

## Lexaria Bioscience Corp.

(LEXX - NASDAQ)

### An Investment That's Easy to Swallow

Based on our DCF model and a 15% discount rate, Lexaria is valued at approximately \$15.00 per share. Our model applies a weighted average 13% probability of ultimate approval and commercialization of products employing DehydraTECH. The model includes contributions from the United States and Rest of World.

Current Price (9/17/2021) **\$6.32**  
Valuation **\$15.00**

Lexaria is a biotechnology company seeking to enhance the bioavailability of a broad variety of drug agents with its DehydraTECH (DHT) technology using oral and topical delivery. The approach combines lipophilic APIs with specific fatty acid and carrier compounds followed by dehydration using a proprietary process.

DHT offers several attractive features vs other drug delivery technologies: substantial improvement in bioabsorption both in terms of time to measurable plasma levels & AUC, brain permeation for some APIs, masking of unwanted taste & reduction of unwanted side effects. As the technology does not employ a covalent bond, the combined product is not a new molecular entity and can rely on previously conducted safety and efficacy data to obtain regulatory approval.

Lexaria receives revenues from licensing & product sales which can in part fund R&D operations which require minimal capital. R&D activities are pursuing both preclinical and clinical programs. The lead program is investigating CBD for the reduction of hypertension with three active clinical trials. Other DHT candidates include antivirals, nicotine, PDE5 inhibitors, NSAIDS, hormones, colchicine & others.

We forecast penetration into global markets for hypertension, nicotine delivery and antiviral product categories. Our valuation assumes a 2024 regulatory approval and commercialization of DehydraTECH CBD in the US and developed markets.

### INITIATION SUMMARY DATA

52-Week High **12.50**  
52-Week Low **3.97**  
One-Year Return (%) **N/A**  
Beta **1.54**  
Average Daily Volume (sh) **1,158,268**

Shares Outstanding (mil) **5.73**  
Market Capitalization (\$mil) **36.2**  
Short Interest Ratio (days) **2.18**  
Institutional Ownership (%) **7.6**  
Insider Ownership (%) **10.0**

Annual Cash Dividend **\$0.00**  
Dividend Yield (%) **0.00**

5-Yr. Historical Growth Rates  
Sales (%) **N/A**  
Earnings Per Share (%) **N/A**  
Dividend (%) **N/A**

P/E using TTM EPS **N/A**  
P/E using 2020 Estimate **N/A**  
P/E using 2021 Estimate **N/A**

Zacks Rank **N/A**

Risk Level **Above Average**  
Type of Stock **Small-Growth**  
Industry **Medical**

### ZACKS ESTIMATES

#### Revenue

(In millions of USD)

	Q1	Q2	Q3	Q4	Year
	(Nov)	(Feb)	(May)	(Aug)	(Aug)
2020	\$0.0 A	\$0.0 A	\$0.0 A	\$0.3 A	\$0.3 A
2021	\$0.3 A	\$0.2 A	\$0.2 A	\$0.2 E	\$0.9 E
2022					\$1.2 E
2023					\$1.5 E

#### Earnings per Share

	Q1	Q2	Q3	Q4	Year
2020	-\$0.35 A	-\$0.37 A	-\$0.50 A	\$0.31 A	-\$1.42 A
2021	-\$0.24 A	\$0.10 A	-\$0.50 A	-\$0.23 E	-\$0.94 E
2022					-\$0.93 E
2023					-\$0.93 E

## INITIATION

We are initiating coverage of Lexaria Bioscience Corp. (NASDAQ: LEXX) with a valuation of \$15.00 per share. This present value is based on cash flows related to probability adjusted estimates related to the completion of the hypertension, nicotine and antiviral programs, partnership with consumer, medical and pharmaceutical companies, approval by regulatory authorities and commercialization of approved products. Lexaria is advancing a number of programs using its proprietary DehydraTECH (DHT) drug delivery technology, primarily in cannabidiol (CBD) for hypertension (HTN), nicotine for oral pouches and nicotine replacement therapy (NRT), antivirals and related compounds for COVID and other viral diseases. The company also has relationships with several consumer products companies which provide growing revenues to the company in the CBD and nutraceuticals spaces.

Lexaria's DHT takes advantage of the digestive and circulatory system's fast track pathway for long chain fatty acids (LCFAs) to deliver a variety of drug compounds to the blood plasma. LCFAs are able to bypass absorption into the blood via the capillary system and instead form into triglycerides which are transported into lymph vessels as chylomicrons via the lymphatic lacteals. This route allows for more rapid delivery to the circulatory system and bypasses the liver, improving bioavailability.

DHT employs a relatively simple structure that combines an API with an LCFA. LCFAs can be any number of edible oils that are mixed with the API then combined together with a carrier compound by way of a dehydration synthesis reaction in commercial dryers. Lexaria has almost exclusively used high oleic acid sunflower oil as the LCFA source for its formulations, although its patents cover many other fatty acid source compounds. Carrier compound excipients are added which may improve passage through the digestive system and allow the mixed product to be rendered as a powder for later use in a capsule or emulsification.

DHT is amenable to lipophilic APIs and has been investigated in a number of compounds including cannabinoids, nicotine, antivirals, PED5 inhibitors, human hormones, non-steroidal anti-inflammatory drugs (NSAIDs) and vitamins among others. Many of these drugs have low bioavailability or take a long time to enter the bloodstream. In addition to rapidly and efficiently shuttling desired compounds into the bloodstream, DHT also provides other benefits including taste masking, improved delivery across the blood brain barrier (BBB), reduced levels of drug required for efficacy and reduced risk of side effects.

Lexaria is conducting several preclinical and clinical studies to advance DHT with CBD for hypertension. Two animal studies have generated successful results and three human studies have been completed or substantially completed and have provided evidence of safety and efficacy. Two other human studies are being prepared to begin this autumn which are expected to produce data over the next year. Four preclinical studies have been successfully completed in the antiviral program which have examined compounds such as remdesivir and colchicine in cell-based and animal studies. The company's longest standing relationship is in the nicotine space. In recent years, with increasing restrictions on smoking, nicotine delivery in oral pouch (snus) avoids risks of lung cancer and provides an alternative when smoking is not allowed. New alternatives for NRT are in demand as existing offerings suffer from slow onset and low bioavailability.

Lexaria offers a portfolio of indications that take advantage of DHT's simple but elegant approach to drug delivery. DHT substantially improves the rapidity and quantity of API transport to the blood plasma and brain using the body's natural process for distributing fatty acids via the oral route. Products from [Cannadips](#), [Impact Naturals](#) and [Amari Botanicals](#) among other consumer goods companies that use Lexaria's technology are being sold online and at retailers including Albertson's, Safeway and Hudson News stores. Interest in using DHT extends across many categories beyond the primary pharmaceutical focus of the company from foods to beauty products and nutraceuticals, and across a range of formats from oral ingestible to oral buccal/sublingual to topical products.

Target markets for APIs that can benefit from DHT are immense. Hypertension affects about 150 million persons in North America and over a billion around the globe. Many of these individuals are untreated or do not benefit from existing medications. DHT with CBD offers a natural alternative to hypertension control for many who are unresponsive to existing medicines or could benefit from the product in combination with currently prescribed therapies. Viruses are omnipresent in our daily lives and their impact extends beyond the over 200 million cases and 4.3 million deaths from COVID around the globe. Every year from 10 to 50 million Americans catch the flu and around 1 billion global cases occur with hospitalization rates of 1 – 2%.<sup>1</sup> There are also many other viruses that cause severe symptoms, hospitalization and death. The need for orally administered anti-viral medications is critical to keeping hospital beds open and treating those in areas with less developed health care infrastructure. There are ap-

<sup>1</sup> Based on [CDC Figures](#)

proximately one billion smokers around the world and around 40 million in the United States. There is significant demand for nicotine replacement products, substitutes for nicotine when smoking is prohibited and less risky alternatives to smoking. This need opens the door for DHT technology which can address many of the shortcomings related to nicotine addiction including rapid binding to receptors in the brain and inconspicuous consumption.

On May 31, 2021, Lexaria held \$8.5 million in cash on its balance sheet after raising gross proceeds of \$11 million in January 2021. The funds have enabled Lexaria to continue multiple preclinical and clinical studies clearing a path for partnership and further development. The company holds no debt and has a market capitalization of just over \$35 million. We expect the company to consume from \$3.5 to \$4 million in cash annually, providing a multi-year runway with existing cash reserves. The company also disclosed that it had received an additional ~\$4 million in funds from warrant exercises during the fourth quarter.

We anticipate that partnerships and pivotal data will emerge over the next several years with registrational submissions by 2023 and commercialization in 2024 for DHT CBD in hypertension potentially using the 505(b)(2) pathway. Other development products in nicotine and antivirals are expected to come to market in subsequent years. Existing revenues from partners in the consumer goods space provide current revenues and are forecast to grow at a modest rate offsetting cash burn and providing support for the technology.

Key reasons to own Lexaria shares:

- **Patent portfolio supporting DehydraTECH in multiple compositions**
- **DehydraTECH provides marked improvements over other methods of API delivery**
  - **Improved bioavailability**
    - **Fewer side effects**
    - **Lower drug cost**
  - **More rapid delivery to blood plasma**
  - **Able to cross the blood brain barrier**
  - **Flavor masking allows for use of fewer excipients**
  - **Allows select infused or injected drugs to be administered orally**
  - **Approaching infusion levels of drug bioavailability**
    - **Can generate substantial savings converting infused medicines to oral**
- **DehydraTECH can augment performance of numerous APIs**
  - **Cannabidiol (CBD)**
  - **Nicotine**
  - **Anti-virals**
  - **PDE5 inhibitors**
  - **NSAIDS**
  - **Hormones**
  - **Vitamin D3**
- **Existing license and product revenues provide supportive cash flow**
  - **Relationships with several consumer packaged goods (CPG) manufacturers**
  - **Double digit revenue growth**
- **Low cost technology that can produce up to 400,000 CPG units per day at existing facility**
- **Collaborations with Fortune 100 companies Altria and British American Tobacco**

In the following sections we review the various APIs being pursued by Lexaria and the studies conducted on their behalf. A review of the lead indication in hypertension is presented along with discussion of the disease's prevalence, treatment and risk factors. We report on relevant preclinical and clinical data, trial design and development history for DehydraTECH in hypertension and provide a summary of other potential combinations with the technology. Following an in-depth discussion of our model assumptions, we provide an appraisal of Lexaria's valuation generating a target price of \$15.00.

## TECHNOLOGY, INDICATIONS & CLINICAL TRIALS

### Scientific Background

Drug delivery is a critical aspect of administering medicines; however, safe and effective delivery of a drug agent to a target site presents many challenges. Many compounds are poorly soluble, toxic to certain tissues or can break down as they pass through the body. If administered orally, they may also transit the gastrointestinal (GI) system and reach the bloodstream only after an extended period, frequently after being partially metabolized via passage through the liver. A drug's efficacy and side effect profile can vary significantly depending upon the drug delivery system and route used to transit to the tissues and cells to where it is needed.

Drugs can be administered to the body via numerous routes with some of the most common being oral, intravenous, transdermal and inhaled. Oral administration presents several advantages over other alternatives, including ease of delivery, patient preference, cost effectiveness and favorable absorptive properties of the GI tract among others. However, oral administration also suffers from drawbacks in part due to losses during first pass metabolism and a delay between administration and entry into the blood plasma. Primary disadvantages include slow onset, low bioavailability, and irregular absorption and inconsistent pharmacokinetics (PK).

Bioavailability is the proportion of a dose of medicine that reaches systemic circulation unchanged after administration. It can be impacted by numerous factors, including method of administration, formulation and physicochemical characteristics. For oral administration, GI conditions may significantly influence the rate of absorption depending on fed or fasted states and GI health. The intravenous route offers high bioavailability and rapid onset; however, it usually requires a visit to a hospital, medical assistance and presents a risk of infection.

To address the difficulties faced by oral and intravenous administration, drug delivery must offer rapid entry into the blood plasma and present a predictable PK profile. Bioavailability must be high in order to limit side effects and to ensure sufficient drug infiltrates target tissues. It must also be cost effective, especially in the CPG industry.

Orally administered drugs commonly cross the intestinal wall and then navigate the portal circulation to the liver. Following this route, the agent undergoes first pass metabolism, thereby reducing its concentration. It must also traverse the epithelial membrane of the small intestine delaying its entry into the bloodstream. The small intestine presents a large surface area and consumed contents remain here for a relatively long period. A drug may be absorbed by passive diffusion for small molecules or active transport for larger ones. Lipophilic drugs transit cell membranes to access the bloodstream, while water-soluble drugs enter through paracellular spaces.

To improve oral delivery of lipophilic drugs, industry has turned to drug delivery vehicles such as oils, dispersions, surfactants, self-emulsifying formulations, emulsions and liposomes<sup>2</sup> with varying degrees of success. Lipids and oils in particular exhibit many attractive characteristics in drug delivery. Oil can solubilize material amounts of a lipophilic drug, increase the proportion of this drug into the intestinal lymphatic system and increase absorption from the GI tract.

Drugs with a narrow therapeutic index merit special treatment as variations in dose or blood concentration may cause serious therapeutic failures and/or adverse drug reactions that are life-threatening.<sup>3</sup> For this class, improved consistency in drug absorption and bioavailability are primary considerations.

A key aspect of drug delivery often overlooked is flavor masking. Many APIs have a bitter taste that must be concealed, especially for pediatric or animal health populations. The natural aversion to bitter tastes is thought to have evolved to protect against accidental poisoning. However, despite the health benefits of many medicines, taste can interfere with proper administration. A variety of approaches are used to conceal the taste of a medicine, including sweetener or excipient addition, complexation, coating, matrix entrapment or prodrug formation. Other remedies for taste masking include the use of cyclodextrin, sweeteners, amino acids and flavoring agents. In other circumstances, lipophilic vehicles, lecithin, polymers and coating agents such as starch, gelatin, ethyl cellulose may also be used to hide unpleasant taste. A lipophilic drug can be masked by placing it into a lipoidal matrix. Oil based liquids can also provide masking qualities by coating the taste buds. Fatty acids are able to mask bitter tastes through the formation of hydrogen bonds and hydrophobic interactions with bitter substances.<sup>4</sup>

<sup>2</sup> Gershanik, T., Benita, S. Self-dispersing lipid formulations for improving oral absorption of lipophilic drugs. *European Journal of Pharmaceutics and Biopharmaceutics* 50 (2000) 179±188

<sup>3</sup> Regulatory Science Research Report: [Narrow Therapeutic Index Drugs](#). US Food & Drug Administration.

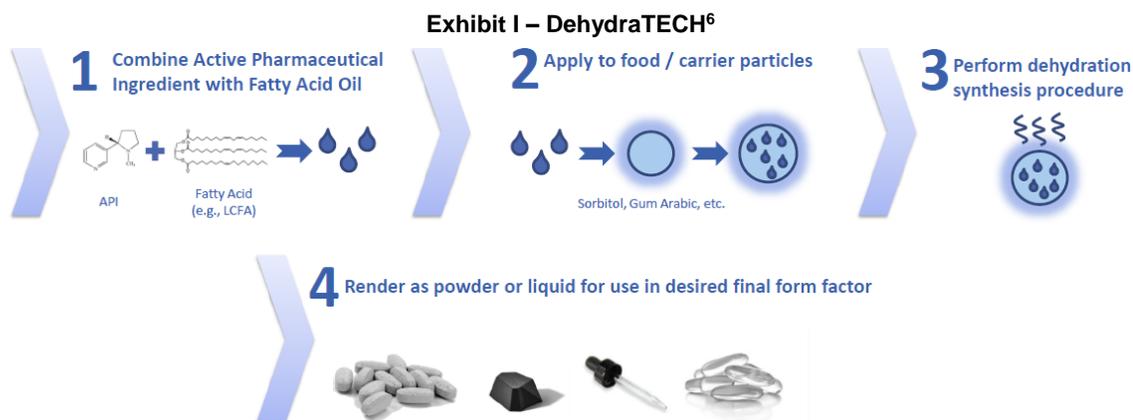
<sup>4</sup> Ogi, K. *et al.* Long-Chain Fatty Acids Elicit a Bitterness-Masking Effect on Quinine and Other Nitrogenous Bitter Substances by Formation of Insoluble Binary Complexes. 12Sept15 <https://doi.org/10.1021/acs.jafc.5b03193> American Chemical Society.

## DehydraTECH (DHT)

In response to the limitations of standard oral administration approaches that achieve only limited bioavailability and slow onset of action, new techniques have been developed. DehydraTECH (DHT) is a simple but elegant approach which allows for higher delivery rates compared with other technologies.

DHT creates a molecular association between API and LCFAs together with emulsifier compounds which enhances the bioavailability of the lipophilic active agent. The bioavailable active agent can be a protective colloid, an edible oil or fat and a taste masking agent. The resulting compound provides several benefits including taste masking, rapid delivery to the lymphatic then circulatory system and high levels of bioavailability.

DHT overcomes earlier mechanisms that dissolve a lipophilic compound in a water-miscible organic solvent. Earlier approaches suffered from the lipophilic compound precipitating out as a solid or liquid emulsion that exhibited low bioavailability. Physicochemical solubilization techniques such as micellar solubilization lack sufficient solubility to offer formulations that can deliver therapeutically effective doses. DHT uses LCFAs that are classified as GRAS<sup>5</sup> and attaches them to lipophilic API through an as yet uncharacterized molecular association. API can be any number of lipophilic substances including cannabidiol, nicotine, darunavir and efavirenz among others.



The DHT molecule is able to transit the GI system, first in the mouth where the long chain fatty acids exert a neutralization effect that blunts the taste of the API and blocks receptors that detect bitterness. As the molecule moves through the esophagus, stomach and intestine, it is routed through the lymphatic system, entering through the lymphatic lacteals. Furthermore, the DHT molecule has demonstrated the ability to cross the blood brain barrier and permeate brain tissues for certain APIs, which is believed to be facilitated by way of fatty acid transport proteins that line the vasculature of the human brain responding to the LCFAs that comprise the DHT molecule.

## Indications

Lexaria is pursuing several indications with DHT. The lead and largest opportunity indication is hypertension which is a condition that affects over a billion people worldwide. DHT is also being investigated in antiviral drug delivery in an effort to simplify administration and reduce the burden on hospitals and health care workers especially during a pandemic. Nicotine delivery via oral pouches is another target area for the technology as is nicotine replacement therapy (NRT). With increasing limitations on smoking and well-known health risks, non-combustible tobacco products such as snus have become an alternative for smokers that is inconspicuous and has no risk of lung cancer. Other medicines of interest that can utilize the technology include PDE5 inhibitors for erectile dysfunction, human hormones for hormone imbalances, ibuprofen and naproxen to address pain and Vitamin D3 to address vitamin deficiencies. The company has also examined the use of DHT to deliver colchicine, which is used to treat emergent pericarditis in children and gout. Below, we discuss Lexaria's most advanced indications in hypertension, nicotine and antivirals.

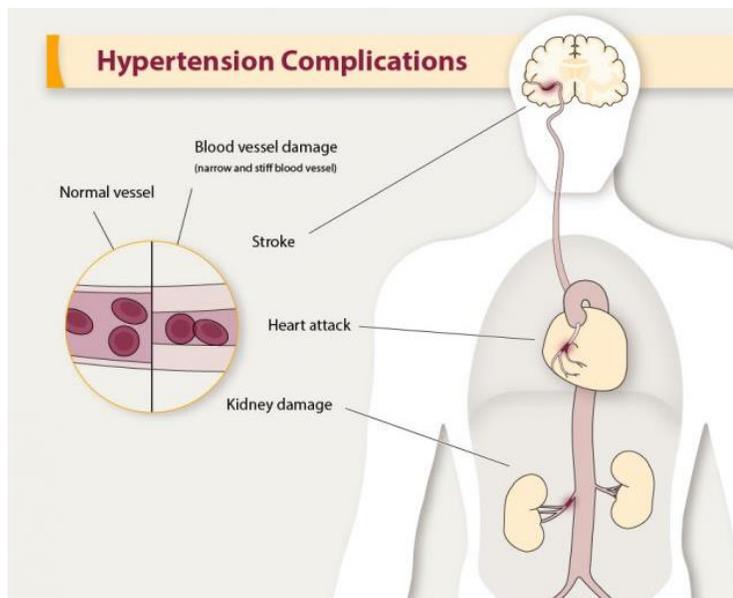
<sup>5</sup> Generally recognized as safe (GRAS) is a FDA designation that a chemical or substance added to food is considered safe by experts and is exempt from the usual Federal Food, Drug, and Cosmetic Act (FFDCA) food additive tolerance requirements.

<sup>6</sup> Source: Lexaria Bioscience Corporate Presentation 3Q:21

## Hypertension (HTN)

Hypertension (HTN) is a condition where blood pressure is elevated, usually above 140/90 millimeters of mercury (mm Hg) as measured by a blood pressure monitor or a provider. Normal blood pressure averages 120/80 mm Hg. The first number is the systolic pressure, which occurs when the left ventricle pumps blood out of the heart. The second number is the diastolic pressure, which occurs between heartbeats, as the heart relaxes and chambers refill. HTN, when experienced over an extended period of time, can cause a number of health issues including fatal heart attack or stroke. Consistently higher than normal pressure can damage the arteries' inner lining and can reduce their elasticity. If there is a weak area of an artery, high blood pressure can cause a bulge or aneurysm which could burst and cause internal bleeding. There is an extended list of injuries that can occur as a result of HTN, including heart damage, such as coronary artery disease, brain damage, such as stroke, kidney failure, sexual dysfunction, vision loss and other conditions. In some cases when blood pressure exceeds 180/120 mm Hg, it is considered a hypertensive crisis that requires immediate medical attention.

Exhibit II – Hypertension Complications<sup>7</sup>



### Incidence/Prevalence

The World Health Organization (WHO) estimates that there are 1.13 billion people worldwide with HTN, making it a common condition. Studies conducted by the National Health and Nutrition Examination Survey during 2017 and 2018 found HTN prevalence of 45% among adults and positive correlation with age.<sup>8</sup> 48.3% of the hypertensive population is able to control it,<sup>9</sup> demonstrating an unmet need for an important public health challenge due to its association with cardiovascular disease. Using data collected over the 2013 to 2016 period, the US National Center for Health Statistics estimated that 108 million adults have hypertension. Of this total, an estimated 82 million of the US adults with HTN do not have it under control. The WHO estimates that prevalence of HTN in Europe is just over 40%. Another study found that control is on average under 15% in each of the five<sup>10</sup> European countries investigated.<sup>11</sup> Two studies, EURIKA<sup>12</sup> and EUROASPIRE,<sup>13</sup> identified a proportion of hypertensive patients with controlled blood pressure ranging from 27% to 47%. This low level of blood pressure control across the globe highlights the need for new approaches to lower blood pressure.

<sup>7</sup> Source: Centers for Disease Control and Prevention Website. High Blood Pressure Symptoms and Causes, accessed May 2020. <https://www.cdc.gov/bloodpressure/images/hypertension-complications-medium.jpg>

<sup>8</sup> National Center for Health Statistics. [National Health and Nutrition Examination Survey](#). July 2020

<sup>9</sup> [Hypertension Prevalence and Control Among Adults: United States, 2015-2016](#). NCHS Data Brief, No. 289. October 2017.

<sup>10</sup> These included Sweden, Spain, England, Germany and Italy.

<sup>11</sup> Wolf-Maier, K., *et al.* Hypertension Treatment and Control in Five European Countries, Canada, and the United States. *Hypertension*. 2004;43:10-17

<sup>12</sup> Borghi, C., *et al.* Lack of Control of Hypertension in Primary Cardiovascular Disease Prevention in Europe: Results From the EURIKA Study. *Int J Cardiol*. 2016 Sep 1;218:83-88.

<sup>13</sup> Kotseva, K., *et al.* The EUROASPIRE surveys: lessons learned in cardiovascular disease prevention. *Cardiovasc Diagn Ther*. 2017 Dec; 7(6): 633-639.

### Treatment

To combat this deadly but conventional disease, a broad variety of treatments have been developed and approved. Treatment spans a wide range and frequently begins with recommendations for lifestyle changes such as weight loss, exercise and a diet high in fruits and vegetables. If this is ineffective, medications such as diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) or calcium channel blockers will be prescribed. There are dozens of medications available for this indication in a wide variety of classes. Despite the varied approaches and choices available, in many cases treatment is ineffective, highlighting the need for new approaches for controlling HTN.

**Exhibit III – Product Classes Used for Hypertension<sup>14</sup>**

Classes of Hypertension Medications			
Loop diuretics	Central agonists	Calcium channel blockers	Angiotensin converting Enzyme (ACE) inhibitors
Beta blockers	Alpha-blockers	Alpha-beta-blockers	Angiotensin II receptor blockers (ARBs)
Vasodilators	Renin Inhibitor	Thiazide diuretics	Potassium-sparing diuretics

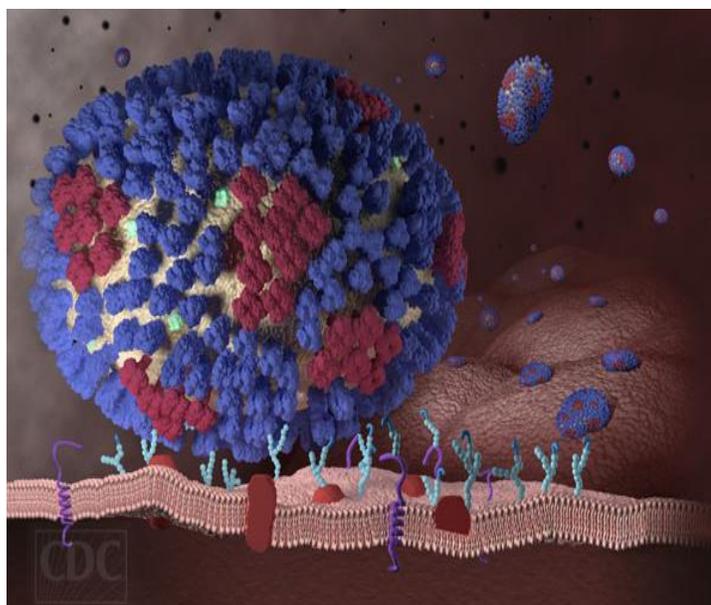
### Risk Factors & Symptoms

There are a number of risk factors for HTN including obesity, excessive intake of alcohol and salt, lack of exercise, poor sleeping habits, diabetes, stress and others. Family history also plays a role. In some cases, other medical conditions can contribute to high blood pressure such as pregnancy, heart defects and kidney disorders. High blood pressure usually subsides when the underlying condition resolves. One of the reasons HTN is so common is that the symptoms are usually undetectable, earning its moniker: the silent killer. In some cases, high blood pressure may cause headache, blurred vision, dizziness and shortness of breath. High blood pressure may also affect the heart which can cause shortness of breath, chest pain and heart attack and can also impact the kidneys, resulting in fluid retention and kidney failure. Since detectable symptoms without diagnostic measurement are uncommon, screening for blood pressure is a routine part of an office visit.

### Viruses

Viruses are small infectious agents that use host cells to replicate and spread. They are not considered life by most biologists as they lack a cell wall, are unable to replicate on their own and cannot survive for extended periods in the extracellular environment. They do have some characteristics of life, such as carrying genetic material, reproduction and evolution. The small particles, on the order of 20 to 300 nanometers, require a host to survive. The host can be animal, plant, bacteria or archaea that provides the cellular machinery required for the virus to propagate and spread. The microscopic particles are present everywhere on earth and can cause disease or provide synergistic benefits to their hosts.

**Exhibit IV – Influenza Virion<sup>15</sup>**



<sup>14</sup> Source: Zacks analyst compilation from various sources.

<sup>15</sup> Source: Centers for Disease Control <https://www.cdc.gov/flu/resource-center/freeresources/graphics/images.htm>

With the emergence of COVID and SARS-CoV-2, viruses now receive daily attention and treating viral infections has become an urgent need. Vaccines are excellent approaches to halting viral spread as they prime the immune system to eradicate the invader as soon as it enters the system. However, in many cases, vaccines are unavailable, ineffective or have not been administered to individuals with the virus. In these cases, treatment is required to attenuate the spread of the virus in the body and to limit an excessive immune response. Many of the treatments for COVID and other viral infections are infused. This includes monoclonal antibodies such as casirivimab and imdevimab and antivirals such as remdesivir. While infusion is an effective method of administration achieving near 100% bioavailability almost immediately, it requires a relatively high level of resources in personnel, equipment, refrigeration, time and hospital space. During pandemic conditions in areas with limited resources, infusion may not be possible and convenient alternatives are needed that are able to rapidly enter the bloodstream in sufficient quantities to have a therapeutic effect.

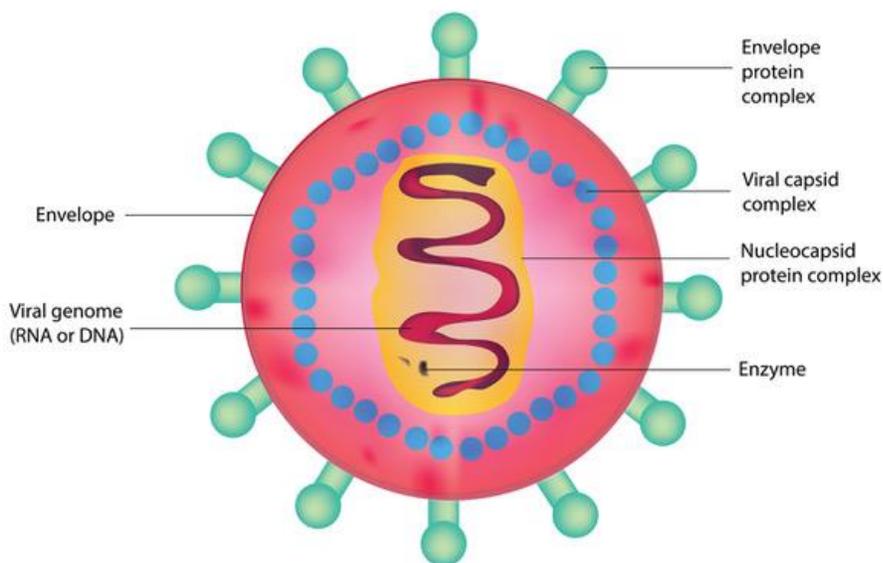
Viruses exist to reproduce and are constantly evolving to evade a host's immune system. One of the ways to expand and evolve is to spread as broadly as possible to new hosts through a variety of mechanisms. Viruses can spread through touch, respiratory droplets, direct contact, bodily fluids, insects and other vectors. While viruses cannot maintain their structure indefinitely outside a host, some have evolved to remain active on an object for extended periods.

### Structure

Viruses contain an RNA or DNA genome that is surrounded by a protective, virus-coded protein coat. The virus particle, called a virion, is frequently surrounded by an envelope, which surrounds the nucleocapsid and capsid providing a protective layer. The capsid is the protein shell that encloses the nucleic acid which encodes the genetic information required for protein synthesis.

### Exhibit V – Viral Structure<sup>16</sup>

#### Structure of Typical Virus



### Prevalence

Viruses are everywhere. They infect all living organisms and are found all over the earth. According to researchers at the NIH, viruses outnumber bacteria ten to one. Other sources estimate that there are 10 nonillion individual viruses on Earth, and are found in all habitable locations from seawater, to the atmosphere, in soil and of course in us.<sup>17</sup> While only a small proportion of these viruses negatively affect human health, the ones that are harmful can have devastating effects. There have been near 220 million reported cases of COVID globally and from 10 to 40 million influenza cases annually.

<sup>16</sup> Source: Shutterstock.com

<sup>17</sup> Wu, K. There are more viruses than stars in the universe. Why do only some infect us? National Geographic.

### *Treatment*

Vaccines are preferred as a preventive approach to viral infection, which enhance the body's immune system to clear the virus. However, in many cases effective vaccines do not exist or have not been administered and the body has to fight the virus without help. There are few medicines that can slow a viral infection but there is treatment for the symptoms and some classes of drugs are able to suppress viral replication. Treating symptoms is important as uncontrolled viral infection can be deadly. The body may mount an excessive immune response which can lead to cell damage, tissue-damaging inflammation and potentially death if not suppressed. In other cases, a viral respiratory infection can lead to a bacterial infection such as pneumonia<sup>18</sup> which can also be deadly. And in yet other scenarios, a viral infection may disable the immune system allowing other opportunistic diseases to take hold, such as in HIV.

In the anti-viral space, many medications including remdesivir, darunavir and efavirenz have been used to suppress viral outbreaks. Some of the viruses these medications have addressed include COVID-19, hepatitis, Ebola, HIV and others. One of the shortcomings of this class of drug is that they require infusion and there is a severe loss in bioavailability if administered via alternate routes.

### **Nicotine**

Nicotine is an alkaloid, fat soluble molecule that naturally comes from plants in the nightshade family. The most common source is *Nicotiana tabacum*, or the tobacco plant which is grown globally, particularly in China, India and Brazil. The chemical compound is an oily liquid that will mix with water and has a boiling point of 247 °C. Nicotine will burn at a temperature below its boiling point, and its vapors will combust at 35 °C in air despite a low vapor pressure. As a result, most nicotine is burned when a cigarette is smoked; however, enough is inhaled to provide the desired effects. When exposed to heat, a portion of the nicotine is transferred to the small airways and alveoli of the lung. The drug is dissolved and transferred across cell membranes at a rate dependent on pH to reach the bloodstream then the brain in a process that only takes seconds.

**Exhibit VI – Tobacco Plant<sup>19</sup>**



### *Nicotine Mechanism of Action*

Nicotine acts as an agonist on nicotinic acetylcholine receptors (nAChRs) which are found throughout the body, autonomic ganglia, at neuromuscular junctions, in the adrenal medulla and the brain. The receptors are also located on the pre-synaptic axon terminals of the central nervous system. This action facilitates neurotransmitter release and thereby mediates the complex actions of nicotine in tobacco users.

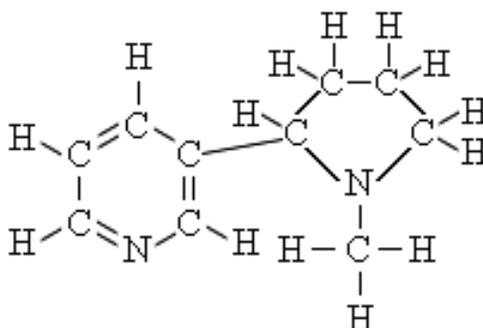
Neurotransmitters are released when nicotine acts on receptors. These include dopamine, glutamate, acetylcholine and gamma aminobutyric acid. These produce short-term euphoric effects and elicit pleasure, increased attention

<sup>18</sup> It is estimated that over 90% of those who died in the 1918 influenza epidemic died from secondary bacterial infections.

<sup>19</sup> Source: Shutterstock.com.

and mental processing ability and improved working memory. Nicotine binds to nAChRs located in muscles and in the ventral tegmental area of the brain. As the stimulant interacts with the receptors, this causes release of dopamine in the nucleus accumbens providing the sense of pleasure that the smoker seeks. Nicotine interferes with the normal binding of acetylcholine, which is an important neurotransmitter and increases the level of activity with the nAChRs. This increase in activity creates an imbalance which triggers a reaction to reduce the production of acetylcholine. Over time, the receptors become desensitized and the number of receptors increases in response to constant nicotine exposure.<sup>20</sup> As the number of receptors increase, tolerance emerges and higher levels of nicotine are required to achieve the same effect.

**Exhibit VII – Nicotine Chemical Structure (C<sub>10</sub>H<sub>14</sub>N<sub>2</sub>)<sup>21</sup>**



When an individual stops smoking, the receptors are not activated due to the absence of nicotine and the pleasure response ceases. This causes withdrawal symptoms including severe cravings, anxiety, anger, increased appetite, impatience, irritability, poor concentration, restlessness, weight gain and insomnia. The brain receptors are also accustomed to stimulation by nicotine in certain settings such as while drinking or after a meal, triggering the urge to smoke.

***Nicotine Replacement Therapies (NRT)***

Although the harm from smoking is associated with the smoke, it is the nicotine that produces the pharmacological effects that lead to addiction. Nicotine replacement products include a variety of administration types to replace the nicotine that is lost when a patient stops smoking. They can include patches, gums, lozenges, sprays, inhalers and tablets and are most commonly used in an attempt to quit smoking. NRT does not precisely reproduce the exposure of arterial nicotine absorbed in the body through smoking, resulting in some symptoms of withdrawal. While smoking can deliver nicotine to the brain in seconds, NRT approaches can take many minutes or hours to achieve the same effect and the user can suffer withdrawal symptoms during the delay. Electronic cigarettes are another approach used for nicotine replacement but are not approved by the FDA. These devices include a system that vaporizes or nebulizes liquid sealed in a cartridge. Medical experts and regulatory authorities are concerned with e-cigarettes regarding labeled and measured nicotine content and insufficient information of the effect of the vaporized liquid and whether or not it may be harmful.

Lexaria's partners Altria (NYSE: MO) and British American Tobacco (NYSE: BTI) may use DHT in snus. Snus is similar to dip or snuff in that it is placed between the lip and gum and in many cases lacks the nitrosamine preservatives and curing byproducts that are associated with chewing tobacco. The product is not ignited, thereby bypassing the impact of smoke on the lungs. The pasteurized tobacco leaves are placed in a pouch and deliver nicotine via the oral mucosa. While no health agency will vouch for the safety of a tobacco product, snus does avoid the greatest risk of cancer to both the user and those around them from smoke. It also provides a way for smokers and others addicted to nicotine to satisfy their cravings in situations where smoking is prohibited. In 2019 the FDA [authorized](#) the marketing of snus smokeless tobacco products under the modified risk tobacco product pathway. Based on evidence provided by the applicant, Swedish Match, the sponsor can make the claim that "Using [their product] instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis." The FDA implicitly recognizes that the use of Swedish Match's snus product will reduce risk and harm compared with smoking. The available scientific evidence demonstrated that relative to cigarette smoking, exclusive use of Swedish Match smokeless tobacco products involves a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.

<sup>20</sup> Govind, AP, et al. Nicotine-induced upregulation of nicotinic receptors: underlying mechanisms and relevance to nicotine addiction. *Biochem Pharmacol.* 2009 Oct 1;78(7):756-65.

<sup>21</sup> Purdue University, Department of Chemistry website. <https://www.chem.purdue.edu/jmol/molecules/nicotin.html>

## Hypertension Studies

Lexaria has disclosed details of five 2021 studies examining DHT CBD for hypertension, plus a recent addition of a sixth study to commence in the Fall of 2021 that is currently in the early planning stages. Two of the studies are animal studies that assessed the rate of absorption and speed that DHT 2.0 delivered CBD to the bloodstream and brain in Sprague Dawley rats. The more important human studies were designed to examine the impact of different doses of DHT CBD on subjects for blood pressure, heart rate and other secondary endpoints.

**Exhibit VIII – Summary of DehydraTECH CBD Studies for Hypertension<sup>22</sup>**

Study	Type	Report Date	Detail	Location	Dose
HYPER-A21-1	Animal	May-21	Absorption rate, speed & tolerability	USA	
HYPER-A21-2	Animal	May-21	Absorption rate, speed & tolerability	USA	
HYPER-H21-1	Human	Jul-21	24 subject BP & heart rate analysis, PK	Europe	1x300 mg/day
HYPER-H21-2	Human	Sep-21	16 subject BP & heart rate analysis, other	Europe	3x150 mg/day
HYPER-H21-3	Human	1H 2022	16 subject stress test, acute pulmonary HTN	Europe	1x300 mg/day
HYPER-H21-4	Human		In early design stages		

### Animal Results

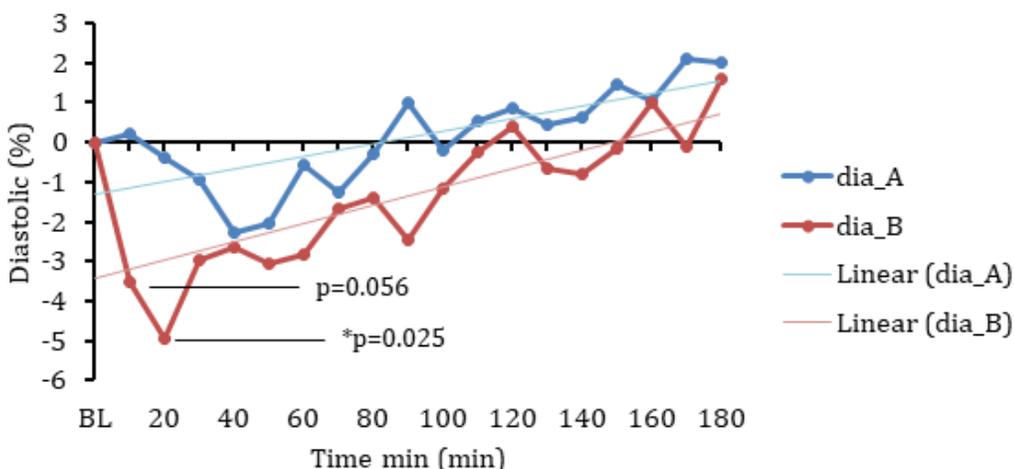
In early May 2021, results from the HYPER-A21-1 study were shared in a [press release](#). In comparison with a control formula using medium chain triglycerides, DHT 2.0 formulations were able to deliver up to 22x more CBD into the bloodstream and up to 17x more CBD into the brain tissue. In each arm of the study, ten male Sprague-Dawley rats were dosed orally at a level of 25 mg/Kg CBD; multiple measurements were made of delivery into the bloodstream and tissues comparing the DHT formulations to certain controls over the following 120 minutes.

In late May 2021, the animal [results](#) from HYPER-A21-2 indicated absorption up to 27x greater for CBD delivery to the bloodstream during the study measurement period compared with the industry standard control. The study measured the effectiveness of the DHT 2.0 formulation, which offers improved performance over previous compositions.

### HYPER-H21-1

HYPER-H21-1 is a randomized, double blind study that is evaluating 24 subjects with untreated pre- or mild hypertension dosed with 300 mg of CBD using DHT and conventional formulations and measured over a three hour period. Measurements were taken every 10 minutes for blood pressure and heart rate. Primary endpoints for the study are time series blood pressure and heart rate analysis. Secondary endpoints include speed and rate of absorption of CBD and its main metabolites. The study will also evaluate inflammatory markers associated with cardiovascular disease and nitric oxide (NO). NO measurements are included to provide mechanistic insight into the anticipated reduction of blood pressure as a result of vasodilation.

**Exhibit IX – Changes in Diastolic Blood Pressure Over Time (Control dia\_A/DHT dia\_B)<sup>23</sup>**

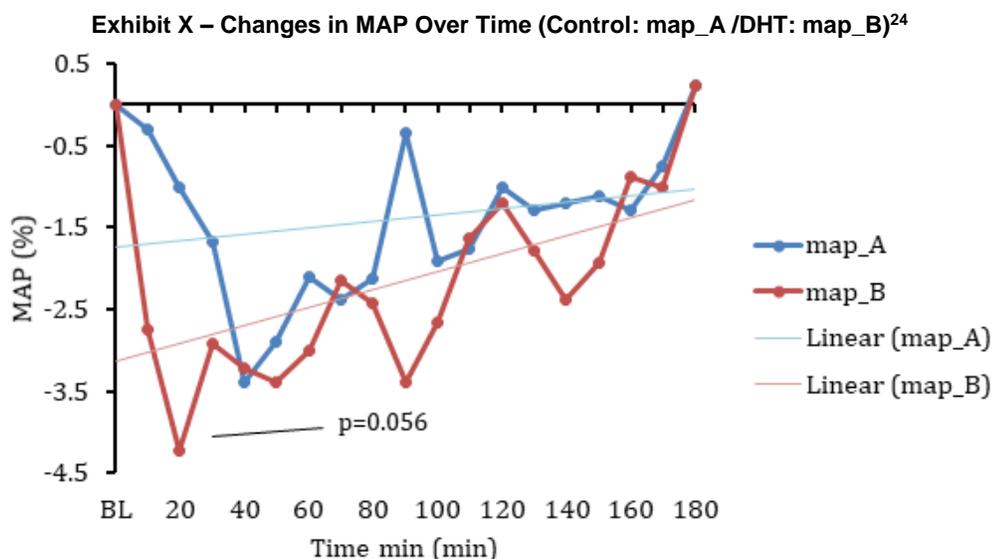


<sup>22</sup> Source: Company press releases and Zacks analyst compilation

<sup>23</sup> Source: Lexaria [press release](#), July 29, 2021. Changes in diastolic blood pressure between generic CBD control (dose A) and DehydraTECH-CBD (dose B). Data are grouped means (n=24) with linear regression.

In a July 29th [release](#), management updated investors with partial results from the trial. DHT CBD enabled a rapid and sustained drop in blood pressure. The effect was most pronounced in systolic pressure and in Stage 2 hypertensive subjects. Blood pressure was reduced for both males and females and provided the most substantial effect in the first hour of the study. Below are the mean results of diastolic blood pressure over time from the study.

A second evaluation compares the change in mean arterial pressure (MAP) between the DHT CBD formulation and control. As with the impact on diastolic blood pressure, the largest impact was noted in the first 20 to 30 minutes after administration.



Secondary analysis is underway and will focus on inflammatory and oxidative markers associated with cardiovascular disease and biomarkers for NO. Final results are expected to be released in the next several months.

### HYPER-H21-2

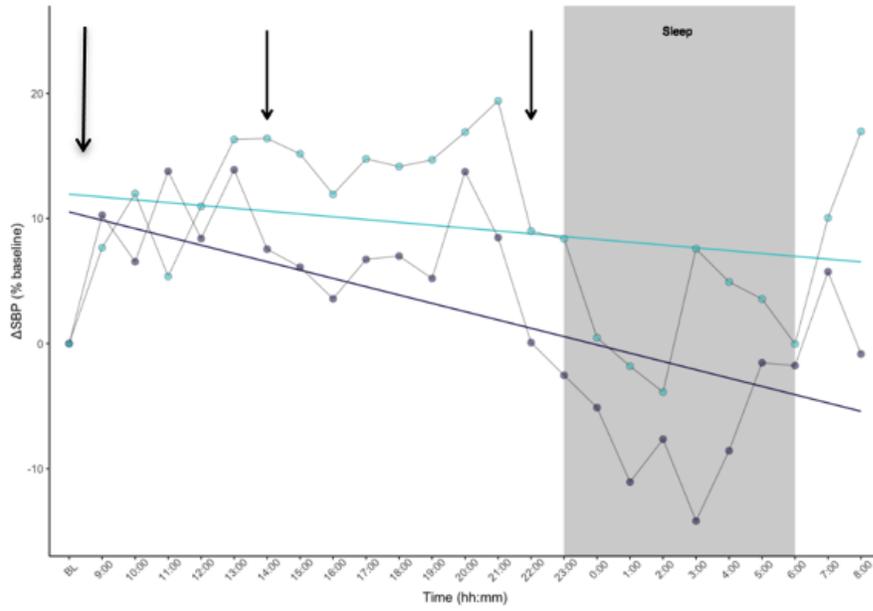
HYPER-H21-2 is a randomized, double blind study enrolling 16 subjects classified as either pre- or mildly hypertensive. This study, which is also being conducted in Europe, targets males and females from 45 to 70 years of age. It differs from the first study in that 150 mg will be administered in three separate doses and data collected over a 24 hour period. One objective of the study was to learn whether multiple doses would produce a different effect compared with a single dose.

Primary endpoints for this study are the same as in the first human study with measurement of blood pressure and heart rate. Secondary endpoints introduce new variables including central arterial stiffness, physical activity and sleep quality (total sleep time, total wake time and sleep efficiency). Dosing for HYPER-H21-2 was [completed](#) in July and initial results were published September 7<sup>th</sup>.

Initial [results](#) of the trial showed as much as a 23% decrease in blood pressure with DHT CBD compared with placebo. This was equivalent to a 20 mmHg difference between the DHT-CBD and placebo arm. Over the 24 hour monitoring period, subjects averaged a reduction of 7.0% (p=0.001) in systolic pressure using DHT CBD vs. placebo. Dosing was 150 mg in three intervals indicated by the downward pointing arrows in the following exhibits.

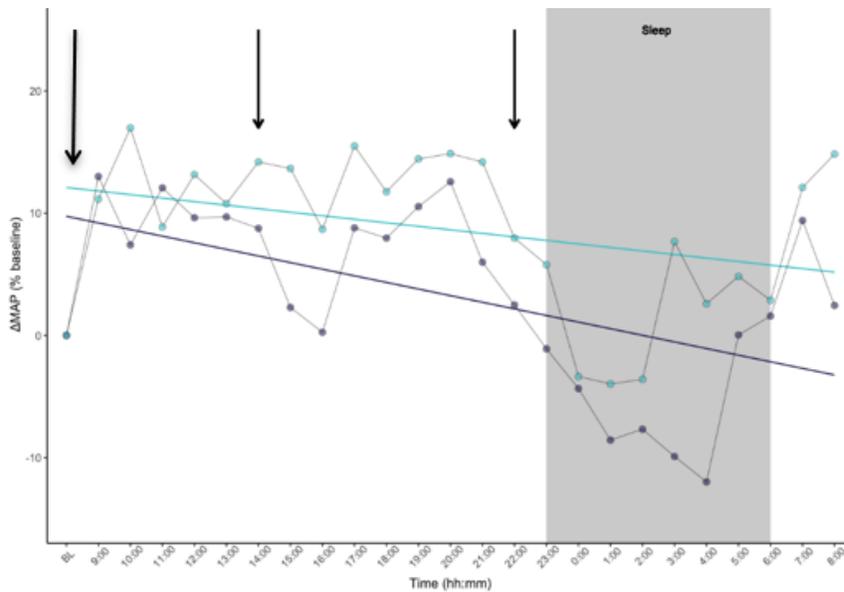
<sup>24</sup> Source: Lexaria [Press Release](#), July 29, 2021.

**Exhibit XI – Change in Systolic Blood Pressure (Purple=DHT CBD/Blue=Placebo)<sup>25</sup>**



Note the increasing separation of the placebo and the treatment arm in each of the charts representing the straight line averages.

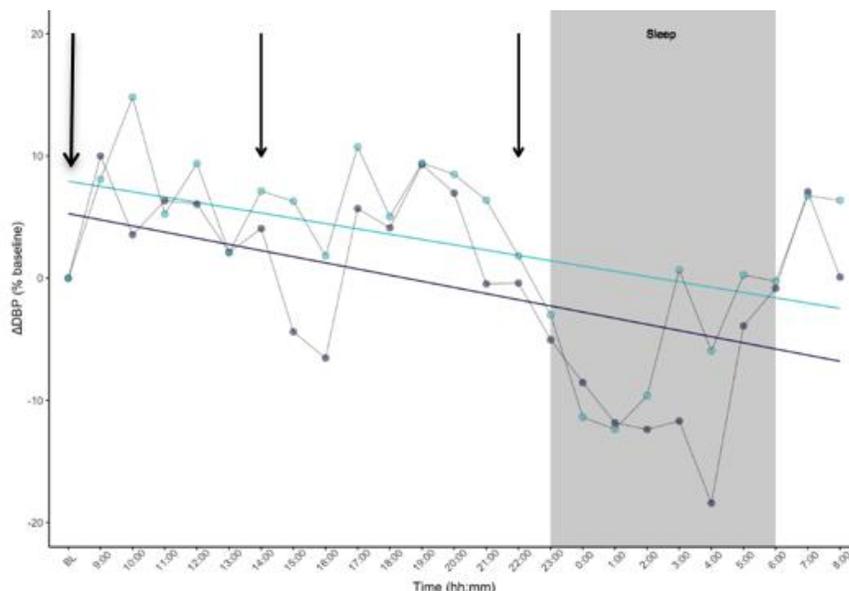
**Exhibit XII – Change in Mean Arterial Pressure (Purple=DHT CBD/Blue=Placebo)<sup>26</sup>**



<sup>25</sup> Source: Lexaria [Press Release](#) September 7, 2021

<sup>26</sup> Source: Lexaria [Press Release](#) September 7, 2021

Exhibit XIII – Change in Diastolic Blood Pressure (Purple=DHT CBD/Blue=Placebo)<sup>27</sup>



Safety continued to be a strong point and DHT CBD was well tolerated by all of the subjects with no serious adverse events or side effects that differed between the groups. This compares with other common blood pressure medications such as diuretics that can cause excessive urination, beta blockers that can cause erectile dysfunction, calcium-channel blockers that can cause leg swelling, and ACE inhibitors that can lead to persistent cough in a small segment of the treated population.

Additional data is expected to be released after further analysis which will include blood pressure subset analyses, sleep quality and other undisclosed data.

### HYPER-H21-3 and HYPER-H21-4

HYPER-H21-3 is a double-blinded, placebo controlled, randomized human clinical study designed to monitor effectiveness of a 300 mg dose of DHT-CBD relative to placebo on blood pressure in volunteers under conditions of hypoxic pulmonary vasoconstriction. Data from this study may demonstrate utility of DHT-CBD for blood pressure reduction in pulmonary edema/hypertension that results from traveling to high altitude regions of the world. HYPER-H21-3 is expected to start after the conclusion of HYPER-H21-2.

Lexaria may pursue other studies to further define DHT CBD safety and efficacy in hypertension. Lexaria is in early stages of designing a fourth human clinical study (HYPER-H21-4) that would likely include a 4-week minimum study duration, with two or three doses of DHT per day. Many approved hypertension drugs require weeks or months of dosing before they provide maximum benefit to the patient; Lexaria will investigate whether or not multi-week dosing of DHT leads to additive benefits not visible in a study duration of 24 hours or less. The goal of this stage of work is to develop a body of research that clearly and convincingly demonstrates the ability of DHT in hypertension to attract a well-funded partner that can both shepherd the product through clinical trials and commercialize it following regulatory approval.

### DHT CBD Next Steps

Following the significant initial results from HYPER-H21-2, the company [announced](#) its intent to begin work to prepare and submit an Investigational New Drug (IND) application to advance DHT CBD into formal, FDA-recognized trials. Lexaria has hired a regulatory and quality assurance consultant to help prepare the document and to help conduct the additional non-clinical, clinical and related product development IND-enabling work required before the IND filing. Recent work conducted includes the human and animal PK studies. Molecular characterization efforts will streamline the body of evidence required for the IND application. An anticipated fourth human clinical trial will also generate data in support of the application. Management disclosed its intent to pursue the abbreviated 505(b)(2) pathway if circumstances permit. This pathway is supported given previous CBD approvals.

<sup>27</sup> Source: Lexaria [Press Release](#) September 7, 2021

## Preclinical Antiviral Drug Studies

DehydraTECH is being used in conjunction with leading classes of antiviral drugs in preclinical studies to combat common viruses. In early 2020, Lexaria filed for a new patent to use DHT for the delivery of antivirals for viral infectious diseases such as SARS-CoV-2 (COVID), human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), Middle East Respiratory Syndrome (MERS), severe acute respiratory syndrome (SARS), influenza, herpes and hepatitis. In a July 22<sup>nd</sup> press release, Lexaria provided a summary of tested and published data for candidates in the antiviral drug class. Two studies were announced in December 2020 later designated VIRAL-A20-2 and VIRAL-A20-3.

The VIRAL-A20-2 study was an animal research PK study. 40 animals were dosed over a 48 hour period with DHT-processed remdesivir and ebastine to identify if DHT transports the antiviral to the bloodstream faster and more efficiently. Results from the study were released in May.

VIRAL-A20-3 began in April 2021 to evaluate the effectiveness of DHT-processed remdesivir and ebastine with non-DHT-processed versions in a SARS-CoV-2 infected human cell culture study. The assessment used an *in vitro* screening assay in infected cells. The primary goal of the work was to ensure that DHT did not negatively impact the efficacy of the compounds before moving to the *in vivo* part of the testing. A primate cell line, VERO-E6, was used.

The formulations used in the previous two studies are being further characterized in a molecular study conducted by Canada's National Research Council (NRC). Nuclear Magnetic Resonance and Liquid Chromatography-High Resolution Mass Spectrometry studies are being performed. The results are critical for confirming the non-covalent nature of the molecular association between the LCFAs and API. Eliminating the possibility of a covalent bond between the LCFAs and the API is important as the existence of such a bond renders the new molecule a new chemical entity (NCE) whereas its absence supports the use of existing research and documentation. NCEs require separate preclinical studies, pharmacokinetic, pharmacodynamic, absorption, distribution, metabolism and excretion studies as well as animal *in vivo* work before they can be cleared for clinical trials. If no covalent bond exists, then previous work on target API may be relied upon to satisfy regulatory requirements for entry into the clinic.

**Exhibit XIV – DehydraTECH Delivery Improvement for Evaluated Candidates<sup>28</sup>**

Drug	AUC Improvement vs. Standard	Drug Class	Indication
Remdesivir	82% (p=0.12)	Reverse transcriptase inhibitor	Broad spectrum antiviral
Ebastine	204% (p=0.027)	Protease inhibitor	H1 antihistamine
Darunavir	54% (p=0.036)	Protease inhibitor	HIV Antiviral
Efavirenz	42% (p=0.028)	Reverse transcriptase inhibitor	HIV Antiviral
Colchicine	167% (p=0.0028)	Tubulin polymerization/microtubule inhibitor	Inflammation/pain

Lexaria conducted a pilot study using DHT-formulated antivirals compared to concentration-matched controls administered via oral gavage to male Sprague Dawley rats. 40 animals were used, divided into four groups. A protease inhibitor (darunavir) and a non-nucleoside reverse transcriptase inhibitor (efavirenz) were administered to the rats in either the DHT or control formulation. Drug levels in the bloodstream using AUC were measured over a 24 hour period.

Results showed a 54% improvement in AUC compared to control for darunavir and a 16% improvement compared to control for efavirenz. The theoretical maximum AUC for each was also calculated and included in the following exhibit. Safety and tolerability was excellent as reported by study investigators with all animals displaying normal activity and behavior throughout the study with no adverse effects noted.

**Exhibit XV – AUC Levels for Darunavir & Efavirenz in Animal Model<sup>29</sup>**

Drug	AUC Level (Last) (hr*ng/mL)	AUC Improvement	Control	AUC Level t=∞ (hr*ng/mL)	AUC Improvement	Control
Darunavir	721 ±332	54% p=0.036	469 ±252	726 ±211	35% p=0.062	536 ±223
Efavirenz	752 ±203	16% p=0.11	650 ±148	1,072 ±40	42% p=0.028	757 ±103

<sup>28</sup> Analyst compilation of Lexaria data

<sup>29</sup> Analyst compilation of Lexaria data

## Oral Nicotine

Lexaria is [conducting](#) a tolerability and PK study designated NIC-A21-1 in animals evaluating oral nicotine. The study recently migrated from an *in vitro* cell based study to the active *in vivo* study in Sprague-Dawley rats. Animal dosing began in July and is expected to produce results in September or October. Substantial successful work has been conducted in nicotine delivery by Altria; however, it was not cleared for use by Lexaria. While the studies did show efficient and safe delivery of nicotine to the brain, the studies will have to be repeated if the approach is to be used with other partners besides Altria.

## Nicotine Partnerships

Lexaria's longest standing relationship is with the tobacco industry. The company has been working with both Altria and British American Tobacco to improve the performance of non-combustible nicotine products. With increased smoking regulation and restriction, demand for alternative nicotine products has emerged that are less conspicuous such as snus and smokeless tobacco. These technologies require rapid and even delivery of nicotine to the nicotinic acetylcholine receptors be effective and on par with the nearly instantaneous delivery achieved from smoking. To this end, Lexaria has applied its DehydraTECH approach to the snus category.

Lexaria has licensed nicotine molecules to Altria Ventures, which is owned by Altria Group. In 2019, Altria executed an agreement to pursue new oral, reduced risk nicotine products using DehydraTECH which provided for exclusive rights to use the technology in the United States and non-exclusive rights outside the United States. The agreement included an initial \$1 million upfront payment. Altria will additionally pay a royalty to Lexaria for all of its products that use DehydraTECH. Altria was originally on track to obtain exclusive rights for using the technology in the United States, but did not keep up with the investment requirement and now has non-exclusive rights in the US.

Lexaria is also working with British American Tobacco (BAT) to investigate the feasibility of using DehydraTECH in nicotine products. An agreement was signed in August 2020 which designed a research and development framework that has been funded by BAT.

Management has also hinted at the possibility of other partners in the nicotine space that may be interested in licensing the technology. The agreements with Altria and BAT are both non-exclusive and allow Lexaria to sign other deals for use of DehydraTECH in nicotine delivery.

## Intellectual Property

Lexaria began filing patents for DehydraTECH in 2014 and has since increased the number of patent applications to approximately 60 with 21 patents granted worldwide. The substance of the patents center on the use of DehydraTECH in a variety of products including those that are ingested or topically administered such as CBD, food, beverage, patches, creams, lotions *et cetera*. Patents have been filed specifically for the use of DHT with cannabinoids for the treatment of heart disease. The patent estate also includes intellectual property that addresses the manufacturing and processing methods used to combine the long chain fatty acids with active pharmaceutical ingredients. This includes heating and drying methods and use of excipients and substrates. Below we summarize Lexaria's key patents.

### Exhibit XVI – Key Lexaria Patents<sup>30</sup>

Title	Patent #	Date	Region
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	9,474,725	25-Oct-16	US
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	9,839,612	12-Dec-17	US
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	9,972,680	15-May-18	US
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	9,974,739	22-May-18	US
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	10,084,044	25-Sep-18	US
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	10,103,225	16-Oct-18	US
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	10,381,440	13-Aug-19	US
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	10,374,036	6-Aug-19	US
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	10,756,180	25-Aug-20	US
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	2015274698	15-Jun-17	AUS
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	2017203054	30-Aug-18	AUS
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	2018202562	30-Aug-18	AUS
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	2018202583	30-Aug-18	AUS
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	2018202584	10-Jan-19	AUS
Food and Beverage Compositions Infused With Lipophilic Active Agents and Methods of Use	2018220067	30-Jul-19	AUS
Methods for Formulating Orally Ingestible Compositions Comprising Lipophilic Active Agents	2016367036	30-Jul-19	AUS
Stable Ready-to-Drink Beverage Compositions Comprising Lipophilic Active Agents	2016367037	15-Aug-19	AUS
Stable Ready-to-Drink Beverage Compositions Comprising Lipophilic Active Agents	IN 365854	30-Apr-21	India
Stable Ready-to-Drink Beverage Compositions Comprising Lipophilic Active Agents	2017-554607	30-Jun-21	Jap
Food and Beverage Compositions Infused with Lipophilic Active Agents and Methods of Use	2017-517203A	10-Jun-15	Jap

<sup>30</sup> Source: Analyst compilation of data from corporate materials, uspto.gov and Google patent search.

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## Peers and Competitors

Lexaria is exposed to a number of verticals ranging from the cannabinoid (CBD) industry to nicotine and antivirals. We also classify the company as a drug and nutraceutical delivery platform which includes its own set of peers and competitors. In the CBD space, the active ingredient is being developed along with DehydraTECH in a number of areas including consumer edibles and nutraceuticals.

There are many companies developing and commercializing CBD products including Botanix Pharma which is sponsoring clinical trials using CBD for skin conditions, Preveceutical which is advancing a CBD nose-to-brain delivery system for pain, inflammation, seizures and neurological disorders and Zynerba Pharma with its CBD cell for Fragile X syndrome. Other companies developing CBD-based therapies are Ananda Scientific for neuropathic pain and opioid replacement/withdrawal therapy that is using a unique drug delivery platform that addresses bioavailability, absorption and stability issues related to CBD. Aphios Pharma employs a proprietary nano-encapsulation approach to solve delivery problems for indications in chemotherapy-induced peripheral neuropathic pain, opioid addiction, and multiple sclerosis. Other delivery technologies such as Echo Pharmaceuticals' Alitra formulation brings forward oral CBD compounds for MS, chronic pain, and behavioral Alzheimer's Disease.

Other peers are focused on drug delivery technologies outside of the products and indications targeted by Lexaria. Two firms using in-house technologies to cross the blood brain barrier include Denali Therapeutics' transport vehicle and Bioasis Technologies with its xB<sup>3</sup> peptide that both employ receptor mediated transcytosis. Lipocine uses its oral formulation Lip'ral technology to improve delivery and absorption of already approved drugs in the intestine.

Lexaria's DHT technology demonstrates many competitive benefits as compared with the technologies mentioned above. These include the rate and extent of systematic and blood brain barrier permeation, cost effectiveness, safety and taste masking.

Of special consideration is [Jazz Pharmaceuticals](#), which recently acquired GW Pharma for \$7.2 billion. The latter had developed and obtained FDA approval for Epidiolex, a CBD treatment for seizures that places them in a strong position to advance another CBD-based pharmaceutical product such as DehydraTECH CBD for hypertension.

Switzerland-based [VESIsorb](#) offers a naturally self-assembling colloidal droplet delivery system that improves the bioavailability of poorly absorbed ingredients. The platform can combine with omega-3 fatty acids, coenzyme Q10, curcumin, phytocannabinoids, gamma tocopherols and many other bioactive ingredients. The company has a presence in nutritional supplements, food and beverage, pharmaceuticals, animal health, cosmeceuticals and medical foods.

Other companies such as Columbia Care and Emerald Health offer CBD brands and products for pain, nausea and other indications as well as conduct research and development into new products.

Below we highlight several of the key companies involved in drug delivery, CBD product sales and pursuing similar indications and markets as Lexaria.

**Exhibit XVII – Peers and Competitors<sup>31</sup>**

Ticker	Company	Price	MktCap (MM)	EV	Therapeutic Area
AZN	AstraZeneca	\$55.56	\$172,138	\$180,577	Diversified pharma; Seloken for HTN
BIOAF	Bioasis	\$0.20	\$15	\$13	Peptide-based delivery system for crossing BBB (xB <sup>3</sup> )
BTI	British American Tob	\$36.70	\$78,269	\$124,411	Provides tobacco & nicotine products worldwide
BXPHF	Botanix Pharma	\$0.06	\$53	\$37	CBD-acne, plaque psoriasis, atopic dermatitis
CCHWF	Columbia Care	\$4.08	\$1,480	\$1,830	Retailer for various oral CBD products
DNLI	Denali Tx	\$52.83	\$6,426	\$5,117	Transferrin receptor large molecule BBB transport vehicle
EMHTF	Emerald Health	\$0.10	\$24	\$6	Synthetic CBD product sales and development
GILD	Gilead Sciences	\$71.61	\$89,785	\$111,174	Diversified biopharma; remdesivir
JAZZ	Jazz Pharma	\$133.22	\$8,175	\$13,773	Epidiolex CBD for certain childhood seizures
LPCN	Lipocine	\$1.16	\$102	\$56	Lip'ral technology for insoluble drugs to oral formulations
MO	Altria Group	\$48.61	\$89,641	\$116,005	US sales of cigarettes & oral tobacco products
NVS	Novartis	\$83.48	\$186,723	\$206,195	Diversified healthcare Co; Diovan, Exforge for HTN
PODD	Insulet	\$292.45	\$20,142	\$20,505	Insulin delivery using Omnipod system
PRVCF	Preveceutical	\$0.02	\$10	\$11	CBD gel, intranasal administration
QNNTF	Quantum Genomics	\$4.50	\$162	\$130	BAPAI firibastat for hard to treat hypertension
RHHBY	Roche	\$46.07	\$314,658	\$312,403	Brain shuttle for antibodies
SLGL	SolGel	\$9.47	\$193	\$175	Silica-based delivery technology; microencapsulation process
SQZ	SQZ Biotech	\$14.48	\$406	\$221	Oncology drug delivery via cell compression
ZYNE	Zynerba Pharma	\$4.23	\$174	\$89	CBD transdermal gel, Fragile X & other rare neuro-psych
pvt	Senopsys				Taste masking of drug products
pvt	Vesisorb				VESIsorb: improved bioavailability using lipid based formula
pvt	Ananda Scientific				CBD-neuropathic pain, opioid replacement & withdrawal
pvt	Aphios				CBD-opioid addiction
pvt	Boehringer Ingelheim				Diversified pharma; Micardis for HTN
pvt	Echo Pharma				CBD-Oral form, Rett syndrome, epilepsy, schizophrenia
pvt	Kalytera				CBD-multiple formulations in GVHD & other indications
pvt	PolyActiva				Biodegradable polymer conjugate; glaucoma, anti-inflammatory
pvt	PureForm Global				Non-hemp CBD in liquid & powder form
pvt	Satipharm				CBD-gelatin beads in pediatric epilepsy
pvt	Serina Tx				Polymer delivery system for small molecule. Lead in PD & RLS
pvt	Souvie Biodelivery				Exosome-based platform; cell delivery in auto-immune & sepsis
LEXX	Lexaria Bioscience	\$6.32	\$32	\$24	DehydraTECH for lipophilic drug delivery to plasma and brain

<sup>31</sup> Price and market capitalization data is as of September 17, 2021.

## Financial and Operational Results

### Corporate Milestones

Highlights year-to-date include:

- [Announcement](#) of 1-for-30 reverse split - January 2021
- [Uplisting](#) to Nasdaq Capital Market - January 2021
- [Pricing](#) and [closing](#) of \$11M public offer - January 2021
- Al Reese, Jr. [appointed](#) to Board of Directors - January 2021
- CBD beverage shelf stability [results](#) - March 2021
- Gregory Downey [appointed](#) CFO - April 2021
- [Issuance](#) of warrants for 300,000 common shares - April 2021
- HYPER-H21-1 [underway](#) - April 2021
- First ever patent [granted](#) in India: DehydraTECH beverage - May 2021
- HYPER-H21-2 [starts](#) - June 2021
- 2021 Annual Meeting [results](#) - June 2021
- Voluntary [delisting](#) from CSE - July 2021
- [First](#) and [second](#) patents granted in Japan - July 2021
- HYPER-H21-2 dosing [complete](#) - July 2021
- \$3.8 million in proceeds [received](#) from warrants – July 2021
- Ibuprofen study results – 3Q:21
- Topline results from HYPER-H21-2 study – September 2021
- Results from nicotine animal study (canines) – September/October 2021
- THC (THC-A21-1) animal study results – 4Q:21
- Sildenafil/PDE5 inhibitor (PDE5-A21-1) animal study results – 4Q:21
- Launch of CBD HTN human study (HYPER-H21-3) – 4Q:21

Lexaria began the year with the [announcement](#) of a reverse stock split, effective on January 11, 2021. The reverse split was conducted on a 1-for-30 basis on the outstanding 90.0 million shares consolidating to 3.0 million shares. Lexaria's issued convertible securities were also subject to the reverse split with the exercise prices of outstanding convertible securities adjusted accordingly. Lexaria was also [uplisted](#) to the Nasdaq Capital Market the next day.

January 12<sup>th</sup> saw the [announcement](#) of the pricing of a public offer of 1,828,571 units, with each unit comprising one share of common stock and one warrant to purchase one share of common stock at \$5.25 per unit. Warrants have an exercise price of \$6.58 per share, are immediately exercisable, and expire five years from issuance date. The underwriter was granted 30-day option to purchase up to an additional 274,285 shares of common stock and/or warrants to purchase up to the same amount of common stock. H.C. Wainwright & Co. acted as sole book-running manager for the offer. Gross proceeds of \$11.04 million were ultimately received as indicated in a January 15<sup>th</sup> [update](#). The underwriter exercised full option to purchase both additional 274,285 common shares, as well as warrants to purchase 274,285 common shares. Wainwright was also issued five-year warrants to purchase 166,781 shares of common stock with an exercise price of \$6.58 per share. Pursuant to certain tail rights held by Bradley Woods & Co. Lexaria paid Bradley Woods \$316,999.62 and issued Woods five-year warrants to purchase 60,385 shares of common stock at an exercise price of \$6.58 per share.

Mr. Al Reese, Jr., was [appointed](#) to Lexaria's Board of Directors, as announced in a January 15<sup>th</sup> [press release](#). Mr. Reese brings over 40 years of experience in public and private businesses including as a CFO of a former Nasdaq-listed energy company where he arranged over \$10 billion in financing over his 20-year tenure. He was also a Director and Chairman of the Audit Committee of a Texas community bank. Reese is a CPA and received his bachelor's in business administration from Texas A&M University and his MBA from University of Houston.

On March 24, 2021, Lexaria issued a [press release](#) reporting results from a shelf-stability study. DehydraTECH CBD beverages demonstrated 93.4% of target CBD potency a year after production. The beverages also exhibited zero microbial growth over the period. Furthermore, the samples had intra-beverage variance less than 1% in CBD potency across various fractions (top, middle and bottom) without mixing or agitation, indicating a very stable emulsion.

On April 15, 2021, Lexaria [announced](#) the appointment of its new Chief Financial Officer, Gregory Downey, as former finance chief Allan Spissinger passed the baton. Downey received an option grant for the issuance of up to 12,000 common shares in addition to other customary incentives. In the same press release, Lexaria announced the issuance of share purchase warrants representing up to an aggregate of 300,000 common shares to three unrelated third party consultants, effective April 16, 2021. The warrants are exercisable, immediately, for a period of up to three years at an exercise price of \$9.00 per share.

Lexaria commenced its human clinical study of DehydraTECH CBD in hypertension, [announced](#) in an April 22, 2021 press release. Study design for HYPER-H21-1 had already been completed as well as university hospital and ethics board approvals and shipment of clinical test articles to clinical sites. HYPER-H21-1 is first of several human clinical studies planned by Lexaria intended to validate DehydraTECH CBD's effect in hypertension, and is a randomized, double-blind, controlled study expected to enroll 24 subjects with symptoms of either pre-hypertension or mild hypertension. A single 300 mg dose of DehydraTECH 2.0 CBD formulation will be compared against a non-dehydraTECH control of matched concentration. Time series blood pressure and heart rate analyses are primary objectives of the study. Secondary objectives include pharmacokinetic speed and rate of absorption of CBD and main metabolites as well as assessment of inflammatory markers of cardiovascular disease and nitric oxide biomarkers.

On July 5, 2021, Lexaria [announced](#) that it would voluntarily delist from the Canadian Securities Exchange to focus trading on the Nasdaq Capital Markets, effective on market close July 7, 2021. The release indicated that since Lexaria's shares began trading on the Nasdaq in January 2021, that the overwhelming majority of trading has moved to that exchange. With the majority of trading occurring on the Nasdaq, Lexaria can save fees, time and effort through the consolidation of the dual listing.

On June 7, 2021, Lexaria provided an [update](#) on HYPER-H21-1 progress, stating that 24 volunteers, ranging in age between 45 to 65, were dosed and the treatment was well tolerated with no serious adverse events (SAEs) or side effects observed or reported. In the same press release, the company announced that a subsequent study, designated HYPER-H21-2, would commence immediately. Several weeks later in a July 27 follow-up, Lexaria [reported](#) that HYPER-H21-2 had completed its patient dosing and in September initial results from the trial were shared in a [press release](#).

Encouraging early results from HYPER-H21-1 were [published](#) on July 29<sup>th</sup>. The difference between the DehydraTECH and control arm at the 20-minute mark was statistically significant at the 2.5% level. In contrast to HYPER-H21-1, HYPER-H21-2 evaluated 16 volunteers who were pre or mildly hypertensive and received three separate doses of 150mg DehydraTECH 2.0 CBD versus placebo. HYPER-H21-2 also differed by monitoring blood pressure reduction continuously over 24 hours. Central arterial stiffness, physical activity and sleep quality are also being assessed.

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## MANAGEMENT PROFILES

### **Mr. Christopher Bunka – Chairman, Chief Executive Officer and Director**

Mr. Bunka has been Chairman of the Board and CEO since 2006 and was primarily responsible for the corporate pivot from older business activities to bioscience. Mr. Bunka is a serial entrepreneur and has been involved in several private and public companies since the late 1980's. He was well known for more than a decade as a part-time business commentator in print and radio, as well as an author. He has extensive experience in the capital markets, corporate governance, project acquisition and corporate finance. He is a named inventor on some of Lexaria's pending patents. Since 1988, Mr. Bunka has been the CEO of CAB Financial Services Ltd., a private holding company located in Kelowna, Canada. He is a venture capitalist and corporate consultant.

### **Mr. John Docherty – President and Director**

Mr. Docherty was appointed President of Lexaria effective April 15, 2015. Prior to Lexaria Mr. Docherty was former President and Chief Operating Officer of Helix BioPharma Corp. (TSX: HBP), where he led the company's pharmaceutical development programs for its plant and recombinantly derived therapeutic protein product candidates. Mr. Docherty is a senior operations and management executive with over 20 years' experience in the pharmaceutical and biopharmaceutical sectors. He has worked with large multinational companies and emerging, private and publicly held start-ups. At Helix, Mr. Docherty was also instrumental in the areas of investor/stakeholder relations, capital raising, capital markets development, strategic partnering, regulatory authority interactions and media relations, and he also served as a management member of its board of directors. Prior to this, Mr. Docherty was President and a board member of PharmaDerm Laboratories Ltd., a Canadian drug delivery company that developed unique microencapsulation formulation technologies for use with a range of active compounds. Mr. Docherty has also held positions with companies such as Astra Pharma Inc., Nu-Pharm Inc. and PriceWaterhouse Coopers' former global pharmaceutical industry consulting practice. He is a named inventor on issued and pending patents and he has a M.Sc. in pharmacology and a B.Sc. in Toxicology from the University of Toronto. He has served as a director of Lexaria since April 29, 2016.

### **Mr. Gregory Downey – Chief Financial Officer**

Mr. Downey ascended to the position of CFO after serving two years as Lexaria's Controller. He had previously served as CFO of several public companies over the past decade. He holds a Certified Management Accountant designation and is a member of the Chartered Professional Accountants of British Columbia. Mr. Downey has over 35 years of diverse financial experience in the mining, oil and gas, manufacturing, construction and the public sectors. He served 8 years as CFO for several public companies and has provided business advisory and financial accounting services to many medium and large size organizations. Mr. Downey obtained his Certified Management Accountant (CMA) designation in 1992 and is a member of the Chartered Professional Accountants of British Columbia.

## RISKS

All investments contain an element of risk which reflects business uncertainty and opportunity. Some investments exhibit higher predictability, with current cash flows and established sales. These enterprises will have a lower level of perceived risk while other companies that are developing an undefined, new technology have a much higher level of perceived risk.

The biotechnology space includes companies at both ends of the spectrum, from mega-cap pharmaceutical and device powerhouses that have dozens of established products, to small operations with a handful of employees conducting pre-clinical studies. Many of the risks faced by the large and small firms are similar; however, there are some hazards that are particular to smaller companies that have not yet established themselves or their products. The typical risks faced by companies operating in the biotechnology space include risks related to liquidity, financing & trading, clinical trials, regulatory, personnel, intellectual property, marketing, and geopolitics.

### **Pandemic Risk**

The pandemic has disrupted economic and other activity in the United States and around the globe. It has also caused significant volatility in financial markets. Economic activity worldwide has contracted and may take many quarters to reverse. While the financial markets have not declined in tandem with economic growth, risk perception may increase and financial markets may begin to reflect a lower level of economic activity and decreased availability of capital. Early stage clinical firms lacking revenues rely on capital markets to sustain development efforts and may be sensitive to changes in risk perception and trading dynamics.

As the pandemic has progressed, it has negatively impacted supply chains, led to restrictions for clinical trials and led to the imposition of travel restrictions. As a company that requires the manufacture of drugs that cross international borders between the US and Canada, Lexaria may suffer delays in distribution of product and delays with its clinical trials. Risks pertaining to the company's supply chain may be impacted by future developments in the pandemic. The risk of variants, and difficulties in vaccinating the greater population leave subsequent waves of infection as a possibility.

### **Liquidity, Financing & Trading**

Access to financing comes and goes in cycles. During periods of improving confidence and plentiful liquidity, capital may be easy to obtain; however, during a crisis or a period of heightened risk perception, even companies with bright prospects may be in trouble if they depend on financial markets to fund their work. Pre-revenue biotech firms rely primarily on equity issuance to fund their operations. The duration of drug development is considerable, and can last as long as 12 to 15 years before product revenues come in the door. Funds can be sourced through debt or grants and tax credits; however, these sources may reduce the flexibility of the company and can create difficulties if debt is unable to be repaid.

If capital is not readily available when needed, a company may be forced to suspend research and development, sell equity at a substantial discount to previous valuations and dilute earlier shareholders. A lack of funding may leave potentially promising therapies without a viable route forward or force a company to accept onerous terms. Lexaria is in a relatively enviable position in that its capital needs are minimal for planned research and development and the company is generating consumer product related revenues that offset expenses

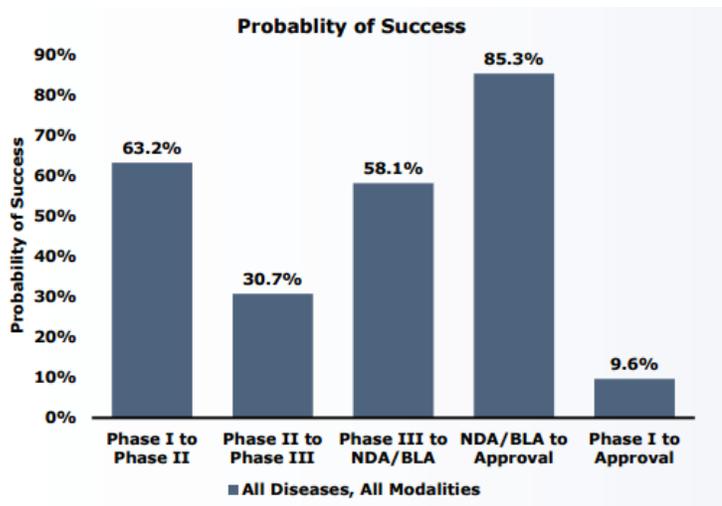
Trading volumes are lower for smaller biotech firms, creating liquidity risk for the investor and large transactions may have a material impact on share price. In periods of crisis or heightened risk perception, share price may be volatile. Companies with smaller capitalizations are typically considered riskier and changes in sentiment may adversely affect their trading prices and volumes. Smaller firms may also have less visibility, compete for investor dollars in a shallow market and be excluded from market indices. Lexaria has 5.7 million shares outstanding as of the end of its 2021 fiscal year and insiders hold over 10% of shares outstanding. This low level of float may result in significant price movement and sensitivity if shares are purchased or sold.

Lexaria management has guided toward a cash runway sufficient to fund announced programs and conduct the preparatory work to file an investigational new drug application with the FDA. As of end of May 2021, Lexaria held \$8.5 million in cash, equivalents and bank deposits. Following the end of the third quarter 2021, warrants were exercised which generated cash of approximately \$4 million providing an additional buffer.

## Clinical Trials

For smaller early-stage companies, investing in drug development is a lengthy process. The timeframe for conducting pre-clinical research to eventually commercializing a drug frequently takes from 12 to 15 years depending on market and company-specific conditions. On average, only one in a thousand compounds in discovery is eventually approved, creating a high hurdle for success.

Exhibit XVIII – Success of Phased Trials and Regulatory Approval<sup>32</sup>



The future of a drug development company is largely dependent on the data produced from clinical trials. Due to the cost, magnitude and complexity typical of this work, partners are often sought to share risk. Lexaria is seeking partnerships with consumer goods, medical and pharmaceutical companies in North America and around the globe. If successful, the deals would provide upfronts, milestones and royalties would further support development efforts. Partners may have competing demands which can adversely affect the work they are managing on behalf of the firm. Contract research organizations (CROs) and subcontractors must abide by strict execution and trial parameters that if violated can jeopardize trial success. Subcontractors supervise and execute research, biometric and pharmacovigilance, which are complex tasks. Patient recruitment may be difficult. Clinical investigational centers need sufficient capacity and the candidate drug needs to be manufactured according to current Good Manufacturing Practices (cGMP) and available to administer. Finally, clinical endpoints need to reach statistical significance to justify regulatory approval.

Lexaria is recognizing product and license revenues from its consumer products relationships. However, this is insufficient to offset anticipated research and development expenses. The company is planning further preclinical and clinical studies in hypertension, nicotine, antivirals and several other compounds that have poor bioavailability and would benefit from the DehydraTECH technology.

## Development and Commercialization

Some biotechnology firms' share prices have performed well during the pandemic, with relatively unfettered access to financing despite the economic contraction; however, many clinical trials have also been delayed and disrupted due to restrictions and reallocation of trial site resources. Biotechnology firms frequently have global aspirations and must navigate clinical trials, regulatory approval and marketing regulations in multiple geographies. Companies that have a long history of research success and experience in drug development, with opinion leaders and experts advocating for the product in the field will hold a more favorable position compared to those that do not.

Lexaria lacks sufficient capital to advance its candidates into late stage clinical trials and will be reliant on partners to conduct these studies for its pharmaceutical-based products. Partners will also be needed to move the candidates through the regulatory approval process and commercialization. While partnership can bolster the expertise supporting the candidates' later stage activities, partnership itself carries risk. Commercialization through partnership, even with a large pharmaceutical firm, does not guarantee that the program will receive the investment necessary from the partner to maximize the candidate's value.

<sup>32</sup>Clinical Development Success Rates 2006-2015. David Thomas, Justin Burns, John Audette, Adam Carroll, Corey Dow-Hygelund, Michael Hay.

## Regulatory and Compliance Risks

Lexaria has exposure to cannabidiol (CBD) which can be derived from the marijuana plant. In the United States, it is illegal, under federal law, to grow, cultivate and sell marijuana. Despite this, a majority of states have approved adult use regulations for the plant and its derivatives. Lexaria has not cultivated, produced or distributed marijuana or related products in the United States and its exposure to this industry is limited to ancillary involvement based on out-licensing of DehydraTECH to state licensed entities. The regulation of CBD products is constantly changing and new rules and requirements could reduce sales of products and increase operating costs for the CBD value chain.

## Legislative

Companies with exposure to the United States' healthcare system have experienced legislative disruption with the Patient Protection and Affordable Care Act (PPACA) of 2010 and the Health Care and Education Reconciliation Act. These legislative actions impose non-deductible excise taxes on pharmaceutical manufacturers or importers that sell branded prescription drugs to government programs, which can increase drug prices as levies are passed through to consumers. Prior to the PPACA, Congress had adopted the Medicare Prescription Drug, Improvement and Modernization Act of 2003. The Act modified Medicare reimbursement and coverage policies for prescription drugs.

## Personnel

Biotechnology companies rely on the expertise and leadership of their executives to make both technical and strategic decisions and investments. Due to the highly competitive nature of the industry, talented personnel are sought and firms with the best resources are in the strongest position to attract talented leaders. Leadership turnover can be high in small biotech firms. Lexaria recently promoted Mr. Greg Downey to CFO after the departure of the previous CFO, Mr. Allan Spissinger. Change in management is disruptive and can dramatically change the course of a firm. Personnel turnover can place a small company at a disadvantage when compared to larger firms with more specialized employees and executives. Furthermore, there can be risks and challenges associated with adding talent as the firm grows in size, especially with capital constraints. The size of the firm, volatility of stock price and a large component of compensation made up of equity-based compensation can deter certain talent from joining the firm or make it difficult to retain. We see both CEO Chris Bunka and President John Docherty as critical to the success of Lexaria Biosciences programs.

## Intellectual Property

Intellectual property is the lifeblood of biotechnology development. Even with an approved patent on file, intellectual property protection is not guaranteed. The patent application process requires time, capital and the disclosure of substantial detail on the company's technology which is eventually made public. Despite submission of an application, patents may not be granted. Patent protection requires legal resources that a startup biotech firm may not have. Furthermore, countries differ in the degree and type of intellectual property protection. Some firms may in- or out-license intellectual property, which exposes parties holding the patent to risk of adherence and litigation regarding the parameters of the licensing. Finally, patent protection is temporary and there is no guarantee that the firm will benefit from the patent protection before it expires.

## Market

Successful marketing of approved drug candidates relies on adoption by patients and providers. The approved drug must present convincing clinical trial data and maintain a favorable reputation among prescribers. Marketing is expensive and requires an experienced sales force and a presence in the marketing area. Marketed products remain under surveillance and any unexpected adverse effects damage the product's reputation. Furthermore, the risk of a competing or superior therapy is a continuous threat. Insurance coverage is also important. Rapidly obtaining a preferred position on health plan and payor formularies is critical to achieving target penetration rates. If health plans and payors cannot agree on appropriate pricing for the drug and the compound fails to offer a significant benefit above standard of care, the product may not be available on formularies. Once on the market, product liability risk presents and insurance will be needed to contain this risk.

Lexaria's value is derived from the marketing of consumer, medical and pharmaceutical products internationally. The lead and most valuable segment is the use of CBD in hypertension, which if successful will be regulated as a drug. The company is also involved in the nicotine industry which is also regulated, but under a different regime. Product and licensing revenues from consumer products using CBD, supplements and nutraceuticals are generat-

ing revenues for Lexaria with further growth dependent on expansion of their commercial distribution network. While Lexaria does not directly assume marketing risks, revenues can be impacted if licensees are unable to commercialize their product successfully.

### **Geopolitical**

Recent trade tensions between the US and China threaten the world economy and have been exacerbated during the ongoing pandemic. There has been a cross-pollination of capital and drug development between China and North America in recent years which may slow as a result of the trade and political dispute between the countries. This conflict may reduce the availability of capital, partnerships and future development deals between companies in the two nations. The UK seceded from the European Union in 2020, potentially creating additional difficulties for companies seeking to obtain approval and marketing rights throughout Europe. Previously, a drug approved under the centralized procedure in the European Union would be approved in all member states. However, with the withdrawal of the UK, additional efforts and expense may be required to obtain marketing approval in this large European market. International firms are also exposed to risk of currency fluctuations.

## VALUATION

Lexaria has established itself as a leader in API delivery in the CPG market, harnessing the natural route of drug delivery using a LCFAs' natural route through the GI system. The company is taking this expertise and applying it to pharmaceutical products that require FDA approval. Existing revenues come from DHT manufacturing and licensing of the technology. Future revenues are expected from DHT CBD, DHT nicotine and other fat soluble drugs that have poor bioavailability and slow onset, such as remdesivir. Lexaria has selected markets with immense potential that measure in the billions. Even a small market share in a few of the categories would provide substantial value to shareholders.

Revenues of almost \$1 million are expected for fiscal year 2021, which are generated through relationships with a variety of consumer packaged goods (CPG) companies. We anticipate revenues from these sources to grow in the 20 to 30% range over the next few years as existing partners expand distribution and as new ones are added. Licensing revenue gross margins are forecast in the 95% range and product revenues in the 35% range.

Our primary value driver is success in the CBD hypertension space. Hypertension is a common ailment and is frequently uncontrolled, providing a large addressable market. After a reduction to the total hypertensive population to reflect the uncontrolled population, we generate an addressable market of about 46 million in the US and 73 million in the EU (including the UK). Hypertension treatment is a large and diverse market; however, we believe that there is a space for all effective approaches, especially ones that have demonstrated safety and are derived from natural sources. In both markets we anticipate penetration of 10 basis points in year one (2024) rising to 40 basis points in year four where it will remain steady over the forecast period. Applying an annual treatment cost of \$6,000 in the United States, revenues start at \$283 million in year one and rise to \$1.2 billion by year six. In the EU + UK, with an annual treatment cost of \$3,000 revenues of \$225 million in year one to \$1.0 billion in year six. We anticipate royalties of 15% of revenues for DHT CBD. For the purposes of our model and valuation we assume that the royalty represents the totality of economic value of the arrangement which includes upfronts, milestones and royalties.

Lexaria peer Jazz Pharmaceuticals markets [Epidolex](#), an FDA approved CBD formulation for treating seizures. As they have already performed safety work sufficient to obtain approval, it may be possible for Lexaria to partner with Jazz to expand the label to include DHT CBD for hypertension using the [505\(b\)\(2\)](#) approval pathway. If this approach is successful, we see FDA and EMA approval granted by 2024.

Lexaria has multiple opportunities in the nicotine space both in the non-combustible snus category and in nicotine replacement therapy. The first is for snus, which is estimated to be a \$155 million market and anticipated to grow 15% over the next several years. We see DHT being sold in non-combustible tobacco form by 2024 through relationships with tobacco manufacturers. Penetration in the first year of commercialization is forecast at 5% or approximately \$12 million in product revenues. This is expected to rise to 35% or \$126 million by 2027 with stable penetration and 5% market growth thereafter. Nicotine replacement therapy is another area with potential for using DHT. Sales of over the counter and FDA approved NRT was recently estimated at \$2.4 billion.<sup>33</sup> We model first sales in this category in 2024 with initial penetration of 2% rising to 6% by 2028 through the efforts of an as yet to be determined pharmaceutical partner. This is equivalent to sales of \$52 to \$177 million over the same period. Royalties are forecast at 15% of product revenues and will represent all economic value to Lexaria including upfronts, milestones and royalties.

Our third in-development value driver is from a basket of lipophilic drugs that are now either infused or have poor oral characteristics, providing an unmet need that can be addressed by DHT. The basket includes several candidates that Lexaria has already successfully tested in pre-clinical work including remdesivir, ebastine, darunavir, efavirenz and colchicine. We estimated market size of these products based on the most recent available annual sales numbers. Together this group generates an estimated \$5.95 billion in revenues and is growing at an estimated rate of 2% per annum. We see relationships developing with pharmaceutical partners culminating in marketing approval by 2025 and an initial 75 basis point penetration into this market. Penetration is expected to increase to 300 basis points by year four (2028). Revenues from the relationship are expected to start at \$48 million in year one and rise to over \$200 million by year three. Since more of the development work will fall on the partner, we forecast a lower share of economic value for Lexaria of 9%. This royalty represents the totality of upfronts, milestones and royalties to be received from the relationship.

<sup>33</sup> Source: As smokers spark up e-cigs to quit, traditional aids suffer. Reuters, Jilian Miller. January 2015.

On the cost side of the coin, we see research and development costs rising to approximately \$3 million in 2022 and \$3.5 million in 2023. In future years, 3% annual growth is expected for this line item. Selling, general and administrative expenses are forecast at \$2.9 million in 2022 and \$3.0 million in 2023. After 2023, a 4% inflation rate is applied to SG&A expenses

Taxes are set at 30% and assessed following the use of tax loss carryforwards of approximately \$40 million. Our revenue and cost estimates generate annual cash flows which we discount to present using a 15% rate. We apply a probability of regulatory approval and commercial success to the portfolio of candidates. A 12% probability of success is applied to the DHT CBD program, 10% to each of the two nicotine programs, 15% to the basket of antiviral candidates and 100% to CPG revenues. After weighting the probabilities by potential revenues in each category, we produce a 13% overall probability of success.

To the balance of 5.7 million shares outstanding we add issued warrants, options and additional shares to reflect future anticipated issuances to bring the total to 9.5 million which we use for our calculations. Based on the assumptions identified above, we generate a valuation of \$15.00 per share.

## CONCLUSION

Lexaria has designed and developed an elegant approach to swiftly deliver medicines, nutraceuticals and other fat soluble active molecules using its DehydraTECH technology. The approach is able to deliver APIs via oral and topical routes to blood plasma more rapidly and with higher bioavailability compared with competing technologies. DHT confers additional benefits including taste masking, evasion of first pass metabolism and ability to cross the blood brain barrier. Lexaria's technology is a low-cost process that establishes a molecular association between the lipophilic API and long chain fatty acids that creates a compound able to exploit a fast track route to the blood plasma and the brain.

DHT exploits a heating process to molecularly associate long chain fatty acids such as oleic acid with fat soluble drugs and an emulsifier. The product is formed into a wide range of oral dosage formats such as capsules which are administered and pass through the gastrointestinal system. DHT molecules are protected from digestion in the stomach and small intestine and are instead taken up by the lacteals, which are lymphatic vessels of the small intestine that absorb fats. The lymphatic system transports dietary lipids throughout the body, into the bloodstream and into the brain, bypassing liver metabolism. This route delivers the DHT payload to blood plasma more quickly and in higher concentrations than is possible if passing through the liver.

This DHT technology is already being used in revenue generating products in the consumer product segment. Growth in CPG should reach double digit rates for the near future. Partners pay either a license fee to use DHT to manufacture their products or purchase DHT-manufactured product from Lexaria. While these sources are expected to produce revenues of near \$1 million per year in 2021, they will only partially offset the pharmaceutical-related research and development expenses that the company is incurring over the next few years. There are several active programs both preclinical and clinical that are investigating DHT to be used in new indications and for already approved compounds.

The most important program Lexaria is pursuing is DHT CBD for hypertension. Hypertension affects over a billion persons around the globe and fewer than half are diagnosed and treated. The CBD approach may address and improve upon several unmet needs in this population including medication cost, side effects, desire for natural product, varied mechanism of action and hard to treat patients. In addition, DHT CBD's ability to permeate brain tissues is believed to contribute significantly to its powerful effectiveness in reducing blood pressure given the importance of central mediation for blood pressure maintenance and control. First human studies have begun and the company is on the cusp of compiling an IND for further safety and efficacy testing toward use as a registered pharmaceutical. A partner will be pursued and Jazz Pharmaceuticals in particular may be amenable to working together. Jazz is commercializing an approved CBD product for seizures and has the technical and regulatory experience necessary to expand its portfolio of indications to include hypertension using Lexaria's DHT. Furthermore, partnering with Jazz could also be beneficial to enable a fast path to market approvals via the 505(b)(2) abbreviated NDA pathway.

The nicotine program is another important value driver that emerged from long term relationships with multiple global tobacco manufacturers. With increased pressure to reduce combustible tobacco use, less risky and inconspicuous alternatives such as snus can fill the gap. Nicotine replacement therapy is another avenue that can be pursued. Both of these approaches require rapid delivery of sufficient nicotine to the brain to quell the urge to smoke. DHT has demonstrated the ability to achieve these ends and additional data will be available in the near term.

Antivirals and other treatments for viral infections are critical to a well-functioning health system. For success, these medicines require rapid and sufficient delivery to the patient's system, usually via infusion. However, there are numerous shortcomings. Oral formulations can address many of these hurdles, however, approved approaches have low bioavailability, unpleasant side effects or simply do not exist. DHT has the potential when combined with several leading products including remdesivir, ebastine, darunavir, efavirenz and colchicine among many others to avoid the cost and complexity of infusion and rapidly deliver the medicine to the desired tissue with a high degree of bioavailability.

Despite being at an early stage of development, Lexaria has a multitude of options for its DHT platform. CPG is already generating revenues and could see dramatic growth if its partners continue to increase distribution. Hypertension is a massive market with a majority of the disease going untreated. There are also numerous other lipophilic compounds that could benefit from a DHT oral form that are being considered.

Lexaria, in contrast to many early stage research and development companies, is already generating revenues from its CPG business. Including recent warrant exercises, it also has over \$10 million in cash on the balance sheet to fund development work. While the company will need to find a partner to advance its pharmaceutical DHT iterations into late stage clinical trials, it is developing numerous relationships that we think will yield results.

Key reasons to own Lexaria shares:

- **Patent portfolio supporting DehydraTECH in multiple compositions**
- **DehydraTECH provides marked improvements over other methods of API delivery**
  - **Improved bioavailability**
    - **Fewer side effects**
    - **Lower drug cost**
  - **More rapid delivery to blood plasma**
  - **Able to cross the blood brain barrier**
  - **Flavor masking allows for use of fewer excipients**
  - **Allows select infused or injected drugs to be administered orally**
  - **Approaching infusion levels of drug bioavailability**
    - **Can generate substantial savings converting infused medicines to oral**
- **DehydraTECH can augment performance of numerous APIs**
  - **Cannabidiol (CBD)**
  - **Nicotine**
  - **Anti-virals**
  - **PDE5 inhibitors**
  - **NSAIDS**
  - **Hormones**
  - **Vitamin D3**
- **Existing license and product revenues provide supportive cash flow**
  - **Relationships with several consumer packaged goods (CPG) manufacturers**
  - **Double digit revenue growth**
- **Low cost technology that can produce up to 400,000 CPG units per day at existing facility**
- **Collaborations with Fortune 100 companies Altria and British American Tobacco**

Based on our analysis of Lexaria and its DHT technology, we are optimistic on the continued development of the multiple active programs. We anticipate that a partnership will materialize on several fronts, including for indications in hypertension, nicotine delivery and treatment of viral diseases among others. Our valuation work employs a probabilistic approach for the programs underway, assuming various levels of success based on data generated to date and program maturity. With multiple opportunities, even a small chance of success in each provides a large potential market for this platform technology. We initiate on Lexaria Bioscience Corp. with a valuation of \$15.00 per share.

## PROJECTED FINANCIALS

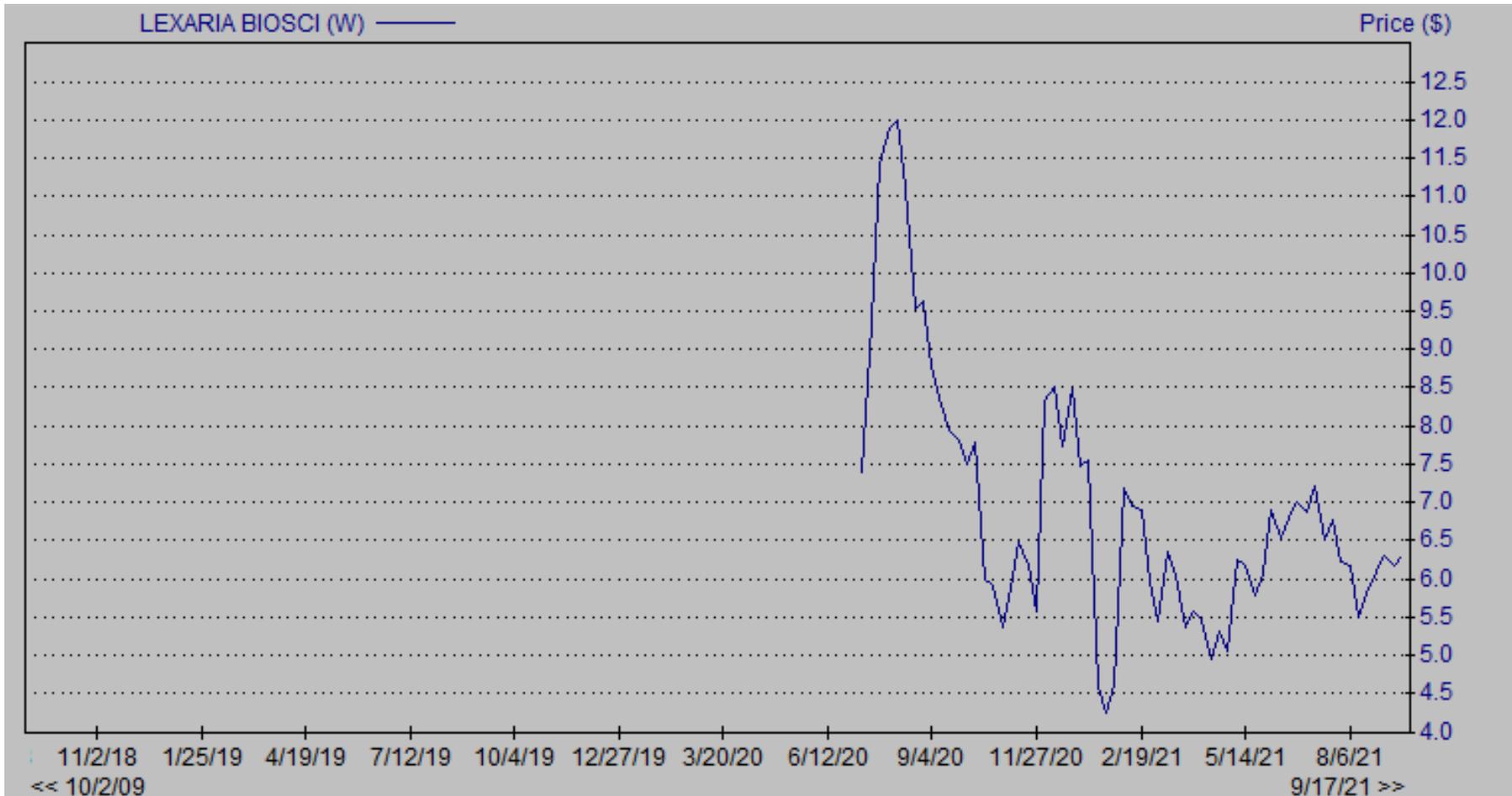
### Lexaria Bioscience Corp - Income Statement

Lexaria Bioscience Corp.	2020 A	Q1 A	Q2 A	Q3 A	Q4 E	2021 E	2022 E	2023 E
<b>Total Revenues</b>	<b>\$385</b>	<b>\$296</b>	<b>\$192</b>	<b>\$204</b>	<b>\$250</b>	<b>\$942</b>	<b>\$1,220</b>	<b>\$1,510</b>
YOY Growth	73%	2761%	412%	460%	-17%	145%	30%	24%
<b>Gross Profit</b>	<b>\$285</b>	<b>\$231</b>	<b>\$161</b>	<b>\$144</b>	<b>\$163</b>	<b>\$699</b>	<b>\$799.0</b>	<b>\$984.5</b>
Research & Development	\$387	\$192	\$176	\$454	\$192	\$1,015	\$3,000	\$3,500
General & Administrative	\$3,936	\$775	\$1,047	\$2,186	\$1,180	\$5,188	\$2,900	\$3,000
Other	\$46	(\$23)	(\$1,481)	\$70	\$0	(\$1,433)	\$0	\$0
<b>Income from operations</b>	<b>(\$4,085)</b>	<b>(\$713)</b>	<b>\$418</b>	<b>(\$2,567)</b>	<b>(\$1,210)</b>	<b>(\$4,071)</b>	<b>(\$5,101)</b>	<b>(\$5,516)</b>
<i>Operating Margin</i>						-432%		
Discontinued operations	\$135	\$3.0	\$0.0	\$0.0	\$0.0	\$3.0	\$0	\$0
<b>Pre-Tax Income</b>	<b>(\$3,949)</b>	<b>(\$710)</b>	<b>\$418</b>	<b>(\$2,567)</b>	<b>(\$1,210)</b>	<b>(\$4,068)</b>	<b>(\$5,101)</b>	<b>(\$5,516)</b>
<b>Net Income</b>	<b>(\$3,949)</b>	<b>(\$710)</b>	<b>\$418</b>	<b>(\$2,567)</b>	<b>(\$1,210)</b>	<b>(\$4,068)</b>	<b>(\$5,101)</b>	<b>(\$5,516)</b>
<i>Net Margin</i>	-1027%	-240%	218%	-1258%	-484%	-432%	-418%	-365%
<b>Reported EPS</b>	<b>(\$1.42)</b>	<b>(\$0.24)</b>	<b>\$0.10</b>	<b>(\$0.50)</b>	<b>(\$0.23)</b>	<b>(\$0.94)</b>	<b>(\$0.93)</b>	<b>(\$0.93)</b>
Basic Shares Outstanding	2,773	3,001	4,053	5,104	5,200	4,340	5,500.0	5,900.0

Source: Company Filing // Zacks Investment Research, Inc. Estimates

# HISTORICAL STOCK PRICE

Lexaria Bioscience Corp – Share Price Chart<sup>34</sup>



<sup>34</sup> Source: Zacks Research System

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