KAZIA THERAPEUTICS

A Diversified Oncology Drug Development Company

Kazia Corporate Overview

January 2025

NASDAQ: KZIA | X: @KaziaTx

Forward Looking Statements

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Company Overview

A late-clinical-stage oncology drug development company

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Paxalisib

Brain-penetrant pan-PI3K / mTOR inhibitor

- Well-validated class with five current FDA-approved therapies
- Only brain-penetrant PI3K inhibitor in development

In development for multiple brain cancers

- Clinical trials ongoing in brain metastases, childhood brain cancer, glioblastoma, IDH-mutant glioma, and primary CNS lymphoma

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

- Glioblastoma alone sized at US$ 1.5 billion per annum
- Commercial licensee in place for China
- Licensee for intractable seizures in rare CNS diseases

Advanced breast cancer trial launched 1Q CY2025

EVT801

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

Phase 1 final data anticipated CY2025

Corporate Highlights

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)

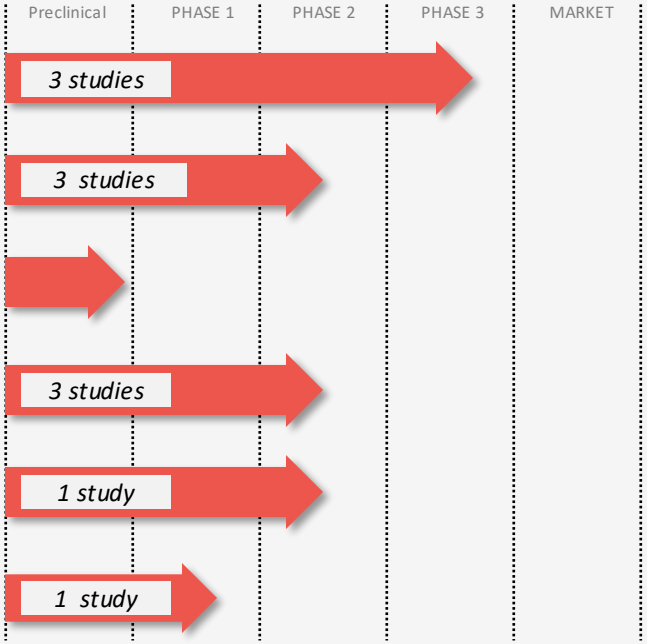
Pipeline – Two Differentiated Assets

CY2025 positive clinical data updates driving strong interest in oncology community

Paxalisib

Investigational, small molecule, potent, brain-penetrant inhibitor of PI3K / mTOR

licensed from: Genentech IN BUSINESS FOR LIFE



	Collaborators / Sponsors	Anticipated
Glioblastoma & IDH-mutant glioma *Common primary brain cancer*	Weill Cornell Medicine; Global Coalition for Adaptive Research; The University of Sydney	*Further Update* **CY25**
DIPG/Advanced Solid Tumors *Childhood brain cancer*	Pacific Pediatric Neuro-Oncology Consortium; St. Jude Children's Research Hospital; ANZCHOG	*Further Update* **CY25**
AT/RT *Childhood brain cancer*	Johns Hopkins	*Further Update* **CY25**
Brain Metastases *Cancer that spreads to brain from elsewhere*	NIH National Cancer Institute; Dana-Farber Cancer Institute; Memorial Sloan Kettering Cancer Center	*Further Data* **CY25**
Primary CNS Lymphoma *Form of non-Hodgkin's lymphoma*	Dana-Farber Cancer Institute	*Initial Data* **CY25**
Cancers Outside the CNS *Advanced Breast Cancer*	QIMR Berghofer Medical Research Institute	*Study Launch* **1QCY25**

EVT801

Investigational, small molecule, highly specific inhibitor of VEGFR3

licensed from: evotec

	Collaborators / Sponsors	Anticipated
Advanced Solid Tumors *Patients w/ highly treatment-resistant cancer*	Institut Universitaire du Cancer de Toulouse Oncopole; Centre Léon Bérard	*Final Data* **CY25**

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

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Paxalisib Mechanism of Action

Only brain-penetrant drug in development within the dual PI3K/mTOR inhibitor class

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

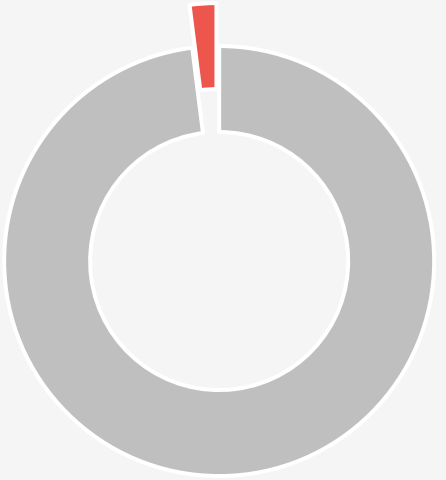
	Glioblastoma	**90%**
	Breast	**80%**
	Lung	**75%**
	Endometrial	**60%**
	Ovarian	**60%**
	Prostate	**45%**

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

Zydelig (idelalisib) tablets	• Chronic lymphocytic leukemia • Follicular lymphoma
Aliqopa (copanlisib) 60 mg vial for injection	• Follicular lymphoma
Copiktra (duvelisib)	• Chronic lymphocytic leukemia • Follicular lymphoma
PIQRAY (alpelisib) tablets	• Breast cancer
UKONIQ umbralisib 200 mg tablets	• Follicular lymphoma

3 **Paxalisib is the only brain-penetrant dual PI3K/mTOR inhibitor in development**

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



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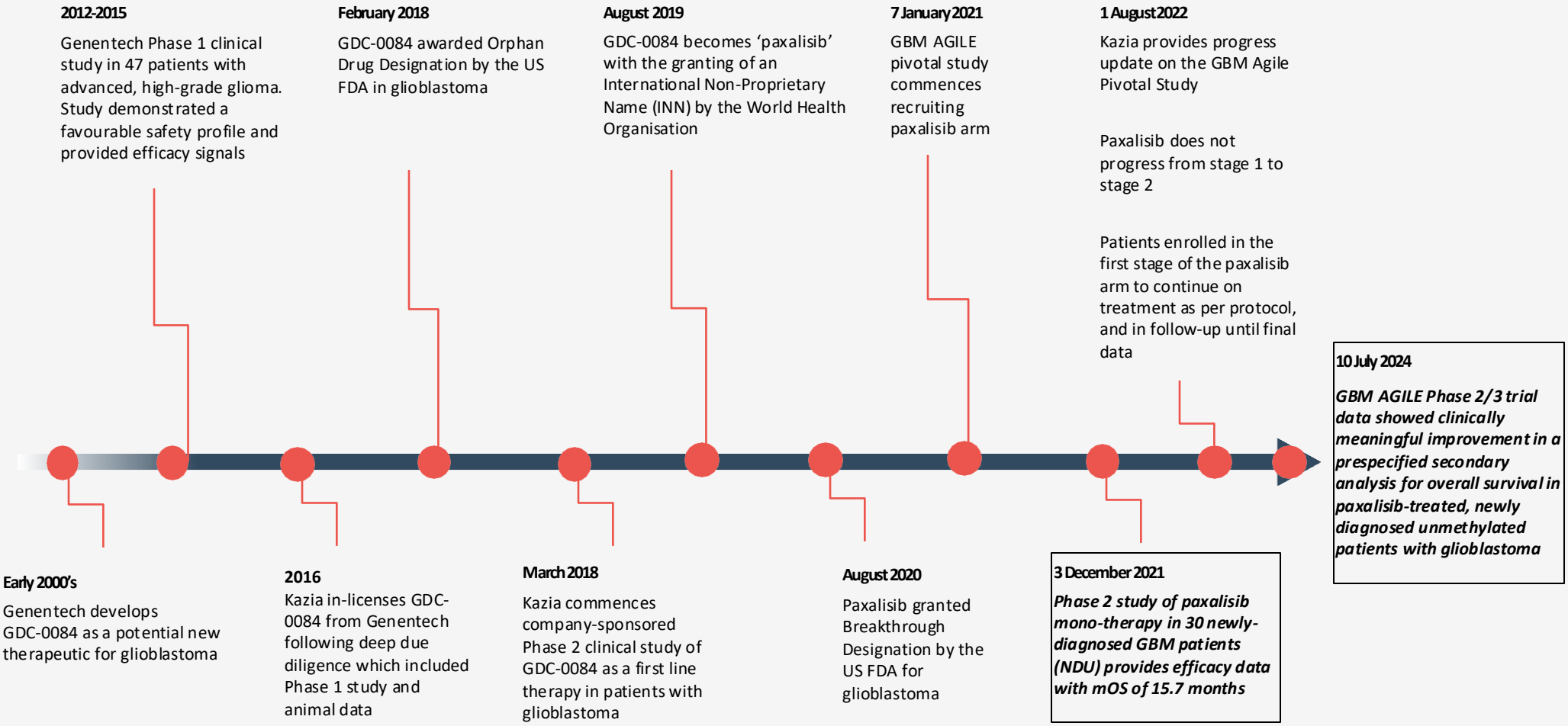
Paxalisib – *Development History*

Growing Body of Clinical Evidence Demonstrating Activity in GBM



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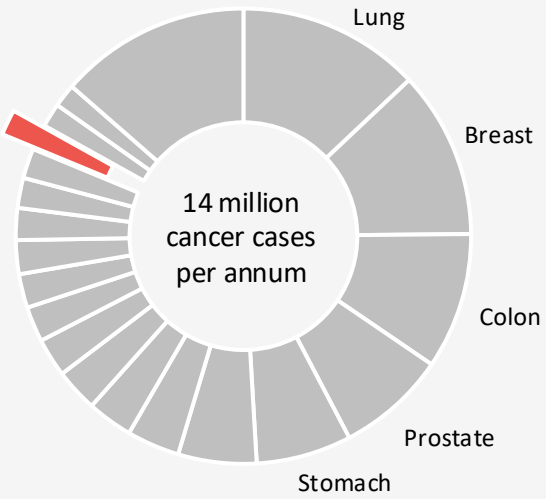
Glioblastoma

Background & Market potential

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

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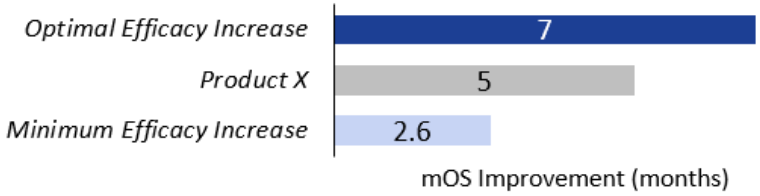
Primary Market Research Outcomes

Physicians indicated a 2-month minimum and 12-month optimum increase in efficacy for newly diagnosed unmethylated GBM treatments, but adoption would be high regardless

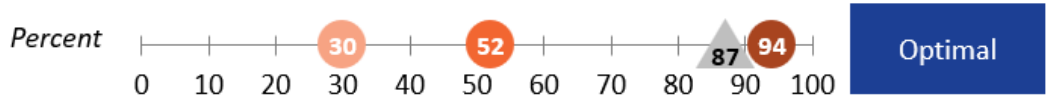
Physician receptivity to optimal and minimal mOS efficacy for ND* GBM

(N=15 Physicians)

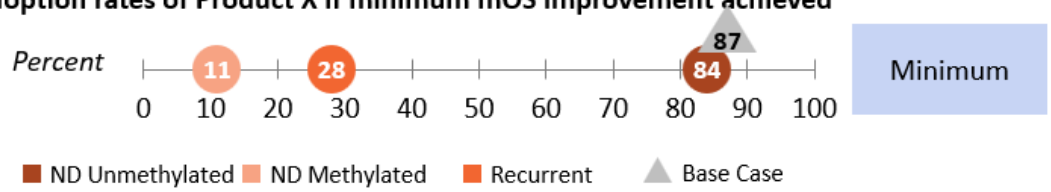
Optimal and minimal mOS increase in newly diagnosed GBM patients



Adoption rates of Product X if optimal mOS improvement achieved



Adoption rates of Product X if minimum mOS improvement achieved



Key Takeaway

- Due to the high unmet need for a more efficacious therapy for Newly Diagnosed Unmethylated (NDU) GBM patients, physicians indicated high adoption rates if Product X (paxalisib)* is approved by the FDA and achieved their suggested minimum mOS improvement of 2-3 months for newly diagnosed unmethylated GBM patients

Source: Data on file. Company-sponsored market research performed in 2021

* There is no guarantee that the Paxalisib data generated to date will support an FDA approval for commercial use

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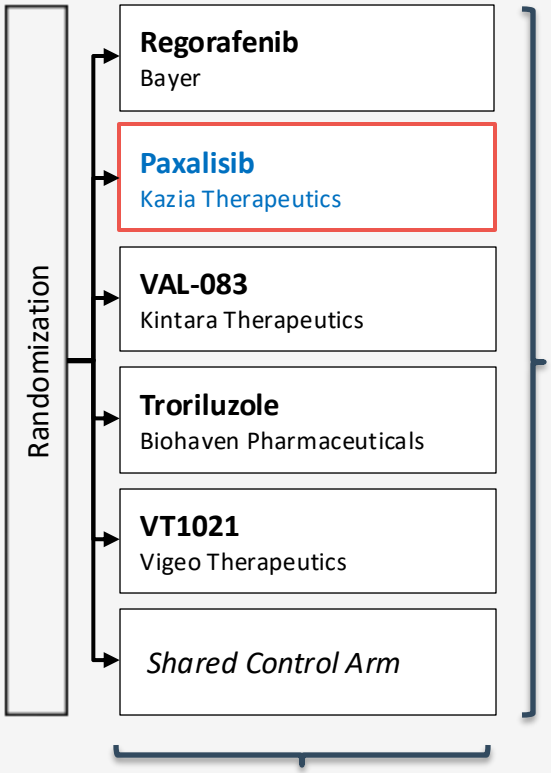
GBM AGILE study data –
Primary and secondary analysis

Paxalisib and GBM-Agile

International, multi-center, adaptive, phase 2/3 study evaluating promising therapeutics in patients with glioblastoma

Key Points

- A 'platform study', sponsored by GCAR 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



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

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

- Completed — *Negative outcome (Sep 2022)*
- **Final Top Line Data** — ***July 2024***
- Completed — *Negative outcome (Oct 2023)*
- Ongoing — *Joined study in Jan 2022*
- Ongoing — *Joined study in Jan 2022*

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

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

GCAR: Global Coalition for Adaptive Research

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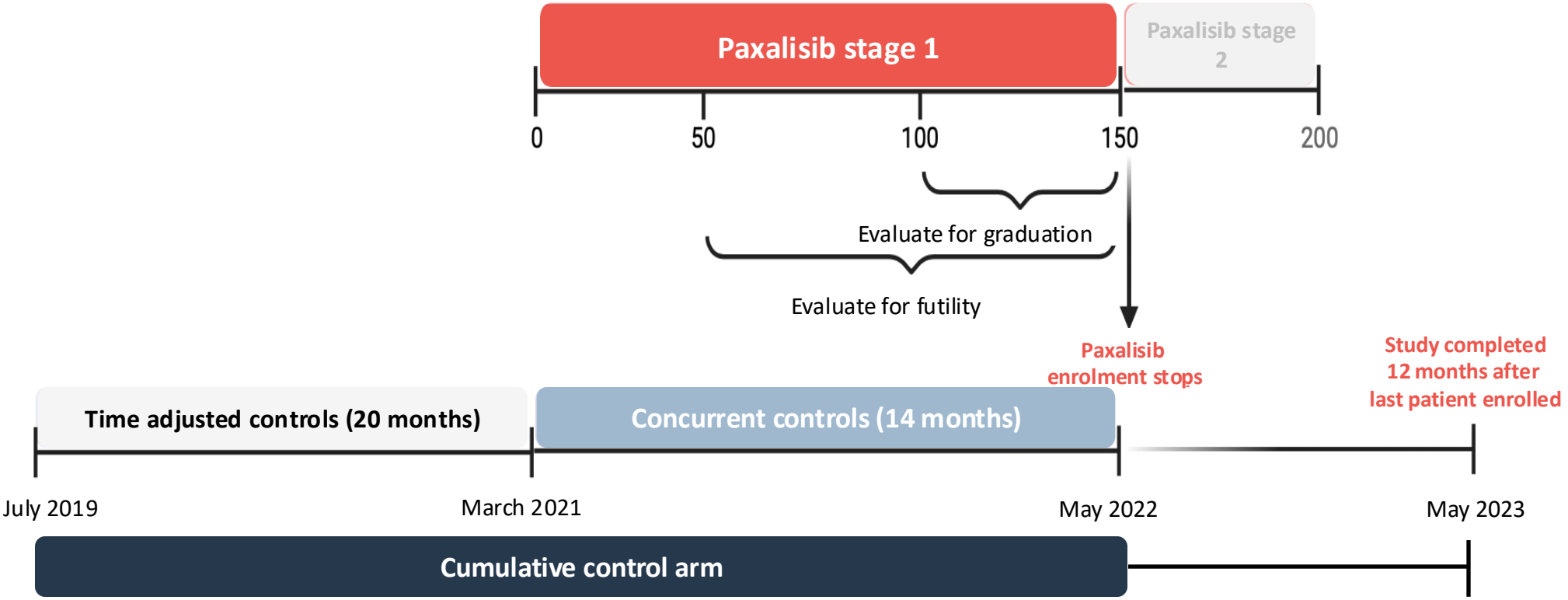
Paxalisib & GBM-Agile

Study schema; Paxalisib arm (n=154) enrolled Newly Diagnosed Unmethylated GBM patients (NDU) and Recurrent GBM patients



Important notes:

- The cumulative control arm is a combination of concurrent control patients and the "Time adjusted control" patients that were enrolled in the study before the Paxalisib arm joined the study
- Bayesian Primary Analysis uses data from the cumulative control arm, while Prespecified Secondary Analysis uses data from the concurrent control arm (i.e.. Compares paxalisib data with standard of care)
- All patients (Paxalisib, concurrent control, and cumulative control) were censored on May 2023 if still alive

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Paxalisib & GBM-Agile

Concurrent Control versus Cumulative Control

Cumulative controls: Patients randomized to control from the start of the entire GBM AGILE study (June 2019) to the date the last patient was randomized to paxalisib. Cumulative control patients are censored one year after the last patient was enrolled in paxalisib arm (May 2023)

Concurrent controls: Patients randomized to the control arm from the date of inclusion of paxalisib (April 2021) onto the study until the date the last patient was randomized to paxalisib. Concurrent control patients are censored one year after the last patient was enrolled in paxalisib arm (May 2023)

Paxalisib and GBM-Agile

Summary of OS in NDU Patients: Primary and Secondary Analyses

	Primary OS analysis	Prespecified Secondary OS analysis		
		Main analysis	Sensitivity analysis I	Sensitivity analysis II
Method	Bayesian piecewise exponential model	Frequentist methods and standard Kaplan-Meier curve	Frequentist methods and standard Kaplan-Meier curve	Frequentist methods and standard Kaplan-Meier curve
Population	ITT	ITT	ITT	ITT
Number for analysis	Paxalisib: 54 Cumulative control: 75	Paxalisib: 54 Concurrent control: 46	Paxalisib: 54 Concurrent control: 46	Paxalisib: 54 Concurrent control: 46
Median OS	Paxalisib: 14.77 Cumulative control: 13.84	Paxalisib: 15.54 Concurrent control: 11.89	Paxalisib: 15.54 Concurrent control: 11.70	Paxalisib: 14.39 Concurrent control: 11.89
Hazard ratio	0.89 (0.54, 1.38)	0.76 (0.45, 1.26) 24% hazard reduction	0.67 (0.40, 1.13) 33% hazard reduction	0.73 (0.45, 1.18) 27% hazard reduction

Important notes:

Although the primary OS analysis did not meet statistical significance compared to the cumulative control arm, the prespecified OS analyses were consistent with an encouraging 30% hazard ratio reduction

An efficacy signal was not detected in the recurrent disease population [median OS of 9.69 months for concurrent SOC (n=113) versus 8.05 months for paxalisib (n=100)]

Source: Data on file

Paxalisib and GBM-Agile

Treatment Emergent Adverse Events (TEAE) NDU Patients

Common Adverse Events Summary

- In the paxalisib arm, the most frequently reported treatment emergent adverse events (TEAEs) were hyperglycemia (65%); fatigue (60%); lymphocyte count decreased (50%); white blood cell count decreased (40%), nausea (38%); decreased appetite and diarrhea (37% each); stomatitis (33%); constipation, platelet count decreased, and rash maculopapular (31% each)
- In the concurrent standard of care (SOC) arm, the most frequently reported TEAEs were fatigue (48%), nausea (43%), constipation (39%), and vomiting (25%)

TEAEs reported by ≥ 20% of patients

Preferred Term	Paxalisib (N=52)	Concurrent SOC: (N=44)
Patients with any TEAE	50 (96)	40 (91)
Hyperglycemia	34 (65)	5 (11)
Fatigue	31 (60)	21 (48)
Lymphocyte Count Decreased	26 (50)	8 (18)
White Blood Cell Count Decreased	21 (40)	4 (9)
Nausea	20 (38)	19 (43)
Decreased Appetite	19 (37)	7 (16)
Diarrhea	19 (37)	2 (5)
Stomatitis	17 (33)	0 (0)
Constipation	16 (31)	17 (39)
Platelet Count Decreased	16 (31)	5 (11)
Rash Maculo-Papular	16 (31)	1 (2)
Alanine Aminotransferase Increased	15 (29)	4 (9)
Neutrophil Count Decreased	15 (29)	7 (16)
Headache	13 (25)	6 (14)
Alopecia	12 (23)	5 (11)
Seizure	12 (23)	8 (18)
Anemia	11 (21)	5 (11)
Aspartate Aminotransferase Increased	11 (21)	2 (5)
Vomiting	11 (21)	11 (25)

Source: Data on file

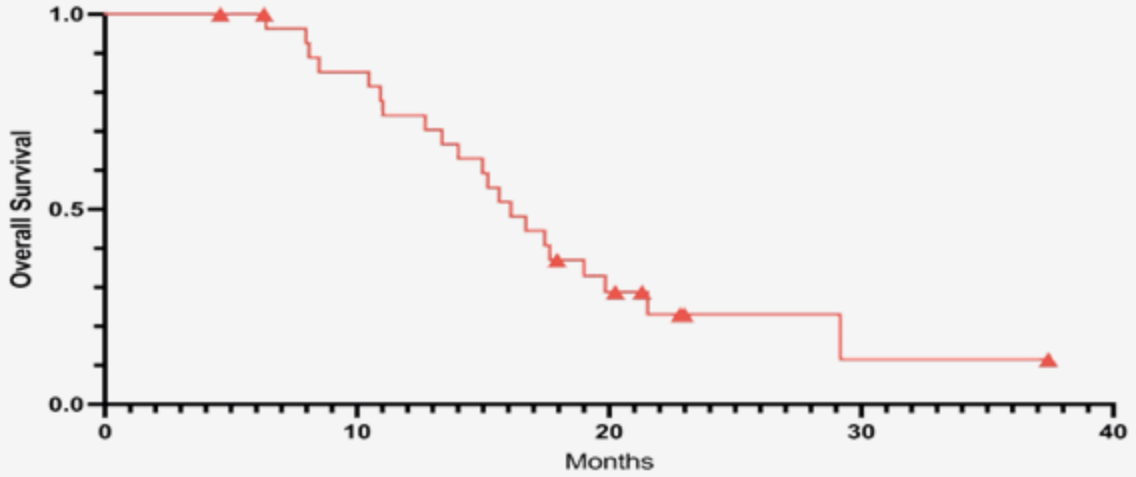
Recap and next steps for Paxalisib in glioblastoma

Paxalisib in Glioblastoma Phase 2 Clinical Study

Encouraging median OS (mOS) in Newly Diagnosed Unmethylated GBM patients

Overall Survival (OS)

(n=30)



Median OS: **15.7 months** (11.1-19.1)

Historical mOS for existing therapy: **12.7 months** (Hegi et al. 2005)

Note: Figures for existing therapy are for temozolomide, per Hegi et al. (2005); No head-to-head studies have been published

Paxalisib in Glioblastoma Phase 2 Clinical Study

Encouraging safety profile

Number of Patients at Any Dose (n=30) Experiencing AEs 'Possibly' or 'Likely' Related to Paxalisib (affecting ≥10% of patients)

Term	Gr 1	Gr 2	Gr 3	Gr 4	Total (%)
Fatigue	3	13	2		18 (60%)
Stomatitis	4	7	3		14 (47%)
Decreased appetite	6	6	1		13 (43%)
Hyperglycemia	3	1	6	2	12 (40%)
Nausea	4	6	1		11 (37%)
Rash, maculo-popular	1	1	7		9 (30%)
Diarrhea	7	1			8 (27%)
Vomiting	4	2	1		7 (23%)
Rash	2	4	1		7 (23%)
Neutrophils decreased	3	3		1	7 (23%)
Platelets decreased	6	1			7 (23%)
Weight decreased	5	2			7 (23%)
Lymphocytes decreased	2	3			5 (17%)
Dehydration		4	1		5 (17%)
Dysgeusia		4			4 (13%)
Cholesterol increased	4				4 (13%)
ALT increased	1		2		3 (10%)
Triglycerides increased	1	2			3 (10%)
Malaise	2	1			3 (10%)

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	Paxalisib in Kazia sponsored phase 2 study
(n=54)	(n=30)
Median OS: **15.54 months***	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	STUPP historical control
(n=46)	(N/A)
Median OS: **11.9 months***	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:

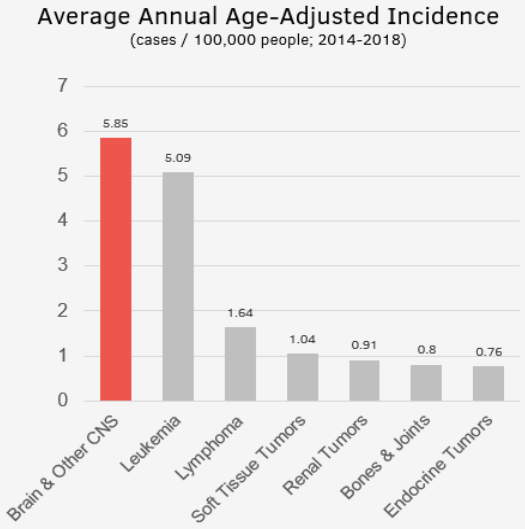
- The FDA's current position is that data on Overall Survival would generally not be appropriate for accelerated approval but could be considered to support a traditional/standard approval
- The Agency further commented that the secondary endpoint OS data from the GBM-AGILE study may be supportive and 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 providing an update in 1Q25

Childhood Brain Cancers

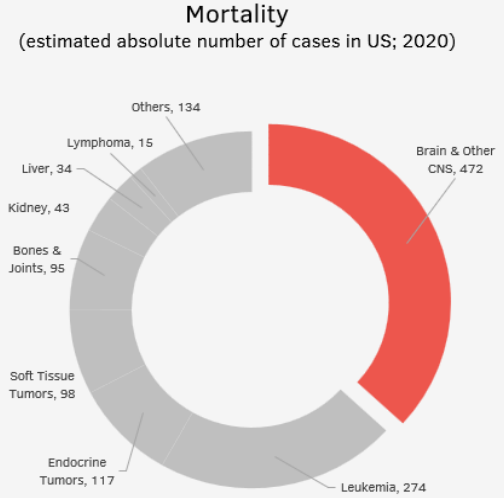
Paxalisib in Childhood Brain Cancer

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

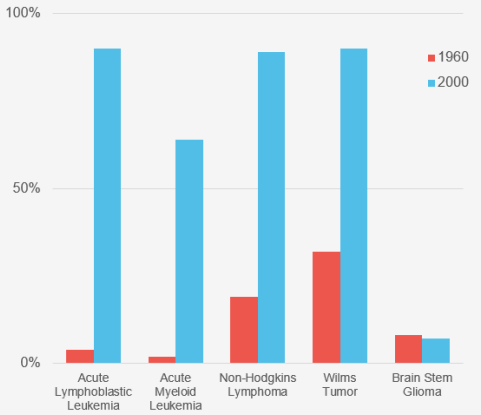
1 Brain cancer is the most common malignancy of childhood



2 Brain cancer represents about one third of childhood cancer deaths



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

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Summary of Paxalisib in Childhood Brain Cancer

Kazia is actively pursuing three forms of childhood brain cancer

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

Paxalisib in Diffuse Midline Gliomas

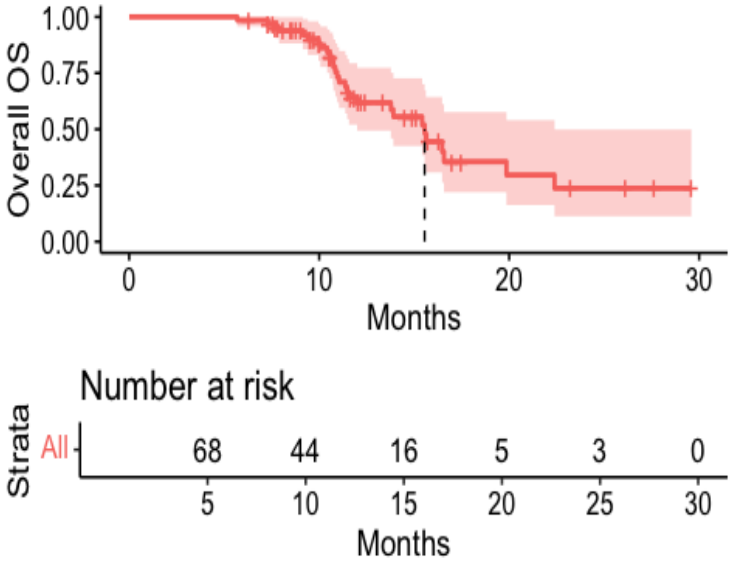
Follow-up Phase 2 data presented at ISPNO 2024 Annual Meeting

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[1]

- 68 patients with biopsy-proven DMG were enrolled in the PNOC 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 clinical update 1HCY2025

Overall Survival - Cohort 2 (post RT)

Median OS 15.6 months [CI 95%; 12.0, 22.4]



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)

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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

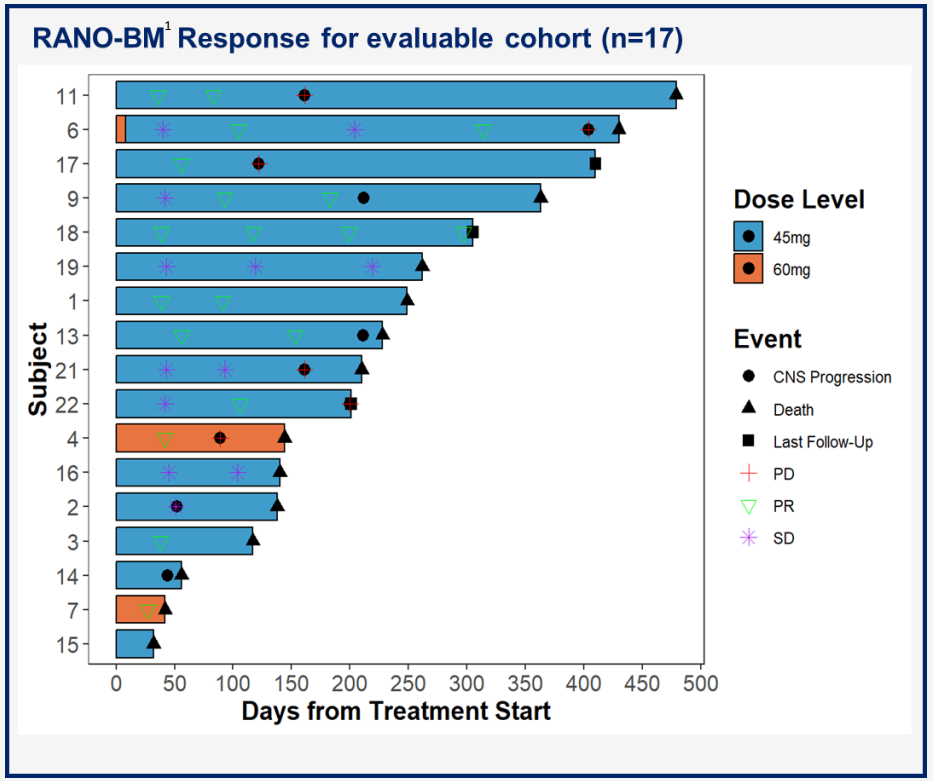
Coordinate and plan next clinical study in conjunction key thought leaders and FDA

*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

- 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%)[2] 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

* American Society for Radiation Oncology

1. Response assessment in neuro-oncology brain metastases (RANO-BM)
2. Zhou et al. 2021, Kim et al. 2020

Other Solid Tumors

Triple Negative Breast Cancer

Triple Negative Breast Cancer Treatment Landscape

Projected TNBC market to exceed $1.5 Billion by 2030

2.3 million[1]

Cases / year
Breast cancer
most commonly
diagnosed cancer

American Cancer Society says nearly

300,000

new cases of invasive BC in US

Triple negative breast cancer

TNBC

most aggressive form of breast cancer

Characteristics

Higher early relapse rate, increased metastases risk and higher mortality rate

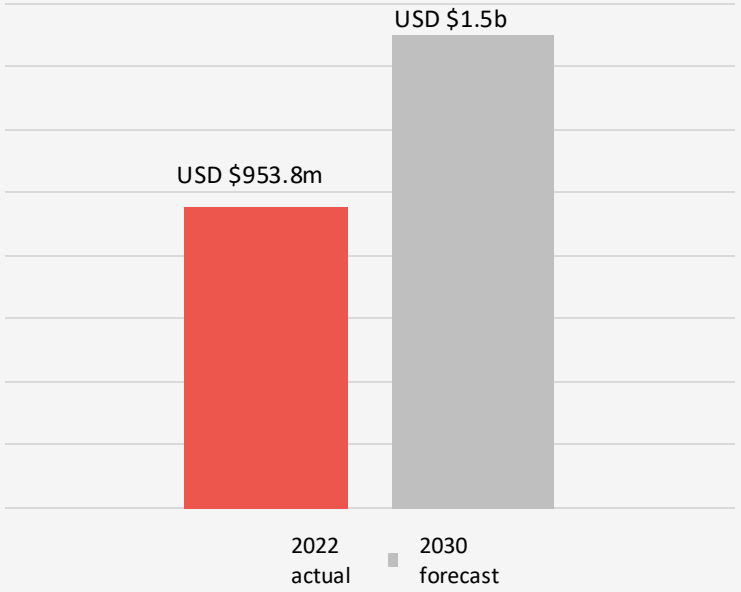
15-20%

Of all breast cancers attributed to TNBC

TNBC market valued at USD $953.8m in 2022. Predicted to grow to **USD**

$1.5b by 2030[2]

TNBC market growth forecast[2]



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

KAZIA THERAPEUTICS

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[1]) 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 tumour, making it more susceptive to immunotherapy

- Preliminary data from our collaboration was presented at San Antonio Breast Cancer Symposium 4Q CY2024

Combination Paxalisib + KEYTRUDA® (pembrolizumab) data in TNBC[1] preclinical models

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

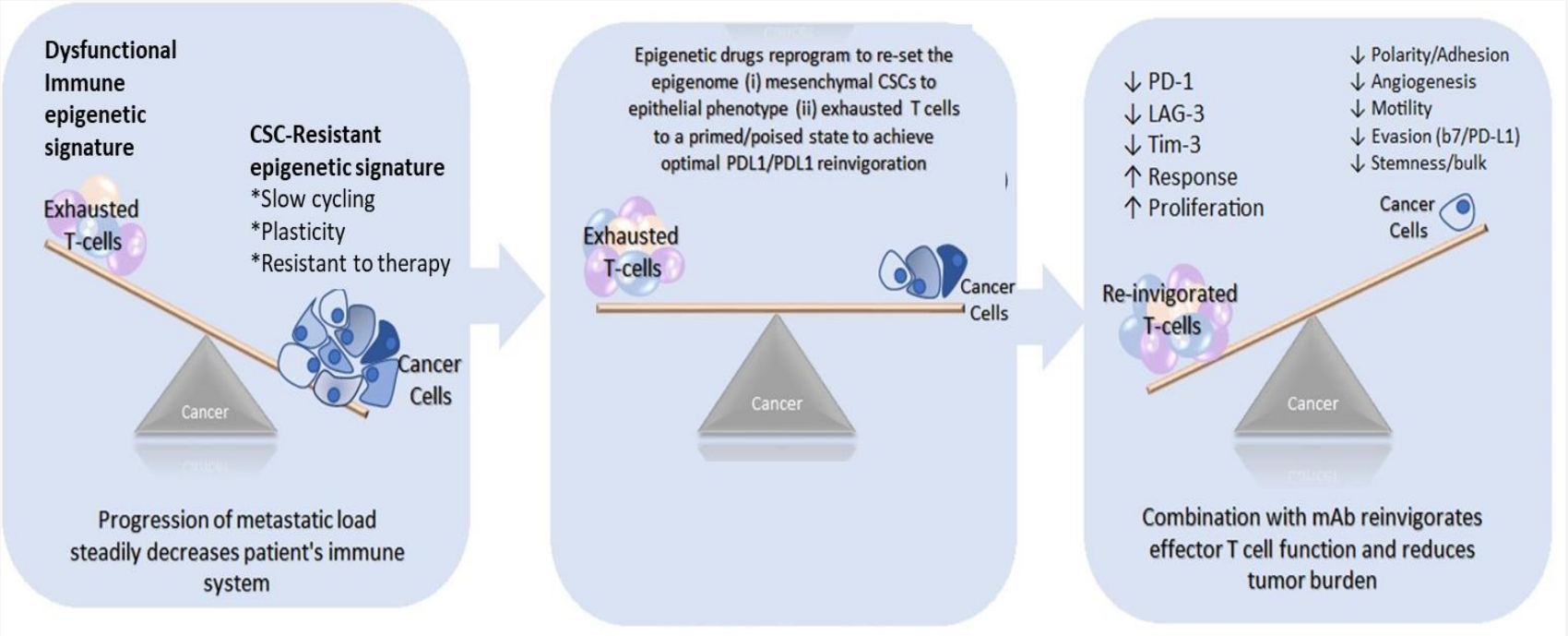
Paxalisib influence on immune system (example, T cells, B cells, NK cells) and within the tumor and its micro-environment

Intellectual Property (IP) update

1. Triple Negative Breast Cancer

Current challenges with immunotherapy in advanced breast cancer

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

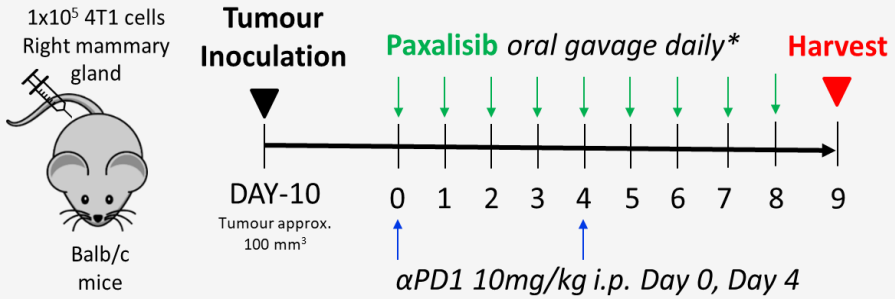


Potential Solution: Targeting BOTH PI3K & mTOR inhibit critical cancer inflammation switch signature; induces “viral mimicry”, making the cancer cells and cancer stem cells (CSC) immune visible; re-program “epigenetic memory” on the CSC epi-genome & in parallel, re-invigorate T cells

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

* αPD1: pembrolizumab or "Pembro"

Kazia-sponsored Clinical Study Overview

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.

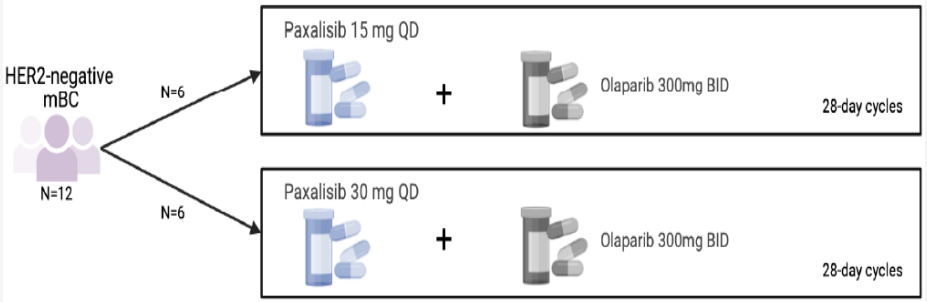
Secondary Objectives:

- 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

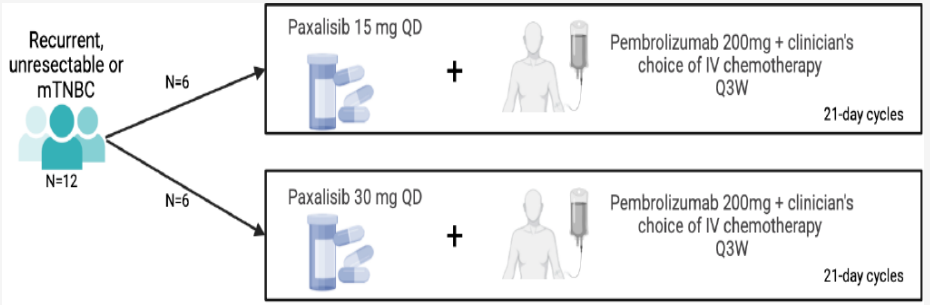
Arm A: Paxalisib plus Olaparib
28 Day Cycle



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

Arm B: Paxalisib plus Pembrolizumab/chemotherapy
21 Day Cycle

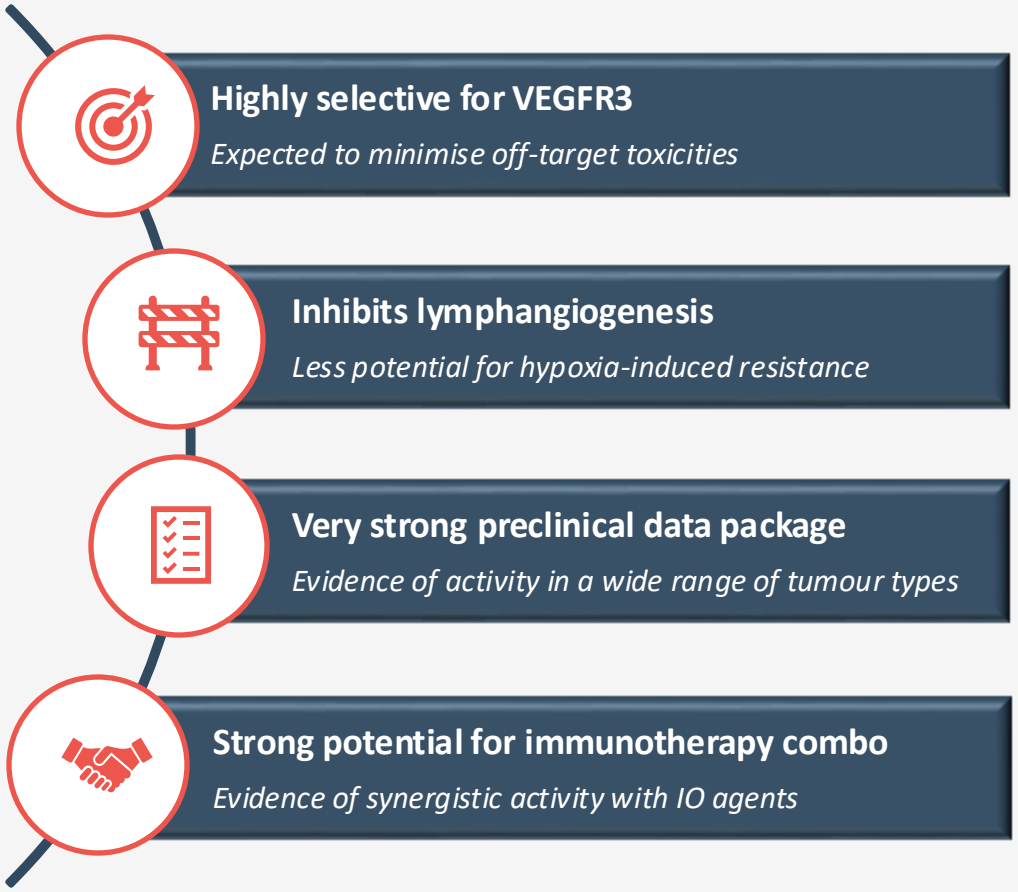


Participant disease characteristics:

- 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) ≥ 10
- Have not received prior PD-1/PD-L1 therapy
- Meet all current prescribing criteria for commencing pembrolizumab therapy

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

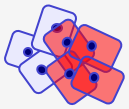
EVT801 Mechanism of Action

By targeting VEGFR3^{pos} 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

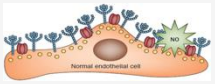
EVT801 activity on tumor microenvironment

Normalization of tumor (lymph)-angiogenesis ⬆



Hypoxia ⬇

CD8^{pos} T-cell infiltration ⬆



Endothelial cell immunotolerance ⬆

Tumor associated macrophages ⬇

EVT801
(SAR131675)

Cytokines involved in MDSC frequency ⬇

Myeloid-derived suppressor cells ⬇

Tumor metastasis

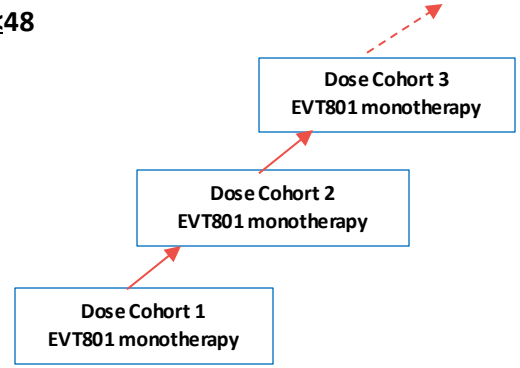
⬇

Multiple cooperative modes of action

Data from Tacconi & al. with SAR131675

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

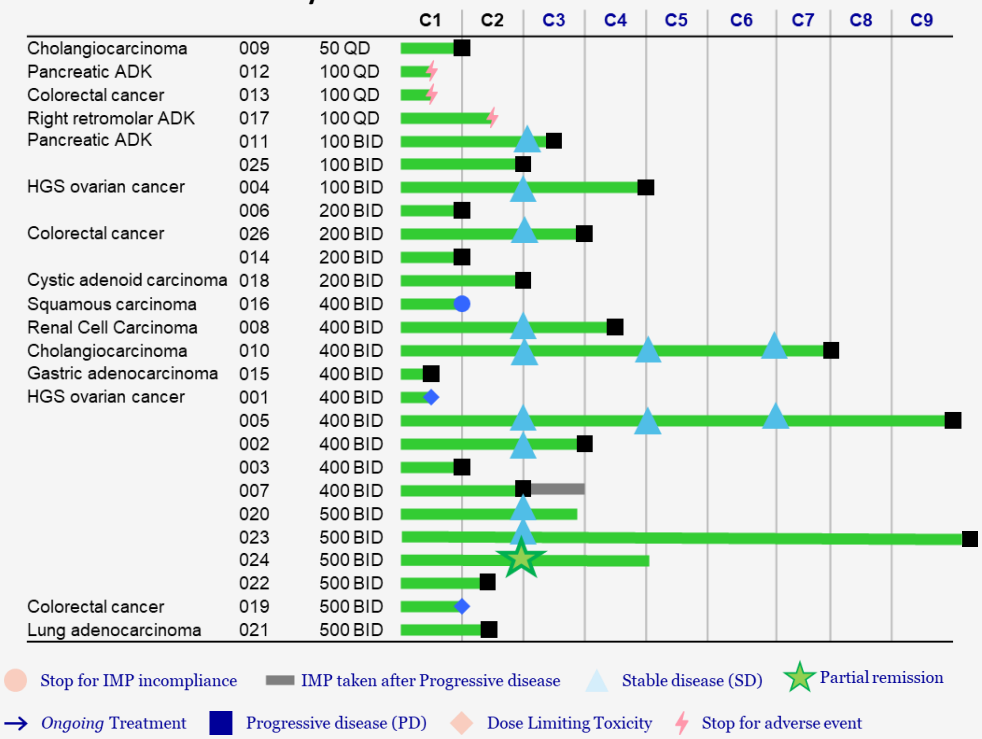
CENTRE LEON BERARD

INSTITUT UNIVERSITAIRE DU CANCER DE TOULOUSE Oncopole

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



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

KAZIA THERAPEUTICS

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 tumours 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)

2024 Corporate Update

Paxalisib Licensing and Collaborations

Opportunistic partnering and strategic collaborations continue to add value

Licensing

Summary	Simcere	Sovargen
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

QIMR Berghofer Medical Research Institute

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

Johns Hopkins University

- Paxalisib alone and in combination with other targeted agents is active in preclinical models of AT/RT[1]
- 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 glioblastoma program	• FDA meeting in Dec2024 confirmed standard approval pathway with single pivotal registrational study in NDU GBM patients • Finalize protocol, assess costs/timelines and select strategic CRO partner
Execute paxalisib pediatric and brain metastasis programs	• PNOC team to complete PK/biomarker data analysis and provide update 2Q CY2025 • Complete analysis and close out MSKCC clinical brain metastasis study
Paxalisib in other key oncology indications	• Launch Kazia-sponsored phase 1b clinical study in advanced breast cancer patients • Provide additional preclinical data and updates from the QIMR collaboration throughout the year
EVT801 program	• Complete analysis stage one of EVT801 Phase 1 clinical study • Discuss and plan for Phase 2 study in advanced ovarian cancer patients while seeking potential partners
Corporate business development	• Continue to be opportunistic in terms of global and regional licensing for paxalisib and EVT801

1. Triple Negative Breast Cancer

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