



**UNITED STATES**  
BIOPHARMACEUTICALS  
**2020**



Research and Development - Contract Services - Drug Discovery  
Academic Research Regulations and Compliance - East Coast Hubs - Logistics and Distribution

# Dr. Trevor P. Castor



President & CEO  
APHIOS



## How has Aphios evolved since its founding and how has nature influenced the development of your therapeutics?

Aphios' vision is to develop biotechnology products for improving health and treating chronic diseases in an environmentally sustainable manner. Aphios was established in 1993 with an initial focus on developing enabling technology platforms for improving drug discovery, drug manufacturing, drug delivery and pathogenic drug safety focused on the inactivation of viruses and pathogens in the blood supply and our bodies. Aphios is a combination of two Greek words, which means virus free. We spent approximately a decade developing, validating and patenting these platforms and from there, we started developing therapeutic products based on these platforms. In 2003, we began our first big clinical trial for our patented product Zindol for chemotherapy induced nausea and vomiting. That was influenced by nature, because it was a ginger based product. Currently Zindol is on the marketplace as a dietary supplement, while we focus on attaining FDA approval.

We also developed a technology for manufacturing Taxol, a potent anti-cancer agent. Today, we have several products in development, including APH-0812, for which we were just awarded a US patent. It is a combination therapy of a protein kinase C (PKC) modulator and histone deacetylase (HDAC) inhibitor in a nanoparticle that is targeted for HIV latency.

## Can you elaborate on the Aphios' partnership with LSU Health Shreveport?

We have a partnership with LSU Health

Shreveport to develop drugs for Alzheimer's disease and cognitive disorders, as well as for the transplantation of kidneys and the liver. Together we have developed and patented a technology and product for improving the length of which an organ can be preserved before transplantation.

## What is Aphios strategy for pushing its products forward and taking them to market?

Aphios' strategy is to license as early as possible. We collaborate with strategic partners and/or license our enabling technology platform to research and develop novel drugs, and for the reformulation of existing drugs to reduce toxicity and improve efficacy and therapeutic index, while extending product life. We will also collaborate with strategic investors and corporate partners to further the development and commercialization of our therapeutic products.

## What are your thoughts on the current developments in the neurodegenerative space and the potential for making important strides forward?

There is an association between amyloid plaques and tau entanglements in Alzheimer's disease (AD). The question remains how to prevent this from happening or to reduce it once it does happen. There are three critical neural enzymes that affect amyloid plaques. They are Beta-secretase, Gamma-secretase, and Alpha-secretase. Pharmaceutical companies have focused on Beta-secretase and Gamma-secretase, but these have been difficult to translate into effective clinical treatments for AD.

Aphios' approach is to upregulate Al-

pha-secretase, which positively impacts amyloid precursor protein, (APP) processing. Both Beta-secretase and Gamma-secretase cleave APP to form insoluble amyloid plaques that set in motion tau fiber assembly. In contrast, Alpha-secretase cleaves APP into a harmless and more soluble product, that supports new synapse formation and is more readily cleared from the brain. Thus, unlike current strategies, which aim to suppress amyloid plaque formation by minimizing Beta- and Gamma-secretase activities, our strategy is to activate Alpha-secretase, which will effectively eliminate the substrate for Beta-amyloid generation, and at the same time lead to positive amyloid precursor processing, to both prevent and reduce amyloid plaques in AD.

## Can you elaborate more on Aphios' platforms?

We are leading the way in developing green, enabling biotechnology and nanotechnology drug delivery platforms and enhanced therapeutic products for health maintenance and the treatment of chronic diseases. We source our biodiversity from nature – medicinal plants, marine organisms, or humans. We use supercritical fluid solvents, as a replacement for organic solvents. When compressed, these fluids exhibit enhanced thermodynamic properties of penetration, selection, solvation, and expansion. We manipulate these fluids on a cellular level to increase process selectivity and speed while reducing processing steps, toxic organic usage and manufacturing costs.

This technology is especially relevant with the ongoing corona virus pandemic. Our pathogen inactivation technology can clear viruses from the blood supply, and our photoluminescence molecular flashlight therapeutic can inactivate viruses within our body.

## What trends are you currently seeing?

Cannabis-based drugs are becoming a huge trend in the market. Aphios is developing FDA-approved, cannabis-based drugs for treating unmet central and peripheral nervous system disorders of opioid addiction and pain. Cannabinoids have a lot of potential to affect the body. ■

# Commercializing Neuroscience

## VC BETS BIG ON THE BRAIN

→ Often referred to as 'the final frontier' of medicine, neuroscience is unquestionably complex. So much so, that stories of high profile failures and headlines of big pharma deprioritizing programs have seemingly muted enthusiasm for the field. Amgen scrapped its R&D program to focus on cancer in 2019, following in the footsteps of Pfizer's decision to do the same in 2018. Others, like Bristol-Myers Squibb, GlaxoSmithKline and AstraZeneca announced cutbacks on CNS disorders a few years earlier.

Amgen's head of R&D, David Reese, explained that the reason for the companies exit rested on several factors, including the industry's "fairly rudimentary" understanding of neurological diseases, the long development programs some of these drugs require, and the clearer opportunities Amgen saw with oncology, inflammation and cardiovascular medicines. There is no doubt neuroscience presents some unique challenges: uncertain diagnoses, long progressive burdens of disease, multiple etiologies and complicated clinical trials are a few of them. As a consequence, there remain few, if any, novel treatments for diseases like Alzheimer's, Parkinson's and depression, each of which affect millions of patients.

Despite the flurry of headlines of a pull-back from big pharma, neuroscience has quietly become a hot space for startups. Across a range of neurologic conditions, investors have been fueling entrepreneurs to discover and develop novel therapeutic strategies. According to Bio's 2019 Industry Analysis report, neurology startups received US\$1.5 billion in venture funding in 2018, second only to oncology. This suggests financiers expect payoffs in the not-too-distant future, perhaps through a big pharma buyout. Their bet may be well placed too, as industry watchers foresee big pharma lured by emerging treatments

for epilepsy, mood disorders and genetic diseases of the central nervous system.

Because there is so much downside risk, the upside potential of investing in the sector is exponential. Patient unmet needs from neurologic disorders are staggering, and the cost to society is enormous. As most OECD countries experience a 'greying' of their populations, the burdens of many of these later-onset neurologic conditions will skyrocket. This creates an imperative to act, and to invest, in new therapies.

Psychiatric disorders such as schizophrenia have gone long periods without advances in treatment. Given the disease affects 1% of the population according to the Mayo Clinic, there is substantial need for disruption in the area. Terran Biosciences is at the forefront of trying to solve this debilitating disorder. The company is developing therapeutics and neuroimaging software to deliver novel treatment solutions and aid in the diagnosis of patients with psychiatric and neurological diseases. "We have seen renewed interest in the space over the last couple of years, and a few groups are really pushing forward on new mechanisms to address the large unmet need. Terran's lead compound, TR-01, is an alpha-2 ( $\alpha_2$ ) adrenergic receptor antagonist, which can be added onto the current standard of care therapies. This makes it the only drug in development as an adjunctive therapy for schizophrenia, and is designed to give patients a new safe and more effective option for improving their current treatment," said chief business officer Dustin Tetzl.

Massachusetts based Aphios are working to develop therapeutics products for CNS disorders. Its approach, as characterized by President and CEO Dr. Trevor Castor, is to: "Upregulate Alpha-secretase, which positively impacts amyloid precursor protein (APP) processing. Both Beta-secretase and Gamma-secretase cleave APP to form insoluble amyloid plaques that set in motion tau fiber assembly. In contrast, Alpha-secretase cleaves APP into a harmless and more soluble product that supports new synapse formation and is more

readily cleared from the brain. Thus, unlike current strategies, which aim to suppress amyloid plaque formation by minimizing Beta- and Gamma-secretase activities, our strategy is to activate Alpha-secretase, which will effectively eliminate the substrate for Beta-amyloid generation and, at the same time, lead to positive amyloid precursor processing to both prevent and reduce amyloid plaques in Alzheimers disease."

**"The human body has an endo-cannabinoid system to satisfy the CB1 and CB2 receptors. Cannabis-based drugs can thus supplement the body's endo-cannabinoids. There are approximately 65 different cannabinoids, all of which have different potential impacts on the human body. We believe that cannabinoids are great for treating opioid addiction, as some of the same receptors that interact with methadone, the treatment that is used on opioid addicts, interact with cannabinoids. If the receptors can be satisfied by a non-opioid drug, it will be able to alleviate the craving for opioids."**

**- Dr.Trevor Castor,  
President and CEO,  
Aphios**

A huge element of this expansion of basic neuroscience understanding has come from the explosion in NIH funding for neuroscience in the first decade of the 2000s. In the 1990s, the NIH channeled US\$954 million into neurology research. In the 2000s, this number spiked to over US\$8 billion. This was a larger increase than in any other therapeutic area, and has created a wave of insights a decade later that the industry is currently in the process of translating into new therapies.

Developments in neuroscience are always uncertain, but some experts, such as Roche CEO Bill Anderson, believe we are on the cusp of major breakthroughs: "Neuroscience has the potential to be in the 2020s what oncology has been in the last decade."

If such is the case, it will be an exciting road forward for all involved. ■