

Nemus Bioscience is developing Bio-engineered Medicines using Cannabinoid Molecules in a Pro-drug of THC to offer a Revolutionary Treatment for Glaucoma Patients with a Dual Benefit of Lowering Intraocular Pressure and Providing Neuroprotection



Dr. Brian Murphy, MD, MPH, MBA
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Interview conducted by:
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CEOCFO: *Dr. Murphy, you have almost two decades of experience in drug development and evaluation, both from academic and industry perspectives. What attracted you to Nemus Bioscience?*

Dr. Murphy: There were multiple reasons to see Nemus as an attractive opportunity. Probably the first and foremost was the diversity for growth in the cannabinoid-based therapeutic space. Cannabinoids are proving to have utility across multiple organ systems in the body leading to diverse treatment opportunities. The second reason is that many of these opportunities are in disease targets of unmet medical need and in particular to Nemus: ophthalmology, neurology, analgesics, and infectious diseases. There are not that many therapeutic molecular targets that have the versatility to impact human health on as many levels. A third reason was the company affiliation with the University of Mississippi. The University has had the only federal license to grow, cultivate, and research cannabis and cannabinoids autonomously for the past fifty years. They bring a wealth of intellectual capital to our drug development programs and pipelines. The last reason that brings this all together was the mission of the company and that mission is devoted to improving health for people with diseases that are currently underserved by using precision medicine. That is, to deliver these molecules to patients in an optimized way that is more targeted than just smoking the plant.

CEOCFO: *Are your compounds strictly from the University or also in-house?*

Dr. Murphy: Currently, given our relationship with Ole Miss, the University is acting as the discovery arm of R&D. They are responsible for the patents related to the bio-engineered molecules that we are using. We currently have a global, exclusive relationship with the University related to the patents, indications and routes of administration that we have in-licensed from them.

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CEOCFO: *Cannabinoid-based therapies are starting to get a great deal of attention these days. Before we get into what Nemus is actually doing, would you explain cannabinoid-based therapies, what sets you apart from conventional drugs, and what sets you apart from others developing cannabinoid-based therapies?*

Dr. Murphy: Cannabinoid based therapies revolve around the fact that there are more than 100 identified cannabinoid-related molecules that can be extracted from the cannabis plant. These molecules essentially exert their effects mainly through the activation of cannabinoid receptors that are in the body. There are basically two types of cannabinoid receptors, CB-1 and CB-2. These two receptors are located in almost every major organ of the body. However the central nervous system seems to have a preponderance of CB-1 type receptors while the immune system seems to have a preponderance of CB-2 type receptors. The cannabinoid-based therapeutic companies are working to understand the interaction of their particular cannabinoid molecules with these receptors, and to understand what the physiologic outcome is in either activating or blocking these receptors. Another challenge is to develop a formulation for these molecules that best balances safety and efficacy by having reliable bioavailability and consistent pharmacokinetics. In other words, can you get the drug to the various organs and from a safety perspective, are the drug levels within a therapeutic window as opposed to having significant peaks and troughs that could be impacted by other drugs patients are taking or even what foods they are eating. These are the topline issues in drug development amongst people doing cannabinoid-based drug development. I think what sets cannabinoid therapeutic developers apart from those developing conventional drugs is nothing. If you are in the cannabinoid biopharmaceutical space, we consider these molecules to be on the critical path of regulatory-approved drug development, despite being originally derived from a plant. Cannabinoid molecules used as medicines actually date back thousands of years for multiple uses, especially related to pain management as seen in gout and arthritis. What Nemus is doing involves taking these molecules and re-engineering them into acceptable pharmaceutical products. This really falls under the rubric of botanical-based medicine. There is a long history of pharmaceutical products being developed from plants. Many anti-cancer therapies are derived from plants, there is also theophylline for asthma and COPD, and digoxin for heart failure: all derived from a plant. I would say as far as the comparison between cannabinoids and conventional drugs or differences, there really is not a difference necessarily in the regulatory approval process. We are following the same regulatory pathways, the same principles and regulations, for getting cannabinoid molecules approved as a drug, just as if it were any other type of medicinal product.

CEOCFO: *Are you working with plant-based cannabinoids, synthetic or both?*

Dr. Murphy: I think what separates Nemus from other companies developing cannabinoids is that our cannabinoids are both chemically and biosynthetically derived. We are the only company developing across the spectrum of our pipeline, biosynthetically derived API (Active Pharmaceutical Ingredients) through our 2016 affiliation with Teewinot Life Sciences and Albany Molecular Research Inc. One other difference that sets Nemus apart from other companies is that we have global

composition of matter and methods of use intellectual property (IP) for our lead molecule THCVHS, which is a pro-drug of THC. The patent footprint ranges from Asia, with Hong Kong and Japan, to Australia, North America, the United Kingdom, and a dozen countries in the EU. Some other cannabinoid companies do not have a global patent estate nor composition of matter patents. They may have patents based on the genetic composition of plants or they may have patents in the delivery system but we have composition of matter, methods-of-use, as well as method of IP for our pro-drug of THC. We look to have the same situation for our analog of CBD. I think the way we derive our API, our patent situation, and the global nature of our patents, sets us apart as being unique from a lot of the other cannabinoid companies out there.

CEOCFO: *What is the mode of delivery?*

Dr. Murphy: One of the hallmarks of cannabinoid molecules is that they are very lipophilic or fat soluble, so delivery through an oral route of administration can often be complicated by variability in absorption, metabolism or drug-drug interactions. This also includes variability seen when ingested compounds undergo first-pass metabolism by the liver. Working with the University of Mississippi, Nemus has licensed bio-engineered cannabinoids to make them more hydrophilic or water soluble to give these molecules versatility for routes of administration that can potentially avoid first-pass metabolism in the liver and the irregularities that are associated with oral administration of cannabinoids. On a molecular or cellular level, having these molecules be more hydrophilic also allows them to transfer across membranes better and there is no better example of this than our pro-drug of THC being used in the eye for glaucoma. If you were to take pure THC and make it into an eye-drop, it would resemble a drop of cooking oil. It hits the outer barrier of the eye, the cornea, and very little of that drug reaches key organs in the eye. Whereas, if you use a pro-drug approach with THC, the drug not only can get into the anterior chamber of the eye but we also find that the drug is able to penetrate into the posterior chamber of the eye as well. That is very important because the eye is very dense with cannabinoid receptors, especially CB-1 receptors located on the organs that regulate intraocular pressure in the eye which is key in treating glaucoma. By virtue of re-engineering these molecules to be more hydrophilic, we have the versatility of an ocular formulation for the eye, developing an intranasal spray, working on embedding the drug in a matrix so that it can be used for buccal administration, which is essentially a tape that adheres to the gingiva or gum in your mouth, and dissolves over fifteen or twenty minutes with the cannabinoid absorbed directly into the blood stream, avoiding the GI track. We also have the ability for transdermal administration as well as trans-membranous administration, either by a rectal or vaginal suppository. Bio-engineering provides great options on potential routes of administration.

CEOCFO: *You have drug candidate programs in pre-clinical stages of development, especially for glaucoma. Would you tell us about the market size, is glaucoma considered an area of unmet need and what was the impetus for applying your technology to this indication?*

Dr. Murphy: Our lead candidate right now is a molecule that is a pro-drug of THC. We use the identifier NB1111. This pro-drug of THC is designed for the treatment and management of glaucoma. The current western market for glaucoma is in excess of \$3 billion. The reason I say

the western market is because a lot of the drugs either in development or currently approved for glaucoma, focus on lowering intraocular pressure because in western society, glaucoma is typically the type where you see an elevated pressure within the eye. It is hypertensive glaucoma. The drugs relieve that pressure thereby increasing blood-flow to the retina and the optic nerve to preserve vision. However, in eastern societies, especially Japan, at least 90% of the patients with glaucoma have something called normo-tensive glaucoma. They have a situation where retinal ganglion cells are dying but they are not dying because pressure in the eye is unduly elevated. You can also see this in segments of other Asian societies in China and Korea, although not to the same degree as in Japan. We feel that NB1111 could be an ideal therapy for Asian glaucoma markets as well as in western nations because as seen in animal data to-date, NB1111 not only effectively lowers intraocular pressure, but cannabinoids as a class of molecules, have been shown to be intrinsically neuro-protective. Protecting retinal ganglion cells of the optic nerve is really the holy grail of treating glaucoma. We feel that the pro-drug of THC is positioned in a way that it could offer a dual benefit to patients: lowering intraocular pressure and also providing neuroprotection. The glaucoma market is currently one that could be categorized as a “non-responder” market in that more than half of patients require more than one drug to manage their condition. This unmet need could possibly be filled by a cannabinoid medication that given the NB1111 product profile, could act as a first-line or adjunctive therapy in the glaucoma treatment space. Human study data will be valuable in further guiding the positioning direction for this pro-drug of THC.

CEOCFO: *Where are you in the process with NB1111?*

Dr. Murphy: We are working with AMRI to produce drug product and then to formulate the molecule, initially as an eyedrop. We have successfully demonstrated synthetic scale-up capacity with an API purity of 99.7% which meets FDA criteria for purity. From the formulation stage, we want to do a bit more animal testing then enter human trials. Our target for having a pre-IND meeting and then subsequent IND filing, is in Q-4 this year to Q-1 of next year. In addition, Nemus is looking at a number of options right now to see how we can expedite the critical path to human data and we would update the investment community at the appropriate time pending that analysis.

CEOCFO: *Would you tell us about your NB2111 for chemotherapy-induced peripheral-neuropathy? What are you doing that would potentially aid in easing the suffering of these patients?*

Dr. Murphy: In the United States there are roughly four million patients a year that undergo chemotherapy and a significant portion of them do develop chemotherapy-induced peripheral neuropathy. We are currently looking at a way to formulate an analog of cannabidiol, NB2111, to address these pain management needs. In 2017, we issued data updates about this analog of CBD in multiple animal studies and the main takeaway was that this drug was able to deliver analgesia or pain relief equivalent to morphine and that of oxycodone. As an added finding, we also found that this drug, unlike opioids, did not display attributes of addiction in this validated animal model. This means alleviation of pain comparable to opioids but does not display qualities of addiction like opioid counterparts. We are potentially looking at a molecule that in

animal experiments to-date, traverses the blood-brain barrier and can enter all major organ systems of the body. There is a dual potential here, not only to be a choice for analgesia, but also potentially a candidate therapy to help patients with chronic pain wean off opioids into a cannabinoid-class of molecule that controls pain but are not as addictive.

CEOCFO: *As CEO, what are you doing to get the word out to the medical and investment communities? Are you attending conferences and going on road shows to explain the value that Nemus brings to the table?*

Dr. Murphy: The last few years we have focused on fundraising which is typical of any startup biotech. When you are in fundraising mode, you sometimes must limit a lot of media that may be perceived as marketing events. We focused instead on reporting scientific advances and information that impacted development. Now we are in a more stabilized capital position thanks to our new relationship with Emerald Health Sciences. Therefore, we will be able to generate more communications through media portals as well as continuing our information outflow through scientific channels both through medical and basic science meetings in an effort to raise the profile of the potential therapeutic advantages of using pharmaceuticalized cannabinoids among the medical and investor communities. Additionally, there may be investors in the cannabis market who may be interested in the cannabinoid pharmaceutical space as a longer-term investment play. With regulatory approval comes insurance coverage for the therapy, validation on purity and consistency of the product, along with the knowledge that the drug has met a rigorous outcomes program showing the efficacy and safety profile of the drug. We anticipate that these attributes could be highly desirable by many different groups, but particularly patient populations looking for tested and validated therapies for their conditions.

CEOCFO: *In closing, why is Nemus Bioscience a company to watch?*

Dr. Murphy: I think Nemus is exciting because we are looking to take bio-engineered cannabinoids developed for specific conditions and then scale-up manufacturing utilizing biosynthetic methods which can have a positive effect on our cost-of-goods sold. Nemus is working to provide a demonstrable value-proposition for our investors balanced by our research and intellectual capital to help patients in global markets, especially those with serious unmet needs. The recent investment by Emerald Health Sciences also provides much needed financial stability so that the company can execute on our vision and technology. I would say right now in the pharmaceutical field, there are two significant transformational moments. One is CAR-T immunotherapy for cancer. The other is the coming age of cannabinoid-based medicines, which I believe, will be the next once-in-a-generation transformational moment in pharmaceuticals.

