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Kazia Therapeutics Announces Presentation of Promising Phase I Data Evaluating Concurrent Paxalisib and Radiation Therapy in Patients with Solid Tumor Brain Metastases or Leptomeningeal Metastases Harboring PI3K Pathway Mutations at the American Society for Radiation Oncology 66th Annual Meeting

Treatment with 45mg paxalisib and radiotherapy demonstrated 67% partial response (PR)

Over two-thirds of the patients at maximum tolerated dose (MTD) achieved intracranial response which compares favorably to historical response rates for whole brain radiation therapy alone

Sydney, October 2, 2024 – Kazia Therapeutics Limited (NASDAQ: KZIA), an oncology-focused drug development company, announced the presentation of data from a Phase I study (NCT04192981) evaluating concurrent paxalisib and radiation therapy (RT) in patients for the treatment of solid tumor brain metastases (BM) or leptomeningeal metastases (LM) harboring PI3K pathway mutations at the American Society for Radiation Oncology 66th Annual Meeting (ASTRO 2024), which is taking place from September 29 - October 2, 2024, in Washington, D.C.

"The encouraging response rates observed from this Phase 1 study suggests that the concurrent administration of the investigational brain penetrant PI3K inhibitor, paxalisib, in combination radiation therapy appears to be a viable treatment approach for addressing the tumor radioresistance in patients harboring PI3K pathway mutations," said John Friend, M.D., Chief Executive Officer of Kazia Therapeutics. "Additional data, including circulating tumor DNA (ctDNA) from this study will be presented at an upcoming 2024 scientific congress and discussions for a potential pivotal registration study to evaluate this unique combination therapy for patients with PI3K mutant brain metastases are ongoing."

Presentation details:

Title:	Multi-Center Phase I Study of Concurrent Paxalisib and Radiation Therapy in Patients with Solid Tumor Brain Metastases (BM) or Leptomeningeal Metastases (LM) Harboring PI3K Pathway Mutations
Presenter:	Brandon S. Imber, M.D., M.A., Memorial Sloan Kettering Cancer Center
Abstract	1094
Scientific Session Title:	CNS 4: Brain Mets and LMD
Session Date/Time:	October 1, 5:15-6:15 PM ET

Summary Results from Part II of Phase 1 Study

- Concurrent daily administration of paxalisib with brain radiotherapy was generally well-tolerated at a maximum dose of 45 mg per day in advanced solid tumor patients with brain metastases and PI3K pathway mutations;

- The most commonly reported adverse events in the study were nausea, vomiting and hyperglycemia;
- Established proof-of-principle for molecularly-selected, rational combination studies in radiation oncology to assess safety and ultimately efficacy;
- Treatment with 45mg paxalisib and radiotherapy demonstrated a 67% PR; and
- Over two-thirds of the patients at MTD achieved intracranial response which compares favorably to historical response rates for WBRT alone.

The Phase 1 study (n=17 evaluable) was a two-part, investigator-initiated trial evaluating the use of paxalisib with radiation therapy for the treatment of patients with PI3K pathway mutation brain metastases from solid tumors. Part I of the study established the MTD of paxalisib in combination with radiation therapy, while also demonstrating promising signs of clinical activity in all nine evaluable patients. Part II was a follow-on expansion cohort to further evaluate safety and efficacy of the MTD (45mg daily) combined with radiation therapy in up to 12 additional patients.

Approximately 200,000 cancer patients develop brain metastases in the United States each year. Radiotherapy is the mainstay of treatment for brain metastases, and generally consists of either stereotactic radiosurgery (SRS) or whole brain radiotherapy (WBRT) or some combination thereof. The efficacy in patients who receive WBRT differs according to the type of tumor and the number and volume of brain metastases, but several recent publications cite overall response rates of 20-45%. The increasing incidence of brain metastasis and the low response rates to existing treatments underscores the need for new treatment options.

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 has been completed and preliminary data was presented at 15th Biennial Ovarian Cancer Research Symposium in September 2024. 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, Kazia's strategy and plans with respect to its programs, including paxalisib and EVT801, the potential benefits of paxalisib as an investigational PI3K/mTOR inhibitor, timing for any regulatory submissions or discussions with regulatory agencies, and the potential market opportunity for paxalisib. 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 SEC, and in subsequent filings with the United States Securities and Exchange Commission. 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.