ASX ANNOUNCEMENT

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First FDA Breakthrough Therapy designation in PSMA PET imaging granted to Cu-64 SAR-bisPSMA in biochemical recurrence of prostate cancer

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 patients with cancer, is pleased to announce that the United States (US) Food and Drug Administration (FDA) granted ^{64}Cu-SAR-bisPSMA Breakthrough Therapy designation for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level.

Breakthrough Therapy designation is a process designed to expedite the development and review of drugs that are intended to treat a serious condition, and preliminary clinical evidence indicates that the drug/agent of interest may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s)[1]. This designation is intended to get promising drugs developed and to the market as quickly and safely as possible, so that they can be available to optimise the treatment of the patients who need them most[2]. The benefits of a product having Breakthrough Therapy designation include[1]:

- All Fast Track designation features
- Intensive guidance on an efficient drug development program
- Organisational commitment from the FDA involving senior managers for a more proactive, collaborative, cross-disciplinary review

While Fast Track designation can be granted based on early-stage or nonclinical data, Breakthrough Therapy designation requires preliminary clinical evidence of a treatment effect that may represent considerable additional clinical benefit over available products in a serious condition[3]. Breakthrough Therapy designation is also a positive indicator of potential eligibility for Priority Review due to overlapping qualifying criteria. Priority Review is requested at the time of the New Drug Application (NDA) submission and can substantially shorten the FDA's review timeline for an NDA[3].

The FDA Breakthrough Therapy designation was supported by data from the Phase II Co-PSMA trial[4], Phase I/II COBRA trial[5] (see About Co-PSMA and About COBRA sections below) and real-world evidence[6], which collectively indicate enhanced diagnostic performance of ^{64}Cu-SAR-bisPSMA over standard-of-care (SOC) PSMA PET in patients with biochemical recurrence (BCR) of prostate cancer.

Clarity is currently progressing two registrational Phase III trials with ^{64}Cu-SAR-bisPSMA, AMPLIFY (NCT06970847)[7] and CLARIFY (NCT06056830)[8], both of which have successfully completed recruitment and are now in patient follow-up. Topline data from both pivotal trials are anticipated to be released in the first half of calendar year (CY) 2027. As pivotal trials, the final study results are intended to provide sufficient evidence to support an application to the US FDA for approval of ^{64}Cu-SAR-bisPSMA as a new diagnostic imaging agent in prostate cancer patients prior to undergoing definitive therapy (CLARIFY) and with BCR (AMPLIFY).

Dr Alan Taylor, Executive Chairperson of Clarity Pharmaceuticals, commented, "Receiving this Breakthrough Therapy designation is one of the most significant milestones in our prostate cancer program to date. Its importance is further amplified given fewer than half of designation requests across all therapeutic areas are successful[9]. The FDA's award of the first Breakthrough Therapy designation in the history of PSMA PET imaging highlights both the unmet need for more accurate detection of recurrent prostate cancer lesions and the significance of the data generated to date, which indicates improved diagnostic performance of ^{64}Cu-SAR-bisPSMA compared to SOC PSMA PET in patients with BCR of prostate cancer.

"Although PSMA PET represents a major advance over conventional imaging for prostate cancer detection, currently approved products miss metastatic disease in many patients, particularly in those with small volume disease. According to their respective FDA-approved prescribing information, the two leading PSMA PET agents demonstrate these limitations across different clinical settings. In initial staging, sensitivities as per the FDA-approved label are 47% for ^{68}Ga-PSMA-11[10] and 35% for ^{18}F-DCFPyL[11] (averages across readers). In BCR, PET positivity rates on the FDA-approved label are only 36% and 35%, respectively, in patients with PSA<0.5 ng/mL, and only increase to 56% and 50%, respectively, in patients with PSA 0.5 to < 1.0 ng/mL[10,11], meaning that disease detection is still missed in up to half the patients even at these higher PSA levels. The Co-PSMA data that had participants with a median PSA level of 0.43 ng/mL and a ^{68}Ga-PSMA-11 detection rate of 36% is comparable to the FDA-approved label. The detection rate for ^{64}Cu-SAR-bisPSMA in Co-PSMA in the same patient group was more than double that of ^{68}Ga-PSMA-11 at 78%[4].

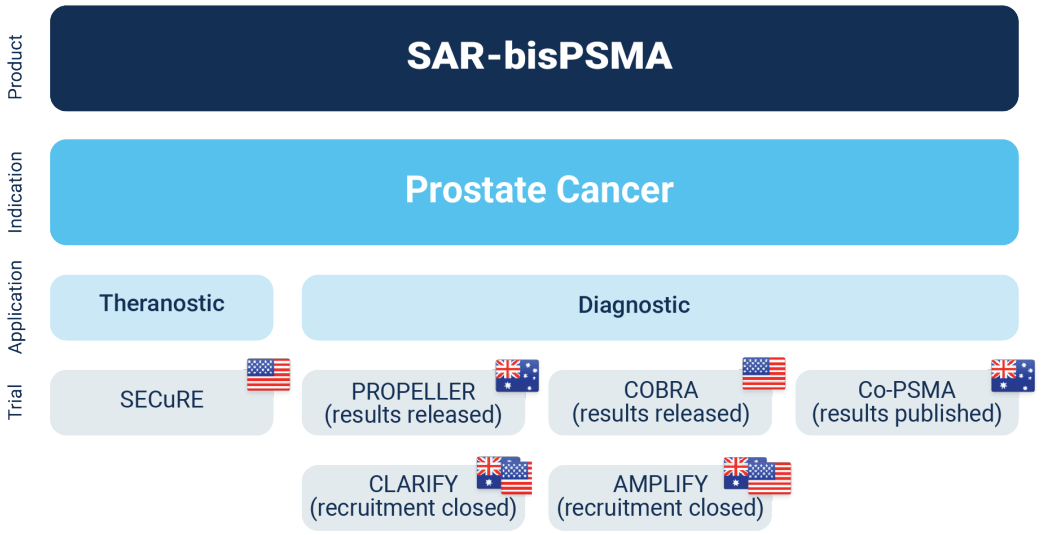
"With innovation, scientific rigour and highest standards of clinical development at the core of our Company, our lead product, ^{64}Cu-SAR-bisPSMA, is testament to this approach. Our proprietary sarcophagine (SAR) Technology, derived from the benchtop of Australian science, is a platform technology that enables us to successfully use the 'perfect pairing' of copper-64 (for imaging) and copper-67 (for therapy). The potential benefits of copper-64 and copper-67 have been discussed in scientific literature for decades, but their adoption in the clinic had been limited due to issues with copper isotopes leaking from conventional chelators into the body. The SAR Technology is designed to overcome this challenge, opening new opportunities in Targeted Copper Theranostics (TCTs). Being able to successfully employ copper-64 with its longer half-life of 12.7 hours, compared to the gallium-68 and fluorine-18 isotopes with half-lives of 1-2 hours, enables extended imaging timepoints of up to 30 hours post-injection. Differentiating further, we went back to the benchtop and optimised the well-known PSMA target, developing a novel, bivalent bisPSMA agent and subsequently filing a patent for the composition of matter in June 2018, providing us with patent protection until at least 2038. The combination of the secure chelating SAR Technology, optimal imaging timepoints with copper-64 and the bivalent bisPSMA agent is what makes ^{64}Cu-SAR-bisPSMA stand out from the FDA-approved PSMA PET products in the market, with the potential to improve the detection of prostate cancer and facilitate more informed, individualised clinical management in these patients. The longer product shelf-life (compared to Ga-68 and F-18 based products) also translates into supply chain benefits through centralised and regional manufacture as well as broad geographic distribution, which can improve patient access to this important imaging tool.

"The Breakthrough Therapy designation is supported by the Co-PSMA[4] and COBRA[5] trials as well as real-world evidence[6]. A key study contributing to this milestone is Co-PSMA, which investigated ^{64}Cu-SAR-bisPSMA against ^{68}Ga-PSMA-11 in a head-to-head and intra-patient comparison design. This investigator-initiated trial (IIT) was conducted by Prof Louise Emmett, a globally renowned nuclear medicine physician, at St Vincent's Hospital in Sydney. The quality and significance of this work have been recognised globally with the manuscript selected as an Editor's Choice article by the editors of European Urology, a world-leading clinical journal in the field of Urology with an impressive impact factor of 29.7. The data were showcased at the annual European Association of Urology (EAU) Congress and as a Top-Rated Oral Presentation at the European Association of Nuclear Medicine (EANM) Congress 2026, which underscore the significance of the findings for both the urology and nuclear medicine fields. We are proud to have supported this IIT and are committed to supporting high-quality research involving ^{64}Cu-SAR-bisPSMA in the future.

"The field of PSMA PET imaging has evolved rapidly over the past few years, quickly becoming a blockbuster market with sales of around US$2 billion per year in the US alone, and this is expected to further grow to over US$3 billion by 2029. The substantial and growing PSMA PET market represents a significant opportunity for Clarity, but our ambition extends well beyond market size. Our focus remains firmly on developing products that will improve the outcomes of patients with cancer, and this Breakthrough Therapy designation is an important step in the progress we are making towards this goal.

"We would like to take this opportunity to acknowledge and thank the investigators who have contributed their knowledge, time and resources to the ^{64}Cu-SAR-bisPSMA trials, our team of dedicated and driven individuals who continue tirelessly progressing this program towards launch and, importantly, the participants and their families who took part in our trials and special access cases to date."

Overview of Clarity's SAR-bisPSMA clinical trial program



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 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.

About Co-PSMA

Co-PSMA ("Comparative performance of ^{64}Copper [^{64}Cu] SAR-bisPSMA vs. ^{68}Ga-PSMA-11 PET CT for the detection of prostate cancer recurrence in the setting of biochemical failure following radical prostatectomy") was an IIT led by Prof Louise Emmett at St Vincent's Hospital, Sydney, evaluating the performance of Clarity's diagnostic product, ^{64}Cu-SAR-bis-PSMA, in a head-to-head comparison to SOC ^{68}Ga-PSMA-11 product in prostate cancer patients with PSA of 0.2 – 0.75 ng/mL. Eligible patients were required to have had radical prostatectomy with no salvage therapy. SOC ^{68}Ga-PSMA-11 PET/CT per institutional protocol was followed by ^{64}Cu-SAR-bisPSMA PET/computed tomography (CT) (at 1 hour and 24 hours post-injection, same-day and next-day imaging, respectively), on the same digital PET camera[4].

The primary endpoint of the Co-PSMA study was to assess the difference in mean per patient lesion number. Secondary endpoints included management impact questionnaires between ^{64}Cu-SAR-bisPSMA and ^{68}Ga-PSMA-11 and accuracy of the PET findings determined using a comprehensive reference standard, including biopsy, response to targeted treatment without androgen deprivation therapy (ADT), PSA rise without treatment or corroborative imaging[4].

The study enrolled 50 participants (median PSA 0.43 ng/mL [interquartile range: 0.31–0.63]). In addition to meeting its primary endpoint, the study also demonstrated improved diagnostic performance of next-day ^{64}Cu-SAR-bisPSMA PET across multiple parameters (minimal differences were observed between 1-hour ^{64}Cu-SAR-bisPSMA and ^{68}Ga-PSMA-11 PET). The mean per-patient lesion for ^{64}Cu-SAR-bisPSMA (24-hour imaging) was 1.26, compared to 0.48 for ^{68}Ga-PSMA-11, with a difference of 0.78 (95% confidence interval [CI]: 0.52 – 1.04), ratio 2.63 (95% CI: 1.64 – 4.20) (primary endpoint; $p < 0.0001$). On a per patient level, 36% (18/50) of participants were positive on ^{68}Ga-PSMA-11 PET/CT, compared to 78% (39/50) on ^{64}Cu-SAR-bisPSMA PET/CT (next-day imaging). The patient-level true positive rate also favoured ^{64}Cu-SAR-bisPSMA next-day imaging (71% vs. 29% for ^{68}Ga-PSMA-11, against the composite reference standard). In total, ^{68}Ga-PSMA-11 identified 24 lesions across all participants, while 24-hour ^{64}Cu-SAR-bisPSMA imaging detected 63 lesions. The increase in the number of lesions identified by ^{64}Cu-SAR-

bisPSMA was noted in the prostatic bed region (local recurrence), pelvic/extrapelvic lymph nodes and bone.[4]

At 24 hours, ^{64}Cu-SAR-bisPSMA demonstrated higher lesion uptake compared to ^{68}Ga-PSMA-11 (median maximum standardised uptake value [SUVmax] 13.6 vs. 5.3), and lower background bladder activity (median SUVmax 12.0 vs. 34.5, respectively), improving tumour-to-background contrast. These imaging attributes likely contributed to an almost perfect agreement across the three independent blinded readers for the ^{64}Cu-SAR-bisPSMA scans, whereas the agreement was lower for ^{68}Ga-PSMA-11. This means the readers reached the same conclusions when assessing the ^{64}Cu-SAR-bisPSMA scans far more often than when assessing the ^{68}Ga-PSMA-11 scans in a blinded fashion (near perfect level of agreement for ^{64}Cu-SAR-bisPSMA, Cohen's Kappa 0.94 vs. 0.75 for ^{68}Ga-PSMA-11)[4].

Importantly, these imaging findings informed clinically meaningful changes in planned patient management, with a marked difference between ^{64}Cu-SAR-bisPSMA and ^{68}Ga-PSMA-11 (planned management changes observed in 44% of patients following ^{64}Cu-SAR-bisPSMA imaging). The two most common modifications in treatment plan were changes from observation to active treatment (12/22) and changes in the radiation field (9/22). Active planned management increased from 66% based on ^{68}Ga-PSMA-11 results to 90% based on ^{64}Cu-SAR-bisPSMA findings. This highlights the potential impact of ^{64}Cu-SAR-bisPSMA on the management of patients with BCR and at these PSA levels[4].

Key data from the abstract was released in February 2026 and presented at the EAU Congress in March 2026. The manuscript was selected as an Editor's Choice article in European Urology (impact factor of 29.7) in March 2026. The results were also showcased as a Top-Rated Oral Presentation at the EANM Annual Congress 2026 in October, highlighting the significance of its findings for the fields of urology and nuclear medicine.

About COBRA

COBRA was a Phase I/IIa, multi-centre, single arm, non-randomised, open-label study of ^{64}Cu-SAR-bisPSMA in participants with BCR of prostate cancer and negative or equivocal findings on institutional SOC conventional imaging. The primary objectives of the trial were to investigate the safety and tolerability of ^{64}Cu-SAR-bisPSMA as well as its ability to correctly detect recurrence of prostate cancer. Patients underwent PET/ CT scans on same-day and next-day imaging (1-4 hours and 24±6 hours post-injection, respectively), which were interpreted by three blinded central readers. To determine the efficacy of ^{64}Cu-SAR-bisPSMA imaging, same-day and next-day imaging results of the central readers were assessed against a composite reference standard that was determined by an independent, blinded, central expert panel. The reference standard consisted of histopathology, follow-up SOC imaging and/or confirmed PSA response to focal therapy[12].

Fifty-two participants with negative or equivocal SOC scans were enrolled and imaged, of whom 42 were included in the calculation of the efficacy endpoints. The median PSA at study entry was 0.9 ng/mL (range 0.25 – 17.60). The study demonstrated that ^{64}Cu-SAR-bisPSMA was safe and effective in detecting lesions in patients with BCR of prostate cancer who were negative or equivocal on SOC imaging (e.g. bone scan, CT or PET with approved PSMA imaging agents) at screening[12].

The primary efficacy endpoints were patient-level correct detection rate (CDR, defined as the proportion of true positive participants out of all scanned participants who had at least one evaluable reference standard datapoint) and region-level positive predictive value (PPV, defined as the proportion of true positive regions out of all positive regions on the ^{64}Cu-SAR-bisPSMA PET/CT scan with corresponding evaluable reference standard). The CDR range across the central readers in patients that were negative or equivocal on SOC imaging on same-day imaging was 19.0–26.2% (95% confidence interval [CI] 8.6–42.0), increasing to 26.2–33.3% (95% CI 13.9–49.5) on next-day imaging. The region-level PPV on same-day imaging range was 39.1–44.8% (95% CI 19.7–64.3), and on next-day imaging it was 32.7–43.3% (95% CI 20.3–62.6). The CDR and PPV results were substantially impacted by the large number of lesions that were detected, but unable to be biopsied as this would not be clinically appropriate, despite these patients being negative or equivocal SOC imaging. The study had biopsies performed in 9 patients, of whom 7 (almost 80%) had a positive result based on histopathology. This trial was the first study in the BCR setting, showing such considerable effects of ^{64}Cu-SAR-bisPSMA even in patients who had failed SOC imaging[12].

^{64}Cu-SAR-bisPSMA was able to identify approximately 91% more lesions (median increase) on next-day imaging compared to same-day imaging (ranges across the readers for the total number of lesions: 53–80 on same-day vs.

82–153 on next-day imaging). The number of lesions in the pelvic lymph node region more than doubled on next-day imaging compared to same-day imaging (median increase of 108.3% across all readers comparing same-day vs. next-day imaging). The ranges of CDR and patient-level detection rate (DR, defined as the proportion of participants with a positive ^{64}Cu-SAR-bisPSMA PET/CT scan out of all scanned participants) were both higher on next-day imaging compared to same-day imaging. The DR range on same-day imaging was 44–58% (95% CI 30–71.8), increasing on next-day imaging to 58–80% (95% CI 43.2–90)[12].

The same-day and next-day ^{64}Cu-SAR-bisPSMA scans were compared with follow-up conventional SOC PSMA PET scans in 20 participants (13 participants with ^{68}Ga-PSMA-11 scans and 7 with ^{18}F-DCFPyL scans) during the follow-up period. The median time from same-day ^{64}Cu-SAR-bisPSMA imaging to follow-up SOC PSMA PET was 73.5 (range: 29-180) days. Both same-day and next-day ^{64}Cu-SAR-bisPSMA imaging demonstrated a higher number of PET-positive lesions in a higher proportion of patients (26 and 53 lesions in 14 and 18 participants, respectively) compared with the follow-up SOC PSMA PET (20 lesions in 12 participants), indicating earlier and improved detection of recurrent prostate cancer lesions with ^{64}Cu-SAR-bisPSMA compared with SOC PSMA PET agents[12].

Following ^{64}Cu-SAR-bisPSMA PET imaging, investigators indicated that they would change the treatment plan of approximately half of the patients (48%). Of these patients, nearly two-thirds (62.5%) proceeded to receive systemic and/or focal therapy or biopsy. Taken altogether, the findings from the COBRA trial have important clinical implications as the localisation of recurrence may lead to different treatment pathways for these patients.

About AMPLIFY

AMPLIFY (^{64}Cu-SAR-bisPSMA Positron Emission Tomography: A Phase 3 Study of Participants with Biochemical Recurrence of Prostate Cancer) is a non-randomised, single-arm, open-label, multi-centre, diagnostic clinical trial of ^{64}Cu-SAR-bisPSMA PET in participants with rising or detectable PSA after initial definitive treatment at clinical sites across the US and Australia[7].

The aim of this registrational study is to investigate the diagnostic ability of ^{64}Cu-SAR-bisPSMA PET/CT to detect recurrence of prostate cancer in men with PSA levels above 0.2 ng/mL. The study co-primary endpoints are participant-level CDR and region-level PPV assessed independently for same-day and next-day imaging (1-4 hours and approximately 24 hours post-administration, respectively)[7].

AMPLIFY commenced in May 2025, seeking to enrol approximately 220 participants, and the first trial participant was imaged in the same month at XCancer with Dr Luke Nordquist (Omaha, NE). The target number of participants in the AMPLIFY study was achieved in March 2026. All trial participants are expected to complete their follow-up in the coming weeks with topline data anticipated in the first half of CY2027.

About CLARIFY

CLARIFY (Positron Emission Tomography Using ^{64}Cu-SAR-bisPSMA in Participants With High-risk Prostate Cancer Prior to Radical Prostatectomy: A Prospective, Single-arm, Multi-center, Blinded-review, Phase 3 Diagnostic Performance Study) is the first Phase III registrational trial for Clarity, being conducted in the US and Australia. It is a non-randomised, open-label study of ^{64}Cu-SAR-bisPSMA in participants with untreated, histopathology-confirmed prostate cancer with high-risk features who are proceeding to radical prostatectomy (removal of the prostate) with pelvic lymph node dissection (removal of lymph nodes from the pelvic region)[8].

The target number of participants in the CLARIFY study was achieved in October 2026. All trial participants are expected to complete their follow-up in the coming weeks with topline data anticipated in the first half of CY2027.

Disclaimer

^{64}Cu-SAR-bisPSMA and ^{67}Cu-SAR-bisPSMA are unregistered products. Their safety and efficacy 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.

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[13]. Prostate cancer is the second-leading cause of cancer death in American men. The American Cancer Society estimates there will be about 333,830 new cases of prostate cancer in the US in 2026 and around 36,320 deaths from the disease[14].

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.

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