

# Novogen is an Australian biotechnology company listed on both the Australian Securities Exchange (NRT) and NASDAQ (NVGN).

Novogen owns two proprietary drug technology platforms that are first-in-class and which the Company believes will be the foundation that will enable us to grow into a major global biopharmaceutical force.

Both technologies target essential functions, that lie at the heart of cells behaving abnormally. These essential functions are present across a wide range of degenerative diseases, including cancer, genetic disorders and autoimmune diseases.

These are entirely novel drug targets and Novogen believes addressing them will revolutionize the treatment of many of the common diseases affecting our community and for which no curative treatments currently exist.

# "We are building a global bio-pharmaceutical business around two first-inclass drug technology platforms." Dr. Graham Kelly, Executive Chairman

# Super-benzopyrans (SBPs)

Most of the long-standing anti-cancer drugs that 40 years on remain the backbone of chemotherapy, are derived from plants or soil organisms. In this same way, hormones. These hormones control a wide range of plant functions through their ability either to inhibit or activate a wide range of enzyme pathways and gene

functions. The fact that humans share 25% of their DNA with plants accounts for the ability of these simple plant hormones to modify a wide range of human biological functions including the function of

human genes. Some of those functions are inhibitory (eg. killing cancer stem cells), while others are promotional (eg. activating normal stem cells).

Novogen has run a simple strategy - identify selective functions and then magnify them to the point of being drug-like. That magnification goal is achieved through the creation of compounds

considerably more complex in their structure than the original plant hormone.

That is our SBPs family of drugs. Small molecules where the insertion of a range of chemical groups has led to much greater electron-donating and electron-receiving

function. That creates molecules with greater binding-affinity to their targets and thereby greater ability to inhibit or activate the target. This happens whether it be in a cancer cell, a stem cell from the muscle of a patient with muscular dystrophy, or a

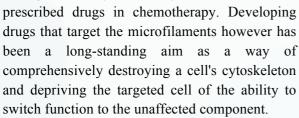
normal stem cell in the brain of a patient suffering from stroke.

SBPs work by targeting an enzyme that regulates the movement of hydrogen ions across cell membranes. Inhibiting this enzyme robs key functions within the cancer cell of hydrogen, leading to the death of the cancer cell.

## Anti-tropomyosins (ATMs)

These drugs are first-in-class, targeting an entirely new drug target across oncology and autoimmune diseases. The target is the cell's cytoskeleton (or architectural framework), essential for signal transduction, cell migration

and cell division. The cytoskeleton skeleton has two main components microtubules microfilaments. Currently the microtubules are targeted by standard chemotherapy drug families, the taxanes and vinca alkaloids and remain among the mostly commonly

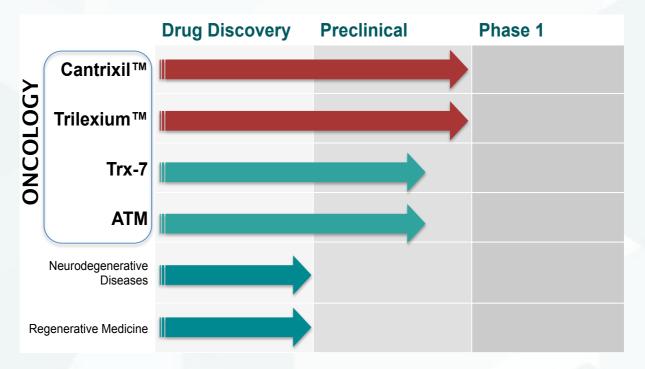


The breakthrough came recently with the discovery that the microfilaments of cancer cells could be destroyed selectively by targeting a particular isoform of a tropomyosin protein known as Tm5NM1. While this isoform is found

in both normal cells, cancer cells and certain autoimmune diseases such as ulcerative colitis, it has been high-jacked by abnormally functioning cells for their survival; normal cells can survive without it. Our lead ATM drug is high ontarget and prevents the Tm5NM1 protein from dimerizing. This leads to complete disintegration of

the microfilaments. When used in combination with an anti-microtubule drug such as vincristine or paclitaxel, the destruction of the cancer cell's cytoskeleton is comprehensive.

# Drug Pipeline



### **VISION**

"Our vision is for the SBP and ATM drug technologies to provide a combination chemotherapy regimen that will become the standard first-line therapy for most forms of cancer. Used together they will provide comprehensive killing of the full hierarchy of tumor cells, thereby preventing or stalling disease relapse and the development of refractory cancer." Dr. Graham Kelly, Executive Chairman

## Oncology

#### Cantrixil<sup>TM</sup>

Cantrixil is owned by CanTx Inc., the Connecticut-based, joint venture company between Novogen and Yale University. Cantrixil has been developed as a groundbreaking intra-cavity product, to be delivered as a non-irritant anti-cancer agent into the peritoneal and pleural cavities to treat malignancy. Cantrixil is a construct of the SBP molecule, TRX-E-002-1, in a cyclodextrin (Captisol] polymer. The polymer dissolves within the cavity, releasing the drug molecule. A particular feature of TRX-E-002-1 is its ability to kill both cancer stem (CD44+ve) cells and their daughter cancer (CD44-ve) cells.

The primary indication of **Cantrixil** is first-line therapy of ovarian cancer used in combination with carboplatin. This combination in an animal model of intra-peritoneal human ovarian cancer has proved highly effective in providing complete remission of the cancer.

First-in-man studies will be conducted in patients with recurrent, late-stage cancers of the abdomen. In particular, platinum- and taxane-refractory ovarian cancer, malignant ascites and peritoneal carcinomatosis associated with colorectal, ovarian, pancreatic and breast cancer. There is currently no standard of care for malignant ascites and peritoneal carcinomatosis. Cantrixil is believed to be the only experimental drug being tested in this area of significant unmet clinical need.

#### Trilexium<sup>TM</sup>

**Trilexium** is a construct of the SBP drug, **TRX-E-009-1**, in a proprietary formulation that optimizes the bioavailability of the molecule across the gut mucosa. **TRX-E-009-1** has been selected for its potent cytotoxicity against neural cancer stem cells. The primary clinical indications are primary brain cancers of both adults and children and also neuroblastoma of children.

#### Trx-7

**Trx-7** is an SBP analog that has been selected for its high cytotoxic activity against prostate cancer cells. It is formulated in the same proprietary formulation developed for Trilexium. It is being developed for the treatment of docetaxel-refractory prostate cancer.

#### **ATM-001**

**ATM-001** is the lead ATM drug candidate that is being developed as a treatment for prostate cancer, melanoma and neuroblastoma. The concept is to use ATM-001 in combination with an anti-microtubule drug (vincristine, paclitaxel] in order to deliver comprehensive destruction of the cancer cell's cytoskeleton and to be used ultimately in further combination with **Trilexium** or **Trx-7**.

## Degenerative Disease

The same family of SBP compounds that are potent killers of cancer stem cells, conversely have the opposite effect on stem cells associated with a range of genetic disorders. These are where disease process is either associated with abnormal stem cell activity, or the stem cells are behaving normally but have become exhausted trying to repair the damage. Muscular dystrophy diseases, motor neurone disease, and Alzheimer's are just some of the conditions in question.

While the mechanism by which this happens is yet to be determined, Novogen is developing SBP compounds with the ability to promote the function of stem cells within a range of genetic disorders. This is not theoretical.... Novogen has achieved proof-of-concept and is actively pursuing a program to develop potent drugs with this activity. This function represents one of the strands of biological activity that has been teased out of the original plant hormone and then magnified to become more drug-like.

Many companies are taking the approach of stem cell therapy to treat these disorders. This involves the transplantation of adult or embryonic stem cells, and is an approach fraught with challenges, not the least being that the underlying disease state has the potential to nullify any benefit of the transplanted stem cells. The Novogen approach is to promote the body's own stem cells to address the underlying disease process.

## Regenerative Medicine

This is an extension of the degenerative diseases program, the difference being that the SBP compounds are now being used to promote the activity of normal tissue stem cells. Novogen is focusing on the recruitment and activation of neural stem cells in order to repair brain injury (stroke, trauma) spinal cord injury and peripheral nerve damage.