

ASX RELEASE

13 January 2020

## **KAZIA PRESENTS AT BIOTECH SHOWCASE**

**Sydney, 13 January 2020** – Kazia Therapeutics Limited (ASX: KZA; NASDAQ: KZIA), an Australian oncology-focused biotechnology company, is pleased to provide a copy of a presentation to be made to Biotech Showcase in San Francisco, CA later today.

[ENDS]

### **About Kazia Therapeutics Limited**

Kazia Therapeutics Limited (ASX: KZA, NASDAQ: KZIA) is an innovative oncology-focused biotechnology company, based in Sydney, Australia. Our pipeline includes two clinical-stage drug development candidates, and we are working to develop therapies across a range of oncology indications.

Our lead program is paxalisib (GDC-0084), a small molecule inhibitor of the PI3K / AKT / mTOR pathway, which is being developed to treat glioblastoma, the most common and most aggressive form of primary brain cancer in adults. Licensed from Genentech in late 2016, paxalisib entered a phase II clinical trial in 2018. Interim data was reported in November 2019, and further data is expected in 1H 2020. Paxalisib was granted orphan designation for glioblastoma by the US FDA in February 2018.

TRX-E-002-1 (Cantrixil), is a third-generation benzopyran molecule with activity against cancer stem cells and is being developed to treat ovarian cancer. TRX-E-002-1 is currently undergoing a phase I clinical trial in Australia and the United States. Interim data was presented at the ESMO Congress in September 2019, and the study remains ongoing. Cantrixil was granted orphan designation for ovarian cancer by the US FDA in April 2015.

This announcement was authorized for release to the ASX by James Garner, Chief Executive Officer, Managing Director.

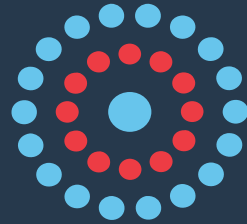
### **Board of Directors**

**Mr Iain Ross** Chairman, Non-Executive Director

**Mr Bryce Carmine** Non-Executive Director

**Mr Steven Coffey** Non-Executive Director

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



**KAZIA**  
THERAPEUTICS



A company developing  
innovative, high-impact  
drugs for cancer

Presentation to Biotech Showcase




San Francisco, CA  
13 January 2020

# 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.

# Corporate Overview



 <b>Company Description</b>	Oncology-focused, mid-clinical-stage, small-molecule biotechnology company, headquartered in Sydney, Australia
 <b>Pipeline</b>	<b>Paxalisib</b> – brain-penetrant PI3K / mTOR inhibitor in phase II for glioblastoma <b>Cantrixil</b> – cancer stem cell-targeting agent in phase I for ovarian cancer
 <b>Financials</b>	Listed on NASDAQ (KZIA) with a market capitalization of ~US\$ 35 million Current assets at 30 June 2019 of ~US\$ 5.5 million, augmented by ~US\$ 2.8 million PIPE in October 2019

# Investment Rationale

1

Our lead program, paxalisib, was **designed by Genentech**, the world's most successful cancer drug developer, and has completed a **successful phase 1 human trial**, showing it to be generally safe and providing signals of efficacy

2

Paxalisib is a PI3K inhibitor, a well-validated and well-understood class of cancer therapies with **four FDA-approved products**; unique differentiating feature of GDC-0084 is the **ability to cross the blood-brain barrier**

3

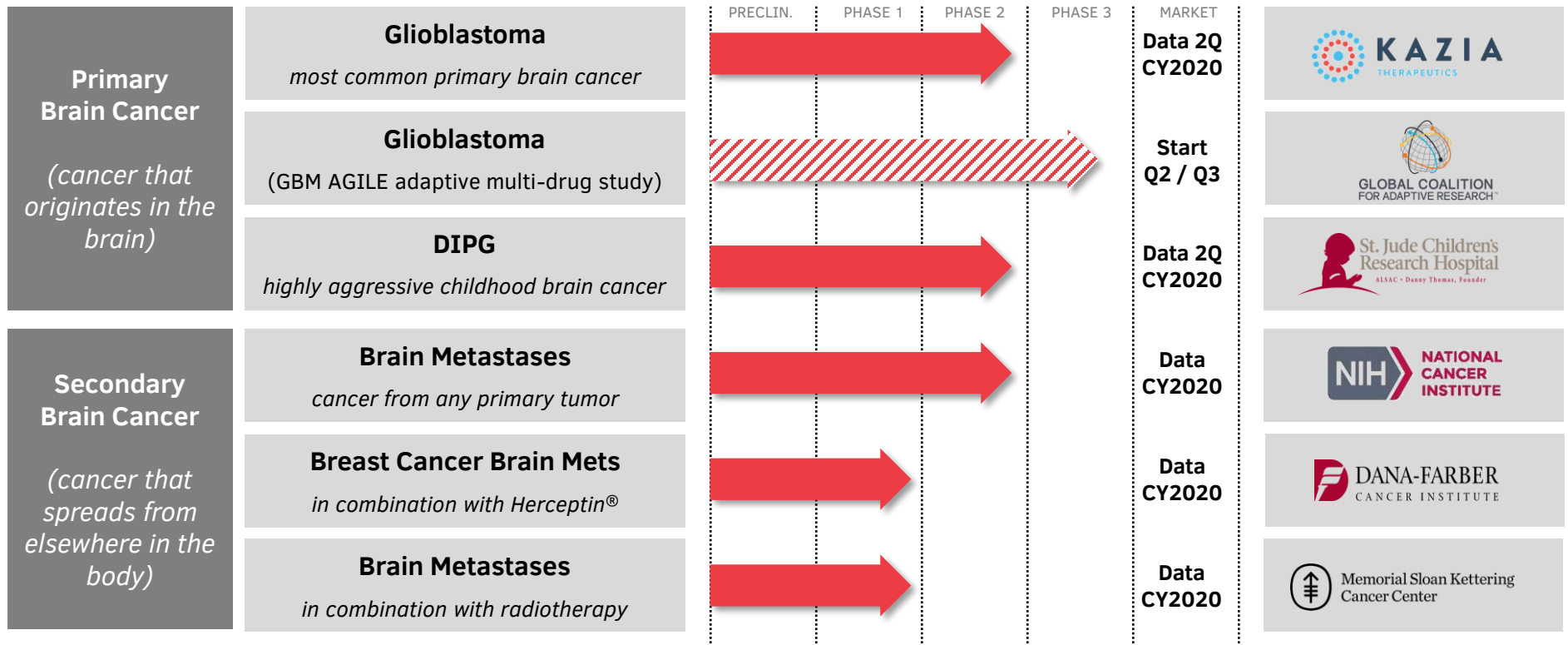
**Five clinical trials** of paxalisib are currently underway at leading US hospitals, of which four are primarily funded by external parties, covering a broad range of primary and secondary brain cancers to provide **multiple shots on goal**

4

Paxalisib has reported preliminary evidence of **clinical efficacy**, and has a clear **path-to-market** via the multi-drug adaptive study, GBM AGILE; glioblastoma represents a commercial opportunity of ~US\$ 1.5 billion

# Six ongoing trials across two assets; lead program covers full range of brain cancers

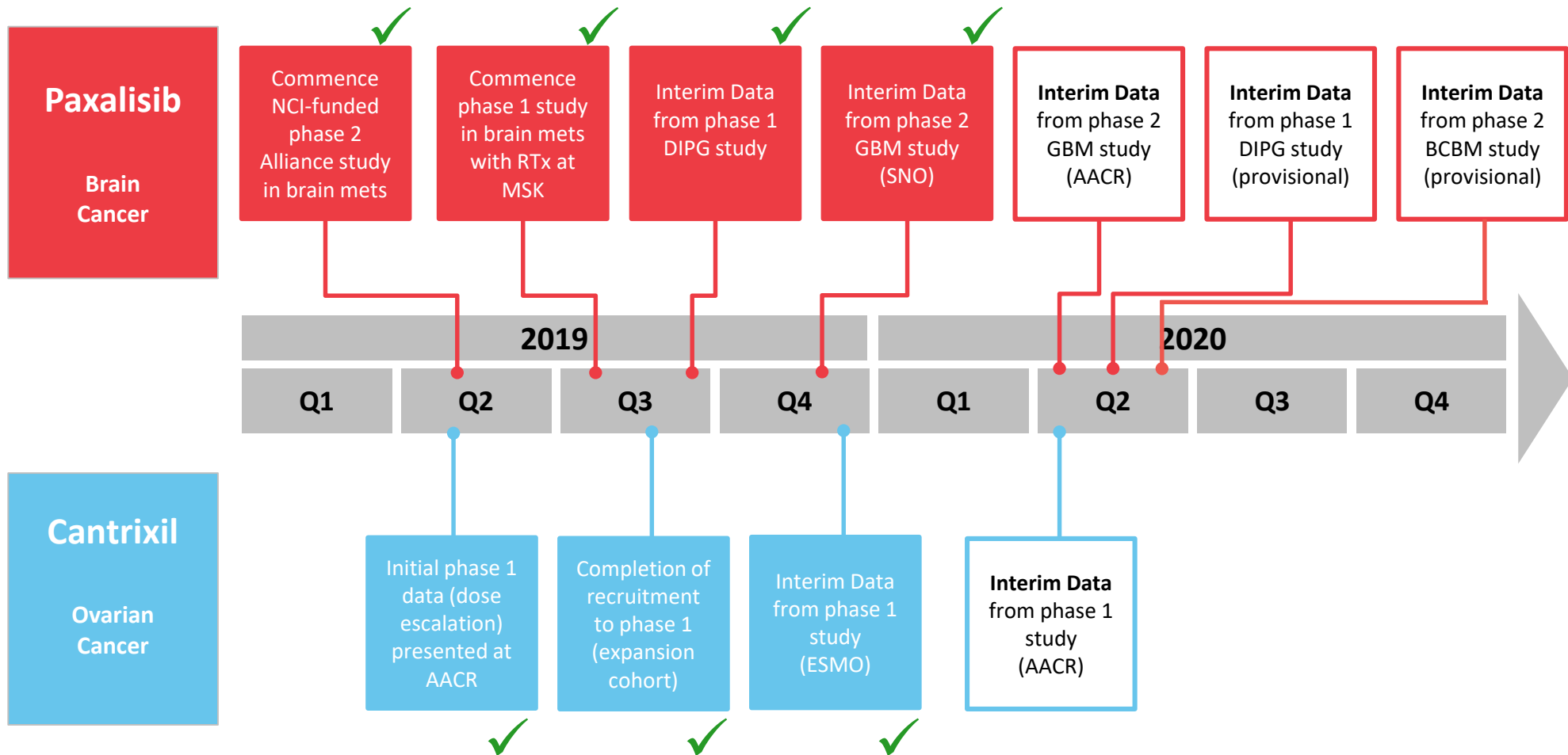
## Paxalisib (GDC-0084)



## Cantrixil (TRX-E-001)



# Kazia has delivered all milestones to date, with multiple data read-outs expected over 6-12 months



Note: forward-looking milestones are forecast and indicative but subject to revision

# Paxalisib (GDC-0084)

Phase II

Glioblastoma Multiforme  
& Other Brain Cancers

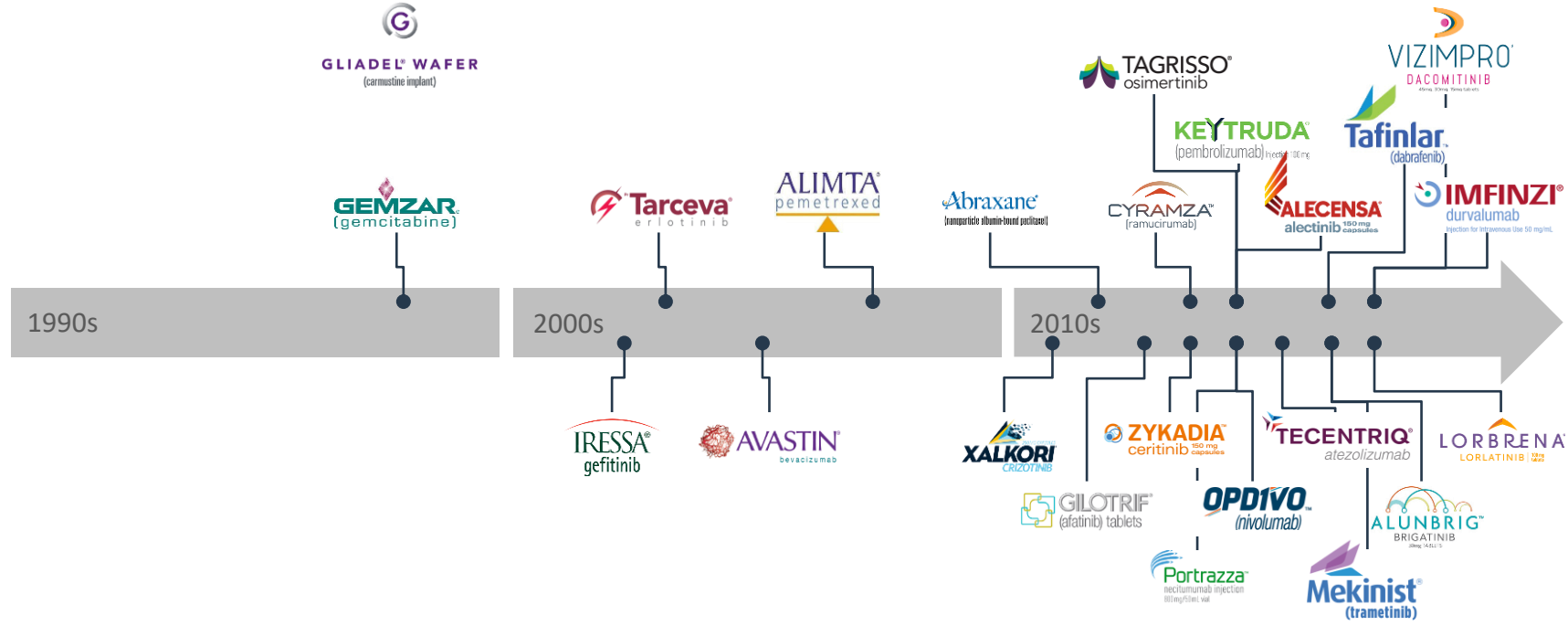


# Treatment of brain cancer has improved little in recent decades, unlike other cancers

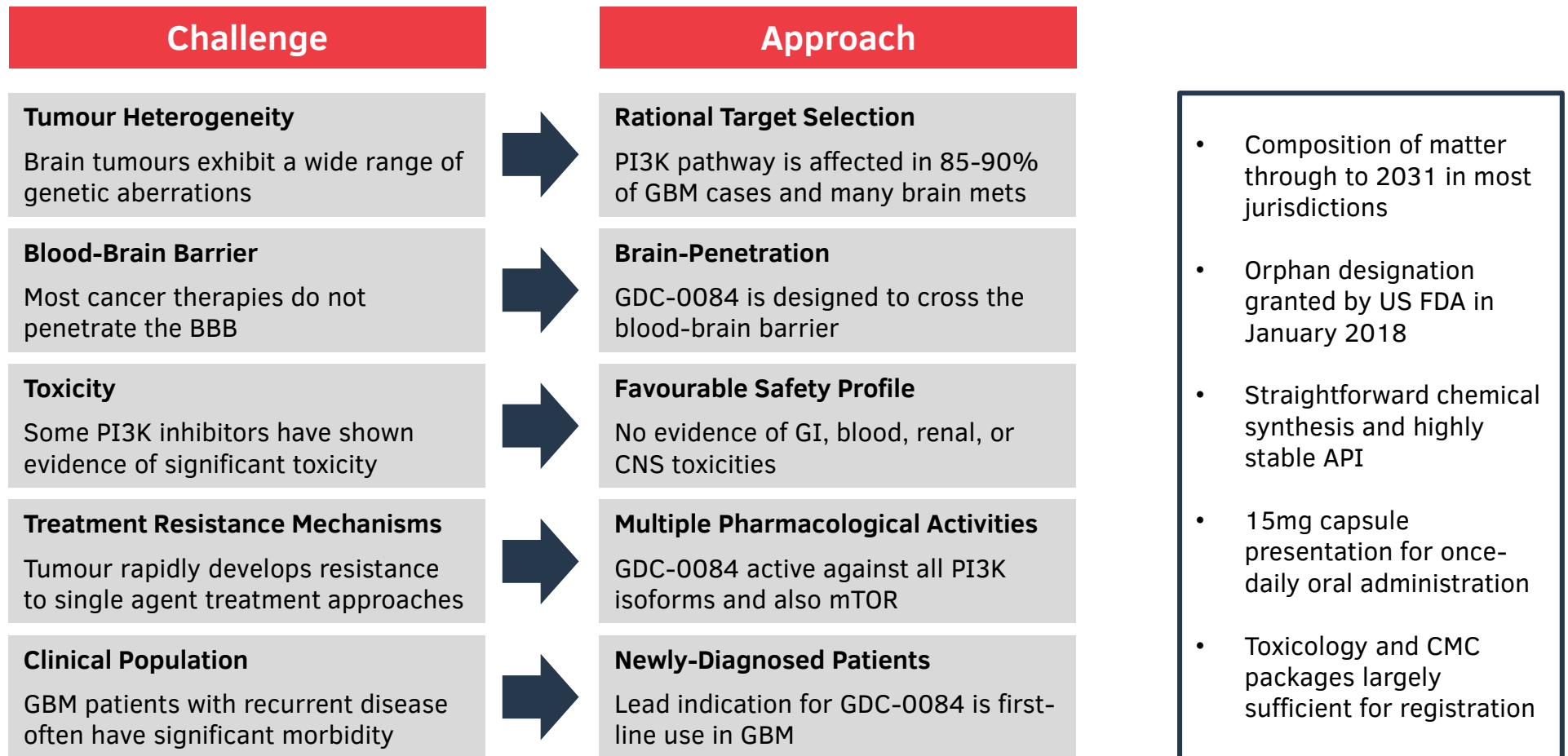
**Brain Cancer**  
(glioblastoma)



**Lung Cancer**



# Paxalisib was designed specifically to overcome challenges associated with brain cancer treatment



# PI3K class is well-established, but paxalisib is unique in its ability to cross the blood-brain barrier



Zydelig (idelalisib)



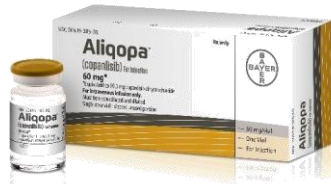
FDA Approved **July 2014** ✓  
(blood cancers)  
[accelerated approval]

Does not cross blood-brain barrier ✗

Potentially fatal liver toxicity and diarrhoea ✗



Aliqopa (copanlisib)



FDA Approved **September 2017** ✓  
(blood cancers)  
[accelerated approval]

Does not cross blood-brain barrier ✗

Potentially fatal infections ✗



Copiktra (duvelisib)



FDA Approved **October 2018** ✓  
(blood cancers)  
[accelerated approval]

Does not cross blood-brain barrier ✗

Potentially fatal infections & diarrhoea ✗



Piqray (alpelisib)



FDA Approved **May 2019** ✓  
(breast cancer)  
[accelerated approval]

Does not cross blood-brain barrier ✗

Limited toxicities to date ✓



GDC-0084

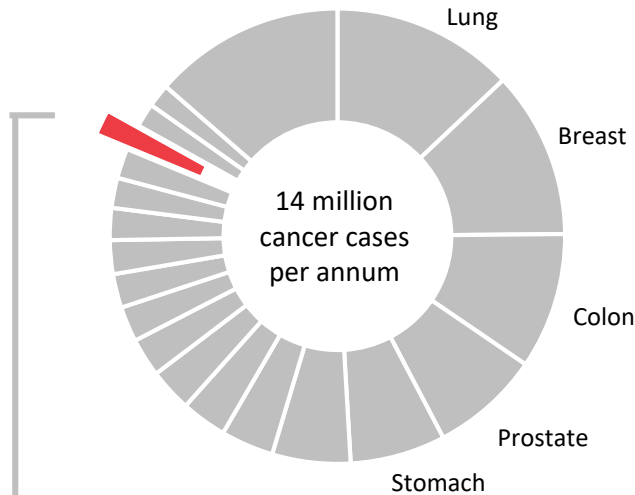


In phase II human trials under US FDA oversight (brain cancer)

Does cross blood-brain barrier ✓

Appears generally safe and well-tolerated thus far ✓

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



## Glioblastoma Multiforme

133,000 cases per annum worldwide

Indicative Market Opportunity

**US\$ 1+ billion**

**No clear cause**  
or strong risk factors

**3-4 months**  
untreated survival

**12-15 months**  
average survival with treatment

Any age, but most common in  
**60s**

Five-year survival  
**3 – 5%**  
(breast cancer: 90%)



Sen. John McCain



Sen. Ted Kennedy



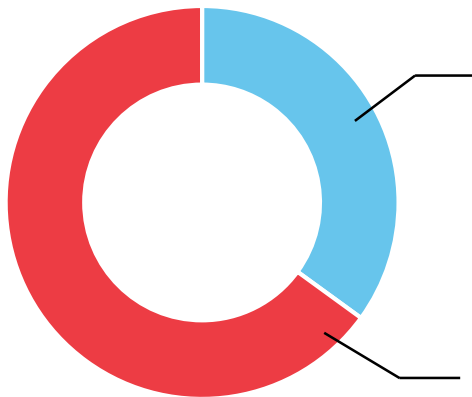
Beau Biden



Dan Case

# Temozolomide is only FDA-approved drug for GBM; it is ineffective in ~65% of cases

Standard of Care ('Stupp Regimen')



**~35% of patients respond to temozolomide**

*Extends overall survival from 15 to 22 months*

**~65% of patients don't respond to temozolomide**

*Extends overall survival from 12 to 13 months*



**Paxalisib is being developed for the ~65% of newly-diagnosed GBM patients who will not respond to existing chemotherapy with temozolomide**

*For these patients, there is no effective pharmacological treatment currently available*

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

Note: Temozolomide is only approved therapy for newly-diagnosed patients; Avastin (bevacizumab) is approved for use in recurrent setting

# A phase 1 human trial of paxalisib in GBM showed favourable safety and multiple efficacy signals

## Safety

- Phase I safety trial conducted by Genentech
- 47 patients enrolled with advanced glioma (grade 3/4); average of three prior lines of therapy
- Most common adverse events were oral mucositis and hyperglycemia (common effects of PI3K inhibitors)
- No evidence of liver, bone marrow, kidney toxicity, or mood disturbances
- Data presented at American Society for Clinical Oncology annual meeting in Chicago, June 2016

## Efficacy Signals

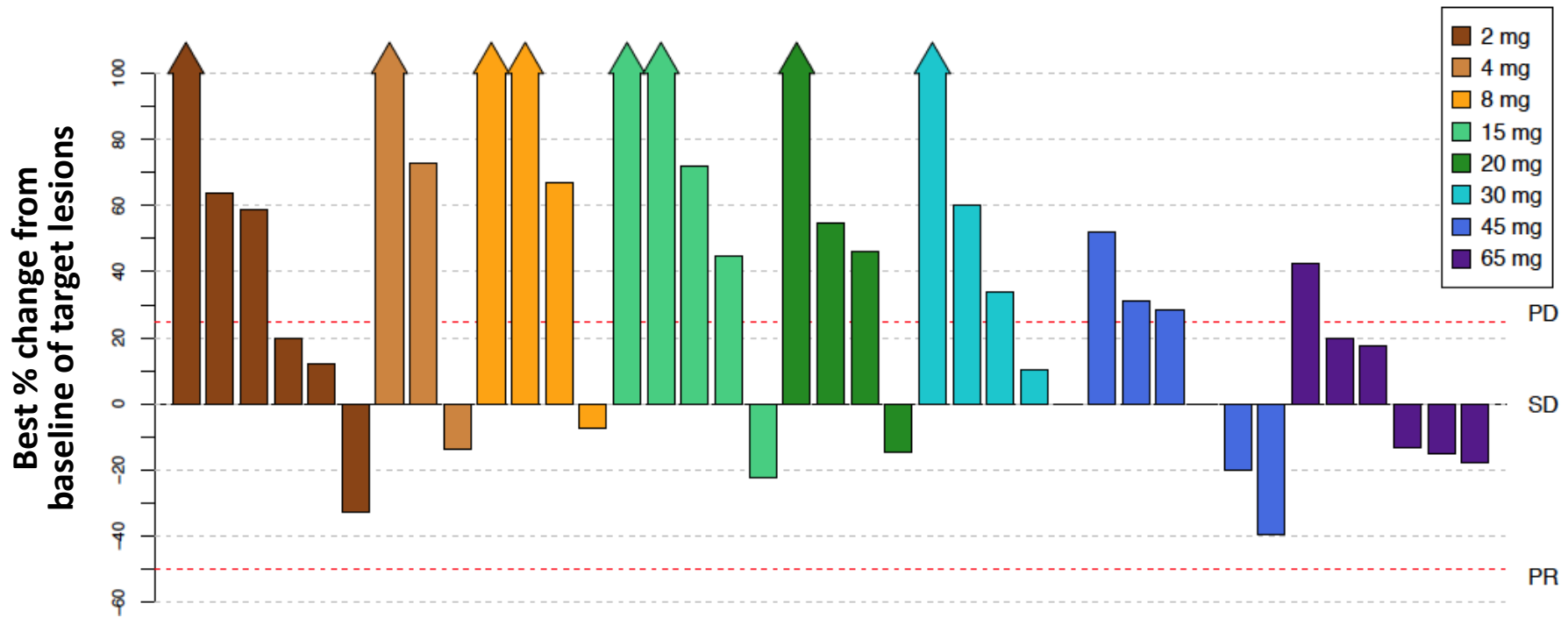
	Paxalisib	Comparison
Arresting Tumour Growth	<b>40%</b> Achieved 'stable disease'	<b>21-52%</b> in studies of Avastin in similar patients
Potentially Delaying Progression	<b>21%</b> Remained on study for >3 months	Median progression-free survival of <b>1 month*</b>
Slowing Tumour Metabolism	<b>26%</b> Showed 'metabolic partial response' on FDG-PET	Potentially better predictor of clinical response than MRI <sup>†</sup>



\* Taal et al., Lancet Oncology (2015): ORR and mPFS of Lomustine in 2L GBM were 2/41 (5%) and 1 months, respectively (n = 46)

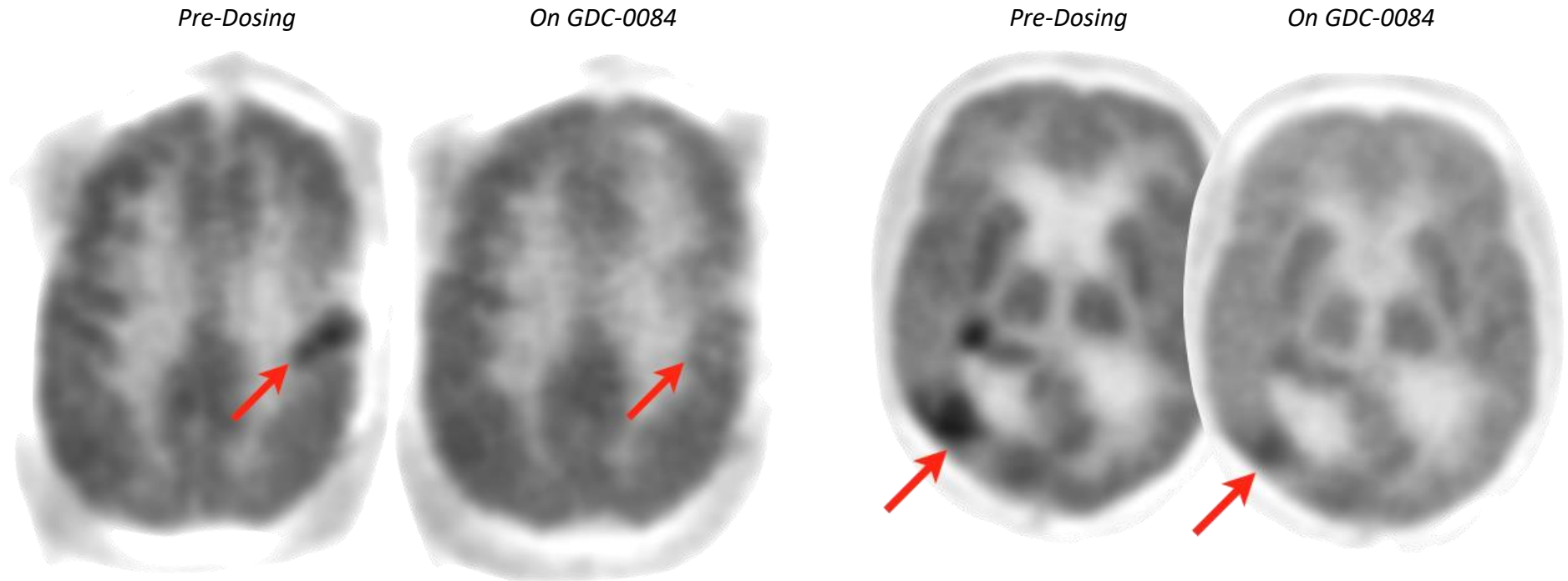
† Schwarzenberg J, et al. Clin Cancer Res; 20(13); 3550-9

# Response rate showed dose-dependent reduction in tumor growth (consistent with mode of action)



CR / PR: 0  
SD: 19 (40%)  
PD: 26 (55%)

# 7 / 27 patients (26%) showed a 'metabolic partial response' on FDG-PET



Analysis courtesy of Professor Ben Ellingson, UCLA Brain Tumor Imaging Laboratory



# Safety profile appeared acceptable and consistent with PI3K class

Dose level	30 mg N = 7				45 mg N = 8				65 mg N = 6			
	Grade 1	Grade 2	Grade 3	All Grade	Grade 1	Grade 2	Grade 3	All Grade	Grade 1	Grade 2	Grade 3	All Grade
Any Adverse Events	2 (29%)	2 (29%)	2 (29%)	6 (86%)	2 (25%)	3 (38%)	2 (25%)	7 (88%)	1 (17%)	0	4 (67%)	5 (83%)
FATIGUE *	1 (14%)	0	1 (14%)	2 (29%)	2 (25%)	3 (38%)	0	5 (62%)	1 (17%)	2 (33%)	0	3 (50%)
HYPERGLYCAEMIA	2 (29%)	0	1 (14%)	3 (43%)	0	2 (25%)	0	2 (25%)	0	1 (17%)	2 (33%)	3 (50%)
NAUSEA	1 (14%)	0	0	1 (14%)	1 (12%)	1 (12%)	0	2 (25%)	2 (33%)	0	0	2 (33%)
RASH **	0	0	0	0	1 (12%)	2 (25%)	0	3 (38%)	2 (33%)	3 (50%)	0	5 (83%)
HYPER TRIGLYCERIDAEMIA	1 (14%)	1 (14%)	0	2 (29%)	1 (12%)	1 (12%)	0	2 (25%)	0	1 (17%)	0	1 (17%)
MUCOSITIS ***	0	0	0	0	1 (12%)	2 (25%)	1 (12%)	4 (50%)	1 (17%)	0	2 (33%)	3 (50%)
HYPO PHOSPHATAEMIA	0	0	0	0	1 (12%)	1 (12%)	0	2 (25%)	0	0	1 (17%)	1 (17%)
DECREASED APPETITE	0	0	0	0	3 (38%)	1 (12%)	0	4 (50%)	0	0	0	0
DIARRHOEA	0	1 (14%)	0	1 (14%)	0	1 (12%)	0	1 (12%)	2 (33%)	0	0	2 (33%)
VOMITING	0	0	0	0	1 (12%)	0	0	1 (12%)	1 (17%)	0	0	1 (17%)
CHOLESTEROL INCREASED	0	2 (29%)	0	2 (29%)	0	1 (12%)	0	1 (12%)	0	0	0	0
HYPER CHOLESTEROLAEMIA	0	0	0	0	0	0	0	0	0	1 (17%)	0	1 (17%)
PTL decreased	0	0	0	0	2 (25%)	0	0	2 (25%)	1 (17%)	0	0	1 (17%)
DIZZINESS	0	0	0	0	0	1 (12%)	0	1 (12%)	0	0	0	0
DRY MOUTH	0	0	0	0	2 (25%)	0	0	2 (25%)	0	0	0	0
DRY SKIN	0	0	0	0	1 (12%)	0	1 (12%)	2 (25%)	0	0	0	0
DYSGEUSIA	0	0	0	0	2 (25%)	0	0	2 (25%)	0	0	0	0
DYSPNOEA	0	0	0	0	2 (25%)	0	0	2 (25%)	0	0	0	0
PRURITUS	0	0	0	0	0	0	1 (12%)	1 (12%)	1 (17%)	0	0	1 (17%)
WEIGHT DECREASED	0	0	0	0	1 (12%)	0	0	1 (12%)	1 (17%)	0	0	1 (17%)

\* FATIGUE includes FATIGUE and ASTHENIA.

\*\* Rash includes rash and rash maculo-paular

\*\*\*MUCOSITIS includes MUCOSAL INFLAMMATION and STOMATITIS

# A broad-based clinical program is underway across multiple forms of brain cancer

## Paxalisib (GDC-0084)

### Primary Brain Cancer (brain cancer that begins in the brain)

#### Glioblastoma

*Most common and most aggressive brain tumour*

**Phase II**

[NCT03522298](https://clinicaltrials.gov/ct2/show/study/NCT03522298)



#### Glioblastoma

*(planned pivotal study for approval [in set-up])*

**Phase II / III**

[NCT03970447](https://clinicaltrials.gov/ct2/show/study/NCT03970447)



#### DIPG

*Highly aggressive childhood brain tumour*

**Phase I**

[NCT03696355](https://clinicaltrials.gov/ct2/show/study/NCT03696355)



### Secondary Brain Cancer (brain cancer that spreads from elsewhere in the body)

#### Brain Metastases

*Cancer that has spread from any primary tumour*

**Phase II**

[NCT03994796](https://clinicaltrials.gov/ct2/show/study/NCT03994796)



#### Breast Cancer Brain Mets

*(combination with Herceptin®)*

**Phase II**

[NCT03765983](https://clinicaltrials.gov/ct2/show/study/NCT03765983)

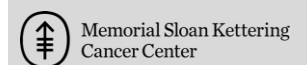


#### Brain Metastases

*(combination with radiotherapy)*

**Phase I**

[NCT04192981](https://clinicaltrials.gov/ct2/show/study/NCT04192981)



*Funded by Kazia*

*Funded Primarily Through Partnerships and External Funding*

# Paxalisib is currently in a phase 2a study in newly-diagnosed GBM; aim to start pivotal study in 2020

## Step 1: Dose Optimisation

6 – 24 patients  
12 months

Primary objective is to determine the appropriate dose for newly-diagnosed patients (phase 1 was in end-stage patients)

### Complete



- Top-line data reported May 2019
- Dose of 60mg determined (higher than 45mg dose found in phase I)

## Step 2: Expansion Cohort

20 patients  
6 months

Primary objective is to generate supportive data for FDA and to provide confirmatory signals of efficacy in newly-diagnosed population

### Ongoing

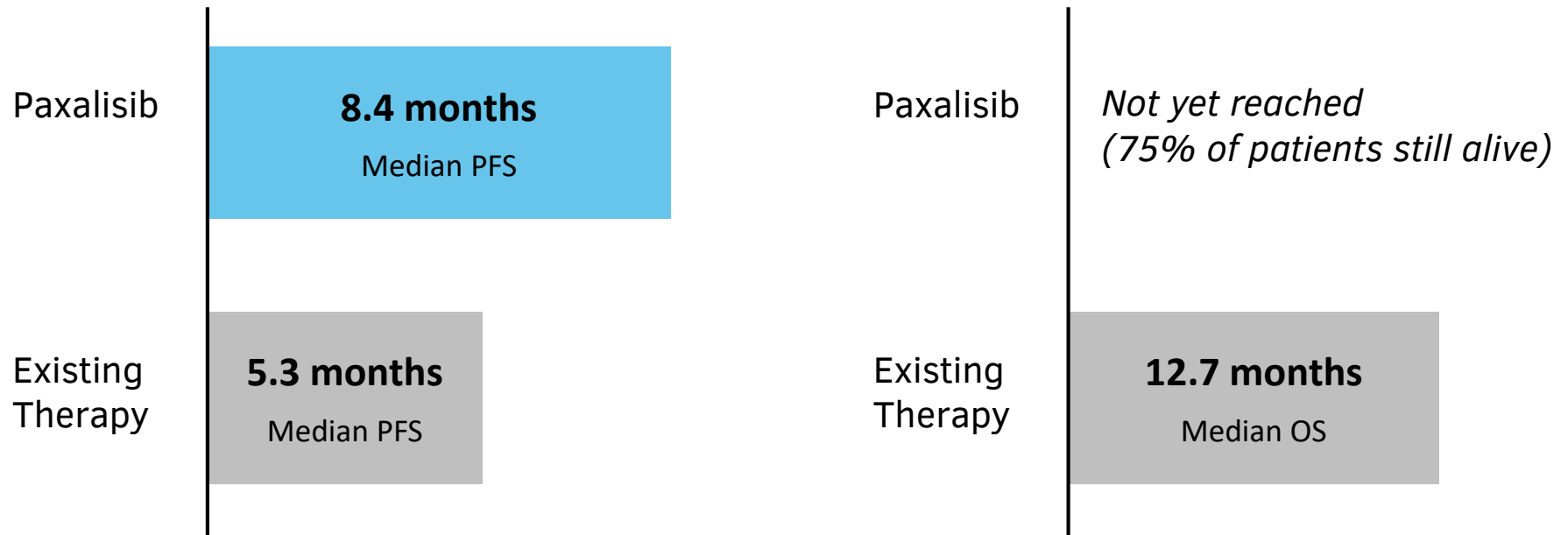
- Completion of recruitment anticipated in 4Q CY2019
- Data unlikely to be rate-limiting for pivotal study

- Newly-diagnosed patients with the unmethylated MGMT promotor (i.e. resistant to temozolomide)
- Paxalisib administered once daily, orally, as monotherapy in place of temozolomide
- Primary objective is dose determination (Step 1) and time to progression (Step 2)

# Interim analysis of the phase 2 study shows evidence of delaying tumour progression

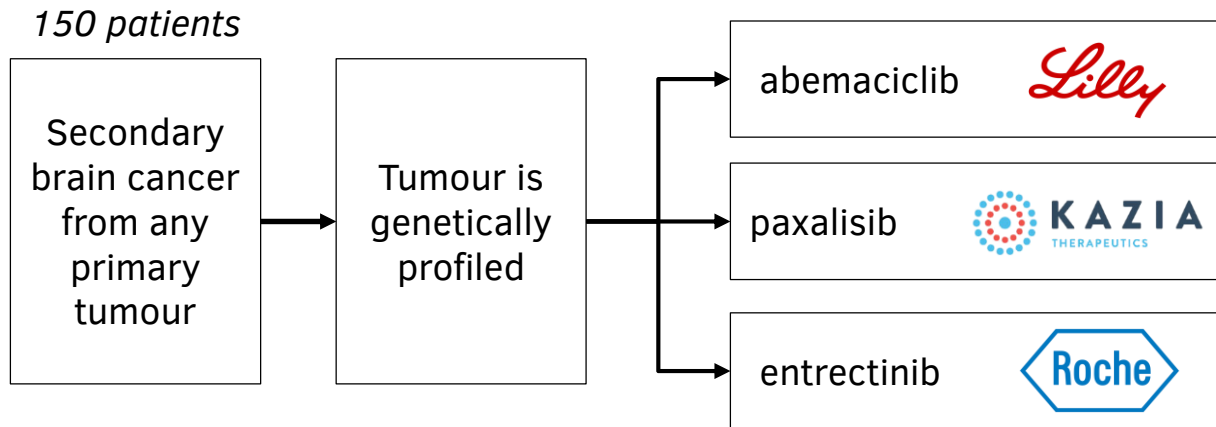
Progression-Free Survival (PFS)

Overall Survival (OS)



Note: figures for existing therapy are for temozolomide, per Hegi et al. (2005); comparison between different studies is never perfectly like-for-like

# The NCI-funded Alliance study in brain metastases is a cutting-edge, multi-drug clinical trial



- 'Precision medicine' study in which treatment is guided by the specific genetic make-up of each individual patient's tumour
- Accepts patients with brain metastases from any primary tumour (estimated to be ~200,000 patients per annum in US)

Funded by  
US National Cancer Institute



Executed by Alliance for Clinical  
Trials in Oncology



Led by Dr Priscilla Brastianos, a  
world expert on brain mets



# The St Jude study in DIPG has the potential for breakthrough designation and early approval

## Step 1: Dose Escalation

6 – 24 patients

Primary objective is to determine the appropriate dose for pediatric use (mg/kg dosing)

### Complete

- Top-line data reported Sept 2019
- Dose of 27 mg/m<sup>2</sup> determined (comparable dose and safety profile to adult studies)

## Step 2: Expansion Cohort

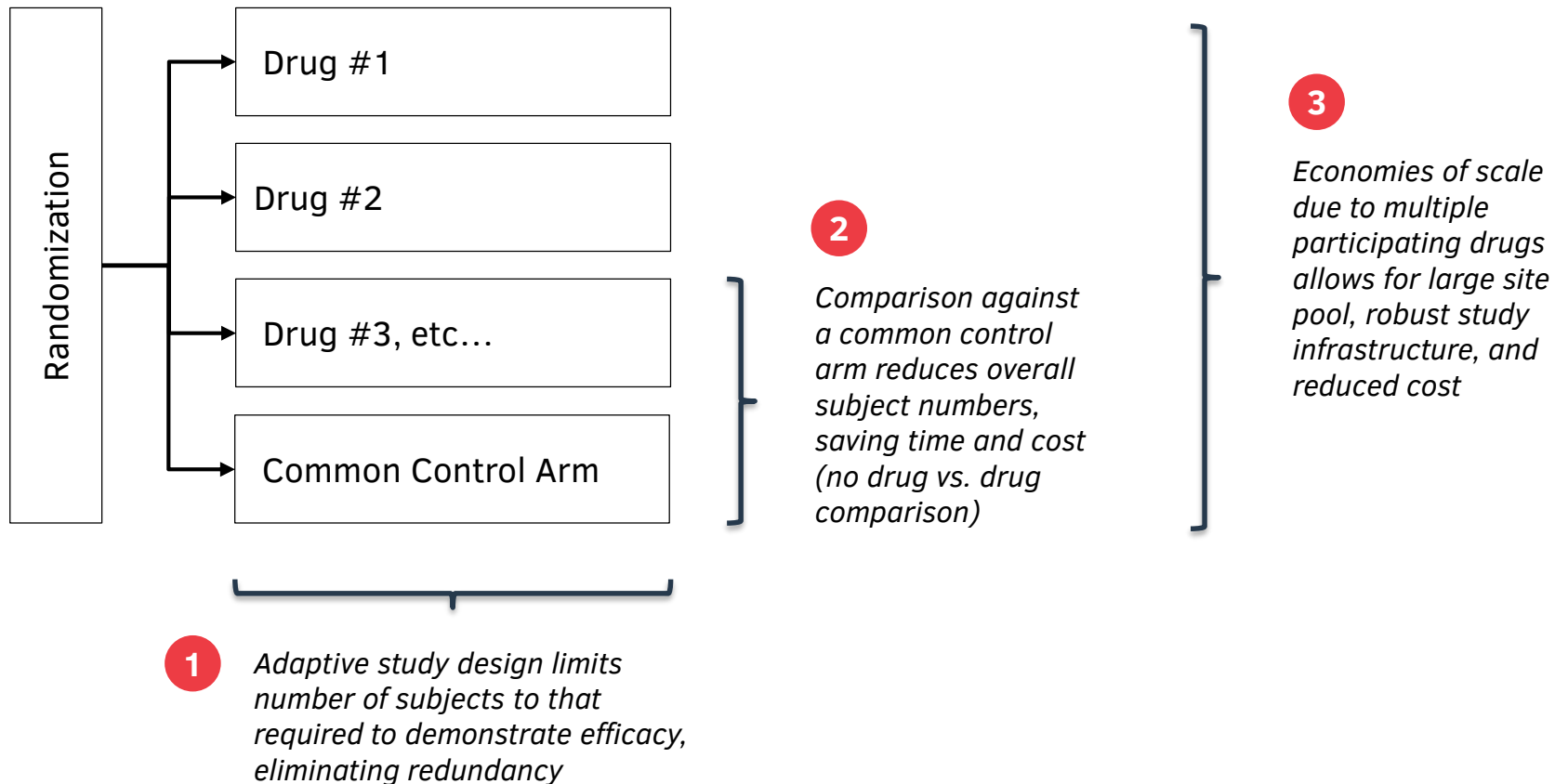
12 patients

Primary objective is to provide initial evidence of clinical efficacy

### Not Yet Started

- All patients with DIPG or high-grade gliomas (2 – 22 years of age), following radiotherapy
- Paxalisib given once daily, orally, as monotherapy
- Primary objective is dose determination (Step 1) and time to progression (Step 2)
- Given no FDA-approved therapies for DIPG, a successful result could lead to discussion of early approval

# GBM AGILE is an adaptive multi-drug registrational study, with strong FDA support



# GBM AGILE features a two-stage design



- Primary endpoint of both stages is overall survival (OS); final analysis performed on all patients from both stages, compared to all control patients recruited to date
- Stage 1 is the primary efficacy analysis; Stage 2 is a confirmatory component
- Study is designed to provide definitive data to support product registration if a candidate drug is efficacious

- Sponsored by Global Coalition for Adaptive Research (GCAR), a 501(c)(3) non-profit
- Paxalisib expected to be second drug to join the study
- Extensive funding support from National Brain Tumor Society, Cure Brain Cancer Foundation, and other bodies

## Current Status

- GBM AGILE: Recruiting
- Paxalisib Participation: In planning, with enrolment expected to commence in Q2 / Q3 CY2020

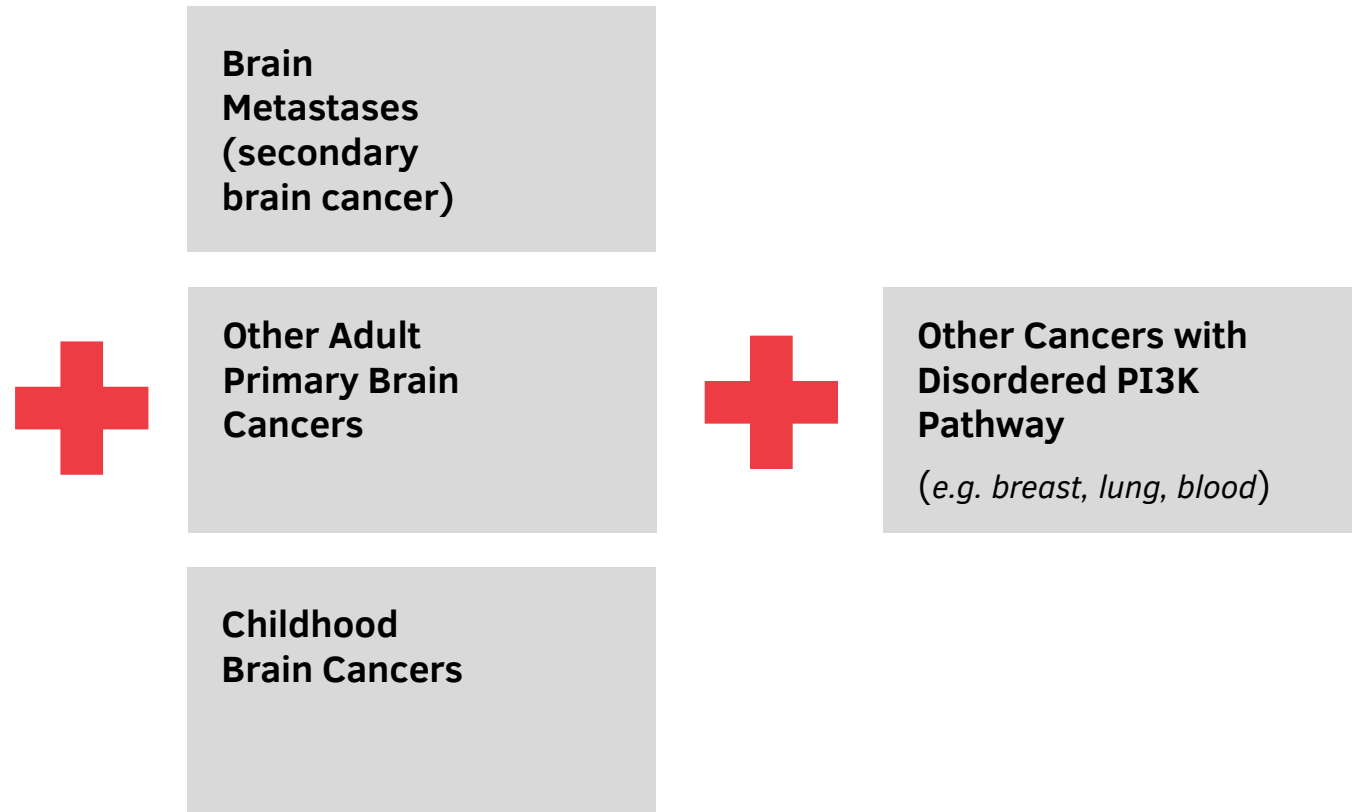


# Brain cancer represents a significant commercial opportunity for paxalisib with limited competition

## Path to Market



## Expansion Opportunities



## 'Blue Sky' Potential

**Other Cancers with Disordered PI3K Pathway**  
*(e.g. breast, lung, blood)*

**Cantrixil**

Phase I

Ovarian Cancer

# A second program, Cantrixil, is currently in a phase 1 study in ovarian cancer, with data reporting this year



## Part A: Dose Escalation

- 3 to 42 patients in up to 8 cohorts
- Seeks to establish maximum tolerated dose and understand safety profile

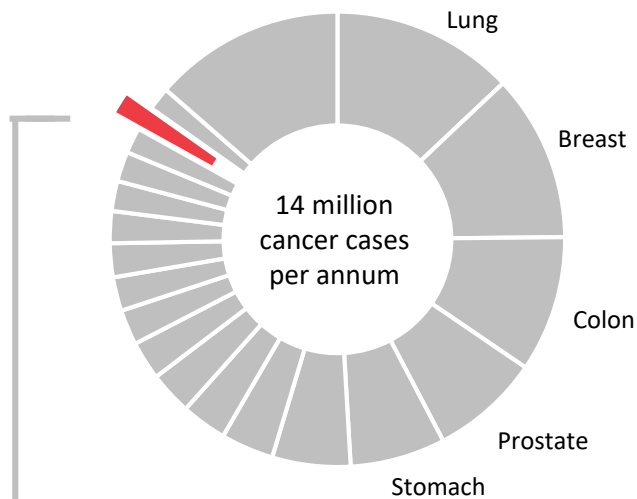


## Part B: Dose Expansion

- 12 patients, all at MTD
- Seeks to provide potential efficacy signals
- Near full recruitment

- MTD of 5 mg / kg established
- Advanced, platinum-resistant population
- 2 / 9 patients (22%) with partial response (PR) on combination with chemotherapy
- PFS = 5.5 months (versus 3.4 months for historical controls)
- Mainly low-grade GI toxicities

# Ovarian cancer remains a disease of high unmet medical need



**Ovarian Cancer**  
239,000 cases per annum worldwide

Indicative Market Opportunity  
**US\$ 1.5 billion**

Cause of death for  
**1 in 100**  
women

**>60%**  
of patients have disease spread at diagnosis

**10%**  
of cases are primarily genetic in origin

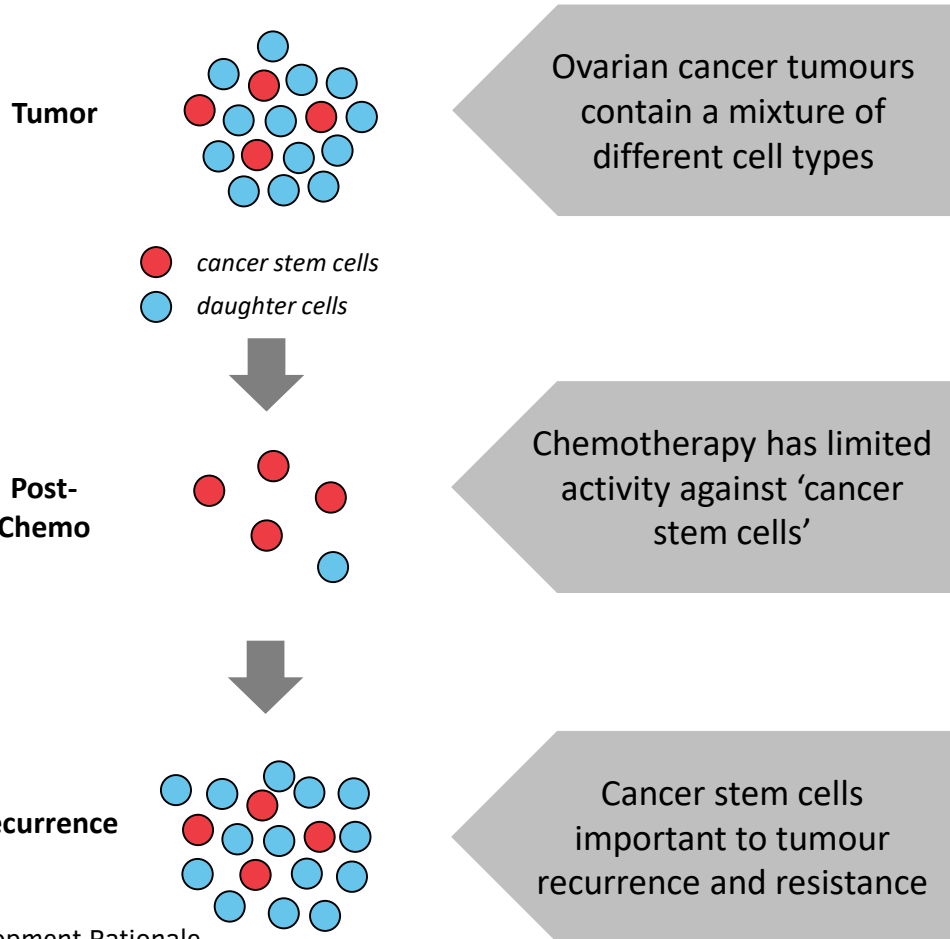
**80%**  
of patients are over 50 years of age

Five-year survival  
**45%**  
(breast cancer: 90%)

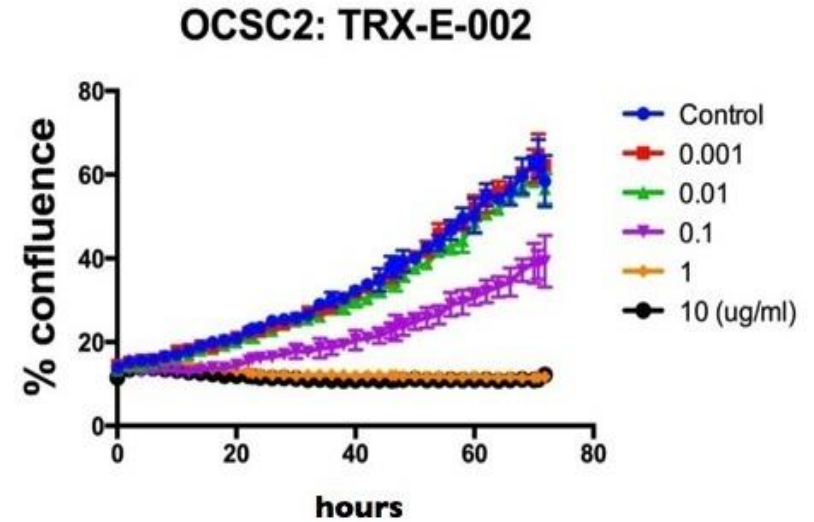
**Chemotherapy only curative in ~20% of ovarian cancers**

**More than half of patients with advanced disease will recur within 1-4 years**

# Cantrixil has been developed to target 'cancer stem cells' which are often resistant to chemotherapy



Development Rationale



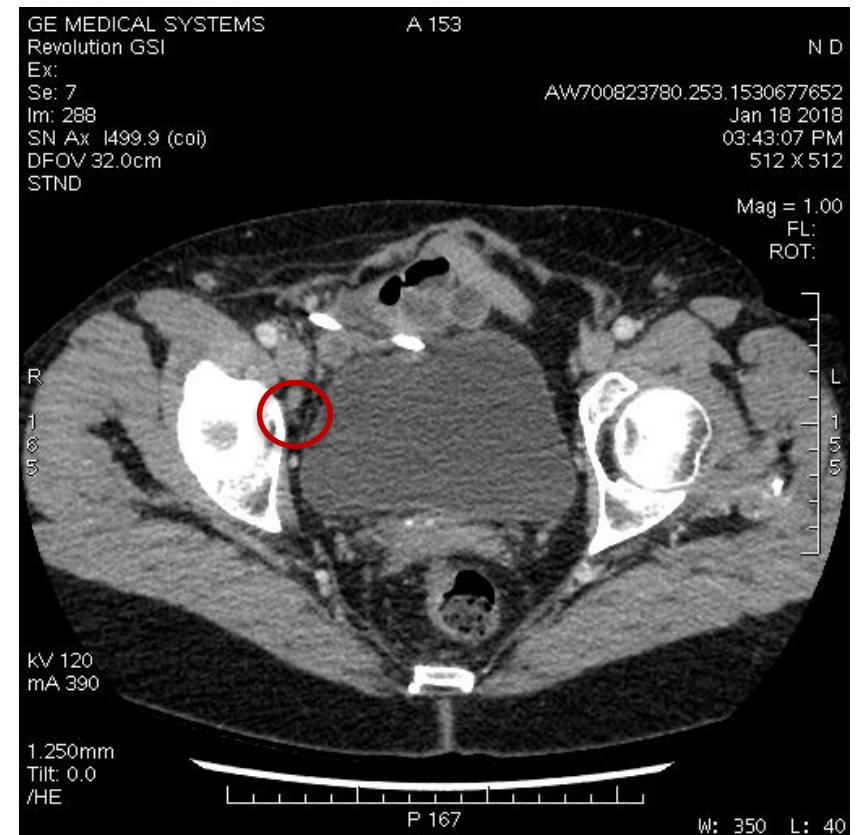
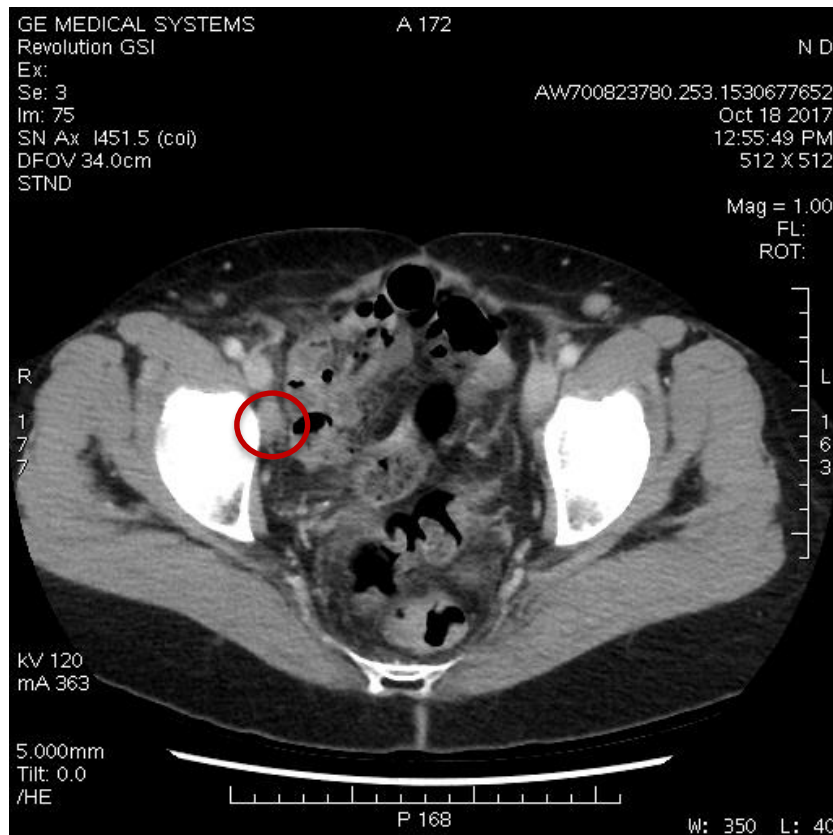
**Cantrixil shows dose-dependent inhibition of CD44<sup>+</sup> / My88<sup>+</sup> ovarian cancer stem cells**

**Yale** | Data courtesy of Prof Gil Mor, Yale University

# Part A has already shown evidence of activity with several partial responders to date

October 2017 (baseline)

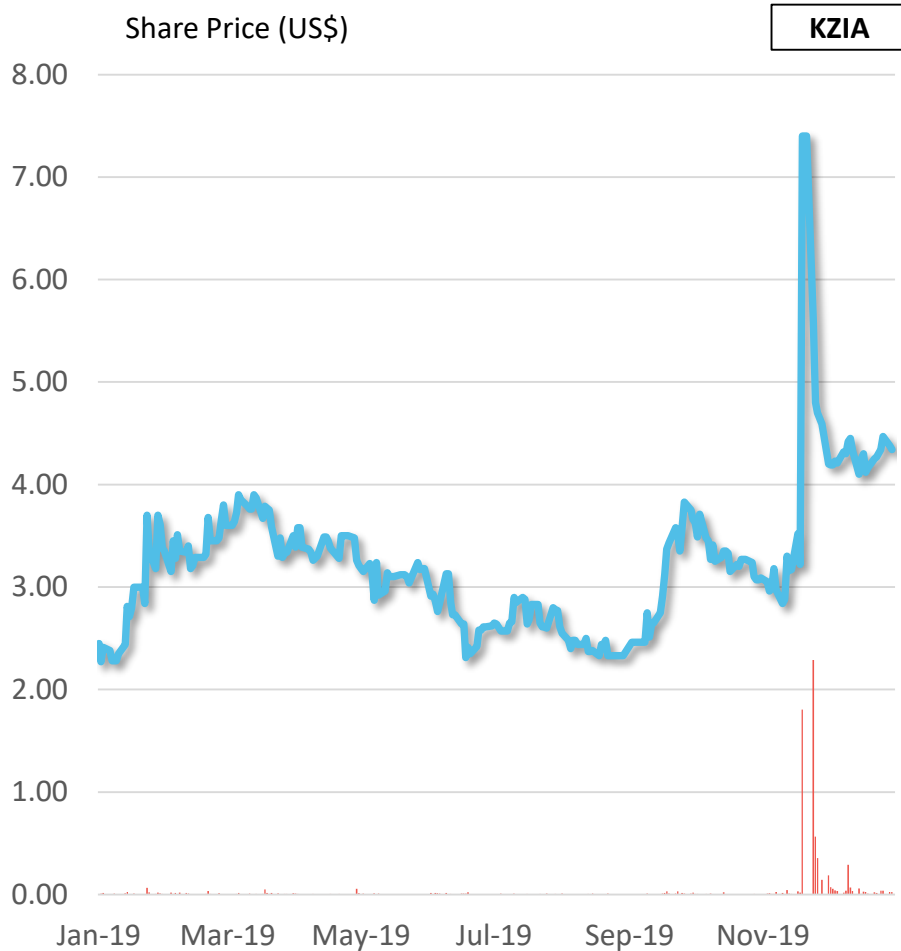
January 2018



Source: images courtesy of Professor Jim Coward, Icon Cancer Centre

# Corporate Summary

# Recent institutional placement leaves the company well funded for next round of data read-outs



<b>Market Capitalisation</b>	~US\$ 35 million
<b>Listing</b>	NASDAQ: KZIA (1:10 ratio) ASX: KZA

**Successful placement in October 2019**

<b>Current Assets</b> (30 June 2019)		AU\$ 7.5 million
	+	
<b>Institutional Placement</b> (October 2019)		AU\$ 4.0 million
	↓	
<i>Funded for multiple value-driving data readouts during 1H 2020</i>		



# A strong team brings international experience in big pharma and early-stage biotech

## Board



**Iain Ross**  
Chairman

*Executive and Board roles in pharma and small biotech*



**Bryce Carmine**  
Deputy Chairman

*36 years executive experience in Eli Lilly*



**Steven Coffey**  
Non-Executive Director

*Chartered accountant with extensive governance experience*



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

*Physician / MBA; Extensive drug development experience*



## Scientific Advisory Board



**Professor Sir Murray Brennan**  
Emeritus Chairman of Cancer Surgery at Memorial Sloan Kettering Hospital, New York



**Dr Karen Ferrante**  
Former Chief Medical Officer at Millennium Pharmaceuticals



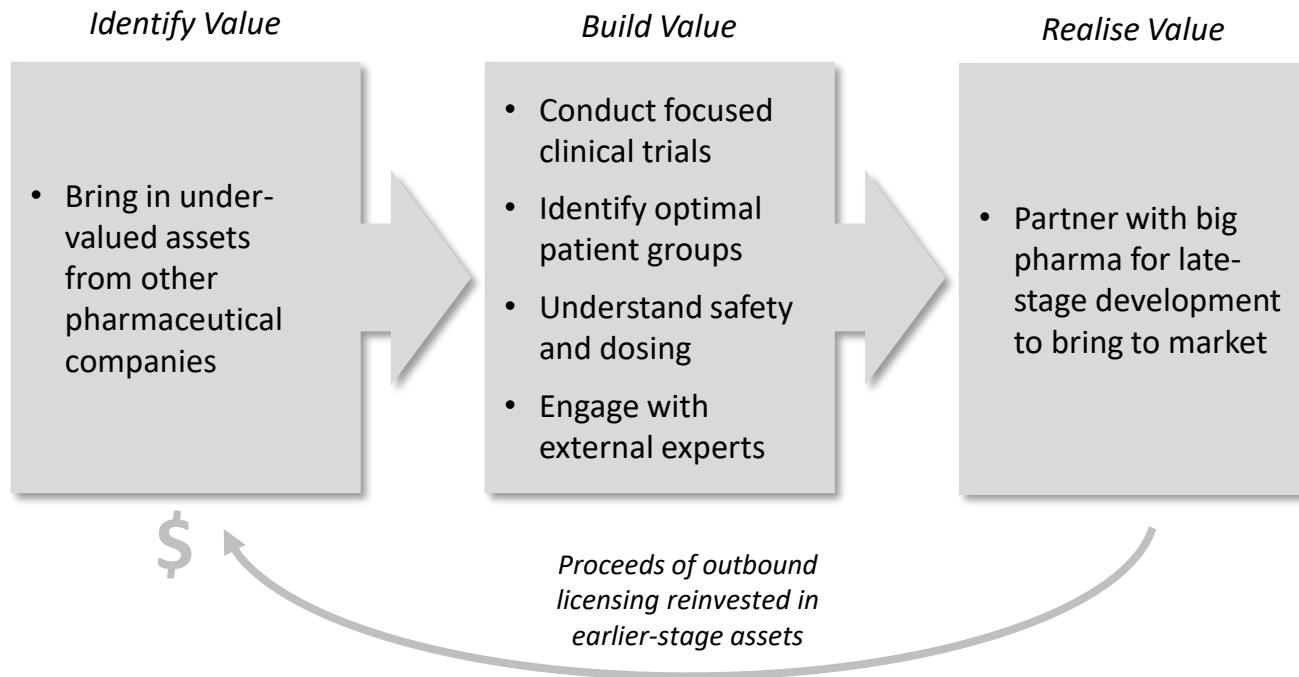
**Professor Peter Gunning**  
Head of School of Medical Sciences at University of New South Wales



**Professor Alex Matter**  
Former Global Head of Oncology Research at Novartis



# Kazia has implemented a strategy of developing high-quality assets from external sources













**Reduce cycle time and accelerate returns:** 2-4 years to get to value inflection

**Improve portfolio strength:** access the best global innovation









**Mitigate risk:** bring in assets which already partially de-risked

# The partnering market for new oncology drugs is active and driven by emerging data

## Select CY2019 Licensing Transactions

Licensee	Licensor	Stage	Asset(s)	Deal Value (US\$)
 GILEAD	 CARINA BIOSCIENCES	Discovery	Lipid kinase inhibitors	\$470M
 Johnson & Johnson	 Genmab	Preclinical	Anti-CD38 antibody	\$275M
 Jazz Pharmaceuticals	 RedX Pharma	Preclinical	RAS-RAF-MAPK inhibitors	\$207M
 Boehringer Ingelheim	 LUPIN	Clinical	MEK inhibitor	\$700M
 Mallinckrodt Pharmaceuticals	 SILENCE THERAPEUTICS	Discovery	Complement modulator	\$2.0B

## Select CY2019 M&A Transactions

Acquirer	Target	Stage	Asset(s)	Deal Value (US\$)
 Pfizer	 ARRAY BIOPHARMA	Commercial	BRAF inhibitors	\$11.0B
 MERCK	 Peloton Therapeutics	Clinical	HIF-2 $\alpha$ inhibitors	\$2.2B
 AMGEN	 NUEVOLUTION	Discovery	Discovery platform	\$167M
 Boehringer Ingelheim	 AMAL THERAPEUTICS	Clinical	Cancer vaccine platform	\$367M

# The next six months will be an exciting period for Kazia, and a crucial inflection point for our programs

<b>February 2020</b>	Half-Year Financial Report
<b>1Q CY2020</b>	Completion of patient dosing in Cantrixil phase 1 study
<b>1Q CY2020</b>	Completion of recruitment to paxalisib phase 2 study in glioblastoma
<b>2Q CY2020</b>	Potential initial efficacy data from St Jude paxalisib DIPG study
<b>2Q CY2020</b>	Potential initial efficacy data from Dana-Farber paxalisib breast cancer mets study
<b>2Q CY2020</b>	Further efficacy data from ongoing phase 2 study of paxalisib in glioblastoma
<b>2Q CY2020</b>	Further efficacy data from ongoing phase I study of Cantrixil in ovarian cancer
<b>2Q / 3Q CY2020</b>	Commencement of recruitment to GBM AGILE pivotal study
<b>3Q CY2020</b>	Full-Year Financial Statements

Note: all milestones are indicative and subject to periodic revision in light of operational factors and emerging data



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