KAZIA THERAPEUTICS

Beyond Inhibition.
Reprogramming Cancer Control.

Corporate Update Call

September 1, 2026

NASDAQ: KZIA | X: @KaziaTx

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Agenda

- Paxalisib Overview
- Investment Framework
- New Data
  - Stage IV TNBC
  - HR+/HER2- Breast Cancer
  - Stage IIb/III TNBC
  - pMMR Colorectal Cancer
- Clinical Trial Expansions
- Investment Framework Recap
- Summary & Next Steps

Overview

Asset Overview	Brain-penetrant, oral, once daily small molecule dual PI3K/mTOR inhibitor with epigenetic and immunomodulatory activity
Origin	Discovered by Genentech (GDC-0084); In-licensed by Kazia Therapeutics
Development Stage	Clinical
Lead Indications	Advanced Breast Cancer (ABC, Phase 1), Glioblastoma (GBM, Phase 3), Childhood Brain Cancer (Phase 2 / Preclinical)
Formulation	Oral, capsule
Key Differentiators	Oral once-per-day dual PI3K/mTOR inhibitor in clinical development for ABC; addresses key mechanisms of immunotherapy resistance; as well as ability to cross the blood brain barrier (BBB) as a potential therapy for primary and secondary brain cancers
Mechanism of Action	PI3K/mTOR kinase inhibitor that disrupts core oncogenic signalling driving tumor growth and survival, while also affecting tumor epigenetic regulation, transcriptional state, and the immune microenvironment beyond its core kinase inhibition
FDA Designations	Fast Track and Orphan Drug for GBM; Fast Track for PI3K-altered brain metastases with radiation; and Rare Pediatric Disease and Orphan Drug for select pediatric gliomas, including diffuse intrinsic pontine glioma (DIPG) and atypical teratoid/rhabdoid tumor (AT/RT)
IP	Patent protection projected until 2043; coverage in over 40 jurisdictions, including U.S., Europe, Japan, China, and India; three patent families: paxalisib molecule *per se* (granted), synthesis of paxalisib (granted), and secondary medical uses / combination treatments (pending)

Kazia-Sponsored Clinical Phase 1b Study Overview

Multi-center, open-label, randomized trial

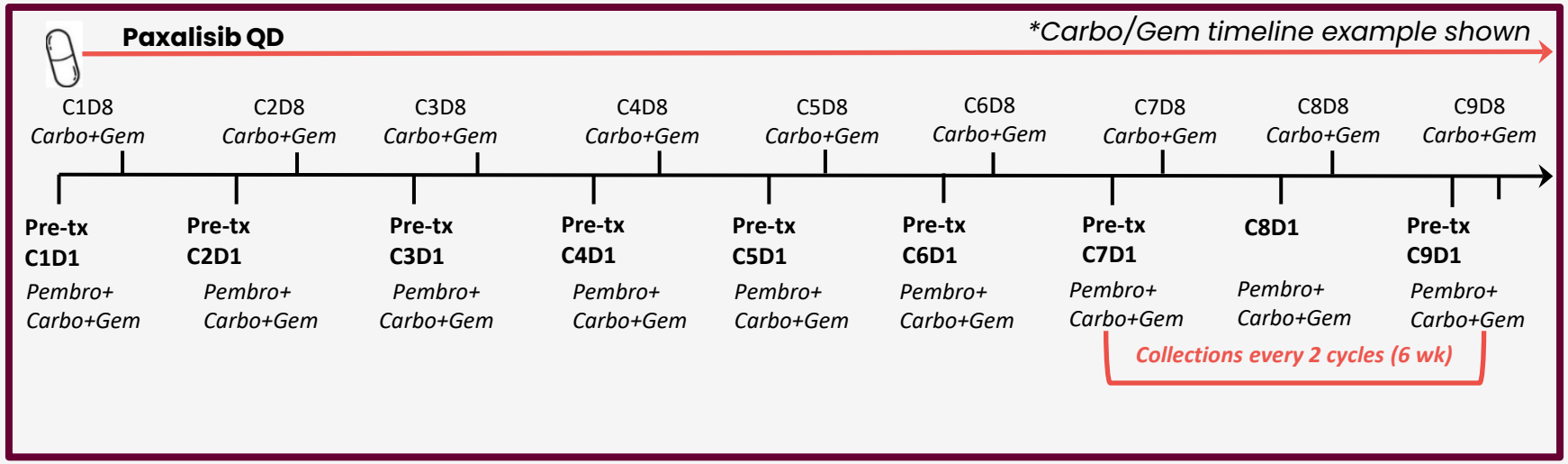
Arm B

- Recurrent, unresectable or metastatic TNBC
- Confirmed that tumors express PD-L1 with a combined positive score (CPS) ≥ 1
- Meet all current prescribing criteria for commencing pembrolizumab therapy

Total enrollment: 36

Paxalisib + Pembrolizumab / Chemotherapy (21-Day Cycle)

- Paxalisib 15mg QD + pembrolizumab 200mg + clinician's choice of IV chemotherapy QW3, n=18
- Paxalisib 30mg QD + pembrolizumab 200mg + clinician's choice of IV chemotherapy QW3, n=18



Endpoints

Primary

- Safety and tolerability of paxalisib in combination with pembro / chemotherapy
- Determine recommended Phase 2 dose (RP2D)

Secondary

- Progression free survival and overall response rates
- To assess the utility of novel liquid biopsy assessments

Trial ID: ACTRN12624001340527

Investment Framework

Key elements underpinning our potential for value creation

Early clinical validation creates multiple paths to significant value

Stage IV TNBC clinical observations + potential expansion into >$40B of additional oncology markets

6/6
Stage IV TNBC Patients

Immune Restoration

Reduced and reprogrammed terminally exhausted CD8+ T cells

6/6
Stage IV TNBC Patients

Metastatic Biology Disrupted

Reduced circulating tumor cell (CTC) clusters associated with metastatic dissemination

Extensive Preclinical Data & IP to Support Expanded Indications

HR+ / HER2- breast cancer • Early-stage high-risk TNBC • pMMR CRC

>$40B
Potential Market Opportunity

6/6
Stage IV TNBC Patients with Clinical Benefit

1 Complete Response • 4 Partial Responses • 1 Stable Disease

Ongoing Complete Metabolic Response with Persistent Biological Reprogramming

Reductions in terminally exhausted CD8⁺ T cells and CTC clusters persist alongside complete metabolic response

WHY THIS MATTERS

Early clinical observations support a potentially differentiated mechanism with applicability beyond TNBC.

Not all PI3K/mTOR inhibitors are created equal. Paxalisib's ability to reprogram tumor and immune biology appears distinct and is not a class effect, supporting potential expansion across multiple solid tumors.

Potential Value Creation Pathway

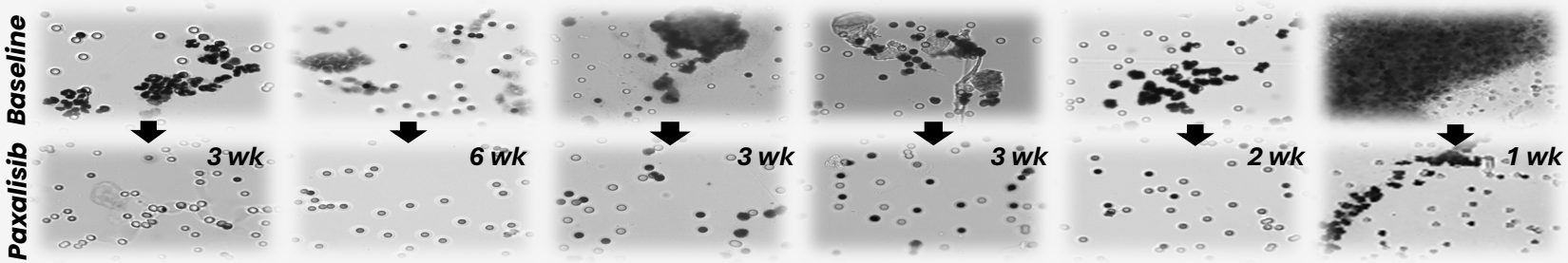
Stage IV TNBC	Additional Data	Broader Indications	Strategic Optionality
Clinical validation	Increased confidence	Expand addressable market	Development / Partnering

Data on file

New Data: Stage IV TNBC Highlights

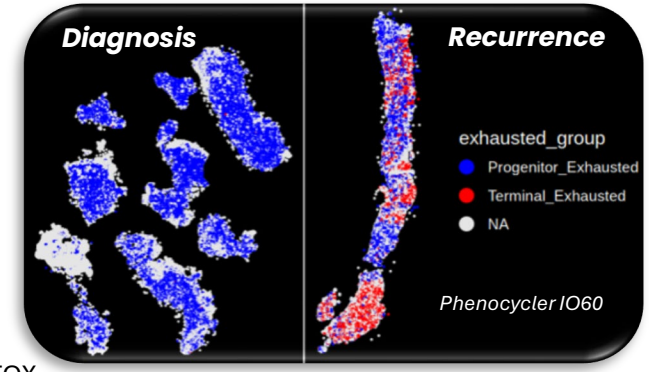
Translational evidence in 6/6 evaluable patients: paxalisib targeting CTC clusters and terminally exhausted T cells

1 Early disruption of CTC clusters by paxalisib combination treatment in Stage IV TNBC



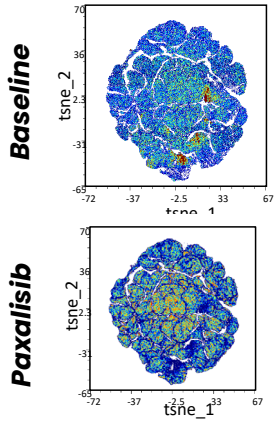
2 Increased terminally exhausted CD8⁺ T cells in progression of TNBC

TNBC disease progression is associated with increased CD8⁺PD1⁺LAG3⁺TOX⁺ terminally exhausted T cells

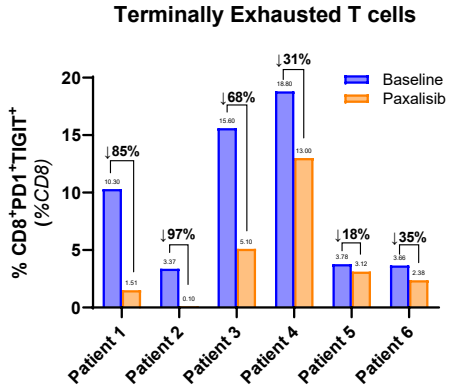


Progenitor: CD8, PD1, TCF-1
Terminal: CD8, PD1, LAG3, TOX

3 Paxalisib rapidly reduces terminally exhausted CD8+ T cells in Stage IV TNBC after 1-3 week treatment



- ↓ PD1
- ↓ TIGIT
- ↓ TIM3
- ↓ LAG3
- ↓ CD160



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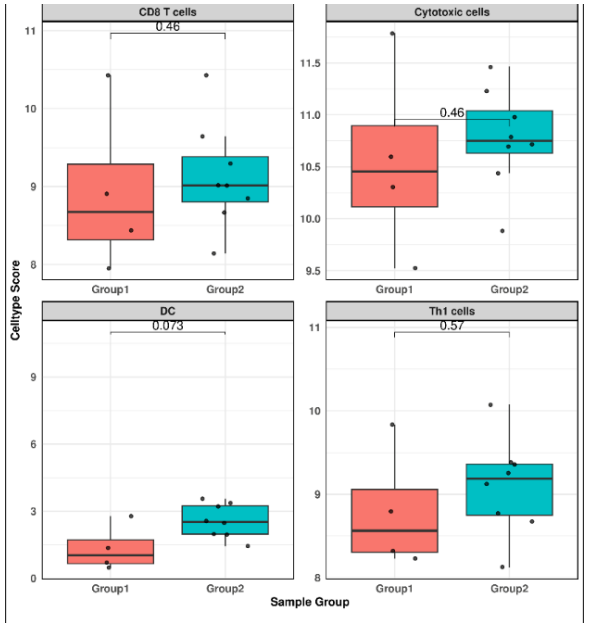
New Data: Stage IV TNBC Highlights (Cont.)

Translational evidence: paxalisib combination reinvigorating the immune landscape

Nanostring RNA profiling of PBMCs isolated from longitudinal patient bloods pre- and post-paxalisib treatment

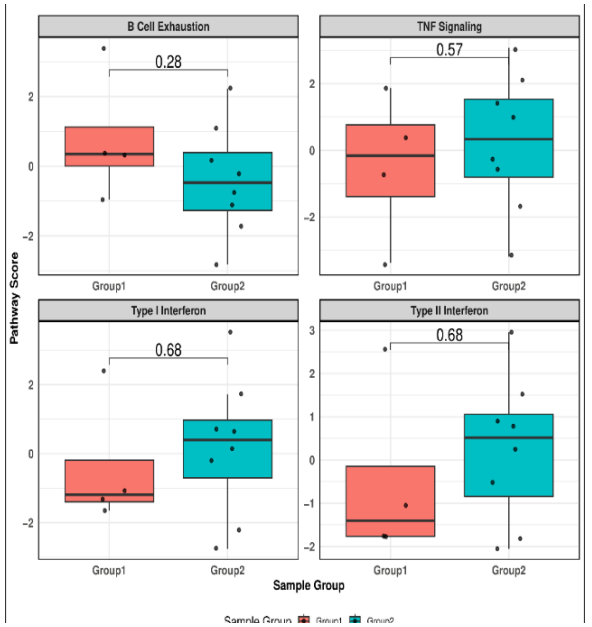
Increased cytotoxicity, IFNγ, DCs



Group 1: Pre-treatment Group 2: Post-treatment

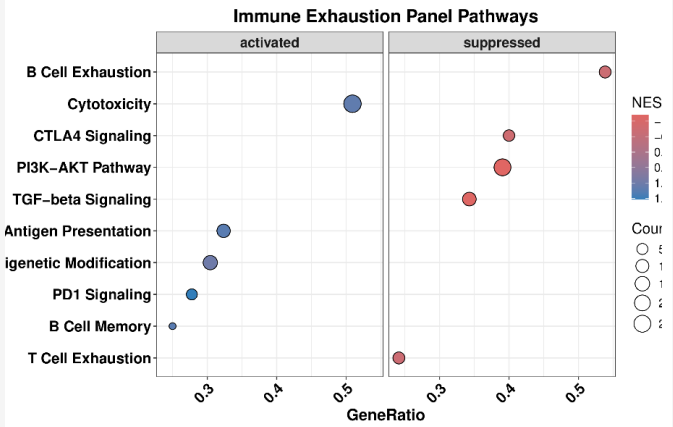
- Increased anti-tumor immune cells
  - ↑ Cytotoxic T cells
  - ↑ Th1 IFNg producing cells
  - ↑ Antigen presenting DCs

Increased antigen presentation, reduced B cell exhaustion



- ↑ Activation of Type I/ II IFN
- ↑ TNF signalling indicative of enhanced cytotoxicity
- ↑ Antigen presentation
- ↓ B cell exhaustion

Inhibition of T cell exhaustion, increased adaptive immune activation



- Global activation of adaptive immune responses
- Inhibition of immunosuppressive signalling (B and T cell exhaustion)
- Confirmation of paxalisib induced inhibition of its target, the PI3K-AKT pathway

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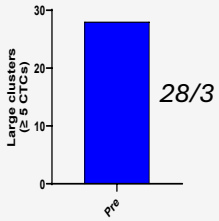
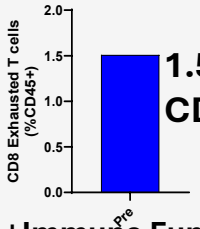
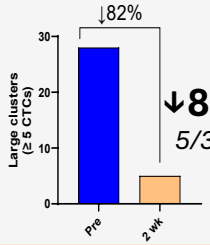
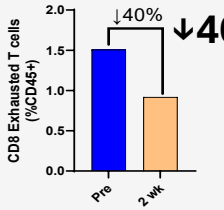
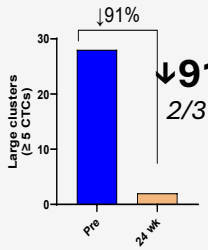
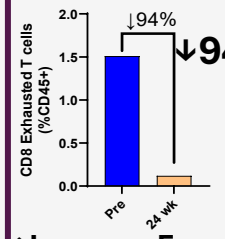
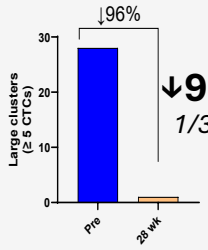
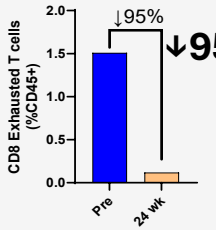
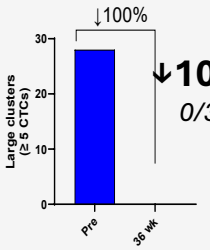
New Data: Stage IV TNBC Highlights (Cont.)

Early efficacy readout predicts complete metabolic response

MAR 25, 2025	JUL 23, 2025	AUG 6, 2025	AUG 20, 2025	AUG 21, 2025	NOV 10, 2025	JAN 21, 2026*	FEB 26, 2026	APR 15, 2026	AUG 4, 2026
PET Scan Multiple bilateral pulmonary nodules New FDG avid skeletal metastatic disease	**BLOOD** **High CTC Clusters** *(Large clusters ≥5 CTCs)*  *28/3 ml* **High % Ex T cells**  **1.5%/ CD45+** **↓Immune Function** Low Granzyme A,B High IL-6 (CTC inducer) (Plasma)	**Paxalisib** **+** **Pembrolizumab** **+** **Chemotherapy** **Treatment Started**	**BLOOD** **Reduced Clusters**  **↓82%** *5/3 ml* Mesenchymal Vim+NRF2+Snail+ **↓92%** **Reduced Ex T cells**  **↓40%** **↑Immune Function** ↑ Granzyme A,B ↓IL-6 (CTC inducer) (Plasma)	**PET Scan** Reduction in pulmonary nodules Resolution of the FDG activity in the left ilium No new FDG activity within the axial or appendicular skeleton	**PET Scan** **COMPLETE RESPONSE** No evidence of metastatic malignancy	**BLOOD** **Reduced Clusters**  **↓91%** *2/3 ml* **Reduced Ex T cells**  **↓94%** **↑Immune Function** ↑ Granzyme A,B ↓IL-6 (CTC inducer) (Plasma) ***PET Scan confirmed CR**	**BLOOD** **Reduced Clusters**  **↓96%** *1/3 ml* **Reduced Ex T cells**  **↓95%** **↑Immune Function** ↑ Granzyme A,B ↓IL-6 (CTC inducer) (Plasma)	**BLOOD** **Reduced Clusters**  **↓100%** *0/3 ml* **↑Immune Function** ↑ Granzyme A,B ↓IL-6 (CTC inducer) (Plasma)	**PET Scan** **COMPLETE RESPONSE** No FDG active locally recurrent, nodal metastatic, or avid distant metastatic disease.

SCAN Matched | **SCAN Predicted** | **SCAN Predicted**

Data on file

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New Data: Stage IV TNBC Individual Patient Responses

Patient	Age	Dose	Disease Sites	Response	Time to Response
1	61	30mg	1 target lesion, left upper lobe of lung	Partial	~5 months
2	47	30mg	Lung, liver, bone, lymph node lesions	Partial	~3 months
3	45	15mg	5 target lesions	Partial	~3 months
4	70	15mg	2 target lesions	Stable disease	~5 months
5	43	30mg	CNS target lesions	Partial (Near complete resolution of dural metastases)	~6 months
6	44	30mg	Lung and skeletal target lesions	Complete	~3 months

Key Takeaway:
Responses were observed across visceral, skeletal and CNS metastases.

Data on file

New Data: Stage IV TNBC Safety Profile Supports Continued Clinical Development

0

Paxalisib-Related Serious Adverse Events (SAEs)

0

Suspected Unexpected Serious Adverse Reactions (SUSARs) or Significant Safety Issues (SSIs) Reported

13

Total SAEs Reported

- 1 patient had 1 SAE
- 1 patient had 3 SAEs
- 1 patient had 9 SAEs
- 3 patients had 0 SAEs

Reported SAEs:

Unrelated (10)

Port-related infection (polymicrobial port colonization)
Chest wall pain (non-cardiac)
Parainfluenza
Lung infection
Nausea
Fatigue
Catheter-related infection
Diarrhea
Sepsis (2 events)

Unlikely Related (3)

Infectious colitis / diarrhea
Diarrhea
Low-grade fevers (Temps: 37.5° - 37.9° C / 99.5° - 100.22° F)

No SAEs were considered treatment-related and no suspected serious safety signals were reported.

Data on file

New Data: Stage IV TNBC Highlights (Cont.)

Clinical evidence: first-in-human signals from six evaluable patients

100% of evaluable patients (6/6) showed clinical benefit.

Selective immune reinvigoration

- Terminally exhausted $CD8^+$ T cells reduced in **100% of evaluable patients (6/6)**
- **Median 51% reduction** (range 18–97%) within ~3 weeks
- **Total $CD8^+$ T-cell numbers unchanged**, indicating selective reduction of dysfunctional T cells

Robust disruption of metastatic CTC clusters

- **100% of evaluable patients (6/6)** showed reductions in CTC clusters
- **Median 83% reduction** (range 76–90%) by 6–7 weeks of treatment

Clinical implication

- Early, consistent pharmacodynamic responses suggest **paxalisib extends beyond PI3K/mTOR inhibition**
- Supports our hypothesis of paxalisib's ability to target **immune dysfunction** and **metastatic dissemination**, two key drivers of TNBC
- One expanded access patient demonstrated durable complete metabolic response and robust reductions in CTC clusters and exhausted terminally exhausted $CD8^+$ T cells

Data on file

Advancing Paxalisib Programs

One biological opportunity, multiple high-value markets

HR+ / HER2- BREAST CANCER	TNBC	pMMR CRC
Large population • Relapse • CNS disease	Metastasis • Brain metastases • Immune escape • Recurrence	Large population • Limited I/O response • Resistance • Major unmet need
• Large, biologically defined population with substantial unmet need in advanced / metastatic disease • Represents ~60-70% of all breast cancers • ~322,000 new invasive cases of breast cancer are expected in the US alone in 2026 • 5-year relative survival rate of ~35% for distant HR+ / HER2- disease • Predicted market of ~$17B by 2030	• Rare, fast-growing, and aggressive form of breast cancer • Accounts for approximately 10-15% of all breast cancer • 5-year survival rate of 12% for metastatic TNBC • Predicted market of ~$6B by 2030	• ~85% of colorectal cancers is pMMR / MSS, representing the overwhelming majority of CRC patients • ~159,000 new cases are expected in the US alone in 2026 • 5-year relative survival rate of 13-18% for distant stage CRC • Predicted market of ~$18B by 2030

Innovation Highlights:

- IP filed on all three indications
- Compelling preclinical data
- Ready for clinical advancement
  - Trial design with comparative drugs
  - Liquid biopsy early efficacy readout biomarkers
- PI clinicians in place (multi-center)
- Rapid recruitment (12 months)

NIH, American Cancer Society, Cancer.gov, published literature/DelveInsight

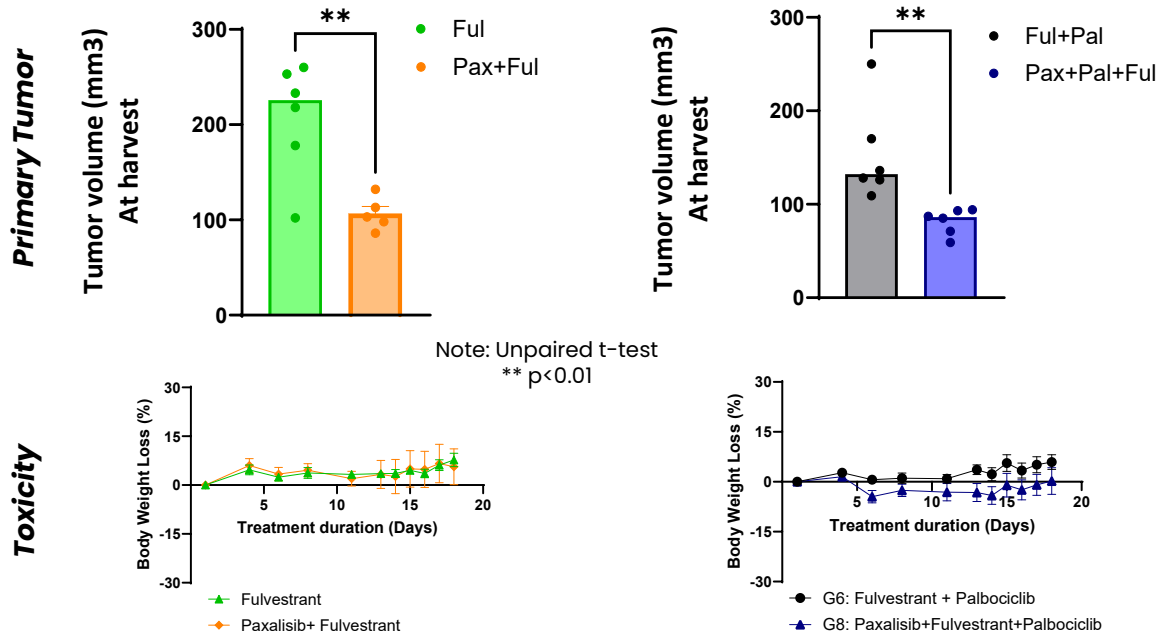
New Data: HR+ / HER2- Innovation & Highlights

Key Highlights

- Patent protected
- Extensive preclinical safety and efficacy evidence supporting paxalisib in combination with standard of care (SOC) in HR+ / HER2- breast cancer patients (both wild-type and mutant)
- Subpopulation with elevated novel PI3K/mTOR marker enriched in HR+ / HER2- breast cancer that is tightly coupled with poor survival identified; axis uniquely targeted by paxalisib
  - Identified a novel epigenetic MOA that allows paxalisib (and not gedatolisib) to uniquely sensitize the CDK4/6 resistant subpopulation to overcome recurrence and metastases
  - Abstract submitted to upcoming conference
- Potential for paxalisib to treat HR+ / HER2- patients with brain mets accounts for 10% HR+ / HER2-
- Clinical-trial ready

Scientific Evidence

Paxalisib + Fulvestrant +/- CDK4/6 inhibitor reduces tumor burden without toxicity



Data on file

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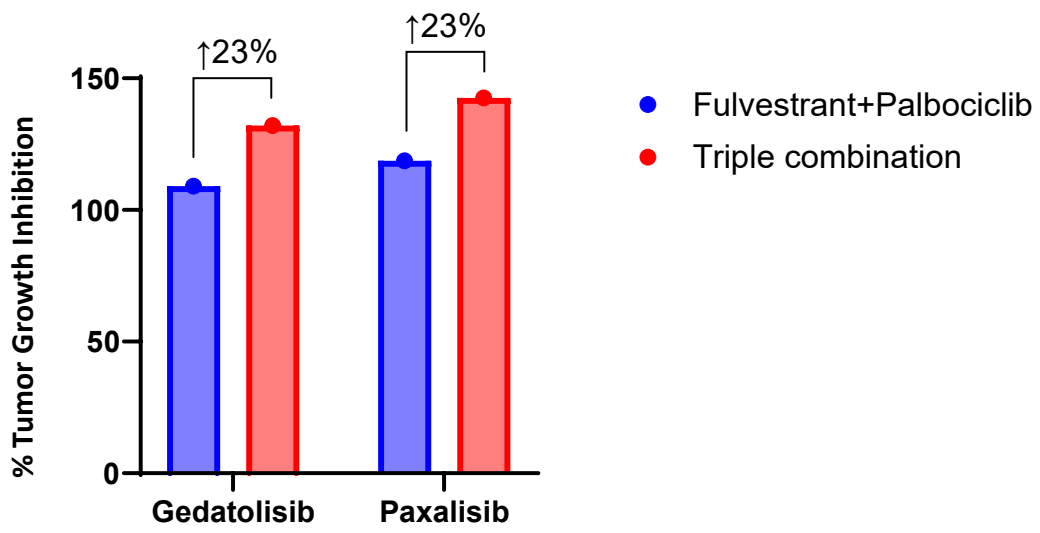
New Data: HR+ / HER2- Innovation & Highlights (Cont.)

Scientific Evidence

Comparison of tumor growth inhibition following treatment with Gedatolisib and Paxalisib in combination with Fulvestrant + Palbociclib in the MCF7 HR$^+$ xenograft model



Paxalisib shows identical efficacy to gedatolisib in preclinical studies.

Data on file

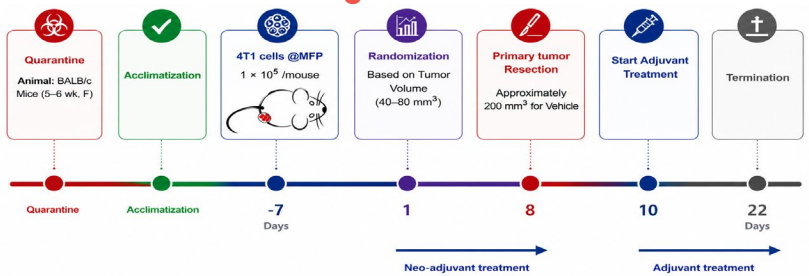
New Data: Stage IIb/III TNBC Innovation & Highlights

Key Highlights

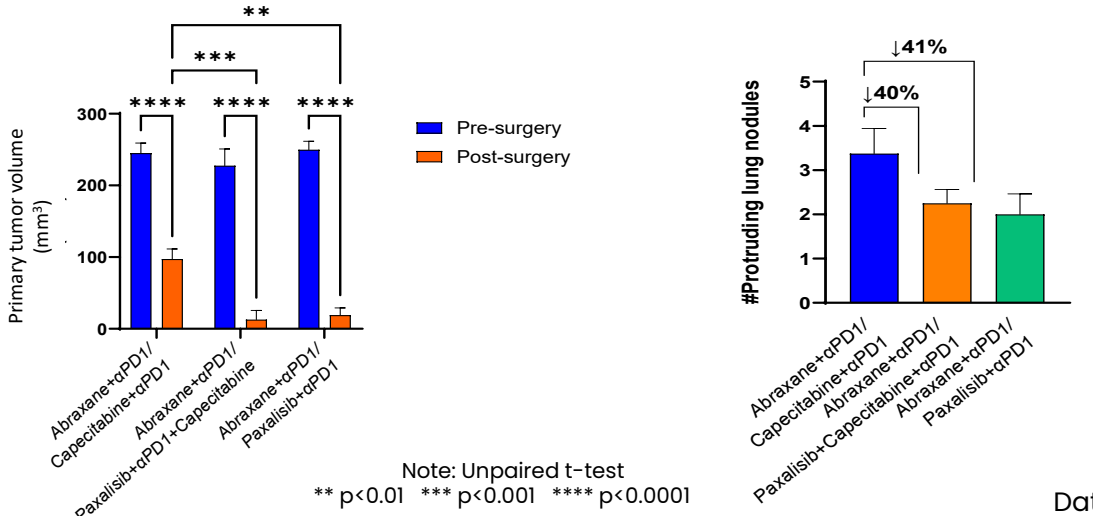
- Patent protected
- Significant residual disease and local recurrence suppressed by paxalisib combination therapy in the 4T1 neoadjuvant / adjuvant surgical metastasis model
- Significant reduction in distant metastatic recurrence
- A quarter-dose chemotherapy combination cuts tumor burden without toxicity
- Patient CTC clusters disrupted ex vivo, with attenuation of the aggressive phenotype in early-stage TNBC
- Novel liquid biomarkers to select patients and read out response early
- Early access partners for spatial ATAC sequencing
- Excitingly, epi-reprogramming of durable immune responses seen for the first time in the lymph node
- Clinical-trial ready — protocols in place

Scientific Evidence

Establishment of a clinically relevant preclinical neoadjuvant / adjuvant 4T1 surgical model



Paxalisib combination therapy suppresses residual disease, local and distant recurrence in a preclinical neoadjuvant / adjuvant 4T1 surgical model



Note: Unpaired t-test
** p<0.01 *** p<0.001 **** p<0.0001

Data on file

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New Data: pMMR CRC Innovation & Highlights

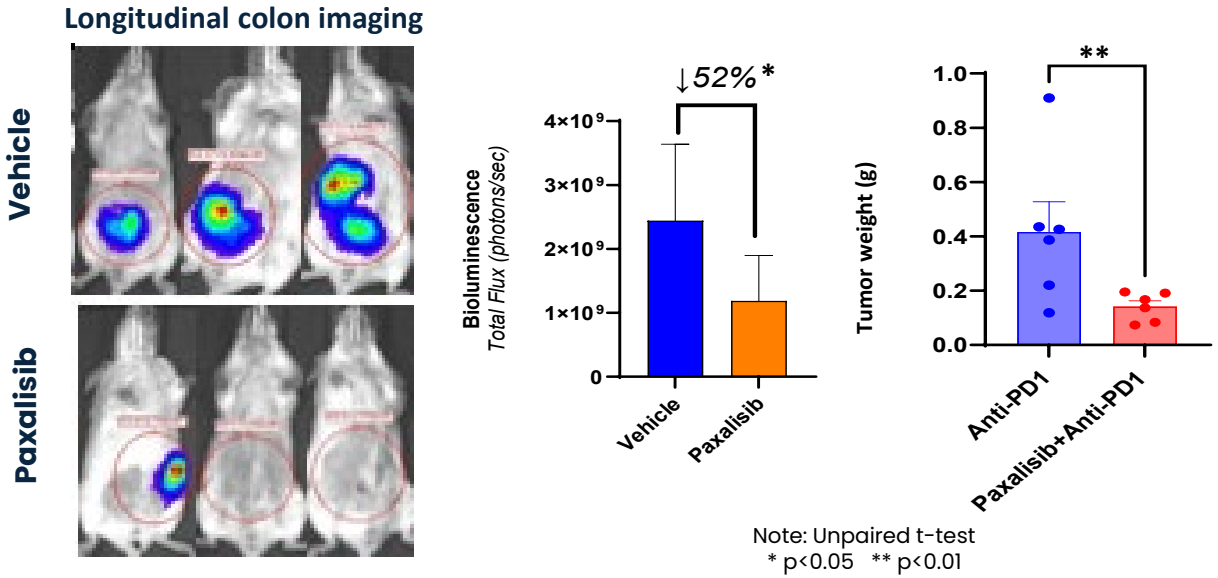
Key Highlights

- Patent protected
- 52% reduction in tumor burden with paxalisib as a single agent (p = 0.035), well tolerated throughout
- A further 50% reduction in tumor volume when added to anti-PD-1, versus anti-PD-1 alone (p = 0.022)
- Novel liquid biomarkers to select patients and monitor response, where none exist today
- Targets the pMMR majority — the 85-90% of colorectal cancer patients who derive limited benefit from checkpoint inhibitors today
- Early access partners for spatial ATAC sequencing
- Clinical-trial ready — protocols in place

Scientific Evidence

Paxalisib monotherapy and αPD1 combination suppresses primary tumor burden in pMMR+ CRC preclinical models

Monotherapy ***Combination***



Note: Unpaired t-test
* p<0.05 ** p<0.01

Data on file

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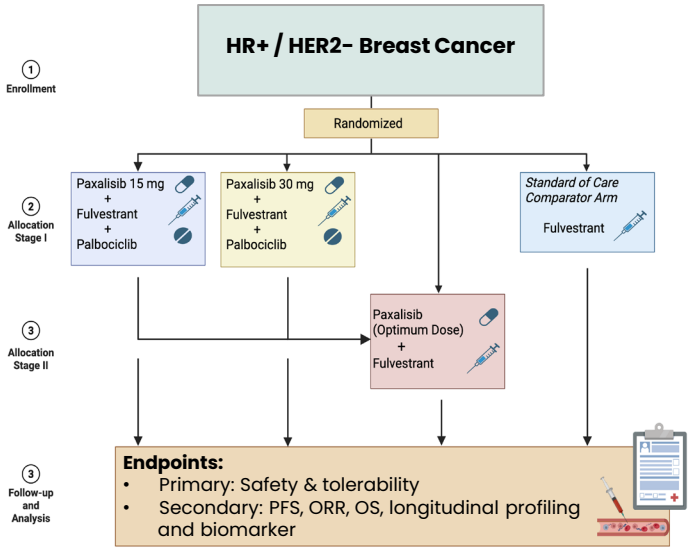
Clinical Trial Ready

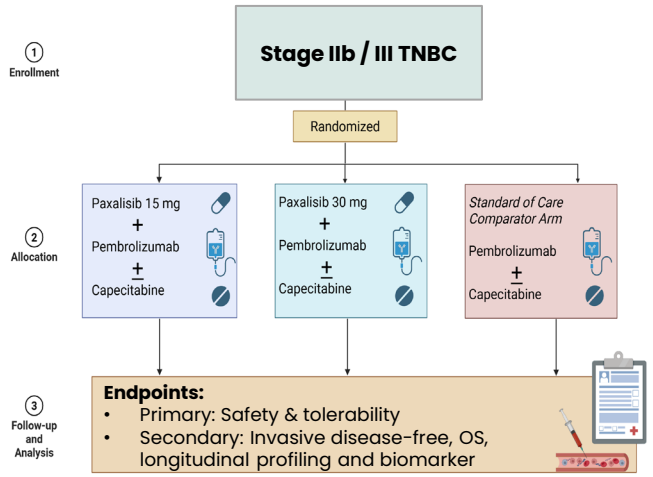
HR+ / HER2- Breast Cancer

Paxalisib + Fulvestrant + Palbociclib for pre-treated HR+ / HER2- metastatic breast cancer (Second line setting)



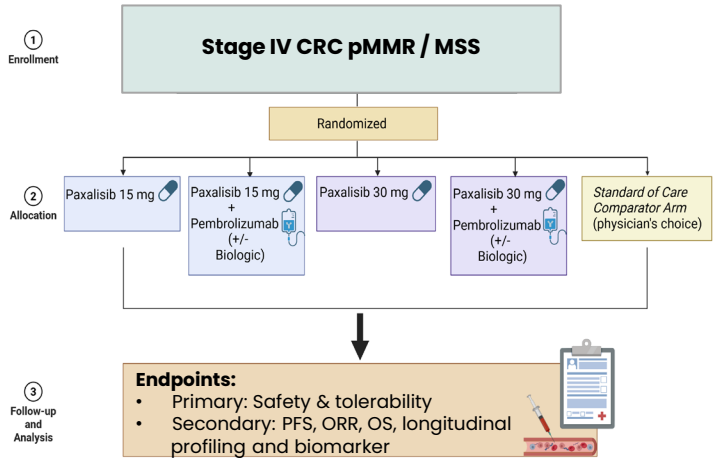
Stage IIb / III TNBC
(in adjuvant, followed by neoadjuvant setting)

Paxalisib + Pembrolizumab + Capecitabine for high-risk Stage IIb / III TNBC in the adjuvant setting (First line setting)



pMMR CRC

Paxalisib Monotherapy and Paxalisib + Pembrolizumab vs. Standard of Care in pre-treated pMMR / MSS metastatic CRC (Third line setting)



KAZIA THERAPEUTICS

Investment Framework Recap

Key elements underpinning our potential for value creation

Early clinical validation creates multiple paths to significant value

Stage IV TNBC clinical observations + potential expansion into >$40B of additional oncology markets

6/6
Stage IV TNBC Patients

Immune Restoration

Reduced and reprogrammed terminally exhausted CD8+ T cells

6/6
Stage IV TNBC Patients

Metastatic Biology Disrupted

Reduced circulating tumor cell (CTC) clusters associated with metastatic dissemination

Extensive Preclinical Data & IP to Support Expanded Indications

HR+ / HER2- breast cancer • Early-stage high-risk TNBC • pMMR CRC

>$40B
Potential Market Opportunity

6/6
Stage IV TNBC Patients with Clinical Benefit

1 Complete Response • 4 Partial Responses • 1 Stable Disease

Ongoing Complete Metabolic Response with Persistent Biological Reprogramming

Reductions in terminally exhausted CD8⁺ T cells and CTC clusters persist alongside complete metabolic response

WHY THIS MATTERS

Early clinical observations support a potentially differentiated mechanism with applicability beyond TNBC.

Not all PI3K/mTOR inhibitors are created equal. Paxalisib's ability to reprogram tumor and immune biology appears distinct and is not a class effect, supporting potential expansion across multiple solid tumors.

Potential Value Creation Pathway

Stage IV TNBC	Additional Data	Broader Indications	Strategic Optionality
Clinical validation	Increased confidence	Expand addressable market	Development / Partnering

Data on file

Summary & Next Steps

Summary

- Brain-penetrant dual pan-PI3K/mTOR inhibitor in development (Only 2% of small-molecule drugs are brain-penetrant)
- Designed to be best-in-class pan-PI3K pathway inhibitor with modest mTOR activity (dual targeting required to inhibit cancer cell proliferation & migration in TNBC cell model)
- Overcoming metastasis and drug resistance in combination with immunotherapy (epigenetic reprogramming of dormant cancer cells and improved cancer immune visibility)
- Generally well tolerated (evaluated in 550 adult and pediatric patients across Phase 1-3 clinical trials and expanded access programs)

Clinical and Translational Epigenetic Data Demonstrate That Paxalisib:

- Reduces CTC and CTC-clusters as well as aggressive mesenchymal phenotypes (observable impact on metastatic biology)
- Enhances activity when combined with immune checkpoint inhibition (combination-enabling potential)
- Modulates immune exhaustion markers (evidence of tumor microenvironment reprogramming)

On Strategy

- Positioned as a backbone therapy within the emerging category of functional epigenetic reprogramming therapeutics

Next Steps

- **Advanced Breast Cancer**: 1) Provide additional preclinical data and updates throughout the year, 2) ongoing updates from Phase 1b advanced breast cancer clinical study (ACTRN12624001340527) throughout 2026, 3) expand into other clinical indications including HR+ / HER2- breast cancer and early-stage high-risk TNBC and 4) participate in upcoming scientific conferences
- **Colorectal Cancer:** 1) Execute clinical development plan with Phase 2 clinical trial in pMMR CRC to evaluate paxalisib as monotherapy and in combination with pembrolizumab and 2) participate in upcoming scientific conferences
- **Glioblastoma**: 1) Anticipated follow-up FDA Type C meeting to discuss commercial and development path forward and 2) finalize clinical development plan based on FDA feedback
- **Pediatric & Brain Metastasis Programs**: 1) PNOC022 team to complete PK / biomarker data analysis and provide update, 2) data release / updates from other brain met trials, and 3) initiate enrollment for PNOC035 (AT/RT clinical study)

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