ASX Announcement

Race Executes Contract to Commence Phase 2 Extramedullary AML Trial

- **Contract Research Organisation Parexel has been appointed to support an Australian trial of Bisantrene in Acute Myeloid Leukemia (AML) patients with extramedullary disease**
- **The study led by Associate Professor Anoop Enjeti will underpin future Phase 2/3 trials in the USA and EU with the aim of achieving orphan drug approval for Bisantrene for the treatment of extramedullary AML. First patient is expected to be treated Q4 CY 2021**
- **Study follows the investigator-initiated Phase 2 clinical trial of Bisantrene, conducted at Israel's Sheba Medical Center which reported promising results in patients with extramedullary AML in June 2020**

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2 June 2021 – Race Oncology Limited ("Race") is pleased to announce it has appointed the Contract Research Organisation (CRO), Parexel International, to support an open label Phase 1/2 clinical trial in patients with relapsed or refractory (r/r) extramedullary Acute Myeloid Leukemia (AML).

The trial will be led by Principal Investigator Associate Professor Anoop Enjeti, Director of Haematology at the Calvary Mater Newcastle and John Hunter Hospitals.

Dr Enjeti is a highly experienced clinical haematologist having designed and led more than 25 clinical trials. Dr Enjeti is the co-chair of the MDS/AML working party for the Australasian Lymphoma and Leukemia Group (ALLG) for Cooperative Clinical Trials.

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.

A recent Phase 2 clinical trial in r/r AML patients treated with Bisantrene by a team led by Prof Arnon Nagler of the Chiam 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).

Clinical Trial Design

This open label Phase 1/2 trial will recruit approximately 60 patients with ^{18}F-FDG PET/CT imaging-identified extramedullary AML at 10 clinical sites across Australia using a two-stratum (arm) design. The first stratum will utilise Bisantrene 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 Bisantrene in combination with azacitidine, a standard of care drug.

The second stratum will use Bisantrene as a low dose FTO-targeted agent in combination with the oral hypomethylating agent, Inqovi® (decitabine and cedazuridine) for patients unable to tolerate high intensity chemotherapy. Published preclinical data from the City of Hope Hospital by Prof Chen's team identified that Bisantrene 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 for both strata 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. Key secondary endpoints include safety and tolerability of Bisantrene, overall and event-free survival, and the level of FTO expression with response to treatment.

Indicative Costs and Timelines

The trial is expected to take 36 to 40 months to complete with full patient recruitment over approximately 18 months. Treatment of the first patient is targeted for Q4 CY 2021, subject to human ethics approval of the study and patient recruitment.

Race will pay Parexel an initial fee of $1.11 million under the Start Up Agreement (SUA). Additional payments will be made to Parexel under a Master Service Agreement (MSA) throughout the study upon reaching key milestones and will depend on the number of patients recruited and other operational variables.

Due to the adaptive nature of this study, the total study costs cannot be determined at this stage.

Race CSO Daniel Tillett said: *"We are excited to begin this study with the twin aims of exploring the use of Bisantrene to treat FTO overexpressing cancers and bring it to market as a heart safer orphan drug treatment for AML. This trial will be transformational for Race and our shareholders."*

Race CEO & MD Phillip Lynch said: *"This study supports our Pillar 3 registration ambition to see Bisantrene's historical safety and efficacy in AML demonstrated with superior drug combinations that may benefit patients who remain challenged by initial treatment failures."*

Clinical Trial Summary

Study Title	An open label Phase 1/2 study of high dose Bisantrene with cytarabine arabinoside (Ara-C) or low dose Bisantrene with oral decitabine for treatment of relapsed or refractory Acute Myeloid Leukemia (r/r AML) patients with extramedullary disease (BISECT)
Phase of Development	Phase 1/2
Active Ingredient	Bisantrene dihydrochloride
Study Description	A two stratum trial of Bisantrene in patients with extramedullary AML 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 relapsed and/ or refractory Acute Myeloid Leukemia (R/R AML) presenting with non-CNS extramedullary disease.
Number of Subjects	Stratum 1: up to 30 patients Stratum 2: 4 -10 patients (dose escalation); up to 30 patients in the expansion phase
Study Period	36 – 40 months
Study Design	This is 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 decitabine (Inqovi®) (Stratum 2) in patients with extramedullary r/r AML. As the patient population is considered relapsed and/or refractory to existing treatments, 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: Achievement of a morphological overall response, i.e. complete response (CR) or complete response with incomplete count recovery (CRi), after commencing cycle 1 and before commencement of cycle 2. 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 status, event free survival, overall survival
Participating Centres	10 ALLG participating sites across Australia
Start Date	First patient In: Q4 CY2021
End Date	Last Patient In (anticipated): Q2 CY2023

Q&A

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

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

Does this trial target FTO in AML 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 Bisantrene (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 stratum?

There is currently no standard of care treatment for the extramedullary form of AML. As approximately 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.

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 biotech companies. Race believes that Parexel will be able to support Race's aspirations for the regulatory approval of Bisantrene in both the USA and EU markets in a cost and time efficient manner.

Why run this trial in Australia and not the USA if the aim is to gain FDA approval?

Three reasons – cost, control and speed. Australia is an attractive location to run early stage trials with excellent trial infrastructure and regulatory reputation. The 43.5% R&D tax rebate provides a very competitive environment as regards minimising trial costs. The results from this trial will be used in the regulatory approval process in the USA and EU allowing the trial size and cost in these more expensive jurisdictions to be minimised.

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.

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 in Q4 CY 2021.

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

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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About Parexel

Headquartered near Boston, Massachusetts and in Durham, North Carolina, Parexel has over 16,000 employees, with offices that support clients in over 100 countries around the world.

With integrated consulting expertise, Parexel provides global Phase I-IV clinical research programs designed with the end in mind to navigate regulatory and market access hurdles more smoothly and cost-effectively.

About Race Oncology (ASX: RAC)

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

Bisantrene 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 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.

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