ASX RELEASE

15 April 2020

POSITIVE INTERIM DATA FROM PAXALISIB PHASE II STUDY

CONFERENCE CALL RECORDING AND TRANSCRIPT

Sydney, 15 April 2020 – Kazia Therapeutics Limited (ASX: KZA; NASDAQ: KZIA), an Australian oncology-focused biotechnology company, is pleased to provide an audio recording and transcript of the investor conference call on the positive interim data from the paxalisib phase II study in glioblastoma, held by Kazia's Chief Executive Officer, Dr James Garner on Thursday, 9 April 2020.

The recording and transcript are available on the Kazia Therapeutics website via the following link: https://www.kaziatherapeutics.com/investorcentre/corporatepresentations

[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 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

Q&A

What is the significance of the data reported here? How should these results be interpreted?

Kazia has previously referred to the published paper by Hegi et al. on temozolomide, which reports a median PFS of 5.3 months and a median OS of 12.7 months[1]. This paper remains the definitive reference point for this patient population when treated with temozolomide, the existing standard of care. In effect, it shows that patients receiving standard treatment will typically progress in about 5.3 months and will pass away in little over a year.

The current phase II study of paxalisib has reported a PFS of 8.5 months and an OS of 17.7 months. Comparisons between studies are always confounded by differences in patient population, study design, calculation methodology, and other variables. However, the magnitude of these differences strongly suggests that paxalisib is offering superior benefit to patients. Were this difference in OS to be replicated in a randomized, controlled trial, the magnitude of improvement would represent approximately a 40% increase in life expectancy. As previously noted, the precise quantification of this benefit will be the focus of the planned GBM AGILE study.

OS has long been considered the 'gold standard' measure of effectiveness for a new cancer drug[2], although a number of novel therapies have been approved in recent years without demonstrating an OS benefit. The implication that paxalisib may be able to achieve this objective provides a powerful endorsement to its further development.

Are the results statistically significant?

'Statistical significance' is a mathematical term that refers specifically to a comparison between different arms in a single study. In common with most oncology studies at this stage of development, this study is only a single-arm study and so it is not possible to formally assess statistical significance.

Is it possible that this study could provide a basis for product approval without conducting a further pivotal study?

While these data are highly encouraging, Kazia expects that confirmation from a larger number of patients in a randomized, controlled trial will be required to secure product approval from FDA and other regulatory agencies.

In December 2019, Kazia announced that it had begun setup work to bring paxalisib into GBM AGILE, an ongoing platform study designed to provide data for registration of new drugs in glioblastoma. Our plan is to use GBM AGILE as a path-to-market for paxalisib, and recruitment is expected to commence in 2H CY2020.

---

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

[2] US Food and Drug Administration. *Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics – Guidance for Industry* (December 2018)

How would a survival benefit of this magnitude compare to other cancer drugs, and would it be sufficient to engage the support of clinicians and payors?

Each disease is specific, and so it is difficult to compare the potential efficacy of paxalisib with other drugs in other disease areas. Nevertheless, Kazia takes the view that, if paxalisib continued to demonstrate in a pivotal study an OS improvement of approximately this magnitude, both in proportional and absolute terms, it would provide the basis of a highly competitive commercial product.

For reference, the OS benefit associated with a number of FDA-approved and commercially successful cancer treatments are indicated below:-

Drug	Indication	OS Improvement
Avastin (bevacizumab)	Metastatic colorectal cancer	15.6 → 20.3 months
Avastin (bevacizumab)	Recurrent glioblastoma	(no improvement)
Abraxane (paclitaxel)	Pancreatic cancer	6.7 → 8.5 months
Nexavar (sorafenib)	Liver cancer	7.9 → 10.7 months
Stivarga (regorafenib)	Metastatic colorectal cancer	5.0 → 6.4 months

(all figures taken from product Prescribing Information)

How robust is the comparison to data from previous clinical studies?

Ideally, the gold standard for definitive determination of efficacy is a randomised, controlled trial (RCT), in which patients are randomly allocated to receive either the treatment under investigation (in this case, paxalisib), or a comparator of some kind (either placebo or an existing treatment). The investigational treatment is then compared with exactly matched patients in the same clinical trial.

However, in common with the majority of cancer studies at this stage of development, the present study only contains a single arm and all patients receive paxalisib. The reasons for this approach are various, and include both ethical and operational considerations. A recent published analysis determined that more than 60% of oncology studies are single-arm rather than RCT[3]. Moreover, a separate analysis demonstrated that success in a single-arm phase II study was strongly predictive of subsequent success in a phase III study, and that an RCT phase II study was not superior to a single-arm design[4].

As such, the emerging data must necessarily be compared to results from previous studies to assess treatment effect, and this reliance on 'historical controls' is also standard practice in the development of new cancer drugs. Such comparisons are of course imperfect: there are often differences in the way that studies have been run, the statistical calculation of endpoints, and the composition patient population.

[3] BR Hirsch et al. *JAMA Intern Med*. (2013);173(11):972-979
[4] JG Monzon et al. *Eur J Cancer*. (2015);51(17):2501-2507

Nevertheless, the natural history of glioblastoma is generally well-understood, and there have not been significant improvements in the prognosis of the disease since the Hegi paper was published. In this context, Kazia considers the emerging data from this study to be a positive signal.

What is the difference between progression-free survival (PFS) and overall survival (OS)?

For a given patient, progression-free survival (PFS) describes the time until either progression of the disease (recurrence or growth of the tumour) or death, whichever is first. Overall survival (OS) describes the time until death from any cause.

In clinical trials of experimental cancer drugs, median PFS and median OS are commonly used as endpoints. The median PFS is the time point at which 50% of patients have progressed or died. For example, a median PFS of 5.4 months means that half of the patients will progress in less than 5.4 months and half will last longer. The median is used in preference to the more common mean because it reduces the impact of outliers. Similarly, the median OS is the time point at which 50% of patients have passed away.

These are interim data. Is it expected that the headline figures (PFS of 8.5 months and OS of 17.7 months) may change substantially in subsequent read-outs?

As additional patients complete their participation, it is possible that these data points will change, either for the better or otherwise. The PFS data matures more quickly than the OS data, since patients typically progress before passing away, and so this data point may be considered more stable. The fact that inclusion of additional patients in the PFS analysis does not materially change the figure may be interpreted as validating.

Why was one of the patients withdrawn from the study, and what is the impact on the results?

One patient was poorly compliant with study procedures and a decision was made by the Principal Investigator to withdraw that patient from the study. Since the patient's exposure to paxalisib was confined to a matter of days, and given that any data associated with this patient was considered questionable, they have been excluded entirely from this analysis.

Kazia has conducted sensitivity analyses to explore the impact of including all available data from this patient versus removing them from the analysis, and the impact on PFS and OS is negligible.

How does this study compare to the phase I study performed by Genentech?

Prior to Kazia's licensing of the GDC-0084 asset, Genentech completed a phase I dose escalation study (NCT01547546). There are important differences between this study and the phase I study:-

- The phase I included patients with both grade III and grade IV glioma. Glioblastoma is essentially equivalent to grade IV glioma. This study has only enrolled patients with glioblastoma (grade IV glioma).

- The phase I patients were very advanced and had failed on average three prior lines of therapy, making them an extremely treatment-resistant group. The present study has enrolled newly-diagnosed patients who are expected to respond better to treatment.
- The phase I study included patients with both methylated and unmethylated MGMT promotor status. The unmethylated MGMT promotor is associated with a worse prognosis. This study has only enrolled patients with unmethylated MGMT promotor status.
- The phase I study did not report PFS or OS.

What are the next steps for the paxalisib program, and what does this data mean for GBM AGILE, the planned pivotal study?

This phase II study remains ongoing. At present, Kazia expects to report further interim data in 2H CY2020, and final data in 1H CY2021.

In the meantime, as previously indicated, Kazia has begin preparatory work associated with the addition of paxalisib to the ongoing GBM AGILE study in glioblastoma. GBM AGILE is a platform study that is being run independently of any one company, under the leadership of many of the leading world experts in the field. It is designed to provide data to support registration of new drugs in glioblastoma and is strongly supported by the US FDA. It is expected that GBM AGILE will recruit up to 200 patients on paxalisib, in a randomized, controlled trial against temozolomide, the existing standard of care. The patient population will be highly consistent with that examined in this phase II study, and the primary endpoint will be overall survival.

For clarity, GBM AGILE has been adopted in place of a previously-planned company-sponsored phase III study, and it is expected that it will provide the path-to-market for the commercial product.

Investors are referred to Kazia's announcement in December 2019 and its investor newsletter in March 2020 for additional information. At present, Kazia expects that GBM AGILE will begin recruiting paxalisib patients in 2H CY2020, prior to finalization of the ongoing phase II study.

How is progress on the other paxalisib clinical trials?

In addition to this clinical trial, four other studies with paxalisib are underway in DIPG and in brain metastases. All of these studies have recruited patients. Kazia is working with investigators in the hope of providing interim data from several of these studies during CY2020 and will update investors accordingly in due course.

What are Kazia's plans for publication of final data from this study?

Kazia expects that final data from this phase II study will be published in a peer-reviewed journal in CY2021, after completion of all analyses.

In the meantime, the phase I study originally conducted by Genentech has been accepted for publication by the journal *Clinical Cancer Research*, and publication is expected soon. In

addition, the post hoc analysis of imaging data from that study by Professor Ben Ellingson at UCLA has separately been accepted for publication in the same journal. Professor Ellingson's work was previously the subject of a prize-winning oral presentation at the Society for Neuro-Oncology annual meeting in November 2019, as announced at the time by Kazia.

What is the competitive landscape for glioblastoma? How do these results compare to other drugs in development for the disease?

Kazia is not presently aware of any investigational new drug in the global pipeline which is (a) in active development for single-agent adjuvant use in newly-diagnosed glioblastoma patients, (b) further advanced than paxalisib, and (c) which shows superior evidence of activity on currently available data.

What is the level of partnering interest for paxalisib? Is Kazia in discussion with pharma partners?

Kazia continues to entertain exploratory discussion with several potential partners for the paxalisib asset. The timing and terms of any future transaction will be designed to ensure the most expeditious development of the drug, and the optimal return to Kazia shareholders.

Does Kazia expect this or other studies to be affected by the ongoing COVID-19 outbreak?

Kazia works with large, world-class, highly-experienced partners in the conduct of its studies, and each of these collaborators have put in place measures to mitigate the impact of COVID-19. At this stage, we see minor operational disruption, but no suggestion that the timelines or data integrity of our clinical studies are likely to be fundamentally affected. We will continue to keep investors informed as the situation develops.