

ASX:NRT  
NASDAQ:NVGN

Novogen Ltd  
(Company)

ABN 37 063 259 754

### Capital Structure

Ordinary Shares on  
issue:

483 M

### Board of Directors

**Mr John O'Connor**  
Chairman  
Non-Executive Director

**Mr Bryce Carmine**  
Deputy Chairman  
Non-Executive Director

**Dr James Garner**  
Chief Executive Officer  
Managing Director

**Mr Ian Phillips MNZM**  
Non-Executive Director

**Mr Iain Ross**  
Non-Executive Director

**Mr Steven Coffey**  
Non-Executive Director

### MARKET RELEASE

10 January 2017

#### NOVOGEN PRESENTS AT BIOTECH SHOWCASE CONFERENCE

Sydney, 10th January 2017 – Australian oncology-focused biotechnology company Novogen Ltd (ASX: NRT; NASDAQ: NVGN) is pleased to release the presentation that CEO, Dr James Garner presented at the Biotech Showcase Conference being held in San Francisco.

[ENDS]

Media and Investor Relations	Investor Relations (US)
Glen Zurcher E: <a href="mailto:glen.zurcher@irdepartment.com.au">glen.zurcher@irdepartment.com.au</a> T: +61 420 249 299	Robert Kennedy E: <a href="mailto:robert.kennedy@novogen.com">robert.kennedy@novogen.com</a> T: +1 212 519 9832 / +1 646 662 3574

### About Novogen Limited

Novogen Limited (ASX: NRT; NASDAQ: NVGN) is an emerging oncology-focused biotechnology company, based in Sydney, Australia. Novogen has a portfolio of four development candidates, diversified across three distinct technologies, with the potential to yield first-in-class and best-in-class agents across a range of oncology indications.

The lead program is GDC-0084, a small molecule inhibitor of the PI3K / AKT / mTOR pathway, which is being developed to treat glioblastoma multiforme. Licensed from Genentech in late 2016, GDC-0084 is anticipated to enter phase II clinical trials in 2017. Three further molecules have been developed in-house from two proprietary drug discovery platforms (superbenzopyrans and anti-tropomyosins) to treat ovarian cancer and a range of solid tumours. Cantrixil, the most advanced of these, commenced a first-in-human clinical study in patients with ovarian cancer in late 2016, while Anisina and Trilexium are in preclinical development.

For more information, please visit: [www.novogen.com](http://www.novogen.com)

# Novogen Limited

Presentation to 9<sup>th</sup> Annual Biotech Showcase Conference

Dr James Garner  
Chief Executive Officer  
[james.garner@novogen.com](mailto:james.garner@novogen.com)

San Francisco, CA  
9 January 2017

# Forward-Looking Statements

This presentation contains “forward-looking statements” within the meaning of the “safe-harbor” provisions of the Private Securities Litigation Reform Act of 1995. Such statements involve known and unknown risks, uncertainties and other factors that could cause the actual results of the Company to differ materially from the results expressed or implied by such statements, including changes from anticipated levels of customer acceptance of existing and new products and services and other factors. Accordingly, although the Company believes that the expectations reflected in such forward-looking statements are reasonable, there can be no assurance that such expectations will prove to be correct. The Company has no obligation to sales, future international, national or regional economic and competitive conditions, changes in relationships with customers, access to capital, difficulties in developing and marketing new products and services, marketing existing products and services update the forward-looking information contained in this presentation.

# Novogen is a biotech company dedicated to driving sustainable, long-term growth in shareholder value

## Focus on unmet medical need

Robust pipeline of novel therapies, targeting oncology patients poorly served by existing treatment options

## Financially sound

Listed on ASX and NASDAQ, with cash runway for continuing operations

## Clinical stage

Two clinical stage programs: GDC-0084 and Cantrixil, with rich flow of milestones over next 12-18 months

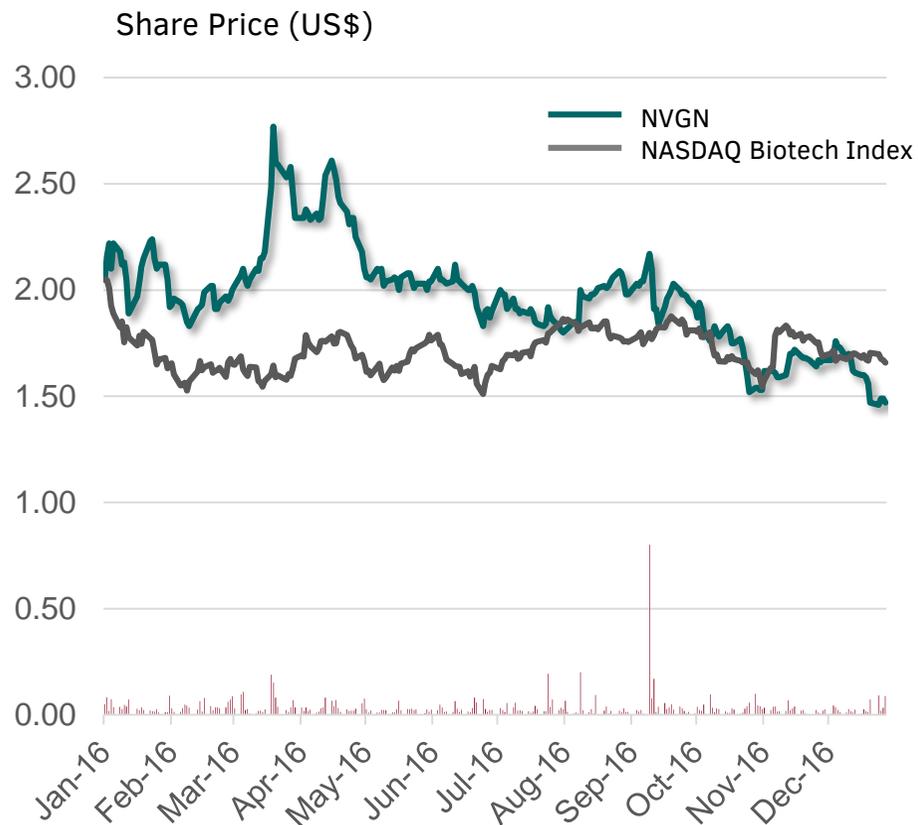
## Strong management and Board

Lean team of internationally-experienced pharma executives, overseen by seasoned Board

# 2016 has been a transformative year for Novogen



# Novogen is listed on ASX and NASDAQ, and is well-funded



**Cash at Bank\***  
 US\$ 25 million

**Debt**  
 Nil

**Market Capitalisation**

US\$ 33 million

**Listing**

ASX: NRT  
 NASDAQ: NVGN (1:25 ratio)

**Average Daily Volume**

ASX: ~570,000 /day  
 NASDAQ: ~50,000 /day

**Shares on Issue**

483 million  
 (35% US, 65% Australia)

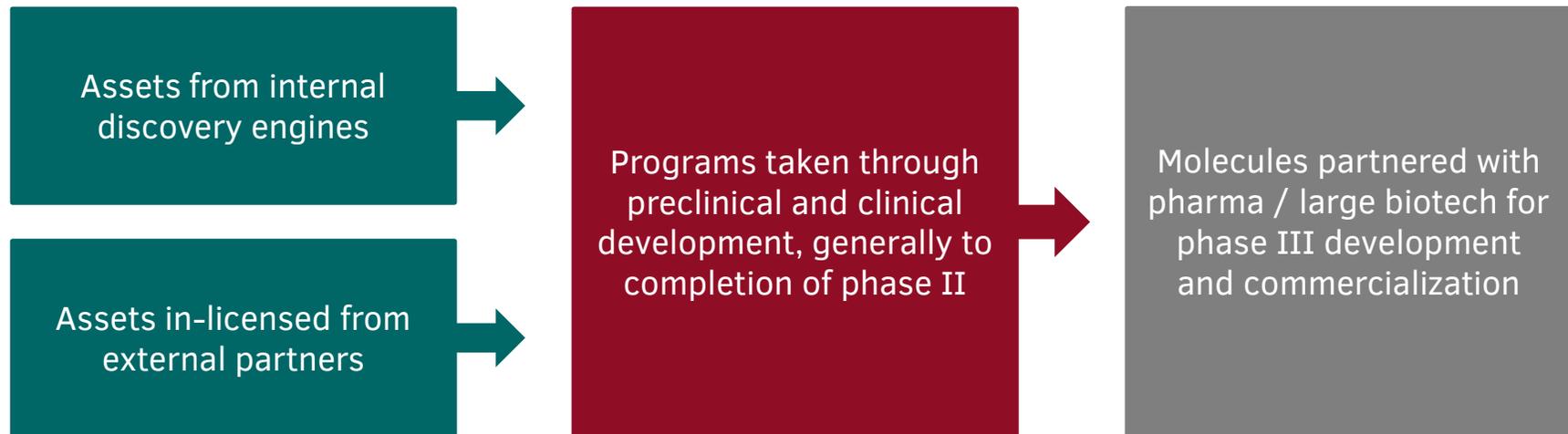
**Outstanding  
 Options / Warrants**

~60 million

\* Last reported as at 30 June 2016.

GDC-0084 was in-licensed on 31 October comprising upfront cash payments of US\$ 5 m combined with the acquisition of a neuro-oncology company for AU\$ 600,000

# Novogen has focused on oncology, with a clear strategy for building and managing a high-value portfolio



# Novogen has built a strong management team with international experience in big pharma



**Dr James Garner**  
Chief Executive Officer & Managing Director

*Physician / MBA; Extensive pharma drug development experience*



**Dr David Brown**  
Chief Scientific Officer

*Twenty years of drug discovery and development experience*



**Dr Gordon Hirsch**  
Chief Medical Officer

*Physician / MBA; Twenty years of pharmaceutical industry experience*



**Dr Peng Leong**  
Chief Business Officer

*Eighteen years of business development and investment banking experience*



**Dr Andrew Heaton**  
VP, Drug Discovery

*Twenty years of medicinal chemistry experience*



**Cristyn Humphreys**  
Chief Financial Officer

*Chartered accountant with twenty years of experience in corporate roles*

# Our newly-appointed Scientific Advisory Board brings global expertise and experience to Novogen

**Professor Sir  
Murray Brennan**



**Dr Karen  
Ferrante**



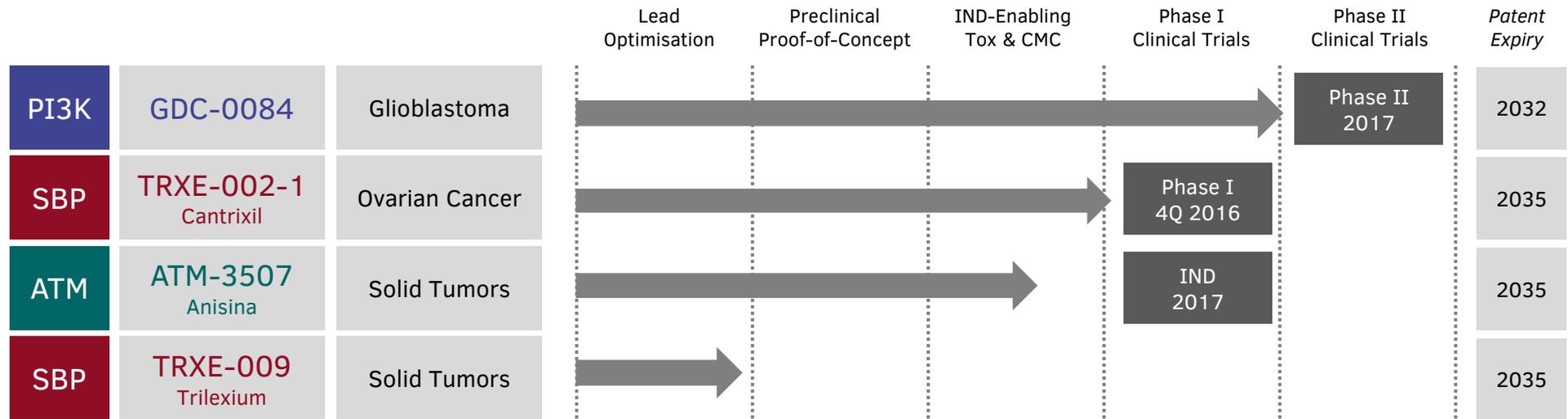
**Professor  
Peter Gunning**



**Professor  
Alex Matter**



# Novogen now has a well-diversified portfolio of assets, stretching from preclinical to mid-stage clinical

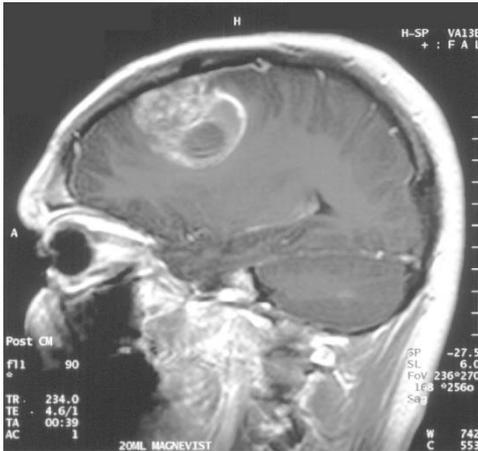


PI3K Technology	Brain-penetrant PI3K inhibitor with some mTOR activity, targeting PI3K / Akt / mTOR pathway, which is shown to be upregulated in majority of GBM cases and many other tumor types
ATM Technology	First-in-class program targeting cancer-specific tropomyosin isoform in cytoskeletal microfilaments of cancer cells, leading to apoptosis
SBP Technology	First-in-class program based on earlier clinically-validated isoflavone chemotype (e.g. phenoxidiol, MEI Pharma), but with distinct IP space and greater preclinical activity

# Glioblastoma Multiforme (GBM) is the most common form of primary brain cancer

## Presentation

- Usually presents with non-specific symptoms (e.g. headaches, nausea)
- Rapid clinical progression to permanent neurological defect and coma



Source: GLOBOCAN 2012

## Epidemiology

- Approximately 12,500 incident cases per annum in United States
- Limited understanding of causes and risk factors
- Generally more common in people >50 years of age, and slightly more common in males

## Prognosis

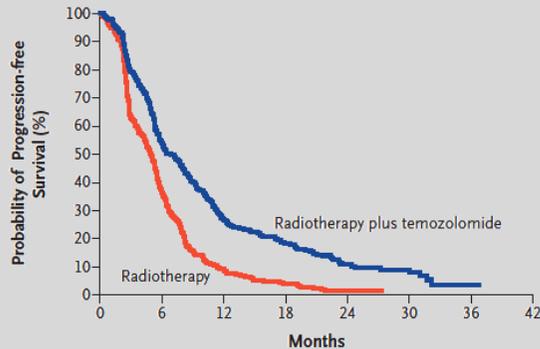
- Median survival following diagnosis = 12-15 months with best available treatment (~3 months without treatment)
- 5-year survival rate = 3-5%
- Limited improvement in prognosis over last 15-20 years

# Current GBM standard of care is ineffective in ~65% of patients

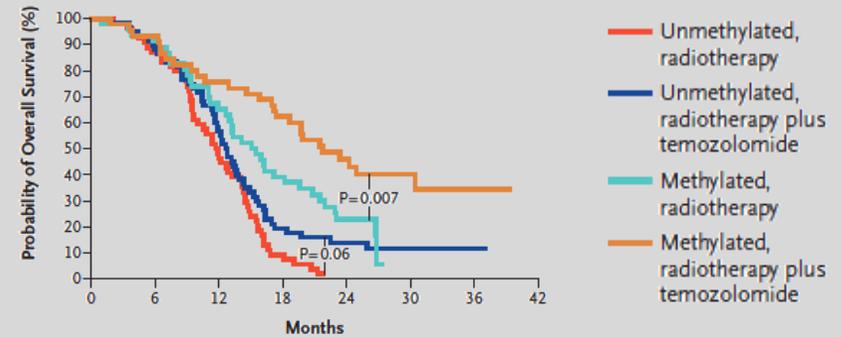
Standard of Care ('Stupp Regimen')



Temozolomide is clearly efficacious...



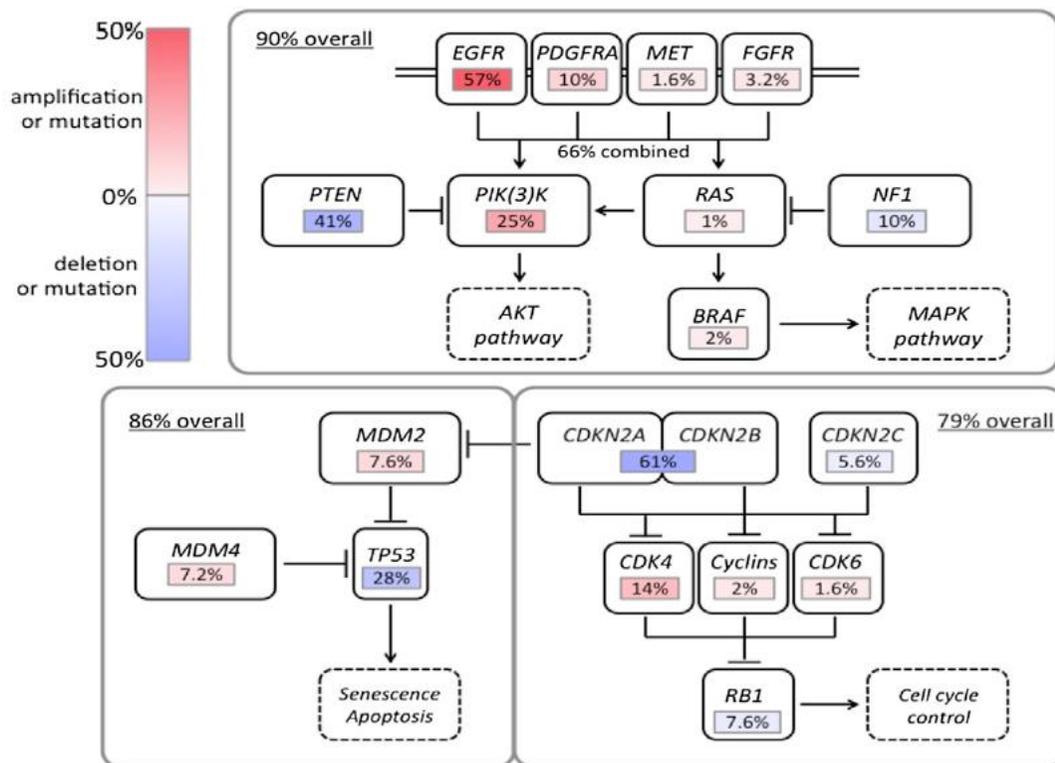
...but only in ~35% of patients who are sensitive



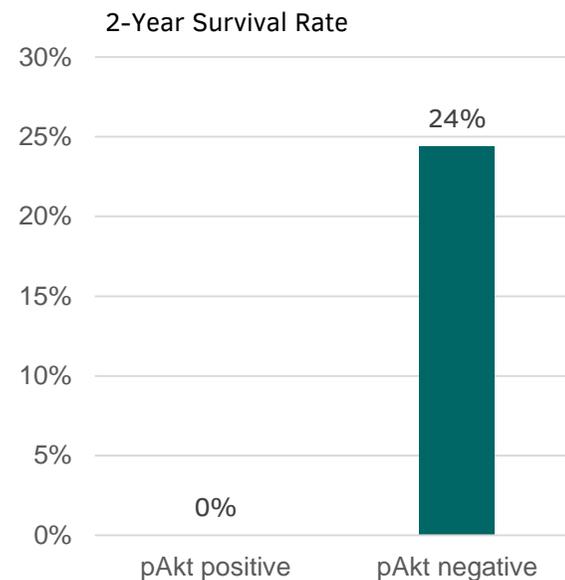
Source: ME Hegi, A-C Diserens, T Gorlia, et al. (2005). *N Engl J Med* 352:997-1003

# The PI3K / Akt / mTOR pathway is activated in ~80% of GBM cases

## Canonical Oncogenic Pathway for GBM



## Worse Prognosis



Higher pAkt expression (downstream signal of PI3K) predicts a worse response in GBM

Source: CW Brennan, RGW Verhaak, A McKenna, et al. (2013) Cell 155:462-477; Y Suzuki, K Shirai, K Oka, et al. (2010) J Radiat Res. 51:343-348

# PI3K inhibitors are well-validated, with one marketed product and extensive clinical data

## Zydelig (idelalisib) on market



## Other PI3K inhibitors in clinical trials

### Review

*Nature Reviews Clinical Oncology* **10**, 143-153 (March 2013) | doi:10.1038/

Development of PI3K inhibitors: lessons learned from early clinical trials

Jordi Tabernero  
Targeting PI3K/AKT/mTOR pathway in non small cell lung cancer

The pleiotropic effects of PI3K inhibitors on angiogenesis, tumor growth, and metastasis: implications for clinical trials

Commentary

Claudia Fu  
Show n

The PI3K/AKT/mTOR pathway in breast cancer: targets, trials and biomarkers

Elisavet Paplomata

Winship Cancer Institute of Emory University, Atlanta, GA, USA

Ruth O'Regan [roregan@emory.edu](mailto:roregan@emory.edu)

Winship Cancer Institute of Emory University, Atlanta, GA, USA

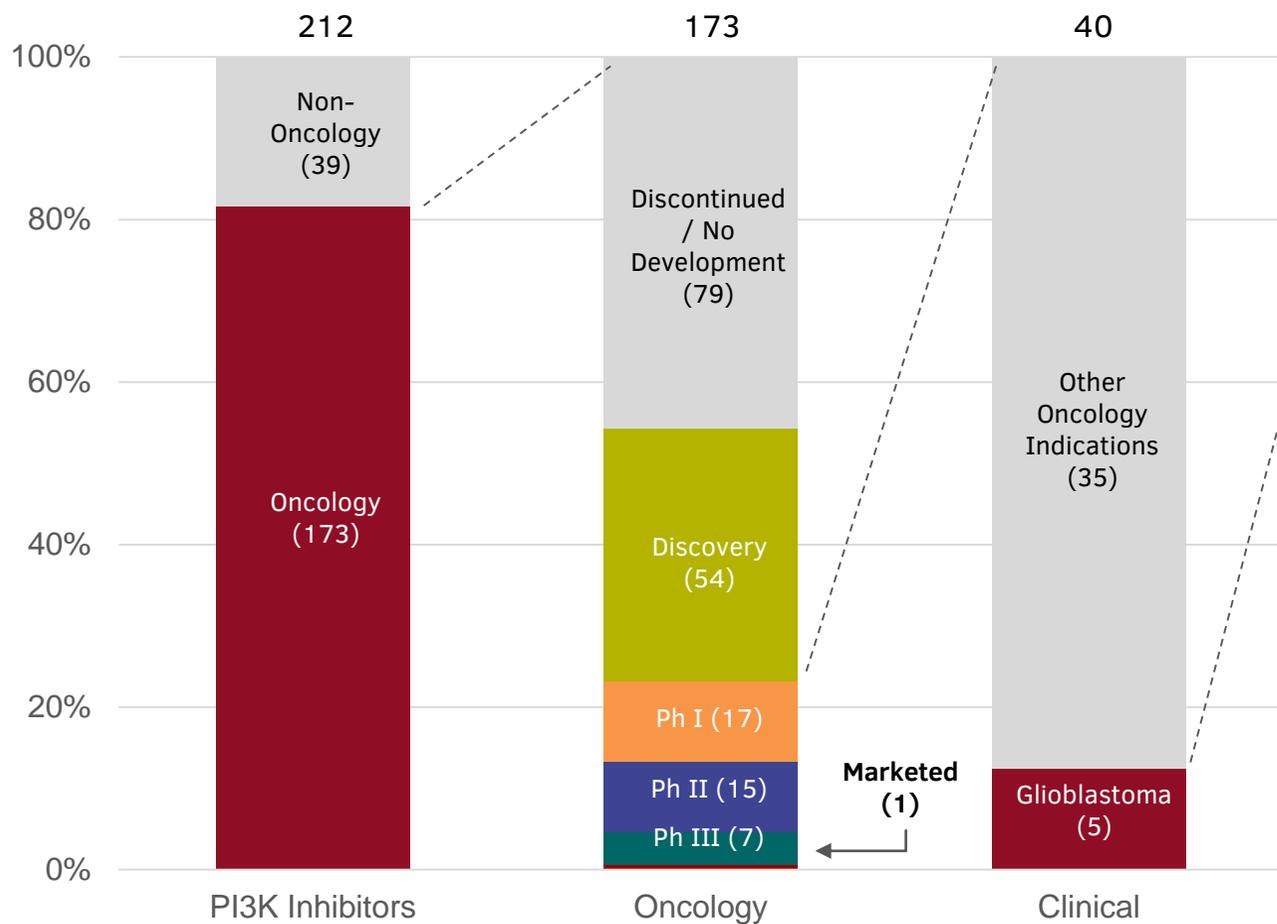
Abstract

The phosphoinositide 3 kinase (PI3K)/Akt/mammalian (or mechanistic) target of rapamycin (mTOR) pathway is a complicated intracellular pathway, which leads to cell growth and tumor proliferation and plays a significant role in endocrine resistance in breast cancer. Multiple compounds targeting this pathway are being evaluated in clinical trials. These agents are generally well tolerated and can be used in combination with targeted therapies, endocrine therapy or cytotoxic agents. The identification of subtypes of tumors more likely to respond to these therapeutics cannot be overemphasized, since breast cancer is a very heterogeneous malignancy. Activation of pathways such as KRAS and MEK can act as escape mechanisms that lead to

GDC-0084 differentiated from other PI3K inhibitors by:-

- Ability to cross blood-brain barrier
- Optimised balance of PI3K and mTOR activity

# GDC-0084 is among the most advanced PI3K inhibitors in active development for GBM

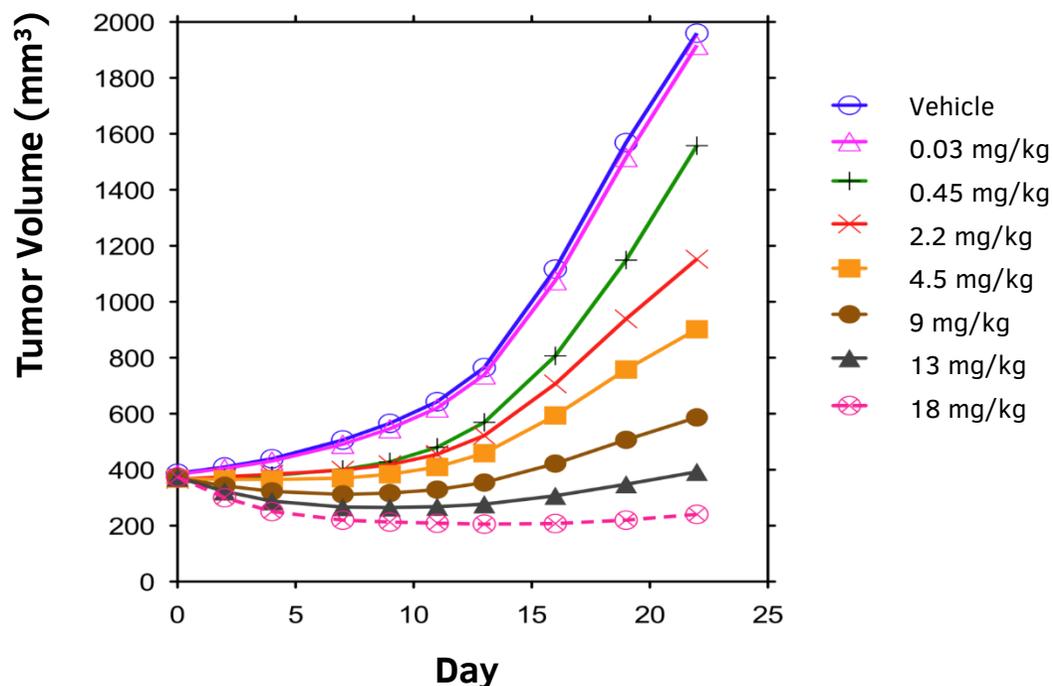


<b>Genentech</b> GDC-0084	Completed P1 in GBM (n=47)
<b>NOVARTIS</b> buparlisib	P1/2a in GBM due to complete in Oct 2016
<b>PIOUR</b> PQR-309	Single-site P2 in GBM underway; read-out in Jan '18
<b>CASCADIAN THERAPEUTICS</b> sonolisib	Discontinued
<b>EXELIXIS</b> voxtalisib	Discontinued

Source: Thomson Reuters Cortellis Competitor Intelligence

# GDC-0084 shows single-agent activity in preclinical models of glioblastoma

## Illustrative Dose-Dependent Activity in U87 Model



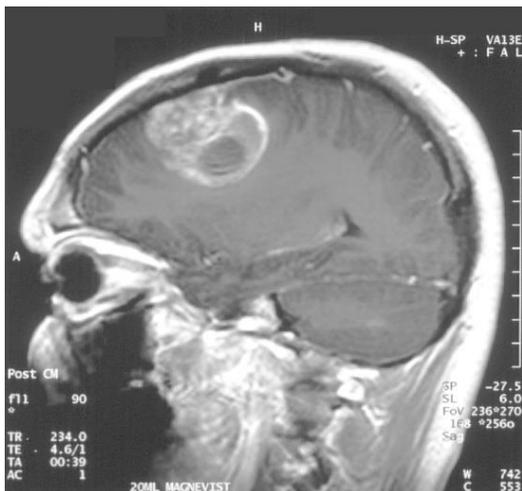
## General Findings

Widespread activity in a range of PDX models; appears unaffected by MGMT promotor status

Clear dose - PI3K inhibition - response relationship seen in most experiments

GDC-0084 even moderately active in GS2 intracranial model (intact BBB, no PI3K dysregulation) which is resistant to other test articles

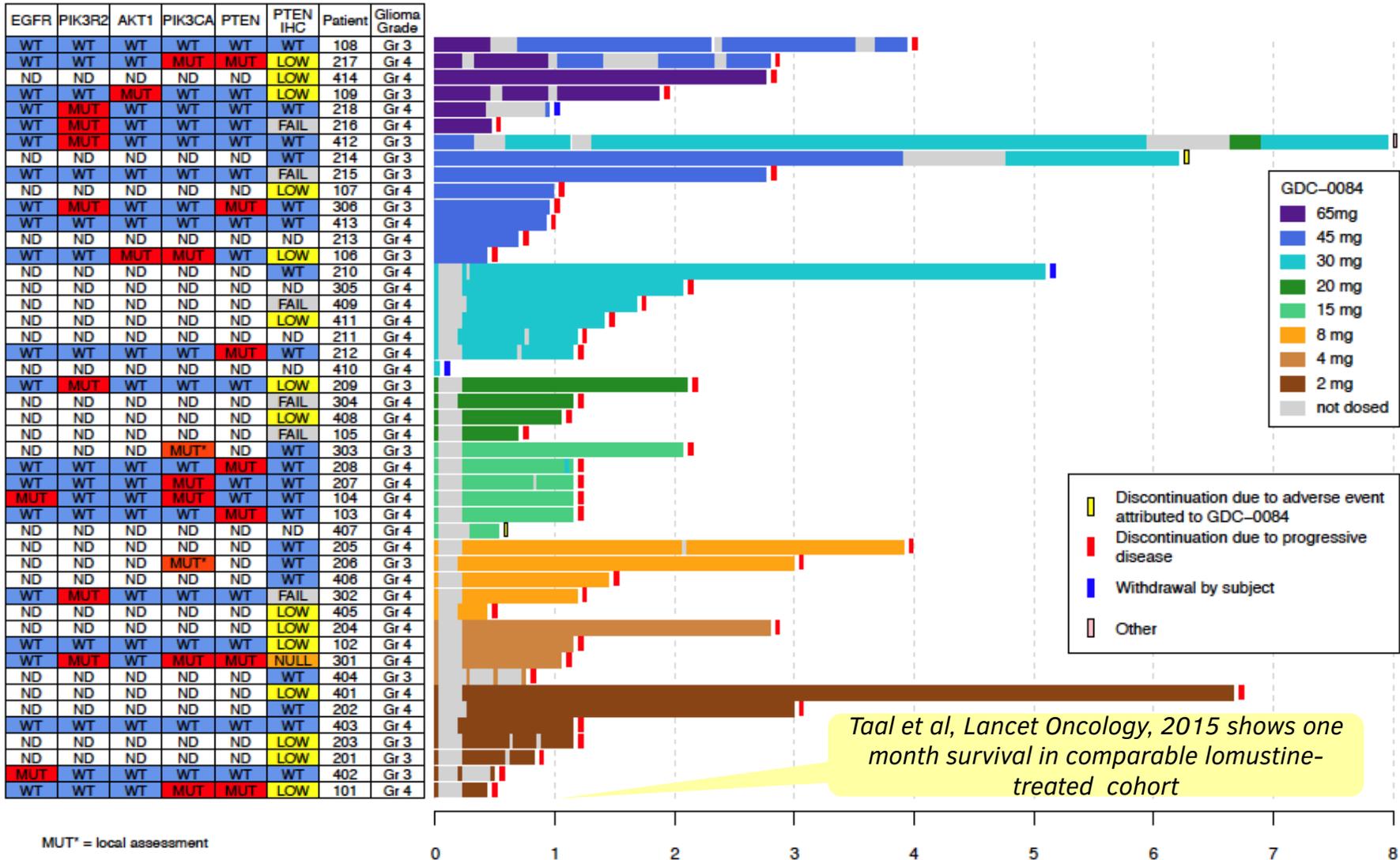
# GDC-0084 has successfully completed a phase I study which established dose and safety profile



## Phase I Study

- 47 patients enrolled at 4 centres (MD Anderson, UCLA, Dana-Farber, and Vall d'Hebron)
- Patients were grade 3 or 4 gliomas with at least one (and in most cases, several) lines of prior therapy
- 45mg established as Maximally Tolerated Dose (MTD) for phase II study
- Pharmacokinetic profile consistent with daily dosing
- Safety profile consistent with other PI3K inhibitors, with hyperglycemia and mucositis / stomatitis the most common adverse events
- Promising signals of pharmacodynamic response on FDG-PET, an exploratory radiological marker

# Time on study exceeded historical controls for the majority of patients



MUT\* = local assessment



# Brain metastases from non-CNS tumors represent long-term upside potential

## Overview

- Estimated 100,000 - 200,000 cases/year in US
- ~10-25% adult cancer patients develop symptomatic brain mets
- Lung, breast and melanoma represent the majority of brain mets
- Frequency of brain mets increasing with better systemic control and longer survival
- Few (if any) drugs available to treat brain metastasis

## Example: Breast Cancer

- ~30-44% of metastatic HER2-positive metastatic breast cancer patients have brain metastases
- Brain metastases represent the cause of death in ~50% of HER2-positive breast cancer patients
- ~40-50% of breast cancer brain metastases have disordered PI3K pathway
- Therapies that are effective for the primary tumor (e.g. Herceptin) are often ineffective for brain metastases

## Next Steps

- Use GBM as a 'gateway indication', with the potential to explore registration post-phase II via accelerated approval / breakthrough designation, subject to clinical results
- Meanwhile, conduct preclinical exploration of brain metastases in partnership with identified researchers to demonstrate preclinical proof-of-concept and augment economic value of the asset

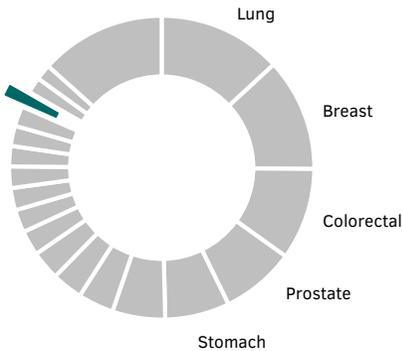
Source: E Lim & N Lim (2012). *Oncology*. 26(7):652-9; PK Brastianos, SL Carter, S Santagata, et al. (2015). *Discovery* 5:1164

# Ovarian cancer remains a disease of high unmet medical need

## High Incidence

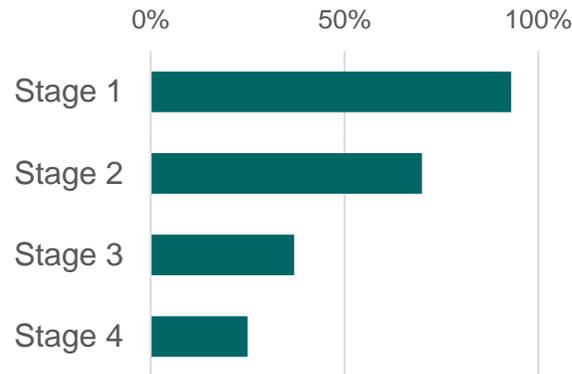
### Ovarian Cancer

- 17<sup>th</sup> most common tumour worldwide
- 7<sup>th</sup> most common tumour in women
- ~240,000 new cases per annum
- 1.7% of all new cancer cases
- Overall lifetime risk is 1.6% for women
- Genetic cause (BRCA1 or BRCA2) in ~10% of cases
- More common in women who have not borne children
- 80% of cases occurring in women >50 years of age



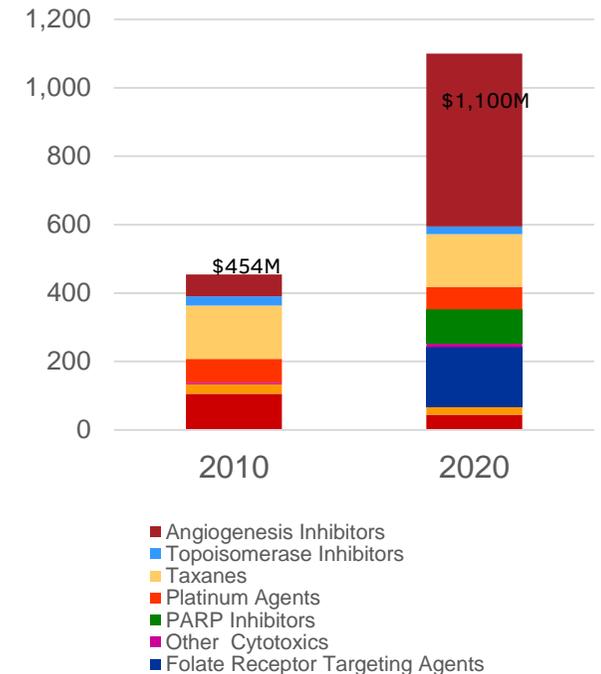
## Poor Prognosis with Existing Therapies

### Five-Year Survival



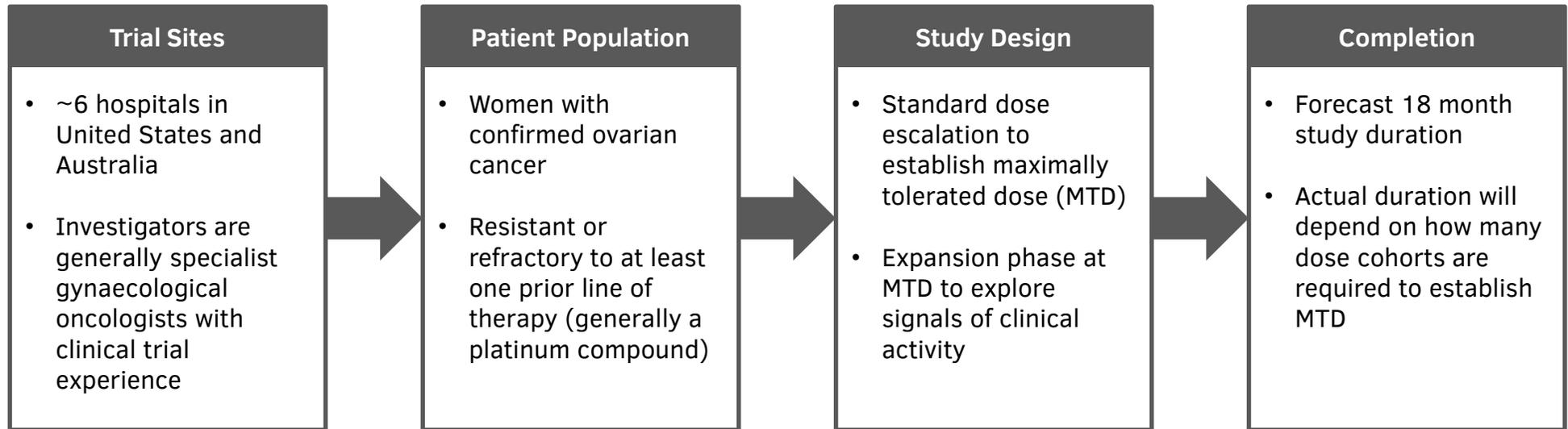
## Growing and Evolving Market

### Market Size (US\$ ,000)



Source: GLOBOCAN; Holschneider & Berek (2000), *Sem Surg Onc* 19(1):3-10; Decision Resources

# Phase I study is designed to establish safety and tolerability, and explore potential efficacy



Study performed under Investigational New Drug (IND) application with United States Food & Drug Administration (FDA) – provides careful validation and supports eventual product approval in United States

In addition to standard efficacy measures (via CT scan), study will measure exploratory biomarkers to seek signals of clinical activity

# Work continues at full pace with Anisina and Trilexium

## Anisina (ATM-3507)

### Current Status

- IND-enabling activities (CMC, toxicology, regulatory) well underway
- Final preclinical studies underway to optimise phase I clinical trial design
- Initiating GMP manufacture

### Plans for 2017

- Submission of IND and initiation of phase I clinical study in 2H 2017

## Trilexium (TRXE-009-1)

### Current Status

- Preclinical development ongoing
  - Broad activity against multiple cancer types
  - High potential to combine with targeted therapies
- Development of a clinical formulation underway (intravenous liposomal formulation favoured)

### Plans for 2017

- Initiation of IND-enabling activities in mid-2017

# 2017 will be an important year for Novogen, with a rich series of value-driving events



## Key Milestones for 2017

IND submission and approval for Anisina

Initiation of Anisina phase I study

Initiation of GDC-0084 phase II study

Full recruitment of Cantrixil phase I study

Initiation of IND-enabling activities for Trilexium

# Novogen now has a diversified portfolio and is positioned for growth



- **Focus on unmet need:** pipeline of novel therapies, targeting oncology patients, poorly served by existing treatment options
- **Building a sustainable model:** leveraging oncology expertise, developing commercially attractive, in-house and external assets
- **Diversified portfolio:**
  - Multiple assets in various stages of development – from pre-clinical through to phase II-ready
  - Across technologies / development platforms
- **Strong management and board:** lean team of internationally-experienced pharma executives
- **Financially sound:** listed on ASX and NASDAQ, with cash runway
- **News flow:** rich series of value-driving milestones over 12-18 months

