Inspired by Nature,
Enabled by Science®

APHIOS®

APHIOS® PHARMA LLC

Trevor P. Castor, PhD
President & CEO

December, 2018

3-E Gill Street, New Boston Park, Woburn, MA 01801 USA
Tel: (781) 932-6933; Fax: (781) 932-6865; Cell: (781) 858-7520
www.aphios.com www.aphioshwc.com tcastor@aphios.com

Inspired by Nature,
Enabled by Science®

APHIOS®

Forward Looking Statements

This Business Presentation may contain forward looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, and is subject to the safe harbors created thereby. All such forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from those in forward looking statements.

Inspired by Nature,
Enabled by Science®

APHIOS®

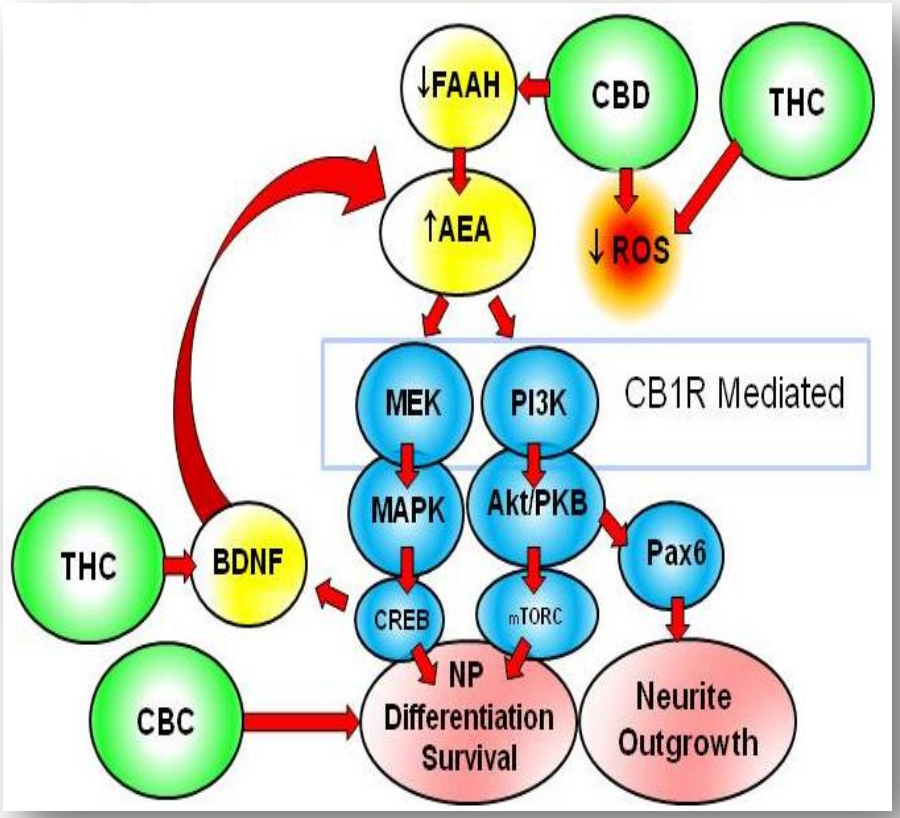
Aphios Pharma LLC

- Aphios Pharma LLC ('Aphios Pharma'), a wholly-owned subsidiary of Aphios Corporation, is dedicated to the discovery, delivery, development and commercialization of cannabis-based drugs
- Aphios Pharma will obtain a world-wide exclusive license from Aphios Corporation to its intellectual property and know-how on green enabling technology platforms for improved fractionation and drug discovery, and manufacturing and formulation of cannabis-based drugs for opioid addiction and chemotherapy induced peripheral neuropathic pain (CIPNP)
- Aphios Pharma will utilize these technology platforms in a DEA-Compliant Schedule I facility following current Good Manufacturing Practices (cGMP) of the US FDA to develop FDA-approved drugs for opioid addiction and CIPNP

Inspired by Nature,
Enabled by Science®

Cannabis Interaction with our Central and Peripheral Nervous Systems

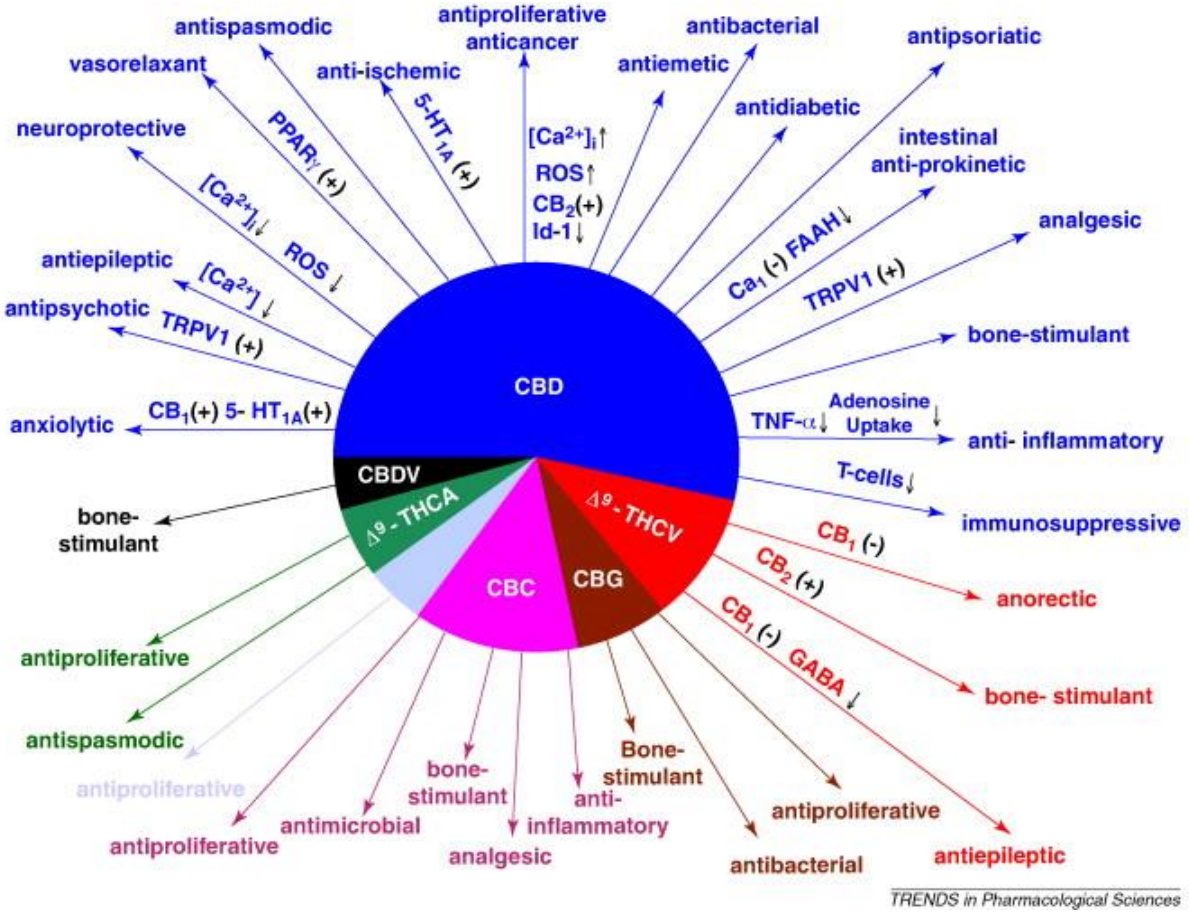
- Cannabis has a complicated interaction with nervous system disorders through cannabinoid receptors, CB1 and CB2
- Cannabis consists of 60 - 100 bioactive compounds including Δ9-THC, Δ9-THCA, CBD, CBDA, and CBC
- Humans have an inherent endo-cannabinoid system – anandamide (AEA) is stimulated by fatty acid hydrolase (FAAH) enzyme and CBD



Inspired by Nature,
Enabled by Science®

APHIOS®

Bioactivities of Non-Psychotropic Cannabinoids



Inspired by Nature,
Enabled by Science®

The Problem

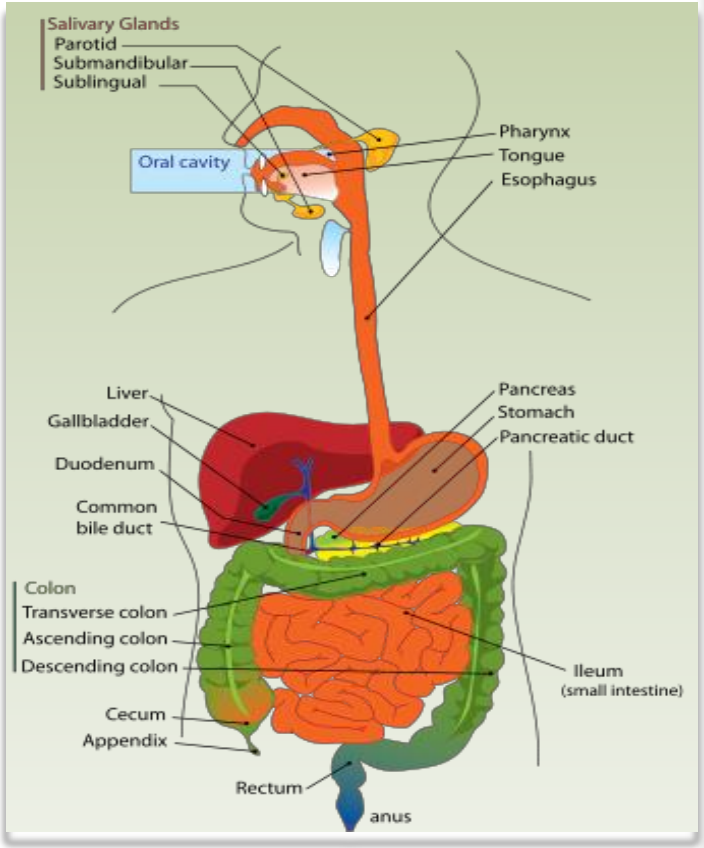
- **Synthetic Prescription Drugs:** Cancer pain and opioid addiction are only treated with synthetic drugs, such as opioids, that have significant adverse side-effects such as addiction
- **Lack of specificity:** Medical marijuana, which works anecdotally but only partially for opioid addiction and cancer pain, is a complex mixture of cannabinoids and other compounds
- **Difficult-to-deliver orally**: Cannabinoids are difficult to administer orally because they are hydrophobic with poor bioavailability (~ 6%) which results in over 90 percent loss in excretions from the body
- **Shelf stability**: Cannabinoids are oxygen sensitive and unstable which cause reduction in bioactivity and therapeutic efficacy
- **Burdensome process:** Current DEA, NIH and FDA regulatory environments are burdensome to the development of cannabis-based drugs

Inspired by Nature,
Enabled by Science®

APHIOS®

Our Solution

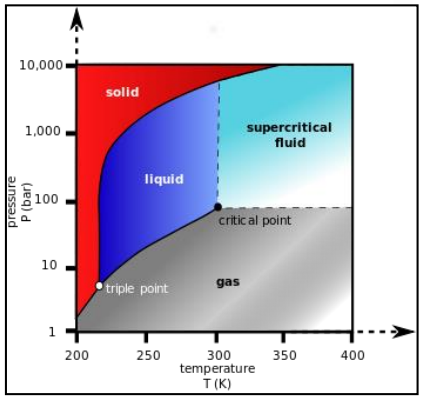
- Establish and confirm best cannabis-based drugs or combinations for treating opioid addiction and chemotherapy induced peripheral neuropathic pain (CIPNP)
- Isolate and manufacture specific cannabis drugs using supercritical carbon dioxide extraction and chromatographic purification technologies
- Nanoencapsulate these drugs in biodegradable polymer nanospheres to significantly improve oral bioavailability
- Nanoencapsulate cannabis drugs in the lipid membrane of phospholipid nanosomes to improve their transport across mucosal membranes



Inspired by Nature,
Enabled by Science®

APHIOS®

SFS-CXF™ (SuperFluids™ - Critical Fluid Extraction and Fractionation)



[US Patent Nos. 6,569,640B1; 5,854,064

SFS-CXF™ improves and accelerates drug discovery by:

- Cellular disruption and then rapid polarity-guided extraction and fractionation of partially purified natural molecules
- Increases recovery & diversity of secondary metabolites
- Reduces interference from nuisance compounds
- Increased probability of clean "hits" with reduced false positives and negatives
- Automating high throughput preparation of partially purified natural molecules

Inspired by Nature,
Enabled by Science®

APHIOS®

SFS-CXP™ (SuperFluids™ Critical Fluid Extraction and Purification Process) for Cannabinoid Manufacturing

[US Patent Nos. 5,750,709; 5,440,055]

Process

- Selective SuperFluids™ extraction (CO_2 with or without alcohol)
- SuperFluids™ extraction combined with online SuperFluids™ chromatographic purification

Characteristics

- Reduced number of extraction and chromatographic purification steps
- Decreased processing times from several days to < 24 hrs
- Significantly reduces use of organic solvents requiring disposal
- Green technology with higher overall yields and lower costs

Inspired by Nature,
Enabled by Science®

APHIOS®

SFS-CFN™ (SuperFluids™ Critical Fluid Nanosomes) Process for Cannabinoid Nanoencapsulation

[US Patent Nos. 8,703,727; 5,776,486; 5,554,382]

The CFN Process

- Phospholipids are solvated in SuperFluids™
- Target such as CBD is added to phospholipid-rich SFS stream
- Mixture is decompressed through a nozzle
- Nanosomes are thermodynamically formed, encapsulating target
- SFS replaces organic solvent and acts like a homogenizing agent

Inspired by Nature,
Enabled by Science®

APHIOS®

SFS-PNS™ (SuperFluids™ Polymer Nanospheres) Process for Cannabinoid Nanoencapsulation

[US Patent Nos. 8,440,614; 8,070,467; 7,708,915; 7,147,806]

Process

- **Step 1** - Polymers are dissolved in SuperFluids™
- **Step 2** - Mixture is injected into aqueous solution
- **Step 3** - Polymer nanospheres are formed

Characteristics

- Retention of cannabinoid activities
- Sustained or controlled release of cannabinoids
- Elimination of toxic organic solvents
- No residual organic solvents in final product
- Reduced processing steps and costs

Uses

- Oral and depot delivery of cannabinoids
- Sustained or controlled release of cannabinoids

Inspired by Nature,
Enabled by Science®

APHIOS®

APHIOS PHARMA SOLUTION

Cannabis

cGMP Manufacturing

Nanoformulation

Clinical Trials

Patient

Inspired by Nature,
Enabled by Science®

APHIOS®

APH-1501 for Opioid Addiction

- CDC reports a 200% increase in the rate of deaths involving opioid pain relievers and heroin over the period 2000-2014; estimated market size will be $1.8 Billion by 2020
- Unlike buprenorphine and methadone, CBD is not an opioid and does not exhibit any psychotropic effects
- CBD acts as an activator of 5-HT_{1A} serotonin receptors, is an anxiolytic, and accelerates the agonist effects of naloxone
- CBD has been shown to alleviate cue-induced opioid addiction behaviors and allosterically modulate the μ and δ-opioid receptors

Inspired by Nature,
Enabled by Science®

APHIOS®

APH-1502 for Chemotherapy Induced Peripheral Neuropathic Pain [CIPNP]

- The global neuropathic pain market was $5.2 B in 2015 and is estimated to reach $8.3 B by 2024; the CIPNP segment is estimated to be 42.4% revenue share in the global neuropathic pain market
- APH-1502 is a nanoencapsulation of CBD in biodegradable polymer nanospheres [US Patent, 2014]
- Nanoencapsulation is being used to protect the CBD during the stomach passage; the residence time in the stomach will be short compared to CBD release rate from polymer nanospheres
- Nanoencapsulation of CBD improves stability, oral bioavailability while sustaining or controlling release

Inspired by Nature,
Enabled by Science®

APHIOS®

Intellectual Property & Know-How

- **Drug Discovery:** US Patent Nos. 6,569,640; 5,854,064
- **Drug Manufacturing:** US Patent Nos. 5,750,709; 5,440,055
  - **Drug Crystallization:** U.S. Patent Nos. 6,051,694; 6,221,153
- **Drug Delivery:**
  - **Biodegradable Polymer Nanospheres:** US Patent Nos. 9,034,347; 8,703,727; 8,629,177; 8,440,614; 8,070,467; 7,708,915; 7,147,806
  - **Critical Fluids Nanosomes:** US Patent Nos. 8,637,074 ; 5,776,486; 5,554,382
- File and prosecute new patents on drug discovery, manufacturing, delivery, drug use, route of administration, and schedule-of-use

Inspired by Nature,
Enabled by Science®

APHIOS®

Competition

- Our primary competition is GW Pharmaceuticals of England which has a mixture of CBD and THC for multiple sclerosis, and an FDA-approved purified CBD product for childhood epilepsy

- Other competition includes pharmaceutical companies with synthetic cannabis drugs such as AbbVie, Par Pharmaceuticals and Insys
- Companies with non-cannabis based drugs against similar disease targets such as Biogen, Sanofi, Pfizer and Merck

Inspired by Nature,
Enabled by Science®

APHIOS®

Management Team

Dr. Trevor P. Castor, President and Chief Executive Officer, has over 30 years of diversified management, marketing and business experience in the biotech, energy and environmental industries

Mr. James J. Falese, Chief Financial Officer and Controller, has over 30 years of experience in biotech accounting, financial analysis and strategic planning

Dr. Judith L. Palmer-Castor, Director, Clinical and Regulatory Affairs, has over 20 years of teaching, research, regulatory and clinical experiences in academia and industry

Inspired by Nature,
Enabled by Science®

APHIOS®

Scientific Advisors

Dr. Arthur D. Lander, M.D., Ph.D., a neuroscientist, is a Professor of Developmental and Cell Biology and a Professor of Biomedical Engineering at the University of California, Irvine

Dr. Gordon M. Cragg, Ph.D., a natural product chemist, served as Chief of the Natural Products Branch, National Cancer Institute (NCI), NIH and is currently serving as an NIH Special Volunteer

Dr. Glenn T. Hong, Sc.D., Founder, Counter-Current Systems, Inc., is a chemical engineering and supercritical fluid expert

Dr. Jonathan Steven Alexander, Ph.D. is a Professor of Molecular & Cellular Physiology, Medicine, Neurology, Anesthesiology and OMFS at Louisiana State University

Inspired by Nature,
Enabled by Science®

APHIOS®

Key Opinion Leader

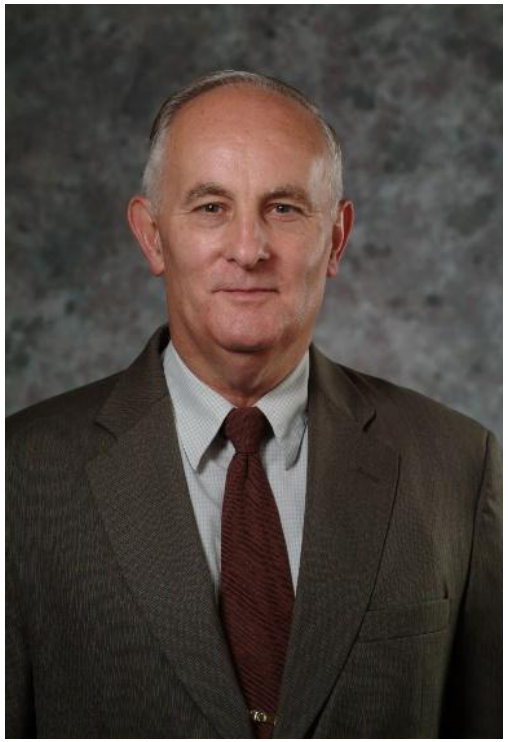
Dr. Staci A. Gruber, Associate Professor of Psychiatry, Harvard Medical School, McLean Hospital, Belmont, MA

"I am enthusiastic about Aphios Pharma's plans to manufacture and deliver cannabinoids for clinical research studies which follow cGMP. Aphios has a proven track record .... and this latest endeavor represents an important milestone for patients exploring cannabinoid-based therapies... Aphios is clearly invested in facilitating research and clinical endeavors which are likely to advance the science of cannabinoid-based medicines, and with the launch of this program, Aphios stands uniquely poised to make highly significant contributions to science and medicine."

Inspired by Nature,
Enabled by Science®

APHIOS®

Key Opinion Leader



Dr. Jerry W. King, retired University Professor and Supercritical Fluid Technology expert and author, Fayetteville, AR

"Aphios under the leadership of Dr. Trevor P. Castor has pioneered the application of supercritical fluid technologies: to drug delivery systems, the extraction of bioactive natural and marine products, nanoparticulate synthesis, and more recently in the field of cannabis science & technology. .... Under Dr. Castor's leadership, Aphios has a successful record of developing extraction and formulation technologies as applied to drugs such as Taxol, THC, several bioactive marine products which will now be focused in this new company on cannabidiol on a nanoscale to achieve solubilization and facilitate sustained release of CBD."

Inspired by Nature,
Enabled by Science®

APHIOS®

Business Model

- Utilize 505B(2) pathway of US FDA to accelerate clinical trials
- Conduct Phase 2 clinical trial and license product on a global or regional basis
- Agreements will be structured as a combination of upfront payments, R&D and milestone payments
- Conduct Phase 3 clinical trial, obtain FDA approval and commercialize product with direct sales force

Average Upfront Payments by Stage and Phase (Recap, 2013)

Inspired by Nature,
Enabled by Science®

APHIOS®

Investment

- We expect to raise convertible debt/equity of $5 million from private investors
- We anticipate having to raise additional capital through private and public investors in the next 3 years

Use of Funds ($USD)

Cost Unit	FY19	FY20
G&A	1,478,294	3,199,114
BD	458,227	761,316
COGS	1,716,954	2,301,629
R&D	1,294,590	14,924,185
FA	466,248	1,265,515
Amount	**$5,414,313**	**$22,451,759**

Inspired by Nature,
Enabled by Science®

APHIOS®

Summary

- We plan to develop FDA-approved, cannabis-based drugs for treating highly unmet disorders – opioid addiction and cancer pain -- that are only partially and anecdotally addressed by medical marijuana
- We expect to raise convertible debt/equity of $5 million to file an IND with the FDA in 2019
- We anticipate raising a second round of capital to conduct Phase 2 clinical trials in 2020
- We expect to license out these products to strategic corporate partners within a 2-3 year period, at which time investors may have an opportunity to exit
- Alternatively, we plan to file for an IPO and commercialize these products with a direct sales force, which may provide investors with another opportunity to exit

Inspired by Nature,
Enabled by Science®

APHIOS®

Contact Information

Dr. Trevor P. Castor, President and CEO

Aphios Pharma LLC
3-E Gill Street, New Boston Park
Woburn, MA 01801 USA

Office Phone: 001 (781) 932-6933
Office Fax: 001 (781) 932-6865

E-mail: tcastor@aphios.com
Websites: www.aphios.com/www.aphioshwc.com