KAZIA THERAPEUTICS

# Presentation to Bell Potter Healthcare Coference

Dr James Garner
Chief Executive Officer

Sydney, NSW
10 November 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.

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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**

- Under development for glioblastoma, most common and aggressive form of brain cancer
- International phase III underway
- Developed by Genentech, Inc
- US$ 1.5 billion target market
- Eight further studies ongoing across various forms of brain cancer
- Commercial partnership in place with Simcere Pharmaceutical for Greater China region

## Diversified Clinical-Stage Pipeline

**EVT801**

- Under development for advanced cancer (lung, liver, kidney, and other cancers are future targets)
- Phase I study underway in France
- Developed by Sanofi and Evotec SE
- Targets lymphangiogenesis, and shows preclinical evidence of synergy with immuno-oncology therapies

## Strong Corporate Fundamentals

- Listed on ASX (KZA) and on NASDAQ (KZIA)
- ~AU$ 200 million market cap.
- Cash position @ 30 Sept 2021: ~AU$ 19.6 million
- Lean operating model, with ~75% of cashflow devoted directly to clinical trials
- Multiple fundamental-driven institutional investors on registry

# 2021 in Review

*A Year of Achievements*

**3**

Major cross-border licensing deals in FY2021

**$15M**

Revenue in FY2021

**11**

Ongoing clinical studies across two clinical programs

**179%**

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

**Phase III**

Paxalisib pivotal study commenced in Jan ‘21

**3**

New paxalisib trial partnerships executed in FY2021

**>200**

Patients now treated with paxalisib

**Phase I**

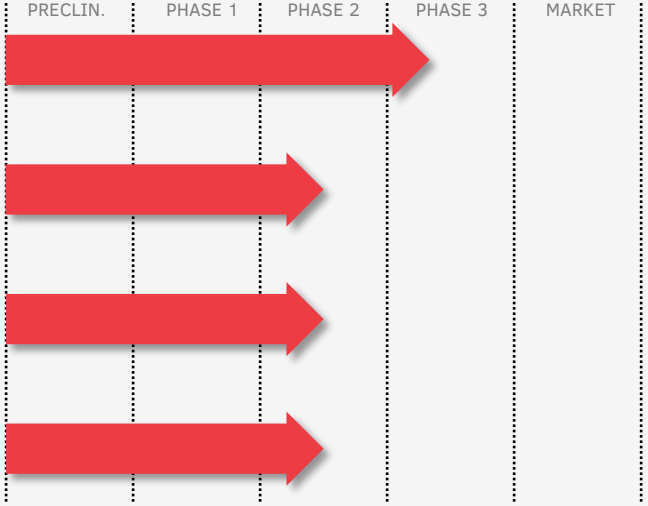
EVT801 commenced human trials in Nov 2021

# Pipeline

*Two world-class assets in clinical trials by end CY2021*

**Paxalisib (GDC-0084)**
Small molecule, brain-penetrant inhibitor of PI3K / mTOR

*licensed from:* Genentech IN BUSINESS FOR LIFE




**Glioblastoma**
*Most common primary brain cancer*

Weill Cornell Medicine · GLOBAL COALITION FOR ADAPTIVE RESEARCH

**DIPG**
*Highly aggressive childhood brain cancer*

Pacific Pediatric Neuro-Oncology Consortium · St. Jude Children's Research Hospital

**Primary CNS Lymphoma**
*Uncommon form of non-Hodgkin's lymphoma*

DANA-FARBER CANCER INSTITUTE

**Brain Metastases**
*Cancer that spreads to brain from elsewhere*

NIH NATIONAL CANCER INSTITUTE · DANA-FARBER CANCER INSTITUTE · Memorial Sloan Kettering Cancer Center

**EVT801**
Small molecule inhibitor of VEGFR3

*licensed from:* evotec

**Advanced Solid tumors**
*Patients with cancer resistant to other drugs*

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# Operating Model

*In-licensing advanced assets drives earlier value realization*

**License under-valued assets from larger organisations**

**Develop value through innovative clinical trial approaches**

**Partner for late-stage development and commercialisation**

**2016**
Paxalisib licensed from Genentech

**2021**
EVT801 licensed from Evotec

**2016 - 2021**
Paxalisib taken from phase I to phase III in GBM

**2021**
Paxalisib partnered with Simcere in China

**2021**
Legacy Cantrixil assert partnered with Oasmia

***A Proven Strategy***

TESARO™

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

**$360 million** → **$5.1 billion**

IPO (2012) — Acquisition (2018)

ARRAY BIOPHARMA

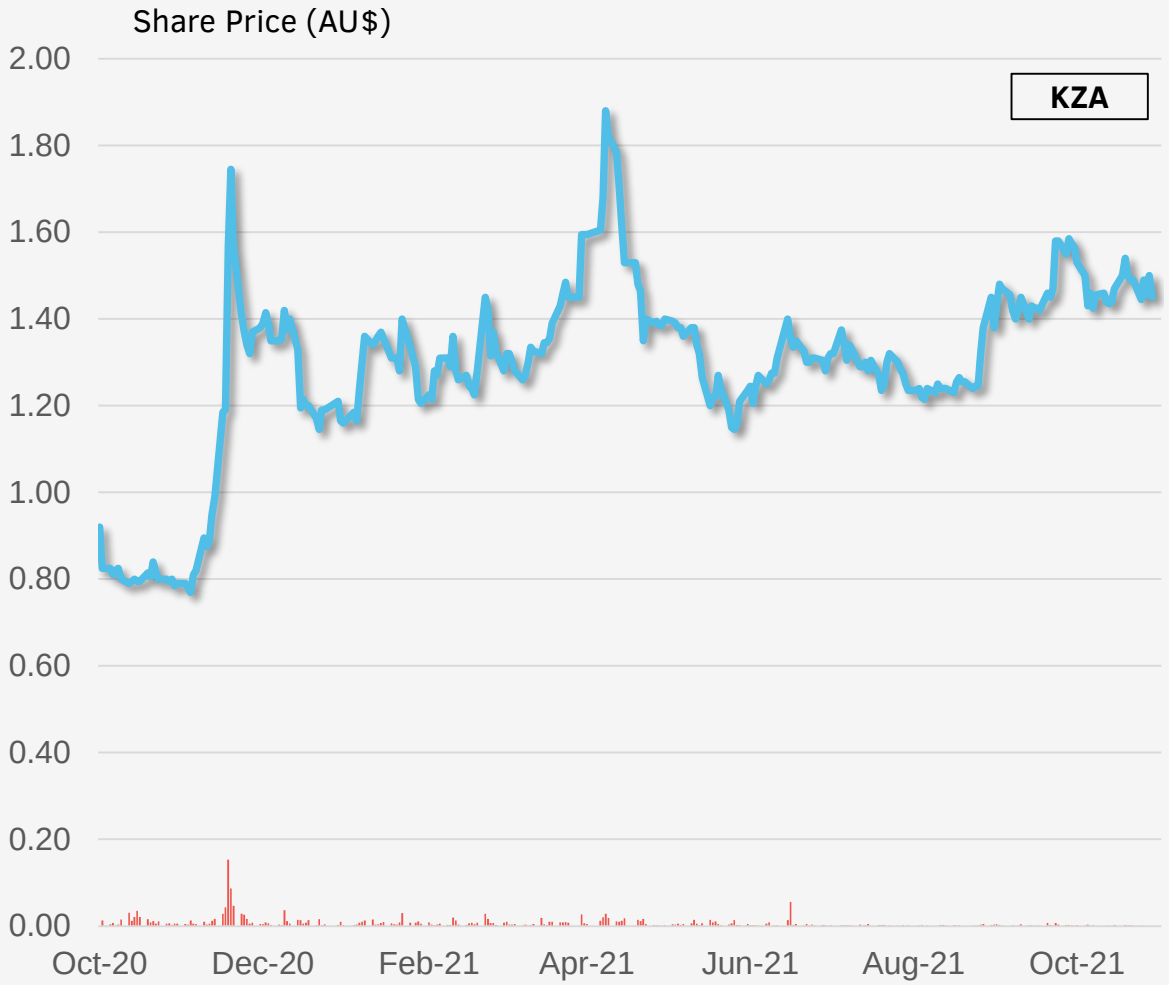
**Dec 2014** – reclaims binimetinib from Novartis
**Sep 2017** – licenses encorafenib from Novartis
**Jun 2018**– combination approved by FDA

**$49 million** → **$11.4 billion**

Raised at IPO (2000) — Acquisition (2019)

# Financial Metrics

*Value-driving news flow for investors*



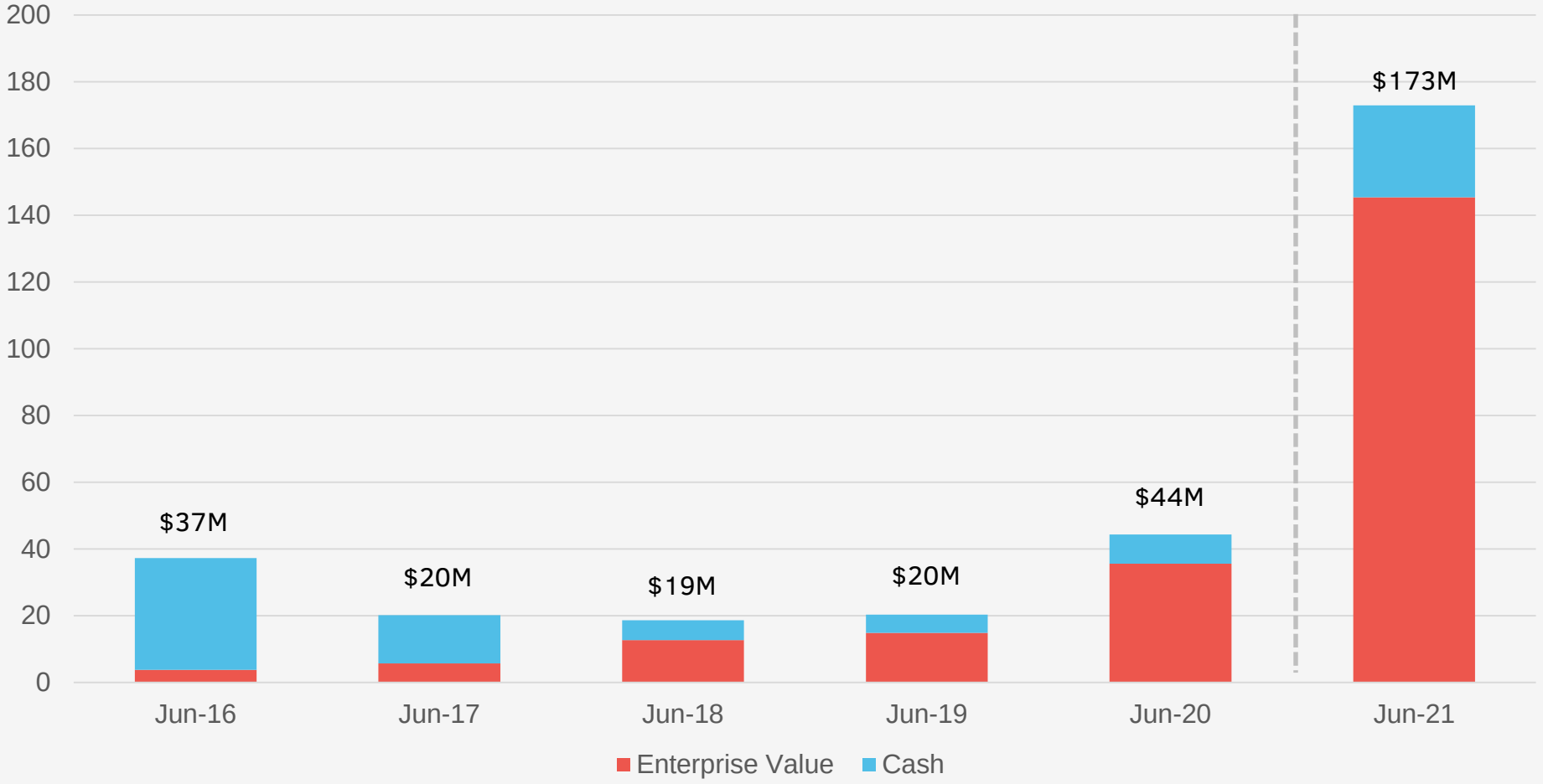

| **Market Capitalisation** | **AU$ 200M** |
|---|---|

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

| **Balance Sheet** | AU$ |
|---|---|
| Cash (at 30 Jun 21) | $19.6M |
| Monthly Burn Rate | ~$1.25M |

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

# Kazia's enterprise value has increased by approximately 37x in the last five years




Source: Company Annual Reports; Marketwatch



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# CY2021 Milestones and Newsflow

*Multiple catalysts across two clinical programs*

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

*Italics* – updated guidance

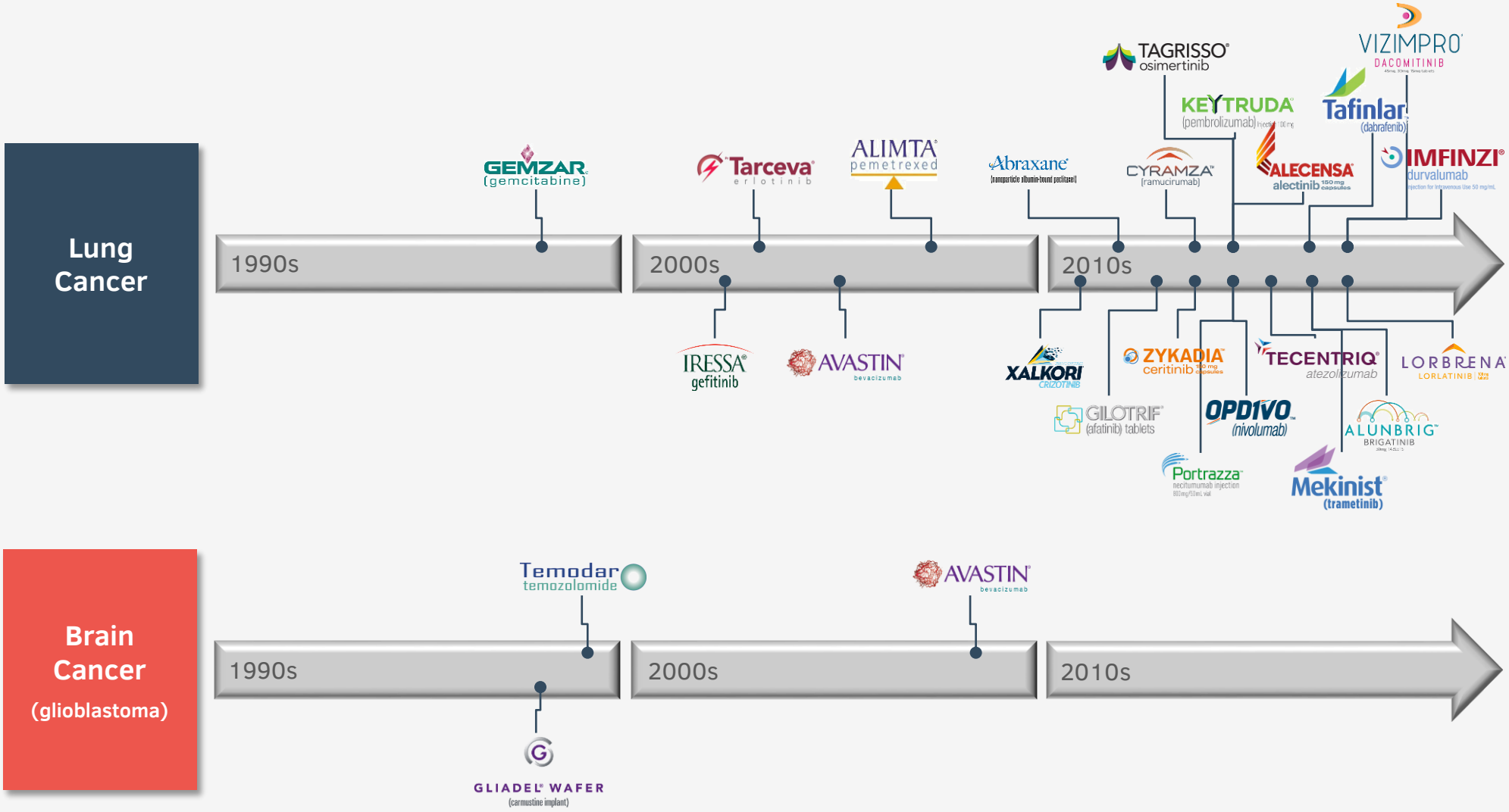
Note: all guidance is indicative, and subject to amendment in light of changing conference schedules, operational considerations, etc.

# Paxalisib

Brain Cancer

Phase III

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



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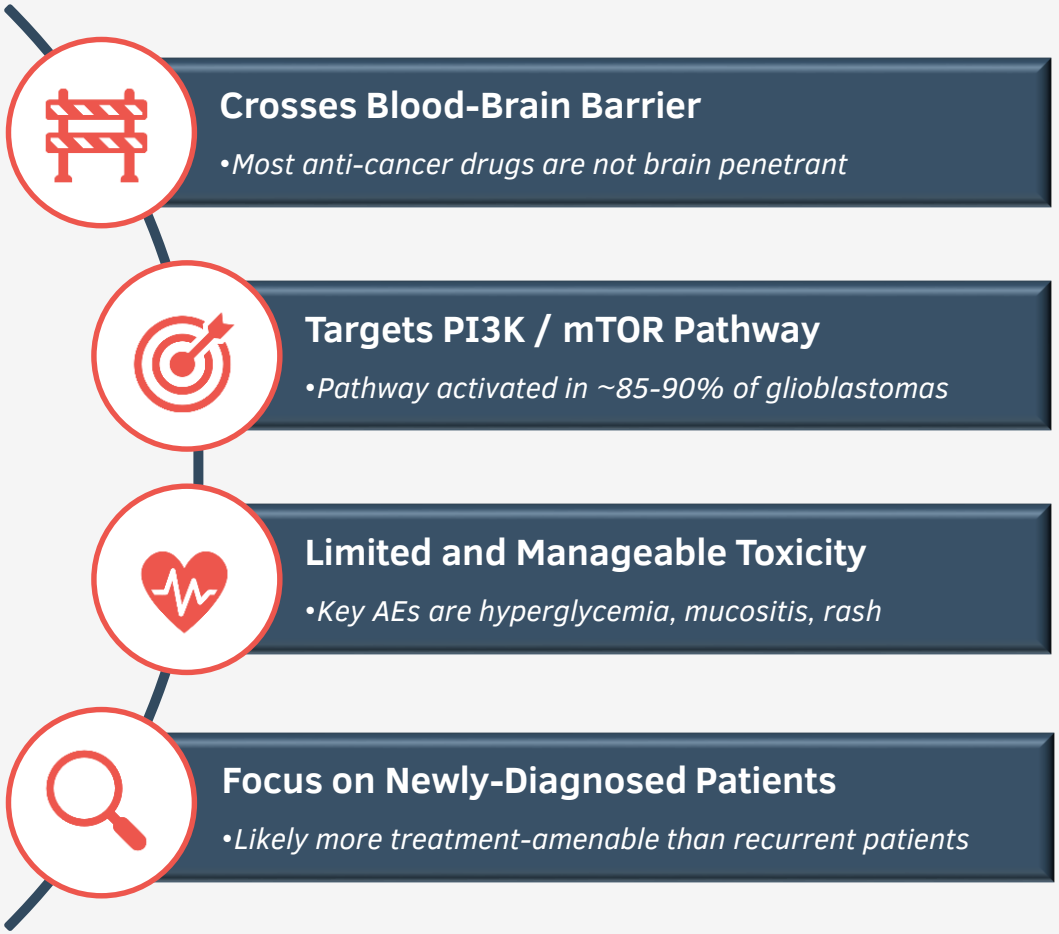
# Paxalisib was designed specifically to overcome key challenges in the treatment of brain cancer



**Crosses Blood-Brain Barrier**

•*Most anti-cancer drugs are not brain penetrant*

**Targets PI3K / mTOR Pathway**

•*Pathway activated in ~85-90% of glioblastomas*

**Limited and Manageable Toxicity**

•*Key AEs are hyperglycemia, mucositis, rash*

**Focus on Newly-Diagnosed Patients**

•*Likely more treatment-amenable than recurrent patients*

**Oral Presentation**

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

**Strong IP Protection**

Composition-of-matter to 2031 in most jurisdictions

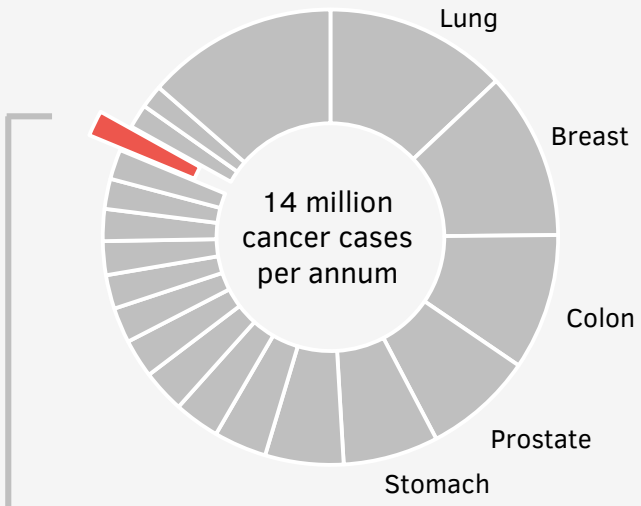
**Low Cost of Goods**

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**

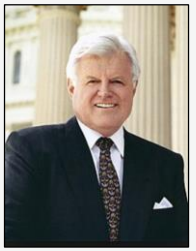
average survival with treatment

Five-year survival

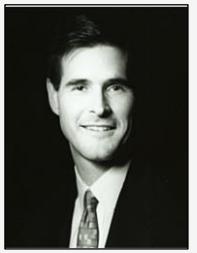
**3 – 5%**

(breast cancer: 90%)


Sen. John McCain


Sen. Ted Kennedy


Beau Biden


Dan Case



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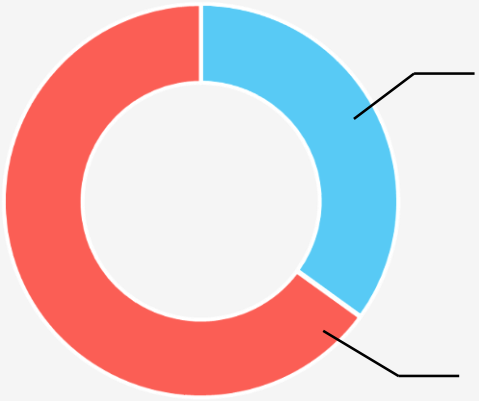
# Temozolomide is only FDA-approved drug for GBM; it is ineffective in ~65% of cases

*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



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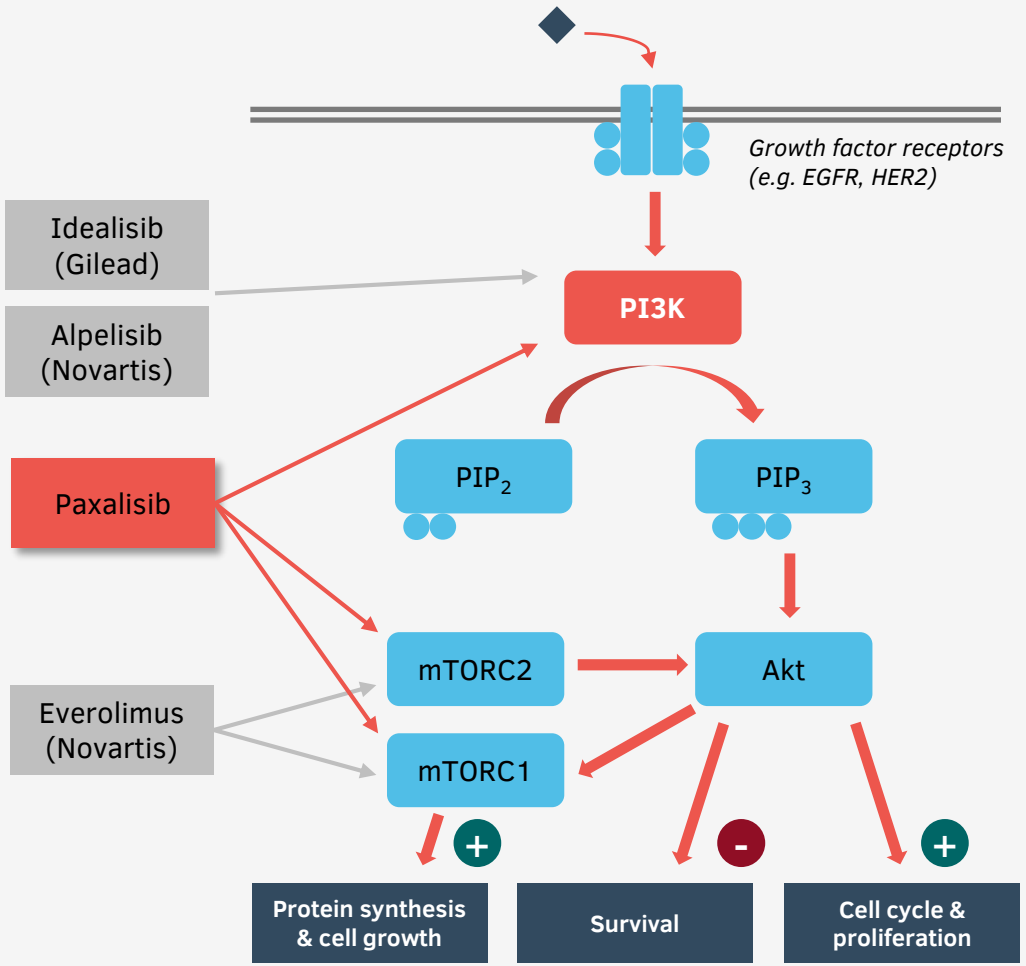
# The PI3K / Akt / mTOR pathway is a critical signalling mechanism for many tumor types




**Comparative Potency vs Other PI3K Inhibitors**

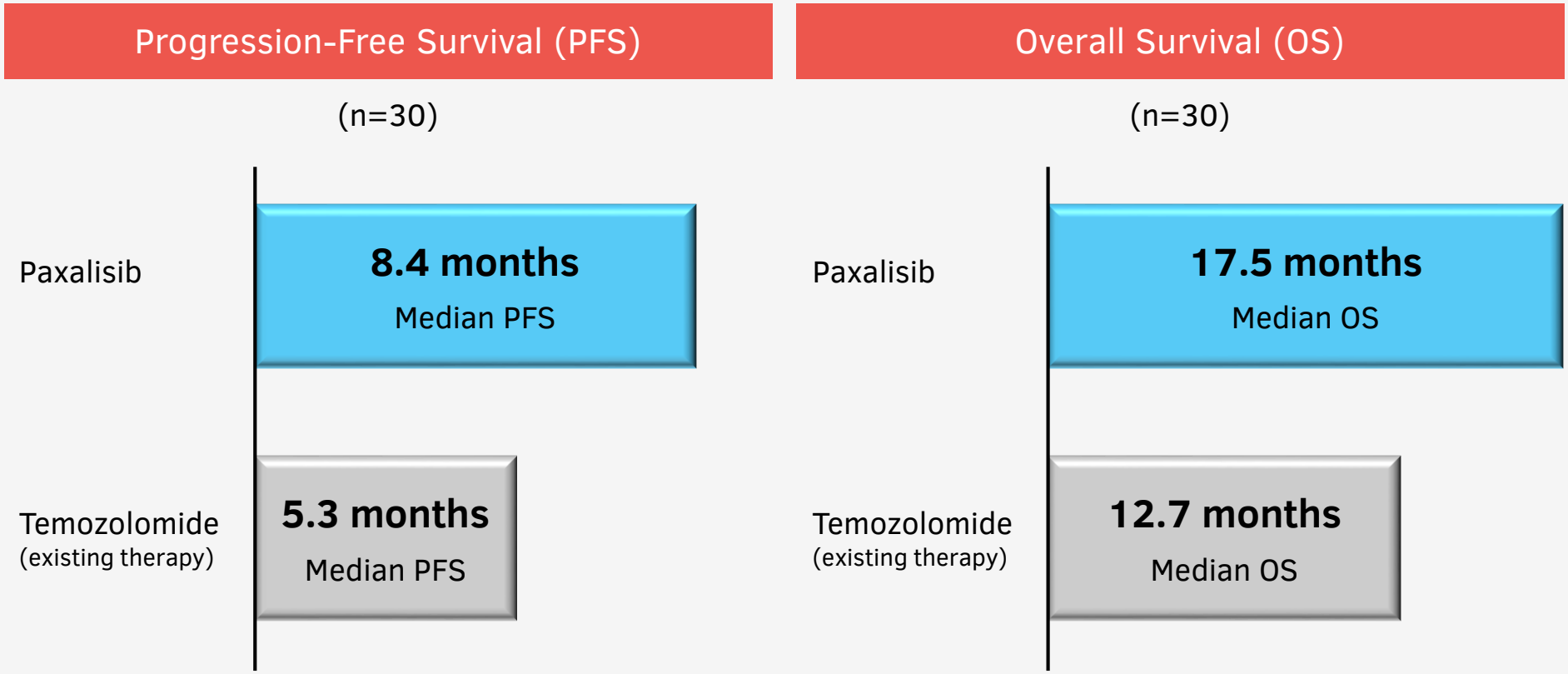
| | $IC_{50}$ (nM) | | | | |
|---|---|---|---|---|---|
| | p110α | p110β | p110γ | p110δ | mTORC 1/2 |
| **Paxalisib** | **2** | **46** | **10** | **3** | **70** |
| Idelalisib | 820 | 565 | 89 | 2.5 | >1,000 |
| Alpelisib | 5 | 1200 | 250 | 290 | >9,100 |
| Buparlisib | 52 | 166 | 262 | 116 | 4,600 |
| Pilaralisib | 39 | 383 | 23 | 36 | >15,000 |
| Taselisib | 0.3 | 9.1 | 1.0 | 0.1 | 1,200 |
| Pictilisib | 3 | 33 | 75 | 3 | 580 |

Note: lower $IC_{50}$ 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) | Aliqopa (copanlisib) | 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* | ✗ | ✗ | ✗ | ✗ | ✗ | ✓ |
| *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 |

# 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

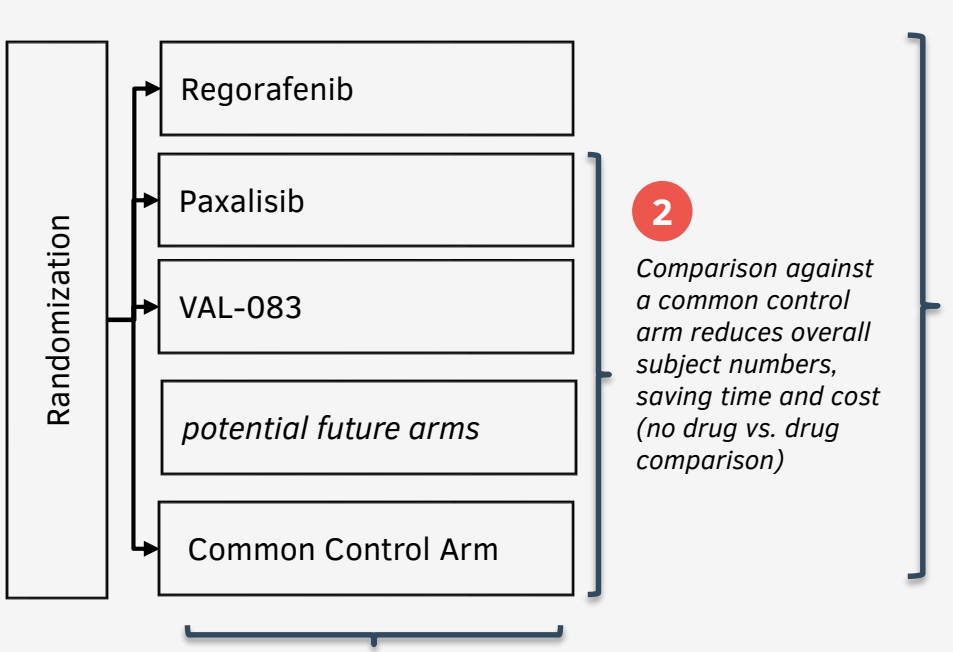
# Nine clinical studies are active across multiple forms of brain cancer

| Registration | Indication | Phase | N | Status | Sponsor |
|---|---|---|---|---|---|
| **Primary Brain Cancer** | | | | | |
| NCT03522298 | Glioblastoma | II | 30 | Follow-up | KAZIA THERAPEUTICS |
| TBD | Glioblastoma (combination with ketogenic diet) | II | 33-60 | Start-up | Weill Cornell Medicine |
| NCT03970447 | Glioblastoma (GBM AGILE) | II / III | Up to 200 on paxalisib | Recruiting | GLOBAL COALITION FOR ADAPTIVE RESEARCH |
| NCT03696355 | DIPG and DMGs | I | 27 | Follow-up | St. Jude Children's Research Hospital |
| TBD | DIPG and DMGs | II | TBD | Start-up | Pacific Pediatric Neuro-Oncology Consortium |
| NCT04906096 | Primary CNS Lymphoma | II | 25 | Recruiting | DANA-FARBER CANCER INSTITUTE |
| **Secondary (Metastatic) 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, 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*



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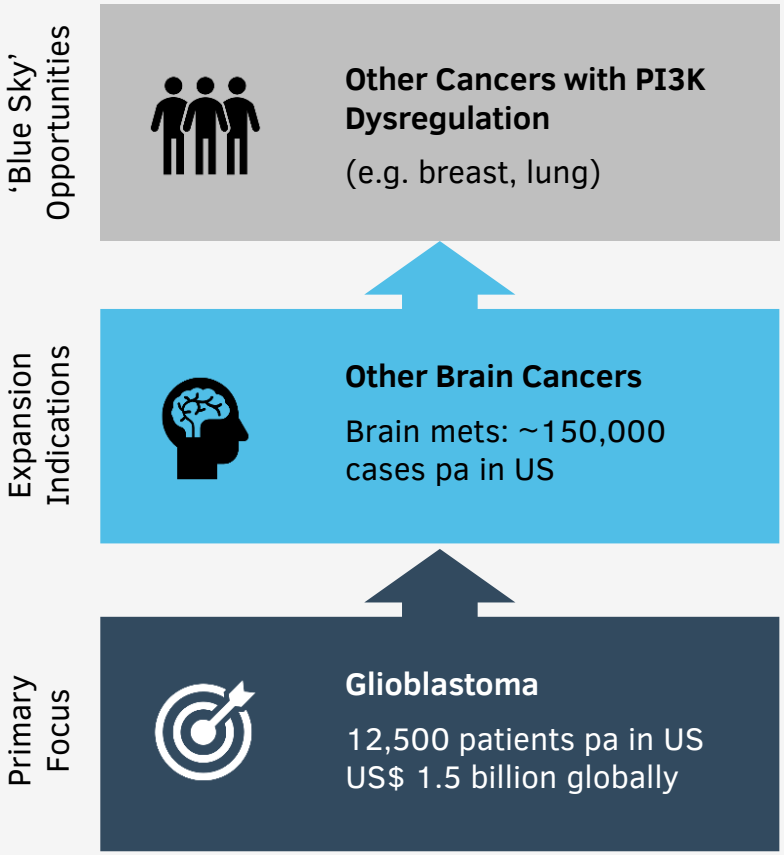
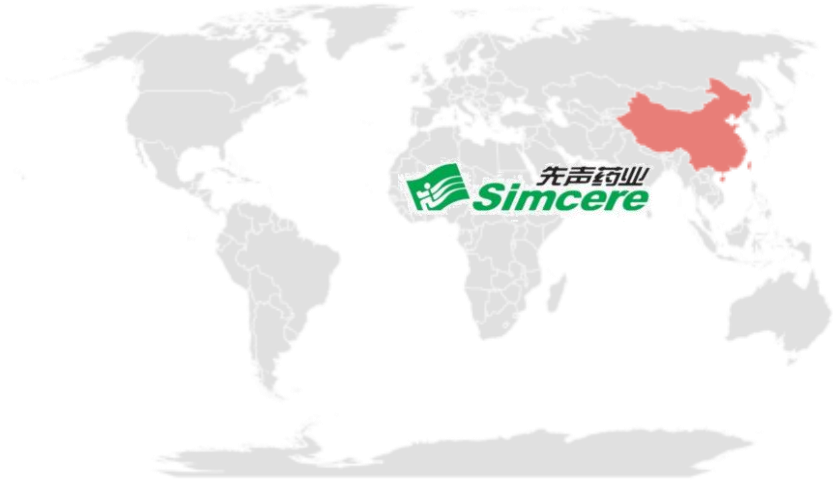
# Commercial opportunity is substantial, with one commercial partnership already in place




**Partnership with Simcere Pharmaceutical for Greater China signed in March 2021**

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



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# 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 and positive phase I data

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 for glioblastoma alone, with limited competition and very high unmet-need

# EVT801

Solid Tumors

Pre-Phase I

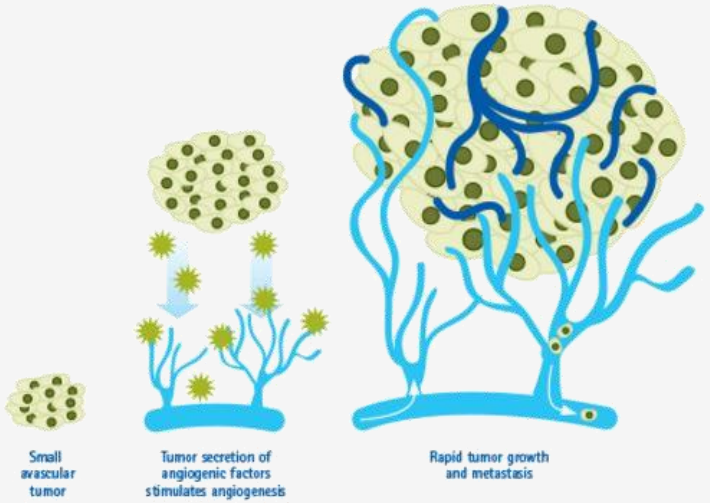
# Targeting angiogenesis is a well-established approach in the treatment of cancer

| Product | Company | Target | Indications | Annual Sales (US$)* |
|---|---|---|---|---|
| AVASTIN bevacizumab | Genentech A Member of the Roche Group | VEGF-A | • Colorectal cancer<br>• Lung cancer<br>• Breast cancer | **$7 billion** |
| Nexavar (sorafenib) tablets | BAYER | VEGFR<br>PDGFR<br>RAF kinases | • Hepatocellular carcinoma<br>• Renal call carcinoma<br>• Thyroid cancer | **$1 billion** |
| SUTENT capsules sunitinib malate | Pfizer | VEGFR<br>PDGFR | • Renal cell carcinoma<br>• Gasto-intestinal stromal tumor | **$750 million** |
| Votrient pazopanib tablets (200 mg) | NOVARTIS | VEGFR<br>PDGFR<br>c-Kit | • Renal cell carcinoma<br>• Soft tissue sarcoma | **$1 billion** |
| Inlyta axitinib 1mg and 5mg tablets | Pfizer | VEGFR<br>c-Kit<br>PDGFR | • Renal cell carcinoma | **$400 million** |
| LENVIMA (lenvatinib) capsules 10 mg and 4 mg | Eisai | VEGFR | • Renal cell carcinoma<br>• Hepatocellular carcinoma<br>• Endometrial carcinoma | **$300 million** |
| CABOMETYX (cabozantinib) tablets | EXELIXIS | c-Met<br>VEGFR2<br>RET | • Renal cell carcinoma<br>• Hepatocellular 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




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**



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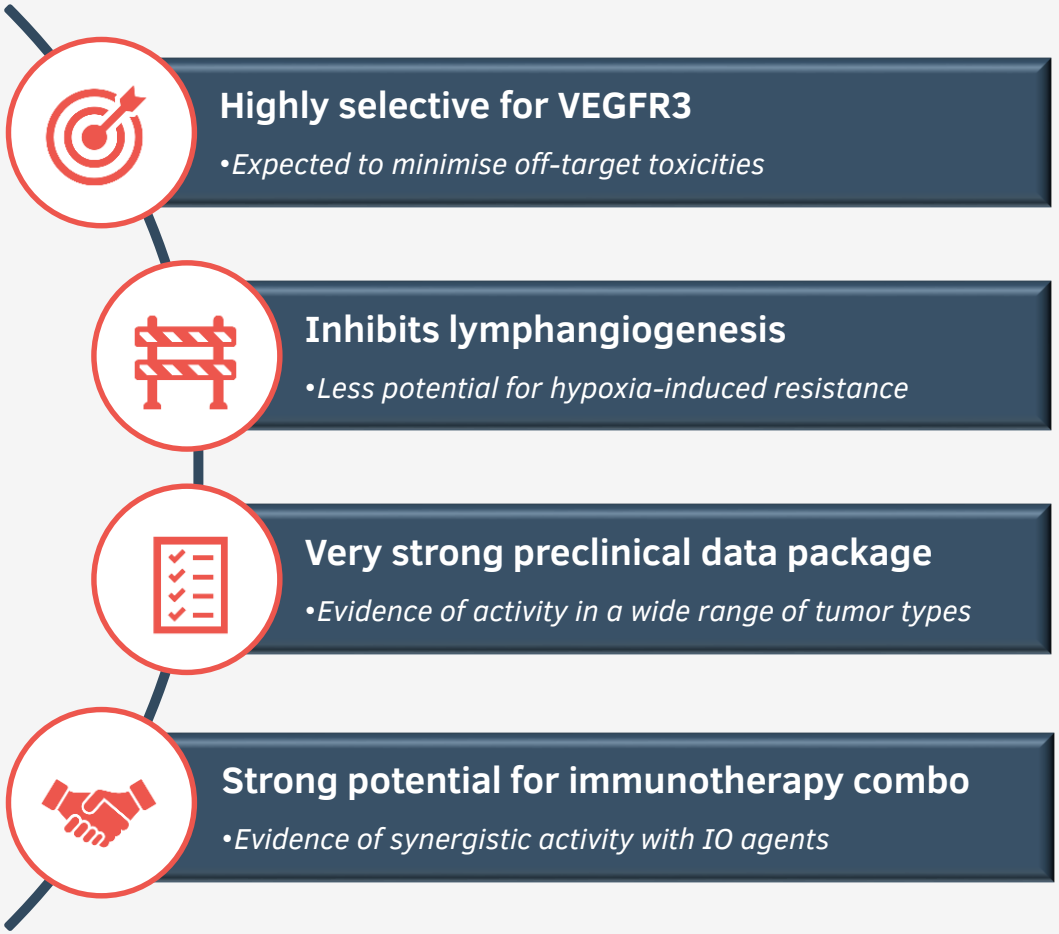
# EVT801 is a selective VEGFR inhibitor, primarily inhibiting lymphangiogenesis (formation of new lymphatic vessels)




**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

# 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

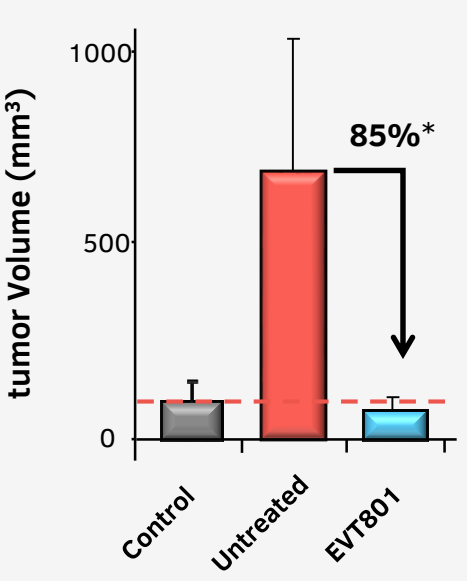
**Conclusions**

- 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*

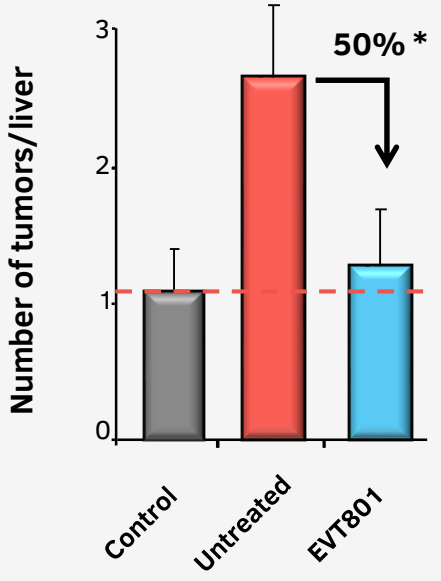
85% reduction




**Metastasis**

*Number of Tumors in the Liver*

50% reduction




* Statistically significant ($p<0.05$)

Data on file



KAZIA THERAPEUTICS

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

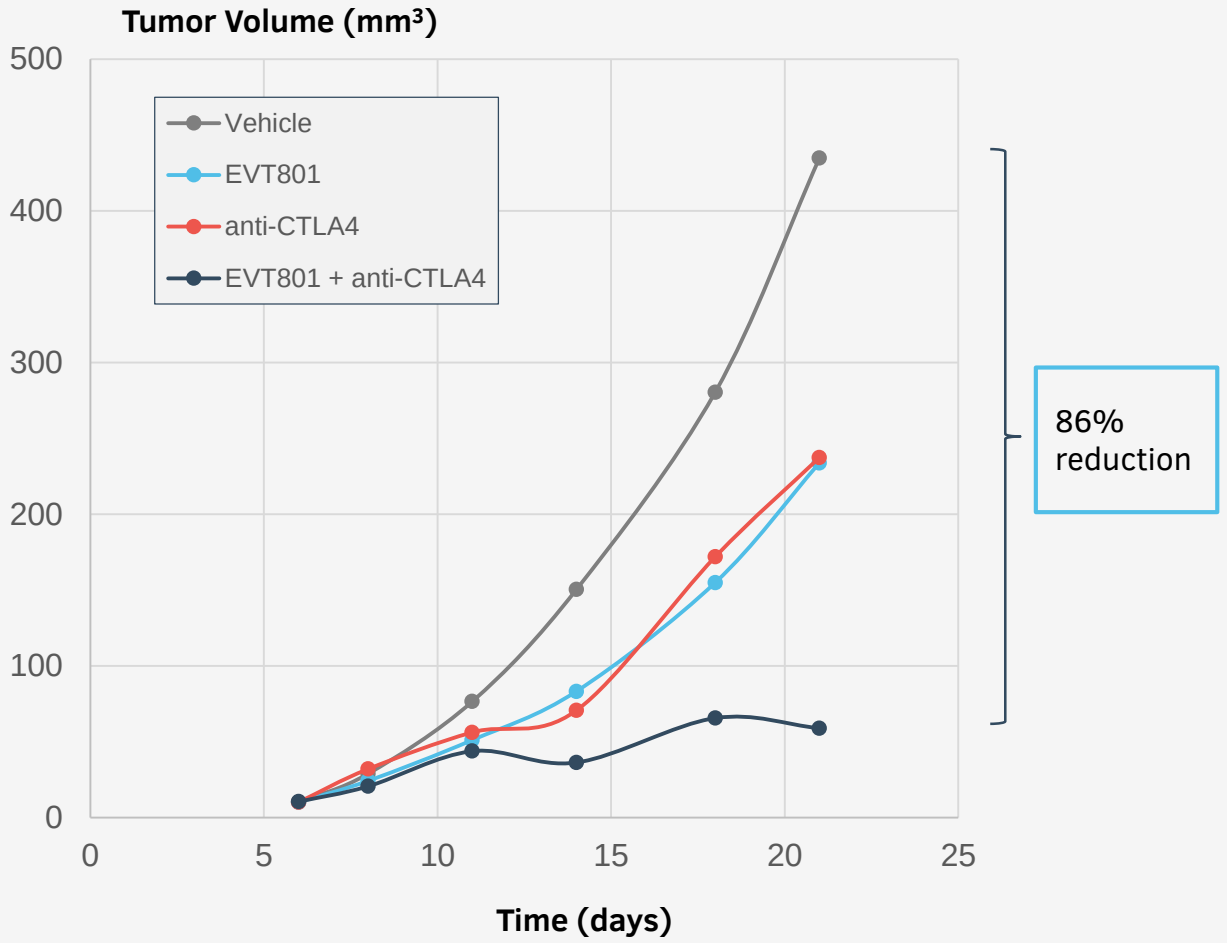
*Synergistic activity in combination with anti-CTLA4 mAb*

**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 commenced a phase I clinical trial in November 2021

- Up to 60 patients with advanced solid tumors, resistant to existing therapies
- Endpoints will include safety and tolerability, mechanism of action, and preliminary efficacy
- EVT801 administered initially as monotherapy; plan for early transition to immunotherapy combination
- Rich suite of biomarkers investigated to provide deep understanding of EVT801 activity
- First Patient In (FPI) November 2021

| 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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