skin.

CUV could seek breakthrough status for EPP and Vitiligo in the US, in our view. It has recently raised funds for a NDA in the US

Fig. 6: Photodermatoses

Disorder	Wavelength (nm)	Symptoms	Prevalence
Polymorphous Light eruption	300-600	Subactute rash, itching, generalised erythema. Transient in spring, diminshing in intensity through summer	10-20% of Caucasian Population, 18% of Europeans
Actinic Prurigo (HLA positive)	300-600	Subacute rash, itching, erythema generalised	Unknown, seen in American Indian and Mexican Popn
Chronic Actinic Dermatitis			16.5 per 100,000
Solar Urticaria	350-550	Acute oedematous reaction, anaphylactic reaction to UV light, most prominent in Spring and Summer	3.1 per 100,000
Discoid Lupus Erythematosis	300-650	Chronic and Recurrent light sensitive episodes of LE on exposed body surfaces	27.7 per 100,000
Erthyropoietic Protoporphyria	408-620	Acute phototoxicity after light exposure	1 per 75,000
Congenital Erythropoietic Porphyria	410		1 per 100,000

Wavelength = corresponds to wavelength of light that at which disease is seen
Source: PubMed, Nomura research

Vitiligo

CUV has previously announced that it is investigating the effectiveness of afamelanotide in Non-Segmental Vitiligo. This is a new medical indication for afamelanotide. CUV plans to use afamelanotide as an adjunct to the current mainstay of treatment, narrowband UVB (NB-UVB), as well as testing afamelanotide as a single treatment option. NSV is a de-pigmenting disease that affects c10mn persons in the US and EU. CUV's afamelanotide is being evaluated as a combination therapy with narrowband UVB light therapy in two clinical studies in patients with NSV. In early Phase II trial results presented at a recent conference, the NB-UVB plus afamelanotide group showed earlier onset of repigmentation compared to controls. We believe the NSV market is currently USD1.4bn pa, consisting of generic treatments and UVB. We believe the current lack of high-margin branded pharma treatments in the Vitiligo market could mean that should it be approved, then CUV's afamelanotide would be of interest to established dermatology companies, because these companies have salesforces and associated infrastructure that already detail product to dermatologists.

EPP

CUV has succeeded in enrolling a large number of patients into its EPP trials, considering the rarity of this disease. This may be an indication of the potential patients' willingness to participate, in our view. This is despite the fact that a patient may receive a placebo injection, and hence be subjected to high levels of pain as a part of their disease process. In our view, since high unmet medical need forms a pivotal criterion for the lead regulatory agencies during the evaluation of new therapies, this factor should assist CUV in obtaining approval for afamelanotide. Photodermatology is the subspecialty which focuses on skin disorders which are triggered or aggravated by UV or light of a particular wavelength. In Phase II and Phase III trials, afamelanotide has been shown to mitigate or prevent the symptoms in polymorphous light eruption, solar urticaria, and EPP. These photodermatoses vary in onset, character and severity. CUV has focussed its program on those photodermatoses which are most severe in nature and for which there is no current therapy, such as EPP.

C. Mesoblast

We believe MSB may apply for breakthrough status for its MPC in the as a part of bone-marrow transplantation, amongst others

Mesenchymal precursor cells (MPCs, also known as mesenchymal stem cells) are adult stem cells that have the ability to become solid organs and tissues such as bone, heart muscle and cartilage. They do not have immunological markers and will therefore cause no immune reaction when injected into a foreign host. This means MPCs can be harvested as a generic product for any recipient from any donor. The proprietary technology being commercialised by MSB enables the efficient extraction, isolation and scale-up of MPCs. This technology has allowed for the potential application of commercial, off-the-shelf MPCs harvested from relatively few, non-specific donors in a wide range of serious medical issues. MSB aims to capitalise on its patents that relate to the identification, extraction and culture of adult mesenchymal precursor cells. We

believe MSB may apply for breakthrough status for its MPC in the as a part of bone-marrow transplantation, amongst others.

Bone marrow trial

In July 2011, MSB was US FDA approved to start a Phase III trial for bone-marrow transplantation. We believe the trial should run for c24 months, with results available 3-6 months after that. There are 12,500 unrelated allogeneic bone-marrow transplants per year in the US. In the US, MSB believe that an additional c20,000 potential patients do not receive transplants because of a lack of matched donors in current donor registries. MSB's MPCs could allow these patients to potentially receive a transplant from donors who have lower levels of matching. In effect, MSB's MPCs could expand the donor pool for unrelated allogeneic bone-marrow transplants. Although few in number, bone-marrow transplants are very expensive procedures, with the potential price for the MSB stem cells ranging from USD50K to USD100K.

D. Prima Biomed

PRR could seek breakthrough status for ovarian cancer in the US, in our view

PRR intends to commercialise an ovarian cancer recurrence immunotherapeutic vaccine. As a part of this C-Vac process, PRR sensitises the patient's own dendritic immune cells against components of the patient's ovarian cancer, namely Mucin-1. These sensitised dendritic cells then attach to ovarian cancer cells, and transport them to the immune system complexes, where the cancer cells are destroyed.

We believe that immunotherapy is an interesting technology in that it uses the body's own processes to destroy cancer cells, thus decreasing the side-effect profile of the treatment compared to external chemotherapeutic agents.

CVac is a personalized immunocellular therapy which targets Mucin-1 over-expressing cancer cells. To date, PRR has advanced its CVac therapy to phase 2 and 3 trials for the treatment of epithelial ovarian cancer in remission. Recently, PRR announced that it intends to commence three separate phase 2 clinical trials to evaluate the use of CVac for the treatment of resectable pancreatic cancer, metastatic colorectal cancer, and triple-negative breast cancer.

PRR has begun a Phase III clinical trial in CVac (CAN-004). We believe final data from this Phase III clinical trial is likely to be released in CY16. The World Health Organisation (WHO) predicts that c61,000 females (aged 0-75 years) in the major markets were diagnosed with ovarian cancer in 2010, of which c70% have stage III-IV cancer. We believe approximately 75% of these females, or 33,000 patients, will be eligible for an immunotherapy vaccine after their cancer goes into remission post optimal surgical/radiotherapy treatment. This is the updated target market for CVac, which has the aim of extending remission.

E. Starpharma

SPL could seek breakthrough status for dendrimer-docetaxel in the US, in our view

SPL has previously announced positive preclinical trial results of its potential anti-cancer drug dendrimer-docetaxel, when compared with industry-standard docetaxel, known as Taxotere. The dendrimer-docetaxel trial was due to begin in 2013.

According to SPL, SPL's dendrimer-docetaxel: 1) is more effective in treating breast cancer in animals than Taxotere (a statistically significant result); 2) has a 60x longer duration of effect than Taxotere; and 3) has an improved solubility profile compared to Taxotere. It is hoped that the increased water solubility provided by SPL's dendrimer technology will allow the development of a docetaxel formulation which would not require pre-medication with high doses of cortisone and would avoid the need for inclusion of formulation components thought to cause the severe allergic reactions and fluid retention experienced by some patients. In CY10, Taxotere generated sales of EUR2.1bn for Sanofi-Aventis. We believe SPL will aim to perform a Phase I/II trial in dendrimer-docetaxel and then license the product should the trial be successful.

What is docetaxel?

Docetaxel is an anti-cancer chemotherapy drug. This is approved for the treatment of breast cancer, non-small-cell lung cancer, advanced stomach cancer, head and neck cancer and metastatic prostate cancer. Docetaxel is also being investigated to treat small-cell lung, ovarian, bladder, and pancreatic cancers, soft tissue sarcoma and melanoma. Docetaxel is given intravenously. Premedication with a corticosteroid starting

a day prior to docetaxel infusion is given to reduce the severity of fluid retention and allergic reactions. SPL management states that the need for this premedication may be reduced through the development of a dendrimer-docetaxel complex. This would likely have positive pharmacoeconomic benefits.

What are dendrimers?

Dendrimers are a class of synthetically produced, highly branched, spherical nanostructures that can be used as carrier molecules. A variety of dendrimers exist, and each has biological properties that alter its biodistribution. Dendrimers are composed of combinations of core types such as ethylene diamine (EDA), diaminobutyl (DAB), polyamidoamine (PAMAM) and polypropylimine (PPI), and different surface residues such as amine, carboxyl, and alcoholic groups. Dendrimers are produced in an iterative sequence of reaction steps, in which each additional iteration leads to a higher-generation dendrimer.

Other potential dendrimer-pharmaceutical opportunities for SPL

SPL has updated the market that it is looking at a number of pharmaceutical agents in combination with the company's dendrimer technology. In addition to dendrimer-docetaxel, these include anti-cancer drugs (including gemcitabine, 2010 global sales of cUSD1.2bn) and recombinant antibodies.

Appendix A-1

Analyst Certification

I, David Stanton, hereby certify (1) that the views expressed in this Research report accurately reflect my personal views about any or all of the subject securities or issuers referred to in this Research report, (2) no part of my compensation was, is or will be directly or indirectly related to the specific recommendations or views expressed in this Research report and (3) no part of my compensation is tied to any specific investment banking transactions performed by Nomura Securities International, Inc., Nomura International plc or any other Nomura Group company.

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Materially mentioned issuers

Issuer	Ticker	Price	Price date	Stock rating	Sector rating	Disclosures
Alchemia	ACL AU	AUD 0.32	28-Jun-2013	Buy	Not rated	
Clinuvel Pharmaceuticals	CUV AU	AUD 1.81	28-Jun-2013	Buy	Not rated	A4,A5
Mesoblast	MSB AU	AUD 5.30	28-Jun-2013	Buy	Not rated	A6
Prima BioMed	PRR AU	AUD 0.07	28-Jun-2013	Buy	Not rated	
Starpharma Holdings	SPL AU	AUD 0.82	28-Jun-2013	Buy	Not rated	

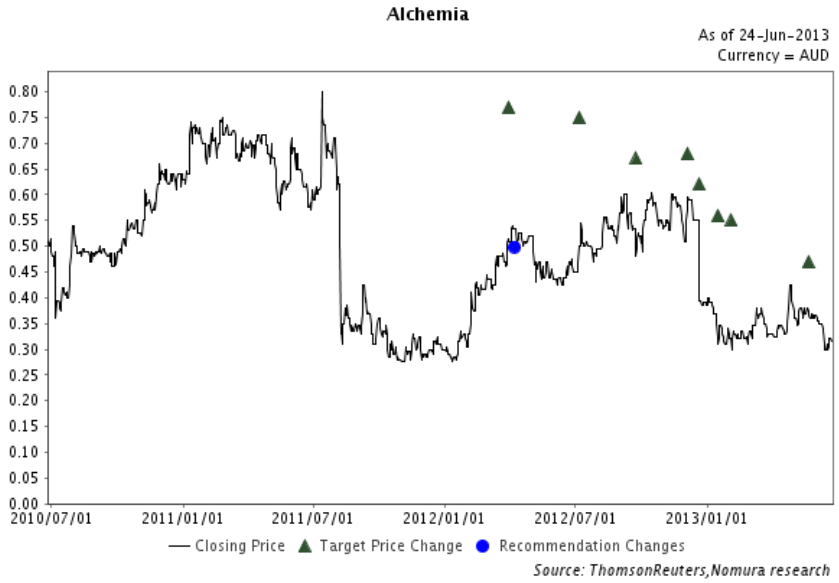
A4 The Nomura Group had an investment banking services client relationship with the issuer during the past 12 months.

A5 The Nomura Group has received compensation for investment banking services from the issuer in the past 12 months.

A6 The Nomura Group expects to receive or intends to seek compensation for investment banking services from the issuer in the next three months.

Alchemia (ACL AU) **AUD 0.32 (28-Jun-2013)** Buy (Sector rating: Not rated)

Rating and target price chart (three year history)



Date	Rating	Target price	Closing price
22-May-13		0.47	0.375
04-Feb-13		0.55	0.32
16-Jan-13		0.56	0.31
21-Dec-12		0.62	0.395
04-Dec-12		0.68	0.57
24-Sep-12		0.67	0.48
06-Jul-12		0.75	0.50
30-Mar-12	Buy		0.51
30-Mar-12		0.77	0.51

For explanation of ratings refer to the stock rating keys located after chart(s)

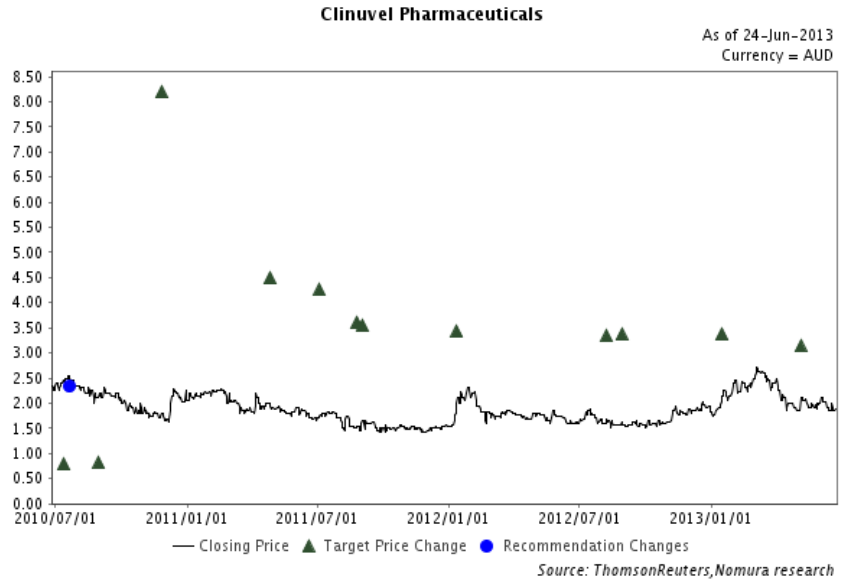
Valuation Methodology Our AUD0.47 TP is based on the risk-weighted valuation of the company's product opportunities plus cash and less R&D expenses. We have valued the generic fondaparinux opportunity (AUD0.33/sh) in line with our forecasts for the growth of the fondaparinux market in the US market, as well as potential entry into other developed markets. In addition, we have valued other opportunities (AUD0.24/sh)for ACL, namely HA-Irinotecan, and have added cash (AUD0.04/sh) and subtracted R&D expenses (-AUD0.14/sh).

Risks that may impede the achievement of the target price For ACL's leading product, generic fondaparinux, there is still uncertainty around the potential level of growth in most of its prospective markets. ACL's rate of earnings growth is dependent

on the sales and marketing support provided by its partner Dr Reddy's Laboratories. Should ACL enter further clinical trials in new methods of drug delivery, we note that early results give no real enough indication of a product's true viability, and full foresight on future market conditions is difficult to obtain. For irinotecan, there is still a good deal of uncertainty around the viability of ACL's HA-iriontecan in most of its prospective markets. Early clinical trials, although positive, give no real enough indication of a product's true viability and full foresight on future market conditions is difficult to obtain. To date, all preclinical and Phase II trials have shown indications for product viability. As it stands, there have been no significant adverse effects or health issues and Phase II trials indicate a product with the potential for market viability. Therefore, we believe this is an investment opportunity for investors with a higher risk appetite.

Clinuvel Pharmaceuticals (CUV AU) **AUD 1.81 (28-Jun-2013)** Buy (Sector rating: Not rated)

Rating and target price chart (three year history)



Date	Rating	Target price	Closing price
06-May-13		3.14	2.10
16-Jan-13		3.39	2.15
29-Aug-12		3.38	1.63
08-Aug-12		3.34	1.69
12-Jan-12		3.44	1.99
02-Sep-11		3.56	1.65
26-Aug-11		3.62	1.54
04-Jul-11		4.26	1.75
26-Apr-11		4.50	2.00
26-Nov-10		8.20	1.80
30-Aug-10		0.82	2.10
12-Jul-10	Buy		2.45
12-Jul-10		0.80	2.45

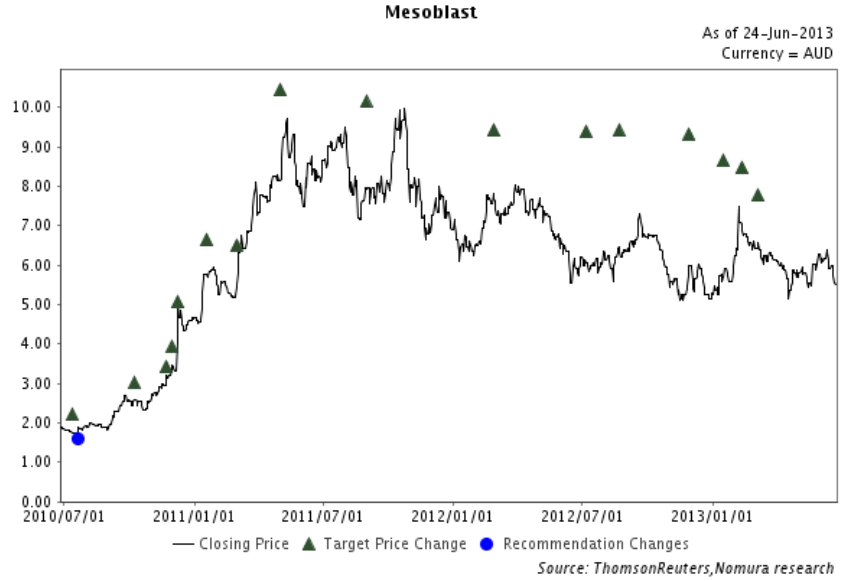
For explanation of ratings refer to the stock rating keys located after chart(s)

Valuation Methodology Our risk-weighted valuation for EPP is AUD1.61/share. Regarding NSV, starting from potential approval in 2016, We believe that if an eventual maximum of 10% of US and EU patients were to use afamelanotide, the risk-weighted NPV for the NSV opportunity for CUV is AUD1.53/share. Our risk-weighted valuation of the CUV pipeline (AUD3.14) is our TP.

Risks that may impede the achievement of the target price We believe that any delay or failure to progress in clinical trials would present downside risk to our target price. That said, faster-than-expected progression to production of CUV's photoprotective technology could provide an upside boost.

Mesoblast (MSB AU) **AUD 5.30 (28-Jun-2013)** Buy (Sector rating: Not rated)

Rating and target price chart (three year history)



Date	Rating	Target price	Closing price
06-Mar-13		7.78	6.45
11-Feb-13		8.49	7.04
16-Jan-13		8.66	5.69
29-Nov-12		9.33	5.98
22-Aug-12		9.41	6.45
06-Jul-12		9.39	6.05
27-Feb-12		9.44	7.80
31-Aug-11		10.15	7.95
02-May-11		10.45	8.15
01-Mar-11		6.51	5.42
18-Jan-11		6.66	5.76
08-Dec-10		5.08	4.05
30-Nov-10		3.92	3.46
22-Nov-10		3.44	3.19
08-Oct-10		3.01	2.60
12-Jul-10	Buy		1.74
12-Jul-10		2.21	1.74

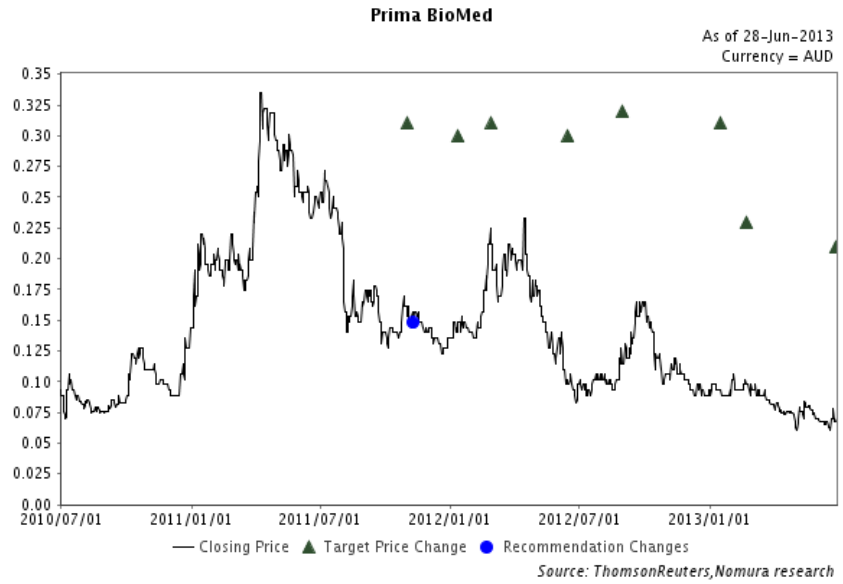
For explanation of ratings refer to the stock rating keys located after chart(s)

Valuation Methodology We calculate that the NPV of the potential near-term opportunities developed by MSB is AUD24.52. We believe the probability of MSB getting its product onto market depends on its clinical trial stage. Hence, our risk-weighted valuation is AUD7.78 per share.

Risks that may impede the achievement of the target price There is still a good deal of uncertainty around MSB's viability in most of its prospective markets. Pre-clinical trials, although positive, give no firm indication of a product's true viability and full foresight on future market conditions is difficult to obtain. In its favour, MSB's base product is found naturally in the body, and we see little reason to believe that injections of concentrated numbers would cause serious health issues or be relatively less effective in doing their natural job.

Prima BioMed (PRR AU) **AUD 0.07 (28-Jun-2013)** Buy (Sector rating: Not rated)

Rating and target price chart (three year history)



Date	Rating	Target price	Closing price
28-Jun-13		0.21	0.068
22-Feb-13		0.23	0.098
16-Jan-13		0.31	0.093
31-Aug-12		0.32	0.115
15-Jun-12		0.30	0.098
28-Feb-12		0.31	0.212
12-Jan-12		0.30	0.148
01-Nov-11	Buy		0.153
01-Nov-11		0.31	0.153

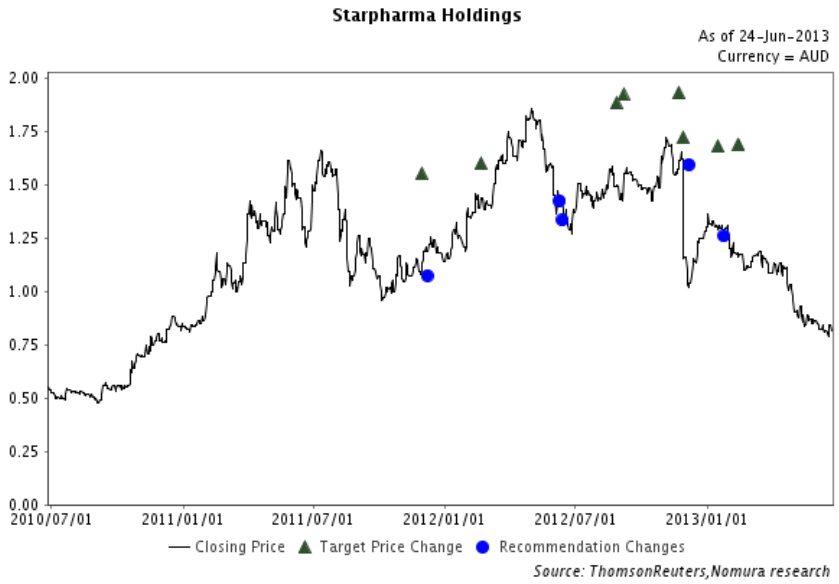
For explanation of ratings refer to the stock rating keys located after chart(s)

Valuation Methodology We ascribe a 61.2% risk-weighting for the C-Vac ovarian cancer opportunity, as PRR has begun a Phase III clinical trial. Our risk-weighted valuation for PRR is AUD0.21 per share.

Risks that may impede the achievement of the target price There is still a good deal of uncertainty around PRR's viability in most of its prospective markets. Early clinical trials, although positive, give no real enough indication of a product's true viability and full foresight on future market conditions is difficult to obtain.Therefore we believe this is an investment opportunity for investors with a higher risk appetite.

Starpharma Holdings (SPL AU) **AUD 0.82 (28-Jun-2013)** Buy (Sector rating: Not rated)

Rating and target price chart (three year history)



Date	Rating	Target price	Closing price
14-Feb-13		1.69	1.16
16-Jan-13	Buy		1.285
16-Jan-13		1.68	1.285
28-Nov-12	Neutral		1.62
28-Nov-12		1.72	1.62
22-Nov-12		1.93	1.57
06-Sep-12		1.92	1.53
27-Aug-12		1.88	1.49
05-Jun-12	Buy		1.36
01-Jun-12	Neutral		1.45
20-Feb-12		1.60	1.44
29-Nov-11	Buy		1.10
29-Nov-11		1.55	1.10

For explanation of ratings refer to the stock rating keys located after chart(s)

Valuation Methodology We ascribe a risk-weighting for the SPL opportunities, depending upon the stage of clinical trials. We ascribe AUD0.55 for VivaGel (BV) prevention, AUD0.18 for VivaGel Microbicide (STI), AUD0.51 for VivaGel (coated condom), AUD0.33 for drug delivery, AUD0.18 for agrochemicals, AUD0.04 for other anti-cancer opportunities,(AUD0.24) for R&D and AUD0.14 for cash. Our risk-weighted valuation for SPL is AUD1.69 per share.

Risks that may impede the achievement of the target price There is still a good deal of uncertainty around SPL's viability in most of its prospective markets. Early clinical trials, although positive, give no real enough indication of a product's true viability and full foresight on future market conditions is difficult to obtain. As it stands, there have been no significant adverse effects or health issues and most trials indicate a product with the potential for market viability. Therefore, we believe this is an investment opportunity for investors with a higher risk appetite.

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STOCKS

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SECTORS

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Explanation of Nomura's equity research rating system in Japan and Asia ex-Japan

STOCKS

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