

## **ProstACT SELECT Study of TLX591 Interim Readout: Positive Results Confirm Safety and Tolerability**

- The study has achieved its primary objectives, confirming the safety and tolerability profile of TLX591 administered in two doses, two weeks apart in combination with standard of care (SoC)
- Preliminary activity demonstrates meaningful PSA<sup>1</sup> reduction; monitoring of patients is ongoing, including for rPFS<sup>2</sup>
- Findings reinforce the potential advantages of this first-in-class radio-antibody drug conjugate (rADC) investigational therapy, consistent with previous clinical studies of TLX591<sup>3</sup>

*Melbourne (Australia) – 19 October 2023.* Telix Pharmaceuticals Limited (ASX: TLX, Telix, the Company) today announces positive preliminary results from the Phase I ProstACT SELECT study of its rADC therapy candidate TLX591 (Lutetium (<sup>177</sup>Lu) rosopatamab tetraxetan) for prostate-specific membrane antigen (PSMA) positive metastatic castration-resistant prostate cancer (mCRPC).

The purpose of the SELECT study (ClinicalTrials.gov ID: [NCT04786847](#)) was to evaluate the utility of PSMA imaging to select patients for rADC-based PSMA therapy and to confirm the biodistribution of the rADC investigational therapy. The primary clinical objective was to determine whole body distribution and organ radiation and assess the safety and tolerability of TLX591, when administered in combination with SoC in second-line mCRPC.

The evaluable population was 28 patients (of a total 30 enrolled in the study). Patients received two (2) single intravenous (IV) infusions of TLX591, fourteen (14) days apart. Cohort 1 (5 patients) received a 27mCi dose followed by a 76 mCi dose for accuracy of biodistribution determination. Cohort 2 (23 patients) received two 76mCi doses.

The study achieved its primary objectives, confirming the safety and tolerability profile of TLX591 administered in two cycles, 14 days apart (total cumulative dose 152mCi). The results reinforce the clinical utility of the short, fractionated dosing regimen.

### **Key results and observations**

#### ***Dosimetry and biodistribution***

- Consistent lesion delineation between TLX591 and <sup>68</sup>Ga-PSMA-11 imaging, within the detection sensitivity and resolution limits of SPECT<sup>4</sup>
- Excellent uptake and retention in tumour and metastases up to 14 days post injection
- Radiation exposure to key organs is well within prescribed safety limits
- The highest absorbed dose was in the liver (clearance organ), with minimal uptake in exocrine (salivary) glands
- Long retention period is evidence of internalisation and ability to efficiently deliver payload to tumour

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<sup>1</sup> Prostate-specific antigen.

<sup>2</sup> Radiographic progression-free survival.

<sup>3</sup> Bander et al. *J Clin Oncol*. 2005; Tagawa et al. *Clin Cancer Res*. 2013; Tagawa et al. *Cancer*. 2019; Batra et al. *Urol Oncol*. 2020; Niaz et al. *Oncologist*. 2020.

<sup>4</sup> Single-photon emission computed tomography.

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## ***Hematologic profile and adverse events***

- Grade 3 thrombocytopenia (25%) and neutropenia (38%) events in line with profile expected for this class of therapy. Similarly for Grade 4 hematologic events – thrombocytopenia (25%) and neutropenia (4%)
- Serious adverse events (SAEs) observed were generally lower than in earlier studies conducted at the same dose level, reflective of the SELECT study being conducted in a healthier patient population
- Hematologic events were transient and reversible
- Four patients (17%) received intervention in the form of platelets, growth factors or both
- All treatment related non-hematologic events were Grade 1 or Grade 2 and generally mild

## ***Preliminary anti-tumour activity***

- 64% of patients (baseline PSA and full dose) had a PSA reduction, with 27% demonstrating a 30% reduction and 18% demonstrating a 50% reduction. PSA and rPFS monitoring is ongoing

Scott T. Tagawa, MD, Professor of Medicine and Urology in New York said, “Preliminary results from the ProstACT SELECT study build on prior studies of TLX591 and underline the potential advantages of an antibody-based approach. Latest data provides further evidence of the long retention and internalisation of TLX591 in the tumour (and metastases), which may maximise the cell-killing effect of the <sup>177</sup>Lu radioisotope at the site of the tumour.”

Nat Lenzo, MD, GenesisCare Group Clinical Director Theranostics and top recruiter onto the ProstACT SELECT study commented, “It is really exciting to see development of this next-generation PSMA-targeting radiotherapeutic progressing. This study confirms the suitability of the short, simple treatment duration with two doses administered two weeks apart which is attractive to physicians and patients. The safety and tolerability data also demonstrates the potential for this therapy to reduce undesirable side effects, while delivering a hematologic toxicity profile that is both tolerable and manageable.”

Colin Hayward, Telix Chief Medical Officer, added, “TLX591 is being designed to integrate with current standard of care, demonstrative of Telix’s continued innovation in prostate cancer treatment. The SELECT study provides further validation of the potential of TLX591, a first-in-class rADC therapy and the use of PSMA imaging with small molecules to select patients for antibody-based PSMA therapy.”

Investigation of TLX591 is continuing in the Phase III ProstACT GLOBAL study (ClinicalTrials.gov ID [NCT04876651](https://clinicaltrials.gov/ct2/show/study/NCT04876651)), open for enrolment in Australia and expected to commence in the United States in 2024.

## **About Telix Pharmaceuticals Limited**

Telix is a biopharmaceutical company focused on the development and commercialisation of diagnostic and therapeutic radiopharmaceuticals and associated medical devices. Telix is headquartered in Melbourne, Australia with international operations in the United States, Europe (Belgium and Switzerland), and Japan. Telix is developing a portfolio of clinical-stage products that aims to address significant unmet medical needs in oncology and rare diseases. Telix is listed on the Australian Securities Exchange (ASX: TLX).

Visit [www.telixpharma.com](http://www.telixpharma.com) for further information about Telix, including details of the latest share price, announcements made to the ASX, investor and analyst presentations, news releases, event details and other publications that may be of interest. You can also follow Telix on [LinkedIn](https://www.linkedin.com/company/telix-pharmaceuticals).

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TLX591 has not received a marketing authorisation in any jurisdiction. Telix's lead product, gallium-68 (<sup>68</sup>Ga) gozetotide (also known as <sup>68</sup>Ga PSMA-11) injection, has been approved by the U.S. Food and Drug Administration (FDA),<sup>5</sup> by the Australian Therapeutic Goods Administration (TGA),<sup>6</sup> and by Health Canada.<sup>7</sup> Telix is also progressing Marketing Authorisation Applications for <sup>68</sup>Ga-PSMA-11 in the United Kingdom, the European Union<sup>8</sup> and Brazil.

## Telix Investor Relations

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*This announcement has been authorised for release by the Telix Pharmaceuticals Limited Disclosure Committee on behalf of the Board.*

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<sup>5</sup> Telix ASX disclosure 20 December 2021.

<sup>6</sup> Telix ASX disclosure 2 November 2021.

<sup>7</sup> Telix ASX disclosure 14 October 2022.

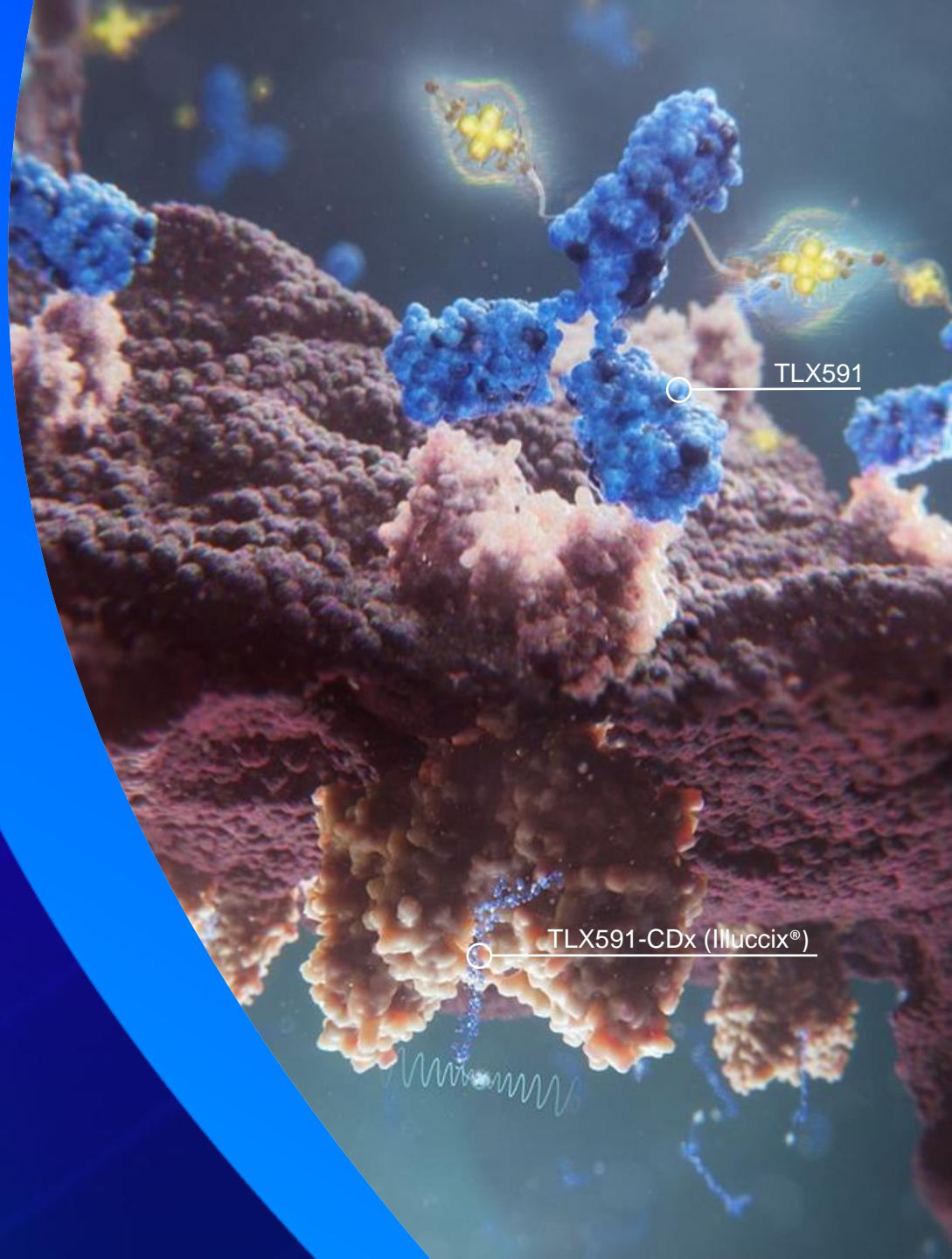
<sup>8</sup> Telix ASX disclosure 3 April 2023.



# TLX591 Program Update

## ProstACT SELECT Study Preliminary Results (NCT04786847)

19 October 2023



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Telix’s lead product, Illuccix® (TLX591-CDx) for prostate cancer imaging, has been approved by the Australian Therapeutic Goods Administration (TGA), the U.S. Food and Drug Administration (FDA), and Health Canada. With the exception of Illuccix as noted above, no Telix product has received a marketing authorisation in any jurisdiction.

Full United States prescribing information for Illuccix can be found at <http://illuccixhcp.com/s/illuccix-prescribing-information.pdf>

All figures are in AU\$ unless otherwise stated and provided on an unaudited basis.

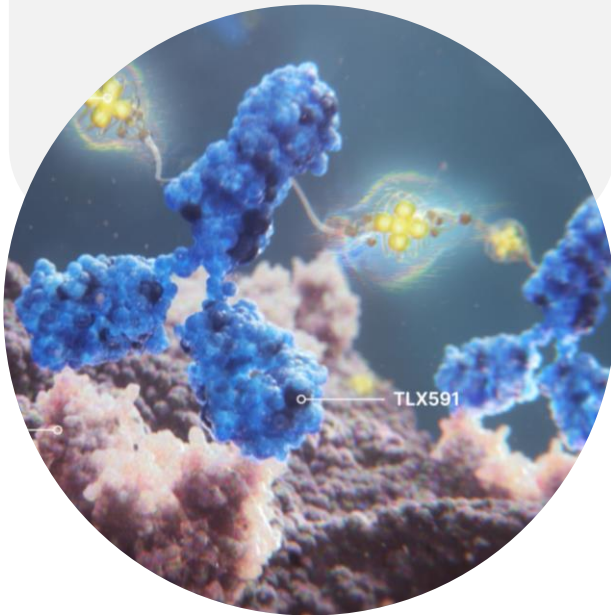
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# TLX591: Rationale

First-in-class/best-in-class radiopharmaceutical therapy using a biologic to target PSMA

TLX591:  
Lutetium ( $^{177}\text{Lu}$ )  
rosopatamab tetraxetan



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

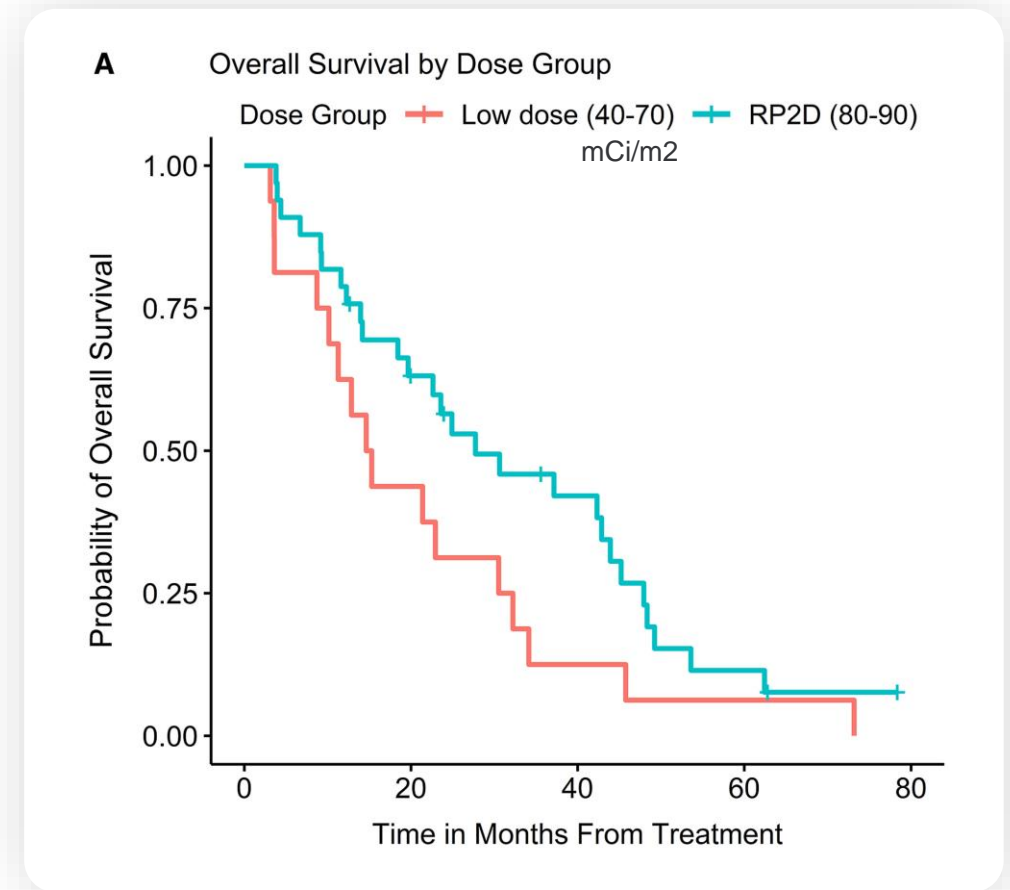
- PSMA is a validated target in prostate cancer<sup>1</sup>
- TLX591 utilises a **PSMA-targeted monoclonal antibody (mAb) approach**. This is significantly different targeting and pharmacology to anti-PSMA small molecules
- mAbs are distinguished by their internalisation, long retention and functional selectivity for tumour-expressed PSMA<sup>2</sup>
- This enables a short, patient-friendly dosing regimen and low occurrence of off-target side effects, while delivering a meaningful therapeutic index<sup>3</sup>
- ProstACT SELECT is a Phase I safety and dosimetry study, and one of three ProstACT studies underway
- SELECT interim clinical findings reinforce data published to date and highlight the clinical potential of this asset

# TLX591 data generated to date

## Published data demonstrates anti-tumour effect and overall survival benefits

- TLX591 has been previously evaluated in over 200 prostate cancer patients in five Phase I and Phase II studies
- Evidence of anti-tumour effect and a clear dose-response profile for key measures of activity
  - Prostate-specific antigen (PSA) response
  - Overall survival (OS) – **published 40+ months** median survival in end-stage (heavily pre-treated) patients
- Well tolerated with predictable and transient reductions in hematological parameters, with subsequent recovery

**Fractionated dosing manages hematologic safety while delivering a highly targeted and potent radiation dose to prostate cancer metastases<sup>1</sup>**



# Active TLX591 Studies

Exploring patient selection, early-stage and advanced disease



**Radiogenomics study  
(Phase I)**

*“Treat the scan”*

Aims to demonstrate correlation between imaging and therapy to optimise patient selection. Supports indication expansion based on a “theranostic” approach.

Low dose study – 2 x 2.8GBq (76mCi)



**Combination with EBRT<sup>1</sup> in  
oligometastatic early recurrence  
(Phase II)**

*Early data in front line care*

Efficacy data in patients in their first recurrence. Uniquely positions Telix as the leading radiopharmaceutical company combining external beam radiation and a PSMA-targeting therapy

In partnership with GenesisCare – recruiting



**Phase III study in patients with  
mCRPC<sup>2</sup> progressing on 1st line  
novel androgen agents**

***TLX591 + Standard of Care (SoC) vs.  
SoC alone***

Product designed to be “patient-centric”, only requires two treatments with TLX591 compared to six treatments with competitor products.  
Potential for less off-target toxicity

Global study enrolling ~400 patients,  
APAC recruiting

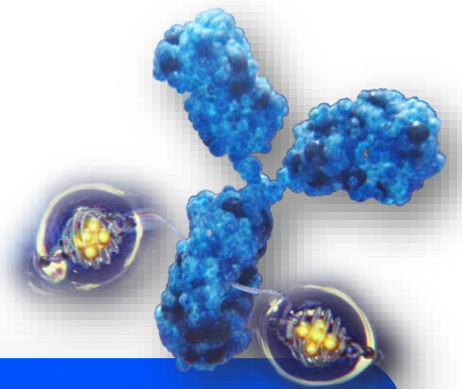


1. External-beam radiation therapy.
2. Metastatic castration-resistant prostate cancer.



# ProstACT SELECT: Study purpose and design

## Correlation between imaging and therapy to optimise patient selection



### The SELECT study enables us to:

- Compare biodistribution between small molecule PSMA agents and mAb-based therapy > *critical for patient selection for therapy*
- Safety profile > *further evaluate safety and tolerability in a mid-stage patient population reflective of ProstACT GLOBAL*
- Capture activity data > *although not an efficacy study, patients will continue to be monitored enabling the generation of activity data*

### Clinical Goals:

- **Primary objective:** Determine whole body distribution and organ radiation and assess the safety and tolerability of TLX591
- **Patient population:** Evaluate TLX591 in mCRPC patients that are PSMA positive, and previously treated with ARPI<sup>1</sup>



**Full analysis set: 28 patients<sup>2</sup>**

Patients selected with <sup>68</sup>Ga-PSMA-11 imaging

**Day 1:**  
First dose TLX591  
(2.8GBq)

**Days 1-13:**  
Safety evaluation,  
dosimetry imaging

↓  
**Day 14:**

Second dose of TLX591 (2.8GBq) upon confirmed safety



**Imaging to assess biodistribution and dosimetry, as well as close safety monitoring following each dose**

ClinicalTrials.gov ID: [NCT04786847](https://clinicaltrials.gov/ct2/show/study/NCT04786847)



1. Androgen receptor pathway inhibitor.

2. Cohort 1 (5 patients) received a 27mCi dose (for imaging biodistribution) followed by a 76 mCi dose. Cohort 2 (23 patients) completed two 76mCi doses.

# ProstACT SELECT: Key findings from interim readout

## Primary and secondary objectives achieved to date



### Objectives met

Demonstrated safety profile and tolerability with two doses administered two weeks apart (total cumulative dose 152mCi)



### Patient-friendly dosing

Short, simple regimen of two doses, administered two weeks apart



### Uptake

Highest absorbed dose in the liver (clearance organ), minimal uptake in exocrine (salivary) glands



### Retention

TLX591 retained in the tumour with high activity remaining at two weeks



### Hematology

Lower rates of hematologic events than in earlier studies

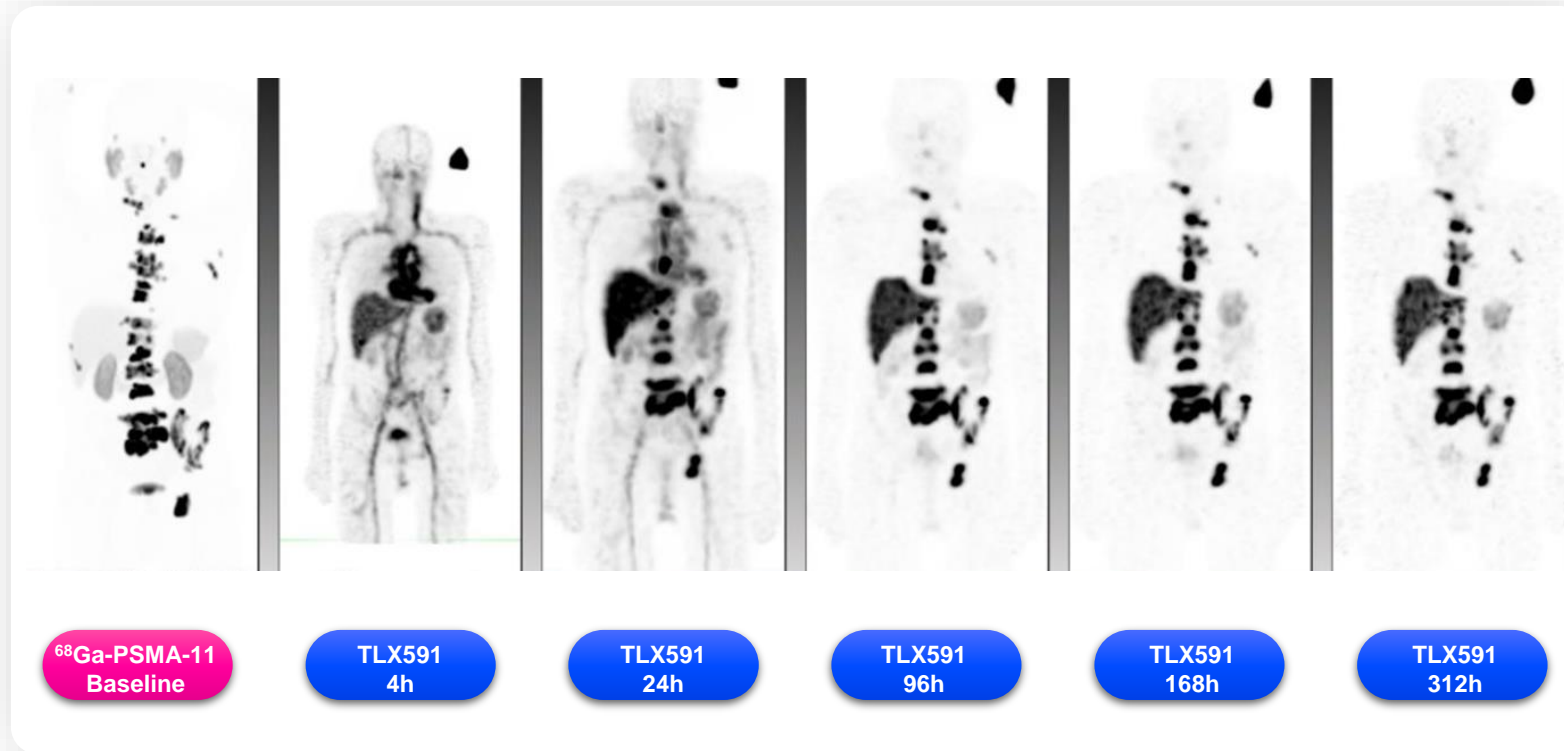


### Preliminary efficacy

64% of patients (baseline PSA and full dose) had a PSA reduction, with 27% demonstrating a 30% reduction and 18% demonstrating a 50% reduction. PSA and rPFS monitoring is ongoing

# Example: High disease burden patient

Patient with 98% drop in PSA



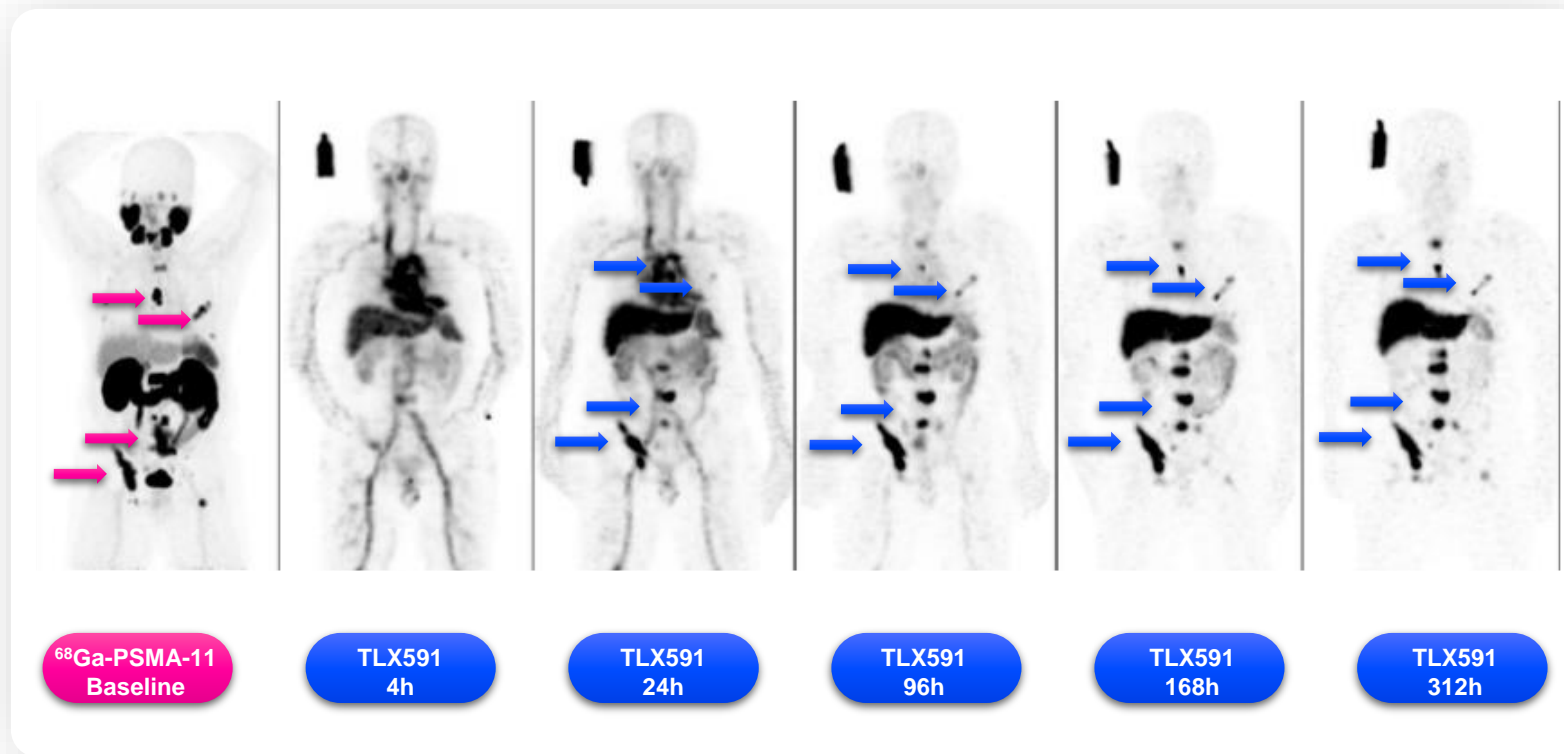
Patient representative scan - individual results may vary.

## Key observations

- Data shows excellent uptake and retention in tumour and metastases up to 14 days post-injection
- Uptake consistent between TLX591 and <sup>68</sup>Ga-PSMA-11 imaging - demonstrates the small molecule-based imaging agent and the antibody-based therapeutic agent are reaching the same target, an important point when considering a companion diagnostic for patient selection and monitoring
- Long retention period evidence of internalisation, and ability to deliver payload to tumour, maximising cell-killing effect
- Patient had prior therapy with abiraterone
- PSA nadir 334 days after first dose

# Example: Moderate disease burden patient

PSA dropped to 33% of baseline value



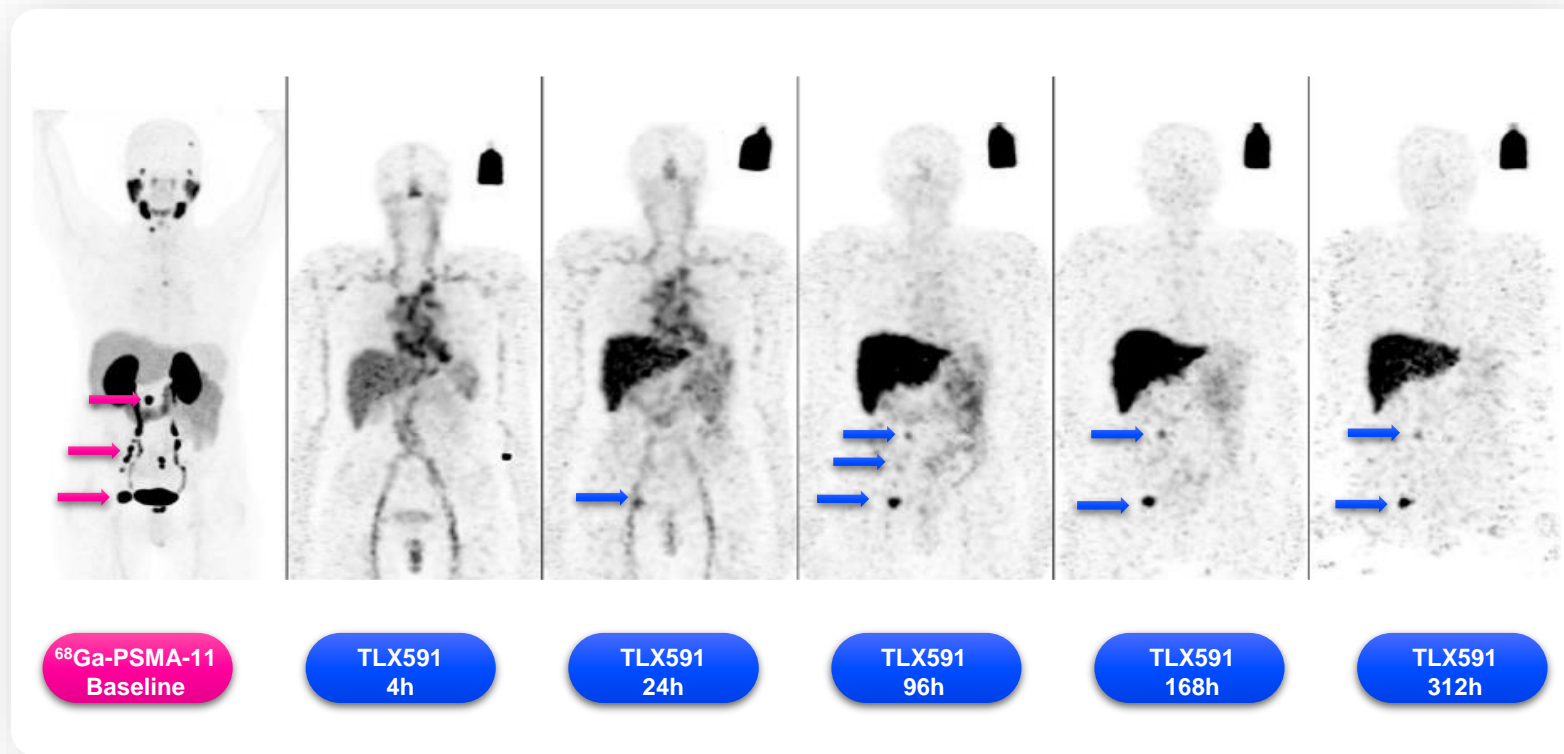
Patient representative scan - individual results may vary.

## Key observations

- Stage IV gleason 8 disease in 2015.
- Treated with Denosumab and Zoladex. No other concomitant medications for prostate cancer
- Treated with 2 x 76mCi TLX591 doses 2 weeks apart
- Good bone uptake over the course of 2 weeks
- PSA nadir was 54 days after first dose

# Example: Low disease burden patient

PSA dropped to 61% of baseline value



Patient representative scan - individual results may vary.

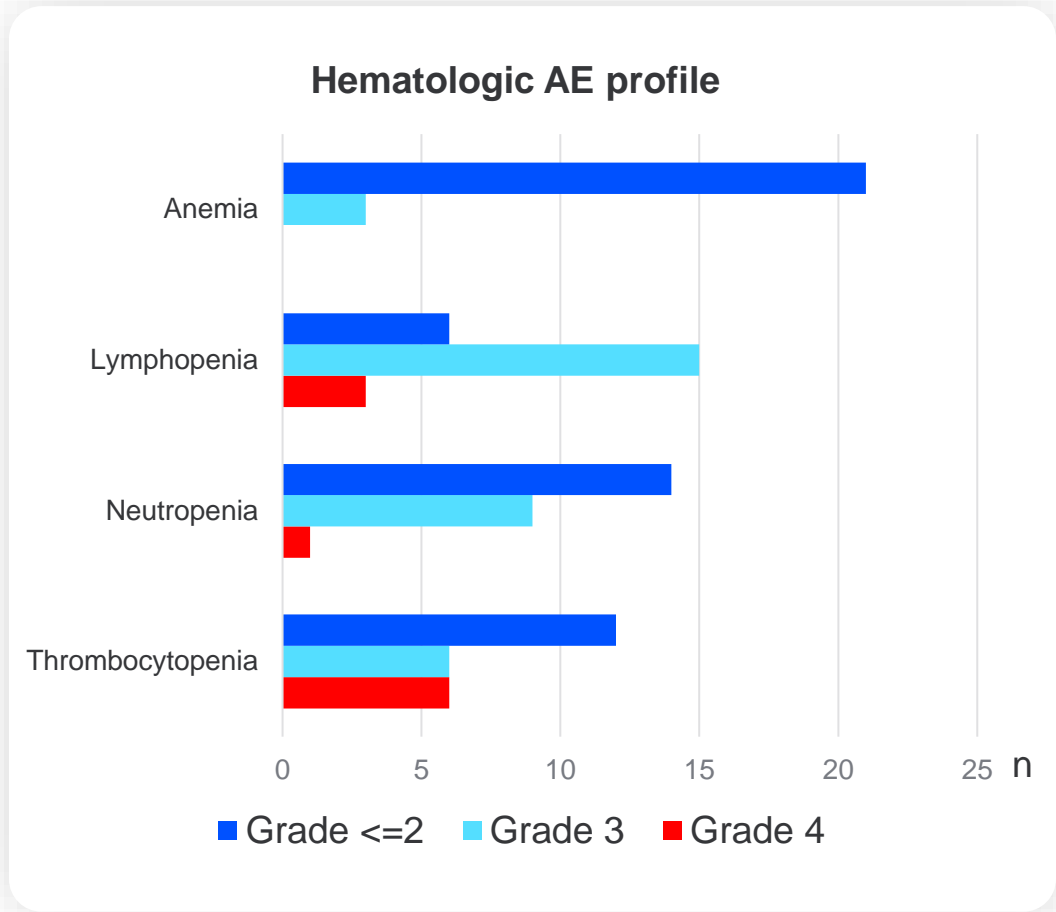
## Key observations

- Diagnosed in 2013 with Gleason 9 disease. Had radiotherapy at diagnosis
- Previously treated with enzalutamide five years before study entry. No other anti-prostate cancer drugs
- Nodal disease in the pelvis and abdomen
- PSA nadir 168 days after first dose

# Safety data

## Safety and tolerability confirmed

### Key observations



#### Hematologic laboratory profile

- Grade 3 thrombocytopenia (25%) and neutropenia (38%) events in line with profile expected for this class of therapy
- Grade 4 thrombocytopenia (25%) and neutropenia (4%) were transient
- Four patients (17%) received intervention for hematologic toxicity in the form of platelets, growth factors or both

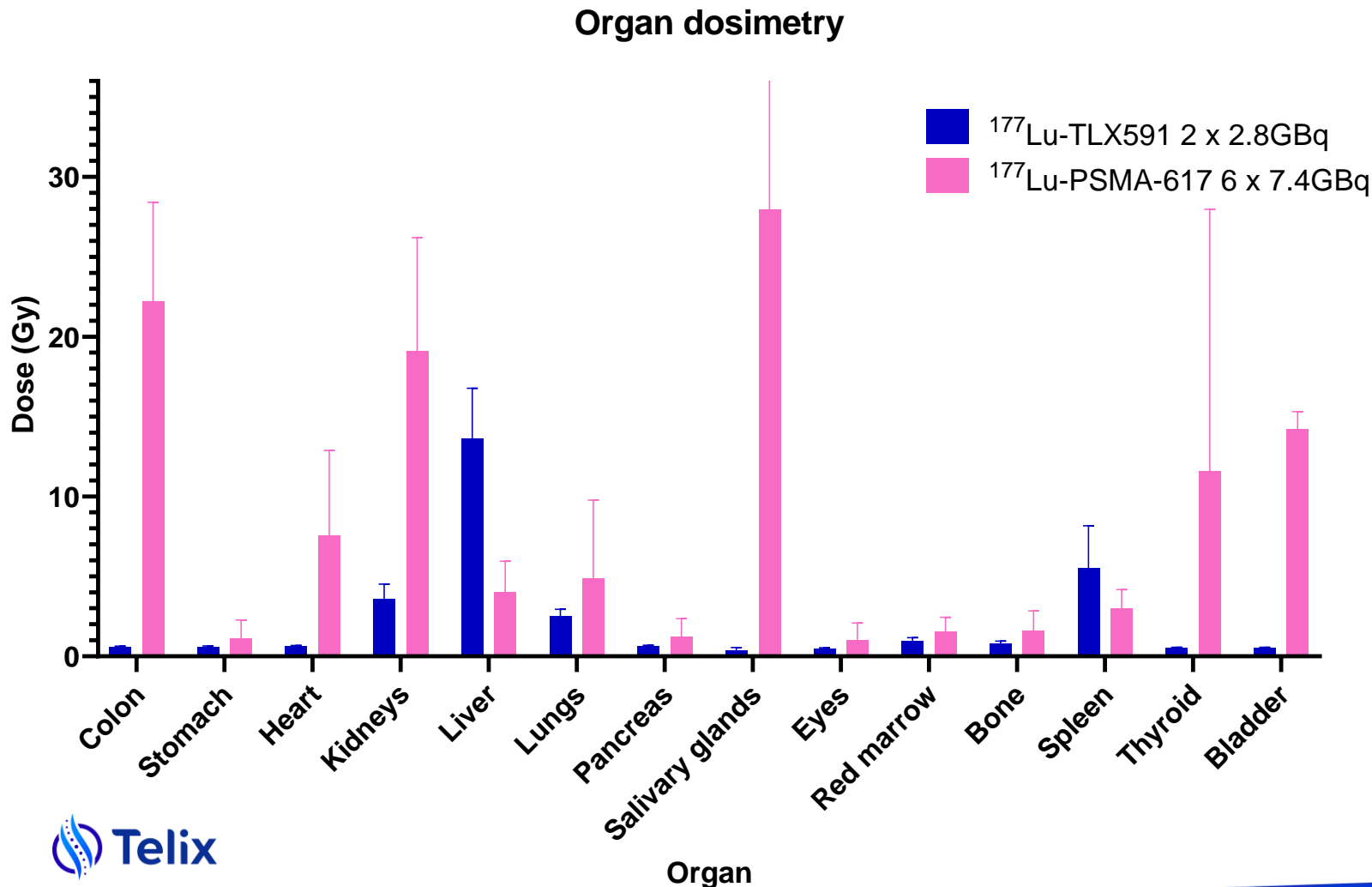
#### Non-hematologic events

- All drug-related non-hematologic events were grade 1 or grade 2
- The most prevalent non-hematological adverse events were fatigue (76%), nausea (20%) and loss of appetite (20%)

# Comparative dosimetry: TLX591 is highly targeted

$^{177}\text{Lu}$ -TLX591 compared with  $^{177}\text{Lu}$ -PSMA-617

## Key observations



- TLX591 significantly lower total dose in many organs compared to  $^{177}\text{Lu}$ -PSMA-617 especially in the salivary glands, kidneys, colon and bladder wall
- Lower dose has potential to avoid renal and salivary gland toxicities
- Bone marrow dose is below the 2Gy external beam threshold as suggested by ICRP 41 (International Convention on Radiation Protection)
- Liver dose is also well below the 32Gy limit

# Summary and next steps

## Competitive safety and tolerability profile, anti-tumour activity

### SELECT data supports the potential benefits of an antibody-based approach

- **Patient friendly dosing regimen** – supports compliance to treatment and ease of integration with standard of care
- **Internalisation and long retention** – delivering a payload to the tumour, potentially maximising cell killing effect
- Safety and tolerability profile – **low occurrence of patient-centric off-target side effects**, which impact quality-of-life
- Lower rates of hematologic toxicity than in earlier studies
- **Supply, access and radiation protection** are potential real-world advantages, due to lower lutetium dose and hepatic clearance



Prostate **ACT**  
GLOBAL

### Investigation of TLX591 is continuing in the Prostate ACT GLOBAL Phase III study

- Open for enrolment and screening patients in first APAC sites
- Additional sites being on-boarded
- Prostate ACT GLOBAL to expand into international sites in 2024, pending regulatory approval(s)



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