ASX RELEASE

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KAZIA EXECUTES AGREEEMENT TO COMMENCE GBM AGILE PIVOTAL STUDY

Sydney, 16 October 2020 – Kazia Therapeutics Limited (ASX: KZA; NASDAQ: KZIA), an Australian oncology-focused biotechnology company, is pleased to announce that it has executed a definitive agreement with the Global Coalition for Adaptive Research (GCAR) to commence Kazia's participation in the GBM AGILE pivotal study in glioblastoma. The study will open a new arm with Kazia's investigational new drug, paxalisib (formerly GDC-0084), and will now move into an operational phase with recruitment of patients to the paxalisib arm expected to begin in Q1 CY2021.

Key Points

- GBM AGILE (NCT03970447) is intended to serve as the pivotal study for registration of paxalisib in key markets
- Dr Ingo Mellinghoff (Memorial Sloan Kettering Cancer Center) and Dr Eudocia Q Lee (Dana-Farber Cancer Institute) have been named as Principal Investigators for the paxalisib arm; Dr Timothy Cloughesy (UCLA) is the Principal Investigator for the overall study
- Kazia will pay an initial fee of US$ 5 million to GCAR, with further milestone payments payable throughout the course of the study
- The duration of paxalisib's enrollment period in GBM AGILE is expected to total approximately 30 – 36 months, plus follow-up, but will depend on emerging study data, recruitment rates, and other variables

Kazia CEO, Dr James Garner, commented, "we have spent the last nine months or so working closely with the GCAR team to plan paxalisib's entry into GBM AGILE, and we are very gratified to now be moving into the operational phase of the study. GBM AGILE is truly a ground-breaking clinical trial, driven by some of the world's leading experts in the field, and we are proud to be a part of it. We expect GBM AGILE to provide definitive clinical evidence for the approval of paxalisib by regulatory agencies in key markets. This is a faster, more cost effective, and higher quality study than any company of our size could mount independently, and we are confident that it will provide the best possible opportunity for paxalisib to demonstrate its potential in this very challenging disease."

Dr Meredith Buxton, Chief Executive Officer at GCAR added, "We are pleased to welcome paxalisib into GBM AGILE. Our mission is to help drive the development of new therapies for glioblastoma, by creating an efficient model for testing and confirming new potentially beneficial treatments for

patients with GBM. We look forward to continuing to work closely with the Kazia team to bring paxalisib into the study and support its evaluation."

Principal Investigators

Dr Ingo Mellinghoff and Dr Eudocia Q Lee will serve as Principal Investigators for the paxalisib arm. Dr Timothy Cloughesy is the Principal Investigator for the overall study.

Dr Mellinghoff is the Chair of the Department of Neurology at Memorial Sloan Kettering Cancer Center in New York, NY. He is a highly experienced neuro-oncologist with an extensive track record of published research in brain tumours, and is a Professor at the Gerstner Sloan Kettering Graduate School of Biomedical Sciences and the Graduate School of Medical Sciences at Weill Cornell University. His laboratory focuses on the study of biochemical pathways that regulate the growth of brain cancer, and he has participated in numerous clinical trials for glioblastoma and other forms of brain cancer.

Dr Mellinghoff commented, "we have seen little progress in the treatment of glioblastoma for over two decades, and the need for new therapies is urgent. We have seen encouraging signals from the paxalisib program thus far, and my colleagues and I look forward to exploring its potential in the GBM AGILE pivotal study."

Dr Lee is a neuro-oncologist at Dana-Farber Cancer Institute in Boston, MA, Director of Clinical Research at the Center for Neuro-Oncology at Dana-Farber, and an Assistant Professor of neurology at Harvard Medical School. She is a widely published clinical researcher, with a primary research interest in tumours of the brain and spinal cord, and their neurologic complications. Dr Lee has been an investigator in previous clinical trials of paxalisib in glioblastoma and has first-hand clinical experience with the drug.

Dr Lee added, "GBM AGILE has been designed to provide a definitive assessment of the efficacy of new drugs for glioblastoma. Paxalisib has already been evaluated in two clinical trials in this disease, and GBM AGILE will now greatly enrich our understanding of how best to use it for the benefit of patients."

GBM AGILE

GBM AGILE (Glioblastoma Adaptive Global Innovative Learning Environment) is an international platform study that has been established specifically to facilitate the approval of new medicines for glioblastoma.

The scientific leadership of GBM AGILE comprises many of the leading experts in glioblastoma, and they have worked in collaboration with the US FDA on its development. It is sponsored by the Global Coalition for Adaptive Research (GCAR), a US-based 501(c)(3) non-profit organisation. At present, the study is underway in 30 sites in the United States and Canada, with plans to launch in Europe and China during CY2021. One drug candidate is currently participating, and paxalisib will be the second candidate to join the study.

GBM AGILE is an adaptive study, so the number of patients recruited, and their allocation within the study, will be continuously adjusted in the light of emerging results. It is expected that between 50 and 200 patients will receive paxalisib, depending on the safety and efficacy of the drug. The data

from these patients will be compared against data from an estimated several hundred patients in a shared control arm, allowing for considerable operational efficiency.

The paxalisib arm of GBM AGILE will recruit newly diagnosed patients with unmethylated MGMT promotor status, which is the same population that has been investigated in Kazia's ongoing phase II study. In addition, GBM AGILE will recruit recurrent patients to the paxalisib arm. The drug may ultimately be considered efficacious in either or both of these patient groups, and Kazia will frame any future application for regulatory approval on the basis of this data.

Dr Mellinghoff added, "we see interesting signals of activity in the phase I study of paxalisib in recurrent glioma patients, and so my colleagues and I consider it important to evaluate the drug also in this later-stage group, where the unmet medical need is very substantial. Including both newly diagnosed and recurrent patients in GBM AGILE enables us to observe how paxalisib performs across the spectrum of the disease, and provides us with a significant amount of additional data as we move towards registration."

The primary endpoint of GBM AGILE is overall survival (OS), which is considered the gold standard endpoint for the assessment of new cancer therapies.

Indicative Costs and Timelines

Kazia will initially pay a fee of US$ 5 million to GCAR in consideration for paxalisib joining GBM AGILE. Additional payments will be due throughout the duration of the study, dependent on the attainment of key milestones. The full financial terms of the agreement between Kazia and GCAR are considered commercially confidential. In addition, the total cost of the study will depend on the number of patients ultimately recruited and other operational variables.

Kazia and GCAR expect that necessary regulatory filings and submissions to institutional review boards will be actioned during 4Q CY2020. First patient in to the paxalisib arm is currently anticipated to occur early in CY2021.

The duration of paxalisib's participation in GBM AGILE is unpredictable due to the adaptive nature of the study. As an indicative base case estimate, Kazia expects at this stage that paxalisib will enrol patients for between 30 – 36 months, plus follow-up. However, this figure could change, either in an upward or downward direction, depending on emerging data from the study as well as operational matters such as recruitment rates.

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, 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 most recently at AACR in June 2020, and further data is expected in 2H 2020. Five additional studies are in start-up or ongoing in other forms of brain cancer. 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.

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 has completed a phase I clinical trial in Australia and the United States with the final data expected in the second half of calendar 2020. Interim data was presented most recently at the AACR conference in June 2020. Cantrixil was granted orphan designation for ovarian cancer by the US FDA in April 2015.

For more information, please visit www.kaziatherapeutics.com.

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

CLINICAL TRIAL SUMMARY

Study Title	A Trial to Evaluate Multiple Regimens in Newly Diagnosed and Recurrent Glioblastoma (GBM AGILE)
Phase of Development	Phase II / III
Investigational Product	Paxalisib (GDC-0084), among other agents
Disease Area	Newly diagnosed glioblastoma (GBM) (WHO grade IV glioma) Recurrent glioblastoma
Registration	NCT03970447
Study Description	GBM AGILE is an international, seamless Phase II / III response adaptive randomization platform trial designed to evaluate multiple therapies in newly diagnosed (ND) and recurrent GBM.
Number of Subjects	**Stage 1** – up to 150 patients (adaptive randomization) **Stage 2** – 50 patients (fixed randomization)
Study Design	This is an open-label, randomized controlled trial. The study is composed of two stages, which will run sequentially, with seamless transition from Stage 1 to Stage 2. **Stage 1** – a phase II 'screening stage' will evaluate paxalisib within newly-diagnosed unmethylated and recurrent patient populations, compared against a common control for each group. Stage 1 will stop recruiting patients if it reaches its maximal sample size, drops for futility, or evinces inadequate safety. If paxalisib reaches an efficacy threshold for graduation from Stage 1, it will seamlessly move into Stage 2 within either or both patient groups. **Stage 2** – a phase III 'confirmation stage', with fixed randomization. The primary analysis of paxalisib's efficacy uses all patients in both stages and all control patients in the trial in the graduating patient population, suitably adjusted for any possible time trends.
Patient Population	GBM AGILE recruits patients in three groups:- **Newly Diagnosed Unmethylated** **Newly Diagnosed Methylated**

	Recurrent The paxalisib arm will recruit patients from the newly diagnosed unmethylated and recurrent groups. The balance of patients between these two groups will depend on emerging data as the study progresses, but the total number of patients assigned to paxalisib will not exceed 200. Paxalisib may ultimately 'graduate' from GBM AGILE with a positive result in zero, one, or two of the patient groups.
Endpoints	The primary endpoint of the study is overall survival (OS)
Participating Centres	GBM AGILE is currently underway in 30 sites across the United States and Canada. It is expected that the study will open sites in the European Union and China in CY2021.
Start Date	First Patient In (paxalisib arm): Q1 CY2021
End of Recruitment	Last Patient In (anticipated): Q4 CY2022

Q&A

In addition to GBM AGILE, will Kazia also conduct its own registration study for paxalisib?

No. It is expected that GBM AGILE will serve as a single pivotal study for registration purposes.

FDA Guidelines stipulate a general need for two adequate, well-controlled clinical trials to register a new pharmaceutical product. How confident is Kazia that GBM AGILE, as a single trial, will be sufficient?

Although FDA Guidelines describe a general requirement for two clinical trials, it is common for oncology drugs to achieve registration after a single trial. Section 115(a) of the FDA Modernization Act provides for FDA to accept a single clinical trial under certain circumstances.

Although GBM AGILE is a single, seamless trial from an operational standpoint, and although the efficacy analysis is performed on the aggregate patient sample, the fact that it is statistically divided into two stages, notionally comprising a phase II and a phase III stage, means that it reduces type I error to a level consistent with two conventional pivotal studies.

What does it mean to say that GBM AGILE is an 'adaptive' study?

Conventional clinical trials define a target number of patients at the outset, based on certain assumptions around treatment effect, drop-out rate, etc. Often, the number of patients ends up greater or less than was actually required, leading to inefficiency and, on occasion, the failure of potentially efficacious drugs.

An adaptive study is one that dynamically adjusts the number of patients in the study according to emerging data, so that only the number necessary to answer the question are recruited. This is considered a more efficient approach to drug development, and one that has received considerable interest and support from clinicians, industry, and regulatory agencies.

What is a 'platform' study?

A platform study or master protocol study is one that allows for testing of more than one investigational drug, and will typically open and close different arms over time as different drugs enter and leave the study. It provides considerable operational efficiency, particularly in less common diseases such as glioblastoma. Paxalisib is already participating in a similar trial – the Alliance study in brain metastases (NCT03994796), which currently includes three experimental arms.

How does GBM AGILE differ from Kazia's phase II study of paxalisib in glioblastoma?

Some of the key differences between the two studies can be summarized as follows:-

	Kazia Phase II	GBM AGILE
Study Design	• Single-arm trial	• Randomised, controlled trial
Patient Population	• Newly diagnosed unmethylated	• Newly diagnosed unmethylated • Recurrent
Primary Endpoint	• Safety and tolerability	• Overall survival
Number of Patients	• 30	• Up to 200 on paxalisib
Geography	• United States	• United States • Canada • European Union • China

How did Kazia become aware of GBM AGILE, and what has been the process to get to this point?

A number of clinicians who are currently participating in Kazia's phase II study of paxalisib in glioblastoma have leadership roles in GBM AGILE. They have recommended inclusion of paxalisib and have facilitated the necessary introductions and relationships. In late CY2019, Kazia presented paxalisib data to GCAR's Arm Selection Committee and was invited to join the study shortly thereafter.

How confident is Kazia that data from GBM AGILE will be acceptable to regulatory agencies for product registration?

GCAR has consulted extensively with FDA and with other national regulatory agencies. FDA has indicated that it expects data from GBM AGILE to be suitable for product registration, should efficacy be demonstrated, and assuming that other matters such as manufacturing and preclinical toxicology are of appropriate standard.

Paxalisib will be the second drug to join GBM AGILE. Does this mean that only one drug can be successful, and that paxalisib will have to show superiority to other agents?

No. The study is designed to compare participating drug candidates against a common control arm, but not to make drug-versus-drug comparisons. It is possible that several successful drug candidates will eventually emerge from the GBM AGILE study, and this could only be of benefit to patients.

For comparative purposes, a total of approximately twenty new drugs have been approved in lung cancer over the past decade. Kazia hopes and expects that a number of new drugs will become available for patients with glioblastoma over the next few years, and the company intends to do everything possible to ensure that paxalisib is one of them.

Academic-led studies can sometimes be operationally challenging. How confident is Kazia in GCAR's ability to execute this complex study?

Kazia has conducted extensive discussions with the GCAR team and believes that it brings world-class professionalism to the study. GCAR has engaged IQVIA, one of the world's leading

contract research organisations, to execute the study, and has selected top tier sites to participate. GCAR is profoundly motivated by the desire to accelerate availability of new treatment options for patients with glioblastoma, a commitment which Kazia wholly shares.

How much will GBM AGILE cost?

Kazia will fund the participation of paxalisib in GBM AGILE through a commercial agreement with GCAR. However, the adaptive design, and the economies released by shared infrastructure and a common control arm, mean that the cost of participation will be very substantially lower than the cost of a comparable standalone, company-run study. The commercial terms remain confidential.

The agreement between Kazia and GCAR does not create any royalty obligations or other post-trial financial commitments in relation to the commercialization of paxalisib.

What does GBM AGILE mean for partnering?

Kazia continues to believe that paxalisib is a highly attractive asset to pharma partners, and continues to engage actively with a number of companies.

Kazia believes that the best way to realise commercial value for shareholders is to keep all options open, and so the company is proceeding with GBM AGILE as a path-to-market, in parallel with its partnering activities. Should a partnering transaction occur, it is entirely feasible that Kazia's involvement with GBM AGILE could be transitioned in whole or in part to another company at any point during the study.