ASX Announcement

RC220 Bisantrene GLP Non-clinical Toxicology and Safety Pharmacology Program Successful

- Non-clinical toxicology and safety studies of RC220 bisantrene successfully completed by Attentive Science and Agilex Biolabs on-time and on-budget
- RC220 bisantrene demonstrated an excellent safety profile for a chemotherapeutic oncology drug, including when administered via peripheral intravenous infusion
- Complete data package supports initiation of human clinical trials using RC220 bisantrene in H2 2024 and US FDA IND application in 2025.

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26 June 2024 – Race Oncology Limited ("Race") is pleased to announce that the Good Laboratory Practice (GLP) toxicology and safety pharmacology studies have been successfully completed for RC220 bisantrene, the company's flagship formulation of bisantrene for peripheral intravenous (IV) infusion. No unexpected or unacceptable toxicities were observed, and the completed data package supports the use of RC220 bisantrene in human clinical trials.

In October 2023, Race contracted Attentive Science (USA) and Agilex Biolabs (Australia) to undertake the regulatory-standard GLP non-clinical toxicology and safety pharmacology studies required to advance RC220 bisantrene into human clinical trials (ASX Announcement: 05 October 2023). These studies aimed to: (i) demonstrate in two animal species that RC220 bisantrene is safe and amenable to administration via peripheral IV infusion in humans, and (ii) establish an acceptable starting dose for Phase I clinical studies. This GLP program has been delivered on time and on-budget.

In the GLP toxicology studies, three doses of RC220 bisantrene (low, medium and high; reflecting the expected dose-range in humans) were administered via peripheral veins and showed similar systemic effects to those seen when using the historical bisantrene formulation administered via a central line.

Examination of the animals after a four-week post-dose recovery period showed that all observed toxicities were reversible. Importantly, there were no RC220 formulation-specific adverse macroscopic or histological findings at the sites of infusion. This finding confirmed that, unlike the historical bisantrene formulation, peripheral IV administration of RC220 bisantrene was devoid of adverse infusion site or vein reactions. Safety pharmacology studies also confirmed that at all three dose-levels evaluated, RC220 bisantrene had an acceptable respiratory and cardiovascular safety profile.

Data from these studies will be used to support regulatory and ethics submissions for evaluation of RC220 bisantrene in human clinical trials, including the upcoming Phase 1a/1b trial in Australia, Hong Kong & South Korea (ASX Announcement: 20 June 2024), an investigator-sponsored Phase 1/2 AML trial and a US FDA Investigational New Drug (IND) application in 2025.

Race Chief Executive Officer, Dr Daniel Tillett commented: *"Receiving clear confirmation of the safety of RC220 bisantrene in these studies and identifying a suitable starting dose for our upcoming trial is another major milestone in bringing our new drug product to cancer patients. I congratulate and thank the Race preclinical team, Attentive Science and Agilex Biolabs for completing these studies on time and on-budget."*

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Q&A

What are the next steps to starting human clinical trials with RC220 bisantrene?

Having completed the GMP manufacturing of RC220 bisantrene (ASX Announcement: 26 March 2024) and contracting with CRO George Clinical (ASX Announcement: 20 June 2024), the next step is submission of the human ethics application in Q3 CY2024. Once ethics approval has been received, clinical site governance approval is required before site activation, with first patient recruitment forecast for late Q4 CY2024. This timeline assumes efficient processing of documents by the appropriate regulatory bodies.

Why did it take so long to generate the non-clinical GLP safety data?

The GLP studies took under 9 months to complete. This is unusually fast for non-clinical GLP toxicology and safety studies of investigational oncology drugs, as they can often take more than 12 months. The rapid progression through these studies was due to the dedication and professionalism of the Race preclinical team, Attentive Science and Agilex Biolabs. Furthermore, this work was completed on a modest budget – considerably less than expected in the industry for a new oncology drug candidate, thanks to careful planning by the Race preclinical team, Attentive Science and Agilex Biolabs.

Can we rely on animal data to know that RC220 bisantrene can be delivered via a peripheral vein in humans?

Yes. In early historical clinical trials where bisantrene was infused into the peripheral veins of patients, drug precipitation problems were observed due to the lower solubility of bisantrene at pH 7 or higher (neutral to alkaline). Bisantrene dihydrochloride solutions precipitates (crystalise) when the pH rises above pH 6 if the drug concentration is high. Since the blood of mammals (animals and humans) is close to pH 7.4, peripheral infusion resulted in a rapid, local precipitation of bisantrene in the vein, causing serious inflammation and blockage. While the precipitation problem can be overcome by using central line infusion into the aorta or heart (where high blood flow dilutes the bisantrene before it can precipitate), it is riskier and less convenient for patients and clinicians than peripheral IV infusions.

The pH-dependent precipitation of bisantrene is the same in both human and animal blood. Having found in the GLP toxicology and other studies that the RC220 bisantrene formulation doesn't precipitate when infused into the peripheral vein of animals, we are very confident that it also won't precipitate when infused into the peripheral vein of a patient.

When will the patent for RC220 bisantrene be submitted?

Soon. Race aims to maximise the value of all IP. Since patents have a limited 20-year life from the filing date, delaying filing of the patent until the composition must be disclosed (e.g. to regulatory authorities) maximises the lifetime and commercial value of the RC220 bisantrene formulation.

How can I learn more?

Race Chief Executive Officer Dr Daniel Tillett explains more in a video interview here:
https://announcements.raceoncology.com/link/DexRmP

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About Race Oncology (ASX: RAC)

Race Oncology (ASX: RAC) is an ASX-listed clinical stage biopharmaceutical company with a dedicated mission to be at the heart of cancer care.

Race's lead asset, bisantrene, is a small molecule chemotherapeutic. Bisantrene has a rich and unique clinical history with demonstrated therapeutic benefits in both adult and paediatric patients, a well characterised safety profile, and compelling clinical data demonstrating an anticancer effect and less cardiotoxicity over certain anthracyclines, such as doxorubicin.

Race is advancing a reformulated bisantrene (RC220) to address the high unmet needs of patients across multiple oncology indications, with a clinical focus on anthracycline combinations, where we hope to deliver cardioprotection and enhanced anti-cancer activity in solid tumours. Race is also exploring RC220 as a low intensity treatment for acute myeloid leukaemia.

Race is investigating the effect of bisantrene on the m^6A RNA pathway, following independent research published by the City of Hope identifying bisantrene as a potent inhibitor of FTO (Fat mass and obesity-associated protein). Dysregulation of the m^6A RNA pathway has been described in numerous peer reviewed studies as a driver of a diverse range of cancers.

Race Oncology has collaborated with Astex, City of Hope, MD Anderson, Sheba City of Health, UNC School of Medicine, University of Wollongong and University of Newcastle, and is actively exploring partnerships, licence agreements or a commercial merger and acquisition to accelerate access to bisantrene for patients with cancer across the world.

Learn more at www.raceoncology.com.

If you have any questions on this announcement or any past Race Oncology announcements, please go to the Interactive Announcements page in our Investor Hub https://announcements.raceoncology.com

Race encourages all investors to go paperless by registering their details with the Company's share registry, Automic Registry Services, at www.automicgroup.com.au.

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