

(NASDAQ market code: NVGN)

Novogen (NRT) Spec Buy

PHENOXODIOL IS PHENOMONAL

Shareprice:	\$2.10	Y/end June	2002a	2003e	2004e	2005e
Shares now	95.4m	Sales revenue \$m	23.1	27.5	31.9	32.4
Market Cap A\$m	\$200m	NPAT \$m	-14.7	-16.7	-16.2	-19.7
Risk	High	EPS c	-0.15	-0.18	-0.17	-0.21
		PER x	N/a	N/a	N/a	N/a
		DPS c	0.0	0.0	0.0	0.0
		Yield %	0.0	0.0	0.0	0.0

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Key Points

An investor presentation held by Marshall Edwards Inc on October 7th 2002 has revealed some very exciting developments regarding phenoxodiol.

Phenoxodiol is a very promising compound with very potent anti-cancer properties. There are plenty of anti-cancer compounds on the market and in development, but what is exciting about phenoxodiol is the low toxicity profile combined with the very effective anti-cancer properties.

Phenoxodiol's mechanisms of action to kill cancer cells is ubiquitous to all cancer cells. As a result, Marshall Edwards is embarking upon several phase II clinical trials to treat various forms of cancer. These include leukemia, ovarian cancer, renal carcinoma and pancreatic cancer.

Yale University and Marshall Edwards are jointly researching the therapeutic effects of phenoxodiol on ovarian cancer. Standard therapy for ovarian cancer is surgery and chemotherapy, however to date, the overall improvement in the survival for patients with ovarian cancer has been minimal. Scientists at Yale University are extremely enthusiastic about the potential of phenoxodiol as a novel weapon in the fight against cancer, in particular ovarian cancer.

Phenoxodiol must still prove in the phase II trials statistically significant positive results, however all early indications are looking extremely promising. The dual mechanism of killing cancer cells combined with its low toxicity profile makes phenoxodiol one of the most exciting anti-cancer compounds under development. Speculative Buy.

Phenoxodiol

It has now become apparent that phenoxodiol has two crucial mechanisms of action:

1. It inhibits the anti-apoptotic proteins FLIP and IAP by binding to death receptors on the cell.
2. It increases the pro-apoptotic protein BAX.

Apoptosis (programmed cell death) is essential for tissue homeostasis, that is the balance between cell proliferation and apoptosis. An imbalance in tissue homeostasis such as unwanted tissue atrophy (i.e. cells dying via apoptosis too rapidly resulting in ageing) or excessive cell proliferation (i.e. tissue becomes immortal resulting in cancer) causes a disease state.

The main difference between normal cells and cancer cells is its sensitivity to apoptosis. In cancer cells, the ability for those cells to die via apoptosis is inactivated by a series of protein interactions in the cell. Phenoxodiol makes cancer cells sensitive to apoptosis via the two modes of actions detailed above, thus reversing the cancer process and transforming a cancer cell back into a normal cell that is programmed to die.

Not all cancers express death receptors which trigger apoptosis, thus up until now phenoxodiol has been less effective against these types of cancers, with only one of its two mechanism of action (via the increased production of BAX) able to kill the cancer cell. Recently scientists at Marshall Edwards have discovered a method of rendering all cancer cells susceptible to phenoxodiol via both mechanisms of action.

Two commonly used chemotherapeutic drugs are cisplatin and gamma-interferon. By combining phenoxodiol with either cisplatin or gamma-interferon it is believed that all cancer cells will be susceptible to phenoxodiol because cisplatin and gamma-interferon both increase the number of death receptors on the cell. With the death receptors now present on the cell surface, phenoxodiol can kill the cancer cell via both mechanisms, making it a much more potent anti-cancer compound.

Clinical Trials

Marshall Edwards are embarking on a number of clinical trials in 2002/03. Phenoxodiol is being administered in two forms:

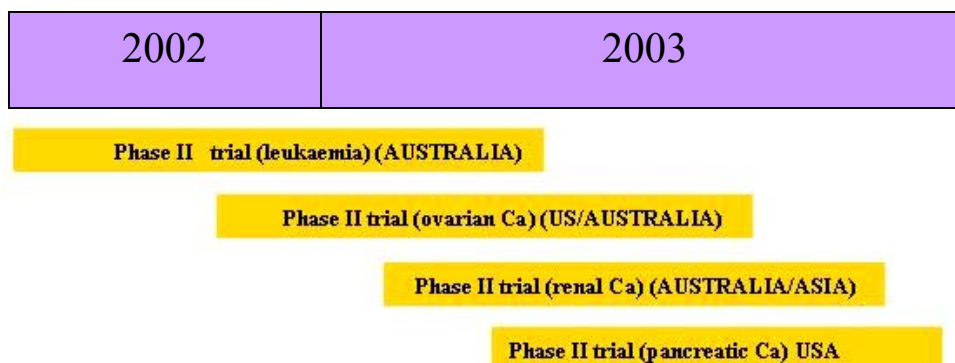
1. Oral for long term cancer therapy
2. IV for short term cancer therapy

Normally, an oral formulation is very difficult to develop because the digestive tract destroys the drug, or the drug does not pass through the gut wall or, the stomach conjugates sugar molecules onto the drug rendering it inactive. However, phenoxodiol is of a similar chemical structure to steroids, thus acts very similar to the oral contraceptive pill in the stomach. Developing an effective oral formulation would be of a similar challenge to developing the oral contraceptive pill.

In addition, the each phase II clinical trial is being developed in two parts:

- Part A – phenoxodiol as a monotherapy
- Part B – phenoxodiol in combination with either cisplatin or gamma-interferon

Phase II Clinical Program



Ovarian Cancer

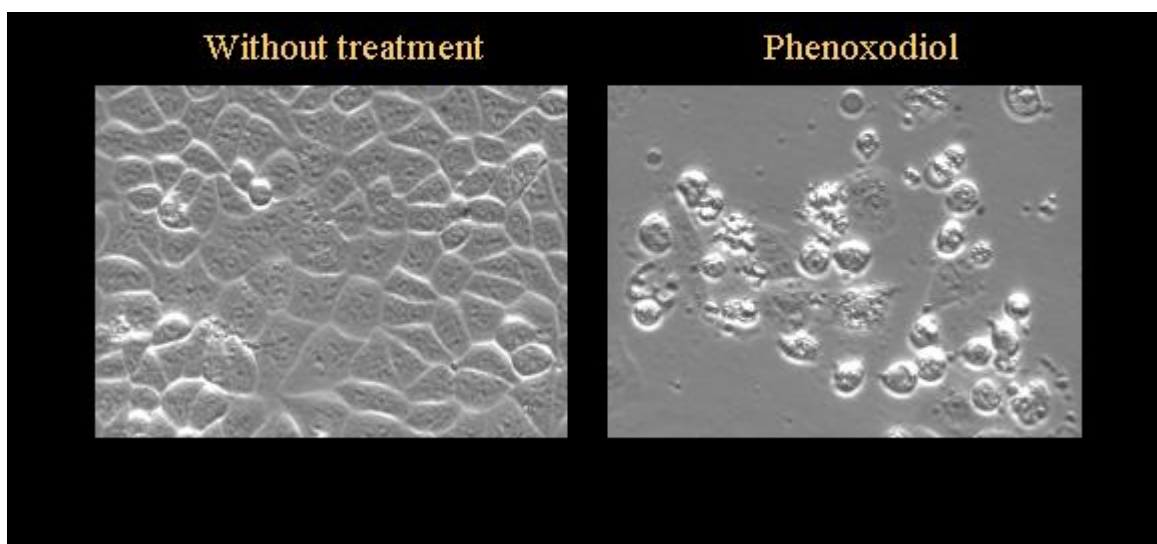
Marshall Edwards and Yale University have a research collaboration agreement to co-develop phenoxodiol as a novel treatment for ovarian cancer.

Ovarian cancer will affect 1 in 70 women in the USA and kill 1 in 100 this year. It is the leading cause of death from gynaecologic cancers. Standard treatment for ovarian cancer is surgery followed by chemotherapy. The overall improvement in the survival for patients with ovarian cancer has been minimal because

1. microscopic disease remains after surgery in the peritoneal cavity;
2. incomplete eradication of disease with systemic chemotherapy; and
3. dose and duration of intra-peritoneal chemotherapy is limited by toxicity to normal cells.

The reason ovarian cancer is becoming more prevalent is due to the lack of an effective screening system. Symptoms include abdominal pain, abdominal swelling, and loss of appetite, all of which can be attributed to various sequale.

Scientists at Yale University are extremely excited about phenoxodiol because of its novel mechanisms of action to treat cancers. The pictures below show ovarian cancer cells without treatment, and 24 hours after phenoxodiol treatment. There was no toxicity in non-cancerous cells.



As the pictures above indicate, the cancer cells have had a violent reaction to phenoxodiol in less than 24 hours.

Phenoxodiol must still prove in the phase II trials statistically significant positive results, however all early indications are looking extremely promising. The dual mechanism of killing cancer cells combined with its low toxicity profile makes phenoxodiol one of the most exciting anti-cancer compounds under development.

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