ASX Announcement

Race Expands FTO Targeting Phase 1b/2a Extramedullary AML & MDS Trial to Europe

- **BISECT (RAC-006) Phase 1b/2a clinical trial of Zantrene in AML & MDS patients with extramedullary disease expanded to include five additional clinical trial sites in Italy & Spain.**
- **Addition of new sites will accelerate patient recruitment and responds to European investigator interest in both Zantrene and EMD AML & MDS.**
- **A revised clinical support contract which now covers the extended European trial has been signed with global Clinical Research Organisation, Parexel.**

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08 June 2022 – Race Oncology Limited ("Race") is pleased to announce it is expanding the FTO-targeted BISECT (RAC-006) clinical trial in extramedullary Acute Myeloid Leukaemia (EMD AML) and Myelodysplastic Syndromes (MDS) to include five additional trial sites in Spain and Italy and has signed a new clinical support agreement with global Clinical Research Organisation, Parexel International to support the additional trial monitoring activities.

BISECT (RAC-006) is an open label Phase 1b/2a clinical trial in patients with EMD AML and MDS which recently received Ethics and Governance approval to commence patient recruitment at the Calvary Mater Hospital Newcastle (ASX announcements: 6 April 2022 and 12 May 2022). The intention to expand the BISECT trial to Europe was announced at the 2021 Race Annual General Meeting (ASX Announcement: 23 November 2021).

The total study costs are expected to be in the range of A$7.7 million to a maximum of A$15.4 million. The final cost is dependent on the location and number of patients screened and enrolled in the trial. Due to the adaptive (Bayesian) design of this study, the total study costs cannot be precisely determined, but are expected to be lower than the maximum cited here.

Payments will be made to Parexel throughout the study upon reaching key milestones as patients are recruited and other operational variables are achieved.

Race CMO Dr David Fuller said: *"We are pleased that we have received strong interest in our BISECT (RAC-006) EMD AML and MDS study from experienced European haematologists. These clinicians identify a significant unmet need for the treatment of EMD AML and MDS and want to be actively involved in EMD clinical research. We look forward to activating these sites once we have cleared the necessary European Regulatory and Ethics approval process."*

Race CEO & MD Phillip Lynch said: *"This study supports our Pillar 3 FDA registration ambitions and builds on Zantrene's historical safety and efficacy in AML. The clinical use of*

Zantrene using superior drug combinations offers hope to patients with difficult to treat forms of AML and MDS."

Extramedullary AML

Extramedullary AML occurs when leukaemia spreads from the bone marrow and forms solid tumours in tissues such as the skin, breast, kidney, brain, or other organs. 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. There are more than 10,000 patients diagnosed with MDS each year in the USA, which is approximately half the rate of AML.

Clinical Trial Design

This open label Phase 1b trial with a Phase 2a dose expansion phase will recruit up to 60 patients with ^{18}F-FDG PET/CT imaging-identified extramedullary AML at 10 clinical sites 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 of Zantrene in combination with Ara-C, a standard of care 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 (Los Angeles, California), by Professor Chen's Laboratory identified that inhibition of FTO synergizes with decitabine to better kill AML cells[3]. Subsequent preclinical work by Race in collaboration with the Verrills' Laboratory (Newcastle, Australia) validated these findings in the EMD setting. Using a mouse model of EMD AML, Associate Professor Verrills demonstrated that optimal dosing of decitabine and Zantrene can 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.

Full details of the trial will be published on www.clinicaltrials.gov.

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., Dong, L., Li, Y., Gao, M., Han, L., Wunderlich, M., et al. (2020). Targeting FTO Suppresses Cancer Stem Cell Maintenance and Immune Evasion. *Cancer Cell*, *38*(1), 79–96.e11.

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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 Acute Myeloid Leukemia Patients with Extramedullary Disease. BISECT (*BI*S*ECT* (*BI*S*antrene E*xtramedullary *C*hemo*T*herapy)
Phase of Development	Phase 1b with Phase 2 dose expansion
Active Ingredient	bisantrene dihydrochloride (Zantrene)
Study Description	A two-stratum trial of Zantrene in patients with extramedullary AML or MDS and 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 or MDS 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 without 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 AML where the true response rate is expected to be <20% applying a 90% power.
End Points	**Primary (Stratum 1):** Achievement of a complete response (CR) or complete response with incomplete count 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	10 sites in Australia & Europe

Q&A

Why was Parexel chosen as the CRO to support this trial?

Parexel has the global reach and experience to support this complex trial, both in Australia and internationally. Importantly for Race, Parexel has a specialised division dedicated to supporting and understanding the needs of small and medium sized biotech companies.

What is ASTX727 and why was it chosen for the trial?

ASTXZ727 (trademark INQOVI®) is an oral formulation of decitabine, a nucleoside metabolic inhibitor, and cedazuridine, a cytidine deaminase inhibitor and has been approved by the FDA for treatment of adult patients with MDS. It is currently in late-stage clinical trials for AML patients. Astex Pharmaceuticals will provide ASTX727 free of charge to Race for use in Australia, Italy, Spain, Germany and the USA. Additional countries may be included, subject to agreement with Astex.

Why run this trial in both Australia and Europe?

Three reasons – cost, control and speed. Australia remains an attractive location to run early stage trials with excellent clinical trial infrastructure and regulatory reputation. The 43.5% R&D tax rebate provides a very competitive environment as regards minimising trial costs. The inclusion of European sites will accelerate the trial and bring greater clinical attention to Zantrene's potential. European trial costs are similar to Australia. In addition (subject to approval) we plan to claim a sizable proportion of the European costs through the R&D tax rebate.

Will you need to do a separate Phase 3 trial in the US to enable FDA registration?

No. By utilising the FDA 505(b)(2) approval pathway our clinical advisors have indicated that FDA approval can be obtained using a limited number of Phase 2 trials. Race intents to run three limited Phase 2 trials in Australia, USA and the EU and seek Fast Track FDA designation and EMA label approval for this orphan indication.

Does this trial target FTO in AML & MDS patients?

Yes. This trial builds on the preclinical studies of our advisor Professor Jianjun Chen of the City of Hope Hospital. His team discovered in AML cells that inhibition of FTO synergises with the hypomethylating standard of care drug, decitabine. This combination will be clinically explored in patients unable or unwilling to tolerate high intensity chemotherapy (Stratum 2). This synergy has been confirmed in both cell cultures and animal models of EMD AML by Associate Professor Nikki Verrills of the University of Newcastle (ASX Announcement: 17 March 2022).

When can shareholders expect progress updates on the trial?

This trial is open label in nature, so patient outcome results are obtained by Race as patients are treated. We intend to announce progress updates on a regular basis, but not at the individual patient level.

-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

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