ASX ANNOUNCEMENT
27 October 2022

KAZIA'S PAXALISIB DEMONSTRATES POSITIVE MONOTHERAPY EFFICACY SIGNALS IN PRECLINICAL MODELS OF MELANOMA

Sydney, 27 October 2022 – Kazia Therapeutics Limited (NASDAQ: KZIA; ASX: KZA), an oncology-focused drug development company, is pleased to announce the presentation of new data from an ongoing research collaboration with the Huntsman Cancer Institute at the University of Utah in Salt Lake City, UT.

A poster presentation by Dr Gennie Parkman and colleagues, working in the laboratory of Professor Sheri Holmen, has shown paxalisib to be active *in vitro* and *in vivo* against a range of preclinical models of metastatic melanoma, the most aggressive form of skin cancer. Dr Parkman's data suggested substantial activity for paxalisib as monotherapy, and greater activity in combination with MEK and BRAF inhibitors, two classes of drugs that are commonly used for a substantial proportion of melanoma patients.

"This is among the most promising single agent data that we have seen in our research," commented Professor Sheri Holmen, lead investigator on the project. "Despite the widespread adoption of immunotherapy in recent years, there remains substantial unmet need in melanoma, particularly in those patients who develop brain metastases. We look forward to exploring the potential of paxalisib further in our research, and hopefully seeing the drug transition to a clinical trial in the near future."

A copy of Dr Parkman's poster is available via the Kazia website:
https://www.kaziatherapeutics.com/site/pdf/1a6a7cef-bde8-42b0-91c7-e5db0f658838/Poster-at-Int-Congress-of-the-Society-for-Melanoma-Research.pdf

The research by the University of Utah team was presented at the 19th International Congress of the Society for Melanoma Research, held in Edinburgh, Scotland from 17-20 October 2022. The collaboration remains ongoing, with additional preclinical studies anticipated as a prelude to potential future clinical trials.

Key Points

- Approximately 100,000 Americans are diagnosed with invasive melanoma each year. It is the fifth most common cancer in the US, and one of the most common cancers

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in young adults. Despite marked progress in treatment of the disease, around 7,500 patients die from melanoma in the US each year.

- Australia has the highest rates of melanoma in the world, and it is the most common cancer in young Australians (aged 15-39 years). It is estimated that there will be more than 17,700 new cases diagnosed in Australia in 2022, and 1,281 deaths.

- Approximately 50% of melanoma cases harbor a genetic mutation known as BRAF. Such patients are often treated with a combination of two drugs, known as a MEK inhibitor and a BRAF inhibitor respectively.

- Despite receiving BRAF / MEK inhibitor therapy, most patients eventually progress. Activation of the PI3K / Akt / mTOR pathway, which is the target of paxalisib, has been identified as a key resistance mechanism to these therapies, and has also been found to promote brain metastases.

“We are honored to be collaborating with Professor Holmen’s team at the Huntsman Cancer Institute,” commented Dr James Garner, Chief Executive Officer at Kazia. “Although brain cancer, in various forms, has been the primary focus of paxalisib’s clinical development thus far, we have always believed that the drug offers the potential to treat cancers that metastasize to the brain, and indeed cancers outside the central nervous system. This promising data from one of the leading US melanoma research centers points towards an important new opportunity for paxalisib. We look forward to working closely with the team to move this collaboration forward.”

Melanoma

Approximately 1 in 50 people will be diagnosed with melanoma during their lifetime. Most cases are localised to the skin and can be cured through surgical resection. However, about 20% of cases spread (metastasise) and require more complex and ongoing treatment.

Melanoma represents approximately 1% of all skin cancers, but accounts for the majority of deaths from skin cancer. For melanoma that is confined to the skin at the time of diagnosis, the five-year survival rate is 99.5%. However, for melanoma that has spread to distant sites (metastatic melanoma), the five-year survival rate falls to 32%.

Approximately 50% of patients harbour activating mutations in the BRAF gene. Such patients are typically treated with the combination of a BRAF inhibitor and a MEK inhibitor. The most common drugs used are Tafinlar® (dabrafenib) / Mekinist® (trametinib) (manufactured by Novartis), Braftovi® (encorafenib) / Mektovi® (binimetinib) (manufactured by Pfizer), and Zalboraf® (vemurafenib) / Cotellic® (cobimetinib) (manufactured by Genentech). The introduction of such targeted therapies has improved the average survival of patients with BRAF-mutant metastatic melanoma from approximately 6 months to approximately 24 months. However, there remains a need for additional therapeutic options to further improve survival.

Next Steps

Kazia anticipates further data from the ongoing collaboration with the Huntsman Cancer Institute in CY2023. Depending on the results, Kazia may evaluate future opportunities to launch a clinical trial of paxalisib in melanoma.

A broad clinical program exploring paxalisib in multiple forms of brain cancer is ongoing. During 2022, two ongoing clinical trials of paxalisib in the treatment of brain metastases have reported positive interim results and have graduated to expansion cohorts.

In addition, six other clinical trials of paxalisib in other forms of adult and pediatric brain cancer are ongoing, with multiple data read-outs anticipated throughout CY2023.

For More Information, Please Contact:-

Jane Lowe
IR Department
jane.lowe@irdepartment.com.au
Phone: +61 411 117 774

About Kazia Therapeutics Limited

Kazia Therapeutics Limited (NASDAQ: KZIA; ASX: KZA) is an oncology-focused drug development company, based in Sydney, Australia.

Our lead program is paxalisib, a 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 II study in glioblastoma reported promising signals of efficacy in 2021, and a pivotal study for registration, GBM AGILE, is ongoing, with final data expected in CY2023. Other clinical trials are ongoing in brain metastases, diffuse midline gliomas, and primary CNS lymphoma, with several of these having reported encouraging interim data.

Paxalisib was granted Orphan Drug Designation for glioblastoma by the US FDA in February 2018, and Fast Track Designation for glioblastoma by the US FDA in August 2020. In addition, paxalisib was granted Rare Pediatric Disease Designation and Orphan Designation by the US FDA for DIPG in August 2020, and for atypical teratoid / rhabdoid tumours (AT/RT) 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 compelling evidence of synergy with immuno-oncology agents. A phase I study commenced recruitment in November 2021.

For more information, please visit www.kaziatherapeutics.com or follow us on Twitter @KaziaTx.

This document was authorized for release to the ASX by James Garner, Chief Executive Officer, Managing Director.

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 Kazia’s strategy and plans with respect to its programs, including paxalisib. Such statements are based on Kazia’s 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 the 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 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.