



ASX: NRT  
NASDAQ: NVGN

# Roadshow Presentation

## Sept 2014

# Forward-Looking Statements

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# Company History

- 1994** Australian company founded by G. Kelly; drug discovery based on benzopyran drug structure; listed ASX
- 1998** Listed NASDAQ
- 1998-2008** Develop 4 anti-cancer drugs; 1 (idrinoxil) taken to Phase 3 pivotal study
- 2001** Spin-out Marshall Edwards Inc as focused oncology company; IPO and NASDAQ listing; Novogen to focus on non-oncology drug discovery
- 2006** G. Kelly leaves Novogen and Marshall Edwards
- 2008** Phase 3 trial fails
- 2011** Decision to focus on oncology; all IP transferred to Marshall Edwards (now MEIPharma); Novogen staff retrenched and company prepared as shell
- 2011** Kelly and two ex-Novogen senior scientists leave Novogen and establish private company Triaxial Pharmaceuticals; objective to advance benzopyran drug technology
- 2012** Triaxial achieves breakthrough in development of super-benzopyran structures
- 2012** Novogen acquires Triaxial as reverse takeover
- 2012** Novogen and MEIP demerge



# Novogen

## Goal

**To develop and commercialize a new generation of anti-cancer drugs designed to:**

- Improve the effectiveness of first-line chemotherapy in order to prevent tumor recurrence
- Extend the effectiveness of chemotherapy across most cancer types
- Deliver high on-target activity with minimal unwanted side-effects and no immune-suppression



# Novogen

## Vision

To become a major bio-pharmaceutical company based on two ground-breaking and first-in-class drug technology platforms in the fields of:

**Oncology**

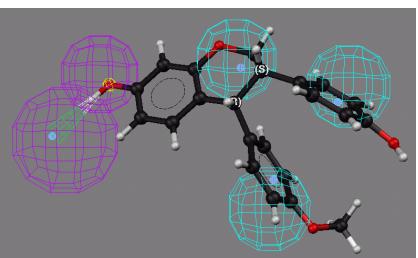
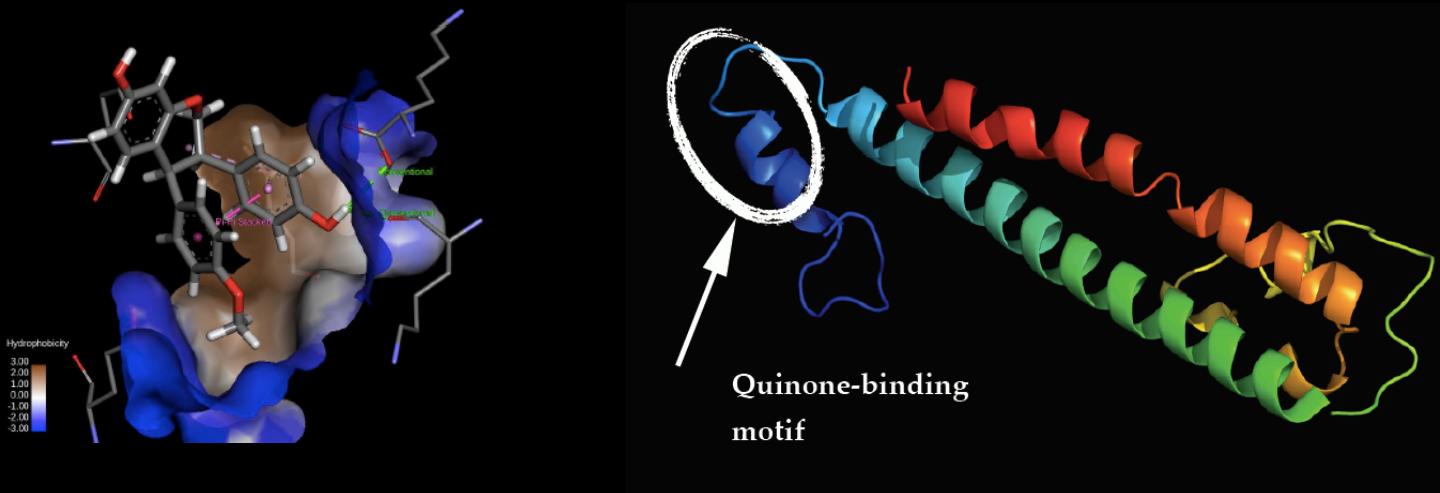
**Degenerative Diseases**

**Regenerative Medicine**

# Two Proprietary Technologies

Super-Benzopyrans	Anti-Tropomyosins
First-in-class molecules with pleiotropic effects	First-in class compounds to disassemble microfilament component of cancer cell cytoskeleton
<b>Primary effect:</b> <b>ONCOLOGY</b> Cytotoxic to both (parent) cancer stem cells and (daughter) somatic cancer cells.  First anti-cancer drugs to kill the full heterogeneity of tumor cell sub-populations	<b>Primary effect:</b> <b>ONCOLOGY</b> Highly synergistic with anti-microtubular drugs producing complete destruction of cancer cell cytoskeleton.
<b>Secondary effect:</b> <b>DEGENERATIVE DISEASES</b> <b>REGENERATIVE MEDICINE</b> Promotion of activity and function of tissue stem cells	<b>Secondary effect:</b> <b>AUTOIMMUNE DISEASES</b> New drug target for diseases associated with abnormal cytoskeleton function

# Super-Benzopyrans Molecular target



Quinone-binding motif of tumor-associated NADH oxidase (tNOX).

tNOX is splice variant of constitutive NADH and is restricted to tumor cells.

Pan-cancer oncogene.

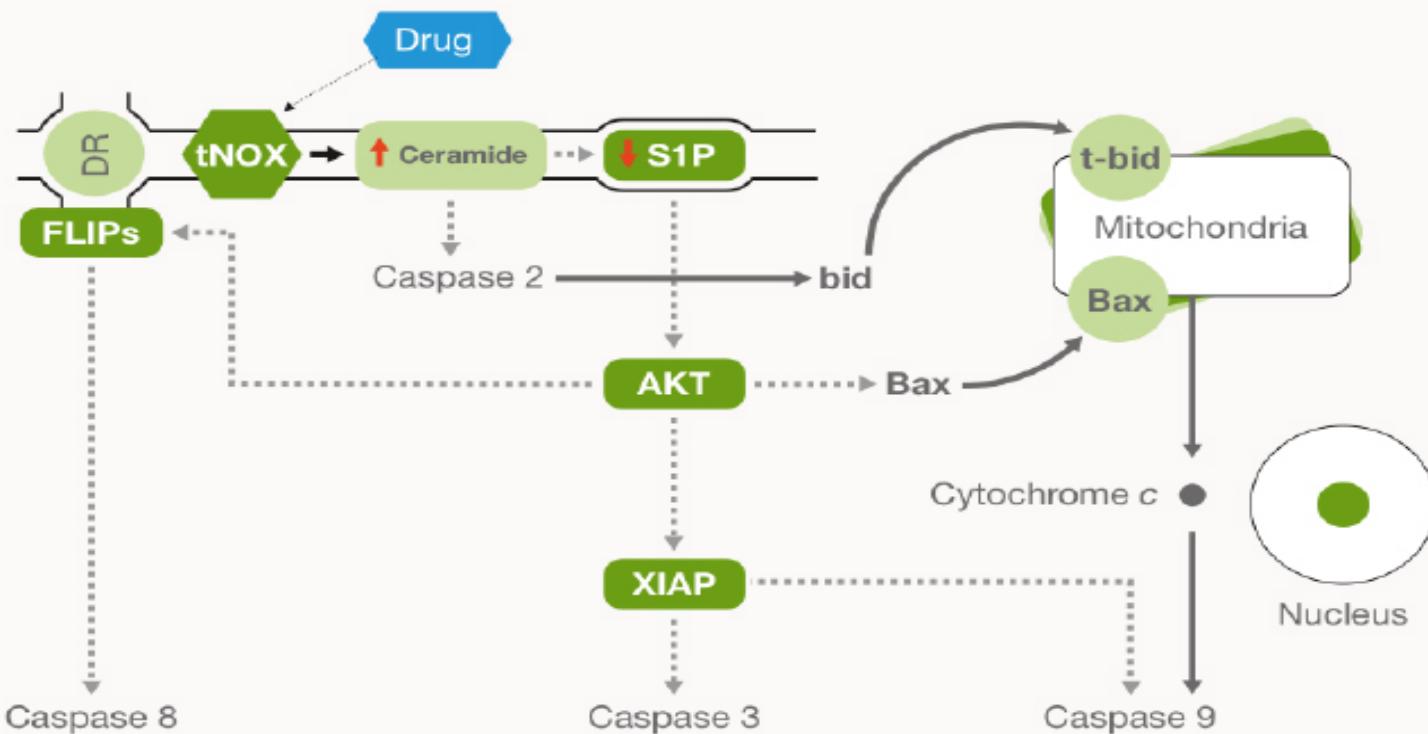
Regulates electron ( $H^+$ ) transfer across cell membranes within cancer cell.

Inhibition leads to disruption of sphingomyelin pathway, depolarisation of mitochondrial membrane and DNA fragmentation.

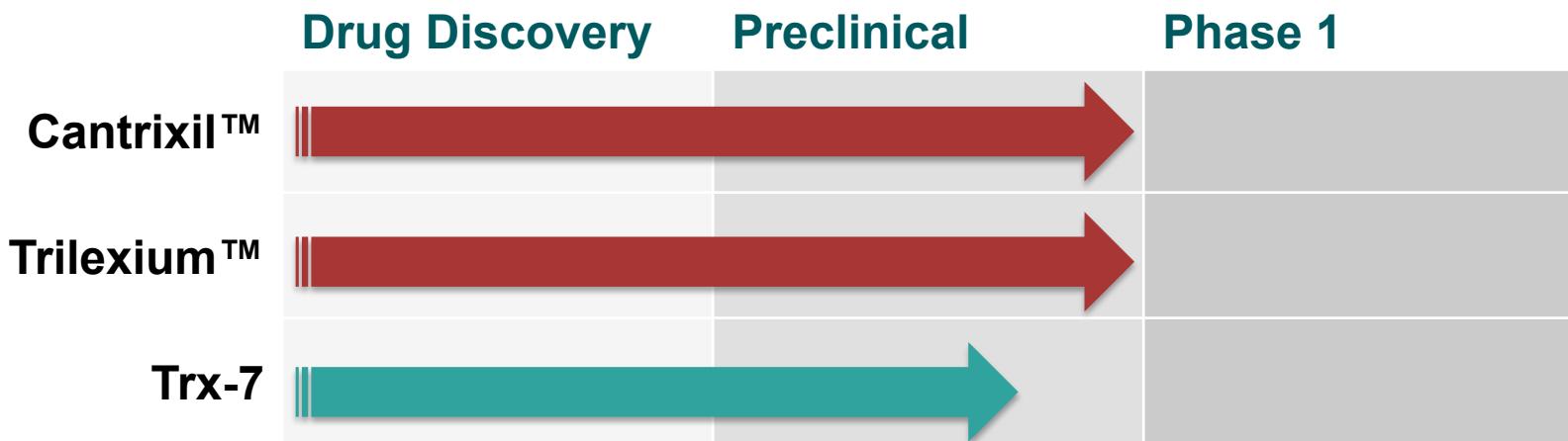
Cell death caspase 2- and 3-dependent.

# Super-Benzopyrans Mechanism of action

## NADH Oxidase (tNOX) Inhibitors Mechanism of Action: Caspase-Mediated Apoptosis



# Super-Benzopyran Oncology Pipeline

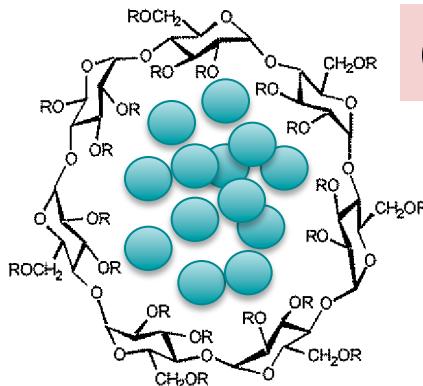


# Cantrixil

 canTx

# Compound Overview

# A new approach to the treatment of intra-abdominal cancers



# **Construct of Trx-E-005-1 in Captisol**

### ***Method of use:***

- intra-peritoneal infusion
  - In combination with cytotoxic chemotherapy

## ***Primary clinical indications:***

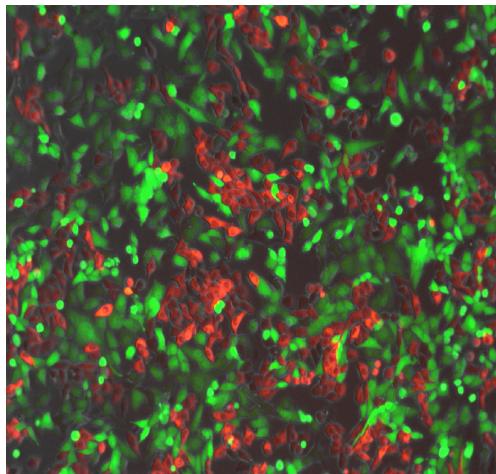
- Ovarian cancer
  - Malignant ascites associated with colo-rectal cancers

## **Rationale:**

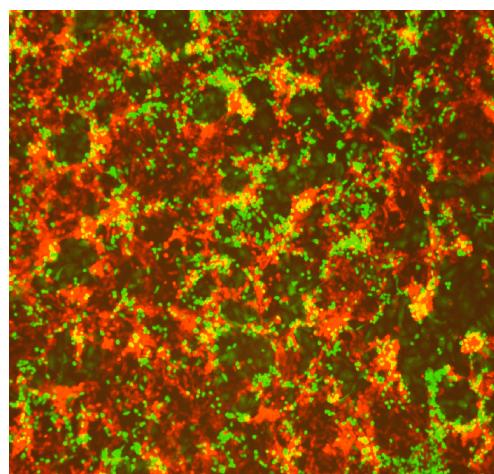
- to destroy **the full hierarchy** of cells within tumors
  - to destroy the cancer stem cells, to prevent tumor recurrence

# Cantrixil

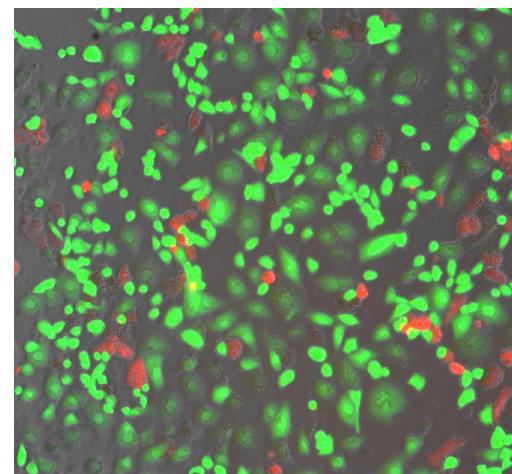
*in vitro* images show significant unmet need for therapy that kills both stem cells and daughter cells within ovarian cancer tumors



Ovarian cancer tumors are composed of slow-dividing cancer stem cells (**CD44+**) and fast-dividing daughter cells (**CD44-**)



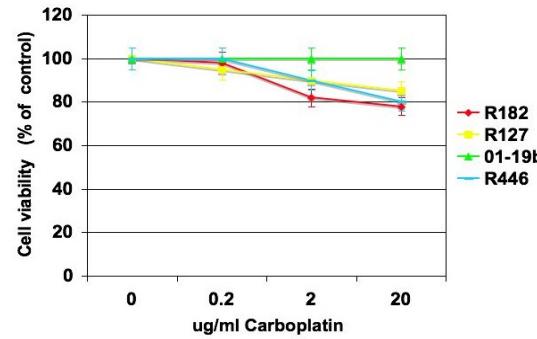
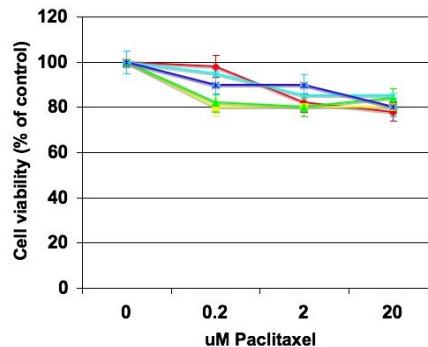
**72-hour culture untreated**  
**CD44-** cells dominate due to rapid cell division



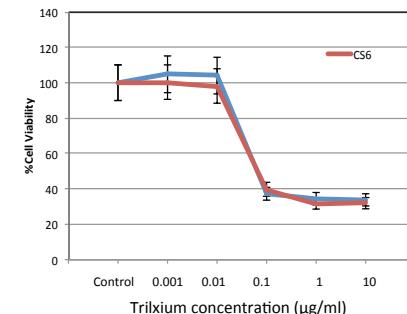
**72-hour culture treated with paclitaxel**  
**CD44-** cells killed  
**CD44+** cells unaffected

# Cantrixil

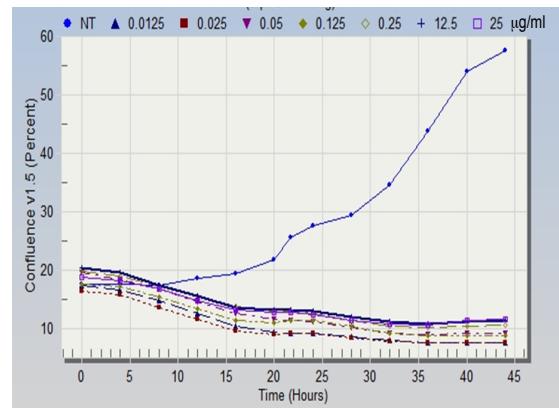
Kills ovarian cancer cells refractory to taxanes and platinums



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



*Same cells highly sensitive to TRX-E-005-1*

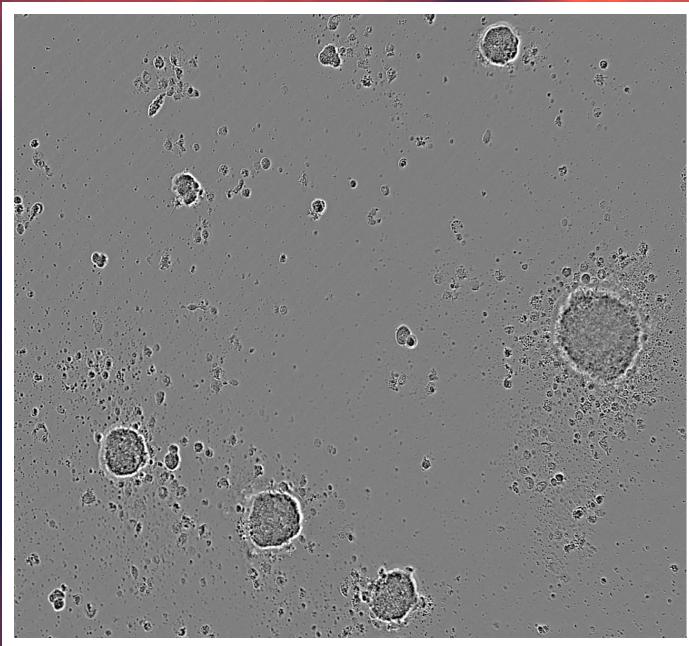


- Killing effect of TRX-E-005-1 on highly-resistant ovarian cancer stem cell line.
- Note complete cytotoxicity at all dose levels plus early response to drugs

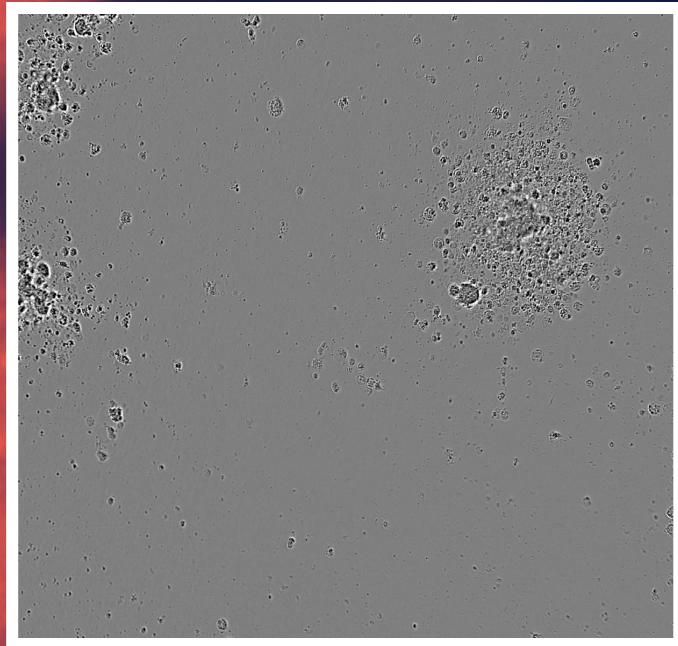
# Cantrixil

*in vitro* results

Control



Cantrixil



CD44+ ovarian cancer stem cell spheroids

# Cantrixil

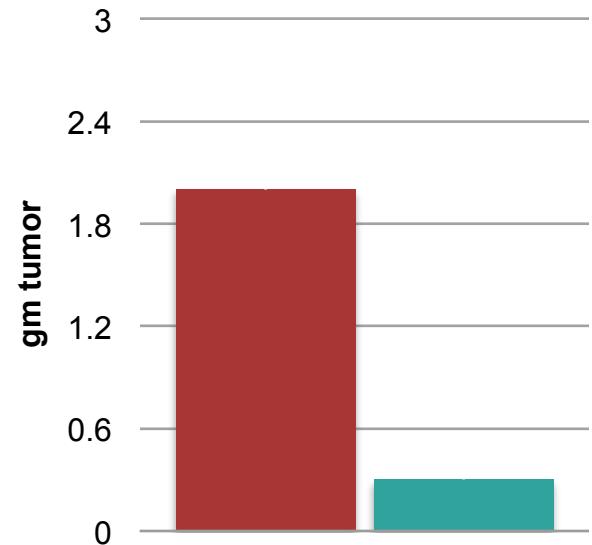
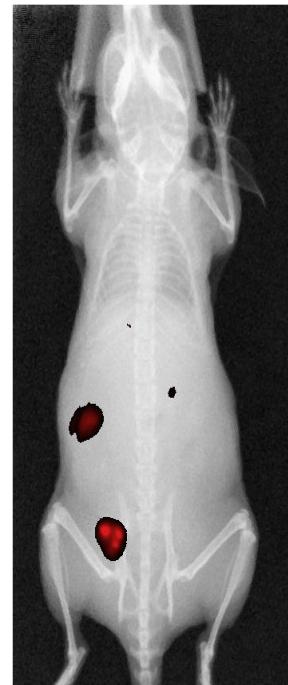
## *in vivo* results

Inhibits carcinomatosis in mice following IP injection of ovarian cancer stem cell spheroids

Control



Cantrixil



**IND lodgement Date:** **2Q 2015**

**Est. Study Start Date:** **3Q 2015**

**Disease:** Late-stage, refractory ovarian cancer

**Study Location(s):** Yale-New Haven Cancer Center  
Smilow Cancer Hospital at Yale-New Haven

**Study Design:** Monotherapy; IP infusion; continuous daily Rx

**Endpoint:** Disease progression

### A new approach to the treatment of neural cancers

#### Trx-E-009-1

##### **Method of use:**

- Gastro-intestinal administration (proprietary formulation)
- In combination with standard cytotoxic chemotherapy

##### **Targets:**

- Neural cancers
  - GBM
  - Astrocytoma
  - Medulloblastoma
  - Neuroblastoma
- Various solid cancers

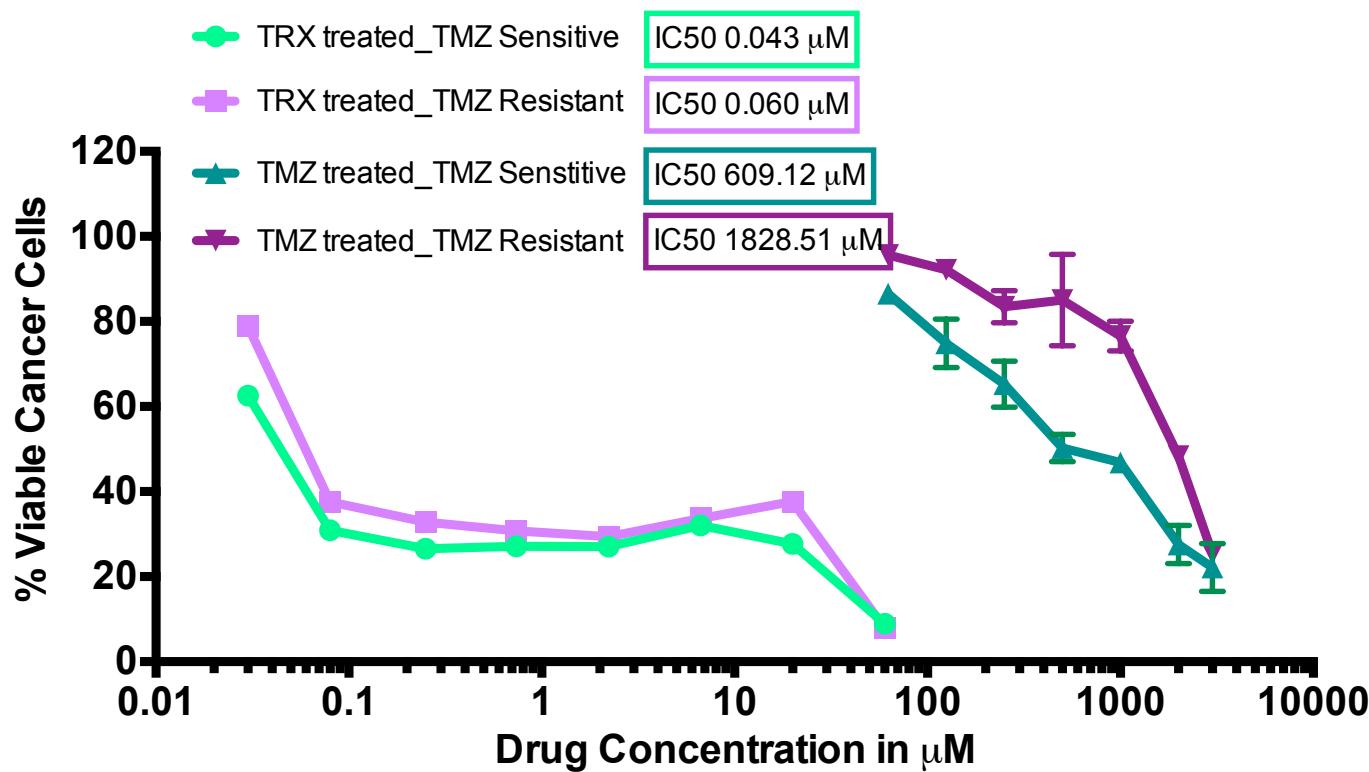
##### **Rationale:**

- To destroy the full hierarchy of cells within primary neural (brain and peripheral) cancers
- Destroy cancer stem cells, to prevent tumor recurrence

# Trilexium

## *in vitro* results

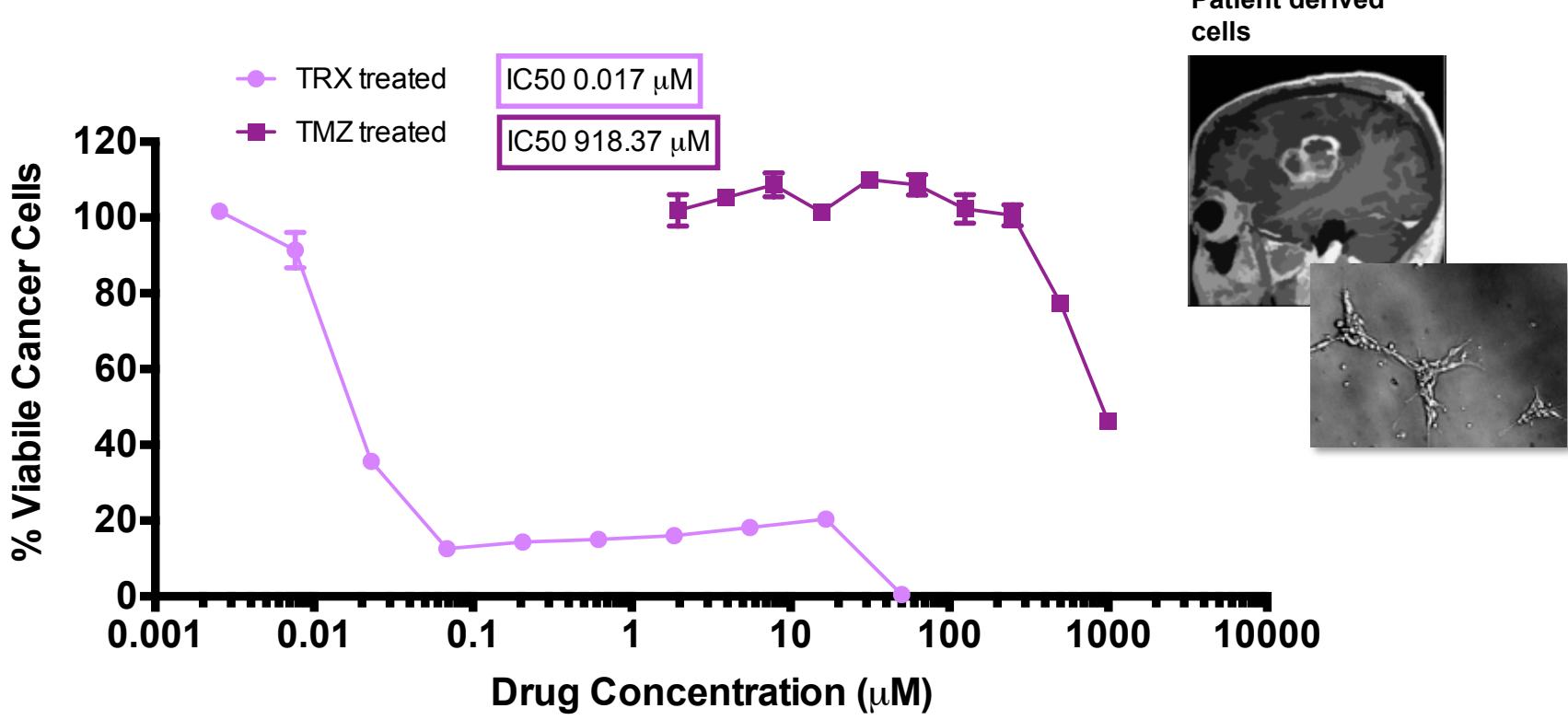
**Trilexium (TRX) kills GBM cells at drug concentrations much lower than those achieved by Temozolomide (TMZ)**



# Trilexium

## *in vitro* results

**Trilexium (TRX) kills GBM explant-derived cells from patients who failed to respond to TMZ**



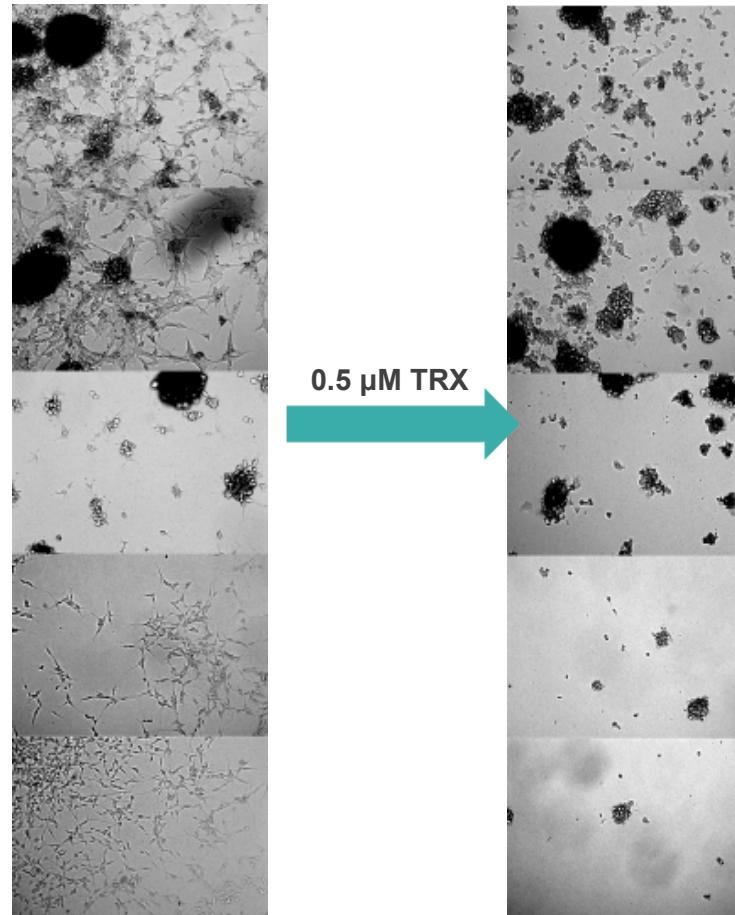
# Trilexium

## *in vitro* results

Trilexium kills GBM stem-like cells

GBM explants grown in culture conditions designed to promote stem cell-like characteristics

Courtesy of  
**Dr. Moonsoo Jin**  
Weill Cornell Medical School  
(unpublished)



# Trilexium

## Clinical Development Plans

**IRB Submission Date:** **1Q2015**

**Est. Study Start Date:** **2Q2015**

**Disease:** Safety/MTD-finding study in patients with late-stage solid tumors (post-TMZ GBM preferentially)

**Study Location(s):** 2 Australian sites

**Study Design:** Monotherapy; daily for 3 weeks of 4 week treatment course

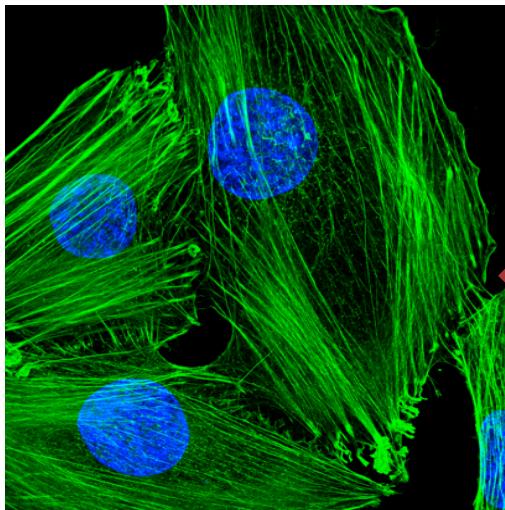
**Endpoint:** Disease progression

# ATM Platform

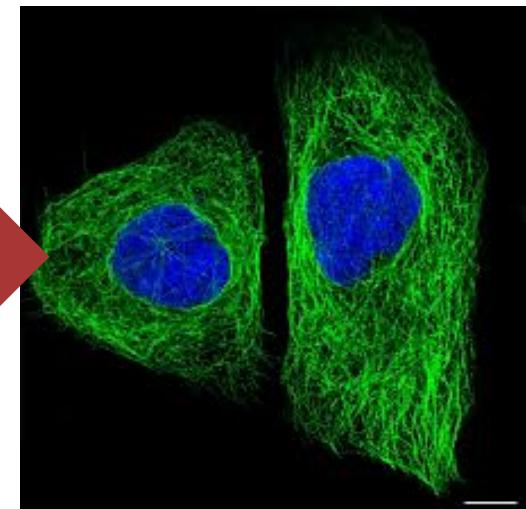
## Platform overview

Providing the first opportunity to comprehensively destroy the cancer cell's cytoskeleton

Microfilaments



Microtubules



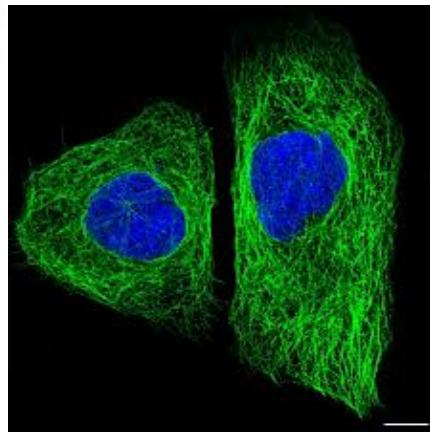
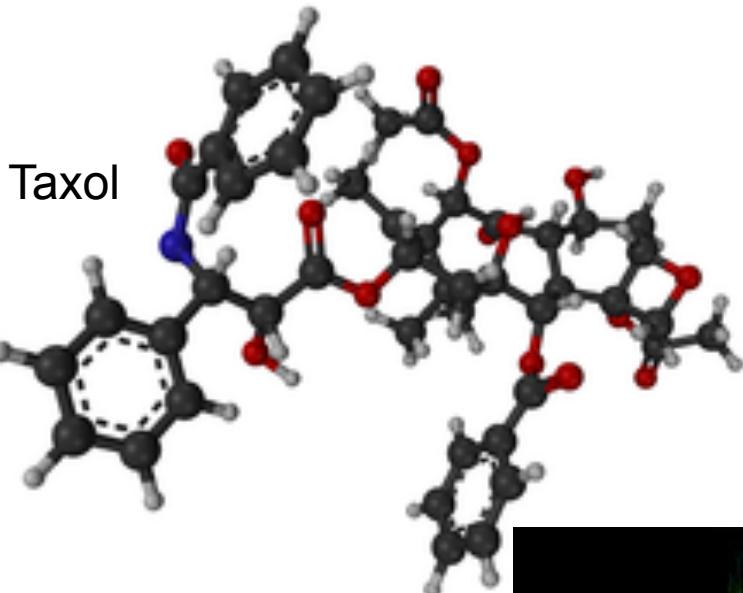
Cytoskeleton

NOVEL DRUG TARGET

ACCEPTED DRUG TARGET

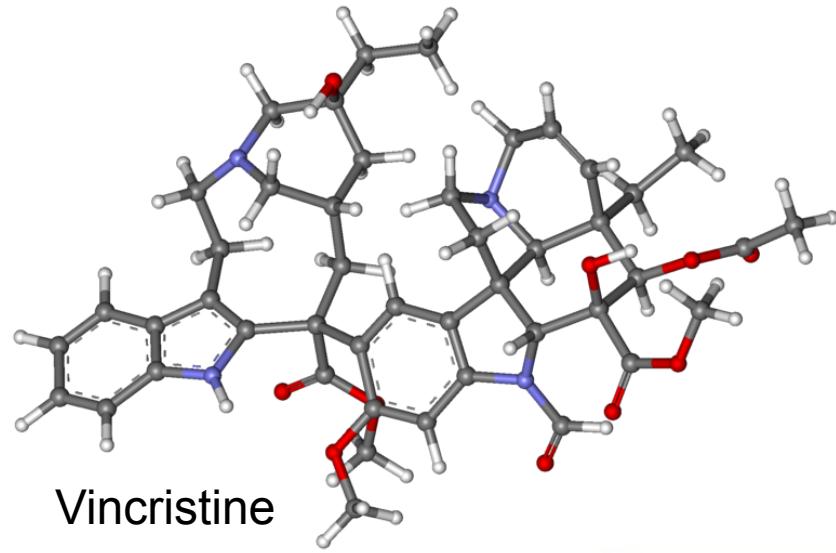
# ATM Platform

## Proven Efficacy of Targeting the Cytoskeleton



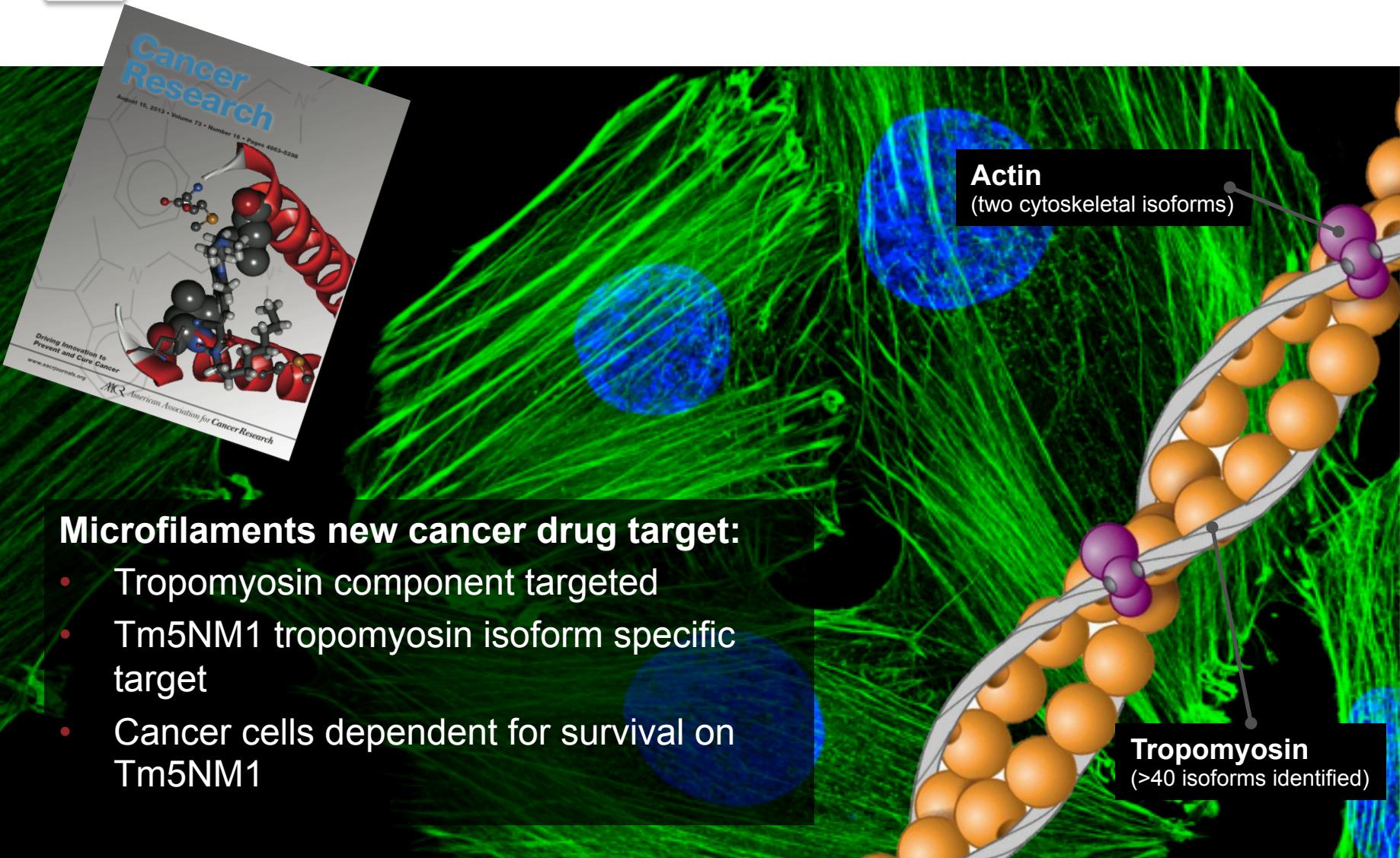
**Anti-microtubule cancer drugs** are a drug development success story despite:

- **Limited sensitivity of cancer phenotypes**
- Rapid development of drug-resistance
- **Significant toxicity**



# ATM Platform

Destroying the microfilaments by selectively targeting the  
**Tm5NM1 tropomyosin isoform**

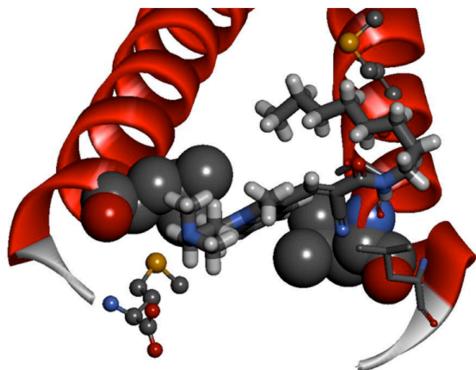


# ATM Platform

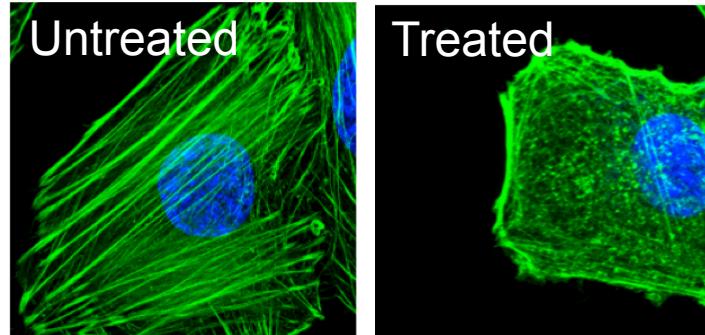
## Blocking Tm5NM1 kills cancer cells

### ATM compounds:

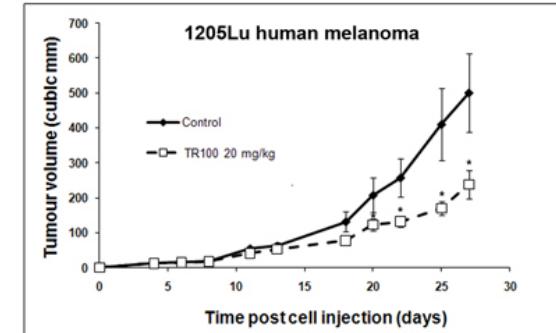
i) Bind to the C-terminus  
of Tm5NM1



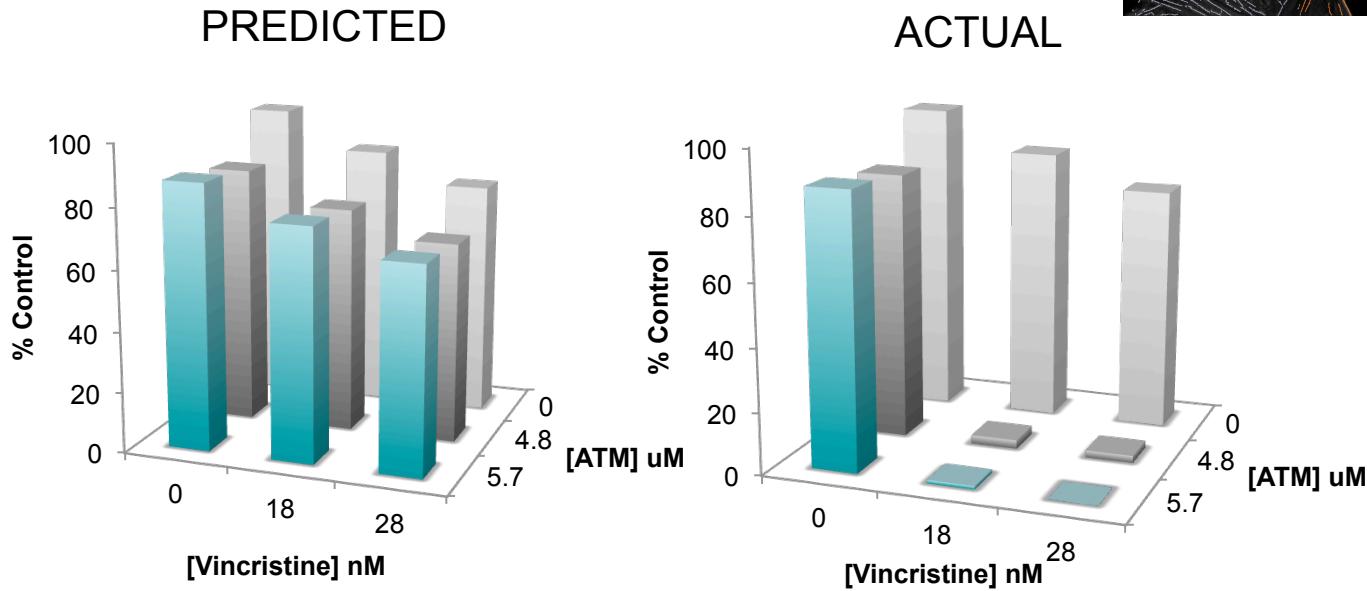
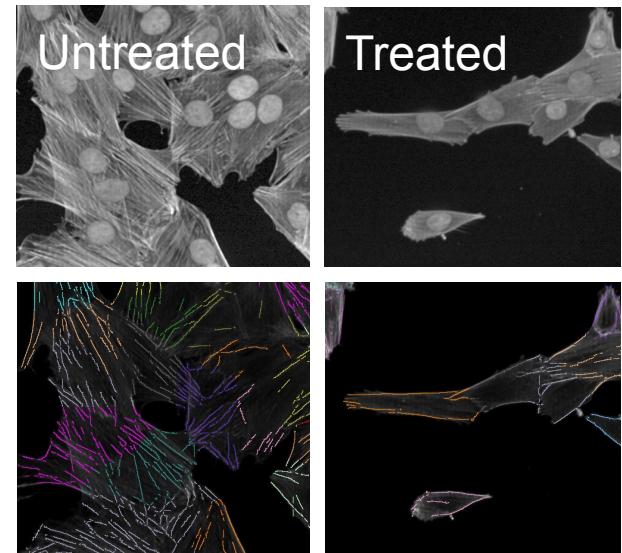
ii) Impact Tm5NM1  
Organization and function



iii) Reduce tumor cell growth



# Targeting the “whole” cytoskeleton. A new paradigm in cancer therapy



- ATMs act **synergistically** in combination with the microtubule targeting compound vincristine.
- Combination well tolerated in animal studies suggesting no increased off-target toxicity

# ATM Platform

## Clinical Strategy

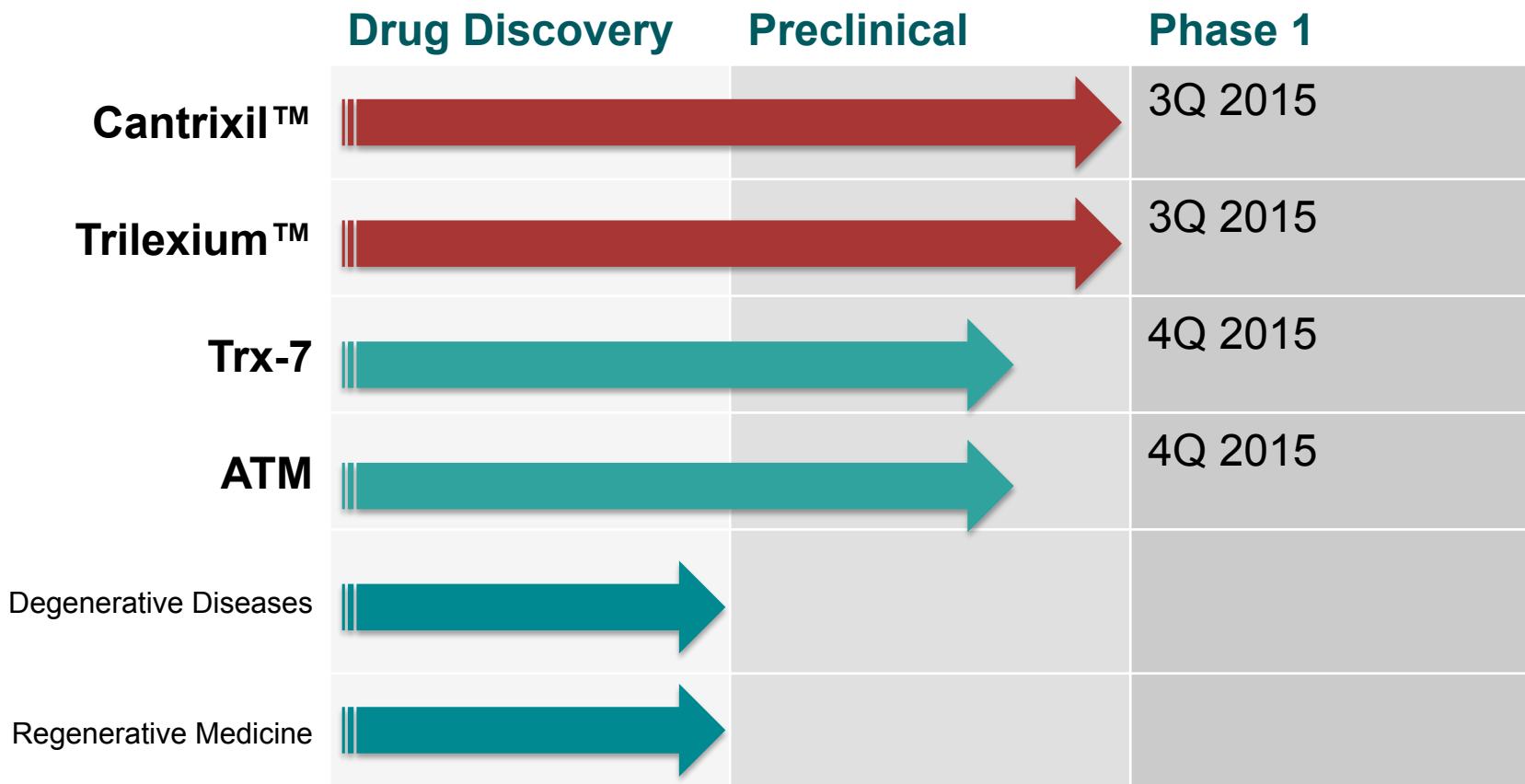
### Clinical targets:

- Prostate cancer
- Melanoma
- Neuroblastoma

### Proposed method of use:

- Oral dosing
- Combination with vincristine to deliver comprehensive destruction of the cancer cell cytoskeleton without exacerbation of toxicity

# Value drivers





# Value Proposition

**Two first-in-class drug technologies**

**One technology offering first drugs to kill cancer stem cells AND their daughter cells in order to prevent cancer relapse**

**Second technology hitting entirely new cancer cell target**

**Two first-in-man trials within 12 months; 4x within 18 months**

**Proprietary IP**

**Lean, low-cost operation**

**Experienced CEO and senior executive team**

**READY TO GO**



ASX: NRT  
NASDAQ: NVGN

# Roadshow Presentation

## Sept 2014