ASX Announcement

Race Submits Human Ethics Application to Commence Phase 2 Extramedullary AML & MDS Trial

- **Study follows the Phase 2 trial of Zantrene® conducted at Chaim Sheba Medical Center which reported promising results in patients with extramedullary AML**
- **Underpins future registration trials in the USA and EU with the aim of achieving orphan drug approval for Zantrene for the treatment of AML and MDS**
- **Study is led by Associate Professor Anoop Enjeti (Calvary Mater Hospital, Newcastle) with the support of the Contract Research Organisation, Parexel.**

---

1 November 2021 – Race Oncology Limited ("Race") is pleased to announce it has submitted the first human ethics application to the Hunter New England Human Research Ethics Committee (NSW, Australia) seeking approval to commence an open label Phase 2 clinical trial of Zantrene (bisantrene dihydrochloride) in patients with extramedullary Acute Myeloid Leukaemia (AML) or Myelodysplastic Syndromes (MDS).

This trial (named BISECT) will be led by Associate Professor Anoop Enjeti, Director of Haematology at the Calvary Mater Newcastle and John Hunter Hospitals and is designed to use 10 high volume MDS/AML referral sites with all sites expected to be active by Q3 CY 2022. Dr Enjeti is a highly experienced clinical haematologist, having designed and led more than 25 clinical trials and is the co-chair of the MDS/AML working party for the Australasian Lymphoma and Leukaemia Group (ALLG) for Cooperative Clinical Trials.

This open label Phase 2 trial will recruit up to 60 patients with extramedullary AML or MDS using a two-stratum (arm) design. The first stratum will utilise high dose Zantrene over 7 days followed by one or more cycles of consolidation treatment of Zantrene in combination with cytarabine arabinoside (Ara-C).

The second stratum builds on work from the Chen Laboratory, City of Hope, which identified that Zantrene is able to synergize with decitabine to provide increased efficacy in mouse models of AML[1,2]. This stratum will use low dose Zantrene targeting FTO in combination with the oral hypomethylating agent, ASTX747 (decitabine and cedazuridine) for patients unable to tolerate high intensity chemotherapy. This stratum has been expanded to include both extramedullary AML and MDS patients.

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[3]. 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.

A Phase 2 clinical trial of Zantrene in relapsed or refractory (r/r) AML patients by a team led by Professor Arnon Nagler of the Chaim Sheba Medical Center, Israel reported a 100% clinical response rate (4/4 patients) in those patients with the extramedullary form of this deadly cancer (ASX announcement: 16 June 2020).

Myelodysplastic Syndromes (MDS)

MDS are a group of blood cancers which affect the production of normal blood cells in the bone marrow. These include chronic myelomonocytic leukaemia (CMML), juvenile myelomonocytic leukaemia (JMML), atypical chronic myeloid leukaemia (aCML) and myelodysplastic/ myeloproliferative neoplasms unclassifiable (MDS/MPN)[4].

MDS has a very high risk (1 in 3) of the patient progressing to 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 2 trial 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, ASTX747 for MDS/AML patients unable to tolerate high intensity chemotherapy. Published preclinical data from the City of Hope Hospital by Professor Chen's Laboratory identified that Zantrene is able to synergize with decitabine[2]. In mouse models of AML the combination provided improved therapeutic efficacy with, lower toxicity compared to when either drug was used alone[3].

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

Indicative Timelines

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

A/Prof Anoop Enjeti said "*I am delighted to be involved with this important and novel study for patients with extramedullary AML and MDS which - due to improvements in diagnostic imaging - has been recognised to occur in up to 22% of AML patients. There is currently no agreed standard treatment for this patient population and this is one of the first therapeutic*

trials to focus on this important disease area. This study will improve our knowledge of extramedullary AML and hopefully result in a new treatment approach."

Race CMO Dr David Fuller said *"We are excited to commence this important study that explores treatment for a poorly served population of AML and MDS patients. This is a novel study design and the use of Zantrene in both high and low dose levels is unique. The high dose stratum extends our legacy AML credentials, while the low dose represents the start of our FTO targeted clinical program."*

Race CEO & MD Phillip Lynch said: *"This study supports our Pillar 3 registration ambition to see Zantrene's historical safety and efficacy in AML demonstrated with superior drug combinations that may benefit patients who remain challenged by initial treatment failures. It is pleasing to be able to open up this trial to MDS patients who are equally in need of new improved treatment options."*

Clinical Trial Summary

Study Title	An open label Phase 2 study of high dose bisantrene with cytarabine arabinoside (Ara-C) or low dose bisantrene with oral decitabine for treatment of Acute Myeloid Leukemia patients with extramedullary disease (BISECT)
Phase of Development	Phase 2
Active Ingredient	Zantrene® (bisantrene dihydrochloride)
Study Description	A two-stratum trial of Zantrene in patients with extramedullary AML or MDS 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:** 4 -10 patients (dose escalation stage); up to 30 patients in the expansion stage
Study Period	36 – 40 months
Study Design	A two strata Phase 2, open-label 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 (ASTX747) (Stratum 2) in patients with extramedullary AML or MDS. 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 RR 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. **Other Secondary:** FTO and other biomarker status, event free survival, overall survival
Participating Centres	10 sites

Q&A

What is ASTX747 and why was it chosen for the trial?

ASTXZ747 (trademark INQOVI®) is a 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 /Otsaka Pharmaceuticals intends to provide ASTX747 free of charge for this trial.

Will this trial support orphan drug registration of Zantrene under the FDA 505(b)(2) pathway?

Yes. The Stratum 1 patients will be treated as per the historical Zantrene AML trials (i.e. 250 mg/m^2/day over 7 days). This trial will build the modern and historical data.

Stratum 2 may provide clinical evidence for the use of Zantrene in patients too old or ill to be able to tolerate high intensity chemotherapy.

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 with Zantrene (CS1) synergises with the hypomethylating standard of care drug, decitabine. This combination will be clinically explored in patients unable to tolerate high intensity chemotherapy (Stratum 2).

Why was the trial split into two stratums?

There is currently no standard of care treatment for the extramedullary form of AML or MDS. As more than 50% of AML patients are not healthy enough to tolerate high intensity chemotherapy, we wanted to ensure we could offer a treatment option for all patients enrolled in the trial. In addition, success with the low intensity FTO-targeted regime could potentially be an attractive alternative for healthier patients unwilling to undertake intense chemotherapy.

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 with high unmet medical need.

When can shareholders expect progress updates on the trial?

This trial is open label in nature, so patient outcome results are obtained as patients are treated. We intend to announce progress updates on a regular basis, but not at the individual patient level. The first patient is expected to begin treatment soon after human ethical approval is obtained.

References

1. Prof Chen recently joined Race's Scientific Advisory Board (ASX Announcements: 16 April 2021).

2. 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.

3. 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.

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

-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. The Company also has compelling clinical data for the use of Zantrene 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 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