ASX Announcement

Race Receives Governance Approval for Extramedullary AML & MDS Human Trial

- **Governance approval received for the lead site in Race's clinical trial of Zantrene® for the treatment of patients with extramedullary AML and high risk MDS**
- **Site meeting scheduled for 31 May 2022 to initiate trial and allow recruitment of the first patient**
- **The first clinical trial in the world to investigate the targeting of FTO as a potential cancer therapy using an AML & MDS population.**

---

12 May 2022 – Race Oncology Limited ("Race") is pleased to announce it has received Research Governance Office (RGO) approval from the Calvary Mater Newcastle Hospital for its open label clinical trial of Zantrene® (bisantrene dihydrochloride) in patients with extramedullary Acute Myeloid Leukaemia (AML) or high-risk Myelodysplastic Syndrome (MDS). Human ethics approval for this trial has been granted (ASX Announcement: 5 April 2022).

Representatives of the Race Oncology clinical team, the contract research organisation Paraxel, and associated clinical teams of the Calvary Mater Hospital are scheduled to meet for site initiation and training on the 31 May 2022. Completion of this site training will enable the first patient to be recruited into the trial.

This open label Phase 1 trial with a dose expansion Phase 2 stage will recruit up to 60 patients with extramedullary AML or MDS using a two-stratum (arm) design at trial sites in Australia and Europe (ASX Announcement: 1 November 2021).

Extramedullary AML

Extramedullary AML occurs when the leukaemia spreads from the bone marrow and forms solid tumours in tissues such as the skin, breast, kidney, brain and others. A 2020 prospective positron imaging trial identified that up to 22% of AML patients have the extramedullary form[1]. Extramedullary AML patients have no clinically approved treatments and limited experimental treatment options, with many clinical trials explicitly excluding this difficult to treat form of AML.

Myelodysplastic Syndromes (MDS)

MDS are a group of blood cancers that affect the production of normal blood cells in the bone marrow. These include chronic myelomonocytic leukaemia (CMML), atypical chronic myeloid leukaemia (aCML) and myelodysplastic/myeloproliferative neoplasms unclassifiable (MDS/MPN)[2].

MDS has a very high risk (1 in 3) of the patient progressing to AML and high risk MDS is considered to be an earlier stage of AML. The annual rate of MDS is 40 to 50 clinical cases per million people[2], which is approximately half the case rate of AML.

Clinical Trial Design

This open label Phase 1 trial with a Phase 2 dose expansion phase will recruit up to 60 patients with ^{18}F-FDG PET/CT imaging-confirmed extramedullary AML at up to 10 clinical sites in Australia and Europe using a two-stratum (arm) design. The first stratum will utilise Zantrene as a high dose, single agent treatment over 7 days in patients with extramedullary AML who are able to tolerate high intensity chemotherapy, followed by one or more cycles of consolidation treatment using Zantrene in combination with Ara-C, a standard of care AML drug.

The second stratum will use Zantrene as a low dose FTO-targeted agent in combination with the oral hypomethylating agent, ASTX727, for MDS or AML patients unwilling, or unable to tolerate high intensity chemotherapy. Published preclinical data from City of Hope Hospital / Beckman Research Institute by Professor Chen's Laboratory identified that FTO inhibition synergized with decitabine in leukaemic cells[3]. Subsequent preclinical work by Race in collaboration with the Verrill's Laboratory validated these findings in the EMD *in vivo* setting. Using a mouse model of EMD AML, A/Prof Verrills demonstrated that optimal dosing of decitabine and Zantrene is able to synergistically target extramedullary AML tumours as well as AML lesions in the bone marrow and spleen (ASX Announcement: 17 March 2022).

The trial primary endpoint will be complete response (CR) and complete response with incomplete haematological recovery (CRi), with the clinical aim of bridging the patient to an allogeneic hematopoietic stem cell transplant (Stratum 1), and safety and tolerability of the decitabine/Zantrene regimen (Stratum 2). Key secondary endpoints include safety and tolerability of Zantrene, overall and event-free survival, and the correlation of FTO expression or other biomarkers with response to treatment.

Indicative Timelines and Reporting

The trial is expected to take 36 to 40 months with full patient recruitment completed over approximately 18 months.

This trial is open label in nature, so patient outcome results are obtained soon after patients are treated. We intend to announce progress updates on the trial on a regular basis, but not at the individual patient level. The first patient is expected to be recruited soon after site initiation.

RACE ONCOLOGY

Clinical Trial Summary

Study Title	An Open-label Two Strata Study of High Dose Bisantrene in Combination with Cytarabine Arabinoside (Ara-C) or Low Dose Bisantrene in Combination with Oral Decitabine/Cedazuridine for the Treatment of Leukemia Patients with Extramedullary Disease. BISECT (*BI*S*ECT*: *BI*Santrene *E*xtramedullary *C*hemo*T*herapy)
Phase of Development	Phase 1b with Phase 2 dose expansion
Active Ingredient	Bisantrene dihydrochloride (Zantrene®)
Study Description	BISECT: A two-stratum trial of Zantrene in patients with extramedullary AML, MDS or CMML diagnosed by ^{18}F-FDG PET/CT imaging.
Principle Investigator	A/Prof Anoop Enjeti
Sponsor	Race Oncology
Indication/population	Adult men and women ≥18 years of age with AML, MDS or CMML presenting with non-CNS extramedullary disease.
Number of Subjects	**Stratum 1:** up to 30 patients **Stratum 2:** up to 10 patients (dose escalation stage); up to additional 20 patients in the expansion stage
Study Period	36 – 40 months
Study Design	A two strata open-label non-randomized study of high dose bisantrene treatment given as a monotherapy induction and in combination with Ara-C as consolidation (Stratum 1) and lower dose bisantrene in combination with oral decitabine/cedazuridine (ASTX727) (Stratum 2) in patients with extramedullary AML, or high risk MDS and CMML. As the patient population is considered to have no existing treatment options, a comparator arm will not be used.
Statistical methods	Bayesian Optimal Interval (BOIN) model-based design based on observed response rate of 30% for R/R AML where the true response rate is expected to be <20% with a 90% power.
End Points	**Primary (Stratum 1):** Achievement of a complete response (CR) or complete response with incomplete hematological recovery (CRi). **Primary (Stratum 2):** Tolerability and safety. **Key Secondary:** Achievement of a PET/radiologic overall response, i.e. complete or partial metabolic response, after cycles 1, 2 and 4 (Stratum 1) and after cycles 4, 6, 9 and 12 (Stratum 2). **Other Secondary:** number of patients bridged to transplant and time to transplant (Stratum 1), pharmacokinetics, FTO and other biomarker status, event free survival, overall survival
Participating Centres	Up to 10 sites in Australia and Europe.

References

1. Stölzel, F., Lüer, T., Löck, S., Parmentier, S., Kuithan, F., Kramer, M., et al. (2020). The prevalence of extramedullary acute myeloid leukemia detected by 18FDG-PET/CT: final results from the prospective PETAML trial. *Haematologica*, *105*(6), 1552–1558.

2. www.leukaemia.org.au/blood-cancer-information/types-of-blood-cancer/myelodysplastic-syndromes/

3. Su, R. *et al.* (2018). R-2HG Exhibits Anti-tumor Activity by Targeting FTO/m6A/MYC/CEBPA Signaling. *Cell* 172, 90-105.e23.

-ENDS-

About Race Oncology (ASX: RAC)

Race Oncology is an ASX listed precision oncology company with a Phase 2/3 cancer drug called Zantrene®.

Zantrene is a potent inhibitor of the Fatso/Fat mass and obesity associated (FTO) protein. Overexpression of FTO has been shown to be the genetic driver of a diverse range of cancers. Race is exploring the use of Zantrene as a new therapy for melanoma and clear cell renal cell carcinoma, which are both frequent FTO over-expressing cancers.

In breakthrough preclinical research, Race has also discovered that Zantrene protects from anthracycline-induced heart damage, while in tandem acting with anthracyclines and proteasome inhibitors to improve their ability to target breast cancer. Race is evaluating this discovery.

The Company also has compelling clinical data for Zantrene as a chemotherapeutic agent and is in clinical trial in Acute Myeloid Leukaemia (AML).

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

Learn more at www.raceoncology.com

Release authorised by:

Phil Lynch, CEO/MD on behalf

of the Race Board of Directors

phillip.lynch@raceoncology.com

Media contact:

Jane Lowe

+61 411 117 774

jane.lowe@irdepartment.com.au