RACURA ONCOLOGY

ASX Announcement

Sheba Medical Center Grants Approval for the EMILI 2b/3 AML Trial

- **Sheba Medical Center in Israel has granted site ethics approval for the pivotal EMILI Phase 2b/3 trial of RC220 in relapsed or refractory acute myeloid leukaemia (R/R AML)**
- **Racura Board has approved the initiation of the EMILI trial with the Phase 2b (up to 68 patients) fully funded from existing cash**
- **Governance approval process at Sheba is well advanced, with site activation and trial initiation expected by end of 2026, with the first patient to be enrolled and treated in Q1 2027**
- **Additional sites in Europe, USA and Australia to be activated in 2027, subject to regulatory approvals and feasibility**

18 November 2026

Racura Oncology Ltd (ASX: RAC; "Racura" or the "Company") is pleased to announce that the Institutional Helsinki Committee (human research ethics committee) of the Sheba Medical Center, Israel, has approved the pivotal EMILI Phase 2b/3 trial of RC220 in adults with relapsed or refractory acute myeloid leukaemia (R/R AML). The approval is subject to minor updates to the patient informed consent documents, which do not change the trial design, and allows Sheba, under the supervision of Principal Investigator Professor Arnon Nagler, to progress towards site activation and patient enrolment, subject to final institutional governance approval. The Israeli Ministry of Health has agreed that separate approval is not required for the EMILI trial as bisantrene has previously been evaluated at Sheba in two past Phase 2 clinical trials.[1,2]

The Board of Racura has approved initiation of the EMILI trial, comprising a Phase 2b dose-optimisation stage to meet the requirements of the US Food and Drug Administration's (FDA) Project Optimus, followed by a Phase 3 dose expansion and efficacy stage. The Phase 2b stage is funded from the Company's existing cash. Progression to Phase 3 will depend on the Phase 2b results, funding, and consultation with regulatory authorities at an End-of-Phase 2 meeting.

AML is an aggressive cancer of the blood and bone marrow. For patients with AML, the main curative option is an allogeneic haematopoietic stem cell transplant from a donor (allo-HSCT). To proceed to transplant, patients generally need their leukaemia brought under control first.[3] EMILI is designed to test whether a single course of RC220 over seven days can achieve this outcome in patients with R/R AML.

Sheba has a long association studying bisantrene in AML. Investigators at Sheba led by Professor Nagler have completed two earlier studies using RC110, a prior formulation of (E,E)-bisantrene. In a Phase 2 monotherapy study, four of ten patients with R/R AML (40%) responded, including one complete remission.[1] In a Phase 1b/2 study of bisantrene combined with fludarabine and clofarabine, six of 15 evaluable patients (40%) responded, including five complete remissions (ASX Announcement: 4 August 2025).[2] These were small, single-centre, non-randomised studies, and while their results do not predict the outcome of the EMILI trial, they did inform its design.

Racura CEO and MD, Dr Daniel Tillett, commented: *"Ethics approval from the Sheba Medical Center is an important step towards starting EMILI, our seamless Phase 2b/3 trial of RC220 in relapsed or refractory AML. EMILI will open first at Sheba, where Professor Arnon Nagler and his team have studied bisantrene in AML patients for many years. With this approval, our focus now turns to activating Sheba with other sites to follow, with the aim of generating the data needed to select the right RC220 dose for the pivotal Phase 3 stage. I thank Professor Nagler, his team and colleagues, the Sheba Helsinki Committee, and the Racura clinical and preclinical teams for their hard work and dedication in reaching this important milestone."*

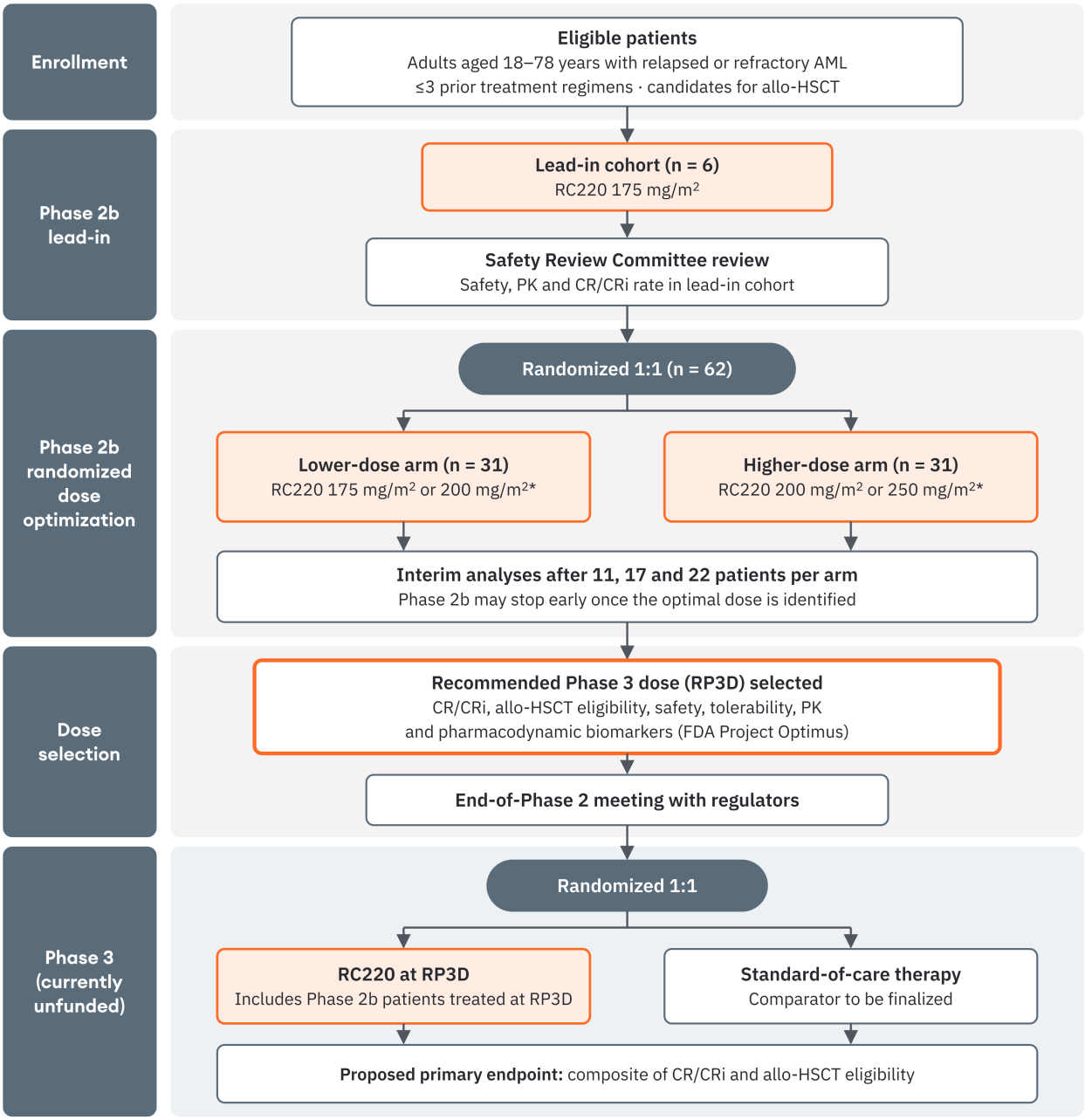
EMILI Trial Overview

EMILI is a pivotal, multicentre, adaptive, seamless Phase 2b/3 trial evaluating RC220 monotherapy (RC220 given on its own) as a single-cycle salvage induction therapy, with the intent of bringing relapsed or refractory AML into remission so that a patient can proceed to a potentially curative allogeneic-HSCT. Eligible patients are adults aged 18 to 78 years with R/R AML who have received no more than three prior treatment regimens and are candidates for allogeneic-HSCT. RC220 will be given as a 2-hour intravenous infusion, once daily, on Days 1 to 7 of a single treatment cycle.

The Phase 2b stage will enrol up to 68 patients. It begins with a lead-in cohort of six patients treated with RC220 at 175 mg/m² (milligrams per square metre of body surface area, the standard way of dosing many cancer drugs). After the Safety Review Committee (SRC) reviews the lead-in cohort data, a further 62 patients will be randomised 1:1 (31 per arm) to one of two dose levels, either 175 mg/m² and 200 mg/m², or 200 mg/m² and 250 mg/m², depending on the rate of complete remission (CR) or complete remission with incomplete blood count recovery (CRi)[3] seen in the lead-in cohort. Interim analysis of the Phase 2b data will be conducted after 11, 16 and 21 patients have been dosed per arm to establish if the optimal dose has been identified and the Phase 2b can end early.

The aim of the Phase 2b stage is to identify the recommended Phase 3 dose (RP3D) by assessing efficacy, safety, tolerability, pharmacokinetics (how the body absorbs, distributes and clears a drug) and pharmacodynamic biomarker activity (the drug's measurable effects on its biological targets). This is designed to address the US FDA's Project Optimus initiative, which asks cancer drug developers to compare more than one dose and choose the one with the best balance of benefit and side effects, rather than simply the highest dose patients can tolerate.[4] The Phase 2b assessment includes CR and CRi rates and

the proportion of patients who become eligible for allogeneic-HSCT. The EMILI trial design is summarised in Figure 1.



*Dose pair set by the lead-in CR/CRi rate: 175 vs 200 mg/m² if the pre-specified criterion is met; otherwise 200 vs 250 mg/m². RC220 is given as a 2-hour intravenous infusion once daily on Days 1–7 of a single treatment cycle. Phase 3 sample size, comparator and statistical design will be finalized after regulatory consultation.

Figure 1. EMILI seamless Phase 2b/3 trial design. In both stages, RC220 is given as a 2-hour intravenous infusion once daily on Days 1 to 7 of a single treatment cycle. Allo-HSCT: allogeneic haematopoietic stem cell transplant; AML: acute myeloid leukaemia; CR: complete remission; CRi: complete remission with incomplete blood count recovery; PK: pharmacokinetics; RP3D: recommended Phase 3 dose; SRC: Safety Review Committee.

Following the Phase 2b stage and an End-of-Phase 2 (EOP2) meeting with regulators, the trial will seamlessly transition to the randomised Phase 3 stage comparing RC220 at the RP3D against standard-of-care therapy in a 1:1 ratio, with patients treated at the RP3D in Phase 2b included in the Phase 3 RC220 arm. The proposed Phase 3 primary efficacy endpoint is a composite of remission (CR or CRi) and eligibility for allogeneic-HSCT. The Phase 3 sample size, comparator therapy and statistical design will be finalised after regulatory consultation.

Exploratory analyses will measure changes in MYC protein levels and MYC-regulated gene expression in patients' leukaemia cells. Additional sites in Europe and the United States are expected to open in 2027, subject to the required regulatory and ethics approvals, with sites in Australia also planned to open in 2027, subject to feasibility.

Importance of MYC as a Target in Cancer

MYC acts as a master switch for cell growth and division. In healthy cells its activity is tightly controlled, but in cancer cells MYC is often switched on permanently, through extra copies of the gene, chromosomal rearrangements or overactive growth signals, making it one of the most commonly dysregulated genes in human cancer.[5] In a landmark mouse study, switching off MYC function caused established lung tumours to regress rapidly, while the effects on normal tissues were mild and reversed once MYC function was restored.[6] These and other findings have made MYC one of the most sought-after targets in cancer drug development.

Despite four decades of research, MYC has been extremely difficult to drug and continues to be described as "undruggable" by the pharmaceutical industry.[7] Unlike enzymes such as kinases, the MYC protein has no well-defined binding pocket into which a conventional small-molecule drug can bind. MYC lacks a fixed shape, and it acts inside the cell nucleus by pairing with a partner protein, MAX, across a large, flat surface that is hard to block.[7] No drug that directly targets MYC has yet been approved. One of the first direct MYC inhibitors to reach the clinic, the peptide OMO-103, completed a Phase 1 trial in patients with advanced solid tumours. While OMO-103 was found to be safe, its clinical activity was limited.[8]

(E,E)-bisantrene uses a different approach to inhibit MYC. Rather than targeting the MYC protein directly, it binds to G-quadruplex structures in the control region of the MYC gene and reduce MYC expression in preclinical models (ASX Announcements: 2 October 2025, 22 April 2026 and 12 November 2026). Whether RC220 can suppress MYC activity in patients is one of the key questions the EMILI trial will be able to answer.

Why is AML Useful for Exploring MYC Inhibition?

AML is an excellent clinical indication in which to explore whether RC220 can inhibit MYC activity in cancer patients, for four primary reasons.

1. MYC is a key driver of AML. AML cells largely depend on MYC to sustain their growth and the self-renewal of leukaemia stem cells, and suppressing MYC expression has strong anti-leukaemic effects in laboratory

models.[9] The MYC protein is overexpressed in around 90% of patients with newly diagnosed AML, and higher MYC levels are associated with shorter remissions and poorer patient survival.[10]

2. (E,E)-bisantrene can inhibit MYC gene transcription and activity in AML models. In a recent preclinical collaborative study conducted by researchers at the University of Newcastle and Racura, (E,E)-bisantrene was found to be able to reduce MYC gene and protein levels in AML cells in a dose- and time-dependent manner and reduce activity of MYC-regulated cell-cycle pathways. Bisantrene was active at very low (nanomolar) concentrations in most of the AML cell lines tested and prolonged survival in mouse models of AML, including an AML model derived from a patient's leukaemia.[11] These results build on earlier studies showing bisantrene is active against patient-derived AML cells and in mouse models of AML (ASX Announcement: 6 March 2024) and are supported by laboratory studies which show that (E,E)-bisantrene binds to a folded DNA structure called a G-quadruplex in the control region (promoter) of the MYC gene and is able to inhibit MYC transcription in both breast and lung cancer cells (ASX Announcements: 2 October 2025, 22 April 2026 and 12 November 2026).

3. Bisantrene has already shown clinical activity in AML. An earlier formulation of bisantrene was approved for AML in France in 1988 (ASX Announcement: 13 May 2024) with an objective response in 40% of patients. This response rate was repeated in each of the two recent Sheba Phase 2 AML studies.[1,2] The EMILI trial will explore if clinical activity correlates with MYC overexpression and if RC220 is able to reduce MYC activity in patients.

4. AML allows direct and rapid measurement of MYC gene expression and activity in patients. In most solid tumours, measuring a drug's effect on its molecular target requires repeated tumour biopsies. This is impractical in most cases during dosing. In AML, leukaemia cells circulate in the blood, so the EMILI trial can measure changes in MYC protein levels and MYC-regulated genes directly from patients' leukaemia cells taken from blood samples before, during and after treatment. Because treatment response is assessed after a single treatment cycle, these biomarker changes can be readily compared with clinical outcomes.

Demonstrating the inhibition of MYC gene transcription in patients was highlighted as a key objective of the AML clinical program in the Company's Clinical Program Update (ASX Announcement: 17 November 2025). Clinical evidence of the mechanism would also be highly relevant to Racura's HARNESS-1 and CPACS solid tumour clinical programs, where demonstrating a direct effect on MYC activity in the patient's cancer is more complex.

Next Steps

Racura and Sheba will now make the minor updates to the informed consent documents requested by the Institutional Helsinki Committee. In parallel, Sheba's institutional governance review (the hospital's review of the trial's contractual, financial and operational arrangements) has started and is well advanced. Once governance approval is granted, Racura will conduct the trial initiation visit, at which the Sheba team is trained on the protocol and the site is formally opened for patient enrolment. Governance approval and

trial initiation are expected to be completed by the end of 2026 with the first patient expected to be enrolled and treated in Q1 2027. These timelines depend on completing the remaining approvals and identifying eligible patients.

Other upcoming EMILI milestones include the appointment of a contract research organisation to manage the multinational trial, regulatory clearance from the FDA, European regulatory approval through the European Medicines Agency (EMA) Clinical Trials Information System, and the activation of additional trial sites. Racura will announce these milestones as they are achieved. All timelines are estimates and subject to change.

EMILI Trial Information

EMILI will be registered on ClinicalTrials.gov, and the trial identifier will be provided in a future update.

Enquiries about EMILI can be directed by email to Racura Oncology via trials@racuraoncology.com.

Investor Webinar

Racura will hold an online investor webinar on Thursday, 19 November 2026 at 12:00pm (AEDT). Racura CEO and Managing Director, Dr Daniel Tillett, and EMILI lead, Dr Anupa Kudva, will discuss the EMILI trial and today's ethics approval, followed by a Q&A session with investors.

Registration link: https://us02web.zoom.us/webinar/register/WN_qg3XNP9zRzKscrwpvagYHA

Once registration is completed, an email detailing how to access the webinar will be sent to your registered email address.

References

1. Canaani J, Danylesko I, Shemtov N, Zlotnick M, Lozinsky K, Benjamini O, et al. A phase II study of bisantrene in patients with relapsed/refractory acute myeloid leukemia. Eur J Haematol. 2021;106(2):260–6. doi:10.1111/ejh.13544 (ClinicalTrials.gov: NCT03820908)
2. Danylesko I, Shimoni A, Avigdor A, Kedmi M, Amitai I, Shem-Tov N, et al. Bisantrene in combination with fludarabine and clofarabine as salvage therapy for adult patients with refractory or relapsed acute myeloid leukaemia (AML)—an open-label, phase I/II study. Br J Haematol. 2025;207(4):1425–34. doi:10.1111/bjh.70035 (ClinicalTrials.gov: NCT04989335)
3. Döhner H, Wei AH, Appelbaum FR, Craddock C, DiNardo CD, Dombret H, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. Blood. 2022;140(12):1345–77. doi:10.1182/blood.2022016867
4. US Food and Drug Administration. Optimizing the dosage of human prescription drugs and biological products for the treatment of oncologic diseases: guidance for industry. 2024 Aug [cited 2026 Nov 15]. Available from: https://www.fda.gov/media/164555/download
5. Dang CV. MYC on the path to cancer. Cell. 2012;149(1):22–35. doi:10.1016/j.cell.2012.03.003
6. Soucek L, Whitfield J, Martins CP, Finch AJ, Murphy DJ, Sodir NM, et al. Modelling Myc inhibition as a cancer therapy. Nature. 2008;455(7213):679–83. doi:10.1038/nature07260
7. Dang CV, Reddy EP, Shokat KM, Soucek L. Drugging the 'undruggable' cancer targets. Nat Rev Cancer. 2017;17(8):502–8. doi:10.1038/nrc.2017.36
8. Garralda E, Beaulieu ME, Moreno V, Casacuberta-Serra S, Martínez-Martín S, Foradada L, et al. MYC targeting by OMO-103 in solid tumors: a phase 1 trial. Nat Med. 2024;30(3):762–71. doi:10.1038/s41591-024-02805-1
9. Zuber J, Shi J, Wang E, Rappaport AR, Herrmann H, Sison EA, et al. RNAi screen identifies Brd4 as a therapeutic target in acute myeloid leukaemia. Nature. 2011;478(7370):524–8. doi:10.1038/nature10334
10. Ohanian M, Rozovski U, Kanagal-Shamanna R, Abruzzo LV, Loghavi S, Kadia T, et al. MYC protein expression is an important prognostic factor in acute myeloid leukemia. Leuk Lymphoma. 2019;60(1):37–48. doi:10.1080/10428194.2018.1464158
11. Murray HC, Miller K, Brzozowski J, Kiltschewskij D, Roy I, Panicker N, et al. (E,E)-bisantrene suppresses MYC expression and displays anti-leukemic activity in acute myeloid leukemia. bioRxiv. 2026 Sep 16. doi:10.64898/2026.09.10.750805
12. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. ICH harmonised guideline: guideline for good clinical practice E6(R3). 2025. Available from: https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf
13. Orphan Drug Act. Protection for drugs for rare diseases or conditions. 21 U.S.C. § 360cc.

-ENDS-

Q&A

What does EMILI stand for?

EMILI stands for *Evaluation of a MYC-silencing Intervention in Acute Myeloid LeukemIa*. The name reflects the trial's two aims: to evaluate RC220 as a treatment for relapsed or refractory AML, and to test whether the MYC gene expression inhibition mechanism of action is observed in patients.

Does the EMILI trial need to treat all 68 patients to progress to the Phase 3 stage?

No. The trial has three interim assessments after 11, 16 and 21 patients are treated in each dose arm. If one arm shows significantly better outcomes or safety, the Phase 2b stage can end early and the trial progress seamlessly to the Phase 3 stage.

How long will the Phase 2b stage of the EMILI trial take?

This is difficult to answer as it depends on the number of patients that need to be treated to establish the optimal dose. Our expectation at this time is in the range of 18 to 24 months, subject to the usual uncertainties that accompany all clinical trials (i.e. speed of patient recruitment and site activation).

How soon will investors be updated on the MYC-suppressing activity of RC220 in patients?

We expect that we will be able to measure the effects of RC220 on MYC gene expression and activity in AML samples from the first patient, but for robust conclusions we expect we will need data from between 12 and 18 patients. We will update our investors on this aspect as soon as possible.

Does ethics approval mean RC220 will work in R/R AML?

No. An ethics committee assesses whether a trial is ethically and scientifically acceptable and whether participants are adequately protected.[12] It does not determine whether RC220 is effective. The efficacy and safety of RC220 in R/R AML will be determined by the EMILI trial itself.

Why is EMILI a seamless Phase 2b/3 trial rather than two separate trials?

A seamless trial design allows the dose-finding (Phase 2b) and confirmatory efficacy (Phase 3) stages to run under a single protocol. The trial can move rapidly into Phase 3 without starting a new study, and patients treated at the selected dose in Phase 2b can contribute to the Phase 3 RC220 arm. The transition to Phase 3 will depend on the Phase 2b results, funding, and consultation with regulators such as the FDA and EMA.

Does RC220 have any regulatory designations for AML?

Yes. The US FDA has granted Orphan Drug Designation to RC220 for the treatment of AML (ASX Announcement: 11 June 2024). This provides benefits including eligibility for seven years of US market exclusivity on approval.[13]

About Racura Oncology

Racura Oncology (ASX: RAC) is a late-stage clinical biopharmaceutical company with a mission to silence cancer.

Racura's lead asset, (E,E)-bisantrene, is a clinically derisked small-molecule anticancer agent that primarily acts by stabilising G4-DNA and RNA structures, driving potent inhibition of c-MYC gene expression, a key cancer gene dysregulated in up to 70% of all cancers. Bisantrene has shown therapeutic activity in cancer patients and has a well-characterised safety profile. Racura's discoveries have supported composition-of-matter IP filings that, if granted, could provide up to 20 years of patent protection for (E,E)-bisantrene.

Racura is advancing RC220, its proprietary formulation of (E,E)-bisantrene, to address significant unmet need across multiple MYC-driven oncology indications. The Company's clinical programs include the EMILI Phase 2b/3 trial in acute myeloid leukaemia, the HARNESS Phase 1 trial in combination with osimertinib for EGFRm NSCLC, and the CPACS Phase 1 trial in combination with doxorubicin, where Racura aims to deliver both anthracycline cardioprotection and enhanced anticancer activity.

Racura has collaborated with Astex, Emory University, Purdue University, MD Anderson Cancer Center, Sheba Medical Center, University of North Carolina School of Medicine, University of Wollongong, and University of Newcastle. Racura is actively exploring partnerships, licence agreements, and potential commercial merger and acquisition opportunities to accelerate global patient access to RC220. Learn more at www.racuraoncology.com.

If you have any questions on this announcement, or any past Racura Oncology announcements, please visit the Company's Interactive Announcements page.

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

Release authorised by

Daniel Tillett, CEO/MD

info@racuraoncology.com

Media Contact

Cherie Hartley +61 418 737 020

cherie.hartley@irdepartment.com.au