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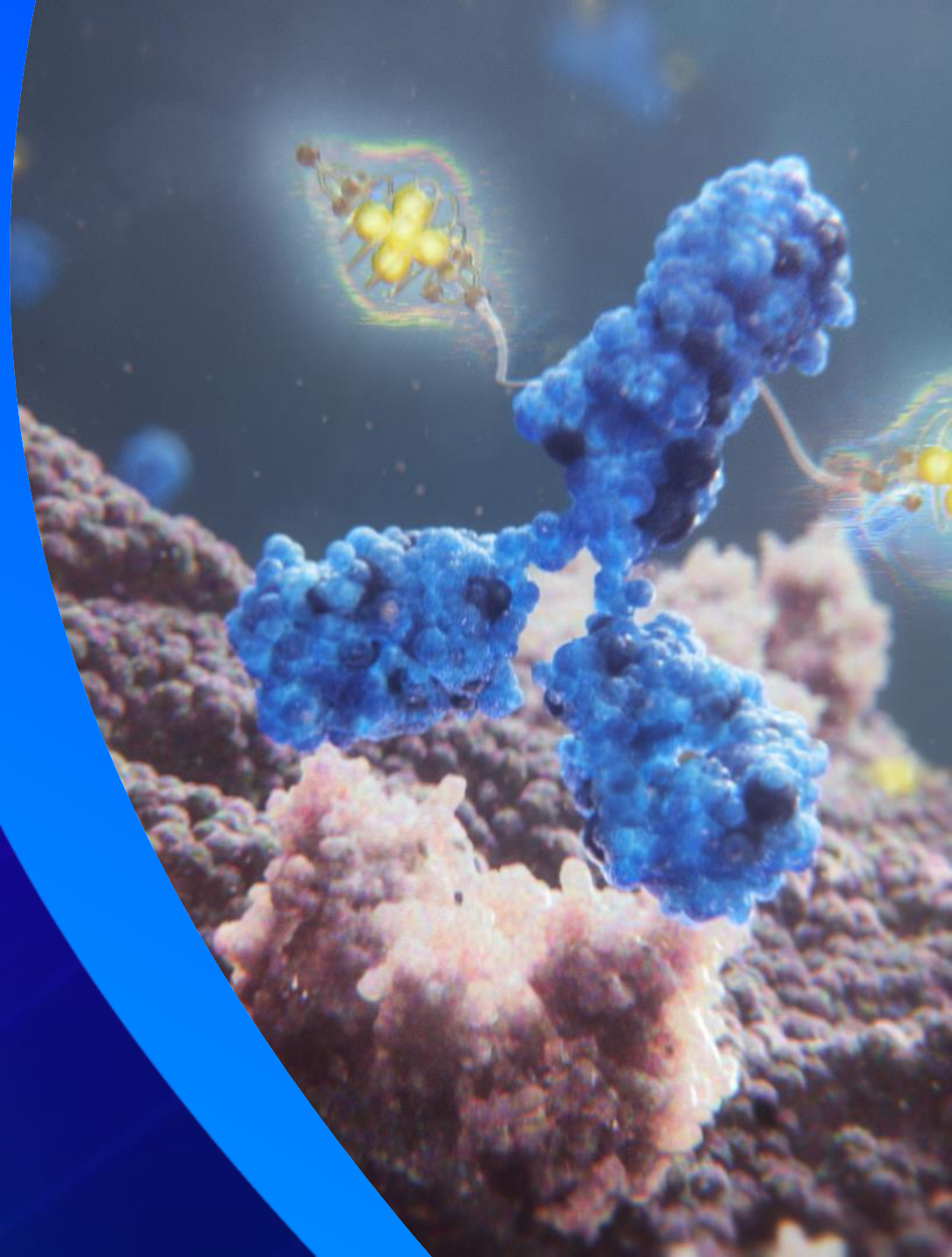
TLX591-Tx: Development overview and data highlights

Lutetium (^{177}Lu) rosopatamab tetraxetan

March 2026



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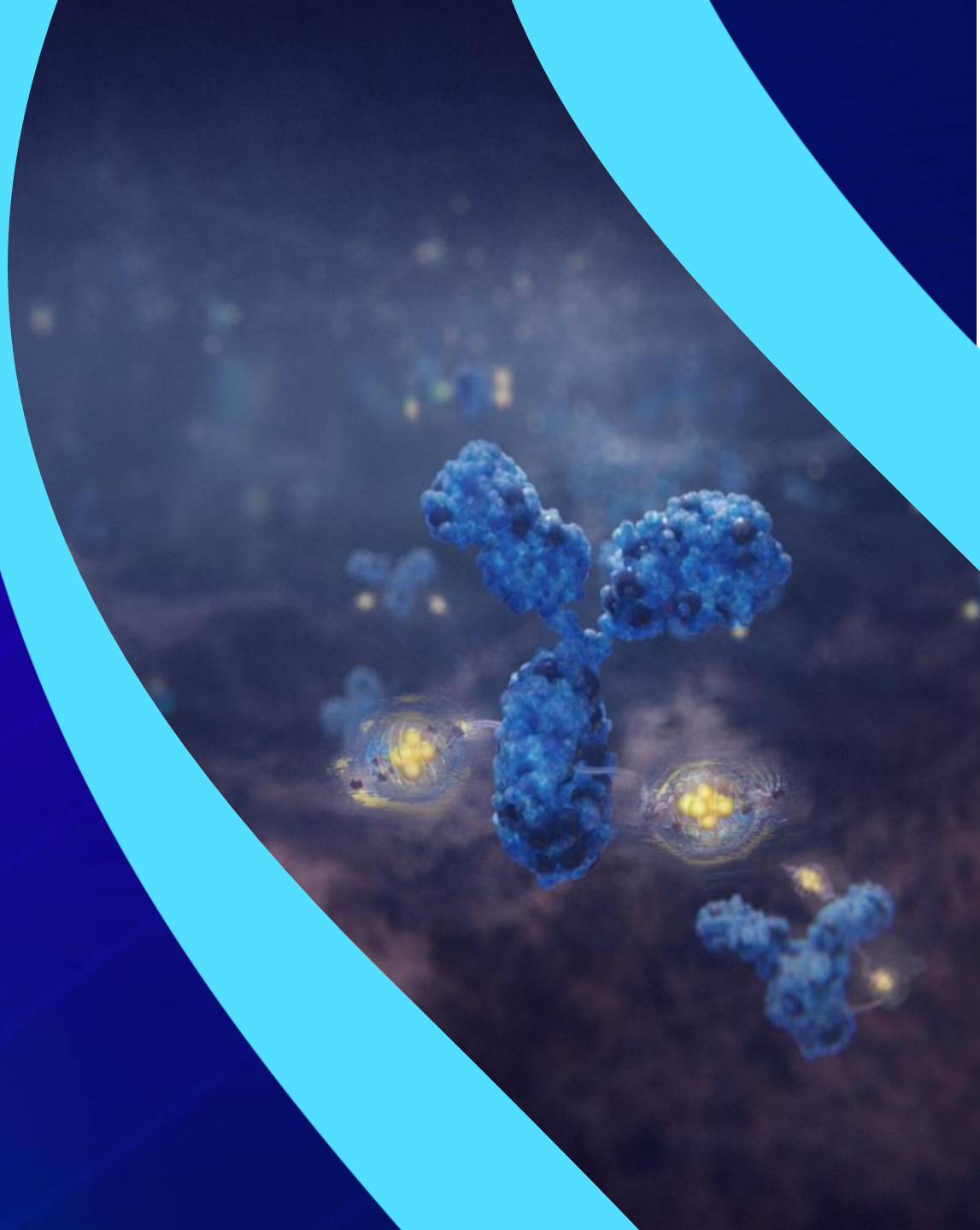
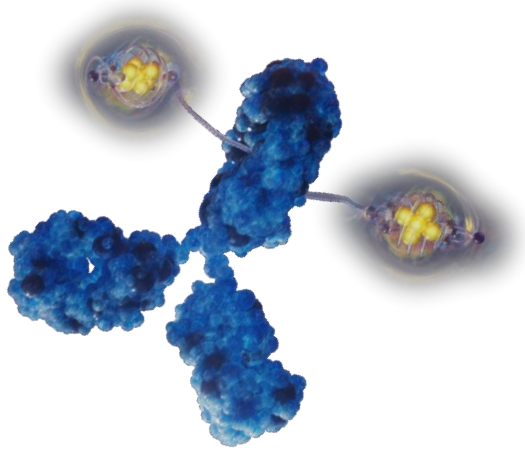
1. TLX591-Tx Overview



TLX591-Tx is a novel PSMA therapy for prostate cancer

Differentiated therapeutic radiopharmaceutical using a biologic to target PSMA

TLX591-Tx:
Lutetium (^{177}Lu) rosopatamab tetraxetan



TLX591-Tx is a radio antibody-drug conjugate (rADC) for metastatic castration-resistant prostate cancer (mCRPC) expressing prostate-specific membrane antigen (PSMA)

- PSMA is a validated target in prostate cancer[1]
- TLX591-Tx utilises **a PSMA-targeted monoclonal antibody (mAb) approach** with differentiated targeting and pharmacology versus approved PSMA-targeted small molecules
- mAbs are distinguished by their internalization, prolonged retention and high specificity for tumor-expressed PSMA[2]
- Enables a short, patient-friendly dosing regimen and low occurrence of off-target side effects, while delivering a meaningful therapeutic index[3]
- Anticipated (typical) course of therapy uses ^{177}Lu supply chain far more efficiently with ~1/9th injected activity compared with current products

1. Dorff et al. *Am Soc Clin Oncol Educ Book.* 2019.
2. New Class of Radiopharmaceutical Therapy Makes Headway in Prostate Cancer (onclive.com).
3. Sun et al. *Curr Oncol Rep.* 2021.

TLX591-Tx aims to address key unmet needs

Potential to overcome limitations of 1st generation small molecule approach

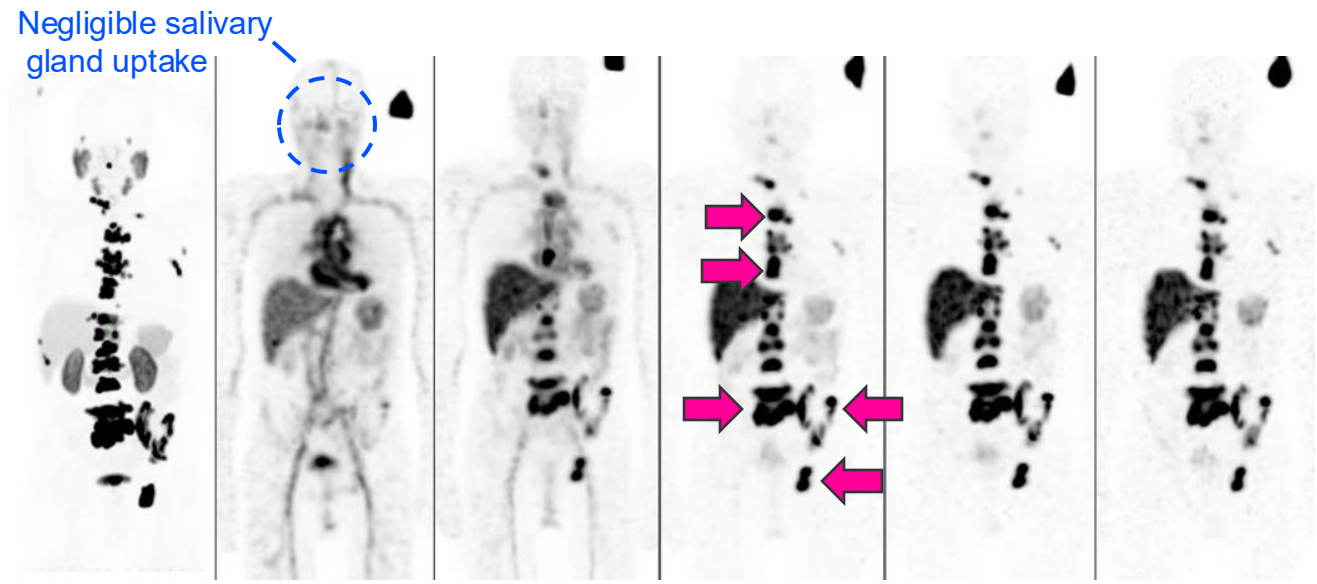
ProstACT™

SURVIVAL Promising overall survival demonstrated in early studies, median OS 42.3 months[1]

DOSING Simple 2-dose regimen[2]
Lower cumulative radiation exposure (152 mCi vs. 1,200 mCi)

QoL[3] Limited off target side effects: renal toxicity, dry mouth, dry eye, ganglia irritation.
Predictable hematological response[4]

TLX591-Tx biodistribution on SPECT imaging[4]



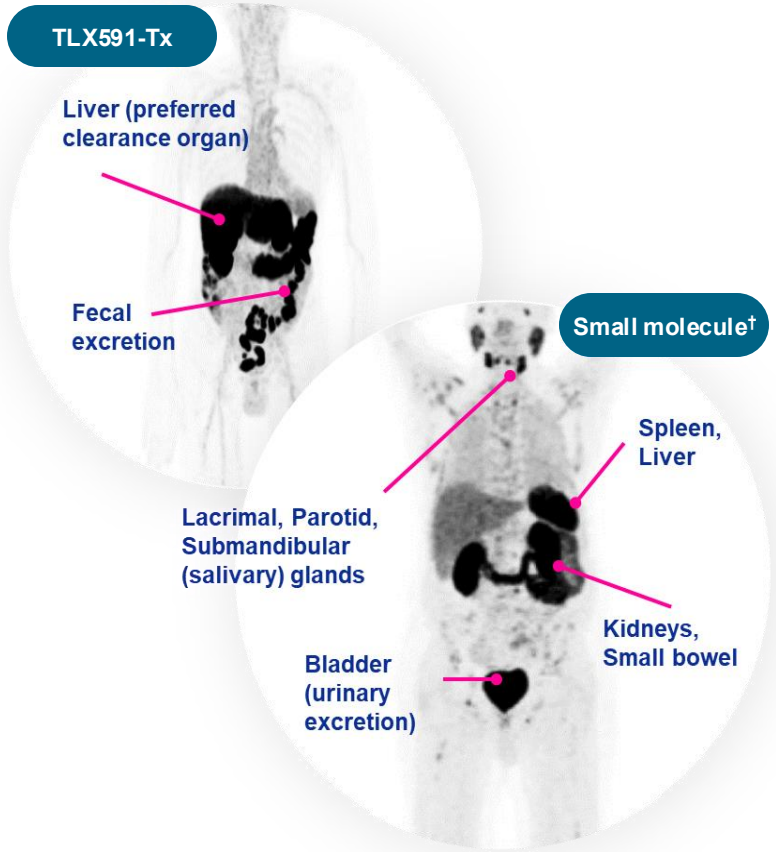
Patient representative scans - individual results may vary.

1. Tagawa, et al. *Cancer*. 2019 (Open label, single-arm Phase 1/2 clinical trial in 17 patients with advanced mCRPC).
2. ClinicalTrials.gov ID: NCT06520345.
3. Quality of life.
4. ProstACT SELECT data on file. Clinical Study Report 08-Dec-2025.

TLX591-Tx rADC versus 1st generation small molecule RLT

Key differences underpin PSMA tumor targeting, internalization, and prolonged retention[6]

	rADC	1st Generation RLT
Radiopharmaceutical description	TLX591-Tx[1-4]	Small Molecule[5]
Recommended adult dose	2 x 76 mCi (14 days apart)	6 x 200 mCi* (6 weeks apart)
Molecule size	Antibody Large (mw ~150,000)	Small molecule (mw ~1,200)
Terminal half-life ($t_{1/2}$)	5.6 days	1.7 days
Off-target organ exposure	Liver, spleen	Salivary glands, kidneys, GI tract, other sites
Route of excretion and time	Liver 80% cleared within 44+/-15 hours	Kidneys ~70% excreted in 12 hours

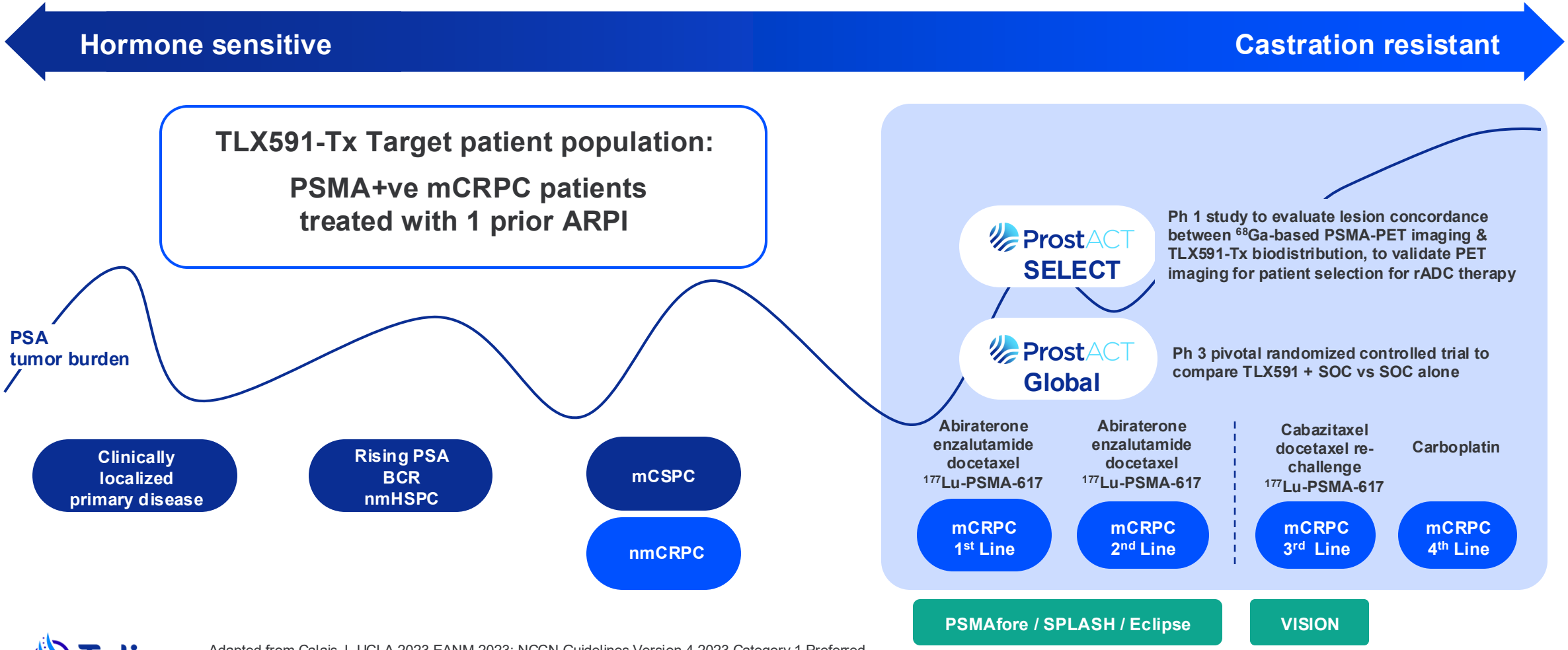


*^{177}Lu-PSMA617 prescribing information. Administered every 6 weeks for up to 6 treatments, solution for injection contains 200 mCi (7.4 GBq) at time of use.[5]
*^{68}Ga-PSMA-11.[2] GI=gastrointestinal; mw=molecular weight; PSMA=prostate-specific membrane antigen; rADC=radio-antibody drug conjugate; RLT=radio-ligand therapy.

1. Sartor O, et al. Presented at: American Society of Clinical Oncology Annual Meeting; May 31-June 4, 2024; Chicago, IL. TPS5115. **2.** Sun M, et al. *Curr Oncol Rep*. 2021;23(5):59. **3.** Data on file. Telix Pharmaceuticals Limited. **4.** Tagawa ST et al. *Cancer*. 2019;125(15):2561-2569. **5.** Lu177-PSMA617. Prescribing information. 2022. Novartis Pharmaceuticals Corp. 6. Differences described are not derived from head-to-head clinical studies, cross-trial comparison should be interpreted as not being definitive.

TLX591-Tx is positioned to integrate with SOC for 1–2 L mCPRC

55k incident U.S. mCPRC patients per annum[1], ARPIs and taxanes as current standard of care



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Adapted from Calais J. UCLA 2023 EANM 2023; NCCN Guidelines Version 4.2023 Category 1 Preferred Scher 2015, PLoS1; Nezolosky 2018, Journal of Clinical Oncology; ASCO Cancer.NET, Prostate Cancer Statistics, accessed November 2023.

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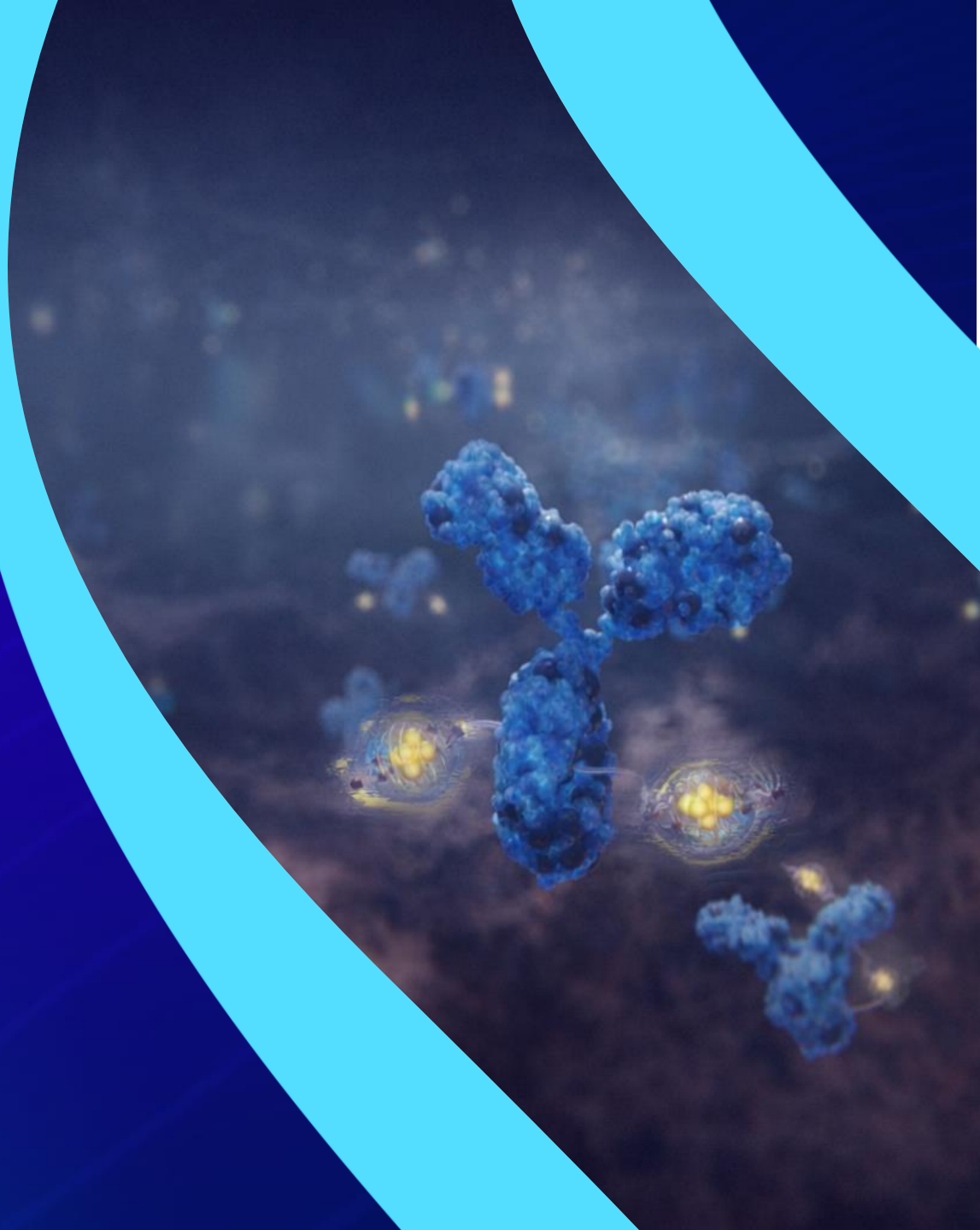
2. Published Data Highlights and Phase 1 ProstACT SELECT Results Recap



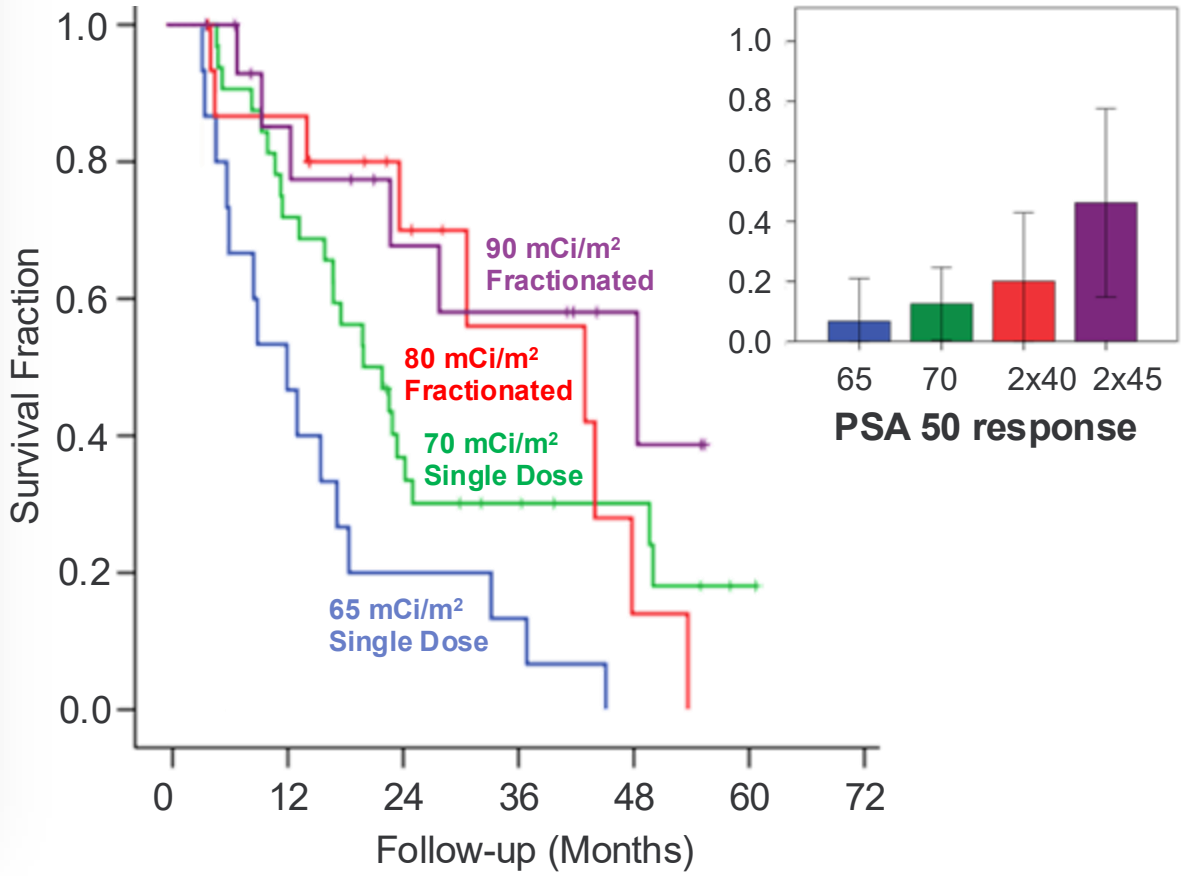
Dose expansion trials established efficacy signal

Demonstrated anti-tumor effect and overall survival benefit of monotherapy in mCRPC[1,2]

- Evidence of anti-tumor effect and clear dose-response profile for key measures of efficacy[2]
  - Prostate-specific antigen (PSA) response
  - Overall survival (OS) – **published 42.3 months** median survival in later-stage (heavily pre-treated) patients

Fractionated dosing regimen manages hematologic safety while delivering a highly targeted and potent radiation dose

Overall survival by cohort, 80 patients[2]



1. Vallabhajosula et al. Curr Radiopharm. 2016.
2. Tagawa et al, Cancer. 2019. Tagawa et al, Clin Cancer Res. 2013.

Safety profile established across monotherapy trial publications

Demonstrated acceptable and manageable safety profile

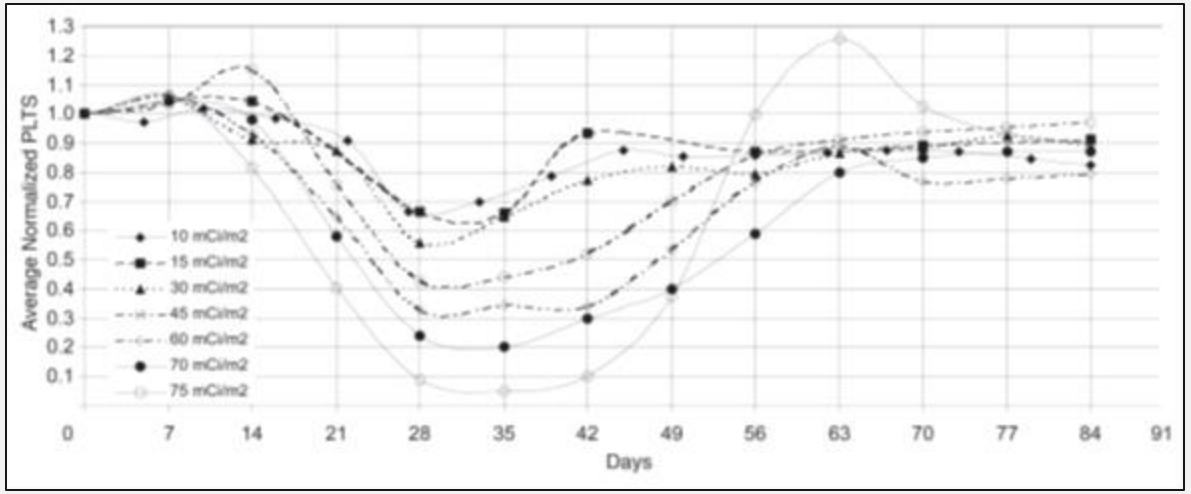
Incidence of AEs in monotherapy studies, all grades[1-2]

Body System / Adverse Event	Bander 2005; 177Lu-TLX591 N=35	Tagawa 2013; 177Lu-TLX591 N=47	Tagawa 2019; 177Lu-TLX591 N=49
Thrombocytopenia	35	36	46
Neutropenia	35	36	40
Decreased Leukocytes	NR	40	38
Anemia	NR	24	27
Fatigue	16	17	23
Fever	1	1	NR
Nausea	5	5	13

N = number of subjects; NR = no reaction.

- Well-tolerated with predictable and transient hematological toxicity[1]
  - Post-treatment platelet counts followed a consistent pattern regardless of the number of doses administered
  - Reduction in platelet counts generally began 2.5-3 weeks post-treatment with nadirs occurring at 4-5 weeks
  - In majority of subjects, mean platelet counts returned to 80-95% of pre-treatment values by a median of Day 26
- The most common non-hematologic event is fatigue

Platelet counts at different doses of TLX591-Tx[2]



1. Tagawa et al, Cancer. 2019. Tagawa et al, Clin Cancer Res. 2013.
2. Bander et al. J Clin Oncol. 2005.

Phase 1 ProstACT SELECT trial design

A multicenter, phase 1 open label study to evaluate safety, tolerability, biodistribution, dosimetry, & preliminary efficacy of TLX591-Tx + SOC in patients with PSMA+ mCRPC[1]

Eligible patients
- Confirmed progressive mCRPC
- ≥1 PSMA-positive metastatic lesion on ^{68}Ga-PSMA-11 PET/CT scan
- Progressed on 1 prior ARPI in mCSPC, nmCRPC, or mCRPC treatment settings
  - Eligible for ARPI switch
- Taxane-naïve
  - May have received one line of prior taxane in mHSPC
- ECOG status 0, 1, 2

Cohort 1 TLX591-Tx + SOC n = 5

1 imaging dose 27mCi

1 therapeutic dose 76mCi

sequential assignment

Cohort 2 TLX591-Tx + SOC n = 25

therapeutic dose 76mCi

therapeutic dose 76mCi

Endpoints

Primary (Cohorts 1 & 2)
- Safety & tolerability
- Whole body biodistribution & organ dosimetry

Secondary (Cohort 2)
- Efficacy
  - rPFS
  - PSA response

Exploratory (Cohort 2)
- QoL
- Pain management

1-Year Long Term Safety Follow Up
(Overall Survival not assessed)

- Concomitant standard of care (SOC) only, as determined by the Principal Investigator (PI):
  → ARPIs abiraterone or enzalutamide were permitted therapeutics.

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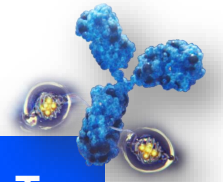
1. ClinicalTrials.gov ID: NCT04786847

ProstACT SELECT provided important insights in 1L / 2L mCRPC[1]

Supporting the differentiated clinical profile of TLX591-Tx



Study Goal: To evaluate lesion concordance between ^{68}Ga (gallium)-based PSMA-PET-imaging and TLX591-Tx dosimetry for the purpose of validating PET imaging for patient selection for rADC therapy

Objectives met

Confirmed safety & tolerability profile in combination with SOC; Meaningful PSA reduction & median rPFS 8.8 months[1]

Patient-friendly dosing

Short, simple regimen of two doses (76 mCi), administered 14 days apart (total cumulative dose 152mCi) [1]

Uptake

Radiation exposure to key organs well within safety limits; Highest absorbed dose was in the liver (clearance organ), with minimal uptake in salivary glands[1]

Retention

Long retention period as potential signal of internalization and ability to deliver payload to tumor[1]

Hematology

Hematologic profile consistent with prior studies; Events were transient and clinically manageable[1]

Targeted patient selection

PSMA+ve patient selection via PSMA-PET imaging across a range of mCRPC tumor burdens[1]

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1. ProstACT SELECT data on file. Clinical Study Report 08-Dec-2025

ProstACT SELECT Cohort 2 baseline demographics

Patient Population

- **Median age 75**
- **Predominantly Caucasian**
- **Heterogeneous mix of prior ARPI & docetaxel therapy in mCSPC or 1L mCRPC treatment settings; most patients had 2 lines of prior therapy**

	Cohort 2 (n=25)
Age Group, n (%)	
Cohort 2	75 (58 – 85)
Race, n (%)	
Asian	n=1
Arabic	n=1
Black or African American	n=0
White	n=18
Other Not Specified	n=1
Not Reported	n=4
Country, n (%)	
Australia	n=25 (100%)

	Cohort 2 (n=25)
ECOG performance status, n (%)	
0	n=15 (60%)
1	n=8 (32%)
2	n=2 (08%)
Sites of metastases, n (%)	
Node	n=6 (27%)
Bone	n=11 (50%)
Visceral	n=13 (59%)
Prior docetaxel therapy, n (%)	
Yes	n=5 (25%)
No	n=20 (75%)
Prior ARPI therapy, n (%)	
Abiraterone	n=7 (28%)
Enzalutamide	n=7 (28%)
ARPI Doublet Abiraterone + Enzalutamide	n=2 (8%)

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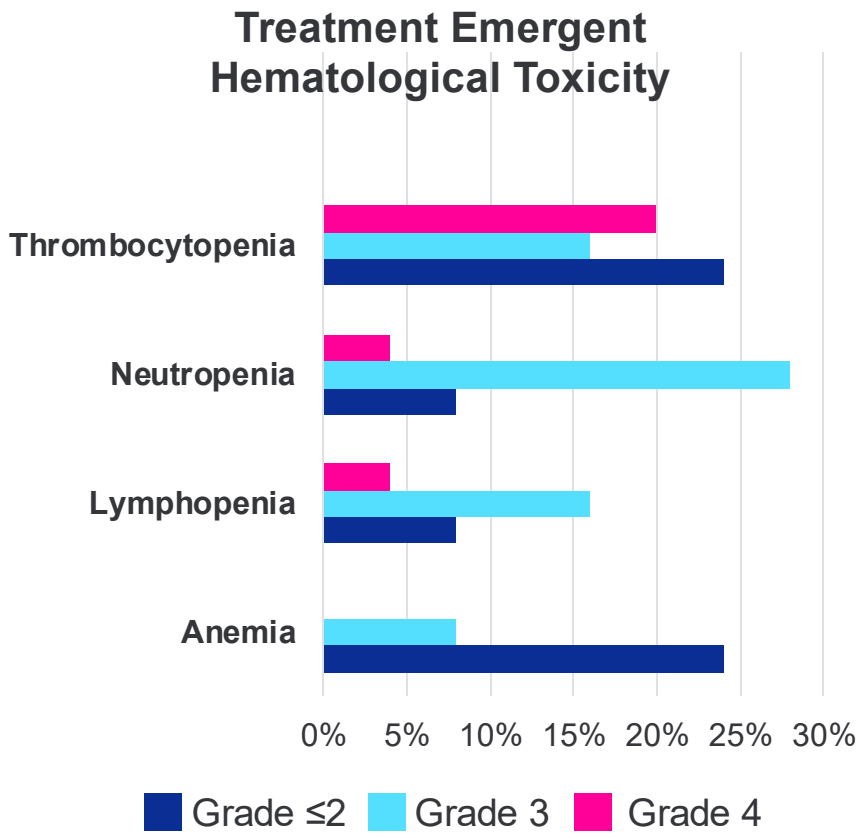
1. ProstACT SELECT data on file. Clinical Study Report 08-Dec-2025

Acceptable safety and tolerability profile, in line with prior studies

Hematologic events were transient and manageable, non-hematologic events were G1 or G2



Key Observations

23 of 25 participants administered 2 doses of 76 mCi

Hematologic laboratory profile[1]

- Grade 3 thrombocytopenia (16%) (4 / 25) and neutropenia (28%) (7 / 25) events in line with profile expected for this class of therapy
- Grade 4 thrombocytopenia (20%) (5 / 25) and neutropenia (4%) (1 / 25) were transient
- Six patients (24%) received intervention for hematologic toxicity in the form of platelets, growth factors or both

Non-hematologic Events[1]

- All drug-related non-hematologic events were Grade 1 or Grade 2
- Most prevalent non-hematologic events were fatigue (72%), nausea (28%) and loss of appetite (20%)

Note: Two patient deaths deemed unrelated to TLX591 occurred during the study: 1 death died due to intracerebral hemorrhage (Cohort 1); 1 death due to disease progression (Cohort 2)

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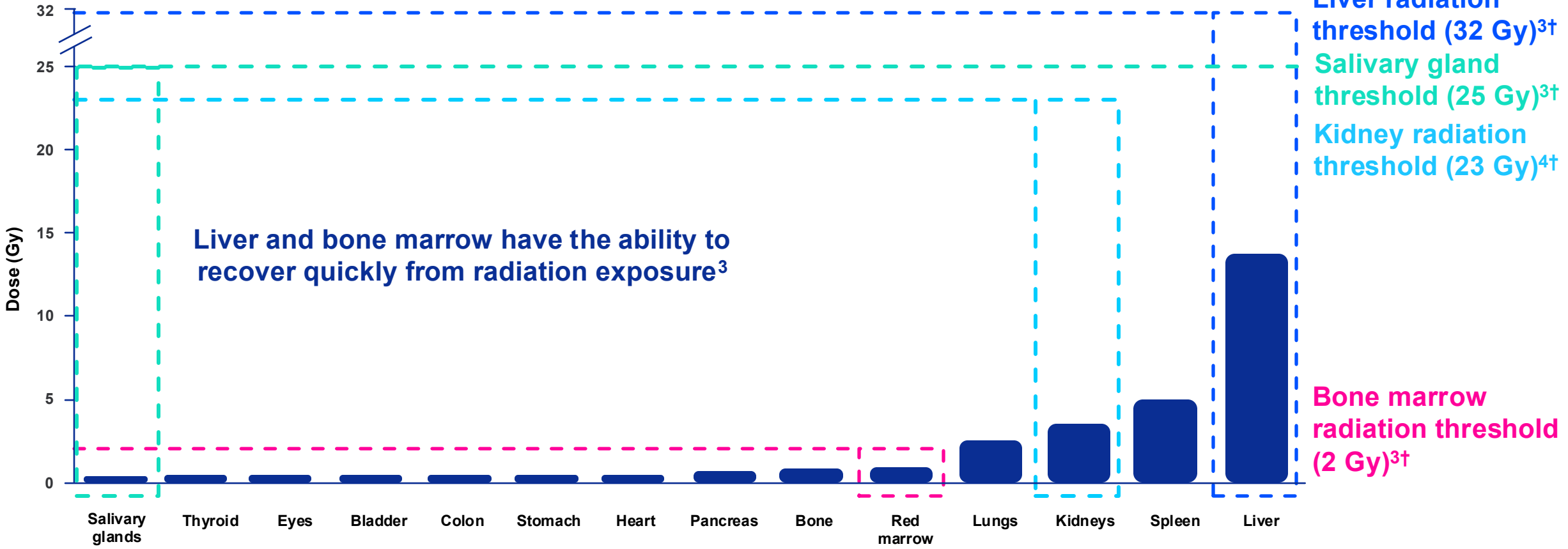
1. ProstACT SELECT Clinical Study Report 08-Dec-2025.

Liver, kidney and red marrow received radiation doses below recommended thresholds in ProstACT SELECT study[1,2]



Abbreviated ProstACT SELECT study design: A phase 1 study (N=28) to evaluate the safety, tolerability, biodistribution, and dosimetry of ^{177}Lu-TLX591 in patients with PSMA-expressing mCRPC.

*In cohort 2 of ProstACT SELECT (n=23), patients received 76 mCi of ^{177}Lu-TLX591 x 2 doses 14 days apart

†External beam radiation limits.

1. ProstACT SELECT data on file. Clinical Study Report 08-Dec-2025. **2.** Lenzo N, et al. *J Nucl Med.* 2024;65(suppl 2). Abstract 241503. **3.** Wahl RL, et al. JNuclMedicine. 2021; 62 (12, suppl 3): 23S-35

4. https://www.fda.gov/media/144845/download 5.

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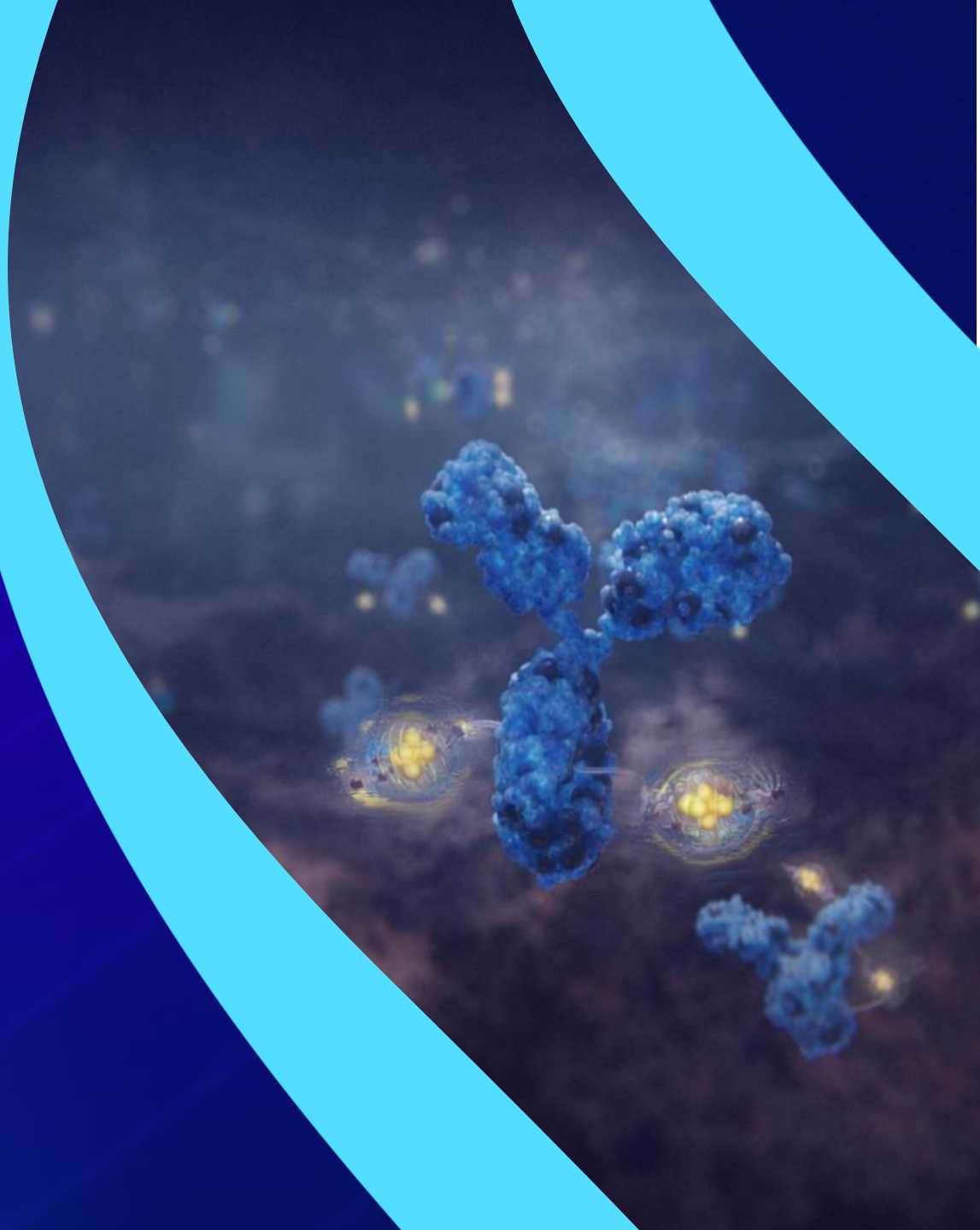
3. Phase 3 ProstACT GLOBAL Trial Design



ProstACT GLOBAL phase 3 trial design[1]

Two-part study design assessing safety and efficacy of 591 + SOC combinations

Part 1: Safety & Dosimetry Lead-In (n = 30)

Eligibility

- Confirmed mCRPC
- Progressed on 1 prior ARPI in mCSPC, nmCRPC, or 1L mCRPC treatment settings
- Docetaxel in mCSPC if ≥6 months prior

76mCi ← 14 days → 76mCi

Fractionated dosing

TLX591-Tx + SOC
- abiraterone (10)
- enzalutamide (10)
- docetaxel (10)

N = 30

Primary
- Safety
- Tolerability

Secondary
- Pharmacokinetics
- Biodistribution
- Dosimetry

Exploratory
- ORR
- rPFS
- PSA Resp
- OS

Characterize safety & dosimetry profiles of TLX591-Tx + SOC combinations

Part 2: Randomized Treatment Expansion (n = 490)

2:1

TLX591-Tx + SOC
- abiraterone
- enzalutamide
- docetaxel

N = 327

SOC
- abiraterone
- enzalutamide
- docetaxel

N = 163

Primary
- rPFS

Key Secondary
- OS

Other Secondary
- ORR
- SSE
- PSA Resp
- HRQoL

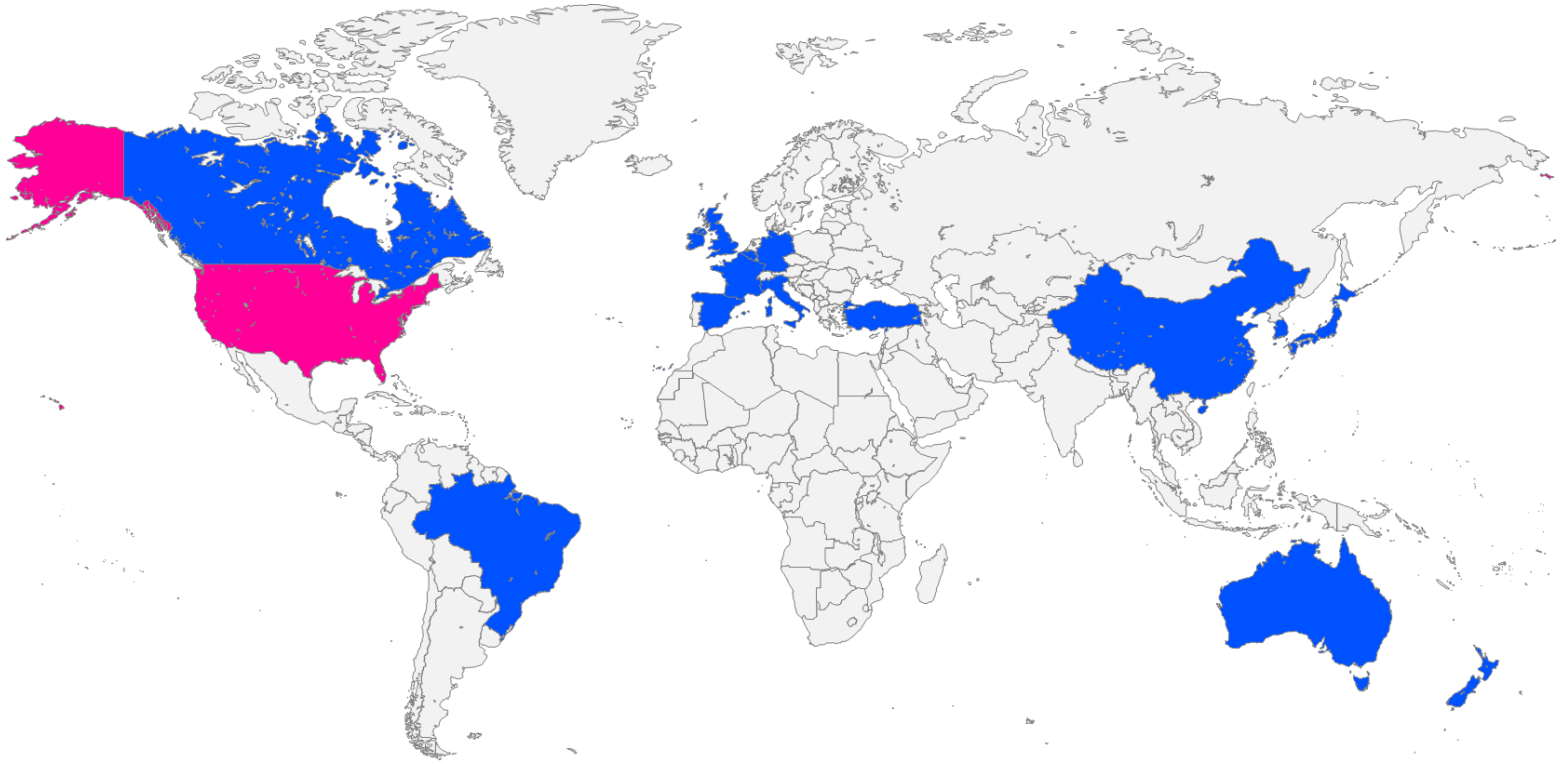
Interim Analysis

1. ClinicalTrials.gov ID: NCT06520345.

ProstACT Global study design reflects global clinical practice

Typical clinical practice following disease progression on first ARPI

Predominantly ARPI Switch[2] | **Predominantly Docetaxel[3,4,5,6,7,8]**



- **Pragmatic study design** allows Investigator to combine TLX591 with either
  - ARPI (abiraterone or enzalutamide)

    or

  - Chemotherapy (docetaxel)
- **U.S.:** Largest prostate cancer market[1]; real-world analysis indicates 57% of patients with prior ARPI exposure receive another ARPI as next therapy[2]
- **ROW**: Guidelines support docetaxel post-progression on first ARPI

1. Clarivate Prostate Cancer Market Forecast, July 2025
2. Narayan V. et al, Treatment Patterns and Survival Outcomes Among Androgen Receptor Pathway Inhibitor- Experienced Patients with Metastatic Castration Resistant Prostate Cancer, Clin Genitourin Cancer, Volume 22, Issue 6, 102188 December 2024
3. 2025 Canadian Urological Association-Canadian Uro-oncology Group Guideline: Metastatic castration-resistant prostate cancer
4. 2025 ESMO Treatment Guidelines / EAU Prostate Cancer Guidelines
5. 2025 Chinese Society of Clinical Oncology Guideline
6. Korean Guidelines for the Management of Metastatic Prostate Cancer
7. Japanese Clinical Practice Guidelines for Prostate Cancer 2023
8. Fontes et al. Treatment Patterns Among Patients with advanced Prostate Cancer in Brazil: An Analysis of a Private Healthcare System Database, World J. Oncology 2022 Dec; 13(6):350-358

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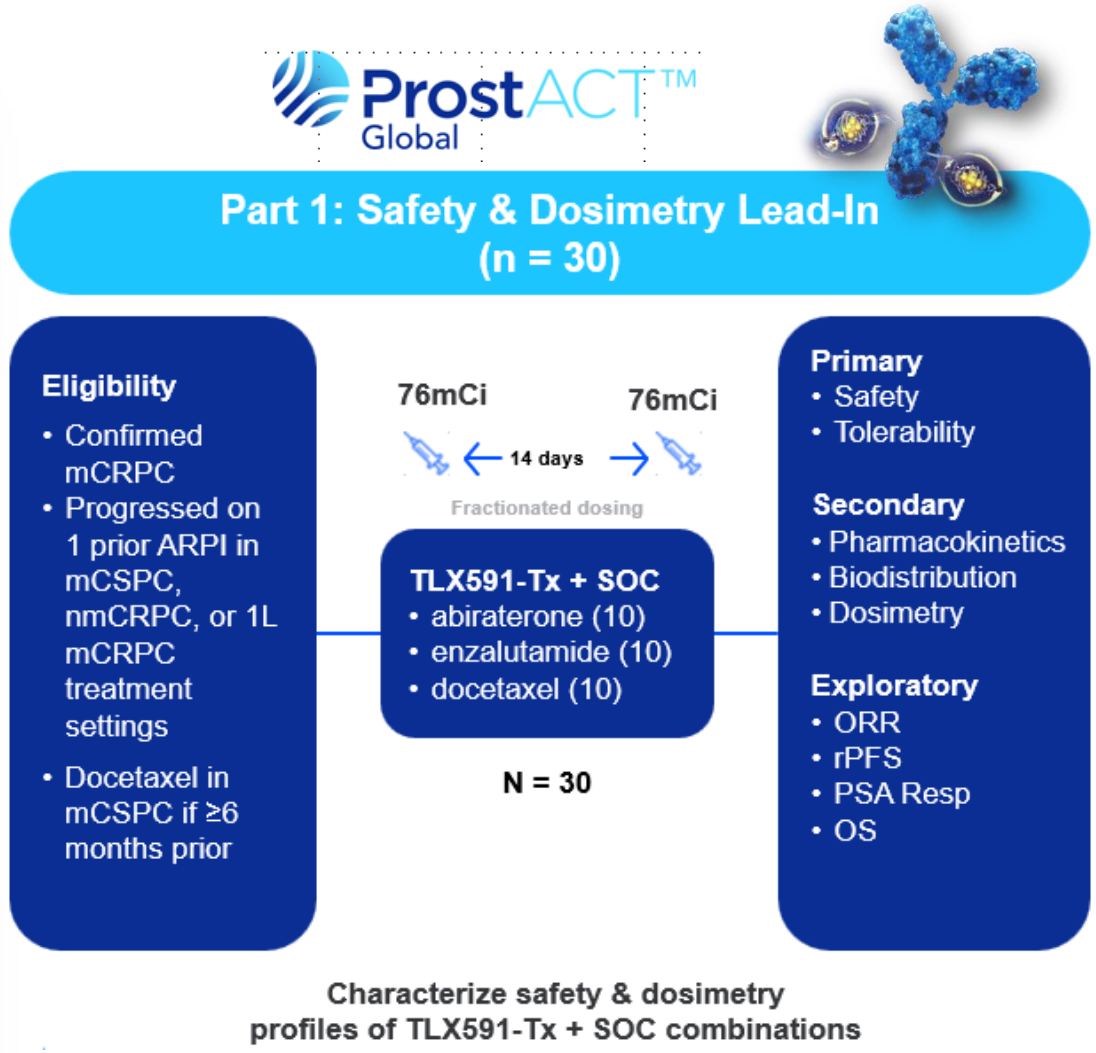
ProstACT Global part 1 safety & dosimetry lead-in

Readout - What to Expect

- **Primary Endpoints**
  - Safety (AEs / SAEs)
  - Tolerability
- **Secondary**
  - Pharmacokinetics & biodistribution
  - Organ & tumor dosimetry

Purpose of Part 1:

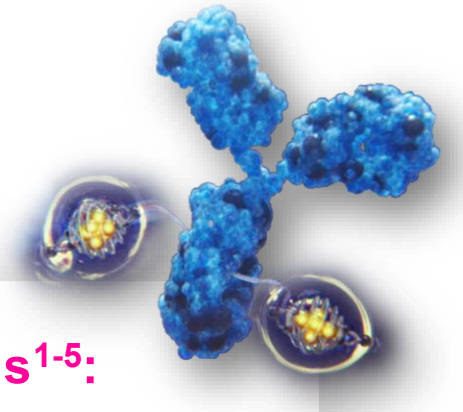
- Demonstrate an acceptable safety profile of TLX591-Tx in 3 SOC combinations
- No new safety signals compared to prior studies
- Data readout aligned to FDA submission to seek clearance to open Part 2 in the U.S.
- Part 2 is enrolling patients in Australia, Canada and New Zealand, following Independent Data Monitoring Committee (IDMC) review



1. Part 1 data will also be submitted to EMA to request clearance to open Part 2 in the E.U.

Summary: TLX591-Tx

A novel PSMA therapy with an extensive body of clinical evidence



Radio antibody-drug conjugate (rADC) approach addresses key unmet needs[1-5]:

- **Patient friendly dosing regimen** – supports compliance to treatment and ease of integration with standard of care
- **Internalization and long retention** – delivering a payload to the tumor, potentially maximising cell killing effect
- Safety and tolerability profile – **low occurrence of off-target side effects**, which impact quality-of-life, transient and manageable hematological profile
- **Supply, access and radiation protection** are potential real-world advantages, due to lower lutetium dose and hepatic clearance

- **ProstACT GLOBAL Part 1 safety and dosimetry readout aligned to FDA Part 2 submission**
- **Part 2 is enrolling patients in Australia, Canada and New Zealand, following Independent Data Monitoring Committee (IDMC) review**

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1. Sartor O, et al. Presented at: American Society of Clinical Oncology Annual Meeting; May 31-June 4, 2024; Chicago, IL. TPS5115. **2.** Sun M, et al. *Curr Oncol Rep*. 2021;23(5):59.
3. ProstACT SELECT data on file. Clinical Study Report 08-Dec-2025 **4.** Tagawa ST et al. *Cancer*. 2019;125(15):2561-2569. **5.** Differences described are not derived from head-to-head clinical studies, cross-trial comparison should be interpreted as not being definitive.

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