ASX ANNOUNCEMENT

5 March 2025

SECuRE trial update: 92% of pre-chemo participants experience greater than 35% drop in PSA levels across all cohorts. Cohort Expansion Phase commences.

HIGHLIGHTS

- Safety Review Committee (SRC) meeting confirms end of the Dose Escalation Phase and commencement of the Cohort Expansion Phase (Phase II stage) of the SECuRE study.
- Based on the efficacy and safety assessment of all cohorts and the focus on earlier stages of treatment, the SRC confirmed expansion at 8 GBq dose level and recommended to increase the number of cycles from up to 4 to up to 6.
- Cohort 4 of the Dose Escalation Phase of the SECuRE trial, assessing multiple administrations of ^{67}Cu-SAR-bisPSMA, is complete. Prostate-specific antigen (PSA) levels are continuing to drop in 3 participants, with reductions ≥80% observed in 3 cases so far. A complete response was achieved in a participant in cohort 4 following 2 doses of 12 GBq of ^{67}Cu-SAR-bisPSMA to date, based on the Response Evaluation Criteria in Solid Tumors v1.1 (RECIST).
- Across all cohorts, 68% of participants have shown reductions in PSA levels, despite the vast majority of the participants (77%) only receiving a single dose of ^{67}Cu-SAR-bisPSMA. The majority of participants that did not respond to the treatment had received chemotherapy in the metastatic castration-resistant prostate cancer (mCRPC) stage, were part of the lowest dose cohort (cohort 1) and had some of the highest PSA levels at study entry.
- ^{67}Cu-SAR-bisPSMA has shown a favourable safety profile across all cohorts. The majority of reported adverse events (AEs) were Grade 1-2, with anaemia and thrombocytopenia being the most prevalent among the haematological events. Most AEs have now resolved. One Dose Limiting Toxicity (DLT) in 1 participant occurred at the highest dose in cohort 4, a transient Grade 4 thrombocytopenia, which improved to Grade 3 after 2 weeks. This participant had bone metastases, a high baseline PSA [1503.12 ng/mL] and had previously been treated with chemotherapy and multiple lines of ^{177}Lu-PSMA-617. A PSA drop of 10.7% was observed following the administration of 1 cycle of ^{67}Cu-SAR-bisPSMA.
- In the group of 13 participants who had not received chemotherapy in the mCRPC setting, all but 1 participant had PSA drops of 35% or more, predominantly with single doses of ^{67}Cu-SAR-bisPSMA. PSA reductions of 80% or more were achieved in almost half of these patients. The majority of participants had received ≥3 lines of therapy prior to enrollment in the study (63.6%). Disease control based on radiographic assessment (RECIST) was achieved in 11 of the 12 (92%) pre-chemotherapy participants who had evaluable disease at baseline.
- The SECuRE trial protocol has been amended to bring ^{67}Cu-SAR-bisPSMA to participants at earlier stages of their disease, in the pre-chemotherapy setting. The amendment incorporates an increase in the number of participants in the Cohort Expansion Phase of the trial from 14 to 24, with a subset of participants planned to receive the combination of ^{67}Cu-SAR-bisPSMA with enzalutamide, an ARPi.

Clarity Pharmaceuticals (ASX: CU6) ("Clarity" or "Company"), a clinical-stage radiopharmaceutical company with a mission to develop next-generation products that improve treatment outcomes for children and adults with cancer, is pleased to announce the completion of the Dose Escalation Phase of the SECuRE trial (NCT04868604)[1]. The SRC recommended the trial progress to the Cohort Expansion Phase (Phase II) at the 8 GBq of ^{67}Cu-SAR-bisPSMA dose level based on the safety and efficacy data demonstrated in every cohort of the study.

Across cohorts 1-4 of the SECuRE study, 68% of participants have shown reductions in PSA levels, despite the vast majority of the participants (77%) only receiving a single dose of ^{67}Cu-SAR-bisPSMA. Most of these participants had a high level of bone metastases at study entry (77.3%), a high median PSA of 112.86 ng/mL (range 0.1-1503.1) and were heavily pre-treated with ≥3 lines of therapy (63.6%). Disease control based on radiographic assessment (complete response + partial response + stable disease) was achieved in 78% of the participants so far (including 2 partial responses and 1 complete response observed to date based on the RECIST assessment). The complete response was seen in a patient dosed twice at 12 GBq. This is the second complete response recorded following ^{67}Cu-SAR-bisPSMA treatment, first being the patient previously reported to have a complete response following 2 doses at 8 GBq (first dose administered through the SECuRE trial, and a second dose administered under the the United States [US] Food and Drug Administration [FDA] Expanded Access Program [EAP]).

Safety profile of ^{67}Cu-SAR-bisPSMA is favourable across cohorts 1-4 with the majority of AEs being Grade 1-2. Anaemia and thrombocytopenia were the most prevalent AEs among the haematological events. No overall trends in other haematological parameters or renal safety were observed in any of the cohorts. Only 1 DLT has been reported in the trial (transient Grade 4 thrombocytopenia, which improved to Grade 3 after 2 weeks) in a patient in the highest dose cohort (cohort 4). This participant had a baseline PSA of 1503.12 ng/mL, had been treated with multiple lines of therapy, including chemotherapy in the mCRPC setting and multiple doses of ^{177}Lu-PSMA-617, and had bone metastases prior to entering the study. The participant's baseline characteristics may have contributed to the lowering of the platelet levels. Despite the unfavourable prognosis of this participant, which included a very high PSA and being heavily pre-treated, 1 cycle of ^{67}Cu-SAR-bisPSMA was still able to reduce his PSA by 10.7% (to 1341.80 ng/mL).

Pre-chemotherapy participants

Thirteen participants across cohorts 1-4 in the SECuRE trial were naïve to taxanes in the mCRPC setting (pre-chemotherapy), including 2 in cohort 1 and 3 in cohort 2. The majority of pre-chemotherapy participants had bone metastases (69.2%) with a median PSA of 42.41 ng/mL (range 0.1-182.4) at study entry. Almost half of these participants received ≥3 lines of therapy prior to trial enrolment (46.2%).

Despite the heavy disease burden and the majority of participants only receiving single doses of ^{67}Cu-SAR-bisPSMA, there was an outstanding result observed in the pre-chemotherapy setting. Out of the total of 13 pre-chemotherapy participants across all cohorts, 12 had PSA drops greater than 35%. PSA reductions greater than 50% were reached in 61.5% (8/13) of participants, and reductions of 80% or more were achieved in 46.2% (6/13) of participants. Disease control based on the RECIST assessment was also observed in 11 out of 12 pre-chemotherapy participants (92%) who had measurable disease at baseline. One participant reached a complete response with 2 doses of 12 GBq in cohort 4, 2 participants had partial responses (cohort 2 and cohort 4), and 8 participants achieved stable disease at this time.

Three participants in the pre-chemotherapy setting of the SECuRE trial had previously been treated with actinium-225 based radioligand therapies (RLT) and, in 1 case, in combination with lutetium-177 based therapy. All 3 participants showed reductions in PSA levels following treatment with ^{67}Cu-SAR-bisPSMA in the trial. Notably, 1 of these 3 participants showed a PSA reduction of 83.4% following the administration of 2 doses of 12 GBq of ^{67}Cu-SAR-bisPSMA in cohort 4, despite being heavily pre-treated. The lines of therapy administered to the patient prior to the SECuRE trial enrollment included androgen deprivation therapy (ADT), 2 androgen receptor pathway inhibitors (ARPIs), autologous cellular immunotherapy, and investigational agents (immunotherapy and ^{177}Lu-PSMA-I&T plus ^{225}Ac-J591).

Safety assessment in pre-chemotherapy participants was comparable to the overall patient population with most AEs being Grade 1 and Grade 2.

Cohort Expansion Phase

Based on the data from cohorts 1-4, the SRC recommends the SECuRE trial progress to Cohort Expansion (Phase II) at an 8 GBq dose level, with an increase in the total number of cycles from up to 4 to up to 6. This recommendation is based on the favourable safety profile of ^{67}Cu-SAR-bisPSMA observed to date.

Cohort 2 (single dose of 8 GBq of ^{67}Cu-SAR-bisPSMA) with 3 participants had the highest rate of PSA response in the trial, and all participants in the cohort had disease control based on the RECIST assessment (including one partial response). The PSA reductions were 81.4%, 95.2% and 99.4%. Only 1 participant in this cohort developed ^{67}Cu-SAR-bisPSMA-related AEs (Grade 1 dry mouth and altered taste, both improved, and Grade 2 fatigue, resolved). No haematological toxicity was reported in the cohort.

The first patient to receive 2 doses of ^{67}Cu-SAR-bisPSMA at 8 GBq (first dose through the SECuRE trial and second dose under the US EAP) achieved a complete anatomical, molecular and biochemical response (assessed by the RECIST criteria, positron emission tomography [PET] and PSA, respectively). He had been heavily pre-treated (chemotherapy in the neoadjuvant setting, ADT, 2 ARPIs and an investigational agent) prior to entering the SECuRE study. The patient's recent follow up showed that he remains with undetectable PSA for almost 16 months, having received his first dose of ^{67}Cu-SAR-bisPSMA over 20 months ago (June 2023). A recent PSMA PET showed no signs of recurrent or metastatic disease. Most AEs related to ^{67}Cu-SAR-bisPSMA were mild or moderate, with the majority having either improved or resolved over time.

Based on these safety and efficacy data, where exceptional efficacy signals were observed at lower radiation doses, 8 GBq was chosen as an optimal dose for the Cohort Expansion Phase.

The SECuRE trial protocol has been amended to include evaluation of mCRPC participants who have not received chemotherapy in the metastatic (pre-chemotherapy) setting. This amendment is aligned with Clarity's strategy of bringing ^{67}Cu-SAR-bisPSMA to participants with earlier stages of the disease and is based on the promising safety and efficacy data, especially in pre-chemotherapy participants of the SECuRE trial.

The protocol amendment also incorporates an increase in the number of participants in the Cohort Expansion Phase of the trial from 14 to 24, in which a subset of participants will receive the combination of ^{67}Cu-SAR-bisPSMA with enzalutamide, an ARPI. These changes are aimed at optimising the development of all of Clarity's products in prostate cancer, following ongoing discussions with and advice from many important global medical experts in the field of prostate cancer, including the Company's Clinical Advisory Board members, Prof Louise Emmett and Prof Oliver Sartor, as well as the SRC.

Clarity's Executive Chairperson, Dr Alan Taylor, commented, "The SECuRE trial continues to generate extraordinary results, and we thank our team, Principal Investigators, members of the SRC, and especially the participants who have contributed to the study. Seeing the safety profile and already observing impressive signs of efficacy (despite the majority of participants only receiving a single cycle of ^{67}Cu-SAR-bisPSMA and the primary focus of the Dose Escalation Phase being safety assessments), we are thrilled to progress to Phase II, the Cohort Expansion Phase, of our theranostic SECuRE trial.

"Dose escalation trial design has not been routinely used in other RLT studies. By pioneering this approach with the SECuRE trial, Clarity was looking to systematically evaluate the safety of ^{67}Cu-SAR-bisPSMA in the context of its therapeutic effect. By gradually increasing the dose from one cohort to the next, we have minimised the risk of AEs and established a favourable safety profile for patients, while also demonstrating that ^{67}Cu-SAR-bisPSMA is effective.

"We are looking forward to executing our strategy of bringing ^{67}Cu-SAR-bisPSMA to earlier lines of prostate cancer therapy with the recent protocol amendment, given the exciting data in pre-chemotherapy participants. We are also increasing the number of participants in the Cohort Expansion Phase. This decision is partly motivated by the

increased demand from oncologists to include their participants into the trial, but it is also led by our decision to explore potential benefits of using a combination of ^{67}Cu-SAR-bisPSMA with enzalutamide, following consultation with world-leading prostate cancer oncologists and nuclear medicine physicians.

"With our focus on treating earlier stage disease (pre-chemotherapy in the mCRPC setting), it is an incredible outcome to have 12 out of 13 pre-chemotherapy participants in the trial experiencing greater than 35% reductions in PSA and almost half of the 13 experiencing drops of 80% or greater. PSA reductions were seen across all cohorts, including the lowest 4 GBq cohort where all pre-chemotherapy participants exhibited greater than 50% drops in PSA from a single dose. Remarkably, one of those participants has had 4 additional doses under EAP and achieved disease control for over 2 years since first treatment. The results from 3 pre-chemotherapy participants who received 8 GBq of ^{67}Cu-SAR-bisPSMA have been outstanding with a favourable safety profile and excellent efficacy, where PSA reductions were greater than 80% for all participants and above 95% for 2 out of the 3 participants, with all of them achieving radiographic disease control and 1 showing a complete response to date.

"The very compelling safety and efficacy data for SAR-bisPSMA that we continue generating stems from Clarity's strong adherence to the highest level of scientific and clinical research. At the heart of this rigorous approach is the dimer "bis" molecule developed at the benchtop of Australian science and translated into the clinic. When optimising the PSMA molecule, the goal was to create an ideal candidate for both therapy and diagnosis of prostate cancer. We wanted to overcome the shortfalls of the current generation of PSMA-targeting products, increasing not only the amount of product in the lesions, but also how long the product is retained in the lesions over time. We are now seeing these results in the clinic with ^{67}Cu-SAR-bisPSMA in the SECuRE trial and with ^{64}Cu-SAR-bisPSMA in our diagnostic trials.

"The recent receipt of 3 Fast Track Designations from the US FDA for our optimised SAR-bisPSMA molecule, one of which was based off the data presented here, is testament to the high quality of this data, but also reflects a critical need for novel solutions in prostate cancer management. With an estimated combined market value of approximately US$10-15 billion by 2030 for PSMA-targeted products, we are hoping to address the evident high unmet need in this segment, from first diagnosis to the treatment of metastatic disease, and improve treatment outcomes for men with prostate cancer around the world.

"We look forward to swiftly recruiting into the next phase of the SECuRE trial, moving towards a Phase III pivotal trial. We are very excited about what the future holds for this promising product and are working tirelessly to bring it to people who need it most in a timely manner, whilst adhering to the highest standards of clinical research."

About the SECuRE trial

The SECuRE trial (NCT04868604)[1] is a Phase I/IIa theranostic trial for identification and treatment of participants with PSMA-expressing mCRPC using ^{64}Cu/^{67}Cu-SAR-bisPSMA. ^{64}Cu-SAR-bisPSMA is used to visualise PSMA-expressing lesions and select candidates for subsequent ^{67}Cu-SAR-bisPSMA therapy. The trial is a multi-centre, single arm, dose escalation study with a cohort expansion involving approximately 54 participants in the US and Australia. The overall aim of the trial is to determine the safety and efficacy of ^{67}Cu-SAR-bisPSMA for the treatment of prostate cancer.

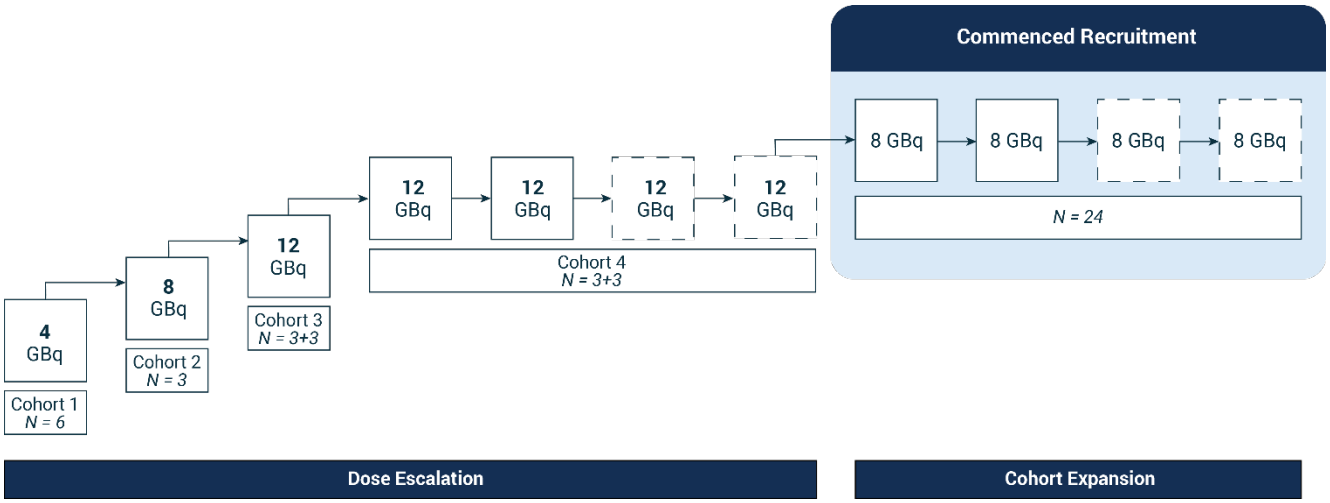
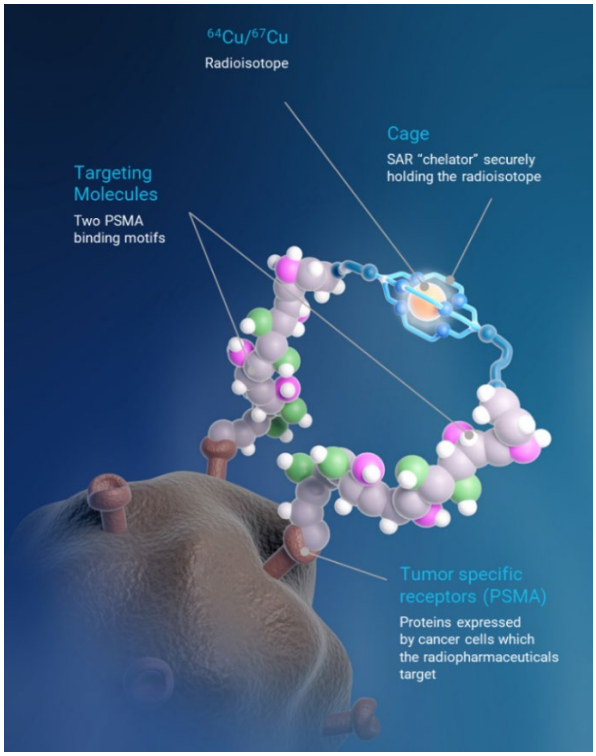


Figure 1. SECuRE Study Design.

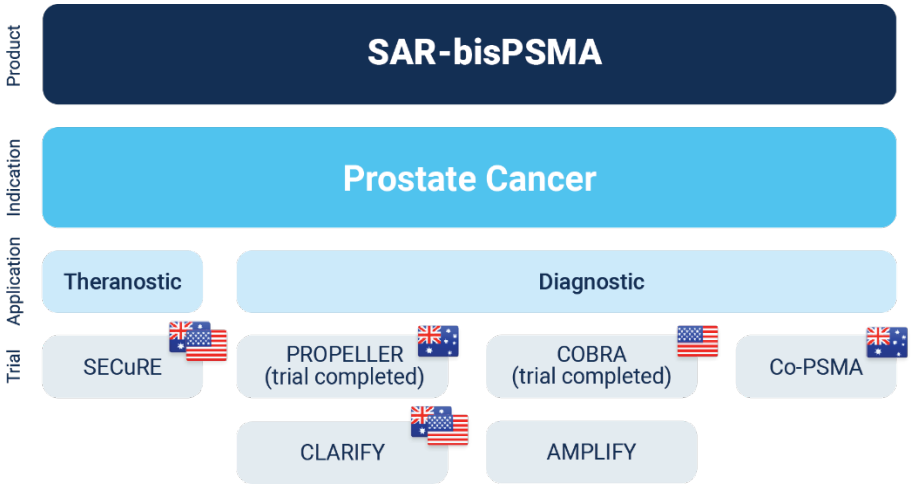
About SAR-bisPSMA

SAR-bisPSMA derives its name from the word "bis", which reflects a novel approach of connecting two PSMA-targeting agents to Clarity's proprietary sarcophagine (SAR) technology that securely holds copper isotopes inside a cage-like structure, called a chelator. Unlike other commercially available chelators, the SAR technology prevents copper leakage into the body. SAR-bisPSMA is a Targeted Copper Theranostic (TCT) that can be used with isotopes of copper-64 (Cu-64 or ^{64}Cu) for imaging and copper-67 (Cu-67 or ^{67}Cu) for therapy.



^{67}Cu-SAR-bisPSMA and ^{64}Cu-SAR-bisPSMA are unregistered products. The safety and efficacy of ^{67}Cu-SAR-bisPSMA and ^{64}Cu-SAR-bisPSMA have not been assessed by health authorities such as the US FDA or the Therapeutic Goods Administration (TGA). There is no guarantee that these products will become commercially available.

Overview of Clarity's SAR-bisPSMA clinical program



About Prostate Cancer

Prostate cancer is the second most common cancer diagnosed in men globally and the fifth leading cause of cancer death in men worldwide[2]. Prostate cancer is the second-leading causes of cancer death in American men. The American Cancer Institute estimates in 2025 there will be about 313,780 new cases of prostate cancer in the US and around 35,770 deaths from the disease[3].

About Clarity Pharmaceuticals

Clarity is a clinical stage radiopharmaceutical company focused on the treatment of serious diseases. The Company is a leader in innovative radiopharmaceuticals, developing Targeted Copper Theranostics based on its SAR Technology Platform for the treatment of cancers in children and adults.

www.claritypharmaceuticals.com

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References

1. ClinicalTrials.gov Identifier: NCT04868604, https://clinicaltrials.gov/ct2/show/NCT04868604
2. Global Cancer Statistics 2022: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries, https://acsjournals.onlinelibrary.wiley.com/doi/10.3322/caac.21834
3. American Cancer Society: Key Statistics for Prostate Cancer, https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html

This announcement has been authorised for release by the Executive Chairperson.