ASX RELEASE

7 June 2021

STUDY OF PAXALISIB IN PRIMARY CNS LYMPHOMA AT DANA-FARBER CANCER INSTITUTE ENROLS FIRST PATIENT

Sydney, 7 June 2021 – Kazia Therapeutics Limited (NASDAQ: KZIA; ASX: KZA), an oncology-focused drug development company, is pleased to announce that a phase II study of Kazia's investigational new drug, paxalisib, in primary CNS lymphoma has been initiated at Dana-Farber Cancer Institute, with the first patient successfully enrolled to the study.

Key Points

- Lymphoma is a cancer of white blood cells. It occurs in the lymphatic system and can spread almost anywhere in the body; primary CNS lymphoma (PCNSL) occurs exclusively in the brain and central nervous system
- The PI3K inhibitor class, to which paxalisib belongs, is well validated in lymphoma outside the brain; three of the four FDA-approved PI3K inhibitors are treatments for forms of lymphoma, but they are assumed ineffective for PCNSL since they cannot cross the blood-brain barrier
- DFCI study (NCT04906096) is an open-label phase II clinical trial of paxalisib in PCNSL, and is expected to recruit up to 25 patients, taking up to 2 years to complete
- Kazia will provide support including study drug and a financial grant

Dana-Farber Cancer Institute (DFCI) is a world-leading cancer treatment and research centre, based in Boston, Massachusetts. It is a principal teaching affiliate of Harvard Medical School and has been designated a Comprehensive Cancer Center by the US National Cancer Institute. DFCI participates in as many as 600 clinical trials at any given time and has been an important contributor to the development of many important new cancer therapies.

The Principal Investigator for the study, Dr Lakshmi Nayak, commented "our center has a strong research focus in primary CNS lymphoma. We are very interested to explore the potential for a brain-penetrant PI3K inhibitor in this disease. Patient outcomes in PCNSL remain far from optimal, and there is a pressing need for new treatment options."

Kazia CEO, Dr James Garner, commented, "we are delighted to see this study underway, and congratulate Dr Nayak and her team on getting it launched. With paxalisib now in an international pivotal study for glioblastoma, we are increasingly focused on identifying other

groups of patients who may benefit from the drug. There is a very sound rationale to explore PCNSL in this disease, and we are looking forward to seeing the study progress."

Primary CNS Lymphoma

Lymphoma is a haematological malignancy (blood cancer) that originates from lymphocytes, a type of white blood cell involved in the immune system. PCNSL is a specific form of the disease that originates in the brain and central nervous system.

Three of the four PI3K inhibitors approved by the US Food and Drug Administration (FDA) are treatments for various forms of lymphoma, provide a strong validation for PI3K as a target in this disease. Paxalisib is the only PI3K inhibitor in mainstream development with the ability to penetrate the blood-brain barrier, and as such has a unique rationale for development in PCNSL.

The incidence of PCNSL has been increasing with time. Patients are typically in their 60s or older, and the disease is slightly more common in men.[1] The mainstays of treatment comprise chemotherapy and radiotherapy, but recurrence is common and only approximately 30% of patients remain alive five years after diagnosis.[2] Many of the drugs used to treat lymphoma elsewhere in the body are ineffective in PCNSL due to their inability to cross the blood-brain barrier.

DFCI Clinical Trial

The CNS Lymphoma Center (CNSLC) at Dana-Farber / Brigham and Women's Cancer Center is the first centre of its kind in the world dedicated to providing comprehensive care and research for patients with primary or secondary CNS lymphoma. With the most advanced treatment options available — including surgery, chemotherapy, stem cell transplant, radiation therapy, immunotherapy, and targeted therapies, and with extensive clinical trial options — CNSLC is uniquely qualified to treat patients with CNS lymphoma and advance the outcome of patients with these tumors.

The principal investigator for the study is Dr Lakshmi Nayak, Director of the CNS Lymphoma Center at Dana-Farber Cancer Institute. Dr Nayak is an Assistant Professor of Neurology at Harvard Medical School and a board-certified neuro-oncologist. Her research interests focus on metastatic brain cancer, glioblastoma, and PCNSL, and she is extensively published in the field of brain cancer. She has been an investigator for multiple clinical trials of experimental drugs in this disease area.

Paxalisib Clinical Program

The initiation of this trial in PCNSL brings the number of ongoing clinical studies of paxalisib in brain cancer to eight.

---

[1] J Rubenstein et al. (2008) *Leuk Lymphoma* 49(0 1):43-51

[2] MS Shiels et al. (2016) *Br J Haematol*. 174(3):417-424

Sponsor	Phase	Indication	Registration
Kazia Therapeutics	II	Glioblastoma	NCT03522298
Global Coalition for Adaptive Research	II / III	Glioblastoma	NCT03970447
Alliance for Clinical Trials in Oncology	II	Brain metastases	NCT03994796
Dana-Farber Cancer Institute	II	Breast cancer brain metastases (*with Herceptin*)	NCT03765983
Dana-Farber Cancer Institute	II	Primary CNS lymphoma	NCT04906096
Pacific Pediatric Neuro-Oncology Consortium	N/A	DIPG & DMGs	TBD
St Jude Children's Research Hospital	I	DIPG (childhood brain cancer)	NCT03696355
Memorial Sloan Kettering Cancer Center	I	Brain metastases (*with radiotherapy*)	NCT04192981

About Kazia Therapeutics Limited

Kazia Therapeutics Limited (NASDAQ: KZIA; ASX: KZA) is an oncology-focused drug development company, based in Sydney, Australia.

Our lead program is paxalisib, a brain-penetrant 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 commenced recruitment to GBM AGILE, a pivotal study in glioblastoma, in January 2021. 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.

Kazia is also developing EVT801, a small-molecule inhibitor of VEGFR3, which was licensed from Evotec SE in April 2021. Preclinical data has shown EVT801 to be active against a broad range of tumour types and has provided compelling evidence of synergy with immuno-oncology agents. A phase I study is expected to begin in CY2021.

For more information, please visit www.kaziatherapeutics.com or follow us on Twitter @KaziaTx.

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

CLINICAL TRIAL SUMMARY

Study Title	Paxalisib (GDC-0084) In Recurrent or Refractory PCNSL
Phase of Development	Phase II
Investigational Product	Paxalisib (GDC-0084)
Disease Area	Recurrent or refractory primary central nervous system lymphoma (PCNSL)
Registration	NCT04906096
Principal Investigator	Associate Professor Lakshmi Nayak *Dana-Farber Cancer Institute, Boston, MA*
Study Description	This is an open-label, phase II study to determine the efficacy of paxalisib (GDC-0084) in patients with recurrent or refractory primary central nervous system lymphoma (R/R PCNSL).
Number of Subjects	25 patients
Study Design	This is an open-label, single-arm study. Eligible patients with R/R PCNSL will be administered paxalisib as monotherapy for up to 24 months, in dosing regimen similar to that used for other adult brain cancers. Results will evaluated against historical controls appropriate to the enrolled patient population.
Patient Population	Relapsed / refractory primary CNS lymphoma (R/R PCNSL)
Endpoints	The primary endpoint of the study is overall response rate (ORR), which measures the growth or shrinkage of tumour on a brain scan during and after treatment.
Participating Centres	Dana-Farber Cancer Institute – Boston, MA Brigham & Women's Hospital – Boston, MA
Start Date	First Patient In: June 2021
End of Recruitment	Last Patient In (anticipated): 1H CY 2023