THE AUSTRALIAN



# Phase III trials: When the science project has to ‘grow up and get a job’

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- Success in late-stage Phase III trials opens doors to regulatory approval, commercial partnerships and revenue streams
- Disappointing outcomes can derail years of R&D and weigh heavily on share prices
- Several ASX companies are undertaking late-stage trials, with Dimerix working particularly hard on its trial design

The journey from lab to clinic is a costly and complex one for biotech companies, encompassing years of R&D and clinical testing with the final hurdle to jump being a phase III trial.

Often referred to as pivotal trials because of their importance, phase III typically evaluates a treatment's safety and effectiveness in larger patient populations.

Some companies also conduct combined phase II/III trials, which can be designed to generate the pivotal evidence needed for regulatory approval.

Morgans healthcare analyst Iain Wilkie said the stakes were particularly high in these late-stage trials.

Positive results can provide critical support for approval submissions to regulatory bodies such as the US Food and Drug Administration (FDA) or Australia's

Therapeutic Goods Administration (TGA), open doors to commercial partnerships and new revenue streams.

However, a disappointing outcome can derail years of R&D and weigh heavily on a company's share price, which unfortunately we've seen with several ASX companies.

"The way I think about it is phase III is where the nice little science project has to grow up and get a job," Wilkie told Stockhead.

## Getting phase III right

Wilkie said the design of a phase III trial could be critical to its eventual success. He said often phase III trial failures were not necessarily unexpected, with weaknesses in earlier clinical data or trial design providing warning signs.

"The dirty little secret for most phase III flops is that some of them aren't really surprises," Wilkie said.

He said issues could include inconsistent signals in phase II data, endpoints that regulators might be less likely to support or patient populations so broad that demonstrating a meaningful treatment effect became difficult.

Wilkie said with phase III trials often representing the most expensive stage of drug development, companies needed to ensure they were carefully designed and aligned with needs of regulators, doctors and the organisations or individuals ultimately paying for a treatment.

"Phase III is the time you have to prove a drug will work to the regulator but also the doctors along with the end payer, so it might be an insurance company, government or private patient paying for treatment," he said.

"The winners tend to design their pivotal trials with the regulator and customer in mind from day one and it's worth a company taking that bit of extra time to know what they want."

With several ASX biotechs now advancing treatments through pivotal trials, here's a look at some working towards clinical and commercial success.

## Dimerix ticking boxes to ensure success

Dimerix (ASX:DXB) is an example of a company working to maximise the likelihood of phase III trial success.

DXB is advancing its lead drug candidate DMX-200 through phase III development for focal segmental glomerulosclerosis (FSGS), a rare and progressive kidney disease.

The trial is titled Angiotensin II Type 1 Receptor and Chemokine Receptor 2 Targets for Inflammatory Nephrosis or ACTION3 for short.

The double-blinded, placebo-controlled study is evaluating the safety and efficacy of DMX-200 in patients with FSGS who are receiving a stable dose of an angiotensin II receptor blocker (ARB).

The trial is designed to assess changes in proteinuria, or excess protein in the urine, alongside kidney function measured by estimated glomerular filtration rate (eGFR) slope.

A phase II study saw 86% of patients see a reduction in proteinuria when administered DMX-200 versus the placebo.

"We've undertaken a number of activities that maximise our probability of success in this phase III clinical study and that included a blinded interim analysis in 2024, which demonstrated the drug was doing better than placebo at that point in time," CEO Dr Nina Webster told Stockhead.

"Earlier this year a blinded statistical review confirmed that the study remained statistically powered by more than 90% to demonstrate a statistical significance in its primary endpoint of proteinuria treatment effect in DMX 200.

"That means for its primary endpoint if DMX-200 continues to reduce proteinuria in patients as we expect, there is a greater than 90% chance of showing a significant

statistical reduction in that effect at the end of the trial."

DXB has also supported Project PARASOL, an international collaboration involving researchers, clinicians and regulators examining the relationship between proteinuria and long-term kidney outcomes in FSGS.

The collaboration's analysis of patient data from renal registries provided further evidence supporting proteinuria as an endpoint in ACTION3 and informed the company's regulatory discussions with the FDA.

"The FDA has also agreed that proteinuria is an appropriate endpoint for DMX 200 for regulatory approval in ACTION3," Webster said.

"That was supported by the recent approval of another FSGS therapy in the US providing clear evidence of that proteinuria endpoint."

DXB has completed recruitment of its adult cohort in ACTION3, with 333 patients randomised across 219 clinical sites in 21 countries.

The final adult participant started treatment in March 2026, transitioning the study from recruitment into treatment and follow-up. The final adult patient is expected to complete dosing in March 2028.

Recruitment of a separate paediatric cohort of patients aged 12 to 17 is continuing, potentially supporting future expansion into adolescent indications in key markets.

## Countdown to Actinogen Alzheimer's results

After 15 years of R&D **Actinogen Medical (ASX:ACW)** is expected to release topline results this month from the phase IIb/III XanaMIA trial of its lead drug candidate Xanamem in Alzheimer's disease.

The readout could be transformational for ACW, potentially providing important clinical evidence for a new approach to treating one of the most challenging neurodegenerative diseases, with no cure and limited options for slowing underlying progression.

ACW describes Xanamem as a potent oral inhibitor of 11β-HSD1, an enzyme involved in regulating cortisol levels in the brain.

By reducing excess cortisol in brain regions associated with memory and cognition, the treatment aims to slow cognitive decline while preserving normal cortisol levels elsewhere in the body.

“Drug development is a highly regulated and incremental process that takes many years and hundreds if not thousands of contributors in companies and hospitals, and of course the patients and their families who participate in the trials,” CEO Dr Steve Gourlay told Stockhead.

ACW has advanced Xanamem from its Australian base, supported by local investors who have contributed ~$150 million to the program.

It is a level of investment Gourlay said would likely have been five times higher had development taken place in the US.

"We are enormously grateful to all of those who have contributed to the Xanamem program and helped to get it to the end of this, the first pivotal clinical trial in Alzheimer’s disease," he said.

## CSL and Telix broad late-stage pipelines

At the big end of town, the ASX healthcare sector's largest company **CSL (ASX:CSL)** has a broad R&D pipeline spanning immunoglobulins, haematology, cardiovascular and renal disease, immunology and vaccines.

Its pipeline includes several phase III development programs, including clazakizumab, an antibody being investigated to reduce cardiovascular complications in patients with end-stage kidney disease.

Other late-stage programs include expanded uses for its plasma-derived immunoglobulin therapy Hizentra as well as treatments targeting surgical bleeding and acquired fibrinogen deficiency.

Radiopharmaceuticals company **Telix Pharmaceuticals (ASX:TLX)** is advancing multiple pivotal late-stage programs targeting prostate, brain and kidney cancers.

Its lead program, ProstACT Global, is evaluating TLX591 in advanced prostate cancer, with Part One complete and Part Two underway.

TLX said it was the first phase III trial to evaluate a PSMA-targeted radio antibody-drug conjugate (rADC) in combination with standard of care.

The company is also advancing TLX101 in glioblastoma through its pivotal phase II/III IPAX BrIGHT trial, which TLX described as the first radiopharmaceutical to reach Phase III development in the brain cancer.

Meanwhile, TLX250 is being evaluated in the pivotal phase II/III LUTEON trial in kidney cancer, marking what TLX said was the first targeted radiopharmaceutical to reach phase III development in the disease.

TLX is also investigating whether PSMA-PET imaging could improve prostate cancer detection before biopsy through its phase III BiPASS trial, which combines its imaging agents Illuccix or Gozellix with MRI.

The company's pipeline could expand further through its proposed merger with Germany's ITM, which would bring ITM-11 into the fold. This is a radiopharmaceutical therapy for neuroendocrine tumours that has completed a phase III trial, with another underway.

## Clarity's trials for diagnostic radiopharmaceutical

**Clarity Pharmaceuticals (ASX:CU6)** is preparing for topline results from two phase III trials of its lead diagnostic radiopharmaceutical, 64Cu-SAR-bisPSMA, in prostate cancer.

CU6 is developing a portfolio of copper-based radiopharmaceuticals designed to help clinicians detect and treat cancer, with its lead candidate targeting prostate-specific membrane antigen (PSMA), a protein commonly found on prostate cancer cells.

The company's technology uses copper-64 for diagnostic imaging and copper-67 for targeted radiation therapy, with the aim of combining more precise cancer detection with targeted treatment.

The two phase III trials, named CLARIFY and AMPLIFY, are evaluating 64Cu-SAR-bisPSMA in different prostate cancer settings across Australia and the US.

CLARIFY is investigating men with high-risk prostate cancer before surgery while AMPLIFY is focused on men whose cancer has returned following initial treatment.

The studies will assess the agent's sensitivity and specificity, as well as its ability to detect prostate cancer, including comparisons with available standard-of-care PSMA imaging agents.

CU6 expects to report topline results from both phase III trials during the first half of next year.

"We are very excited to reach this incredible point of reporting our topline data in two phase III registrational trials for a product that we developed at the benchtop of Australian science less than a decade ago," executive chairman Dr Alan Taylor said.

"The product, SAR bisPSMA, will look to enter the very large prostate cancer imaging market, which is about US$2 billion today in the US alone.

"Importantly, the three agents that make up that market have all failed to meet their pre-specified primary endpoint thresholds for sensitivity, with all three agents reporting sensitivities of 27-40% in their registrational phase III clinical trials.

"The two phase III trial readouts will complement a number of head-to-head trials completed to date which all showed superiority over standard of care imaging, as we look to have this product join the ranks to become one of Australia's most successful pharmaceutical achievements."

## Neurizon seeks ALS breakthrough with trial

Neurizon Therapeutics (ASX:NUZ) is advancing its lead drug candidate NUZ-001 in a late-stage trial for amyotrophic lateral sclerosis (ALS), the most common form of motor neurone disease (MND).

NUZ is carrying out its pivotal phase II/III trial via a US platform called Healey. The company is in Regimen I of the trial, which is one of the largest late-stage clinical trials underway in ALS.

The multi-site Healey trial is being run by the Sean M. Healey & AMG Center for ALS at Mass General Brigham in the US and aims to accelerate development of potential new ALS therapies.

The trial tests multiple investigational drugs simultaneously and shares infrastructure across sites, improving efficiencies and enabling faster results.

In the double-blinded, placebo-controlled, adaptive study, participants are randomised 3:1 to receive NUZ-001 or placebo at 78 US sites.

The first participant was dosed in February 2026 with enrolment closing in July 2026 after the arm was expanded from 160 participants to 250 in May. Topline results are expected in late Q2 CY27.

NUZ has said the trial could potentially act as a registrational trial, with positive results supporting FDA approval for NUZ-001.

## Clinuvel has two trials underway

Clinuvel Pharmaceuticals (ASX:CUV)is advancing two phase III studies to determine whether its lead drug Scenesse (afamelanotide) can help restore pigmentation in people with vitiligo.

Scenesse is already approved in Australia, the US and Europe for erythropoietic protoporphyria (EPP), a rare genetic disorder that causes severe sensitivity to light but is not yet approved for vitiligo.

CUV is investigating its use alongside narrowband UVB phototherapy, an established treatment for vitiligo that stimulates pigmentation.

The first study, CUV105, is a non-pivotal phase III trial involving 210 patients with Fitzpatrick skin types III-VI. It is comparing Scenesse combined with UVB phototherapy against phototherapy alone, with full results expected in H1 2027.

CUV is also preparing CUV107, a planned pivotal phase III registration study involving 300 patients with darker skin types (Fitzpatrick IV-VI).

The trial is intended to further assess efficacy, safety and the durability of repigmentation, potentially supporting future regulatory applications.

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*Disclosure: Iain Wilkie owns shares in Telix Pharmaceuticals, Clarity Pharmaceuticals and Neurizon Therapeutics. Nadine McGrath owns shares in CSL.*

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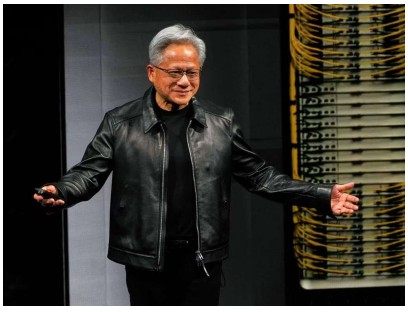

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