

## ASX Announcement

# First Patient Enrolled in Phase 2 CERE-CALM Clinical Trial

- First patient enrolled in Phase 2 CERE-CALM trial, marking an important milestone in the development of Ceretas' non-invasive therapeutic ultrasound platform
- CERE-CALM is evaluating focused ultrasound neuromodulation as a treatment for patients with Alzheimer's disease
- Randomised, double-blind, sham-controlled Phase 2 trial targets 66 patients (min. 60) and designed to assess treatment efficacy, safety and tolerability
- Builds on encouraging Phase 1 clinical results, which demonstrated favourable safety and tolerability, alongside signs of improvement in behavioural symptoms
- Patient recruitment underway at Cognivus Research in Sydney, with additional clinical sites at St Vincent's Hospital Sydney and the John Hunter Medical Institute expected to commence recruitment shortly
- Targeting significant unmet medical need, with behavioural and psychological symptoms affecting over 90% Alzheimer's patients and placing considerable pressure on caregivers and healthcare systems
- Significant market opportunity – Alzheimer's is the most common cause of dementia, which impacts 57m people globally with a new case diagnosed every 3 seconds
- Fully funded trial expected to complete in H1 CY28, with results to inform next stage of clinical development and broader commercialisation strategy

**Brisbane, Australia, 29 October 2026 – Ceretas Limited (ASX:CTS)** ("Ceretas" or "the Company"), an Australian medical technology company developing a portable, non-invasive therapeutic ultrasound platform to treat Alzheimer's disease and other neurodegenerative conditions, is pleased to advise that the first patient has been enrolled in its Phase 2 CERE-CALM clinical trial.

The milestone represents an important step in the clinical development of Ceretas' therapeutic ultrasound platform, with the Company progressing patient enrolment in a Phase 2 study designed to evaluate the safety and efficacy of low-intensity focused ultrasound neuromodulation for behavioural and psychological symptoms of dementia (BPSD) in patients with Alzheimer's disease.

CERE-CALM is a randomised, double-blind, sham-controlled Phase 2 trial targeting 66 participants (minimum 60) across multiple clinical sites in Australia. The study will assess the safety, tolerability and efficacy of focused ultrasound neuromodulation in reducing

behavioural and psychological symptoms associated with Alzheimer's disease. The trial is fully funded, with \$3.4 million of the Company's IPO proceeds allocated to CERE-CALM.

Patient recruitment is underway at Cognivus Research in Sydney, with recruitment at St Vincent's Hospital in Sydney and the John Hunter Medical Research Institute expected to commence shortly. The trial is anticipated to complete in the first half of CY2028.

The commencement of CERE-CALM follows encouraging results from a first-in-human Phase 1 study undertaken by researchers at The University of Queensland's Queensland Brain Institute (QBI) in 2024. The study, involving 12 patients with Alzheimer's disease, found the treatment to be fast, safe and well tolerated, with preliminary signals of improvement in behavioural symptoms.

Behavioural and psychological symptoms affect over 90% of patients with Alzheimer's disease and can include agitation, aggression, anxiety, depression and apathy. These symptoms represent a significant source of distress for patients and caregivers and are associated with increased hospitalisation and earlier admission to residential aged care.

Ceretas' technology is being developed as a non-invasive therapeutic approach targeting neural circuits associated with these symptoms, with the potential to address an area of substantial unmet clinical need.

#### **Management commentary:**

**Ceretas CEO/MD Dr Rachel de las Heras said:** *"The enrolment of our first patient in CERE-CALM represents an important milestone for Ceretas as we advance our therapeutic ultrasound technology through clinical development.*

*"Behavioural and psychological symptoms are among the most challenging aspects of Alzheimer's disease, placing a considerable burden on patients, families and healthcare systems. There remains a significant need for new treatment approaches that can safely and effectively manage these symptoms.*

*"Our earlier Phase 1 study provided encouraging evidence of safety and tolerability, together with early signals of clinical benefit. CERE-CALM is designed to build on those findings through a larger, placebo-controlled study, providing an important opportunity to further evaluate the therapeutic potential of our technology.*

*"With recruitment now underway and additional clinical sites preparing to commence, our focus is on progressing patient enrolment and executing the study efficiently. We believe this program represents an important step towards establishing Ceretas' technology as a potential new treatment option for patients living with Alzheimer's disease."*

#### **CERE-CALM trial overview:**

CERE-CALM is a Phase 2 randomised, double-blind, sham-controlled trial evaluating low-intensity focused ultrasound neuromodulation for the treatment of the behavioural and psychological symptoms of dementia (BPSD) in adults aged 50 and over with probable

Alzheimer's disease and BPSD. Participants receive six treatments over 12 weeks, comprising four weekly sessions followed by two monthly sessions.

The primary endpoint is the change in overall neuropsychiatric symptom burden as measured by Neuropsychiatric Inventory (NPI) total score from baseline to week 6, comparing active treatment with sham control. Secondary endpoints include caregiver distress at week 6 and week 12, durability of treatment effect at week 12, and overall safety and tolerability. The trial targets 66 participants (minimum 60), randomised 2:1 to active treatment or sham control.

The details of the CERE-CALM trial are provided on the Australian and New Zealand public clinical trial registry: [www.anzctr.org.au](http://www.anzctr.org.au), with the trial code ACTRN12626000738325.

Enquiries can be directed via email to Ceretas: [clinicaltrialsenquiries@ceretas.com.au](mailto:clinicaltrialsenquiries@ceretas.com.au).

## **Q&A:**

### **What is neuromodulation?**

Neuromodulation is a technique used to influence the activity of nerves and neural circuits in the brain. Different regions of the brain control functions such as memory, emotions, behaviour and movement.

Ceretas is developing a non-invasive approach that uses low-intensity focused ultrasound to influence activity in specific brain regions associated with behavioural and psychological symptoms of Alzheimer's disease. The objective is to improve how these neural circuits function and potentially reduce symptoms experienced by patients.

### **How does Ceretas' therapeutic ultrasound technology work?**

Ceretas' technology delivers precisely targeted, low-intensity ultrasound waves through the skull to specific areas of the brain, without requiring surgery.

The ultrasound is designed to influence neural activity in targeted brain circuits, potentially improving symptoms such as agitation, aggression and anxiety.

Unlike conventional drug-based treatments, this approach does not rely on medication to produce a therapeutic effect. The technology is being developed as a portable treatment platform, with the potential to support broader clinical use if its safety and effectiveness are demonstrated.

### **What are the behavioural and psychological symptoms of dementia (BPSD)?**

BPSD refers to a range of changes in behaviour and mood commonly experienced by people living with dementia, including agitation, aggression, anxiety, depression, apathy and can change the way someone feels and behaves.

These symptoms affect the majority of people with Alzheimer's disease and can become increasingly difficult to manage as the condition progresses.

Beyond their impact on patients, BPSD can place significant emotional and physical pressure on families and caregivers and is a major contributor to hospitalisation and earlier admission to residential aged care.

### **Why is there a need for new treatments for BPSD?**

Managing behavioural symptoms remains one of the most challenging aspects of Alzheimer's care.

Existing treatment approaches include behavioural interventions, supportive care and medications. However, drug-based treatments can have limited effectiveness for certain symptoms and may be associated with significant side effects, particularly in older and more vulnerable patients.

Ceretas is investigating whether focused ultrasound neuromodulation could provide an additional, non-invasive treatment option that reduces symptoms while maintaining a favourable safety and tolerability profile.

### **What is the CERE-CALM trial designed to demonstrate?**

CERE-CALM is a Phase 2 clinical trial evaluating the safety and effectiveness of Ceretas' focused ultrasound technology in patients with Alzheimer's disease experiencing behavioural and psychological symptoms.

The study is targeting 66 participants, with a minimum of 60, who will receive either active ultrasound treatment or a sham procedure (placebo). This allows researchers to compare outcomes between the two groups and assess whether improvements are attributable to the treatment.

The trial will primarily measure changes in behavioural and psychological symptoms, while also assessing caregiver distress, the duration of any treatment benefit and overall safety.

### **What does treatment involve for patients?**

Participants in the CERE-CALM trial will receive six treatment sessions over a 12-week period, comprising four weekly sessions followed by two monthly sessions.

Treatment involves delivering low-intensity focused ultrasound to targeted areas of the brain using Ceretas' non-invasive technology.

The procedure does not require surgery, and the study will assess whether repeated treatment can produce meaningful and sustained improvements in behavioural symptoms.

### **What have previous clinical studies demonstrated?**

In 2024, researchers at The University of Queensland's Queensland Brain Institute completed a first-in-human Phase 1 study involving 12 patients with Alzheimer's disease.

The study found that focused ultrasound treatment was fast, safe and well tolerated, with encouraging preliminary signs of improvement in behavioural symptoms.

These findings provided an important foundation for further clinical investigation. CERE-CALM is designed to build on this early evidence through a larger, randomised and controlled study capable of providing a more rigorous assessment of potential clinical benefit.

### **What happens if the Phase 2 trial is successful?**

Positive results would provide important evidence supporting the potential of Ceretas' technology as a treatment for behavioural and psychological symptoms associated with Alzheimer's disease.

The findings would help guide the Company's next stage of clinical development, including the design of subsequent studies and engagement with regulatory authorities regarding the requirements for potential approval.

In parallel, Ceretas is progressing development of its next-generation therapeutic ultrasound device, supporting its longer-term objective of developing a scalable, non-invasive treatment platform for Alzheimer's disease and other neurological conditions.

**This announcement is authorised for release by the Board of Directors.**

**- ENDS -**

### **For further information please contact**

#### **Dr Rachel de las Heras**

Chief Executive Officer & Managing Director

[racheldelasheras@ceretas.com.au](mailto:racheldelasheras@ceretas.com.au)

+61 (0)437 338 079

#### **Henry Jordan**

Six Degrees Investor Relations

[henry.jordan@sdir.com.au](mailto:henry.jordan@sdir.com.au)

+61 (0)431 271 538

## **About Ceretas**

Ceretas (ASX:CTS) is a clinical-stage medical technology company developing a portable, non-invasive therapeutic ultrasound platform to treat Alzheimer's disease and other neurodegenerative conditions.

The Ceretas device directs low-intensity focused ultrasound through the skull to act on brain tissue via two mechanisms: neuromodulation, targeting neural circuits involved in memory, cognition and the behavioural and psychological symptoms of dementia; and blood-brain barrier opening, which may facilitate clearance of disease-associated proteins and enhance delivery of therapeutic agents to the brain.

The technology is based on more than a decade of research at The University of Queensland and the Queensland Brain Institute (QBI). In 2024, QBI researchers completed a first-in-human Phase 1 trial of low-intensity focused ultrasound neuromodulation in 12 Alzheimer's participants, finding the treatment to be fast, safe and well tolerated, with encouraging early signals of benefit for behavioural symptoms. The results were published in Brain Communications in December 2025.

Ceretas has commenced its Phase 2 CERE-CALM trial (ACTRN12626000738325), evaluating the platform in Alzheimer's patients with behavioural and psychological symptoms of dementia. QBI researchers are separately running their Phase 2 AGIFUS trial (ACTRN12626000687392), evaluating the same technology in Alzheimer's-related agitation, funded independently by Queensland Health.