



**KAZIA**  
THERAPEUTICS



## A Diversified Oncology Drug Development Company

Kazia Corporate Overview

August 2025

# Forward Looking Statements

This presentation contains forward -looking statements, which can generally be identified as such by the use of words such as “may,” “will,” “estimate,” “future,” “forward,” “anticipate,” “plan,” “expect,” “explore,” “potential” or other similar words. Any statement describing Kazia's future plans, strategies, intentions, expectations, objectives, goals or prospects, and other statements that are not historical facts, are also forward-looking statements, including, but not limited to, statements regarding: the timing for interim or final results and data related to Kazia's clinical and preclinical trials, or third-party trials evaluating Kazia's product candidates, timing and plans with respect to enrolment of patients in Kazia's clinical and preclinical programs, the potential benefits of paxalisib and EVT801, the potential results of combination studies of paxalisib and other collaborations, timing for any regulatory submissions or discussions with regulatory agencies, the potential market opportunity for paxalisib and EVT801, and Kazia's strategy and plans with respect to its business and programs. Such statements are based on Kazia's expectations and projections about future events and future trends affecting its business and are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements, including risks and uncertainties: associated with clinical and preclinical trials and product development, the risk that interim data may not be reflective of final data, related to regulatory approvals, and related to the impact of global economic conditions, including disruptions in the banking industry. These and other risks and uncertainties are described more fully in Kazia's Annual Report, filed on Form 20-F with the SEC, and in subsequent filings with the SEC. Kazia undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise, except as required under applicable law. You should not place undue reliance on these forward-looking statements, which apply only as of the date of this presentation.

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# Company Overview

*A late-clinical-stage oncology drug development company*



## Corporate Highlights

### Paxalisib

**Advanced breast cancer trial launched 1Q CY2025**

Potential best in class PI3K pathway inhibitor

- Designed to be best in class PI3K pathway inhibitor with modest mTOR activity
- Only brain-penetrant PI3K inhibitor in development

Overcoming immunotherapy drug resistance

- Reduced primary tumor burden & metastasis in combination with checkpoint inhibitor or PARP inhibitor in 4T1 TNBC model

Unique asset being evaluated in multiple trials

- Multiple signals of clinical activity across several cancer types
- Fast Track, Orphan Drug, and Rare Pediatric Disease Designations from US FDA

Rich potential commercial opportunity

- TNBC market predicted to grow to USD \$1.5b by 2030
- Commercial licensee in place for China
- Licensee for intractable seizures in rare CNS diseases

### EVT801

**Phase 1 final data anticipated CY2025**

Selective VEGFR3 inhibitor

- Designed to avoid off-target toxicity of older, non-selective angiokinase inhibitors
- Primarily targets lymphangiogenesis

Completed phase 1 for advanced solid tumors

- Preliminary data from adaptive, biomarker study at 2 leading cancer sites in France presented at 2024 AACR Ovarian Cancer Research Symposium

Potential use in multiple solid tumor types

- Potential indications include: ovarian cancer, renal cell carcinoma, liver cancer, colon cancer, and sarcoma

Potential combination with immunotherapy

- Strong evidence of synergy in preclinical data supports potential of monotherapy or combination use

Licensing-driven business model focused on high quality, differentiated clinical-stage assets sourced from Genentech (paxalisib) and Sanofi / Evotec (EVT801)

Lean virtual pharma model, with ~75% of cashflows applied directly to clinical trials

Potential opportunities for non-dilutive income via additional partnering activity

Delisted from Australian Securities Exchange (ASX) in Nov 2023; now solely listed on NASDAQ (KZIA)

# Pipeline – Two Differentiated Assets

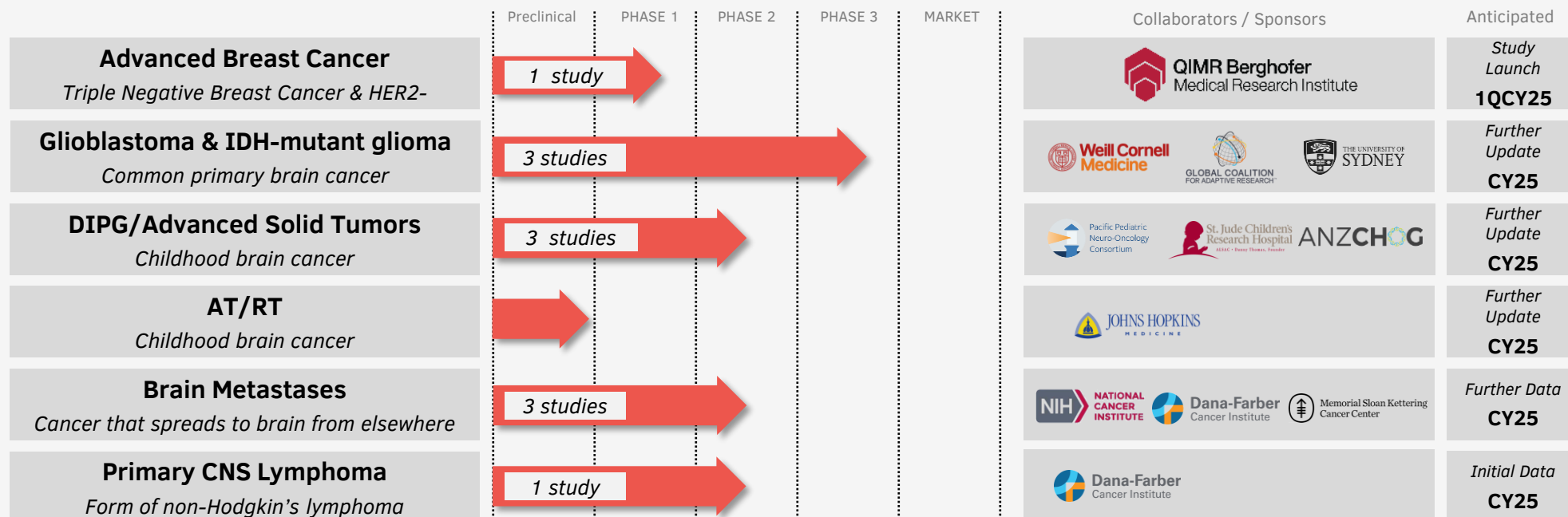
*Clinical progress in rare, resistant and relapsing cancers*

## Paxalisib

Investigational, small molecule, potential best-in-class, brain-penetrant inhibitor of PI3K / mTOR

licensed from:

**Genentech**  
IN BUSINESS FOR LIFE



## EVT801

Investigational, small molecule, highly specific inhibitor of VEGFR3

licensed from:

evotec









IDH: Isocitrate dehydrogenase, DIPG: Diffuse Intrinsic Pontine Glioma, AT/RT: Atypical Teratoid Rhabdoid Tumor, CNS: central nervous system, TNBC: triple negative breast cancer, VEGFR3: vascular endothelial growth factor receptor 3

# Paxalisib Mechanism of Action

*A brain-penetrant PI3K pathway inhibitor with modest mTOR activity, by design*

## 1 The PI3K pathway is activated in many forms of cancer

|   |              |     |
|---|--------------|-----|
|    | Glioblastoma | 90% |
|    | Breast       | 80% |
|    | Lung         | 75% |
|    | Endometrial  | 60% |
|  | Ovarian      | 60% |
|  | Prostate     | 45% |

## 2 Five PI3K inhibitors have already been approved by FDA



- Chronic lymphocytic leukemia
- Follicular lymphoma



- Follicular lymphoma



- Chronic lymphocytic leukemia
- Follicular lymphoma



- Breast cancer



- Follicular lymphoma

## 3 Paxalisib – Unlocking the full potential of PI3K pathway inhibition

**The only brain-penetrant dual pan-PI3K/mTOR inhibitor in development**

*Only 2% of small-molecule drugs are brain-penetrant*

**Designed to be best in class PI3K pathway inhibitor with modest mTOR activity**

*Dual targeting required to inhibit cancer cell proliferation & migration in TNBC cell model*

**Overcoming metastasis and drug resistance in combination with immunotherapy**

*Epigenetic re-programming of dormant cancer cells and improved cancer immune visibility*

Source: Data on file

# Paxalisib – Development History

*Expanding the clinical footprint of paxalisib into solid tumors beyond CNS*

**2012-2015**

Genentech **Phase 1** clinical study in 47 patients with advanced, **high-grade glioma**. Study demonstrated a favourable safety profile and provided efficacy signals

**February 2018**

GDC-0084 awarded **Orphan Drug Designation** by the US FDA in glioblastoma

**August 2019**

GDC-0084 becomes '**paxalisib**' with the granting of an International Non-Proprietary Name (INN) by the World Health Organisation

**7 January 2021**

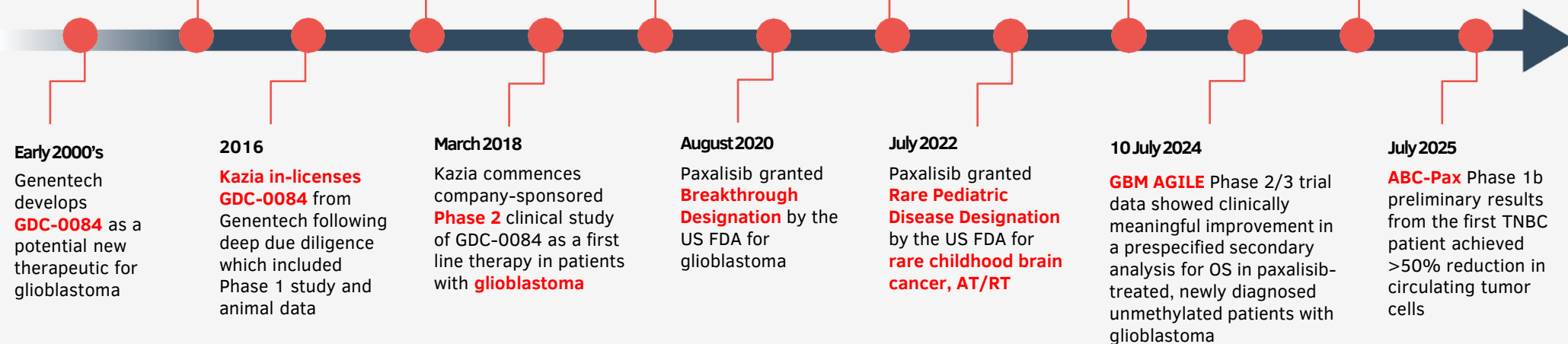
**GBM AGILE** pivotal study commences recruiting paxalisib arm

**July 2023**

Paxalisib received **Fast Track Designation** by the US FDA for solid tumor **brain metastases** with PI3K pathway mutations in combination with radiation therapy

**January 2025**

Kazia commences **Phase 1b ABC-Pax study** of paxalisib in combination with immunotherapy in patients with **triple negative breast cancer (TNBC)**



# Advanced Breast Cancer

# Invasive breast cancer - unmet need

*Most worldwide common cancer among women*

**2.3 million<sup>1</sup>**

Cases / year  
Breast cancer  
most commonly  
diagnosed cancer

**~1 in 8**

Women in the US  
will be diagnosed  
with invasive  
breast cancer

American Cancer  
Society says

**>300,000**

new cases of  
invasive BC in  
US<sup>2</sup>

## Incidence

Increased over  
the last decade  
by 1% annually,  
with steeper  
increase among  
women <50 years  
old

| Current age          | Diagnosed with<br>invasive breast cancer | Dying from<br>breast cancer |
|----------------------|--|-----------------------------|
| 20                   | 0.1% (1 in 1,344)                        | <0.1% (1 in 19,247)         |
| 30                   | 0.5% (1 in 198)                          | <0.1% (1 in 2,192)          |
| 40                   | 1.6% (1 in 62)                           | 0.1% (1 in 723)             |
| 50                   | 2.5% (1 in 41)                           | 0.3% (1 in 348)             |
| 60                   | 3.6% (1 in 28)                           | 0.5% (1 in 217)             |
| 70                   | 4.2% (1 in 24)                           | 0.7% (1 in 141)             |
| 80                   | 3.1% (1 in 32)                           | 1.0% (1 in 103)             |
| <b>Lifetime risk</b> | <b>13.1% (1 in 8)</b>                    | <b>2.3% (1 in 43)</b>       |

Probability is among those who have not been previously diagnosed with cancer and reflects the likelihood of diagnosis/death within 10 years of current age. Percentages and "1 in" numbers may not be numerically equivalent due to rounding.

**Source:** DevCan, Version 6.7.5.  
©2024, American Cancer Society, Inc., Surveillance and Health Equity Science

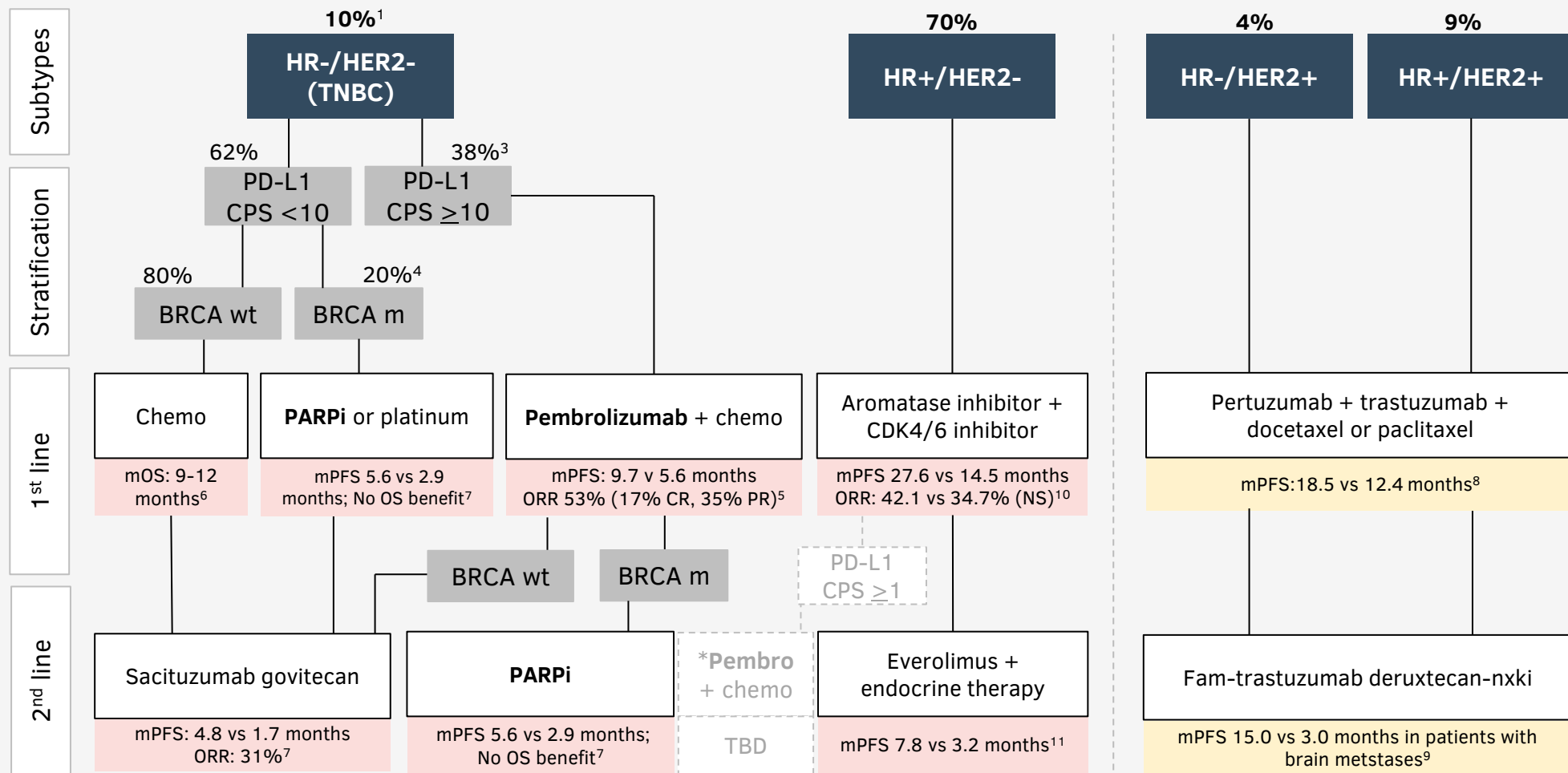
1. National Institutes of Health (NIH): Current and future burden of breast cancer: Global statistics for 2022 and 2030

2. [Cancer.org](https://www.cancer.org) 2024



# Advanced breast cancer treatment landscape

*Modest results for HER2- subtypes, despite checkpoint and PARP inhibitors*

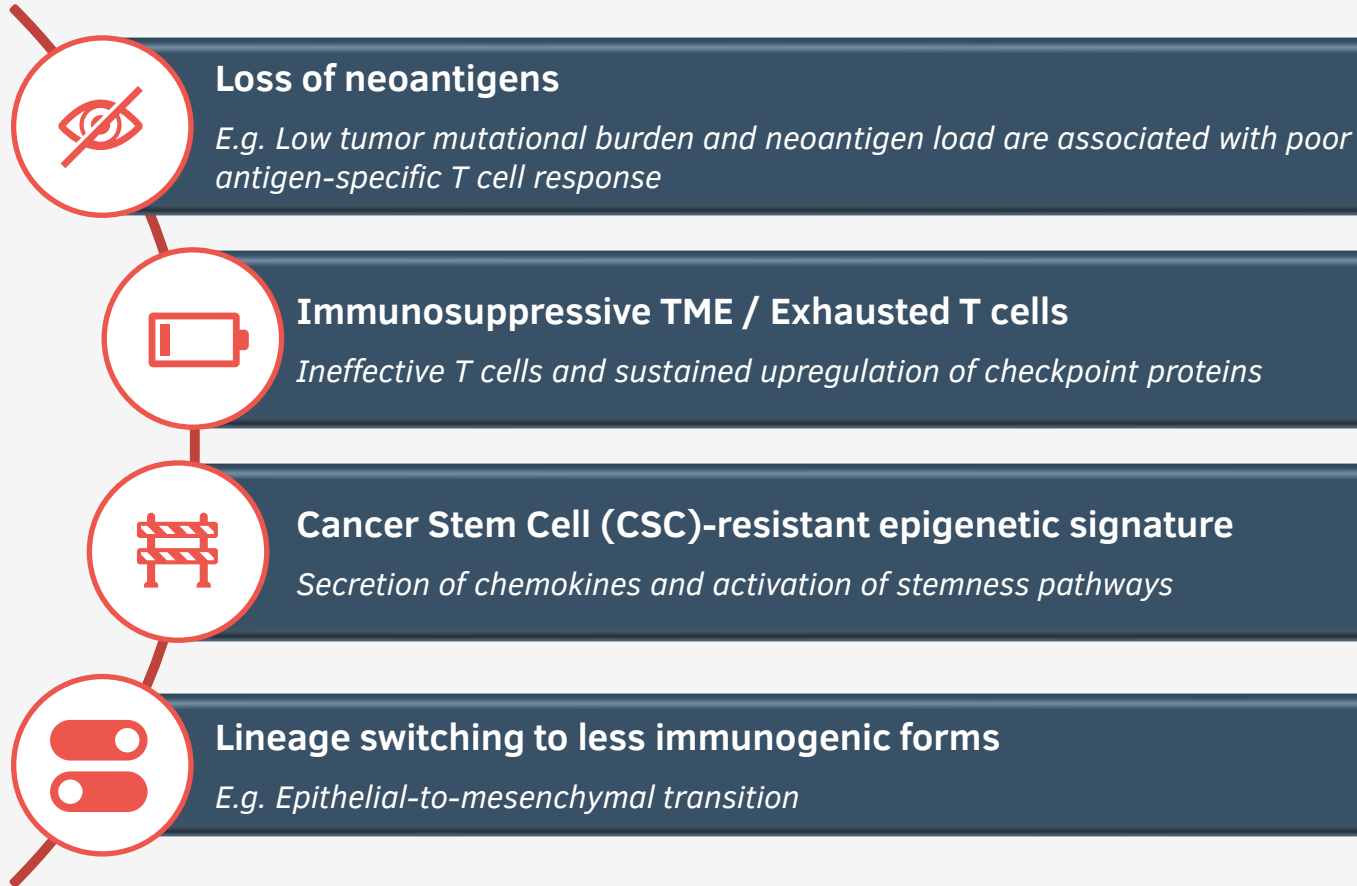


1. BC subtypes and distribution: (7% unknown subtype) [Cancer.org](https://www.cancer.org); 2. Treatment: NCCN Guidelines Version 4.2025, simplified and with focus on preferred regimens; 3. <https://www.pdl1portal.com/tnbc/>; 4. [Pavesi et al. 2022](https://doi.org/10.1093/annonc/ndz001); 5. [Keytruda.com](https://doi.org/10.1093/annonc/ndz001); 6. [Khosravi-Shani et al 2017](https://doi.org/10.1093/annonc/ndz001); 7. [Gacia-Saenz et al 2025](https://doi.org/10.1093/annonc/ndz001); [Bardia et al 2024](https://doi.org/10.1093/annonc/ndz001); 8. [Baselga et al 2012](https://doi.org/10.1093/annonc/ndz001); 9. [Jacobson 2022](https://doi.org/10.1093/annonc/ndz001); 10. [Wu et al 2020](https://doi.org/10.1093/annonc/ndz001); 11. [Yardley et al 2013](https://doi.org/10.1093/annonc/ndz001)

\* Potential future regimen, depending on Keynote B49 readout ([NCT04895358](https://doi.org/10.1093/annonc/ndz001)); CPS = Combined Positive Score; wt = wildtype; NS = not statistically significant

# Resistance, recurrence and metastatic spread

*Cancer Stem Cells and a functioning immune system play a critical role in recurrence and metastatic spread of cancers*



# PI3K-mTOR inhibition may overcome metastasis and immunotherapy drug resistance

## PI3K-mTOR inhibition

### ↓ Metastasis-initiating cells & EMT

- ↓ Highly aggressive CD44<sup>high</sup>/CD24<sup>low</sup> cancer stem cell phenotype
- ↓ Persister cancer cell phenotype (p65, FOXQ1, NRF2, and NNMT)
- ↓ Drug resistance markers (ABCB5, SNAIL, and ALDH1)
- ↓ EMT (reduced expression of mesenchymal marker and increased expression of the epithelial marker)

### ↓ Inflammation

- Inhibits IL-6 and NF-κB inflammation signature

### ↑ Immune reinvigoration

- Epigenetic reprogramming of repressed T-cells
- Increased total tumor-infiltrating lymphocyte with reduction of exhausted T cells and Tregs

### ↑ Cancer immune visibility

- Increases expression of several viral mimicry genes, most profoundly GBP2
- Disrupts both the catalytic and noncatalytic axes of EZH2

## PI3K-mTOR inhibition + Immunotherapy

### ↓ Primary tumor burden

### ↓ Metastases

# Paxalisib (GDC-0084)

*Designed to be best in class PI3K pathway inhibitor with modest mTOR activity*

## Paxalisib

- Potent, selective, oral, once a day dosing, no unexpected toxicities
- Pan PI3K inhibitor activity and modest mTOR, by design
  - Dual targeting required to inhibit cancer cell proliferation and migration in vitro
- Robust brain penetration
- More than 550 adult and pediatric patients have received paxalisib through phase 1-3 clinical trials or expanded access programs (8 clinical trials ongoing)

## Relevant marketed or active clinical PI3K inhibitor programmes

|                          | Paxalisib (Kazia)                | Alpelisib (Novartis)                          | Gedatolisib (Celcuity)  | WXFL-10030390 (Jiatan) <sup>2</sup> |
|--------------------------|----------------------------------|---|---|-------------------------------------|
| <b>Targets</b>           | Pan-PI3K / mTOR                  | PI3Kα only                                    | Pan-PI3K / mTOR   | PI3K / mTOR                         |
| <b>Development stage</b> | P3 (GBM)<br>P1 (TNBC & HER2- BC) | Marketed (HER2- BC)                           | P3 (HER2- BC)   | P2 in China (solid tumors)          |
| <b>Safety</b>            | No unexpected toxicities         | Severe Hyper-sensitivity warning <sup>3</sup> | Grade 4 neutropenia reported in combo with palbociclib <sup>1</sup> | Unknown                             |
| <b>RoA</b>               | Oral (QD)                        | IV  | IV  | Oral                                |
| <b>Brain penetration</b> | Yes                              | Poor  | Partial   | Unknown                             |

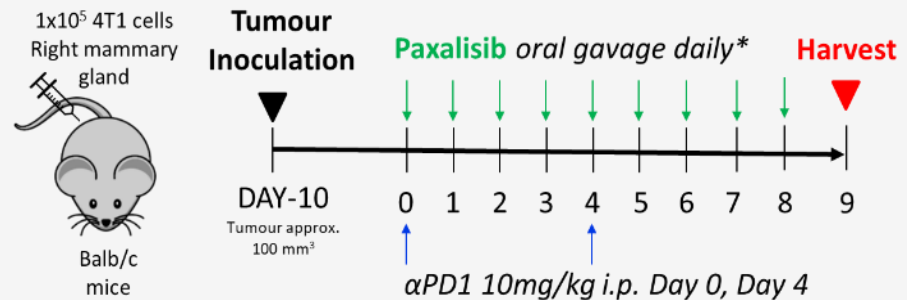
RoA = route of administration

1. [Layman et al 2024](#) 2. GlobalData 3. [Pigray](#)

# Pre-clinical studies combining Paxalisib with either checkpoint inhibitor or PARP inhibitor resulted in highly consistent and statistically significant signals of efficacy

## 4T1 mouse model:

- Standard model for TNBC
- Immunotherapy resistant model
- Highly tumorigenic and invasive



## Checkpoint Inhibitor

- Reduced tumor volume
- ↓ Lung metastases
- ↓ Lymph node metastases
- ↓ Liver inflammation
- ↓ Lung inflammation
- ↓ Liver and spleen EMH
- No observed toxicity

## PARP inhibitor

- Reduced tumor volume
- ↓ Lung metastases
- ↓ Lymph node metastases
- ↓ Liver inflammation
- ↓ Lung inflammation
- ↓ Liver and spleen EMH
- No observed toxicity

# Kazia-sponsored clinical study overview

*PAX-ABC STUDY: KZA-0084-ABC001*

Phase 1b, multi-center, open-label, randomized study to evaluate the safety, tolerability, and clinical activity of combining paxalisib with olaparib or pembrolizumab/chemotherapy in approximately 24 patients with advanced breast cancer

## Primary Objectives:

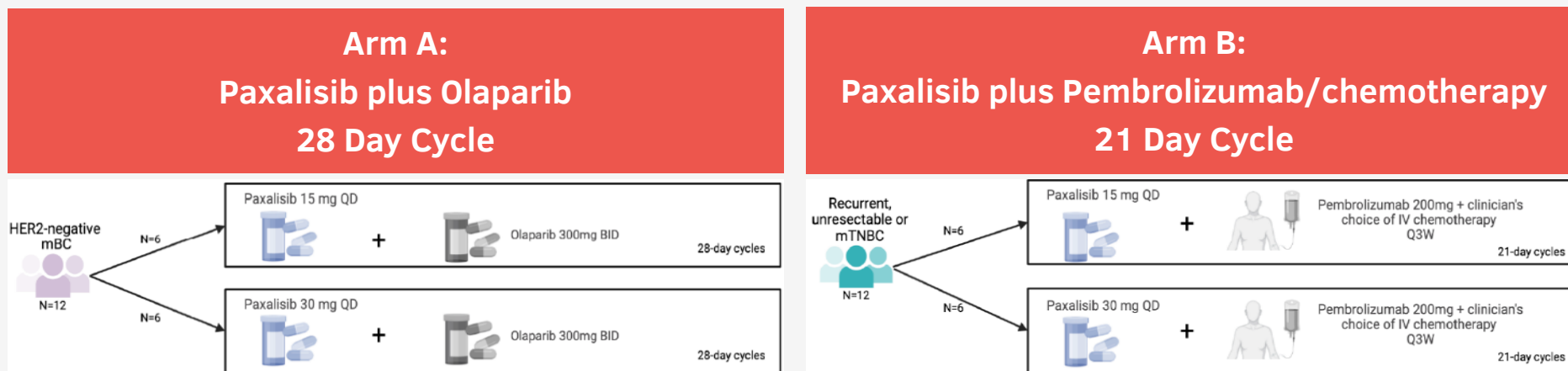
- To evaluate the safety and tolerability of paxalisib administered in combination with either olaparib or pembrolizumab/chemotherapy as per their labelled indications in patients with advanced breast cancer.
- To determine a recommended phase 2 dose (RP2D) of paxalisib for daily administration in combination with either olaparib or pembrolizumab/chemotherapy.

## Secondary Objectives:

- To assess the utility of novel liquid biopsy assessments by monitoring circulating tumor cells in the blood as a predictor of recurrence and to examine immune cell signature as a predictor of immune reinvigoration
- To document measures of clinical activity including progression and response rates

# Kazia-sponsored clinical study overview

KZA-0084-ABC001



## Participant disease characteristics:

- HER2-negative stage IV (metastatic) breast cancer diagnosis based on pre-existing documented histopathology and medical imaging results
- Confirmed gBRCAm (BRCA1, BRCA2 or both)
- Prior treatment with chemotherapy in the metastatic setting
- Meet all current prescribing criteria for commencing olaparib therapy

## Participant disease characteristics:

- Recurrent, unresectable or metastatic TNBC, based on pre-existing documented histopathology and medical imaging results
- Confirmed that tumors express PD-L1 with a combined positive score (CPS)  $\geq 10$
- Meet all current prescribing criteria for commencing pembrolizumab therapy

# Early efficacy data from first TNBC patient in Phase 1b trial

*Combination regimen results in >50% reduction in circulating tumor cells (CTCs)*

## Background

### Patient profile

- 61-year-old woman with metastatic triple-negative breast cancer localized to the left upper lobe of the lung

### Regimen

- Paxalisib, pembrolizumab (Keytruda ®), standard chemotherapy

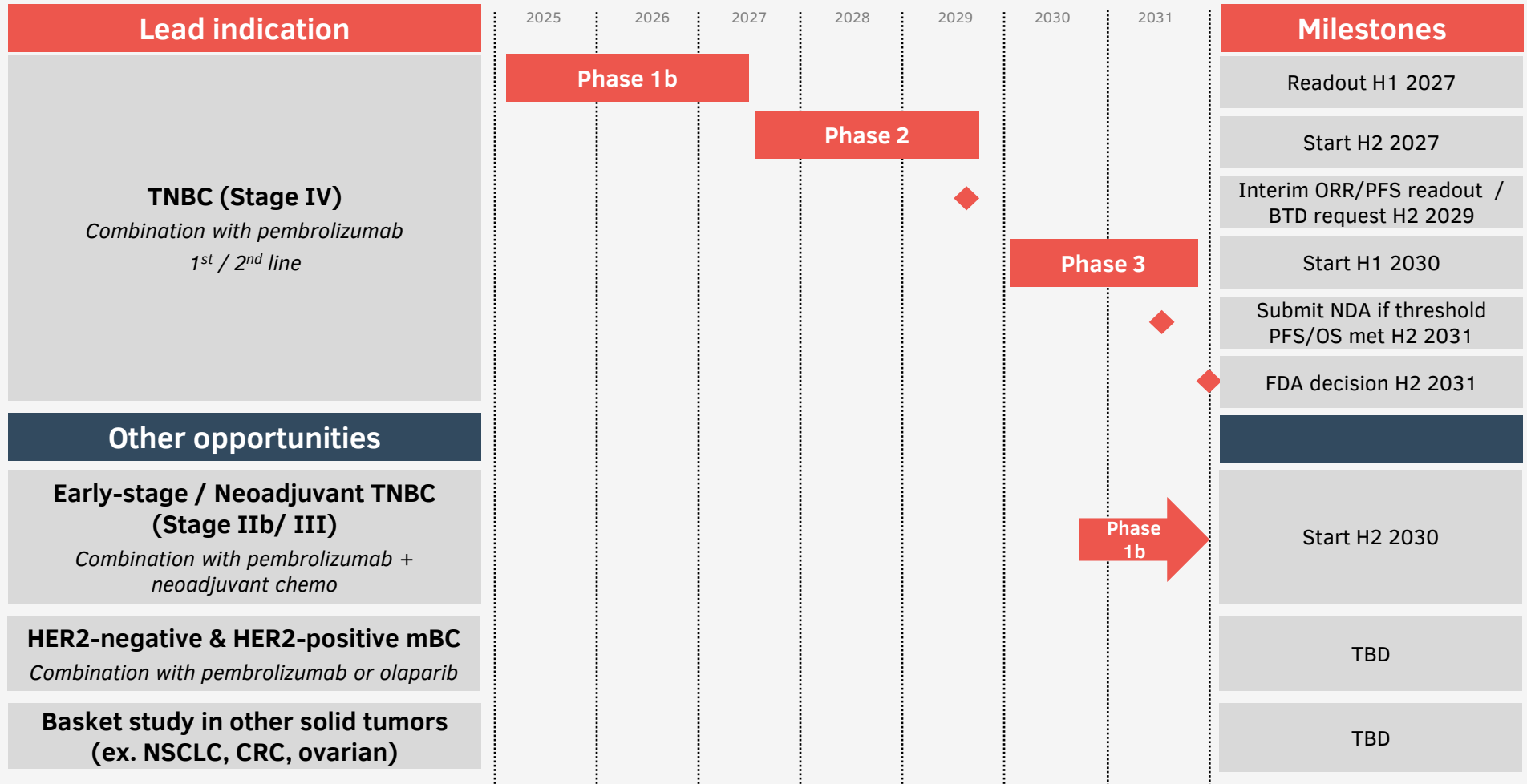
## Results at Day 21 (end-of-cycle 1)

- >50% reduction in total circulating tumor cells count
- Comparable reduction in CTC clusters — these aggregates are associated with heightened metastatic potential
- Reduction in the mesenchymal phenotype of the remaining CTCs; this phenotype is one of the hallmarks of aggressive metastatic seeding cancer cells
- Such results are not typically seen with chemotherapy or immunotherapy therapies

**First-in-human data reflects mechanistic synergy consistent with the preclinical data**

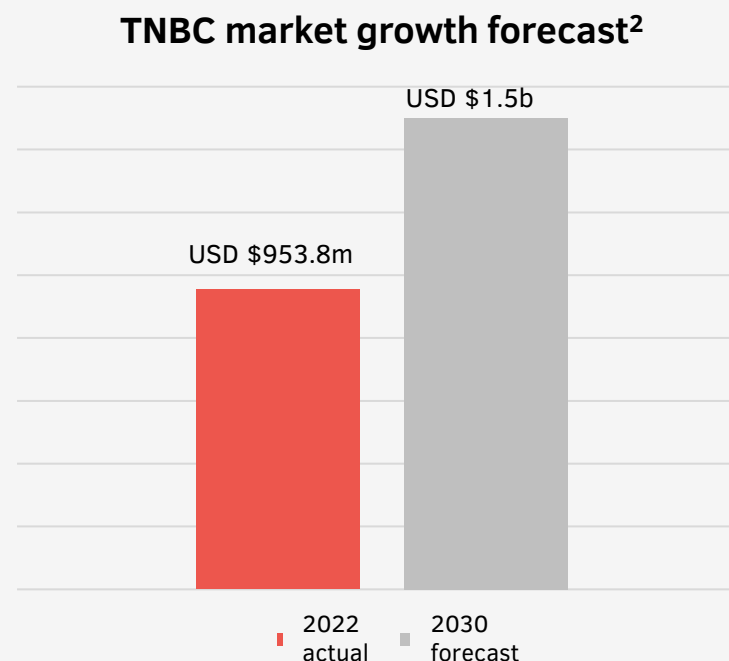
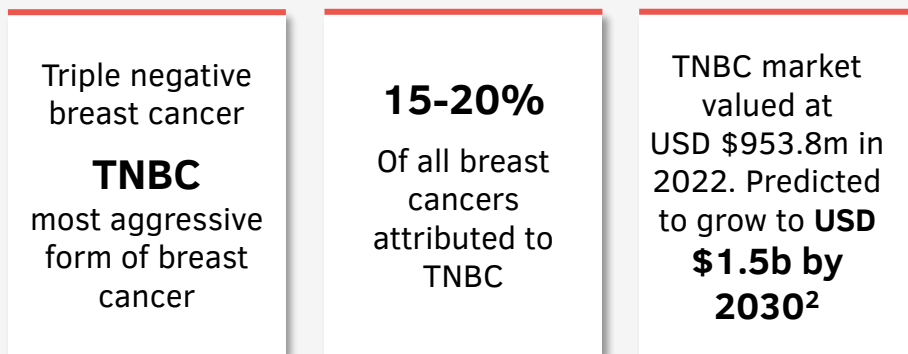


# Development plan & timeline



# Triple negative breast cancer market

*Projected TNBC market to exceed \$1.5 Billion by 2030*



1. National Institutes of Health (NIH): Current and future burden of breast cancer: Global statistics for 2022 and 2030

2. <https://www.databridgemarketresearch.com/reports/global-triple-negative-breast-cancer-market>

# Intellectual property

## QIMR Berghofer Collaboration

- Kazia has obtained an exclusive, worldwide, sub-licenseable, royalty-bearing license to the relevant patents from QIMR
- Patent Overview (WO2024/108256A1)
  - PI3K inhibitors in combination with immunotherapy (including PARP inhibitors) for treating or delaying the progression of cancer, or a recurrence
  - PI3K inhibitors results in epigenetic reprogramming of the repressed T-cells
  - PI3K inhibitors can inhibit the formation and maintenance of cancer stem cells (CSC), and in inducing mesenchymal to epithelial transition (MET), making them useful in treating solid tumors including recurrent cancers
- **Priority date: Nov 2022**

# Paxalisib in triple negative breast cancer

*QIMR Berghofer Medical Institute collaboration*

*“In treatment-resistant pre-clinical models of breast cancer, paxalisib (4T1 mouse model, TNBC<sup>1</sup>) has shown encouraging results in inhibiting both the primary tumor burden and metastasis by reinvigorating the immune system within the tumor microenvironment” – Professor Sudha Rao, Group Leader, QIMR Berghofer*



- Leading transcriptional biology and epigenetics expert, Prof Rao identified an entirely novel effect of PI3K inhibition:
  - Immune modulator of the tumor and the surrounding microenvironment
  - Administration of PI3K inhibitors such as paxalisib, at doses and frequencies different to those conventionally used, appears to activate or reinvigorate the immune system in the tumor, making it more susceptible to immunotherapy
- Preliminary data from our collaboration was presented at San Antonio Breast Cancer Symposium 4Q CY2024

Combination  
Paxalisib +  
KEYTRUDA®  
(pembrolizumab)  
data in TNBC<sup>1</sup>  
preclinical  
models

Combination  
Paxalisib +  
LYNPARZA®  
(olaparib) data in  
advanced breast  
cancer  
preclinical  
models

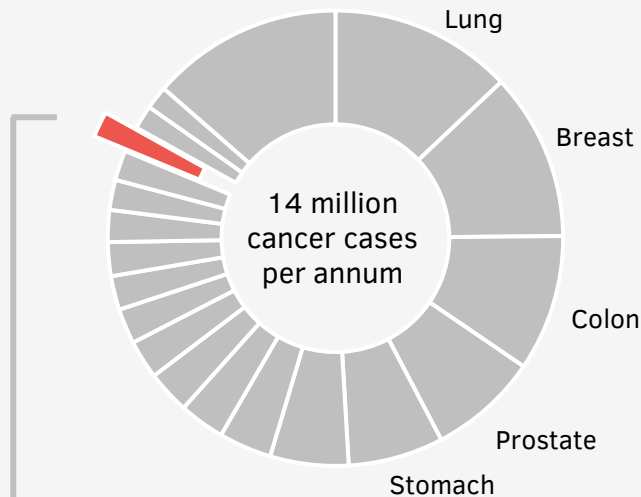
Paxalisib  
influence on  
immune system  
(example, T cells,  
B cells, NK cells)  
and within the  
tumor and its  
micro-  
environment

Intellectual  
Property (IP)  
update

# Glioblastoma

# Glioblastoma Overview

*The most aggressive malignant brain cancer*



## Glioblastoma Multiforme

133,000 cases  
per annum  
worldwide

GBM treatment market size  
(2022)

**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**

Survival,  
if untreated

Five-year  
survival

**3 – 5%**

(breast cancer:  
90%)

*“Even a few months increase in overall survival makes a huge difference for my patients, so efficacy of an approved therapeutic makes the largest impact.”*

US Neuro-Oncologist

Source: Data on file. Market research performed 2021

# Paxalisib in Glioblastoma

*Consistent median Overall Survival data in two studies of NDU glioblastoma patients*

Compelling Paxalisib data in NDU patients  
when compared to SOC

Paxalisib in  
GBM Agile

(n=54)

Median OS: **15.54  
months\***

Paxalisib in  
Kazia sponsored  
phase 2 study

(n=30)

Median OS: **15.7  
months**

Standard of Care data GBM AGILE study (left)  
and STUPP historical controls (right) in NDU  
patients

Concurrent SOC  
GBM Agile

(n=46)

Median OS: **11.9  
months\***

STUPP historical  
control

(N/A)

Median OS: **12.7  
months**

\*GBM Agile; Prespecified secondary analysis of median Overall Survival

# Paxalisib in Newly Diagnosed Unmethylated GBM Next Steps

## **FDA Type C meeting was held in December 2024 to discuss next steps with key highlights of the discussion below:**

- The FDA's current position is that data on Overall Survival would generally not be appropriate for accelerated approval but could be considered to support a traditional/standard approval
- The Agency further commented that the secondary endpoint OS data from the GBM-AGILE study may be supportive and informative for designing and executing a pivotal registrational study in pursuit of a standard approval
- The Company aligned with the FDA on key aspects of the design of a proposed registrational/pivotal phase 3 study in Newly Diagnosed Unmethylated GBM patients
- Kazia is finalizing the protocol for the pivotal phase 3 study and discussing with a number of global contract research organizations (CRO) with experience in the Neuro-oncology drug development space. Anticipate further updates in CYQ25



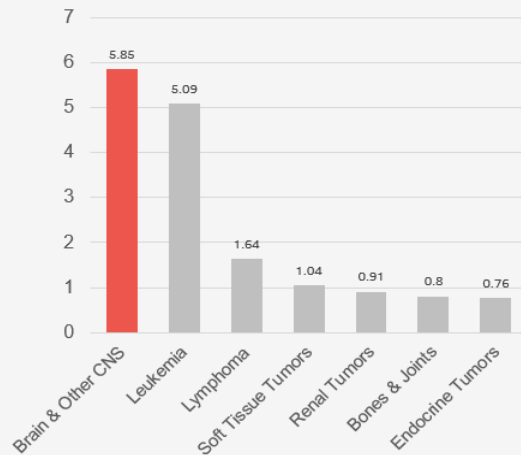
# Childhood Brain Cancers

# Paxalisib in Childhood Brain Cancer

*High unmet need especially in patients with diffuse midline gliomas (DMGs)*

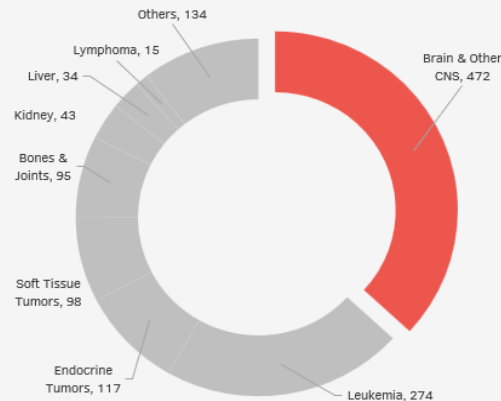
## 1 Brain cancer is the most common malignancy of childhood

Average Annual Age-Adjusted Incidence  
(cases / 100,000 people; 2014–2018)

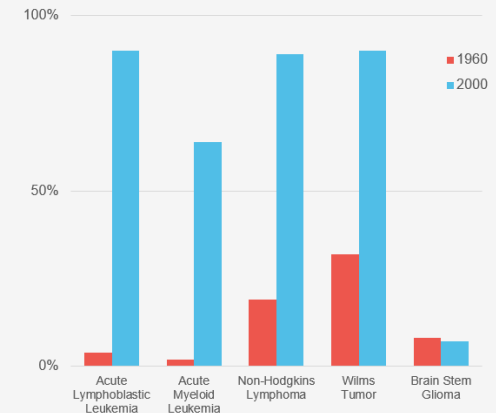


## 2 Brain cancer represents about one third of childhood cancer deaths

Mortality  
(estimated absolute number of cases in US; 2020)



## 3 Prognosis of childhood brain cancer, especially DMGs, has improved little in recent decades



### FDA-Approved Drug Therapies

|                                     |     |
|-------------------------------------|-----|
| Diffuse Midline Gliomas             | Nil |
| Atypical Teratoid / Rhabdoid Tumors | Nil |
| Medulloblastoma                     | Nil |

Source: CBTRUS; CDC; Ages 0–14 shown; Adamson PC, *CA Cancer J Clin.* 2015;65:212–220

# Summary of Paxalisib in Childhood Brain Cancer

*Kazia is actively pursuing three forms of childhood brain cancer*

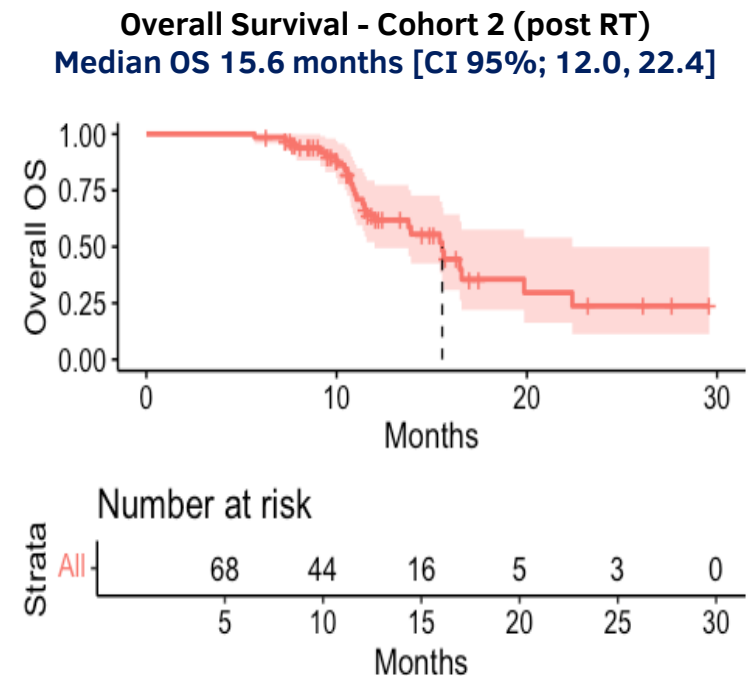
|                               | Diffuse Midline Gliomas<br>(DMG, DIPG)  | Atypical Teratoid /<br>Rhabdoid Tumors (AT/RT)   | Advanced Childhood Cancer<br>(PI3K/mTOR activated)  |
|-------------------------------|---|--|---|
| <b>Preclinical Research</b>   | <i>Positive preclinical data in combination with ONC201</i>   | <i>Positive preclinical data as monotherapy and in combination (AACR 2022, 2023, 2024)</i> | <i>Research proposals under discussion</i>  |
| <b>Clinical Trials</b>        | <i>Phase 1 monotherapy clinical trial at St Jude Children's Research Hospital completed</i>                   | <i>Clinical trial design/execution discussions ongoing between PNOC and Kazia</i>          | <i>Additional clinical trial opportunities under discussion for medulloblastoma and HGG</i>                           |
|                               | <i>PNOC022, Phase 2 clinical trial in combination with ONC201, ongoing</i>                                    |  | <i>Phase 2 clinical trial in combination with chemotherapy for treatment of high-risk malignancies commenced 2024</i> |
| <b>Regulatory Interaction</b> | <i>Orphan Drug Designation (ODD) and Rare Pediatric Disease Designation (RPDD) granted by FDA in Aug 2020</i> | <i>ODD and RPDD granted by FDA in June and July 2022, respectively</i>                     | <i>Regulatory strategy under discussion</i>   |

# Paxalisib in Diffuse Midline Gliomas

## *Follow-up Phase 2 data presented at ISPNO 2024 Annual Meeting*

In spite of research that has helped improve treatment for DIPG patients, the prognosis remains poor—with the median survival range being from 8-11 months<sup>1</sup>

- 68 patients with biopsy-proven DMG were enrolled in the PNOG Phase 2 study between November 2021 and June 2023 (median age 9 years [range 3-37], n=41 female [60%])
- Updated Median OS from time of diagnosis was 15.6 months (Confidence interval (CI) 12.0, 22.4)
- Cohort 3 enrolled 30 recurrent patients (in conjunction with radiation therapy) had median OS 8.7 months [CI 95% 8.5, NA]
- Most common grade 3 and above treatment-related adverse events were decreased neutrophil count (n=4); mucositis (n=3); and colitis, drug reaction with eosinophilia and systemic symptoms, decreased lymphocyte count, hyperglycemia, and hypokalemia (n=2)
- Next Steps: Further PK and biomarker analyses ongoing for subsequent cohorts; anticipate further update CY2025



Central imaging review analysis of PFS ongoing

1. Hargrave, D., Bartels, U. & Bouffet, E. Diffuse brainstem glioma in children: critical review of clinical trials. Lancet Oncol 7, 241-8 (2006)

# Brain Metastases

# Paxalisib in Brain Metastasis

*MSKCC-sponsored Phase 1 trial's interim analysis showed encouraging clinical activity of paxalisib in combination with radiation therapy (NCT04192981)*

**12-13 August 2022**

Data from first stage presented at **2022 Annual Conference on CNS Clinical Trials and Brain Metastases**, Toronto, Canada from 12-13 August 2022



All 9 patients evaluated for efficacy exhibited a clinical response, according to RANO-BM criteria, with breast cancer representing the most common primary tumor

**July 2023**

**Fast Track Designation granted by US FDA** for paxalisib in combination with radiation therapy in patients with solid tumor brain metastases and PI3K pathway mutations



Based on the interim stage 1 data from the MSKCC-sponsored Phase 1 trial's interim analysis.

**February 2024**

**Announced early conclusion**, based on Stage 2 positive safety data and **promising clinical response** findings observed to date.



Preliminary data presented at two scientific congresses\* in CY2024

Coordinate and plan next clinical study in conjunction key thought leaders and FDA

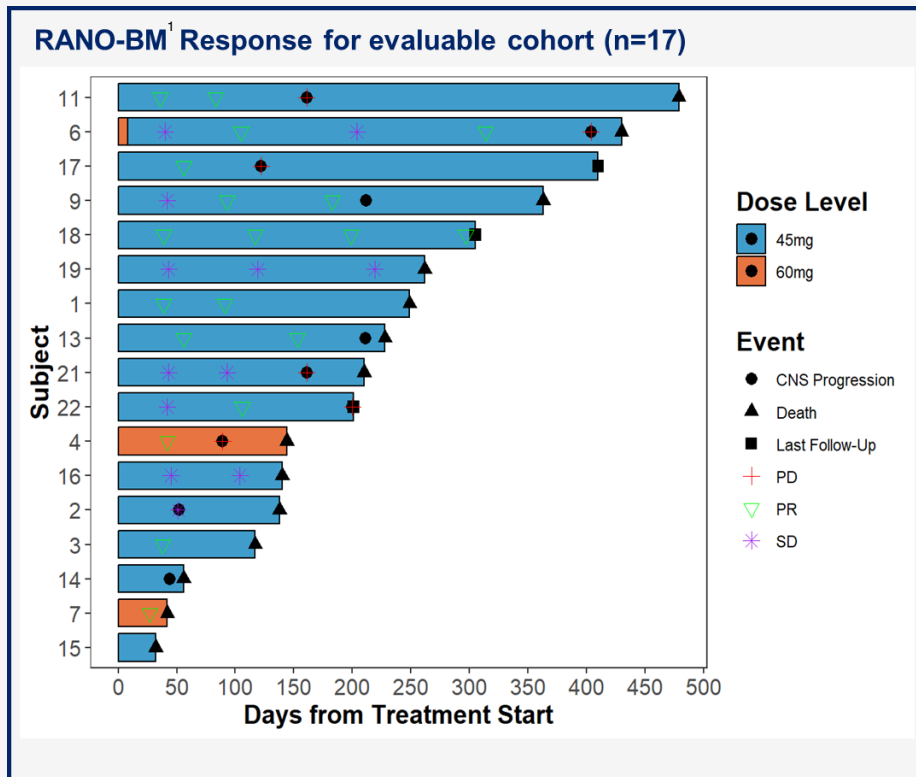
\*ASTRO 2024 Annual Meeting & 2024 SNO Annual Meeting

# Paxalisib in Brain Metastasis

MSKCC-sponsored Phase 1 trial's interim analysis presented at 2024 ASTRO\* & Society of Neuro-oncology meetings showed encouraging clinical activity of paxalisib in combination with radiation therapy (NCT04192981)

Robust response signal seen for concurrent paxalisib and brain RT

## Overall Summary



\* American Society for Radiation Oncology

1. Response assessment in neuro-oncology brain metastases (RANO-BM)

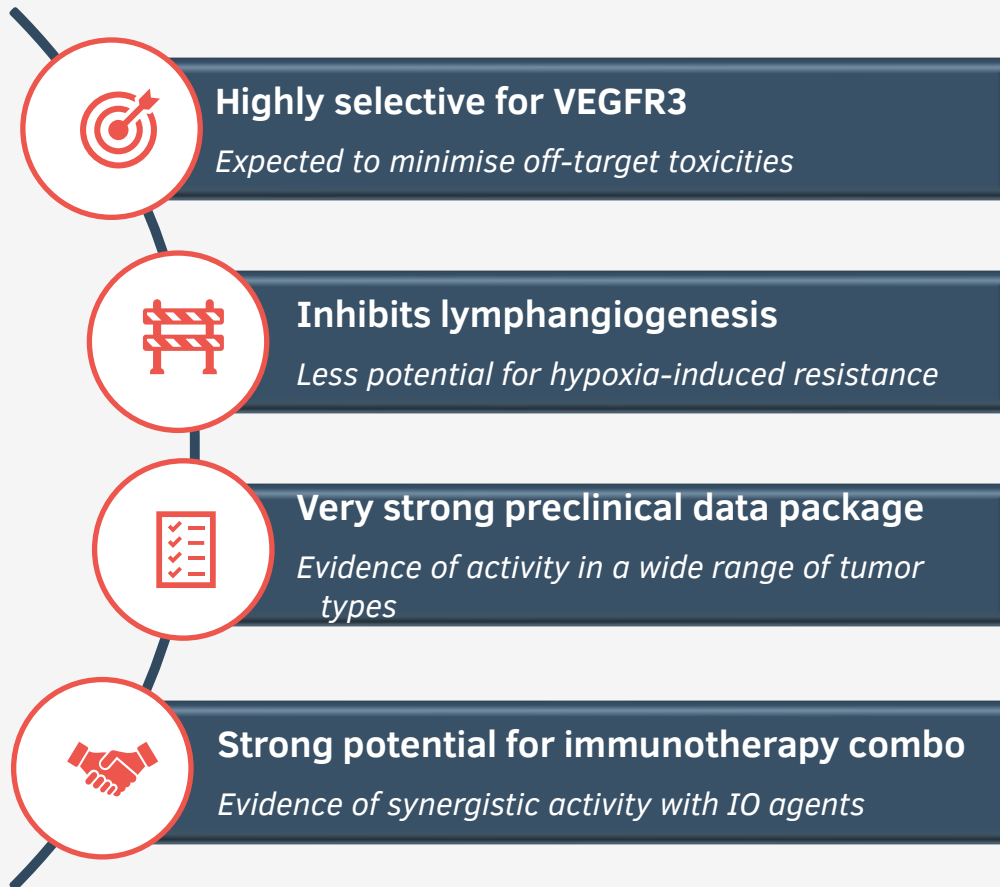
2. Zhou et al. 2021, Kim et al. 2020

- Primary objective of identifying the maximum tolerated dose (MTD) was met:
  - Concurrent daily administration of paxalisib with brain radiotherapy was generally well-tolerated at a maximum dose of 45 mg per day in advanced solid tumor patients with brain metastases and PI3K pathway mutations
- Over two-thirds of the patients at MTD achieved intracranial response which compares favorably to historical response rates (20-40%)<sup>2</sup> for WBRT alone
- Future goals include:
  - Extending the duration of PI3K inhibition, neoadjuvant, adjuvant and maintenance (ideally with complementary systemic therapy options)
  - Integrating PI3K inhibition with CNS tumor types with relevant pathway driver mutations and potentially SRS

EVT801



# EVT801 is a highly 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

## Favourable Preclinical Toxicology

Limited evidence of toxicity in one-month GLP studies

## In Clinical Development

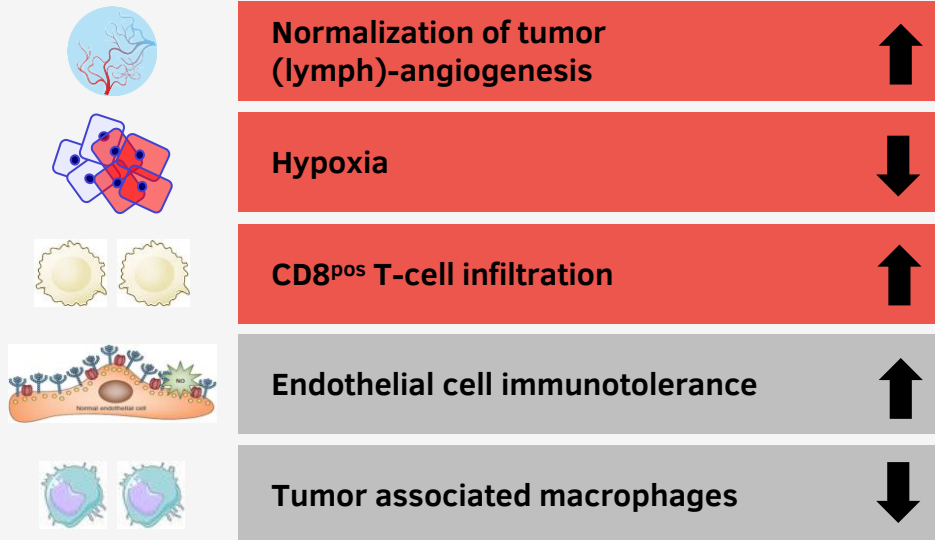
Phase 1 clinical trial completed

# EVT801 Mechanism of Action

*By targeting VEGFR3<sup>pos</sup> tumor blood vessels, EVT801 may induce tumor blood vessel normalization, reduce hypoxia, and improve CD8 T-cells infiltration*

*Schematic overview based on pre-clinical data*

## EVT801 activity on tumor microenvironment



EVT801  
(SAR131675)

Cytokines involved  
in MDSC frequency



## Tumor metastasis



Multiple cooperative  
modes of action

Myeloid-derived  
suppressor cells

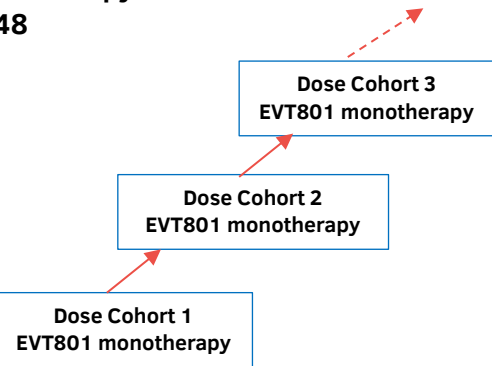


# EVT801: Phase 1 dose-finding trial; KZA 0801-101 (NCT05114668)

## Staged development in patients with advanced cancer

### STAGE 1

Monotherapy dose escalation  
n≤48



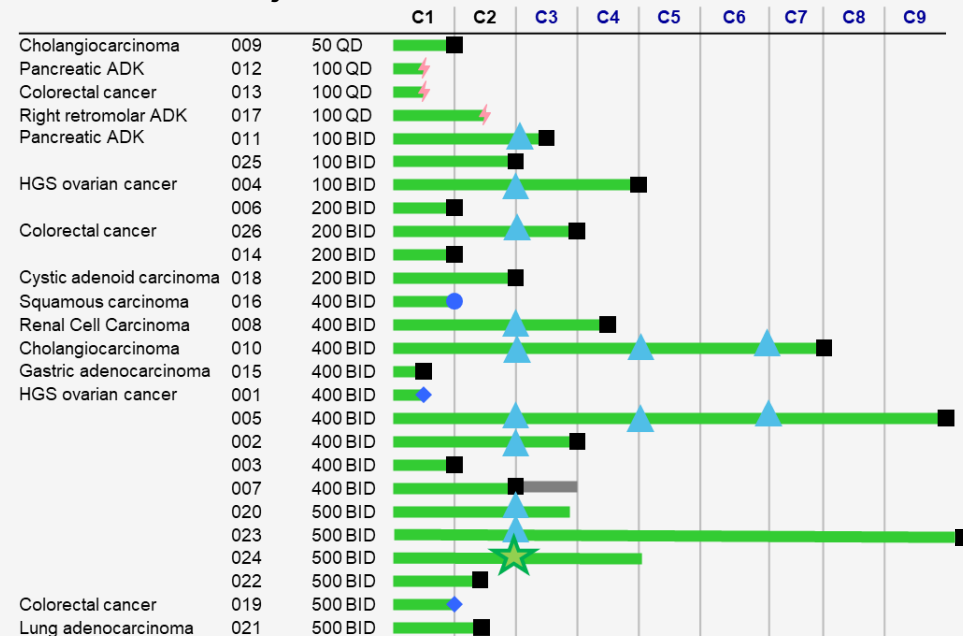
- Up to 8 cohorts
- Single-patient cohorts initially, expand to 3+3 when toxicity is encountered
- Mixed population of advanced solid tumors
- Doses from 50mg QD to 800mg BID



### Phase 1 study in advanced cancer patients completed

- Primary objective of stage one of the study was successfully met:
  - MTD has been reached at 500mg BID
  - The recommended dose for phase 2 is 400 mg BID\* in continuous monotherapy administration

### Number of cycles of treatment: Status on 11 October 2024



- Stop for IMP noncompliance
- IMP taken after Progressive disease
- ▲ Stable disease (SD)
- ★ Partial remission
- Ongoing Treatment
- Progressive disease (PD)
- ◆ Dose Limiting Toxicity
- ⚡ Stop for adverse event

MTD = Maximum Tolerated Dose; RP2D = Recommended Phase 2 Dose

\*Human active dose prediction based on predicted human clearance of 2.5 mL/min/kg: 375 mg BID\*

# EVT801 Key Points

- 1 Well-understood mechanism (anti-angiogenesis) with unique differentiating feature (high VEGFR3 selectivity)
- 2 Strong preclinical data package, with observed activity in multiple tumors and favourable toxicology
- 3 Potential for combination use with immuno-oncology therapies
- 4 Phase 1 completed demonstrating encouraging safety and tolerability profile to date:
  - Clinical and biomarker data presented at AACR Ovarian Cancer Research Symposium September 2024
  - Primary and secondary objectives successfully met, with MTD and RP2D identified
  - Encouraging signal of activity observed in High Grade Serous (HGS) ovarian cancer as well as strong VEGFR3 biomarker expression
- 5 Next clinical trial under discussion with scientific thought leaders:
  - Consolidate safety data at RP2D and our hypotheses on EVT801 mode of action
  - Validate HGS ovarian cancer as indication of choice for clinical trial phase 2 as monotherapy or in combination with standard-of-care (ex. PARPi)

# 2025 Corporate Update

# Paxalisib Licensing and Collaborations

*Opportunistic partnering and strategic collaborations continue to add value*

## Licensing

### Summary



|                                  |   |  |
|----------------------------------|---|--|
| Territories and responsibilities | To develop and commercialize Paxalisib in Greater China, Hong Kong, Macau, and Taiwan                                 | To develop, manufacture and commercialize Paxalisib as a potential treatment for intractable epilepsy in focal cortical dysplasia type 2 (FCD T2) and tuberous sclerosis complex (TSC) disease |
| Upfront payment                  | US\$11m, comprising US\$7m in cash and a US\$ 4m equity investment  | US\$1.5 million  |
| Milestone payments               | Contingent milestone payments of up to US\$ 281 million in GBM + further milestones payable in indications beyond GBM | Potential milestone payments of up to US\$19 million upon the achievement of development and regulatory milestones   |
| Royalties on net sales           | Mid-teen percentage royalties on commercial sales   | A percentage of sub-licensing revenues and royalties on net sales of products incorporating paxalisib  |

## Key Collaborations



Cutting edge preclinical program to evaluate Paxalisib in combination with immuno-therapies for Advanced Breast Cancer



- Paxalisib alone and in combination with other targeted agents is active in preclinical models of AT/RT<sup>1</sup>
- US FDA has awarded Orphan Drug Disease and Rare Pediatric Disease Designations in AT/RT
- If Paxalisib were to be approved, Kazia could be entitled to receive a pediatric priority review voucher which are tradeable and have historically commanded prices in excess of USD \$100 million.

1. Atypical Teratoid Rhabdoid Tumor

# Kazia Therapeutics: 2025 Corporate Focus

## *Objectives for value creation*

|   |  |
|---|--|
| Progress paxalisib in advanced breast cancer              | <ul style="list-style-type: none"><li>• Launch Kazia-sponsored phase 1b clinical study in advanced breast cancer patients</li><li>• Provide additional preclinical data and updates from the QIMR collaboration throughout the year</li></ul>                  |
| Advance paxalisib glioblastoma program                    | <ul style="list-style-type: none"><li>• FDA meeting in Dec2024 confirmed standard approval pathway with single pivotal registrational study in NDU GBM patients</li><li>• Finalize protocol, assess costs/timelines and select strategic CRO partner</li></ul> |
| Execute paxalisib pediatric and brain metastasis programs | <ul style="list-style-type: none"><li>• PNOC team to complete PK/biomarker data analysis and provide update CY2025</li><li>• Complete analysis and close out MSKCC clinical brain metastasis study</li></ul>   |
| EVT801 program  | <ul style="list-style-type: none"><li>• Complete analysis stage one of EVT801 Phase 1 clinical study</li><li>• Discuss and plan for Phase 2 study in advanced ovarian cancer patients while seeking potential partners</li></ul>                               |
| Corporate business development                            | <ul style="list-style-type: none"><li>• Continue to be opportunistic in terms of global and regional licensing for paxalisib and EVT801</li></ul>  |



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THERAPEUTICS

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