23 September 2024

Kazia Therapeutics Announces Presentation of EVT801 Clinical Data at 15th Biennial Ovarian Cancer Research Symposium

Sydney, September 18, 2024 – Kazia Therapeutics Limited (NASDAQ: KZIA), an oncology-focused drug development company, is pleased to announce the presentation of data highlighting promising clinical activity of EVT801 in high grade serous (HGS) Ovarian Cancer at the 15th Biennial Ovarian Cancer Research Symposium, co-presented by American Association of Cancer Research (AACR) and the Rivkin Center for Ovarian Cancer Research on Saturday, September 21, 2024 in Seattle Washington.

Dr. John Friend, CEO Kazia Therapeutics presented preliminary data from a Phase 1 first-in-human clinical trial evaluating the safety and tolerability of EVT801, a highly selective small molecule VEGFR3 inhibitor targeting tumour angiogenesis. The Phase 1 study met its primary objectives, with the maximal tolerated dose identified at 500mg twice a day (BID). The Phase 1 study also identified the recommended Phase 2 dose starting at 400mg BID. It was observed that EVT801 was tolerated across all doses, with the majority of toxicities being mild to moderate and transient in nature.

Key points of the presentation included:

- A total of 26 patients were treated across 6 dosing cohorts ranging from 50mg once daily (QD) to 500mg twice daily (BID)
- Patients with eleven different cancer types (ex. colon, renal cell, pancreatic) were enrolled in the study, with heavily pretreated advanced ovarian cancer being the most prevalent indication (11 patients)
- Biomarkers have shown strong VEGFR3 expression in multiple indications, including ovarian cancer
- Encouraging clinical activity in High Grade Serous ovarian cancer patients with forty-six percent (46%) having stable disease or for at least three cycles, including two patients who received 9 cycles
- One patient had a partial response (-39% decrease) after 2 cycles of EVT801 therapy

Dr John Friend, CEO of Kazia Therapeutics, commented: "I was honored to participate at the Ovarian Cancer Research Symposium and present our findings to fellow clinicians and ovarian cancer researchers from around the globe. Ovarian cancer is often diagnosed at late stages with poor patient prognosis, so the data from the Phase 1 study is extremely encouraging and gives us confidence that we could potentially have a first-in-class VEGFR-3 inhibitor with EVT801."

Abstract: **Phase I study of EVT801, a VEGFR-3 inhibitor, shows promising clinical activity in HGS ovarian cancer**
https://www.xcdsystem.com/rivkin/program/ZR7NvO4/index.cfm?pgid=1697
September 21, 2024 – 11:30am-1:30pm

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 EVT801 as a VEGFR3 inhibitor and the potential market opportunity for EVT801. 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.

Phase I study of EVT801, a VEGFR-3 inhibitor, shows promising clinical activity in HGS ovarian cancer

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Abstract #P110

EVT801: A differentiating anti-tumour approach

Targeting tumour angiogenesis with the selective VEGFR-3 inhibitor EVT801 in combination with cancer immunotherapy
Cancer Research Communications (2022) 2 (11): 1504–1519.

EVT801 activity on tumour microenvironment

- Normalization of tumor (lymph)-angiogenesis ↑
- Hypoxia ↓
- CD8^{pos} T-cell infiltration ↑
- Endothelial cell immunotolerance ↑
- Tumour associated macrophages ↓

Data from Tacconi & al. with SAR131675

Tumour metastasis ↓

Multiple cooperative modes of action

EVT801 (*SAR131675*)*

↓ Cytokines involved in MDSC frequency

↓ Myeloid-derived suppressor cells

** SAR131675, a close analogue of EVT801*

EVT801 MoA hypothesis: by inhibiting VEGFR3^{pos} tumour blood vessels formation, EVT801 would induce tumour blood vessels normalization, reducing hypoxia and improving CD8 T-cells infiltration

NCT05114668: EVT801 in Phase I clinical trial KZA-0801-101

Approvals from regulatory bodies obtained in September 2021

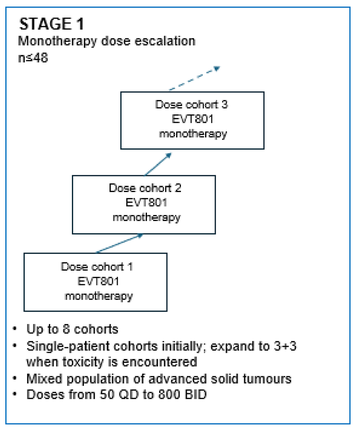
- First-Patient-In in Oct 2021
- 2 clinical sites in France :
  - Toulouse (IUCT): PI = Dr Gomez-Roca
  - Lyon (CLB): PI = Dr Philippe Cassier

32 patients enrolled in stage 1

- 6 screening failure
- 26 patients treated
- 6 cohorts at different doses
  - 50mg QD to 500mg BID
- 11 patients with ovarian carcinoma

Clinical trial design

A Phase 1, First-in-Human, Open-Label Study to Assess the Safety, Tolerability and Pharmacokinetics of EVT801 in Patients with Advanced Solid Tumours



- Up to 8 cohorts
- Single-patient cohorts initially; expand to 3+3 when toxicity is encountered
- Mixed population of advanced solid tumours
- Doses from 50 QD to 800 BID

INSTITUT UNIVERSITAIRE DU CANCER DE TOULOUSE Oncopole

CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD

Clinical trial main objectives

Primary Objective:

- To evaluate the safety and tolerability of EVT801 in subjects with advanced or metastatic solid tumours.
- To determine the maximum tolerated dose (MTD) and / or a recommended Phase 2 dose (RP2D) of EVT801 when administered daily to subjects with advanced or metastatic solid tumours.

Secondary Objectives:

- To characterize the pharmacokinetics (PK) of EVT801 following administration in an oral capsule formulation.
- To identify active metabolites of EVT801 in plasma.
- To determine preliminary anti-tumour activity of EVT801 via assessment of overall response rate (ORR).

Exploratory Objectives:

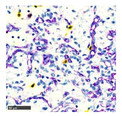
- To calculate progression-free survival (PFS) and overall survival (OS) for patients treated with EVT801.
- To identify biomarkers for EVT801 patient characterization in blood and/or in tissue
- To investigate potential mode of action and pharmacodynamics biomarkers of EVT801
- To correlate progressive disease (PD) response and overall response rate (ORR) to VEGFR3 expression in tumour samples.

Based on protocol v5.0 dated 25 Nov 2023

EVT801 Biomarkers strategy

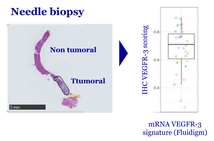
Patients characterization based on VEGFR-3 expression in archival tissues and/or biopsies

- VEGFR-3 signature by IHC: VEGFR-3/CA9/CD8/CD31/ PD-L1



VEGFR-3 & response to immune checkpoint therapies mRNA signatures by Fluidigm

- VEGFR-3 gene signature
- PD-1 response gene signature on archival tissues and/or biopsies



Circulating pharmacodynamic biomarkers

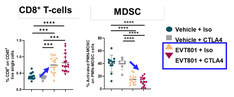
- Bulk RNA sequencing on blood cells at C1D1 vs C2D1 (Paxgene tube)

Safety biomarkers to control hypertension

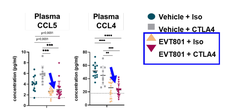
- Blood pressure measurement to control that EVT801 does not induce hypertension (as demonstrated in preclinical model)

Circulating endpoint biomarkers

- **Immunomonitoring** based on CD8$^+$ T-cells / MDSC ratio at C1D1 vs C2D1



- **Proteins signature** based on chemokines involved in inflammation & angiogenesis at C1D1 vs C2D1



Data were obtained on orthotopic 4T1 tumor mouse model

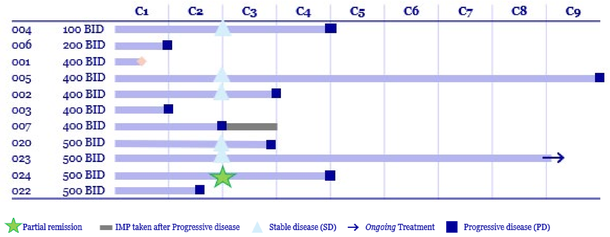
Resting samples will include

- Frozen whole blood & plasma
- Frozen PBMCs
- FFPE biopsies

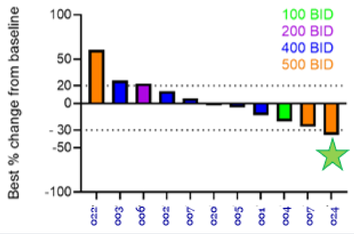
Overview of patient's follow-up Focus on Ovarian cancer patients

- 11 patients with ovarian cancer (10 with high grade serous ovarian cancer (HGS-OC) and 1 with low grade serous ovarian cancer) that have received multiple lines of previous treatments were included among the 32 patients enrolled.
- This represents a consequent subpopulation with the same disease that allows to perform statistical analysis on clinical and biomarkers data
- To date, samples of 6 of these patients have been analyzed for biomarkers

Number of cycles of treatment
Status on 11th of September 2024



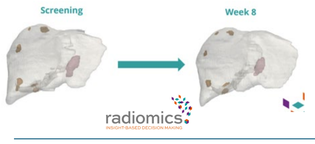
Tumor best responses plot



- **These 11 patients with ovarian cancer had an average age of 67 years (range: 56-76) and a median time from diagnosis of nine years.**
- **Forty-six percent (46%) of the ovarian cancer patients had stable disease or better for at least three cycles of EVT801 therapy.**
- **Patient 024 had a partial response (-39% decrease) at the end of cycle 2**

Case study: Analysis of patient 024 – 3D renderings by Radiomics.org

The 3D renderings show the evolution of the lesions from screening to week 8 with a significant reduction of volume



The volumetric analysis shows a partial response from screening to week 8

Lesion	Screening	Week 8 (Week 8-to/to)	
Liver lesions	4,83 cm3	3,16 cm3	-34,5 %
Abdominal lymph node	7,22 cm3	4,47 cm3	-38,2 %
Total	12,06 cm3	7,63 cm3	-36,7%

Potential disease response= -39%

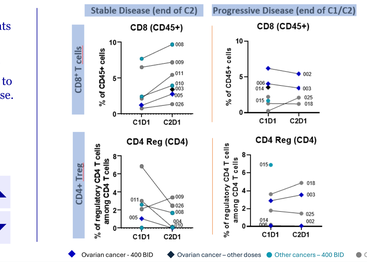
- Some of the quantified radiomics features are **clearly impacted by the treatment**
- Following EVT801 treatment:
  - The lesions became more homogenous & less dense intensity-wise
  - The lesions became more compact

Immunomonitoring: analysis on patients with Stable Disease vs Progressive disease

Working hypothesis: patients with stable disease have an increase of circulating CD8$^+$ T-cells and a decrease of CD4$^+$ Treg-cells in comparison to patients with progressive disease.

Circulating CD8^{pos} T-cell ▲

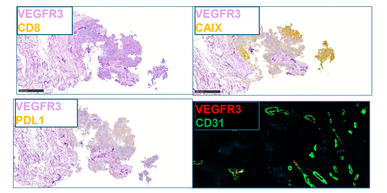
Circulating CD4^{pos} Treg-cell ▼



- **Patients with stable disease in comparison to patients with progressive disease :**
  - **Tendency of an increase of circulating CD8$^+$ T-cells**
  - **Tendency of a decrease of circulating CD4$^+$ Treg-cells.**
- **Blood immunomonitoring should be performed at different cycles of treatment(not only after one cycle) during the phase 2 clinical trial to confirm these trends**

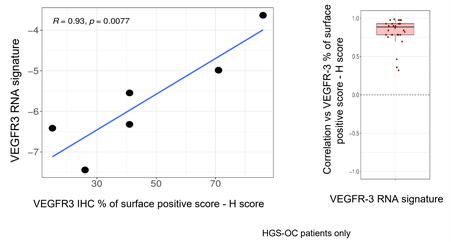
VGFR3 expression in patients with High Grade Serous Ovarian Cancer enrolled in EVT801 clinical trial phase 1

Immunohistochemistry: a case study



	VEGFR3 H-score	CD8 quantification	CAIX quantification
Score	71	0,07	35,2
Status	High	Immune desert	High

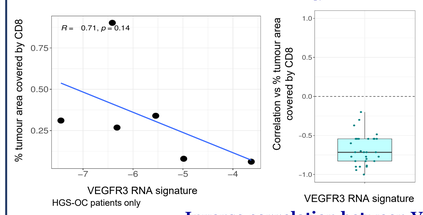
Aggregated VEGFR3 gene signature correlation with VEGFR3 histology



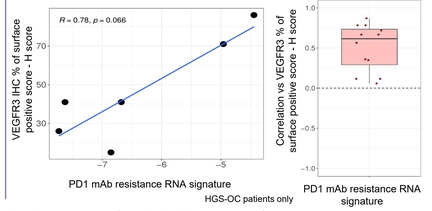
High correlation between VEGFR3 staining by histology and VEGFR3 gene signature allowing to compare RNA signatures with other histology readouts

Correlation between VEGFR3 and immune profile in patients with High Grade Serous Ovarian Cancer enrolled in EVT801 clinical trial phase 1

Individual and aggregated VEGFR3 gene signature Anti-correlation with CD8 histology



Individual and aggregated PD1 mAb resistance gene signature correlation with VEGFR3 histology



Inverse correlation between VEGFR3 expression & CD8 expression
Positive correlation between VEGFR3 expression & PD1 mAb response signature

Conclusion and next steps

- **Stage 1 is complete - primary and secondary endpoints achieved:**
  - 32 patients included in the study with 26 patients treated
  - 6 dosing cohorts completed ranging from 50mg QD to 500mg BID
  - MTD identified as 500mg BID with 400mg BID being RP2D as monotherapy
  - Patients with eleven different cancer types (ex. colon, renal cell, pancreatic) were enrolled in the study, with advanced ovarian cancer being the most prevalent indication (11 patients).
  - Number of patients have remained on treatment for two or more cycles with 9 reaching cycle 3 or greater (two reached cycle 9)
- **EVT801 was well tolerated across all doses with majority of toxicities being mild to moderate and transient in nature:**
  - Reinforces the safety profile of EVT801 observed during the preclinical toxicology studies
- **Biomarkers have shown strong VEGFR3 expression in some indications, and we have observed encouraging clinical activity in High Grade Serous ovarian cancer**
- **Next clinical trial will be pivotal to:**
  - Consolidate safety data at RP2D and our hypotheses on EVT801 mode of action
  - Validate High Grade Serous Ovarian Cancer as indication of choice for clinical trial phase 2 for standalone therapy or in combination with standard-of-care