ASX Announcement

Race Executes Contract to Commence Phase 1b/2 AML Trial at Chaim Sheba Israel

- **Phase 1b/2 relapsed/refractory (R/R) Acute Myeloid Leukemia (AML) trial will use Bisantrene drug combination with known superior efficacy in AML cells**
- **The study will be led by Professor Arnon Nagler of the Chaim Sheba Medical Center, Israel, who conducted the Phase 2 single agent Bisantrene R/R AML trial which demonstrated a 40% clinical response**
- **Trial has human ethics approval with first patient expected to be treated in Q3 CY 2021**

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22 June 2021 – Race Oncology Limited ("Race") is pleased to announce it has executed an agreement with The Sheba Fund for Health Services and Research, Chaim Sheba Medical Center to commence a Phase 1b/2 trial in relapsed/refractory Acute Myeloid Leukaemia (R/R AML). This investigator-led trial will be supervised by Professor Arnon Nagler, who was the Principal Investigator on the Phase 2 investigator-initiated trial which reported an impressive 40% response rate as a single agent in R/R AML (ASX Announcement: 16 June 2020).

This Phase 1b/2 trial will use Bisantrene in a novel three drug combination which in preclinical studies showed superior efficacy in AML cells (ASX Announcement: 10 May 2021). The trial has received human ethics approval and the first patient is expected to be treated in quarter 3 CY 2021.

The trial will run in parallel with a separate Australian Phase 2 trial in patients with extramedullary AML that is expected to begin treating patients in Q4 CY 2021 (ASX Announcement: 2 June 2021).

Both trials form key components of Race's '3 Pillar' strategy announced at the 2020 AGM (ASX Announcement: 30 November 2020).

Relapsed or Refractory Acute Myeloid Leukemia

Primary refractory or relapsed acute myeloid leukemia is associated with poor prognosis and remains a major therapeutic challenge. Primary refractory AML is defined by the absence of complete remission (CR), manifested by blast count of ≥5% in bone marrow after one or two cycles of intense induction chemotherapy.

Up to 30% of adults with newly diagnosed AML fail to achieve CR after two courses of intensive chemotherapy.

Even when CR is achieved through intense chemotherapy, approximately half of the younger and 80% of the older patients relapse. In both clinical situations, refractory

and/or relapsed AML, active disease remains a major therapeutic challenge despite recent advances.

Clinical Trial Design

An open-label, Phase 1b/2 study of intravenous FluCloXan (Fludarabine, Clofarabine, Bisantrene dihydrochloride (Xan)) in cohorts of adult patients with R/R AML using a Simon's 2-stage design: a Phase 1b lead-in dose escalation stage to establish the maximum tolerated dose (MTD) or recommended Phase 2 dose (RP2D) of FluCloXan and a Phase 2 expansion stage to determine efficacy and confirm safety of the FluCloXan regimen at the RP2D in up to 17 subjects.

Phase 1b, Dose-Escalation (Lead-in Stage)

A two-cohort dose escalation schema using a 3 + 3 design will be employed.

Cohort 1 will enroll three subjects to receive the FluCloXan regimen for four consecutive days. If no dose limiting toxicities (DLTs) have occurred in the first three subjects by day 30 of their first cycle of treatment, then dose escalation to Cohort 2 will occur.

Phase 2, Expansion (Efficacy Stage)

Up to 17 subjects will be enrolled into a Phase 2 expansion efficacy cohort using a 2-stage Simon design. Initially, 9 subjects will be enrolled and treated with the recommended dose of FluCloXan regimen determined in Stage 1. If no subject responds according to the response criteria outlined in the European Leukemia Net (ELN) guidelines, in the first 9 subjects, the study will be terminated for futility. If at least one subject shows a response, 8 more subjects will be enrolled and treated. If three or more of subjects treated in Stage 2 respond, the null hypothesis can be rejected.

Efficacy assessments will be based on bone marrow examination at a minimum of two time points on Day 21 and on Day 30. A further bone marrow examination may be performed on Day 42 at the investigator's discretion, based on the patient's disease and performance status and/or on peripheral blood hematology results during the treatment course and between Day 21 to 42.

Treatment will be terminated upon any sign of progressive/recurrent disease and/or referral for starting pre-transplant conditioning therapy for (allogeneic) stem cell transplantation.

Subjects who do not progress or experience any dose limiting toxicities may receive a second course of treatment for the same duration as in their first cycle.

All subjects will be actively followed up every three months for a further 12 months following completion of Cycle 1 for disease free survival (DFS) and overall survival (OS).

While the focus of this trial is not aimed at targeting FTO driven cancers, the FTO expression status will be examined for each patient as part of an exploratory trial endpoint.

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 Q3 CY 2021, subject to patient recruitment. Given its open-label status, Race expects that data will be reported at interim points throughout the trial.

Race will pay Chaim Sheba a maximum fee of USD $668,739 over the study's life. Payments will be made to Chaim Sheba throughout the study upon reaching key milestones with the final trial cost dependent on the number of patients recruited and other operational variables.

Chaim Sheba Professor Arnon Nagler said: "*Relapsed and refractory Acute Myeloid Leukaemia remains a significant challenge for patients and although there have been therapeutic advances in recent years, clinical outcomes are often suboptimal. This trial follows on from the Bisantrene monotherapy study sponsored by the Sheba Medical Centre, which reported promising results last year. In this new trial, we're using a combination approach as identified by MD Anderson's Professor Borje Andersson and published recently in the Journal of Clinical and Experimental Oncology. We hope to see that this combination approach will provide synergistic therapeutic benefit and enable patient dosing at lower levels than where either drug is used on its own.*"

Race CMO Dr David Fuller said: *"We are delighted to be extending our successful collaboration with Prof Nagler and the team at Chaim Sheba using this novel combination approach for relapsed or refractory Acute Myeloid Leukaemia which remains an area of high unmet medical need. This study is an important part of our AML development plan for Bisantrene."*

Race CEO & MD Phillip Lynch said: *"This study builds on our Pillar 3 ambitions 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. We hope to see the study confirming Bisantrene's continued application as a differentiated chemotherapeutic with contemporary clinical relevance."*

Clinical Trial Summary

Study Title	An Open-label, Phase 1b/2, Two-stage, Study of Xantrene® (Bisantrene) in combination with Fludarabine and Clofarabine as Salvage Therapy for Adult Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML)
Phase of Development	Phase 1b/2
Active Ingredient	Bisantrene dihydrochloride, Fludarabine, Clofarabine (FluCloXan)
Study Description	Phase 1b/2 study of FluCloXan, in cohorts of adult patients with R/R AML using a 2-stage design: a Phase 1b lead-in dose escalation stage to establish the MTD or RP2D of FluCloXan and a Phase 2 expansion stage to determine efficacy and confirm safety of the FluCloXan regimen at the RP2D.
Principal Investigator	Professor Arnon Nagler
Sponsor	Race Oncology
Indication/population	Adult men and women 18 to 65 years of age with relapsed and/ or refractory Acute Myeloid Leukemia (R/R AML) without central nervous extramedullary disease.
Number of Subjects	Phase 1b: up to 12 patients in the dose determining phase Phase 2: up to 17 patients in the expansion phase
Study Period	36 – 40 months
Study Design	A two-cohort dose escalation schema using a standard 3 + 3 design will be employed followed by an expansion phase at the RP2D. As the patient population is considered relapsed and/or refractory to existing treatments, a comparator arm will not be used.
Statistical methods	Simon 2 stage
End Points	Primary Phase 1b Dose Escalation: number of subjects experiencing a DLT in each cohort Phase 2 Expansion: Overall Response Rate (ORR) defined as the proportion of subjects with CR and CRi between Day 30 to Day 42 Secondary: Transplant/allo-HSCT rates (for transplant/allo-HSCT-eligible subjects); Combined CR and CRi and PR response rate; Morphologic leukemia-free state (MLFS); Partial remission (PR); Stable disease (SD); Progressive disease (PD); Relapse; Disease free survival (DFS); Overall survival (OS); Time to next treatment (for transplant/allo-HSCT-ineligible subjects); Molecular mutations including FTO overexpression status
Participating Centres	1 - Chaim Sheba Medical Center, Tel Hashomer, Israel
Start Date	First patient in: Q3 CY2021
End Date	Last patient In (anticipated): Q3 CY2023

Q&A

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

No. This trial uses an optimised drug combination discovered by the MD Anderson Cancer Center under a preclinical research project sponsored by Race Oncology. While this trial will not be used for FDA registration of Bisantrene, it will potentially provide oncologists with data on an optimal drug combination to use in the clinic.

Does this trial target FTO in AML patients?

No. While the trial is not FTO directed, the FTO expression status of the patients cancers in the trial will be determined to see if response correlates with FTO expression levels.

When can shareholders expect progress updates on the trial?

Q3 2021. The trial has received human ethics approval and Trialog has drug ready to supply in Israel. Prof Nagler's team is highly skilled in treating AML and has recent experience using Bisantrene in AML patients. It is Race's expectation that the first patient should be treated in the near future subject to recruitment. The Company will be updating our shareholders on progress at key points in the trial.

Why is this trial being run in Israel and not Australia or the USA?

AML has become a very competitive area to recruit patients as many companies are pursuing development of new drugs and treatments for R/R AML. It would not be possible to recruit patients for this combination treatment in Australia before 2024/25 because of competing trials. Prof Nagler's personal experience using Bisantrene provides Race with a unique opportunity to run this trial now.

Will this trial be treating patients with extramedullary AML?

Yes. While the recently announced Australian AML trial will be exclusive to extramedullary AML patients, this trial will be open to all R/R AML patients including those with the extramedullary form of the disease. The only exception is those with CNS involvement as Bisantrene is not currently thought to cross into the brain and so would be likely be unsuitable for this patient population.

-ENDS-

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.

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