ASX RELEASE

1 June 2020

KAZIA PRESENTS INTERIM PAXALISIB PHASE II DATA AT ASCO SHOWING POSITIVE OVERALL SURVIVAL SIGNAL

Sydney, 1 June 2020 – Kazia Therapeutics Limited (ASX: KZA; NASDAQ: KZIA), an Australian oncology-focused biotechnology company, is pleased to share a poster presentation of interim data from the ongoing phase II study of paxalisib (formerly GDC-0084) in glioblastoma, the most common and most aggressive form of primary brain cancer. Top-line data from this interim analysis was previously announced to ASX on 7 April 2020.

Key Points

- Analysis of Stage 1 of the study (n=9) shows median overall survival (OS) of 17.7 months. This compares very favourably with temozolomide, the existing standard of care, which has a reported median OS of 12.7 months in this patient population
- Progression-free survival (PFS) in Stage 1 was 8.4 months, which represents a clinically material advantage over the 5.3 months associated with temozolomide
- The longest-treated patient remains on therapy and progression-free some 19 months after diagnosis
- Safety profile is consistent with prior clinical experience. Rash, mucositis, and hyperglycemia are the most common toxicities, and 60mg, once daily, orally, was confirmed as the maximum tolerated dose (MTD)

Professor Patrick Wen from Dana-Farber Cancer Institute, who was the lead author on the poster presentation, commented, “These are encouraging early signals. We anticipate paxalisib will move into a pivotal study later this year and look forward to reviewing further data as it emerges.”

Kazia CEO, Dr James Garner, added, “We are pleased to be able to share these extremely promising data with clinicians and partners, albeit in the novel forum of a virtual academic meeting. As we have previously said, the gold standard for any new cancer drug is the ability to extend life, and we are seeing evidence from this study that paxalisib may achieve this very challenging goal. We expect to begin recruitment to the international GBM AGILE pivotal study in the second half of this year. In the meantime, we expect several further data read-outs over the next two quarters.”

Summary of Paxalisib Data in Comparison to Temozolomide (existing standard of care)

	Temozolomide (FDA-approved treatment)	**Paxalisib** (Stage 1 of Phase II Study)
Progression-Free Survival (PFS) *Measures ability of a drug to slow growth of a tumour*	5.3 months	8.4 months
Overall Survival (OS) *Measures ability of a drug to prolong life*	12.7 months	17.7 months

ASCO Conference

The American Society of Clinical Oncology Annual Meeting is one of the premier scientific conferences in the world for research and treatment of cancer. It is typically attended by more than 30,000 clinicians, researchers, industry executives, and patient advocates. In 2020, the meeting is being conducted in a virtual format due to the ongoing COVID-19 pandemic.

The Kazia data is presented in Abstract 2550 (NCT03522298). In addition to Kazia's paxalisib poster, abstracts are being presented by the Global Coalition for Adaptive Research on the GBM AGILE clinical trial (Abstract TPS2579; NCT03970447), and by the Alliance for Clinical Trials in Oncology on their genomically-guided study in brain metastases (Abstract TPS2573; NCT03994796), in which paxalisib is one of three participating drug candidates.

The Kazia poster is available for download via the Kazia website at https://kaziatherapeutics.com/researchpipeline/publicationspresentations

Background

The reported overall survival (OS) figure of 17.7 months represents a strong signal of clinical efficacy. The existing, FDA-approved standard of care, temozolomide, is associated with an OS of 12.7 months in this patient population[1]. Comparison between different studies is always imprecise, but the magnitude of the numerical difference provides powerful evidence that treatment with paxalisib may extend life in this patient group.

The reported progression-free survival (PFS) figure of 8.4 months compares favourably with the PFS of 5.3 months that is associated with temozolomide in this patient population. In April 2020, Kazia reported an interim analysis showing a PFS of 8.5 months in the overall study population (n=30). This poster only reports the first stage of the study (n=9), and the figure in this part of the study was 8.4 months.

[1] ME Hegi, A-C Desirens, T Gorlia, et al. *N Engl J Med* (2005); 352:997-1003

Before losing patent protection, temozolomide achieved peak sales in excess of US$ 1 billion per annum, which provides an indication of the commercial opportunity associated with a new treatment for glioblastoma.

The Kazia study is being conducted in newly-diagnosed glioblastoma patients, following surgery and radiotherapy. Only those patients with an unmethylated MGMT promotor have been recruited. This genetic marker renders patients effectively resistant to temozolomide and is present in approximately two-thirds of patients.

Thirty patients were enrolled to this study, comprising 9 in Stage 1 , and 21 in Stage 2. Data reported here are provisional figures from Stage 1 (for OS) and from the entire study population (for PFS), but may change as ongoing patients proceed through the study. The study has been conducted at leading centers of excellence in the United States.

The safety of paxalisib remained broadly consistent with prior experience, with hyperglycaemia (raised blood sugar), oral mucositis (mouth ulcers), and low-grade rash among the most common drug-related toxicities.

In addition to this phase II study in glioblastoma, four other studies are underway with paxalisib in different forms of brain cancer, and it is anticipated that several of these will provide initial efficacy data during CY 2020.

Investors are referred to Kazia's announcement of 7 April 2020 for further discussion of these results.

Next Steps

The phase II study remains ongoing, with approximately half of the total enrolled patient population still receiving drug at the time of analysis and a number of additional patients still in follow-up. Kazia expects to complete the study in 1H CY2021.

Kazia had previously had an abstract accepted the AACR Annual Meeting, which had originally been scheduled for April 2020. This meeting has now been rescheduled to several virtual meetings, and Kazia will present a poster at the 'AACR Virtual Annual Meeting II' on 22-24 June 2020.

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 paxalisib (formerly 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 in adults. Licensed from Genentech in late 2016, paxalisib entered a phase II clinical trial in 2018. Interim data was reported in April 2020, and further data is expected in 2H 2020. Paxalisib was granted orphan designation for glioblastoma by the US FDA in February 2018.

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. Interim data was presented at the ESMO Congress in September 2019, and the study remains ongoing. Cantrixil was granted orphan designation for ovarian cancer by the US FDA in April 2015.

This document was authorized for release to the ASX by James Garner, Chief Executive Officer, Managing Director.

CLINICAL TRIAL SUMMARY

Study Title	A Phase 2 Study to Evaluate the Safety, Pharmacokinetics, and Efficacy of the PI3K/mTOR Inhibitor GDC-0084 Administered to Patients With Glioblastoma Multiforme Characterized by Unmethylated O6-methylguanine-methyltransferase Promoter Status Following Surgical Resection and Standard Concomitant Chemoradiation Therapy With Temozolomide
Phase of Development	Phase II
Investigational Product	Paxalisib (GDC-0084)
Disease Area	Newly-diagnosed glioblastoma (GBM) (WHO grade IV glioma)
Registration	NCT03522298
Study Description	This is a two-part study intended to support transition from an advanced recurrent disease population (as investigated in the phase I study) to newly-diagnosed patients (the target population for commercial launch). It is designed in two stages:- **Stage 1** – a dose escalation component to establish a maximum tolerated dose (MTD) and recommended dose for further study in newly-diagnosed patients; groups of patients will be administered increasing doses of GDC-0084 until unacceptable toxicity is encountered **Stage 2** – a dose expansion cohort, in which all patients will be treated at the MTD, and which is designed to elicit confirmatory signals of clinical efficacy
Number of Subjects	**Stage 1** – 9 patients (enrolment complete) **Stage 2** – 21 patients (enrolment complete)
Study Design	This is a single-arm, exploratory study. Stage 1 is designed as a standard '3+3' dose escalation protocol. The first cohort of 3 patients receive 60mg of GDC-0084, once daily in capsule form. If this dose is tolerated for at least 28 days, an additional 3 patients will receive 75mg, and subsequent cohorts may increase at 15mg intervals until unacceptable toxicity occurs. If a dose-limiting toxicity (DLT) is observed in a given cohort, it will be expanded to 6 patients, and if two DLTs are observed at a given dose level then the previous dose will be declared the MTD.

	Stage 2 will enroll all patients at the MTD. Half of the patients will receive paxalisib with food, and half on an empty stomach, in order to assess potential food effects.
Patient Population	All patients had newly-diagnosed glioblastoma, which had been treated with surgery and radiotherapy according to the standard-of-care 'Stupp regimen'. All patients had unmethylated MGMT promotor status, which renders them essentially resistant to temozolomide, the only FDA-approved drug treatment for newly-diagnosed glioblastoma. This group represents approximately two thirds of the total GBM population.
Endpoints	The primary endpoint of Stage 1 was safety and tolerability, since it is a dose escalation study. PFS and OS were included as exploratory efficacy endpoints. The primary endpoints of Stage 2 were PFS and OS.
Participating Centres	**UCLA – Jonsson Comprehensive Cancer Center** Los Angeles, CA **University of Colorado Cancer Center** Denver, CO **Dana-Farber Cancer Institute** Boston, MA **John Theurer Cancer Center** Hackensack, NJ **Stephenson Cancer Center** Oklahoma City, OK **MD Anderson Cancer Center** Houston, TX
Start Date	First Patient In: September 2018
End of Recruitment	Last Patient In: February 2020