# Kazia Therapeutics Announces Phase II/III Clinical Trial Results for Paxalisib in Glioblastoma

***GBM AGILE trial data shows clinically meaningful improvement in a prespecified secondary analysis for overall survival in paxalisib-treated, newly diagnosed unmethylated patients with glioblastoma***

Sydney, July 10, 2024 -- Kazia Therapeutics Limited (NASDAQ: KZIA), an oncology-focused drug development company, is pleased to announce results from GBM-AGILE, a phase II/III study that included an evaluation of paxalisib versus standard of care (SOC) for patients with glioblastoma (NCT03522298), a life-threatening brain cancer, where there is an urgent unmet need for new therapeutics.

**GBM AGILE STUDY**

GBM AGILE is an adaptive phase II/III global trial sponsored by the Global Coalition for Adaptive Research (GCAR), a nonprofit organization comprised of some of the world's foremost clinical, translational, and basic science researchers, from institutions such as Memorial Sloan Kettering Cancer Center and Dana-Farber Cancer Institute. The trial is designed to efficiently screen for and characterize the response of glioblastoma (GBM) patients to novel investigative agents. Utilizing a complex innovative design, Bayesian principles are applied to the primary endpoint (Overall Survival) comparison of the investigational agents to patients receiving Standard of Care (SOC) enrolled from the study start (also referred to as cumulative control population). In general, secondary analyses and endpoints are assessed based on established statistical models in comparison to the control patients enrolled at the same time as the investigational agent (concurrent control population).

Paxalisib is the third drug candidate to complete its evaluation in the study and was evaluated in newly diagnosed glioblastoma patients with unmethylated MGMT promoter status as well as in patients with recurrent disease.

**GBM AGILE Paxalisib Results**

Kazia CEO, Dr John Friend stated, "We are excited to have shown a 3.8 month improvement in overall survival, an approximate 33% improvement, for newly diagnosed unmethylated patients with GBM compared to the concurrent standard of care arm. Having comparable Overall Survival data across two independent studies is a compelling outcome in this difficult to treat glioblastoma population. We look forward to discussing possible approaches for an accelerated approval pathway for paxalisib with the FDA."

A total of 313 newly diagnosed unmethylated (NDU) patients and recurrent patients being treated at top US cancer hospitals were randomized in Stage 1 to either a paxalisib treatment arm (60 mg/day) or the SOC concurrent control arm from January 2021 to May 2022. The cumulative control arm was enrolled from July 2019 (GBM Agile study start date) to May 2022.

For the primary analysis the median Overall Survival (OS) was 14.77 months for paxalisib-treated NDU patients (n=54) versus 13.84 months for cumulative SOC NDU patients (n=75).

For a prespecified secondary analysis in the NDU patients, median OS was 15.54 months in the paxalisib arm (n=54) versus 11.89 months for concurrent SOC (n=46). In addition, a prespecified sensitivity analysis in NDU patients showed similar median OS difference between paxalisib treated patients (15.54 months) and concurrent SOC patients (11.70 months).

The secondary analysis results are consistent with the previously reported Company-sponsored phase II study, where median OS was 15.7 months (n=27) for paxalisib treated NDU patients compared to 12.7 months historically reported with temozolomide in this patient group (Wen 2022).

Paxalisib was well tolerated in GBM-AGILE, and no new safety signals were identified in this patient population.

An efficacy signal was not detected in the recurrent disease population (median OS of 9.69 months for concurrent SOC (n=113) versus 8.05 months for paxalisib (n=100). Similar results in this population have been reported in the other two drug candidates that have completed the GBM AGILE trial. Kazia is currently pursuing further analyses of this data to elucidate potential signals for further consideration.

Based on the totality of data available from all completed paxalisib clinical studies in newly diagnosed unmethylated GBM patients, Kazia will request a meeting with the US Food & Drug Administration (FDA) to discuss the results and determine if a potential path to accelerated approval is appropriate for paxalisib.

Paxalisib has previously received orphan drug designation and fast track designation from the FDA for glioblastoma in unmethylated MGMT promoter status patients, following radiation plus temozolomide therapy.

Full data including secondary endpoints from the paxalisib arm of the GBM AGILE study is expected to be presented at a scientific meeting later this year.


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**About Kazia Therapeutics Limited**

Kazia Therapeutics Limited (NASDAQ: KZIA) 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, has been completed with presentation of paxalisib arm data expected later in 2024 at a major medical conference. Other clinical trials involving paxalisib are ongoing in brain metastases, diffuse midline gliomas, and primary CNS lymphoma, with several of these trials having reported encouraging interim data.

Paxalisib was granted Orphan Drug Designation for glioblastoma by the 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 harboring 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 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 is ongoing and presentation of preliminary data at a medical conference is anticipated in CY2024. For more information, please visit www.kaziatherapeutics.com or follow us on X @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 investigator-initiated trials of Kazia's product candidates, the potential benefits of Kazia's product candidates, including paxalisib, 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, 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.