ASX ANNOUNCEMENT

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# SABRE topline results: $^{64}$Cu-SAR-Bombesin is effective in detecting prostate cancer recurrence in patients with negative SOC imaging

## Highlights

- Topline data from Clarity's diagnostic Phase II trial, SABRE, showed that $^{64}$Cu-SAR-Bombesin was safe, well tolerated and effective at detecting prostate cancer in patients with biochemical recurrence (BCR) who are negative or equivocal on standard-of-care (SOC) scans, including prostate-specific membrane antigen (PSMA) Positron Emission Tomography (PET).
- SAR-Bombesin targets the gastrin-releasing peptide receptor (GRPR), a promising pan-cancer target expressed in a number of indications, including prostate cancer. Unlike PSMA-targeted agents, $^{64}$Cu-SAR-Bombesin may be particularly valuable for imagining prostate cancer with known biological heterogeneity, which prostate cancer is known to be.
- The trial enrolled 53 patients. $^{64}$Cu-SAR-Bombesin identified lesions in approximately 35% and 28% of participants on same-day and next-day imaging, respectively (average across readers). Forty-nine lesions in total were identified on $^{64}$Cu-SAR-Bombesin PET/computed tomography (CT) scans (average across readers and imaging days).
- The participant-level correct detection rate (CDR) was 14.9% (95% confidence interval [CI]: 6.2, 28.3) on same-day imaging and ranged from 4.3% to 14.9% (95% CI: 0.5-28.3) on next-day imaging across the readers. Region-level positive predictive value (PPV) ranged from 22.6% to 47.1% (95% CI: 9.6-72.2) on same-day imaging and from 22.2% to 37.5% (95% CI: 2.8-61.7) on next-day imaging. The CDR and PPV results were substantially impacted by the large number of lesions that were detected, but unable to be verified by biopsies (not clinically feasible in many cases) and by the low sensitivity of follow-up SOC imaging.
- Despite biopsy not being SOC for this patient population, approximately 16% of patients who were positive on $^{64}$Cu-SAR-Bombesin PET/CT were biopsied in the SABRE study. All lesions assessed by histopathology were positive for prostate cancer, indicating a 100% true-positive rate among those biopsied lesions.
- As an example, in one participant, $^{64}$Cu-SAR-Bombesin PET/CT detected multiple lesions, two of which were confirmed as prostate cancer by biopsy. No lesions were detected on a prior SOC screening $^{18}$F-DCFPyL PSMA PET/CT scan, and on a follow-up $^{18}$F-DCFPyL PET/CT scan conducted approximately 11 weeks later only one bone lesion was detected. A follow-up CT scan conducted approximately 3 months after the $^{64}$Cu-SAR-Bombesin scans confirmed the presence of multiple cancerous lesions.
- Only two participants had adverse events (AEs) related to $^{64}$Cu-SAR-Bombesin, with all being mild (Grade 1) and resolving within 2 days of onset.
- Based on these positive results, Clarity has commenced discussions with key medical experts to determine the most effective pathway for registration of $^{64}$Cu-SAR-Bombesin and to explore its development in a range of large oncology indications with high unmet needs.

**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 positive topline results from the diagnostic Phase II SABRE trial (NCT05407311)[1] with $^{64}$Cu-SAR-Bombesin in participants with PSMA-negative BCR of prostate cancer following definitive therapy. SAR-Bombesin targets the GRPR present on cells of a range of cancers, including prostate cancer.

## SABRE trial design

**SABRE** (Copper-64 **SA**R-Bombesin in **B**iochemical **Re**currence of prostate cancer) was a Phase II multi-centre, single arm, non-randomised, open-label copper-64 labelled SAR-Bombesin PET imaging trial of patients with PSMA-negative BCR of prostate cancer following definitive therapy. To be considered for inclusion in the study, candidates were required to demonstrate negative or equivocal findings for prostate cancer on approved PSMA PET ($^{68}$Ga-PSMA-11 or $^{18}$F-DCFPyL), anatomical imaging (CT and/or magnetic resonance imaging [MRI]) and any other SOC imaging, if available. The primary objectives of the trial were to investigate the safety and tolerability of the product as well as its ability to correctly detect recurrence of prostate cancer.

Study participants were dosed with 200 MBq of $^{64}$Cu-SAR-Bombesin and underwent PET/CT scans at 1-4 hours and 24 ± 6 hours post-dose (same-day and next-day imaging, respectively). The scans were interpreted by three blinded central readers. To determine the efficacy of $^{64}$Cu-SAR-Bombesin imaging, the same-day and next-day PET/CT 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 prostate-specific antigen (PSA) response to focal therapy.

The primary efficacy endpoints were participant-level CDR (defined as the proportion of true-positive participants out of all scanned participants who had at least one evaluable reference standard datapoint collected) and region-level PPV (defined as the proportion of true-positive regions out of all positive regions on the $^{64}$Cu-SAR-Bombesin PET/CT scan with corresponding evaluable composite reference standard data), assessed independently for same-day and next-day imaging timepoints.

The design of the SABRE study followed advice from regulators to achieve the highest standards in clinical research in the BCR setting. Based on this guidance, the expert panel, who determined the reference standard, was blinded to the results of the $^{64}$Cu-SAR-Bombesin scans and distinct from the central readers assessing the $^{64}$Cu-SAR-Bombesin scans. This approach removed potential biases in the assessment of the reference standard, which was not the case for other studies conducted in this setting.

The SABRE study design also adopted a conservative approach to the analysis of both co-primary endpoints. If a lesion identified on the $^{64}$Cu-SAR-Bombesin scan was not biopsied, and it was also not present on follow-up SOC imaging (a suboptimal reference standard with known low sensitivity and in a patient population that was negative on SOC imaging at screening), it was considered as false-positive in the analysis by default.

## Topline results

Fifty-three patients with negative or equivocal SOC scans at screening (which included approved PSMA PET and anatomical imaging) were enrolled and imaged. Forty-seven participants were evaluable for the primary efficacy endpoints. Approximately half of the participants enrolled had PSA less than or equal to 1.0 ng/mL at study entry.

The average detection rate across readers using $^{64}$Cu-SAR-Bombesin PET/CT was 35.2% on same-day imaging (24.5%-43.4% range) and 27.7% on next-day imaging (17%-37.7% range). Approximately 47 lesions were identified on same-day imaging (40-59 range) and approximately 52 on next-day imaging (24-95 range), despite these patients having negative or equivocal SOC scans prior to study entry, highlighting the potential clinical benefit that imaging with $^{64}$Cu-SAR-Bombesin can provide. The most common site of lesion detection was in the lymph nodes (LNs) and the prostate regions.

The participant-level CDR was 14.9% (95% CI: 6.2, 28.3) on same-day imaging and ranged from 4.3% to 14.9% (95% CI: 0.5-28.3) on next-day imaging across the readers. Region-level PPV ranged from 22.6% to 47.1% (95% CI: 9.6-72.2) on same-day imaging and from 22.2% to 37.5% (95% CI: 2.8-61.7) on next-day imaging.

The CDR and PPV results were substantially impacted by the large number of lesions that were detected on the $^{64}$Cu-SAR-Bombesin scans, but unable to be verified due to the lack of effective diagnostic options available for comparison and biopsy not being clinically appropriate in most cases. Three patients underwent biopsy (the 'gold standard' for verifying lesions) due to the findings of the $^{64}$Cu-SAR-Bombesin scan and a total of four biopsies were performed. All biopsies were positive for prostate cancer, including two pelvic LNs, one extra-pelvic LN and one bone lesion.

Administration of $^{64}$Cu-SAR-Bombesin at 200 MBq was shown to be safe and well tolerated. Only two participants had AEs related to $^{64}$Cu-SAR-Bombesin with all being mild (Grade 1) and resolving within 2 days of onset.

### Case study

A participant with BCR of prostate cancer presented with a baseline PSA of 22.3 ng/mL, negative SOC PSMA PET ($^{18}$F-DCFPyL, **Figure 1**, left image) and equivocal CT at screening. Imaging with $^{64}$Cu-SAR-Bombesin (middle image) revealed substantial disease burden with lesions detected in the pelvic LNs, extra-pelvic LNs, visceral/soft tissue, and bone. Subsequent biopsies of a right pelvic bone lesion and a supradiaphragmatic LN confirmed malignancy at both sites. A follow-up $^{18}$F-DCFPyL PET scan, conducted approximately 4 months after the screening with $^{18}$F-DCFPyL, failed to detect lesions in all regions except for the bone.

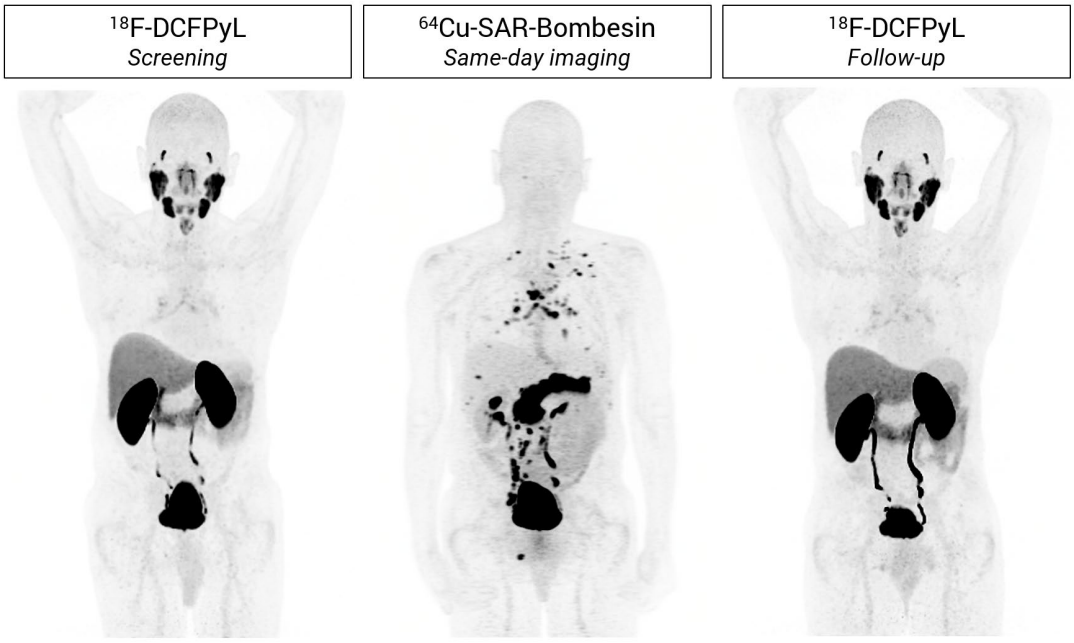


**Figure 1. Detection of extensive metastatic disease by $^{64}$Cu-SAR-Bombesin in a participant with BCR of prostate cancer.** The initial $^{18}$F-DCFPyL PSMA PET at screening was negative (left image), whereas same-day imaging with $^{64}$Cu-SAR-Bombesin (middle image) detected widespread disease, including lesions in the right pelvic bone and a supradiaphragmatic LN, which were confirmed as prostate cancer by biopsy. A follow-up $^{18}$F-DCFPyL scan approximately 11 weeks later (right image) was still unable to detect the extensive recurrence identified by the $^{64}$Cu-SAR-Bombesin scan. Maximum intensity projection of PET imaging. Images are shown with consistent scaling for visual comparison.

**Clarity's Executive Chairperson, Dr Alan Taylor, commented,** "The SABRE trial represents an important milestone for Clarity, setting a new benchmark by seeking to identify lesions that do not express PSMA. This trial, which is Clarity's first sponsored study with $^{64}$Cu-SAR-Bombesin, has now shown that this product can provide a solution where the current diagnostic options fall short and improve lesion detection beyond what is achievable with SOC PSMA-targeted imaging. Prostate cancer is characterised by significant biological heterogeneity, where some patients, or even individual lesions within the same patient, may lack PSMA expression and remain undetectable on PSMA-targeted imaging. A PET agent targeting an alternative receptor, such as GRPR, which is expressed in up to 100% of prostate cancers[2-6], may allow for better staging and hence more accurate treatment of BCR prostate cancer. As seen in the SABRE trial, some patients have widespread metastatic disease that remains completely undetectable by all available SOC imaging for extended periods. These patients deserve access to advanced diagnostic tools, such as $^{64}$Cu-SAR-Bombesin PET, that can reveal otherwise hidden disease and open the door to more informed and effective treatment options.

"We are very pleased with these results of the SABRE trial as a first look into this extraordinary patient population that has virtually invisible disease using SOC imaging and therefore, by definition, a very high unmet medical need. The data confirms that $^{64}$Cu-SAR-Bombesin is safe, well tolerated, and effective at detecting prostate cancer recurrence. Up to approximately 43% of participants had a positive $^{64}$Cu-SAR-Bombesin PET/CT, demonstrating the potential scale of the diagnostic gap this novel agent may help address with no disease identified by SOC imaging. These results are also corroborated by the findings of an earlier investigator-initiated trial (IIT), BOP, conducted by Prof Louise Emmett at St Vincents Hospital Sydney, where $^{64}$Cu-SAR-Bombesin PET/CT identified disease recurrence in 44% of participants with BCR of prostate cancer and negative or equivocal $^{68}$Ga-PSMA-11 PET/CT[7].

"The lack of any suitable diagnostic options for these men is made clear by the difficulty faced in validating lesions detected by $^{64}$Cu-SAR-Bombesin. Given we identified a large number of lesions with our product, it was not feasible nor ethical to verify all lesions with biopsy. Verification of the findings by other means, such as SOC imaging, was further complicated by the very nature of the trial, which specifically enrolled patients who were negative or equivocal on all available SOC imaging. These inherent challenges led to a high number of lesions not being confirmed as true-positives in the study. However, the fact that prostate cancer was confirmed in all $^{64}$Cu-SAR-Bombesin PET-positive lesions that were biopsied strongly reinforces the potential clinical value of this agent and the need it may fulfill within the current diagnostic landscape. SABRE has provided valuable insights into the performance of $^{64}$Cu-SAR-Bombesin relative to available SOC imaging. The study findings, including the potential for significantly improved lesion detection, will be carefully considered in the design of a registrational trial.

"We now have three exceptional diagnostic agents in various stages of clinical development, $^{64}$Cu-SAR-bisPSMA, $^{64}$Cu-SARTATE and $^{64}$Cu-SAR-Bombesin, and all three are showing impressive efficacy compared to SOC imaging. We look forward to sharing additional data readouts from all trials and progressing discussions with key medical experts to determine the most effective pathway for registration, particularly with this asset, $^{64}$Cu-SAR-Bombesin, as the pathway to commercialisation for $^{64}$Cu-SAR-bisPSMA and $^{64}$Cu-SARTATE is clearly defined and quickly progressing. We have already explored additional indications expressing GRPR with high unmet needs where $^{64}$Cu-SAR-Bombesin may significantly improve the diagnostic landscape, and we have seen some promising data on the benefits of $^{64}$Cu-SAR-Bombesin PET/CT in breast cancer patients from the C-BOBCAT IIT, also conducted by Professor Louise Emmett. Results from this study showed high lesion uptake of $^{64}$Cu-SAR-Bombesin in women with lobular subtype of metastatic breast cancer in comparison to SOC imaging (i.e. CT, bone scan and $^{18}$F-FDG PET/CT), indicating that our imaging agent could offer improved diagnostic options in this indication[8].

"These encouraging findings from the SABRE, BOP and C-BOBCAT trials, as well as other trials with GRPR-targeted agents in other cancers, highlight the broad potential of $^{64}$Cu-SAR-Bombesin to become a best-in-class diagnostic agent in a number of indications. This reinforces our drive to advance Targeted Copper Theranostics in areas of significant clinical need, as these areas lack not only accurate diagnostics, but also

effective therapeutics. The detection of GRPR-expressing cancers could represent a significant opportunity to enable more comprehensive disease assessment across varied tumour phenotypes. We look forward to working with key regulatory groups, such as the US Food and Drug Administration (FDA), to explore various avenues and indications with SAR-Bombesin further as we continually strive to improve diagnostic and theranostic options for patients and their clinicians."

### About SAR-Bombesin

$^{64}$Cu-SAR-Bombesin is a highly targeted pan-cancer radiopharmaceutical with broad cancer application. It targets the GRPR present on cells of a range of cancers, including but not limited to prostate, breast and ovarian cancers. GRPR is found in up to 100% of prostate cancers, including prostate cancers that don't express PSMA (PSMA-negative)[2-6]. The product utilises 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-Bombesin 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.

### Disclaimer

$^{64}$Cu-SAR-Bombesin is an unregistered product. The safety and efficacy of $^{64}$Cu-SAR-Bombesin has not been assessed by health authorities such as the US FDA or the Therapeutic Goods Administration (TGA). There is no guarantee that this product 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[9]. 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[10].

Approximately 20-25% of prostate cancer patients with BCR have low or no uptake of PSMA-targeting tracer[11-14]. These patients are unlikely to show meaningful uptake of PSMA-targeted products, such as $^{68}$Ga-PSMA-11. Given the prostate cancer indication is one of the largest in oncology, there is a significant unmet medical need in this segment.

### 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.*