# Kazia Therapeutics Announces First Patient Dosed in Phase 1b Trial of Paxalisib in Advanced Breast Cancer

*Trial is expected to provide key insights on how paxalisib therapy can be combined with established immunotherapies and standard of care chemotherapy to improve patient outcomes in advanced breast cancer*

Sydney, Australia – June 5, 2025. Kazia Therapeutics Limited (NASDAQ: KZIA) ("Kazia" or the "Company"), an oncology-focused biotechnology company developing innovative therapies for difficult-to-treat cancers, today announced that the first patient has been dosed in a Phase 1b clinical trial sponsored by Kazia. The study evaluates paxalisib, the Company's dual PI3K/mTOR inhibitor, in combination with olaparib or pembrolizumab for patients with advanced breast cancer.

This multi-center, open-label, randomized trial is designed to assess the safety, tolerability, and preliminary efficacy of multiple paxalisib-based treatment combinations. The study also includes deep biomarker profiling to support future development and early signals of clinical activity.

"The start of patient dosing in this Kazia-sponsored study marks an important milestone in the evolution of paxalisib beyond brain cancer and into broader solid tumor applications," said Dr. John Friend, Chief Executive Officer of Kazia. "By leveraging the dual inhibition of PI3K and mTOR, this trial builds on compelling preclinical data showing epigenetic modulation in aggressive breast cancer pre-clinical models. We believe the combinations explored here may provide a more effective therapeutic strategy by simultaneously targeting tumor metabolism, DNA repair, and immune evasion."

## About the Study

This Phase 1b trial (ACTRN12624001340527) will enroll patients with advanced breast cancer into two treatment arms:

- Arm A: Patients are randomized to receive either 15mg or 30mg of paxalisib (once daily) in combination with olaparib (300mg orally, twice daily), administered in 28-day cycles.
- Arm B: Patients are randomized to receive paxalisib (15mg or 30mg once daily) and pembrolizumab (200mg IV every 21 days) alongside standard-of-care chemotherapy: either nanoparticle albumin-bound paclitaxel or a gemcitabine-carboplatin regimen, depending on clinical indication.

Participants will be evaluated for:
- Adverse events and overall tolerability
- Changes in circulating tumor cells ("CTCs") and CTC clusters
- Immune cell signatures and overall immune function
- Clinical activity and tumor response signals

## Strategic Significance

• For investors, this trial expands the clinical footprint of paxalisib into solid tumors beyond the central nervous system, targeting a significant commercial opportunity in advanced and metastatic breast cancers, including triple-negative breast cancer.
• For potential partners and acquirers, the novel biomarker-driven design provides an early window into how paxalisib may enhance or sensitize tumors to immune checkpoint inhibitors and DNA repair-targeted therapy.
• For the scientific community, the study is structured to generate translational data that may clarify the mechanistic interactions between dual PI3K/mTOR inhibition, immune modulation, and chemotherapy-induced cytotoxicity.

"The integration of paxalisib into combination regimens reflects our strategy of building value through differentiated science and high-quality collaborations," added Dr. Friend. "As this study progresses, we aim to share interim updates that may further underscore the potential of paxalisib to impact multiple indications with poor prognoses."

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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 2/3 study in glioblastoma (GBM-Agile) was reported in 2024 and discussions are ongoing for designing and executing a pivotal registrational study in pursuit of a standard approval. 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 results of its Phase 1b clinical trial evaluating paxalisib in combination with olaparib or pembrolizumab for patients with advanced breast cancer, the potential benefits of paxalisib as an investigational PI3K/mTOR inhibitor, timing for any regulatory submissions or discussions with regulatory agencies, the potential market opportunity for paxalisib and Kazia's intent and efforts to regain and/or maintain compliance with the applicable Nasdaq continued listing requirements and standards. 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 the impact of global economic conditions, and related to Kazia's ability to regain and/or maintain compliance with the applicable Nasdaq continued listing requirements and standards. 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