ASX RELEASE

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KAZIA PRESENTS POSITIVE CANTRIXIL PHASE I DATA AT AACR CONFERENCE

Sydney, 1 April 2019 – Kazia Therapeutics Limited (ASX: KZA; NASDAQ: KZIA), an Australian oncology-focused biotechnology company, is pleased to provide investors with a poster presentation summarising data from Part A of the ongoing phase I study of Cantrixil (TRX-E-002-1) in ovarian cancer. The poster will be presented at the American Association of Cancer Research (AACR) Annual Meeting in Atlanta, GA at 1:00pm EST on Monday 1 April 2019. The poster number is CT019.

Dr James Garner, Chief Executive Officer of Kazia Therapeutics commented, "we are delighted to be able to share positive results from the first part of the Cantrixil phase I study in ovarian cancer, and it is very encouraging to have been selected to do so at a conference as prestigious as AACR."

Key Points

- Part A of the study was performed at five sites in the United States and Australia. Fourteen patients were enrolled in total, of which eleven received at least one dose of Cantrixil
- A Maximum Tolerated Dose (MTD) of 5mg/kg was determined. This is well within the predicted therapeutic range, based on preclinical data, and supports moving forward with subsequent clinical development
- Of nine patients evaluable for efficacy, five (56%) achieved stable disease after two cycles of Cantrixil monotherapy. One of these five patients subsequently achieved a partial response when Cantrixil was administered with chemotherapy, as intended per protocol
- Main side effects were gastrointestinal in nature, with abdominal pain and fatigue being the most common drug-related observations, although not generally dose-limiting
- An expansion cohort is currently underway to seek efficacy signals, and is planned to enroll 12 patients, all of whom will receive a dose of 5 mg/kg; initial data from this cohort is expected in 2H of calendar 2019

Dr Garner continued, "phase I studies are always primarily safety studies. The data from this study shows that Cantrixil has a safety profile very suitable for further development, and we have been able to reach a dose well within the predicted therapeutic range. It is extremely positive that we have seen some preliminary evidence of efficacy at this early stage in development, and the ongoing Part B of the study should give us much more information."

The AACR Annual Meeting is one of the largest and most prestigious cancer research meetings in the world. Clinical trial abstracts are selected for presentation if they contain impactful new data with the potential to influence treatment practice. The conference brings together more than 20,000 representatives from academia, industry, government and advocacy organisations from across the globe.

The phase I study of Cantrixil commenced in December 2016 and is registered on clinicaltrials.gov as NCT02903771. It is structured in two parts: Part A aimed to understand the safety profile of Cantrixil and to establish the Maximum Tolerated Dose (MTD), while Part B will recruit 12 patients at the MTD to seek preliminary signals of efficacy. Recruitment to Part B remains ongoing, and Kazia expects to report initial data from this component of the study in the second half of calendar 2019.

Following the recent opening of an additional site, the study is currently being conducted at six hospitals in the United States and Australia:-

Site	**Principal Investigator**
United States	
Lifespan Cancer Institute, Providence, RI	Dr. Don Dizon
Stephenson Cancer Center, Oklahoma City , OK	Assoc. Prof. Kathleen Moore
Mary Crowley Cancer Research Centre, Dallas, TX	Dr. Minal Barve
Australia	
ICON Cancer Care, Brisbane, QLD	Assoc. Prof. Jermaine Coward
Westmead Hospital, Sydney, NSW	Prof. Paul Harnett
Flinders Medical Centre, Adelaide, SA	Dr. Ganessan Kichenadasse

Daniel Berg, Clinical Program Director for Cantrixil, commented, “we are fortunate to be working with some of the leading specialists in this disease area. Ovarian cancer remains a disease with significant unmet clinical need, and we believe Cantrixil may represent an important addition to therapeutic protocols.”

The study protocol was designed such that patients received two cycles (six weeks) of therapy with Cantrixil alone, followed by up to six cycles (eighteen weeks) of Cantrixil administered in combination with standard-of-care chemotherapy. In total, 14 patients were enrolled in Part A. However, three patients were withdrawn before receiving a first dose of Cantrixil due to rapid disease progression or other aspects of their pre-existing condition, leaving 11 patients evaluable for safety. Of these, nine patients completed the first cycle of treatment with Cantrixil, making them evaluable for determination of the MTD.

The study enrolled patients at doses ranging from 0.24 mg/kg to 20 mg/kg, and 5 mg/kg was determined to be the maximum tolerated dose. This is within the therapeutic range that would be predicted from preclinical data. The main adverse events were gastrointestinal in nature, and included abdominal pain, ileus, and bowel obstruction. Diarrhoea, nausea, and vomiting were also seen, but were not generally dose-limiting.

All patients had recurrent or persistent ovarian cancer and had failed at least two prior lines of therapy, including platinum therapy, prior to study entry, representing a very advanced

population. After two cycles of treatment with Cantrixil, five of nine evaluable patients (56%) achieved stable disease, according to the industry-standard RECIST criteria, which means that the tumour remained approximately the same size over time and had not progressed. One of these patients subsequently achieved a partial response when Cantrixil was administered with standard-of-care chemotherapy, which means that the tumour was reduced in size by 30% or more.

Four out of nine patients (44%) remained on study drug for the entire 24-week duration of the study (approximately six months), without experiencing progression of their disease. For comparison, data from other studies in a similar patient group has found a progression-free survival of approximately 3.4 to 4.7 months. This further suggests the possibility that Cantrixil may help to delay disease progression.

Ovarian cancer is diagnosed in approximately 240,000 women each year worldwide and is the eighth most common cause of cancer death in women. Conventional treatment typically includes surgery, radiotherapy, and chemotherapy. However, the five-year survival rate remains low, at approximately 45%, reflecting the fact that the disease is often advanced at the time of diagnosis.

[ENDS]

About Kazia Therapeutics Limited

Kazia Therapeutics Limited (ASX: KZA, NASDAQ: KZIA) is an innovative oncology-focused biotechnology company, based in Sydney, Australia. Our pipeline includes two clinical-stage drug development candidates, and we are working to develop therapies across a range of oncology indications.

Our lead program is GDC-0084, a small molecule inhibitor of the PI3K / AKT / mTOR pathway, which is being developed to treat glioblastoma multiforme, the most common and most aggressive form of primary brain cancer in adults. Licensed from Genentech in late 2016, GDC0084 entered a phase II clinical trial in March 2018. Initial data is expected in early calendar 2019. GDC-0084 was granted orphan designation for glioblastoma by the US FDA in February 2018.

TRX-E-002-1 (Cantrixil), is a third-generation benzopyran molecule with activity against cancer stem cells, and is being developed to treat ovarian cancer. TRX-E-002-1 is currently undergoing a phase I clinical trial in Australia and the United States. Initial data was presented in June 2018 and the study remains ongoing. Cantrixil was granted orphan designation for ovarian cancer by the US FDA in April 2015.

Poster # CT091, AACR Meeting, Atlanta GA 2019

ClinicalTrials.gov identifier: NCT02903771

Phase I Study of Intra-peritoneal Cantrixil (TRX-E-002-1) in Patients with Persistent or Recurrent Ovarian Cancer, Fallopian Tube Cancer or Primary Peritoneal Cancer

Jermaine Coward[1], Ganessan Kichenadasse[2], Paul Harnett[3], Kathleen Moore[4], Minal Barve[5], Daniel Berg[6], James Garner[6], Don Dizon[7]

1. ICON Cancer Care, South Brisbane, QLD, Australia; 2. Flinders Medical Centre, Adelaide, SA, Australia; 3. Westmead Adults Hospital, Westmead, NSW, Australia; 4. Oklahoma Health Sciences Center, Oklahoma City, OK, USA; 5.Mary Crowley Cancer Center, Dallas, TX, USA; 6. Kazia Therapeutics Ltd, Sydney, NSW, Australia; 7. Lifespan Cancer Institute, Rhode Island Hospital, Providence, RI, USA.

BACKGROUND

- Despite initial response to surgery/platinum-based chemotherapy, ~75% of stage III/ IV patients with epithelial **ovarian cancer** will experience disease recurrence likely due to cancer stem cell (CSC) involvement.[1,2]
- **TRX-E-002-1 (Cantrixil)** is the active enantiomer of a novel third generation benzopyran molecule that shows potent cytotoxicity against the two main sub-populations of ovarian cancer cells, namely ovarian cancer stem-like (CD44+ve) cells & ovarian somatic cancer (CD44-ve) cells.[3]
- Pre-clinical studies suggest TRX-E-002-1 induces cell death by both caspase-dependent & caspase-independent apoptosis. The mechanism may involve tumour-associated NADH oxidase (ENOX2) & disruption to trans-membrane electron-transport mediated energy production.[3]
- We opened this Phase I open-label, 2-part, progressive design, dose-escalation multi-center study (NCT02903771) investigating the safety, tolerability, pharmacokinetics & activity of TRX-E-002-1 monotherapy and in combination with standard of care therapy (Figure 1).

OBJECTIVES

1. To determine the maximum tolerated dose (MTD) of TRX-E-002-1 monotherapy delivered weekly via intraperitoneal (i.p.) administration
2. To evaluate safety, tolerability, pharmacokinetic (PK) characteristics & anti-tumour activity of TRX-E-002-1 monotherapy & in combination with standard chemotherapy.

METHODS

PART A: Dose Escalation Phase (N= ≤42)

Determine MTD of TRX-E-002-1 monotherapy (defined as observing no dose limiting toxicities [DLTs] or unacceptable adverse events [AEs] → Cycle 1.
Establish disease response → Cycle 2.
Assess outcomes with combination TRX-E-002-1 & standard of care → Cycles 3-8.

PART B: Expansion Cohort Phase (N=12)

More subjects are recruited and treated with TRX-E-002-1 at the MTD:
- As monotherapy → Cycle 1,2.
- In combination with standard of care → Cycle 3-8.

Figure 1. Study design for PART A and PART B of the study protocol.

Eligibility

- Adult females with recurrent or persistent epithelial ovarian, fallopian tube or primary peritoneal cancer.
- Must have completed ≥2 prior regimens for their cancer.

Treatment

- Cycle 1 & 2: Monotherapy TRX-E-002-1 (0.24–20 mg/kg i.p. infusion; 3 weeks per cycle; on days 1, 8 & 15 of each cycle).
- Cycle 3-8: Combination TRX-E-002-1 (0.24–20 mg/kg as above) with standard of care (intravenously (i.v.) on days 4, 11 & 18 of each cycle).

RESULTS: PART A (dose escalation study)

Establishing the MTD

- 14 subjects were enrolled into 6 dose level cohorts (Figure 2); 11 received ≥1 dose of study drug (safety set).
- Of these 11 subjects, 9 completed ≥3 doses of therapy per protocol (evaluable for MTD determination & efficacy).
- An MTD of 5 mg/kg was established on the DLT of ileus syndrome (n=2) & safety signals of bowel obstruction (n=3) & abdominal pain (n=2).

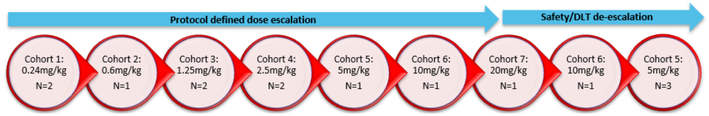


Figure 2. Dose escalation & de-escalation in study cohorts.

Adverse events

- A total of 161 AEs recorded; 66 were study drug related; 95 were not (Figure 3).
- Most AEs were mild (n=43) or moderate (n=29) with only 6 AEs being deemed severe:
  - The severe AEs were neutropenia (n=1), bowel obstruction (n=2), nausea (n=1), vomiting (n=1) & abdominal pain (n=1).
- A total of 12 SAEs were recorded:
  - Bowel obstruction (n=2), small bowel obstruction, sub-acute small bowel obstruction, diarrhoea, florid cellulitis at site of IP port, death due to disease progression of ovarian cancer, worsening of abdominal pain, ileus (n=1 for each event) were not drug related.
  - Ileus syndrome, worsening of right upper quadrant abdominal pain, abdominal pain (n=1 for each event) were drug related.

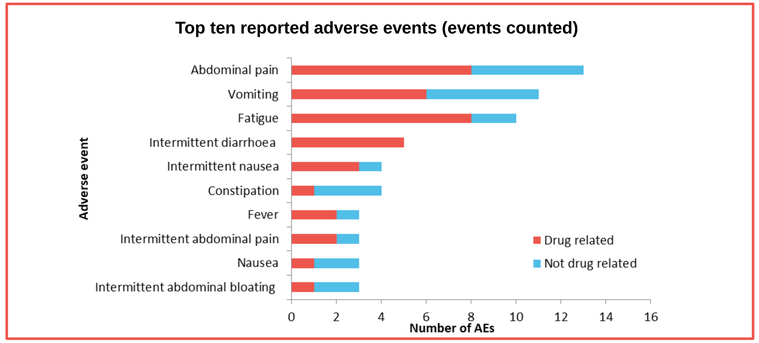


Figure 3. Top ten adverse events reported & relationship to drug.

Pharmacokinetic profile of TRX-E-002-1

- Rapid increase of systemic TRX-002-1 to peak concentrations from 9.81 to 6,100 ng/mL over ~0.4 to 4.6 hrs.
- Plasma concentrations <10 % maximal concentration by 24 hr.
- Terminal ½ life: (range) 2.47 to 5.65 hr (Figure 4).

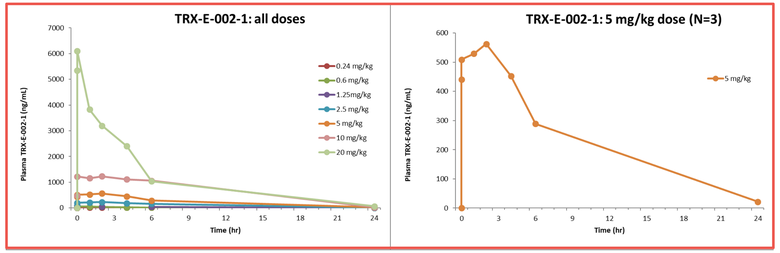


Figure 4. Time-dose concentration profile for TRX-E-002-1 2.5mg/kg after single dose (Day 1, Cycle 1).

The authors would like to thank the patients & their families for participating in the study.

This study is funded by Kazia Therapeutics Ltd, Australia

Anti-cancer activities: Tumour evaluation (MTD population)

- Best overall response (OR): after monotherapy = stable disease; after combination therapy = partial response (Figure 5).

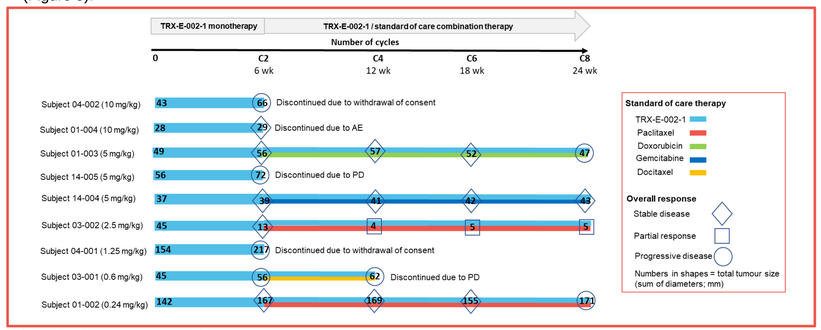


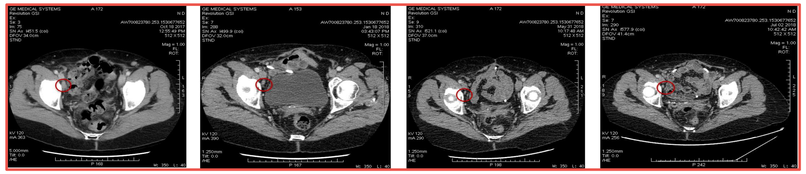
Figure 5. Time on treatment & tumour response.

Subject Case #03-002: Preliminary findings

- 67-yr old Caucasian female with BRCA wildtype high grade (stage IIIC), platinum-resistant, ovarian serous carcinoma (Aug'14); left adnexal, diaphragmatic & omental nodules.

Anti-cancer activities (RECIST and CA-125) & safety outcomes

- By 24 weeks (2 cycles of TRX-E-002-1 monotherapy, 6 cycles of TRX-E-002-1/paclitaxel combination therapy, a CT chest scan & CA-125 assessment confirmed continuing response within all areas of nodal disease (Figure 6).
- On completion of 12-week follow up period, both the CA-125 (16 from baseline 38) & target lesion (5 mm from baseline 22 mm) remained stable.



A. Oct 2017 (baseline) B. Jan 2018 (end Cycle 4) C. May 2018 (end of study) D. Jul 2018 (follow up)

Figure 6. CT images show progressive reduction, from baseline over 9-month period, in size of right iliac nodal disease.

CONCLUSIONS

- A MTD of 5 mg/kg has been established for the investigational drug TRX-E-002-1 based on the limiting toxicity of ileus syndrome & safety signals of bowel obstruction & abdominal pain.
- PK investigations demonstrate a single dose of TRX-E-002-1 results in rapid systemic availability of drug with plasma concentrations reaching <10% maximal concentrations by 24 hours.
- Based on tumour evaluation outcomes from Part A of the study, IP administered TRX-E-002-1 has clinical potential for the treatment of platinum resistant, recurrent or persistent epithelial ovarian, fallopian tube or primary peritoneal cancer.
- Part B (expansion cohort) remains ongoing with 9/12 subjects (75%) enrolled as of March 2019.

REFERENCES

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