

**epm**  
Therapeutics

Investor Presentation

# **Developing Novel Treatments for Unmet Rare Diseases**

January 2024

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# Executive Summary

**EPM 's Innovative Cannabinoid Chemistry**

**Prader-Willi Syndrome (PWS)**

**EPM301: A Solution to PWS**

**Plan for Efficiently Accruing Value for Exit**

**Science and Team with Unparalleled Pedigree**

## Executive Summary

# EPM's Innovative Cannabinoid Chemistry

EPM is developing a series of synthetic cannabinoid derivatives, which have shown therapeutic potential in a number of animal models.



# **EPM301: Cannabidiol Acid Methyl Ester**

## **EPM301 is a New Chemical Entity (NCE)**

EPM301 is EPM's lead compound and is protected by method use claims. EPM301 is one of a family of 14 fully synthetic cannabinoid molecules (eight that are novel and have composition of matter coverage).

## **EPM301 is a CBDA Analogue with Increased Stability**

EPM301 is a synthetic cannabidiol acid (CBDA) analogue that has increased stability compared to CBDA.

## **EPM301 has Demonstrated Efficacy in Multiple in Vitro and in Vivo models**

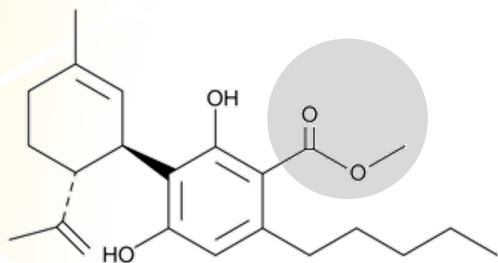
Demonstrated efficacy in various animal models including GI, Metabolic, CNS and Dermatological disorders (see EPM publications list).

## **EPM Carefully Selected a Lead Indication for EPM301**

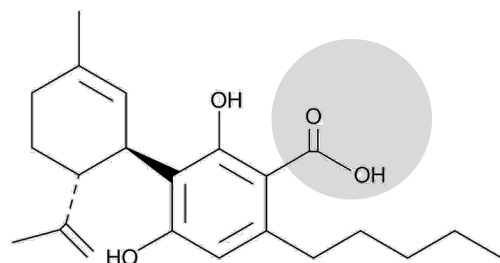
As a result of the pre-clinical activity demonstrated by EPM301, the EPM team evaluated a number of options in order to select an appropriate lead indication considering market size, chance of success and significant unmet clinical need.

# Product Profile: Chemistry & Formulation

## Fully Synthetic Cannabidiol (CBD)



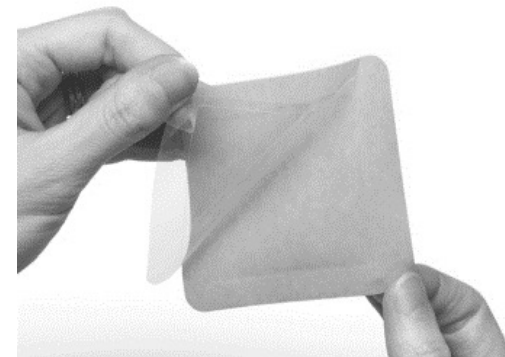
**EPM301**



**CBDA**

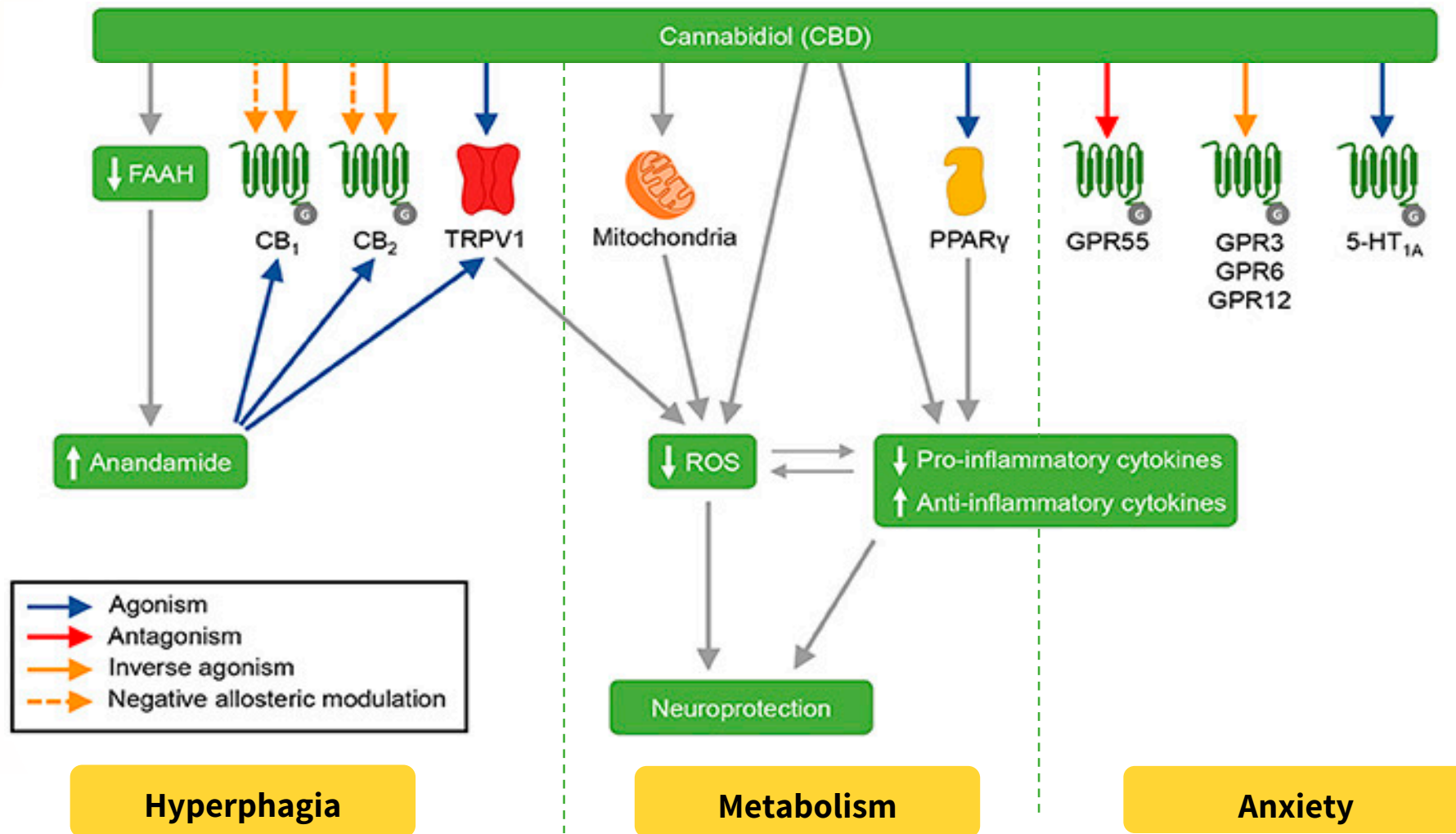
- EPM301 is patent protected for use in the management of PWS patients.
- EPM301 has demonstrated stability in ethanol at 3 different storage conditions (RT, 4°C and -20°C) for at least 12 months.
- The manufacture of EPM301 has been successfully scaled up from a laboratory quantity of 5 g to a batch size of 100 g.

## Delivery Systems



- Initially formulated as an oral solution.
  - Suitable for pediatrics/adolescents
- Plans to develop an alternative more efficient formulation as a transdermal patch.
  - Suitable for pediatrics/adolescents/adults
  - Suitable for application by caregivers

## Product Profile: Mechanism of Action (MOA) of CBD in PWS



# EPM: Collaboration with Recognized Supply Partners

## Enhanced Its Science Pedigree by Collaborating with Leading Academics

EPM has worked with leading global Academic Research Centers including Centers in the UK, Canada and Israel.

## Drug Development Efforts Have Benefitted by Our Work with Leading Companies

EPM has worked with leading Contract Research Organizations from around the globe, including Recipharm (Sweden), NCK (Denmark), LabCorp (United Kingdom) to Charles River Labs (U.S.).



## Executive Summary

# Prader-Willi Syndrome (PWS)

Prader-Willi Syndrome (PWS) is a rare genetic disorder for which there are no FDA approved treatments for hyperphagia (excessive appetite) the most debilitating symptom of PWS patients.



# Prader-Willi Syndrome (PWS)

## Disease

- A rare genetic disorder affecting development and growth with substantial unmet need.
- Caused by genetic defect on Chromosome 15.
- Approximately 30,000 patients in the United States<sup>1</sup>
- No FDA approved treatments for the most significant symptoms of PWS.

## Signs & Symptoms

- Hyperphagia (excessive appetite): is the most debilitating symptom according to caregivers.
- Growth: Short stature, intellectual disability.
- Behavioral: anxiety, cognitive rigidity, irritability.
- Sleep abnormalities.



# PWS: Market Dynamics<sup>1</sup>

## Epidemiology


The prevalent population of PWS is estimated to be 47,560 across 7MM<sup>2</sup> in 2018. United States accounts for the highest PWS cases. Among the EU5 countries Germany had the highest population of PWS, followed by Italy.

## Therapeutic Alternatives

At present, pharmacological management of PWS focuses largely on the use of human growth hormone (HGH) supplementation which is approved in the US. Central nervous system and cardiovascular agents are used with increasingly frequency in older patients.

## Market Outlook

The global market of PWS was estimated to be \$2.1 B in 2018. Hormone treatment holds the highest patient share amongst the therapeutic options for the treatment of PWS.



**PWS estimated  
market opportunity  
of \$900 million<sup>3</sup> in  
the United States**

# PWS: Most Significant Unmet Need.... Hyperphagia Control

*“Hyperphagia prevents individuals with PWS and their families from enjoying many normal community experiences, and often leads to obesity, the complications of which are the leading causes of death in PWS”*

**Lynne Bird, MD**

Clinical Geneticist, Rady Children’s Hospital ,San Diego

***“The most important unmet need for people with PWS is treatment of their hyperphagia. This would not only help prevent and reduce morbidity and mortality but could improve the emotional well-being and quality of life of themselves, family members and caregivers. It might also allow use of less restrictive practices for control of the food environment, saving residential and care costs”***

**Dr. Tony Goldstone MA MRCP PhD FTOS**

Head, PsychoNeuroEndocrinology Research Group Faculty of Medicine, Imperial College, London

# PWS: Current Available Treatments

There is currently no cure for Prader-Willi Syndrome, treatment is based on treating the symptoms of the disorder as they arise.

- Strict supervision of diet (there are no medical means of curbing appetite).
- Plenty of physical activity to help maintain the child's body weight within the normal range.
- Growth hormone (GH) treatment to overcome the hormone deficiency that contributes to the child's short stature.
- Hormone therapy to increase muscle mass.
- Hormone therapy to boost inadequate sex hormone levels.
- Medication to help control any obsessive and compulsive behaviors.
- Orthopedic treatment for scoliosis or kyphosis.



# PWS: Current Development Programs<sup>1</sup>

Company	Drug	Indication	Status
<b>Levo Therapeutics, Inc.</b>	LV101	Hyperphagia, anxiousness and distress associated with PWS	Complete response letter from FDA- need new clinical trial
<b>Soleno Therapetutics, Inc.</b>	DCCR	Hyperphagia associated with PWS	Phase 3 clinical trial showed no significant difference between the DCCR treated patients and placebo treated patients
<b>Acadia Pharmaceuticals</b>	ACP-101	Hyperphagia	Moving ahead to compare the drug ACP-101 with a placebo in a double-blind study as part of the Phase 3 study
<b>Sanonia</b>	Tesomet	Hyperphagia	Phase 2b clinical trial paused due to lack of funding
<b>Aardvark Therapeutics, Inc.</b>	ARD-101	Hyperphagia	Open label Phase 2 <sup>a</sup> study still recruiting
<b>Gedeon Richter Plc</b>	RGH-706	Hyperphagia	Phase 2 study currently recruiting
<b>ConSynance</b>	CSTI-500	Hyperphagia	Phase 1



# EPM301 in PWS: Rationale and Logic

## 1. Multifactorial MOA Characteristics

Supports scientific rationale for treatment of PWS given the multiple symptomologies.

## 2. Botanical CBD Read-Across Data

In refractory seizure studies, decreases in appetite and weight have been reported as adverse events<sup>1</sup>.

## 3. Extensive Literature

Studies and associated data have shown that the endocannabinoid system (ECS), including CBD, is involved in the control of appetite and weight<sup>2,3</sup>.

## 4. Pre-Clinical Studies

Results in a mouse model demonstrated that treatment with EPM301 reduced body weight and food intake.

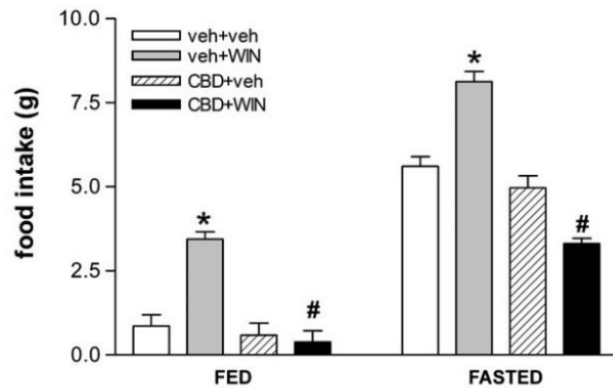
## EPM301: “Reverse Engineering” from Botanical CBD Studies



Supportive evidence from a botanically-derived CBD in the treatment of refractory seizure studies reported **appetite suppression in up to 22% of patients versus 5% in placebo<sup>1</sup>**

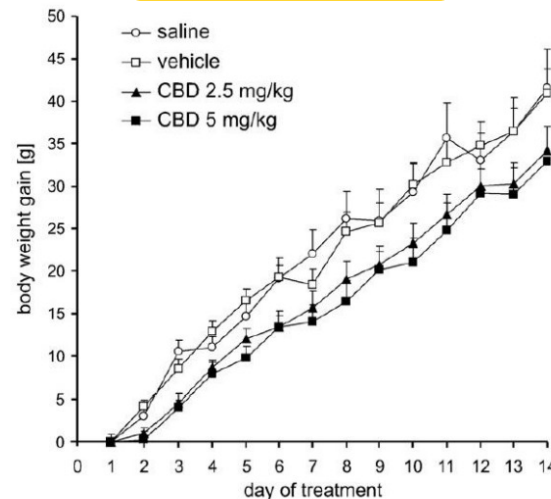
# Scientific Evidence for CBD in the Treatment of Core PWS Symptoms

## Hyperphagia



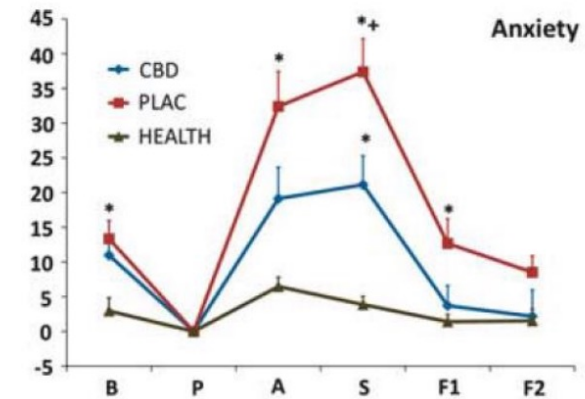
Cannabidiol inhibits hyperphagia induced by CB<sub>1</sub> agonist<sup>1</sup>

## Metabolism



Cannabidiol inhibits body weight gain via CB<sub>2</sub> receptors<sup>2</sup>

## Anxiety



Subjects with social anxiety disorder (SAD), treatment with cannabidiol results: lower anxiety compared to placebo<sup>3</sup>

# Executive Summary

## **EPM301: A Solution to PWS**

EPM's lead compound, EPM301 has demonstrated efficacy in treating Hyperphagia in a mouse model of PWS.

# EPM's Approach to PWS

## Targeting Hyperphagia the Leading Problem with PWS

EPM is targeting Hyperphagia in PWS patients and aims to reduce food intake along with body weight and increase energy levels.

## Received Orphan Drug Designation (ODD)

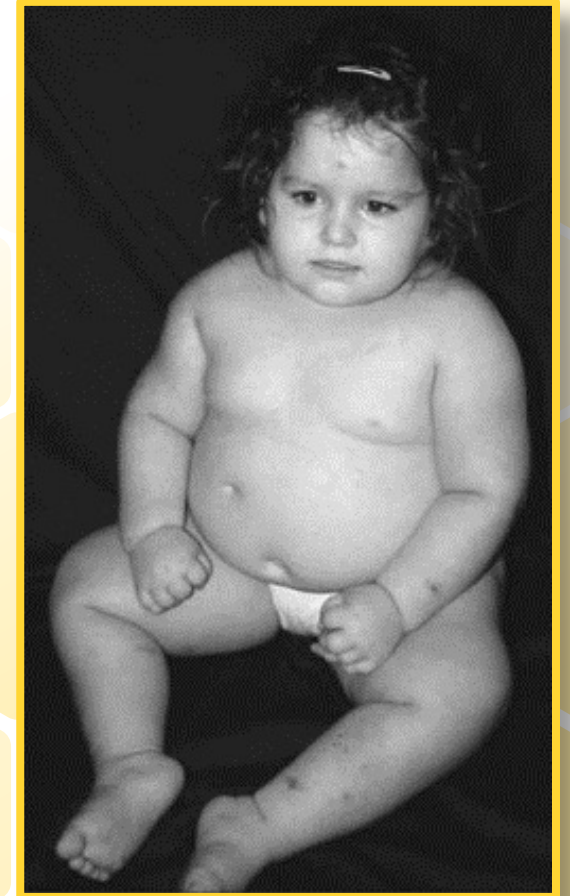
An Orphan Drug Application was submitted to the FDA in Q3 2022 and ODD approval was granted in Q1 2023.

## PWS May Be Springboard to EPM's Future Pipeline

PWS may have future relevance to building a successful pipeline for EPM with new molecules targeting metabolic and other related disorders.

## EPM301 Pre-Clinical Data is Supportive of a Clinical Benefit in PWS

Pre-clinical studies in murine models that mimic PWS suggest potential therapeutic efficacy in treating hyperphagia, obesity and its metabolic abnormalities in PWS patients.





# EPM301: Pre-Clinical Results in Mouse Models of PWS

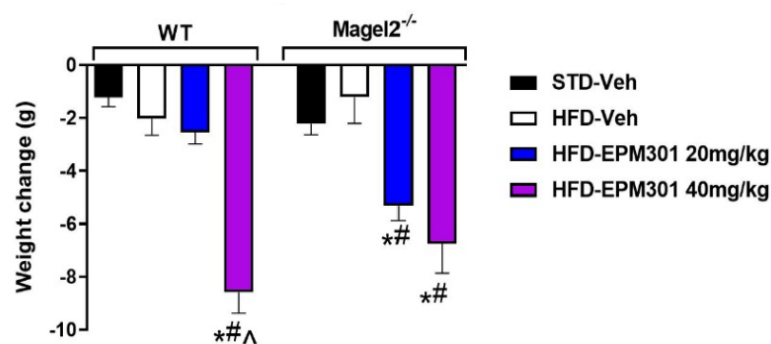
## Magel2 Null Mice, a Valid PWS Model Combined with Varied Diets

Magel2 null mice and their healthy wildtype (WT) siblings were either fed with a high fat diet (HFD) or with a standard (STD) diet for 14-16 weeks.

## Dosage of EPM301 and Control

First experiment involved dosing EPM301 at 20 & 40 mg/kg/day via IP injections for 28 days compared to vehicle. The second, dosing EPM301 20 mg/kg/day or vehicle were given via IP injections for 18 weeks.

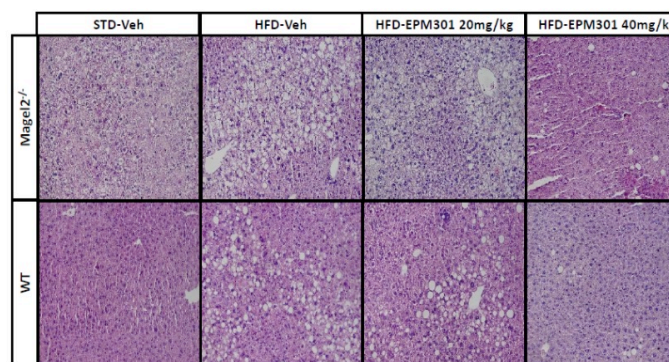
**EPM301 treatment reduced weight and reduced fat in the liver in Magel2 null mice and their WT siblings and reduced food intake in Magel2 null mice**



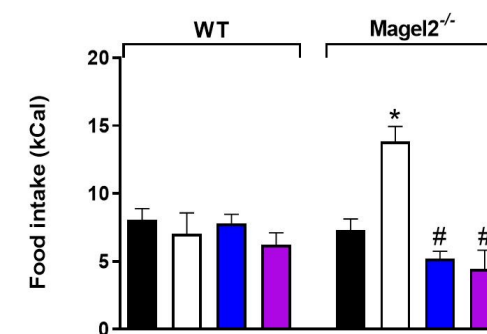
\* p<0.05 (difference between STD and HFD mice – HFD-Veh or HFD-CBDA-ME (EPM301))

# p<0.05 (difference between HFD-Veh and HFD-EPM301)

^ p<0.05 (difference between 40mg/kg and 20mg/kg EPM301)



Full research can be found in: Ben-Cnaan E, et al. The Metabolic Efficacy of a Cannabidiolic Acid (CBDA) Derivative in Treating Diet- and Genetic-Induced Obesity. Int. J. Mol. Sci. 2022; 23(10):5610



# Addressing Community Needs in Rare Disease

## Advocacy Groups



## Community Awareness

- Will incorporate all relevant and meaningful unmet patient needs into the clinical program.
- Support and study awareness including educating families / communities.
- EPM support to enhance research in PWS.
  - PWSA USA Conference
  - FPWR Research Symposium & Family Conference
  - IPWSO Conference

# Plan for Efficiently Accruing Value for Exit

EPM plans to expand their patent portfolio and complete the studies required for an IND filing and conduct a Phase 1/2a clinical trial in PWS patients.

# **EPM301: Achievements and Near-term Milestones to IND Filing**

## **Cannabinoid Synthesis Program**

Initial synthesis scale-up is complete, with pharmaceutical scale-up to 5,000 g continuing.

## **Solubility and Stability Evaluated**

EPM has completed a solubility profile and stability assessment of EPM301.

## **Preliminary Oral Formulation Development Completed**

EPM has completed an assessment of potential oral formulations of EPM301.

## **Preliminary Toxicity Study Completed**

EPM has completed a gene toxicity program and has also demonstrated that EPM301 was well tolerated when administered via the IV route to rats. (see EPM301: Toxicity and Safety Study).

## **Complete pre-IND Tasks and Submit IND**

EPM will continue conducting the IND-enabling non-clinical studies for filing an Investigational New Drug (IND) application with the U.S. Food and Drug Administration.

# Use of Proceeds: Completion of IND-enabling PWS Studies of EPM301

## EPM301 CMC Development

Manufacture of GMP API supplies, toxicology supplies and GMP clinical supplies for the Phase 1 study.

## EPM301 Non-Clinical Toxicology Program

Conduct of 4-week toxicology studies in 2 species, plus associated non-clinical safety studies.

## Regulatory Activities

Pre-IND meeting with the FDA and preparation and submission of the IND to support the Phase 1 study.

Item	Estimated Cost	% of Total
<b>R&amp;D Expense</b>	<b>\$4.822.500</b>	<b>80,7%</b>
CMC Development	\$1.400.000	23,4%
Non-Clinical Toxicology Program	\$2.600.000	43,5%
Regulatory Activities	\$150.000	2,5%
Transdermal Patch Drug Development	\$100.000	1,7%
Other R&D expenses	\$250.000	4,2%
R&D Team	\$322.500	5,4%
<b>G&amp;A Expenses</b>	<b>\$1.157.000</b>	<b>19,3%</b>
<b>Total Seed Round</b>	<b>\$5.979.500</b>	<b>100,0%</b>

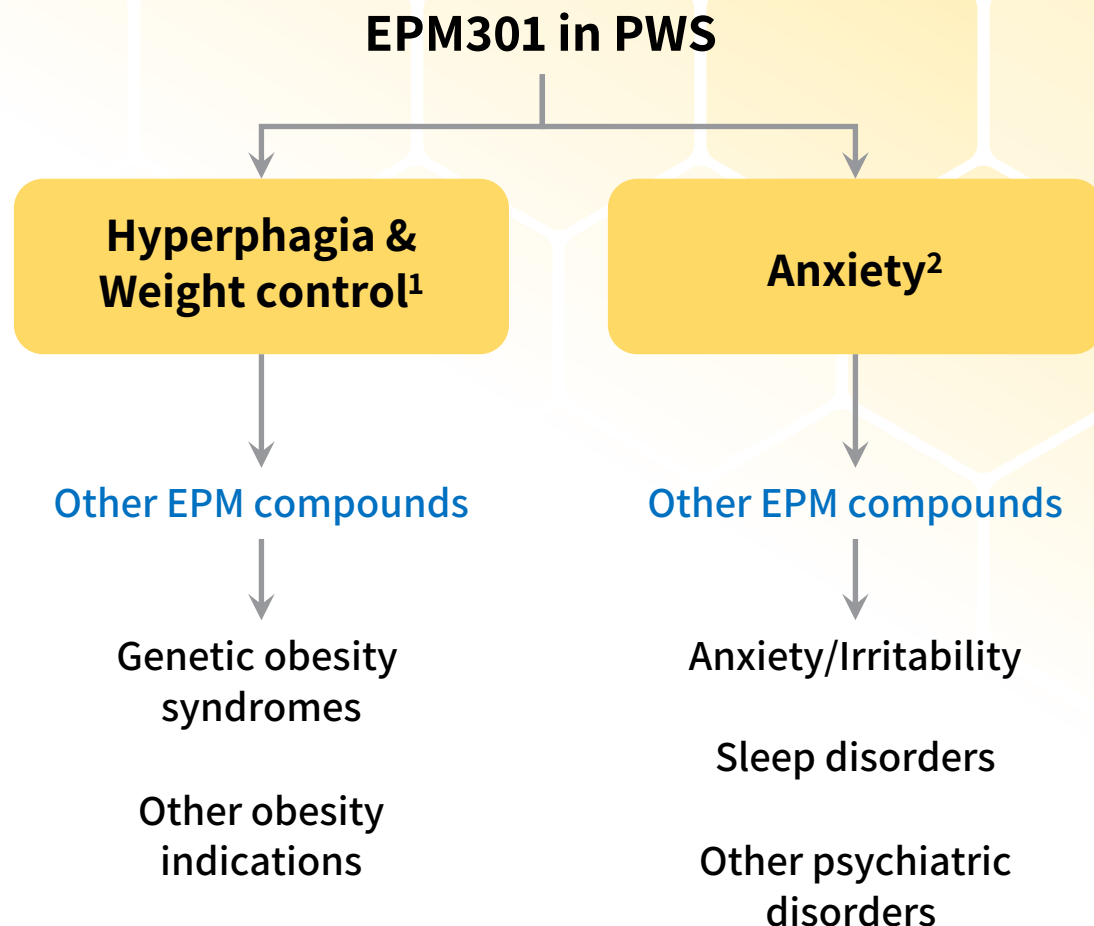


# EPM301: PWS Drug Development

Key Steps	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
<b>PWS Drug Development</b>										
Upscaling synthesis and producing clinical grade 5kg batches										
Continuation ICH storage evaluations & shipments										
Formulation development, active and placebo batches and CTM batch										
CTB stability 24 months										
IND-enabling non-clinical safety program										
Pre-IND meeting request and preparation										
IND preparation & submission										
First in Human clinical trial (SAD, MAD, FE) in HV's & PWS patients										
Initiation of clinical trial Phase 2a on PWS subjects										

# EPM301: Clinical Translation and Future Opportunities

- Obesity market expected to reach \$37.1B across 7MM3 by 2031
- KOLs emphasized the greatest unmet need is therapies with increased efficacy and weight loss maintenance.
- Current late-stage pipeline products employ the GLP-1RA MOA.
- Double and triple-agonist mechanisms are a dominant trend.



- The global anxiety disorders and depression treatment market is likely to reach \$16.1 B by 2032.
- Around 284 million people worldwide suffer from anxiety, yet only 36% seek therapy.
- North America accounts for the largest market share of treatments accounting for over 45%.

# Executive Summary

## Science and Team with Unparalleled Pedigree

EPM has recruited a Management team, Board of Directors and Scientific Advisory Board with a history of successful drug development in both the Biotech and Pharmaceutical sector.

# EPM: Cannabinoid Development Programs

## Development Pipeline Diversified on Molecules and Indications

EPM has a pipeline of programs evaluating various different cannabinoid acid esters, including EPM301 and CBGA ester, THCA ester and CBNA ester.

Molecules Group	Chemical Discovery	Pre-Clinical Models	IND-Enabling Studies (Formulation, Toxicology, CMC)
CBDA-ME			
CBGA-ME			
THCA-ME			
CBNA-ME			

# Valuable Intellectual Property Portfolio

## EPM Continues to Generate Multiple Layers of IP Coverage

EPM plans to leverage its proprietary platform to seek multiple layers of IP coverage (synthesis, formulation, composition of matter, use, mode of administration, therapeutic indications, etc).

## EPM Has Submitted Extensive Patent Applications to International Patent Offices

EPM has active patent applications, worldwide, for both medical and non-medical uses of its family of compounds.

## EPM Has Been Granted Four Patents

Four patents have already been granted to EPM in the United States, Mexico, Australia and the European Union.

## Broad Geographic Reach in Over 15 Major Countries

EPM's core IP is protected in over 15 key countries due to our work with leading intellectual property law firms.

**FENWICK**

**WEBB+CO**  
PATENT ATTORNEYS



# Management Team

**Peter Welburn, PhD**  
Chief Executive Officer



A senior pharmaceutical executive with over 30 years of international experience in R&D roles and general management in Biotech and Pharmaceutical companies. From 2011 to 2014 Dr. Welburn served as the General Manager of LEO Pharma Australia & New Zealand following the acquisition of Peplin by LEO Pharma.

**Phil Rose**  
President and COO



Phil has held operational positions in the United States of increasing responsibility in sales, marketing and administration for pharmaceutical companies such as Eli Lilly, GSK (VP Hospital Sales), Bausch Health (Vice President and General Manager for North America) and Obagi (President and CEO). Phil specializes in financial and product development strategy to maximize commercial potential. Phil is also a practicing Registered Pharmacist.

**Joseph Tam, PhD**  
Scientific Advisor



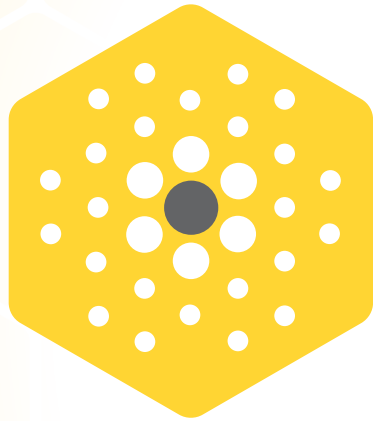
Prof. Tam is a world-renowned leader in the field of cannabis-based solutions. He is Head of the Obesity and Metabolism Laboratory at the Hebrew University of Jerusalem and Head Director of the Multidisciplinary Center of Cannabinoid in Israel. Prof. Tam received the NCATS Director's Awards from the National Institute of Health, and the Chowers Prize for Endocrinology by the Israel Endocrinology Society.

**Jaime Rodriguez**  
Director



Mr. Rodriguez is a result driven industry agnostic executive with extensive knowledge across multiple geographies. Has proven experience in world class companies as a consultant at Bain & Company and as Chief Strategy Officer in publicly traded organizations. Mr. Rodriguez serves in several Board of Directors and Advisory Committees sharing knowledge with entrepreneurs and businessman. Currently is the General Manager at family office for one of Mexico's prominent families.

# Appendix



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# EPM301: Toxicity and Safety Study

## Objective

To determine the toxicity of CBDA-ME, when given via a single intravenous (bolus; 1-2 minutes) injection into the rat tail vein in the Maximum Tolerated Dose (MTD) phase followed by 7 consecutive days of repeat dosing (single dose/day/rat) in the Dose Range Finding (DRF) phase

## Results

- MTD: 100 mg/kg/day
- No unscheduled deaths reported
- No notable sex differences were observed at 25, 50 or 100 mg/kg/day in the DRF study
- Following transient clinical signs were observed at all dose levels:
  - Abnormal respiratory rate, abnormal gait, decreased activity, subdued behavior, salivation, ploughing and low carriage
  - All signs had recovered by 3 hours post-dose on each dosing occasion

## Overall Conclusion

**EPM301 was well tolerated when administered via IV to rats.**

# EPM Publications

**Prader-Willi Syndrome** Ben-Cnaan, E. et al. The metabolic efficacy of a cannabidiolic acid (CBDA) derivative in treating diet- and genetic-induced obesity. International Journal of Molecular Sciences (2022). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9144717/>

**Anxiety and Nausea** Pertwee, R. G. et al. Cannabidiolic acid methyl ester, a stable synthetic analogue of cannabidiolic acid, can produce 5-HT<sub>1A</sub> receptor-mediated suppression of nausea and anxiety in rats. Br. J. Pharmacol. 175, 100–112 (2018). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5740240/>

**Nausea** Rock, E. M. et al. Evaluation of repeated or acute treatment with cannabidiol (CBD), cannabidiolic acid (CBDA) or CBDA methyl ester (HU-580) on nausea and/or vomiting in rats and shrews. Psychopharmacology (Berl). 237, 2621–2631 (2020). <https://pubmed.ncbi.nlm.nih.gov/32488349/>

**Neuropathic Pain** Zho.Y.F, et.al. An evaluation of the anti-hyperalgesic effects of cannabidiolic acid-methyl ester in a preclinical model of peripheral neuropathic pain, British Journal of pharmacology (2020). <https://bpspubs.onlinelibrary.wiley.com/doi/abs/10.1111/bph.14997>

**Major Depressive Disorders** Hen-Shoval, D. et al. Acute oral cannabidiolic acid methyl ester reduces depression-like behavior in two genetic animal models of depression. Behav. Brain Res. 351, 1–3 (2018). <https://pubmed.ncbi.nlm.nih.gov/29860002/>

**Sleep-wake Cycle** EPM301 possess wake-promoting pharmacological properties and enhances the levels of wake-related neurochemicals. Murillo-Rodríguez, E. et al. Sleep and neurochemical modulation by cannabidiolic acid methyl ester in rats. Brain Res. Bull. 155, 166–173 (2020). <https://pubmed.ncbi.nlm.nih.gov/31838151>