



Trevor P. Castor, PhD

President & CEO

Aphios Pharma LLC

Developing cannabis-based, FDA-approved drugs for Cancer Pain, Opioid Use Disorder, Anxiety and Multiple Sclerosis

APHIOS[®] PHARMA LLC

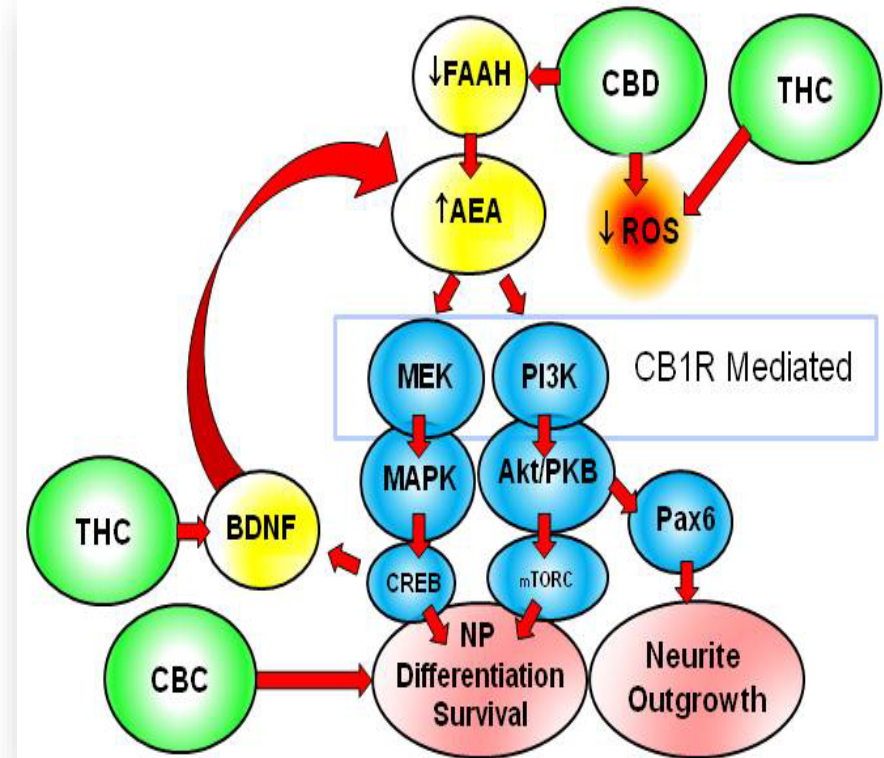
Inspired by Nature, Enabled by Science[®]

- We are dedicated to the discovery, delivery, development and commercialization of cannabis and hemp-based drugs for Central and Peripheral Nervous System disorders
- Our initial product targets are Pain including Cancer Induced Peripheral Neuropathic Pain (CIPNP), Opioid Use Disorder (OUD), Anxiety, and Multiple Sclerosis



The Problem: Internal Cannabinoids

- We, as humans, have an inherent endocannabinoid or internal cannabinoid system – anandamide (AEA) is stimulated by fatty acid hydrolase (FAAH) enzyme
- Unbalances in our internal endocannabinoid system can create unbalances in our health and our abilities to respond to negative health intrusions
- Cannabis and hemp can help. Cannabis consists of 60 - 100 bioactive compounds including Δ 9-THC and CBD. Hemp primarily contains CBD
- Cannabis/Hemp have complicated interactions with the Peripheral and Central Nervous Systems and can help rebalance our endocannabinoid system



Cannabis Interactions with the Peripheral and Central Nervous Systems

The Problem: Pain, Anxiety, Opioids

- Millions suffer from pain and anxiety
 - 50% of cancer patients experience untreated pain
 - Pain from diseases such as MS, age, and injuries
- Opioids can be an effective treatment, yet Opioid Use Disorder is a massive problem
 - Common treatments for Opioid Use Disorder are ineffective
- Cannabis can be an effective treatment, but.



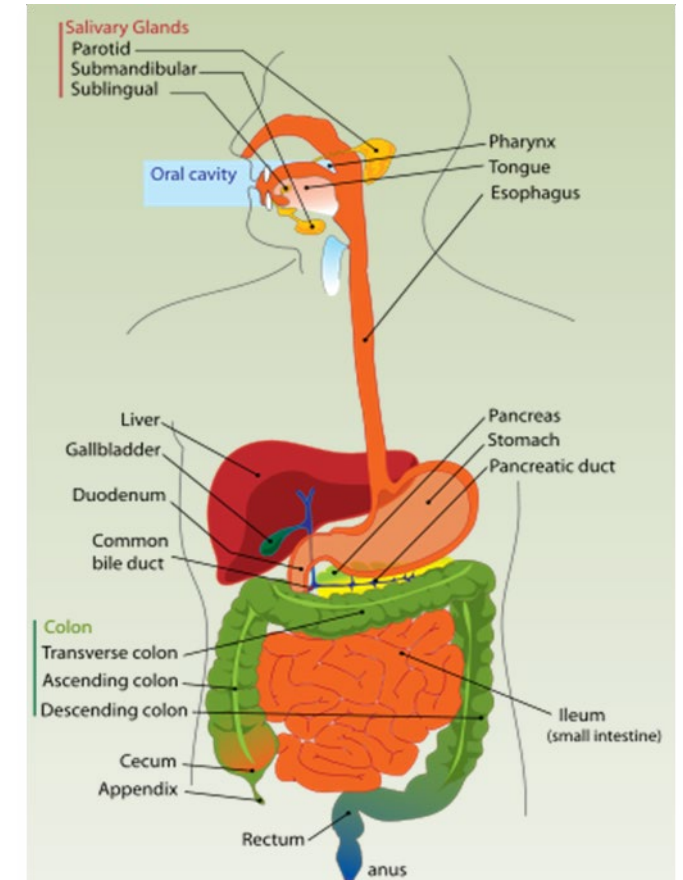
- When inhaled, cannabinoids in this form of composition is not consistent. It is very short-lived or rapidly metabolized. When taken orally, they are rapidly metabolized. They are difficult to formulate. They are hydrophobic with poor bioavailability. There is a 90 percent loss from the first pass. We need to keep them stable from degradation. We can encapsulate them in nanoparticles.



Bioactivities of Non-Psychotropic Cannabinoids

Our Solution: Sustained Release Nanoparticles

- Keep specific, bioactive cannabinoids in the body longer
 - Improve stability from oxygen degradation, and protect from enzymes in digestive tract and stomach acids
 - Prevents first-pass metabolism by liver enzymes, and keep nanoparticles in circulation longer using pegylation
 - Sustained release from breakdown of biodegradable polymers increases bioavailability from ~6%, reduces dosing, improves compliance and efficacy
- Transition acute impact drugs into a sustained release drugs for chronic indications



The Market: Opportunity

Market	Pain	Opioid Use Disorder	Anxiety	Multiple Sclerosis
Characteristics	<ul style="list-style-type: none"> - Chemotherapy induced Peripheral Neuropathic Pain - 50% cancer patients - 42.4% of pain mkt 	<ul style="list-style-type: none"> - 500K deaths in 2 decades - OUD drugs are opioids - CBD alleviate cue-induced OUD and satisfies opioid receptors 	<ul style="list-style-type: none"> - Generalized anxiety disorder - Affects 13% people in US - Lower productivity, higher drug/alcohol use 	<ul style="list-style-type: none"> - 400K US, 500K EU - Neuroinflammation and Neurodegeneration targets
TAM	\$9.9B by 2027	\$4.9B by 2027	\$19.8B by 2028	\$42B by 2028
SAM	\$4.5B by 2027	\$2.5B by 2027	\$2.0B by 2028	\$1B by 2028
Growth Rate	5.6% CAGR	8.7% CAGR	2.4% CAGR	6.3% CAGR



The Market: Competition



Primary competition is **Jazz Pharma** which recently acquired GW Pharma for \$7.2B. We differ from GW Pharma by using proprietary and patented nanotechnology platforms to improve the delivery and efficacy of cannabinoids through oral and topical administration



Secondary competition includes pharmaceutical companies with synthetic cannabis drugs such as AbbVie and Par Pharmaceuticals



Tertiary competition includes pharmaceutical companies that have non-cannabis-based drugs against similar disease targets such as Biogen, Sanofi, Pfizer and Merck

Traction: Research & Collaborations

- Development of a Δ 9-THC, A Natural Cannabinoid Product, NCI, NIH, and Nanoencapsulated Δ 9-THC for Marijuana Addiction, NIDA, NIH
- Development of cGMP Manufacturing Process for CBD from *Cannabis sativa*, NIDA, NIH
- Collaboration with Rhodes Pharma to nanoencapsulate Δ 9-THC in biodegradable polymer nanospheres & phospholipid nanosomes
- Collaboration with Alexza Pharmaceuticals to manufacture Δ 9-THCA
- Collaboration with Prosulus Pharma to manufacture transdermal patches of Δ 9-THC



Aphios' SuperFluids™ CO₂ Extraction and Chromatography Purification Pilot Plant

Traction: Manufacturing & Agreements

- Developed proprietary technologies for manufacturing and nanoencapsulation of pharmaceutical-grade cannabinoids
- Established supercritical fluid manufacturing facility for 1,000 kg pharma-grade cannabinoids per year under cGMP and fully-equipped Schedule I BSL-2 labs
- Inventory of 1.8 kilograms of cannabinoids (CBD, CBDA, Δ 9-THC, Δ 9-THCA, CBG, CBC, CBN)
- Sixteen (16) patents on drug discovery, manufacturing and nanotechnology drug delivery and four (4) pending
- Mutual Nondisclosure Agreements (mNDAs) with GW Pharma, Erie Management Group, Fujimoto Pharmaceuticals

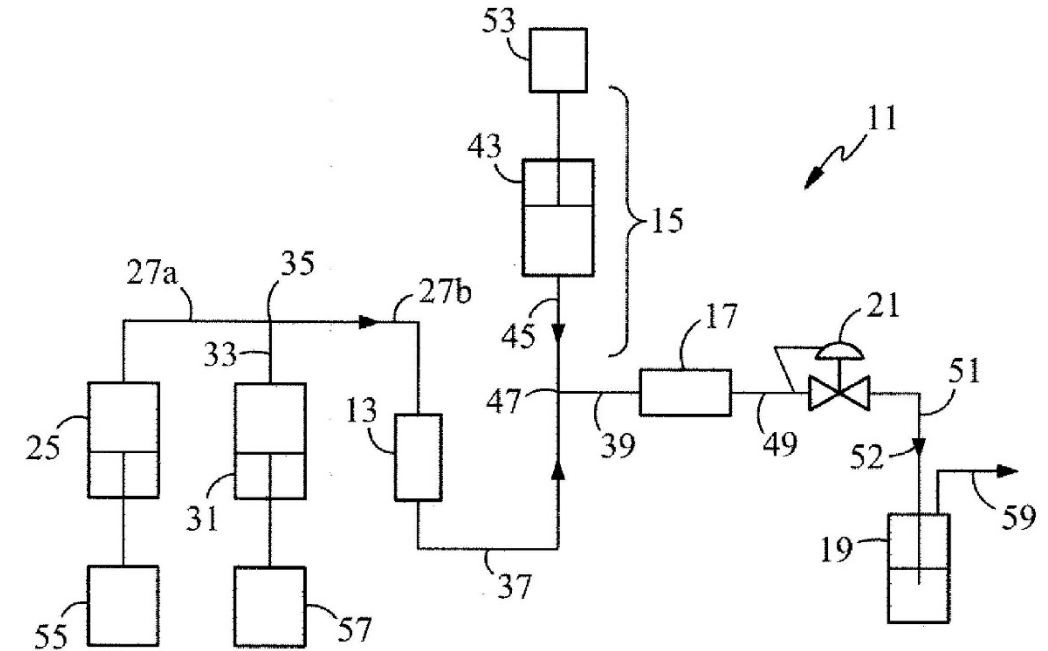


Aphios' SuperFluids™ Polymer Nanospheres Encapsulation Apparatus

Traction: Intellectual Property

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- **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 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
 - **Phospholipid Nanosomes:** US Patent Nos. 9,981,238; 8,637,074; 5,776,486; 5,554,382
- Provisional patent applications on drug discovery, manufacturing, delivery, use and route of administration.



Schematic of Aphios' SuperFluids™ Polymer Nanospheres Encapsulation Apparatus

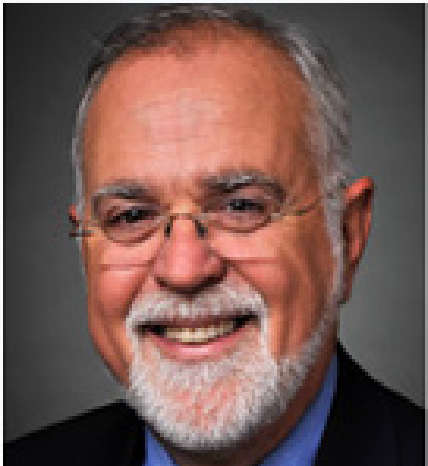
Our Team: Management



Dr. Trevor P. Castor
*President and Chief
Executive Officer*
*Over 30 years of diversified
business experience in
biotechnology*



**Dr. Judith L. Palmer-
Castor**
*Director, Clinical and
Regulatory Affairs*
*Over 20 years of regulatory
and clinical experience*



Dr. Val R. Livada
Business Advisor
*Ret. Senior Lecturer Sloan
School of Management,
MIT, Cambridge, MA*



Ms. Catherine Prillo
Controller
*Over 30 years of
accounting, financial
analysis and strategic
planning experience*

Our Team: Scientific Advisors



Dr. Arthur D. Lander
MD/PhD, Neuroscientist
Prof. of Developmental and
Cell Biology and Biomedical
Engineering Univ. of
California, Irvine



Dr. Glenn T. Hong
Chemical Engineer
Founder, Counter-Current
Systems
MIT grad and Supercritical
Fluid Expert



Dr. Gordon M. Cragg
Natural Product Chemist
Ex-Chief of the Natural
Products Branch, National
Cancer Institute (NCI), NIH
Currently serving as an NIH
Special Volunteer



Dr. Jonathan Steven
Alexander
Biologist
Professor of Molecular &
Cellular Physiology, Medicine &
Neurology, Multiple Sclerosis &
AD Researcher
Louisiana State University

Our Team: Key Opinion Leader

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"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."

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

Our Team: Key Opinion Leader



"I have read through your SBIR Phase I grant submission titled "Nanoformulation of CBD for Chemotherapy Induced Peripheral Neuropathic Pain (CIPNP)" with attention to your efforts to improve the pharmacokinetics of CBD using Aphios Patented nanoformulation to improve the pharmacodynamics of CBD in a model of CIPN-induced pain. There is a great need for novel medications in CIPN in order to reduce the under-utilization of these effective chemotherapeutics. The neuropathy and pain induced by chemotherapeutics results in dose limiting and incomplete destruction of the cancer.I am excited about and intrigued with the potential of the nanoformulations of CBD."

Dr. Todd W. Vanderah, Professor and Head, Department of Pharmacology, University of Arizona

Our Team: Key Opinion Leader



“We are quite interested and excited about your planned research on nanoencapsulated Cannabidiol (CBD) to develop an “Opioid Addiction Therapeutic.” It is my understanding that this product could also have an analgesic effect, thus providing a prophylactic as well as therapeutic role for patients. In 2017, I was appointed by Alabama Governor Robert Bentley to serve on the Governor’s Task Force on Opioid Addiction and Abuse. I would be delighted to provide your team with advice on both progressing your molecule to and in the clinic. At that stage, we would explore participating in your clinical trials to bring much needed non-opioid therapeutics to people suffering from Opioid Use Disorder.”

Dr. Brent Boyett DMD, DO, DFSAM, Chief Medical Officer and Founder
Drug & Alcohol Treatment Centers, Pathway Healthcare

Our Team: Key Opinion Leader



“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.”

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

Our Plan: Development Strategy

- **Isolate and manufacture** specific cannabis drugs using patented environmentally-friendly supercritical carbon dioxide extraction and chromatographic purification technologies
- **Nanoencapsulate** these drugs in biodegradable polymer nanospheres utilizing patented supercritical fluid technologies to significantly improve oral bioavailability and sustain release over 8-24 hours
- Conduct **rigorous Phase 2 clinical trials** to demonstrate safety and efficacy



Aphios' SuperFluids™ Critical Fluid Fractionation (SFS-CXF) Technology

Our Plan: Development Strategy

	Y01	Y02	Y03	Y04
Manufacturing of Pharmaceutical Grade CBD				
Scale-up of Polymer Nanospheres (PNS™) Technology				
Nanoencapsulation of Purified CBD				
<i>In Vitro</i> and <i>In Vivo</i> Studies				
Investigational New Drug (IND) Enabling Studies				
File IND with the FDA for Nanoencapsulated Cannabinoids				
Conduct Phase 2 Clinical Trials under 505b(2) Pathway				
Conduct Phase 3 Pivotal Clinical Trials on Safety & Efficacy				
Obtain FDA approval of New Drug Application (NDA)				

Our Plan: Funding History, Ask and Exit

\$46
M

Spent by Aphios Corporation to develop enabling technology platforms and knowledge used in the manufacturing and nanoencapsulation of cannabinoids

\$7.9
M

In peer-reviewed grants from National Cancer Institute, National Institute on Drug Abuse and National Center for Complimentary and Integrative Health, NIH

\$1
M

Crowdfunding of \$1M to continue development studies and fund raising to raise up to \$30M for cGMP manufacturing, conduct IND-enabling studies, file an IND with the FDA and conduct Phase 2 clinical trials

Exit

Investors will be able to exit in 3 years in a M&A in 2025. Alternatively, we plan to do an IPO to raise \$100M in 2026 to complete clinical trials and file an NDA with the FDA

Our Plan: Exit Strategy

- Aphios Pharma LLC strategic commercialization and exit plans will follow one or more of three strategic options:
 - (1) Establish a strategic corporate partnership or M&A with a multinational pharmaceutical company such as Jazz Pharma, Merck, Biogen, AbbVie, Pfizer to develop and commercialize nanocannabinoids on a world-wide basis.
 - (2) In this option, we will seek to out-license nanocannabinoids as early as possible in the development cycle, on a regional basis.
 - (3) In this option, we will raise \$100M in an IPO to continue clinical development and commercialization of nanocannabinoids for CIPNP, anxiety, opioid use disorder, and/or Multiple Sclerosis
- Investors in the A round can exit on the execution of an M&A in Option 1 or IPO in Option 3



Exit Strategy: Multiple Opportunities



**Thank you for Your
Interest**



Dr. Trevor P. Castor, CEO

- Massive problem and opportunity
- Vastly experienced team and key support
- Proprietary and patented nanotechnology
- Benefitting from decades of development
- Multiple exit opportunities