



NOVOGEN

ASX: **NRT**
NASDAQ: **NVGN**





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Why invest in Novogen?

- ❑ Two proprietary drug technologies. Both with **blockbuster** potential
- ❑ Targeting significant unmet clinical needs capable of expediting approval via **Breakthrough Therapeutic** status
- ❑ One of only a handful of companies with drugs capable of killing cancer stem cells
- ❑ Unique approach globally in developing the next generation of cytotoxic chemotherapies
- ❑ Broad therapeutic potential across cancer, degenerative disorders, autoimmune disease and regenerative medicine
- ❑ Low-cost operation with virtual business model
- ❑ Experienced management team and Board
- ❑ Low entry cost for significant upside potential

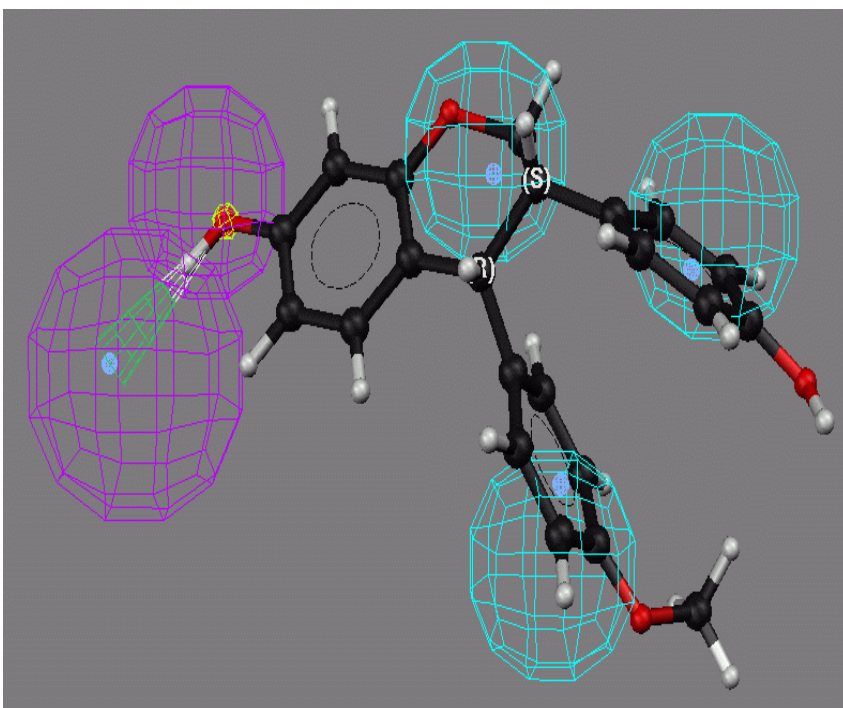
Enabling
cytotoxic chemotherapy
finally to deliver on its promise of
eradicating
most forms of cancer



Vision

To become a major global biotechnology R&D company on the back of two first-in-class drug technology platforms that will provide meaningful survival benefits for most forms of adult and paediatric cancer and which will become standard of care first-line therapies for most forms of cancer based on their abilities to **eradicate the full hierarchy of cells within a cancer.**

Two first-in-class drug technologies

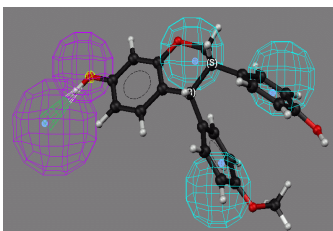


Super-Benzopyrans

Anti-Tropomyosins



Two first-in-class drug technologies



Super-Benzopyrans



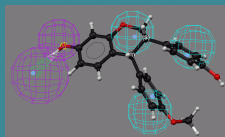
Anti-Tropomyosins

Potent ability to kill cancer stem cells

- ❑ to prevent cancer recurrence
- ❑ potential to become standard of care for first-line therapy across most forms of cancer
- ❑ manageable toxicity

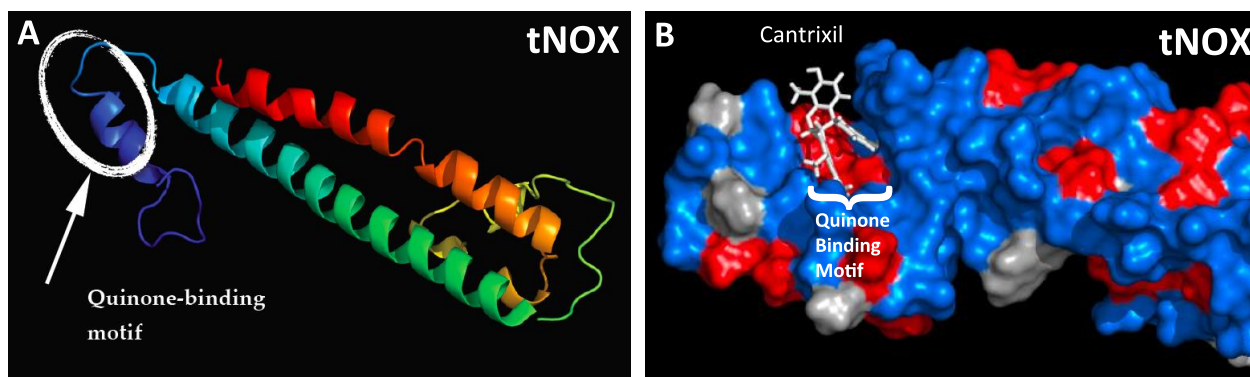
First-in-class drugs targeting the cancer cell's micro-filaments

- ◆ complement the action of the most widely used drugs (taxanes/vinca alkaloids) in oncology
- ◆ potential to become standard of care in combination with taxanes/vinca alkaloids



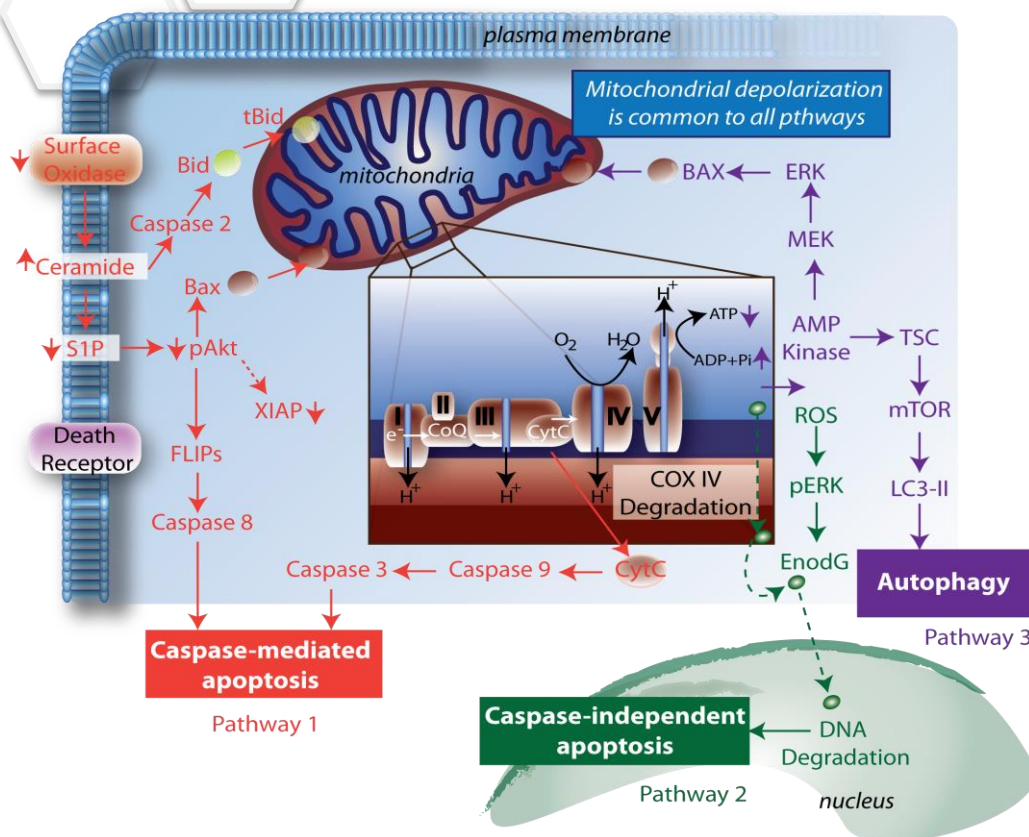
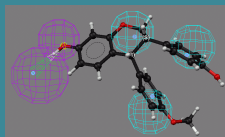
Super-benzopyrans

Molecular target: the heritage of these compounds is plant auxins (simple benzopyrans) With pleiotropic functions embracing both up- and down-regulation of enzyme phosphorylation activity and gene transduction activity in both plants and animals.

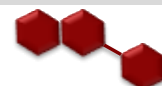


Super-benzopyrans are complex derivatives of the plant auxin, genistein. They retain the central genistein pharmacophore 'privileged scaffold' and therefore the potential for the same multiplicity of functions. The primary anti-cancer function molecular target is believed to be the quinone-binding motif of a splice variant of NADH oxidase known as ENOX2.

Super-benzopyrans



Phenoxodiol



Pathway 1, 2

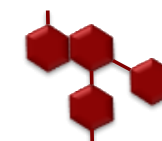
Triphendiol



Pathway 1, 2

Pathway 2, 3

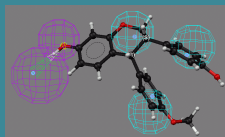
NV-128



Pathway 2, 3

Pathway 3, 4

Structural modifications to the central benzopyran pharmacophore yields compounds activating different cytotoxic pathways involving caspase-mediated and caspase-independent apoptosis and autophagy. Preliminary evidence suggests different ENOX2 isoforms are involved. The above 3 examples are the original simple benzopyran structures now owned by MEI Pharma Inc.



Super-benzopyrans

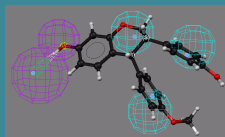
Super-benzopyrans (eg. TRXE-205):

MOA

- Target plasma membrane-bound ENOX2
- Disturbing the plasma membrane sphingomyelin pathway with increased ceramide production
- Pro-apoptotic pathways up-regulated
- Mitochondrial membrane depolarization and fragmentation
- Caspase-mediated apoptosis

BIOLOGY

- *Pan* anti-cancer activity
- Potent cytotoxicity against ovarian and GBM cancer stem-like cells
- Some activity against normal tissue stem cells (skin, bowel, bone marrow) but 100-fold high therapeutic index
- No chemo-sensitizing activity (contrast to 'simple' benzopyrans)



Super-benzopyrans

3 lead candidate drugs

TRXE-002

Equipotent activity across broad range of cancer phenotypes.

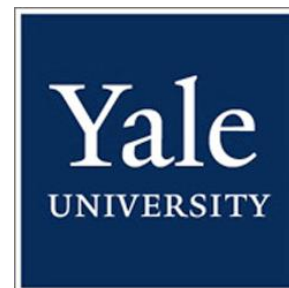
Licensed to **CanTx Inc.** API in **Cantrixil**

TRXE-009

Pan anti-cancer but specifically highly active against cancer cells of neural origin (GBM stem cells, medulloblastoma, DIPG, neuroblastoma)

TRXE-025

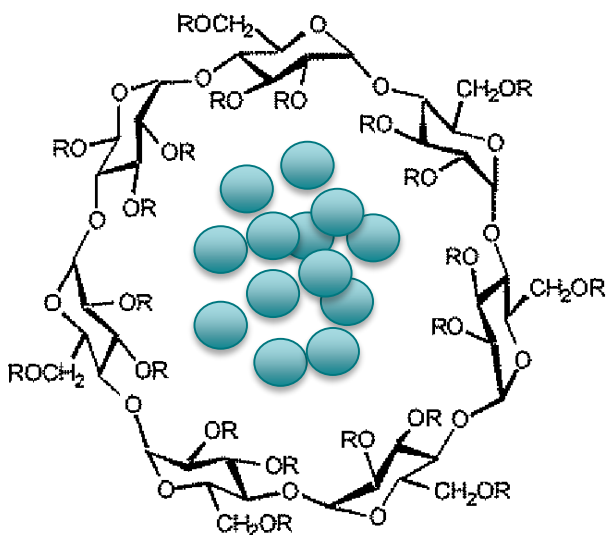
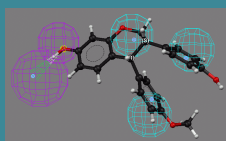
Pan anti-cancer but specifically highly active against prostate cancer cells.



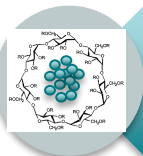
Providing access to
facilities and
expertise

Joint venture Novogen & Yale
85% **15%**

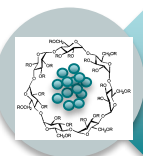
Novogen licence to canTx
TRXE-002 only
for use in Cantrixil only



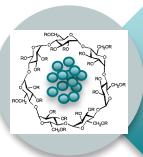
**Construct of
TRXE-002 in
Captisol**



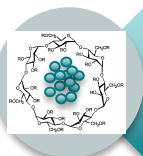
**Designed for installation into
cavities (peritoneal; pleural)**



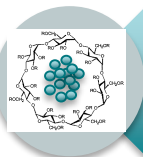
**Captisol dissolves to release
TRXE-002**



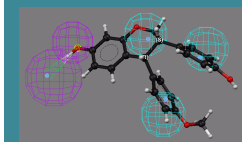
**TRXE-002 kills both cancer stem
cells and somatic cancer cells**



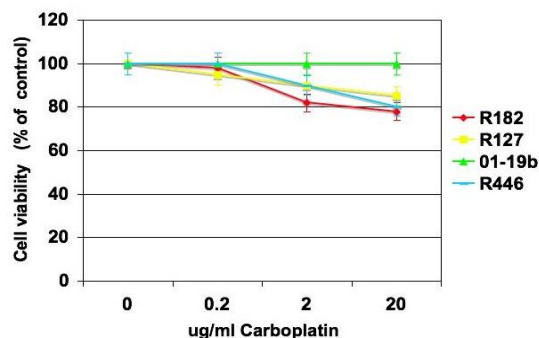
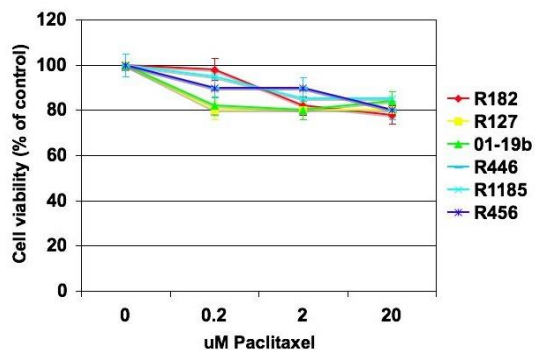
Pan anti-cancer cytotoxic



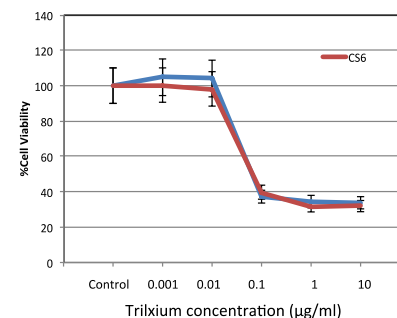
Non-irritant. Low toxicity



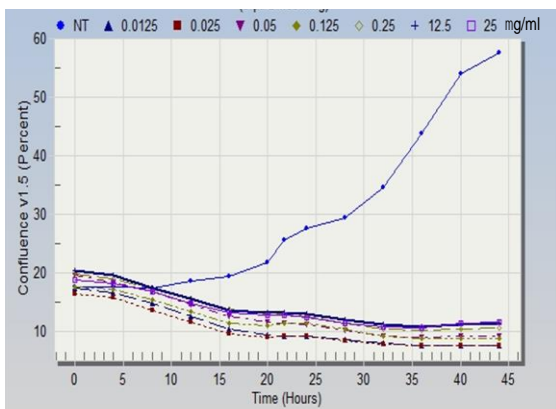
Proof of concept 1: TRXE-002 kills ovarian cancer stem cells that are highly resistant to paclitaxel and carboplatin.



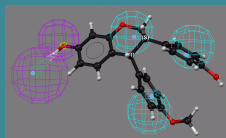
Ovarian cancer stem cells inherently resistant to standard drugs paclitaxel and carboplatin



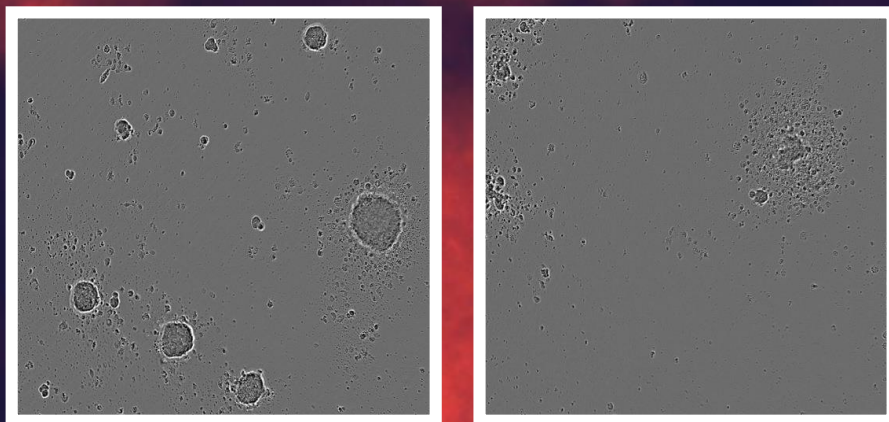
Same cells highly sensitive to TRXE-002



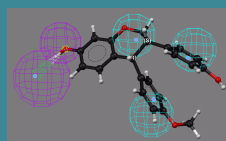
- Killing effect of TRXE-002 on highly chemo-resistant ovarian cancer stem cell line.
- Note complete cytotoxicity at all dose levels plus early response to drugs



Proof of concept 2: Cantrixil construct can destroy 3-dimensional tumor structures comprising ovarian cancer stem cells.



Human ovarian cancer stem cell spheroids comprising tens of thousands of cells (cancer stem cells + somatic cancer cells) completely destroyed by Cantrixil



Proof of concept 3: Cantrixil works as an effective first-line therapy in a highly stringent animal model of human ovarian cancer.



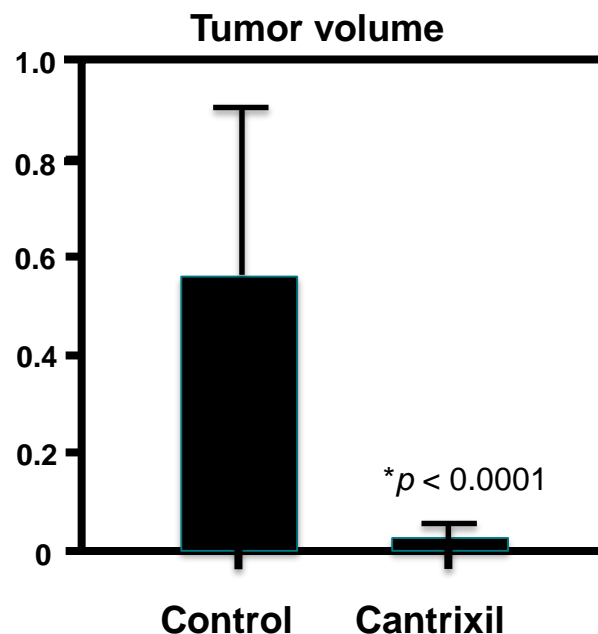
control

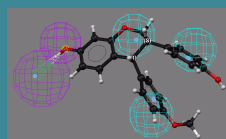


Cantrixil

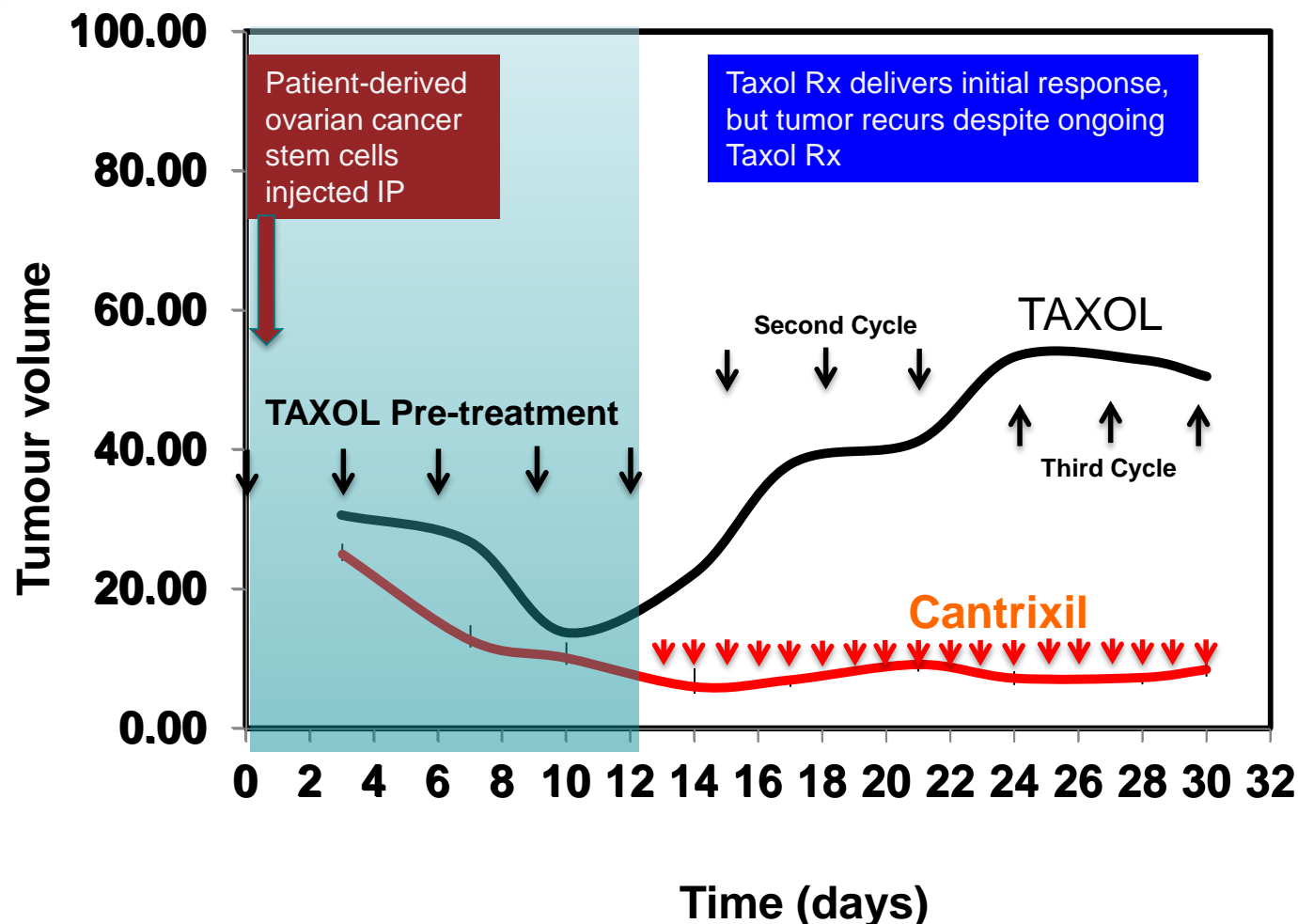


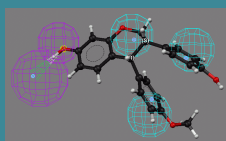
Patient-derived human ovarian cancer (CD44+) stem cells injected into abdomen. Cantrixil Rx commenced once tumors established at Day 4





Proof of concept 4: Cantrixil blocks the development of carcinomatosis in a stringent mouse model of refractory ovarian cancer.





Ovarian cancer indications

Chemo-sensitive disease



First-line therapy

Chemo-resistant disease

&

Recurrent disease



Second-line therapy

(15% of patients failing 1st line)



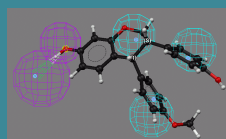
Salvage therapy

(late-stage refractory cancer)



Salvage therapy

(carcinomatosis; malignant ascites)



First-in-man clinical trial

Adaptive Phase 1 design with expanding option

Parallel cohorts of:

- late-stage refractory ovarian cancer
- malignant ascites

4 sites - Australia

Cantrixil 3x-weekly intra-peritoneal injections

Endpoints:

- ◆ Safety
- ◆ Pharmacokinetics
- ◆ Clinical response

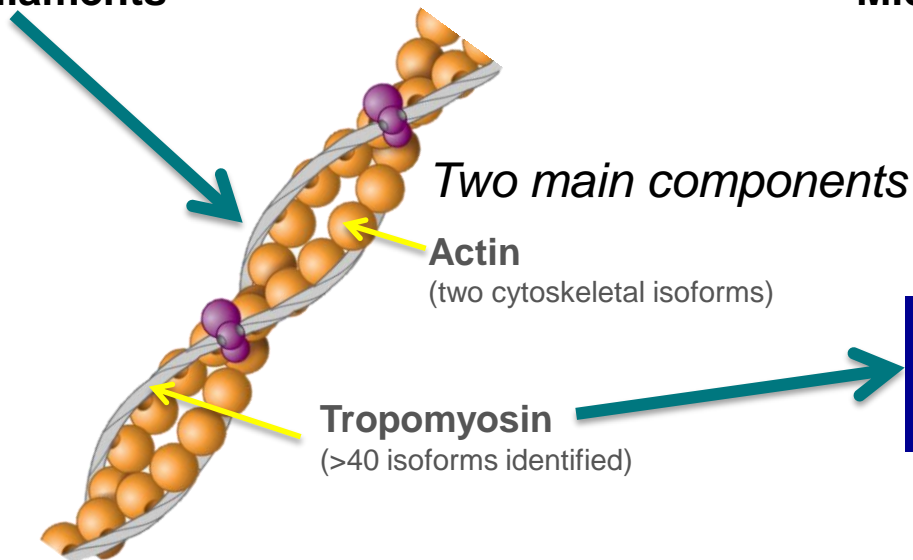
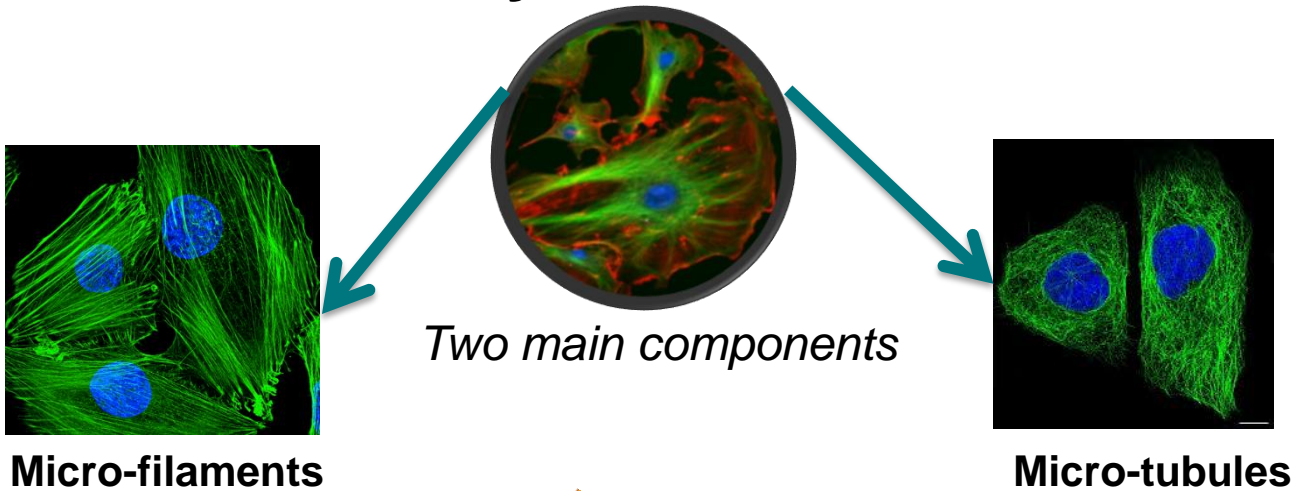
Start: Mid-2015

Finish: 4Q16 (approx.)



ATM program

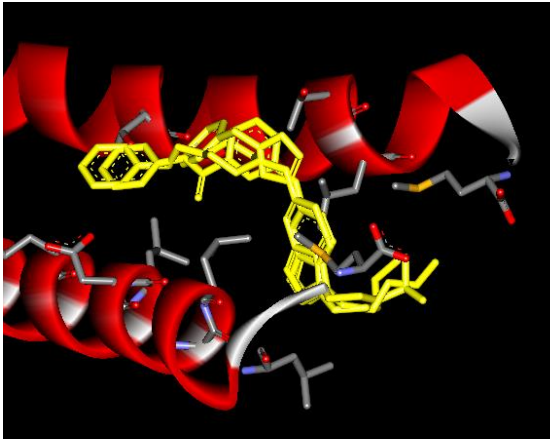
Cytoskeleton



Tm5NM1 tropomyosin isoform essential for survival of cancer cells but not normal cells

ATM program

Lead candidate ATM3507



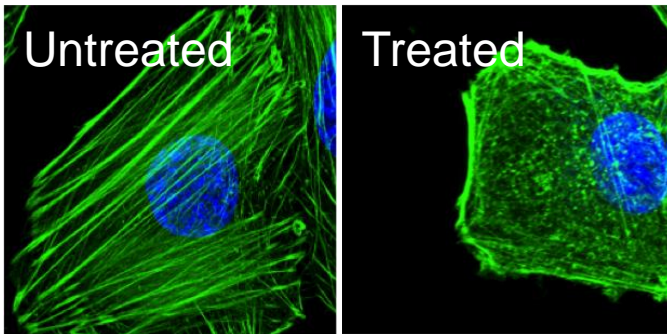
Blocks dimerization of C- and N-terminals
of adjoining Tm5NM1 proteins



Highly on-target destruction of cancer cell
micro-filaments

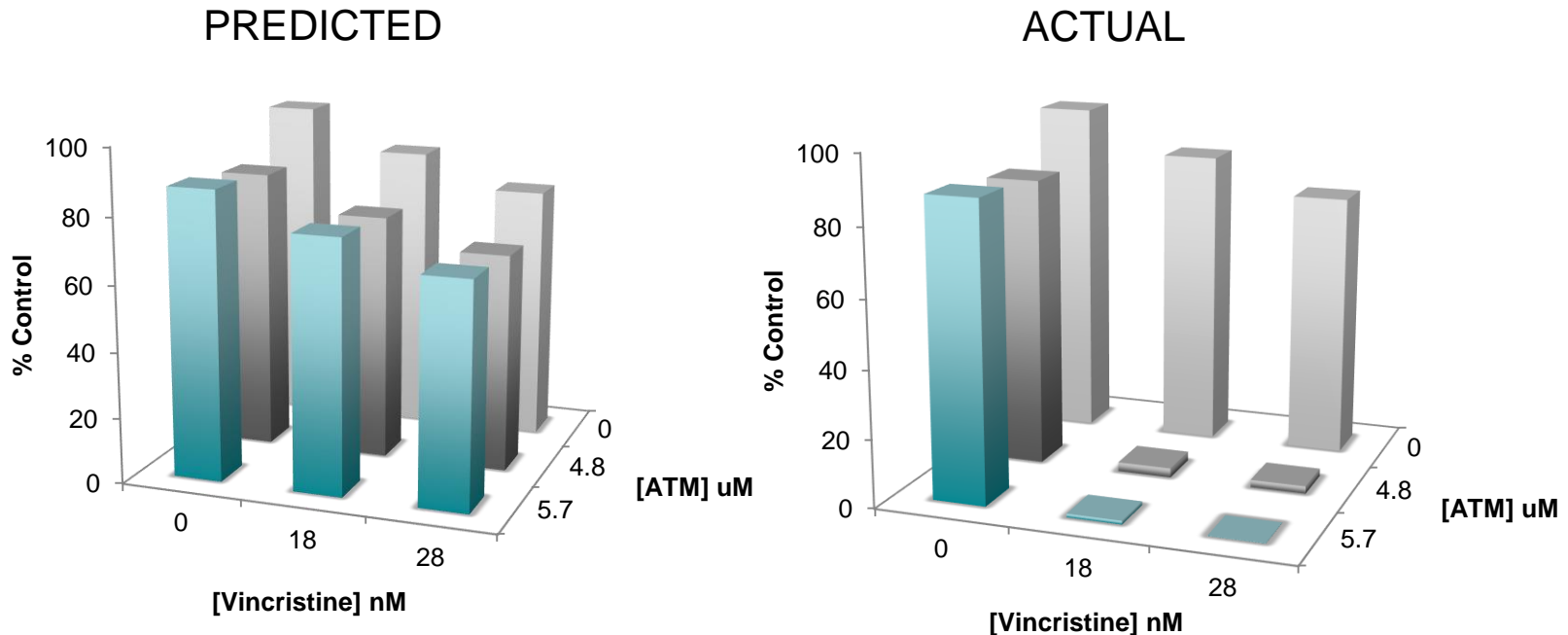


Cell death



ATM program

ATM3507 potently synergizes action of anti-microtubular drugs through comprehensive destruction of the cancer cell cytoskeleton



Dr Timothy Cripe- Nationwide Children's Hospital/ The Kids Cancer Project

- Potent efficacy in human melanoma xenograft when ATM drug and vincristine dosed in combination
- Animals tolerate combined treatment well.

The future of cancer therapy



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