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PESG RESEARCH RELEASES MARKET COMMENTARY ON:

INNOCAN PHARMA, AN UP-AND-COMING LEADER IN CBD VETERINARY SOLUTIONS

MARCH 2022

FUTURE MARKETS RESEARCH TANK

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METHADOLOGY

The market analysis for this report focused on CBD-based veterinary solutions and related Pharmacokinetics and the transition to integrating CBD as an API rather than a sub-pharma ingredient to ease symptoms in pets. Market analysis data was captured relating to total addressable market, trends, published research, five leading veterinary pharma companies (determined by revenue) & and their respective patent portfolios, related patent landscape not assigned of the five leaders, CBD related FDA announcements, and merger and acquistions highlights. All market analysis was derived from data that exclusively or primarily focused on the United States Market. All research was compiled from third party, publicly available sources.

INNOCAN PHARMA (CSE: INNO), (FSE: IP4), (OTC: INNPF) is a pharmaceutical tech company based in Israel that focuses on the development of drug delivery platforms combining cannabidiol ("CBD") with other pharmaceutical ingredients. *Innocan* has addressed the perceived low bioavailability of cannabinoids by developing several new drug delivery platforms including an injectable Liposome technology aimed at the burgeoning Veterinary Services industry. *Innocan* plans to pursue licensing discussions when its data set is complete, accessing a substantial $52B market and new potential growth driver for the company.

THE VETERINARY CBD MARKET, PARTICULARLY IN THE US, IS A GREENFIELD FOR NEW ENTRANTS:

- The Veterinary Services market, at US$52 bn, is large, healthy and growing.
  - Companion animal services (the segment targeted by *Innocan*) totalled US$39.1 bn revenue in 2021.
- A number of trends related to the further growth of veterinary services will positively impact pharmaceutical manufacturers and other suppliers to the industry:
  - Growth in pet ownership and increased willingness to spend money on veterinary services
  - Price elasticity in veterinary services due to the growing use of pet insurance
  - Advancements in animal health technology and longer life spans of pets

- Increased demand for routine care and chronic disease management of older companion pets[8]
- Increased humanization of pets leading to a greater demand for luxury services[10]

- There is existing and significant black and grey market demand for CBD based solutions for pet illnesses:
  - Consumers seek to purchase cannabidiol for human and companion animal (pet) consumption for the potential treatment of pain, anxiety, depression, and psychological disorders.[5]
- Due to growing demand, the number of companies operating in the industry is projected to rapidly expand:[10]
  - Major institutions have given the market attention and produced promising research results relating to the application of CBD pharma to solving key animal ailments.
  - There is existing revenue, research & development, investment and merger & acquisition activity surrounding related non-CBD animal pharmaceuticals solving similar problems as proposed by CBD based alternatives.
- There is substantial runway for new market participants:
  - Key animal pharma players are not yet established in the CBD animal pharma field. No key players have a leadership position, despite most having successful non-cbd veterinary pharmaceutical brands.

BACKGROUND: CBD

Cannabidiol (CBD) is a phytocannabinoid discovered in 1940. It is one of 113 identified cannabinoids in cannabis plants, along with tetrahydrocannabinol (THC), and accounts for up to 40% of the plant's extract. As of 2019, clinical research on CBD included studies related to anxiety, cognition, movement disorders, and pain, but there is insufficient high-quality evidence that cannabidiol is effective for these conditions.[1]

CBD can be taken internally in multiple ways, including by inhaling cannabis smoke or vapor, by mouth, and as an aerosol spray into the cheek. It may be supplied as CBD oil containing only CBD as the active ingredient (excluding tetrahydrocannabinol [THC] or terpenes), CBD-dominant

hemp extract oil, capsules, dried cannabis, or prescription liquid solution. CBD does not have the same psychoactivity as THC, and may change the effects of THC on the body if both are present.[2]

CBD BASED VETERINARY PHARMACEUTICALS

Cannabidiol (CBD) based Veterinary Pharmaceuticals is a new commercial category in the United States due to the fact that Cannabidiol in any form was classified as a narcotic, thus restricting research and development. This changed recently (2018) when the US federal Government reclassified cannabidiol that is accompanied by low and no levels of THC as a non-scheduled narcotic e.g., Hemp, paving the way for research and development, FDA approvals and patent awards for cannabidiol based pharmaceuticals.

In the United States, the cannabidiol drug Epidiolex was approved by the Food and Drug Administration in 2018 for the treatment of two epilepsy disorders. While the 2018 United States Farm Bill removed hemp and hemp extracts (including CBD) from the Controlled Substances Act, the marketing and sale of CBD formulations for medical use or as an ingredient in dietary supplements or manufactured foods remains illegal under FDA regulation, as of 2021.[3]

In other parts of the world cannabidiol and cannabidiol receptors research has happened without being impeded by US laws. Many credit Israeli firm, Tikun Olam, with spearheading the research to successfully separate CBD from THC in 2012.[4]

The “black” and “grey” markets for CBD based products have been growing in the US especially with the decriminalization of cannabis and cannabidiol at the state level. CBD based products are readily available in state sanctioned retail, and in the black market being distributed in states that still consider cannabis and cannabidiol a narcotic. There are no definitive quantification of the black and grey cannabis and cannabidiol markets but judgementally they represent billions of dollars in sales. Consumers are purchasing cannabidiol for human and companion animal (pet) consumption for the potential treatment of pain, anxiety, depression, and psychological disorders.[5]

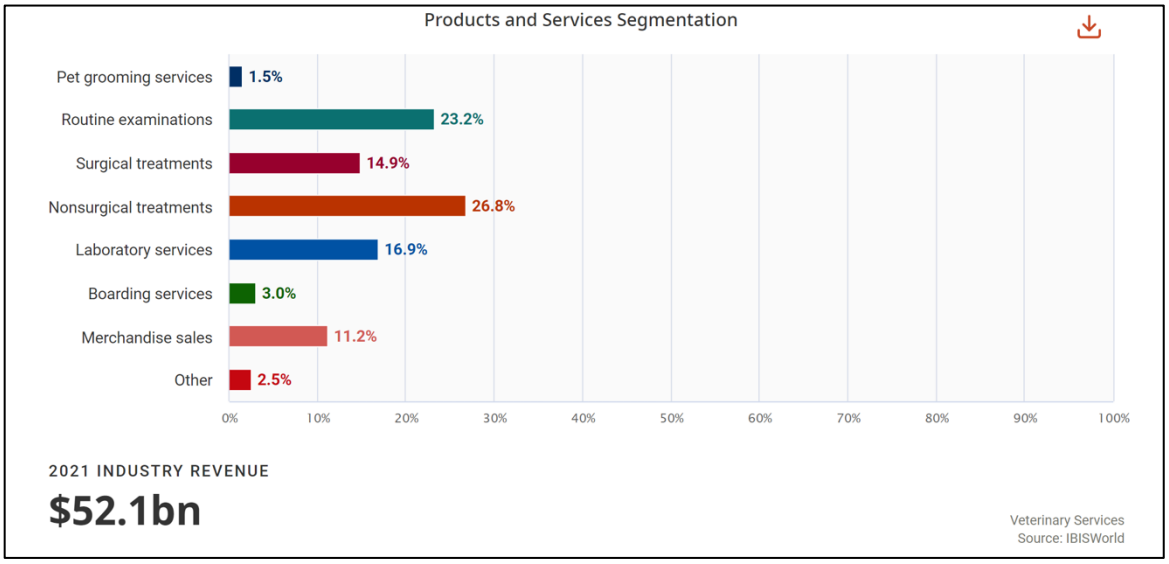
CBD PHARMACOLOGY

The oral bioavailability of CBD varies greatly across species and it is linked to the presentation and the time of administration. A 24-hour kinetic examination in dogs showed that the absorption of the cannabidiolic acid (CBDA) does occur, and that this molecule is absorbed least twice as well as CBD post oral ingestion.[6]

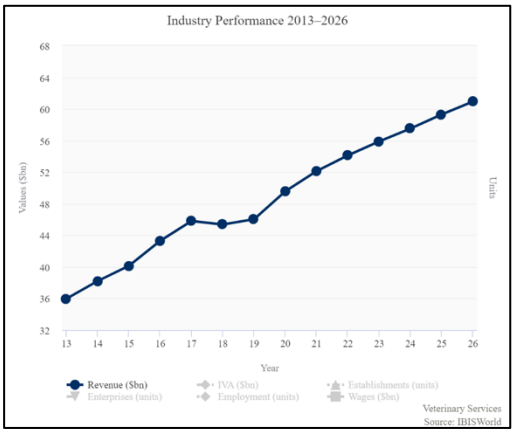
It was found that the major metabolites of CBD in humans (7-OH-CBD and 7-COOH-CBD) are not prevalent in dogs, while 6-OH-CBD was found to be the primary metabolite in dogs receiving a CBD-enriched cannabis-derived herbal extract, suggesting that canine and human CBD metabolic route might be somewhat different.[7]

VETERINARY SERVICES MARKET OVERVIEW

Veterinary Services is a large, mature industry with US$52 bn in total revenues in 2021. Companion animals, comprised 75% of this total or $39.1bn revenue. US$34 bn was spent on animal health products worldwide in 2020, more than double 2006 totals. Almost 60% of the market was generated by classic pharmaceuticals, while the rest was made up of biologicals and medicinal feed additives. Spending on companion animals comprised 33% of the spend or roughly US$11 bn.[29]



Over the past 5 years, Veterinary Services has surged at an annualized rate of 3.8% including an approximate 5.1% increase in 2021 due to the increase in pet ownership and per capita disposable income during the COVID-19 pandemic. Revenue is forecast to grow at an annualized rate of 3.2% to $60.9 billion over the next 5 years.



Overall demand for Veterinary Services is expected to increase in line with an increase in the popularity of pet health insurance, advancement in medical technologies, longer pet lifespans, humanization of pets and overall growth in pet ownership:

PET HEALTH INSURANCE

As more pet owners purchase pet health insurance, they will be able to afford high-cost procedures such as surgery or preventative medicine and the frequency of veterinary visits is likely to increase. Households with a dog or cat currently visit a veterinarian 2.6 and 1.6 times per year, respectively, according to data from the American Veterinary Medical Association.

According to the latest report from the North American Pet Health Insurance Association, close to 3.1 million pets were covered by insurance in North America in 2020 (latest data available). While this figure is significantly lower than pet ownership, considering the American Pet Products Association estimates 85.0 million households own a pet, growth in the number of insured pets will likely continue to grow and provide opportunities for the industry during the outlook period. Due to pet insurance lowering out-of-pocket costs for pet owners, insured pets will likely receive more high-cost treatments, boosting industry revenue.[8]

LONGER PET LIFESPANS

With improved medical care and advances in medical technology, comes an increase in the average lifespan of companion pets. Consequently, the demand for routine care and chronic disease management of older companion pets has increased and will continue to grow. Improving medical technologies and procedures have enabled veterinarians to purchase

enhanced diagnostic tools to perform specialized medical procedures in-house. As a result, many practices now offer ophthalmology, internal medicine, surgery and dentistry, among other specialty services.[8]

HUMANIZATION OF PETS

85% of US dog owners consider their dogs to be family members.[8, 9] Consequently, many pet owners are increasingly willing to pay for pet treatments that were once reserved for humans, such as full serum chemistry profiles, complete blood counts, blood pressure screenings, thoracic and abdominal pet radiographs, thyroid profiles, urinalysis, and fecal parasite screenings. To meet demand, veterinarians will likely include biannual wellness exams for aging pets to lower the risk of heart, kidney and liver diseases as well as decreased mobility. Additionally, many veterinarians are expected to specialize in internal medicine, including cardiology, dermatology, eye care, gastroenterology, endocrinology and urology, among other fields, to provide advanced care for elderly pets.[8] Veterinarians are increasingly expected to include wellness programs with customized packages for aging pets in their product portfolio.

GROWTH IN PET OWNERSHIP

Pet ownership is expected to rise over the next 5 years due in part to advances in pet nutrition and care, including vaccinations and preventative care, that have led to longer pet lifespans.

Moreover, the surge in pet ownership during the coronavirus pandemic is anticipated to result in a sustained increase in the addressable market for industry operators. According to the Insurance Research Council's, Consumer Responses to the Pandemic and Implications for Insurance report, 30.0% of Americans adopted a pet during the pandemic. 67.0% of US households, or 84.9 million homes, have at least 1 pet, providing steady demand for routine veterinary services. 63.4M (50%) US Households own at least 1 dog. This trend is anticipated to boost the base market for industry services, which is likely to benefit industry operators during the outlook period.[8]

CBD RESEARCH ENVIERNMENT

CBD based research is on-going and has received more focus in academic and government research environments in the US due to 2018 federal legislation designating hemp as non-class 1 narcotic. Research on animals so far has been mostly focused on dogs.

Colorado State University (CSU) has established itself as a leader in animal CBD research, publishing several studies on (1) CBD delivery systems in pharmacokinetics including CBD-infused oil, microencapsulated oil beads, and CBD-infused transdermal cream and (2) the use of CBD to treat medical issues common in pets including Epilepsy and Osteoarthritis.

TREATMENT OF EPILEPSY

Epilepsy is currently reported to affect approximately 5% of the canine population; of that number approximately 30% of dogs are poorly controlled on routine anti-epileptic drugs (AEDs).

Recent CSU CBD research studies have demonstrated the anti-convulsive properties in both canine and human patients: [13]

- **Enrollment ends May 31, 2022 - 12-week CBD Canine Epilepsy Trial Study:** This study will determine a dose of CBD that will reduce the seizure frequency in canine patients to 50% or less.
- **CSU Summary of CBD Research (2020):** Human and animal trials examined the mechanism by which CBD exerts its anticonvulsant effect to better understand which patients would benefit from its use.[11]
- **CBD Epilepsy Pilot Study - May 2019:** A small study with 16 pet dogs assessed the short-term effect of CBD on seizure frequency. [12]

TREATMENT OF OSTEOARTHRITIS

According to the American College of Veterinary Surgeons, Osteoarthritis (OA) is the most common form of arthritis in dogs, affecting approximately ¼ of the population. It is a chronic joint disease characterized by loss of joint cartilage, thickening of the joint capsule and new bone

formation around the joint (osteophytosis) and ultimately leading to pain and limb dysfunction. The majority of OAs in dogs occur secondarily to developmental orthopedic disease, such as cranial cruciate ligament disease, hip dysplasia, elbow dysplasia, OCD, patella (knee cap) dislocation. In a small subset of dogs, OA occurs with no obvious primary causes and can be related to genetic and age. Other contributing factors to OA include bodyweight, obesity, gender, exercise, and diet. [15]

A recent pharmacokinetic and clinical study, evaluating the Safety and Clinical Efficacy of Cannabidiol Treatment in Osteoarthritic Dogs suggests that 2 mg/kg of CBD twice daily can help increase comfort and activity in dogs with OA.[14]

RECENT PHARMACOKINETIC STUDIES HAVE REINFORCED THE BENEFITS OF IV VERSUS ORAL ADMINISTRATION[16]

Recent studies have shown that CBD has a high protective index, comparable to that of phenobarbital and phenytoin. Because CBD has been reported to possess both anticonvulsant and antiepileptic activity, its pharmacokinetics were studied in dogs after the administration of 2 iv doses (45 and 90 mg) and 1 oral dose (180 mg) to dogs. After iv administration, CBD was rapidly distributed, followed by a prolonged elimination. It has a terminal half-life of 9 hr. CBD plasma levels declined in a triphasic fashion. The total body clearance of CBD was 17 liters/hr (after the 45-mg dose) and 16 liters/hr (after the 90-mg dose). This clearance value, after its normalization to blood clearance using mathematical equations, approaches the value of the hepatic blood flow; the extraction ratio in the liver is 0.74. CBD was observed to have a large volume of distribution, approximately 100 liters. In the dose range of 45 to 90 mg, the increase in the AUC was proportional to the dose, a fact that indicates that the pharmacokinetic profile of CBD in this dose range was not dose dependent. In 3 of the 6 dogs studied, CBD could not be detected in the plasma after oral administration. In the other 3, the oral bioavailability ranged from 13 to 19%. The results of this study show that CBD is barely absorbed after oral administration to dogs. This low bioavailability may be due to a first pass effect.

CBDA AND THCA ARE ABSORBED OR ELIMINATED DIFFERENTLY THAN CBD OR THC [17]

Cannabidiol (CBD)-rich hemp extract use is increasing in veterinary medicine with little examination of serum cannabinoids. Many products contain small amounts of Δ9-tetrahydrocannabinol (THC), and precursor carboxylic acid forms of CBD and THC known as cannabidiolic acid (CBDA) and tetrahydrocannabinolic acid (THCA).

Examination of the pharmacokinetics of CBD, CBDA, THC, and THCA on 3 oral forms of CBD-rich hemp extract that contained near equal amounts of CBD and CBDA, and minor amounts (<0.3% by weight) of THC and THCA in dogs was performed. In addition, we assess the metabolized psychoactive component of THC, 11-hydroxy-Δ9-tetrahydrocannabinol (11-OH-THC) and CBD metabolites 7-hydroxycannabidiol (7-OH-CBD) and 7-nor-7-carboxycannabidiol (7-COOH-CBD) to better understand the pharmacokinetic differences between 3 formulations regarding THC and CBD, and their metabolism. 6 purpose-bred female beagles were utilized for study purposes, each having an initial 7-point, 24-h pharmacokinetic study performed using a dose of 2 mg/kg body weight of CBD/CBDA (~1 mg/kg CBD and ~1 mg/kg CBDA). Dogs were then dosed every 12 h for 2 weeks and had further serum analyses at weeks 1 and 2, 6 h after the morning dose to assess serum cannabinoids. Serum was analyzed for each cannabinoid or cannabinoid metabolite using liquid chromatography and tandem mass spectroscopy (LC-MS/MS). Regardless of the form provided (1, 2, or 3) the 24-h pharmacokinetics for CBD, CBDA, and THCA were similar, with only Form 2 generating enough data above the lower limit of quantitation to assess pharmacokinetics of THC. CBDA and THCA concentrations were 2- to 3-fold higher than CBD and THC concentrations, respectively. The 1- and 2-week steady-state concentrations were not significantly different between the 2 oils or the soft chew forms. CBDA concentrations were statistically higher with Form 2 than the other forms, showing superior absorption/retention of CBDA. Furthermore, Form 1 showed less THCA retention than either the soft chew Form 3 or Form 2 at weeks 1 and 2. THC was below the quantitation limit of the assay for nearly all samples. Overall, these findings suggest CBDA and THCA are absorbed or eliminated differently than CBD

or THC, respectively, and that a partial lecithin base provides superior absorption and/or retention of CBDA and THCA.

CONCLUSIVE PHARMACOKINETIC STUDIES ARE NEEDED[18]

CBD has gained widespread popularity as a treatment for OA in pets; however, there is minimal scientific evidence regarding safe and effective dosing. A recent study determined plasma and tissue pharmacokinetics after oral CBD oil suspension administration in Hartley guinea pigs (Cavia porcellus), which spontaneously develop OA at 3 months of age. Further studies, including work in female guinea pigs, are needed to determine the efficacy of CBD for OA.

RECENT CBD RESEARCH WITH HUMANS

There has also been research relating to CBD's pharmaceutical impact on humans. The following are key research initiatives in this area.

THE PHARMACOKINETICS AND THE PHARMACODYNAMICS OF CBD[20]

There is increasing interest in the use of cannabinoids for disease and symptom management, but limited information available regarding their pharmacokinetics and pharmacodynamics to guide prescribers.

Cannabis medicines contain a wide variety of chemical compounds, including the cannabinoids delta-9-tetrahydrocannabinol (THC), which is psychoactive, and the non-psychoactive CBD. Cannabis use is associated with both pathological and behavioural toxicity and, accordingly, is contraindicated in the context of significant psychiatric, cardiovascular, renal or hepatic illness. The pharmacokinetics of cannabinoids and the effects observed depend on the formulation and route of administration, which should be tailored to individual patient requirements. As both THC and CBD are hepatically metabolized, the potential exists for pharmacokinetic drug interactions via inhibition or induction of enzymes or transporters. An important example is the CBD-mediated inhibition of clobazam metabolism. Pharmacodynamic interactions may occur if

cannabis is administered with other central nervous system depressant drugs, and cardiac toxicity may occur via additive hypertension and tachycardia with sympathomimetic agents. More vulnerable populations, such as older patients, may benefit from the potential symptomatic and palliative benefits of CBD but are at increased risk of adverse effects.

The limited availability of applicable pharmacokinetic and pharmacodynamic information highlights the need to initiate prescribing cannabis medicines using a 'start low and go slow' approach, carefully observing the patient for desired and adverse effects. Further clinical studies in the actual patient populations for whom prescribing may be considered are needed, to derive a better understanding of these drugs and enhance safe and optimal prescribing.

REGULATORY ENVIRONMENT

The US Food and Drug Administration (FDA) has taken a more cautious approach to regulation compared to the rapid advancement of the research environment. The FDA approved the first and only CBD based drug for Epilepsy in humans in 2018. The agency has refrained from issuing notice of another CBD based pharma solution since. The FDA continues to accept CBD submissions and issue announcements warning and naming companies illegally selling CBD products.

The opening of the legalized environment for CBD research came through the passage of the Agriculture Improvement Act in 2018. This law changed certain federal authorities relating to the production and marketing of hemp, defined as cannabis (Cannabis sativa L.), and derivatives of cannabis with extremely low (less than 0.3 percent on a dry weight basis) concentrations of the psychoactive compound delta-9-tetrahydrocannabinol (THC). These changes included removing hemp from the Controlled Substances Act, which means that it will no longer be an illegal substance under federal law.[24]

In June 2018, the FDA approved Epidiolex®, the first CBD based pharma solution. Epidiolex® was designed for the treatment of 2 severe pediatric seizure disorders, Lennox-Gastaut syndrome and Dravet syndrome. The approval comes at the end of a 4 year series of trials showing the benefits of CBD in relieving the symptoms of these seizure disorders, which are highly resistant to existing treatments.[22]

The FDA recognizes the potential opportunities that cannabis or cannabis-derived compounds may offer and acknowledges the significant interest in these possibilities. However, the FDA has determined that some companies are marketing products containing cannabis and cannabis-derived compounds in ways that violate the Federal Food, Drug and Cosmetic Act (FD&C Act) and that may put the health and safety of consumers at risk. The agency has taken steps to improve the efficiency of regulatory pathways for the lawful marketing of appropriate cannabis and cannabis-derived products.

Over the past several years, the FDA has issued several warning letters to firms that market unapproved new drugs that allegedly contain CBD. As part of these actions, FDA has tested the chemical content of cannabinoid compounds in some of the products, and many were found to not contain the levels of CBD they claimed to contain. The warning letters include CBD products that are especially concerning from a public health perspective due to the route of administration, including nasal, ophthalmic and inhalation. Examples of FDA focus areas include violations relating to the addition of CBD to food, and the impermissible marketing of CBD products as dietary supplements. The FDA also addressed CBD products illegally marketed for pets, including a product for use in the eye.[26]

In July 2020, *Innocan* received notice from the FDA that the company's over-the-counter Relief & Go Pain Relief spray product has successfully received technical validation and approval to commence marketing in the USA. *Innocan*'s pain relief formulation contains a combination of Magnesium oil, Methyl salicylate, Menthol and CBD. The Relief & GO Pain Relief spray is designed

to target pain-related muscle and provide relief for joint pain. The unique formulation is administered with a simple dose of spray, roll-on or lotion.[23]

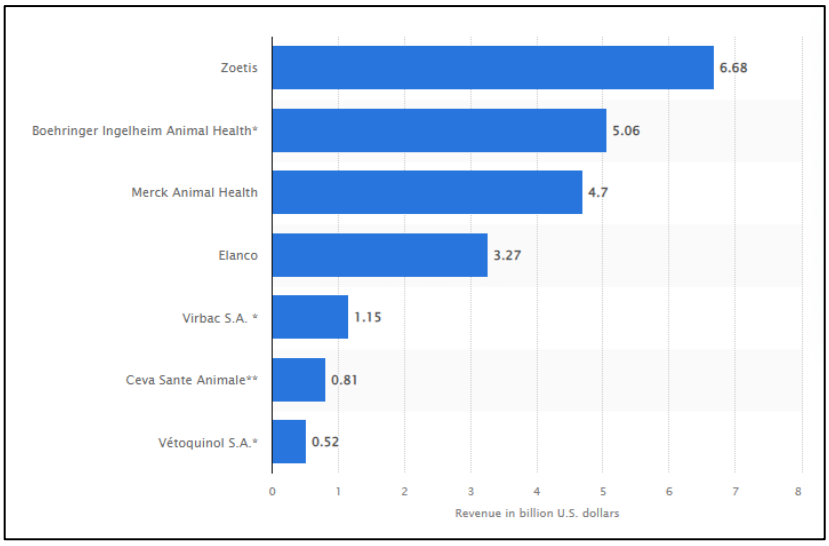
VETERINARY PHARMA COMPETITIVE LANDSCAPE

The veterinary pharmaceutical industry consists of several well-established manufacturers. Several of these companies are divisions of even larger parent companies that also manufacture pharmaceuticals for humans.

This section highlights the revenue, related animal products, CBD patents, and CBD pharmacokinetic patents for the 5 largest in the world. They are: Zoetis, Boehringer Ingelheim, Merck Animal Health, Elanco and Virbac. The biggest 4, Zoetis, Boehringer Ingelheim, Merck Animal Health and Elanco all distribute branded pharma non-steroidal anti-inflammatory drugs.

3 vet pharma companies hold CBD patents: Zoetis (2), Boehringer Ingelheim (10), and Merck Animal Health (3). None hold Cannabidiol pharmacokinetic patents. In addition to the 15 total patents held by the big 3 manufacturers (as above), there are an additional 9 US patents related CBD and animals. Search results for pharmacokinetics, CBD identified an additional 3 patents. There were no patent search results for the combination of the 3 terms: pharmacokinetics, CBD and animals.

LEADING ANIMAL HEALTH COMPANIES IN 2020, BASED ON REVENUE



ZOETIS INC.

Zoetis Inc. Is a public company traded on NYSE: ZTS. Zoetis is a global company focused on animal pharmaceutical products. Revenue and Fiscal Year Ended December 31, 2021 was US$7.8 bn.
2 of the company's largest product categories are vaccines and anti-infectives. The company was a subsidiary of Pfizer, the world's largest drug maker, but with Pfizer's spinoff of its 83% interest in the firm it is now a completely independent company. Zoetis promotes itself as the largest global animal health company.[30]

Related canine pharma products: Rimadyl® (carprofen - non-steroidal anti-inflammatory drug of the propionic acid class that was previously for use in humans and animals, but is now only available to veterinarians for prescribing as a supportive treatment for various conditions in only animals. Carprofen reduces inflammation by inhibition of COX-1 and COX-2; its specificity for COX-2 varies from species to species.) - For the relief of pain and inflammation associated with osteoarthritis and for the control of postoperative pain associated with soft tissue and orthopedic surgeries.[30]

CANNABIDIOL PATENT SEARCH RESULTS:

- **US6949572B2 - Triamide-substituted heterobicyclic compounds**
  Brief Summary of Invention: Microsomal triglyceride transfer protein catalyzes the transport of triglyceride, cholesteryl ester, and phospholipids and has been implicated as a putative mediator in the assembly of Apo B-containing lipoproteins, biomolecules which contribute to the formation of atherosclerotic lesions. Specifically, the subcellular (lumen of the microsomal fraction) and tissue distribution (liver and intestine) of MTP have led to speculation that it plays a role in the assembly of plasma lipoproteins, as these are the sites of plasma lipoprotein assembly. The ability of MTP to catalyze the transport of triglyceride between membranes is consistent with this speculation, and suggests that MTP may catalyze the transport of triglyceride from its site of synthesis in the endoplasmic reticulum membrane to nascent lipoprotein particles within the lumen of the endoplasmic reticulum.[31]\

- **US7572797B2 - Amino substituted pyrazine derivatives for the treatment of pain** Brief Summary of Invention: This invention relates to pyrazine derivatives. More particularly, this invention relates to heteroaryl substituted N-[6-amino-5-aryl-pyrazin-2-yl]-carboxamide derivatives and to processes for the preparation of, intermediates used in the preparation of, compositions containing and the uses of, such derivatives.[32]
- **Cannabidiol pharmacokinetics patent search results:** None found

BOEHRINGER INGELHEIM

Boehringer Ingelheim (parent of Boehringer Ingelheim Animal Health) is the world's largest privately held pharmaceutical company. It generated €19.6 bn revenue in 2020. The company's key areas of interest are: respiratory diseases, metabolism, immunology, oncology and diseases of the central nervous system. Boehringer Ingelheim is the parent company of Boehringer Ingelheim Animal Health division; established in 1955 as the company acquires Pfizer's veterinary program. Boehringer Ingelheim Animal health claims to be market leader in parasiticides, vaccines and therapeutics.[33]

Related pet pharma products: Previcox® (firocoxib - is a nonsteroidal anti-inflammatory drug of the COX-2 inhibitor (coxib) class, currently approved for use in dogs and horses. Firocoxib was the first COX-2 inhibitor approved by the U.S. Food and Drug Administration for horses. Firocoxib is not intended or approved for use in human medicine.) for the relief of pain and inflammation associated with osteoarthritis as well as specific types of post-operative pain in dogs.[33]

CANNABIDIOL PATENT SEARCH RESULTS:

- Boehringer Ingelheim holds ten patents related to CBD, all in with different focuses related to CB2 receptors. All these patents on file a the US Patent Office have the same Brief Summary of Invention: The present invention provides novel compounds which bind to and modulate the CB2 receptor. The invention also provides methods and pharmaceutical compositions for treating inflammation by way of the administration of therapeutic amounts of the compounds of the invention. Lastly, the invention provides a method and pharmaceutical compositions for treating

pain by way of the administration of therapeutic amounts of the compounds of the invention.[34, 35, 36, 37, 38, 39, 40, 41, 42, 43,]

- US9315454B2 - Compounds which modulate the CB2 receptor[34]
- US8299111B2 - Compounds which modulate the CB2 receptor[35]
- US8829034B2 - Compounds which modulate the CB2 receptor[36]
- US7595397B2 - Compounds which modulate the CB2 receptor[37]
- US8889670B2 - Heterocyclic compounds which modulate the CB2 receptor[38]
- US7928103B2 - Compounds which modulate the CB2 receptor[39]
- US8173638B2 - Compounds which modulate the CB2 receptor[40]
- US8629157B2 - Pyrrolidine compounds which modulate the CB2 receptor[41]
- US8546563B2 - Compounds which modulate the CB2 receptor[42]
- US8957063B2 - Amine and ether compounds which modulate the CB2 receptor[43]
- Cannabidiol pharmacokinetics patent search results: None found

MERCK & CO., INC. ./ Merck Sharp & Dohme (MSD)

Is an American multinational pharmaceutical company headquartered in Kenilworth, New Jersey. Merck & Co. (parent of Merck Animal Health) is a publicly traded company (NYSE: MRK). Revenue in 2021 was US$48.7 bn. The company develops medicines, vaccines, biologic therapies and animal health products. Merck Animal Health focuses on companion animals, food animals, food fish.[44]

Related pet pharma products: Dogs and Cats - No results found – others found in parasite, vaccines, insulin therapy.

- **Equine - BANAMINE® (North America):** The original brand of flunixin meglumine (Flunixin is a nonsteroidal anti-inflammatory drug, analgesic, and antipyretic used in horses, cattle and pigs. It is often formulated as the meglumine salt. In the United States, it is regulated by the U.S. Food and Drug Administration, and may only be lawfully distributed by order of a licensed veterinarian. There are many trade names for the product), Banamine® is an

injectable non-steroidal anti-inflammatory drug (NSAID). It is used to reduce inflammation and pain associated with musculoskeletal disorders, and visceral pain associated with colic in horses and has a rapid onset of activity.[44]

CANNABIDIOL PATENT SEARCH RESULTS:

- **US20090029984A1 - Synergistic combination for the treatment of pain (cannabinoid receptor agonist and opioid receptor agonist)** Abstract: The invention relates to a pharmaceutical dosage form comprising an analgesic combination for simultaneous or sequential use which comprises a peripherally restricted cannabinoid CB1 receptor agonist having a brain Cmax to plasma Cmax ratio of less than 0.1 and an opioid receptor agonist, as well as to a method for treating pain using said pharmaceutical dosage form.[45]
- **US8143246B2 - 1-(4-(pyridin-2-yl) benzyl) imidazolidine-2,4-dione derivatives** BACKGROUND - The present invention relates to 1-(4-(pyridin-2-yl)benzyl)imidazolidine-2,4-dione derivatives, to pharmaceutical compositions comprising the same and to the use of these 1-(4-(pyridin-2-yl)benzyl)imidazolidine-2,4-dione derivatives in therapy, especially in the treatment of pain.[46]
- **US20100144723A1 - 1-(biphenyl-4-ylmethyl) imidazolidine-2,4-dione.** BACKGROUND - The present invention relates to 1-(biphenyl-4-ylmethyl)imidazolidine-2,4-dione derivatives, to pharmaceutical compositions comprising the same and to the use of these 1-(biphenyl-4-ylmethyl)imidazolidine-2,4-dione derivatives in therapy, especially in the treatment of pain.[47]
- **Cannabidiol pharmacokinetics patent search results:** None found

ELANCO ANIMAL HEALTH INC.

Elanco is a public company traded on NYSE: ELAN. Elanco focuses primarily on pets and farm animal pharmaceutical products. Revenue fiscal year Ended December 31, 2021 was US$4.76 bn.[48]

Related pet pharma products: DERAMAXX (deracoxib - is a nonsteroidal anti-inflammatory drug of the coxib class, used in dogs to treat pain associated with osteoarthritis, or to prevent pain following orthopedic or dental surgery) helped manage the pain and inflammation of canine OA for over 15 years.

Galliprant (grapiprant - is a small molecule drug that belongs in the piprant class. This analgesic and anti-inflammatory drug is primarily used as a pain relief for mild to moderate inflammation related to osteoarthritis in dogs) is a first-in-class prostaglandin receptor antagonist (PRA), a non-COX inhibiting NSAID. It specifically targets the EP4 receptor, the primary mediator of canine OA pain and inflammation. You can start treatment from the earliest diagnosed stages.[48]

CANNABIDIOL PATENT SEARCH RESULTS:

- **US7410970B2 - Substituted 1,4, -di-piperidin-4-yl-piperazine derivatives and their use as neurokinin antagonists** Abstract - The invention concerns substituted 1,4-di-piperidin-4-yl-piperazine derivatives having neurokinin antagonistic activity, in particular NK1 antagonistic activity, their preparation, compositions comprising them and their use as a medicine, in particular for the treatment of emesis, anxiety, depression, pain, pancreatitis and IBS.[49]
- **Cannabidiol pharmacokinetics patent search results:** None found

VIRBAC

Is a French company, operating in more than 100 countries. Virbac has a US subsidiary but not a US office. The company is dedicated to animal health - food producing animals, and companion animals. Virbac is publicly traded (Euronext: VIRP) and generated revenue of €948 min in 2020.[50]

Related pet pharma products: No results found – others in neutering and nutrition

Cannabidiol patent search results: No results found

Cannabidiol pharmacokinetics patent search results: None found

ADDITIONAL PATENT SEARCH RESULTS RELATED TO CANNABIDIOL, ANIMALS:

US20190142884A1 - Method of reducing stress and anxiety in equines

Brief Summary of Invention: A method of reducing stress and anxiety in an equine comprising administering a therapeutically effective amount of a water-based cannabinoid formulation is provided, where the formulation contains no tetrahydrocannabinol. While many cannabinoids are suitable, the formulation may contain pure cannabidiol as the primary or only cannabinoid.[51]

US20210077455A1 - Use of cannabinoids in the treatment of a neurodegenerative disease or disorder

Brief Summary of Invention: The present invention relates to the use of cannabinoids in the treatment of a neurodegenerative disease or disorder. In particular the cannabinoids cannabidiolic acid (CBDA) and cannabidivarin (CBDV) were able to produce neuroprotective effects in a mouse model of neurodegenerative disease. In particular these effects were associated with the symptoms associated with amyotrophic lateral sclerosis (ALS). Furthermore, the combination of the cannabinoid tetrahydrocannabinol (THC) with the drug olexisome provided a synergistic disease modifying effect in a mouse model of neurodegenerative disease. In particular these effects were associated with the symptoms associated with ALS.[52]

US20200281890A1 - Compositions comprising cannabidiol, tetrahydrocannabinol, terpenes, and flavonoids and use thereof in the treatment of insomnia

Brief Summary of Invention: Compositions comprising two or more cannabinoids, a terpene, and a flavonoid suitable for use in treating insomnia are disclosed. In preferred embodiments, the cannabinoids are cannabidiol and tetrahydrocannabinol, while the terpenes and flavonoids are selected from compounds that naturally occur in Cannabis extracts. Methods of treating insomnia by administering such compositions by a variety of routes are also disclosed.[53]

US20190247324A1 - One or a Combination of Phyto-Cannabinoids in the Treatment of Epilepsy - Google Patents

Brief Summary of Invention: This invention relates to the use of one or more cannabinoids in the treatment of epilepsy and more particularly to the use of one or a combination of cannabinoids in the treatment of generalized or partial seizure. In one embodiment it relates to the use of the cannabinoid THCV, as a pure or isolated compound, or as a plant extract in which significant amounts of any THC naturally present has been selectively removed. In another embodiment the phytocannabinoid is CBD.[54]

US20200078333A1 - Healthier Aging in Domesticated Animals

Brief Summary of Invention: This invention provides compositions, systems and methods that improve and/or optimize the health and performance of animals, especially mammals including humans, canines, equines, felines, etc. Key aspects of the principal invention and its parts include the monitoring, management and modulation of the body's natural cannabinoid systems through its native mechanisms thereby optimizing its processes by supplementation with endogenously occurring components and/or by administering synthetic compounds. The invention selects from multiple available resources to modify and/or rebalance an individual system or it may be applied across interconnected systems. The encompassing system that is intricately involved in the operations and intensities, e.g., the balancing of most other systems of our bodies, relates to cannabinoid compounds and their receptors. The cannabinoid pathways can be coordinated in rebalancing multiple and various metabolic pathways. Compositions comprising compounds that slow degradation of native endocannabinoids, that stimulate their production and/or compounds that act on cannabinoid receptors within the body are featured in systems and methods of this invention. The activated and rebalanced cannabinoid systems then become adept at modulating and the rebalancing of the numerous systems in which they participate to improve one or more systems including, but not limited to: normal and/or abnormal stresses of life, environmental influences, genomic or epigenomic irregularities and/or normal or accentuated processes of aging. Specifically targeted systems may include, but are not limited to, those involved in: cellular and/or mitochondrial metabolism, corticosteroid synthesis and effects,

appetite, allergy and immunity, sleep and waking, etc. Practicing the invention selects from multiple approaches that may be used independently or in concert to compensate for a variety of concerns. Supplementing dietary intake to rebalance metabolism and/or its metabolic responses—including immunogenic or allergic responses to pathogenic and/or environmental stresses is one focus. Additional features of the invention may include: compensating for failing or decreasing androgen hormone levels as an animal continues to age, rebalancing the organism.[55]

US20200179269A1 - Vaporizable compositions comprising cannabinol

Brief Summary of Invention: Vaporizable compositions based on specific components in cannabis extracts and in particular comprising cannabinol and optionally sleep-inducing terpenes, are provided. Such compositions, comprising low to medium concentration of CBN, are particularly useful in treating sleep disorders such as insomnia.[56]

US10172809B2 - Topical regional n€-affective therapy in mammals with cannabinoids

Brief Summary of Invention: A method of treating a disease state or condition in mammals other than humans via topical brainstem afferent stimulation therapy via the administration of a cannabinoid drug(s) to the back of the neck region and/or spine to provide regional n€-affective therapy is disclosed. In certain preferred embodiments, the cannabinoid drug(s) are not psychoactive or substantially not psychoactive. In certain embodiments, the cannabinoid drug(s) are incorporated into a pharmaceutically acceptable topical carrier, e.g., a cream or mousse. In certain preferred embodiments, the cannabinoid drug(s) comprises cannabidiol.[57]

US20180161285A1 - Composition and Method for Treating Seizure Disorders

Brief Summary of Invention: The invention provides compositions and methods for treating seizure disorders such as epilepsy in humans and animals using, in a first embodiment, the combination of (i) an effective amount of a barbiturate drug, such as phenobarbital or primidone, which solely enhances GABAergic inhibition in a patient suffering a seizure disorder; and (ii) phytocannabinoid cannabidiol (CBD) in a dosage amount sufficient to overcome the hepatic

metabolic effect stimulated by the barbiturate drug and provide bioavailable CBD to the patient in clinically efficacious amounts.[58]

US20210052512A1 - Cannabidiol preparations and its uses

Brief Summary of Invention: Cannabidiol (CBD) is a cannabinoid designated chemically as 2-[(1R,6R)-3-Methyl-6-(1-methylethenyl)-2-cyclohexen-1-yl]-5-pentyl-1,3-benzenediol. Its empirical formula is C21H30O2 and its molecular weight is 314.46. CBD is a cannabinoid that naturally occurs in the Cannabis sativa L. plant. CBD is a white to pale yellow crystalline solid which is insoluble in water and soluble in organic solvents. The present invention encompasses the surprising recognition that certain CBD preparations which are prepared from a botanical origin are more effective in treating diseases or disorders than preparations of CBD which are synthetic or purified to the extent no other impurities in the form of other cannabinoids are present. Prior CBD compositions have been prepared such that no psychoactive components, e.g., tetrahydrocannabinol (THC), remain in the final CBD preparation. Surprisingly, the absence of such minor impurities reduces the efficacy of CBD treatment. Such CBD preparations are characterized by chemical components and/or functional properties that distinguish them from prior CBD compositions. One or more components of the preparations described herein provide an unexpectedly synergistic effect when utilized in combination.[59]

OTHER PATENT SEARCH RESULTS RELATED TO PHARMACOKINETICS, CANNABIDIOL:

(Note: “animals” was dropped from the search after no results were found when included)

US8758826B2 - Cannabinoid receptor binding agents, compositions, and methods

Brief Summary of Invention: A composition comprising a cannabinoid receptor binding agent attached to a particle for the treatment of skin conditions. The particle may be a nanoparticle, such as nanocrystalline cellulose. The particle may further be modified with functional moieties. Drug delivery properties may be modified by coating the particles or using vesicles to deliver the cannabinoid receptor binding agent and particle. A substrate may be used to deliver the composition to the skin.[60]

US20190015382A1 - Low dose therapeutic treatment

Brief Summary of Invention: Some embodiments of the invention relate to a system for delivering to a subject at least one pre-determined amount of THC, the system comprising: a memory which stores a scheduled regimen for delivery of THC to the subject, the scheduled regimen defining: a maximal amount of THC to be delivered, the amount being 0.75 mg THC or less, and a time period within which that amount is delivered, the time period being 2 hours or longer; a decision module which decides, according to the scheduled regimen, if a delivery should take place; and an inhaler device for delivering THC to the subject, the inhaler device comprising a controller which carries out delivery of THC based on the decision made by the decision module.[61]

US10772837B2 - Modified release multi-layer tablet cannabinoid formulations

Brief Summary of Invention: The present invention provides modified release pharmaceutical compositions, and methods for administering the compositions to a user, including humans. The composition may contain a combination of ingredients in proportions calculated to achieve therapeutic effect, including at least the following ingredients: one or more natural or synthetic cannabinoids, one or more release modifying agent(s), and one or more pharmaceutically acceptable excipient(s). The composition may be in a multi-layered solid dosage form to provide fast, controlled and also sustained release of specific ingredients. More specifically, the invention relates to modified release pharmaceutical compositions comprising cannabinoids and a process for preparation thereof. More specifically, the invention may control drug release in accordance with the therapeutic purpose and pharmacological properties of active substances.[62]

M&A ACTIVITY (VETERINARY PHARMACEUTICALS, CANNABINOID PHARMACEUTICALS)

Merck & Co. (US$47.9 bn 2021 Total Revenue) is very active in the M&A space, a smaller set of its transactions are in the focus of this report. Just in the last 5 years Merck Animal Health has closed 5 transactions:

- In April 2017, Merck Animal Health acquired Vallée S.A., a Brazilian animal health product manufacturer.[63]
- In December 2019, Merck Animal Health acquired Vaki, an aquaculture company, from Pentair.[64]
- In June 2020, Merck Animal Health acquired Quantified Ag, a data and analytics company that monitors cattle body temperature and movement in order to detect illness early. [65]
- In August 2020, Merck Animal Health acquired IdentiGEN, engaged in DNA-based animal traceability.[66]
- In February 2021, Merck Animal Health acquired PrognostiX Poultry. [67]

Elanco (US$3.273 bn 2020 Total Revenue) has been very active in the M&A area having done at least 8 transactions from 2010 and 2021.

These transactions include:

- Pfizer Animal Health (Acq 2010)
- Janssen Pharmaceutica Animal Health (Acq 2011)
- ChemGen Corp (Acq 2012); Lohmann SE (Acq 2014)
- Lohmann Animal Health (Acq 2014)
- Novartis Animal Health (Acq 2014)
- Bayer Animal Health (Acq 2019)
- Aratana Therapeutics (Acq 2019)
- Kindred Biosciences (Acq 2021) [48]

A noteable transaction directly related to cannabinoid pharma took place in February 2021. Jazz Pharmaceuticals PLC (US$3.1bn 2021 Total Revenue) purchased GW Pharmaceuticals (US$527 million 2020 Total Revenue) in a deal valued at $7.2 billion. The merger of the companies formed a global neuroscience powerhouse that brought GW's lead epilepsy drug, Epidiolex, into Jazz's pipeline. Epidiolex, which is derived from its cannabinoid product platform, was the first plant-derived cannabinoid medicine ever approved by the FDA. In addition to Epidiolex, GW's pipeline includes the Phase III candidate nabiximols, which is being assessed for the treatment of spasticity associated with multiple sclerosis and spinal cord injury. The company also has earlier-stage cannabinoid product candidates for autism and schizophrenia. [68]

Other M&A activity related to key players:

In May 2018, Zoetis Inc. (US$7.8 bn 2021 Total Revenue) announced its intention to acquire Abaxis (specialized in point-of-care blood testing for both human and veterinary purposes) for $1.9 billion in cash.69

Boehringer Ingelheim Animal Health (€ 4bn 2019 Total Revenue) is a multinational animal health company, formed in January 2017 when Merial was acquired by Boehringer Ingelheim and merged with Boehringer Ingelheim's existing animal health assets. [70]

INNOCAN AND THE FUTURE OF VETERINARY PHARMA

It's apparent that the veterinary pharma industry offers substantial economic opportunities for the nimble competitor. Given the attractive attributes of its emerging drug technologies, Innocan is poised to take a leadership role in this nascent sector. The company is well positioned to capture the substantial economic benefits that intersect the evolution of CBD and the pet industry.

Innocan has developed several new drug delivery platforms to tackle the perceived low bioavailability of CBD head on and significantly improve upon current delivery mechanisms. Current CBD administrating platforms have low bioavailability of between 6 and 35%.[72] Innocan's LPT and exosome drug delivery platforms promise to improve bioavailability performance.

(1) Liposome Platform Technology (LPT) Injectable Cannaboids

Liposomes are spherical vesicles composed of a few layers of lipids that can carry drugs through the human vascular system.[72] Innocan's LPT Injectable CBD drug delivery platform injects CBD directly into the bloodstream, facilitating exact dosing and the prolonged and controlled release of CBD into the patient's bloodstream.

Innocan has led several successful research trials that open the door to a wide range of therapeutic possibilities for LPT:

LPT CLINICAL RESEARCH[72]

- March 8, 2022 – Innocan's CBD LPT injection was provided as a treatment to a dog suffering from osteoarthritis of the hip and elbow joint (causing inability of the dog to walk and stand up, as well

as intense pain and a low activity rate). This treatment led to a decrease in pain and improved activity and vitality, as reported by the dog's owner. The CBD was administered to the dog as Innocan's CBD-loaded (LPT) remained in the dog's plasma for 28 days, strengthening the promise in the controlled release of CBD using Innocan's drug delivery platform.

- November 18, 2021 – Trial on dogs, demonstrated prolonged plasma concentration for at least 6 weeks after a single administration.
- October 19, 2021 – Presence of CBD in mice brains, 41 days after being injected.
- September 3, 2021 – Trial on large animals that demonstrated a similar pharmacokinetic profile as was demonstrated in a previous small animal study.
- August 3, 2021 – Presence of high level CBD for at least 3 weeks in the plasma.

It's important to note that Innocan holds the worldwide exclusive option to license the research results and products derived from this technology.

(2) CLX Cannaboids Loaded Exosome Therapy (CLX)

Exosomes are microscopic particles that are created when stem cells are multiplied. These exosomes act as "guided missiles" targeting specific damaged organs and have an important role in cell-to-cell communications. Exosomes are promising nanocarriers for drug delivery and targeted therapy. Innocan, in collaboration with Tel Aviv University, is developing a novel CBD Loaded Exosome Technology. This delivery mechanism may provide a highly synergistic effect of regenerating and anti-inflammatory properties targeting the recovery of infected lung cells and the Central Nervous System (CNS). Innocan has signed an exclusive agreement with Ramot, the commercial arm of Tel Aviv University, to obtain exclusive international research and licensing rights for the products to be manufactured.

CSX CLINICAL RESEARCH[72]

- On January 14, 2001, Innocan announced the successful completion of large-scale production of exomes. Innocan managed to perform the production of trillions of exosomes in a short period of time in a 3-dimensional bioreactor. This may lead to large scale exosome production for the CLX. This successful research is expected to pave the way for larger tests and studies.

COMMERCIAL APPLICATIONS AND MONETIZATION

Both of Innocan's LPT and CSX technologies have commercially feasible applications in the veterinary services realm to combat maladies like anxiety, inflammation and pain management. According to Iris Bincovich, CEO of Innocan, "large animals generally react to medical treatment in a similar way as humans do." The company is enthusiastic that Innocan's drug delivery platform (LPT) demonstrates therapeutic efficacy. The global canine arthritis treatment market in 2019 was estimated at US$1.9 bn and it expected to grow at a CAGR of ~ 4% during the forecast period of 2019-2029 (Future Market Insights, "Canine Arthritis Treatment Market", October 2019). The size of this market represents a tremendous first mover opportunity for Innocan.

CBD as a medical solution for animals is still in its infancy. Although many substantial Pharma companies are active in Veterinary Services, Innocan stands alone in targeting the intersection of Veterinary Services and CBD. As Innocan moves to begin the licensing and monetization of its technology, the company will likely become a viable acquisition target for deep pocked competitors. M&A activity has been propelled forward across pharmaceuticals given historically low interest rates and the availability of cheap financing and the increased risk and inflating costs implicit in research and development. In many cases, especially for public pharma companies beholden to quarterly profit estimates, it makes more sense to acquire a developed technology then to assume the cost and risk in inherent in R&D, especially for a nascent marketplace.

Several recent transactions highlight market interest in cannabis and differentiated technologies, respectively. Pfizer's $6.7B acquisition of Arena in December 2021, provided the company with an entrance into the Cannabis space. In November 2021, Lonza acquired an exosome manufacturing facility from Codiak Biosciences. Certainly Innocan could be high on a Pharma CEO's wish list, especially as the company moves to monetize its LPT technology in 2022. Whether as a buyout target or through pursuing the monetization of its LPT and CSX technologies, Innocan is certainly well positioned for financial success.

APPENDIX

Professional Associations & Societies Related to Veterinary use of Cannabis

- Veterinary Cannabis Society - Veterinary Cannabis Society Home - Veterinary Cannabis Society
- Vetcann - Frequently Asked Questions – Veterinary Medicinal Cannabis Network (vetcann.org)
- Cannabmed - About Cannabmed | Medical Cannabis | ICEERS
- Remevet - REMEVET – Continuous Learning Resources for the Veterinary Zootechnician

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