ASX Announcement

Race Initiates New Collaboration to Understand Zantrene Cardioprotection Mechanism

- **Important step in understanding how Zantrene can protect the heart from chemotherapy-induced damage**
- **Collaboration will use state-of-the-art biochemical, cellular and mouse models of cardioprotection**
- **Program led by leading international cardio-oncologist Dr Brian Jensen of the McAllister Heart Institute, University of North Carolina at Chapel Hill, USA**

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2 March 2023 – Race Oncology Limited ("Race") is pleased to announce that it has begun a new collaborative research project with the University of North Carolina at Chapel Hill (USA) to uncover at the molecular level how Zantrene® protects the heart from chemotherapy. Distinguished cardiologist-scientist and cardio-oncology key opinion leader (KOL) Dr Brian Jensen will lead the project.

Understanding the molecular mechanisms of how Zantrene can mitigate the cardiotoxicity of current standard of care chemotherapies will aid the selection of optimal dosing in the clinic. Dr Brian Jensen, a cardiologist and physician-scientist with a career focus in cardio-oncology, has published widely on the mechanisms of chemotherapy-induced reductions in cardiac function, with a particular focus on the role of alpha-adrenergic receptors[1].

The project is expected to take 12 months with a budged cost of US$101,261.74.

Zantrene Protects the Heart from Doxorubicin-Induced Cardiotoxicity

Anthracyclines are some of the most effective anti-cancer treatments and are used more broadly than any other class of chemotherapeutic agent[2]. These drugs are used to treat millions of cancer patients every year, including those with leukemias, lymphomas, neuroblastoma, kidney, liver, stomach, uterine, thyroid, ovarian, sarcoma, bladder, lung and breast cancers. Clinically, the most important anthracyclines are doxorubicin, daunorubicin, epirubicin and idarubicin[3]. Although they are highly effective anti-cancer drugs, the anthracyclines cause serious and permanent damage to the heart in many patients.

Race Oncology reported that Zantrene (bisantrene) is able to protect human heart muscle cells (cardiomyocytes) from anthracycline-induced cell death (ASX announcement: 22 November 2021). Notably, Zantrene is also able to synergise with anthracyclines to better kill breast cancer cells, making it the first reported chemotherapeutic agent to show both

anticancer and cardioprotective effects. Importantly, Race confirmed that the cardioprotective effects seen in cells translated to significant protection of mouse hearts in an established model of doxorubicin-induced cardiotoxicity (ASX announcement: 30 June 2022). Based on these preclinical findings, Race is planning on undertaking both observational and interventional Phase 1/2b clinical trials of Zantrene in breast cancer patients treated with doxorubicin and cyclophosphamide (AC therapy) (ASX announcement: 9 December 2022).

Chief Scientific Officer, Dr Daniel Tillett said: *"Race is extremely pleased to be working with Dr Jensen and his world-leading cardio-oncology research group. Discovering how Zantrene protects the heart from the highly effective, but cardiotoxic, drugs like doxorubicin is critical for our aims of using its cardioprotective effects in the clinic."*

Dr Brian Jensen said: *"Understanding how therapeutics like bisantrene [Zantrene] work at the molecular level can provide crucial insights into their efficacy and potential side effects. Such investigations will enable us to develop more targeted treatments that both improve cancer outcomes and minimize cardiovascular risk. I am honoured to be part of this effort, working alongside the Race team and other collaborators, to better understand the pharmacology of bisantrene and to pave the way toward new cardioprotective therapies."*

Chief Executive Officer, Damian Clarke-Bruce said: *Deeply understanding the cardioprotective mechanism of action of Zantrene is a critical aspect of our pharma partnering discussions.*

The preclinical discovery that Zantrene in combination with chemotherapy can protect the heart while better treating cancer has the potential to significantly change standard of care cancer treatment and have a meaningful impact on the lives of patients."

References

1. Beak JY, Huang W, Parker JS, Hicks ST, Patterson C, Simpson PC, Ma A, Jin J, Jensen BC. An oral selective alpha-1A adrenergic receptor agonist prevents doxorubicin cardiotoxicity. *JACC: Basic Transl. Sci.* (2017), 2(1):39– 53.

2. Weiss RB. The anthracyclines: will we ever find a better doxorubicin? *Semin Oncol.* (1992), 9(6):670-86.

3. Venkatesh P, Kasi A. Anthracyclines. (2021) In: StatPearls. Treasure Island (FL): StatPearls Publishing.

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About Dr Brian Jensen

Brian Jensen is an Associate Professor of Medicine and Pharmacology at the University of North Carolina School of Medicine. Dr Jensen is a physician-scientist with a clinical and investigative focus on heart failure. He has clinical certification in Advanced Heart Failure/Transplantation and directs the UNC Cardio-oncology clinic. His laboratory uses mouse and cell culture models to study the molecular response to myocardial injury with a focus on mitochondrial function and cellular metabolism.

Dr Jensen received his B.A. in Philosophy from Pomona College and his MD (Highest Honours and Distinction) from the University of North Carolina School of Medicine. He completed his Internal Medicine residency at Brigham and Women's Hospital (Harvard School of Medicine) and his Cardiovascular Medicine fellowship at the University of California, San Francisco, where he was a postdoctoral research fellow studying cardiomyocyte hypertrophy and adrenergic receptor biology in Paul Simpson's lab. Dr Jensen has more than 55 publication with an h-index of 31.

https://www.med.unc.edu/pharm/directory/brian-jensen-md/

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.

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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