ASX RELEASE
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GBM AGILE PIVOTAL STUDY COMMENCES RECRUITMENT TO PAXALISIB ARM

Sydney, 7 January 2021 – Kazia Therapeutics Limited (ASX: KZA; NASDAQ: KZIA), an Australian oncology-focused biotechnology company, is pleased to announce that the GBM AGILE pivotal study (NCT03970447) has commenced recruitment to the paxalisib arm.

Key Points

- GBM AGILE is an international adaptive, multi-drug study, designed to expedite the development of new therapies for glioblastoma
- Kazia executed a definitive agreement with the Global Coalition for Adaptive Research (GCAR) in October 2020 to bring paxalisib into GBM AGILE
- Lead investigators for the paxalisib arm are Professor Ingo Mellinghoff (Memorial Sloan Kettering Cancer Center) and Dr Eudocia Q Lee (Dana-Farber Cancer Institute)
- Positive data from GBM AGILE is expected to support registration of paxalisib in the US and other key markets

Kazia CEO, Dr James Garner, commented, "we are delighted to have recruitment underway, and this marks an important milestone for Kazia as we begin the new year. The GBM AGILE study has secured the support of leading clinicians in the glioblastoma field, and has increasingly won the confidence of regulators and industry participants, so we are excited to be a part of it. If the data from GBM AGILE is positive, we expect it to provide a basis for registration in glioblastoma, and it therefore represents an important step towards commercialisation of the drug.

Clinical Trial Design

The paxalisib arm of GBM AGILE will recruit newly diagnosed patients with the unmethylated MGMT promotor, a genetic marker that denotes near-total resistance to temozolomide, the existing FDA-approved standard of care. In addition, the study will recruit recurrent patients who have progressed despite treatment with temozolomide. The adaptive design allows GBM AGILE to balance between these two patient groups according to emerging data, so it is possible for paxalisib to emerge successful in one or both populations. The primary endpoint of GBM AGILE is overall survival, which is considered the gold standard for the evaluation of new cancer therapies, and which is the preferred approval endpoint for regulators such as the US FDA.

The study will recruit up to 200 patients on paxalisib in total, and these will be compared against a roughly similar number of patients in a control group, with patients being randomly allocated between the groups. The total data set for paxalisib will therefore include up to approximately 450 patients from GBM AGILE. The duration of paxalisib's enrolment is initially estimated to be approximately 30-36 months. However, the adaptive design of GBM AGILE means that if a definitive conclusion is evident at an earlier stage, the study will conclude at that point, with a commensurate reduction in timelines and cost.

Further information was provided in Kazia's announcement to the ASX on 16 October 2020.

Operational Update on GBM AGILE

GBM AGILE commenced operation in July 2019. The first drug to join the study was regorafenib (Bayer), which is an approved therapy for other solid tumours. Kazia Therapeutics' paxalisib and Kintara Therapeutics' VAL-083 commenced recruitment in January 2021.

At present, GBM AGILE is operational in over 30 centres across the United States and has screened over 370 patients to date. The study is expected to open sites in Canada, Europe, and China during CY2021.

The first site to open to the paxalisib arm is the Henry Ford Cancer Institute in Detroit, MI, under the oversight of Dr Tom Mikkelsen. It is expected that other sites will rapidly open to the paxalisib arm as they receive approval from their Institutional Review Boards.

Paxalisib Clinical Program

GBM AGILE is one of eight ongoing clinical trials of paxalisib in brain cancer.

Indication	Phase	Sponsor	Registration
Glioblastoma	II	Kazia Therapeutics	NCT03522298
Glioblastoma	II / III	Global Coalition for Adaptive Research	NCT03970447
DIPG & DMGs	I	St Jude Children's Research Hospital	NCT03696355
DIPG & DMGs	N/A	Pacific Pediatric Neuro-Oncology Consortium	(TBD)
Breast Cancer Brain Metastases	II	Dana-Farber Cancer Institute	NCT03765983
Brain Metastases	II	Alliance for Clinical Trials in Oncology	NCT03994796
Brain Metastases	I	Memorial Sloan-Kettering Cancer Center	NCT04192981
Primary CNS Lymphoma	II	Dana-Farber Cancer Institute	(TBD)

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 GBM AGILE, a pivotal study in glioblastoma, in October 2020. Seven additional studies are active in various 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. 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) (Kazia Therapeutics) Regorafenib (Bayer) VAL-083 (Kintara Therapeutics)
Disease Area	Newly diagnosed glioblastoma (GBM) (WHO grade IV glioma) Recurrent glioblastoma
Registration	NCT03970447
Principal Investigator	Professor Timothy Cloughesy (global study PI) *University of California, Los Angeles* Professor Ingo Mellinghoff (paxalisib arm co-PI) *Memorial Sloan Kettering Cancer Center, New York* Assistant Professor Eudocia Q Lee (paxalisib arm co-PI) *Dana Farber Cancer Institute, Boston*
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 in which it participates (newly-diagnosed unmethylated and recurrent). **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 more than 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