NOVOGEN LIMITED (ASX: NRT)



ASX RELEASE 18 June 2014

# Novogen and CanTx Announce Potency of Intra-Peritoneal Trx-1 Confirmed Against Chemo-Resistant Ovarian Cancer Stem Cells

## Companies expect to commence first-in-human studies of Trx-1 in ovarian cancer in 1H15

Yale researchers present the latest in vitro and in vivo results at Drug Discovery and Therapy 2014 World Congress

BOSTON (June 17, 2014) – Australian oncology drug development company Novogen Limited [ASX:NRT; NASDAQ:NVGN] and CanTx Inc., its joint venture with Yale University, today announced the success of proof-of-concept pre-clinical studies confirming the potency of experimental drug, Trx-1, in the treatment of primary ovarian cancer when delivered into the peritoneal cavity. Based on the potency seen in animal models to date, and the potential to prevent recurrence, Novogen and CanTx believe that Intra-Peritoneal Trx-1 could be utilized as a first-line therapy for ovarian cancer.

Trx-1 is being developed for the treatment of ovarian cancer, particularly for its ability to kill chemo-resistant ovarian cancer stem cells. Novogen and CanTx plan to file an Investigational New Drug application (IND) with the FDA in early 2015 and to start a Phase 1 study by mid-2015.

The data presented yesterday shows that Trx-1 can significantly retard the growth of highly chemo-resistant, human ovarian cancer stem cells in an animal model considered to be highly representative of the human situation.

Gil Mor, M.D. Ph.D., Professor of Obstetrics, Gynecology and Reproductive Science at Yale School of Medicine presented his group's research on Trx-1 to date at the Drug Discovery and Therapy 2014 World Congress. The conference is taking place in Boston, June 16 to 19, 2014.

"Ovarian cancer is the most lethal of all the gynecologic malignancies. These tumors are made up of two distinct kinds of cells: cancer stem cells that initiate and perpetuate the tumor and which resist all forms of chemotherapy, and their daughter cells that, in most patients, respond initially to chemotherapy. Where there is an initial response to therapy, it is because the chemo-sensitive daughter cells that make up the bulk of the tumor have responded. But the parent cancer stem cells then respond by generating a new generation of daughter cells that now display the same level of chemo-resistance as the parent cells. This is why when ovarian cancer recurs it is so difficult, if not impossible, to treat," Prof. Mor explained. Prof. Mor and his colleagues at Yale have identified and cloned the two main subtypes of ovarian cancer cells representative of ovarian tumor complexity. CD44-/MyD88- epithelial ovarian cancer (EOC) cells represent the bulk of ovarian cancer cells: they are rapidly-dividing, short-lived, and can respond to chemotherapy. CD44+/MyD88+ EOC cells are slow-growing, very long-lived, exhibit tumor-initiating (stem cell-like) properties, and are highly chemotherapy-resistant. These latter cells are the source of tumor recurrence.

Prof. Mor said, "An obvious strategy is to be more successful in treating primary disease, so that we stop the development of recurrent disease. We need to be able to kill the ovarian cancer stem cells before they have the chance to produce a second generation of highly chemo-resistant daughter cells."

The animal model developed at Yale involves injecting human CD44+/MyD88+ (cancer stem) cells into the peritoneal cavity of mice, where they quickly establish highly aggressive multiple tumors comprising both CD44+/MyD88+ cells and recurrent CD44-/MyD88- cells, all highly chemo-resistant. This animal model is representative of the human situation where ovarian cancer generally is confined to the abdomen and the cells are free to spread, leading to multiple tumors often involving dozens or even hundreds of individual tumors. Faced with the challenge of treating such scattered tumor load, the injection of anti-cancer drugs directly into peritoneal cavity is an approach clinicians have long considered.

"This is the first time that we've seen a compound have such a profound effect on tumor growth and tumor burden in this highly aggressive ovarian cancer animal model," Mor added. "The current animal studies were all about proving the concept that an intraperitoneal administration of Trx-1 was capable of reducing tumor burden and carcinomatosis, the main cause of patient mortality. We achieved this objective by preventing the renewal and survival of human ovarian cancer stem cells," Mor added. "This is a first important step in our goal of making progress in the treatment of this insidious disease. We believe that this now provides the platform for delivering a killer blow by combining Trx-1 with conventional chemotherapy as a first-line therapy and successfully removing all the cellular components of the tumor."

"This is an exciting outcome that shows what can come of commercial collaboration between industry and academia," said Graham Kelly, Ph.D., CEO of both Novogen and CanTx. "This result elevates our hopes for Trx-1 beyond the usual recovery of patients with late-stage ovarian cancer, to the exciting prospect of incorporating it into first-line therapy in combination with conventional chemotherapy."

## **About Ovarian Cancer**

The American Cancer Society estimates that over 22,000 women will be diagnosed with ovarian cancer during 2013 and 14,230 American women will die from the disease. It ranks fifth in cancer deaths among women, accounting for more deaths than any other cancer of the female reproductive system. This cancer mainly develops in older women. About half of the women who are diagnosed with ovarian cancer are 63 years or older. It is more common in white women that in African-American women.

### **About Novogen Limited**

Novogen is a public, Australian drug-development company with shares traded on both the Australian Securities Exchange ('NRT') and NASDAQ ('NVGN'). The Company has two main drug technology platforms: super-benzopyrans (SBPs) and anti-tropomyosins (ATMs). SBP compounds have been created to have a uniform cytotoxic effect against both cancer stem cell and are being developed in the first instance for the treatment of ovarian cancer, glioblastoma and prostate cancer. ATM compounds target the cancer cell cytoskeleton and are being developed for the treatment of melanoma and neuroblastoma.

Further information is available on the Company's website, www.novogen.com.

### About CanTx, Inc.

CanTx Inc. is a joint venture between Novogen and Yale University. Novogen owns 85% of CanTx. Novogen has provided a license to CanTx to access the Novogen library of super-benzopyran drugs for the development of an intra-peritoneal treatment of cancers such as ovarian and pancreatic cancers that are limited to the abdominal cavity. CanTx is based in New Haven, CT. Further information is available on the Company's website, <u>www.can-tx.com</u>.

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