

ASX RELEASE

19 January 2022

KAZIA CORPORATE PRESENTATION

Sydney, 19 January 2022 – Kazia Therapeutics Limited (NASDAQ: KZIA; ASX: KZA), an oncology-focused drug development company, is pleased to provide its latest corporate presentation, which will be used for investor meetings over the coming months.

For More Information, Please Contact:-

In the United States:

Joe Green Edison Investor Relations <u>igreen@edisongroup.com</u> Phone: +1 646-653-7030 <u>In Australia:</u>

Jane Lowe IR Department

jane.lowe@irdepartment.com.au

Phone: +61 411 117 774

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. Eight additional studies are active in various 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 immuno-oncology agents. A phase I study commenced recruitment in November 2021.

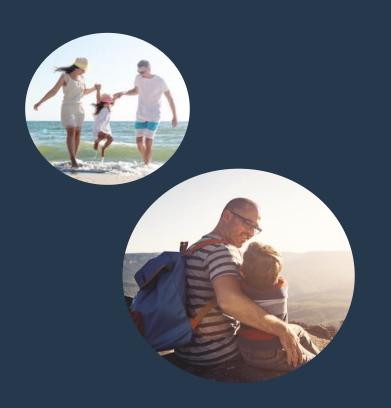
Board of Directors

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

For more information, please visit <u>www.kaziatherapeutics.com</u> or follow us on Twitter @KaziaTx.

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





A Diversified Oncology
Drug Development Company

Corporate Introduction

January 2022

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

An oncology drug-development company



Lead Program in Phase III for Glioblastoma

Paxalisib

- Potential first-in-class therapy for the most common and aggressive form of brain cancer, GBM
- US\$ 1.5 billion target market in lead indication, with substantial potential for additional indications
- International phase III underway
- Eight further studies ongoing across various forms of brain cancer
- Commercial partnership in place with Simcere for Greater China



Diversified Clinical-Stage Pipeline

EVT801

- Potential best-in-class therapy for US\$ 10 billion category
- Under development for advanced cancer (lung, liver, kidney, and other cancers are future targets)
- Adaptive phase I study underway in Europe
- Highly selective VEGFR3 that targets lymphangiogenesis, with preclinical evidence of synergy with PD-1 and CTLA-4 inhibitors



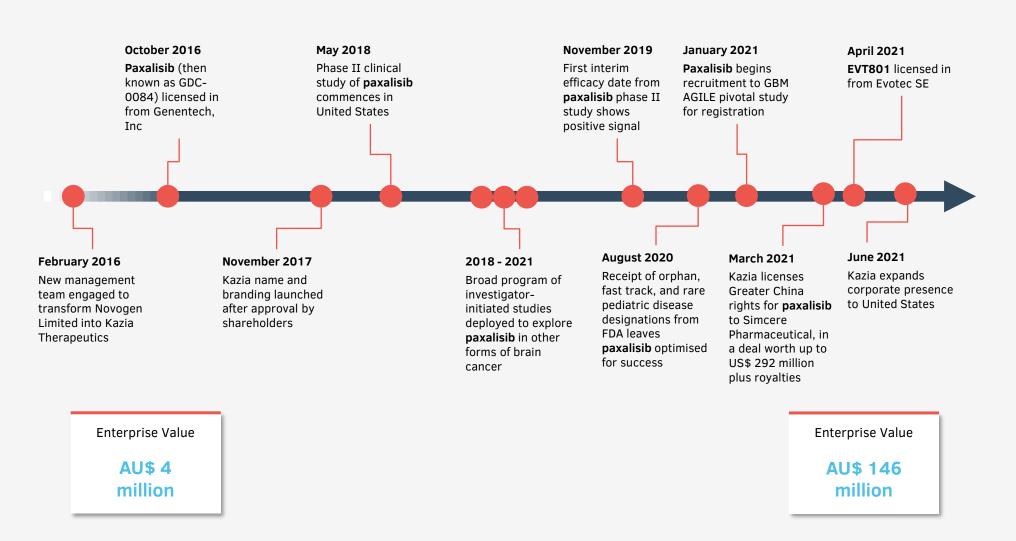
Strong Corporate Fundamentals

- Listed on ASX (KZA) and on NASDAQ (KZIA)
- ~US\$ 125 million market cap.
- Funded through to 40 CY2022
- Lean operating model with majority of cashflow devoted directly to clinical trials
- Multiple fundamental-driven institutional investors on registry



Corporate History

Kazia has shown remarkable growth in five years



2021 in Review

A Year of Delivering Milestones

3

Major cross-border licensing deals in FY2021

\$15M

Revenue in FY2021

5

Clinical studies
initiated across a
variety of oncology
indications

179%

Total shareholder return (TSR) (Jul 20 to Jun 21)

Phase 3

Advanced Paxalisib to pivotal GBM study in Jan '21 3

New paxalisib trial partnerships executed in FY2021

>200

Patients now treated with paxalisib

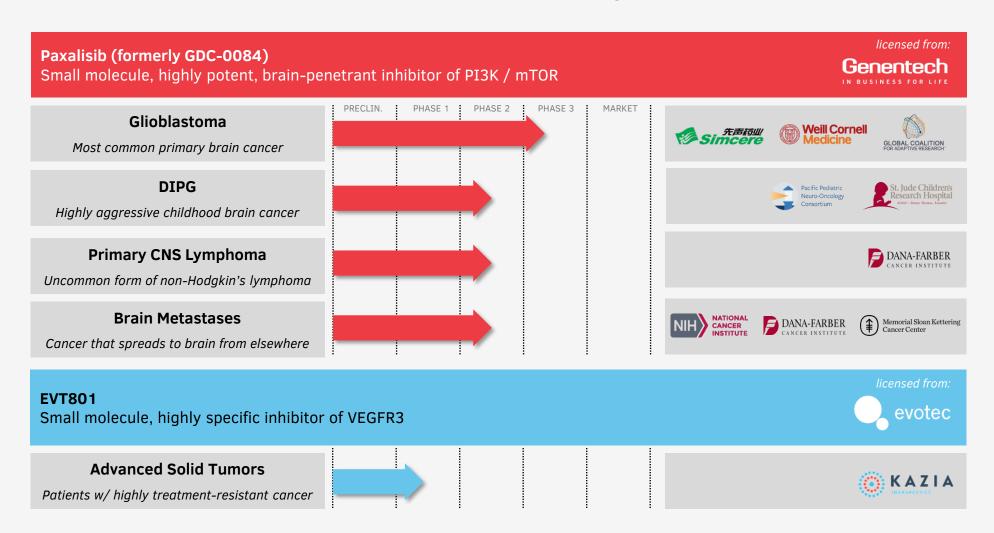
Phase 1

Advanced EVT801 into human trials in Nov 2021



Pipeline

Two world-class assets in clinical trials by end CY2021





Operating Model

In-licensing advanced assets drives earlier value realization



License undervalued assets from larger organisations

2016

Paxalisib licensed from Genentech

2021

EVT801 licensed from Evotec



Develop value through innovative clinical trial approaches

2016 - 2021

Paxalisib taken from phase I to phase III in GBM



Partner for late-stage development and commercialisation

2021

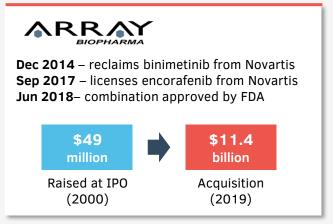
Paxalisib partnered with Simcere in China

2021

Legacy Cantrixil assert partnered with Oasmia

A Proven Strategy







Leadership

160+ years of international drug development experience

Board



Iain Ross Chairman







Executive and Board roles in pharma and small biotech

Red Pharma





Bryce CarmineDeputy Chairman



36 years executive experience in Eli Lilly



Steven CoffeyNon-Executive Director



Chartered accountant with extensive governance experience



Dr James GarnerChief Executive Officer
& Executive Director





Physician / MBA; Extensive drug development experience



Management Team



Dr James GarnerChief Executive Officer
& Executive Director







BAIN &



Dr John FriendChief Medical Officer

Physician / MBA; Extensive drug

development experience







Industry physician with >25 years experience in oncology drug development



Karen Krumeich Chief Financial Officer





Accountant with >20 years experience as a biotech CFO in public and private companies





Kate Hill Company Secretary

Deloitte.

Former audit partner at Deloitte and experienced Board director for multiple public companies



Financial Metrics

Value-driving news flow for investors



Market Capitalisation US\$ 125M

KZIA

↓3%

NBI

↓1%

XBI

↓ 20%

Listing	
ASX (primary)	KZA
NASDAQ (ADSs @ 1:10 ratio)	KZIA
Shares on Issue	130M

Balance Sheet	US\$
Cash (at 30 Sep 21)	\$14.2M
Monthly Burn Rate	~\$1.25M

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



CY2022 Milestones and Newsflow

Multiple catalysts across two clinical programs

Open GBM AGILE paxalisib arm to recruitment in EU and China	1H CY2022
Commence recruitment to paxalisib phase II GBM study at Weill Cornell	1H CY2022
Initial interim data from paxalisib + trastuzumab phase II metastatic HER2+ breast cancer brain metastases trial at Dana-Farber	1H CY2022
Initial interim data from paxalisib phase II brain metastases study with Alliance for Clinical Trials in Oncology	1H CY2022
Initial interim data from paxalisib + radiotherapy phase I brain metastases study at Memorial Sloan-Kettering	1H CY2022
Final data published from Kazia's paxalisib phase II study in GBM	1H CY2022
Additional preclinical data for paxalisib presented at conferences	1H CY2022
Initial interim data from paxalisib phase II PCNSL study at Dana-Farber	2H CY2022
Initial interim data from Kazia's EVT801 phase I trial	2H CY2022

Italics - updated guidance

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



Investment Rationale

A compelling corporate story

High-Quality Late-Stage Pipeline

- Pipeline assets invented by worldclass companies: Genentech (paxalisib) and Sanofi / Evotec (EVT801)
- Targets are wellvalidated (PI3K and angiogenesis)
- Assets are highly potent and differentiated

Valuable Commercial Opportunities

- Glioblastoma alone is a ~US\$ 1.5B market
- Favourable pricing dynamics in orphan indications such as GBM
- Commercial partnership for paxalisib already in place in Greater China with Simcere Pharmaceutical

Efficient, Well-Funded Business

- Board & management team with >160 years of drug development experience
- ~US\$ 14M cash at 30 Sept 2021; funds ongoing projects
- Low overheads;
 ~75% of funds are
 invested directly in
 clinical trials

Rapid Path to Value Realisation

- Paxalisib in phase III and potentially within ~2 years of market launch
- Multiple data read outs from 9x other studies over coming 12-24 months with potential to re-rate
- Demonstrated partnering potential for paxalisib



Paxalisib

Glioblastoma Phase III

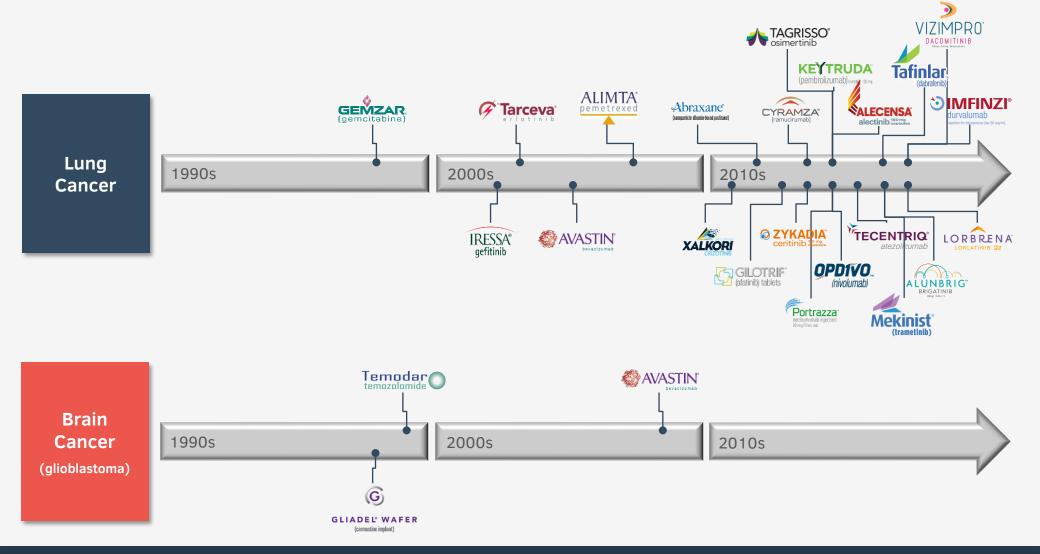
DIPG Phase II

PCNSL Phase II

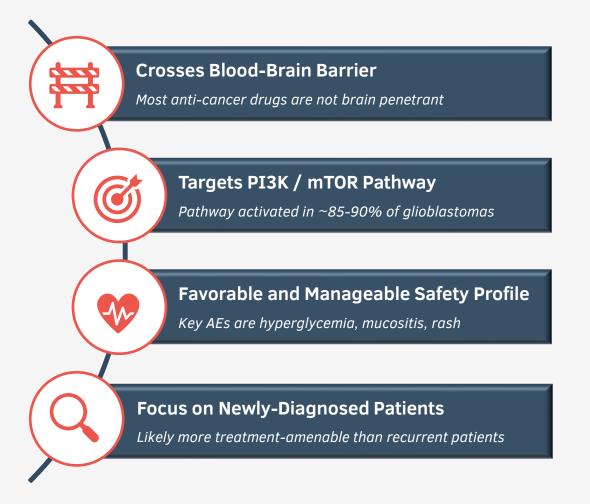
Brain Metastases Phase II



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



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 and Orphan Drug status

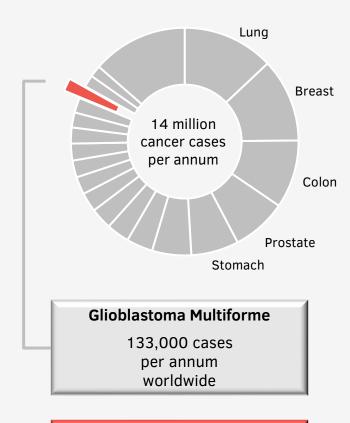
Low Cost of Goods

Straightforward US-based manufacture with excellent stability at ambient temp.

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



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 first-line treatment for GBM; it is ineffective in ~65% of cases

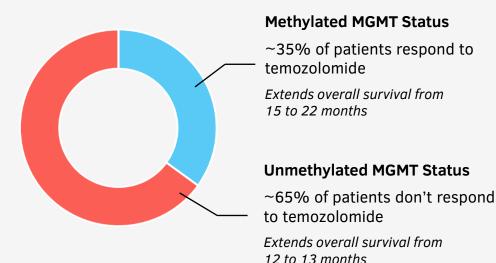
6 weeks

4w

Standard of Care ('Stupp Regimen')

Debulking surgery where possible

Radiotherapy + temozolomide maintenance therapy



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

6 x 28-day cycles

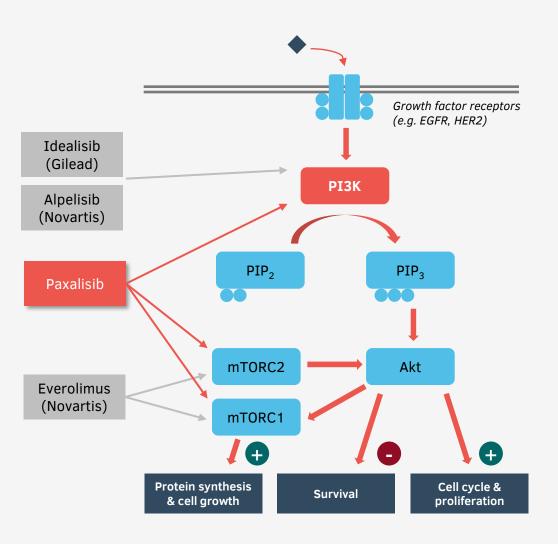
For these patients, there is no effective pharmacological treatment currently available

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



Paxalisib Among Most Potent PI3K Inhibitors

	IC ₅₀ (nM)					
	p110α	p110β	p110γ	p11 0 δ	mTORC 1/2	
Paxalisib	2	46	10	3	70	
Idelalisib	820	565	89	2.5	>1,000	
Alpelisib	5	1200	250	290	>9,100	
Buparlisib	52	166	262	116	4,600	
Pilaralisib	39	383	23	36	>15,000	

Note: lower IC₅₀ implies more potent activity

Source: HF Zhao et al. (2017) Molecular Cancer. 16:100



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













Zydelig (idelalisib)



Copiktra (duvelisib)

Piqray (alpelisib)

Ukoniq (umbralasib)

paxalisib













FDA Approved
July 2014
(blood cancers)

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

FDA Approved
October 2018
(blood cancers)

FDA Approved
May 2019
(breast cancer)

FDA Approved
February 2021
(blood cancers)

In pivotal study for FDA Approval in glioblastoma

Crosses Blood-Brain Barrier





X

X



Safety

Potentially fatal liver toxicity and diarrhoea

Potentially fatal infections

Potentially fatal infections and diarrhoea

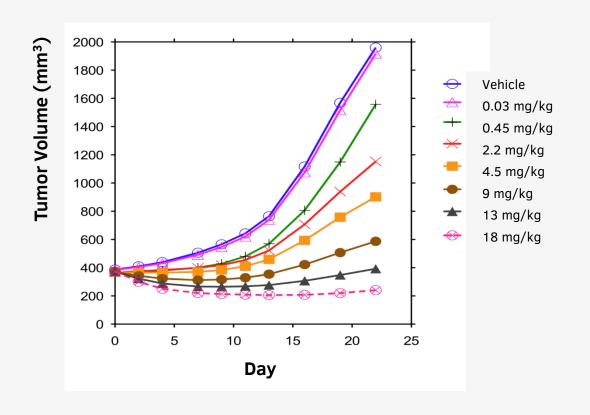
Modest toxicities to date

Serious infections, hepatotoxicity, and diarrhoea Modest toxicities to date



Paxalisib shows convincing 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

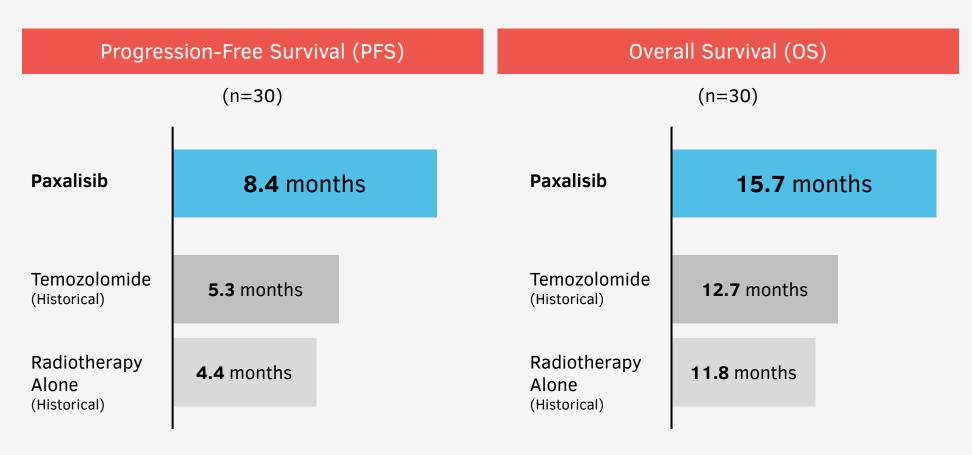
Clear dose - PI3K inhibition - response relationship seen in most experiments

Paxalisib even moderately active in GS2 intracranial model (intact BBB, no PI3K dysregulation) which is resistant to other experimental drugs

Source: data on file



Phase II study of paxalisib mono-therapy in newly-diagnosed GBM provides robust signal of clinical efficacy



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

Safety Profile in the phase 2 clinical study in GBM patients is generally mild to moderate, reversible, and manageable

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

Note: Final data under analysis



Eight unique clinical studies are ongoing across a variety of solid tumours with CNS involvement

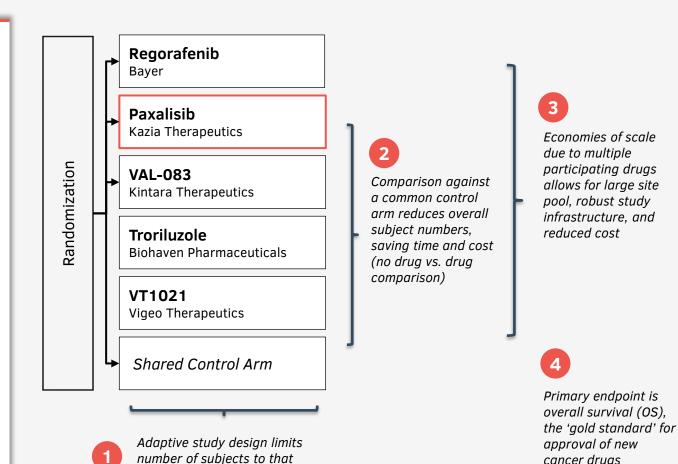
Registration	Indication	Phase	N	Status	Sponsor					
Primary Brain Cancer										
NCT03970447	Glioblastoma (GBM AGILE)	II / III	Up to 200 on paxalisib	Recruiting	GLOBAL COALITION FOR ADAPTIVE RESEARCH					
NCT05183204	Glioblastoma (combination with ketogenic diet)	II	33-60	Recruiting	Weill Cornell Medicine					
NCT03696355	DIPG and DMGs	I	27	Follow-up	St. Jude Children's Research Hospital					
NCT05009992	DIPG and DMGs	II	TBD	Recruiting	Pacific Pediatric Neuro-Oncology Consortium					
NCT04906096	Primary CNS Lymphoma	II	25	Recruiting	DANA-FARBER CANCER INSTITUTE					
Secondary (Metas	static) Brain Cancer									
NCT04192981	Brain Metastases (combination with radiotherapy)	I	Up to 36	Recruiting	Memorial Sloan Kettering Cancer Center					
NCT03765983	Breast Cancer Brain Metastases (combination with trastuzumab)	II	Up to 47	Recruiting	DANA-FARBER CANCER INSTITUTE					
NCT03994796	Brain Metastases ('Alliance' multi-drug study)	II	50	Recruiting	NIH NATIONAL CANCER INSTITUTE					



GBM AGILE international pivotal study is underway Sponsored by GCAR with support of GBM key opinion leaders

Key Points

- A 'platform study', run independently of individual companies, designed to expedite the approval of new drugs for alioblastoma
- 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
- FDA acknowledgement that data expected suitable for registration



required to demonstrate efficacy,

eliminating redundancy

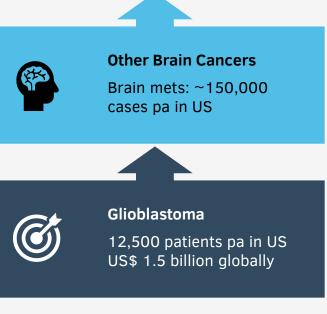
cancer drugs

Paxalisib validated by commercial licensing deal, with significant scope for indication expansion

Other Cancers with PI3K Dysregulation
(e.g. breast, lung)

Other Brain Cancers
Brain mets: ~150,000
cases pa in US

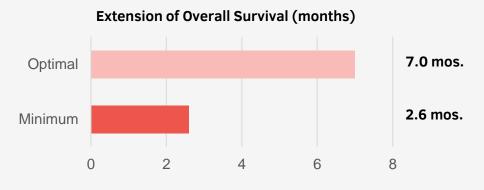
Primary Focus

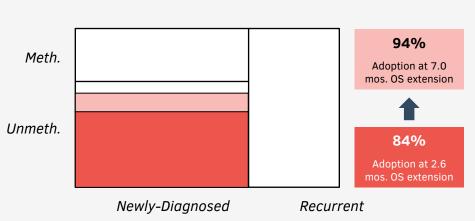




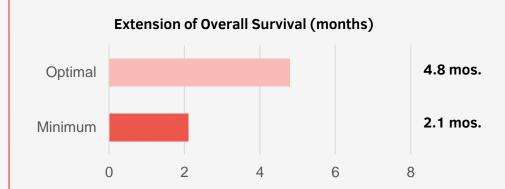
Adoption rate for the commercial product is expected to be very high, due to scarcity of existing treatment options

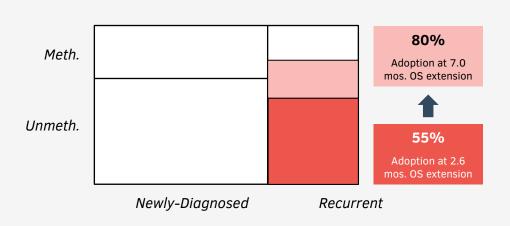
Newly-Diagnosed Unmethylated





Recurrent

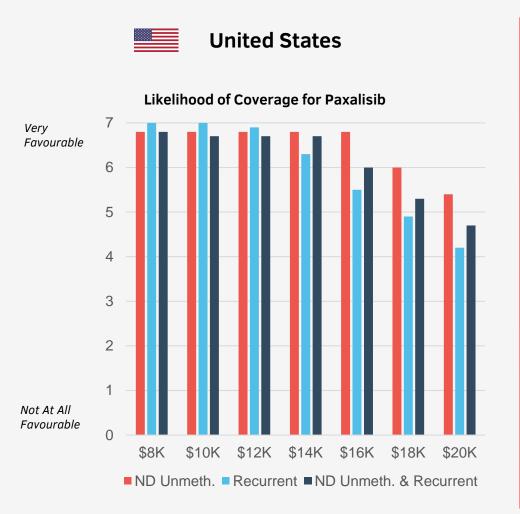


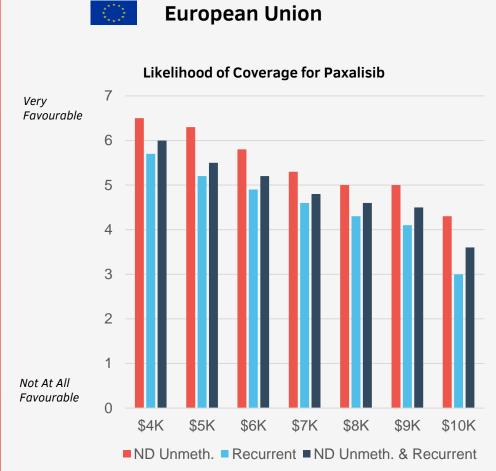


Source: Triangle Insights market research, commissioned by Kazia Therapeutics



Payer interviews support willingness-to-pay up to US\$ 20K in US and up to ~\$10K in EU5





Source: Triangle Insights market research, commissioned by Kazia Therapeutics



Key Points

- Well-validated mechanism (PI3K inhibition) but unique differentiating feature (brain penetration)
- Positive phase II data in GBM, supported by very strong preclinical package and positive phase I data
- Fully-funded international registration study underway with full support of FDA and leading GBM clinicians
- Broad trial program underway with world-class centres in other forms of brain cancer
- Targeting a US\$ 1.5B market for glioblastoma alone, with limited competition and very high unmet-need



EVT801

Solid Tumors

Phase I



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

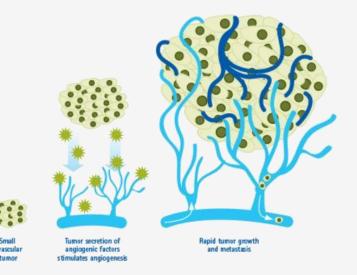
Product	duct Company Target Indications		Annual Sales (US\$)*	
AVASTIN° bevacizumab mongamu.injection for in use	Genentech A Member of the Roche Group	VEGF-A	Colorectal cancerLung cancerBreast cancer	\$7 billion
Nexavar (sorafenib) tablets			Hepatocellular carcinomaRenal call carcinomaThyroid cancer	\$1 billion
SUTENT® sunitinib malate	Pfizer	VEGFR PDGFR	Renal cell carcinomaGasto-intestinal stromal tumor	\$750 million
Votrient° pazopanib tablets (200 mg)	b novartis	VEGFR PDGFR c-Kit	Renal cell carcinomaSoft tissue sarcoma	\$1 billion
Inlyta. axitinib _{lingand} ingtablets	P fizer	VEGFR c-Kit PDGFR	Renal cell carcinoma	\$400 million
Clenvatinib) capsules on grade and	Capsules in my and tony • H		Renal cell carcinomaHepatocellular carcinomaEndometrial carcinoma	\$300 million
CABOMETYX® (cabozantinib) tablets	EXELI <mark>X</mark> IS°	c-Met VEGFR2 RET	Renal cell carcinomaHepatocellular carcinoma	\$750 million

^{*}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



Tumor Hypoxia

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

Limited
Duration of
Effect

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 VEGFR3 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

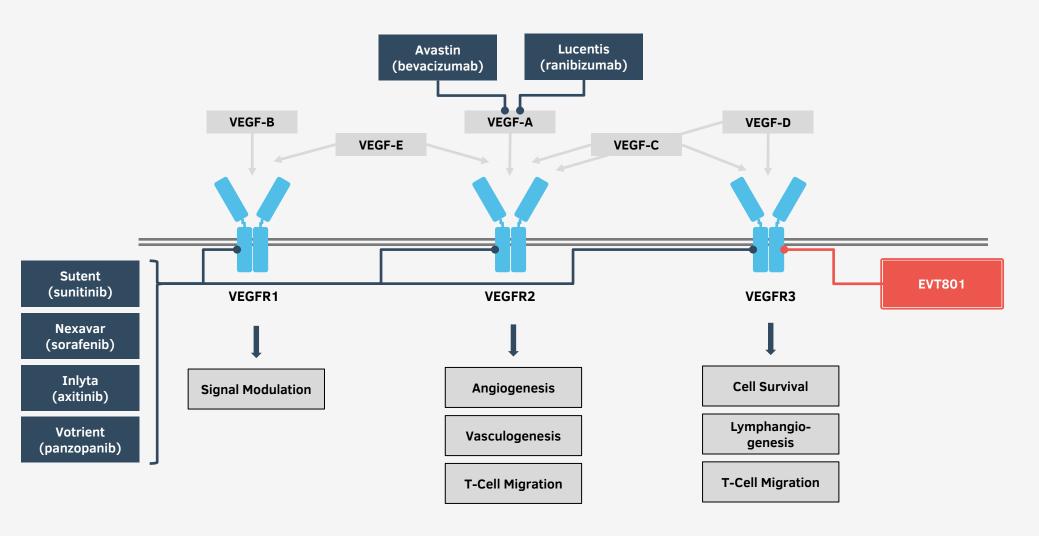
Straightforward manufacture with excellent stability at controlled ambient

Favourable Preclinical Toxicology

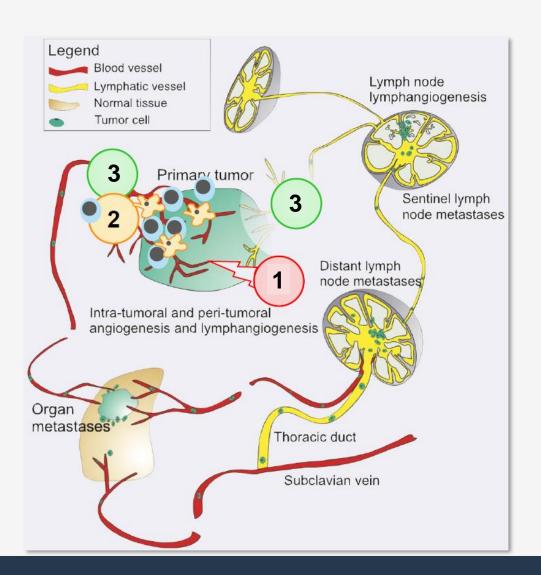
Limited evidence of toxicity in onemonth GLP animal studies



EVT801 selectively inhibits **VEGFR3**



EVT801 is expected to have three primary mechanisms of action



Tumor Killing

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

Increase in Anti-Tumor Immune Activity

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

Inhibition of Metastasis

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



Preclinical data confirms activity of EVT801 (1/2)

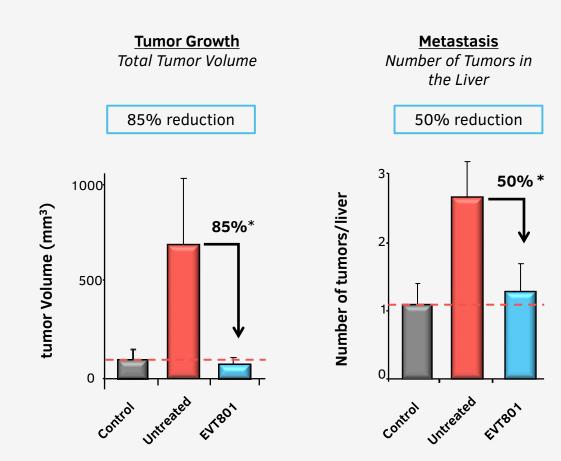
Dramatic single-agent activity in DEN-induced HCC model

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



^{*} Statistically significant (p<0.05)



Preclinical data confirms activity of EVT801 (2/2)

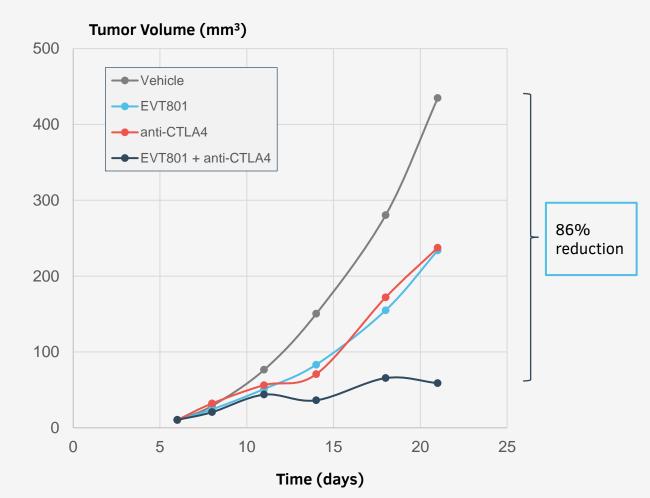
Synergistic activity in combination with anti-CTLA4 mAb

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



Focus in the 'angiokinase inhibitor' class has shifted from anti-angiogenic use to immuno-oncology use

Select VEGFR Inhibitors – FDA Approvals – 2012-2021







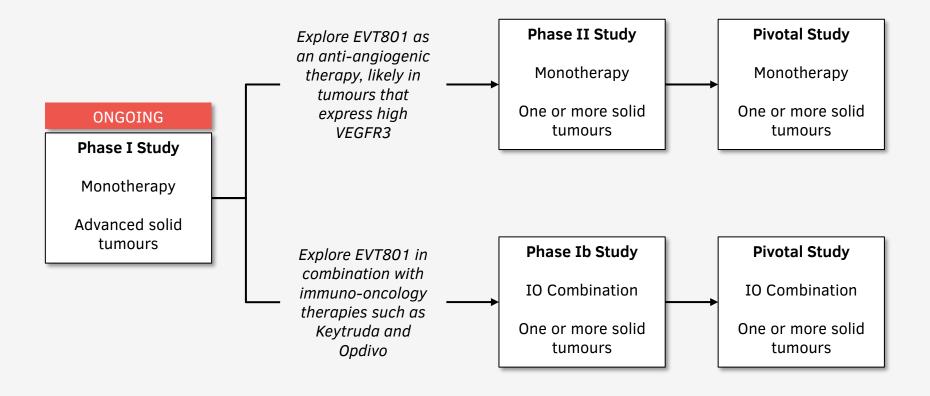
(cabozantinib) tablets

2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Renal Cancer (MonoTx)							Renal Cancer with		
							KEYTRUDA° (pembrolizumab) hjecton 100 mg		
			Thyroid Cancer (MonoTx)	Renal Cancer (MonoTx)		Liver Cancer (MonoTx)	Endomet- rial Ca. with		Renal Cancer with KEYTRUDA
				Renal Cancer (MonoTx)			Liver Cancer (MonoTx)		Renal Cancer with OPDIVO. (nivolumab)

Use of VEGFR inhibitors to target angiogenesis as monotherapy agents Use of VEGFR inhibitors to enhance and augment immuno-oncology therapies



Kazia's strategy for EVT801 aims to explore both areas of opportunity for the drug



Key Points

- Well-understood mechanism (anti-angiogenesis) but unique differentiating feature (VEGFR3 selectivity)
- Very strong preclinical data package, with evidence of activity in multiple tumors and favourable toxicology
- High potential for combination use with immunooncology therapies
- Adaptive phase I study ongoing with anticipated preliminary results 2H CY 2022
- Substantially diversifies Kazia pipeline beyond PI3K and beyond brain cancer





www.kaziatherapeutics.com info@kaziatherapeutics.com