ASX RELEASE

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KAZIA PRESENTATION TO SNO

Sydney, 14 November 2018 – Kazia Therapeutics Limited (ASX: KZA; NASDAQ: KZIA), an Australian oncology-focused biotechnology company, is pleased to provide a copy of the poster which is to be presented at the Society of Neuro-Oncology in New Orleans on Friday 16 November.

[ENDS]

About Kazia Therapeutics Limited

Kazia Therapeutics Limited (ASX: KZA, NASDAQ: KZIA) is an innovative oncology-focused biotechnology company, based in Sydney, Australia. Our pipeline includes two clinical-stage drug development candidates, and we are working to develop therapies across a range of oncology indications.

Our lead program is GDC-0084, a small molecule inhibitor of the PI3K / AKT / mTOR pathway, which is being developed to treat glioblastoma multiforme, the most common and most aggressive form of primary brain cancer. Licensed from Genentech in late 2016, GDC-0084 is due to enter a phase II clinical trial early in 2018. Initial data is expected in early calendar 2019, and the study is expected to complete in 2021.

TRX-E-002-1 (Cantrixil), is a third-generation benzopyran molecule with activity against cancer stem cells, and is being developed to treat ovarian cancer. TRX-E-002-1 is currently undergoing a phase I clinical trial in Australia and the United States. Initial data is expected in the first half of calendar 2018.

Poster #ACTR-51, SNO Meeting, Nov 2018

ClinicalTrials.gov identifier: NCT03522298

Phase 2 study to evaluate the safety, pharmacokinetics and clinical activity of PI3K/mTOR inhibitor GDC-0084 given to glioblastoma (GBM) patients with unmethylated O_6-methylguanine-methyltransferase promoter status

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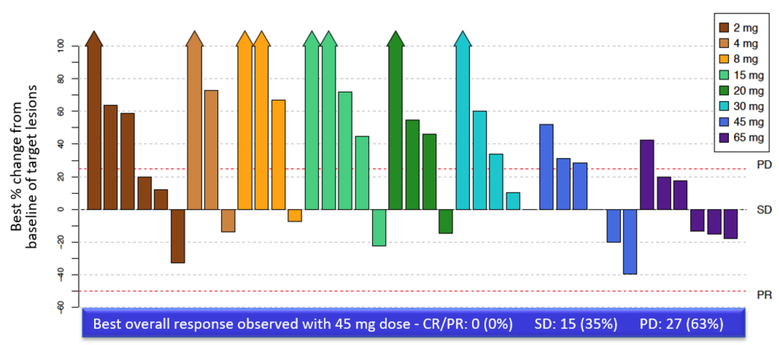
BACKGROUND

- **Glioblastoma multiforme (GBM)** is the most common and aggressive form of primary brain cancer with survival rates of 3-4 months left untreated, and 12-15 months with treatment.
- Standard of care therapy, i.e. debulking surgery + chemoradiation therapy with temozolomide (XRT/TMZ), show a ~65% failure rate[1].
- **GDC-0084** is a potent, oral, selective small molecule inhibitor of class I phosphoinositide 3-kinase and mammalian target of rapamycin (PI3K/mTOR) that crosses the blood brain barrier (BBB)[2,3].
- GDC-0084 has shown efficacy in GBM models driven by activation of the PI3K pathway, which is upregulated in ~85% of GBM cases per the Cancer Genome Atlas[4].
- **Phase I study** (NCT01547546) investigated GDC-0084 given once-daily as an oral (PO) dose in 47 patients with recurrent high-grade gliomas:
  - Maximum tolerated dose (MTD) was 45 mg once daily.
  - GDC-0084 was rapidly absorbed and demonstrated linear- and dose-proportional increases in exposure and 7/8 patients receiving the 45mg dose had drug exposure consistent with anti-tumor activity in pre-clinical models
  - Adverse events (AE) were consistent with established Class I PI3K/mTOR inhibitor class-effects (Table 1).
  - Fluorodeoxyglucose-positron emission tomography (FDG-PET) scans suggested that GDC-0084 crossed the BBB with a uniform distribution throughout the brain.
  - Of the patients who underwent FDG-PET imaging, 7/27 (26%) had metabolic partial response[5].

Table 1. Key adverse events in patients exposed to 45 mg GDC-0084 (n=8).

Preferred Term	Hyperglycemia	Stomatitis/ mucositis	Diarrhea	Nausea/ vomiting	Rash	Fatigue
Grade 3 AE	2 (25%) -	4 (50%) 1 (12%)	1 (12%) -	2 (25%) -	5 (63%)	5 (62%)

Figure 1. Response of patients by dose cohort and exposure to GDC-0084 shows a trend towards stablizing disease at the 45 mg dose.



CR – Complete response; PD - Progressive disease; SD - Stable disease

OBJECTIVES

The **current phase IIa study** (NCT03522298) is investigating the safety, tolerability, recommended phase 2 dose (RP2D), pharmacokinetics (PK) and clinical activity of GDC-0084 in patients with newly diagnosed GBM with unmethylated O^6-methylguanine-methyltransferase (MGMT) promoter status as adjuvant therapy following surgical resection and initial chemoradiation with TMZ.

METHODS

This open-label, multicentre, 2 year study recruiting patients with newly diagnosed GBM from 6-8 sites in the US has 2 stages: Stage 1 (dose escalation) and Stage 2 (expansion cohort) (Figure 2).

Subject eligibility

- Male and female patients ≥ 18 years.
- Histologically confirmed diagnosis of GBM (World Health Organization [WHO] Grade IV astrocytoma) with unmethylated MGMT promoter status.
- Undergone surgical resection of tumor(s) and initial treatment with XRT/TMZ (or XRT only if indicated).

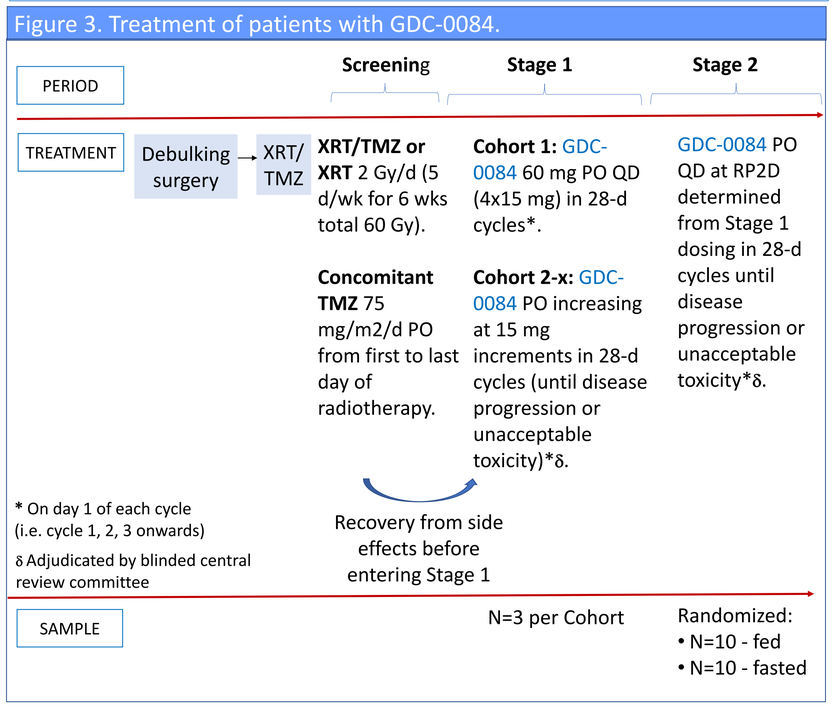
Figure 2. Study design for Stage 1 and Stage 2 of the study protocol.

Stage 1: Dose Escalation	Stage 2: Expansion Cohort
Standard "3+3" design: • to determine the MTD for QD dosing schedule, and safety, tolerability and PK of GCD-0084.	Two-arm, open-label, expansion design to: • characterize safety, tolerability and PK of GDC-0084. • assess single agent activity of GDC-0084. • explore effect of fed vs. fasting state on PK of GDC-0084.
~12 patients (range: 6-24)	~20 patients (2 parallel groups of 10 patients)

Treatment

- Following screening, patients treated with GDC-0084 at doses described in Figure 3 depending on study Stage.
- Patients in Stage 1/2 who discontinue treatment followed every 6 wk until determination of disease progression.
- Subsequent anti-cancer therapy and survival follow-up (FU) collected every 12 wks until death.

Figure 3. Treatment of patients with GDC-0084.



Dose-escalation rules for Stage 1:

- If no patients experience a dose limiting toxicity (DLT; defined *a priori* in protocol) within assessment period (d 1-28), escalation will proceed to the next higher dose in 3 newly-recruited patients.
- If 1 patient experiences DLT, Cohort expanded (max. 6) until a 2nd patient experiences a DLT → MTD 1 dose level below.
- If ≥2 patients experience a DLT at dose level 0 → MTD 45 mg.

KEY STUDY ASSESSMENTS

		CYCLE 1	CYCLE 2	CYCLE 3 onwards				
	SCR (-28 d)	Wk 1 D 1	D 1	Every 4 Wks	Every 8 Wks	Every 8 Wks	EOT/ FU start	Post-EoT FU
KPS	X	X	X	X			X	
MRI		X			X		X	
FDG-PET scan		X						
ECG	X	X	X	X			X	
LVEF	X					X		
aPTT / PT / INR	X	X	X	X			X	
Pregnancy Test	X	X	X	X			X	
PK Sampling		X	X					
Hematol/Chemistry	X	X	X	X			X	
AEs	X	X	X	X			X	X
Disease status								X

SCR: screening; EOT: end of treatment

STUDY ENDPOINTS

Primary safety endpoint: Dose limiting toxicities (DLT).

Key secondary safety endpoints:

- Treatment-emergent adverse events (TEAEs), Grade 3-5 TEAEs, serious adverse events (SAEs), fatal AEs, TEAEs leading to drug discontinuation or study withdrawal.
- Treatment-emergent Grade 3/4 clinical laboratory abnormalities.
- Change/shift in clinical laboratory, vital signs, and electrocardiogram (ECG) parameters.
- Change in corticosteroid use.
- Change in left ventricular ejection fraction (LVEF).
- Change in Karnovsky Performance Status (KPS).

Secondary clinical benefit endpoints:

- Progression free survival (PFS) from first dose (in Stage 1) or randomization (Stage 2) to disease progression (RANO criteria) or death.
- Overall survival (OS) from first dose (in Stage 1) or from randomization (Stage 2) to death.
- Time to progression (TTP) from first dose (Stage 1) or randomization (Stage 2) to disease progression.

Exploratory endpoints will include PK parameters, FDG-PET uptake in tumor and normal brain tissue, and disease control rate.

SUMMARY

Results for this phase IIa study will be available end of 2019.

A future phase IIb study is planned to evaluate clinical activity of GDC-0084 at the RP2D vs TMZ as adjuvant therapy following surgical resection/chemoradiation in 224 patients.

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ACKNOWLEDGEMENTS

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