ASX ANNOUNCEMENT

28 November 2024

Last patient assessment completed for diagnostic SARTATE trial in NETs

Clarity Pharmaceuticals (ASX: CU6) ("Clarity"), 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 last patient has completed their final assessment in the Phase II diagnostic ^{64}Cu-SARTATE trial, DISCO (NCT04438304)[1], for patients with known or suspected neuroendocrine tumours (NETs).

DISCO, which derives from "**D**iagnostic **I**maging **S**tudy of ^{64}**CO**pper-SARTATE Using PET on Patients with Known or Suspected Neuroendocrine Tumours", is assessing the performance of Clarity's SARTATE imaging product as a potential new method to diagnose and manage NETs. The DISCO trial recruited participants with Gastroenteropancreatic NETs (GEP-NETs) across four sites in Australia, comparing the diagnostic performance of ^{64}Cu-SARTATE at approximately 4 hrs and 20 hrs post-administration to ^{68}Ga-DOTATATE at one hour.

The trial was originally planned for up to 63 patients based on an expected discordance level between imaging with Clarity's ^{64}Cu-SARTATE and the current standard of care, ^{68}Ga-DOTATATE. The sample size was adjusted to 45 patients based on the results of the pre-planned early assessment of the images collected during the trial with the aim of generating sufficient evidence to plan for a Phase III trial in this indication. This enabled recruitment to successfully close early.

The trial aims to build on earlier work with SARTATE in patients with NETs, which demonstrated that imaging at later time points, enabled by the longer half-life of copper-64 in comparison to gallium-68, may lead to better identification of disease[2]. Delayed imaging (at 4 hrs and 24 hrs vs 1 hr) showed a progressive increase in lesion-to-liver ratio (Table 1). Figure 1 provides an example of improved lesion detection based on an increase in lesion-to-background ratio observed with delayed imaing[2].

Ratio 1	*Median*	*Ratio 2*	*Median*	*Difference*	*95% CI*	*P**
^{68}Ga-DOTATATE to liver (1 hr)	**3.92**	**^{64}Cu-SARTATE to liver (1 hr)**	**5.45**	**1.35**	**0.7, 2.2**	**0.004**
^{68}Ga-DOTATATE to liver (1 hr)	**3.92**	**^{64}Cu-SARTATE to liver (4 hr)**	**6.70**	**3.86**	**1.5, 6.4**	**0.002**
^{64}Cu-SARTATE to liver (4 hr)	**6.70**	**^{64}Cu-SARTATE to liver (24 hrs)**	**16.69**	**6.75**	**3.4, 10.3**	**0.002**

Table 1. Comparison of lesion-to-liver ratios of ^{68}Ga-DOTATATE and ^{64}Cu-SARTATE. Progressive increase in lesion-to-liver ratio with delayed imaging using ^{64}Cu-SARTATE. *Paired Wilcoxon test on 10 patients. CI = confidence interval.

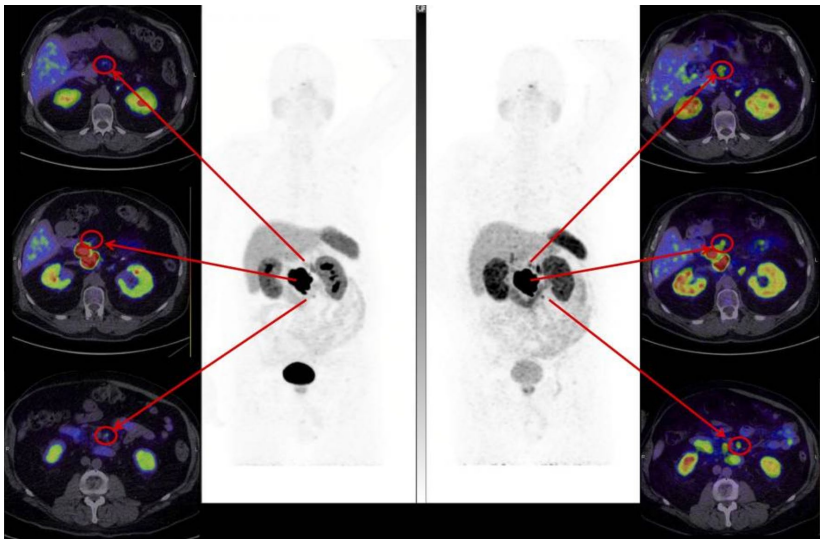


Figure 1. Lesion detection comparing ^{68}Ga-DOTATATE and ^{64}Cu-SARTATE. Hicks et al. (2019) determined superior lesion detection at 4 hrs with ^{64}Cu-SARTATE. High lesion contrast on ^{64}Cu-SARTATE images at 4 hrs (right) better defines regional nodal disease than ^{68}Ga-DOTATATE images at 1 hr (left) in patient with large pancreatic primary tumour.

Clarity's Executive Chairperson, Dr Alan Taylor, commented, "With the recent changes to the U.S. Centers for Medicare and Medicaid Services (CMS) and reimbursement of radio-diagnostics, this market is set to surge. The market opportunity for each radiodiagnostic is now massive, but there are limitations to the current range of products, most notably, the use of short half-life isotopes and short shelf-life products.

"Imaging at a one-hour time point due to the isotope half-life or product shelf-life, as opposed to patient needs, significantly impacts patient care. Firstly, the scheduling of patients may represent a challenge due to the lack of flexibility for imaging. But importantly, later time-point imaging presents significant benefits for doing what cancer diagnostics need to do, and that is finding cancer. At Clarity, we have known this for many years and have demonstrated these benefits time and time again with different products in our Targeted Copper Theranostic (TCT) platform, including SARTATE. We have seen first-hand in clinical trials that once these radiopharmaceutical products are administered, they take time to find the lesion whilst also needing to clear from background organs, providing greater contrast, especially to identify more difficult to find cancers. This is known as signal-to-noise ratio or, in our case, tumour-to-background ratio. We have also seen to date that these physiological characteristics of radiopharmaceutical products in finding the tumour and clearing the background are not overcome with the small number of state-of-the-art whole body positron emission tomography (PET) imaging cameras, despite their increases in sensitivity.

"Copper-64 has comparably low radiation doses to currently used isotopes and involves similar management of patients. However, the longer half-life of copper-64 of 12.7 hours, combined with Clarity's proprietary position in copper-based theranostics, now sets up a foundation for a complete suite of next-generation radiodiagnostics, which could be unmatched in the radiopharmaceutical sector. The opportunity for centralised, multi-layer manufacturing and broad distribution means that every patient with access to PET imaging can potentially have optimal cancer diagnostic care, not limited by isotope half-life.

"We have adopted a dual strategy to date with the SARTATE product. Our initial focus is on the theranostic development of $^{64/67}$Cu-SARTATE for neuroblastoma in children with the CL04 trial currently ongoing (NCT04023331)[3]. Clarity secured two Rare Pediatric Disease Designations (RPDD) and two Orphan Drug Designations (ODD) in this indication. Should Clarity be successful in achieving marketing approval from the U.S. Food and Drug Administration (FDA) for these two products in neuroblastoma, RPDDs may allow the Company to access a total of two tradeable Priority Review Vouchers (PRVs) currently valued at around US$158 million each[4]. Our second strategy is the diagnostic development of ^{64}Cu-SARTATE in a larger market of NETs and other diseases that express the somatostatin receptor 2 (SSTR2) target, followed by therapy in these same indications. We expect the final results from the DISCO study to be available in the first half of 2025, which will inform the design of our registrational Phase III trial in this indication.

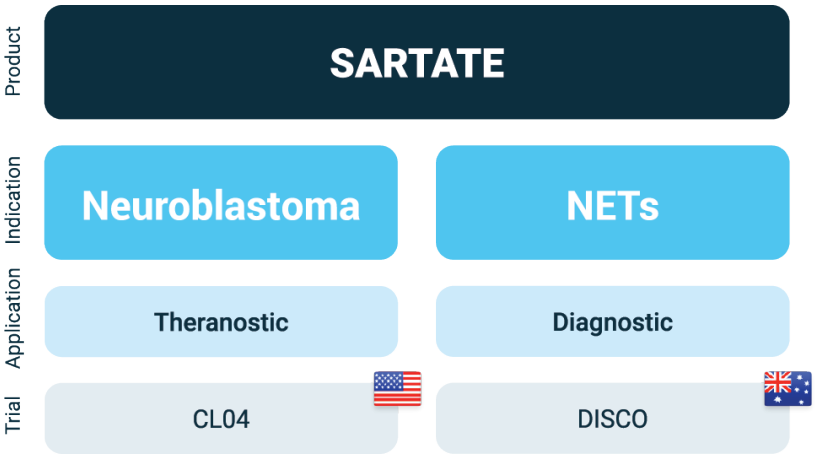
"Patients with NETs are often misdiagnosed and experience delays in receiving the correct diagnosis, which leads to disease progression and identifying the cancer at its later stages. We believe that SARTATE has the potential to become a best-in-class product in this indication, and other indications that have the same target receptor, SSTR2, playing an important role in improving accurate staging, lesion identification and treatment outcomes for these patients. The market for these diagnostics in the United States alone is currently in the hundreds of millions of dollars with products that were commercialised prior to the CMS changes. Our team has been focusing on significantly increasing our diagnostic platform to benefit from our proprietary position and the change in market dynamics for radiodiagnostics brought by the CMS. We think that the advantages of copper-64 based on the potential of a flexible dosing schedule, later time-point imaging and logistical benefits of Clarity's copper-based products could ensure timely diagnosis and enable broader access to critical imaging products for cancer patients around the world."

About SARTATE

SARTATE is a next generation, highly targeted theranostic radiopharmaceutical. It is being developed for diagnosing, staging and subsequently treating cancers that express somatostatin receptor 2 (SSTR2), including neuroblastoma and neuroendocrine tumours (NETs). Like all Clarity products, the SARTATE product can be used with copper-64 (^{64}Cu) for imaging (^{64}Cu-SARTATE) or copper-67 (^{67}Cu) for therapy (^{67}Cu-SARTATE).

^{64}Cu-SARTATE and ^{67}Cu-SARTATE are unregistered products. Their safety and efficacy have not been assessed by health authorities such as the US Food and Drug Administration (FDA) or the Therapeutic Goods Administration (TGA). Individual results may not represent the overall safety and efficacy profiles of the products. There is no guarantee that these products will become commercially available.

Overview of Clarity's SARTATE clinical program



About NETs

NETs, also known as well-differentiated neuroendocrine neoplasms or carcinoids, represent a heterogeneous group of malignant transformations of cells of the diffuse neuroendocrine system[5]. They most commonly occur in the gastrointestinal tract (48%), lung (25%), and pancreas (9%), but may also originate in other areas, including the breast, prostate, thymus and skin[6]. NETs can either be benign or malignant, as well as non-functional and functional[7]. NETs traditionally have been considered uncommon; however, the incidence has been increasing as a worldwide phenomenon[8].

Overall, it is estimated that more than 12,000 people in the United States are diagnosed with a NET each year, and approximately 170,000 people are living with this diagnosis[9]. Patients with NETs present with subtle clinical symptoms, which can lead to a delay in diagnosis of more than 4 years[10]. As such, about 30-75% of NET patients have distant metastases at the time of diagnosis[11]. A 10-year relative survival rate for patients with metastatic GEP-NETs is 3–36%[12].

About Clarity Pharmaceuticals

Clarity is a clinical stage radiopharmaceutical company focused on the treatment of serious disease. The Company is a leader in innovative radiopharmaceuticals, developing targeted copper theranostics based on its SAR Technology Platform for the treatment of cancer in children and adults.

www.claritypharmaceuticals.com

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