10 July 2025

Kazia Therapeutics Reports Early Efficacy Data from First Triple-Negative Breast Cancer Patient Receiving Paxalisib Combination Regimen achieving >50% Reduction in Circulating Tumor Cells in Phase 1b Trial

Kazia Therapeutics (NASDAQ: KZIA) is pleased to announce preliminary results from the first patient in its Phase 1b trial evaluating a combination regimen of Paxalisib, pembrolizumab (Keytruda®), and standard chemotherapy after completing Cycle 1 (21 days) of dosing. The patient, a 61-year-old woman with metastatic triple-negative breast cancer localized to the left upper lobe of the lung, has shown highly encouraging preliminary results at 21 days, with a >50% reduction in circulating tumor cells (CTCs) and a notable decrease in CTC clusters.

The early data in this first patient closely mirror the mechanistic preclinical findings published in Molecular Cancer Therapeutics (https://aacrjournals.org/mct/article/doi/10.1158/1535-7163.MCT-24-0693/762979/Depleting-the-Action-of-EZH2-through-PI3K-mTOR), which highlight that Paxalisib, when combined with immunotherapy, significantly disrupted both single CTCs and multicellular clusters in preclinical models.

Key Highlights

- Patient Profile: 61-year-old female, metastatic triple-negative breast cancer (lung metastasis).

- Investigational Regimen: Paxalisib, pembrolizumab, and chemotherapy.

- Results at Day 21 (End-of-Cycle 1):

  • >50% reduction in total CTC count.

  • Comparable reduction in CTC clusters—these aggregates are associated with heightened metastatic potential.

  • Reduction in the mesenchymal phenotype of the remaining CTCs; this phenotype is one of the hallmarks of aggressive metastatic seeding cancer cells.

  • First-in-human data support potential for potent CTC mobilization suppression by this combination.

Clinical Significance of Patient Data

CTC clusters have long been recognized as critical mediators of metastasis and markers of poor prognosis. They are known to resist apoptosis, evade immune detection, and seed new tumor sites with exceptional efficiency. Notably, standard chemotherapy has been shown in some studies to transiently increase CTC and cluster counts within the first cycle, with levels sometimes doubling before normalizing after cycle two. In contrast, immunotherapy alone has demonstrated variable impact, often showing delayed or modest effects on CTCs, likely due to immune-mediated mechanisms over weeks to months.

In this case, the combination regimen of Paxalisib and immunotherapy achieved a rapid reduction in both CTC numbers and clusters as well as a reduction in the mesenchymal phenotype—an outcome not typically seen with chemotherapy or immunotherapy alone after only 21 days of treatment. This early clinical data reflects mechanistic synergy consistent with the preclinical data described in the MCT manuscript.

Dr. John Friend, MD, Chief Executive Officer of Kazia Therapeutics, said "It is very exciting to see our extensive preclinical research translate into such positive early data in this first patient receiving a combination of Paxalisib and immunotherapy. The degree of reduction in tumor cell dissemination markers in just 21 days gives us strong reason for optimism as we continue this clinical trial."

Dr. Friend continued "CTC clusters are emerging as key drivers of metastatic spread—they're 20–100X more efficient at seeding than single CTCs—and the sharp decline we're seeing is truly encouraging. We believe this combination may offer a meaningful early intervention against systemic disease progression."

Next Steps

- Explore potential relationship between CTC kinetics and radiographic responses

- Enrollment continues in the Phase Ib study, expanding cohort size to assess safety, tolerability, and pharmacodynamics

- Planned comprehensive analysis of immune microenvironment and CTC kinetics across all patients through serial monitoring

- Longer-term follow-up will include imaging, progression-free survival, and assessment of correlation with molecular biomarkers

For investor and media, please contact Alex Star, Managing Director LifeSci Advisors LLC, Astarr@lifesciadvisors.com, +1-201-786-8795.

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 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 advanced breast cancer, 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 paxalisib program, 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, including the risk that interim or early data may not be consistent with final data, risks related to regulatory approvals, risks related to the impact

of global economic conditions, and risks 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