# ASX Announcement

## Race investor briefing and updated presentation

- **Updated investor presentation available which covers recent progress and coming milestones**
- **Investor briefing to be held online on 13 May at 10:30am AEST**

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**5 May 2021** – Race Oncology Limited (ASX: RAC) (**Race**) is pleased to release an updated investor presentation and invite investors to join a special online investor briefing.

### Updated presentation

The attached updated presentation includes:

- An update on the Company's Three Pillar strategy and recent related highlights
- Updates to the Board and extended team slides
- Additional information on the FTO pathway (Pillar 1) for Bisantrene, including relevant comparators
- Coming milestones and the expected activity timeline for Bisantrene's continued development

### Investor briefing invitation

Investors are invited to attend a special briefing session where Managing Director and CEO, Phillip Lynch and CSO and Executive Director, Dr Daniel Tillett will discuss progress on the Company's Three Pillar strategy, as well as the recently announced capital raise and Bonus Options Issue. Details as follows:

| | |
|---|---|
| **When** | Thursday 13 May from 10:30am AEST |
| **Register** | https://us02web.zoom.us/webinar/register/WN_04Io2ZClRrSvGsfoZGlW2Q |
| **Q+A** | Investors will be invited to ask questions during the session. |

-ENDS-

**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.


**Release authorised by:**

Phil Lynch, CEO/MD on behalf

of the Race Board of Directors

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RACE ONCOLOGY

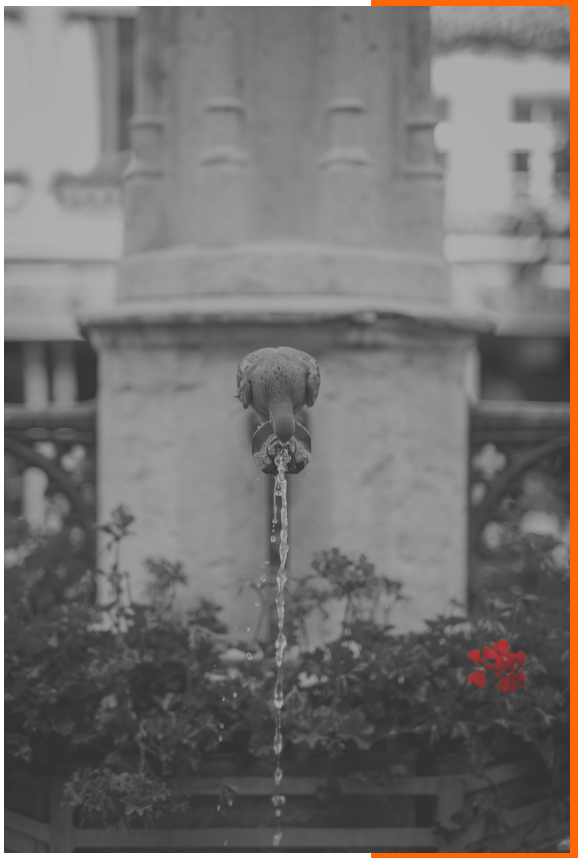
# INVESTOR UPDATE
# 30 APRIL 2021

RACE ONCOLOGY

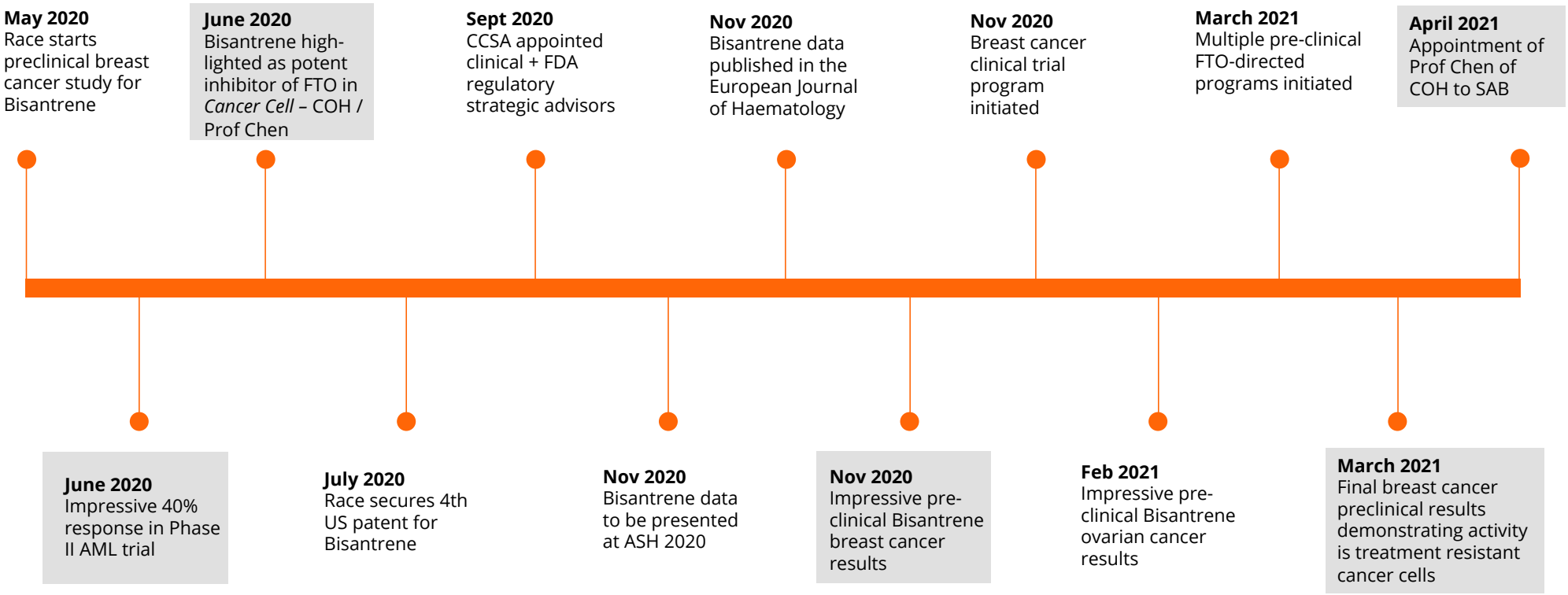
# PRECISION ONCOLOGY

# CORPORATE SNAPSHOT

| ISSUED CAPITAL | |
|---|---|
| Shares | 141.1m |
| Options | 20.9m |
| Shareholders (30 April 2021) | 9133 |
| MARKET CAPITALISATION | |
| Share price (30 April 2021) | $3.07 |
| Market value (30 April 2021) | $433m |
| Cash (31 March 2021) | $6.47m |
| Enterprise value | $426.5m |
| SIGNIFICANT SHAREHOLDERS | |
| Daniel Tillett (Director & CSO) | 9.6% |
| Bill Garner (Founder) | 7.4% |
| Merchant Opportunities Fund | 6.0% |



# 2020-2021 A PIVOTAL PERIOD FOR BISANTRENE



# THREE HEROES

1. The drug
2. The team
3. The three pillars strategy

# 1. THE DRUG. BISANTRENE

Bisantrene is an anti-cancer agent developed in the 1980s by Lederle Laboratories

It was tested in >40 human trials; showed excellent activity in leukemia, breast and ovarian cancer and was approved in France for Acute Myeloid Leukemia (AML)

Since acquiring Bisantrene, Race has

| | | | |
|---|---|---|---|
| Successfully manufactured the GMP drug | Built a strong patent position | Received US Orphan Drug designation (7 years exclusivity) | Secured Rare Paediatric Disease designation and Priority Review Voucher designation |

- Positive single agent R/R AML trial in Israel with a 40% response rate – July 2020
- Released pre-clinical breast cancer data providing evidence to advance into human clinical trials as a potentially safer breast cancer treatment option

# 2. THE TEAM SEASONED BOARD AND EXECUTIVE, KEY OPINION LEADERS

## BOARD

*Dr John Cullity,*
*Non-Executive Chairman*

*Mr Phil Lynch,*
*CEO and Managing Director*

*Dr Daniel Tillett,*
*CSO and Executive Director*

*Mary Harney*
*Non-Executive Director*

## MANAGEMENT

*Mr Phil Lynch,*
*CEO and Managing Director*

*Dr Daniel Tillett, PhD*
*CSO and Executive Director*

*Dr David Fuller*
*Chief Medical Officer*
*(commencing 1 July 2021)*

*Dr Marinella Messina, PhD*
*Clinical Program Director*

# 2. THE TEAM. EXTENDED RACE TEAM

| Business Advisors & Consultants | |
|---|---|
| Accountants | Onyx Corporate Pty Ltd |
| Contracts Lawyer | Elevate Legal |
| IP Manager | Roberts Foster LLP |
| Patent Lawyers | Ditthavong & Steiner P.C. |
| Patent Lawyers | Griffith Hack |
| R&D Tax Lawyers | MJ Associates |
| Investor and Public Relations | IR Department |
| Clinical Manufacturing Manager | DelBioPharma LLC |
| Regulatory Affairs | CCS Associates |
| Quality Assurance | Dianna Goldman Consulting Inc. |
| Calvary Mater Newcastle Hospital | Hunter Medical Research Institute |

| Clinical Advisors | |
|---|---|
| Clinical Advisory Board | Prof. Borje Andersson, MD, PhD, MD Andersson Cancer Centre, USA |
| Clinical Advisory Board | Jaap-Jan Boelens, MD, PhD, Memorial Sloane Kettering, Cancer Centre, USA |
| Clinical Advisory Board | Didier Blaise, MD, Institut Paoli Calmettes, France |
| Clinical Advisory Board | Anoop Enjeti, MBBS MD, PhD Calvary Mater Hospital Newcastle |
| **Scientific Advisors** | |
| Collaborator | Prof Jianjun Chen, PhD, Beckham Institute, City of Hope |
| Collaborator | Nikki Verrills, PhD, University of Newcastle |
| Collaborators | Prof Xu Dong Zhang PhD, A/Prof Lei Jin PhD, University of Newcastle |
| Collaborators | A/Prof. Aaron Sverdlov, MBBS, FRCAP, PhD and A/Prof Doan Ngo PhD, University of Newcastle |

| Industry Partners and Scientific Collaborators | |
|---|---|
| Clinical Manufacturing Drug Product | IrySys LLC |
| Clinical Manufacturing Drug Substance | GVK Bio |
| Clinical Manufacturing Packaging | PCI Pharma |
| Clinical Research Organisation | George Clinical |
| Clinical Research Organisation | Parexel |
| Clinical Research Organisation | Datapharm Australia Pty Ltd |
| Clinical Research Organisation | Novatrials Ltd |
| Clinical Research Organisation | Agilex BioLabs Pty Ltd |
| Clinical Research Organisation | Cyprotex Discovery Limited |

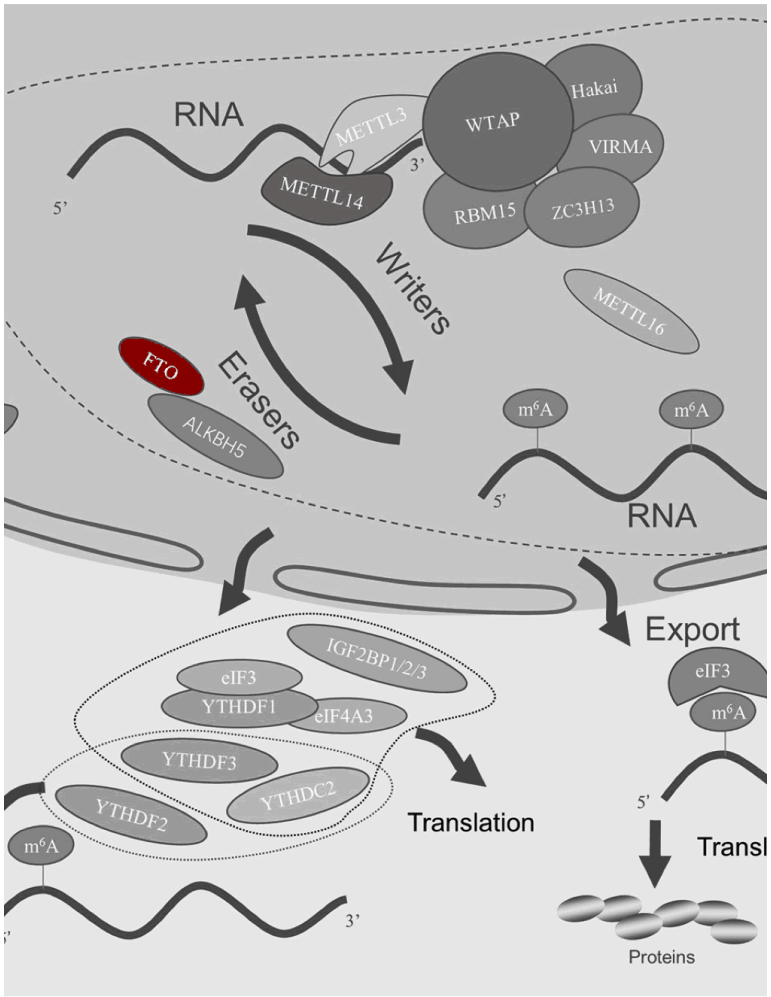
# 3. THE THREE PILLAR STRATEGY

| | |
|---|---|
| GOAL | Plan and progress clinical programs which prove efficacy and utility in targeted indications for Bisantrene, so that its potential is realised through sale to a scaled pharma |

STRATEGIES

| Pillar 1 | Pillar 2 | Pillar 3 |
|---|---|---|
| FTO<br>Melanoma<br>Clear Cell Renal Cell Carcinoma<br>Pre Clinical | Breast Cancer<br>Move to human proof of concept clinical trials<br>Anthracycline replacement | AML Extramedullary<br>R/R Adult & Paediatric<br>MRD<br>Ovarian |

| | |
|---|---|
| ENABLERS | Pre Clinical & Clinical I Collaborators I Regulatory I CMC I IP I Commercial I Board |




# FTO

## CENTRAL ROLE IN CANCER

- Scientific discoveries over the last decade have identified dysregulation (loss of control) of RNA methylation as a key driver of cancer development[1]
- Changes in m$^6$A RNA methylation control the expression of key genes in cancer development and growth[2]
- Fatso/ Fat mass- and obesity-associated Protein (FTO) is an m$^6$A RNA demethylase[1]
- Increases in the expression of FTO drives cancer development and metastasis
- Reduction of FTO activity kills or slows the growth of a wide range of cancers including leukaemia, breast, lung, ovarian, gastric, brain, melanoma, pancreatic, etc – ***difficult to find a cancer where FTO is not an important driver***
- **One of the hottest areas of cancer research**

1. Deng, X., Su, R., Stanford, S., & Chen, J. (2018). Critical Enzymatic Functions of FTO in Obesity and Cancer. Frontiers in Endocrinology, 9, 724–7
2. Huang, H., Weng, H., & Chen, J. (2020). m$^6$A Modification in Coding and Non-coding RNAs: Roles and Therapeutic Implications in Cancer. Cancer Cell, 37(3), 270–28

# FTO INHIBITOR COMPARATIVE OVERVIEW

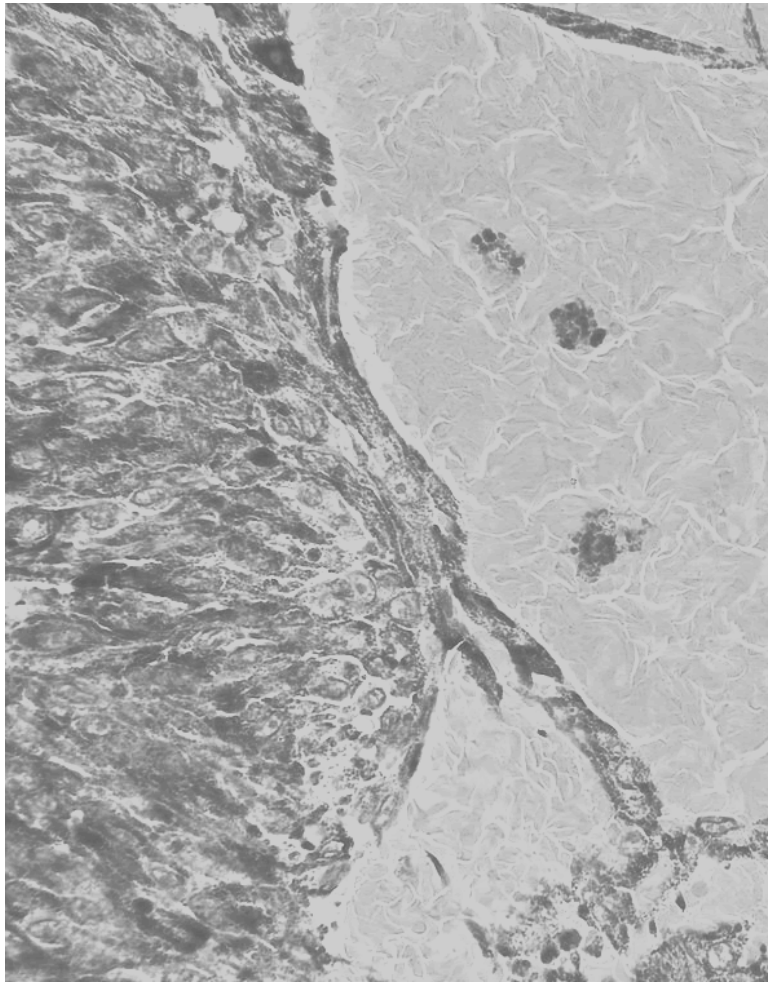
| Drug | $IC_{50}$ (nM) | Potency[1] | Clinical Data | Indications | Efficacy & Known Side Effects | References |
|---|---|---|---|---|---|---|
| **Bisantrene (CS1)** | **142.6** | **1** | **Yes (Phase 3)** | **AML, Breast, Pancreatic, GBM, Skin cancers** | **Leukopenia and myelosuppression at high doses** | doi.org/10.1016/j.ccell.2020.04.017<br>doi.org/10.1016/j.molcel.2020.12.026<br>doi.org/10.1038/s41467-021-22469-6 |
| Dac51 | 400 | 3 | No | Colon and melanoma | Preclinical. No safety or tolerability data from human clinical trials | doi.org/10.1016/j.cmet.2021.04.001 |
| Saikosaponin D | 460 | 3 | No | AML | Preclinical. No safety or tolerability data from human clinical trials | doi.org/10.7150/thno.55574 |
| Brequinar (CS2) | 712.8 | 5 | Yes (Phase 2) | AML | Failed anticancer agent. Failed transplant organ rejection drug. Very immunosuppressive. Variable plasma concentrations | doi.org/10.1016/j.ccell.2020.04.017 |
| Compound 2 | 1460 | 10 | No | Dopamine Neurons | $IC_{50}$ value in μM range. Preclinical. No safety or tolerability data from human clinical trials | doi.org/10.1101/2021.02.23.432419 |
| FB23-2 | 2600 | 18 | No | AML | $IC_{50}$ value in μM range. Preclinical. No safety or tolerability data from human clinical trials | doi.org/10.1016/j.ccell.2019.03.006 |
| FTO-04 | 3400 | 24 | No | GBM Stem cells | $IC_{50}$ value in μM range. Preclinical. No safety or tolerability data from human clinical trials | doi.org/10.1021/acschembio.0c00841 |
| Entacapone | 3500 | 25 | Yes (Approved) | Metabolic cells | $IC_{50}$ value in μM range. | doi.org/10.1126/scitranslmed.aau7116 |
| MA/MA2 | 7000 | 49 | Yes (Approved) | - | $IC_{50}$ value in μM range. | doi.org/10.1093/nar/gku1276 |
| MO-I-500 | 8700 | 61 | No | TNBC | $IC_{50}$ value in μM range. Preclinical. No safety or tolerability data from human clinical trials | doi.org/10.1371/journal.pone.0159072 |

1. Relative to Bisantrene. Compounds with IC50 > 1000nM are unlikely to be useful drugs in the clinic.

# FTO INHIBITORS DRUG SYNERGIES

| Drug | Value[1] (USD) | Indications | Mechanism | References |
|---|---|---|---|---|
| Anti PD-1/ Immune Checkpoint Inhibitors | $20.4 B (2018)<br>$77.4 B (2026) | Melanoma, colon cancer, AML | FTO up regulation increases melanoma growth & decreases anti-PD-1 response. FTO inhibition sensitized melanoma to anti-PD-1 treatment in mice. FTO up regulation increases PD-L1 in colon cancer and AML. FTO inhibition decreases PD-L1 in colon cancer and AML. | doi.org/10.1038/s41467-019-10669-0<br>doi.org/10.1016/j.bbrc.2020.06.153<br>doi.org/10.1016/j.ccell.2020.04.017 |
| TKIs | $19.1 B (2027) | Leukemia | TKI resistance is linked to FTO up regulation in leukemia. FTO inhibition increases TKI sensitivity in leukemia cells. | doi.org/10.1038/s41422-018-0097-4<br>doi.org/10.1158/1541-7786.MCR-20-0541 |
| Alkylating Agents (Cisplatin) | $1.8 B (2026) | Cervical cancer | FTO demethylates β-catenin mRNA and stabilizes the β-catenin in cervical squamous cell carcinoma, thereby inducing chemo-radio therapy resistance. | doi.org/10.1074/jbc.RA119.011009 |
| PARP Inhibitors | $0.8 B (2018)<br>$8.8 B (2027) | Ovarian cancer | FTO inhibition decreases FZD10 mRNA stability and sensitizes the cell to PARP inhibitor | doi.org/10.1158/0008-5472.CAN-18-3592 |
| Hypomethylating Agents | $1.7 B (2020)<br>$2.4 B (2022) | AML | Bisantrene shown to synergize with HMAs in inhibiting AML progression in immune-competent BMT recipient mice, and combinations showed much improved therapeutic efficacy than either treatment alone | doi.org/10.1016/j.ccell.2020.04.017 |
| Radiotherapy | $7.2 B (2021)<br>$11.7 B (2028) | Cervical cancer | FTO induces radio resistance in cervical squamous carcinoma by demethylation of β-catenin mRNA, which stabilizes its expression. | doi.org/10.1002/mc.22782 |
| Proton Pump Inhibitors | $2.7 B (2020)<br>$3.5 B (2026) | Gastric cancer | FTO inhibition induced by omeprazole improved the antitumor efficiency of chemotherapeutic drugs on GC cells | doi.org/10.1042/BSR20200842 |
| Androgen Receptor Antagonists | $13 B (2018) | Prostate cancer | METTL3 knockdown rendered the cells resistant to androgen receptor antagonists. | doi.org/10.1101/2021.01.12.426354 |

1. In house research performed by Race Oncology based on publically available information. All values are approximate and only illustrative of market size.



# PILLAR 1 – FTO & MELANOMA

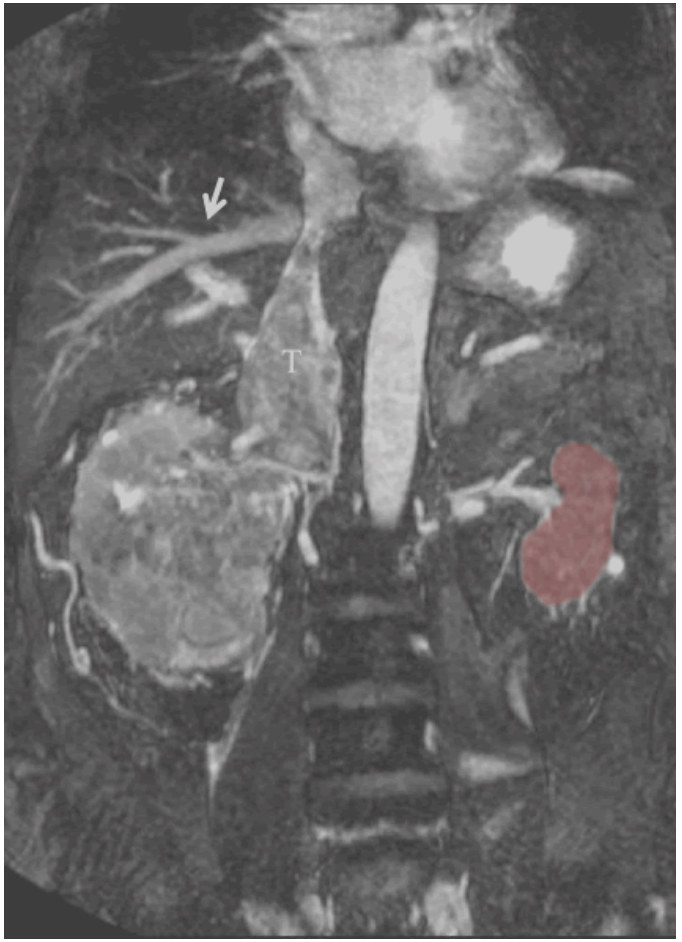
## OPPORTUNITY

- One of the most dangerous cancers: 7000 deaths (USA), 1500 (Aust)[1]
- Major improvements in treatment (BRAF/MEK inhibitors, immune checkpoint), but the 5-year survival rate for advanced melanoma is still as low as ~25%[1]
- **Major problem** - *treatment resistance*
- **FTO**
  - FTO was found to be overexpressed in ~50% of all metastatic melanomas[2]
  - FTO overexpression causes treatment resistance to PD-1 (immune checkpoint) inhibitors[2]
  - **Down-regulation of FTO has been shown to overcome PD-1 resistance[2]**

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

# PILLAR 1 – FTO & CLEAR CELL RENAL CELL CARCINOMA

- 10th most common cancer; often only diagnosed after metastasis[1]
- New treatments. TKI, checkpoint inhibitors[1]
- 5-year survival rate still very low (~12%)[1]
- 90% of ccRCC are caused by mutations in the von Hippel-Lindau (VHL) tumour suppressor gene[2]
- **FTO**
  - FTO was found to be synthetically lethal in cells with inactive VHL[3]
  - **Inhibition of FTO was found to kill VHL(-) ccRCC cancers[3]**




1. www.cancer.net/cancer-types/kidney-cancer/introduction | 2. Young, A. C., Craven, R. A., Cohen, D., Taylor, C., Booth, C., Harnden, P., et al. (2009). Analysis of VHL Gene Alterations and their Relationship to Clinical Parameters in Sporadic Conventional Renal Cell Carcinoma. Clinical Cancer Research, 15(24), 7582–7592. | 3. Xiao, Y., Thakkar, K. N., Zhao, H., Broughton, J., Li, Y., Seoane, J. A., et al. (2020). The m6A RNA demethylase FTO is a HIF-independent synthetic lethal partner with the VHL tumor suppressor. Proceedings of the National Academy of Sciences, 117(35), 21441–21449.

# PILLAR 2 - BREAST CANCER

**Phase 1/2 proof-of-concept (POC) trial in advanced metastatic breast cancer patients**

Preclinical data suggests Bisantrene is able to kill breast cancer cells resistant to current standard of care drugs[1]

Aim to demonstrate activity of Bisantrene in this patient population

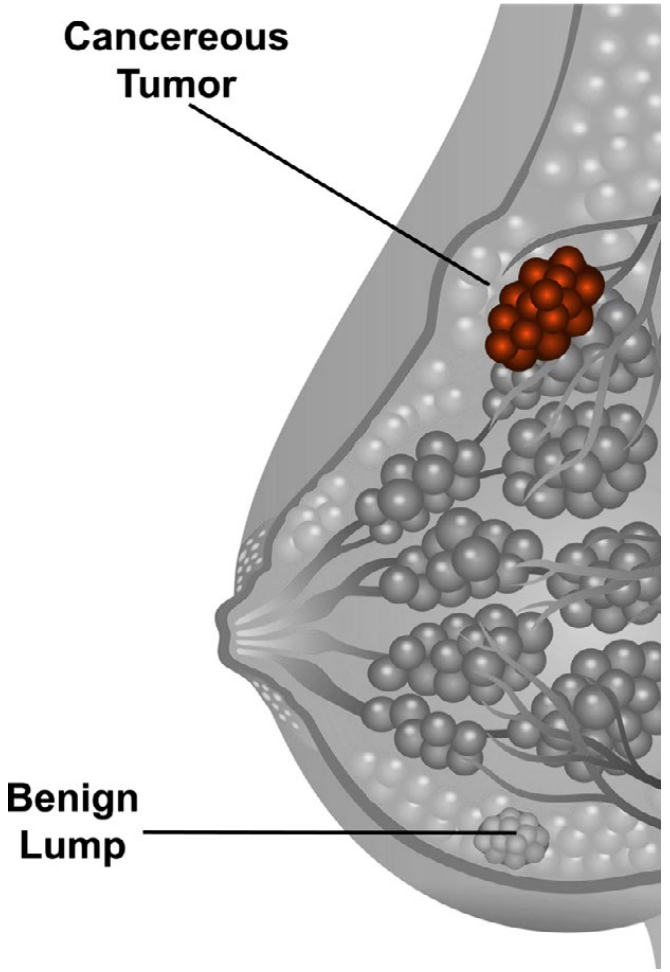
**Phase 2b trial in anthracycline naïve metastatic metastatic breast cancer patients**

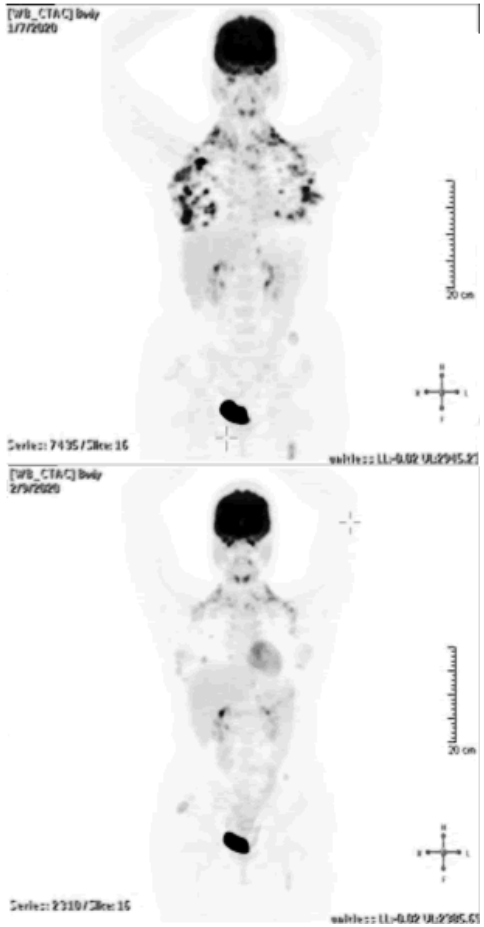
Feasibility study underway with the aim of demonstrating cardio safety and efficacy in a patient population not exposed to anthracyclines

**Preclinical Molecular Study**

Aims to explore the mechanism of action that causes Bisantrene's low cardiotoxicity

Focused on FTO and related pathways

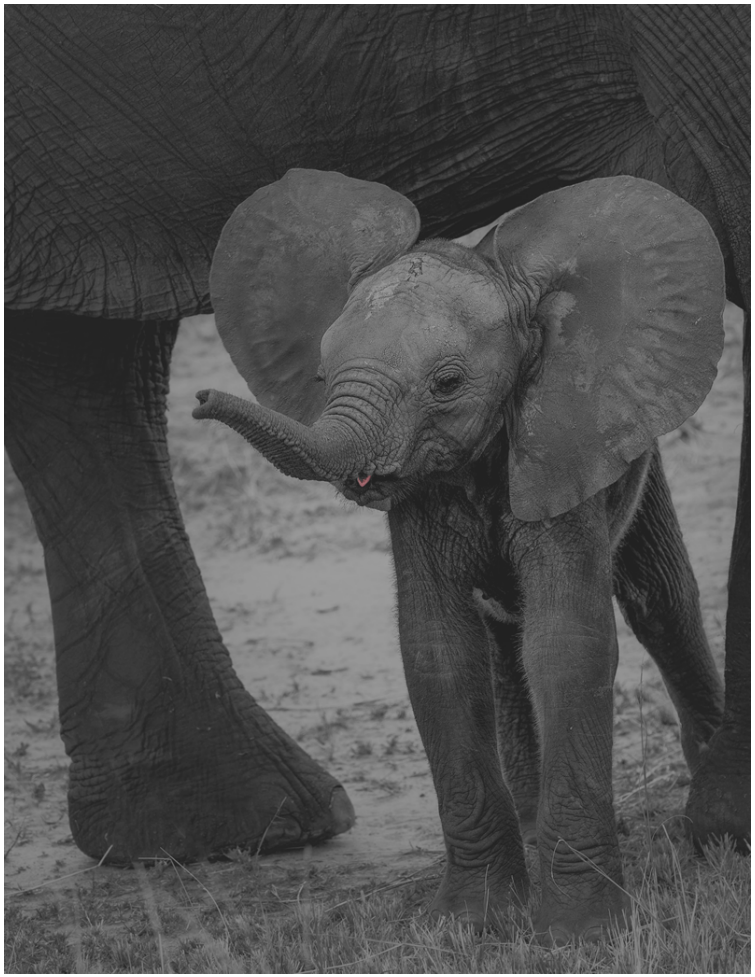




# PILLAR 3 - EXTRAMEDULLARY AML

- **Why extramedullary (EM) AML?**
  - **Recent Israel results** - 4/4 responders had EM AML
  - **Unmet clinical need** - no clinical trials and EM AML patients excluded
  - EM AML patients have a worse outcome than non-EM AML patients
  - PET has shown EM AML is much more common than previously thought (~20%)[1]
  - Small number of patients needed for pivotal trial (50-75)
  - Potential for expansion into paediatric AML; pathway to PRV
  - FDA 505(b)(2) pathway to approval

[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. http://doi.org/10.3324/haematol.2019.223032



# RAPID PROGRESS
## ANNOUNCED ACTIVITIES IN CY 2021

- Positive breast and ovarian cancer preclinical results
- Four preclinical programs launched in collaboration with the University of Newcastle to explore:
  - Use of Bisantrene in combination with standard of care drugs for the treatment of melanoma
  - Use of Bisantrene as a treatment for clear cell renal cell carcinoma
  - Use of Bisantrene in a mouse model of extramedullary AML
  - The molecular mechanism of action of Bisantrenes low cardiotoxicity
- Appointment of Professor Chen of the City of Hope Hospital to Race's scientific advisory board

# NEXT STEPS
## 2021/2022

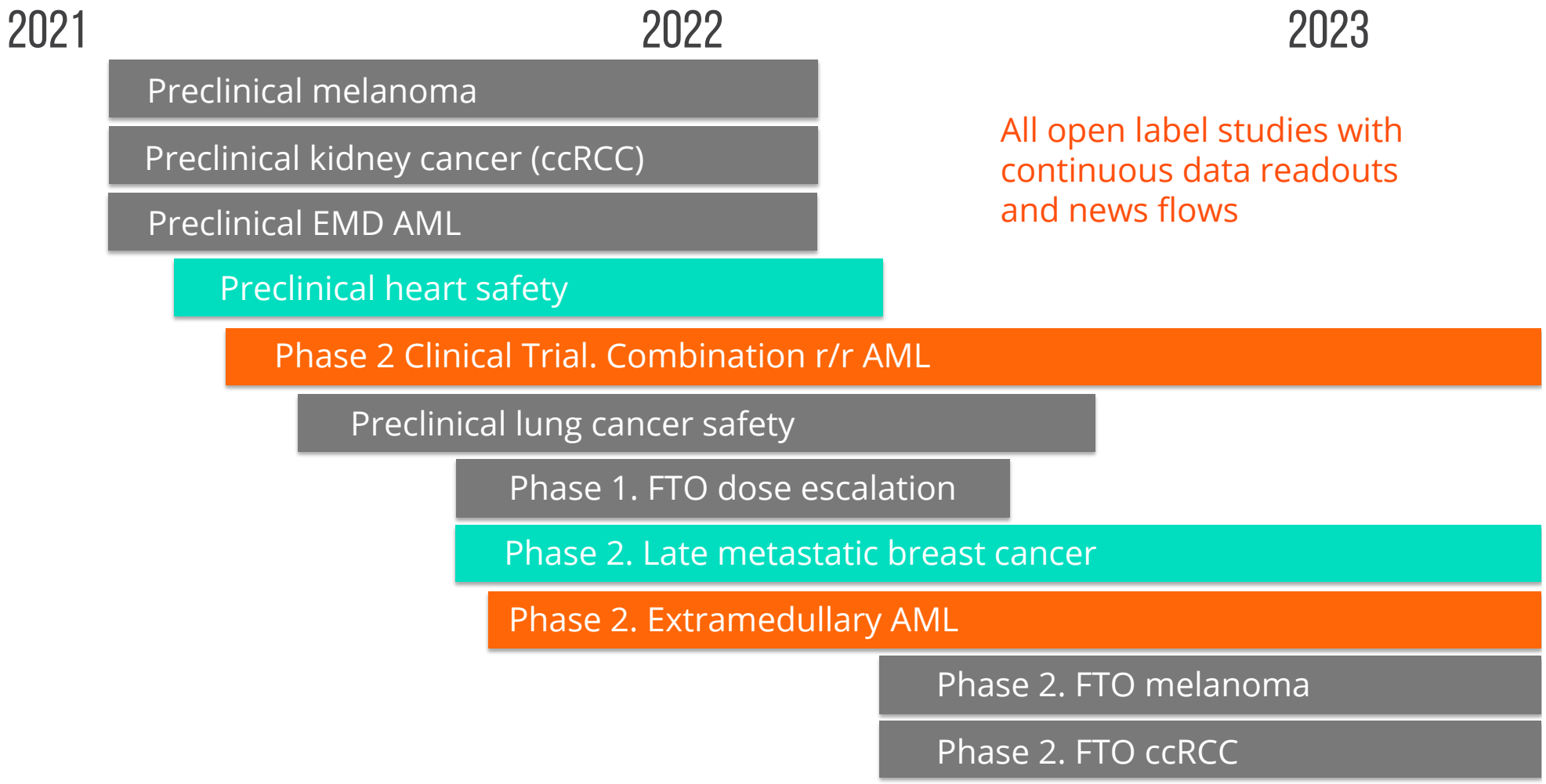
**2021**

- Phase 2 extramedullary AML clinical trial (Australia)
- Phase 2 R/R AML combination clinical trial (Israel)
- Phase 2 clinical trial in late stage metastatic breast cancer (Australia)
- Phase 1 dose escalation trial to determine the optimal Bisantrene dosing for targeting FTO overexpressing cancers
- Preclinical FTO-directed lung cancer program
- Initiation of EU and USA activities to support extramedullary AML clinical trials
- Scaled manufacturing of Bisantrene to support Phase 2/3 trials

**2022**

- Reporting on preclinical programs
- Phase 2 FTO-directed clinical trial of Bisantrene in melanoma
- Phase 2 FTO-directed clinical trial of Bisantrene in ccRCC
- Phase 2b breast cancer trial in anthracycline naïve patients (subject to feasibility)

# ACTIVITY TIMELINE



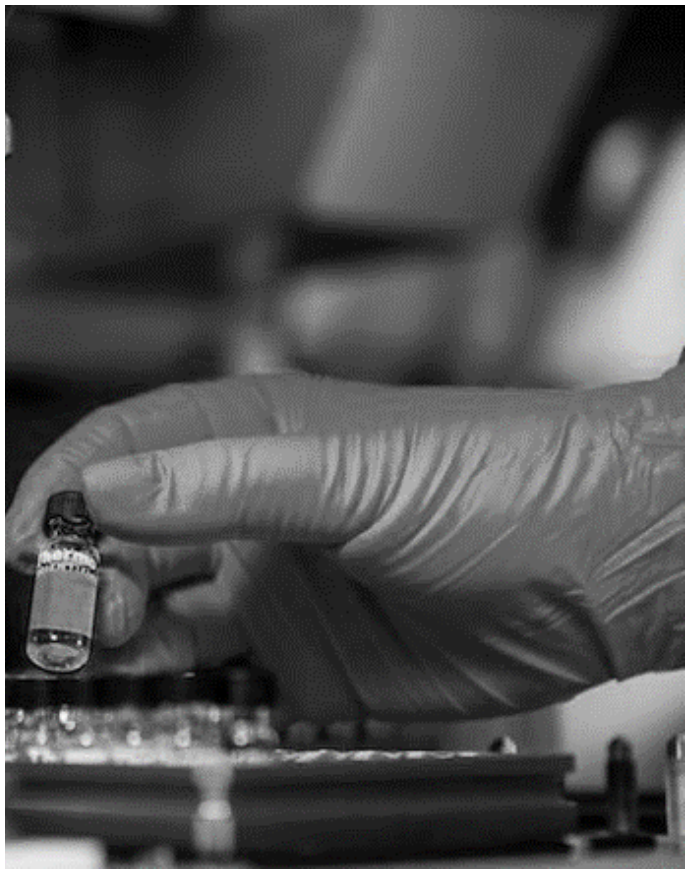
# CONCLUDING COMMENTS

**STRATEGY –** capitalises on FTO opportunity while protecting legacy chemotherapy credentials

**RISK REWARD –** multi leg strategy reduces executional risk and maximises potential for outsized returns

**TEAM –** is focused on shareholder return, via sale / license to pharma partner

**CLINICAL PROGRESS –** will be gated and plans advanced appropriately



RACE ONCOLOGY

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