

ASX Announcement

Race releases complete cardio-protection data presentation and video

- Independent analysis suggests use case for Zantrene in nearly the entire identified target patient population as a cardio-protective oncology drug if anticancer benefits are demonstrated
- If anti-cancer efficacy is demonstrated, sales for Zantrene could represent an overall peak commercial value of ~\$1.7B USD in breast cancer alone within the US (~\$3.4B USD globally)
- Revenue may extend to \$5-8B USD annually if expansion is achieved into additional identified cancer indications and further approvals are obtained in ex-US markets.

14 April 2023 – Race Oncology Limited ("Race") is pleased to release a detailed commercial assessment of the market potential for Zantrene[®] as a cardio-protective agent or dual cardio-protective + anti-cancer agent in breast, endometrial and ovarian cancers.

Zantrene as a cardio-protective agent

Zantrene[®] (bisantrene dihydrochloride) is an anthracene-based anti-cancer agent that was originally developed as a less cardiotoxic alternative to commonly used anthracycline chemotherapeutics such as doxorubicin.

Through work carried out by collaborators at the University of Newcastle, Race discovered that Zantrene protects heart muscle cells from anthracycline-induced damage while also synergising with anthracyclines to better kill breast cancer cells (ASX: 22 November 2021).

Follow-up work demonstrated that Zantrene is able to protect the hearts of mice from anthracycline-induced damage without additional chemotoxicity and myelosuppression (ASX: 30 June 2022.)

Additional preclinical studies are underway in cell and animal models exploring both the mechanism of action and optimal therapeutic usage of Zantrene.

Race announced (ASX: 1 February 2023) that it had received human ethics approval from the Hunter New England Human Research Ethics Committee (NSW, Australia) for the observational stage of a planned Phase 1/2b clinical trial of Zantrene in breast cancer patients receiving doxorubicin and cyclophosphamide (AC therapy) who have two or more cardiovascular risk factors. Details of the trial design and intent have been released previously (ASX Announcement: 9 December 2022). Key supportive contracts for the study were announced on 13 March 2023.

Race Oncology Ltd ABN 61 149 318 749



Triangle Insights research – brief overview

The blinded primary market research, commissioned by Race and conducted by Triangle Insights, provides additional background to the written summary released to ASX on 3 April 2023.

US epidemiology data were consolidated to characterise relevant patient segments and associated anthracycline use. The strong clinical efficacy and survival benefit of anthracyclines was noted to have driven widespread and regular use across a variety of different tumor types.

Given cardiotoxicity associated with anthracycline use remains the largest single concern for oncologists, the research noted there is a large unmet need for cardio-protection or extra survival benefits.

Triangle and Race collaboratively developed multiple blinded Target Product Profiles (TPPs) based on expected potential outcomes (e.g., ability to demonstrate anti-cancer activity). Triangle then conducted blinded stakeholder research with Key Opinion Leaders (KOLs), physicians, and payers to understand potential Zantrene (Product X) utilisation and pricing.

Discussions with oncologists suggested Zantrene may be widely adopted for nearly the entire identified breast cancer target populations if anti-cancer benefits are demonstrated. According to oncologists, Zantrene may be broadly leveraged as a cardio-protective therapy in the absence of anti-cancer data, assuming no impact on the anti-cancer effect of the underlying anthracycline regimen. If anti-cancer benefits are demonstrated, payer discussions suggested pricing on par with recent novel oncology therapeutics, representing an overall peak commercial value of ~\$1.7B USD within breast cancer alone in the US (~\$3.4B USD globally.) Revenue may extend to \$5-8B USD if expansion into additional identified indications is achieved, together with further approvals in ex-US markets.

CEO and Managing Director, Damian Clarke-Bruce commented: "It is pleasing to now be able to share this complete research report to further illustrate what the cardio-protection market potential may look like. This has been defined with three unique clinical scenarios, where Zantrene has demonstrated pre-clinical and historically, early phase therapeutic outcomes. Our thanks go to the Triangle team for taking the time to provide the additional colour on this important piece of research.

It is clear that anthracycline-associated cardiotoxicity remains a major concern for oncologists, and one which can impact the physician's approach to dosing, sequencing and overall treatment regime. We hope that our clinical program will be able to provide a therapeutic option to enable optimal treatment outcomes for cancer patients globally, receiving anthracycline therapy."

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Video resource available

In addition to the presentation appended to this announcement, a video is available to investors, where the Triangle Insights research team provides further context to the slides. To view a copy of the video, please visit: <u>https://www.raceoncology.com/?p=5110</u>.

A copy of the full report follows.

-ENDS-

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 <u>www.raceoncology.com</u>

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 <u>https://announcements.raceoncology.com</u>

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Detailed Summary of Zantrene Commercial Assessment

April, 2023





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Triangle Insights Group – Overview



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Triangle Insights Group is a premier strategy consulting firm providing guidance on critical business issues to life science industry leaders.

The firm's approach combines deep industry knowledge with strong analytical rigor to drive strategic decision-making across client domains.





Average Triangle Insights client satisfaction score



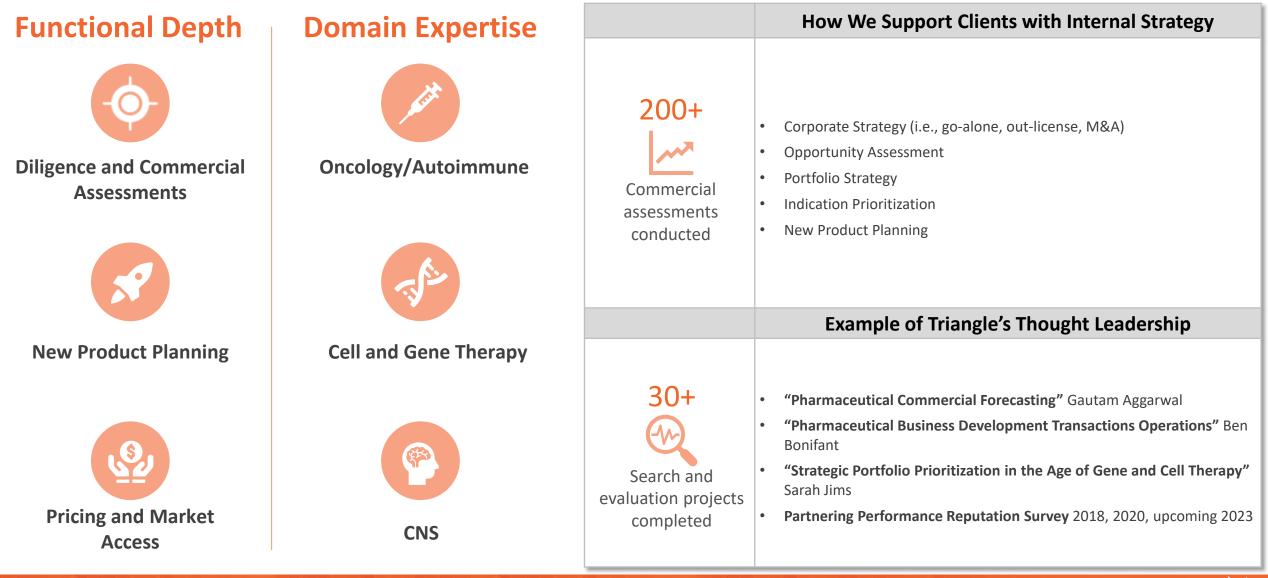
Locations





New York, NY

Triangle Insights Group – Overview



Triangle Insights Group



Chris Apolito Partner



Ben Bonifant Partner

Chris Apolito has over twenty years of pharmaceutical and strategy consulting experience. His previous employers include GlaxoSmithKline, Becton Dickinson, AVOS Life Sciences, and Campbell Alliance. While at GlaxoSmithKline, Chris's scientific accomplishments led to multiple patent authorships and peerreviewed publications. In BD roles, Chris was responsible for corporate strategy and reviewing in-licensing and out-licensing opportunities. For the last fifteen years, Chris has led consulting engagements focused on corporate strategy, R&D portfolio strategy, and commercial assessments across the life science sector.

Degrees: M.B.A., Kenan-Flagler Business School at University of North Carolina | M.S., University of Buffalo | B.S., Biochemistry, University of Rochester Ben Bonifant has 20+ years of experience providing strategic guidance to global pharmaceutical and biotechnology organizations, and to private equity funds. His perspectives are frequently published in life science and strategy journals, and have been used in graduate business programs. Ben has been a guest lecturer at Duke's Fuqua School of Business, the Indiana University Kelley School of Business, and industry conferences in the US, Europe, and Canada.

Parker Guse Principal

Parker Guse is an experienced Principal at Triangle Insights. Since joining Triangle Insights in 2014, he has developed expertise in new product planning, commercial assessment, market access and pricing, corporate strategy, and due diligence. His project experience spans across a variety of therapeutic areas including: oncology, CNS, immunology, orphan diseases, infectious disease, and dermatology. His educational background includes economics, finance, and chemistry.

Degrees: M.B.A., Stanford Graduate School of Business | B.S., Duke University *Degree:* B.A. Economics, University of North Carolina at Chapel Hill

Project Approach

Zantrene



A robust commercial assessment of Zantrene as a cardio-protective and cardio-protective and anti-cancer agent in breast, endometrial, and ovarian cancers was conducted.

Project Approach 1 2 3 Captured 4 **Evaluated** 5 **Defined Strategic Assessed Market Developed Insights & Stakeholder** Commercial Recommendations Questions Landscape Insights Opportunity Collaborated to develop key Consolidated US epidemiology Collaboratively developed • Synthesized insights into "Base • Synthesized the commercial data to characterize relevant various blinded TPPs based on Case" market revenue *implications for Zantrene* strategic questions to be addressed within the patient segments and expected potential outcomes estimates for Zantrene as a Highlighted key considerations commercial assessment to associated anthracycline use (e.g., ability to demonstrate cardio-protective agent, and as associated with the commercial anti-cancer activity) a cardio-protective and antiunderstand Zantrene as a • Prepared summary of clinical opportunity for Zantrene cardio-protective agent, and a cancer agent within breast • Conducted blinded stakeholder pipeline to understand potential • Prepared summary cardio-protective and anticancer future novel treatments which research with KOLs, physicians, observations and cancer agent may displace anthracyclines and payers to understand • Conducted scenario analysis to recommendations for Race potential Zantrene (Product X) *identify bounds of the* Characterized analog drug Oncology utilization and pricing opportunity performance/pricing • Characterized relative size of other potentially relevant market segments for future

development (e.g., ovarian, endometrial, hematologic

cancers)

To gather a thorough understanding of the value of Zantrene, Triangle Insights conducted 30+ interviews with KOLs, medical oncologists, and payers.

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

Primary Research Overview

**Managed care organization (MCO) medical directors provided insights as to potential pricing, coverage, and utilization management criteria for Zantrene Source: Triangle Insights Analysis, Primary Research, November 2022

Managed care organizations play a vital role within US healthcare by mediating pricing and healthcare access between patients and providers.

Managed Care Organization (MCO) Overview

- Within the United States, two types of payer organizations are largely responsible for ٠ the facilitation of private health insurance: managed care organizations (MCOs) and pharmacy benefit organizations (PBMs)
- PBMs are solely involved in the facilitation of pharmacy benefit products (i.e., nonphysician administered therapeutics), whereas MCOs may be responsible for both pharmacy benefit and medical benefit products (physician administered-e.g., Zantrene)
- For further context, an MCO is a company comprised of an administrative body, ٠ doctors, hospitals, and other providers who work together to offer private health care insurance plans and health services to beneficiaries (i.e., patients)
- MCO's serve as a mediator of both pricing and access between their patients and ٠ hospitals/other healthcare spaces

MCO Medical Directors were included in the primary research cohort interview due to their direct impact on medical product pricing, negotiations, and utilization management criteria

MCO Medical Director Role

- Overall, MCO medical directors oversee multiple administrative, clinical, and financial facets and policies within an MCO to ensure patient safety and MCO profitability
- Other responsibilities include (not exhaustive):



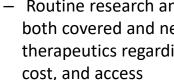
 Development of internal and external MCO patient care policies and responsibilities



 Collaboration with other directors and boards to establish MCO covered therapeutics



 Communication with in-network hospitals and associated provider staff

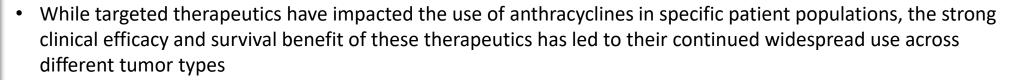


Executive Summary



Zantrene Commercial Assessment – Executive Summary of Project Findings













• Cardiotoxicity associated with anthracycline use remains the largest single concern for oncologists, and the length of anthracycline use is often impacted by these concerns, demonstrating substantial unmet need for a therapeutic

 According to primary research with medical and gynecologic oncologists, Zantrene has an expected use case in nearly the entire identified targeted patient populations as an oncolytic if anti-cancer benefits are demonstrated

- Payer discussions and analogue analysis suggest Zantrene may garner a price point of \$15-20K USD per month if anti-cancer efficacy is demonstrated, **representing an overall peak commercial value of ~\$1.7B USD within breast cancer alone within the US (~\$3.4B USD globally)**
- Substantial revenue upside exists of up to \$5-8B USD with expansion into additional identified indications and further approvals in ex-US markets

Detailed Findings



Despite being highly effective anti-cancer treatments, anthracyclines garner concern from oncologists due to delayed irreversible cardiotoxicity associated with their use.

Anthracycline Overview	Anthracycline Use (On/Off Label)		
 Anthracyclines are highly effective chemotherapeutic agents 	 Anthracyclines* are used broadly for FDA-approved treatment of various cancers On Label Use: 	l indications as well as off-label for th <u>Off Label Use:</u>	
 The mechanism of action involves the interaction with topoisomerase-II leading to cell growth halt and apoptotic cell death 	 Acute lymphocytic leukemia Acute nonlymphocytic leukemia Acute myelogenous leukemia Acute myelogenous leukemia Hodgkin's lymphoma Non-Hodgkin's lymphoma Wilm's tumor Bladder cancer Soft tissue sarcoma Bone sarcoma Thyroid cancer Neuroblastoma Wilm's tumor 	 Advanced Endometrial Cancer Uterine Sarcoma Metastatic Hepatocellular Cancer Advanced Renal Cell Carcinoma Thymomas & Thymic Malignancies 	
 Adverse reactions to anthracyclines include cardiotoxicity, alopecia, nausea/vomiting, myelosuppression, and fetal harm 	 Bladder cancer Breast cancer Breast cancer Ovarian cancer Osteogenic sarcoma AIDS-related Kaposi's sarcoma Multiple myeloma 	 Waldenstrom Macroglobulinemia 	

and Anthropycling Information and Use Cases

Source: FDA Drug Labels; Venkatesh P, Kasi A. Anthracyclines. [Updated 2022 Feb 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Jan 2022; Volkova M, Russell R 3rd. Anthracycline cardiotoxicity: prevalence, pathogenesis and treatment. Curr Cardiol Rev. 2011;7(4):214-220.

Prolonged anthracycline usage is limited by lifetime maximum cumulative dosing due to concerns of anthracycline-associated cardiotoxicity, especially in patients exhibiting risk factors.

Anthracycline-Induced Cardiotoxicity

- Cardiotoxicity is defined as new onset heart failure and/or detection of left ventricular dysfunction in patients treated with anthracyclines
- Cardiotoxicity is a major cause of morbidity and mortality in anthracycline-treated patients
- The likelihood of cardiotoxicity depends on the cumulative dose of the anthracycline, meaning cumulative maximum dose limitations are in place which may impact optimal treatment

Anthracycline	Maximum Lifetime Cumulative Dose	Current SOC Dosing
Doxorubicin	550 mg/m^2	Cancer-specific guidelines often
Daunorubicin	550 mg/m^2	suggest even lower lifetime maximum dosing due to
Epirubicin	900 mg/m^2 heighte	heightened risk of anthracycline- associated cardiotoxicity
Idarubicin	150 mg/m^2	Recommended doxorubicin
Mitoxantrone	140 mg/m^2	dosing for breast cancer: 60-75 mg/m ² for four cycles

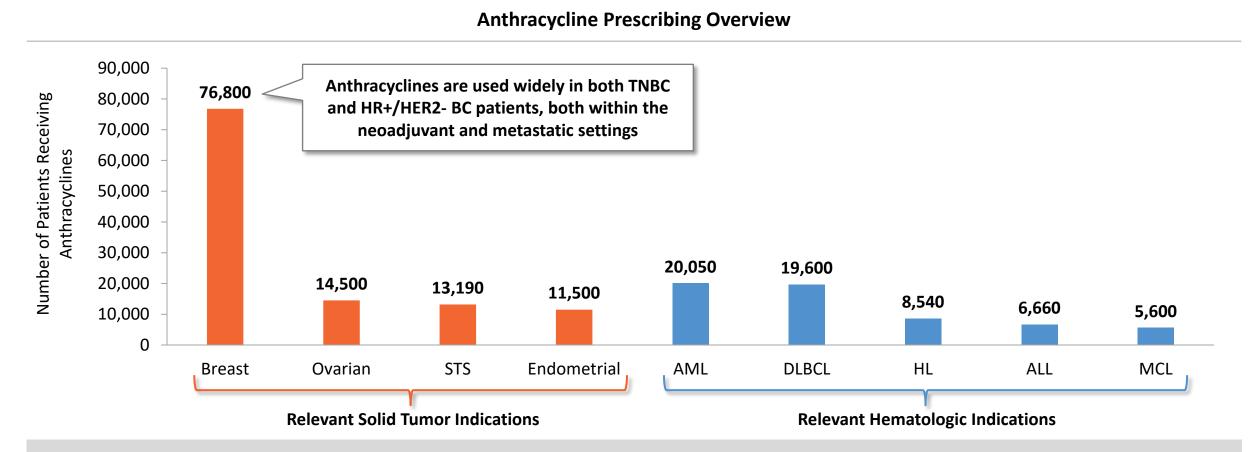
Cardiotoxicity risk factors include: Female Gender High-dose anthracyclines Low-dose anthracycline or high dose radiation to + low dose radiation the chest 60+ Older than 60 years Cardiovascular risk factors Compromised old at cancer diagnosis cardiac function (smoking, hypertension, hyperlipidemia, and obesity)

 $\ensuremath{^*\text{Within}}$ doxorubicin, the primary anthracycline used within breast cancer treatment

Source: Venkatesh P, Kasi A. Anthracyclines. [Updated 2022 Feb 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Jan 2022; Volkova M, Russell R 3rd. Anthracycline cardiotoxicity: prevalence, pathogenesis and treatment. Curr Cardiol Rev. 2011;7(4):214-220.

Anthracycline Cardiotoxicity Risk Factors

Due to their strong efficacy and survival benefits, anthracyclines continue to be widely prescribed across numerous tumor types, with notable total use in breast cancer patients.

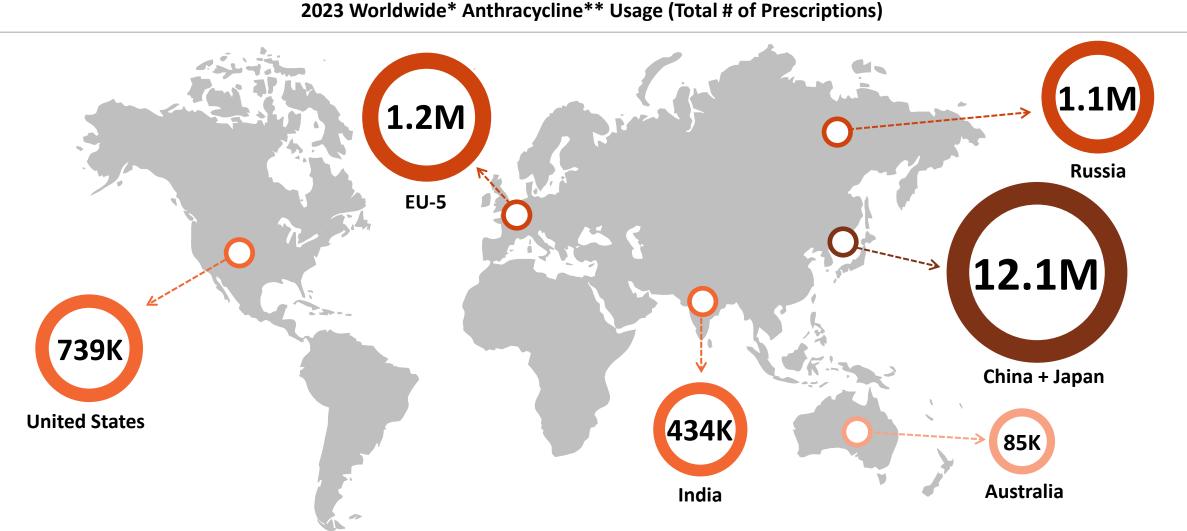


Based on the overall prevalence of the condition and widespread use of anthracyclines, breast cancer was prioritized for the commercial assessment evaluating the utility of Zantrene as both a cardio-protective and anti-cancer therapeutic.

Source: SEER Cancer Stats; Cancer.org; Triangle Insights Analysis, Primary Research, November 2022; Consultant Analysis

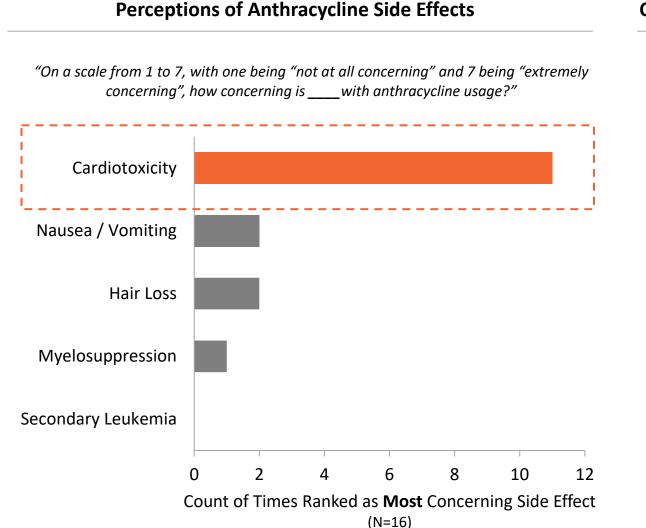
AML = Acute myeloid leukemia, DLBCL = Diffuse large B-cell lymphoma, STS = Soft tissue sarcoma, HL = Hodgkin's lymphoma, ALL = Acute lymphoblastic leukemia, MCL = Mantle Cell lymphoma

While anthracyclines continue to be used widely within the US, the US only accounts for <5% of total global prescriptions.



*Broader global anthracycline usage is higher than just the countries shown above **Anthracyclines included in count: Aclarubicin, Amrubicin. Daunorubicin, Epirubicin, Idarubicin, Pirarubicin, Valrubicin Source: IQIVIA MIDAS AUDITED SU VOLUME Anthracycline Data

Among all the common side effects of anthracyclines, and specifically doxorubicin, cardiotoxicity was by far the most concerning to oncologists.



Oncologist Perspectives on Anthracycline-Induced Cardiotoxicity

- Cardiotoxicity associated with anthracycline use remains the largest single side effect concern for oncologists
- Notably, physicians indicated that cardiotoxicity concerns may impact the total duration of treatment or their broader approach to treatment



"After that lifetime maximum dose [of doxorubicin], there is an exponential increase [in cardiotoxicity]. If we can give a prolonged doses or if the max cumulative dose is double, that would be great."

- Gynecologic Oncologist



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

- Gynecologic Oncologist

Key Takeaway: Substantial unmet need exists for a therapeutic which could alleviate cardiotoxicity concerns

To identify opportunities for which Zantrene may be well-positioned to provide value as a novel therapeutic, a robust prioritization process involving primary and secondary research was conducted.

Zantrene Indication Prioritization Summary

1

2

3

1. On-Label Indication Search

• Broad research of US epidemiology data about oncology indications with on-label usage for common anthracyclines

2. Initial Prioritization

• Focus on indications with the largest relative treatment market

3. Nuanced Prioritization

- Indications were further narrowed down through:
 - Level of anthracycline usage in cancer guidelines
 - KOL feedback from primary research
 - Level of perceived unmet need
 - Trial feasability

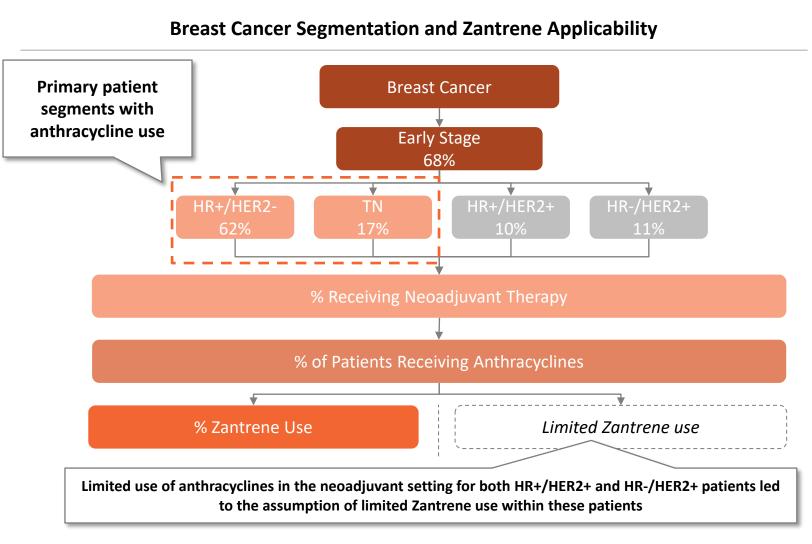
4. Finalized Indication List

- A finalized indication list was provided based on the above criteria:
 - Solid tumor indications: Breast, ovarian, and endometrial cancers, soft-tissue sarcoma
 - Liquid tumor indications: AML and DLBCL

5. Chosen Prioritized Indications

- Collaborative discussions with Race Oncology led to the priotiziation of:
 - Breast, ovarian, and endometrial cancers

Based on the rate of anthracycline use within various subpopulations, Zantrene is well-positioned for use in the neoadjuvant* setting for TNBC and HR+/HER2- breast cancer.



Early-Stage Breast Cancer Treatment

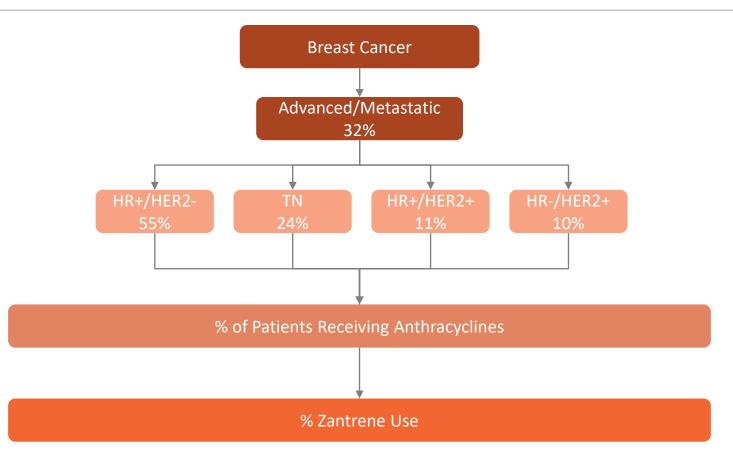
- Surgical resection usually occurs early within breast cancer treatment; however, tumor size drives the potential need for neoadjuvant treatment prior to surgical resection
- Endocrine therapies (aromatase inhibitors) are utilized within patients with HR+ breast cancer subtypes
- HER2+ targeted therapy (Herceptin) is the mainstay of treatment for patients with HER2+ breast cancer subtypes
- Chemotherapy is often used in HER2patients, as there are limited targeted therapy options available
 - Anthracyclines, taxanes, and platinumbased therapy are all common types of chemotherapy

*Neoadjuvant treatment involves the administration of treatment, typically chemotherapy or targeted therapy, prior to the surgical resection of the tumor

HR = hormone receptor; HER2 = human epidermal growth factor receptor 2; TNBC = Triple negative breast cancer (HER2-/HR-) Source: Triangle Insights Analysis, Primary Research, NCCN Guidelines; MD Anderson Treatment Algorithms, November 2022

Additionally, Zantrene is well-positioned for usage within metastatic breast cancer broadly, due to the prevalent use of anthracyclines in these patient populations

Breast Cancer Segmentation and Zantrene Applicability



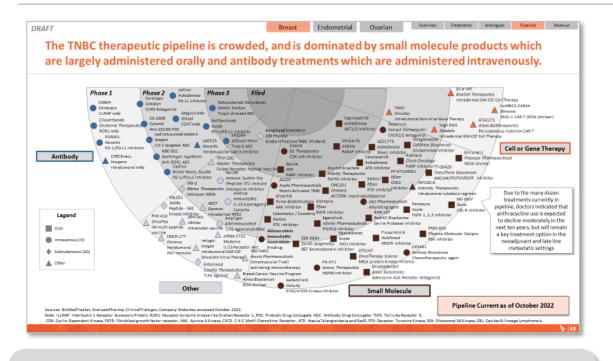
Metastatic Breast Cancer Treatment

- Anthracyclines are generally reserved for later lines (3L+) of treatment for patients with metastatic breast cancer, with liposomal doxorubicin (Doxil) being the preferred anthracycline of choice
- HER2+ and HER2- breast cancer subtypes recommend targeted therapies as both single and combination therapies in earlier lines of treatment (1/2/3L+)
- Many patients with metastatic breast cancer progress to later lines of therapy
 - ~25-40% of patients with HR+/HER2and TNBC progress to lines of therapy in which anthracyclines would be used

Source: Triangle Insights Analysis, Primary Research, NCCN Guidelines; MD Anderson Treatment Algorithms, November 2022

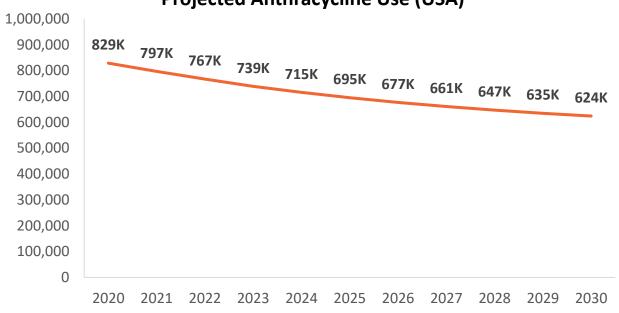
Despite the robust pipeline of breast cancer therapies, anthracyclines are expected to remain a mainstay of neoadjuvant* treatment and later-line metastatic treatment.

Anthracycline Use Expectations



"Anthracycline use in the neoadjuvant setting will stay the same [in the next ten years]. People who will need neoadjuvant treatment will receive Adriamycin-based treatment." - Medical Oncologist

- While the development pipeline for breast cancer therapeutics is robust, it is unlikely anthracyclines will be holistically displaced
- According to IQVIA data, there is an expected global decline in the usage of anthracyclines in the next ten years of about 25%, likely due to the continued addition of novel targeted therapies



— Number of Prescriptions

Projected Anthracycline Use (USA)

*Neoadjuvant treatment involves the administration of treatment, typically chemotherapy or targeted therapy, prior to the surgical resection of the tumor

Source: Triangle Insights Analysis, Primary Research, IQVIA MIDAS Report, BioMed Tracker, November 2022

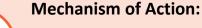
Zantrene

RACE

Zantrene is a small molecule that has demonstrated preclinical efficacy as a cardio-protective and synergistic anti-cancer agent when combined with anthracyclines.

Overview:

- Zantrene is a small molecule drug that has a long history of clinical efficacy as an oncology agent
- Developed in the 1980s as a heart safer alternative to the anthracyclines, never commercialised



- Multiple mechanisms of action including chemotherapeutic, immune stimulating, and putative targeted
- Demonstrated to be cardio-protective in animal and cell models against anthracycline cardiotoxicity via a novel cellular mechanism that is not yet fully understood

Key Features:

- Anthracycline cardio-protective with improved anti-cancer efficacy
- Potential to allow patients to continue treatment beyond the maximum lifetime cumulative dose
- Improved IV formulation developed that allows Zantrene to be delivered by peripheral IV administration

Efficacy Data

- Positive single agent R/R AML trial in Israel with a 40% clinical response rate June 2020
- Historical single agent efficacy in breast, ovarian, and a range of leukemias

To understand the value of Zantrene, three unique clinical performance scenarios were tested: cardio-protection only, cardio-protection + low anti-cancer, and cardio-protection + high anti-cancer.

Cardio-Protection Only Cardio-Protection + Low Anti-Cancer Efficacy Cardio-Protection + High Anti-Cancer Efficacy Therapeutic Product Profile - Product X with Cardio-protective and Anti-Cancer Activity in Therapeutic Product Profile - Product X with Cardio-Protective and Anti-Cancer Activity in Therapeutic Product Profile - Product X for Cardio-protection in Me **Metastatic Breast Cancer** Metastatic Breast Cancer Therapeutic Product Profile - Product X for Cardio-protection in Neoadiuvant HR+/HER2- and Therapeutic Product Profile - Product X with Cardio-pr Therapeutic Product Profile - Product X with Cardio-Protective and Anti-Cancer Activity in TNBC Breast Cancer Neoadjuvant HR+/HER2- and TNBC Breast Cance Neoadiuvant HR+/HER2- and TNBC Breast Cance Mechanism o Action Inhibit At high Produ Patien Primar Patien
 Primar TPP **Efficacy Endpoints** TPP **Efficacy Endpoints** TPP **Efficacy Endpoints** 2-month improvement in median 4-month improvement in median 1 1 PFS PFS (mBC) 30% reduction in the incidence of 30% reduction in the incidence of (mBC) (mBC) • 30% reduction in the incidence of cardiac events cardiac events cardiac events 2 2 • 5% improvement in pCR 2 • 15% improvement in pCR (Neoadjuvant* TN (Neoadjuvant TN 30% reduction in the incidence of (Neoadjuvant TN 30% reduction in the incidence of & HR+/HER2- BC) & HR+/HER2- BC) & HR+/HER2- BC) cardiac events cardiac events

All TPPs blinded Zantrene using the pseudonym "Product X"; No mention of Race Oncology or Zantrene occurred before, during, or after any of the primary research interviews.

Note: BC = Breast Cancer; TN = Triple Negative; mBC = Metastatic Breast Cancer; PFS = Progression free survival; pCR = Pathologic complete response

Medical oncologists thought Product X could further protect breast cancer patients receiving neoadjuvant treatment and could allow for prolonged anthracycline use in the metastatic setting.

Perspectives on Product X (Zantrene) – Cardio-protection Benefit

On a scale of 1-7, where 1 is "not very favorable" and 7 is "very favorable", how would you rate Product X overall?



Metastatic Setting:

- Oncologists were receptive to Product X for patients with metastatic breast cancer due to the prevalence of anthracycline use
- Oncologists believed the cardio-protective benefit of Product X could allow patients to remain on anthracyclines for increased treatment cycles
 - Oncologists noted some patients discontinue anthracycline use, despite the efficacy, due to the development of cardiotoxic side effects



"There are more patients who will potentially benefit from this treatment, because doxorubicin is the standard of care at this point."

- Medical Oncologist

Neoadjuvant Setting:

- Oncologists were more receptive to Product X usage within the neoadjuvant setting as anthracycline use, specifically doxorubicin, is prevalent in patients with HR+/HER2- and triple negative breast cancer
- Oncologists believed Product X provided additional value in the neoadjuvant setting by preventing long-term cardiotoxicity, given the potential for cure in a younger and healthier patient population

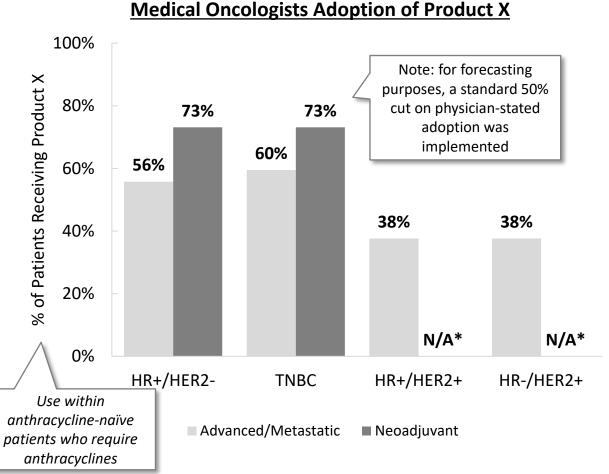


"This is a much better idea, you are talking about patients that you are trying to cure, you don't want them to develop heart failure."

- Medical Oncologist

Medical oncologists expected use of Product X in a majority of patients receiving an anthracycline, assuming a 30% relative reduction in cardiac events.

Product X Adoption: Cardio-Protection Only in the Metastatic and Neoadjuvant Settings



Medical Oncologists Perspectives on Product X Adoption

- A 30% relative reduction in the incidence of cardiac events may lead to widespread adoption of Product X, especially patients with cardiac risk factors
- Product X will likely not be on label for neoadjuvant HER2+ breast cancer subtypes due to the availability and effectiveness of targeted HER2+ therapies, and limited HER2+ patient population



"If we decide to use Doxil, I will use Product X in 100% [of the patients], since you don't want to have any side effects from this treatment."

- Medical Oncologist

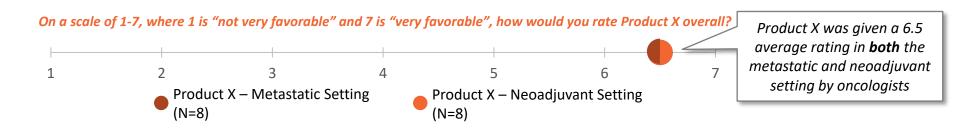


"There are more [TN and HR+/HER2- BC] patients who will potentially benefit from this treatment, because doxorubicin is the standard of care at this point."

- Medical Oncologist

Medical oncologists perceived additional value in Product X as a cardio-protective and anti-cancer agent due to the potential survival benefits in neoadjuvant and metastatic breast cancer patients.

Perspectives on Product X (Zantrene) – Cardio-protection + Anti-Cancer Benefit



Metastatic Setting:

- Nearly all medical oncologists stated their use of Doxil in the metastatic breast cancer setting may increase substantially with the availability of Product X (up to 80% increase in Doxil use)
 - Physicians perceived significant value in both the low anti-cancer (twomonth PFS) and high anti-cancer (four-month PFS) TPPs, expecting equally broad use in either scenario

"I would increase [my Doxil use] because a 4-month PFS is significant. I would say that my usage of Doxil would increase by 80%."

- Medical Oncologist

Neoadjuvant Setting:

- Medical oncologists were the most receptive to the cardio-protection + high anti-cancer profile for breast cancer patients in the neoadjuvant setting because of the perceived additional survival benefit
 - Similar to the metastatic setting TPPs, oncologists held similar perceptions regarding the equally broad use between the low anticancer and high anti-cancer profiles

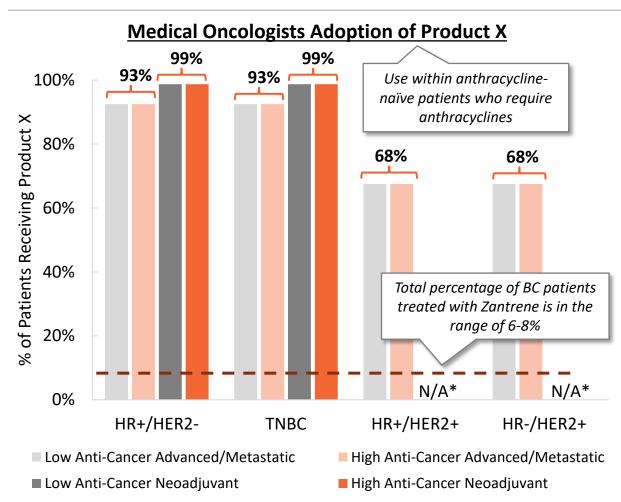


"I can use [Product X] in everyone who are receiving anthracyclines, which is all the patients in the neoadjuvant setting, unless you had a contraindication."

- Medical Oncologist

In the scenario for which Product X demonstrated anti-cancer benefits, the overall anticipated adoption increased to nearly 100% of anthracycline-naïve patients receiving anthracyclines.

Product X Adoption: Cardio-Protection and Anti-Cancer Efficacy Profile in the Metastatic and Neoadjuvant Settings



Medical Oncologists Perspectives on Product X Adoption

- Medical oncologists were highly attracted to the cardioprotective and anti-cancer efficacy profiles, given the potential survival benefits provided to patients
- Physicians expected widespread use of the product regardless of the level on anti-cancer efficacy
- The improvement in PFS and cardio-protection may lead to increased frequency and/or duration of doxorubicin use



"[My overall prescribing of anthracyclines] might change if I'm improving survival, I will increase the use of Doxil by 10-15%"

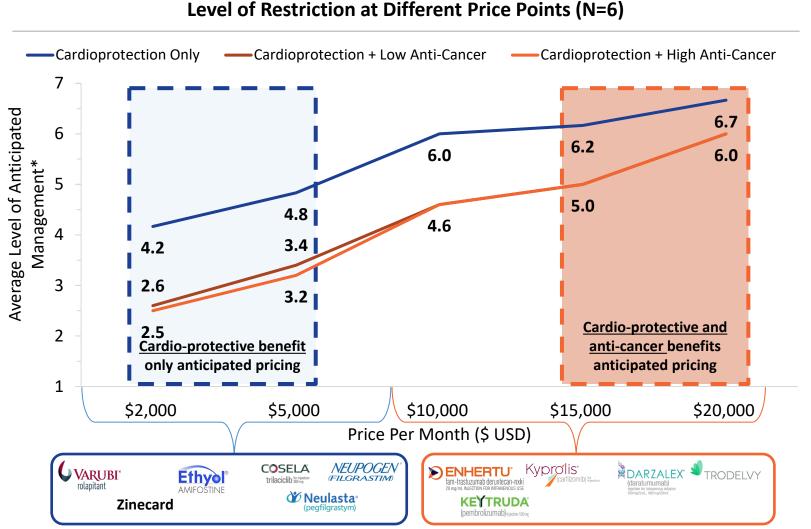
-Medical Oncologist



"This is even better, with no added toxicity. Product X should be used every time you use doxorubicin." -Medical Oncologist

*N/A = not on label

Demonstration of cardio-protective benefits may lead to pricing of \$1-4K USD/month, whereas demonstrating anti-cancer benefit may allow for pricing in the range of \$15-20K USD/month.



Discussion

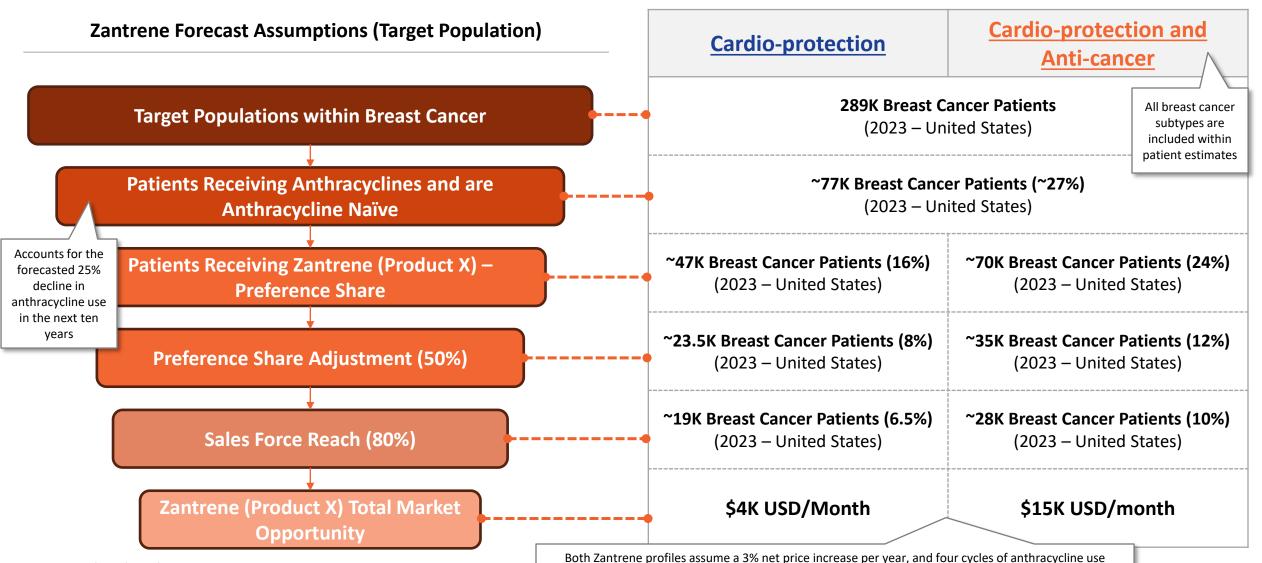
- As a cardio-protective supportive care therapeutic, payers expected pricing in the range of \$1-4K USD per month
- Demonstration of anti-cancer benefits would lead Product X to be considered an, oncolytic, a protected class of therapies that cannot be closely managed
- The price of Product X with anti-cancer efficacy is expected to be similar to new novel anti-cancer therapies (\$15-20K USD per month)

Key Takeaway: Zantrene may have greater pricing potential as an oncolytic rather than as a supportive care agent

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

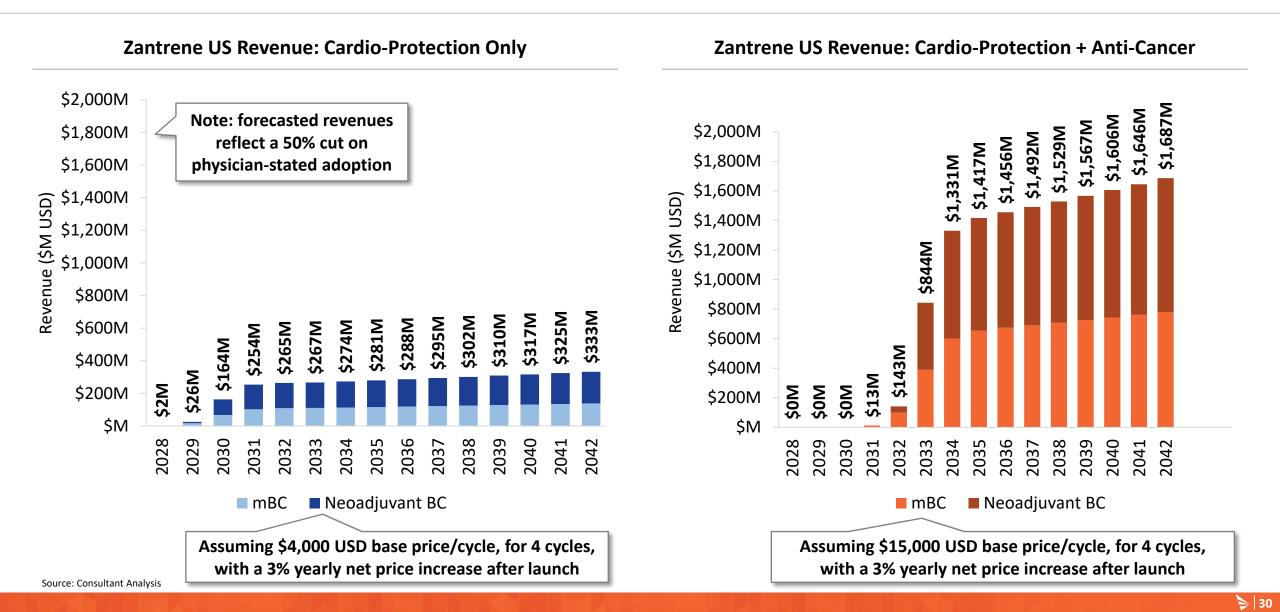
Source: Triangle Insights Analysis, Primary Research, November 2022; Redbook, accessed October 2022

Zantrene commercial forecast estimates utilized a series of population and pricing assumptions such as future anthracycline use, physician utilization, pricing per cycle, and net price increase.



Source: Triangle Insights Analysis

Demonstration of cardio-protective benefits in breast cancer may lead to peak revenues of ~\$300M USD; demonstration of anti-cancer efficacy may increase peak opportunity to ~\$1.7B USD.



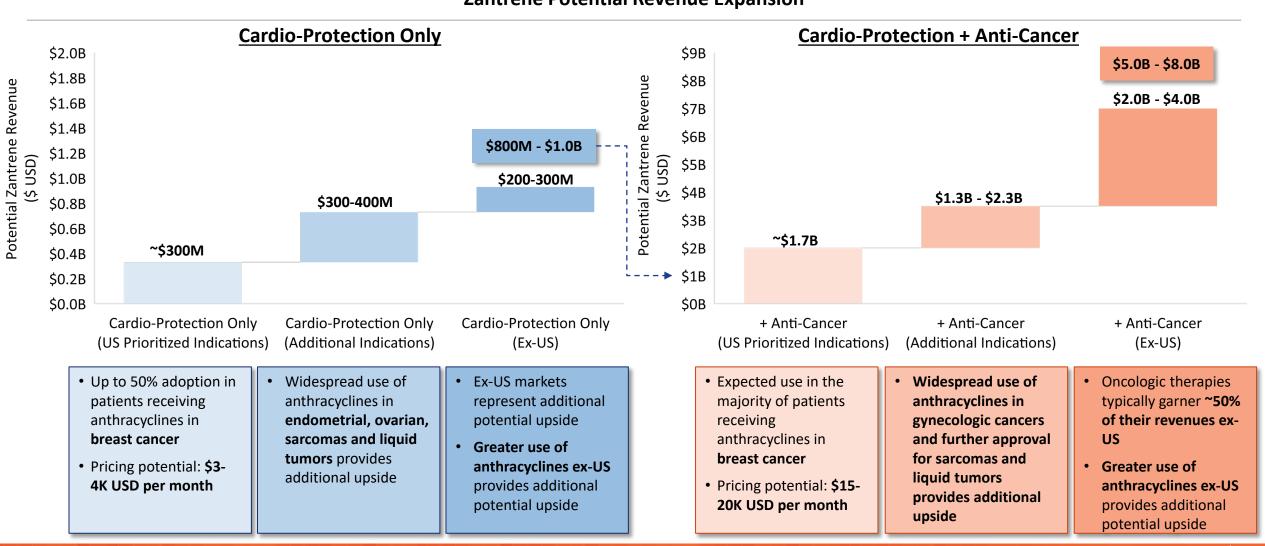
Zantrene's opportunity as a cardio-protective and anti-cancer agent may be dependent upon several key variable including, price per cycle, net price increase, number of cycles, and increased adoption.

Estimated Annual US Net Revenue for Zantrene - Cardio-Protection + Anti-Cancer (\$15,000 USD Price Point)

	Assumptions	Downside Upside		Upside	
Variable		Peak 2042 Annual US Net Revenue (Base Case ~\$1.7B USD)			
Net Price Point Increase (Base: 3% Price Increase/Year)	0% Increase, 6% Increase	\$1.2B	-\$0.5B	+\$0.6B	\$2.3B
# of Anthracycline Cycles (Base: 4 Cycles)	Upside 6 Cycles*			+\$0.8B	\$2.5B
Zantrene Price (Base: \$15K USD)	\$12K USD Downside \$20K USD Upside	\$1.35B	-\$0.35B	+\$0.55B	\$2.25B
Anthracycline Projected Use Volume (Baseline: 25% decline)	Upside: 15% decline Downside: ~35% decline**	\$1.4E	\$1.4B -\$0.3B +\$0 .2B \$1.9B		
\$1.0B \$1.7B \$2.4B \$3.1B (\$ USD)					

*Several oncologists indicated that some patients could receive up to 6 cycles of anthracyclines, especially liposomal doxorubicin (Doxil); **Informed by primary research respondent expectations and varies by indication

Substantial further upside for Zantrene exists outside of breast cancer and within ex-US markets*.



Zantrene Potential Revenue Expansion

*Representative of all ex-US markets (derived through analog assessment of US to ex-US (WW) revenues)

Summary: Based upon a robust commercial assessment, it is estimated the US commercial opportunity of Zantrene as a breast cancer therapeutic may be in the range of ~\$1.7B USD.

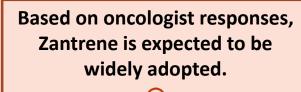
Anthracyclines have prevalent on and off label usage within a variety of oncology indications.

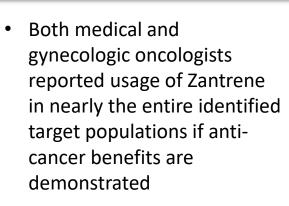


 The strong clinical efficacy and survival benefit of anthracyclines has led to widespread and regular use, both on and off label, across a variety of different tumor types There is a large unmet need for cardio-protection or extra survival benefits.



- Cardiotoxicity associated with anthracycline use remains the largest single concern for oncologists
- Substantial unmet need exists for a therapeutic that can prolong a patient's usage of anthracyclines as utilization of anthracyclines can be cut short due to the cardiotoxic effects associated with prolonged usage





The opportunity for Zantrene is forecasted to be \$1.7B USD within breast cancer alone.



- If anti-cancer benefits are demonstrated, Zantrene pricing may be in the range of \$15K-20K USD per month, representing an overall peak commercial value of ~\$1.7B USD within breast cancer alone in the US (~\$3.4B USD globally)
- Revenue upside of \$5-8B USD exists with expansion into additional identified indications and further approvals in ex-US markets

Appendix

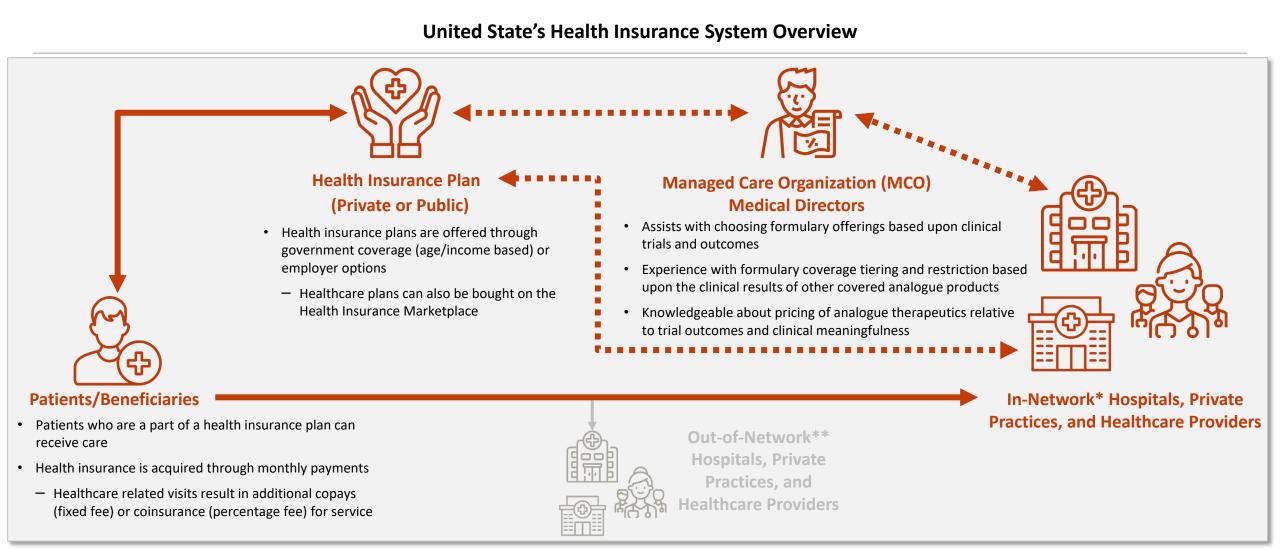


Triangle Insights conducted eight medical oncologist-specific interviews to gather a thorough understanding of the value of Zantrene within breast cancer treatment.

	Region	Years in Practice	Number of Breast Cancer Patients per Year
Medical Oncologist 1	Southeast	25	250 – 300
Medical Oncologist 2	West Coast	23	40 – 50
Medical Oncologist 3	Midwest	30	100
Medical Oncologist 4	Northeast	29	150
Medical Oncologist 5	Midwest	19	75
Medical Oncologist 6	Midwest	30+	60 – 80
Medical Oncologist 7	Northeast	20	45
Medical Oncologist 8	Southeast	20	200

Primary Research Cohort Summary: Medical Oncologists

MCO medical directors play a vital role within the US healthcare system, as they oversee formulary offerings, pricing, and restrictions.



*In-network means that the healthcare provider (hospital or practice) is partnered with the larger health insurance plan - Results in lower copays and coinsurances generally; **Out-of-network includes hospitals or private practices that are not a part of the health insurances network which generally results in a higher cost for service (copay or coinsurance); Sources: Consultant Experience; Kaiser Family Foundation; TheBalance.com

Both public and private health insurance companies utilize a tiering system, with tiers differentiated by drug cost, efficacy, and insurer preference.

Formulary Tiering, Restrictions, and Pricing

- Both public and private health insurance companies provide therapeutics to their beneficiaries (patients) at a fraction of a cost compared to those without health insurance
- Beneficiaries of health insurance plans pay monthly payments for coverage with additional copays (fixed fees) or coinsurance (percentage-based fees) for care, based on the plan type
- Drugs offered by both public and private health insurance companies are often organized in a multi-tiered structure, with tiers differentiated by cost, product efficacy, and brand name
 - Tiers of drugs often differ between health insurance companies, and can vary by the number of tiers offered (3-tier, 4-tier, 5-tier, or other)
 - Formularies, or the list of prescription drugs covered by a health plan, also vary by healthcare insurance provider and are determined by a Pharmacy and Therapeutics (P&T) committee*

Example Humana** 5-tier Insurance Plan						
Tier 1	Tier 2	Tier 3	Tier 4	Tier 5 (Specialty)		
 Preferred, low-cost generic drugs 	 Nonpreferred drugs Low-cost generic drugs 	 Preferred brand- name drugs Some higher-cost generic drugs 	 Nonpreferred brand-name drugs Some nonpreferred, highest-cost generic drugs 	 Highest-cost drugs including most specialty medications 		

Example Humana** E tior Incurance Dia

Tiering of Zantrene

- According to primary interviews with payers, Zantrene as either a cardio-protective agent, or a cardio-protective and anti-cancer agent, can expect to fall within the medical benefit category (specialty tier)
- Zantrene as an anti-cancer drug, rather than a supportive care drug, would likely be classified under the protected oncolytic drug class
 - Protected classes of drugs exist to ensure patients with more severe or persistent disease can receive treatment

Specialty tiers of drugs include medical benefit and pharmacy benefit:



Medical Benefit: Covers administration of drugs that require injections or infusions in an out-patient setting



Pharmacy Benefit: Covers medications that patients can self-administer

*The P&T committee reviews medical literature and clinical trial results to determine which drugs should be included within a health insurance's formulary **Humana is one of the largest health insurance providers in the United States Sources: National Association of Medication Access and Patient Advocacy, Inc.; Medicare.gov; Humana.com