

## ASX Announcement

08 June 2021

ASX Market Announcements  
ASX Limited  
Level 4, North Tower, Rialto  
525 Collins Street  
Melbourne VIC 3000

### Avecho to Present New CBD Data at GCI Virtual Summit

#### Highlights:

- Avecho has today announced it is presenting at the **Global Cannabis Intelligence (GCI) Summit 2021**.
- Presentation includes new data detailing how TPM®, a novel form of Vitamin E, can be used to **increase the dermal absorption of cannabidiol by 3.2 – 5.4 times**.

**Melbourne, Australia, 08 June 2021:** Avecho Biotechnology Limited (ASX:AVE, "Avecho", or "the Company") has today announced its CEO, Dr Paul Gavin, is presenting at the Global Cannabis Intelligence (GCI) Summit 2021 – which will include the release of new data detailing how TPM® can increase the dermal absorption of cannabinoids after topical application.

The GCI Summit is bringing together 1500+ global leaders and decision makers from across the cannabis and psychedelics sector, with a common goal to improve learning, development and advocacy in this space.

The Avecho presentation is titled, '**Overcoming cannabinoid formulation challenges using TPM®, a novel form of Vitamin E**'.

In addition to data showing the increased oral absorption of cannabinoids, the Company will also present new data demonstrating the increased dermal absorption of cannabinoids from topical formulations containing TPM®.

Avecho tested the dermal absorption of CBD from topical formulations previously optimised for drug delivery. **The addition of TPM® in these formulations was shown to increase the dermal absorption of CBD by 3.2 – 5.4 times.**

**Avecho CEO, Dr Paul Gavin said:** *"Topical cannabinoid formulations are currently receiving attention for a range of clinical indications, including dermatology and pain. We are optimistic about this new data and what it tells us about the potential for TPM® to advance the cannabinoid sector at large. It is a great pleasure to be invited to the GCI Virtual Summit 2021 – this is the first time we've presented at a dedicated medicinal cannabis conference and we are grateful for an opportunity to expand our network of potential collaborators and partners."*

**The full presentation may be viewed here: ATTACH PRESENTATION DECK**

**- ENDS -**

This announcement is authorised for release by the Board of Directors of Avecho Biotechnology Limited.

#### Investor + General Enquiries

Ms Melanie Leydin  
Company Secretary  
Avecho Biotechnology Limited  
+61 3 9002 5000

### **About Avecho**

Avecho Biotechnology Limited develops and commercialises innovative Human and Animal Health products using its proprietary drug delivery system called Tocopheryl Phosphate Mixture (**TPM®**). TPM® is derived from Vitamin E using unique, proprietary and patented processes and is proven to enhance the solubility and oral, dermal and transdermal absorption of drugs and nutrients.

Avecho's major projects include delivering TPM® enhanced injectable, oral and topical products for the human health market and is also developing TPM® to enhance the feed efficiency and health of livestock.

See more here - [avecho.com.au](http://avecho.com.au)

### **Forward-Looking Statements**

Certain statements in this announcement are forward looking statements. Forward looking statements can generally be identified by the use of words such as "anticipate", "estimate", "expect", "project", "intend", "plan", "believe", "target", "may", "assume" and words of similar import. These forward-looking statements speak only as at the date of this announcement. These statements are based on current expectations and beliefs and, by their nature, are subject to a number of known and unknown risks and uncertainties that could cause the actual results, performances and achievements to differ materially from any expected future results, performance or achievements expressed or implied by such forward looking statements.

No representation, warranty or assurance (express or implied) is given or made by AVE that the forward-looking statements contained in this announcement are accurate, complete, reliable or adequate or that they will be achieved or prove to be correct. Except for any statutory liability which cannot be excluded, AVE and its respective officers, employees and advisers expressly disclaim any responsibility for the accuracy or completeness of the forward looking statements and exclude all liability whatsoever (including negligence) for any direct or indirect loss or damage which may be suffered by any person as a consequence of any information in this announcement or any error or omission therefrom.

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Global Cannabis Intelligence Virtual Summit

Overcoming cannabinoid formulations challenges  
using TPM<sup>®</sup>, a novel form of Vitamin E

June 2021



# Cannabinoids as medicine

In the past decade, there has been a transformational shift resulting from the recognition of the therapeutic potential of cannabis and cannabis extracts

Many countries around the world have legalized medicinal cannabis extracts for medicinal purposes, while others have also allowed consumer and recreational uses.

Due to the previous illegal nature of cannabis, normal R&D into formulation development has been minimal, and the initial product offerings were simple oil based formulations.

Moving forward, a range of more acceptable dosage forms are required to fulfil the needs of patients, physicians and consumers.



# The problems of formulating cannabinoids

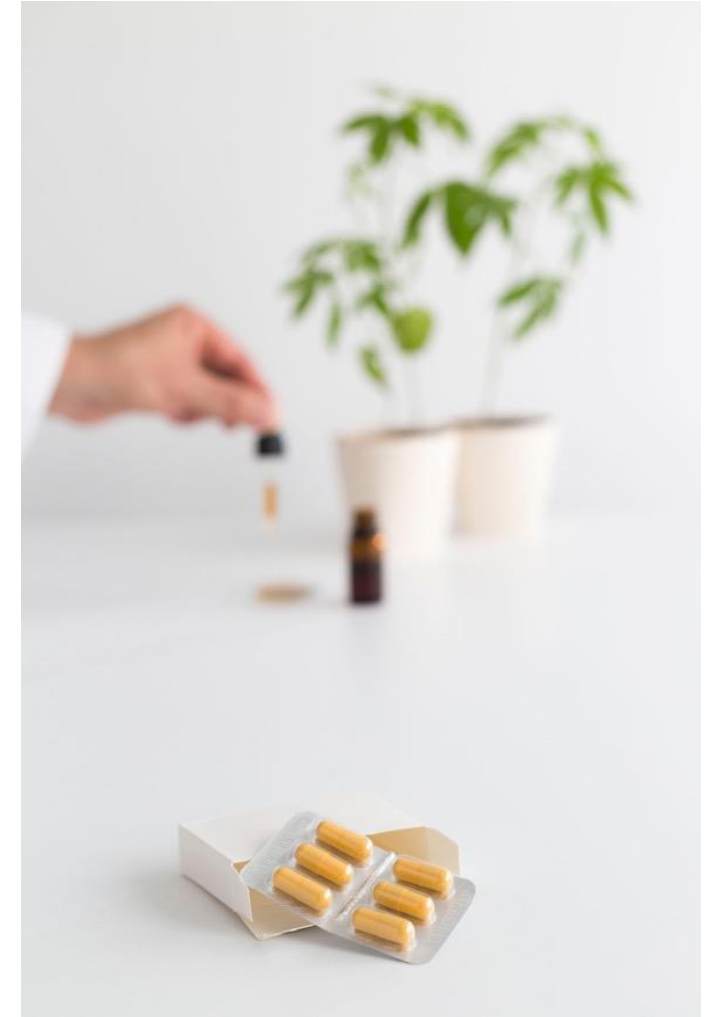
Cannabinoids (the key active compounds in cannabis) are oil soluble molecules with low solubility in water

Oil soluble molecules have poor oral bioavailability, which is also true for cannabinoids (3-10% absorbed)

This presents challenges for developing formulations that can deliver cannabinoids to the body efficiently.

Increasing cannabinoid bioavailability has become a focus for many laboratories around the world, as increasing bioavailability can allow;

- ✓ Greater therapeutic effect
- ✓ New indications, previously untreatable because of high doses required
- ✓ Reduced dosing for cost savings to patients
- ✓ Provide technical/commercial differentiation



# Overview of TPM®

TPM is a proprietary combination of two forms of phosphorylated vitamin E

TPM has enhanced vitamin E activity

TPM is a unique excipient that encapsulates drug molecules

TPM has been used to formulate drugs to improve their:

- solubility
- stability
- oral bioavailability
- dermal/transdermal delivery

TPM has an excellent safety profile making it ideal for drug reformulation

TPM reformulated drugs have:

- improved pharmaceutical properties and performance
- Commercial opportunities for differentiation and patent protection

Propofol TPM®



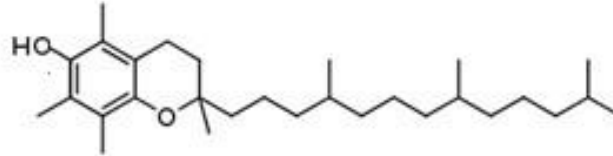
With TPM



Without TPM

# TPM is created from Vitamin E

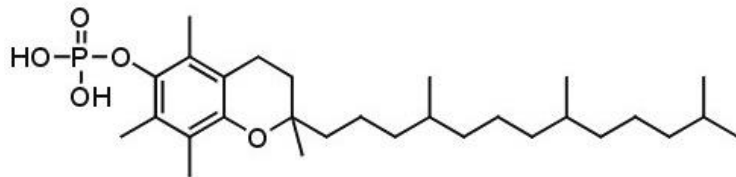
**Vitamin E  
( $\alpha$ -Tocopherol)**



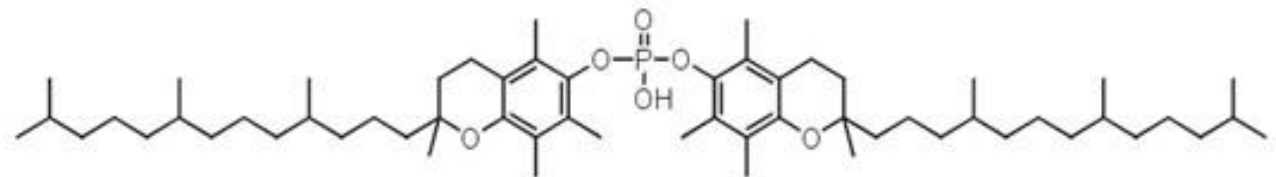
**Phosphorylation  
Process (Patented)**

$C_{29}H_{51}O_5P$   
MW = 510.69

**$\alpha$ -Tocopheryl  
Phosphate (TP)**



**di- $\alpha$ -Tocopheryl  
Phosphate (T2P)**  $C_{56}H_{99}O_6P$   
MW = 923.38



**Tocopheryl Phosphate Mixture (TPM) = mixture of TP & T2P**

# TPM has enhanced Vitamin E activity

## Activity

- Enhanced Vitamin E activity (non-antioxidant roles)
- Anti-inflammatory activity
- Benefits for dyslipidemia
- Improved endothelial dysfunction
- Potential cardio-protection
- Dermal anti-erythema

## Safety

- Metabolized to tocopherol
- Has GRAS status for oral consumption

**$\alpha$ -Tocopheryl phosphate: A novel, natural form of vitamin E**

Robert Gianello<sup>a</sup>, Roksan Libinaki<sup>a</sup>, Angelo Azzi<sup>b</sup>, Paul D. Gavin<sup>a</sup>, Yesim Negis<sup>a</sup>, Jean-Marc Zingg<sup>b</sup>, Phillip Holt<sup>c</sup>, Hooi-Hong Keah<sup>a</sup>, Annike Griffey<sup>a</sup>, Andrew Smallridge<sup>d</sup>, Simon M. West<sup>e</sup>, Esra Ogru<sup>e,\*</sup>

**Effect of tocopheryl phosphate on key biomarkers of inflammation: Implication in the reduction of atherosclerosis progression in a hypercholesterolaemic rabbit model**

Roksan Libinaki,<sup>\*</sup> Sonja Tesanovic,<sup>†</sup> Aileen H. ...

**Cardioprotection with  $\alpha$ -tocopheryl phosphate: Amelioration of myocardial ischemia reperfusion injury is linked with its ability to generate a survival signal through Akt activation**

Subhendu Mukherjee<sup>a</sup>, Istvan Lekli<sup>a</sup>, Manika Das<sup>a</sup>, Angelo Azzi<sup>b</sup>, Dipak K. Das<sup>a</sup>

DOI: 10.1111/1440-1681.12821

WILEY

SPECIAL ARTICLE

**The effect of tocopheryl phosphates (TPM) on the development of atherosclerosis in apolipoprotein-E deficient mice**

... Vinh<sup>2</sup> | Sonja Tesanovic-Klajic<sup>2</sup> | Robert Widdop<sup>2</sup> |

**Modulation of Cell Proliferation and Gene Expression by  $\alpha$ -Tocopheryl Phosphates**

Relev...

**Evaluation of the safety of mixed tocopheryl phosphates (MTP)—A formulation of  $\alpha$ -tocopheryl phosphate plus  $\alpha$ -di-tocopheryl phosphate**

R. Libinaki<sup>a</sup>, E. Ogru<sup>b</sup>, R. Gianello<sup>a,\*</sup>, L. Bolton<sup>c</sup>, S. Geytenbeek<sup>a</sup>

**and Inflammation**

ANELLO,<sup>b</sup>  
MARC ZINGG,<sup>c</sup>

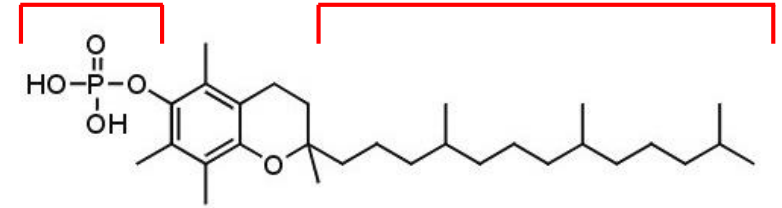


# TPM physicochemical properties

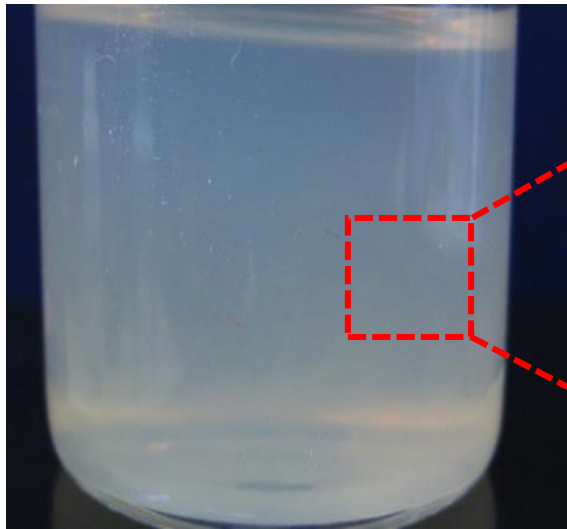
- The addition of the phosphate groups makes TPM<sup>®</sup> more amphipathic in comparison to  $\alpha$ -tocopherol (an oil)
- TPM can self assemble into vesicles ~100-150nm in diameter

Water “loving”

Water “hating”

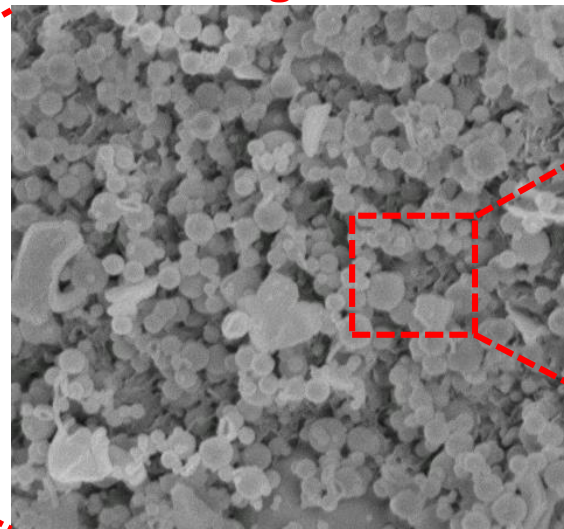


x1 magnification



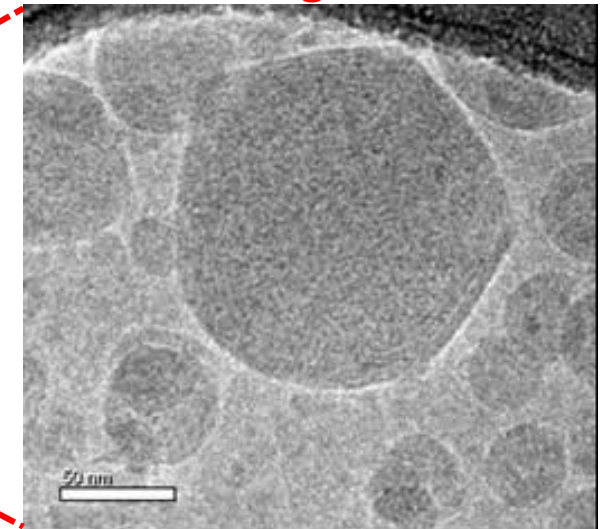
TPM<sup>®</sup> suspension

x25,000 magnification



Cryo-SEM

x500,000 magnification



Cryo-TEM

# TPM dissolves drug molecules

Increased Drug Solubility...

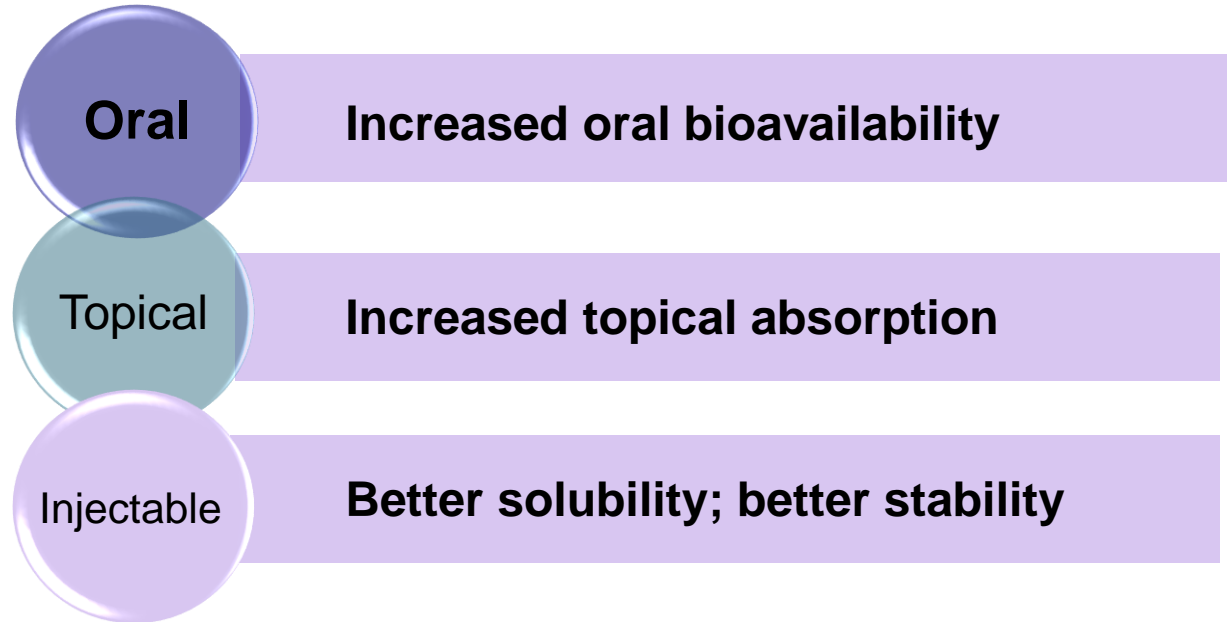


With TPM

Without TPM



Benefits many routes of administration



**Lipid soluble molecules are entrapped within TPM® vesicles at efficiencies greater than 90%**

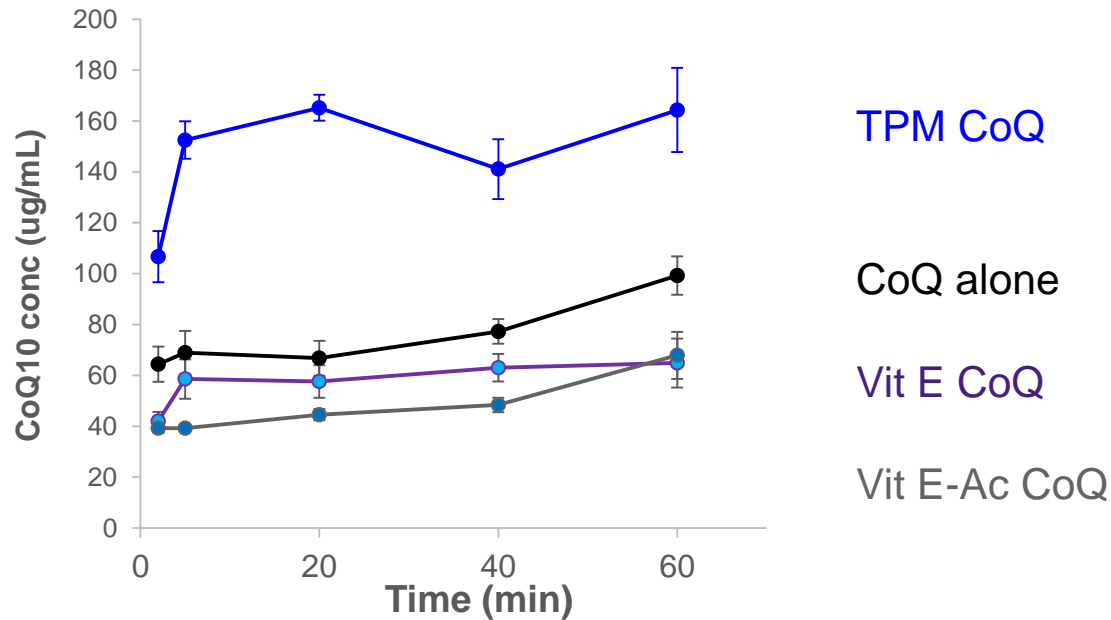
**- Gavin *et al.*, Drug Delivery and Translational Research, 2016**

# Oral Challenges: Low Bioavailability

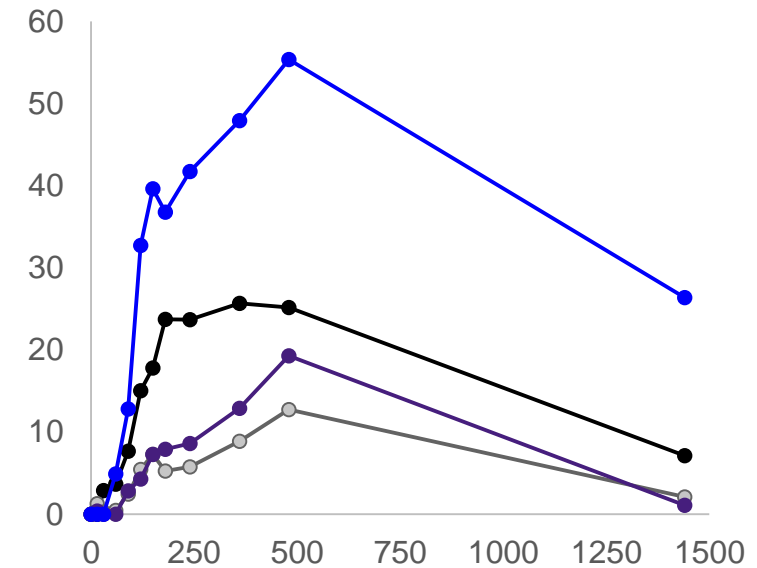
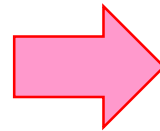
A new lipid excipient, phosphorylated tocopherol mixture, TPM enhances the solubilisation and oral bioavailability of poorly water soluble CoQ<sub>10</sub> in a lipid formulation

Anna C. Pham<sup>a</sup>, Paul Gavin<sup>b,\*</sup>, Roksan Libinaki<sup>b</sup>, Gisela Ramirez<sup>a</sup>, Ben J. Boyd<sup>a,c,\*\*</sup>

- Model lipid soluble drug = CoEnzyme Q<sub>10</sub> (CoQ<sub>10</sub>)



TPM enhances CoQ<sub>10</sub> solubility over other forms of Vitamin E in vitro



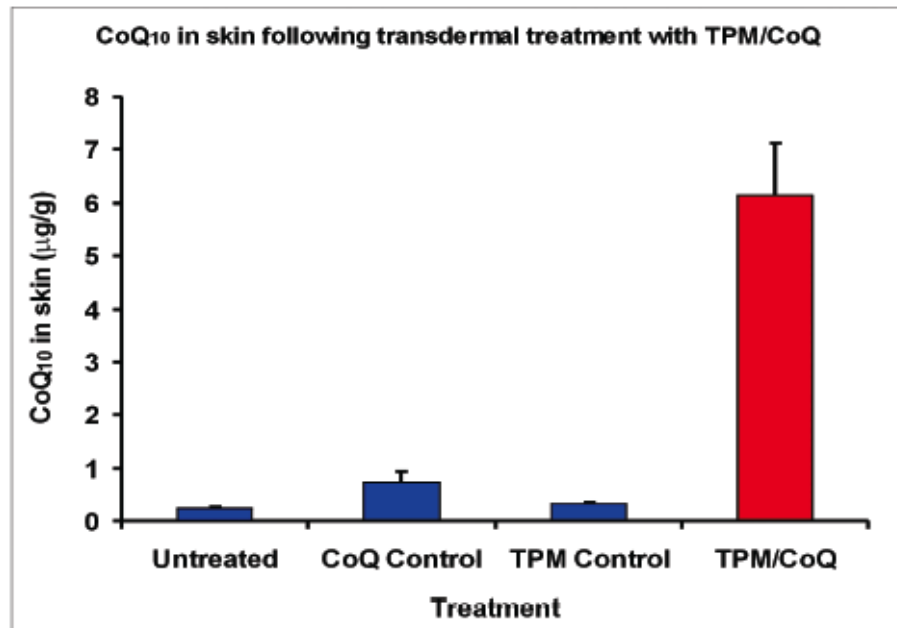
TPM enhances CoQ<sub>10</sub> bioavailability over other forms of Vitamin E in vivo

# Topical Challenges: Poor absorption

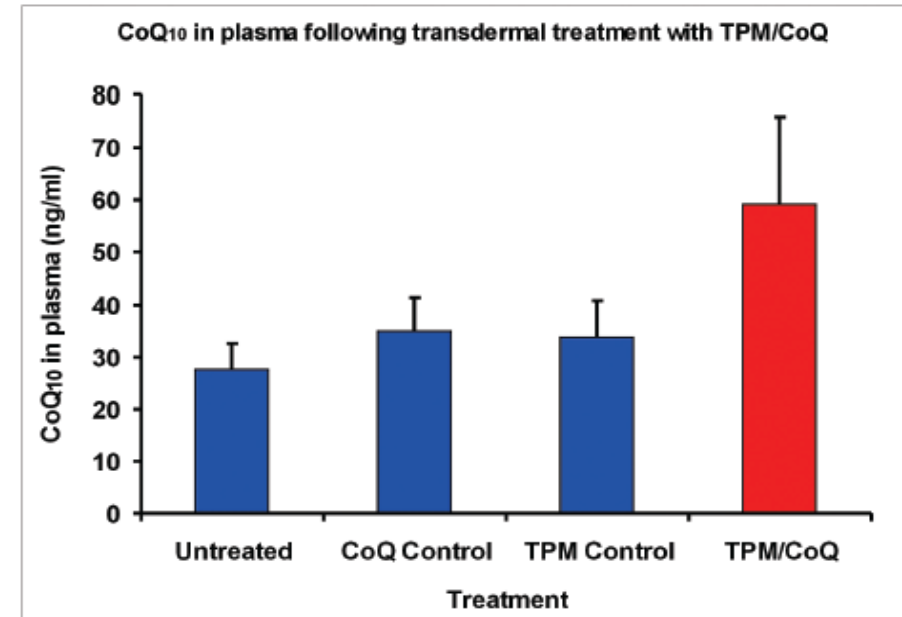
- Model lipid soluble drug = CoEnzyme Q<sub>10</sub> (CoQ<sub>10</sub>)

Tocopheryl phosphate mixture (TPM) as a novel lipid-based transdermal drug delivery carrier: formulation and evaluation

Paul D. Gavin<sup>1</sup> · Mahmoud El-Tamimy<sup>1</sup> · Hooi Hong Keah<sup>1</sup> · Ben J. Boyd<sup>2,3</sup>



TPM enhances CoQ<sub>10</sub> absorption into the skin



TPM enhances CoQ<sub>10</sub> absorption through the skin into plasma

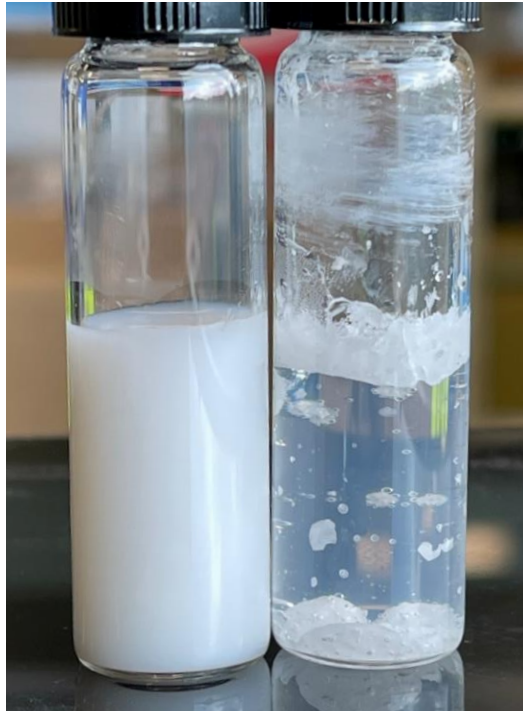
Avecho

# Cannabinoid TPM formulations



# TPM encapsulates and dissolves cannabinoids

## CBD Solubility



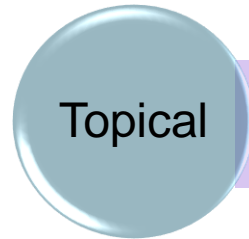
With TPM    Without TPM



## Products under development



**Increased oral bioavailability**



**Increased topical absorption**

**Works with CBD, THC, natural extracts, pure synthetic products**

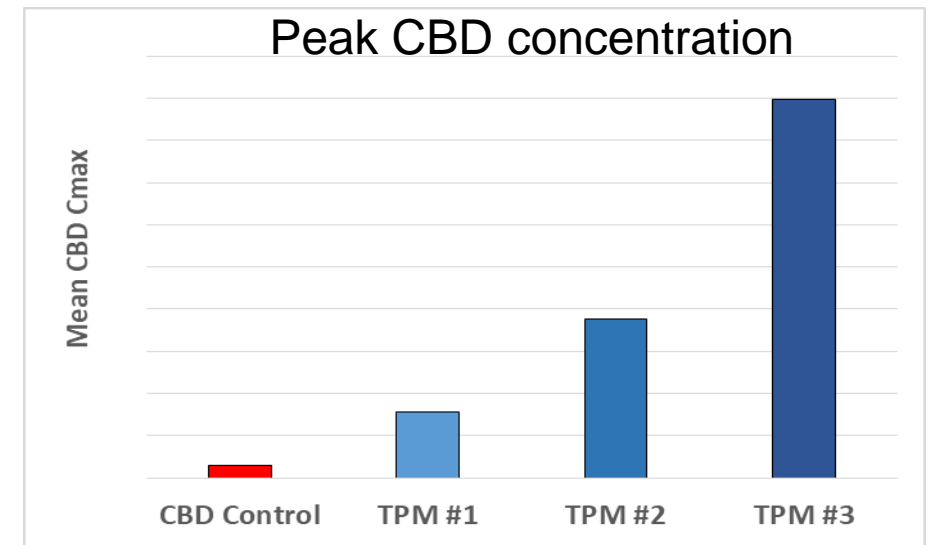
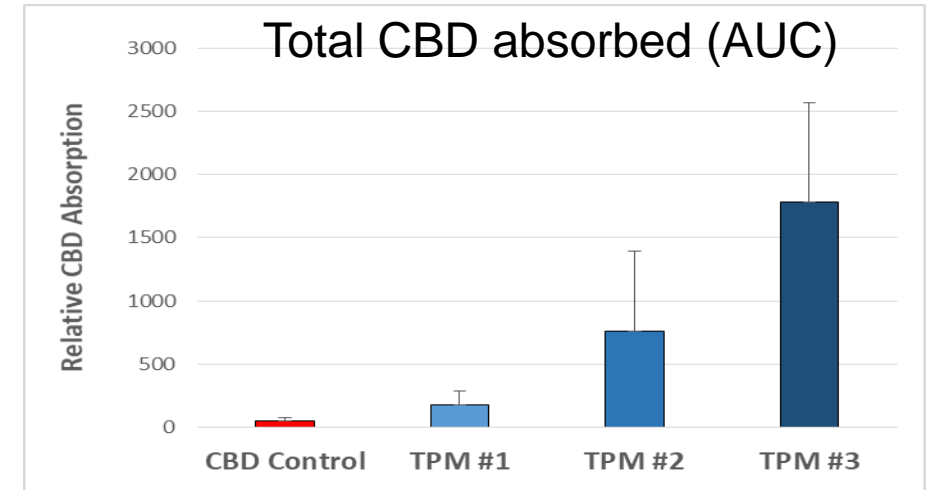
# TPM formulations increase oral bioavailability of CBD

Research conducted at Bioneer:FARMA in Copenhagen

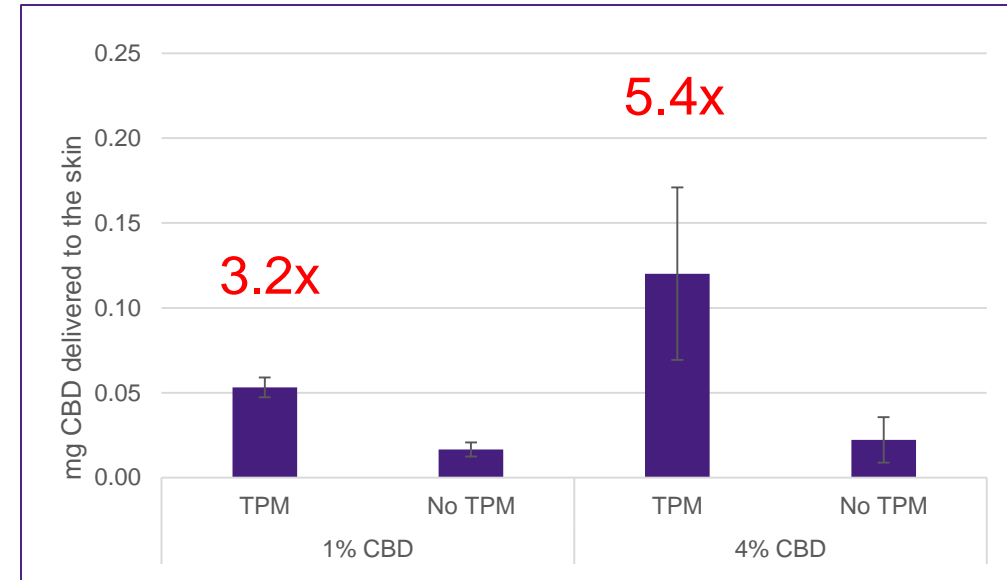
Rats received a single oral dose of CBD and drug content measured in the blood over time. Absorption from TPM formulations compared against CBD in MCT (as sold to patients).

- ✓ All TPM® formulations produced higher mean AUC and Cmax than the commercial CBD formulation.
- ✓ Increases in AUC produced by TPM formulations ranged from **~4-40 times**
- ✓ Increases in Cmax produced by TPM formulations ranged from **~6-41 times**
- ✓ These increases were statistically significant for the best performing TPM formulations.

**TPM® formulations to be taken forward into clinical trials**



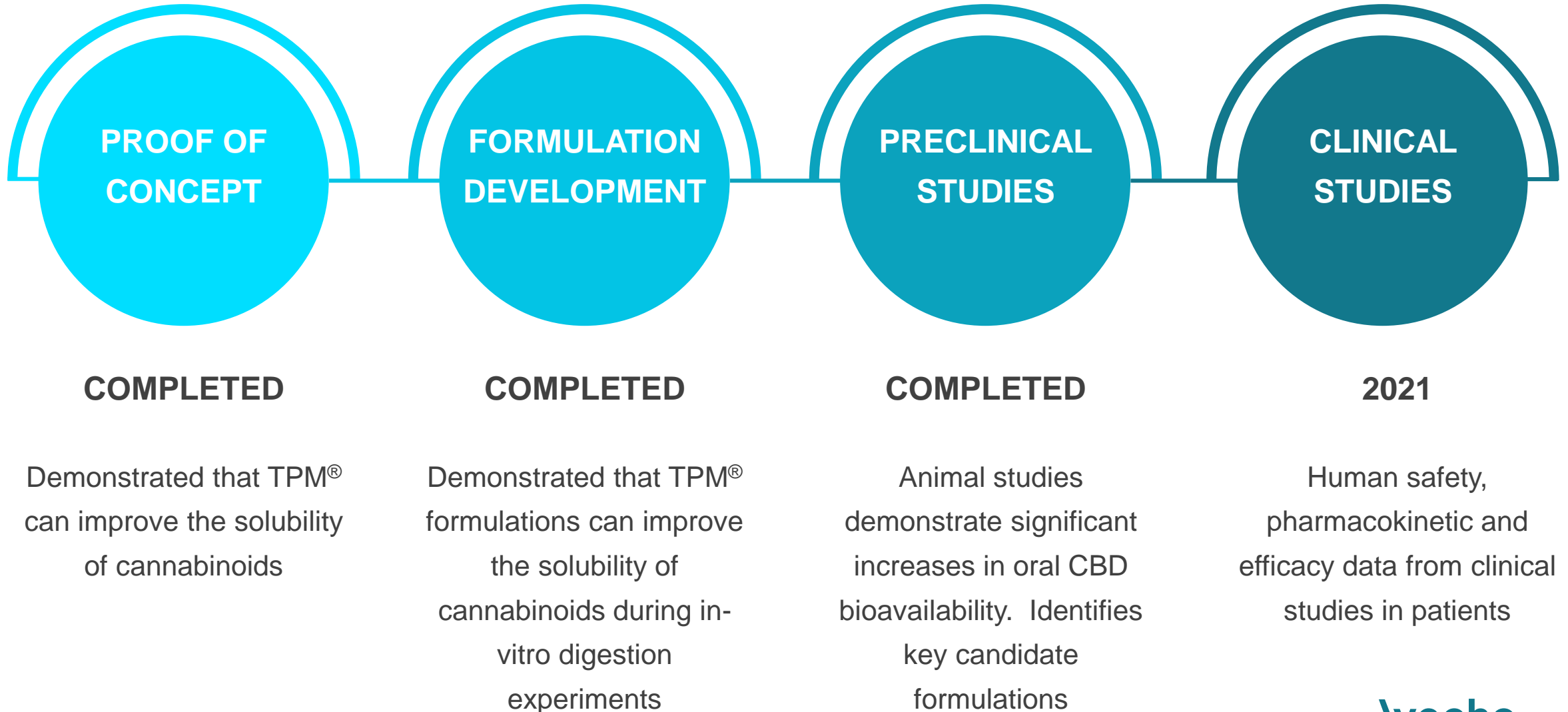
# TPM formulations increase dermal absorption of CBD



- CBD delivery tested from topical vehicles developed for commercial TPM<sup>®</sup> formulations (ie. Voveran TPM)
- Dermal CBD absorption using Franz cells increased by 3-5 times in presence of TPM



# Plan for developing oral TPM formulation of cannabinoids



# Oral Pharmaceutical CBD Product

- 75 mg CBD TPM soft-gel capsule being developed now (Catalent)
- Fill formulation already on observational clinical trial in Australia
- Soft-gel capsules to be tested in Phase I PK study
- Followed by pivotal Phase III study in Australia
- Registration with TGA in Australia to follow.



**Enhanced CBD product to be taken into other territories/markets with partnerships**

# Summary

- ✓ TPM increases the solubility of CBD
- ✓ TPM formulations appropriate for broad range of dosage forms
- ✓ TPM increases the oral bioavailability of CBD
- ✓ TPM increases the dermal absorption of topical CBD
- ✓ TPM activity may be complementary to a range of indications

## Products under development

- CBD soft-gel capsule (Phase I/III) for registration with the TGA
- CBD oil formulation (Observational Study)
- Topical cannabinoid formulations
- Investigating indications that may specifically benefit from TPM (cardiovascular, dermatology)

## **TPM<sup>®</sup> formulations available for use in other markets**

# Questions?

Dr Paul Gavin  
**Chief Executive Officer**  
+61 3 9002 5000  
[pgavin@avecho.com.au](mailto:pgavin@avecho.com.au)

**Melbourne Office**  
Unit A8, 2A Westall Road  
Hallmarc Business Park  
Clayton VIC 3168  
Australia  
Tel: +61 3 9002 5000  
Email: [info@avecho.com.au](mailto:info@avecho.com.au)

