ASX Announcement

Positive Early Preclinical Ovarian Cancer Results

- **Bisantrene found to be more effective compared to doxorubicin and epirubicin in ovarian cancer cell lines**
- **Bisantrene killed ovarian cancer cells resistant to the current standard of care chemotherapeutic agents cisplatin, 5-fluorouracil and chlorambucil**
- **These preclinical results are encouraging and consistent with past Phase II clinical trials which identified Bisantrene as an effective ovarian cancer treatment.**

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23 February 2021 – Race Oncology Limited (ASX: RAC) is pleased to share further interim results of our continuing collaborative preclinical research program with The University of Newcastle. Eminent cancer researcher, Associate Professor Nikki Verrills of the Hunter Medical Research Institute is leading the project.

The aim of this recent preclinical research program is to explore Bisantrene efficacy in ovarian cancer. Bisantrene was the subject of two-Phase II clinical trials in the USA in advanced ovarian cancer patients in the 1980s [1,2]. These trials showed that Bisantrene was able to induce a clinical response in heavily pre-treated ovarian cancer patients, including those resistant to doxorubicin and other standard of care drugs of the period [2].

Early results show Bisantrene to be an effective chemotherapeutic agent in patient-derived ovarian cancer cell lines. Bisantrene was able to kill these cancer cells that were resistant to the current standard of care ovarian drugs, cisplatin, 5-fluorouracil and chlorambucil.

Race's CSO Dr Daniel Tillett commented *"These initial results from Nikki's team further highlight Bisantrene's potential use in ovarian cancer patients as a safer alternative to the commonly used anthracyclines which can be very dangerous to the hearts of patients. It is highly encouraging that bisantrene is able to kill ovarian cancer cells resistant to currently used treatments and these findings support further exploration of the use of Bisantrene in ovarian cancer patients."*

Race's CEO Mr Phillip Lynch added, *"we continue to generate results reconfirming the historical positives for Bisantrene, in this case in ovarian cancer, the 5th most common form of cancer in women [3]. Race Oncology has a broad range of opportunities, ovarian cancer included. This program is further evidence of Race delivering against the Three Pillar strategy, taking counsel, and completing feasibility assessments with a view to mapping promising yet attainable clinical paths for Bisantrene."*

Study Background

Ovarian cancer is the fifth most common cause of cancer-related death among females. Crucially, it is the most lethal gynecologic malignancy in developed countries [3]. Despite many modern advances in cancer therapy, the survival rate of ovarian cancer has not improved markedly over the past several decades. This is a function of the typically late diagnosis of the disease (often only after it has metastasized), and its rapidly developed resistance to standard of care treatments. New treatments are desperately needed.

Materials and Methods

Two cancer cell lines (PEO1 & PEO4) were screened for their sensitivity to Bisantrene and other chemotherapeutic drugs commonly used in ovarian cancer patients (Fig. 1).

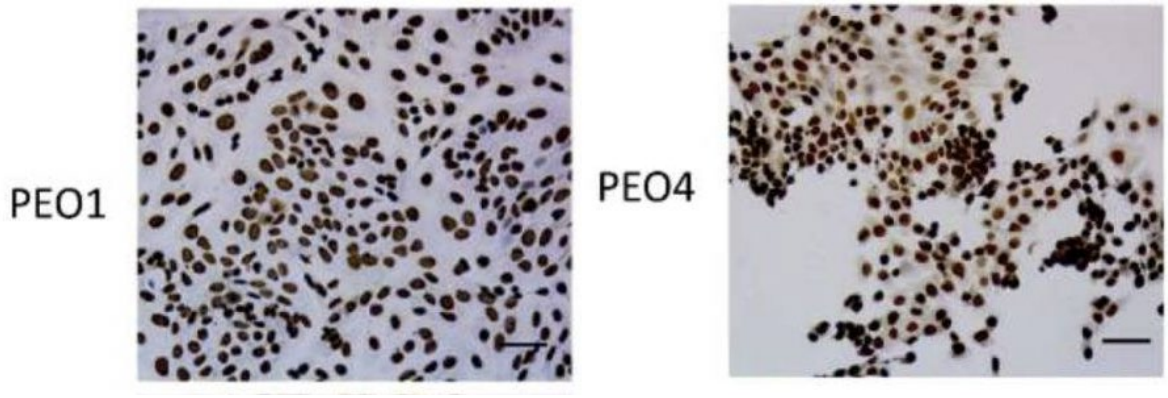

Figure 1. The morphology of PEO1 & PEO4 ovarian cancer cells grown invitro. Scale bars = 50 µm.

PEO1 is an adherent ovarian cancer cell line derived from malignant peritoneal ascites in a patient with a poorly differentiated serous adenocarcinoma. PEO4 was derived from the same patient after relapse and treatment with cisplatin, 5-fluorouracil and chlorambucil and is the cell line resistant to these three drugs [4].

Bisantrene was compared to doxorubicin, epirubicin and cisplatin as a single agent in both PEO1 and PEO4. Cell viability was determined using the resazurin metabolic assay and confirmed by visual inspection under light microscopy. All experiments were replicated a minimum of three times.

Study Highlights

1. Bisantrene is more cytotoxic than doxorubicin and epirubicin in ovarian cancer cells

The study found that Bisantrene showed better cytotoxic (cell killing) effects than either anthracycline, doxorubicin or epirubicin, in both PEO1 and PEO4 ovarian cancer cell lines when compared to the maximum tolerated dose (Figs. 2-4). The IC_{50} (50% cell death) of Bisantrene with the PEO1 & PEO4 cell lines was 173nM & 290nM (Fig 2), respectively. This compares to 207nM & 363nM for doxorubicin (Fig. 3), and 200nM & 265nM for epirubicin required to kill the cells (Fig. 4).

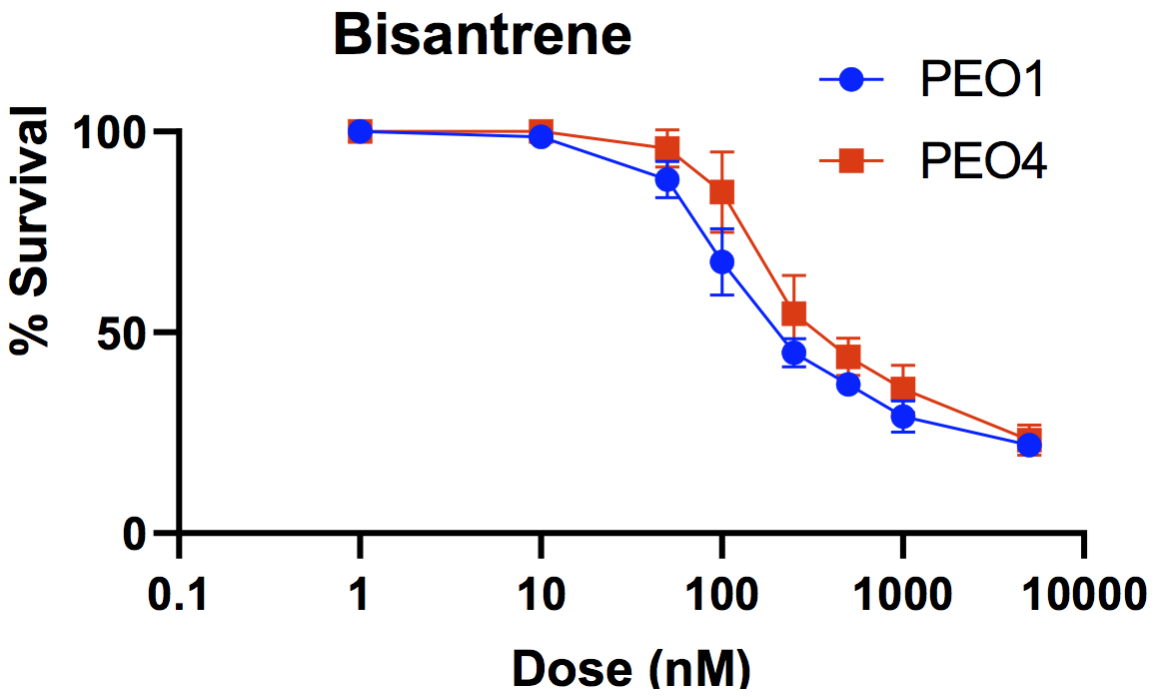

Figure 2. Dose response cytotoxicity of Bisantrene in the PEO1 & PEO4 ovarian cancer cell lines.

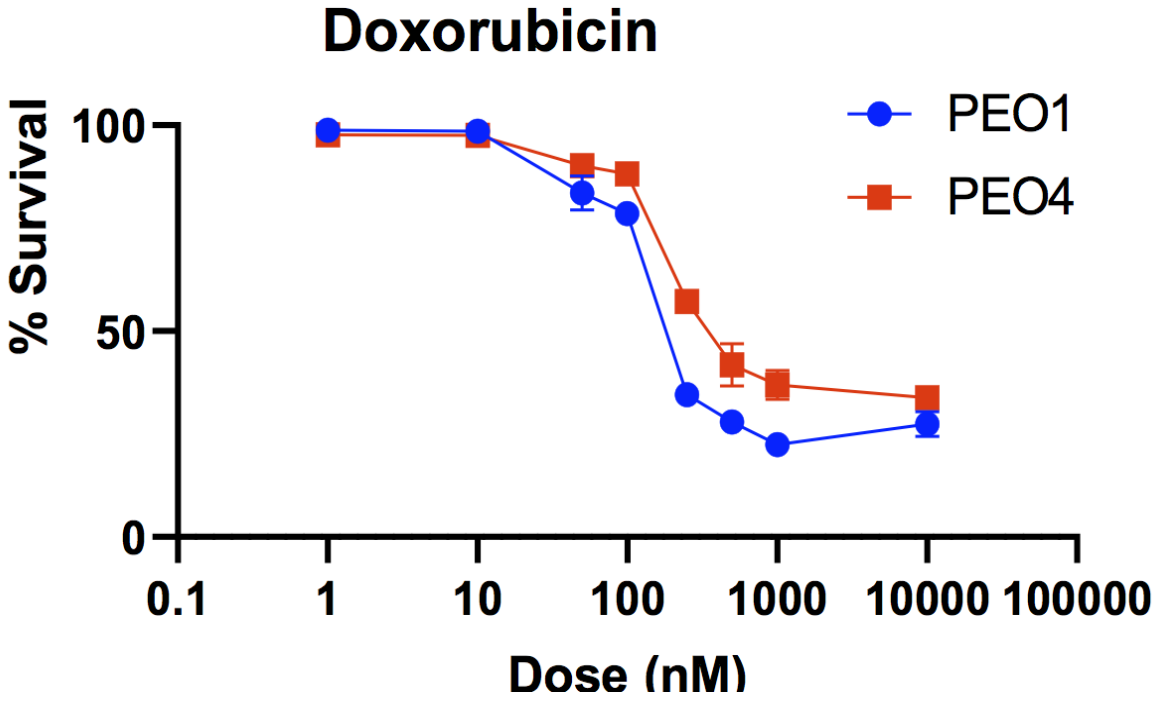

Figure 3. Dose response cytotoxicity of doxorubicin in PEO1 & PEO4 ovarian cancer cell lines.

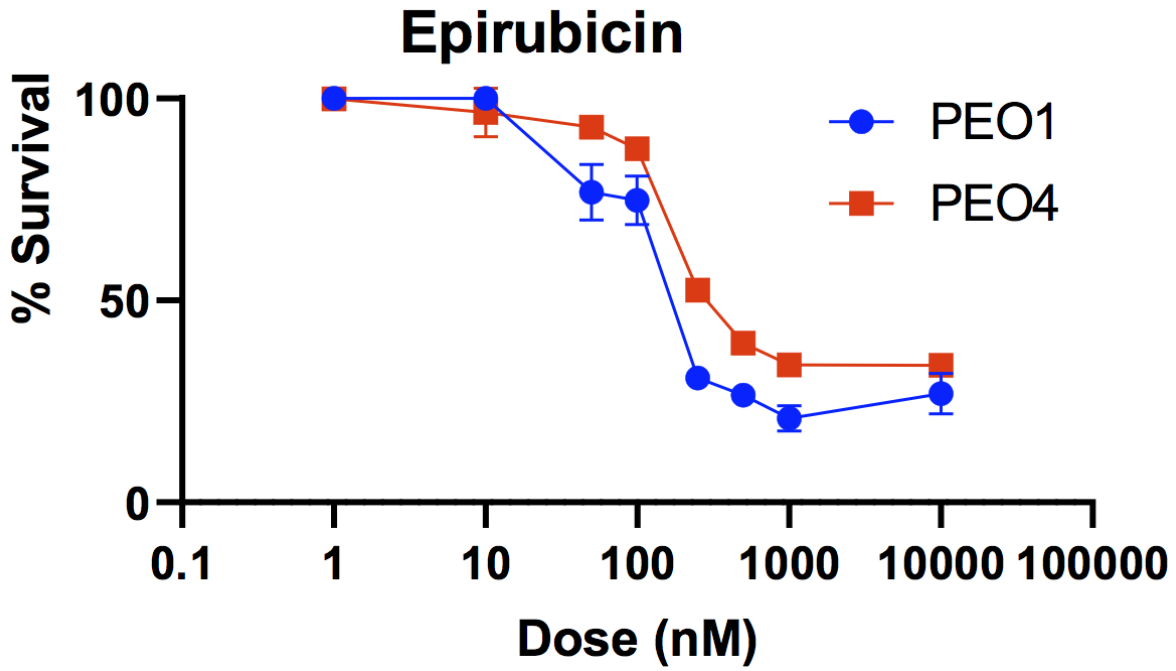

Figure 4. Dose response cytotoxicity of epirubicin in the PEO1 & PEO4 ovarian cancer cell lines.

2. Bisantrene can kill ovarian cancer cell lines resistant to cisplatin, 5-fluorouracil and chlorambucil

The PEO4 cancer cell line is resistant to cisplatin, a commonly used chemotherapeutic drug for ovarian cancer. Bisantrene was almost as effective in the PEO4 resistant cells as the same patient pre-treatment derived PEO1 cancer cells suggesting that Bisantrene may have activity in platinum-resistant ovarian cancer settings (Fig. 5).

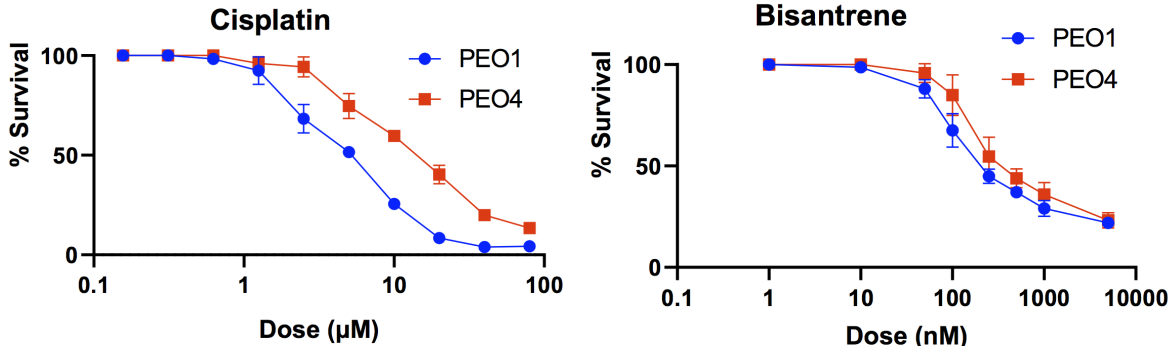

Figure 5. Dose response of cytotoxicity of cisplatin (left) and Bisantrene (right) in the PEO1 & PEO4 ovarian cancer cell lines. Note: 1μM = 1000nM.

Conclusions

- Bisantrene was found to kill ovarian cancer cells confirming the historical Phase II clinical trials
- Bisantrene was able to kill ovarian cancer cells resistant to cisplatin, 5-fluorouracil and chlorambucil
- These data support further assessment of Bisantrene as an alternative chemotherapeutic agent in ovarian cancer patients.

Next Steps

- Further preclinical studies are currently being conducted to elucidate the clinical significance of the overexpression of the fat mass and obesity associated gene (FTO) in ovarian and breast cancer, and expand the range of candidate Bisantrene drug combinations for clinical assessment.
- Publication of these results in a high impact scientific journal upon study completion.
- Update on Race's clinical trial plans under the Three Pillar strategy to be released before the end of Q1 2021.

References

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About Race Oncology (ASX: RAC)

Race Oncology is an ASX listed precision oncology company with a Phase II/III cancer drug called Bisantrene.

Bisantrene is a potent inhibitor of the Fat mass and obesity associated (FTO) protein. Over-expression of FTO has been shown to be the genetic driver of a diverse range of cancers. Race is exploring the use of Bisantrene as a new therapy for melanoma and clear cell renal cell carcinoma, which are both frequent FTO over-expressing cancers. The Company also has compelling clinical data for the use of Bisantrene as a chemotherapeutic agent with reduced cardiotoxicity in Acute Myeloid Leukaemia (AML), breast and ovarian cancers and is investigating its use in these areas.

Race is pursuing outsized commercial returns for shareholders via its 'Three Pillar' strategy for the clinical development of Bisantrene.

See more at www.raceoncology.com.

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