BELL POTTER

18 June 2014

Speculative

Analyst
Tanushree Jain 612 8224 2849

Authorisation
TS Lim 612 8224 2810

Starpharma (SPL)

Sentiment is returning with near term commerciality

Recommendation
Buy (unchanged)
Price
$0.565
Valuation
$1.07 (previously $1.58)
Risk
Speculative

GICS Sector

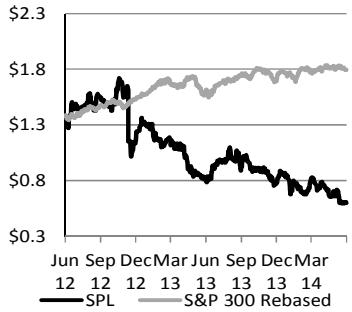
Pharmaceuticals & Biotechnology

Expected Return	
Capital growth	**89.4%**
Dividend yield	**0.0%**
Total expected return	**89.4%**
Company Data & Ratios	
Enterprise value	**$133.4m**
Market cap	**$161.1m**
Issued capital	**285.1m**
Free float	**100%**
Avg. daily val. (52wk)	**$304,641**
12 month price range	**$0.565- $1.11**

Price Performance

	(1m)	(3m)	(12m)
Price (A$)	0.71	0.74	0.82
Absolute (%)	-14.89	-18.37	-26.83
Rel market (%)	-13.15	-18.47	-40.84

Absolute Price



SOURCE: IRESS

Investment View – Attractive at current price levels

SPL remains an attractive story, with multiple shots on goal and meaningful potential for upside. The stock is trading at its 52 week low, having lost some steam over the last 12 months. We believe that investor sentiment is returning to the stock with the first marketing approval received for the VivaGel Coated Condom (VCC) in Japan. We expect multiple catalysts to play out over the next 3 -12 months which could further de-risk the platform technology and demonstrate its commercial viability. Key catalysts include a) launch of VCC in Japan, b) additional regulatory approvals for VCC, c) results from dendrimer-docetaxel Phase I trial, d) licensing deal for Bacterial Vaginosis (BV) symptomatic relief and e) initiation and results from Phase III BV prevention of recurrence trials. We see good risk/reward buying at current levels based on the near term VCC related royalties, upcoming catalysts and a strong cash position of $27.8m which we believe will fund it comfortably through FY15.

Dendrimer-docetaxel – the potential game changer

Phase I dendrimer-docetaxel trial data expected in FY15, if positive, would confirm the ability of SPL's dendrimers to be effective drug delivery agents. Animal results with dendrimer-docetaxel have demonstrated a reduction in some of the frequent dose limiting side effects seen with the original docetaxel drug, as well as increased anti-cancer activity. Similar evidence in humans will give SPL's docetaxel programme a significant edge over other competitive programs. **Results from the trial, in our view, will be a significant inflection point for SPL, with implications for the rest of the pipeline.** Positive data from the trial would set the stage for SPL to secure a commercial partner for its dendrimer-docetaxel programme in FY16.

Valuation methodology changed, revised Valuation $1.07

Previously our valuation was set at the mid-point of our base case & optimistic case DCF range. For all biotech stocks, we no longer use an optimistic case valuation. Therefore we value SPL at our base case. Following changes to our model, we now value SPL using a risk-weighted DCF at $1.07/sh. We retain our Buy recommendation.

Earnings Forecast

Year end 30th June	2012A	2013A	2014E	2015E	2016E
Revenue (A$m)	2.4	9.5	6.3	4.8	16.9
EBITDA (A$m)	-14.4	-5.8	-11.2	-12.0	2.6
NPAT (adjusted) (A$m)	-13.7	-5.2	-11.3	-12.5	1.4
EPS (adjusted) (cps)	-5.10	-1.85	-3.93	-4.35	0.50
EPS growth (%)	N/A	N/A	N/A	N/A	NM
PER (x)	N/A	N/A	N/A	N/A	113.8
EV/EBITDA (x)	-9.3	-23.2	-11.9	-11.1	50.7
Dividend (¢ps)	0.0	0.0	0.0	0.0	0.0
Yield (%)	0.0%	0.0%	0.0%	0.0%	0.0%
Franking (%)	N/A	N/A	N/A	N/A	N/A
ROE (%)	-28.1%	-11.4%	-31.6%	-52.7%	5.6%

NOTE: REVENUE INCLUDES GRANTS AND R&D TAX INCENTIVES. FY16 REVENUE NUMBER INCLUDES POTENTIAL UPFRONT FROM DOCETAXEL AND VIVAGEL SYMPTOMATIC RELIEF DEALS. SOURCE: BELL POTTER SECURITIES ESTIMATES

DISCLAIMER AND DISCLOSURES: THIS REPORT MUST BE READ WITH THE DISCLAIMER AND DISCLOSURES ON PAGE 33 THAT FORM PART OF IT INCLUDING THE FOLLOWING DISCLOSURE.
DISCLOSURE: BELL POTTER SECURITIES ACTED AS LEAD MANAGER IN THE OCTOBER 2011 PLACEMENT AND SPP AND RECEIVED FEES FOR THAT SERVICE.

Contents

Investment Case

We view Starpharma as a diversified pharmaceutical platform technology company with multiple shots on goal and meaningful potential for upside.

We believe that multiple positive catalysts could play out over the next 3 -12 months as investors move from being sceptical about the ability of the company to commercialize its promising technology, to acceptance with the launch of the first VivaGel coated condoms in Japan by Okamoto and to confidence with receipt of regulatory approvals by Ansell for the VivaGel coated condoms in Ex-Japan markets.

The key inflection point for the stock, in our view, will be results from the Phase I dendrimer-docetaxel trial. Consistent with pre-clinical results, if the trial is able to show that dendrimer-docetaxel reduces some of the main dose limiting side effects seen with the original Taxotere drug, as well as provides initial signals of anti-cancer activity, we believe SPL's docetaxel programme will gain a significant edge over other competitive programs. **This, in our view, has the potential to be a game changing event for SPL.** We expect interim data in CY2H14, with top-line data from the trial in CY1H15. Positive data from the trial would set the stage for a potential licensing deal in FY16.

In addition, we expect the Phase III prevention of recurrence of Bacterial Vaginosis (R-BV) trials to start shortly. We expect positive results from this trial in CY2H15 would enable SPL to get a lucrative deal given the high unmet need and no other approved treatments.

The company also plans to submit for registration, in Ex-US jurisdictions, a BV symptomatic relief claim for VivaGel in FY1H15. This will be an OTC (over the counter) product which will not require a prescription to buy. We expect a deal, primarily royalty based with modest commercial milestones, to be inked in FY1H16. We expect SPL can start earning royalties from this indication in FY16.

In summary, we believe that investor sentiment is returning to the stock. We maintain our Buy recommendation on SPL, with a revised valuation of $1.07/sh based on the company getting its first product from the VivaGel portfolio on the market and near-term revenues ensuing from it, other catalysts as stated above which could add value in the near to medium term and a strong cash position of $27.8m which we believe will fund it comfortably through FY15.

We also acknowledge that the stock has a 'wild card' potential in that any of the drug delivery collaborations with numerous companies that it has in place could get converted to a commercialization deal with upfront, milestones and royalties. The timing of this event should it happen is uncertain, but should it eventuate it will be an upside to our valuation.

Key Risks

The key risks to our investment thesis in the near-term are:

- Delays in launch of VivaGel coated condom by Okamoto in Japan;
- Delays in getting regulatory approval for VivaGel coated condom in markets under agreement with Ansell;
- Unsatisfactory results from the Phase I dendrimer-docetaxel trial;
- Delay in the initiation of the Phase III VivaGel R-BV trials;
- Failure to get regulatory approval and license VivaGel for Symptomatic relief of Bacterial Vaginosis;
- Unsatisfactory results from the Phase III VivaGel Prevention of Recurrence of Bacterial Vaginosis trials;

- Termination of any high profile drug delivery or agrochemical collaboration.

What has caused the stock price to fall?

The company reached a peak market capitalization above $500m two years back driven by a deeper understanding of its platform strategy, which offered multiple potential revenue streams across drug delivery, agrochemicals and women's health. Sentiment for the stock was also helped by validation and endorsement of the technology through research partnerships with top global household names in the industry such as Astra Zeneca, Eli Lilly and GlaxoSmithKline.

The stock price has retraced since then primarily due to the following reasons in our view:

- **First regulatory approvals for VivaGel coated condoms taking much longer than expected:** The market had anticipated the license agreements with Okamoto and Ansell for this product to yield early revenue streams from CY2012 based on guidance from the company. However the first of the regulatory approvals was not forthcoming until March 2014.

  This has been a negative overhang on the stock which we believe is now removed with Okamoto receiving regulatory approval in Japan in March and launch expected in CY3Q14. We also expect that first regulatory approvals in some of the Ex-US markets under Ansell's agreement could start coming in before the end of CY2014.

- **Phase III results from Bacterial Vaginosis Treatment trials with VivaGel not meeting FDA stipulated endpoint:** Data from the trials was reported in November 2012. Results from the two trials (500 patients in total) demonstrated that VivaGel (administered once a day for seven days), could effect a statistically significant Clinical Cure at the End of Treatment (5 days post treatment) vs. placebo (~53.6% vs. 19%, $p<0.001$). It also demonstrated a statistically significant reduction in BV symptoms with VivaGel vs. placebo. However, the FDA stipulated primary endpoint of Clinical Cure (i.e. TOC 2-3 weeks post cessation of treatment) was not met (~27.4% vs. ~24.6%).

  The company decided against pursuing the claim of VivaGel as an acute treatment for Bacterial Vaginosis further. Nonetheless, the company is confident that it can pursue a symptomatic relief claim for managing BV related symptoms (in Ex-US markets only). The symptomatic relief opportunity is a bit different being an OTC (Over the Counter) consumer product, whereas the acute treatment opportunity was a prescription (Rx) pharmaceutical product. We are optimistic that SPL can out-license VivaGel for the Ex-US OTC market, given the strong data on symptom resolution seen in trials to date.

- **Phase II results from BV Prevention of Recurrence trial while broadly positive fell short of market expectations:** Results from a 205 patient Phase II R-BV trial released in April 2013, while encouraging did not achieve statistical significance. The results demonstrated that 1% VivaGel, on various measures of efficacy, reduced the overall risk of BV recurrence and re-iterated the strong symptom resolution effect of VivaGel. In our view, the fact that 80% of the women with recurrent BV (a difficult patient population to start with) remained BV free at the end of 4 months of VivaGel treatment is a strong outcome nevertheless and supports moving into Phase III.

  Given, that the results for the most part trended towards statistical significance with p values just above 0.05, we think it's reasonable to assume that an adequately powered trial has a good chance of achieving statistical significance. We acknowledge that a statistically significant Phase II result would have considerably de-risked the asset and potentially allow it to be licensed by now. Nevertheless, we believe SPL's current cash position will allow it to fund the two planned Phase III trials for R-BV. Results from the trial, if positive, will allow SPL to out-license it at attractive commercial terms.

Valuation

We have revisited our assumptions for SPL and changed some aspects of our valuation methodology since we published on the name last in April 2013.

Previously our valuation was set at the mid-point of our base case & optimistic case DCF range. For all biotech stocks, we no longer use an optimistic case valuation. Therefore we value SPL at our base case.

On a broad level the changes to our risk weighted DCF valuation stemmed from a) updating our model with FY13 and 1H14 reported numbers and rolling forward of our DCF model, b) removal of pre-clinical stage and non-core opportunities, c) adding in the BV Symptomatic Relief opportunity, d) Separating out the VivaGel coated condom opportunity into Okamoto and Ansell markets, e) change in assumptions regarding timing of first sales, market size, pricing etc. in our patient driven market revenue models; f) change in assumptions regarding timing of deal and deal terms and g) adjustments in risk weighting.

We value SPL using a risk-weighted DCF sum-of parts model. Our valuation is the sum of NPVs of individual assets based on the different indications targeted by Starpharma's VivaGel, internal lead drug delivery programme dendrimer-docetaxel and internal lead agrochemicals programme dendrimer-glyphosate. We also include the marketed diagnostics/laboratory reagents asset which is a marginal ongoing revenue stream for SPL. Each of the individual DCF models use risk-adjusted revenue numbers based on the probability of success in the clinical trials for each indication. The probability of success we attribute to each indication varies according to the development phase for each.

We value SPL at A$1.07/sh

Our DCF valuation model is based on a WACC of 16.0%. **We assume a terminal growth rate of 1% to arrive at our base case valuation of A$1.07/sh.**

Table 1 - Summary of Valuation

Forecasts	Base case
Enterprise Value from DCF (AUDm)	284.5
Add: Cash at end FY14E (AUDm)	23.4
Less: Debt at end FY14E (AUDm)	0.1
Equity Value (AUDm)	307.8
Total diluted shares at end FY14E (million)	288.3
Value per share (AUD)	**$1.07**
Current Share price (AUD)	$0.57
Expected Capital Growth	89.4%

SOURCE: BELL POTTER SECURITIES ESTIMATES

Table 2 - Valuation Sensitivity Analysis to WACC and Terminal Growth Rate

		WACC				
		15.00%	16.0%	17.00%	18.0%	19.00%
Terminal Growth	-0.5%	$1.16	$1.05	$0.95	$0.87	$0.80
	0.0%	$1.17	$1.05	$0.96	$0.87	$0.80
	0.5%	$1.18	$1.06	$0.96	$0.88	$0.80
	1.0%	$1.18	$1.07	$0.97	$0.88	$0.81
	1.5%	$1.19	$1.07	$0.97	$0.89	$0.81
	2.0%	$1.20	$1.08	$0.98	$0.89	$0.81
	2.5%	$1.21	$1.09	$0.99	$0.89	$0.82

SOURCE: BELL POTTER SECURITIES ESTIMATES

At a WACC of 16%, for every 0.5% change in terminal growth rate, our base case valuation changes minimally by ~A$0.01. We also established that at a terminal growth rate of 1%, every 1% change in WACC, caused an A$0.08-A$0.12 change in our valuation.

Table 3 - SPL- Probability-Weighted Sum-of-parts Valuation Summary

Asset	Stage	First Fiscal Year of sales (Est.)	Peak Market share	Peak Sales Global (US$m)	Probability of success	Probability adjusted NPV (A$m)	Value per share (A$)	% Mix
VivaGel BV Symptomatic Relief	Regulatory Submission planned	2016 (Ex-US)	15.0%	$56	80.0%	$35	**$0.12**	11.2%
VivaGel BV Prevention of Recurrence	Phase II complete	2017	25.0%	$647	38.0%	$129	**$0.45**	41.8%
VivaGel Coated Condom - Okamoto	Regulatory approval received	2015 (Japan)	10.0%	$21	100.0%	$6	**$0.02**	2.0%
VivaGel Coated Condom - Ansell	Awaiting first regulatory approval	2015 (Ex-US), 2016 (US)	10.0%	$374	80.0%	$89	**$0.31**	29.0%
Dendrimer-Docetaxel (first solid tumour)	Phase I	2020	15.0%	$506	15.0%	$44	**$0.15**	14.1%
Dendrimer-Glyphosate	Field Trials ongoing	2016	10.0%	$763	15.0%	$12	**$0.04**	4.0%
Diagnostics/Laboratory Reagents	On-market	NA	NA	NA	NA	$5	**$0.02**	1.5%
Other Pipeline/Non-allocated	NA	NA	NA	NA	NA	-$35	**-$0.12**	-11.3%
Cash (EOY 2014E)	NA	NA	NA	NA	NA	$23	**$0.08**	7.6%
Debt (EOY 2014E)	NA	NA	NA	NA	NA	-$0.1	**$0.00**	$0.00
Equity Value						**$308**	**$1.07**	**100.0%**

GLOBAL PEAK SALES ARE PRE-RISK ADJUSTMENT AND ROYALTIES. BV = BACTERIAL VAGINOSIS

PEAK SALES FOR COATED CONDOM FOR OKAMOTO AND ANSELL ARE NOT GLOBAL; THEY ARE BASED ON REGIONS UNDER AGREEMENT WITH THEM. PEAK SALES FOR VIVAGEL SYMPTOMATIC RELIEF IS FOR EX-US MARKETS ONLY.

SOURCE: BELL POTTER SECURITIES ESTIMATES

Table 4 - Deal Assumptions for SPL

Asset	Indication	Stage at Licensing	Licensee	Fiscal Year Timing of deal (Est.)	Total Deal Value in USDm (upfront plus milestones)	Upfront (USDm)	Developmental & regulatory Milestones (USDm)	Commercial Milestones (USDm)	Royalty Rate (%)
VivaGel	BV Symptomatic Relief (EX-US)	Registration (pre-launch)	TBC	2016	25	1.5	NA	23.5	20.0%
VivaGel	BV Prevention of Recurrence	Phase III complete	TBC	2017	200	5	35	160	25.0%
VivaGel	Coated Condom (Japan)	Pre Regulatory Approval	Okamoto	2011	0	NA	NA	NA	12.0%
VivaGel	Coated Condom (Ex-Japan)	Pre Regulatory Approval	Ansell	2012	0	NA	NA	NA	12.0%
Dendrimer-Docetaxel	First Solid tumour	Phase I complete	TBC	2016	200	10	90	100	12.0%
Dendrimer-Glyphosate	Crop protection	Pre Regulatory Submission	TBC	2H15/1H16	0	NA	NA	NA	5.0%

NOTE: OUR DENDRIMER-DOCETAXEL DEAL ASSUMPTIONS ARE CONSERVATIVE REFLECTING ITS EARLY STAGE. IT COULD POTENTIALLY HAVE ADDITIONAL VALUE FOR EACH ADDITIONAL INDICATION THAT THE LICENSEE PURSUES. WE DO NOT INCLUDE COMMERCIAL MILESTONES IN OUR MODEL AT THIS STAGE.

ROYALTIES ARE LIKELY TO BE TIERED FOR EACH DEAL. WE ASSUME FLAT RATE AT MID POINT OF RANGE FOR NOW.

SOURCE: BELL POTTER SECURITIES ESTIMATES

Upside Risk to our valuation

We have not modelled SPL's potential revenue flow from its partnerships with Nufarm (agrochemicals), Gowan Company (agrochemicals), Makhteshim Agan (agrochemicals), Astra Zeneca (drug-delivery), Eli Lilly (drug delivery), Elanco (drug delivery), GSK (drug delivery) and from its multiple undisclosed partnerships both in drug delivery and agrochemicals. These partnerships becoming substantial in future and converting to a commercial licensing deal with financial terms would lead to an upside to our estimates.

At this stage, we do not value VivaGel's opportunity in Viral Conjunctivitis and SPL's second internal candidate from drug-delivery Dendrimer-Oxaliplatin, given the early nature of these programmes. These programmes moving ahead into the clinic would be a potential upside to our estimates.

Also, we note that docetaxel (Taxotere) made by Sanofi Aventis is currently approved for multiple indications including breast cancer, head and neck cancer, gastric cancer, prostate cancer and non-small cell lung cancer (NSCLC). SPL has previously reported results from animal studies of dendrimer-docetaxel, which demonstrated that dendrimer-docetaxel has superior efficacy to docetaxel alone across a wide range of tumours namely prostate, lung, ovarian and breast. SPL's closest competitor BIND Therapeutics, which has an improved docetaxel formulation in development, is pursuing NSCLC and prostate cancer indications. At this stage for SPL, we model dendrimer-docetaxel's opportunity for the first solid tumour indication the company may pursue. However, depending on the results from the Phase I trial, which is recruiting patients with various solid tumours, SPL or a potential licensee, may decide to pursue more than one indication in parallel. This could considerably increase the market opportunity for this asset. **We envisage that expanded indications for dendrimer-docetaxel will lead to material upgrades in our numbers.** We will revisit our assumptions on the basis of the Phase I dendrimer-docetaxel trial results.

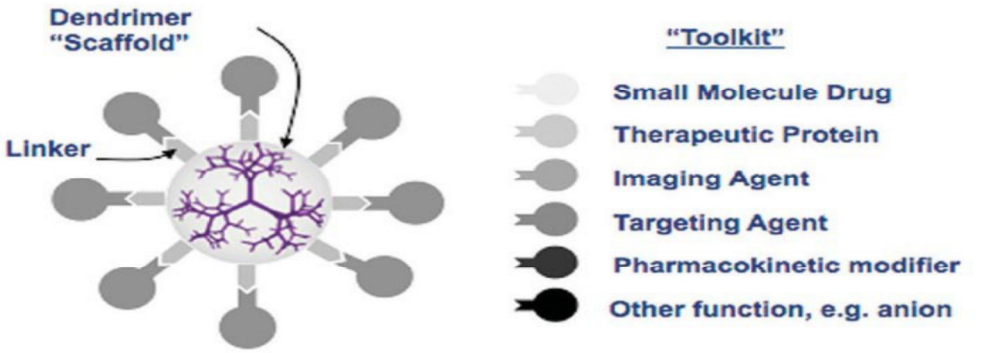
Dendrimers –The technology

Dendrimers fall under the broad heading of nanotechnology, which covers the manipulation of matter in the size range of 1-100 nanometers (one million nanometers equal one millimetre) to create compounds, structures and devices with novel, pre-determined properties.

Starpharma's dendrimers are synthetically produced, highly-branched macromolecules (polymers) with a well-defined stable covalent structure. Dendrimers are constructed by the successive addition of layers to the branching groups. The synthesis of dendrimers involves a core molecule with branching groups to which other branching molecules called monomers are added in spherical layers until the desired structure is reached. Each new layer is called a generation.

The final generation can incorporate additional active groups that give the particular functionality to the dendrimer. The many surface points of attachment can then be functionalised with single or multiple active groups depending on the intended application. This 'polyvalency' property of dendrimers leads to enhanced activity.

Figure 1 - Polyvalency of dendrimers



SOURCE: COMPANY DATA

Dendrimers are synthesised using standard chemical processes. Since the synthesis process is controlled, dendrimers have a high degree of uniformity.

For most of SPL's pharmaceutical dendrimers the monomer used is lysine (an amino acid), which is biofriendly and low cost. The dendrimers used in agrochemicals called the Prisostar dendrimers are different. They are not polylysine and can vary in structure. We give a brief snapshot of how the dendrimers are used in the three main applications SPL is pursuing below:

- **VivaGel for Bacterial Vaginosis (BV):** The compound SPL7013 consists of a polylysine dendrimer scaffold with the active surface groups consisting of 32 naphthalenyl disulphonic acid groups. Each of the naphthalenyl disulphonate surface groups is attached to the branched dendrimer scaffold with an oxyacetamido linkage to the 32 terminal groups.

  In this instance, SPL's dendrimer is used as an active compound itself. In laboratory studies, SPL7013 has been shown to inactivate HIV, HPV and genital herpes (HSV-2) viruses by binding with the virus and preventing it from attaching to the host. In the case of HIV specifically, SPL7013 acted like an entry inhibitor or a fusion inhibitor, where it blocked the gp120[1] protein on the surface of the HIV by binding to it and preventing it from affecting the host. The mechanism of action of VivaGel in BV is thought to be similar with it binding with the harmful bacteria and inactivating them.

[1] Gp120 protein on the surface of the HIV has the function of helping the virus in entering CD4 cells.

- **Dendrimer in drug delivery:** The core of the dendrimers used in drug delivery is identical to SPL7013 dendrimer i.e. made of lysine. In this instance, the dendrimer is used as an inert scaffold which acts as a carrier or transporter of an active drug. The anti-cancer drug (referred to as payload) is conjugated (covalently linked) to the polylysine dendrimer scaffold (the carrier) which then transports it to the tumour tissue.

  Some drugs continue to function when attached to dendrimers, whereas some drugs need to be released before they can work. SPL uses different kinds of linker between the dendrimers and the pharmaceutical drug to control when and where the drug is released.

  In the case of dendrimer-docetaxel (DEP Docetaxel), the linker between drug and dendrimer is designed to release the drug in a controlled manner. The linker used by SPL in its dendrimer-docetaxel is not in the public domain. We understand that SPL considers it an important part of its IP and therefore does not want to disclose it to its competitors.

  Polytheylene glycol (PEG) is also attached to the dendrimer scaffold. It is used to solubilise docetaxel.

  Dendrimers can be used to specifically target tissues, receptors or organs both actively i.e. by attaching a targeting molecule such as an antibody to the dendrimer construct, as well as passively by tailoring the size and chemical properties of the dendrimer. Dendrimer-docetaxel **'passively targets'** the tumour, taking advantage of the leaky vasculature associated with tumour tissue to enter the tumour cells. Owing to their size and decreased lymphatic function of tumours, they are not cleared by the lymphatic drainage and get trapped within the tumour cells where they then release their drug payload i.e. docetaxel.
- **Dendrimer in agrochemicals:** In this instance, SPL's dendrimers called Priostar are added as an additive to the existing agrochemical formulation with the view to improve the characteristics of the formulation such as improve its solubility, stability etc. There is no linker used here. The core is not made of lysine and varies chemically between different agrochemical formulations depending on what function the dendrimers are trying to achieve.

VivaGel Coated Condoms nearing Commerciality

Earlier this year in March, Starpharma's partner Okamoto received the first regulatory approval for a VivaGel coated condom in Japan. We expect the product to be launched in Japan in CY3Q14. We also expect that first regulatory approvals in some of the Ex-US markets under Ansell's agreement could start coming in before the end of CY2014.

This approval was long awaited, removed a negative overhang from the stock and represents near term royalty revenue for SPL. The launch of the coated condom in Japan will also considerably de-risk the VivaGel portfolio and place SPL among the rare breed of small cap biopharma companies listed on the ASX with a considerable revenue generating product on the market.

We expect that further regulatory approvals for VivaGel coated condoms, in markets under the agreement with Ansell, will further validate the dendrimer technology as well as build confidence around Starpharma's ability to commercialise its promising technology.

Background

Starpharma's lead product VivaGel (SPL7013 Gel) is being developed as an anti-microbial coating for Ansell and Okamoto condoms which would offer protection against Sexually Transmitted Infections (STI's). In laboratory studies, SPL7013 has been shown to inactivate HIV, HPV and genital herpes (HSV-2) viruses by binding with the virus and preventing it from attaching to the host.

Agreement with Okamoto: Starpharma entered into an agreement with Okamoto Industries in May 2011, giving it the marketing rights to the VivaGel coated condom in Japan.

Okamoto is the market leader in Japan with ~60% share of the Japanese condom market. Japan is the world's second largest condom market with ~US$500m in annual sales. Condoms are the most popular method of contraception used in Japan owing largely due to the late introduction of oral contraceptives in the country (first approved in 1999). It is estimated that ~75% of married couples in Japan use male condoms.

As per the terms of the agreement, Okamoto will be responsible for registration and launch of the product and will pay royalties to SPL (we estimate it to be tiered in the range of 10-15%, but model a flat rate of 12% for now). The coated condoms marketed by Okamoto will carry the VivaGel brand.

Agreement with Ansell: Starpharma entered into an agreement with Ansell in August 2011, giving it the marketing rights to the VivaGel coated condom in countries excluding Japan and some Asian markets.

Ansell is the world's second largest player in the condom market by sales.

As per the terms of the agreement, Ansell will assume the responsibility for registration, manufacturing and launch of the product as well as bear commercialization costs. SPL will be paid royalties (we estimate it to be tiered in the range of 10-15%, but model a flat rate of 12% for now).

VivaGel coated condom the attraction for Ansell and Okamoto:

The VivaGel coated condom offers more safety and value add to users in terms of extra protection against Sexually Transmitted Infections (STI's). We understand that broadly the product would carry a claim on the lines of 'Vivagel has been shown in labs to inactivate the common STI causing viruses'. **In our view, this offers a strong marketing claim to**

Ansell and Okamoto to differentiate their product. Given that SPL holds the IP for VivaGel and has exclusively licensed it to Ansell and Okamoto, means that their competitors will not have access to VivaGel. The product will enable them to charge a premium pricing and also capture market share. Therefore it should be in the interest of both Ansell and Okamoto to actively push this product and switch consumers over to this line of condom.

The global condom market is projected to reach ~US$5.4bn by 2018. We believe that the growth in the condom market is being more driven due to the concerns regarding spread of Sexually Transmitted Infections rather than for its use as a contraceptive.

Consumer research undertaken by the company and its partners has shown that there is strong interest in the VivaGel coated condom which is encouraging.

According to Okamoto's senior managing director Mr. Seiji Takeuchi, condoms with functional coatings and gels represent the next wave of innovation in the Japanese condom market following on from a decade-long focus on condom thinness.

Also, historically the market has been receptive to condoms with functional coatings which offered some extra benefit. In the 1990s, a condom with a spermicidal coating called Nonoxynol-9 was very popular. It was only in early 2000s that it started dropping in popularity at the back of data showing the condom to be ineffective against HIV and other STIs with possible increased risk of infection from frequent use.

Hence, we are optimistic that the VivaGel coated condom with supportive data around VivaGel's antiviral activity, should also get positive reception.

SPL has patents out to 2027 for the VivaGel coated condom which in all likelihood adds to its attractiveness to these players.

Valuing the opportunity

The key variable in valuing this opportunity is predicting how fast the adoption of the VivaGel coated condom will be. We assume a gradual uptick in sales based on marketing and brand awareness activities undertaken by Okamoto and Ansell. Our base assumption is that the market will be receptive to a condom which offers 'something extra'.

We estimate royalty revenues from VivaGel coated condom growing from US$0.6m in FY15 to US$22m in FY20

Using our patient driven model, we estimate risk adjusted sales of ~US$5m in FY15 growing to ~US$187m in FY20. At a 12% royalty rate, this translates to a royalty revenue stream to SPL of ~US$0.6m in FY15 growing to ~US$22m in FY20. **We estimate that beyond FY20, SPL could get annual royalty revenue streams from the VivaGel coated condom asset in excess of US$30m pa.**

We value SPL's VivaGel coated condom opportunity (Okamoto and Ansell) at A$0.33/sh.

Key market assumptions:

- Our model uses as base our estimated number of women (married and unmarried) of a reproductive age (15-49) who rely on male condoms as a method of contraception.
- We estimate peak penetration of VivaGel coated condom as 10% of that group.
- We assume a box of VivaGel coated condoms containing 12 pieces costs US$12/box in the US and US$8.4/box in Ex-US markets.
- UNFPA assumes that 100 condoms provide 1 year of protection in calculations for cost per male condom. We conservatively assume in our model that each person on average uses ~96 condoms or 8 boxes of 12 each in a year. We assume that 4 out of those boxes is a VivaGel coated condom box in the US and 3 out of those boxes is a VivaGel coated condom box in Ex-US markets.

Bacterial Vaginosis – The late stage opportunity

Starpharma's lead product VivaGel (SPL7013 Gel) is being developed as a topical microbicide for the prevention of recurrence of Bacterial Vaginosis (BV). It is also being positioned as a symptomatic relief product for women suffering with BV in some markets outside of the US.

The company is in advanced stages of preparation for its planned Phase III prevention of recurrent Bacterial Vaginosis (R-BV) trials. Quintiles, one of the leading Contract Research Organisations (CRO) have been engaged to conduct the trials. We expect these trials to start in the next few weeks. We expect positive results from this trial in CY2H15 would enable SPL to get a lucrative deal given the high unmet need and no other approved treatments.

The company also plans to submit for registration, in Ex-US jurisdictions, a BV symptomatic relief claim for VivaGel in FY1H15. We expect a deal, primarily royalty based with modest commercial milestones, to be inked in FY1H16. We expect SPL can start earning royalties from this indication in FY16. The symptomatic relief opportunity is a bit different being positioned as an OTC (Over the Counter) consumer product, whereas the R-BV opportunity will be a prescription (Rx) pharmaceutical product.

Given the late stage nature of SPL's BV opportunity (R-BV and symptomatic relief), it accounts for the major share of our valuation (~53%).

Overview of Bacterial Vaginosis infection

Bacterial Vaginosis is the most common vaginal infection in women of childbearing age (14-49). It is associated with an imbalance in the 'good' and 'harmful' bacteria that are normally found in a women's vagina. Specifically in BV patients the *Lactobacillus* species of bacteria loses its predominance to other bacteria such as those of the *Gardnerella, Mobiluncus* and other anaerobic species. The lactobacilli are largely responsible for maintaining the acidic pH of the vagina.

Disease Prevalence: 29% of US women aged 14-49 have had BV. 30% of BV patients in US have recurrence of symptoms within 3 months of therapy and more than 50% experience a recurrence within 12 months. **Recurrent BV is defined as episodes of 3 BV or more in 12 months.** As an indication BV is an underdiagnosed and undertreated disease.

Symptoms and Risks: The disease is linked to complications like premature delivery, increased risk of sexually transmitted infections (STIs) like HIV and genital herpes, development of pelvic inflammatory disease (PID) and in pregnant women undergoing abortion, it is linked to an increased risk of infection.

Many women with BV have no symptoms. For women with symptomatic BV, the disease affects the quality of life especially if they have chronic and repeated episodes of BV. Common symptoms of BV include:

- Abnormal vaginal discharge
- Unpleasant odour
- Burning during urination
- Itching around outside of vagina

There is no approved treatment for prevention of recurrence of BV

Standard of Care and its quality: There is currently no treatment approved for prevention of recurrence of BV. Current acute treatment options for BV are also few. Hence, there

exists an unmet need for safe and effective treatments and therapies that can prevent the recurrence of the infection.

Current standard of care for BV acute treatment are the antibiotics metronidazole and clindamycin. They are administered either as a pill or applied topically intra-vaginally. They are not optimal since they have high relapse rates and are also associated with side effects including increased risk of thrush (candidiasis), gastrointestinal side effects, adverse reactions with alcohol consumption and are incompatible with condom use.

The high side effects of antibiotics sometimes lead to non-compliance and incomplete treatment which in turn may lead to development of resistance by the bacteria for the antibiotic therapy. Frequent use of antibiotics is also considered to lead to development of resistance.

The high side effects and resistance issues associated with existing antibiotic treatments make them unsuitable for long-term or preventative use.

VivaGel has a compelling proposition to prevent recurrence of BV (R-BV): Since VivaGel is applied topically, unlike antibiotics it does not get absorbed in the patient's bloodstream and therefore is less likely to cause drug interactions and thus is not prone to the side effects or contra-indications seen with antibiotics. We also believe that the resistance issue arising from frequent use of antibiotics is unlikely to be an issue with VivaGel which is based on SPL's dendrimer technology. This allows VivaGel to be used potentially as a chronic use therapy.

Even for antibiotics which are applied topically, contra-indications and warnings of side effects as seen with their oral counterparts still exist as a risk, albeit a reduced one.

The idea here is to use VivaGel as a maintenance therapy for BV. After women (with a history of recurrent BV) are initially cured with antibiotic therapy, they will be put on VivaGel therapy to help in reducing the recurrence of BV.

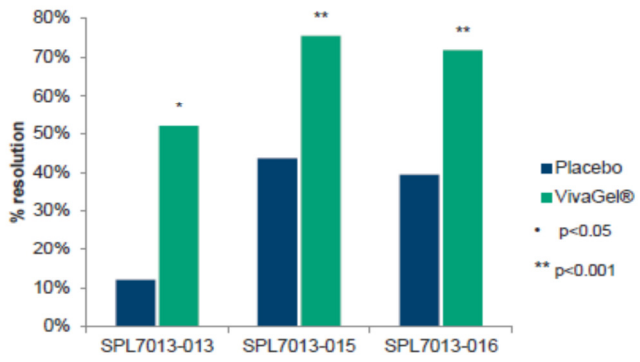
The two Phase III BV treatment trials as well as the Phase II R-BV trial have demonstrated that continuous use of VivaGel is effective in reducing BV symptoms. The Phase II R-BV trial also demonstrated that 1% VivaGel, on various measures of efficacy, reduced the overall risk of BV recurrence. In that trial, more than 80% of women with recurrent BV in the VivaGel 1% group remained free from BV at end of treatment (Week 16).

VivaGel for managing BV Symptoms: In Ex-US markets only, SPL will be pursuing regional approvals of VivaGel for management of BV symptoms. This will be an OTC (over the counter) consumer product. This means that women will not need to see a doctor to get a prescription and will be able to purchase this off-the-shelf in stores. Given that it is women with Symptomatic BV who generally seek treatment, an effective solution for women to reduce or relieve these symptoms is likely to be well received.

Women, who get symptoms of BV for the first time, are more likely to self-medicate (buying an OTC product) rather than going to a doctor for diagnosis. These women would generally consult a doctor if there symptoms persist after self-treatment. All the clinical trials so far have demonstrated the strong BV symptom resolution effect of VivaGel compared to the placebo gel as long as women remained on treatment. In 3 separate VivaGel trials, VivaGel was shown to provide statistically significant results showing greater odour resolution as compared to placebo (See Figure 2 & 3).

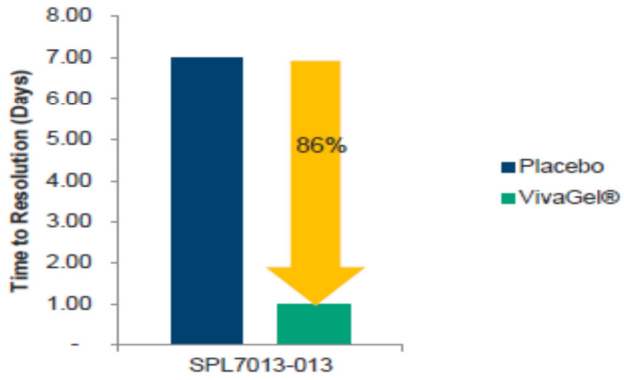
Thus, we expect any industry player looking to augment its women's health offering to be interested in licensing SPL's VivaGel for BV. Some leading companies with women health offerings include Bayer, Eli Lilly, Pfizer, Merck Serono, Johnson & Johnson and Actavis.

Figure 2 - VivaGel - Resolution of Odour in BV patients



SOURCE: COMPANY DATA

Figure 3 - VivaGel - Rapid resolution of BV related odour



SOURCE: COMPANY DATA

The Path Forward – Phase III BV Prevention of Recurrence Trials

The proposed design for the Phase III R-BV trials is very similar to the Phase II R-BV trial and has the nod from both the FDA and the EMA.

In each trial, patients with recurrent BV (3 or more episodes of BV in the last 12 months), will be treated with oral antibiotic metronidazole for 7 days and then screened to ensure that they are free of acute BV. Women will be then randomised to receive either 1% VivaGel or Placebo gel, every second day at bedtime for 16 weeks, followed by a 12 week follow-up period.

We expect the trials will be adequately powered to show statistically significant results given the high placebo effect seen with previous VivaGel BV trials. We understand that each trial will recruit ~600 patients each. One of the trials will have US sites predominantly, while the other trial is expected to have Ex-US sites predominantly.

The primary endpoint of the trial will be Recurrence of BV by or at the End of Treatment Visit (Week 16) as measured by Amsel's criteria.

The four Amsel's criteria are:

- Presence of white to grey homogeneous discharge,
- Whiff test indicating fishy odour with addition of potassium hydroxide,
- Presence of clue cells ≥ 20% of total epithelial cells and
- Vaginal pH greater than 4.5.

The first 3 criteria's above are stipulated by the FDA as the Amsel's criteria for BV diagnosis.

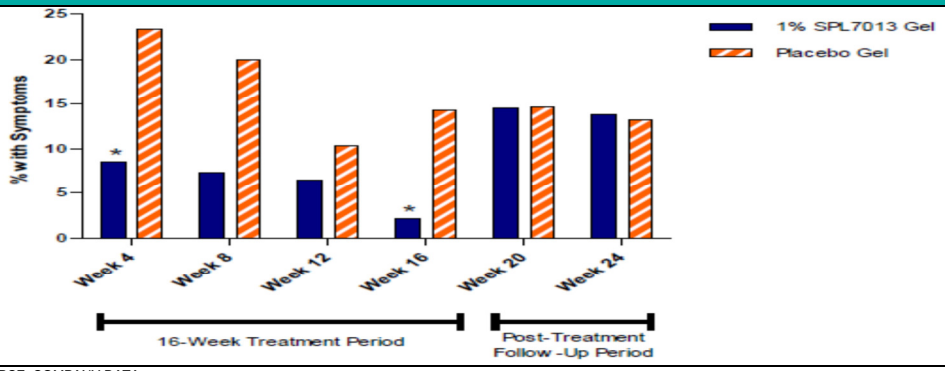
We note that in the Phase II R-BV trial, at week 16 (EOT) when R-BV was assessed using FDA stipulated Amsel criteria of BV diagnosis, the rate of recurrence of BV was only 12% in the 1% VivaGel arm vs. 28% for placebo, and the result was close to statistical significance with p=0.0588. This difference represented a 56% relative risk reduction in R-BV with 1% VivaGel vs. placebo. This is encouraging as the criteria used for diagnosis was regulator specified and we are optimistic that higher number of patients could potentially recreate the Phase II results but with statistical significance.

Lessons learnt from previous VivaGel BV trials?

The previous BV trials have highlighted a few key points which we believe needs to be taken into account by SPL in designing and powering its Phase III R-BV trials.

- **VivaGel is a continuous use product:** In the Phase II R-BV trial, during the 8 week follow up period (after the end of 16 week treatment), the results showed that with the ceasing of treatment, there was no substantial difference between the proportion of women reporting BV symptoms between both the 1% VivaGel group and the placebo group. **This re-iterated the fact that the VivaGel product is a continuous use product and is only effective as long as the patient is on the treatment.**

Figure 4 - Patient Reported BV Symptoms since last visit



SOURCE: COMPANY DATA

- **High placebo effect:** Previous trials have shown that the placebo gel also results in reduction in BV symptoms. The placebo used in the trial is the hydroxyethylcellulose (HEC) placebo gel, which is considered as an inert formulation. Results from VivaGel trials suggest that even the most inert formulations will have some effect on vaginal microflora. Hence, the Phase III trials have to account for this placebo effect and recruit a much higher number of patients in order to have a chance of showing statistically significant difference between results in patients treated with VivaGel and those treated with the placebo. Statistical significance is required from the point of view of satisfying regulatory requirements.

In our view, the dosing regimen as well as the proposed powering of the Phase III trials takes into account the above factors.

Also, as we see it, there are two additional risks which exist based on what we have seen in the Phase II BV trial:

- **Risk of dropout:** In the Phase II R-BV trial although the 1% VivaGel arm (which is the dose being used in the Phase III R-BV trials) did not have a high rate of drop out, there was a large drop out seen in the 3% VivaGel group. This in our view could be one of the reasons why the 3% VivaGel arm had similar results as seen with the placebo arm. According to the company, these drop outs were not treatment related as the patients dropped out before they got the first VivaGel dose. We understand that the drop outs were largely in one site where the patients recruited had low literacy rates. For the Phase III R-BV trials, one of the leading Contract Research Organisations (CRO) Quintiles, have been engaged to conduct the trials. We expect to have better trial management in terms of site qualification, retention strategies, etc. employed by Quintiles. This should reduce the risk of the single site related drop out seen in the Phase II trial. However since we can't completely rule out the chance of a drop out in the planned Phase III R-BV trials, in our view it is very important that the trial be adequately powered to account for it.
- **Safety bar for chronic use product may be higher:** In the Phase II R-BV trial the treatment related Adverse Events (AEs) in the 1% VivaGel group was largely comparable to that in the placebo group (19% vs. 13%) and total AEs in the 1% VivaGel group was substantially lower than that seen with historical antibiotic (metronidazole 16 week study). There were no serious adverse events. The most common AEs seen were genitourinary related and candidiasis. Candidiasis is a

common side effect seen with metronidazole which all the patients in the study were pretreated with. In our view, genitourinary related AEs and candidiasis are likely to be seen in the Phase III trials as well. Acute treatment antibiotics have been approved with much higher rate of AEs compared to what has been seen with VivaGel, therefore we believe VivaGel is a much safer option than conventional antibiotics.

However, since for prevention of recurrence, VivaGel will be required to be used continuously vs. a short term course required for acute treatment, there exists a risk that the safety bar set for VivaGel may be higher. We do not have any precedence given that there is currently no approved treatment for Prevention of BV. Hence, it is unclear to us at this point whether the safety thresholds for a chronic use BV product (i.e. designed to be used continuously) may be more stringent from the regulatory point of view. Having said that, as long as the AEs in the VivaGel arm are comparable to placebo arm there may not be an issue. This will be an issue if the AEs in the 1% VivaGel arm are substantially higher than the placebo arm and will also depend on the type and seriousness of the AEs in the VivaGel arm.

Competitive landscape

There is currently no treatment approved for prevention of recurrence of BV. We are aware of one company called AmVac who has a vaccine in development for treatment as well as prevention of recurrence of Bacterial Vaginosis. We understand that the company is looking to get EU approval in the first instance. We are not aware of any US trials being conducted with the vaccine for Bacterial Vaginosis. Hence, SPL is likely to be the first to market for prevention of recurrence if approved by the FDA.

For symptomatic relief, SPL is targeting the OTC market in Ex-US jurisdictions. Indirectly, the company will face some competition from the approved antibiotics such as Metronidazole and Clindamycin for acute treatment of BV. However, its direct competition will be OTC products which can be clubbed broadly under the heading *'Vaginal pH correction treatments'*. The 'vaginal pH correction' OTC products are intravaginal gels or washes which change the acid balance of the vagina, making it a less hospitable environment for harmful bacteria. There are quite a few of these products available however, most don't have the extent of clinical trials data as SPL has to back their effectiveness claims. In the OTC market, awareness and brand building efforts play a significant role in driving product adoption. Therefore, VivaGel's success in the OTC market will depend on the marketing and distribution capabilities of its licensee. We give a brief snapshot of some of the competition below.

Metronidazole 1.3% for acute treatment of BV: In April 2013, Actavis acquired the rights to higher dose Metronidazole (1.3%) gel from Valeant for acute treatment of Bacterial Vaginosis for up to US$57m in upfront payments, milestone payments and guaranteed royalties for first three years of commercialization. As per the agreement Actavis will continue to pay royalties to Valeant after the first three years at an undisclosed rate. The higher dose Metronidazole is expected to provide an alternative to the current standard of care Metronidazole 0.75%.

FDA approved Metronidazole (1.3%) gel at the end of April 2014. Actavis plans to launch it later this year. The selling point for the 1.3% metronidazole is ease of use and more convenient dosing (single dose, pre-filled disposable applicator administered once intravaginally at bedtime) which is likely to improve patient compliance.

As we mentioned, this is not a direct threat to SPL given metronidazole 1.3% is a prescription product while SPL is targeting the OTC market with symptomatic relief claim.

AMV 100 (Vaccine based on proprietary Gynevac platform) made by Switzerland based AmVac AG: AmVac's Gynevac vaccines are being developed for a wide range of urogenital diseases. The AMV 100 vaccine has inactivated strains of Lactobacilli. AmVac is

a privately held company. We do not have access to clinical trial data on the vaccine, but we understand that one of the key target indications for AMV 100 is treatment as well as prevention of recurrence of Bacterial Vaginosis (BV). BV is one of the main causes of pre-term birth. The company is also targeting complications due to BV including prevention of pre-term birth.

The company has recently submitted a Phase III study protocol for Gynevac with the Hungarian drug administration, with the view to use the results of the study to obtain European regulatory approval. The objective of the Phase III trial is to confirm the safety and efficacy of the vaccine for treatment of BV.

As we mentioned, SPL is likely to be first to market for prevention of recurrence of BV, if approved in the US.

Multi-Gyn ActiGel made by Netherlands based company BioClin: This is an OTC product which treats and prevents vaginal discomforts including Bacterial Vaginosis. It also claims to reduce unpleasant odour and discharge. It is derived from plants and consists of BioClin's 2QR-complex (bioactive polysaccharides). The product claims to restore and keep the vaginal flora healthy and balanced. It restores the optimal vaginal acidity (pH). The Multi-Gyn products are marketed to the consumer through pharmacies and drugstores in more than 30 countries.

Balance Activ's BV Gel or BV Pessaries: This is another OTC product which seeks to restore and maintain the pH levels in the vagina to help relieve the symptoms of BV. The product is a unique formula of lactic acid and glycogen. The BV gel is intravaginally administered while the BV pessaries are inserted intravaginally like a tampon. The company won a National PR Week Award last year for its National BV day campaign, an educational piece designed to raise awareness of the condition and help to remove the taboo surrounding the condition Bacterial Vaginosis.

Lactacyd Pharma with Antibacterials: Lactacyd was founded in France in 1950 by scientists who wanted to create an effective product to prevent irritation. Lactacyd products are based on lactic acid. The Lactacyd Pharma with antibacterials product, contains natural antibacterial agents that help inhibit the growth of bacteria and prevent infections and bad odours. This is in the form of an intimate wash in a mild, soap free formula. It is available at supermarkets and pharmacies.

Valuing the opportunity

We value SPL's VivaGel BV opportunity in Symptomatic Relief at A$0.12/sh and Prevention of Recurrence at A$0.45/sh. For details on risk adjustments used please refer to Table 3 on page 6.

Key assumptions:

- Our patient driven model uses as base our estimated number of women of a reproductive age (15-49) who have symptomatic BV and in the case of prevention of recurrence the sub-population of that which have recurrent BV. We estimate that in the US alone there are ~3.5m BV patients who seek treatment and ~15-30% of that group who have recurrent BV.
- We estimate peak penetration of VivaGel as 15% of the Symptomatic BV patient population in Ex-US markets and 25% for the Recurrent BV patient population globally.
- We estimate peak pre-risk adjusted sales for VivaGel in Symptomatic relief at US$56m (Ex-US OTC markets only) and for prevention of recurrence at US$647m (global).
- We assume that VivaGel for Symptomatic relief gets licensed in FY16 and for Prevention of Recurrence in FY17. For details on our deal assumptions please refer to Table 4 on Page 6.

Drug Delivery with reformulated Docetaxel – The potential game changer

One of the most exciting aspects of the SPL story for us is the versatility of SPL's dendrimers to be effective as drug delivery agents. SPL is using its dendrimer technology to reformulate well-known off patent cancer drugs with the view of improving their therapeutic profile. The anti-cancer drug (referred to as payload) is conjugated (covalently linked) to the dendrimer polymer scaffold (the carrier) which then transports it to the tumour tissue. The linker between drug and dendrimer is designed to release the drug in a controlled manner. Polytheylene glycol (PEG) is also attached to the dendrimer scaffold which is used to solubilise the drug. This development path is less risky since these are approved drugs known to be safe and to work.

The approach of reformulating cancer drugs to make them safer or more efficacious has been commercially successful in the past. One of the most successful precedence of this approach is the drug Abraxane which is a nanoparticle reformulation of paclitaxel (Taxol), a well-known chemotherapy drug used to treat various cancers such as lung, breast and pancreatic cancers. Celgene acquired Abraxane's developer Abraxis BioScience in 2010 for ~US$2.9bn when Abraxane was generating ~$315-$350 million in revenue and was approved only to treat breast cancer. Since then Abraxane's label has been expanded to include treatment of other cancers such as pancreatic cancer. Celgene reported Abraxane sales of US$649m for 2013. Market expectations are that the drug could reach ~US$1bn in sales over the next 2-3 years, becoming a blockbuster drug for Celgene. Another example is of Nektar Therapeutics, a US based company with a similar approach. It is listed on NASDAQ with a current market capitalisation of ~US$1.4bn.

Dendrimer-Docetaxel (DEP docetaxel) is SPL's lead internal programme in drug-delivery with potential to be licensed in FY16.

Externally SPL has multiple partnerships in drug delivery with big names like Eli Lilly, GSK and AstraZeneca and various other undisclosed partnerships. In our view these collaborations indicate the level of interest in the industry around SPL's dendrimer technology. If any of these drug delivery collaborations gets converted to a commercialization deal with upfront, milestones and royalties, it will validate SPL's technology as well as be an upside to our valuation.

SPL initiated the Phase I clinical trial with its dendrimer enhanced formulation of docetaxel in January 2014. This is a dose escalation trial which will establish the Maximum Tolerated Dose (MTD), ascertain any dose limiting toxicities as well as assess initial efficacy of SPL's dendrimer-docetaxel.

The key inflection point for the stock, in our view, will be results from the Phase I dendrimer-docetaxel trial. Data from animal models (pre-clinical), have been very encouraging and has shown the reformulated dendrimer-docetaxel to have reduced side effects vs. original drug as well as increased anti-cancer activity. The ongoing Phase I trial will provide the first evidence of it in humans.

Consistent with pre-clinical results, if the trial is able to show that dendrimer-docetaxel reduces some of the main dose limiting side effects seen with the original Taxotere drug, as well as provides initial signals of anti-cancer activity, we believe SPL's docetaxel programme will gain a significant edge over other competitive programs. **This, in our view, has the potential to be a game changing event for SPL.**

Also, in the case of platform companies, when one drug works typically investors assign value to the rest of the broader pipeline. Hence, we expect that, if the newsflow from the Phase I dendrimer-docetaxel trial is positive; it is likely to increase the value of the overall

drug delivery capability of SPL's dendrimers. Hence, we expect SPL's second lead candidate behind docetaxel i.e. dendrimer oxaliplatin to also benefit from the sentiment irrespective of its early stage. Dendrimer – Oxaliplatin is expected to move ahead into preclinical studies over the next 12 months. We currently do not assign any value to this programme given its early stage.

SPL intends to release interim data points from the docetaxel trial as they are available. We expect interim data in CY2H14, with top-line data from the trial in CY1H15. Depending on the results from the trial, SPL could potentially license the programme in FY16.

SPL has patents out to 2032 for dendrimer-docetaxel, which is likely to increase its attractiveness to a potential licensee.

Why reformulate Docetaxel?

Docetaxel (Taxotere) made by Sanofi Aventis is a leading chemotherapy drug. Docetaxel is a taxane, similar to paclitaxel. It is currently approved for multiple indications including breast cancer, head and neck cancer, gastric cancer, prostate cancer and non-small cell lung cancer (NSCLC). Taxotere's patent expired in 2010. Prior to patent expiry, Taxotere generated ~US$3.1bn in revenue.

The size of the opportunity makes it commercially attractive for SPL to target, however in our view what makes docetaxel a particularly attractive candidate for reformulation, is the fact that it has several dose limiting toxicities. Some of the well-known adverse events associated with docetaxel are neutropenia (low white blood cell count), anaemia (low number of red blood cells), peripheral neuropathy, alopecia (hair loss), thrombocytopenia (low number of platelets in blood) and anaphylaxis (severe allergic reaction).

Docetaxel is administered as a one hour IV infusion every 3 weeks. Docetaxel is not naturally soluble in water and thus requires a solvent called *polysorbate 80* to solubilize it, prior to administration.

Premedication with corticosteroids is generally given to reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions. G-CSF is used to mitigate the risk of haematological toxicities. The frequency of hypersensitivity reactions, severe fluid retention and fatal anaphylactic reactions with docetaxel, despite premedication, led the FDA to issue a "black box" warning on the package insert. It is hypothesized that these reactions were caused by the detergent *polysorbate 80*.

Dendrimer-docetaxel – The benefits as seen in preclinical studies

In preclinical studies, dendrimer-docetaxel has displayed improved pharmacokinetic profile, superior anti-cancer activity with reduced side effects compared to docetaxel alone.

The benefits seen with the dendrimer-docetaxel formulation in preclinical studies include:

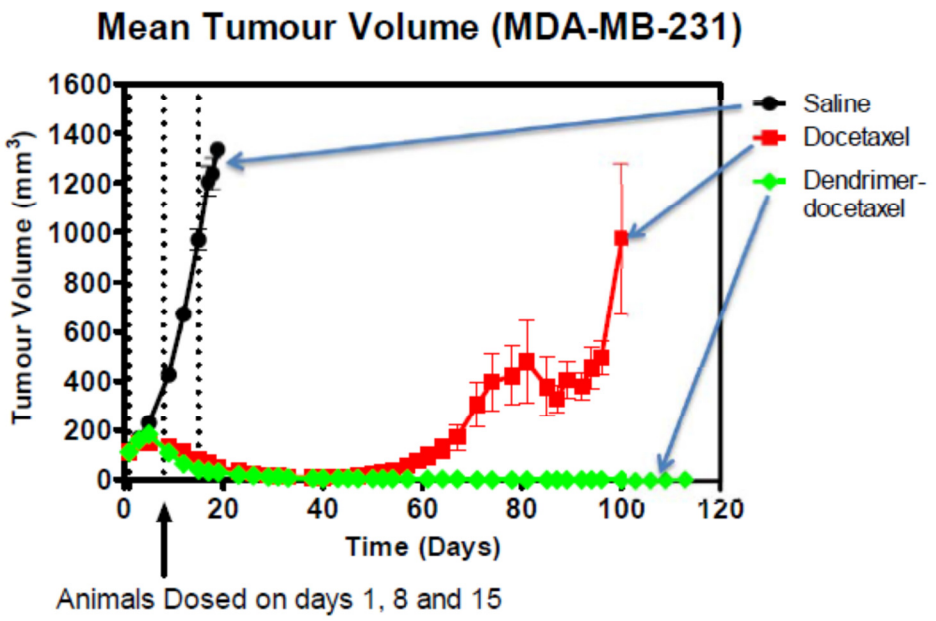
- **Improved solubility in water:** Reformulating docetaxel with SPL's dendrimers improved the water solubility of the drug by 2,000 to 8,000 fold. Increased water solubility removes the need for toxic solvent which is associated with severe side effects including fluid retention and allergic reactions. This would reduce the need for premedication with corticosteroids which have their own side effects.

  Removing the need to use toxic solvent to dissolve docetaxel in water is commercially attractive, as we have seen with Abraxane in the past. Abraxane's key attractiveness was that it removed the need to use the toxic solvent Cremophor which the original paclitaxel drug needed and therefore made the drug less toxic. This in turn enabled a higher dose of paclitaxel to be delivered thereby increasing efficacy of the treatment.

- **Longer plasma half-life:** The plasma half-life of dendrimer-docetaxel was 60 times longer than conventional docetaxel (30 hours for dendrimer formulation vs. 30 mins for Taxotere). Given that dendrimer-docetaxel gets cleared from the blood plasma more slowly than the original Taxotere drug, it will allow greater exposure time of the tumour to the drug. This will likely lead to improved efficacy and will be seen as a benefit as long as increased half-life is not associated with any safety issues.
- **Greater amount of drug delivered to tumour**: At 3 days after IV administration in mouse tumour tissue, levels of docetaxel in tumour tissue was more than 40 times greater than levels seen with original docetaxel alone. For an effective chemotherapy, the amount of drug given to the patient is less important than the amount of drug which gets to the tumour. The 40 times greater accumulation of drug seen with dendrimer-docetaxel indicates a superior selective accumulation displayed by dendrimer-docetaxel in tumours. This implies that less of docetaxel will be in circulation to affect healthy cells, thereby improving efficacy while reducing side effects.
- **Improved efficacy**: In a breast cancer xenograft mice model, 10 mice per group were dosed with dendrimer-docetaxel, docetaxel or saline on days 1, 8 and 15. 60% of animals treated with dendrimer-docetaxel had no evidence of tumour at 94 days. Comparatively at day 60, tumours in 100% of mice treated with docetaxel alone started regrowing. Dendrimer-docetaxel showed significantly better efficacy ($p<0.0001$) than traditional docetaxel.

  In December 2012, SPL reported additional efficacy results from animal studies of dendrimer-docetaxel, which demonstrated that dendrimer-docetaxel had superior efficacy to docetaxel alone across a wide range of tumours namely prostate, lung, ovarian and breast. Results showed that dendrimer-docetaxel resulted in a 26-47% reduction in mean tumour cell survival compared to docetaxel alone.

Figure 5 - Improved efficacy with dendrimer-docetaxel in mice breast cancer model



MOUSE XENOGRAFT (MDA- MB 231); N= 10/GROUP ; ^ P< 0.0001

SOURCE: COMPANY DATA

- **Reduced dose limiting side effect of docetaxel:** One of the most common and dose limiting side effect seen with traditional docetaxel is neutropenia i.e. reduced number of white blood cells (WBCs) in blood following chemotherapy with docetaxel. Neutropenia makes a patient more susceptible to infection. We use the example of metastatic breast cancer to explain the neutropenia side effect of traditional docetaxel.

For the treatment of patients with metastatic breast cancer, the recommended dose of docetaxel is 100 mg/m2 in monotherapy. WBC count of patients on therapy is frequently monitored so that subsequent cycle doses can be adjusted in patients who experience severe neutropenia for more than a week. In practice the dose ranges from 60mg/m2 to 100 mg/m2. Lower doses are likely to be less effective than the recommended 100 mg/m2 dose. If neutropenia persists even at lower doses it may necessitate cessation of treatment.

Neutropenia (<2000 neutrophils/mm3) occurs in virtually all patients given 60 mg/m2 to 100 mg/m2 of Taxotere and severe neutropenia (<500 cells/mm3 for 7 days or more) occurs in 85% of patients given 100 mg/m2 and 75% of patients given 60 mg/m2.

The number of WBCs will start to reduce 5 days after treatment and are usually at their lowest ~7 days after. Neutrophil nadirs occurred at a median of 7 days but this interval may be shorter in heavily pre-treated patients. The next dose of chemotherapy is given only after a person's blood counts have left the nadir and recovered to a safe level.

In October 2013, SPL reported that dendrimer-docetaxel treated rats showed no evidence of neutropenia, while rats treated with traditional docetaxel (taxotere) exhibited severe neutropenia. Furthermore, the dendrimer-docetaxel treated rats showed no evidence of thrombocytopenia (low number of platelets in blood) which was observed in the taxotere treated rats.

The Path Forward – Dendrimer-docetaxel now in the clinic

SPL initiated the Phase I clinical trial with its dendrimer enhanced formulation of docetaxel in January 2014.

The trial will recruit ~25-30 patients with advanced or metastatic solid tumours across 3 centres in Australia. Typically these would be heavily pre-treated patients who have failed previous therapies.

The main objective of the study is to establish the Maximum Tolerated Dose (MTD) of dendrimer-docetaxel, as determined by the occurrence of dose limiting toxicities when given intravenously, once every 3 weeks.

Secondary endpoints include determining the safety, tolerability and pharmacokinetic profile of dendrimer-docetaxel and explore its preliminary anti-cancer efficacy.

The trial is an open label, sequential dose escalation study with two parts a) a dose-escalation phase and b) a dose expansion phase.

Generally, with such two phase protocols, the dose escalation phase would identify initial MTD. In the dose expansion phase, a cohort of patients will be treated at the MTD derived from the dose escalation phase. In the dose expansion phase, the company explores additional safety profile of the drug at the MTD dose, so that a more efficient and accurate dose is selected for Phase II trials. Also, having more patients in the dose expansion phase on the MTD dose, gives a reasonable chance for the company to get some efficacy signals (response to treatment). The company can also have patients with different types of tumours dosed at MTD in the dose expansion phase, which could help the company identify the indication it should pursue in Phase II trials.

The key data point to watch in this trial will be the impact of dendrimer-docetaxel on the well-known dose limiting side effects seen with traditional docetaxel such as neutropenia, alopecia and anaphylaxis.

While we acknowledge that the Phase I studies are typically not designed to demonstrate efficacy as such, the anti-cancer efficacy (complete response, partial response and/or stable disease) data from these trials, will be very important as well. Ideally we would like to see some initial efficacy signals from this trial along with a favourable safety profile.

Consistent with pre-clinical results, if the trial is able to show that dendrimer-docetaxel reduces some of the main dose limiting side effects seen with the original Taxotere drug, as well as provides initial signals of anti-cancer activity, we believe SPL's docetaxel programme will gain a significant edge over other competitive programs. It would considerably raise the commercial prospects of the programme and improve its near term licensing prospects. **This, in our view, has the potential to be a game changing event for SPL and we expect will lead to a re-rating of the stock.**

In the recent update, SPL announced that all the 3 clinical sites have received ethics approval, with one actively enrolling patients. The trial is currently in the dose escalation phase of the study. **The company stated that the first group of patients enrolled at Nucleus Network in Melbourne have received one or more cycles of dendrimer-docetaxel treatment and so far show good tolerability with no evidence of neutropenia.** This early data from the trial gives us comfort and we look forward to additional data points from the trial.

Competitive landscape

We have identified 3 nanopharmaceutical companies who are working on reformulations of docetaxel using nanoparticles. Two of the companies are in preclinical studies with their formulation and thus behind Starpharma in terms of the development stage, however one is considerably ahead of SPL in terms of clinical development. We discuss each of the companies below.

CERULEAN PHARMA

Cerulean Pharma (CERU) recently listed on the NASDAQ (April 2014). The company based in Cambridge, Massachusetts raised US$60m at $7/sh well below its estimated price range of $11/sh to $13/sh. The company has a current market cap of US$141.6m.

Its lead candidate is CRLX101 (currently in mid-stage trials) which is a reformulation of camptothecin. It is currently targeting kidney cancer, ovarian cancer and rectal cancer. In March 2013, a Phase 2b trial of CRLX101 failed to meet the primary endpoint of improvement in overall survival in non-small cell lung cancer.

However, what is relevant to SPL is Cerulean's pre-clinical candidate CRLX301 which is a reformulation of docetaxel.

The company reported some encouraging preclinical data from a prostate cancer xenograft model in 2010 on a nanoparticle formulation of docetaxel called CRLX288. Cerulean's reformulated docetaxel delivered 20 times greater drug to tumour tissue than levels seen with original docetaxel alone. SPL's dendrimer-docetaxel has superior drug accumulation (40 times greater drug than docetaxel alone) than Cerulean's CRLX288. CRLX288 also achieved inhibition of tumor growth in 100% of the animals studied for greater than 100 days post-treatment.

Since then, the company's pipeline only mentions CRLX301 as the docetaxel candidate in preclinical studies with no mention about CRLX288. Also, the company seems to be focused on its lead product and CRLX301 has not advanced into the clinic as yet.

Considering that Cerulean's docetaxel programme has not advanced in the last three years, the failure of the lung cancer study with its lead candidate as well as running mid-stage trials in three different cancer indications with CRLX301, in our view, this candidate is unlikely to move into the clinic anytime soon. Moreover, SPL is in a much more advanced position and therefore we see Cerulean as less of a threat for SPL at this stage.

OASMIA PHARMACEUTICAL AB

Oasmia is a Swedish company listed on NASDAQ OMX Stockholm since June 2010. The company is developing nanoparticle formulations of cancer drugs for both human health

and veterinary use. The company's patented invention XR-17 is a hydrophilic platform which can be used to reformulate a number of anti-cancer agents with a view of improving their solubility and other pharmacokinetic profile.

In human health, its lead candidate is Paclical which is a reformulation of anti-cancer drug paclitaxel. It has completed a Phase III study in ovarian cancer and a marketing application for approval has been submitted in Russia. Another Phase III ovarian cancer trial is currently ongoing which would allow it to seek approval in other jurisdictions. Paclical is also in early stage trials for breast cancer.

The company also has a Phase I trial ongoing with a reformulation of anti-cancer drug doxorubicin in breast cancer.

However, what is relevant to SPL is Oasmia's pre-clinical candidate Docecal which is a reformulation of docetaxel and is being targeted at breast cancer.

As per the company's website the preclinical development of docecal has been completed with clinical trials currently being planned. Its listing prospectus in 2010 mentioned that a Phase I/II study for docecal in prostate cancer will begin in 2010. Since then, there seems to be a change in the lead target indication for docecal from prostate cancer to breast cancer. The candidate is yet to enter clinical trials.

Considering that Oasmia's docetaxel programme has not advanced since 2010 and the fact that we do not have visibility on the preclinical data, it is difficult to say how it would compare with SPL's products. Moreover, SPL is in a much more advanced position and therefore we see Oasmia as less of a threat for SPL at this stage.

BIND THERAPEUTICS

BIND therapeutics (BIND) is a clinical stage, oncology focused, nanomedicine platform company which listed on the NASDAQ in September 2013. The company, based in Cambridge, Massachusetts raised US$70.5m at $15/sh in its IPO. The company has a current market cap of US$164.8m. BIND is developing nanotechnology-based class of therapies called Accurins.

The company's lead asset is BIND-014, which is an Accurin that targets PSMA (Prostate-specific membrane antigen) and contains docetaxel. It is currently in Phase II development for the treatment of non-small lung cancer (NSCLC) and metastatic castrate resistant prostate cancer (mCRPC).

BIND also has collaborations with Amgen, Pfizer, and Astra Zeneca to develop other products using its Accurin delivery technology. These collaborations are in the preclinical stage and in totality could deliver ~$700m in milestones to the company in future.

BIND is SPL's most relevant competitor, with its Accurin-docetaxel (BIND-014) further advanced clinically than SPL's dendrimer-docetaxel.

Given that BIND-014 is more clinically advanced than dendrimer-docetaxel, in our view, it is a bit early to ascertain which drug candidate is likely to have superior clinical benefit.

However, based on the data so far we believe that dendrimer-docetaxel has the potential to be commercially more attractive and have a significant competitive advantage over BIND-014, should it display a superior safety profile in the currently ongoing Phase I trial.

We give a snapshot of BIND-014 technology, preclinical and clinical results so far and a preliminary comparison of BIND-014 with SPL's dendrimer-docetaxel below.

BIND-014

BIND-014 uses the 'affinity targeting' approach for drug delivery, taking advantage of the overexpressed tumour-associated antigen (PSMA) to selectively target the drug to the tumour tissue. BIND-014 is composed of biodegradable polymers which encapsulates docetaxel. It is coated with polyethylene glycol (PEG) and has a ligand called ACUPA

which binds to PSMA. The PEG coating serves as a 'stealth' layer which aids BIND-014's safe passage through the bloodstream and into the tumour cells.

We note here that SPL's approach is different to BIND's. Dendrimer-docetaxel 'passively targets' the tumour, taking advantage of the leaky vasculature associated with tumour tissue to enter the tumour cells. Owing to their size and decreased lymphatic function of tumours, they are not cleared by the lymphatic drainage and get trapped within the tumour cells where they then release their drug payload i.e. docetaxel.

Pre-clinical results on BIND-014

BIND conducted preclinical studies in mice, rats and nonhuman primates to study the pharmacokinetic profile of BIND-014. They used mouse xenograft models of breast cancer, prostate cancer and NSCLC to examine efficacy. The key findings from preclinical studies were:

- Pharmacokinetic and tissue distribution studies in rats showed that BIND's DTXL-TNP (docetaxel targeted polymeric nanoparticle) had a blood circulation half-life of about 20 hours.
- BIND-014 was shown to deliver up to 20 fold more docetaxel to the tumor site than an equivalent dose of Taxotere.
- In tumor-bearing mice, rats, and nonhuman primates, total DTXL plasma concentrations remained at least 100-fold higher with DTXL-TNP than Taxotere for more than 24 hours.
- In a mouse model of prostate cancer, for DTXL-TNP tumor mass decreased by an average of 26%, while the mice treated with docetaxel alone showed 100% increase in tumour mass over the 50 day study period.

Phase I clinical data on BIND-014

BIND-014 was initially tested in Phase I trials in patients with advanced or metastatic solid tumours evaluating two different dosing schedules:

- Once every three weeks (Q3W) and
- Once weekly for three weeks followed by one week of no treatment over a 4-week cycle (Q1W)

The Q3W Phase I dose escalation trial has been completed. 30 patients with refractory advanced or metastatic solid tumours were enrolled. 28 patients were evaluable since 2 patients had disease progression before 1st dose of BIND-014.

6 escalating doses were administered ranging from 3.5 mg/m2 to 75 mg/m2. Patients received a median of 3 cycles (1 cycle = 21 days, range was 1-22 cycles).

Patients were pre-treated with diphenhydramine 50mg, dexamethasone 20mg and ranitidine 50mg.

The primary objective of the study was to establish the Maximum Tolerated Dose (MTD) as determined by the occurrence of dose limiting toxicities and evaluate safety and tolerability of BIND-014. Secondary objectives included exploring plasma PK and preliminary antitumour activity.

Key highlights from the Q3W trial results were:

- The MTD (maximum tolerated dose) was determined to be 60 mg/m2, since dose limiting toxicities of Grade 3 fatigue and Grade 4 neutropenia lasting 5 days were observed at 75mg/m2 dose.
- Treatment related Serious Adverse Events (SAEs) i.e. Grade 3 or above were observed in 14 patients (i.e. 50%), 3 patients (11%) withdrew from the trial and 1 patient (4%) died as a result of Grade 5 sepsis following severe neutropenia. The

patient who died had a stent. 6 patients (21%) had AEs which resulted in either dose modification or interruption.

- Neutropenia was the most common AE and was observed in 10 patients.
- Other common treatment-related adverse events observed included fatigue, diarrhoea, anaemia, alopecia, infusion related reactions, dehydration, leukopenia, nausea and vomiting.
- 1 complete response was observed in a patient with cervical cancer.
- 3 partial responses were observed in patients with NSCLC, biliary and prostate cancer at the MTD dose.

  Stable disease lasting at least 12 weeks was observed in 5 patients with varied tumour types.

Our take:

Phase I trials are small and are not generally designed to fully measure anti-tumour responses. From that perspective, it is encouraging that 9 of 28 patients had a positive response to BIND-014.

On the safety front, however the data does not suggest that BIND-014 has a more favorable safety profile compared to Taxotere.

The nature and frequency of the treatment related adverse events seen with BIND-014 are generally consistent with the treatment-related adverse events associated with Taxotere and other cancer drugs. Dose limiting toxicity of neutropenia as well as fatigue as seen with Taxotere was also observed in patients treated with BIND-014, implying no particular safety benefit in delivering docetaxel with Accurin nanoparticle.

We also note that the MTD of 60 mg/m2 for BIND-014 is lower than that of Taxotere (doses of 75 mg/m2 and 100 mg/m2 also administered).

The Q1W Phase I dose escalation trial results were presented at the American Association of Cancer Research (AACR) 2014 meeting. 27 patients with refractory advanced or metastatic solid tumours were dosed. Each patient received a 60-minute infusion of BIND-014 on days 1, 8 and 15 of a 28-day cycle.

6 escalating doses were administered ranging from 15 mg/m2 to 45 mg/m2. Patients received a median of 6 doses (range was 2-34 doses).

The objective of the study was to establish the Maximum Tolerated Dose (MTD), assess dose limiting toxicities, characterize PK profile of BIND-014 when administered weekly and assess preliminary anti-tumour activity.

Key highlights from the Q1W trial results were:

- The MTD (maximum tolerated dose) was determined to be 40 mg/m2, since dose limiting toxicities of Grade 3 mucositis in 1 patient and febrile neutropenia in 1 patient occurred at 45mg/m2 dose.
- Treatment related Serious Adverse Events (SAEs) i.e. Grade 3 or above across all dose levels were fatigue, anaemia, neutropenia and mucosal inflammation.
- Fatigue was the most common AE. Fatigue was mild to moderate at or below the MTD, and resulted in no discontinuations or dose reductions.
- Other common treatment-related adverse events observed included nausea, anaemia, diarrhea, alopecia, neutropenia, vomiting, decreased appetite, stomatis, dysgeusia, leukopenia, mucosal inflammation and rash.
- 2 partial responses were observed in patients with Breast and gastroesophageal cancer.

Stable disease lasting at least 12 weeks was observed in 5 patients with varied tumour types.

Our take:

As seen with the Q3W dosing schedule, preliminary efficacy signals was observed with 7 out of 27 patients showing a positive response to BIND-014, which is encouraging.

The Q1W MTD dose of 40 mg/m2 translates to a 50% increase in cumulative dose compared to the MTD of BIND-014 of 60 mg/m2 when administered every three weeks

Different tolerability profiles were demonstrated with BIND-014 dosed at Q3W and Q1W. The Q1W schedule demonstrated considerably less neutropenia than Q3W BIND-014 with higher occurrence of fatigue.

In our view, while neutropenia was lower in Q1W it is still not eliminated. There were still SAEs of Grade 3 and 4 observed. We note that Taxotere in practice has a Q3W dosing schedule.

BIND is examining both Q3W and Q1W dosing schedules in its Phase II NSCLC trial. At this stage we are still not convinced that BIND-014 shows a meaningful differentiated safety profile compared to Taxotere.

DENDRIMER-DOCETAXEL VS. BIND-014

Since BIND-014 is more clinically advanced than dendrimer-docetaxel, in our view, it is a bit early to ascertain which drug candidate is likely to have superior clinical benefit.

However, based on the data so far we believe that dendrimer-docetaxel has the potential to be commercially more attractive and have a significant competitive advantage over BIND-014, should it display a superior safety profile in the currently ongoing Phase I trial.

As discussed above, while preliminary efficacy signals were observed in the BIND-014 trials, the data so far does not suggest a considerably superior safety profile versus Taxotere. We note here that BIND-014 requires pre-treatment with corticosteroids and uses the toxic solvent *polysorbate 80* to dissolve docetaxel.

One of the important differentiating factors between dendrimer-docetaxel and BIND-014 is that **dendrimer-docetaxel eliminates the need for docetaxel to be dissolved in the toxic *polysorbate 80* and therefore does not require premedication with corticosteroids** such as dexamethasone which has its own side effects such as elevated glucose, insomnia etc. We also know that in pre-clinical studies neutropenia was not observed in animals treated with dendrimer-docetaxel.

Hence, we are optimistic that the Phase I trial with dendrimer-docetaxel could display a superior safety profile than seen with BIND-014. Our optimism is also based on the fact that dendrimer enhanced version of another cancer drug oxaliplatin in preclinical studies has also shown a lack of the major dose limiting side effects of neutropenia, thrombocytopenia as well as reduced levels of neurotoxicity.

To date dendrimer enhanced reformulations have consistently demonstrated a more favourable safety profile than the original drug which is encouraging. **However, we note that these results are from animal models.** SPL recently reported that the first group of patients enrolled in the Phase I trial have received one or more cycles of dendrimer-docetaxel treatment and so far show good tolerability with no evidence of neutropenia. This preliminary safety signal seen in humans is encouraging although it is likely to be at lower doses. **We look forward to detailed data from the trial to establish SPL's safety benefit in humans.** Total elimination of neutropenia will be 'the holy grail' as far as we are concerned, however given that neutropenia is a side effect related to the mechanism of action of docetaxel, in our view total elimination of this side effect will be quite difficult since some amount of drug will be in circulation outside the tumour cell. Hence, rationally in humans, what we are looking for is reduced frequency of neutropenia and other dose

limiting side effects, which could potentially allow administration of higher dose of docetaxel and therefore improve the efficacy of the treatment.

Also, in terms of pharmacokinetic profile, related to half-life and amount of drug delivered to tumour site, dendrimer-docetaxel has displayed a superior PK profile to BIND-014. Dendrimer-docetaxel had a plasma half-life of 30 hours vs. 20 hours seen with BIND-014. Also, dendrimer-docetaxel was shown to deliver ~ 40 fold more docetaxel to the tumor site than an equivalent dose of Taxotere whereas BIND-014 was shown to deliver up to 20 fold more docetaxel to the tumor site than an equivalent dose of Taxotere. Due to the superior PK profile of dendrimer-docetaxel vis-à-vis BIND-014, we are optimistic that the safety profile of dendrimer-docetaxel could potentially be better than seen with BIND-014.

According to Starpharma, the main points of differentiation between dendrimer-docetaxel and BIND-014 can be seen in the figure below.

Figure 6 - Comparison of BIND-014 and SPL's DEP docetaxel

Competitor Technology / candidate	Aspect	Competitor	Starpharma	Starpharma Benefit
BIND	Manufacture	self loading particle	linear process, controlled, covalent bonds	SPL manufacture is scalable. Bind have problems with scale up – this is a potential major issue with FDA and Partners
Bind	Stability	self loading particle; unlikely to have the scalability or stability to satisfy FDA	Stability of SPL's docetaxel is very good	Tendency for particles to break down over time and under certain conditions; concerns raised by partners
BIND	Drug loading	10%	20-25%	SPL requires less material to be introduced into body.
BIND	Particle Size	60-120nm	10-15nm	SPL particles enter tissues more easily
BIND	Tumour concentration of active	10x	up to 40x	SPL - better efficacy, reduced toxicity
BIND	Half life	~6 hours	50 hours	Higher level of docetaxel delivery to tumour
BIND	Duration of efficacy in models	30 days	>90 days	Efficacy appears to be short-lived following which tumour recurrence occurs

SOURCE: STARPHARMA INVESTOR PRESENTATION

Valuing the opportunity

At this stage for SPL, we model dendrimer-docetaxel's opportunity only in the first solid tumour indication the company may pursue. However, depending on the results from the Phase I trial, which is recruiting patients with various solid tumours, SPL or a potential licensee, may decide to pursue more than one indication in parallel. This could considerably increase the market opportunity for this asset. We will revisit our assumptions on the basis of the Phase I dendrimer-docetaxel trial results.

We value SPL's dendrimer-docetaxel opportunity (first solid tumour) at A$0.15/sh. For details on risk adjustments used please refer to Table 3 on page 6.

Key assumptions:

- We use a patient driven model to estimate the prevalence of the first solid tumour indication which the company may pursue.
- We estimate peak penetration of dendrimer-docetaxel as 15% conservatively. This is the key variable in valuing this opportunity. The uptake of dendrimer-docetaxel will depend on how differentiated its safety profile and efficacy is compared to the original Taxotere drug in late stage clinical trials.

- We assume patients will be on 6 cycles of treatment on average.
- We assume each dose costs US$2000 in the US market and a 30% discount to the US price in Ex-US market. We note here that we are very conservative in this estimate given that Abraxane had a per dose cost of ~US$4200/vial in 2006 for breast cancer and for pancreatic cancer Celgene has announced a US market price for Abraxane of US$6,000-US$8,000 per month recently. However, we note that the high price of Abraxane for pancreatic cancer has led to prominent oncologists raising concerns around the risk-benefit of the drug relative to its high price. Ultimately in the Obamacare regime we expect that unless dendrimer-docetaxel shows significant improvement in overall survival in Phase III trials, the drug is unlikely to command a significant premium. This is another key variable in valuing this opportunity.
- We estimate peak pre-risk adjusted sales for dendrimer-docetaxel (first solid tumour indication) at US$506m (global). We think this is reasonable looking at Abraxane, which was generating ~US$315-$350 million in revenue when it was approved only to treat breast cancer. We note here that docetaxel is more potent than paclitaxel and had higher sales before patent expiry (~US$3.1bn vs. US$1.6bn). We also note that with label expansion of Abraxane to treat other cancers, the sales of the drug have grown to US$649m and market expectations are that the drug could reach ~ US$1bn in sales over the next 2-3 years. Dendrimer-docetaxel in all likelihood could follow a similar path.
- We assume that dendrimer-docetaxel gets licensed in FY16. For details on our deal assumptions please refer to Table 4 on Page 6.

Dendrimer enhanced glyphosate – Lead agrochemicals program

SPL is applying its dendrimer technology (Priostar dendrimers) to improve the formulation and therefore efficiency of crop protection agents. This is likely to reduce the cost and the environmental impact of using such chemicals. This application of its dendrimers is attractive commercially for SPL since it requires minimal investment from SPL but could lead to multiple licensing deals with modest single digit royalty streams attached.

Crop protection products or pesticides include herbicides which are used to control weeds, fungicides which are used to control bacteria and insecticides which are used to protect crops from insects.

The agrochemicals market opportunity is huge given that the world expenditure on pesticides in 2007 was ~US$39.4bn with US accounting for US$12.5bn of it. Herbicides accounted for ~40% of the global pesticide expenditure followed by insecticides (28%) and fungicides (23%).

In the US the expenditures in the agriculture sector accounted for nearly two-thirds of the total expenditure i.e. ~US$7.9bn. Food production is estimated to increase by 60% over 2005/07 levels by 2050. ~85% of the food production over the next 40 years has been estimated to be derived from improved yields which ensure that the demand for fertilizers and pesticides and other inputs which increase yield will grow.

SPL will be targeting the off patent segment where agrochemicals which have gone off patent can be rebranded through a new method of delivery. According to SPL there is more than $5bn worth of crop protection products coming off patent during 2011-2016.

Dendrimer-glyphosate is SPL's lead internal programme in agrochemicals with potential to be licensed in late FY15/ early FY16. SPL has field trials ongoing for its dendrimer-glyphosate programme. Glyphosate is the most commonly used herbicide globally (Trade name Roundup) with annual sales of US$4-5bn.

Externally SPL has multiple partnerships with the major global agrochemical companies such as Nufarm, Gowan, Makhteshim Agan and various other undisclosed partnerships.

Improvements seen with dendrimer formulations

Starpharma has reported initial efficacy results from studies using its proprietary Priostar dendrimer agrochemical formulations.

- In one of the studies, dendrimer-glyphosate formulation demonstrated superior rain-fastness than traditional glyphosate, with a 150%-250% improvement in efficacy following rain, four hours after treatment.
- In another study, the dendrimer-glyphosate formulation showed an increase in the brownout or rate of vegetation dying off. The rate of brownout is a measure of effectiveness. SPL's dendrimer technology when applied to glyphosate increased the performance of glyphosate by ~160-320% compared to glyphosate alone.
- One of the latest field trials show that dendrimer-glyphosate formulations are more effective on hard to control weeds than traditional glyphosate. Two key benefits seen were a) better overall effectiveness with the dendrimer formulation leaving only minimal number of weeds alive (less than 10% survival) at end of study, whereas traditional glyphosate had > 30% survival and b) early feedback of effectiveness to grower with 3 to 4 times as much "brownout" after 5 days of application seen with dendrimer-

glyphosate formulations than traditional glyphosate. This visible evidence of effect enables growers to ascertain that the formulation is working effectively.

- One of the early studies demonstrated the ability of SPL's dendrimers to increase efficacy of glyphosate, offering benefits such as solubility enhancement for more concentrated formulations, improved soil penetration and reduced need for harmful solvents.
- Working with other off-patent agrochemicals, SPL's dendrimer technology has also shown the ability to increase the loading of crop protection products (loading of one herbicide was increased by 50% more with dendrimers).

Through these benefits, SPL's dendrimers can contribute in improving the efficiency of existing agrochemicals as well as reducing the cost and the environmental impact of using such chemicals.

Valuing the opportunity

At this stage for SPL, we only value SPL's dendrimer-glyphosate opportunity in agrochemicals. We value SPL's dendrimer-glyphosate opportunity at A$0.04/sh. For details on risk adjustments used please refer to Table 3 on page 6.

Key assumptions:

- We estimate peak penetration of dendrimer-glyphosate as 10% of the global glyphosate market.
- We estimate peak pre-risk adjusted sales for dendrimer-glyphosate at US$763m (global).
- We assume that dendrimer-glyphosate gets licensed in late FY15/ early FY16. We assume a pure royalty based deal for SPL without any upfront or milestones. We assume a 5% royalty rate on net sales. For details on our deal assumptions please refer to Table 4 on Page 6.

Appendix 1 - Board of Directors

Board of Directors of Starpharma Holdings Limited

We give a snapshot of SPL's Board in the table below.

Table 5 - Starpharma's Board of Directors have a broad range of skills and experience

Directors	Position	Year Appointed	Experience
Robert B Thomas	Chairman and Non-Executive Director	Chairman (2014) and Director (2013)	Currently director of HeartWare Limited a US based medical device company, director of various ASX listed companies including Biotron, Reva Medical, Virgin Australia Ltd and TAL ltd. He also has stockbroking experience, previously serving as CEO and then consultant to Citigroup Corporate and Invetsment Bank and Chairman of Global Corporate and Investment Bank. Citigroup Global Markets, Australia & NZ. He is currently Chairman of Aus Bio Ltd, and a member of the advisory boards of Nomura Australia and Inteq Ltd.
Peter J Jenkins	Non-Executive Director and Deputy Chairman	2000	Consultant physician and gastroenterologist who holds research and clinical positions at the Alfred Hospital and has held similar positions with Baker Medical Research Centre in the past. He is also an executive director of AusBio Ltd, an unlisted public biotechnology company.
Jackie Fairley	CEO & Executive Director	2006	Jackie has more than 20 years of experience in the pharmaceutical and biotechnology industries working in business development and senior management roles with companies including CSL and Faulding (now Hospira). Former CEO of Cerylid Biosciences, Jackie also spent 5 years as a VP for Faulding's injectable division and 5 years with CSL in various executive roles. She holds first class honours degrees in Science and Veterinary Science, and has an MBA from the Melbourne Business School (MBS) where she was the recipient of the Clemenger Medal. In 2010, Jackie was appointed to the board of directors of MBS.
Richard A Hazleton	Non-Executive Director	2006	Former Chairman of US based Dow Corning where he was CEO from 1993 to 2001 and Chairman from 1994. Was Chairman of Dendritic Nanotechnologies from 2004 until 2006 when it was acquired by SPL.
Peter R Turvey	Non-Executive Director	2012	Former Executive Vice President Licensing and Company Secretary of CSL and currently a Principal of Foursight Associates and a director of AusBiotech as well as ASX listed Allied Healthcare Group.
Zita Peach	Non-Executive Director	2011	More than 20 years of commercial experience in the pharmaceutical industry particularly in marketing and business dvelopment, having worked with CSL and Merck Sharpe & Dohme. She is currently the MD and Executive VP, South Asia Pacific for Fresenius Kabi Australia, a leader in infusion therapy and clinical nutrition. Until recently she was VP/Director, Business Development R&D for CSL, a position she held for ten years. Ms Peach is a Non-Executive Director of the ASX-listed Vision Eye Institute Limited.

SOURCE: COMPANY DATA AND BELL POTTER SECURITIES

Starpharma Holdings Ltd. (SPL)

COMPANY DESCRIPTION

Starpharma is a Melbourne-based platform company commercialising the science of nanoscale polymers called dendrimers. Its proprietary dendrimer technology is versatile with wide applicability across multiple sectors including pharmaceuticals, agrochemicals and industrial applications. Starpharma's lead product is VivaGel which is being developed as an anti-microbial coating for Ansell and Okamoto condoms offering protection against Sexually Transmitted Infections (STIs), as well as a topical microbicide to prevent the recurrence of the common vaginal infection in women, Bacterial Vaginosis. SPL is also working on improved formulations of leading cancer drugs as well as agrochemicals both internally and with external partners. Substantial shareholders include Allan Gray, M&G, Acorn Capital and Dow Chemical Company. Their combined holdings represent ~41.8%.

KEY RISKS

We see the following key stock specific risks to our investment thesis on Starpharma:

- **Clinical risk:** There is a risk that SPL's clinical trials primarily the Phase III Prevention of Recurrence of Bacterial Vaginosis trials and the Phase I dendrimer-docetaxel trial may fail to demonstrate meaningful safety and efficacy. This may jeopardise the potential for the company to license the products and/or pursue further clinical development.
- **Technology risk:** SPL is a platform company, with its entire pipeline based on its proprietary dendrimer technology. Any setback clinically or commercially is likely to put the viability of the company's technology at risk.
- **Regulatory risk:** Any further delay in receiving marketing approval for VivaGel coated condom or delay in its launch in various jurisdictions will negatively impact our revenue forecasts. This risk also extends to other pipeline products as well in terms of getting regulatory agreement to conduct clinical trials and then get marketing approval before they can be launched in the market.
- **Partnering risk:** The basic premise behind our investment thesis for SPL is that all its major products get licensed at attractive terms with the partner being responsible for all commercialisation and any further development as required. If SPL fails to secure partnerships at attractive terms, our forecasts will be negatively impacted. Furthermore, if any of SPL's existing collaborations should be terminated, it is likely to shake the markets confidence in SPL's technology and its commercial viability.
- **Commercial risk:** The VivaGel coated condom sales and revenue from partnerships with Okamoto and Ansell could fail to meet our expectations due to poor commercialization effort, delays in launch, unfavourable experience of consumers with the product, better performance of a competing product etc. This will impact our forecasts negatively.
- **Funding risk:** Delays in partnering of products may impact SPL's funding position. Increase in costs of trials beyond what we currently estimate may require SPL to raise additional capital before it can become financially self-sustainable. There is a risk that SPL may not be able to raise sufficient capital to meet its funding needs or at favourable terms.

SPL has $27.81m cash at the end of FY3Q14 and has burned ~$0.7m/month on average over the last twelve months

Starpharma
as at 18 June 2014

Recommendation	Buy, Speculative
Price	$0.565
Valuation	$1.07

Table 6 - Financial summary

Starpharma (SPL) — **Share price (A$)** **$0.565**
As at 18 June 2014 — **Market cap (A$m)** **161.1**

Profit and Loss

Y/e June 30 (A$m)	2012A	2013A	2014E	2015E	2016E
Revenue*	2.4	9.5	6.3	4.8	16.9
EBITDA	**-14.4**	**-5.8**	**-11.2**	**-12.0**	**2.6**
Depreciation & Amortisation	-1.1	-1.1	-1.1	-1.1	-1.1
EBIT	**-15.5**	**-6.8**	**-12.2**	**-13.1**	**1.5**
Net interest & Other Income/(Expense)	1.9	1.6	0.9	0.6	0.5
Pre-tax profit (loss)	-13.7	-5.2	-11.3	-12.5	2.0
Tax	0.0	0.0	0.0	0.0	0.6
NPAT (adjusted)	-13.7	-5.2	-11.3	-12.5	1.4
Less minority interests	0.0	0.0	0.0	0.0	0.0
Net profit (loss) to shareholders	**-13.7**	**-5.2**	**-11.3**	**-12.5**	**1.4**
Reported net profit (loss) to shareholders	-13.7	-5.2	-11.3	-12.5	1.4

* Including grants and R&D tax incentive. FY16 Revenue number includes potential upfront from docetaxel & VivaGel symptomatic relief deals

Cashflow

Y/e June 30 (A$m)	2012A	2013A	2014E	2015E	2016E
Reported NPAT plus discontinued ops.	-13.7	-5.2	-11.3	-12.5	1.4
Non-cash items	1.4	1.9	1.9	1.5	1.5
Working capital	2.4	-6.4	-1.0	2.1	3.2
Other operating cash flow	0.0	0.0	0.0	0.0	0.0
Operating cashflow	**-9.8**	**-9.8**	**-10.4**	**-9.0**	**6.1**
Capex	-0.1	-0.2	-0.3	-0.5	-0.6
Investments	0.0	0.0	0.0	0.0	0.0
Other investing cash flow	0.0	0.0	0.0	0.0	0.0
Investing cashflow	**-0.1**	**-0.2**	**-0.3**	**-0.5**	**-0.6**
Change in borrowings	-0.1	-0.1	0.0	0.0	0.0
Equity issued	33.7	0.9	0.2	0.0	0.0
Dividends paid	0.0	0.0	0.0	0.0	0.0
Other financing cash flow	0.0	0.0	0.0	0.0	0.0
Financing cashflow	**33.7**	**0.8**	**0.2**	**0.0**	**0.0**
Net change in cash	**23.8**	**-9.1**	**-10.5**	**-9.4**	**5.5**
Cash at end of period*	42.8	33.8	23.4	14.0	19.6
Free cash flow	**-9.9**	**-10.0**	**-10.8**	**-9.4**	**5.5**

* Includes effect of exchange rate fluctuations on cash balance

Balance sheet

Y/e June 30 (A$m)	2012A	2013A	2014E	2015E	2016E
Cash	42.8	33.8	23.4	14.0	19.6
Current receivables	1.9	5.3	6.5	4.4	1.2
Inventories	0.0	0.0	0.0	0.0	0.0
Other current assets	0.1	0.2	0.7	0.7	0.7
Current assets	**44.9**	**39.3**	**30.5**	**19.1**	**21.5**
PPE	0.4	0.4	0.6	0.8	1.2
Non-current receivables	0.0	0.0	0.0	0.0	0.0
Intangible assets	9.0	8.8	7.9	7.0	6.1
Other non-current assets	0.0	0.0	0.0	0.0	0.0
Non-current assets	**9.4**	**9.2**	**8.5**	**7.8**	**7.3**
Total assets	**54.3**	**48.6**	**39.0**	**26.9**	**28.8**
Payables	4.5	1.7	2.4	2.4	2.4
Debt	0.1	0.1	0.1	0.0	0.0
Provisions	0.6	0.7	0.7	0.7	0.7
Other liabilities	0.4	0.1	0.1	0.1	0.1
Total liabilities	**5.6**	**2.6**	**3.2**	**3.2**	**3.1**
Shareholders' equity	48.7	46.0	35.8	23.8	25.7
Minorities	0.0	0.0	0.0	0.0	0.0
Total shareholders funds	**48.7**	**46.0**	**35.8**	**23.8**	**25.7**
Total funds employed	**54.3**	**48.6**	**39.0**	**26.9**	**28.8**
W/A shares on issue	267.7	283.3	287.6	288.0	288.1

Valuation data

Y/e June 30	2012A	2013A	2014E	2015E	2016E
Net profit (A$m)	-13.7	-5.2	-11.3	-12.5	1.4
EPS (c)	-5.1	-1.8	-3.9	-4.4	0.5
EPS growth (%)	N/A	N/A	N/A	N/A	NM
P/E ratio (x)	N/A	N/A	N/A	N/A	113.8
CFPS (c)	-3.7	-3.5	-3.6	-3.1	2.1
Price/CF (x)	-15.5	-16.3	-15.6	-18.2	26.5
DPS (c)	0.0	0.0	0.0	0.0	0.0
Yield (%)	0.0%	0.0%	0.0%	0.0%	0.0%
Franking (%)	N/A	N/A	N/A	N/A	N/A
EV/EBITDA	-9.3	-23.2	-11.9	-11.1	50.7
EV/EBIT	-8.6	-19.6	-10.9	-10.2	87.6

Share price now	$0.565
Valuation:	$1.07
Premium (discount) to price	89.4%
Recommendation:	Buy
Risk Rating	Speculative

Profitability ratios

Y/e June 30	2012A	2013A	2014E	2015E	2016E
EBITDA/revenue (%)	N/A	N/A	N/A	N/A	15.6%
EBIT/revenue (%)	N/A	N/A	N/A	N/A	9.0%
Return on assets (%)	-25.2%	-10.8%	-29.0%	-46.5%	5.0%
Return on equity (%)	-28.1%	-11.4%	-31.6%	-52.7%	5.6%
Return on funds empl'd (%)	-28.0%	-11.4%	-31.5%	-52.6%	5.6%
Dividend cover (x)	N/A	N/A	N/A	N/A	N/A
Effective tax rate (%)	0.0%	0.0%	0.0%	0.0%	30.0%

Liquidity and leverage ratios

Y/e June 30	2012A	2013A	2014E	2015E	2016E
Net cash (debt) (A$m)	42.7	33.7	23.3	14.0	19.6
Net debt/equity (%)	N/A	N/A	N/A	N/A	N/A
Net interest cover (x)	N/A	N/A	N/A	N/A	N/A
Current ratio (x)	8.3	16.0	9.8	6.1	6.9

Interims

Y/e June 30 (A$m)	1H13A	2H13A	1H14A	2H14E	1H15E
Revenue*	7.2	2.3	2.8	3.5	2.0
EBITDA	-2.2	-3.5	-5.6	-5.6	-5.8
Depreciation & Amortisation	-0.5	-0.5	-0.5	-0.5	-0.5
EBIT	-2.7	-4.1	-6.1	-6.1	-6.4
Net interest & Other Income (Expense)	0.9	0.7	0.6	0.4	0.3
Pre-tax profit	-1.8	-3.4	-5.6	-5.7	-6.1
Tax	0.0	0.0	0.0	0.0	0.0
NPAT (adjusted)	-1.8	-3.4	-5.6	-5.7	-6.1
Less minority interests	0.0	0.0	0.0	0.0	0.0
Net profit to shareholders	-1.8	-3.4	-5.6	-5.7	-6.1

*Includes R&D Tax incentive

SOURCE: BELL POTTER SECURITIES ESTIMATES

Recommendation structure

Buy: Expect >15% total return on a 12 month view. For stocks regarded as 'Speculative' a return of >30% is expected.

Hold: Expect total return between -5% and 15% on a 12 month view

Sell: Expect <-5% total return on a 12 month view

Speculative Investments are either start-up enterprises with nil or only prospective operations or recently commenced operations with only forecast cash flows, or companies that have commenced operations or have been in operation for some time but have only forecast cash flows and/or a stressed balance sheet.

Such investments may carry an exceptionally high level of capital risk and volatility of returns.

Bell Potter Securities Limited
ACN 25 006 390 7721
Level 38, Aurora Place
88 Phillip Street, Sydney 2000
Telephone +61 2 9255 7200
www.bellpotter.com.au

Research Team

Staff Member	Title/Sector	Phone	@bellpotter.com.au
TS Lim	Head of Research	612 8224 2810	tslim
Industrials			
Sam Haddad	Industrials	612 8224 2819	shaddad
John O'Shea	Industrials	613 9235 1633	joshea
Chris Savage	Industrials	612 8224 2835	csavage
Jonathan Snape	Industrials	613 9235 1601	jsnape
Sam Byrnes	Industrials	612 8224 2886	sbyrnes
Bryson Calwell	Industrials Associate	613 9235 1853	bcalwell
John Hester	Healthcare	612 8224 2871	jhester
Tanushree Jain	Healthcare/Biotech	612 8224 2849	tnjain
Financials			
TS Lim	Banks/Regionals	612 8224 2810	tslim
Lafitani Sotiriou	Diversified	613 9235 1668	lsotiriou
Resources			
Di Brookman	Oil & Gas	612 8224 2859	dbrookman
Stuart Howe	Resources	613 9235 1782	showe
Fred Truong	Resources	613 9235 1629	ftruong
Bernard Lai	Gold	613 9235 1731	blai
Quantitative			
Tim Piper	Research Assistant	612 8224 2825	tpiper
Fixed Income			
Damien Williamson	Fixed Income	613 9235 1958	dwilliamson
Barry Ziegler	Fixed Income	613 9235 1848	bziegler

The following may affect your legal rights. Important Disclaimer:

This document is a private communication to clients and is not intended for public circulation or for the use of any third party, without the prior approval of Bell Potter Securities Limited. In the USA and the UK this research is only for institutional investors. It is not for release, publication or distribution in whole or in part to any persons in the two specified countries. In Hong Kong this research is being distributed by Bell Potter Securities (HK) Limited which is licensed and regulated by the Securities and Futures Commission, Hong Kong. This is general investment advice only and does not constitute personal advice to any person. Because this document has been prepared without consideration of any specific client's financial situation, particular needs and investment objectives ('relevant personal circumstances'), a Bell Potter Securities Limited investment adviser (or the financial services licensee, or the representative of such licensee, who has provided you with this report by arraignment with Bell Potter Securities Limited) should be made aware of your relevant personal circumstances and consulted before any investment decision is made on the basis of this document. While this document is based on information from sources which are considered reliable, Bell Potter Securities Limited has not verified independently the information contained in the document and Bell Potter Securities Limited and its directors, employees and consultants do not represent, warrant or guarantee, expressly or impliedly, that the information contained in this document is complete or accurate. Nor does Bell Potter Securities Limited accept any responsibility for updating any advice, views opinions, or recommendations contained in this document or for correcting any error or omission which may become apparent after the document has been issued. Except insofar as liability under any statute cannot be excluded. Bell Potter Limited and its directors, employees and consultants do not accept any liability (whether arising in contract, in tort or negligence or otherwise) for any error or omission in this document or for any resulting loss or damage (whether direct, indirect, consequential or otherwise) suffered by the recipient of this document or any other person.

Disclosure of interest:

Bell Potter Securities Limited, its employees, consultants and its associates within the meaning of Chapter 7 of the Corporations Law may receive commissions, underwriting and management fees from transactions involving securities referred to in this document (which its representatives may directly share) and may from time to time hold interests in the securities referred to in this document.

Disclosure: Bell Potter Securities acted as lead manager in the October 2011 placement and SPP and received fees for that service.

Biotechnology Risk Warning:

The stocks of biotechnology companies without strong revenue streams from product sales or ongoing service revenue should always be regarded as speculative in character. Since most biotechnology companies fit this description, the speculative designation also applies to the entire sector. The fact that the intellectual property base of a typical biotechnology company lies in science not generally regarded as accessible to the layman adds further to the riskiness with which biotechnology investments ought to be regarded. **Stocks with 'Speculative' designation are prone to high volatility in share price movements.** Clinical and regulatory risks are inherent in biotechnology stocks. Biotechnology developers usually seek US FDA approval for their technology which is a long and arduous three phase process to prove the safety, effectiveness and appropriate application or use of the developed drug and even after approval a drug can be the subject of an FDA investigation of subsequently discovered possible links between the drug and other diseases not previously diagnosed. Furthermore, the Australian exchange listed biotechnology sector is subject to influence by the global biotechnology sector, particularly that in the USA. Consequently, Australian exchange listed biotechnology stocks can experience sharp movements, both upwards and downwards, in both valuations and share prices, as a result of a re-rating of the sector both globally and in the USA, in particular. Investors are advised to be cognisant of these risks before buying such a stock including **Starpharma. For a list of risks specific to Starpharma please refer to Page 31 of this note.**

ANALYST CERTIFICATION:

Each research analyst primarily responsible for the content of this research report, in whole or in part, certifies that with respect to each security or issuer that the analyst covered in this report: (1) all of the views expressed accurately reflect his or her personal views about those securities or issuers and were prepared in an independent manner and (2) no part of his or her compensation was, is, or will be, directly or indirectly, related to the specific recommendations or views expressed by that research analyst in the research report.