ASX ANNOUNCEMENT

24 January 2025

Clarity receives U.S. FDA Fast Track Designation for 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 children and adults with cancer, is pleased to announce that the U.S. Food and Drug Administration (FDA) has granted Fast Track Designation (FTD) for ^{64}Cu-SAR-bisPSMA for positron emission tomography (PET) imaging of prostate-specific membrane antigen (PSMA) positive prostate cancer lesions in patients with biochemical recurrence (BCR) of prostate cancer following definitive therapy.

This milestone builds on Clarity's earlier receipt of an FTD for ^{64}Cu-SAR-bisPSMA in patients with suspected metastasis of prostate cancer who are candidates for initial definitive therapy[1]. These 2 FTDs enable the Company to accelerate the development of its comprehensive diagnostic program with this product.

The FDA's FTD is designed to expedite the development and regulatory review of novel drugs addressing serious conditions with significant unmet medical needs. For ^{64}Cu-SAR-bisPSMA, it provides a number of product development advantages. The designation paves the way for a faster review process once Clarity submits its product approval applications. Additionally, it enables more frequent communication with the FDA, allowing for rapid resolution of queries during development. Furthermore, Clarity can submit completed sections of its application as they are ready, rather than waiting for the entire package to be finished before it can be lodged with the FDA. These benefits would reduce the review time needed to bring this innovative prostate cancer imaging agent to market, potentially improving diagnosis and treatment planning for patients sooner.

The FTD submission highlighted several advantages of ^{64}Cu-SAR-bisPSMA over currently approved PSMA PET agents due to the bivalent structure of bisPSMA and the longer half-life of ^{64}Cu (12.7 hours vs. <2 hours for ^{18}F and ^{68}Ga). These advantages include improved diagnostic performance, flexible imaging schedule and broader availability. The data for this FTD submission was primarily focused on the results of the Phase I/II COBRA study, which assessed the safety and diagnostic performance of ^{64}Cu-SAR-bisPSMA in detecting prostate cancer in patients with BCR of their disease who had a negative or equivocal standard of care (SOC) scan at study entry. Advantages have been shown with same-day and next-day imaging, however, the standout was next-day ^{64}Cu-SAR-bisPSMA PET imaging, showing localised disease in up to 80% of participants and detecting lesions as small as 2 mm. This compares favourably against the current SOC PSMA PET agents, with which the detection of lesions smaller than 5 mm is challenging. The number of lesions detected by ^{64}Cu-SAR-bisPSMA on next-day imaging almost doubled compared to same-day imaging, and ^{64}Cu-SAR-bisPSMA was also able to identify more lesions at much earlier timepoints (**Figure 1**) compared to approved PSMA PET agents.

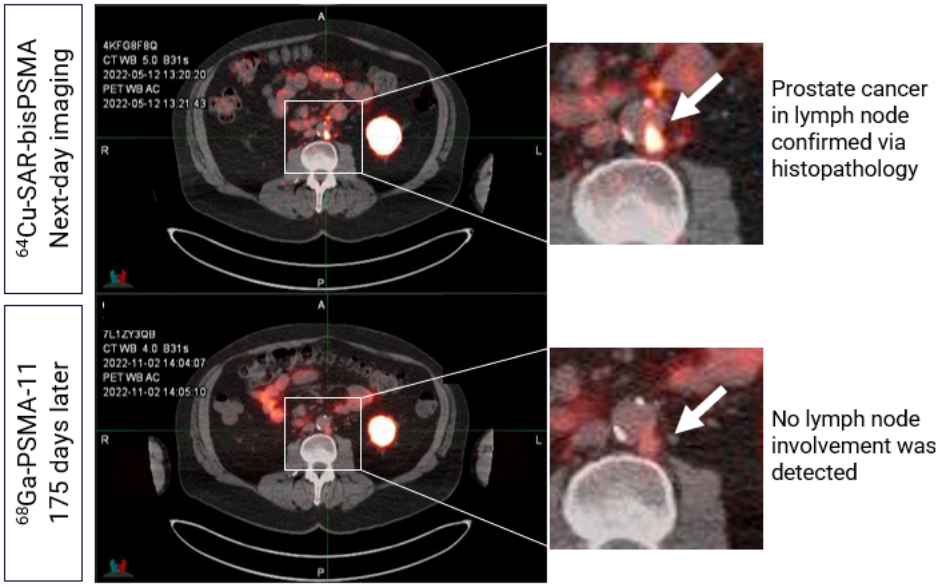


Figure 1. Retroperitoneal lymph node detected by ^{64}Cu-SAR-bisPSMA on next-day imaging (identified by all 3 central readers). Lymph node involvement was not identified on the ^{68}Ga-PSMA-11 scan performed 176 days post-Day 0 (175 days post-Day 1) according to central read. Histopathology, performed on Day 190, confirmed the presence of prostate cancer in the extra-pelvic lymph node region in this patient. PET/computed tomography (CT) fusion.

The COBRA trial paved the way for Clarity's second diagnostic registrational trial, AMPLIFY, and an investigator-initiated trial (IIT) Co-PSMA, led by Prof Louise Emmett at St Vincent's Hospital Sydney. The AMPLIFY trial will be a non-randomised, single-arm, open-label, multi-centre, Phase III diagnostic clinical trial of ^{64}Cu-SAR-bisPSMA PET in approximately 220 participants with rising or detectable PSA after initial definitive treatment. As a pivotal trial, the final study results are intended to provide sufficient evidence to support an application to the FDA for approval of ^{64}Cu-SAR-bisPSMA as a new diagnostic imaging agent in prostate cancer in patients with BCR. The Co-PSMA IIT will aim to build on the evidence generated so far, evaluating the diagnostic performance of ^{64}Cu-SAR-bisPSMA in comparison to SOC ^{68}Ga-PSMA-11 for the detection of recurrent prostate cancer lesions with curative intent.

Clarity's Executive Chairperson, Dr Alan Taylor, commented, "Receiving the second FTD for ^{64}Cu-SAR-bisPSMA and well within the 60-day period following our application submission, reserved by the U.S. FDA for review, is yet another significant milestone in our bisPSMA program. This highlights the high unmet need for novel diagnostics in prostate cancer and the high quality of data we presented to the FDA.

"The market for first-generation diagnostic PSMA PET today is approximately US$2 billion (AU$3.2 billion) in the U.S. alone, with little differentiation between products. It is expected to further grow to US$3 billion (AU$4.75 billion) by 2029. The development pipeline of new products coming to market, outside of ^{64}Cu-SAR-bisPSMA, also offers no differentiation from the existing offering, with some new entrants commercialising the unpatented ^{68}Ga-PSMA-11 agent, which has been capitalised on by three separate groups already.

"Being able to now fast-track the development of ^{64}Cu-SAR-bisPSMA for patients with BCR as well as for patients prior to initial definitive therapy is incredibly exciting. The news is especially timely as we are actively preparing to commence recruitment for our second registrational trial, AMPLIFY, in the coming months. The designation will allow us to work closely with the FDA to facilitate the development process and accelerate the approval of what could become a best-in-class diagnostic.

"The dual targeting structure of bisPSMA enables increased uptake and retention of the product in the lesions, while the longer half-life of copper-64 provides greater flexibility with imaging scheduling, including next-day imaging (something that gallium-68 and fluorine-18 based products cannot support). When combined, these features make ^{64}Cu-SAR-bisPSMA stand out from its competitors who are known to have issues with sensitivity. We have seen 2-

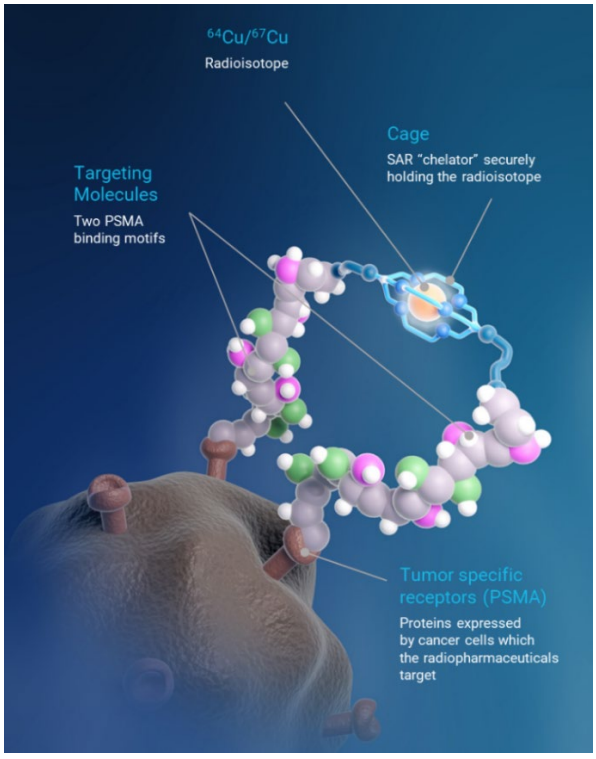
3 times higher uptake in prostate cancer lesions and the identification of more lesions using ^{64}Cu-SAR-bisPSMA compared to ^{68}Ga-PSMA-11 in pre-prostatectomy patients in our PROPELLER study. The COBRA trial results showed great diagnostic performance in the BCR setting, with lesions identified by ^{64}Cu-SAR-bisPSMA in the 2-mm range and visualised many months before SOC PSMA PET agents are able detect them.

"Not only are we developing a product that may have improved diagnostic performance compared to SOC PSMA PET agents, but the longer half-life of copper-64 also enables a longer shelf-life of ^{64}Cu-SAR-bisPSMA than currently used diagnostic radiopharmaceuticals, allowing for centralised manufacture and wider distribution. These attributes have the potential to reduce disparities in prostate cancer care and ensure that most patients, regardless of geographic location, can benefit from the latest advances in diagnostic technology.

"This designation highlights the unique opportunity for ^{64}Cu-SAR-bisPSMA in this very large market by addressing the limitations of the current-generation diagnostic radiopharmaceuticals and providing patients with prostate cancer with a more accurate diagnosis leading to more optimal treatment options. As such, we are fully committed to advancing the development of this best-in-class product to address the critical need for more accurate and accessible diagnostic tools in prostate cancer management."

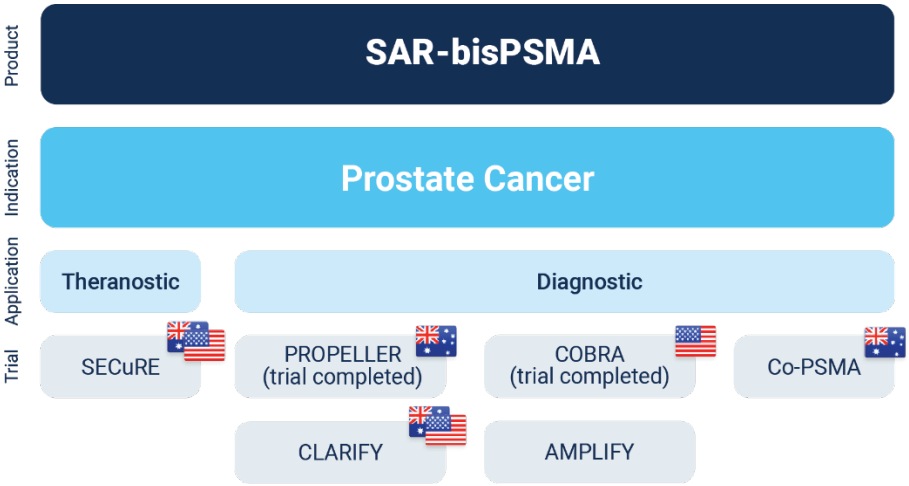
About SAR-bisPSMA

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.



^{64}Cu-SAR-bisPSMA is an unregistered product. The safety and efficacy of ^{64}Cu-SAR-bisPSMA has not been assessed by health authorities such as the U.S. FDA or the Therapeutic Goods Administration (TGA). There is no guarantee that this product will become commercially available. Among 82 patients who received ^{64}Cu-SAR-bisPSMA in PROPELLER and COBRA, 2 adverse reactions were reported in 2 participants (mild occasional metallic taste and moderate worsening of type II diabetes, both resolved)[2,3].

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[4]. 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 U.S. and around 35,770 deaths from the disease[5].

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.

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2. Lengyelova et al. ^{64}Cu-SAR-bisPSMA (PROPELLER) positron emission tomography (PET) imaging in patients with confirmed prostate cancer. ASCO, 2023.
3. Nordquist et al. COBRA: Assessment of safety and efficacy of ^{64}Cu-SAR-bisPSMA in patients with biochemical recurrence of prostate cancer following definitive therapy. EANM, 2024.
4. 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
5. 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.