

## ASX Announcement

### Race releases cardio-protection market potential data

- Triangle Insights conducted blinded primary research with stakeholders to investigate Zantrene's commercial potential as cardio-protective and anti-cancer agent within key cancer types where anthracyclines are typically used
- Assessment suggests that Zantrene is well-positioned for use in metastatic breast cancer broadly, and within the neoadjuvant setting for HR+/HER2- and triple negative breast cancer (HR-/HER2), relative to the profile assessed
- Significant opportunity: may offer >\$5B USD if anti-cancer efficacy is demonstrated, or ~\$1B USD as a supportive care cardio-protective therapeutic.

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**4 April 2023** – Race Oncology Limited (“Race”) is pleased to provide investors with a summary of market research, commissioned to better understand the commercial potential for lead asset, Zantrene® as a cardio-protective and anti-cancer agent in settings where anthracyclines are typically used.

**Non-Executive Chairman, Dr John Cullity commented:** *“This research, conducted by third party life science strategy consulting firm, Triangle Insights Group is highly informative to Race’s understanding of Zantrene’s market potential. To complete this work, Triangle consulted with key stakeholders involved in the treatment and reimbursement chain – from cardio-oncologists to payors.*

*The findings have been entirely useful, informing potential treatment scenarios for Zantrene in breast cancer, an area in which we have promising historical data. While the sample set was modest, this independent assessment provides a valid picture of the market and suggests a positive and wide-ranging financial opportunity.”*

**CEO and Managing Director, Damian Clarke-Bruce commented:** *“The Triangle Insights report indicates a major global commercial opportunity for Zantrene if proven to be a cardio-protective agent with anti-cancer activity in breast cancer. Physicians noted that cardio-protection from anthracycline-induced heart damage is a clear unmet need and that they would embrace treatment options for their patients.*

*The peripheral (intravenous) formulation is critical for this specific opportunity in breast cancer and as we look toward partnerships or potential licencing agreements in the future. The team is working on the formulation and updates on its progress are expected during H1 CY23.*

*By scope, this research project reviewed cardio oncology opportunities, and whilst breast cancer appears to be the obvious approach, the data is directional for further exploration in other cancer types. Being specific to the cardio protection opportunity, this assessment was not scoped to review the other significant area of research and intellectual property potential for Zantrene – the pursuit of the FTO pathway. Investigating and understanding Zantrene’s ability to inhibit FTO remains a core component of our Three Pillar strategy and any relevant FTO-related market assessment may be additive to this research.”*



A longer form copy of the market research report is in the process of being finalised and will be lodged with ASX once available.

Race remains on track to update shareholders on other milestones as set out in its Q2 FY23 quarterly report (ASX announcement: 31 January 2023.)

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**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 cancer.

The Company also has compelling clinical data for Zantrene as a chemotherapeutic agent and is in multiple clinical trials in Acute Myeloid Leukaemia (AML).

Race is pursuing outsized commercial returns for shareholders via its 'Three Pillar' strategy for the clinical development of Zantrene. Learn more at [www.raceoncology.com](http://www.raceoncology.com)

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>

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Race Oncology recently engaged with a third-party life science strategy consulting firm, Triangle Insights Group, to better understand the commercial potential for Zantrene as both a cardio-protective and anti-cancer agent within key cancer types for which anthracyclines are typically used. The following information represents a summary of the research:

Zantrene is a small molecule drug which has demonstrated clinical and pre-clinical efficacy as a highly targeted oncology agent, and as a cardio-protective therapeutic when used alongside anthracyclines. Preclinical data further suggests potential anti-cancer benefits and efficacy across breast, gynecologic cancers, sarcomas, and hematologic malignancies, within patients who are anthracycline naïve. Another potential key feature of Zantrene is its ability to allow patients to continue anthracycline-based treatment beyond the maximum lifetime cumulative dose.

*The following information provides a summary of findings from the commercial assessment of Zantrene:*

Anthracyclines are believed to exhibit their anti-cancer efficacy by interacting with topoisomerase-II, halting cell growth, and causing apoptotic cell death. Anthracyclines are FDA approved in over twenty various cancer types including breast, gynecologic, and hematologic cancers, with frequent off-label use for other cancers (e.g., endometrial cancer, uterine sarcomas, and renal cell carcinoma).

Anthracyclines are a mainstay of cancer treatment due to their highly effective anti-cancer properties, despite cardiotoxic concerns. Among all discussed side effects<sup>1</sup>, cardiotoxicity, which is defined as new onset heart failure and/or detection of left ventricular dysfunction, was the single most concerning adverse effect associated with anthracycline use, according to oncologists.

#### Anthracycline Side Effects Ranked by Reported Levels of Physician Concern

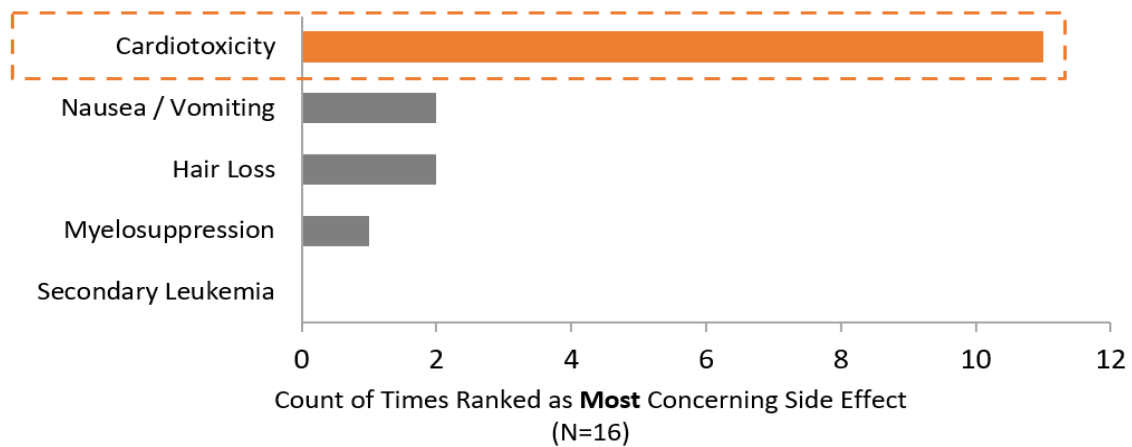


Figure 1 – Primary Research: Oncologist Perceptions on Common Anthracycline Adverse Effects<sup>2</sup>

<sup>1</sup> Included alopecia, nausea/vomiting, myelosuppression, secondary leukemia, and cardiotoxicity.

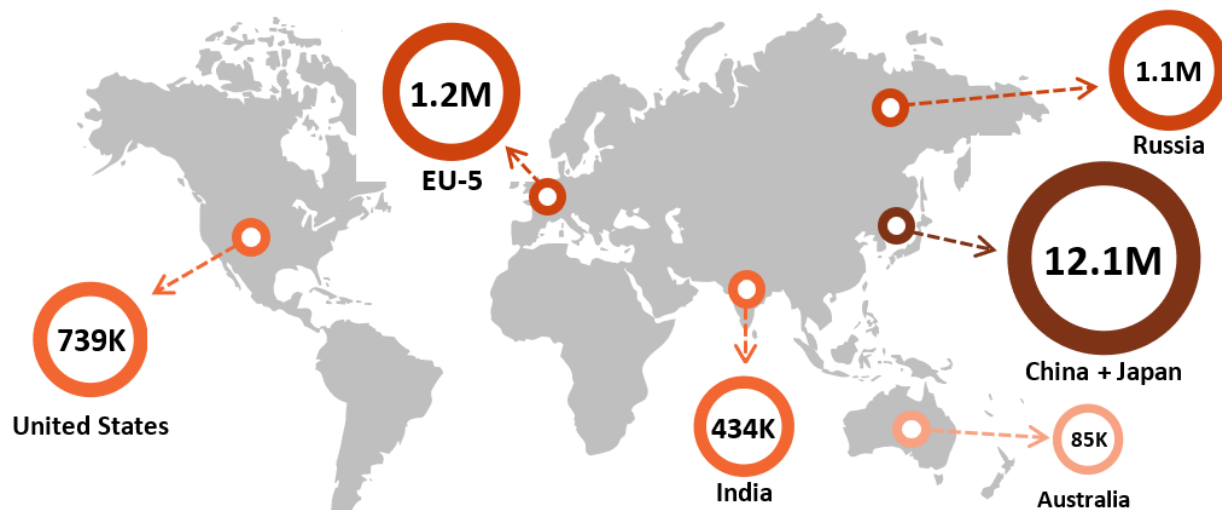
<sup>2</sup> Physicians were asked “On a scale from 1 to 7, with one being “not at all concerning” and 7 being “extremely concerning”, how concerning are each of the following, with regards anthracycline usage?” with corresponding responses ranked by counts of the most concerning side effect (highest rating)

*“Doxorubicin is shown to be the single most effective drug for chemotherapy, but its disadvantage is cardiac toxicity.”*

Furthermore, physicians noted that cardiac concerns may impact standard anthracycline dosing schedules, potentially leading to less-than-optimal patient outcomes. Multiple oncologists stated they have discontinued anthracycline-based treatment in patients, despite positive responses to therapy, solely to prevent anthracycline-associated cardiotoxicity from developing due to the prolonged courses of treatment. The likelihood of developing cardiotoxicity is heightened by approaching the maximum cumulative dose, but also by other risk factors such as sex, age, compromised cardiac function or cardiovascular risk factors such as obesity, smoking, and hypertension. Currently, the only therapeutic available to address cardio-toxicity concerns remains dexrazoxane which has very sparse use due to label restrictions limiting use to patients surpassing the 300mg/m<sup>2</sup> and is not actively promoted. Additionally, there has been historical evidence dexrazoxane may limit the anti-tumor activity of specific anthracycline-based treatment regimens, likely further limiting dexrazoxane use.

Despite hundreds of thousands of anthracycline prescriptions annually within the US, the use of anthracyclines is even more prevalent in ex-US markets.<sup>3</sup> Large commercial upside exists outside the US as the US market comprises approximately 5% of overall globally reported anthracycline prescriptions.

**Global Anthracycline\* Use (Total # of Prescriptions)**



\*Anthracyclines included in count: Aclarubicin, Amrubicin, Daunorubicin, Epirubicin, Idarubicin, Pirarubicin, Valrubicin  
 Figure 2 - Worldwide Anthracycline Use 2023 (IQVIA MIDAS Anthracycline Use Data)

Despite a robust pipeline of products in development across many tumor types for which anthracyclines are used, anthracyclines’ overall efficacy is expected to drive their continued utilization as backbone therapy.

Based on the epidemiological factors of potential target indications, established usage of anthracyclines, and levels of perceived unmet need from Key Opinion Leaders (KOLs) and physician discussions, breast

<sup>3</sup> IQVIA MIDAS Anthracycline Use Data

cancer was selected for this particular commercial assessment, evaluating the utility of Zantrene as a cardio-protective and anti-cancer therapeutic.

Based on the rate of anthracycline use within various subtypes of breast cancer, Zantrene is well-positioned for use in metastatic breast cancer broadly, and within the neoadjuvant setting for HR+/HER2- and triple negative breast cancer (HR-/HER2-).<sup>4</sup> In the United States there are an estimated ~75,000 breast cancer patients who receive anthracyclines annually.

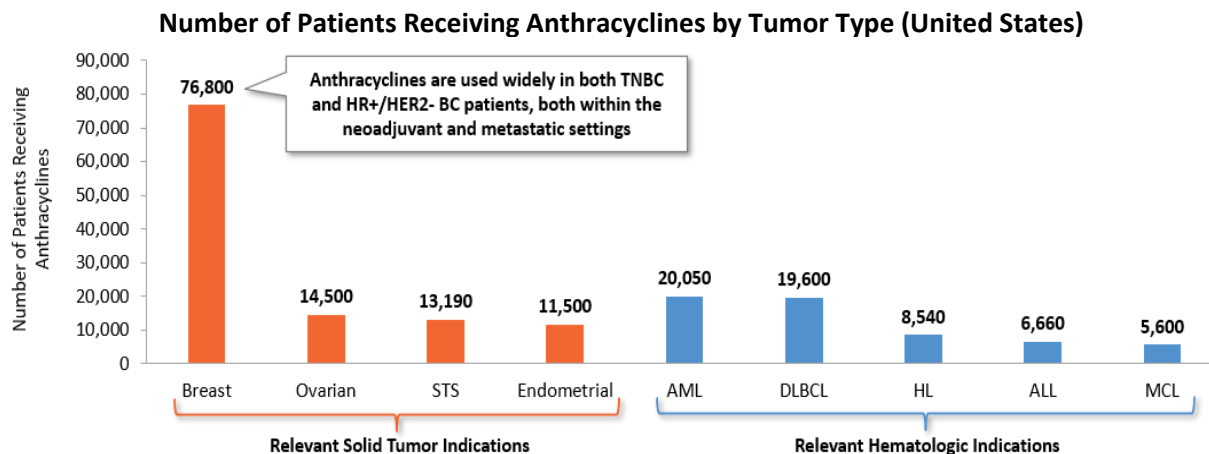


Figure 3 - Relevant Indications<sup>5</sup>

Within metastatic breast cancer specifically, anthracyclines are used in third line or later treatments, with liposomal doxorubicin (Doxil) being the preferred anthracycline of choice by physicians. Because of the nature of metastatic disease, ~25-40% of patients with HR+/HER2- and triple negative breast cancer progress to the line of therapy in which anthracyclines are used. Within the neoadjuvant setting, HR+/HER2- and triple negative breast cancer subtypes often receive taxanes, platinum-based therapy, or anthracycline-based treatment prior to surgical resection, dependent upon tumor size and patient characteristics. Zantrene would likely have limited usage within neoadjuvant HER2+ patients due to the availability of HER2+ targeted therapies that displace the usage of anthracycline-based treatment within this population.

To understand the value of Zantrene, three unique clinical performance scenarios were tested, which included “cardio-protection only”, “cardio-protection and “low anti-cancer”, and “cardio-protection and “high anti-cancer” profiles. Within the target product profiles, Zantrene’s name was blinded, replaced by the pseudonym “Product X”. To test feedback from the interview cohort, the following theoretical product profiles were put forward:

<sup>4</sup> HR = Hormone receptor; HER2 = Human epidermal growth factor receptor 2

<sup>5</sup> STS = Soft tissues sarcoma, AML = Acute myeloid leukemia, DLBCL = Diffuse large B cell lymphoma, HL = Hodgkin’s lymphoma, ALL = Acute lymphoblastic leukemia, MCL = Mantle cell lymphoma

<sup>6</sup> Based on historical data, in the metastatic setting, doxorubicin has demonstrated a median PFS in the range of 6 to 8 months

Sourced from SEER Cancer Statistics, Cancer.org, Triangle Insights Analysis and Primary Research

- **Cardio-protection only profile** included a 30% reduction in the incidence of cardiac events
- **Cardio-protection + low anti-cancer profile** includes an incremental 2-month improvement<sup>6</sup> in Progression Free Survival (PFS) along with a 30% reduction in the incidence of cardiac events
- **Cardio-protection + high anti-cancer profile** includes an incremental 4-month improvement in PFS along with a 30% reduction in the incidence of cardiac events

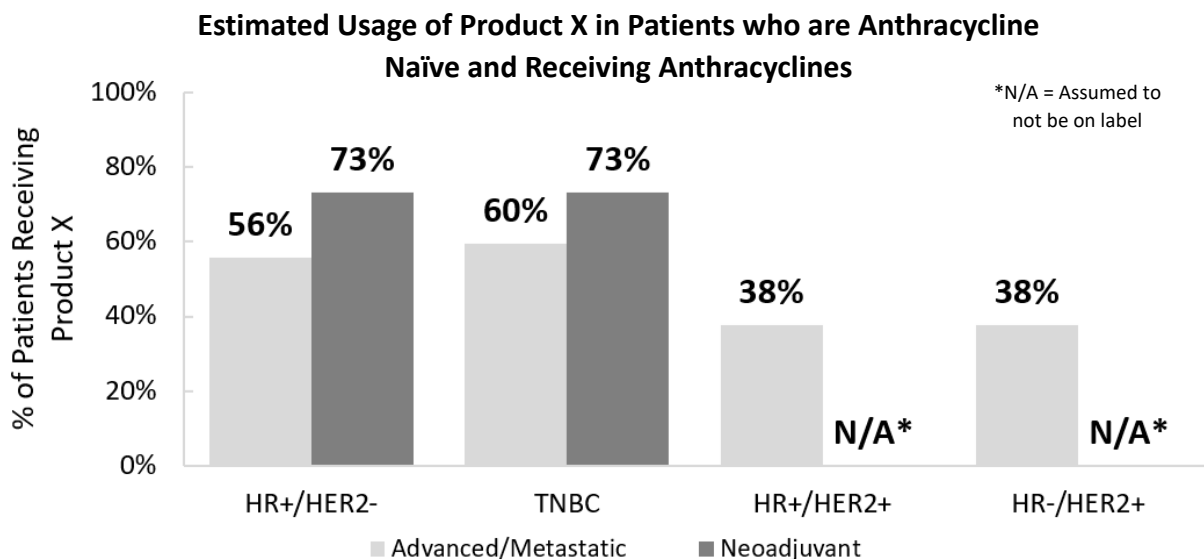


Figure 4 – Primary Research: Medical Oncologist Adoption of Product X (Cardioprotection Only)

Medical Oncologists viewed there to be substantial value in a therapeutic which could limit future cardiotoxic events if taken alongside an anthracycline, mentioning a 30% reduction in the incidence of cardiac events may lead to widespread adoption of Zantrene, especially in patients with underlying cardiac risk factors. Physicians were receptive to the “cardio-protection only” performance scenario, stating Product X usage in approximately 60% of metastatic patients (the yearly incidence of breast cancer patients of all subtypes receiving metastatic anthracycline-based treatment is ~35,500).<sup>6</sup>

In the neoadjuvant setting, oncologists believed Zantrene had strong applicability to HR+/HER2- and triple negative breast cancer patients, estimating the product may be used in up to 70% of anthracycline naïve neoadjuvant patients in these subgroups (the yearly incidence of HR+/HER2 and TNBC patients receiving neoadjuvant anthracycline-based treatment is ~38,000).<sup>7</sup> Multiple oncologists also specifically noted Zantrene could provide significant value within triple negative breast cancer patients as these patients tend to be younger and healthier.

<sup>6</sup> Based on primary research

<sup>7</sup> Based on primary research

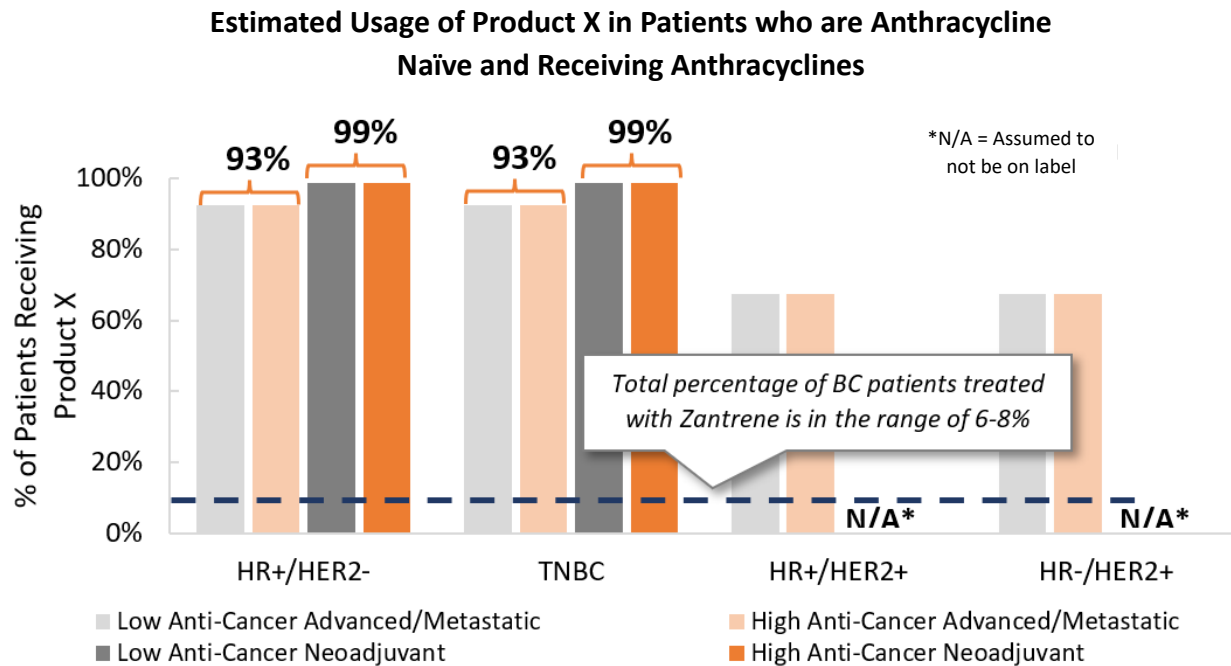


Figure 5 – Primary Research: Medical Oncologist Adoption of Product X (Cardioprotection and Anti-Cancer)

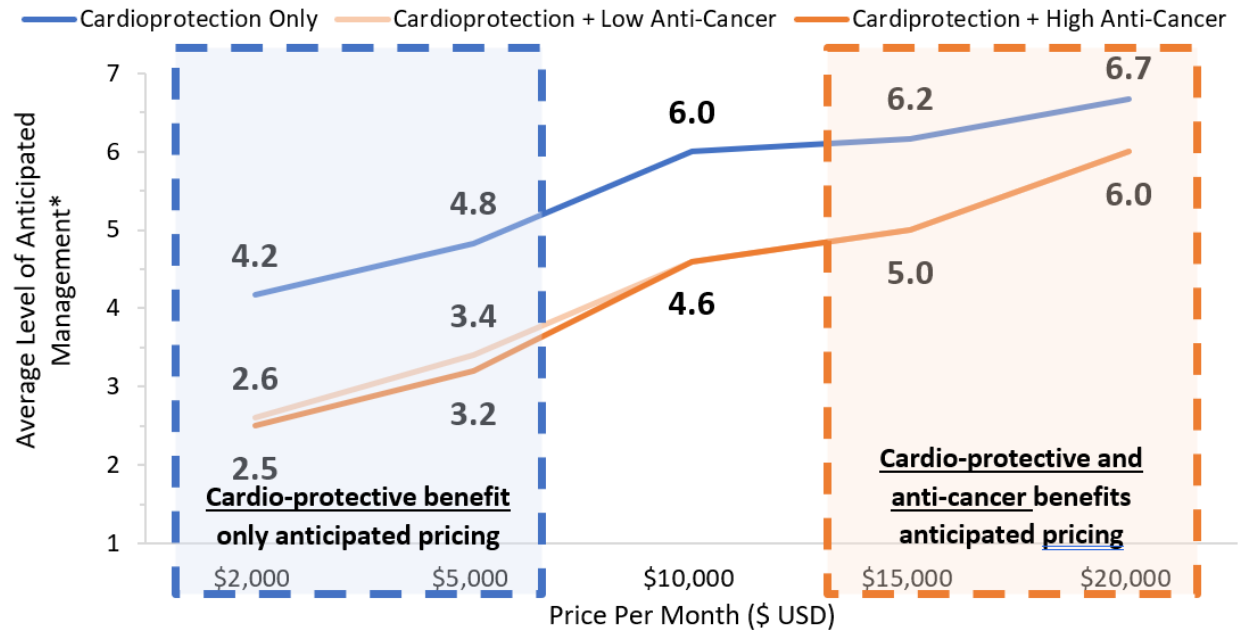
Medical oncologists were further receptive to the anti-cancer target product profiles<sup>8</sup>, noting the potential added survival benefits provided to patients (e.g., PFS and pCR).<sup>9</sup> Achieving a minimum threshold of an incremental two-month PFS would potentially result in widespread utilization of Zantrene. Within metastatic breast cancer specifically, oncologists suggested Zantrene may be applicable for all anthracycline naïve patients across all subtypes. Similarly, oncologists reported a use case in nearly the entirety of the target neoadjuvant patient population (HER2- breast cancer subtypes).

Under all tested scenarios, oncologists specifically noted the potential for Zantrene to increase the overall lifetime cumulative dose of anthracyclines, a benefit which could lead to improved survival outcomes.

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<sup>8</sup> No adoption difference was observed between the low and high anti-cancer profiles of Zantrene.

<sup>9</sup> PFS is the length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease but it does not get worse. pCR refers to the absence of invasive/in situ cancer in the breast and/or axillary lymph nodes. PFS and pCR are common clinical endpoints within breast cancer trials.

**Anticipated Level of Restriction  
 (By Price and Clinical Endpoint)**


\*1-7 scale representing restriction where 1 is very low restriction and 7 is highly restricted

Figure 6 – Primary Research: Anticipated Level of Restriction<sup>10</sup> at Different Price Points

Alongside analogue product pricing analysis, discussions with payers were conducted to further establish potential Zantrene pricing corridors. Based on levels of anticipated management, managed care organization (MCO) medical directors (key decision makers regarding pricing and therapeutic management within the US market) expected Zantrene pricing to be in the range of \$3-4k USD per month as a cardio-protective supportive care therapeutic. Demonstration of anti-cancer benefits would place Zantrene within the protected class of “oncolytics”, allowing for pricing in-line with recently approved anti-cancer therapies (~\$15-20k USD per month). Within the US market, products falling within protected classes are typically managed less restrictively by payers.

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<sup>10</sup> Levels of restriction refers to how closely managed a product may be by payers (e.g., step-edit: requirement for failure of prior therapies; prior authorization: additional criteria required for patient access to therapeutic).



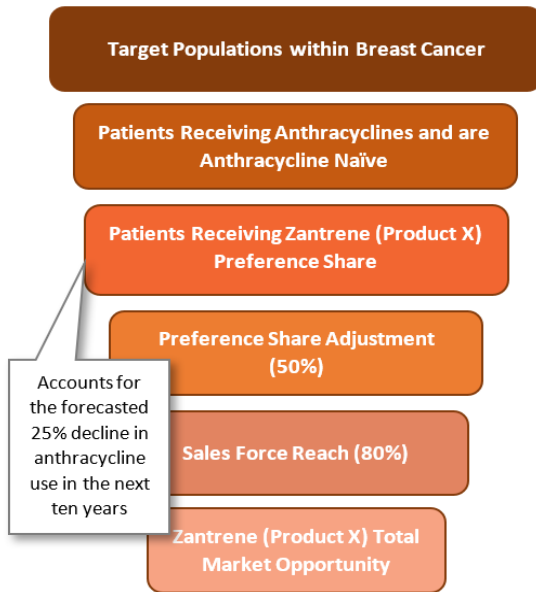
**Zantrene Forecast Assumptions  
 (Not Exhaustive)**


Figure 7 - Zantrene Forecast Assumptions (Not Exhaustive)

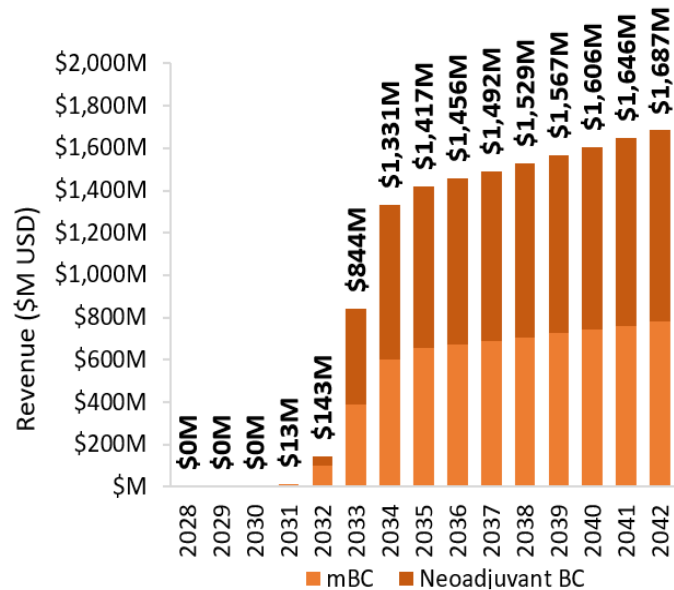
**Estimated Zantrene US Revenue  
 (Cardioprotection + Anti-cancer)**


Figure 8 - Zantrene US Revenue: Cardio-Protection + Anti-Cancer




Based on the expected pricing, volume of anthracycline use, and physician adoption by segment (including a 50% downward adjustment to physician-stated adoption) total peak US revenues for Zantrene may reach ~\$1.7B USD if developed as breast cancer anti-cancer agent, or ~\$200M-300M USD as a supportive care cardio-protective therapeutic in breast cancer (without direct anti-cancer benefits).

Expansion to additional indications for which anthracyclines are commonly used (e.g., hematologic malignancies, sarcomas, and gynecologic cancers) and ex-US markets (~95% of anthracycline use is outside the US), may present further commercial upside.

Assuming expansion to each of these markets and indications, the overall opportunity for Zantrene may be greater than \$5B USD if anti-cancer efficacy is demonstrated, or ~\$1B USD as a supportive care cardio-protective therapeutic.

## Methodology

To understand the commercial potential of Zantrene, a multi-step assessment was conducted by Triangle Insights Group, commissioned by Race Oncology. Secondary research focusing on the consolidation of US epidemiology data, summarization of clinical pipelines, and characterization of analogue drug performance and pricing was completed to characterize the most commercially attractive targeted indications.

KOL Cohort		Primary Physician Cohort	
	University Role(s)		Respondent Role
KOL #1	<b>University of Chicago</b> • Medical Oncologist and Hematologist	<b>Medical Oncologists</b>  12	<b>Med. Oncologists (N = 12)</b> Average Years in Role: 25 Years
KOL #2	<b>University of Pittsburgh</b> • Oncologist within the Comprehensive Breast Cancer Center • Involved with Clinical Investigation at Pitt		Average Breast Cancer Patients per Year (Range): 140 Patients (45 – 350)
KOL #3	<b>University of California San Diego</b> • Medical oncologist specializing in breast cancer • On the leadership board for large breast cancer network trials	<b>Gynecologic Oncologists</b>  8	<b>Gyn. Oncologists (N = 8)</b> Average Years in Role: 16 years
KOL #4	<b>Yale School of Medicine</b> • Involved in Clinical Research • Professor of Clinical Medicine (Medical Oncology) • Principal investigator of a large breast cancer grants program		Average Gynecologic Cancer Patients per Year (Range): 650 Patients (200 – 1000)
KOL #5	<b>Orlando Health Cancer Institute</b> • Medical oncologist within the breast cancer center • Leadership within the Cancer Risk Evaluation at UF Health Cancer Center	<b>Payers (MCO Medical Directors**)</b>  6	<b>MCO Directors (N = 6)</b> Average Covered Lives (Range): 10M Covered Lives (1M – 50M)

To affirm the identified target indications and further understand the clinical value of Zantrene, blinded primary research with stakeholders was conducted. KOLs and oncologists were interviewed within the initial stakeholder cohort to further understand anthracycline usage habits within various oncologic indications, Zantrene trial structure and feasibility, and potential clinical value.<sup>11</sup> Following the characterization and summarization of these findings, discussions with additional oncologists were held to examine different clinical profiles of Zantrene (Product X).<sup>12</sup> Furthermore, discussions with MCO medical directors were held to quantify potential price points and levels of restriction for Zantrene under multiple clinical profiles.<sup>13</sup>

Synthesized findings from stakeholder discussions were leveraged to forecast revenue estimates for Zantrene as a cardio-protective agent, and as an anti-cancer agent in breast cancer. Additional scenario analysis was conducted to identify the bounds of the assessment, with further characterization of the relative size of other potentially relevant market segments for future development (e.g., ovarian, endometrial, and hematologic cancers).

<sup>11</sup> Initial Interview Cohort: N=5 KOLs; N=4 Oncologists

<sup>12</sup> Primary Interview Cohort: N=16 Oncologists

<sup>13</sup> Levels of restriction refers to how closely managed a product may be by payers (e.g., step-edit: requirement for failure of prior therapies; prior authorization: additional criteria required for patient access to therapeutic).

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**About Triangle Insights Group**

Triangle Insights is a premier strategy consulting firm providing guidance on critical business issues to life science industry leaders. Triangle Insights supports clients in the therapeutics, diagnostics, and medical device industries, and have partnered with clients to address needs throughout the commercial lifecycle. Over 25% of all projects completed by Triangle Insights fall are focused on the oncology market.