BBY **Company Research**	21 November 2014

Novogen Limited

NRT A$0.09	**TARGET PRICE** A$0.22	**SPECULATIVE BUY** 0.0X

Novogen Limited is developing a new class of anticancer drugs that it calls super-benzopyrans. The super-benzopyrans have potent activity against cancer stem cells that are resistant to existing chemotherapy drugs.

Dr Dennis Hulme
+61 2 9226 0083
djh@bby.com.au

Targeting the cells that cause cancer recurrence and spread

Novogen Limited's (NRT) lead products are a new type of anticancer drug known as super benzopyrans which effectively kill cancer stem cells from a number of different types of cancer. Cancer stem cells are resistant to existing chemotherapy drugs and are believed to be responsible for tumour recurrence and spread. Impressively, super benzopyrans are the only drugs known to effectively cure ovarian cancer in a cancer stem cell model developed by Yale University. While the drugs are still at a fairly early stage of development, with the first clinical trials to be undertaken in 2015, they have the potential to substantially improve survival in hard-to-treat diseases such as ovarian cancer and aggressive prostate cancer. NRT raised A$1.85M earlier this month, and will need additional funding to complete the planned clinical trials. We initiate coverage with a SPECULATIVE BUY recommendation and a price target of A$0.22/sh.

Cancer stem cells

- Cancer stem cells are a small population of slow–growing cells within a tumour that are highly resistant to chemotherapy drugs. They are able to regenerate a tumour even if the bulk of the tumour is killed by chemotherapy drugs. Cancer stem cells are also believed to be responsible for the spread or metastasis of cancer.

Cantrixil

- NRT's initial trials will be in ovarian cancer where lead drug Cantrixil achieved very impressive results against human ovarian cancer stem cells transplanted in to an animal model. NRT plans to initiate a US-based Phase 1 trial of Cantrixil in ovarian cancer patients in 3Q CY15.
- **Malignant ascites** - Cantrixil is designed to be administered directly into the abdominal (peritoneal) cavity, a protocol that some cancer centres already use to treat ovarian cancer patients. In addition to the ovarian cancer trial, NRT also plans to conduct a clinical trial of Cantrixil in patients with a malignant ascites. This condition occurs when late-stage cancers such as ovarian, pancreatic, bowel and breast cancers spread throughout the abdominal cavity.

Proof of concept for super benzopyran technology

- In addition to Cantrixil, NRT has developed a number of other super benzopyran drugs with potent anticancer activity, including Trilexium which is in preclinical development for brain cancers and Trx-7 which is being developed for prostate cancer. While ovarian cancer is an important commercial target in itself, the upcoming clinical trials will also serve as proof of concept for the capacity of super benzopyran drugs to improve survival rates by killing cancer stem cells.

Company Data

Number of shares	186M
Market capitalisation	$16M
Free Float (%)	
12 month high/low	$0.30/$0.08
Average monthly turnover	$2M
% S&P/ASX 200	n/a
% All Ordinaries	n/a
DDM Ranking	n/a
ESG Score (Ranking)	n/a
GICS Industry Group	Pharmaceuticals, Biotechnology & Life Sciences

BBY vs Consensus

	BBY FY1	Consensus FY1	% Difference
EBITDA ($m)	(4.0)		
NPAT ($m)	(4.7)		
EPS (c/sh)	(2.2)		

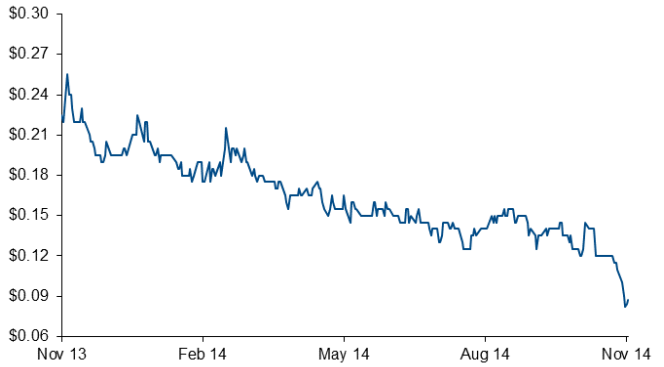
BBY Technical View – as at 21/11/2014

Short Term	Downtrend	Resistance	$0.141
Long Term	Downtrend	Support	$0.076

Earnings summary (AUD)

Year end June	2014A	2015F	2016F	2017F
Revenue ($M)	0.1	0.9	0.9	0.9
EBITDA ($M)	(6.6)	(4.0)	(5.2)	(6.2)
Reported NPAT ($M)	(7.9)	(4.7)	(5.6)	(6.5)
Adjusted NPAT ($M)	(7.9)	(4.7)	(5.6)	(6.5)
Reported EPS (¢)	(4.8)	(2.2)	(2.4)	(2.7)
Adjusted EPS (¢ - FD)	(4.8)	(2.2)	(2.4)	(2.7)
Adjusted EPS growth (%)	nm	nm	nm	nm
Adjusted P/E (x)	(3.1)	(4.0)	(3.6)	(3.2)
Dividend (¢/sh)	0.0	0.0	0.0	0.0
Gross yield (%)	0.0	0.0	0.0	0.0
Net yield (%)	0.0	0.0	0.0	0.0
Franking (%)	0.0	0.0	0.0	0.0
ROIC (%)	(4,377.1)	223.5	191.1	171.7

NRT Share Price Performance



Financial Summary

Novogen Limited Share Price (A$) **$0.09** Mkt Cap (A$M) **16**

Year ending June 30

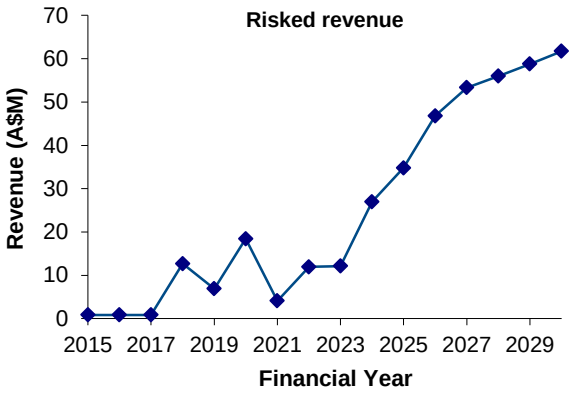
Profit & Loss (A$M)	2014A	2015F	2016F	2017F
Total Revenue	0.1	0.9	0.9	0.9
Growth (%)	(92.2)	nm	0.0	0.0
EBITDA	(6.6)	(4.0)	(5.2)	(6.2)
Growth (%)	(236.6)	38.7	(28.3)	(18.5)
Dep'n and amort'n	(0.1)	(0.6)	(0.6)	(0.5)
EBIT	(6.7)	(4.6)	(5.8)	(6.7)
Net interest expense	(0.7)	(0.1)	0.3	0.1
PBT	(7.9)	(4.7)	(5.6)	(6.5)
Growth (%)	nm	40.4	(17.9)	(17.6)
Tax	0.0	0.0	0.0	0.0
NPAT Underlying attrib.	(7.9)	(4.7)	(5.6)	(6.5)
Growth (%)	nm	40.4	(17.9)	(17.6)
NPAT Reported	(7.9)	(4.7)	(5.6)	(6.5)
Normalised NPAT	(7.9)	(4.7)	(5.6)	(6.5)
Ord Shares	168.6	221.2	238.0	238.0
Options	24.9	25.9	26.9	28.0
Fully Diluted	193.5	236.7	254.1	254.8
FD Wgted Av Shares	166.5	216.7	229.6	238.0

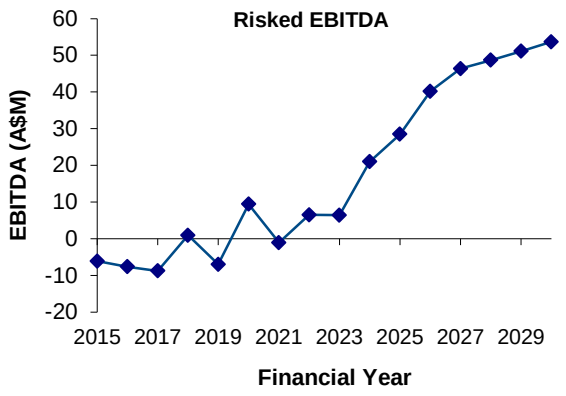
Cashflow (A$M)	2014A	2015F	2016F	2017F
Customer receipts	0.3	0.8	0.9	0.9
Supplier Payments	(6.4)	(4.7)	(5.9)	(6.8)
Net interest paid	0.2	(0.1)	0.3	0.1
Taxes Paid	0.0	0.0	0.0	0.0
Net operating cash flow	(5.7)	(4.0)	(4.7)	(5.8)
Capex	0.0	(0.2)	(0.2)	(0.2)
Net investing cash flow	0.0	(0.2)	(0.2)	(0.2)
Dividends paid	0.0	0.0	0.0	0.0
Net financing cash flow	5.5	6.8	2.1	0.0
Net Change in cash	(0.2)	2.5	(2.8)	(6.0)
Net cash at end of period	2.5	5.0	2.2	(3.8)
Free cash flow	(5.7)	(4.2)	(4.9)	(6.0)
Change in working capital	0.8	(2.8)	2.8	6.0

Balance sheet (A$M)	2014A	2015F	2016F	2017F
Cash	2.5	5.0	2.2	(3.8)
Receivables	0.1	0.2	0.2	0.2
Inventories	0.0	0.0	0.0	0.0
Current assets	2.6	5.3	2.5	(3.6)
Tangible Assets	0.0	0.2	0.3	0.4
Investments	0.0	0.0	0.0	0.0
Goodwill	0.0	0.0	0.0	0.0
Total assets	5.2	7.5	4.2	(2.1)
Payables	0.3	0.3	0.3	0.3
Current Term debt	0.0	0.0	0.0	0.0
Long term debt	0.0	0.0	0.0	0.0
Total liabilities	0.5	4.3	4.5	4.7
Total Shareholder Equity	1.4	3.2	(0.2)	(6.8)

Investment summary	2014A	2015F	2016F	2017F
NPAT reported	(7.9)	(4.7)	(5.6)	(6.5)
NPAT Underlying	(7.9)	(4.7)	(5.6)	(6.5)
EPS Reported	(4.8)	(2.2)	(2.4)	(2.7)
EPS Underlying	(4.8)	(2.2)	(2.4)	(2.7)
EPS Growth (%)	(248.8)	54.2	(11.3)	(13.5)
P/E Underlying (x)	(3.1)	(4.0)	(3.6)	(3.2)
Dividend (¢/sh)	0.0	0.0	0.0	0.0
Payout Ratio (%)	0.0	0.0	0.0	0.0
Gross Yield (%)				
Net Yield (%)				
Franking (%)	0.0	0.0	0.0	0.0

Key Ratios	2014A	2015F	2016F	2017F
Profitability (%)				
EBITDA	(6.6)	(4.0)	(5.2)	(6.2)
EBITDA/Rev (%)	(7,611.4)	(470.7)	(604.0)	(715.5)
EBIT	(6.7)	(4.6)	(5.8)	(6.7)
EBIT/Rev (%)	(7,677.4)	(539.5)	(679.1)	(775.0)
NPAT	(7.9)	(4.7)	(5.6)	(6.5)
NPAT/Rev (%)	(9,124.9)	(548.7)	(646.8)	(760.7)
ROE (%)	(290.2)	(203.3)	(370.6)	186.9
ROA (%)	(127.9)	(73.0)	(99.7)	(630.8)
ROIC (%)	(4,377.1)	223.5	191.1	171.7
Financial Strength				
Debt to equity (%)	0.0	0.0	0.0	0.0
Net debt ($M)	(2.5)	(5.0)	(2.2)	3.8
Net debt to equity (%)	(177.2)	(156.2)	973.9	(56.1)
Net Debt to EBITDA (%)	0.4	1.2	0.4	(0.6)
Interest Cover EBIT (x)	(9.3)	(21.4)	na	na
Current Ratio (x)	4.9	14.5	6.8	(9.7)
Quick Ratio (x)	4.9	14.5	6.8	(9.7)
Valuation				
Operating cash flow	(5.7)	(4.0)	(4.7)	(5.8)
CFPS (¢ - FD)	(3.4)	(1.9)	(2.1)	(2.4)
Price/CF	(4.2)	(4.7)	(4.2)	(3.6)
BV per share ($)	0.0	0.0	0.0	0.0
Price/Book Value (x)	16.2	6.0	(90.3)	(3.1)
NTA ($)	(1.2)	1.3	(1.6)	(7.7)
NTA per share ($)	0.0	0.0	0.0	0.0
Price/NTA (x)	(24.0)	14.9	(13.0)	(2.7)
EV/Sales (x)	(6.7)	12.9	16.2	23.2
EV/EBITDA (x)	0.1	(2.7)	(2.7)	(3.2)
EV/EBIT (x)	0.1	(2.4)	(2.4)	(3.0)





Source: BBY, Company Reports. BBY contributes all company estimates to Bloomberg, Thomson Reuters, FactSet and Capital IQ.

Note: Numbers displayed are a sub-set

The ESG (Environmental, Social, Governance) score is a measure of the sustainability and ethical impact of an investment in this company or product. ESG scores range from 0.1 (min) to 100 (max). ESG scores are provided to BBY by Bloomberg and are only available for those companies that disclose ESG data to Bloomberg.

Investment Case

The concept that cancer stem cells are a key driver of cancer recurrence and spread has gained increased acceptance over the past decade.

NRT is developing a class of drugs that it terms super-benzopyrans (SBP) which have demonstrated potent activity against cancer stem cells in a range of preclinical models of cancer. For example, SBPs are the only drugs that have shown meaningful activity against ovarian cancer stem cells in a model developed by Yale University. The results show that NRTs Cantrixil SBP has the potential to improve the survival of ovarian cancer patients by wiping out cancer stem cells and thereby preventing tumour recurrence. The SBP compounds have been created to kill the full range of cells within a tumour, but particularly the cancer stem cells.

NRT's initial clinical trials of the new super benzopyran drugs will be in ovarian cancer patients with refractory disease, a patient population where none of the currently available treatments are effective. Because there are no alternative treatments for these patients, if the drug is shown to be effective in Phase 2 trials we would expect it to be eligible for the FDA's breakthrough designation and it could potentially receive an initial marketing approval based on Phase 2 trial data.

While ovarian cancer is a significant target market in its own right, it is perhaps more important as a model disease where NRT can demonstrate the potency of its SBP drugs against cancer stem cells. Preclinical studies have already demonstrated the potency of SBP drugs against diseases such as prostate cancer which represent larger potential markets.

If NRT's super benzopyran drugs show efficacy against cancer stem cells in clinical trials we see a high likelihood of a licence deal or M&A transaction for the stock.

History

Novogen has been engaged in a medicinal chemistry program since 1998, seeking to isolate certain properties of naturally occurring plant hormones (genistein) which are involved in regulation of enzymes and gene assembly.

It discovered four benzopyran drugs with potential anti-cancer properties namely phenoxydiol, triphendiol, NV-143 and NV-344. Phenoxydiol was granted IND status by FDA in Feb 2001 as an intravenous formulation and in June 2003 as an oral formulation

The intravenous dose form of Phenoxydiol was effective against ovarian cancer in a Phase 2 trial. However Phenoxydiol in its oral form, when tested for efficacy in ovarian, fallopian and primary peritoneal cancer in a large Multicentre Phase 3 trial (OVATURE Trial) did not show a statistically significant improvement in primary or secondary endpoints. Subsequent studies by NRT suggest that the failure in Phase 3 was due to the low bioavailability for the oral formulation of Phenoxydiol that was used in the Phase 3 trial.

The first generation benzopyran drugs including Phenoxydiol were sold in 2010 to US company and former NRT subsidiary MEIPharma. In 2011, NRT was able to create complex benzopyrans with several log increase in anti-cancer activity. It was subsequently re-capitalised and embarked on further drug discoveries.

It formed a partnership with Yale university in 2013 to develop a new super benzopyran drug for the treatment of advanced ovarian cancer

Cancer stem cells

Initial treatment of cancer with chemotherapy drugs is often successful in shrinking the size of the tumour, but the disease commonly re-occurs at a later date, often with a resistance to the previously-used therapy. One theory that is gaining increasing acceptance suggests that "Cancer Stem Cells" could be responsible for the recurrence and spread of cancer.

The cancer stem cells are slow growing and have stem cell-like properties, including cell surface markers that are characteristic of normal adult stem cells. The cancer stem cells make up only a small proportion of the total population in a tumour, with the remainder comprising rapidly-dividing somatic or daughter cells.

Cancer Stem cells are resistant to the conventional chemotherapy drugs, which target the faster growing daughter cells. As a result, when treatment with the chemotherapy agents is stopped the remaining cancer stem cells start growing and dividing leading to tumour recurrence.

Cancer stem cells have been identified in a number of cancers including ovarian breast, prostate, brain and various blood cancers.

Studies in animal models have shown that a combination of a conventional chemotherapy agent and a drug that targets cancer stem cells can lead to complete killing of all cancer cells and prevent tumour recurrence.

Novogen has a rich pipeline of drugs which target the cancer stem

Cantrixil shows potent activity in a stringent mouse model of ovarian cancer stem cells

NRT's superbenzopyran drugs have high potency in an ovarian cancer stem cell model developed by Professor Gil Mor at Yale University.

Professor Mor and his team demonstrated that ovarian cancers contain a small population of cancer stem cells that are slow-growing and are highly resistant to traditional chemotherapy agents. These cancer stem cells carried the CD44 cell surface marker, whereas the rapidly dividing somatic or daughter cells that comprise the majority of the tumour were CD44 negative.

The researchers at Yale also showed that when they purified CD44+ stem cells from patient tumours and injected the cells into the abdominal cavity (intra-peritoneal) of immune-compromised mice then they quickly develop into highly aggressive tumours that spread throughout the abdomen. These tumours had the same appearance under the microscope as the original tumour; pockets of the larger, slower-growing CD44+ human ovarian cancer stem cells were observed surrounded by CD44-ve daughter cells that were derived from the injected CD44+ cells[1].

The Yale model is unique. The Mor group have spent a considerable time developing what is arguably the most stringent test yet devised for ovarian cancer, because:

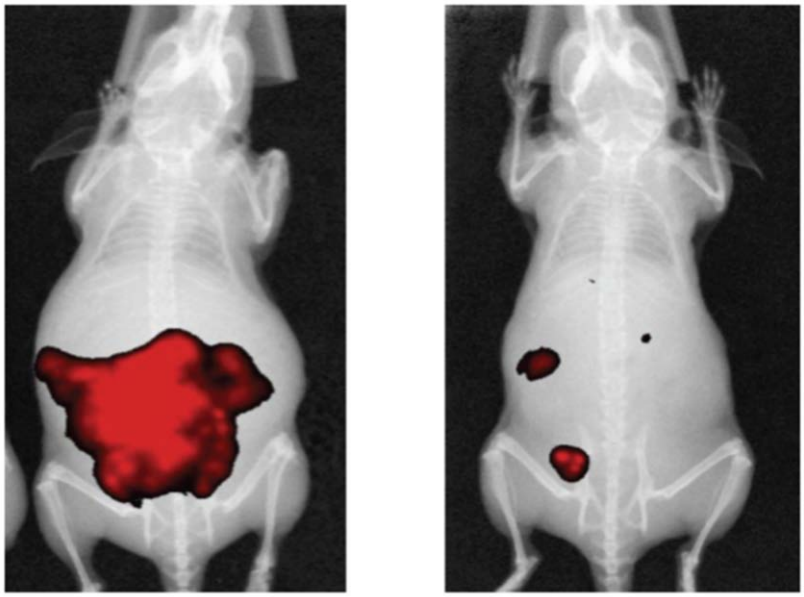
- **It is orthotopic -** The tumour grows in the abdomen of the mouse in exactly the same manner as in women, attaching to the same organs and sparing the same organs and tissue; and resulting in a disseminated carcinomatosis as in women.
- **It is heterogenous -** The mice are injected with human ovarian cancer stem cells (CD44+), but the resulting tumours have an identical histological appearance to that in women, with both CD44+ and CD44- cells.
- **It is drug-refractory -** Once the tumour is seeded, the mouse is treated with paclitaxel (Taxol). A transient anti-cancer effect ensues, followed by rapid growth of tumour despite ongoing Taxol treatment.

Cantrixil delivers a potent anti-cancer effect in this mouse model that is highly representative of human ovarian cancer. The photos of anaesthetized mice in Chart 1 show that 10 days after the injection of the cancer cells, the tumours in control mice receiving no drug grew into a significant tumour mass. Those mice receiving Cantrixil had tumours that either didn't progress or had completely regressed.

Cantrixil is the first drug to provide any meaningful anti-cancer effect against ovarian cancer stem cells in this aggressive tumour model, which underlines its promise as a novel anti-cancer drug. The team at Yale has tested the currently-marketed chemotherapy drugs plus number of new drugs being developed by companies such as Merck and Pfizer, and none of those drugs has shown significant activity against ovarian cancer stem cells in the mouse model.

[1] Alvero,Chen et al.2009, Alvero,Fu et al.2009)

Chart 1. Cantrixil dramatically reduces tumour growth in the Yale ovarian cancer stem cell mouse model



Source: Company announcement

NRT has a deep pipeline of potent super benzopyran anti-cancer drugs

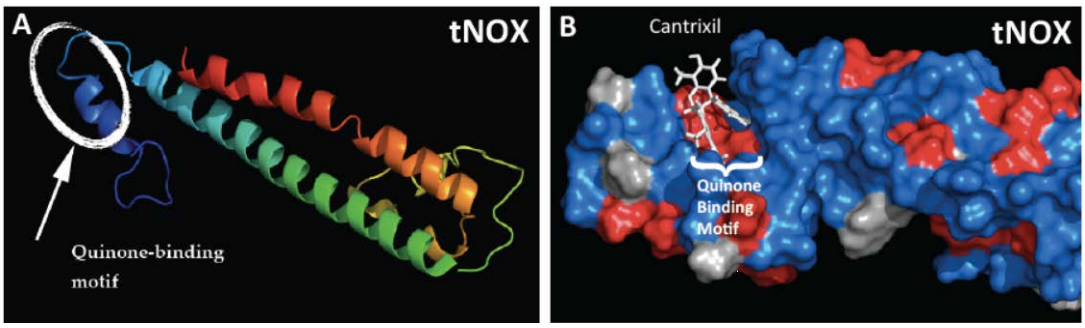
NRT has developed a new class of drugs that it terms super benzopyrans, by modifying the chemistry of the first generation of simple benzopyran drugs that include its former drug candidate phenoxydiol.

Benzopyrans as a drug class trigger cancer cell death by inhibiting a target known as tumour-associated NADPH oxidase, or tNOX. The current SBP drugs in NRT's pipeline bind more strongly to tNOX compared to the older benzopyrans, and have 10-100x higher anticancer activity. Chart 2 shows the binding of NRT's Cantrixil super benzopyran drug to the tNOX enzyme.

NRT has identified three lead SBP drug candidates. Each of these three compounds is cytotoxic against all forms of cancer cells, but small structural changes bring out particularly high anticancer activity against certain types of cancer. The three lead candidates are:

- Cantrixil - a formulation of the super benzopyran TRX-002 formulated in captisol, a sugar (cyclodextrin) membrane. Cantrixil was selected for its high activity against ovarian cancer and is formulated for administration directly into the abdominal (peritoneal) or thoracic cavity.
- Trilexium - a construct of TRX-009 in a proprietary formulation intended to maximise transport across the blood brain barrier. Trilexium was selected for its strong activity against brain cancer cells.
- TRX-7 - which has been selected for its strong activity against prostate cancer cells. It is formulated in the same proprietary formulation as Trilexium.

Chart 2. Chart Heading (Numbered)

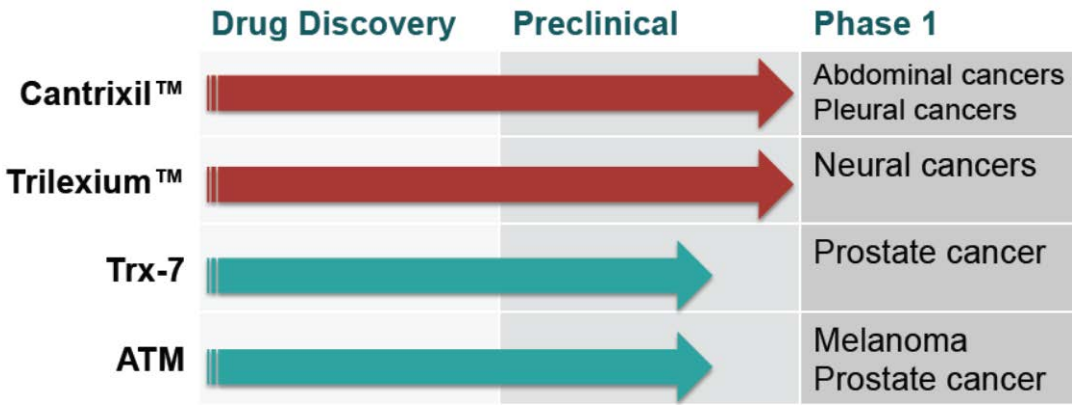


Source: Company announcement

Development plan and pipeline

Chart 3 illustrates the development status of NRT's three lead super benzopyrans, plus a separate class of drugs known as anti tropomyosins (ATM). While all three lead SBPs could potentially be ready for clinical trials in 2015, the company has decided to focus its near-term clinical development program on its most advanced drug, Cantrixil.

Chart 3. Novogen's anti-cancer drug pipeline



Source: company presentation

Cantrixil development plan

NRT is completing pre-clinical toxicology studies to support a US Investigational New Drug application (IND) for Cantrixil and plans to conduct two Phase 1 clinical studies of the drug. Table 1 outlines the Cantrixil development timeline.

The first Phase 1 trial will test the intra-abdominal infusion of Cantrixil in patients with late stage ovarian cancer refractory to standard therapy, but without significant ascites. The trial will be conducted at Yale Cancer Centre, and in select hospitals in Australia and possibly also in the UK.

The trial will be an accelerated dose-escalation design that will provide greater opportunity to achieve an anti-cancer effect. Patients will continue to be treated with Cantrixil until either complete remission or disease progression. If the disease progresses (gets worse), Cantrixil will be administered in combination with another cytotoxic drug.

The second trial will be an Australia-based pilot study of intra-abdominal Cantrixil in patients with advanced cancer of the abdomen (carcinomatosis) associated with malignant ascites (fluid accumulation), due to the spread of diseases such as mesothelioma, ovarian, bowel, gastric, pancreatic or breast cancer. No standard of care exits for these patients, and the survival prospects are 2-6 months.

Table 1. Cantrixil clinical development strategy and timeline

Phase	Status	Indication	Sites	Start	Finish
IND	current		US	Aug-14	May-15
Phase 1	3Q15	late-stage ovarian cancer	US/UK	Aug-15	Aug-16
Pilot study	3Q15	malignant ascites	Australia	Aug-15	Mar-16

Source: company presentation

.

Pre-clinical development of other pipeline drugs

Trilexium

Trilexium has shown good anti-tumour activity against neural cancer stem cells generated from biopsies of tumours that were highly resistant to standard chemotherapy drugs. Studies conducted at university of Hong Kong confirm the anti-cancer activity and next stage involves testing in mouse models where the human cancer cells are growing in the brain. This trial will confirm the ability of Trilexium to cross the blood/brain barrier to target brain tumours. Following this trial, formal preclinical toxicology studies would need to be completed before progressing to IND submission and a Phase 1 clinical trial.

Novogen plans to file for IND in 2015 and could be in a position to initiate a Phase 1 trial in 4Q CY15.

Trx-7

Trx-7 has shown in-vitro activity against prostate cancer cells and Novogen aims to develop the drug further in 2015. Trx-7 is active against a wide range of cancer cell lines, and could eventually become the lead candidate for intravenous applications.

Anti-tropomyosins

In addition to the SBPs, NRT is developing a separate class of drugs known as anti-tropomyosins (ATM). ATMs inhibit a cancer target known as Tm5NM1, which is a cancer-specific form of tropomyosin, a component of the cell skeletal structure known as microfilaments.

A living cell is made up of a skeleton which consists of microfilaments and microtubules. Some anti-cancer drugs target the microtubules, but none currently target the microfilaments. The microtubules are not specific to cancer cells and as a result the conventional drugs lead to side effects. In contrast, NRT's ATM drugs are expected to have fewer side effects because they target a cancer-specific component of the microfilaments.

Novogen plans to develop this technology further with the aim of combining ATM drugs with conventional chemo agents to achieve better response rates by targeting both the microfilament and the microtubule components of the cell skeletal structure.

NRT has identified 6 different families of ATM compounds, and is in the process of identifying lead drug candidates. While these compounds show promising anti-cancer potential, at this stage they are a lower priority than the SBP drugs.

Valuation

We value NRT at A$0.22/sh based on a risk-adjusted discounted cash flow model, which includes our estimates of the future milestone payments and royalty streams for the three lead SBP drugs, Cantrixil, Trilexium and Trx-7. We have extended our cash-flow forecasts out to 2035 but we have not included any terminal valuation due to the ongoing risk of product failure and potential competition from novel products. We assume a long-term A$/US$ exchange rate of 0.83 and apply a discount rate of 15%. We initiate coverage with a price target of A$0.22/sh

For valuation purposes we assume that NRT raises a further A$5M through the issue of 62.5M shares at the current share price of 8¢/sh, plus a further A$2.1M through the exercise of options in November 2015.

The average success rate for small molecule drugs commencing Phase 1 trials is 13%. We use a lower likelihood of success in our valuation model because each drug still has to clear some pre-clinical hurdles before Phase 1 trials commence. In our valuation model we assume:

- 12% likelihood for Cantrixil in ovarian cancer - preclinical efficacy studies in animal models are complete, and the only remaining hurdle is formal preclinical toxicology studies. No toxicity issues have been seen in animal studies to date.
- 8% likelihood for Cantrixil for malignant ascites - the pilot study in patients with malignant ascites will go ahead pending the completion of preclinical toxicology studies. Preclinical efficacy studies are complete for ovarian cancer, but not for the other cancer types that lead to malignant ascites such as bowel, pancreatic and breast cancer.
- 8% likelihood for Trilexium – preclinical efficacy studies in mice with brain cancer need to be completed to show that Trilexium crosses the blood/brain barrier.
- 8% likelihood for Trx-7 in prostate cancer – Trx-7 shows high potency against prostate cancer cell lines that are resistant to standard chemotherapy drugs. However, pre-clinical studies in animal models have not yet been completed.

Table 2 shows our market assumptions for the three lead super benzopyran drugs. We base our estimate of the size of the non-ovarian cancer malignant ascites market on the colorectal (bowel) cancer market. Approximately 10% of colorectal cancer patients develop malignant ascites, and we assume a 30% uptake of Cantrixil among these patients.

In our forecasts for NRT we also assume that:

- NRT earns a 15% royalty on net sales of super benzopyran drugs.
- The drugs are licence to a marketing partner at the completion of Phase 2 trials.
- Each new licence deal includes a US$20M up-front payment and US$140M in milestone payments, in line with the ChemGenex's 2009 licence deal with Hospira for its lead cancer candidate Omapro (omacetaxine mepesuccinate).
- 15% of the revenue from Cantrixil goes to Yale University under the CanTx joint venture.

Table 2. Market assumptions for lead super benzopyran products

Indication	Market launch	Peak market share	Global market size (US$M)	Peak sales in year 4 (US$M)	Likelihood of approval
Cantrixil in ovarian cancer	2022	30%	1,500	$770	12%
Cantrixil - malignant ascites in bowel cancer	2022	3%	8,300	$425	8%
Trilexium in Glioblastoma multiforme	2024	10%	400	$75	8%
TRrx-7 in prostate cancer.	2024	10%	11,300	$2,100	8%

Source: BBY research

Target diseases and addressable markets

Ovarian Cancer

Market research group GBI Research forecast the global ovarian cancer therapeutics market will grow to US$1.9B in 2020 at a Compound Annual Growth Rate (CAGR) of 3.4%.

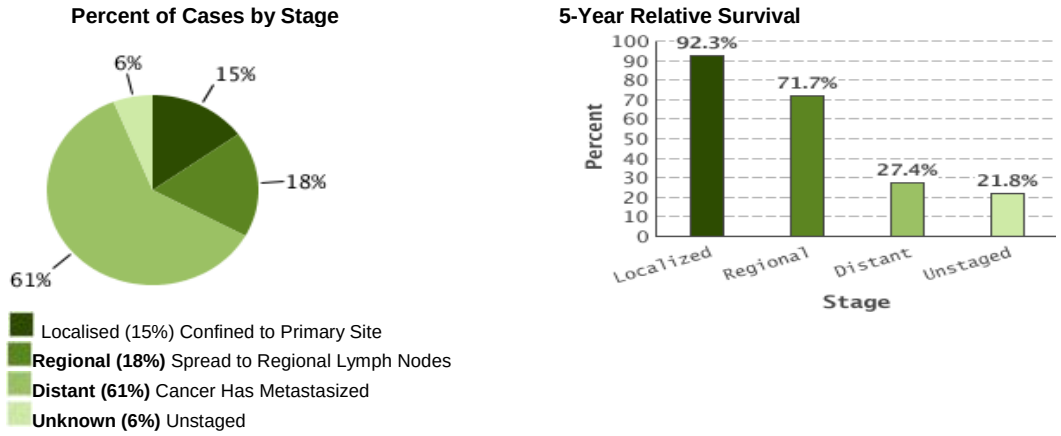
Ovarian cancer is diagnosed annually in nearly 21,980 women in USA and causes an estimated 14,270 deaths annually. It is the deadliest gynaecological malignancy.

In Australia, every 10 hours, a woman dies of ovarian cancer and out of the 1400 Australian women diagnosed every year, only 20% of these women will survive for longer than five years. At the time of diagnosis, the majority of patients present with advanced disease (about 61%) as the disease is often asymptomatic in the early stage.

In most patients with advanced disease, tumour spreads across the lining of the abdomen which leads to accumulation of fluid within the abdominal cavity known as ascites.

The standard treatment includes surgery when the cancer has not spread, and combination of surgery and chemotherapy for advanced widespread disease. The chemotherapy agents can be injected into the blood or can be directly inserted into the abdominal cavity so that there is a local and concentrated action against the tumour. In the past, studies have shown superior survival rates in patients in whom the chemo agent has been inserted directly into the abdominal cavity via a catheter

Chart 4. Most ovarian cancer patients have developed late stage disease by the time the cancer is diagnosed



Source: National Cancer Research Institute www.seer.cancer.gov

Prostate Cancer

Market research group BCC Research estimated the global prostate chemotherapeutics market to be US8.1B in 2012, and forecasts it to grow to US$18.6B in 2017, at a CAGR of 18%.

Prostate Cancer is the most common cancer in men with an annual incidence of 233,000 cases per year in USA in 2014, causing 29,480 deaths. In Australia, about 20,810 Australian men are expected to be diagnosed with prostate cancer in 2014. The majority of cases are localised at diagnosis but a substantial number of cases spread to the bones and other organs.

The treatment options for advanced cases involve using drugs which block the production of the hormone testosterone which is thought to be one of the main drivers of the prostate cancer. Chemotherapeutic agents are used when the tumour cells do not respond to hormone blockage, but they improve survival by only a few months

Glioblastoma Multiforme

A recent MarketWatch report forecasts the GBM chemotherapeutic market to grow rapidly from $301 million in 2013 to $623 million by 2020, at a CAGR of 11%.

Glioblastoma multiforme (GBM) is one of the deadliest brain tumours with a median survival of around 4 months without any treatment.

The National Cancer Institute, USA estimates that 23,380 adults will be diagnosed with brain and other nervous system tumours in 2014 in the US. It also estimates that in 2014, 14,320 of these diagnoses will result in death.

Glioblastoma accounts for about 17 percent of all brain tumours and primarily occurs in adults between the ages of 45 and 70. Standard therapy consisting of surgery, radiotherapy and a chemotherapy agent temzolamide is not very effective and prolongs survival on average by 15 months.

Other Players in the Cancer Stem Cell Space

A number of other companies are developing drugs that target cancer stem cells, but the most advanced products have only reached Phase 2 clinical trials. Some of the leading players are:

Verastem

Verastem is developing a range of small molecules that inhibit focal adhesion kinase (FAK). They claim that FAK is a key regulator of signaling pathways critical to cancer stem cell survival.

Its lead FAK inhibitor is VS-6063 (defactinib). Initial data from an ovarian cancer Phase 1a study of defactinib showed encouraging signs of clinical activity, with 9/22 (41%) having an objective response (partial or complete response) or stable disease for more than 6 months. The drug is currently in a Phase 2 study in mesothelioma and is also in a Phase 1 study with paclitaxel in ovarian cancer.

VS-4718, another oral small molecule FAK inhibitor, is currently in Phase 1 in advanced solid tumours.

OncoMed Pharmaceuticals/Bayer

OncoMed is developing antibodies and small molecule drugs that act against cancer stem cells by targeting the signalling proteins Notch and Wnt.

OncoMed has formed a number of alliances with big pharma companies including Bayer. A Phase 1b trial of their monoclonal antibody Demcizumab has shown good clinical and radiological response rates in patients with Non-Small Cell Lung Cancer and Pancreatic cancers.

Stemline Therapeutics

Stemline has a single small molecule (fused to diphtheria toxin) drug directed at interleukin-3 receptor (IL-3R). This receptor is over-expressed on blast cells of certain haematological cancers. The company has seen some evidence of activity in Phase 1 study. The drug does not target solid tumours.

Geron Corporation

Geron claims that myeloid blast cells express high telomerase activity. It has a single drug, imetelstat, a small molecule telomerase inhibitor that is currently in Phase 1. Earlier this month Geron formed a partnership with J&J to develop imetelstat, including plans for Phase 2 trials in myelofibrosis and myelodysplastic syndrome.

Bionomics (ASX :BNO)

Bionomics is developing a monoclonal antibody (BNC 101) which targets cancer stem cells present in colon and pancreatic cancers and plans to conduct a Phase 1 study in 2015, pending approval.

Bionomics' other potential anti-cancer drug is the vascular disrupting agent BNC105. A Phase 1 trial of BNC105 in ovarian cancer involving combination of BNC105 with standard chemotherapy agents showed that patients with first or second relapse of cancer had a positive response rate of 66.7%

Risks:

Speculative Investment - An investment in NRT should be considered speculative in nature. The success of the Company is dependent on successful development and commercialisation of its pipeline of drug candidates.

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Clinical trials – Clinical trials may not be successful, or recruitment delays may mean that the trials take longer than expected.

Regulatory approval - VLA may not succeed in obtaining regulatory approval for its Cymerus therapeutic products, or may face unexpected delays. Regulators may take a cautious approach to approving the initiation of clinical trials and to the subsequent approval of therapeutic products that are based on iPS cell technology.

Funding – NRT will require additional funding to conduct Phase 2 trials of it drug candidates. There is no guarantee that the funding will be available when required.

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Contact with NRT has been made during the preparation of this report for assistance with verification of facts.

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