ASX Announcement

Racura Oncology Presents MYC Gene Silencing Data by (E,E)-bisantrene at the 2026 American Association of Cancer Research Annual Meeting

- **Mechanism of action data describing how (E,E)-bisantrene silences MYC gene expression was presented at the prestigious American Association of Cancer Research (AACR) Annual Meeting held in San Diego, 17-22 April 2026**
- **Data demonstrates how (E,E)-bisantrene binds to and stabilises G-quadruplex (G4) structures in the c-MYC gene promotor region, leading to silencing of the key cancer driver MYC**
- **Presentation data supports Racura's current and planned clinical trials**

22 April 2026

Racura Oncology Limited ("Racura") is pleased to announce that Dr Sumit Sahni, presented mechanism of action data on (E-E)-bisantrene at the 2026 AACR Annual Meeting. The data discloses results from a range of preclinical studies demonstrating (E,E)-bisantrene silences MYC gene expression by stabilising a G-quadruplex (G4) DNA structure located in the promoter region of the c-MYC oncogene.

The poster presentation entitled *"(E,E)-bisantrene silences c-MYC expression by stabilizing its promotor region G-quadruplex"* is attached to this announcement.

Racura Oncology Senior Scientist, Dr Sumit Sahni commented: *"It was a privilege to be chosen to present Racura's mechanism of action data at the leading annual international cancer conference, AACR. I sincerely thank my preclinical team colleagues and our valued collaborators for their outstanding work that has uncovered the primary mechanism by which (E,E)-bisantrene exerts its anticancer activity. The strong interest and positive reception this work received at the conference is very encouraging."*

-ENDS-

About Racura Oncology

Racura Oncology (ASX: RAC) is a Phase 3 clinical-stage biopharmaceutical company with a mission to silence cancer.

Racura's lead asset, (E,E)-bisantrene, is a small molecule anticancer agent that primarily functions via G4-DNA & RNA binding, leading to potent silencing of the important cancer growth regulator MYC. (E,E)-bisantrene has demonstrated therapeutic activity in cancer patients with a well-characterised safety profile. Recent discoveries made by Racura have enabled composition of matter IP filings that provides for 20 years of patent protection over (E,E)-bisantrene.

Racura is advancing a proprietary formulation of (E,E)-bisantrene (RC220) to address the high unmet needs of patients across multiple oncology indications, with a Phase 3 clinical program in acute myeloid leukaemia (AML), a Phase 1a/b program in mutant epidermal growth factor receptor non-small cell lung cancer (EGFRm NSCLC), and a Phase 1a/b program in combination with the anthracycline doxorubicin, where we aim to deliver both cardioprotection and enhanced anticancer activity for solid tumour patients.

Racura has collaborated with Astex, Emory University, Purdue University, MD Anderson, Sheba City of Health, UNC School of Medicine, University of Wollongong, and University of Newcastle. Racura is actively exploring partnerships, licence agreements, or a commercial merger and acquisition to accelerate access to RC220 for patients with cancer across the world. Learn more at www.racuraoncology.com.

If you have any questions on this announcement, or any past Racura Oncology announcements, please visit our 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.

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(E,E)-bisantrene silences *c-MYC* expression by stabilizing its promotor region G-quadruplex

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BACKGROUND

G-quadruplex (G4) DNA and RNA are important non-canonical nucleic acid secondary structures that play key roles in many cellular processes. They regulate the expression and translation of several oncogenes, including the master cell growth regulator, c-MYC. Bisantrene is a small-molecule anticancer agent that has been shown to be safe and effective in >1500 clinical trial patients. This study characterized the binding and stabilization of a G4 region in the *c-MYC* gene promoter by the pure (E,E)-bisantrene isomer[1] and silencing of *c-MYC* gene expression in cancer cells.

METHODS

Circular dichroism spectroscopy established if (E,E)-bisantrene stabilizes the c-*MYC* promotor G4 structure, and surface plasmon resonance was used to measure the binding affinity. Nuclear magnetic resonance spectroscopy was used to determine the binding stoichiometry of (E,E)-bisantrene with *c-MYC* G4 and molecular dynamics simulations identified a possible 3-dimensional structure of the complex. Changes in *c-MYC* gene expression were assessed by qPCR in selected cancer cell lines after treatment with (E,E)-bisantrene. RNA-seq with pathway analysis was performed in lung cancer cell lines treated with (E,E)-bisantrene.

RESULTS

^{1}H-Nuclear Magnetic Resonance (^{1}H-NMR)

^{1}H-NMR titration indicated that (E,E)-bisantrene binds to *c-MYC* G4 with a 2:1 (E,E)-bisantrene: *c-MYC* G4 stoichiometry (Figure 1).

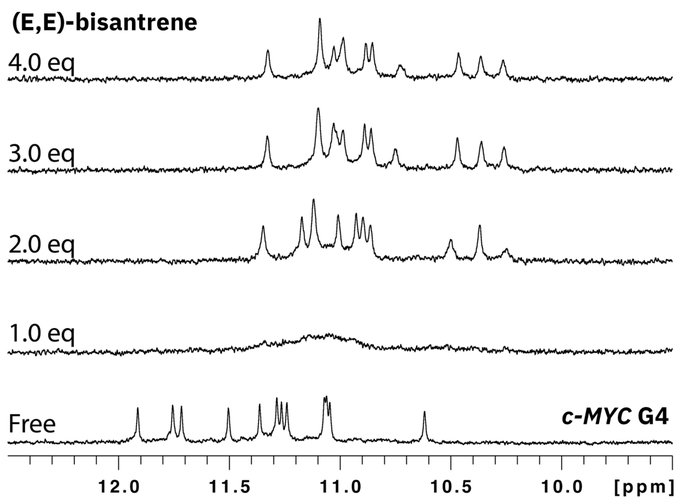


Figure 1: ^{1}H-NMR titration (guanine imino proton region) of *c-MYC* G4 DNA with (E,E)-bisantrene. Conditions: 100 mM K^+, pH 7.0, 25°C; DNA concentration, 150 µM; ratios of (E,E)-bisantrene/*c-MYC* G4 are shown.

[1]Racura ASX Announcement: 2nd Oct 2025

Molecular Dynamics

Molecular dynamics simulations suggested that (E,E)-bisantrene preferentially binds to the *c-MYC* G4 by stacking one molecule on each of the top and bottom G-tetrads (Figure 2).

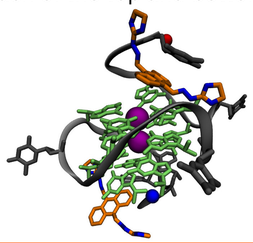


Figure 2: Representative binding mode (34.9% population) of (E,E)-bisantrene (orange sticks) interaction with the *c-MYC* G4 (PDB ID: 2MGN). 5′ and 3′ ends of the DNA chain are indicated by red and blue spheres, respectively. K^+ ions are indicated by purple spheres.

Binding Affinity

Surface Plasmon Resonance (SPR) analysis demonstrated that (E,E)-bisantrene binds to the *c-MYC* G4 with high affinity (Figure 3A) and showed ~1.5-fold selectivity over a related mutant *c-MYC* double stranded DNA (dsDNA) sequence (Figure 3B).

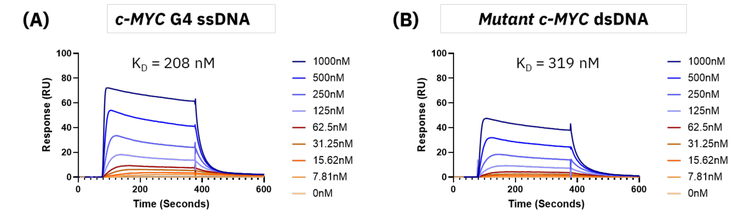


Figure 3: SPR analysis of (E,E)-bisantrene binding to 1000 response units (RU) of: **(A)** *c-MYC* G4 ssDNA (5'-/5Biosg/TGAGGGTGGGTAGGGTGGGTAA-3'), and **(B)** a related mutant *c-MYC* dsDNA sequence (5'-/5Biosg/TGAGAGTGAGTAGAGTGAGTAA-3' and 5'-TTACTCACTCTACTCACTCTCA-3') on a NeutrAvidin-coated sensor chip. (E,E)-bisantrene was injected in a concentration series from 0–1000 nM over multiple sequential injections, each lasting 300 s at a flow rate of 25 µL/min, followed by a 600 s dissociation phase.

G4 Stabilization

(E,E)-bisantrene (Figure 4A) and CX-5461 (Pidnarulex, Figure 4B), an investigational G4 stabilizing comparator, each dose-dependently increased the c-*MYC* G4 melting temperature, confirming binding and stabilization of the c-*MYC* G4.

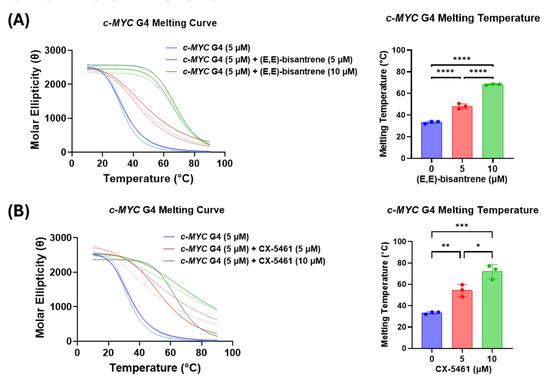


Figure 4: Melting curves of *c-MYC* G4 DNA sequence in the presence of (E,E)-bisantrene **(A)** or CX-5461 **(B)**. Molar ellipticity for *c-MYC* G4 was determined at 265 nm using circular dichroism spectroscopy.

Gene Expression Analysis

Treatment of breast and lung cancer cells with (E,E)-bisantrene for 2 h dose-dependently suppressed *c-MYC* expression (Figure 5).

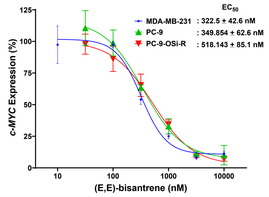
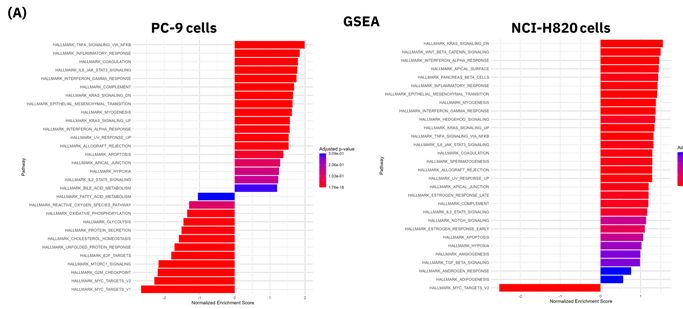


Figure 5: *c-MYC* gene expression levels were determined by qPCR after treatment of breast (MDA-MB-231) and lung (PC-9 and Osimertinib-resistant PC-9) cancer cells with increasing concentrations of (E,E)-bisantrene for 2 h.

RNA-Sequencing & Pathway Analysis

RNA-seq analysis in PC-9 and NCI-H820 non-small cell lung cancer (NSCLC) cells showed thousands of differentially regulated genes following treatment with (E,E)-bisantrene (data not shown). Gene set enrichment analysis of the RNA-seq data showed that the most strongly downregulated pathways were related to c-MYC (Figure 6A). Ingenuity Pathway Analysis identified that transcriptomic profile of (E,E)-bisantrene is similar to the G4-binding comparator CX-5461 (Figure 6B).



(B)

Similarity to Transcriptomic Profile of Another G4-Binder CX-5461			
PC-9 cells		NCI-H820 cells	
Activation z-score	p-value of overlap	Activation Z-Score	p value of overlap
2.514	0.00245	3.841	0.00233

Figure 6: RNA-Sequencing analysis of PC-9 and NCI-H820 lung cancer cells after treatment with (E,E)-bisantrene. **(A)** Gene set enrichment analysis (GSEA) based on the observed transcriptomic profile. **(B)** Similarity of the transcriptomic profile of (E,E)-bisantrene to another G4 binding drug, CX-5461, by Ingenuity Pathway Analysis.

CONCLUSION

(E,E)-bisantrene binds to and stabilizes the G4 DNA structure contained within the *c-MYC* promotor region, leading to silencing of c-*MYC* gene expression. These studies support the clinical evaluation of (E,E)-bisantrene as a new c-MYC targeting G4 drug. Two Phase 1 clinical trials are currently underway exploring the activity of (E,E)-bisantrene in combination with doxorubicin in advanced solid tumors (ClinicalTrials.gov ID: NCT06815575) and in combination with osimertinib in EGFRm NSCLC (ClinicalTrials.gov ID: Pending; Australia New Zealand Clinical Trial Registration #2626000325303).

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