NOVARTIS

Clinical Trial Results Website

Sponsor

Advanced Accelerator Applications

Generic Drug Name

[68Ga]Ga-PSMA-R2 (^{68}Ga-PSMA-R2) (PSMA imaging), [177Lu]Lu-PSMA-R2 (^{177}Lu-PSMA-R2) (PSMA-RLT)

Trial Indication(s)

Prostate specific membrane antigen (PSMA) positive (68Ga-PSMA-R2) progressive metastatic castration-resistant prostate cancer, following previous systemic treatment

Protocol Number

A206T-G01-001 / CAAA602A12101

Protocol Title

A Phase 1/2 open-label, multi-center, dose-escalation study of safety, tolerability, pharmacokinetics, dosimetry, and response to repeat dosing of 177Lu-PSMA-R2 radio-ligand therapy in patients with prostate specific membrane antigen (PSMA) positive (68Ga-PSMA-R2) progressive metastatic castration-resistant prostate cancer, following previous systemic treatment

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase I/II

Study Start/End Dates

Study Start Date: May 2018 (Actual)
Primary Completion Date: May 2021 (Actual)
Study Completion Date: June 2022 (Actual)

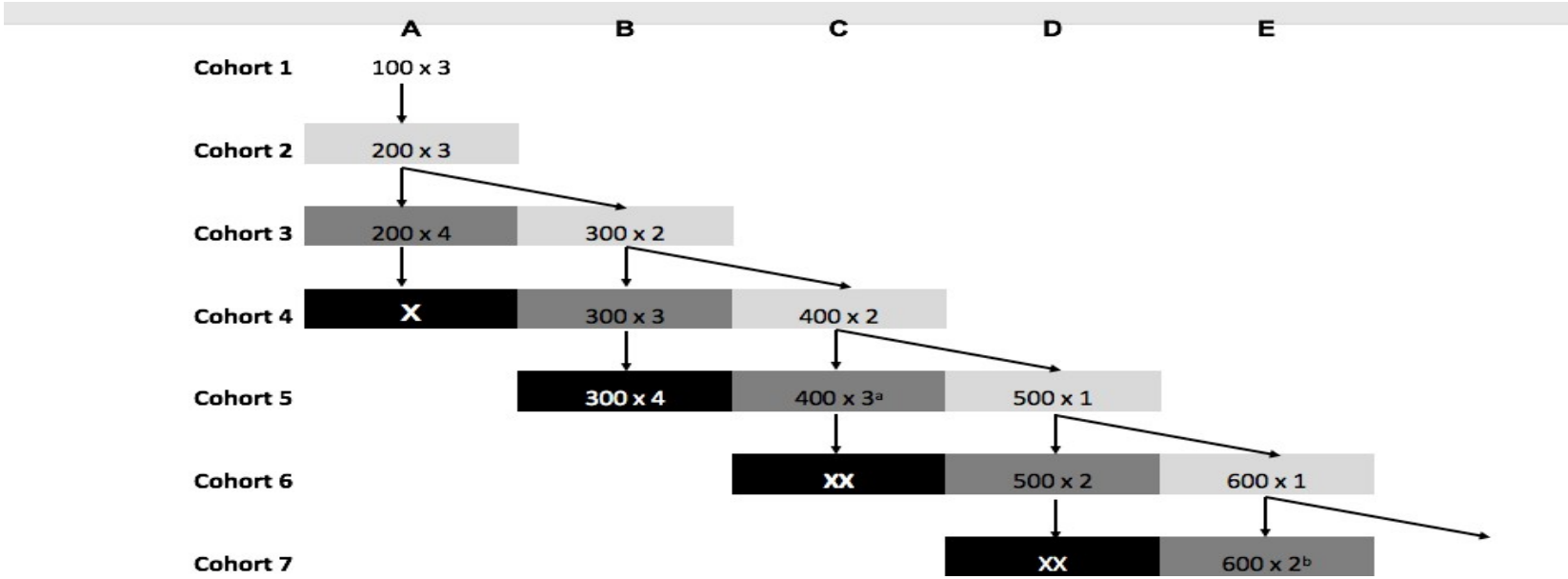
Reason for Termination (If applicable)

Recruitment for PROter A206T-G01-001 (NCT03490838) was halted in Phase I by sponsor decision. Phase II expansion portion of the study was never initiated.

Study Design/Methodology

This was a Phase I/II, open-label, multi-center, dose-escalation and expansion study of 177Lu-PSMA-R2 in patients with adenocarcinoma of the prostate and radiographic CT/magnetic resonance imaging (MRI) or bone scan evidence of metastatic disease. Patients were enrolled who had progression after treatment for their metastatic Castration-resistant Prostate Cancer (mCRPC) including CYP17 inhibitors and/or androgen pathway inhibitors and no more than one line of chemotherapy for the advanced disease, or patients who were ineligible (unfit or unwilling) to receive chemotherapy. All patients had 68Ga-PSMA-R2 PET imaging to document PSMA positive lesion(s).

The study was designed to be executed in 3 periods (screening, treatment -dose escalation and dose expansion, and follow-up) to estimate organ and lesion radiation uptake by dosimetry, characterize the safety profile and determine the MTD and Dose Limiting Toxicity (DLT) of 177Lu-PSMA-R2, as well as detect initial efficacy signals.



Regimens are presented in the format: dose strength (mCi) x number of cycles; Cycle duration is 6 weeks (+2 weeks in case of toxicity or administrative issue); Each subcohort will comprise of 3 patients

Cumulative dose not to exceed:

Level 1: 60% of the average dosimetry driven estimate from preceding cohorts

Level 2: 80% of the average dosimetry driven estimate from preceding cohorts

Level 3: 100% of the average dosimetry driven estimate from preceding cohorts

Data from cycle 1 will be used for determination of DLT. Accordingly, data from up to 3 subcohorts, i.e. 9 patients, can inform DLT decisions (example subcohorts 3B, 4B, 5B for 300 mCi). Please see Table 5 for Dose Escalation and Stopping rules

Dosimetry conducted in:

Cycle 1 of the indicated cohorts

Assumptions

Maximum safe cumulative exposure of 1334 mCi (actual estimates driven by dosimetry data from the study)

Dose strength escalation by 100 mCi per cycle after DLT period of the Level 1 subcohorts (actual increase will be determined based on review of data in consultation with the SRB)

Notes:

X – Subcohort not initiated as maximum number of doses would exceed 4

XX – Subcohort not initiated as additional dose would exceed 100% of the maximum safe cumulative exposure

[a] – Addition of dose exceeds the 80% limit. Interim analysis will be conducted after the cumulative exposure of the prior level (400 x 2) to confirm the findings. If confirmed, an additional dose will be added such that the maximum safe cumulative exposure is not exceeded for the next level (100%)

[b] – Addition of dose exceeds the 80% limit. Interim analysis will be conducted after the cumulative exposure of the prior level (600 x 1) to confirm the findings. If confirmed, an additional dose will be added such that the maximum safe cumulative exposure is not exceeded for the next level (100%)

Screening period: Period up to 28 days during which informed consent form (ICF) signature was obtained and all screening procedures to determine patient eligibility were performed.

Dose Escalation Period (Phase I): At baseline (before receiving the investigational product), all patients underwent physical examination (source documented only), electrocardiogram (ECG), routine blood tests for biochemistry (including amylase, lipase, liver and kidney function parameters) and hematology. Xerostomia/Xerophthalmia and Brief Pain Inventory questionnaires were completed prior to the first infusion of 177Lu-PSMA-R2 and then every 12 weeks until 1 year after disease progression per PCWG3, or early termination whichever occurred first.

Dose escalation was carried out in a modified 3+3 design testing a number of dosing schedules (combination of dose strength and number of doses) using prespecified dose escalation rules. The total radioactivity was injected either in a single dose or in a fractionated regimen of up to 4 doses with each cycle separated by 6 weeks (with a 2-week window in the event of a possible toxicity or administrative issue). To limit the exposure of a large number of patients to subtherapeutic doses, patients were enrolled in groups of 3. Dose-escalation decision was made based on review of DLT, dosimetry and in consultation with the safety review board (SRB). A total of 27 patients were enrolled.

Data from cycle 1 was used for determination of DLT as well as dose escalation. The safety profile of subsequent cycles continued to be carefully monitored to define the potential need for dose adjustment in the corresponding cycles of subsequent cohorts. Dosimetry was conducted during cycle 1 of each cohort testing a new dose strength in order to determine the radiation uptake by critical organs from a single dose as well as the anticipated maximum safe cumulative exposure from multiple doses.

177Lu-PSMA-R2Treatment in the first two cohorts was initiated as follows:

- Cohort-1: 3.70 GBq (100mCi) x 3 times = 11.10 GBq
- Cohort-2: 7.40 GBq (200mCi) x 3 times = 22.2 GBq, if no DLT is reported on Cohort 1

Organ dosimetry data from these two cohorts was used to determine the maximum safe cumulative exposure. Commonly accepted radiation thresholds for critical organs (kidney, salivary glands, bone marrow) based on external beam radiation therapy were used as a guidance to derive these estimates. Dosimetry for subsequent cohorts continued to inform this limit on an ongoing basis.

Following cohort 2, dose escalation was conducted by initiation of two parallel subcohorts – one adding more doses at the same dose strength and the other testing a higher dose strength.

- The addition of more doses was done in such a way that the cumulative dose did not exceed 80% of the maximum safe cumulative exposure.
- The escalation of dose strength did not exceed 100 mCi in each dose of the regimen. No subcohort testing a new dose strength exceeded the cumulative dose of 60% of the maximum safe cumulative exposure.

Following the DLT period of the subcohort testing 80% of the maximum safe cumulative exposure, another subcohort using the same dose strength was initiated in such a way that that the cumulative exposure was approximately 100% (not to exceed 120%) of the maximum safe cumulative exposure.

The DLT information from the subcohorts testing higher number of doses i.e., 80% was used to confirm the findings from the first cohort at that dose strength as well as inform dosing in the future subcohorts. Safety follow-up during Phase I included weekly blood tests for electrolytes, hematology, liver, amylase and lipase, and kidney function tests from the first dose date up to 6 weeks after last dose, or until toxicities were resolved. The safety profile or all ongoing patients were continuously monitored and considered throughout the study.

The adverse events (AEs) and serious adverse events (SAEs), as well as laboratory abnormalities were monitored and recorded from the time the patient signed the ICF to the last day of the final treatment cycle (SAEs considered by the investigator as related to investigational product continued to be collected during safety follow up).

Dosimetry and pharmacokinetics (PK): 3 patients from each cohort testing a new dose strength during dose escalation phase (Phase I) underwent 8 scans [6 planar and 2 SPECT/CT] concomitantly with serial blood samples over a period of eight days. Total urine excreted over a period of 4 days were also collected.

Phase II

Once the RP2D was determined, the Phase II portion of the study was planned to be initiated. However, based on the totality of the available data, the Sponsor's governance board with agreement of SRB recommended to halt recruitment during phase I prior to reaching MTD/RP2D, and not to initiate the phase II expansion part of the study. This recruitment halt was not a consequence of any safety concern; it was an outcome of the sponsor’s strategic assessment of the current and future clinical development plan for 177Lu-PSMA assets in mCRPC.

Follow-up Period: This period started at the End of Treatment (EOT) visit for all patients enrolled in the Phase I portion of the study. Hematology, kidney function tests (BUN and serum creatinine), as well as urinalysis were performed every 12 weeks until 1 year after EOT. Collection of follow-up data continued until early study termination, reached upon completion of one-year safety follow-up for the last enrolled patient.

PRO questionnaires were applied every 12 weeks until one year after disease progression was documented per PCWG3 or early termination, whichever occurred first.

Tumor assessments was collected every 12 weeks up to objective disease progression (per PCWG3). Survival status continued to be collected every 12 weeks along with PRO questionnaires and twice a year thereafter.

All SAEs judged by the Investigator to be related to study treatment as well as further therapies for prostate cancer were collected for all patients at least until completion of the 1-year follow-up period.

Centers

11 centers in 2 countries: United States(9), Spain(2)

Objectives:

This Phase I/II study was intended to investigate the safety, tolerability, and radiation dosimetry of 177Lu-PSMA-R2 and further assess preliminary efficacy data in patients with mCRPC. The Phase I portion of the study aimed to determine the recommended dose or Maximum Tolerated Dose (MTD) of 177Lu-PSMA-R2 for RLT of mCRPC, and the Phase II portion was planned to expand into approximately 60 patients documenting the preliminary activity (anti-tumor response) of repeated treatments administered, continuing safety assessments and collecting QoL data.

Phase I:

Primary Objective:

- Determine the MTD and Recommended Phase II Dose (RP2D) for 177Lu-PSMA-R2

Secondary Objectives:

- Characterize the safety and tolerability of 177Lu-PSMA-R2
- Assess preliminary anti-tumor response based on RECIST v1.1
- Assess preliminary anti-tumor response based on prostate-specific antigen (PSA) levels
- Assess the pharmacokinetic profile of 177Lu-PSMA-R2
- Assess organ and lesion radiation uptake by dosimetry
- Assess preliminary patient reported outcomes related to xerostomia and xerophthalmia

Test Product (s), Dose(s), and Mode(s) of Administration

No reference therapy was administered.

Investigational product for PSMA imaging: 68Ga-PSMA-R2:

The full name of the Investigational Product (IP) is “68Ga-PSMA-R2 kit for radiopharmaceutical preparation”,

The IP was a sterile 2-vial kit which consisted of:

- Vial 1: PSMA-R2, 30 µg, powder for solution for injection, to be reconstituted with a solution of gallium-68 chloride (68GaCl3) in HCl eluted from a GMP 68Ge/68Ga generator;
- Vial 2: Reaction buffer. Vial 2 was to be added to the reconstituted Vial 1.

The kit was to be used in combination with a solution of 68Ga in HCl provided by GMP 68Ge/68Ga generator qualified by the Sponsor for this purpose. The final product 68Ga- PSMA-R2 solution for injection, was directly injected to the patient.

Investigational product for PSMA-RLT: 177Lu-PSMA-R2:

The IP was a radiopharmaceutical product presented as a solution for infusion. The investigational product 177Lu-PSMA-R2 370 MBq/mL solution for infusion was a sterile ready-to-use solution for infusion containing 177Lu-PSMA-R2 as drug substance with a volumetric activity of 370 MBq/mL at reference date and time (calibration time (tc)). Given the fixed volumetric activity of 370 MBq/mL at the date and time of calibration, the volume of the solution was adjusted between 15 mL and 25 mL in order to provide the required amount of radioactivity at the date and time of infusion.

Statistical Methods

Analysis Sets

The Full Analysis Set (FAS) consisted of all patients who entered the study and received at least one dose of 177Lu-PSMA-R2. The safety set in this case was identical to the FAS and so was not defined as a separate set.

Demography and baseline characteristics

Demographic, baseline characteristics and other baseline data was summarized descriptively.

Efficacy analysis

Summaries of PSA response rate 50 at Week 13 were produced including point estimate and 95% confidence interval. This was produced for the primary response definition of a 50% decline in PSA confirmed at least 4 weeks later, and also for the minor response definition of a 30% decline in PSA confirmed at least 4 weeks later. Summary statistics were also produced for changes in PSA as a continuous endpoint at Week 13 as well as maximum reduction in PSA during the study and this data was also presented in waterfall plots at each assessment point (a plot of vertical bars, one bar per patient indicating their % change in PSA ordered from largest increase to largest decrease).

Objective response rate (CR and PR) and duration were assessed in patients with soft tissue lesions and summarized descriptively. ORR (CR+PR) was presented with appropriate 95% confidence intervals. Duration of response was a summary of the number of patients with progression events along with the relevant summary statistics obtained from the Kaplan-Meier estimates (median with 95% confidence intervals).

Safety analysis

Safety evaluations on the safety set were based on the incidence, type, severity, relationship to the IP and consequences (e.g., study discontinuation) of an AE as well as on clinically significant changes in the patient's ECGs, vital signs, and clinical laboratory results as further described in the SAP. ECG parameters include HR, RR interval, PR interval, QRS width and QTc interval. Statistical analysis included descriptive tabulation for categorical descriptive statistics for continuous data, for observed values as well as for changes from baseline in continuous parameters at each measuring time. Clinical laboratory data, ECGs and vital signs were also presented graphically in terms of box plots of absolute values over time and changes from baseline over time, when appropriate. Clinical laboratory data was summarized with respect to the normal ranges of values provided by the laboratory and with respect to pre-defined levels of change in these values.

All adverse events were listed on an individual basis. They were summarized by System Organ Class (SOC) and Preferred Term (PT) at patient level. Patients with more than one adverse event within a particular SOC and PT were counted only once for that SOC and PT.

Only treatment emergent events were included in summaries of AEs, but all adverse events were presented in listings.

Analysis of Biodistribution, Pharmacokinetics and Dosimetry data

The analysis of biodistribution and dosimetry endpoints consisted in descriptive summaries of the derived parameters on the sub-population of full analysis set who underwent dosimetry assessments.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Male patients, 18 years of age or older
- Signed and dated written ICF by the patient or legally acceptable representative prior to any study-specific procedures
- Histologically confirmed adenocarcinoma of the prostate
- Serum testosterone levels < 50 ng/dL after surgical or continued chemical castration
- Metastatic disease documented by CT/MRI or bone scan (not older than 28 days at enrollment) revealing at least one metastatic lymph-node, visceral metastasis and/or bone metastasis
- Positive 68Ga-PSMA-R2 PET/CT scan for central eligibility assessment. Patients who receive 68Ga-PSMA-R2 as part of separate clinical protocol are eligible (must meet all study eligibility criteria)
- Documented progressive mCRPC on or after the last systemic treatment administered for the advanced disease including metastatic disease. Disease progression defined as increasing serum PSA (per PCWG3), radiological progression or ≥ 2 new bone lesions.
- Must have received prior systemic treatment for mCRPC including CYP17 inhibitors and/or androgen-pathway inhibitors (i.e. abiraterone and/or enzalutamide when available) and one and no more than one line of chemotherapy for the advanced disease (unless ineligible (unfit) to receive chemotherapy).
- At least 28 days elapsed between last anti-cancer treatment administration and the initiation of study treatment (except for Luteinizing Hormone-releasing Hormone [LHRH] or Gonadotropin-releasing Hormone [GnRH]), or resolution of all previous treatment related toxicities to CTCAE version 5.0 grade of ≤ 1 (except for chemotherapy induced alopecia and grade 2 peripheral neuropathy or grade 2 urinary frequency which are allowed). Prior major surgery must be at least 12 weeks prior to study entry.
- Eastern cooperative oncology group (ECOG) performance status of 0-2 with a life expectancy ≥ 6 months
- Adequate bone marrow reserve and organ function as demonstrated by complete blood count, and biochemistry in blood and urine at baseline

a. Platelet count of >100 x10e9/L

b. White blood cell (WBC) count > 3,000/mL
c. Neutrophil count > 1,500/mL
d. Hemoglobin ≥ 10 g/dL
e. Serum creatinine < 1.5 x upper limit normal (ULN) or estimated glomerular filtration rate (GFR) > 50 mL/min based upon Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation. Patients with estimated GFR between 50 - 60 mL/min at baseline will require a 99mTc-DTPA GFR test and only patients with non-obstructive pathology will be included in the study.
f. Total bilirubin < 3 x ULN (except if confirmed history of Gilbert's disease)
g. Baseline serum albumin > 30 g/L
h. Aspartate aminotransferase (AST) < 3 times the ULN
- For male patients with partners of childbearing potential, agreement to use barrier contraceptive method (condom) and to continue its use for 6 months from receiving the last dose of IP

Exclusion Criteria:
- Pathological finding consistent with small cell, neuroendocrine carcinoma of the prostate or any other histology different than adenocarcinoma.
- Diffuse bone-marrow involvement (i.e. "superscan" defined as bone scintigraphy in which there is excessive skeletal radioisotope uptake [>20 bone lesions] in relation to soft tissues along with absent or faint activity in the genitourinary tract due to diffuse bone/ bone marrow metastases)
- Prior exposure to radioligand therapy radioisotope therapy (e.g. 89Sr), systemic radiotherapy
or 223Ra-therapy.
- Current severe urinary incontinence, hydronephrosis, severe voiding dysfunction, any level of urinary obstruction requiring indwelling/condom catheters
- Spinal cord compression or brain metastases
- Uncontrolled pain that results in patient's lack of compliance with the imaging procedures
- Uncontrolled cardiovascular history, defined as:
* Congestive heart failure (New York Heart Association [NYHA] II, III, IV)
* Mean resting corrected QT interval (QTc) >450 millisecond (msec), obtained from 3 ECGs recordings, using the screening clinic ECG machine-derived QTc value.
* Any clinically important abnormalities in rhythm, conduction, or morphology of resting ECG (e.g., complete left bundle branch block, third-degree heart block, second-degree heart block, PR interval >250 msec).
* Any factor increasing the risk of QTc prolongation or risk of arrhythmic events such as heart failure, hypokalemia, congenital long QT syndrome, family history of long QT syndrome, or unexplained sudden death under 40 years of age in first-degree relatives, or any concomitant medication known to prolong the QT interval.

- Other known co-existing malignancies except non-melanoma skin cancer or low grade superficial bladder cancer unless definitively treated and proven no evidence of recurrence for 5 years.
- History of deep vein thrombosis and/or pulmonary embolism within 4 weeks of enrollment.
- Known incompatibility to CT or PET scans.
- Any evidence of severe or uncontrolled systemic or psychiatric diseases, including uncontrolled hypertension and active bleeding diatheses, which in the Investigator's opinion makes it undesirable for the patient to participate in the trial or which would jeopardize compliance with the protocol
- Active infection including human immunodeficiency virus (HIV) and untreated hepatitis B, and hepatitis C. Screening for chronic conditions is not required.
- Patients who have received any investigational treatment agent within the last 28 days.
- Known allergies, hypersensitivity, or intolerance to the IP or its excipients
- Known history of myelodysplastic syndrome/leukemia at any time
- Patient is unlikely to comply with study procedures, restrictions and requirements and judged by the Investigator that the patient is not suitable for participation in the study.

Participant Flow Table

Overall Study

	Phase I: Dose Escalation Cohort 1	**Phase I: Dose Escalation Cohort 2**	**Phase I: Dose Escalation Cohort 3A**	**Phase I: Dose Escalation Cohort 3B**	**Phase I: Dose Escalation Cohort 4B**	**Phase I: Dose Escalation Cohort 4C**	**Phase I: Dose Escalation Cohort 5C**	**Phase I: Dose Escalation Cohort 5D**	**Phase I: Dose Escalation Cohort 6E**	**Total**
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)	
Started	3	3	3	3	3	3	3	3	3	27
Completed	0	0	0	0	0	0	0	0	0	0
Not Completed	3	3	3	3	3	3	3	3	3	27
Death	1	1	1	3	3	2	1	1	0	13

Physician Decision	0	0	0	0	0	0	0	2	1	3
Withdrawal by Subject	2	2	1	0	0	0	0	0	0	5
Lost to Follow-up	0	0	0	0	0	0	1	0	0	1
Sponsor Decision	0	0	1	0	0	1	1	0	1	4
Other pre-specified reason defined in the protocol	0	0	0	0	0	0	0	0	1	1

Baseline Characteristics

	Phase I: Dose Escalation Cohort 1	**Phase I: Dose Escalation Cohort 2**	**Phase I: Dose Escalation Cohort 3A**	**Phase I: Dose Escalation Cohort 3B**	**Phase I: Dose Escalation Cohort 4B**	**Phase I: Dose Escalation Cohort 4C**	**Phase I: Dose Escalation Cohort 5C**	**Phase I: Dose Escalation Cohort 5D**	**Phase I: Dose Escalation Cohort 6E**	**Total**
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)	
Number of Participants [units: participants]	3	3	3	3	3	3	3	3	3	27

Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)										
Female	0	0	0	0	0	0	0	0	0	0
Male	3	3	3	3	3	3	3	3	3	27
ECOG Performance Status[1] (units: Participants) Count of Participants (Not Applicable)										
Grade 0	3	3	1	0	2	3	1	2	3	18
Grade 1	0	0	2	3	1	0	2	1	0	9
Number of participants by Total Gleason score (>=6)[2] (units: Participants) Count of Participants (Not Applicable)										
Gleason score = 6	0	0	0	0	1	0	0	0	0	1
Gleason score = 7	1	1	1	0	1	1	0	3	2	10
Gleason score = 8	1	0	0	1	0	1	1	0	1	5
Gleason score = 9	0	2	1	1	1	1	1	0	0	7
Gleason score = 10	0	0	0	1	0	0	1	0	0	2
Gleason score = Missing	1	0	1	0	0	0	0	0	0	2
Age Continuous (units: Years) Mean ± Standard Deviation										
	58.3±12.01	61.0±5.57	74.0±10.44	72.7±6.03	72.0±2.00	65.7±2.31	67.0±6.08	64.7±5.86	64.3±8.14	66.6±7.91

Time since first prostate cancer diagnosis[3] (units: Months) Mean ± Standard Deviation	70.5±52.95	76.7±26.44	176.6±132.16	75.3±54.27	89.4±49.80	40.0±15.47	129.5±78.29	76.1±32.37	120.2±49.29	94.9±65.69
Race (NIH/OMB) (units: Participants) Count of Participants (Not Applicable)										
American Indian or Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	1	0	0	0	0	1
White	2	3	3	3	2	3	3	3	3	25
More than one race	1	0	0	0	0	0	0	0	0	1
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0

[1] The Eastern Cooperative Oncology Group Performance Status (ECOG PS) score classifies participants according to their functional impairment, with scores ranging from 0 (fully active) to 5 (dead). ECOG PS: 0 = Fully active, able to carry on all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
[2] Gleason score can range from 2-10. The higher the Gleason Score, the more likely that the cancer will grow and spread quickly. Scores of 6 (or less) describe cancer cells that look similar to normal cells and suggest that the cancer is likely to grow slowly. A score of 7 suggests an intermediate risk for aggressive cancer. Scores of 8 (or higher) describe cancers that are likely to spread more rapidly, these cancers are often referred to as poorly differentiated or high grade.
[3] Time since first prostate cancer diagnosis is defined as (date of screening – date of first prostate cancer diagnosis + 1) / 30.4375.

Primary Outcome Result(s)

Phase I: Incidence of dose limiting toxicities (DLTs) during first cycle of study treatment.

(Time Frame: Up to 8 weeks after the first 177Lu-PSMA-R2 dose)

	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D	Phase I: Dose Escalation Cohort 6E
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Number of Participants Analyzed [units: participants]	3	3	3	3	3	3	3	3	3
Phase I: Incidence of dose limiting toxicities (DLTs) during first cycle of study treatment. (units: Participants) Count of Participants (Not Applicable)									
	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)

Secondary Outcome Result(s)

Phase I: Number of Participants with Treatment Emergent Adverse Events (TEAEs)

(Time Frame: From randomization till 30 days safety follow-up, assessed up to approximately 4 years)

	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D	Phase I: Dose Escalation Cohort 6E
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Number of Participants Analyzed [units: participants]	3	3	3	3	3	3	3	3	3
Phase I: Number of Participants with Treatment Emergent Adverse Events (TEAEs) (units: Participants) Count of Participants (Not Applicable)									
At least one TEAE	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)
TEAE rel. to 68Ga-PSMA-R2	0 (%)	0 (%)	1 (33.33%)	1 (33.33%)	0 (%)	1 (33.33%)	2 (66.67%)	0 (%)	0 (%)
TEAE rel. to 177Lu-PSMA-R2	2 (66.67%)	2 (66.67%)	2 (66.67%)	3 (100%)	2 (66.67%)	2 (66.67%)	3 (100%)	3 (100%)	3 (100%)
TEAE rel. to the study procedure	0 (%)	3 (100%)	1 (33.33%)	1 (33.33%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (33.33%)
Serious TEAE	1 (33.33%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	2 (66.67%)	0 (%)	0 (%)	0 (%)	0 (%)
Serious TEAE rel. to 68Ga-PSMA-R2	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Serious TEAE rel. to 177Lu-PSMA-R2	0 (%)	0 (%)	1 (33.33%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)

Serious TEAE rel. to the study procedure	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
TEAE leading to study discontinuation	1 (33.33%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Mild TEAE	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)
Moderate TEAE	2 (66.67%)	3 (100%)	2 (66.67%)	1 (33.33%)	3 (100%)	1 (33.33%)	2 (66.67%)	1 (33.33%)	1 (33.33%)
Severe TEAE	0 (%)	1 (33.33%)	1 (33.33%)	2 (66.67%)	2 (66.67%)	0 (%)	0 (%)	0 (%)	0 (%)
Life threatening TEAE	1 (33.33%)	1 (33.33%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
TEAE leading to death	1 (33.33%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
At least one DLT	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)

Phase I: Number of participants with an Objective Response Rate (ORR)

(Time Frame: From date of randomization until date of progression or date of death from any cause, whichever comes first, assessed up to approximately 4 years)

	Phase I: Dose Escalation Cohort 1	**Phase I: Dose Escalation Cohort 2**	**Phase I: Dose Escalation Cohort 3A**	**Phase I: Dose Escalation Cohort 3B**	**Phase I: Dose Escalation Cohort 4B**	**Phase I: Dose Escalation Cohort 4C**	**Phase I: Dose Escalation Cohort 5C**	**Phase I: Dose Escalation Cohort 5D**	**Phase I: Dose Escalation Cohort 6E**
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Number of Participants Analyzed [units: participants]	3	3	3	3	3	3	3	3	3

Phase I: Number of participants with an Objective Response Rate (ORR)
(units: Participants)
Count of Participants (Not Applicable)

ORR in overall population	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (33.33%)
ORR in patients with visceral disease at Baseline	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)

Phase I: Duration of Response (DoR)

(Time Frame: From first documented evidence of CR or PR (the response prior to confirmation) until time of documented disease progression or death due to any cause, whichever comes first, assessed up to approximately 4 years)

	Phase I: Dose Escalation Cohort 1	**Phase I: Dose Escalation Cohort 2**	**Phase I: Dose Escalation Cohort 3A**	**Phase I: Dose Escalation Cohort 3B**	**Phase I: Dose Escalation Cohort 4B**	**Phase I: Dose Escalation Cohort 4C**	**Phase I: Dose Escalation Cohort 5C**	**Phase I: Dose Escalation Cohort 5D**	**Phase I: Dose Escalation Cohort 6E**
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0	0	0	1
Phase I: Duration of Response (DoR) (units: Months) Median (95% Confidence Interval)									2.63 (0 to NA)[1]

[1] Only 1 participant analyzed

Phase I: Number of participants with a Prostate-Specific Antigen (PSA) response rate 30

(Time Frame: Week 13 (12 weeks after the first 177Lu-PSMA-R2 injection))

	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D	Phase I: Dose Escalation Cohort 6E
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Number of Participants Analyzed [units: participants]	3	3	3	3	3	3	3	3	3
Phase I: Number of participants with a Prostate-Specific Antigen (PSA) response rate 30 (units: Participants) Count of Participants (Not Applicable)									
	0 (%)	0 (%)	0 (%)	1 (33.33%)	0 (%)	0 (%)	0 (%)	0 (%)	2 (66.67%)

Phase I: Number of participants with a Prostate-Specific Antigen (PSA) response rate 50

(Time Frame: Week 13 (12 weeks after the first 177Lu-PSMA-R2 injection))

	Phase I: Dose	Phase I: Dose	Phase I: Dose	Phase I: Dose	Phase I: Dose	Phase I: Dose	Phase I: Dose	Phase I: Dose	Phase I: Dose

	Escalation Cohort 1	Escalation Cohort 2	Escalation Cohort 3A	Escalation Cohort 3B	Escalation Cohort 4B	Escalation Cohort 4C	Escalation Cohort 5C	Escalation Cohort 5D	Escalation Cohort 6E
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Number of Participants Analyzed [units: participants]	3	3	3	3	3	3	3	3	3
Phase I: Number of participants with a Prostate-Specific Antigen (PSA) response rate 50 (units: Participants) Count of Participants (Not Applicable)									
	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (33.33%)

Phase I: Maximum plasma concentration (Cmax) of 177Lu-PSMA-R2

(Time Frame: Day 1 (before the start of infusion, at the mid-point, and just before the end of infusion, then at post infusion at approximately 5, 15, 30 minutes, 1, 2, 4, 6, 8, 24, 40 (+/- 4 hours), 48 hours), Day 4 (+2 days) and Day 8 post end of infusion)

	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D	Phase I: Dose Escalation Cohort 6E
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3	Phase I: Dose Escalation Cohort 2 (3	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B (3	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C (3	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D (2	Phase I: Dose Escalation Cohort 6E (3

	cycles at 100 mCi)	cycles at 200 mCi)	(4 cycles at 200 mCi)	cycles at 300 mCi)	(4 cycles at 300 mCi)	cycles at 400 mCi)	(4 cycles at 400 mCi)	cycles at 500 mCi)	cycles at 500 mCi)
Number of Participants Analyzed [units: participants]	3	3	0	3	0	3	0	3	3
Phase I: Maximum plasma concentration (Cmax) of 177Lu-PSMA-R2 (units: ng/mL) Geometric Mean (Geometric Coefficient of Variation)									
	7.16 (46.9%)	12.8 (33.8%)		21.7 (31.2%)		21.9 (25.2%)		32.8 (8.17%)	43.7 (41.2%)

Phase I: Area under the serum concentration-time curve from time zero to the time of last quantifiable concentration (AUCtlast) of 177Lu-PSMA-R2

(Time Frame: Day 1 (before the start of infusion, at the mid-point, and just before the end of infusion, then at post infusion at approximately 5, 15, 30 minutes, 1, 2, 4, 6, 8, 24, 40 (+/- 4 hours), 48 hours), Day 4 (+2 days) and Day 8 post end of infusion)

	Phase I: Dose Escalation Cohort 1	**Phase I: Dose Escalation Cohort 2**	**Phase I: Dose Escalation Cohort 3A**	**Phase I: Dose Escalation Cohort 3B**	**Phase I: Dose Escalation Cohort 4B**	**Phase I: Dose Escalation Cohort 4C**	**Phase I: Dose Escalation Cohort 5C**	**Phase I: Dose Escalation Cohort 5D**	**Phase I: Dose Escalation Cohort 6E**
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Number of Participants	3	3	0	3	0	3	0	3	3

Analyzed [units: participants]						
Phase I: Area under the serum concentration-time curve from time zero to the time of last quantifiable concentration (AUCtlast) of 177Lu-PSMA-R2 (units: hr*ng/mL) Geometric Mean (Geometric Coefficient of Variation)						
	21.3 (53.8%)	36.3 (35.2%)	85.9 (4.81%)	82.7 (39.5%)	126 (32.7%)	207 (17.6%)

Phase I: Area under the serum concentration-time curve from time zero to (AUCinf) of 177Lu-PSMA-R2

(Time Frame: Day 1 (before the start of infusion, at the mid-point, and just before the end of infusion, then at post infusion at approximately 5, 15, 30 minutes, 1, 2, 4, 6, 8, 24, 40 (+/- 4 hours), 48 hours), Day 4 (+2 days) and Day 8 post end of infusion)

	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D	Phase I: Dose Escalation Cohort 6E
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Number of Participants Analyzed [units: participants]	3	3	0	3	0	3	0	3	3

Phase I: Area under the serum concentration-time curve from time zero to (AUCinf) of 177Lu-PSMA-R2 (units: hr*ng/mL) Geometric Mean (Geometric Coefficient of Variation)						
	21.3 (53.8%)	37.9 (37.5%)	86.6 (4.59%)	83.1 (39.8%)	127 (32.7%)	207 (17.5%)

Phase I: Residence times of 177Lu-PSMA-R2 in normal organs

(Time Frame: Days 1 through 8 post-treatment)

	Phase I: Dose Escalation Cohort 1 (Cycle 1)	**Phase I: Dose Escalation Cohorts 2 & 3A (Cycle 1)**	**Phase I: Dose Escalation Cohorts 3B & 4B (Cycle 1)**	**Phase I: Dose Escalation Cohorts 4C & 5C (Cycle 1)**	**Phase I: Dose Escalation Cohorts 5D & 6E (Cycle 1)**
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (Cycle 1 at 100 mCi)	Phase I: Dose Escalation Cohorts 2 & 3A (Cycle 1 at 200 mCi)	Phase I: Dose Escalation Cohorts 3B & 4B (Cycle 1 at 300 mCi)	Phase I: Dose Escalation Cohorts 4C & 5C (Cycle 1 at 400 mCi)	Phase I: Dose Escalation Cohorts 5D & 6E (Cycle 1 at 500 mCi)
Number of Participants Analyzed [units: participants]	3	6	6	6	6
Phase I: Residence times of 177Lu-PSMA-R2 in normal organs (units: MBq-hr/MBq) Median (Full Range)					
Bladder	0.26 (0.14 to 0.59)		1.5 (0.63 to 2.4)	0.84 (0.32 to 0.89)	1.2 (0.46 to 2.9)
Body	5.6 (4.0 to 6.2)	51 (32 to 63)	8.7 (6.4 to 16)	7.1 (7.1 to 8.9)	8.4 (6.3 to 11)
Bone Marrow	0.12 (0.12 to 0.27)	0.12 (0.10 to 0.14)	0.30 (0.26 to 0.34)	0.17 (0.14 to 0.30)	0.22 (0.17 to 0.33)

Brain	0.026 (0.0082 to 0.033)	0.044 (0.020 to 0.053)	0.033 (0.029 to 0.053)	0.040 (0.027 to 0.041)	0.044 (0.022 to 0.058)
Heart, Ventricular Wall	0.17 (0.078 to 0.43)	0.15 (0.11 to 0.21)	0.28 (0.24 to 0.56)	0.16 (0.095 to 0.32)	0.28 (0.11 to 0.42)
Intestine	0.51 (0.45 to 0.58)	0.83 (0.44 to 0.90)	2.4 (1.3 to 6.4)	0.98 (0.89 to 1.8)	1.4 (0.61 to 2.6)
Kidney	0.92 (0.74 to 0.97)	0.48 (0.40 to 0.71)	1.1 (0.90 to 1.7)	0.90 (0.67 to 1.6)	0.97 (0.66 to 1.9)
Lacrimal Gland	0.0016 (0.0013 to 0.0036)	0.0019 (0.0010 to 0.0075)	0.0030 (0.0022 to 0.0052)	0.0025 (0.0021 to 0.0029)	0.0030 (0.0025 to 0.0058)
Liver	0.42 (0.27 to 0.49)	0.22 (0.095 to 0.31)	0.48 (0.43 to 0.92)	0.44 (0.32 to 0.72)	0.68 (0.31 to 1.1)
Lung	0.12 (0.12 to 0.13)	0.20 (0.11 to 0.22)	0.29 (0.11 to 0.64)	0.19 (0.13 to 0.61)	0.21 (0.10 to 0.50)
Salivary Gland	0.024 (0.016 to 0.036)	0.050 (0.049 to 0.095)	0.039 (0.035 to 0.074)	0.038 (0.030 to 0.051)	0.048 (0.024 to 0.080)
Spleen	0.0055 (0.0050 to 0.048)	0.060 (0.031 to 0.13)	0.030 (0.023 to 0.092)	0.11 (0.039 to 0.26)	0.15 (0.020 to 0.31)
Thyroid Gland	0.015 (0.0047 to 0.027)	0.0091 (0.0085 to 0.019)	0.016 (0.014 to 0.034)	0.022 (0.0084 to 0.054)	0.020 (0.0065 to 0.076)

Phase I: Absorbed doses of 177Lu-PSMA-R2 by critical organs

(Time Frame: Days 1 through 8 post-treatment)

	Phase I: Dose Escalation Cohort 1 (Cycle 1)	Phase I: Dose Escalation Cohorts 2 & 3A (Cycle 1)	Phase I: Dose Escalation Cohorts 3B & 4B (Cycle 1)	Phase I: Dose Escalation Cohorts 4C & 5C (Cycle 1)	Phase I: Dose Escalation Cohorts 5D & 6E (Cycle 1)
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (Cycle 1 at 100 mCi)	Phase I: Dose Escalation Cohorts 2 & 3A (Cycle 1 at 200 mCi)	Phase I: Dose Escalation Cohorts 3B & 4B (Cycle 1 at 300 mCi)	Phase I: Dose Escalation Cohorts 4C & 5C (Cycle 1 at 400 mCi)	Phase I: Dose Escalation Cohorts 5D & 6E (Cycle 1 at 500 mCi)
Number of Participants Analyzed [units: participants]	3	6	6	6	6

Phase I: Absorbed doses of 177Lu-PSMA-R2 by critical organs
(units: Gy/GBq)
Median (Full Range)

Adrenal Gland	0.0054 (0.0045 to 0.0063)	0.065 (0.041 to 0.080)	0.0093 (0.0066 to 0.014)	0.0088 (0.0062 to 0.010)	0.0077 (0.0067 to 0.013)
Bladder Wall	0.41 (0.41 to 0.46)	0.36 (0.35 to 0.41)	0.27 (0.24 to 0.37)	0.40 (0.32 to 0.41)	0.36 (0.30 to 0.41)
Bone Marrow	0.0065 (0.0064 to 0.013)	0.056 (0.035 to 0.065)	0.014 (0.014 to 0.019)	0.0091 (0.0086 to 0.016)	0.013 (0.0088 to 0.015)
Brain	0.0016 (0.00056 to 0.0021)	0.0048 (0.0026 to 0.0059)	0.0021 (0.0020 to 0.0034)	0.0026 (0.0017 to 0.0027)	0.0028 (0.0015 to 0.0037)
Colon, Left	0.15 (0.14 to 0.23)	0.42 (0.21 to 0.48)	0.54 (0.52 to 0.77)	0.44 (0.21 to 0.47)	0.31 (0.18 to 0.47)
Colon, Right	0.079 (0.075 to 0.12)	0.25 (0.13 to 0.29)	0.29 (0.28 to 0.41)	0.24 (0.11 to 0.25)	0.17 (0.099 to 0.25)
Esophagus	0.0018 (0.0015 to 0.0023)	0.062 (0.039 to 0.077)	0.0043 (0.0024 to 0.0066)	0.0034 (0.0026 to 0.0051)	0.0042 (0.0017 to 0.0054)
Eye	0.0011 (0.00096 to 0.0017)	0.061 (0.039 to 0.075)	0.0034 (0.0015 to 0.0047)	0.0025 (0.0020 to 0.0039)	0.0029 (0.0011 to 0.0048)
Gallbladder	0.0028 (0.0023 to 0.0034)	0.064 (0.040 to 0.079)	0.0063 (0.0045 to 0.0096)	0.0054 (0.0043 to 0.0062)	0.0057 (0.0029 to 0.0075)
Heart, Ventricular Wall	0.044 (0.021 to 0.11)	0.045 (0.032 to 0.062)	0.074 (0.065 to 0.15)	0.043 (0.026 to 0.085)	0.073 (0.030 to 0.11)
Kidney	0.26 (0.21 to 0.27)	0.14 (0.12 to 0.21)	0.33 (0.19 to 0.50)	0.25 (0.15 to 0.45)	0.24 (0.11 to 0.49)
Lacrimal Gland	0.045 (0.035 to 0.10)	0.053 (0.028 to 0.21)	0.082 (0.061 to 0.14)	0.070 (0.058 to 0.081)	0.083 (0.070 to 0.16)
Liver	0.022 (0.014 to 0.025)	0.015 (0.0072 to 0.020)	0.025 (0.023 to 0.047)	0.023 (0.017 to 0.037)	0.035 (0.016 to 0.056)

Lung	0.0093 (0.0091 to 0.0093)	0.020 (0.011 to 0.020)	0.021 (0.0086 to 0.047)	0.014 (0.0098 to 0.045)	0.016 (0.0079 to 0.037)
Osteogenic Cells	0.0044 (0.0043 to 0.0081)	0.075 (0.047 to 0.090)	0.0099 (0.0088 to 0.014)	0.0068 (0.0065 to 0.011)	0.0095 (0.0060 to 0.010)
Pancreas	0.0026 (0.0021 to 0.0030)	0.065 (0.041 to 0.080)	0.0062 (0.0043 to 0.0092)	0.0053 (0.0043 to 0.0057)	0.0054 (0.0028 to 0.0069)
Prostate Gland	0.0046 (0.0045 to 0.0050)	0.067 (0.043 to 0.082)	0.0070 (0.0059 to 0.0095)	0.0065 (0.0063 to 0.0073)	0.0068 (0.0048 to 0.0081)
Rectum	0.14 (0.13 to 0.22)	0.40 (0.20 to 0.46)	0.51 (0.50 to 0.74)	0.42 (0.20 to 0.45)	0.30 (0.17 to 0.45)
Salivary Gland	0.024 (0.016 to 0.037)	0.055 (0.052 to 0.10)	0.040 (0.036 to 0.074)	0.039 (0.031 to 0.052)	0.048 (0.025 to 0.080)
Small Intestine	0.015 (0.013 to 0.021)	0.094 (0.055 to 0.11)	0.047 (0.047 to 0.070)	0.040 (0.022 to 0.043)	0.028 (0.020 to 0.043)
Spleen	0.0042 (0.0042 to 0.029)	0.040 (0.022 to 0.083)	0.020 (0.015 to 0.056)	0.066 (0.025 to 0.15)	0.087 (0.013 to 0.18)
Stomach	0.0019 (0.0017 to 0.0025)	0.064 (0.040 to 0.078)	0.0048 (0.0028 to 0.0071)	0.0039 (0.0032 to 0.0052)	0.0045 (0.0020 to 0.0058)
Testis	0.0018 (0.0016 to 0.0023)	0.063 (0.040 to 0.077)	0.0038 (0.0021 to 0.0053)	0.0031 (0.0026 to 0.0044)	0.0034 (0.0017 to 0.0054)
Thymus Gland	0.0018 (0.0014 to 0.0021)	0.063 (0.040 to 0.077)	0.0041 (0.0021 to 0.0063)	0.0031 (0.0023 to 0.0049)	0.0039 (0.0015 to 0.0052)
Thyroid Gland	0.065 (0.020 to 0.11)	0.044 (0.039 to 0.088)	0.067 (0.060 to 0.15)	0.092 (0.036 to 0.23)	0.085 (0.028 to 0.32)
Whole-body	0.0077 (0.0066 to 0.0079)	0.069 (0.044 to 0.084)	0.012 (0.010 to 0.017)	0.011 (0.0099 to 0.012)	0.011 (0.0082 to 0.014)

Phase I: Mean change from Baseline in Patient Reported Outcomes (PRO) of Mouth Dryness using Xerostomia Questionnaire

(Time Frame: Baseline, Cycle 1 Day 1, Cycle 3 Day 85, Follow Up 1, Follow Up 2, Follow Up 3, Follow Up 4)

Phase I: Dose	Phase I: Dose	Phase I: Dose	Phase I: Dose	Phase I: Dose	Phase I: Dose	Phase I: Dose	Phase I: Dose	Phase I: Dose

	Escalation Cohort 1	Escalation Cohort 2	Escalation Cohort 3A	Escalation Cohort 3B	Escalation Cohort 4B	Escalation Cohort 4C	Escalation Cohort 5C	Escalation Cohort 5D	Escalation Cohort 6E
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Number of Participants Analyzed [units: participants]	3	3	3	3	3	3	3	3	3
Phase I: Mean change from Baseline in Patient Reported Outcomes (PRO) of Mouth Dryness using Xerostomia Questionnaire (units: Score) Mean ± Standard Deviation									
Cycle 1 Day 1 Change from Baseline									
Cycle 3 Day 85 Change from Baseline		-4.0 ± NA[1234567891011]	4.7 ± 8.96	-2.5 ± 9.19		-8.0 ± NA[1234567891011]	14.0 ± NA[1234567891011]		-0.7 ± 3.06
Follow Up 1 Change from Baseline			-1.0 ± NA[1234567891011]	0.5 ± 13.44	6.0 ± NA[1234567891011]	-8.0 ± NA[1234567891011]	2.5 ± 4.95	-2.3 ± 4.04	2.3 ± 14.64
Follow Up 2 Change from Baseline				-4.5 ± 6.36	0.0 ± NA[1234567891011]	18.0 ± NA[1234567891011]	-2.0 ± NA[1234567891011]		3.3 ± 8.50
Follow Up 3 Change from Baseline				21.0 ± NA[1234567891011]		-7.0 ± 4.24			4.7 ± 7.23

Follow Up 4 Change from Baseline	-1.0 ± NA[1234567891011]	16.0	18.5 ± 26.16

[1] Only 1 participant analyzed
[2] Only 1 participant analyzed
[3] Only 1 participant analyzed
[4] Only 1 participant analyzed
[5] Only 1 participant analyzed
[6] Only 1 participant analyzed
[7] Only 1 participant analyzed
[8] Only 1 participant analyzed
[9] Only 1 participant analyzed
[10] Only 1 participant analyzed
[11] Only 1 participant analyzed

Phase I: Mean change from Baseline in Patient Reported Outcomes (PRO) of Eye Dryness using Xerophthalmia Questionnaire

(Time Frame: Baseline, Cycle 1 Day 1, Cycle 3 Day 85, Follow Up 1, Follow Up 2, Follow Up 3, Follow Up 4)

	Phase I: Dose Escalation Cohort 1	Phase I: Dose Escalation Cohort 2	Phase I: Dose Escalation Cohort 3A	Phase I: Dose Escalation Cohort 3B	Phase I: Dose Escalation Cohort 4B	Phase I: Dose Escalation Cohort 4C	Phase I: Dose Escalation Cohort 5C	Phase I: Dose Escalation Cohort 5D	Phase I: Dose Escalation Cohort 6E
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Number of Participants Analyzed [units: participants]	3	3	3	3	3	3	3	3	3

Phase I: Mean change from Baseline in Patient Reported Outcomes (PRO) of Eye Dryness using Xerophthalmia Questionnaire
(units: Score)
Mean ± Standard Deviation

Cycle 1 Day 1 Change from Baseline								
Cycle 3 Day 85 Change from Baseline	-2.0 ± NA[12345678910111 2]	0.0 ± 0.00	-1.0 ± 1.41		1.0 ± NA[1234567891011 12]	1.0 ± NA[1234567891011 12]		0.0 ± 0.00
Follow Up 1 Change from Baseline		-2.0 ± NA[1234567891011 12]	-0.5 ± 2.12	0.0 ± NA[1234567891011 12]	0.0 ± NA[1234567891011 12]	1.5 ± 0.71	-0.3 ± 0.58	-0.3 ± 0.58
Follow Up 2 Change from Baseline			-0.5 ± 2.12	0.0 ± NA[1234567891011 12]	0.0 ± NA[1234567891011 12]	0.0 ± NA[1234567891011 12]		0.0 ± 0.00
Follow Up 3 Change from Baseline			-2.0 ± NA[1234567891011 12]		0.0 ± 0.00			0.0 ± 0.00
Follow Up 4 Change from Baseline		-2.0 ± NA[1234567891011 12]				2.0 ± NA[1234567891011 12]		0.0 ± 0.00

[1] Only 1 participant analyzed
[2] Only 1 participant analyzed
[3] Only 1 participant analyzed
[4] Only 1 participant analyzed
[5] Only 1 participant analyzed
[6] Only 1 participant analyzed
[7] Only 1 participant analyzed
[8] Only 1 participant analyzed
[9] Only 1 participant analyzed
[10] Only 1 participant analyzed
[11] Only 1 participant analyzed

[12] Only 1 participant analyzed

Safety Results

All-Cause Mortality

	Phase I: Dose Escalation Cohort 1 N = 3	Phase I: Dose Escalation Cohort 2 N = 3	Phase I: Dose Escalation Cohort 3A N = 3	Phase I: Dose Escalation Cohort 3B N = 3	Phase I: Dose Escalation Cohort 4B N = 3	Phase I: Dose Escalation Cohort 4C N = 3	Phase I: Dose Escalation Cohort 5C N = 3	Phase I: Dose Escalation Cohort 5D N = 3	Phase I: Dose Escalation Cohort 6E N = 3
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Total participants affected	1 (33.33%)	1 (33.33%)	1 (33.33%)	3 (100.00%)	3 (100.00%)	2 (66.67%)	1 (33.33%)	1 (33.33%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	From informed consent signature through study completion reached at early termination date on 02-Jun-2022, assessed up to approximately 4 years.
Additional Description	Any sign or symptom that occurs after written informed consent provided.
Source Vocabulary for Table Default	MedDRA 25.0
Assessment Type for Table Default	Systematic Assessment

	Phase I: Dose Escalation Cohort 1 N = 3	Phase I: Dose Escalation Cohort 2 N = 3	Phase I: Dose Escalation Cohort 3A N = 3	Phase I: Dose Escalation Cohort 3B N = 3	Phase I: Dose Escalation Cohort 4B N = 3	Phase I: Dose Escalation Cohort 4C N = 3	Phase I: Dose Escalation Cohort 5C N = 3	Phase I: Dose Escalation Cohort 5D N = 3	Phase I: Dose Escalation Cohort 6E N = 3
Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Total participants affected	1 (33.33%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	2 (66.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders									
Atrial flutter	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders									
Vomiting	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations									
Urinary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations									
Platelet count decreased	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders									
Back pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Osteoarthritis	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Neoplasms benign, malignant and unspecified (incl cysts and polyps)									
Squamous cell carcinoma of lung	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nervous system disorders									
Hypoaesthesia	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders									
Acute respiratory failure	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	From informed consent signature through study completion reached at early termination date on 02-Jun-2022, assessed up to approximately 4 years.
Additional Description	Any sign or symptom that occurs after written informed consent provided.
Source Vocabulary for Table Default	MedDRA 25.0
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Phase I: Dose Escalation Cohort 1 N = 3	**Phase I: Dose Escalation Cohort 2 N = 3**	**Phase I: Dose Escalation Cohort 3A N = 3**	**Phase I: Dose Escalation Cohort 3B N = 3**	**Phase I: Dose Escalation Cohort 4B N = 3**	**Phase I: Dose Escalation Cohort 4C N = 3**	**Phase I: Dose Escalation Cohort 5C N = 3**	**Phase I: Dose Escalation Cohort 5D N = 3**	**Phase I: Dose Escalation Cohort 6E N = 3**

Arm/Group Description	Phase I: Dose Escalation Cohort 1 (3 cycles at 100 mCi)	Phase I: Dose Escalation Cohort 2 (3 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3A (4 cycles at 200 mCi)	Phase I: Dose Escalation Cohort 3B (3 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4B (4 cycles at 300 mCi)	Phase I: Dose Escalation Cohort 4C (3 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5C (4 cycles at 400 mCi)	Phase I: Dose Escalation Cohort 5D (2 cycles at 500 mCi)	Phase I: Dose Escalation Cohort 6E (3 cycles at 500 mCi)
Total participants affected	3 (100.00%)	3 (100.00%)	3 (100.00%)	3 (100.00%)	3 (100.00%)	3 (100.00%)	3 (100.00%)	3 (100.00%)	3 (100.00%)
Blood and lymphatic system disorders									
Anaemia	2 (66.67%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Blood loss anaemia	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eosinophilia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)
Eye disorders									
Dry eye	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)
Xerophthalmia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders									
Abdominal distension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)
Abdominal pain upper	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Constipation	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	1 (33.33%)
Diarrhoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)
Dry mouth	0 (0.00%)	0 (0.00%)	2 (66.67%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	2 (66.67%)
Dyschezia	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Frequent bowel movements	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrooesophageal reflux disease	1 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Nausea	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	1 (33.33%)
Oral pruritus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
General disorders and administration site conditions									
Asthenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	2 (66.67%)	1 (33.33%)	0 (0.00%)
Fatigue	1 (33.33%)	1 (33.33%)	2 (66.67%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	2 (66.67%)
Infusion site coldness	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injection site pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oedema peripheral	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)
Peripheral swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyrexia	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatobiliary disorders									
Liver injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations									
COVID-19	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Nasopharyngitis	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Staphylococcal infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications									
Lip injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Investigations

Alanine aminotransferase increased	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (33.33%)
Amylase decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aspartate aminotransferase increased	1 (33.33%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (33.33%)
Blood alkaline phosphatase increased	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)
Blood bilirubin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Blood chloride increased	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood creatine increased	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Blood fibrinogen decreased	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood glucose increased	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood lactate dehydrogenase increased	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood urea increased	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Electrocardiogram QT prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eosinophil count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)
Eosinophil count increased	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)

Gamma-glutamyltransferase increased	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (33.33%)
Glomerular filtration rate decreased	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immature granulocyte count increased	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immature granulocyte percentage increased	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lipase decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lymphocyte count decreased	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)
Mean cell haemoglobin increased	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutrophil count decreased	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Platelet count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Protein urine present	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Red blood cells urine positive	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary casts	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Urine analysis abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Weight decreased	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
White blood cell count decreased	0 (0.00%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)

White blood cells urine positive	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders									
Decreased appetite	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (66.67%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)
Hyperglycaemia	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperkalaemia	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders									
Arthralgia	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Back pain	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	2 (66.67%)	0 (0.00%)	1 (33.33%)
Bone pain	1 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Coccydynia	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Groin pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Muscular weakness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)
Musculoskeletal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)
Pain in extremity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (66.67%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)									
Cancer pain	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nervous system disorders									
Dizziness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)
Dysgeusia	0 (0.00%)	2 (66.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)
Headache	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Peripheral sensory neuropathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)
Sciatica	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders									
Depression	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Insomnia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders									
Pollakiuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)
Renal failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary incontinence	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary retention	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Reproductive system and breast disorders									
Prostatic pain	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders									
Dyspnoea	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)
Hypoxia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)
Productive cough	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders									
Dry skin	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ingrowing nail	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Rash	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)

Other Relevant Findings

None

Conclusion:

- No further dose-escalation or expansion of 177Lu-PSMA-R2 into Phase II was supported given observed antitumor activity at the current dose range (100 mCi to 500 mCi with cumulative dose given to patients: 100 mCi to 1500 mCi) and Q6W regimen and potential plateauing of tumor uptake.
- 177Lu-PSMA-R2 has an acceptable safety and tolerability profile with no DLTs and no observed correlation between adverse events and increase in dosage.
- Clinical development of 177Lu-PSMA-R2 was stopped upon completion of the 1-year Safety follow-up for all patients following the Sponsor's strategic assessment of the current and future clinical development plan for 177Lu-PSMA assets in mCRPC.

Date of Clinical Trial Report

06-Feb-2023