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KAZIA THERAPEUTICS PROVIDES PRELIMINARY UPDATE FROM ONGOING PHASE 2 STUDY OF PAXALISIB IN PRIMARY CNS LYMPHOMA

Sydney, 02 Nov 2023 – Kazia Therapeutics Limited (NASDAQ: KZIA; ASX: KZA), an oncology-focused drug development company, is pleased to provide a preliminary update from the ongoing investigator-initiated Phase 2 clinical trial (NCT04906096) evaluating paxalisib as monotherapy treatment in patients with relapsed/refractory primary central nervous system lymphoma (r/r PCNSL).

This is an open-label, Phase 2 clinical trial, led by Dr. Lakshmi Nayak MD, of the Dana-Farber Cancer Institute in Boston, MA. Eligible patients with r/r PCNSL will be administered paxalisib as monotherapy for up to 24 months, in an initial dosing regimen of 60mg daily, which is similar to the dosing regimen used for paxalisib clinical trials in other adult brain cancers. The objectives of the study are to assess the clinical efficacy and safety of paxalisib in up to twenty-five (25) patients with r/r PCNSL based on objective response rate (ORR), duration of response (DOR), progression-free survival (PFS) and overall survival (OS). To date, fourteen (14) patients have been enrolled in the study.

Clinical activity has been preliminarily observed in enrolled patients, including partial responses and stable disease. Although early clinical activity was observed in some patients, several heavily pretreated r/r PCNSL patients experienced treatment-related adverse events consistent with those previously reported with paxalisib, that resulted in dose reductions and, in some cases, early termination from the study. As such, the protocol is being optimized by the investigator to initiate starting doses at 15mg twice a day or 30mg once a day with the goal of improving the durability of clinical benefit and overall tolerability.

“We are encouraged by the clinical activity preliminarily observed to date and agree with the lead investigator to reduce the dose with the goal of improving tolerability and durability of response,” stated Dr. John Friend, CEO Kazia Therapeutics. “The investigator has enrolled over half the patients needed to complete this study, and we look forward to receiving additional clinical updates in the future.”

Primary CNS Lymphoma

Primary central nervous system lymphoma (PCNSL) is a rare, poor prognosis subtype of extranodal, non-Hodgkin’s lymphoma (NHL), which accounts for 4% of primary brain tumours. Approximately 90% of PCNSL cases are diffuse large-B cell lymphoma (DLBCL) in origin, with T-cell lymphoma, Burkitt’s lymphoma and poorly characterized low-grade lymphoma representing a much smaller percentage of disease.

Despite an aggressive approach to the initial treatment involving high-dose methotrexate-based chemotherapy, whole-brain radiotherapy (WBRT) and autologous stem cell transplantation (ASCT), nearly 50% of patients recur after two years, with a third of patients becoming refractory early in the course of treatment.

Optimal therapy in the setting of either recurrence or treatment-refractoriness has not yet been established and most patients ultimately die of their disease, underscoring the fact that PCNSL remains a major unmet need in oncology today. The treatment of r/r PCNSL has largely been based on the experience gathered in numerous small retrospective studies and a limited number of prospective clinical trials. The clinical evidence from these approaches have demonstrated limited efficacy and durability.

Lymphoma outside the CNS has been a successful 'use case' for PI3K inhibitors, with four of the five FDA-approved therapies indicated for some form of the disease. There is a rationale for a brain-penetrant agent to examine CNS lymphoma, which is otherwise relatively treatment resistant to existing therapies.

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, an investigational brain-penetrant inhibitor of the PI3K / Akt / mTOR pathway, which is being developed to treat multiple forms of brain cancer. Licensed from Genentech in late 2016, paxalisib is or has been the subject of ten clinical trials in this disease. A completed Phase 2 study in glioblastoma reported early signals of clinical activity in 2021, and a pivotal study in glioblastoma, GBM AGILE, is ongoing, with final data expected in CY2023. Other clinical trials are ongoing in brain metastases, diffuse midline gliomas, and primary CNS lymphoma, with several of these having reported encouraging interim data.

Paxalisib was granted Orphan Drug Designation for glioblastoma by the US Food and Drug Administration (FDA) in February 2018, and Fast Track Designation (FTD) for glioblastoma by the FDA in August 2020. Paxalisib was also granted FTD in July 2023 for the treatment of solid tumour brain metastases harbouring PI3K pathway mutations in combination with radiation therapy. In addition, paxalisib was granted Rare Pediatric Disease Designation and Orphan Drug Designation by the FDA for diffuse intrinsic pontine glioma in August 2020, and for atypical teratoid / rhabdoid tumours (AT/RT) in June 2022 and July 2022, respectively.

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 evidence of synergy with immuno-oncology agents. A Phase I study commenced recruitment in November 2021.

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

Forward-Looking Statements

This announcement may contain forward-looking statements, which can generally be identified as such by the use of words such as "may," "will," "estimate," "future," "forward," "anticipate," or other similar words. Any statement describing Kazia's future plans, strategies, intentions, expectations, objectives, goals or prospects, and other statements that are not historical facts,

are also forward-looking statements, including, but not limited to, statements regarding: the timing for results and data related to Kazia's clinical and preclinical trials, and Kazia's strategy and plans with respect to its programs, including paxalisib and EVT801. Such statements are based on Kazia's current expectations and projections about future events and future trends affecting its business and are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements, including risks and uncertainties: associated with clinical and preclinical trials and product development, related to regulatory approvals, related to Kazia's executive leadership changes, and related to the impact of global economic conditions. These and other risks and uncertainties are described more fully in Kazia's Annual Report, filed on form 20-F with the United States Securities and Exchange Commission (SEC), and in subsequent filings with the SEC. Kazia undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise, except as required under applicable law. You should not place undue reliance on these forward-looking statements, which apply only as of the date of this announcement.

This announcement was authorized for release by Dr John Friend, CEO.