

ASX RELEASE

19 April 2021

## KAZIA CORPORATE PRESENTATION

**Sydney, 19 April 2021** – Kazia Therapeutics Limited (ASX: KZA; NASDAQ: KZIA), an Australian oncology-focused biotechnology company, is pleased to provide its latest corporate presentation, including updates for its newly in-licensed asset, EVT801.

[ENDS]

### About Kazia Therapeutics Limited

Kazia Therapeutics Limited (NASDAQ: KZIA; ASX: KZA) is an oncology-focused drug development company, based in Sydney, Australia.

Our lead program is paxalisib, a brain-penetrant 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 commenced recruitment to GBM AGILE, a pivotal study in glioblastoma, in January 2021. Seven additional studies are active in other forms of brain cancer. Paxalisib was granted Orphan Drug Designation for glioblastoma by the US FDA in February 2018, and Fast Track Designation for glioblastoma by the US FDA in August 2020. In addition, paxalisib was granted Rare Pediatric Disease Designation and Orphan Designation by the US FDA for DIPG in August 2020.

Kazia is also developing EVT801, a small-molecule inhibitor of VEGFR3, which was licensed from Evotec SE in April 2021. Preclinical data has shown EVT801 to be active against a broad range of tumour types and has provided compelling evidence of synergy with immunoncology agents. A phase I study is expected to begin in CY2021.

For more information, please visit [www.kaziatherapeutics.com](http://www.kaziatherapeutics.com) or follow us on Twitter @KaziaTx.

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

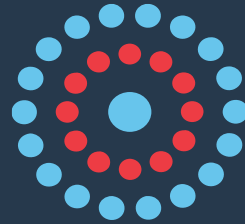
### Board of Directors

**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 Diversified, Clinical-Stage  
Oncology Drug Development  
Company

Corporate Introduction

April 2021

# 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 substantial risks and uncertainties, not all of which may be known at the time. All statements contained in this presentation, other than statements of historical fact, including statements regarding our strategy, research and development plans, collaborations, future operations, future financial position, future revenues, projected costs, prospects, plans, and objectives of management, are forward-looking statements. Not all forward-looking statements in this presentation are explicitly identified as such.

Many factors could cause the actual results of the Company to differ materially from the results expressed or implied herein, and you should not place undue reliance on the forward-looking statements. Factors which could change the Company's expected outcomes include, without limitation, our ability to: advance the development of our programs, and to do so within any timelines that may be indicated herein; the safety and efficacy of our drug development candidates; our ability to replicate experimental data; the ongoing validity of patents covering our drug development candidates, and our freedom to operate under third party intellectual property; our ability to obtain necessary regulatory approvals; our ability to enter into and maintain partnerships, collaborations, and other business relationships necessary to the progression of our drug development candidates; the timely availability of necessary capital to pursue our business objectives; and our ability to attract and retain qualified personnel; changes from anticipated levels of customer acceptance of existing and new products and services and other factors.

Although the Company believes that the expectations reflected in such forward-looking statements are reasonable, there can therefore be no assurance that such expectations will prove to be correct. The Company has no obligation as a result of this presentation to clinical trial outcomes, sales, partnerships, 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, or marketing existing products.

In addition, the extent to which the COVID-19 outbreak continues to impact our workforce and our discovery research, supply chain and clinical trial operations activities, and the operations of the third parties on which we rely, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration and severity of the outbreak, additional or modified government actions, and the actions that may be required to contain the virus or treat its impact.

Any forward-looking statements contained in this presentation speak only as of the date this presentation is made, and we expressly disclaim any obligation to update any forward-looking statements, whether because of new information, future events or otherwise.

# Company Overview



## Diversified, Clinical-Stage Oncology Pipeline

### Paxalisib

- Brain-penetrant PI3K / mTOR inhibitor
- International pivotal study for glioblastoma underway

### EVT-801

- First-in-class selective VEGFR3 inhibitor
- Potential applications in multiple solid tumors
- Phase I clinical trial to commence in CY2021



## Substantial Commercial Opportunity

- Glioblastoma represents ~US\$ 1.5 billion commercial market
- 5x additional clinical trials ongoing with paxalisib in other forms of brain cancer
- Commercial partnership in place for paxalisib in Greater China with Simcere Pharmaceutical
- High-potential indications for EVT-801 include renal cell carcinoma, hepatocellular carcinoma, and soft tissue sarcoma

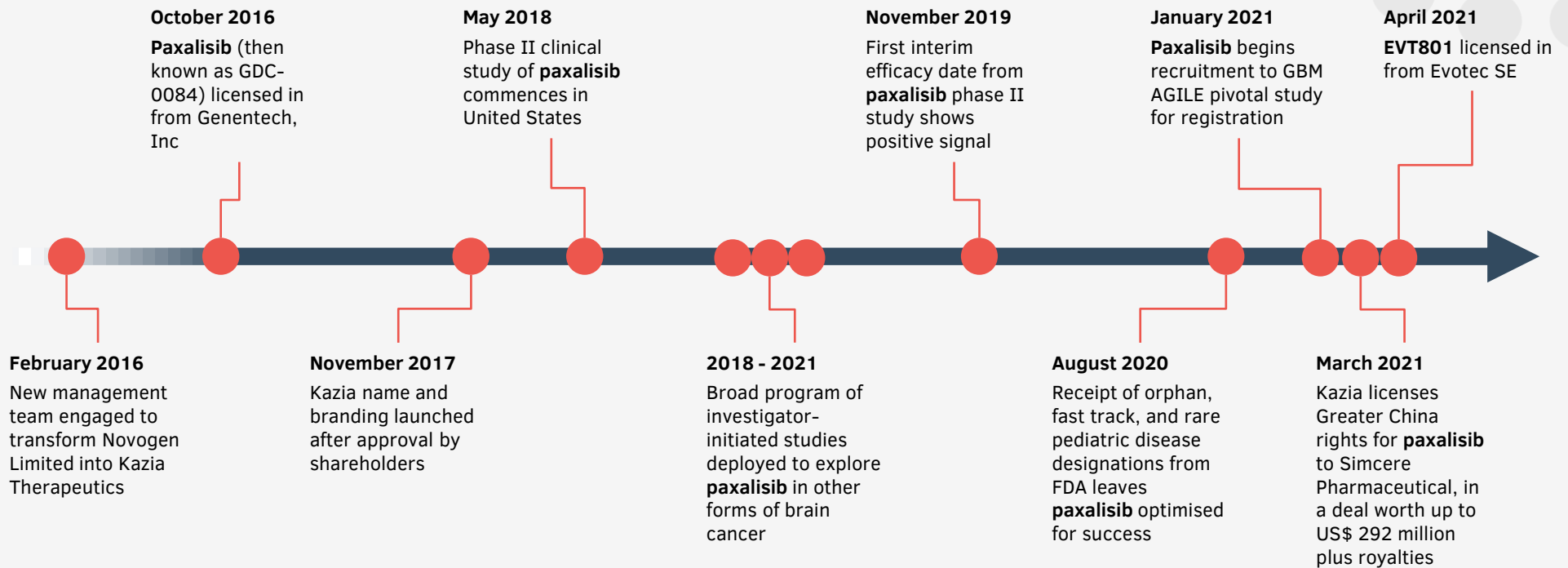


## Strong Corporate Fundamentals

- Listed on ASX (KZA) and on NASDAQ (KZIA)
- ~US\$ 160 million market cap.
- Cash position @ 31 December 2020: ~US\$ 15 million
- Lean operating model, with ~75% of cashflow devoted directly to clinical trials
- Multiple fundamental-driven institutional investors on registry

# Corporate History

*Kazia has shown remarkable growth in five years*



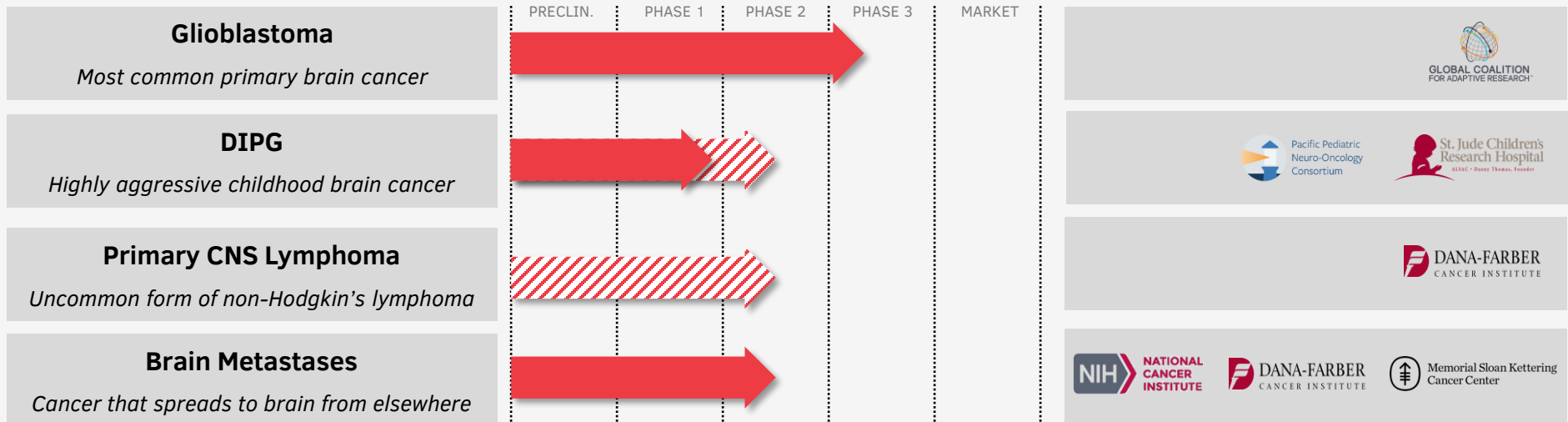
# Pipeline

Two world-class assets in clinical trials by end CY2021

## Paxalisib (GDC-0084)

Small molecule, brain-penetrant inhibitor of PI3K / mTOR

licensed from:



## EVT801

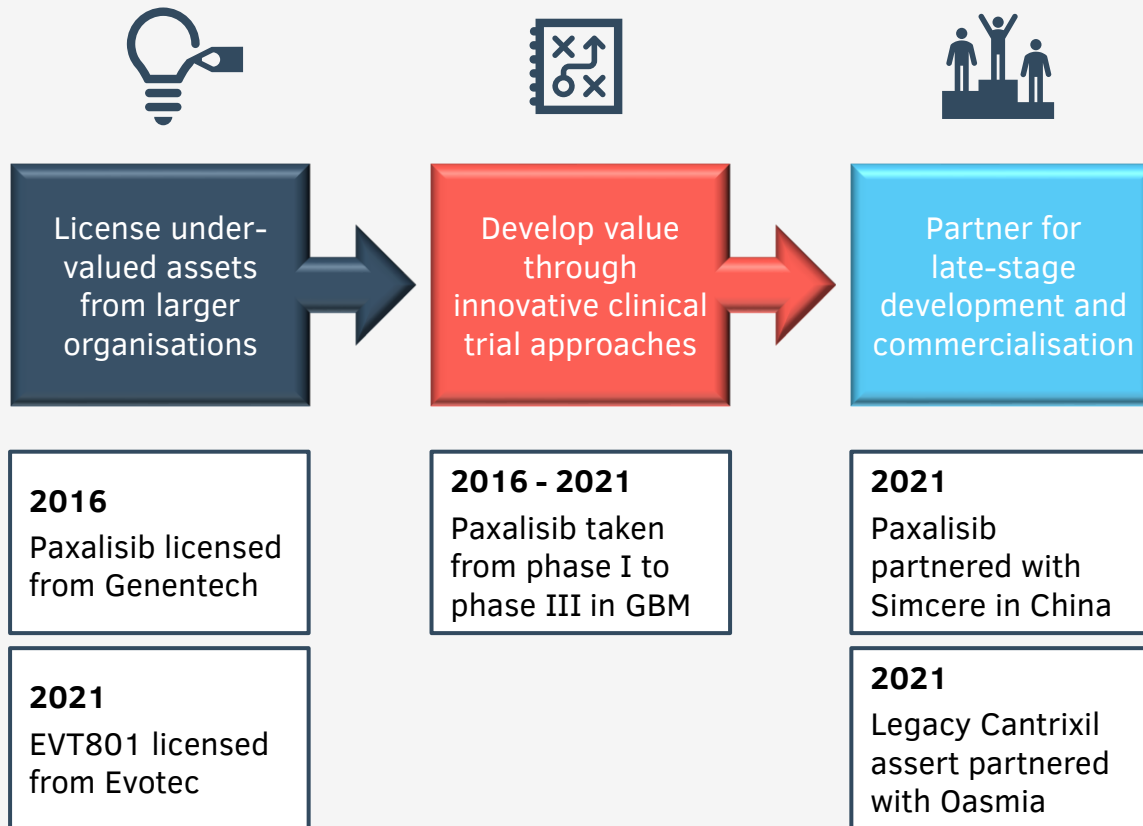
Small molecule inhibitor of VEGFR3

licensed from:



# Operating Model

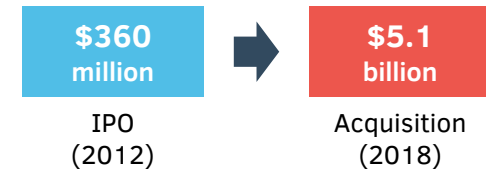
*Partnering-based approach harnesses the best global research*



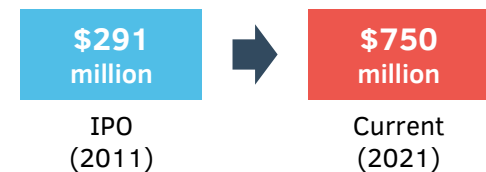
## A Proven Strategy



**Jun 2010** – licensed niraparib from Merck  
**Mar 2017** – Zejula® (niraparib) approved by FDA  
**Dec 2018** – Tesaro acquired by GSK



**Jun 2011** – licensed rucaparib from Pfizer  
**Apr 2018** – Rubraca® (rucaparib) approved



# Leadership

## Extensive international drug development experience

### 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



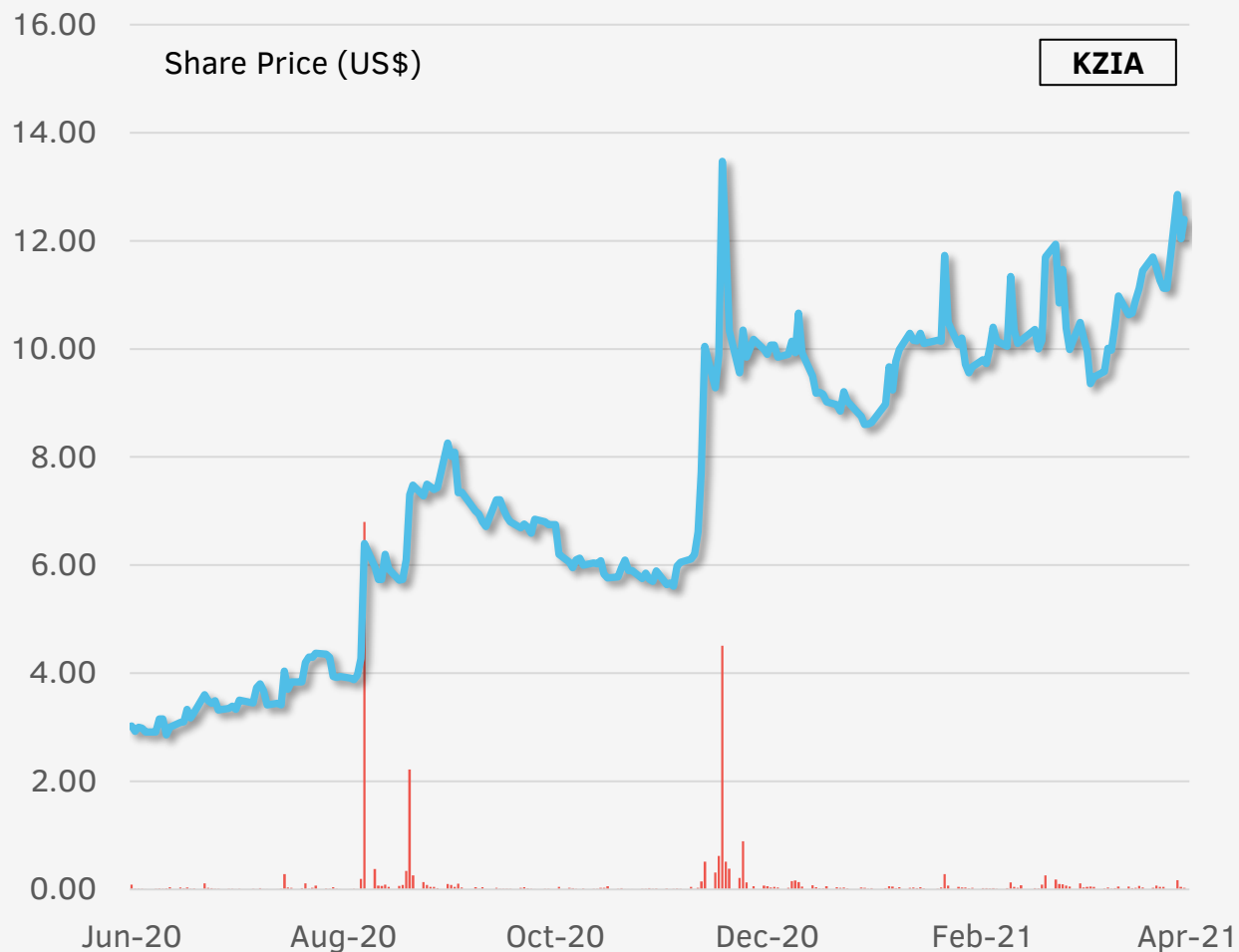
**Professor Alex Matter**  
Former Global Head of Oncology Research at Novartis





# Financial Metrics

*Value-driving news flow for investors*



<b>Market Capitalisation</b>	<b>US\$ 160M</b>
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## Listing

ASX (primary)	KZA
NASDAQ (ADSS @ 1:10 ratio)	KZIA
Shares on Issue	127M

<b>Balance Sheet</b>	<b>US\$</b>
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Cash (at 31 Dec 20)	~\$15M
Partnering Income (Q1 CY21)	\$15M
FY20 Expenditure	~\$9M

## Substantial Shareholders

Willoughby Capital	16%
Quest Asset Partners	9%
Platinum Asset Management	6%
UniSuper	6%
Board and Management	2%

# CY2021 Milestones and Newsflow

## *Multiple catalysts across two clinical programs*

Commence of recruitment to GBM AGILE pivotal study for <b>paxalisib</b>	January 2021	✓
Out-license of <b>Cantrixil</b> legacy asset to Oasmia Pharmaceutical	March 2021	✓
Partnership for <b>paxalisib</b> in Greater China with Simcere Pharmaceutical	March 2021	✓
<b>Paxalisib</b> interim phase II glioblastoma data at AACR Annual Meeting	April 2021	✓
Global in-license of <b>EVT801</b> from Evotec SE	April 2021	✓
Initial interim data from <b>paxalisib</b> phase II BCBM trial at Dana-Farber	2H CY2021	
Commence of recruitment to PNOC <b>paxalisib</b> combination study in DIPG	2H CY2021	
Commence of recruitment to <b>paxalisib</b> phase II PCNSL study at Dana-Farber	2H CY2021	
Initial interim data from <b>paxalisib</b> phase II brain mets study by Alliance Group	2H CY2021	
Initial interim data from <b>paxalisib</b> phase I brain mets study at Sloan-Kettering	2H CY2021	
Final data from <b>paxalisib</b> phase II glioblastoma trial	2H CY2021	
Commence recruitment to <b>EVT801</b> phase I trial	2H CY2021	

Note: all guidance is indicative, and subject to amendment in light of changing conference schedules, operational considerations, etc.

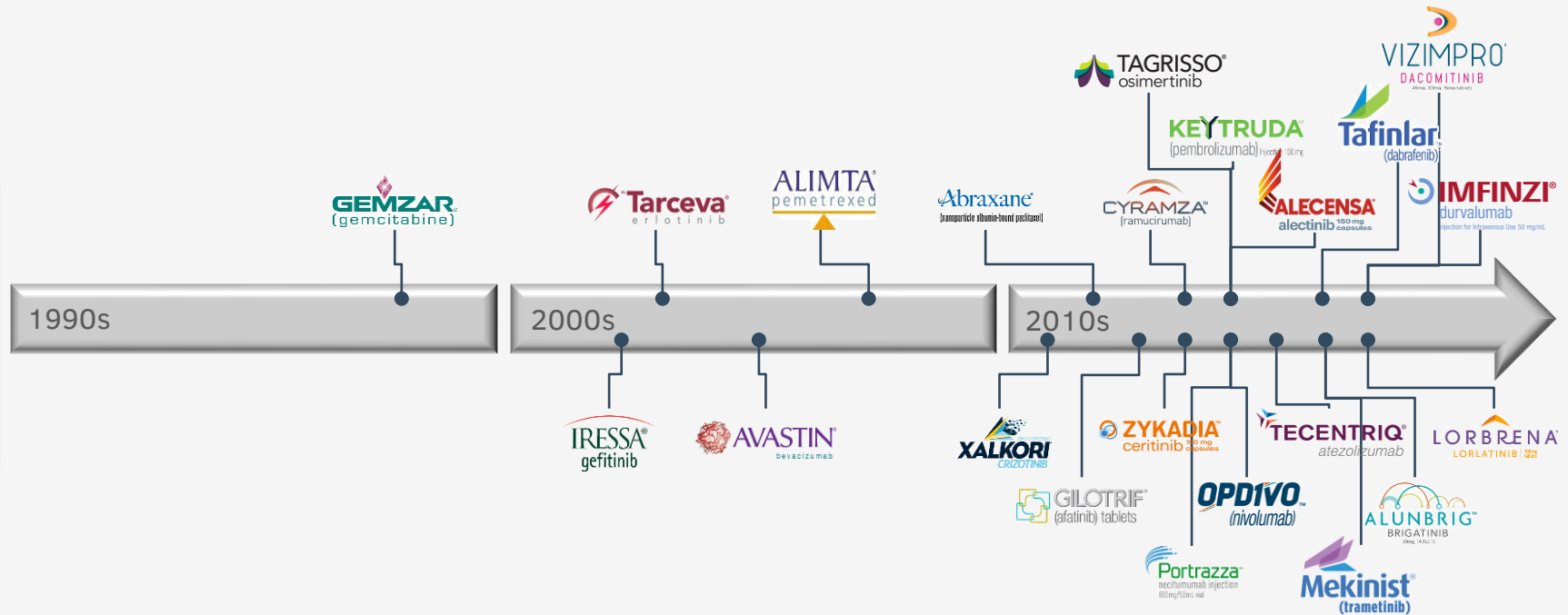
# Paxalisib

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Brain Cancer  
Phase III

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

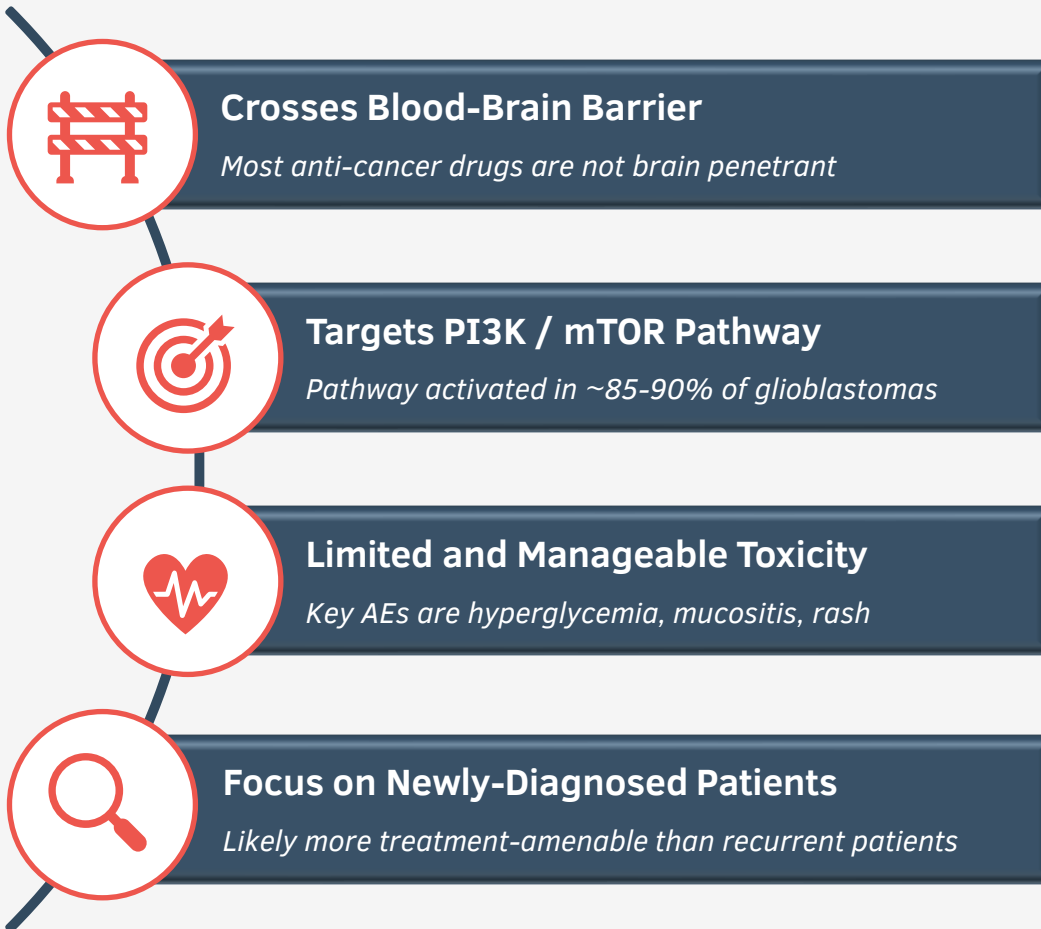
## Lung Cancer



## Brain Cancer (glioblastoma)



# Paxalisib was designed specifically to overcome key challenges in the treatment of brain cancer



## **Oral Presentation**

15mg capsule, taken once daily; no significant food effect

## **Strong IP Protection**

Composition-of-matter to 2031 in most jurisdictions

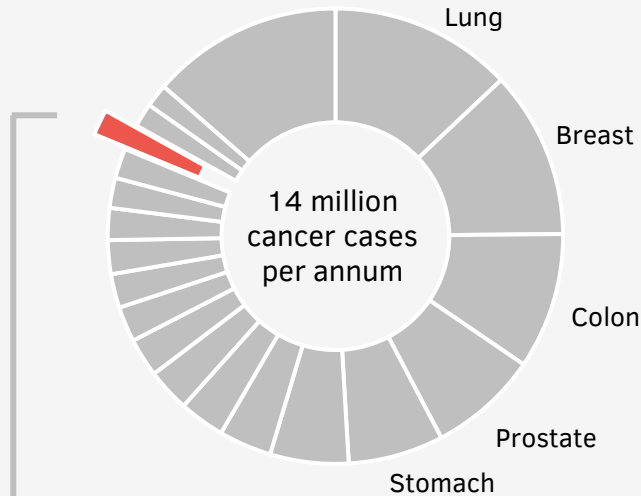
## **Low Cost of Goods**

Straightforward manufacture with excellent stability at controlled ambient

## **Limited Potential for Interactions**

Has been successfully combined with other targeted therapies and RTx

# 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\$ 1.5 billion**

**No clear cause**  
or strong risk factors

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

No clear improvement in prognosis for  
**20 years**

**3-4 months**  
untreated survival

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

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



Sen. John McCain



Sen. Ted Kennedy



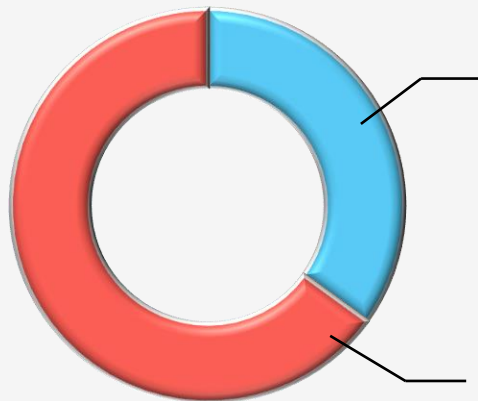
Beau Biden



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*



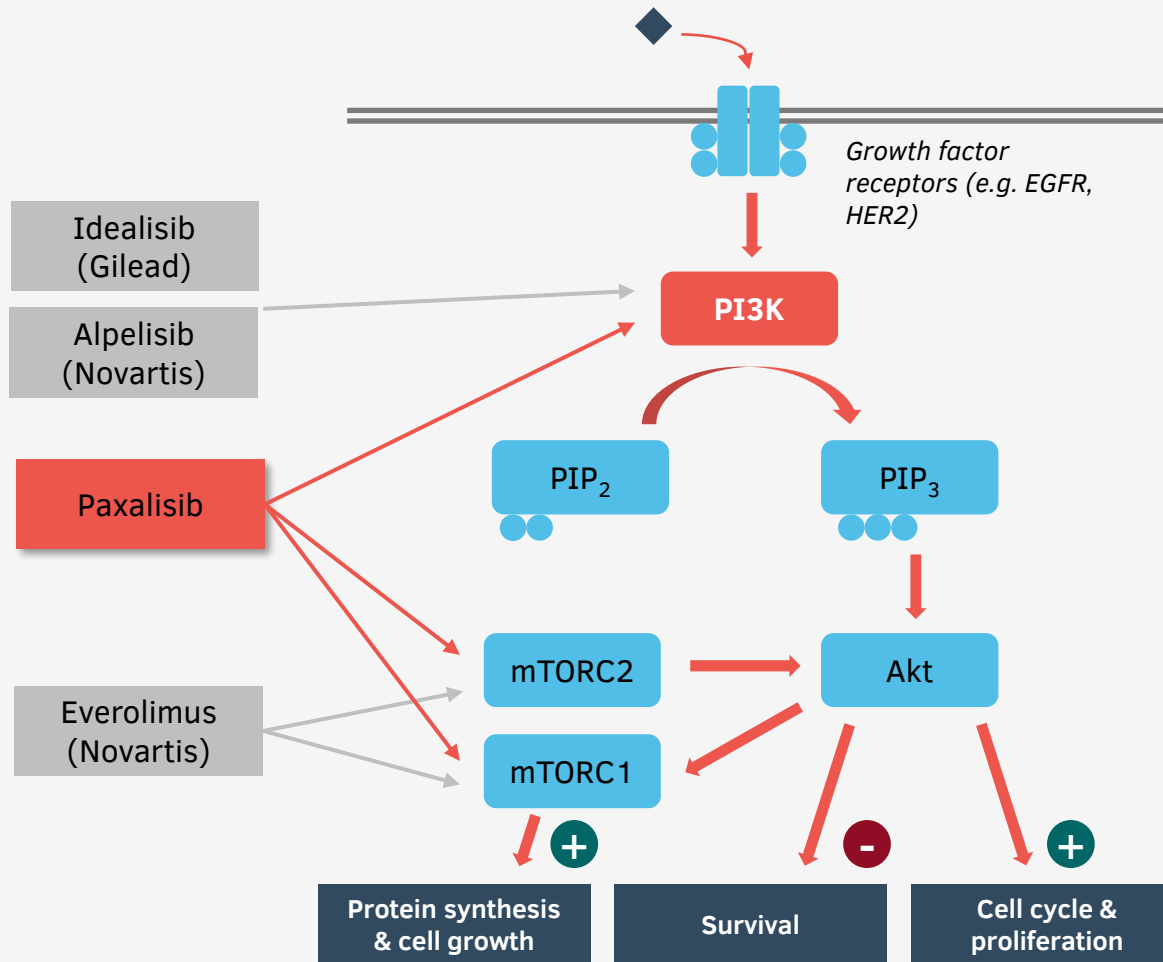
**Paxalisib is being developed primarily for the ~65% of newly-diagnosed GBM patients who will not respond to existing chemotherapy with temozolomide**

*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

# The PI3K / Akt / mTOR pathway is a critical signalling mechanism for many tumor types





# The PI3K inhibitor 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)



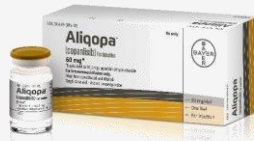
*Crosses  
Blood-  
Brain  
Barrier*

*Safety*

Potentially fatal  
liver toxicity and  
diarrhoea



Aliqopa  
(copanlisib)



FDA Approved  
**September 2017**  
(blood cancers)



Potentially fatal  
infections



Copiktra  
(duvelisib)



FDA Approved  
**October 2018**  
(blood cancers)



Potentially fatal  
infections and  
diarrhoea



Piqray  
(alpelisib)



FDA Approved  
**May 2019**  
(breast cancer)



Modest toxicities to  
date



Ukoniq  
(umbralisib)



FDA Approved  
**February 2021**  
(blood cancers)



Serious infections,  
hepatotoxicity, and  
diarrhoea



**paxalisib**

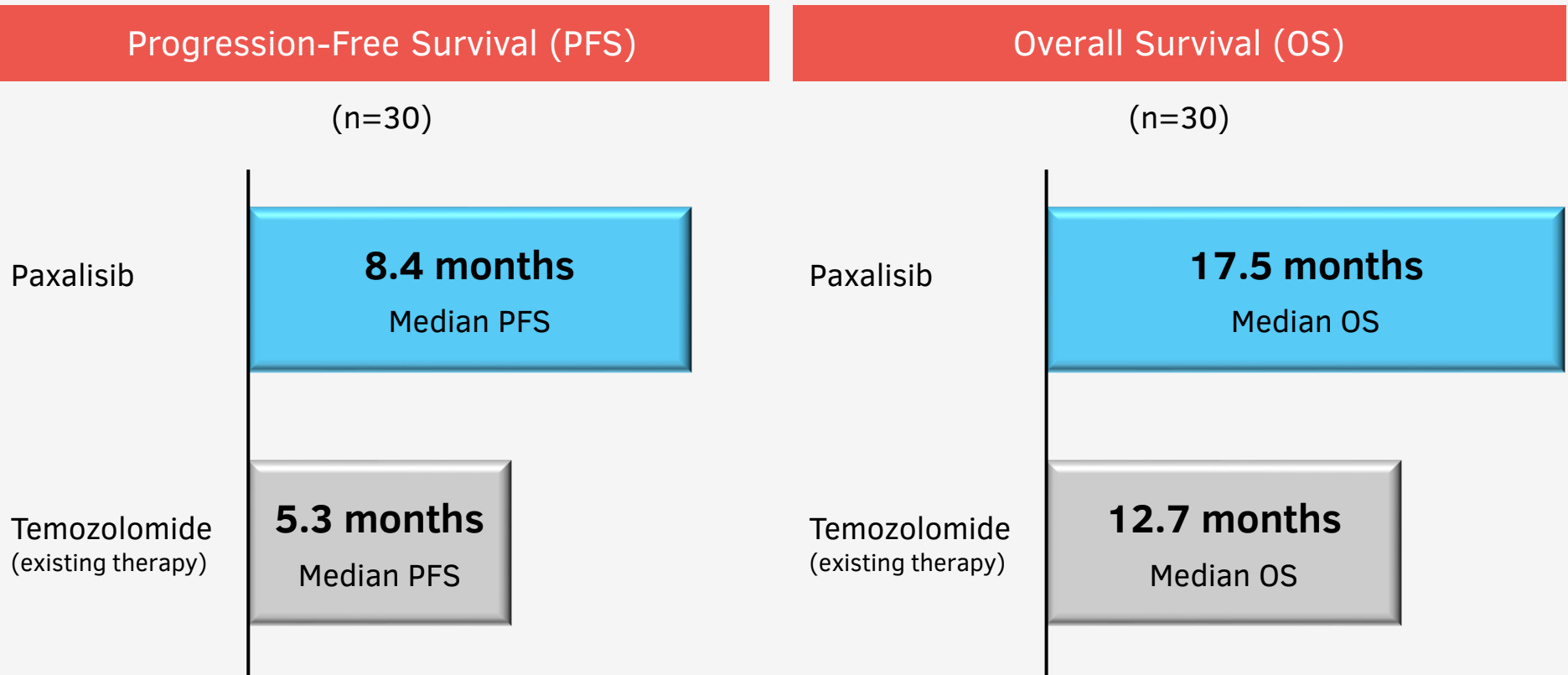


In pivotal study for  
FDA Approval in  
glioblastoma



Modest toxicities to  
date

# Latest phase II data compares well to historical data for temozolomide (existing standard of care)



Presented at Society for Neuro-Oncology Annual Meeting, November 2020

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









# Toxicities are generally mild to moderate, entirely reversible, and manageable with readily-available therapies

Number of Patients at 60mg (n=24) Experiencing AEs 'Possibly' or 'Likely' Related to Paxalisib (affecting ≥2 patients)

Term	Gr 1	Gr 2	Gr 3	Gr 4	Total (%)
Rash	4	6	7		17 (71%)
Fatigue	2	10	2		14 (58%)
Stomatitis	4	6	1		11 (46%)
Decreased appetite	5	5	1		11 (46%)
Nausea	3	5	1		9 (38%)
Hyperglycemia	1	2	5		8 (33%)
Diarrhea	5	1			6 (25%)
Decreased neutrophils	2	3		1	6 (25%)
Vomiting	3	2	1		6 (25%)
Decreased weight	3	2			5 (21%)
Decreased platelets	4	1			5 (21%)
Dehydration		4	1		5 (21%)
Dysgeusia		4			4 (17%)
Decr. lymphocytes	1	2			3 (13%)
Drug reaction			3		3 (13%)
Malaise	2	1			3 (18%)
Incr. cholesterol	2				2 (8%)
Pruritis	1		1		2 (8%)

Presented at Society for Neuro-Oncology Annual Meeting, November 2020

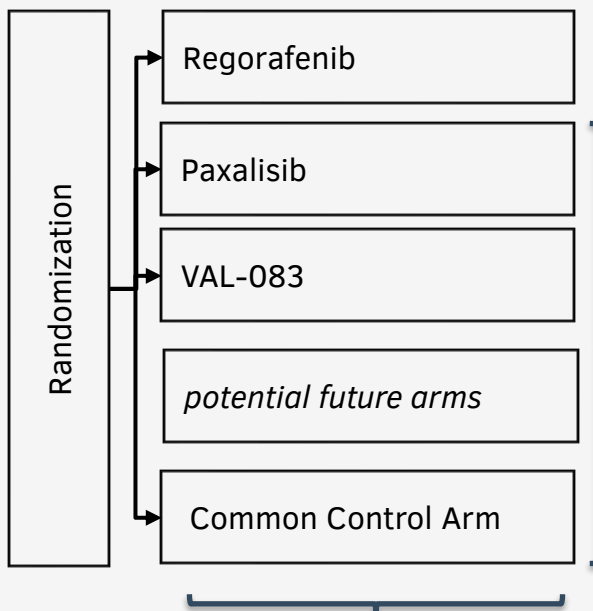
# A broad-based clinical program is underway across multiple forms of brain cancer

Registration	Indication	Phase	N	Status	Sponsor
<b>Primary Brain Cancer</b>					
<a href="#">NCT03522298</a>	Glioblastoma	II	30	Follow-up	 KAZIA THERAPEUTICS
<a href="#">NCT03970447</a>	Glioblastoma (GBM AGILE)	II / III	Up to 200 on paxalisib	Recruiting	 GLOBAL COALITION FOR ADAPTIVE RESEARCH™
<a href="#">NCT03696355</a>	DIPG and DMGs	I	27	Follow-up	 St. Jude Children's Research Hospital <small>ALSAC - Danny Thomas, Founder</small>
TBD	DIPG and DMGs	II	TBD	Start-up	 Pacific Pediatric Neuro-Oncology Consortium
TBD	Primary CNS Lymphoma	II	TBD	Start-up	 DANA-FARBER CANCER INSTITUTE
<b>Secondary (Metastatic) Brain Cancer</b>					
<a href="#">NCT04192981</a>	Brain Metastases (combination with radiotherapy)	I	Up to 36	Recruiting	 Memorial Sloan Kettering Cancer Center
<a href="#">NCT03765983</a>	Breast Cancer Brain Metastases (combination with trastuzumab)	II	Up to 47	Recruiting	 DANA-FARBER CANCER INSTITUTE
<a href="#">NCT03994796</a>	Brain Metastases ('Alliance' multi-drug study)	II	50	Recruiting	 NIH NATIONAL CANCER INSTITUTE

# GBM AGILE international pivotal study is underway, and is expected to provide the basis for regulatory approval

## Key Points

- A 'platform study', run independently of individual companies, designed to expedite the approval of new drugs for glioblastoma
- Multiple drugs are evaluated in parallel, saving time and money
- Not a 'winner-takes-all' approach: multiple drugs can succeed
- Cutting-edge 'adaptive design' avoids redundant recruitment, expediting path to market
- Strong support from FDA and key opinion leaders



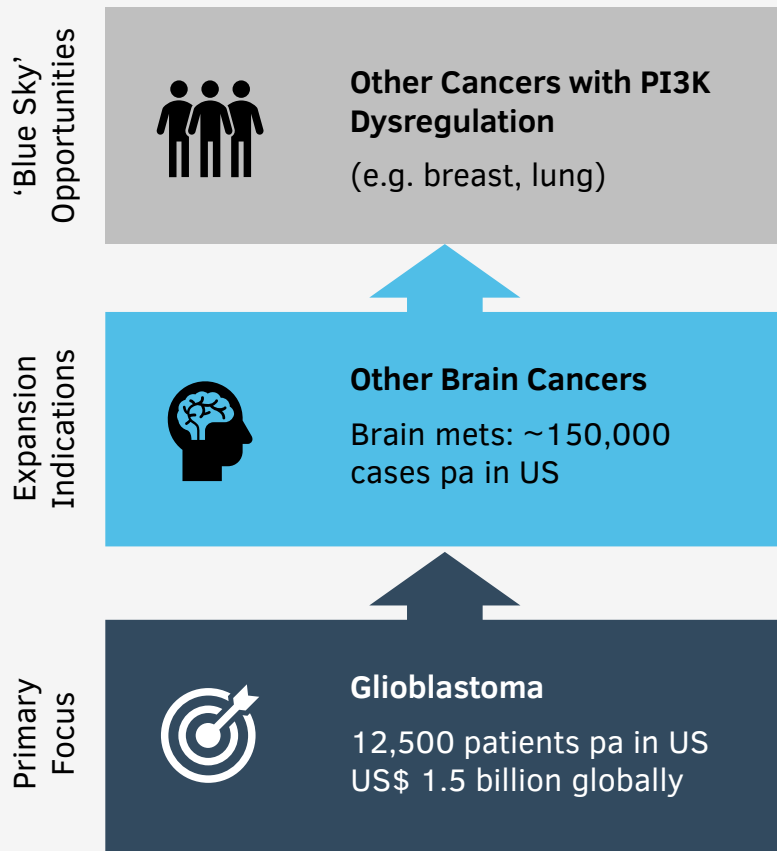
**1** Adaptive study design limits number of subjects to that required to demonstrate efficacy, eliminating redundancy

**2** Comparison against a common control arm reduces overall subject numbers, saving time and cost (no drug vs. drug comparison)

**3** Economies of scale due to multiple participating drugs allows for large site pool, robust study infrastructure, and reduced cost

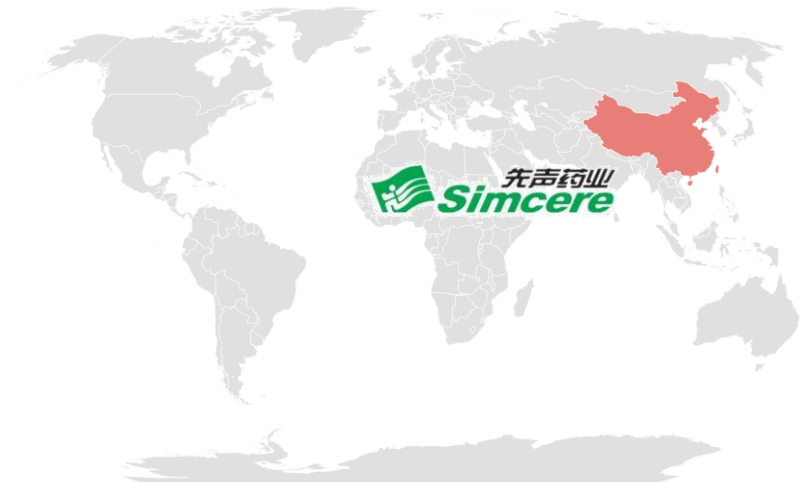
**4** Primary endpoint is overall survival (OS), the 'gold standard' for approval of new cancer drugs

# Commercial opportunity is substantial, with one commercial partnership already in place



## Partnership with Sincere Pharmaceutical for Greater China signed in March 2021

Sincere will develop and commercialise paxalisib for a territory comprising > 1.2 billion people and ~10% of the global pharmaceutical market



# Key Points

- 1 Well-understood mechanism (PI3K inhibition) but unique differentiating feature (brain penetration)
- 2 Positive phase II data in glioblastoma, supported by very strong preclinical package
- 3 Fully-funded international registration study underway with support of FDA and leading clinicians
- 4 Broad trial program underway with world-class centres in other forms of brain cancer; de-risks lead indication
- 5 Targeting a US\$ 1.5B market with limited competition and very high unmet-need











# EVT801

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Solid Tumors  
Pre-Phase I



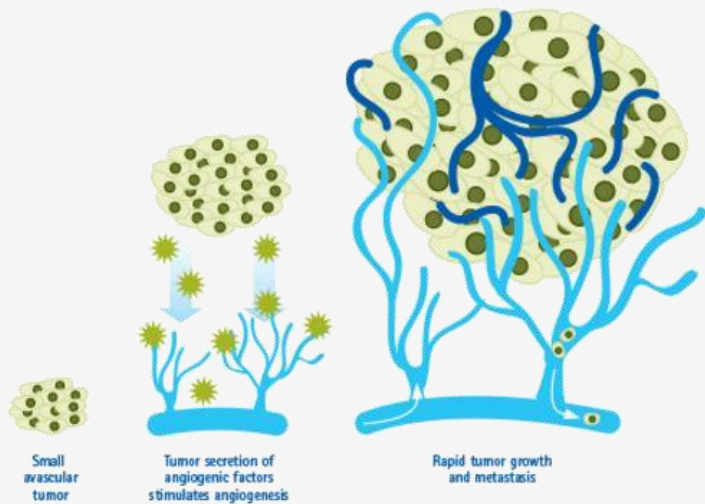
# Targeting angiogenesis is a well-established approach in the treatment of cancer

Product	Company	Target	Indications	Annual Sales (US\$)*
 <p><b>AVASTIN</b><sup>®</sup> bevacizumab 100 MG/4 ML INJECTION FOR IV USE</p>	 <p><b>Genentech</b> A Member of the Roche Group</p>	VEGF-A	<ul style="list-style-type: none"> <li>• Colorectal cancer</li> <li>• Lung cancer</li> <li>• Breast cancer</li> <li>• Other cancers</li> </ul>	<b>\$7 billion</b>
 <p><b>Nexavar</b><sup>®</sup> (sorafenib) tablets</p>	 <p><b>BAYER</b></p>	VEGFR PDGFR RAF kinases	<ul style="list-style-type: none"> <li>• Hepatocellular carcinoma</li> <li>• Renal cell carcinoma</li> <li>• Thyroid cancer</li> </ul>	<b>\$1 billion</b>
 <p><b>SUTENT</b><sup>®</sup> sunitinib maleate capsules</p>	 <p><b>Pfizer</b></p>	VEGFR PDGFR	<ul style="list-style-type: none"> <li>• Renal cell carcinoma</li> <li>• Gasto-intestinal stromal tumor</li> </ul>	<b>\$750 million</b>
 <p><b>Votrient</b><sup>®</sup> pazopanib tablets (200 mg)</p>	 <p><b>NOVARTIS</b></p>	VEGFR PDGFR c-Kit FGFR	<ul style="list-style-type: none"> <li>• Renal cell carcinoma</li> <li>• Soft tissue sarcoma</li> </ul>	<b>\$1 billion</b>
 <p><b>Inlyta</b><sup>®</sup> axitinib 1mg and 5mg tablets</p>	 <p><b>Pfizer</b></p>	VEGFR c-Kit PDGFR	<ul style="list-style-type: none"> <li>• Renal cell carcinoma</li> </ul>	<b>\$400 million</b>

\*approximate, based on company filings and market data

# Despite their proven efficacy, angiogenesis inhibitors are limited by several key challenges

Angiogenesis inhibitors work by reducing the formation of **new blood vessels** around the tumor, starving it of vital nutrients needed for tumor growth, and limiting its ability to spread (metastasise) elsewhere in the body



1

## Tumor Hypoxia

Sustained tumor hypoxia activates adaptive mechanisms, leading to secondary resistance and tumor progression



**Limited Duration of Effect**

2

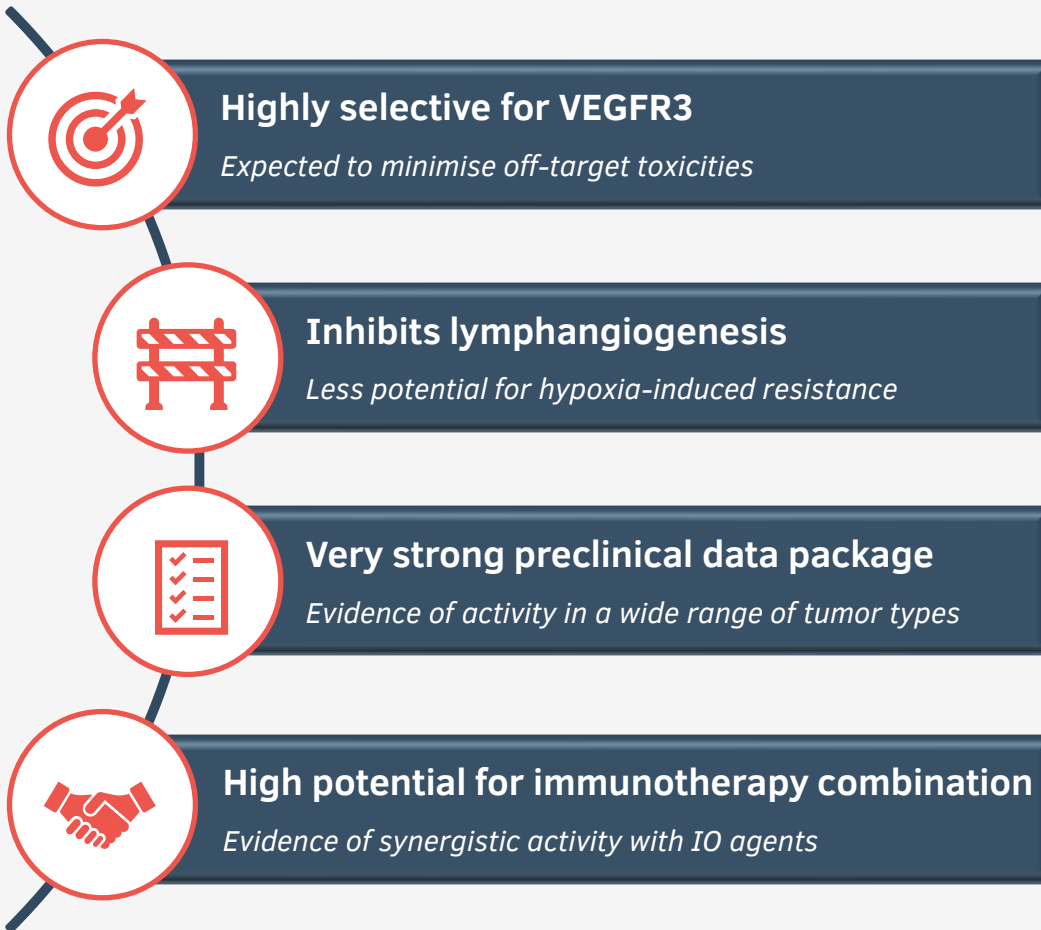
## Off-Target Activity

Most small molecule angiogenesis inhibitors have a broad range of pharmacological activities, leading to substantial toxicity (e.g. hand-foot syndrome)



**Significant Side Effects**

# EVT801 is a selective VEGFR inhibitor, primarily inhibiting lymphangiogenesis (formation of new lymphatic vessels)



## **Oral Presentation**

Administered by mouth once or twice daily

## **Strong IP Protection**

Composition-of-matter to 2032 / 2033 in most jurisdictions

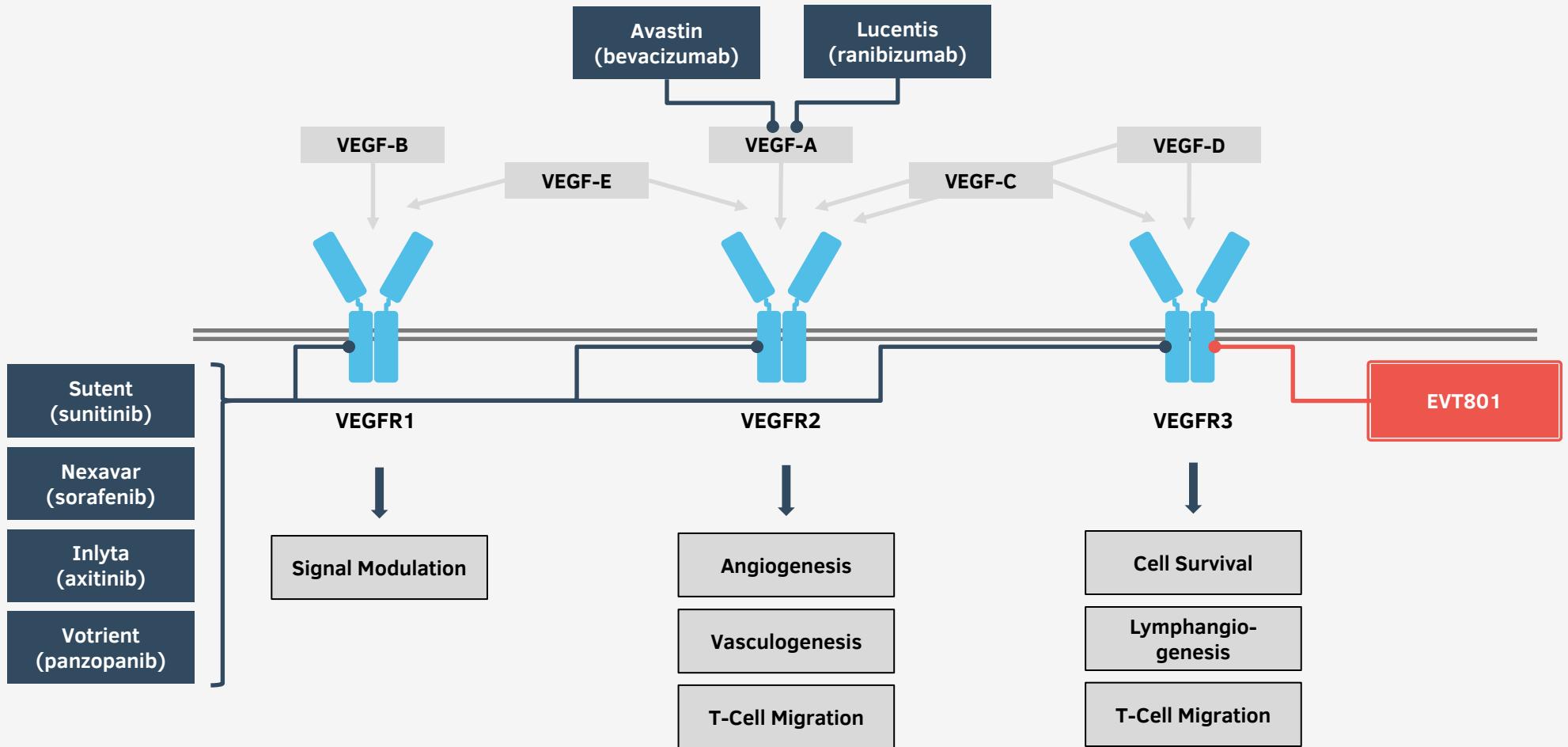
## **Low Cost of Goods**

Straightforward manufacture with excellent stability at controlled ambient

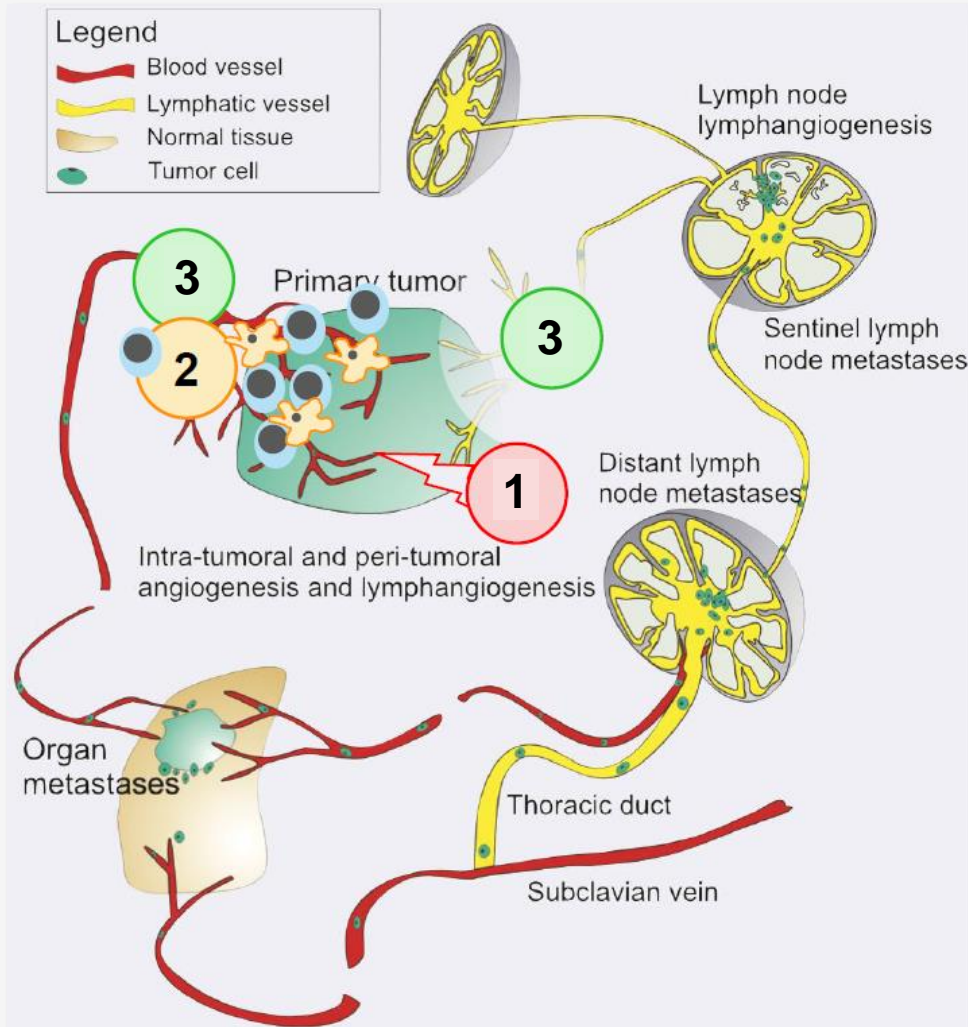
## **Favourable Preclinical Toxicology**

Limited evidence of toxicity in one-month GLP animal studies

# EVT801 selectively inhibits VEGFR3



# EVT801 is expected to have three primary mechanisms of action



1

## Tumor Killing

Direct effect on VEGFR3-expressing tumor cells (typically from endothelial origin, e.g. sarcoma)

2

## Increase in Anti-Tumor Immune Activity

Increased infiltration of effector T-cells, and reduction in immunosuppressive myeloid cells

3

## Inhibition of Metastasis

Stabilisation of tumor vasculature and avoidance of hypoxia decreases potential for metastatic spread

# Preclinical data confirms activity of EVT801 (1/2)

## *Dramatic single-agent activity in DEN-induced HCC model*

### Experimental Methods

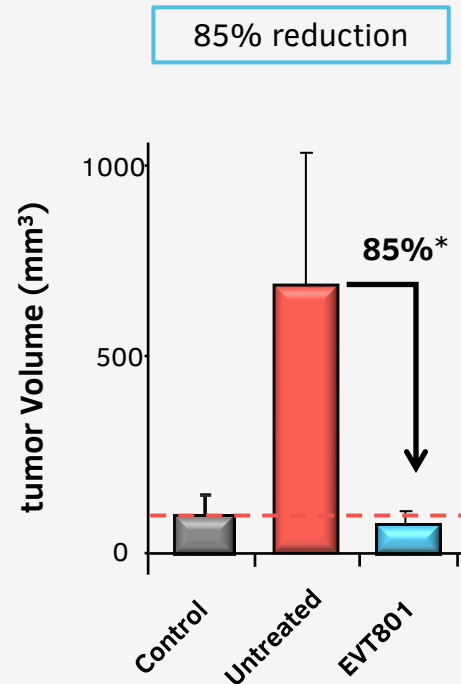
- Syngeneic mouse model
- Hepatocellular carcinoma chemically induced with diethylnitrosamine (DEN)
- Treatment with EVT801 in M10-M12

### Conclusions

- EVT801 monotherapy causes marked reduction in growth of primary tumor versus untreated comparator
- EVT801 appears to have significant anti-metastatic effect

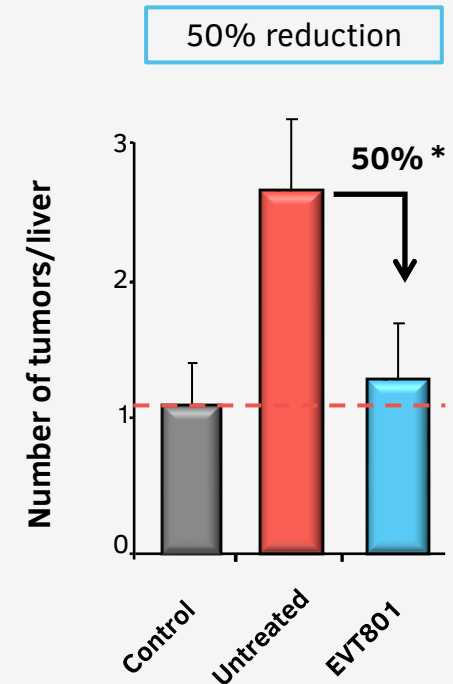
### Tumor Growth

Total Tumor Volume



### Metastasis

Number of Tumors in the Liver



\* Statistically significant (p<0.05)

# Preclinical data confirms activity of EVT801 (2/2)

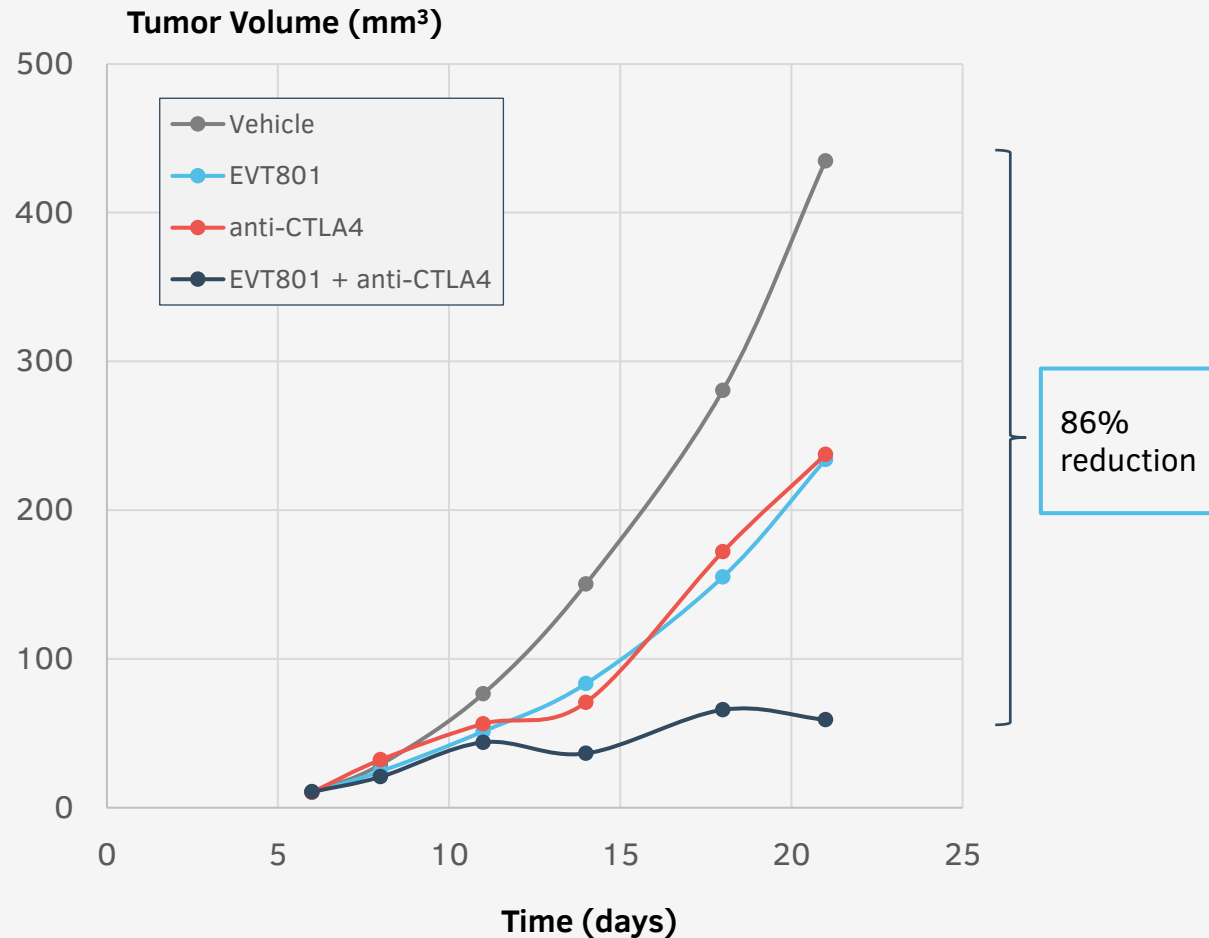
## *Synergistic activity in combination with anti-CTLA4 mAb*

### Experimental Methods

- Orthotopic mouse model
- 4T1 tumor cells inoculated in BALB/c mice (mammary fat pad)
- Treatment with EVT801 on D7-D21 and with anti-CTLA4 on D7, D14, D21

### Conclusions

- EVT801 monotherapy has approximately equivalent activity to anti-CTLA4 antibody
- Combination of EVT801 and anti-CTLA4 antibody is highly synergistic



Data on file

Note: CTLA4 is the target of Yervoy® (ipilimumab), an approved immuno-oncology therapy

# Kazia plans to commence a phase I clinical trial in CY2021



Up to 90 patients with advanced solid tumors, resistant to existing therapies



Endpoints will include safety and tolerability, mechanism of action, and preliminary efficacy



EVT801 administered both as monotherapy and in combination with immuno-oncology therapies



Rich suite of biomarkers investigated to provide deep understanding of EVT801 activity



First Patient In (FPI) by end of CY2021

## Current Status

- |   |   |
|---|---|
| • Investigational product manufactured and ready to ship                      | ✓ |
| • Draft clinical trial protocol prepared and under discussion with clinicians | ✓ |
| • Preclinical toxicology package complete for phase I                         | ✓ |
| • Regulatory documentation prepared   | ✓ |
| • Biomarker assays in advanced development                                    | ✓ |
| • Two sites in EU selected to commence phase I study                          | ✓ |
| • CRO selected for phase I study  | ✓ |



# Key Points

- 1 Well-understood mechanism (anti-angiogenesis) but unique differentiating feature (VEGFR3 selectivity)
- 2 Very strong preclinical data package, with evidence of activity in multiple tumors and favourable toxicology
- 3 High potential for combination use with immuno-oncology therapies
- 4 'Clinic-ready', with phase I study anticipated to start in CY2021
- 5 Substantially diversifies Kazia pipeline beyond PI3K and beyond brain cancer



**KAZIA**  
THERAPEUTICS

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