Kazia Therapeutics Reports Complete Ex Vivo Disruption of Large Circulating Tumor Cell Clusters in Stage IV HER2-Positive Breast Cancer with Paxalisib Monotherapy

Sydney, Australia – September 11, 2025 – Kazia Therapeutics Limited (NASDAQ: KZIA), an oncology-focused drug development company, today announced new findings from a collaborative research program led by Professor Sudha Rao at QIMR Berghofer.

In this ex vivo study, blood samples from Stage IV HER2-positive metastatic breast cancer (mBC) patients were profiled to evaluate the effect of paxalisib, Kazia's investigational PI3K–mTOR inhibitor, on metastatic burden. Paxalisib monotherapy demonstrated a statistically significant reduction in single circulating tumor cells and achieved a complete (100%) disruption of circulating tumor cell (CTC) clusters containing three or more cells."

Key Points

- HER2-positive breast cancer accounts for 15–20% of cases and remains a clinical challenge despite the transformative impact of HER2-targeted therapies, with many patients experiencing resistance, recurrence, or metastasis.
- Immunotherapy has demonstrated success across several solid tumors but has shown limited efficacy in HER2-positive breast cancer, underscoring the need for new therapeutic approaches.
- In this study, liquid biopsy profiling of Stage IV patients revealed that paxalisib treatment effectively disrupted CTCs and CTC clusters, which are considered biomarkers of aggressive disease and metastasis.
- Immunofluorescence analyses showed that paxalisib-treated blood samples from HER2-positive mBC patients achieved complete disruption of highly metastatic CTC clusters (≥3 cells).

"This monotherapy ex-vivo result extends our understanding of paxalisib's potential beyond triple-negative breast cancer into HER2-positive disease," said Dr. John Friend, CEO of Kazia Therapeutics. "The ability to disrupt circulating tumor cell clusters, which are strongly associated with metastasis and poor prognosis, represents a transformative therapeutic avenue. We are particularly excited by the precision medicine aspect of this work, which leverages biomarkers to both track metastatic burden and guide therapeutic decisions. This work underscores Kazia's commitment to expanding paxalisib's utility across multiple subtypes of advanced breast cancer, addressing high unmet need in patients with limited options."

These findings complement Kazia's ongoing Phase 1b trial in Stage IV triple-negative breast cancer (TNBC), where initial patient data announced in July 2025 demonstrated significant reductions in circulating tumor cells and clusters, underscoring the broader potential of paxalisib to address metastatic progression across multiple breast cancer subtypes.

Next Steps

Detailed datasets encompassing metastatic signatures and disrupted progenitor populations in Stage IV HER2-positive breast cancer have been submitted for presentation at an upcoming global oncology meeting in 2025.

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, including the potential presentation at an oncology conference of comprehensive datasets, including analyses of metastatic signatures and disrupted progenitor populations in Stage IV HER2-positive breast cancer patients, 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 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, 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