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# Positive Phase III Interim Analysis Result

Dr Paul Gavin | Chief Executive Officer

## THE TRIAL

# Phase III design — what we're testing

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- 244** participants randomised for the interim cohort
- 3 arms** 75mg CBD | 150mg CBD | placebo
- 8 weeks** of nightly dosing per participant
- 2 endpoints** Insomnia Severity Index (ISI) + subjective sleep efficiency (sSE)
- Blinded** patients, investigators and Avecho all blinded to allocation

### Insomnia — what we're treating

Difficulty falling or staying asleep

**Affects ~10-30% of Australians**

No approved OTC pharmaceutical product currently available in Australia for ongoing use

*Australia's unique Schedule 3 OTC pathway for CBD opens a first-mover commercial opportunity*

*Largest CBD insomnia trial globally; designed to support a TGA submission on positive completion.*

## UNDERSTANDING THE READOUT

# What the interim analysis is

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1

### What gets tested

The interim analysis examines whether the CBD TPM® capsule is improving sleep in the 244 patients dosed to date — measured using two independent primary endpoints (ISI and sSE). Either endpoint succeeding is sufficient.

2

### Who decides

An independent Data Monitoring Board reviews the unblinded data. The DMB is independent of Avecho and the trial investigators. Avecho remains fully blinded throughout the process.

3

### What we'll learn

The DMB will recommend one of three outcomes:

- 1) **Positive** - Continue the trial with a second cohort of patients - confirmed sample size
- 2) **Positive** - Stop the trial for efficacy
- 3) **Negative** - stop the trial for futility

#### Independent Data Monitoring Board (DMB)

- External sleep, safety and biostatistical experts
- Independent of Avecho and trial investigators

The DMB is the sole body with access to unblinded interim data -- standard best practice for pivotal placebo-controlled trials.

## TRIAL DESIGN

# Why this trial is positioned to deliver a clinical signal

*Three key design features have been built into this trial specifically to maximise the probability of a successful result*

**01**

### Two independent primary endpoints

- 1) Insomnia Severity Index (ISI)
- 2) Subjective Sleep Efficiency (sSE)

Only one needs to work for trial success.

**02**

### Adaptive design interim analysis

The interim analysis can recalibrate the trial, adjusting the required patient numbers during the study to ensure the result is conclusive.

**03**

### Placebo-effect control mechanisms

The protocol is designed to minimise damage from the placebo response — improving the chance that genuine drug effect is detected cleanly.

### Supporting design features

**150mg**

Maximum allowed OTC dose tested

**519**

Largest CBD insomnia trial globally

**8 weeks**

Treatment duration per patient

**ISI ≥ 15**

Tight inclusion criteria

**FDA + EMA**

Trial designed to global standards

## WHAT HAPPENS AFTER THE READOUT

## Three possible outcomes

**Stop for futility -- negative**

*The drug is not showing the required effect*

Dosing of further patients ceases — preserving shareholder capital. The CBD asset retains commercial value for alternative indications.

**Trial continues -- positive**

*Base case positive outcome — this is what we are aiming for*

The drug/trial is working, with an observable difference between treatment and placebo. DMB recommends continuing the trial with a confirmed sample size needed to reach statistical significance at completion.

**Stop for efficacy -- positive**

*Upside scenario — not expected, but possible*

The drug/trial is working so well results are highly statistically significant after 244 patients. The DMB can recommend stopping the trial early, declaring Phase III successful.

***The expected positive result was continuing the trial to 519 patients.***

## VERDICT

Positive – DMB recommends trial continues to 519 patients

**What does the recommendation tell us - *Efficacy***

1. Interim analysis met the pre-specified criteria to continue for efficacy — a treatment effect for the CBD TPM capsule versus placebo on at least one of the two primary endpoints
2. Observed data variability is in line with the assumptions used to power the study
3. If the second cohort performs consistently with the first, the completed 519-participant trial is well positioned to meet its primary endpoint
4. By recommending continuation at the originally planned sample size — rather than a larger one — the independent DMB has signalled that Avecho's original assumptions on effect size\* and variability are tracking at, or better than, expectation

**\*Original assumptions were that the product performs as well as approved insomnia drugs**

***Take Away - So far, product performance appears in line with approved insomnia medications***

Positive – DMB recommends trial continues to 519 patients

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### What does the recommendation tell us - *Safety*

- 1) **CBD TPM® capsule** — no serious adverse events across 244 participants at two doses in the interim analysis. Safety profile looks good.

#### Safety burdens of currently approved insomnia medicines

- Dependence, tolerance and withdrawal
- Next-day impairment
- Overdose toxicity
- Complex sleep behaviours
- Risk in older adults

*Take Away - So far, the product safety profile is competitive with approved insomnia drugs*

# Global insomnia: a large, growing market underserved by current therapies

Market context for Avecho's TPM<sup>®</sup>-enhanced CBD capsule for insomnia

**~850M**

adults live with chronic insomnia worldwide — 16.2% of the adult population

**~1 in 3**

adults experience insomnia symptoms at some point

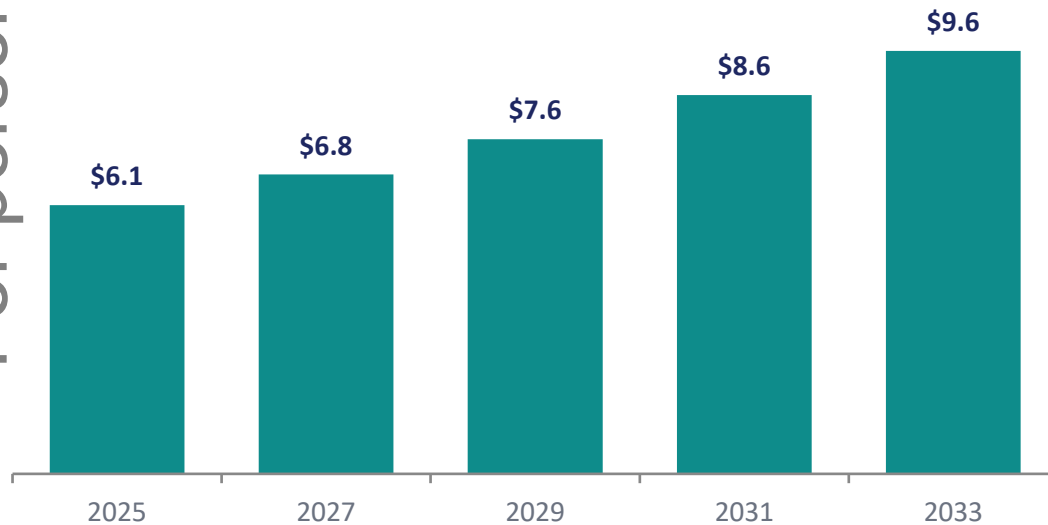
**~US\$9.5bn**

forecast global insomnia treatment market by 2033

**~6% CAGR**

projected annual market growth, 2025–2033

## Insomnia treatment market — global revenue (US\$bn)



## Why this is Avecho's opportunity

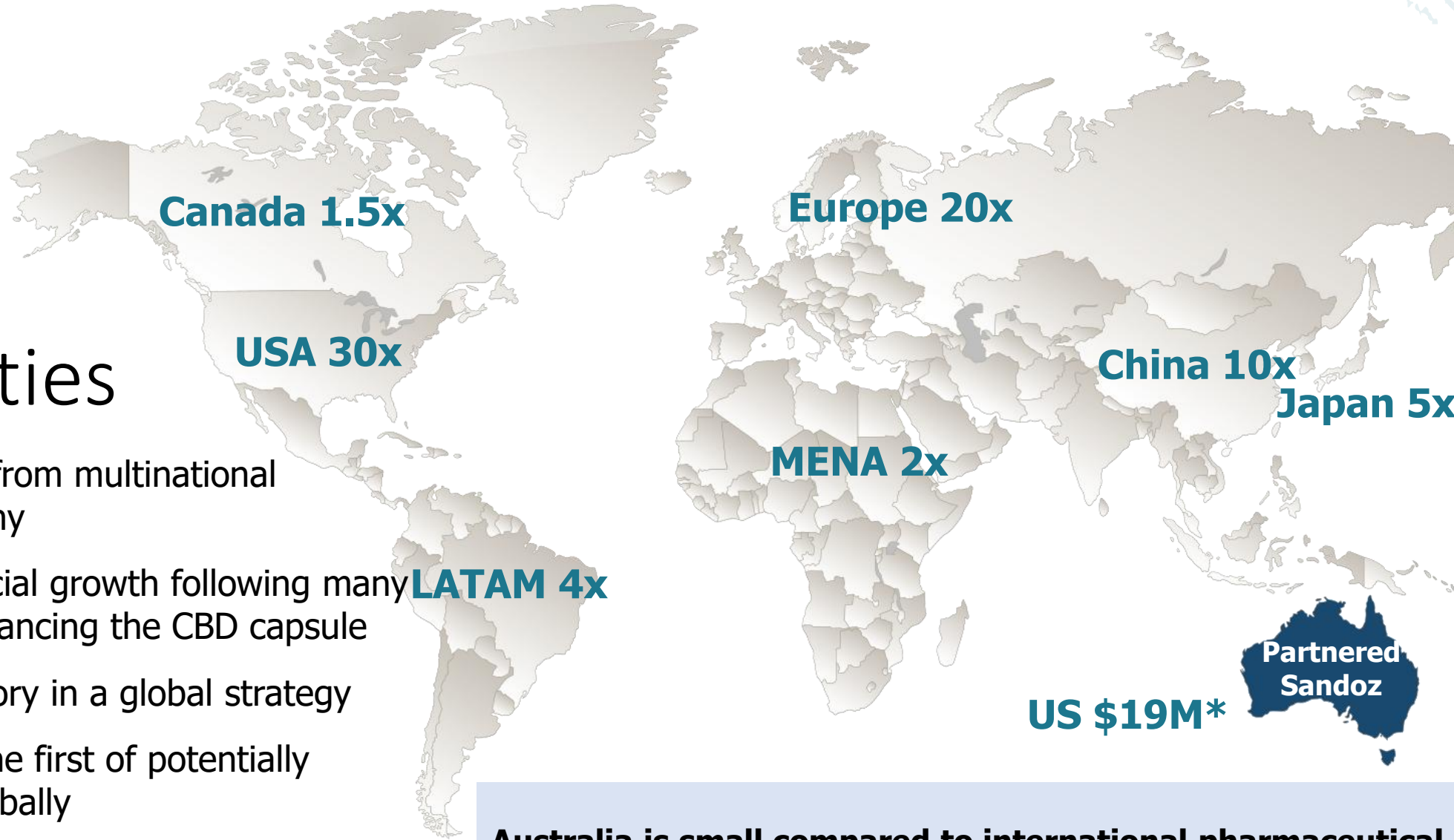
- **A safety-driven gap.** Benzodiazepines, Z-drugs and sedating antihistamines carry dependence, next-day impairment and overdose risk — shifting demand to safer, non-scheduled options. The newest class, orexin antagonists, is the fastest-growing at ~12% CAGR.
- **An open OTC pathway in Australia.** Since Feb 2021 the TGA permits low-dose CBD ( $\leq 150$  mg/day) to be sold pharmacist-only, over the counter — but no product has yet met the efficacy bar required for ARTG registration.
- **First-mover potential.** A successful Phase III is the registration-enabling dataset — positioning Avecho's CBD TPM capsule to be first to that OTC market, with Sandoz as Australian commercial partner.

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# Licensing Opportunities

- Commercial validation from multinational pharmaceutical company
- New phase of commercial growth following many years of hard work advancing the CBD capsule
- Australia the first territory in a global strategy
- > Licensing deal marks the first of potentially several agreements globally

\*For upfront and potential milestone payments prior to commercial sales



**Australia is small compared to international pharmaceutical markets. Huge opportunity for overseas territories**

## BASE CASE IN DETAIL

## Continuing the trial — how we fund it, how we execute

*Trial completion requires ~300 additional patients. The two questions shareholders will ask: how much, and how long?*

 **How we fund it**

- Priority: pharmaceutical licensing deal for an ex-Australian territory — upfront fees from licensing would fund Phase III completion.
- Pro-forma \$6.25M in the bank already

 **How we accelerate**

- ~300 additional patients required to complete the trial
- Plan to open ~10 additional clinical sites — already identified
- With additional sites engaged, recruitment expected to take ~12 months
- Lessons from interim recruitment fully embedded in completion plan

 **What runs in parallel**

- TGA dossier construction (with Sandoz)
- Manufacturing scale-up continues — funded from earlier placement
- Further ex-Australia licensing conversations progress to closure
- Engagement with international regulators (e.g. FDA) for global pathway optionality

## MILESTONES AND TRIGGERS

## Next 12-18 months

## H2 2026

**Trial Continuation**

- Pursue multiple licensing deals
- Open additional trial sites and recommence dosing
- Engagement with overseas regulators (e.g. FDA)
- Scale up and manufacturing

## 2027

**Trial completion and submission readiness**

- Pursue further licensing deals
- Complete Phase III dosing to final patient
- Complete manufacturing work required for TGA submission
- Compile and finalise TGA submission dossier
- Develop product with partners in international territories (specific territories may have their own requirements)

## CLOSING ARGUMENT

# Every part of our thesis has been independently validated

*For years we have claimed big things for this product. At each step, an external body has validated those predictions. One piece of validation remained.*

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Preclinical	US Patent Office	TGA	Sandoz	Market	Interim analysis
<p><i>validated that</i></p> <p><b>TPM Increased CBD absorption</b></p> <p><b>VALIDATED</b></p>	<p><i>validated that</i></p> <p><b>Product is unique</b></p> <p><b>VALIDATED</b></p>	<p><i>validated that</i></p> <p><b>Trial design &amp; submission strategy are sound</b></p> <p><b>VALIDATED</b></p>	<p><i>validated that</i></p> <p><b>Data, trial design, commercial case are compelling</b></p> <p><b>VALIDATED</b></p>	<p><i>validated that</i></p> <p><b>Story is good, value will follow</b></p> <p><b>VALIDATED</b></p>	<p><i>validated that</i></p> <p><b>Evidence the product works for the indication</b></p> <p><b>VALIDATED</b></p>

## INVESTMENT CASE DE-RISKED

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- ✓ **Positive Interim Analysis in Phase III insomnia trial**  
Positive signal for efficacy and safety after 244 patients — de-risks remaining Phase III trial to completion.

- ✓ **Clear registration pathway with the TGA**  
Unique Australian OTC pathway for CBD; trial designed and conducted for TGA submission.

- ✓ **Significant commercial potential in Australia**  
9.5M Australians experience insomnia; addressable market potential >US\$125M per annum. Global opportunity larger

- ✓ **Significant Commercial Partner for Australia**  
Sandoz, world's largest generics pharma — US\$3M upfront, US\$16M in milestones, 14–19% tiered royalties.

- ✓ **Global licensing potential**  
Large commercial opportunity in numerous jurisdictions allows for potentially multiple licensing transactions

- ✓ **Money in the bank**  
Proforma cash position of \$6.25M , provides strong position to execute deals following a positive interim readout

*Stop thinking if this will work – start thinking what this could be*

Avecho

# Questions Welcome

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