

The logo for Tetra Bio-Pharma features the word "TETRA" in a large, bold, green sans-serif font. The letter "E" is stylized with a white cross inside it. Below "TETRA" is the word "BIO-PHARMA" in a smaller, bold, dark green sans-serif font. The background of the slide includes a green checkered pattern at the top, a white checkered pattern below it, and a green molecular structure graphic on the left side.

# **TETRA** **BIO-PHARMA**

Global Leaders in Cannabinoid-Based  
Drug Discovery and Development

**Guy Chamberland**

CEO and Chief Scientific Officer

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**SCIENTIFIC DATA AND  
INFORMATION ABOUT  
PRODUCTS CONTAINING  
CANNABIS OR  
CANNABIS-DERIVED  
COMPOUNDS**

-  
**FDA PUBLIC HEARING**

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31 MAY 2019

OTCQB: TBPMPF

TSX-V: TBP

# Overview of Clinical Trials Sponsored by Tetra Bio-Pharma

## ✓ Phase 1 trials

1. A Double-Blind Phase I Study to Assess Safety, Tolerability and Pharmacokinetics of Single and Multiple Daily Doses of **Cannabis (Delta-9- tetrahydrocannabinol 25 mg/Cannabidiol 5.5) Administered by Smoke Inhalation Using a Pipe** in Healthy Male and Female Volunteers/Fasting State
2. A Double-Blind Phase I Study to Assess Safety, Tolerability and Pharmacokinetics of Single and Multiple Daily Doses of **Cannabis (Delta-9- tetrahydrocannabinol/Cannabidiol) Administered by Vapor Inhalation Using a Vaporizer** in Healthy Male and Female Volunteers/Fasting State
3. A Double-Blind Phase I Study to Assess Safety, Tolerability and Pharmacokinetics of Single and Multiple Daily Doses of Cannabis Formulation administered Orally in Healthy Male and Female Volunteers Under Fasting State.

## ✓ Phase 2 trial

1. A Phase 2 Randomized, Double-Blind, Placebo-Controlled Pilot Study Followed by an Open-Label Extension Phase to Assess Safety And Efficacy Of Oral **Cannabis Oil Capsules** In the Treatment of Patients With Chronic Pain.

# PH 1 Trials - PK Parameters

		THC				CBD			
26.5 mg THC/7.5 mg CBD		T <sub>1/2</sub> hours	T <sub>max</sub> hours	C <sub>max</sub> ng/ml	AUC <sub>T</sub> ng.h/ml	T <sub>1/2</sub> hours	T <sub>max</sub> hours	C <sub>max</sub> ng/ml	AUC <sub>T</sub> ng.h/ml
Smoke	SD	0.42-0.68	0.05-0.17	78.50-93.85	21.21-23.71	0.80-1.66	0.05-0.17	15.85-23.65	7.14-7.38
	MD	0.42-0.81	0.05-0.17	28.4-98.39	9.83-26.66	1.14-1.25	0.05-0.17	5.19-22.23	3.27-9.29
Vapor		2.25	0.10	61.23	34.93	1.63	0.10	17.77	11.15
Oil 10 mg THC/10 mg CBD	SD	2.69	4.36	1.89	8.268	4.95	5.67	0.892	3.781
	MD	6.85	3.79	2.3	11.041	14.42	3.50	0.966	6.458
Sativex Sublingual 10.8mg THC/10 mg CBD		<b>1.40</b>	<b>4.38</b>	<b>4.9</b>	<b>14.91</b>	<b>1.81</b>	<b>4.22</b>	<b>3.33</b>	<b>11.34</b>

➤ 50% efficiency  
 ➤ Smoke THC C<sub>max</sub> ≈ 6-20 x Sativex C<sub>max</sub>  
 ➤ Vapor THC C<sub>max</sub> ≈ 12 x Sativex C<sub>max</sub>

➤ Sativex THC C<sub>max</sub> ≈ 2-3 x oil THC C<sub>max</sub>

OTCQB: TBPME

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# PH1 Trials – AEs with Inhaled Cannabis (1/2)

## Smoked Cannabis:

SD & MD: 100% experienced AEs, dose-related trend was observed in number of AEs with ↑ doses

The most common types of AEs

- SD: nervous system disorders
- MD: euphoria and general disorders

Majority AEs – mild & considered drug-related

Severe AEs:

- SD: 5 in 2 patients (syncope, fatigue, somnolence, feeling abnormal, dizziness)
- MD: 1 (↑ alanine transferase)

Most common AEs (experienced in at least 3 subjects):

- SD; Feeling abnormal, Somnolence, Headache, Dizziness, Fatigue
- MD: Euphoric mood, fatigue, feeling of relaxation, disturbance in attention, dry mouth, nausea

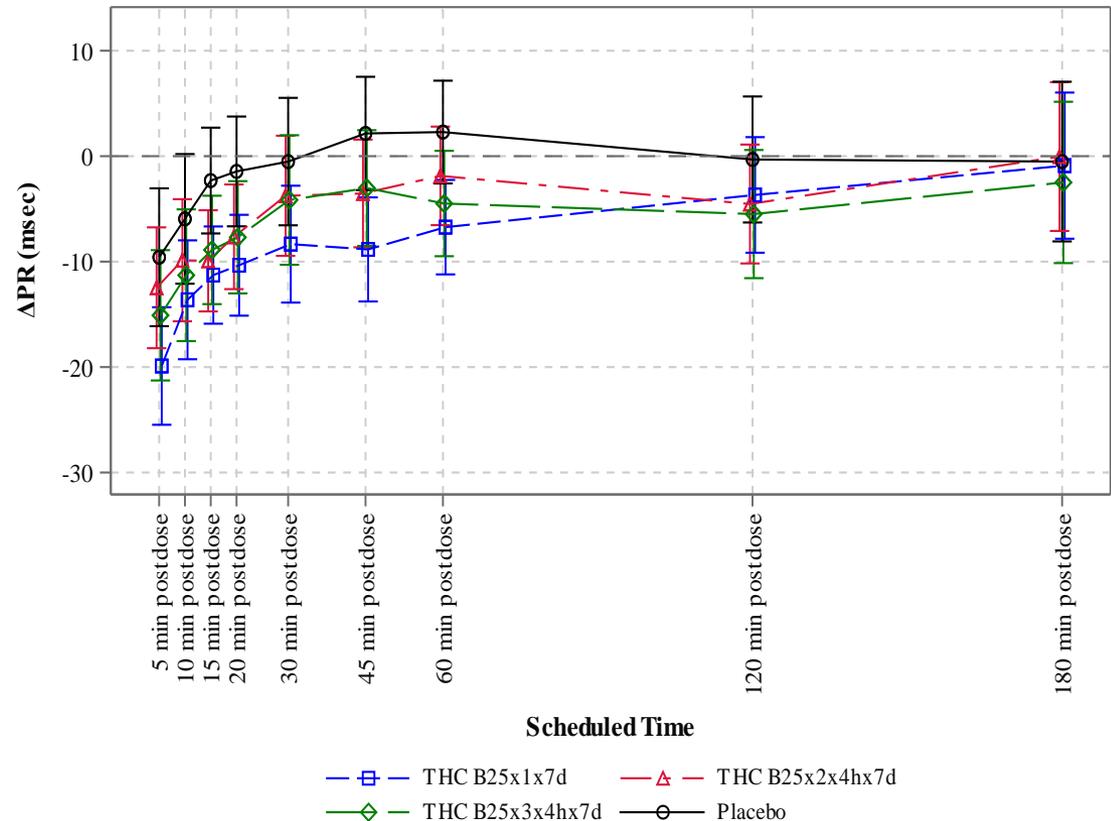
## Vaporized Cannabis:

- 100% experienced AEs
- Most common: euphoric mood (cannabis expected pharmacological effect)
- Majority AEs: drug-related & mild to moderate

# PH1 Trials – AEs with Inhaled Cannabis (2/2)

## Salient Findings:

- **Cardiac function** – assessed in Ph1 smoke MD - substantial heart rate effect observed at the 5-minute time point ( $\Delta HR$ ) = [15.4 bpm to 24.2 bpm];  $\Delta HR$  remained elevated 60 minutes post-dosing.
- **Neurologic** : Dizziness, fainting, headache, fatigue, somnolence, feeling abnormal



➤ **Related to Cmax**

# PH I Trials – AEs with Oral Cannabis Oil (7-Day Repeat Dosing 10 mg-10 mg THC-CBD)

- 2/7 patients experienced at least one AE (dizziness and constipation)
- All AEs severity: mild
- Dizziness and constipation occurred and resolved on day 1 and did not re-occur even with higher CBD concentrations throughout the study duration (7 days of consecutive intake)

➤ **Suggesting mechanism of tolerance**

# PH 2 Trial – AEs and Safety Data with Oral Cannabis Oil

Ratio THC/CBD of interest: 1:20 (< 0.1 mgTHC/ 5 mgCBD)

**NOAEL = 5 mg CBD daily consecutive intake during 6 days**

First time observed adverse effects

AE	CBD daily intake when AE occurred	Number of days of consecutive intake before AE occurrence
Dizziness	5 mg	7 days
Constipation	5 mg	8 days
Decreased appetite	10 mg	11 days
Palpitation	10 mg	24 days
Anxiety	15 mg	35 days
Nausea	15 mg	76 days
Itch	20 mg	40 days

# PH I Trials – Smoked vs Oral Oil

- Programmed titration (cannabis inhaled smoke)
  - Tolerance is observed:
    - No AEs classified as nervous system disorders (following MD by titration) were reported.
    - Negative impact on cognition was not evident after 7 days of repeated dosing (smoke) – Syncope occurred in SD part of Ph1 study (smoke).

	Inhalation	Oral
Neurological AEs	↑	↓
Cardiac AEs	↑	↓

	Single Dose	Multiple Dose (7days)
Neurological AEs	↑	↓
Cardiac AEs	↓	↑

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# Mycotoxin Contamination of Cannabis

- Tetra detected and then quantified mycotoxins in 3 lots of dried cannabis and 1 lot of cannabis oil. Levels ranged between 1 and 10 ug/g (ppb) of Aflatoxins, Ochratoxin A and/or Vomitoxin.
- Several screening tools were developed and validated to map out the organisms growing on a crop and bulk plant supplies. Example: qPCR screening was implemented to detect mycotoxin encoding genes.
- Developed and validated assays to quantify multiple known mycotoxins: T2 toxin, ochratoxin A, Vomitoxin, penicillic acid, etc.
  - Assayed on all raw materials as well as finished products.
- All suppliers of bulk plant materials are subject to our monitoring program.



# Thank You!

- Complete data will be submitted to the FDA through the confidential path

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