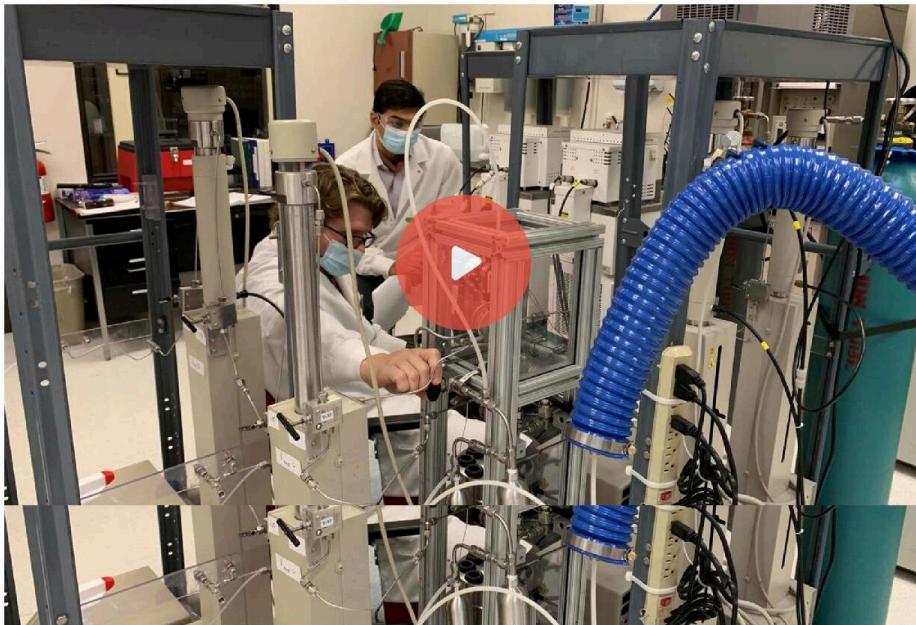


Aphios® Pharma is developing cannabis-based therapeutics for anxiety, pain, opioid use disorder & MS



Highlights

- 1 Green biotech developing sustained release nanoencapsulated cannabinoids for highly unmet chronic medical needs
- 2 ESG opportunity addressing a \$4B market for cancer pain, \$5B for opioid use disorder and \$40B for Multiple Sclerosis
- 3 Aphios has spent \$44 million to date on developing enabling drug manufacturing and drug delivery technologies
- 3 Aphios has spent \$44 million to date on developing enabling drug manufacturing and drug delivery technologies
- 4 Including \$7.9M in peer-reviewed grants from National Cancer Institute, National Institute on Drug Abuse and NCCIH, NIH
- 5 Established supercritical fluid manufacturing facility for 1,000 kg pharma-grade cannabinoids per yr under cGMP
- 6 Fully-equipped Schedule I BSL-2 labs and cGMP suites for formulation and nanoencapsulation of cannabinoids
- 7 Our proprietary manufacturing and nanoencapsulation technologies are protected by 16 issued patents and 4 provisionals
- 8 We are dedicated to sustainability, environmental responsibility and communal curtailment of climate change

Our Team



Travis D. Carter



Trevor P. Castor

Dr. Castor has developed green enabling platforms for improving drug discovery and manufacturing, and nanotechnology drug delivery in an environmentally sustainable manner and nanoencapsulated cannabinoids for cancer pain, MS and opioid use disorder.

Medical marijuana has proven to be partially effective for cancer pain, opioid addiction and Multiple Sclerosis. These effects are acute and not effective for the treatment for chronic diseases such as pain and opioid addiction. With nanoencapsulation, we can improve the delivery and efficacy of cannabinoids.



Dr. Val Livada

Dr. Val R. Livada is Founder and CEO of Weybridge Partners which is focused on successful technology commercialization. He was a Senior Lecturer (retired) on Corporate Entrepreneurship at the Sloan School of Management, MIT, Cambridge, MA.



Judith Castor

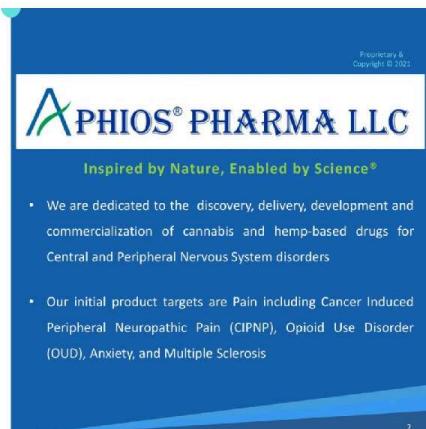
Dr. Judith Palmer-Castor is a behavioral health scientist with a broad range of clinical and regulatory experiences including Phase II/III clinical trials for a cancer supportive care compound, Phase II for HIV and Phase I for Alzheimer's disease.



Catherine Prillo

Catherine Prillo was most recently VP of Accounting at an internationally renowned retail organization where she successfully completed a management-led leveraged buy-out, recapitalization to a Private Equity group and sale to a strategic buyer.

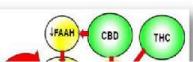
Pitch



Aphios

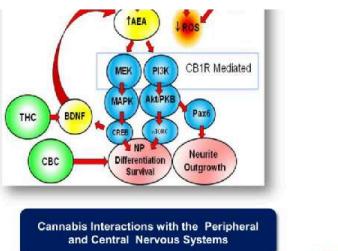
► The Problem: Internal Cannabinoids

- 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 $\Delta 9$ -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



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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.....



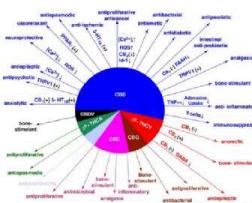
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The Problem: External Cannabinoids

- When Cannabis is smoked or inhaled, cannabinoids are rapidly absorbed. Cannabinoid composition is not consistent making it difficult to dose. The impact is very short-lived or acute and not adequate for chronic use.
- When cannabinoids are taken orally, they are rapidly degraded and excreted from our bodies. They are difficult to administer orally because they are hydrophobic with poor bioavailability (~ 6%) which results in over 90 percent loss from the body
- Cannabinoids can help but we need to keep them in the body longer and protect them from degradation. We can do so by encapsulating cannabinoids in nanoparticles.
- Cancer pain and opioid addiction are only treated with synthetic drugs, such as opioids, that have significant adverse side-effects such as addiction



Bioactivities of Non-Psychotropic Cannabinoids

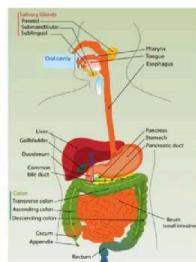
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Our Solution: Sustained Release Nanoparticles

- 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



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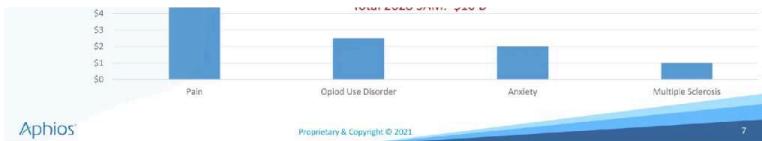
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The Market: Opportunity

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

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Total 2028 SAM- \$10 B



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

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Traction: Research & Collaborations

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



Aphios' SuperFluids™ CO₂ Extraction and Chromatography Purification Pilot Plant

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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, $\Delta 9$ -THC, $\Delta 9$ -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

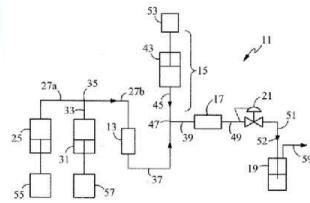
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Traction: Intellectual Property

- Drug Discovery: US Patent Nos. 6,569,640; 5,854,064
- Drug Manufacturing: US Patent Nos. 5,750,709; 5,440,055
- Drug Crystallization: US. 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

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► 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

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► 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

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► Our Team: Key Opinion Leader



"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

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► 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

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► 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**

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► 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

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► 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

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► 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)				

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► Our Plan: Funding History, Ask and Exit



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



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



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



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



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Exit Strategy: Multiple Opportunities



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Thank you for Your Interest

APHIOS® PHARMA LLC

Dr. Trevor P. Castor, CEO

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