ASX ANNOUNCEMENT
26 June 2023

KAZIA CORPORATE UPDATE AND CORPORATE PRESENTATION

Sydney, 26 June 2023 – Kazia Therapeutics Limited (NASDAQ: KZIA; ASX: KZA), an oncology-focused drug development company, is pleased to provide an update on key corporate and clinical initiatives and release a new investor presentation.

Key points

- Dr John Friend completes transition into the CEO role, including a full portfolio review.
- Final data anticipated from GBM AGILE pivotal study of paxalisib in glioblastoma in 2H CY2023.
- Interim data from phase II Pacific Pediatric NeuroOncology Consortium study in diffuse intrinsic pontine glioma (DIPG) and other diffuse midline gliomas (DMGs) now expected to be available in July or August 2023.
- Phase I expansion cohort is enrolling for brain metastases study sponsored by Memorial Sloan Kettering Cancer Center. Two other preeminent cancer centres have joined the study. Preliminary data from expansion cohort is anticipated by 1Q24.

Following his appointment as CEO on 1 May 2023, Dr John Friend has completed his transition into the role. He commented, “In the weeks since my appointment, I’ve worked with the team to review the full set of assets and clinical trials within the Kazia portfolio and the process has strongly reinforced my conviction in the opportunities ahead of us.”

“We believe substantial potential exists across our pipeline and in particular, across three key pillars of development for paxalisib—adult brain cancer, paediatric brain cancer and brain metastases. We are keen to explore paxalisib’s use in patient populations that may have the greatest benefit from a PI3K/AKT/mTOR targeted therapeutic candidate.”

“As we move toward the second half of 2023, critical milestones are approaching for both paxalisib and EVT-801. We look forward to keeping investors updated across our progress on these important programs.”

Clinical programs update

11 clinical trials are currently in progress or in planning for Kazia's two assets, paxalisib and EVT-801, and Kazia continues to execute across all programs. Current program highlights are set out in brief below. Refer to the appended corporate presentation for more detail:

Paxalisib

Kazia's lead program is paxalisib, an investigational brain-penetrant inhibitor of the PI3K / Akt / mTOR pathway, which is being developed to treat multiple forms of brain cancer. Licensed from Genentech in late 2016, paxalisib is or has been the subject of ten clinical trials in various brain cancers.

GBM AGILE Pivotal study

Final data are expected from the GBM AGILE pivotal study of paxalisib in glioblastoma in 2H CY2023. Depending on the results of the study, Kazia may use such data to support submission of a new drug application for marketing authorisation to the FDA.

PNOC022 phase II study

Paxalisib is being studied as an investigational drug for the treatment of the paediatric brain cancers DIPG and other DMGs in a study sponsored by the Pacific Pediatric Neuro-Oncology Consortium (PNOC).

The study team at PNOC has been diligently collecting and preparing the data for interim analysis. At this point, Kazia expects that the data will be available in July or August 2023.

LUMOS2 phase II study

On 8 June 2023, Kazia announced that it is supporting the University of Sydney on a molecularly-guided phase II clinical study evaluating paxalisib in adult patients with recurrent/progressive isocitrate dehydrogenase (IDH) mutant grade 2 and 3 gliomas (G2/3 gliomas).

The study, named LUMOS2, will be sponsored by the University of Sydney, and coordinated by NHMRC Clinical Trials Centre, University of Sydney, in collaboration with COGNO (CoOperative Trials Group for Neuro-Oncology). LUMOS2, an umbrella study with multiple arms, is expected to enroll up to 76 patients and will be a multi-centre study at several Australian sites, with the potential to expand internationally. We anticipate enrollment to commence in 4Q23.

MSKCC phase I clinical study

Paxalisib is the subject of an ongoing phase I clinical study in combination with radiotherapy for the treatment of brain metastases, sponsored by Memorial Sloan Kettering Cancer Center in New York, NY.

Kazia is pleased to confirm that the phase I expansion cohort is enrolling. Two world-renowned cancer centres have joined MSKCC in this study: Miami Cancer Institute and Fred Hutch Cancer Center in Seattle, WA. Preliminary data from the expansion cohort is anticipated by 1Q24.

EVT-801

Phase I study

Kazia is also developing EVT801, a small-molecule inhibitor of VEGFR3, which was licensed from Evotec SE in April 2021. Preclinical data showed EVT801 to be active against a broad range of tumour types and has shown evidence of synergy with immuno-oncology agents. A phase I study commenced recruitment in November 2021.

EVT-801 continues to enroll in the phase I dose finding study. Kazia anticipates stage 1 data in 2H23, which we believe will enable identification of the recommended dose for subsequent phase II trials. Kazia also anticipates reporting preliminary biomarker data focused on high-grade, serous ovarian cancer as part of this data update.

About Kazia Therapeutics Limited

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

Our lead program is paxalisib, a brain-penetrant inhibitor candidate of the PI3K / Akt / mTOR pathway, which is being developed to treat multiple forms of brain cancer. Licensed from Genentech in late 2016, Paxalisib is or has been the subject of ten clinical trials in various brain cancers. A completed phase II study in glioblastoma reported promising signals of clinical activity in 2021, and a potentially pivotal study for registration, GBM AGILE, is ongoing, with final data expected in CY2023. Other clinical trials are ongoing in brain metastases, diffuse midline gliomas, and primary CNS lymphoma, with several of these having reported encouraging interim data.

Paxalisib was granted Orphan Drug Designation for glioblastoma by the US FDA in February 2018, and Fast Track Designation for glioblastoma by the US FDA in August 2020. In addition, Paxalisib was granted Rare Pediatric Disease Designation and Orphan Designation by the US FDA for DIPG in August 2020, and for atypical teratoid / rhabdoid tumours (AT/RT) in June 2022 and July 2022, respectively.

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

This document was authorized for release to the ASX by John Friend, Chief Executive Officer.

Forward-Looking Statements

This announcement may contain 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," "potential," "explore," 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 trials and Kazia's strategy and plans with respect to its programs, including paxalisib and EVT-801. Such statements are based on Kazia's current 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, related to regulatory approvals, related to Kazia's executive leadership changes, 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 announcement.

KAZIA THERAPEUTICS

A Diversified Oncology Drug Development Company

June 2023

ASX: KZA | NASDAQ: KZIA | Twitter: @KaziaTx

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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, related to regulatory approvals, risks related to Kazia’s executive leadership changes, and the 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.

Company Overview

A late-clinical-stage oncology drug development company

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Paxalisib	EVT801
Brain-penetrant pan-PI3K / mTOR inhibitor • Well-validated class with five FDA-approved therapies • Only brain-penetrant PI3K inhibitor in development	Selective VEGFR3 inhibitor • Designed to avoid off-target toxicity of older angiokinase inhibitors • Primarily targets lymphangiogenesis
In development for multiple brain cancers • Clinical trials ongoing in brain metastases, childhood brain cancer, glioblastoma, IDH-mutant glioma, and primary CNS lymphoma	Currently in phase I for advanced solid tumors • Adaptive, biomarker study ongoing at 2 leading cancer sites in France
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	Potential use in many solid tumors • Potential indications include: ovarian cancer, renal cell carcinoma, liver cancer, colon cancer, and sarcoma
Rich potential commercial opportunity • Glioblastoma alone sized at US$ 1.5 billion per annum • Commercial licensee in place for China	Potential combination with immunotherapy • Strong evidence of synergy in preclinical data supports potential of monotherapy or combination use
Final Phase III Data: Anticipated 2H CY2023	**Initial Phase I Data: Anticipated 2HCY2023**

Company is dual-listed on NASDAQ (KZIA) and ASX (KZA) with market cap around US$ 27 million

Licensing-driven business model, with programs sourced from Genentech (paxalisib) and Sanofi / Evotec (EVT801)

Cash runway into 4Q23, with potential opportunities for non-dilutive income via additional partnering activity

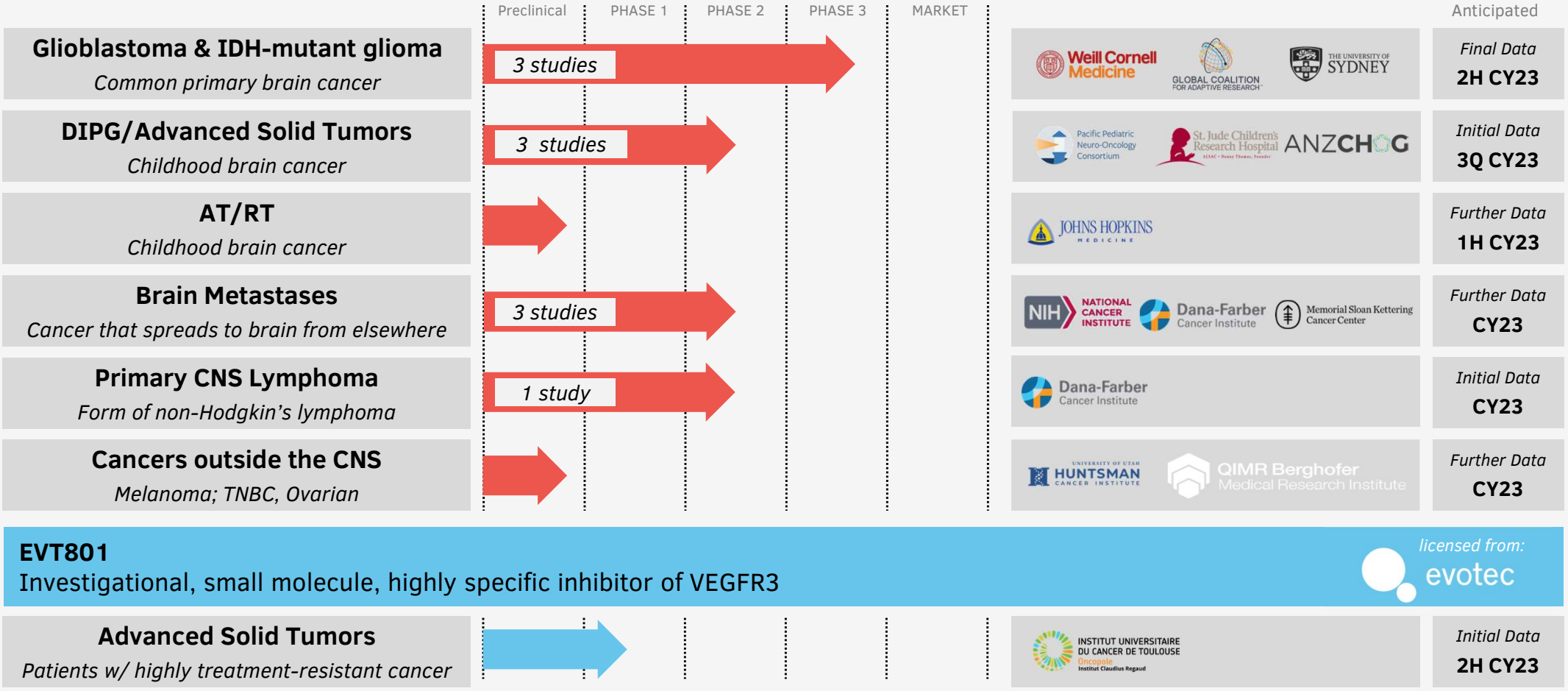
Lean virtual pharma model, with ~75% of cashflows applied directly to clinical trials

Pipeline – Two Differentiated Assets

Lead asset provides a 'pipeline in a molecule'

Paxalisib
Investigational, small molecule, potent, 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

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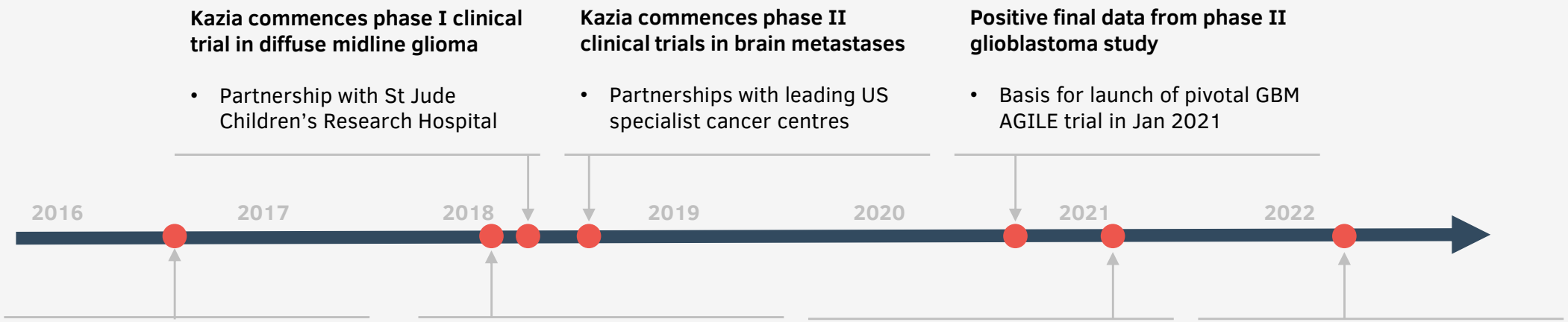
Paxalisib History

Asset licensed from Genentech in 2016



Kazia licenses paxalisib from Genentech, Inc

- $5 million upfront payment
- Royalties on commercial sales
- Asset licensed after strategic review by Genentech refocused R&D on immuno-oncology and tumors outside the brain

Kazia commences phase I clinical trial in diffuse midline glioma

- Partnership with St Jude Children's Research Hospital

Kazia commences phase II clinical trial in glioblastoma

- 6 leading US based cancer centres
- Focuses development on newly-diagnosed patients, a larger commercial opportunity and more treatment-responsive population

Kazia commences phase II clinical trials in brain metastases

- Partnerships with leading US specialist cancer centres

Greater China rights licensed to Simcere Pharmaceutical

- $11 million upfront payment
- Up to $281 million in milestone payments
- Mid- to high-teen royalties on net sales in greater China

Positive final data from phase II glioblastoma study

- Basis for launch of pivotal GBM AGILE trial in Jan 2021

Multiple positive data read-outs in various cancers

- 2 brain mets studies graduate to expansion stages
- Compelling preclinical DIPG data in combination with ONC201 presented
- Positive preclinical data in AR/RT
- Positive preclinical data in melanoma

Collaborations with Leading Brain Cancer Research Centres

Weill Cornell Medicine · St. Jude Children's Research Hospital · Johns Hopkins Medicine · Memorial Sloan Kettering Cancer Center · Hunter Medical Research Institute (HMRI) · Harvard Medical School · Global Coalition for Adaptive Research · Pacific Pediatric Neuro-Oncology Consortium · National Cancer Institute · University of Utah Huntsman Cancer Institute · Dana-Farber Cancer Institute · David Geffen School of Medicine (UCLA)

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CY2023 Milestones and Newsflow

Multiple catalysts across two clinical programs

Preclinical data for paxalisib in melanoma presented at AACR (2023)	1H CY2023	✓
Preclinical data for paxalisib in DMG/DIPG & AT/RT presented at AACR (2023)	1H CY2023	✓
Preliminary data from Kazia's EVT801 phase I trial presented AACR 2023	1H CY2023	✓
Initiate OPTIMISE clinical study in pediatric PI3K/mTOR activated cancers	1H CY2023	✓
Initiate LUMOS2 clinical study in adult IDH-mutant glioma patients w/PI3K/mTOR mutations	1H CY2023	✓
Initial interim data from paxalisib phase II DIPG study with PNOC	3Q CY2023	
EVT801 Stage 1 completion	2H CY2023	
QIMR preclinical data and provisional patent update	2H CY2023	
Initial interim data from paxalisib phase II PCNSL study at Dana-Farber	2H CY2023	
Further interim data from paxalisib brain metastases trials	2H CY2023	
Final data from GBM AGILE pivotal study of paxalisib	2H CY2023	
Paxalisib + radiotherapy Stage 2 data phase I brain mets study at Memorial Sloan-Kettering	1Q CY2024	

Note: all guidance is indicative, and subject to amendment in light of changing conference schedules, operational considerations, etc
Kazia is not the sponsor of all planned/ongoing studies and may have limited control or visibility into study timelines

Paxalisib Mechanism of Action

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

1 The PI3K pathway is activated in many forms of cancer

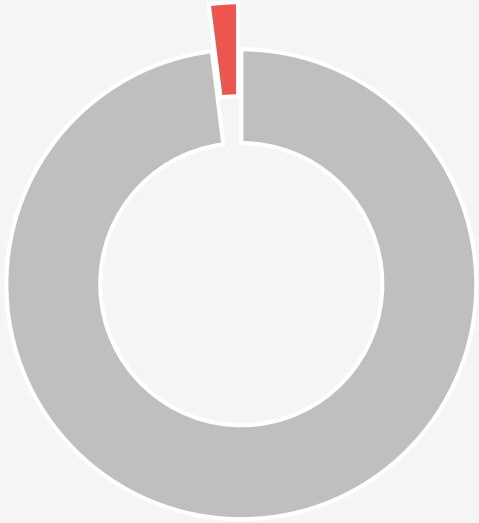
Glioblastoma	**90%**
Breast	**80%**
Lung	**75%**
Endometrial	**60%**
Ovarian	**60%**
Prostate	**45%**

2 Five PI3K inhibitors have already been approved by FDA

Zydelig (idelalisib) 150 mg 100 mg tablets	• Chronic lymphocytic leukemia • Follicular lymphoma
Aliqopa (copanlisib) 60 mg vial for injection	• Follicular lymphoma
Copiktra (duvelisib) 15mg | 25mg capsules	• Chronic lymphocytic leukemia • Follicular lymphoma
PIQRAY (alpelisib) tablets 50 mg · 150 mg · 200 mg	• Breast cancer
UKONIQ umbralisib 200 mg tablets	• Follicular lymphoma

3 Paxalisib is the only brain-penetrant PI3K inhibitor

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



Source: Data on file

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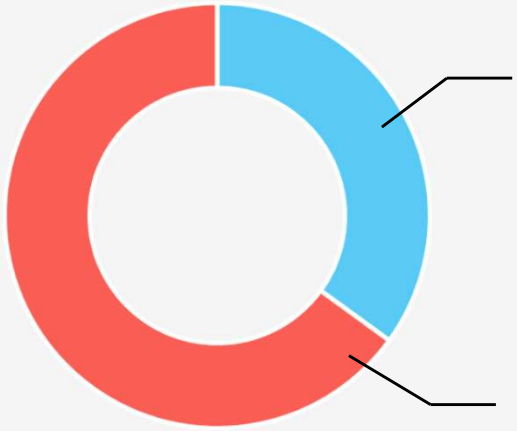
Glioblastoma

Paxalisib in Glioblastoma

High unmet need, especially in 'MGMT unmethylated' patients

Standard of Care ('Stupp Regimen')



Methylated MGMT Status

~35% of patients respond to temozolomide

Extends overall survival from 15 to 22 months

Unmethylated MGMT Status

~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

MGMT: O6-methylguanine-DNA methyltransferase

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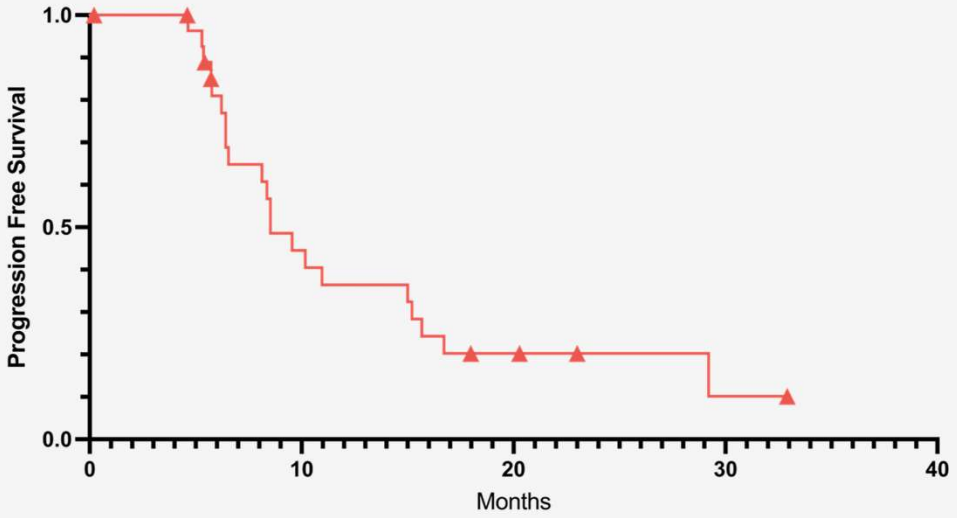
Paxalisib in Glioblastoma

Phase II study suggests encouraging PFS and OS in context of current treatment landscape

Progression-Free Survival (PFS)

(n=30)

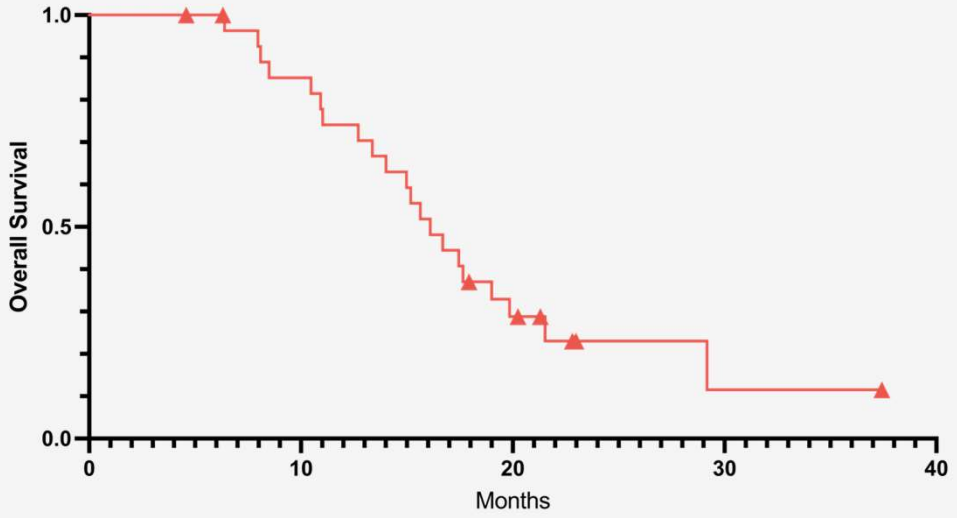


Median PFS: **8.6 months** (6.6-11.0)

Comparator figure for existing therapy: **5.3 months**
(Hegi et al. 2005)

Overall Survival (OS)

(n=30)



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

Comparator figure 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

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Paxalisib in Glioblastoma

Safety profile in Phase II study is favorable for a drug in advanced cancer

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

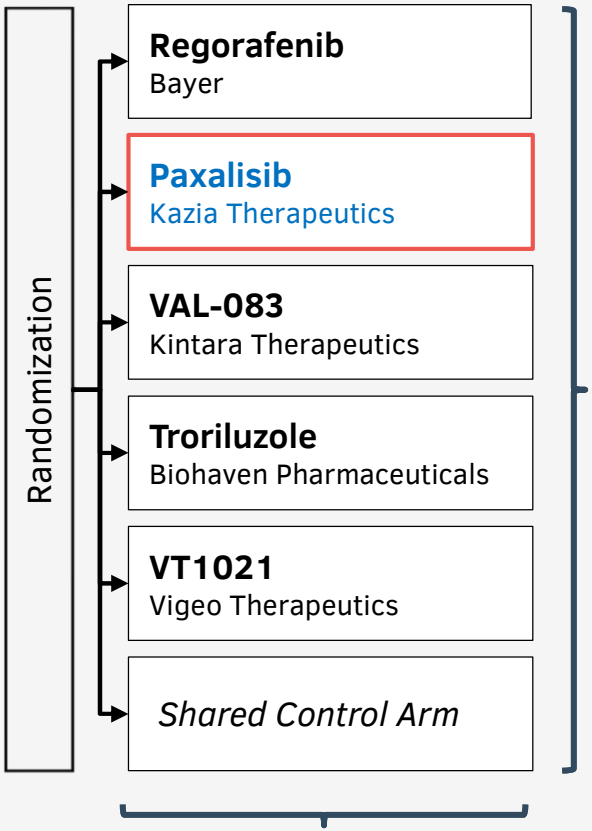
Term	Gr 1	Gr 2	Gr 3	Gr 4	Total (%)
Fatigue	3	13	2		18 (60%)
Stomatitis	4	7	3		14 (47%)
Decreased appetite	6	6	1		13 (43%)
Hyperglycemia	3	1	6	2	12 (40%)
Nausea	4	6	1		11 (37%)
Rash, maculo-popular	1	1	7		9 (30%)
Diarrhea	7	1			8 (27%)
Vomiting	4	2	1		7 (23%)
Rash	2	4	1		7 (23%)
Neutrophils decreased	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

Adaptive multi-drug study, GBM AGILE, is ongoing

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
- FDA acknowledged that GBM-AGILE data may be suitable for registration



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*

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

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

- **Completed** — *Negative outcome (Sep 22)*
- **Ongoing** — *No graduation to Stage 2 (Aug 22)*
- **Ongoing** — *No public information on graduation*
- **Ongoing** — *Joined study in Jan 22*
- **Ongoing** — *Joined study in Jan 22*

GCAR: Global Coalition for Adaptive Research

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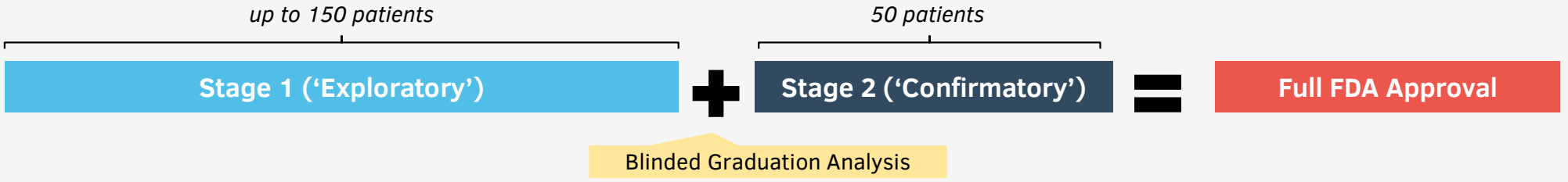
Paxalisib in Glioblastoma

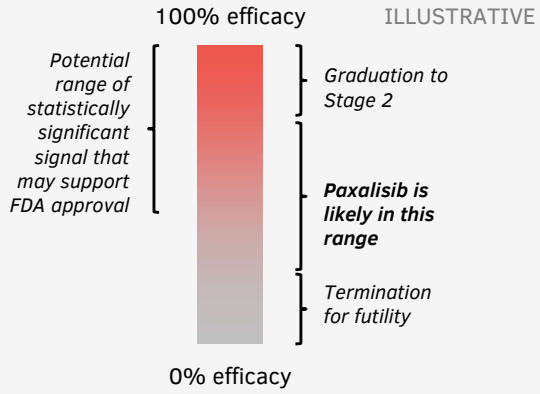
We believe *GBM AGILE's interim analysis may have been premature*

OVERALL STUDY DESIGN



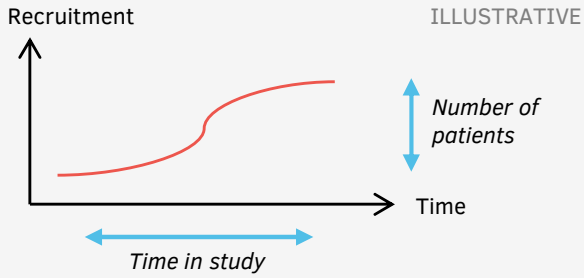
POTENTIAL CONTRIBUTORY FACTORS TO PAXALISIB GRADUATION RESULT

1 Graduation threshold is high



Avastin® (bevacizumab) was approved for recurrent glioblastoma by FDA in 2009 with no evidence of any survival benefit

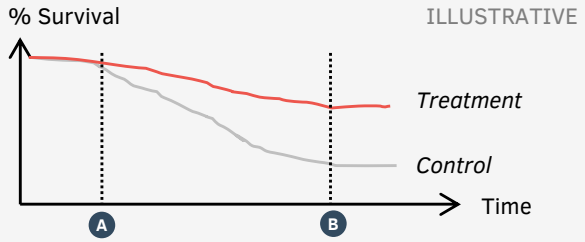
2 Back-loaded recruitment may have reduced statistical power at graduation



Statistical Power = Number of Patients x Time in study

GBM AGILE has recruited ~3-4 times faster than originally anticipated; many paxalisib patients likely have limited time in study

3 Treatment effect typically becomes clearer as study matures



- **A** At an early point in the study, there is limited separation of curves
- **B** As the study matures over time, treatment effect becomes more apparent

Final analysis will be performed 12 months after last patient enrolled; graduation analysis may include <60% of final study information

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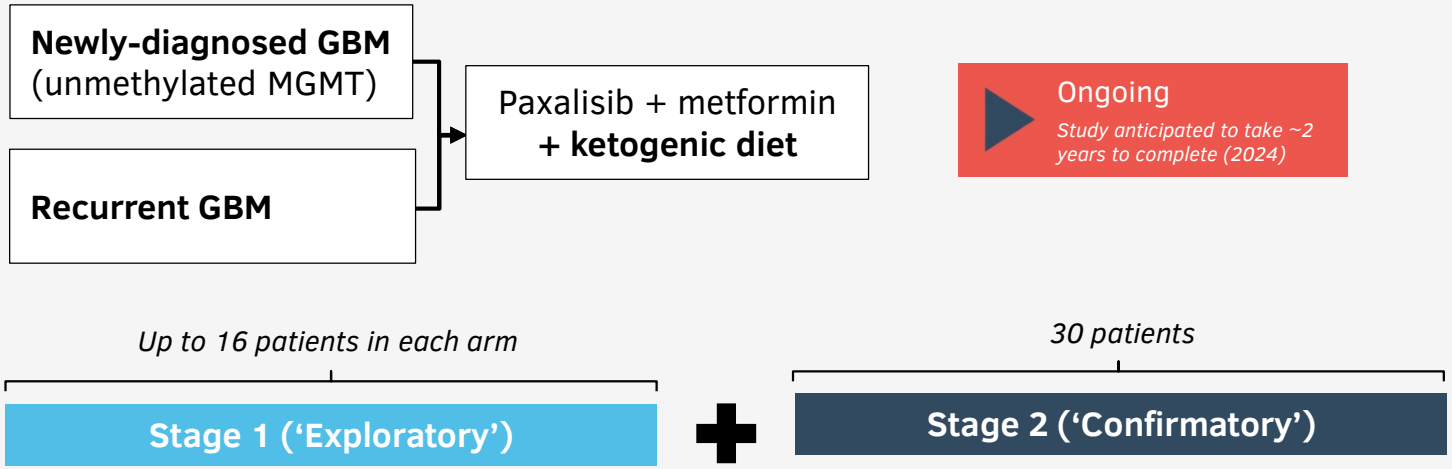
Paxalisib in Glioblastoma

Cornell study to investigate if low-insulin state enhances paxalisib activity

Rationale of conducting the study

- As with most PI3K inhibitors, hyperglycemia is a key toxicity
- Insulin regulated glucose metabolism partly via PI3K-Akt-driven signalling
- Insulin signalling and PI3K inhibition are essentially antagonistic
- The interaction between PI3K inhibition and insulin signalling may drive hyperglycemia and differential efficacy

OVERALL STUDY DESIGN



1. **Primary Endpoint:** progression-free survival at six months (PFS6)
2. **Secondary Endpoints**: Overall survival, insulin levels and metabolic markers

Weill Cornell Medicine

Source: NCT05183204

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Paxalisib in Grade 2/3 IDH-Mutant Glioma

LUMOS 2 Clinical Study

- LUMOS2 is a prospective, multi-center, open-label, multi-arm, phase II, biomarker-directed, signal-seeking, umbrella clinical trial sponsored by University of Sydney
  - Adults with progressive grade 2/3, IDH-mutant glioma at recurrence after prior treatment with radiotherapy and alkylating chemotherapy who are eligible and willing to undergo tumour resection and will undergo genetic/molecular profiling
  - The genetic testing results will serve as a recommendation to be assigned to a treatment arm. Patients with PI3K-related mutations will be randomized to receive paxalisib
  - Primary objective of the study is to determine progression-free survival at six months (PFS6) with overall survival, response rate and health-related quality of life as secondary endpoints.
- Anticipate the first patient to be enrolled 4Q23

Childhood brain cancers

Summary of Paxalisib in Childhood Brain Cancer

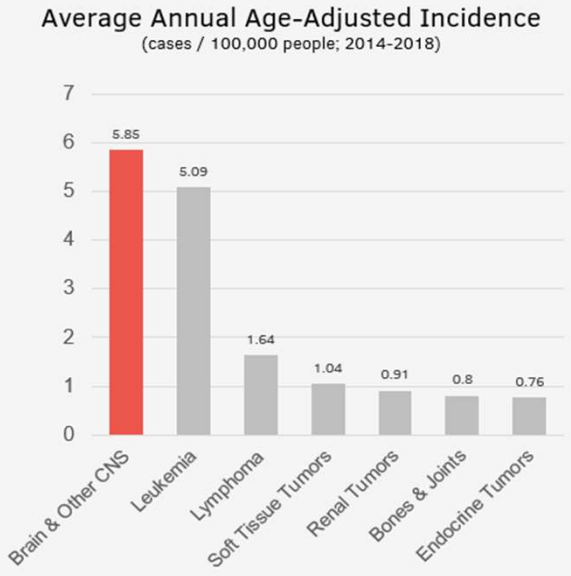
Kazia has interest in at least three forms of childhood brain cancer

	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)	*Research proposals under discussion*
Clinical Trials	Phase I monotherapy clinical trial nearing completion at St Jude Children's Research Hospital	*Clinical trial opportunities under discussion*	*Additional clinical trial opportunities under discussion for medulloblastoma and HGG*
	Phase II clinical trial in combination with ONC201, commenced recruitment in Nov 2021		Phase II clinical trial in combination with chemotherapy for treatment of high-risk malignancies including (but not confined to) brain tumors
Regulatory Interaction	Orphan Drug Designation (ODD) and Rare Pediatric Disease Designation (RPDD) granted by FDA in Aug 2020	Orphan Drug Designation (ODD) granted by FDA in June 2022	*Regulatory strategy under discussion*

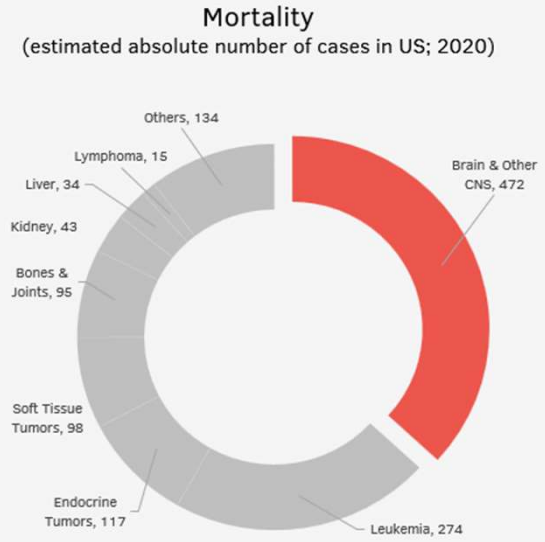
Paxalisib in Childhood Brain Cancer

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

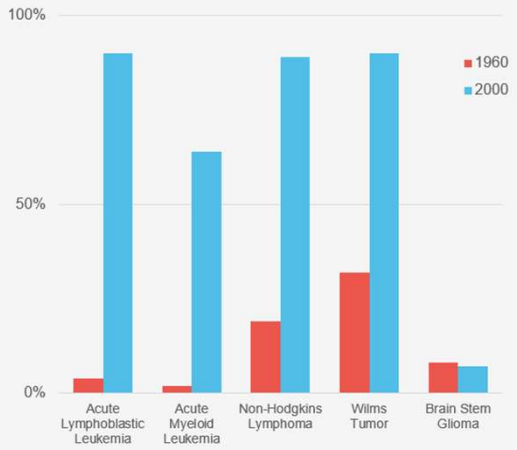
1 **Brain cancer is the most common malignancy of childhood**



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

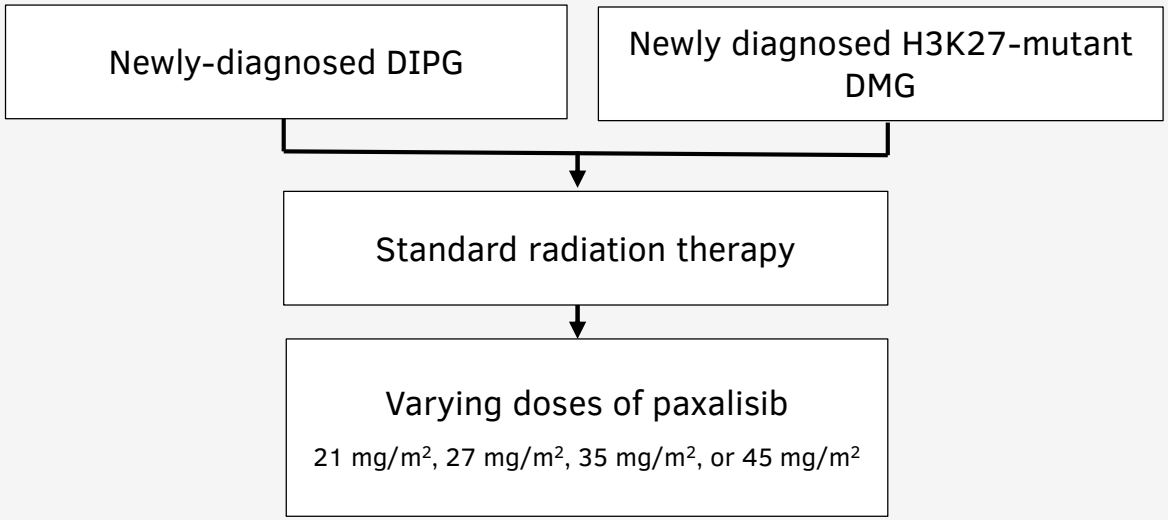
Source: CBTRUS; CDC; Ages 0-14 shown; Adamson PC, *CA Cancer J Clin*. 2015;65:212–220

KAZIA THERAPEUTICS

Paxalisib in Diffuse Midline Gliomas

Phase I trial (St. Jude Children study) showed paxalisib was generally well tolerated in children

OVERALL STUDY DESIGN



Results from Phase I trial

- ✓ **MTD** of paxalisib **has been established**
- ✓ Paxalisib exhibited a generally favorable tolerability profile in children, with toxicity profile (rash, hyperglycemia and neutropenia were the most common reported serious adverse events) being comparable to that observed in adults and consistent with other agents in the same class
- ✓ Data published SNO Scientific Meeting 2020

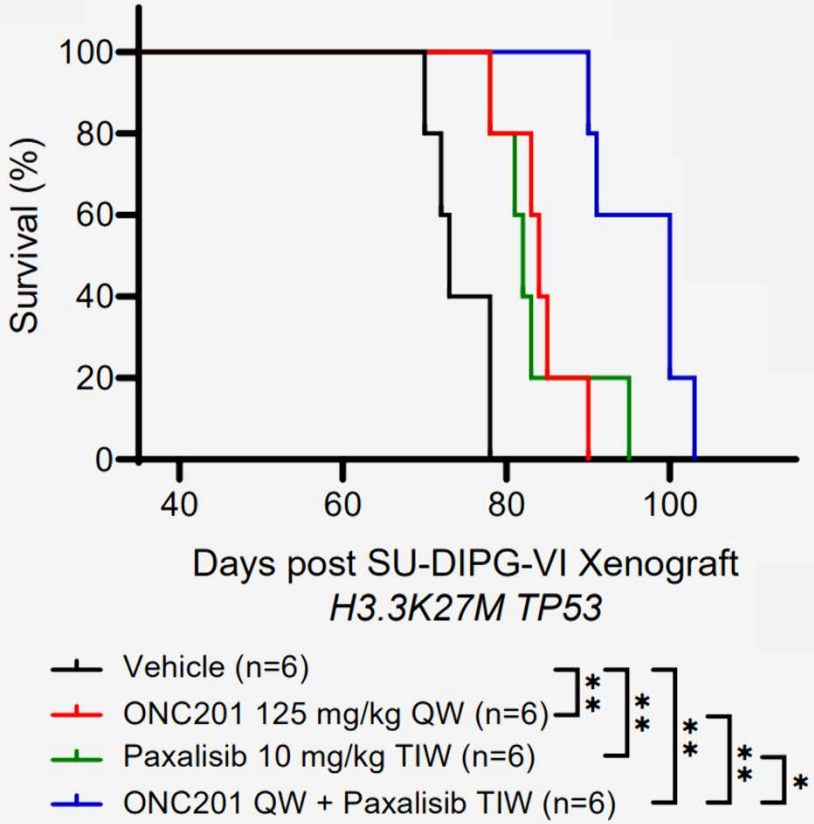
St. Jude Children's Research Hospital
Finding cures. Saving children.

KAZIA THERAPEUTICS

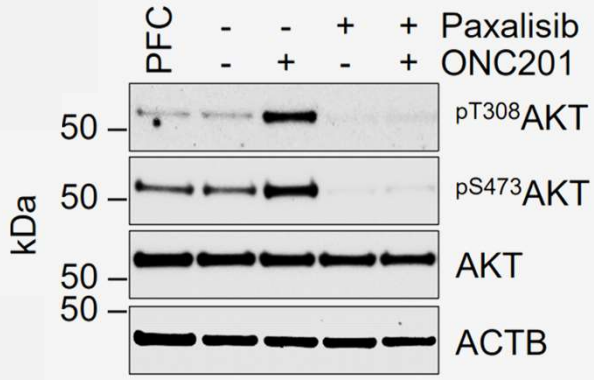
Paxalisib in Diffuse Midline Gliomas

Combination of ONC201 and paxalisib appeared synergistic in preclinical model

The *in vivo* xenograft model demonstrated extended survival with the addition of paxalisib



Addition of paxalisib rescued ONC201 from pAKT activation



Source: Jackson, et al. ONC201 in combination with paxalisib is a therapeutic strategy for diffuse midline glioma. Cancer Research, 2023/5/17

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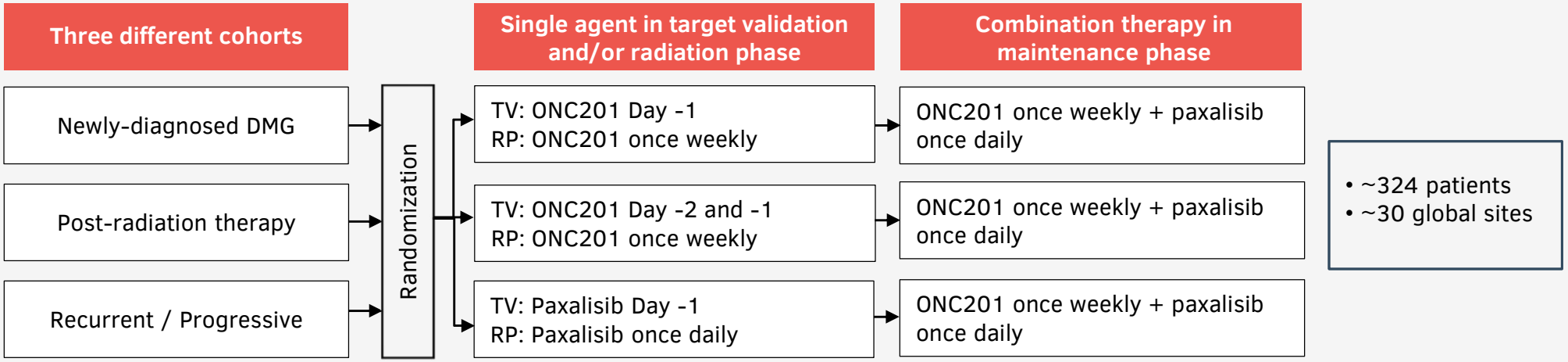
Paxalisib in Diffuse Midline Gliomas

Multi-arm, global site study, PNOC022, is underway

OVERALL STUDY DESIGN



REGULATORY STRATEGY

- ✓ Orphan Drug Designation in DIPG / DMGs
- ✓ Rare Pediatric Disease Designation in DIPG / DMGs
- Evaluate possibility of NDA filing in DIPG / DMGs on the basis of data from PNOC022 study (2H CY2023)
- Successful NDA approval may provide a pediatric Priority Review Voucher (pPRV) – current value ~US$ 110M

Pacific Pediatric Neuro-Oncology Consortium

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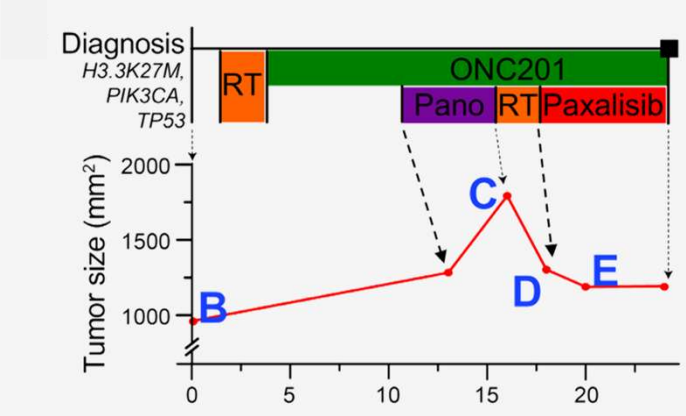
Paxalisib in Diffuse Midline Gliomas

Case studies from compassionate use suggest activity

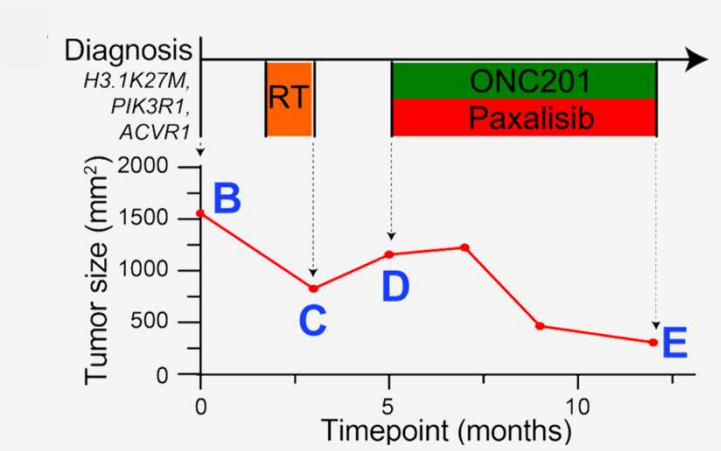
Patient 1

- Commenced ONC201 + paxalisib immediately following re-irradiation
- At 5 months, MRI showed continued regression of primary tumor and clinical improvement
- Patient succumbed unexpectedly of pneumonia, with autopsy showing no evidence of new tumor growth or tumor-related mortality



Patient 2

- Commenced ONC201 + paxalisib following radiotherapy after diagnosis
- Tumor size has decreased by 80% (versus diagnosis) or 68% (versus post-RT)
- Patient has returned to school with marked reduction of DIPG-associated symptoms, and continued tumor regression



Source: Jackson, et al. ONC201 in combination with paxalisib is a therapeutic strategy for diffuse midline glioma. Cancer Research, 2023/5/17

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Paxalisib in Childhood Brain Cancer

Australian phase II study, OPTIMISE, anticipated enrollment in 2H 2023

The trial explores paxalisib in combination with existing chemotherapy agents for the treatment of children with high-risk malignancies, including (but not confined to) brain tumors

18 patients

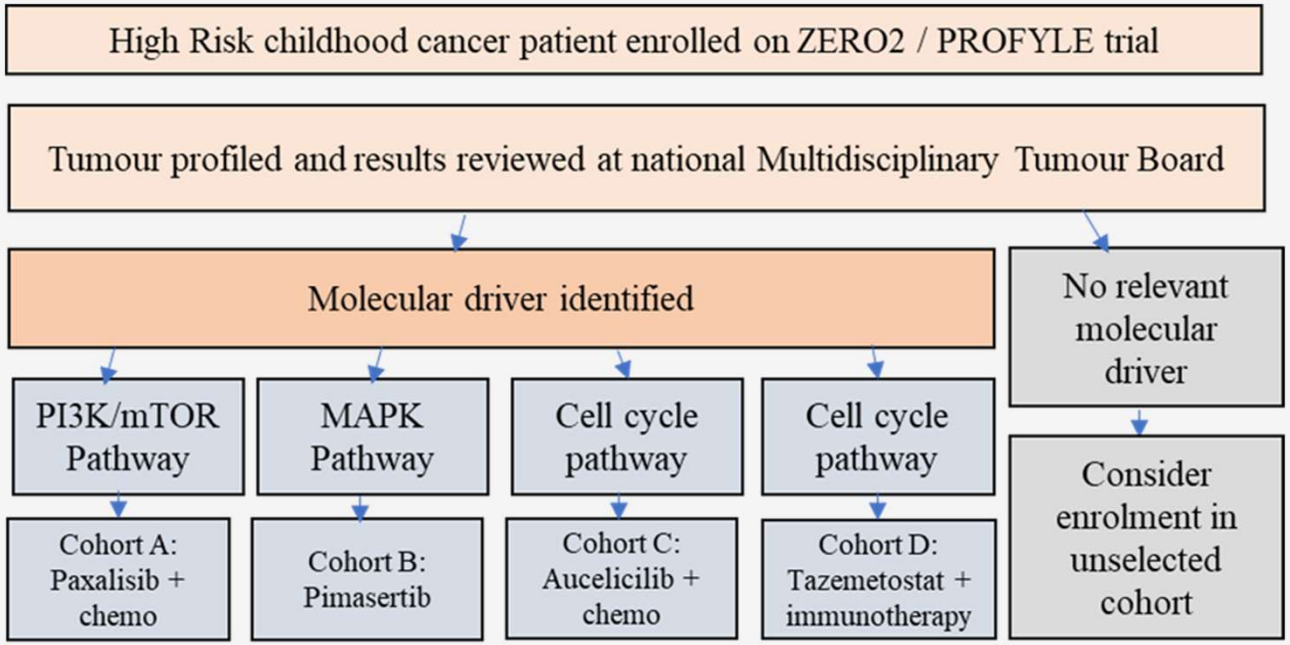
Stage 1 ('Exploratory')

First patient dose:
4Q 2023

+

100 patients

Stage 2 ('Confirmatory')



ANZCHOG
Australian & New Zealand Childrens Haematology/Oncology Group

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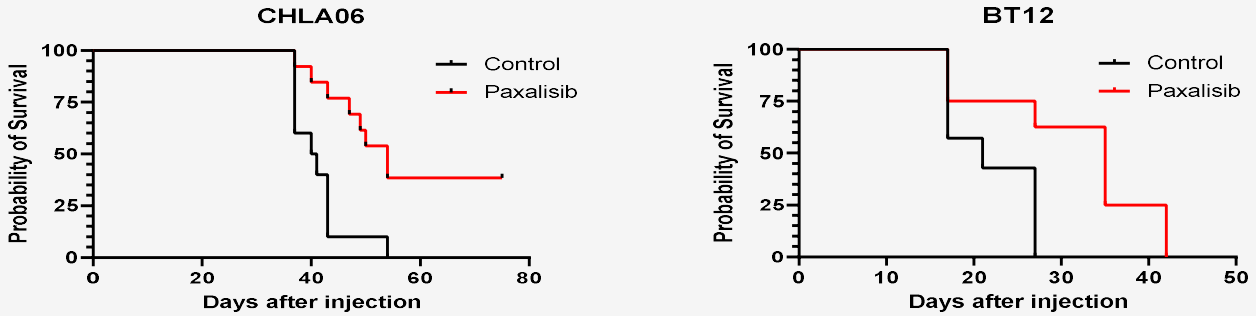
Paxalisib in Atypical Teratoid / Rhabdoid Tumor

Monotherapy showed activity in vivo models

High unmet need

- Atypical Teratoid /Rhabdoid Tumors (AT/RT) are the most common malignant brain tumors of infancy
- Activation of the PI3k-Akt-mTOR pathway is commonly observed in patients with AT/RT
- There are no FDA approved therapies. Current standard of care are surgery, chemotherapy and radiation

Paxalisib monotherapy slowed tumor growth and extended survival in mice bearing AT/RT orthotopic xenograft tumors



Data on additional combination treatments published at AACR 2023

With nucleoside analog, gemcitabine

- Increased apoptosis and synergized to decrease AT/RT cell growth
- Further extended median survival in CHLA-266 orthotopic tumors

With MEK inhibitor, mirdametinib

- Reduced AT/RT growth and viability (Bliss synergy score 16.77)
- Induced high levels of apoptosis and cell senescence
- Decreased mTOR and MAPK pathway activation in mice bearing AT/RT orthotopic tumors

Source: AACR 2022 & ISPNO 2022 Poster Presentations

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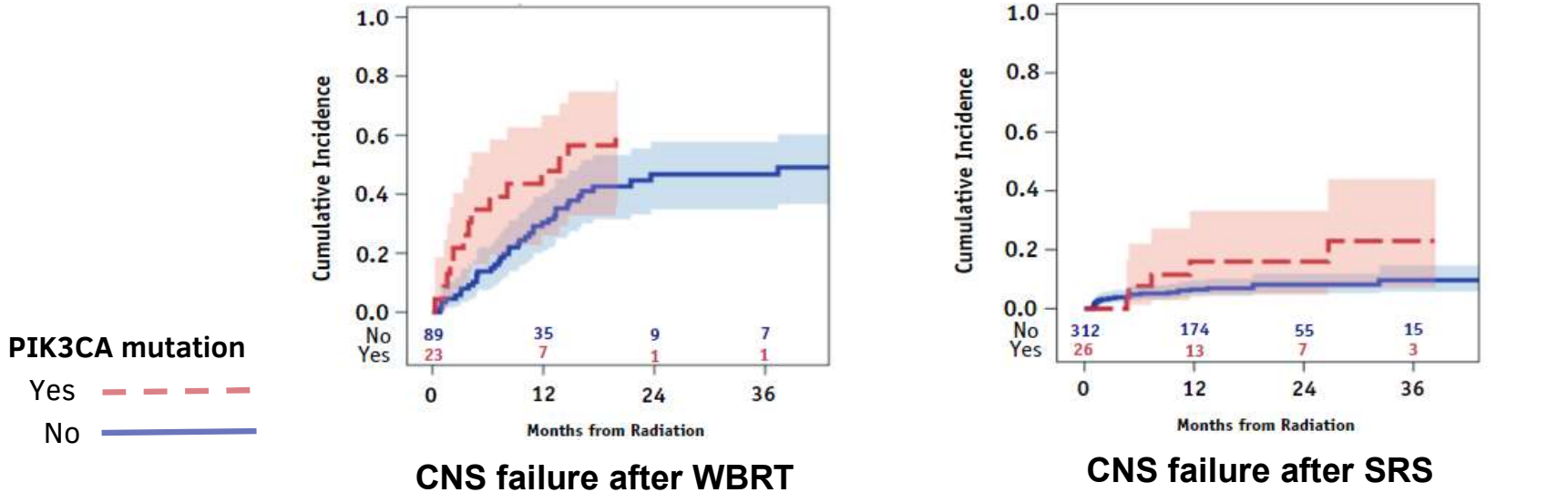
Brain metastases

Summary of Brain Metastases Clinical Studies Underway

Registration	Indication	Phase	N	Status	Sponsor
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

Paxalisib in Brain Metastasis

PI3K pathway mutations are common in brain metastases and associated with a worse prognosis



	+*PIK3CA* mutations at 1 yr	–*PIK3CA* mutations at 1 yr
CNS failure after WBRT, % (95% CI)	48 (26-67)	30 (21-40)
CNS failure after SRS, % (95% CI)	16 (5-33)	7 (CI 4-10)

CI, confidence interval. **SRS**, stereotactic radiosurgery. **WBRT**, whole-brain radiation therapy.

Source: Lockney NA, et al. *Int J Radiat Oncol Biol Phys*. 2018;101(4):833-844.

Paxalisib in Brain Metastasis

Phase I trial's interim analysis showed encouraging clinical activity of paxalisib in combination with radiation therapy

OVERALL STUDY DESIGN

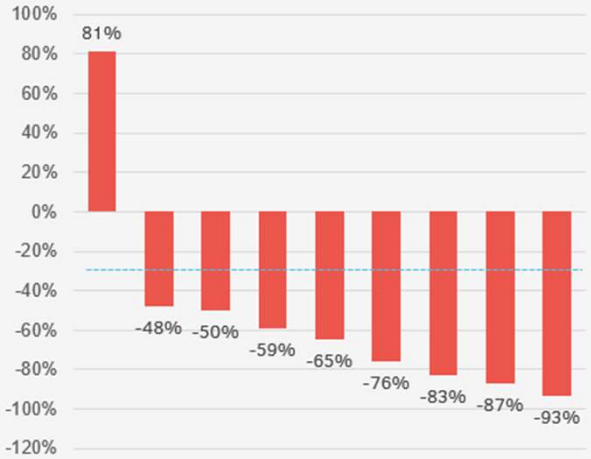
12 patients enrolled (9 evaluable, 3 did not complete protocol treatment)

Additional 12 patients

Stage 1 ('Exploratory') + **Stage 2 ('Confirmatory')**

Interim Analysis

Best Observed Response



- The most common histology was breast cancer
- The Maximum Tolerated Dose of paxalisib when combined with cranial RT has been established
- Robust response with all evaluable patients experiencing partial or complete response per RANO-Brain Mets criteria within 3 months of protocol therapy

Memorial Sloan Kettering Cancer Center

Source: Jonathan Yang, et al, *Neuro-Oncology Advances,* 2022

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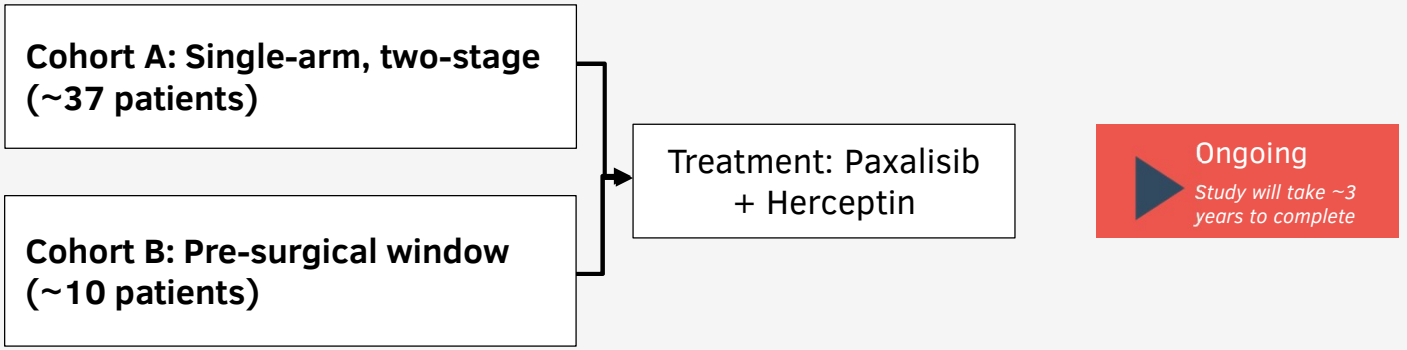
Paxalisib in Brain Metastasis

Phase II trial to evaluate efficacy with trastuzumab in BCBM patients

Rationale of conducting the study

- The PI3K/Akt/mTOR is an important pathway in HER2-positive breast cancer brain metastases (BCBM).
- Mutations in PIK3CA loss are associated with trastuzumab resistance.
- This single-center, phase II study aims to evaluate the efficacy of the combination of paxalisib with trastuzumab for the treatment of CNS metastases in BCBM patients

OVERALL STUDY DESIGN



1. **Primary Endpoints:** progression-free survival at six months (PFS6) and correlation between p-4EBP1 inhibition in brain tumor tissue and PDX model response
2. **Secondary Endpoints**: overall survival, safety and patient-reported outcomes

DANA-FARBER CANCER INSTITUTE

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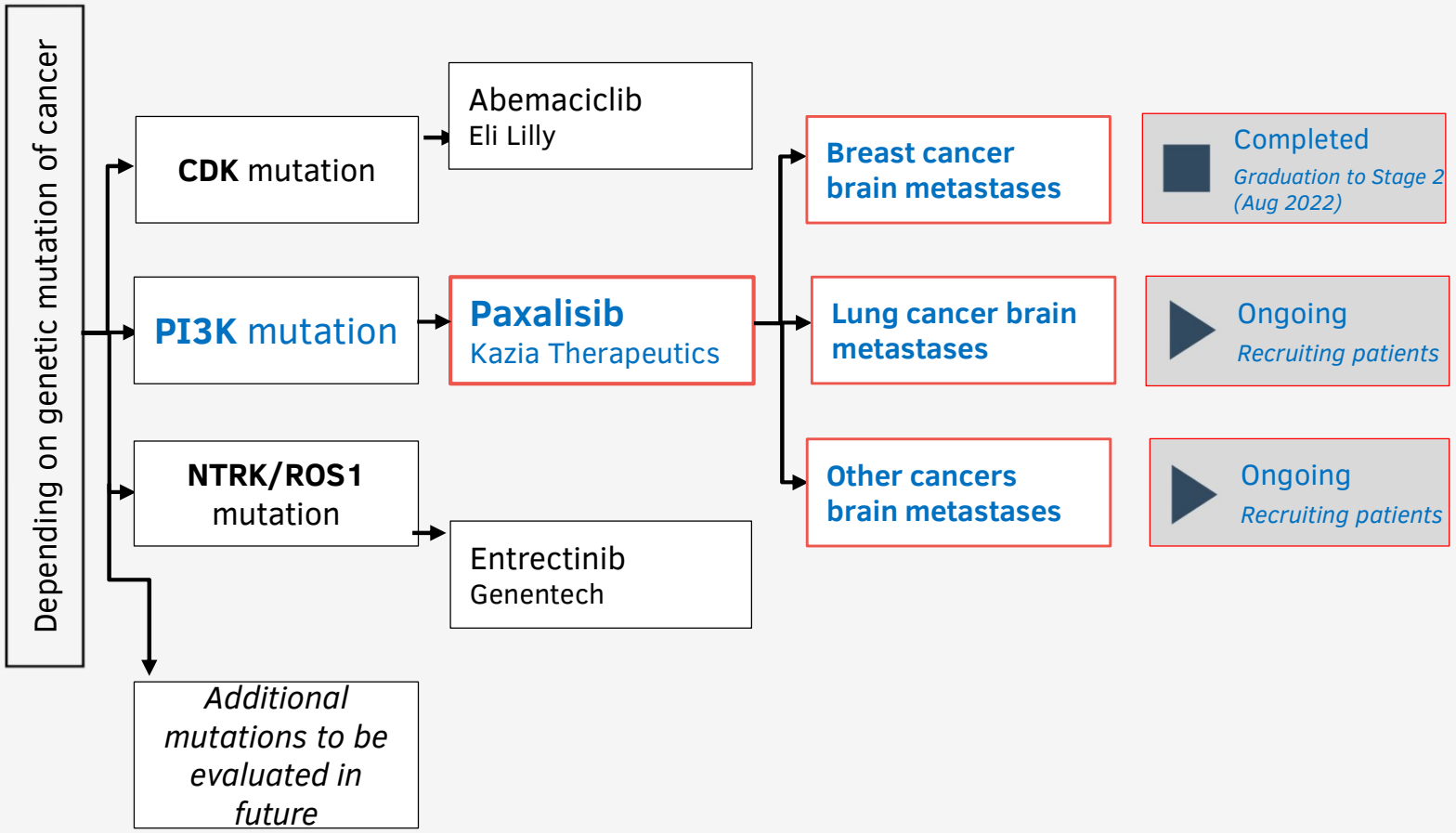
Paxalisib in Brain Metastasis

Genomically guided phase II study of multiple therapies in patients with brain metastases

Rationale of conducting the study

- Approximately 30% of patients with metastatic cancer develop brain metastases
- They have limited treatment options and an average survival range of 3 to 27 months
- Variations in the genetic profiles of tumors in the same location can lead to different responses to treatment



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Primary CNS lymphoma

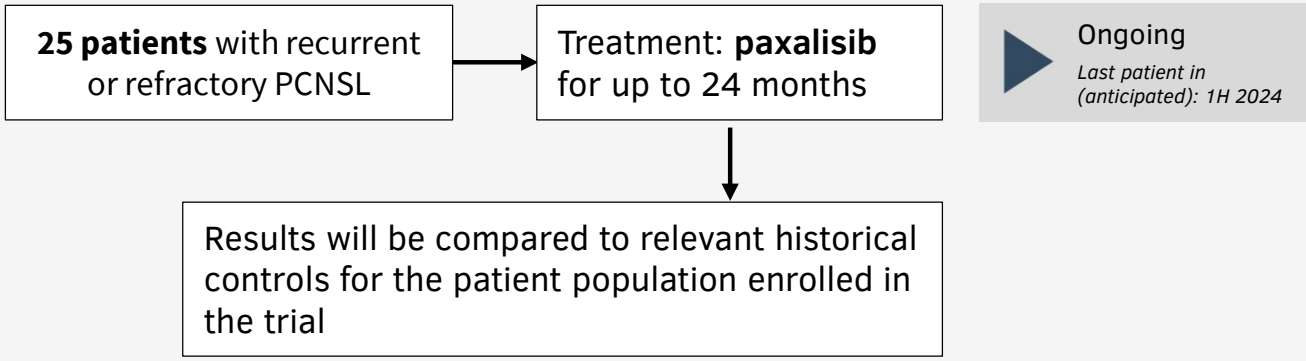
Paxalisib in Primary CNS lymphoma

Phase II trial to evaluate safety and efficacy of paxalisib in PCNSL
Preliminary results anticipated 2H23

Rationale of conducting the study

- PCNSL is a subtype of lymphoma that exclusively occurs in the brain and CNS
- PI3K inhibitors are effective for lymphoma outside the brain, but not for PCNSL because they cannot cross the blood-brain barrier
- Paxalisib is the only PI3K inhibitor in development that can cross the blood-brain barrier, making it a unique candidate for treating PCNSL

OVERALL STUDY DESIGN



1. **Primary Endpoint:** objective response rate
2. **Secondary Endpoints**: progress free survival, safety, overall survival

DANA-FARBER CANCER INSTITUTE

Source: NCT04906096

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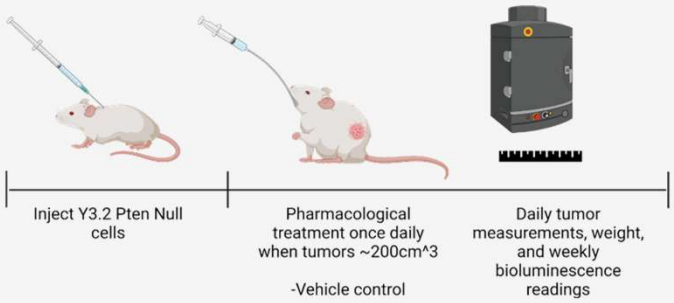
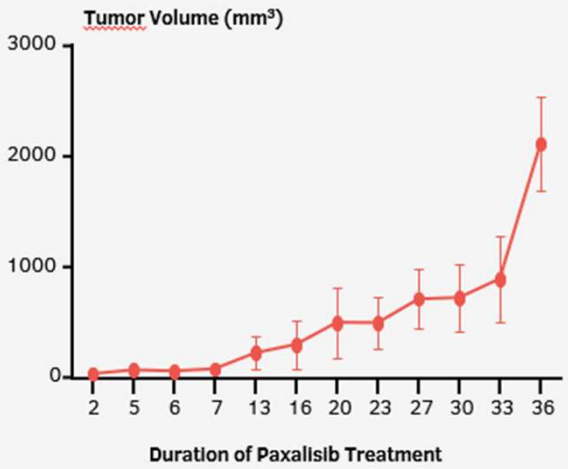
Other solid tumors

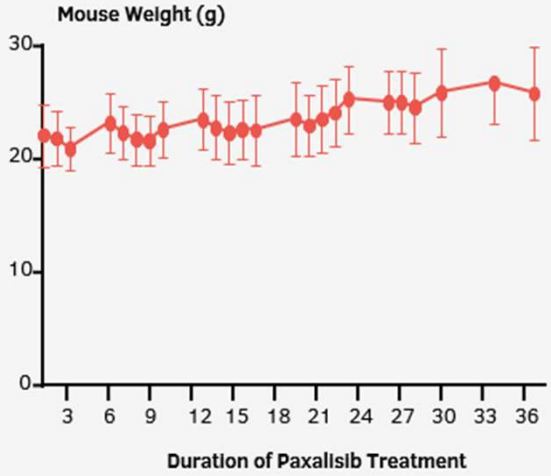
Paxalisib in Metastatic Melanoma

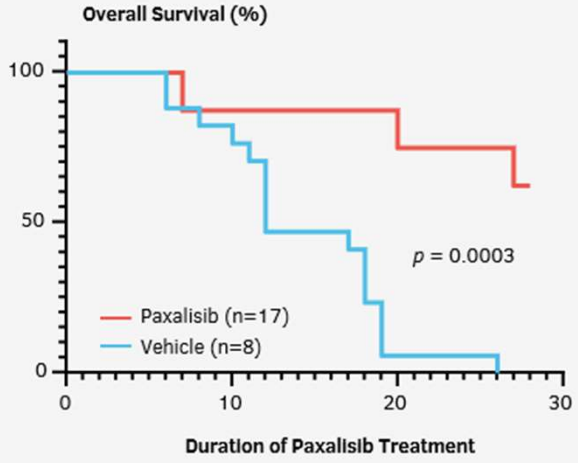
Paxalisib showed potent single agent activity in an in vivo melanoma model



Tumor Volume (Activity)	Animal Weight (Tolerability)	Survival (Efficacy)







Source: AACR 2023 abstracts

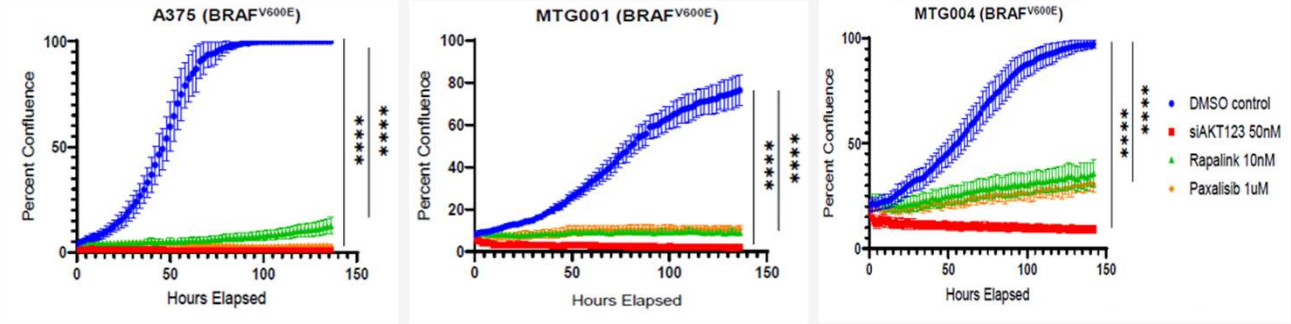
Paxalisib in Metastatic Melanoma

Paxalisib showed potential as therapeutic strategy in refractory melanoma

Unmet need

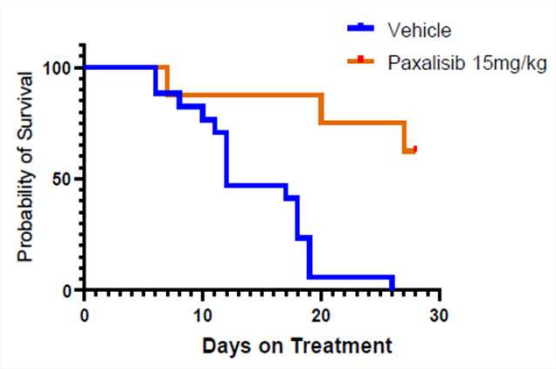
- Melanoma is the 5th most common cancer for men & women in the U.S.
- Approximately 50% of all melanomas harbor an activating BRAF mutation.
- Targeted therapy options for BRAF-mutant melanoma exist, but most patients will experience primary or secondary resistance
- The five-year survival rate of stage IV melanoma remains at 30%, highlighting the need for new therapeutics to treat this disease.

Paxalisib blocked proliferation in vitro (cell confluence assay)

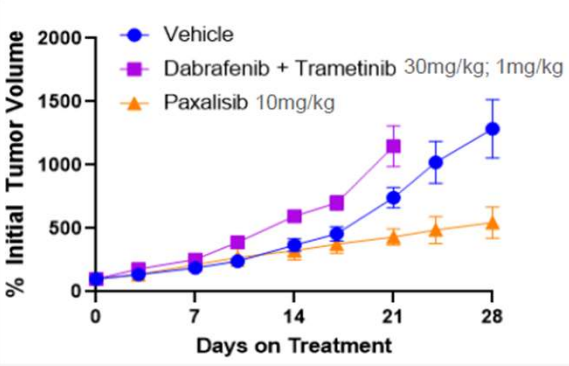


Paxalisib improved survival of BRAF-mutant mouse melanoma, and reduced growth of dabrafenib/trametinib resistant melanoma PDX in vivo

YUMM3.2 Kaplan-Meier Survival Curve



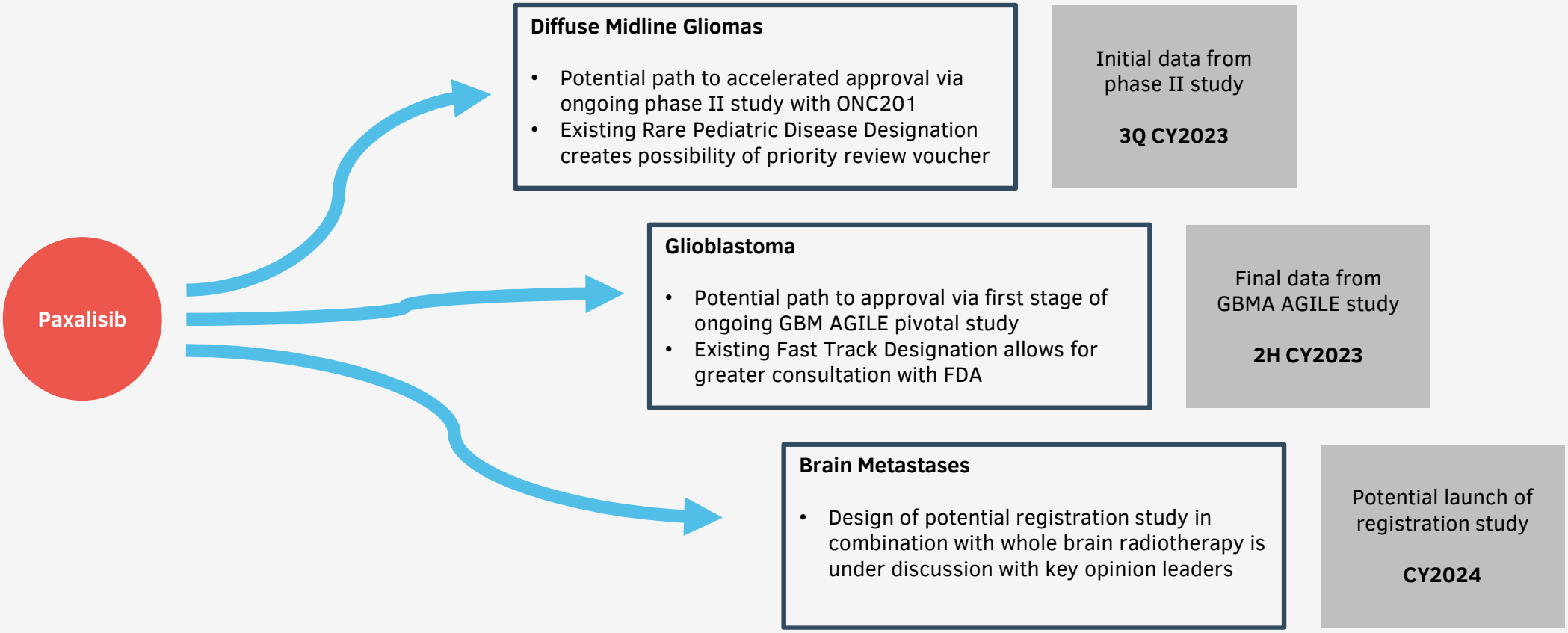
MTG004 Tumor Volume



Source: AACR 2023 abstracts

Paxalisib – Potential Paths to Registration

Multiple opportunities to become a marketed product



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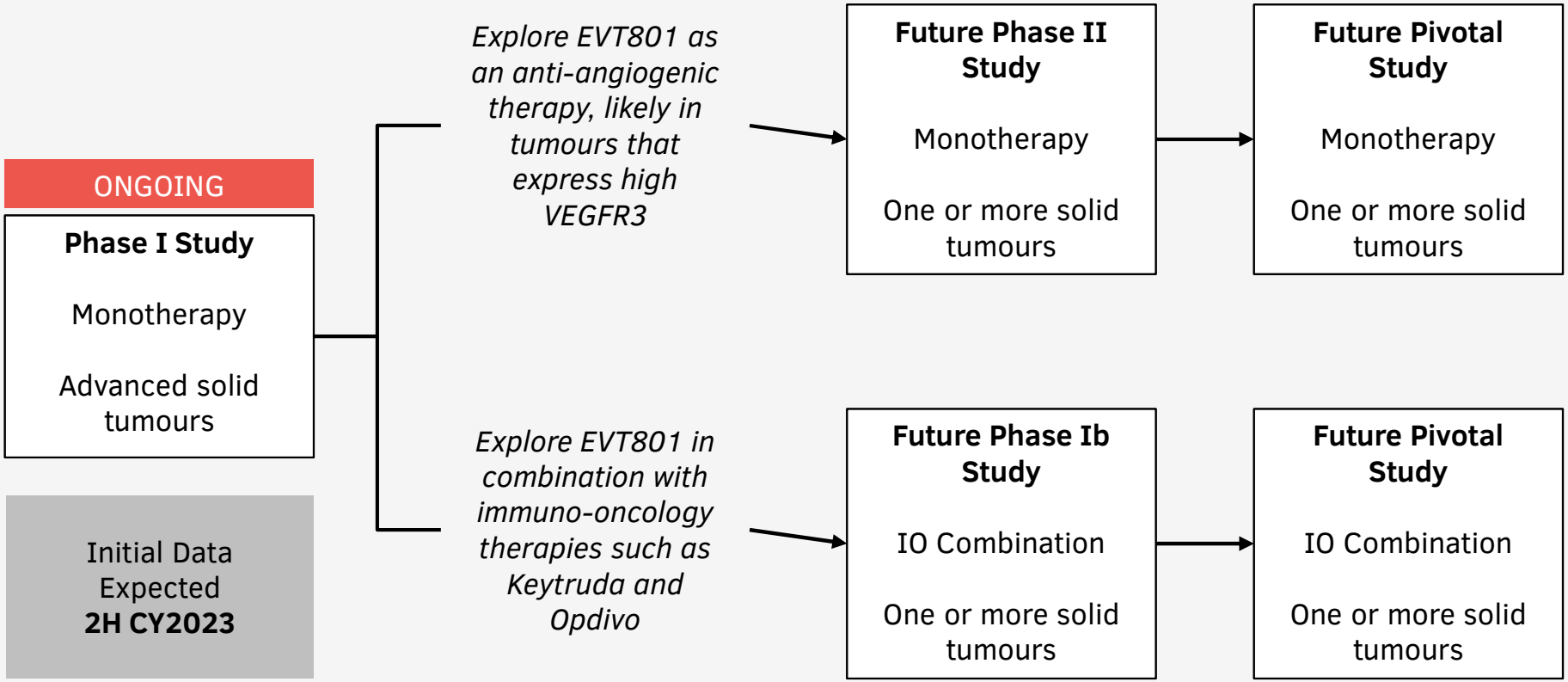
Second Drug in Clinical Trials

EVT801 has potential in a wide range of cancers



Board and Management Team

Extensive experience in drug development

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Bryce Carmine
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Independent Director

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