NOVOGEN

THE FUTURE OF
CANCER THERAPY

Novogen 3 minute update

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

Novogen believes it has the potential to bring a new and considerably more effective way of thinking to the management of many of our community's debilitating diseases.

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 biotechnology company.

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, neurodegenerative, musculodegenerative, metabolic disorders and autoimmune diseases.

These are entirely novel drug targets that 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 biotechnology business around two first-in-class drug technology platforms that have potential reach across many of mankind's most lethal and debilitating degenerative diseases."

Cancer

Forty-four years ago (1971), President Richard Nixon famously declared "war on cancer". Since then, cytotoxic chemotherapy has been the backbone of cancer chemotherapy. Drugs that kill cancer cells by damaging them to the point of destruction remain the go-to form of chemotherapy for almost all forms of inoperable cancer. Cytotoxic chemotherapy is the only validated form of drug therapy that is capable of delivering meaningful prolongation of survival for patients with malignant cancers.

But cytotoxic chemotherapy has its limitations: (a) many forms of cancer remain insensitive to chemotherapy, and (b) it rarely prevents the cancer from recurring. These limitations have driven interest in alternative approaches including targeted therapy, gene silencing, and immunotherapies including cancer vaccines and immune checkpoint inhibitors. The oldest of these, targeted chemotherapy, has been generally disappointing. The newer approaches have yet to prove their worth.

Novogen has taken the approach of seeking to make cytotoxic chemotherapy work better. We believe that a *validated* form of therapy is a sensible and perfectly rational starting point in looking to make improvements.

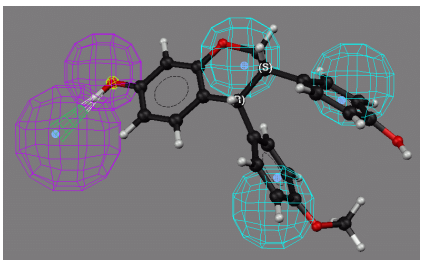
Both Novogen drug technology platforms are being harnessed to achieve this goal.

(a) Super-benzopyrans (SBPs).

The SBPs are a family of small molecule compounds that are proprietary to Novogen. Their primary features are:

- they kill the **FULL** hierarchy of cells within a tumor, **INCLUDING THE CANCER STEM CELLS**
- they work against **ALL** types of cancer
- they are highly selective for cancer cells, with minimal toxicity.

SBPs work by targeting a tumor-specific mutant form of 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 rapidly to the death of the cancer cell.



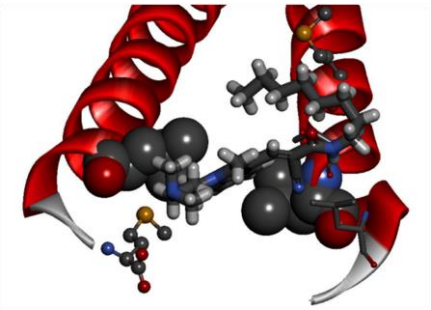
Importantly, the molecular target is common to all forms of cancer and, within different cancers, to both parent cancer (stem) cells and their more prevalent daughter cancer cells.

Novogen has advanced this technology to the point where it can manipulate the structure of the underlying SBP molecule to create drug candidates with elevated activity against specific cancer types. Three lead drug candidates have been created in this way against ovarian cancer (TRXE-002), cancers of neural crest cells (TRXE-009), and prostate cancer (TRXE-0025).

(b) Anti-tropomyosins (ATMs)

The ATMs are a family of small molecules that target the cytoskeleton of cancer cells, destroying the architecture of the cell and resulting in its death.

The ATMs are intended to be used in conjunction with standard-of-care chemotherapies that similarly target the cancer cell cytoskeleton, with the combination of the two providing substantial synergy of effect, resulting in comprehensive destruction of the cancer cell's physical structure.



The cytoskeleton of a cell has two main components –**microtubules** and **microfilaments**. While each component has separate functions, there is enough overlap that destruction of just one component yields incomplete disintegration of the cytoskeleton.

The most widely used cytotoxic drugs in cancer therapy target the microtubules. These drugs are the taxanes (paclitaxel, docetaxel) and the vinca alkaloids (vincristine, vinblastine, vineralbine), standard first-line therapies in cancers of the breast, ovary, lung, prostate, head and neck and various leukaemias.

The advantages of using an ATM drug in combination with an anti-microtubular drugs are:

- 100-fold synergy of anti-cancer effect of either combination drug alone
- anti-cancer effect in cancer cell types (eg melanoma) currently insensitive to anti-microtubular drugs
- ability to lower the dose of anti-microtubular drugs to reduce their toxic side-effects profile without sacrificing anti-cancer potency.

One lead ATM drug candidate has been developed.

(c) Oncology drug pipeline.

TRXE-002

TRXE-002 has been developed as the construct, **Cantrixil™,** employing a cyclodextrin polymer shell. It has been designed as a non-irritant, intra-cavity chemotherapy to be administered directly into the peritoneal and pleural cavities to treat malignancy. The polymer dissolves within the cavity, releasing the drug molecule where its primary effect is locally within the cavity, but where systemic absorption also takes place to deliver a dual anti-cancer effect both directly and indirectly.

Cantrixil is being developed for the treatment of tumors that arise within or spread to the peritoneal and pleural cavities. The first-in-man clinical trial that is scheduled to commence in 2H15 will be in patients with malignant ascites.

TRXE-002 has been licensed by Novogen to **CanTx Inc**, the joint-venture company with Yale University.

TRXE-009

TRXE-009 is a uniquely-targeting anti-cancer drug, showing preferential activity against cancer cells that share a common embryonic link with the neural crest. This includes primary brain cancers, neuroblastoma and melanoma. Clinical trials are being planned for a proprietary formulation of **TRXE-009** known as **Trilexium™** to enter a Phase 1 study in adults with malignant melanoma and glioblastoma multiforme (1H16), and in children with medulloblastoma and diffuse interstitial pontine glioma (1H16).

TRXE-0025

TRXE-0025 displays preferential activity against prostate cancer cells. This drug candidate is undergoing final formulation optimisation studies and is scheduled to enter the clinic in 1H16 in men with castrate-resistant disease.

ATM3507 (Anisina)

Anisina is intended to be used in combination with an anti-microtubular drug (paclitaxel or vineralbine) in adults with solid and non-solid cancers and in children with neuroblastoma. Time to clinic is scheduled to be 1H16.

Degenerative Diseases

The Company's two drug technology platforms are being applied also to a variety of non-oncology degenerative disease applications.

In the case of the SBP platform, we are exploiting the pleiotropic nature of the original plant hormone, genistein, with its known therapeutic potential in a range of therapeutic indications including lysosomal storage diseases (eg San Filippo Syndrome) as well as an ability (discovered by Novogen scientists) to promote the function of dysfunctional or under-performing tissue stem cells.

Alzheimer's disease, fascioscapulohumeral dystrophy (FSHD), nemaline dystrophy and San Filippo Syndrome are 4 clinical indications currently being actively pursued.

In the case of the ATM platform, the same molecular target of Anisina in cancer cells (tropomyosin isoform Tm5NM1) has been implicated in ulcerative colitis. But beyond this disease, the structural integrity of a cell

(its cytoskeleton) is becoming increasingly seen as being integral to many autoimmune disease processes beyond ulcerative colitis. Novogen believes that its world-leading research into the biology of tropomyosin and the ability to target this protein with designer drugs, opens up a major new drug development opportunity.

Regenerative Medicine

This builds on the discovery by Novogen of the ability of its SBP drugs to promote the activity of tissue stem cells. IN this program, this ability is being studied for its therapeutic potential in the recruitment and activation of neural stem cells in order to repair brain injury (stroke, trauma), spinal cord injury, and peripheral nerve damage.