ASX Announcement

Race Initiates FTO Melanoma Preclinical Study

- Race enters collaborative preclinical research program with The University of Newcastle to explore use of Bisantrene as a novel FTO directed treatment for melanoma
- Research designed to identify drug combinations that improve upon current standard of care melanoma treatment with focus on immune checkpoint resistance
- Project is Race's first step under Pillar 1 of its Three Pillar strategy, designed to demonstrate Bisantrene's potential in inhibiting FTO in humans

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19 March 2021 – Race Oncology Limited ("Race") is pleased to announce that it has entered into a collaborative preclinical research program with The University of Newcastle. Eminent melanoma cancer researchers, Professor Xu Dong Zhang and Associate Professor Lei Jin will lead the project.

The aim of this project is to explore the use of Bisantrene as a novel treatment for melanoma using cellular and mouse models to identify drug combinations that improve melanoma treatment, with a focus on treatment resistant cancer patients.

Bisantrene has recently been identified as a potent targeted inhibitor of the Fat Mass and Obesity associated protein (FTO)[1]. Previous studies have observed that FTO is over produced in approximately 50% of metastatic melanoma cancers[2] and the inhibition of FTO can overcome PD-1 immune checkpoint resistance in mouse models of melanoma[2,3]. While there have been major improvements with melanoma treatment in recent decades, the five-year survival rate for advanced melanoma is still as low as ~25%[4].

Race is pursuing Bisantrene therapies targeted at inhibiting FTO in both melanoma and clear cell renal cell carcinoma, as part of its Three Pillar strategy (ASX Announcement 30 Nov 2020). This work could lead to new melanoma treatments with improved safety and efficacy especially in treatment resistant cancers.

The results of this study will support Phase II human trials of a Bisantrene in melanoma, currently scheduled to begin in Australia in early 2022.

This project is to start immediately with results expected to be reported over the coming 12 months.

Chief Scientific Officer, Dr Daniel Tillett said: *"This is an exciting development for Race and we are looking forward to collaborating with Prof Zhang and Jin on this transformational project. Recent scientific developments have identified Bisantrene as a potent targeted agent of FTO which offers the possibility of novel treatment options for patients with drug resistant melanomas that can rapidly be translated into the clinic."*

Melanoma remains one of the most dangerous cancers, with 7000 deaths in the USA and 1,500 deaths recorded in Australia in 2020[4].

1. 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.

2. Yang, S., Wei, J., Cui, Y.-H., Park, G., Shah, P., Deng, Y., et al. (2019). m6A mRNA demethylase FTO regulates melanoma tumorigenicity and response to anti-PD-1 blockade. *Nature Communications*, *10*(1), 1131–14.

3. Li, N., Kang, Y., Wang, L., Huff, S., Tang, R., Hui, H., et al. (2020). ALKBH5 regulates anti-PD-1 therapy response by modulating lactate and suppressive immune cell accumulation in tumor microenvironment. Proceedings of the National Academy of Sciences, 117(33), 20159–20170.

4. www.cancer.net/cancer-types/melanoma/statistics

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About Professor Xu Dong Zhang

One of the world's most eminent researchers in skin cancer, Professor Zhang is the Head of the Melanoma Research Laboratory at the University of Newcastle and Calvary Mater Newcastle Hospital, Professor Zhang has spent the past 15 years searching for a cure for metastatic melanoma. He is the Co-Director of the Priority Research Centre (PRC) for Cancer at the University of Newcastle and Deputy Director of the Cancer Program of the Hunter Medical Research Institute (HMRI).

In 2013, Professor Zhang discovered a key molecule called PIB5PA which is essential for the normal functioning of cells and is commonly reduced in melanoma cells.

Professor Zhang has established important collaborations with several Top 20 Universities in China, including the University of Science and Technology of China, the Sichuan University, and the Sun Yat-sen University. He also holds honorary professorships at a number of other institutions in China, including the Anhui Medical University, the Fourth Military Medical University, and the Shanxi Cancer Hospital and Shanxi Cancer Institute. He is an honorary director of the Cellular and Molecular Biology Laboratory at the Shanxi Cancer Hospital and Shanxi Cancer Institute.

His global reputation is reflected by his H Factor of 31, his invited presentations in many international and national conferences, and his appointment on the editorial board for a number of scientific journals. Prof Zhang has published to over 120 research papers and received in excess of $14 million in grant funding

About Associate Professor Lei Jin

Associate Professor Lei Jin has pioneered studies on overcoming resistance mechanisms of melanoma and colorectal cancer cells to chemotherapy, which has provided a number of insights into resistance mechanisms of melanoma and colorectal cancer to cell death induced by various treatments. He was also among the first to show that p53 (a common tumour suppressor gene) played a pro-survival role in melanoma cells upon endoplasmic reticular stress (a type of cellular 'stress' that occurs in many types of cancer).

More recently, A/Prof Jin has become a leading figure in investigating the roles of non-coding RNAs in regulating cancer cell survival, proliferation, and metabolism. He has published research articles in high-impact journals including Nature Cell Biology, PNAS, Nature

Communications, Cancer Research and Oncogene. He was awarded Hunter Translational Cancer Research Unit Fellowship in 2013 and a highly competitive Cancer Institute NSW Early Career Fellowship in 2014 and Career Development Fellowship in 2017.

About Race Oncology (ASX: RAC)

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

Bisantrene is a potent inhibitor of the Fat mass and obesity associated (FTO) protein. Over-expression 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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