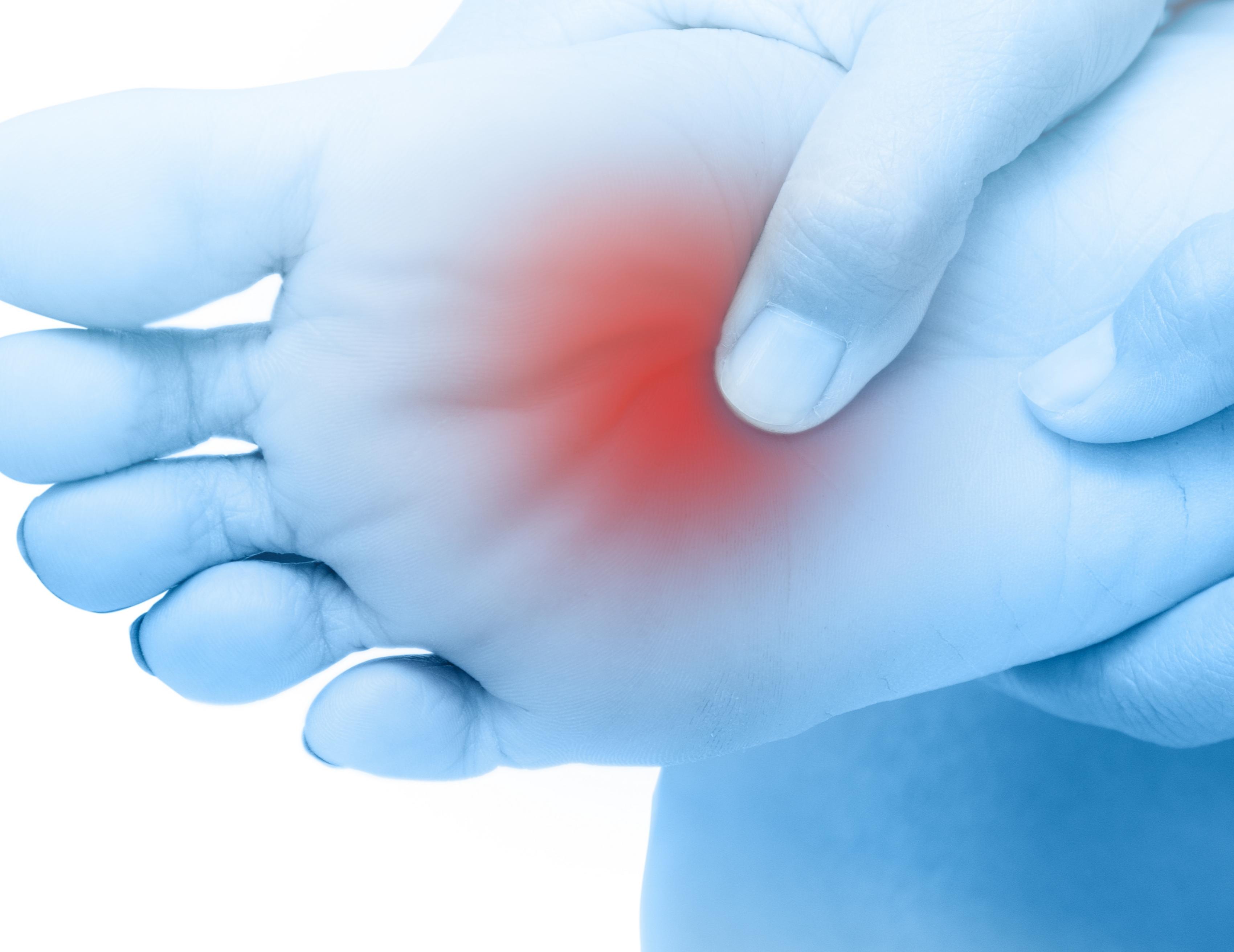
A New Treatment Option for Chronic Pain

WHITE PAPER







Relieving Chronic Pain <u></u>

Chronic pain is one of the most prevalent and <u>costly</u> health problems in the United States. As nearly any injury or illness can lead to chronic pain, it is no surprise that <u>over 20%</u> of Americans currently suffer from the condition. Worldwide, the global chronic pain market was valued at <u>\$77.8 billion in</u> 2019 and is expected to grow to <u>\$151.7 billion by 2030</u>. With over 55.2 million adults nationwide predicted to be diagnosed with chronic pain by 2026, Gb Sciences is proud to be leading the way with first-in-class drugs to treat this debilitating condition.

Problematic Prescriptions

To help patients manage their chronic pain, pharmaceutical companies have been offering different variations of the same four solutions for years:

NSAIDs: Nonsteroidal Anti-inflammatory Drugs, which target

Inflammation, a common underlying cause of chronic pain.



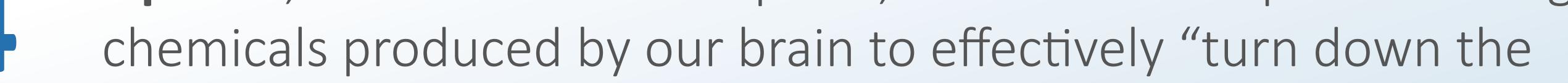
Anti-seizure medications, which dampen pain signals from nerve cells and may be helpful primarily for stabbing or shooting pain resulting from nerve damage.



Antidepressants, which may affect pain because anxiety and depression have been shown to contribute to the severity of, and sensitization to, pain stimuli.



Opioids, which mimic endorphins, are the natural pain-relieving



volume" on the pain signals.



None of those solutions offers a sustainable solution for chronic pain relief. NSAIDs and anti-seizure medications only help with certain kinds of chronic pain, while antidepressants only prevent patients from exacerbating already existing pain. Opioids are effective but patients can develop tolerance to them even with short-term use, and opioid use comes with a high risk of developing potentially deadly addictions.

A Plant-Inspired Path to Pain Relief

Those risks, and a societal change, have patients, doctors, and biopharmaceutical research companies looking for a new approach to chronic pain therapies. Some have found it in cannabis, known for <u>more</u> <u>than a century</u> for its medicinal uses and for its <u>safety</u>.

Since the 1990s, the legalization and acceptance of cannabis use by patients has spread across the country, and biopharmaceutical companies have now begun to use the active ingredients derived from cannabis in the development of medicines for a variety of conditions. Most drugs in development today contain one of the two most abundant (tetrahydrocannabinol (THC) or cannabidiol (CBD)) cannabinoids out of the 113 cannabinoid compounds found in the <u>cannabis plant</u>. However, the cannabis plant contains over 400 potential therapeutic compounds including cannabinoids, terpenes, flavonoids, and alkaloids. Gb Sciences, a plant-based research and drug development company, is looking at all of these ingredients to find new, multi-component solutions to an array of diseases and conditions.

Both THC and CBD are able to affect the human <u>endocannabinoid system</u> (ECS) by mimicking the endocannabinoids that the human body produces normally.

Both the endocannabinoids produced in our bodies and the plant-based cannabinoids bind to cannabinoid receptors that regulate human processes through the ECS such as: mood, sleep, memory, appetite, pain-perception, motor control, inflammation and other immune processes.

Structural differences in the cannabinoids affect their three dimensional shape and their ability to bind to cannabinoid receptors, which leads to



different effects on the body processes. The two primary receptors for cannabinoids are called cannabinoid receptors 1 & 2 (CB1 & CB2); however, there are more than a dozen other cannabinoid-sensitive (TRPV1, TRPV2, TRPA1, TRPM8, TRPA1, dopaminergic, glutamatergic, and GABAergic) receptors that are either directly or indirectly activated or inactivated by cannabinoids. THC binds to CB1 and CB2 receptors, whereas, CBD binds to TRPV1 receptors and indirectly regulates CB1 receptors. THC is a psychoactive chemical that causes most of the intoxicating effects for which cannabis is known, such as the "high" sensation, through binding to CB1 receptors. <u>CBD</u> has no known intoxicating effects, but may be effective in reducing anxiety, inflammation, seizures, and other conditions through binding to TRPV1 or indirectly affecting CB1 and/or CB2 receptor signaling.

A Data-Driven Solution

Gb Sciences, founded in 2014, has built an intellectual property portfolio with more than 60 patents and patent-pending applications for its plantinspired therapeutic mixtures for the treatment of more than 65 clinical conditions, including Parkinson's disease, COVID-related cytokine release syndrome, heart disease, inflammatory bowel disease, and chronic pain.

To discover new therapies, Gb Sciences uses its patent-pending, Al-driven PhAROS[™] drug discovery platform to predict, select, and eliminate certain combinations of compounds for optimal effectiveness.



Gb Sciences also uses data-driven processes like high-throughput screening of tens of thousands of plant-derived mixtures in established cellular and animal models of diseases in order to determine which combinations of ingredients could be the most effective new therapies. The company works with seven university partners worldwide on this challenging discovery and preclinical research, as well as with several companies and CROs on the clinical development work.

Their goal is the development of what Gb Sciences calls Minimum Essential Mixtures (MEM). MEM are plant-based, multi-component formulations that are more effective as mixtures when they are used together than when used separately as single ingredient drugs, which is the definition of molecular synergy (molecules working together synergistically).

The key is to discover the most effective combinations of ingredients, while simplifying the plant extracts down to the compounds needed to achieve the desired therapeutic effects. By simplifying plant extracts down to just the essential ingredients, MEM also have the production and quality control advantages of simpler drugs. To further simplify the process of producing their MEM, Gb Sciences uses identical copies of the plant-based ingredients that are manufactured in large quantities, rather than sourcing from plants to avoid supply chain problems.

Gb Sciences' drug discovery process has identified precise mixtures of cannabinoids and terpenes, most of which contain no THC, to treat conditions including Parkinson's disease, congestive heart failure, cytokine release syndrome, chronic neuropathic pain, Mast Cell Activation Syndrome, and inflammatory bowel disease. Critically, Gb Sciences has been able to demonstrate that these MEM perform more

effectively than the sum of the effects of the components in the MEM measured separately through molecular synergies.



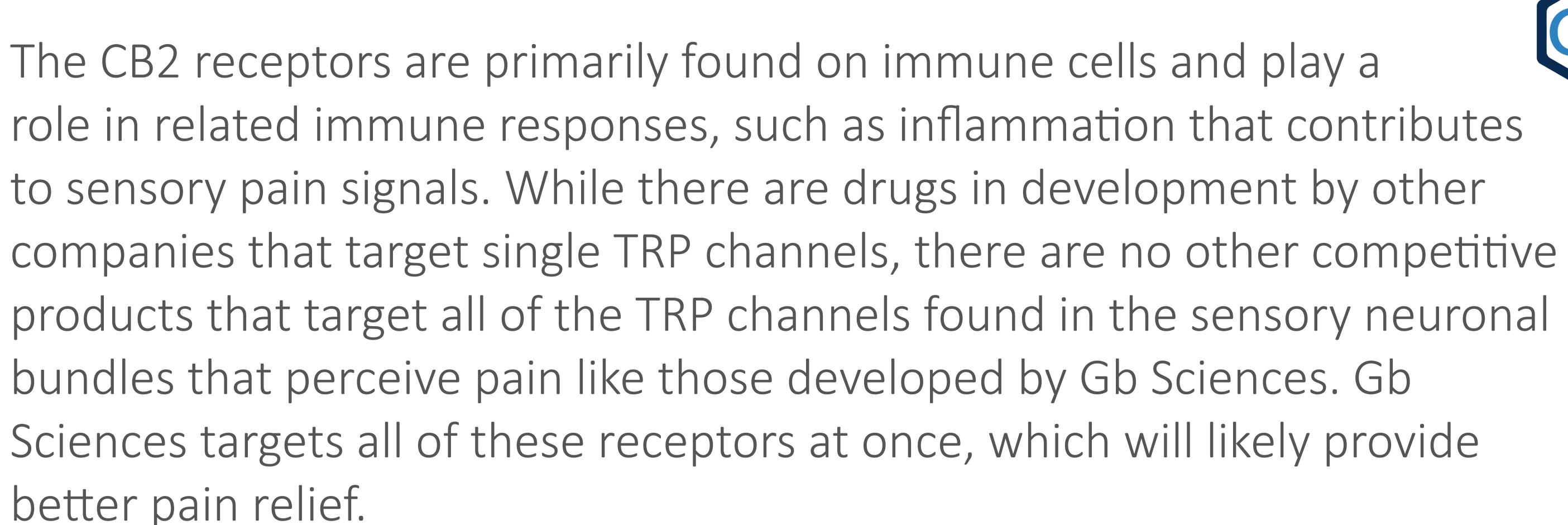
Gb Sciences' chronic pain therapy, which is protected by a U.S. patent and patents-pending, uses a terpene-dominant mixture delivered in an oral, time-released nanoparticle. Gb Sciences' chronic pain therapy is now in preclinical development with the company's university partners at the University of Seville and preclinical research partners at the National Research Council Canada (NRC). Proof-of-concept testing in an animal model demonstrated that a single oral dose of the extended release nanoparticles can provide optimal pain relief for eleven days, far longer

than the several hours of peak pain relief shown when the active ingredient was not delivered within the nanoparticles. The company is working to advance this novel therapy to human clinical trials as soon as possible.

Key Differentiators

Gb Sciences' chronic pain therapies are in a different class from those that are currently marketed; i.e., NSAIDs, repurposed anti-seizure/ antidepressants, and opioids. Gb Sciences' first-in-class chronic pain formulations are also different from the drugs being developed by other

Compared to our competitor's new products in development, Gb Sciences' novel chronic pain solution is differentiated based on the fact that it targets multiple Transient Receptor Potential (TRP) channels and Cannabinoid Receptors (CBRs), simultaneously, to more effectively block the sensing or perception of pain at the TRP channels in the periphery and the CBRs in the brain that process the pain signal. TRP channels play <u>critical roles</u> in sensory physiology, including the feeling or perception of pain. CBRs are found throughout the body, including in the central nervous system (CNS). CB1 receptors are primarily located in the brain and CNS where they affect the processing of the pain signal in the brain responding to sensory neuronal signals from the periphery so that you consciously 'feel the pain'.





Gb Sciences' pain formulations regulate both CB1 and CB2; whereas our competitors have pain therapies in development that target CB1 receptors in the brain or CB2 receptors in the periphery. Furthermore, the majority of the cannabinoid-based pain formulations made by Gb Sciences' competitors are relying on THC, which has psychoactive properties. Two of our competitors' products rely on synthetic THC alone, and an additional six chronic pain products in development combine synthetic THC with opioids. These products have the potential disadvantages of opioids and the psychoactivity of THC.

There is also a novel CBD based product that targets CB2 only to reduce the inflammatory pain signals, and there is a fully synthetic inhibitor of the CB2 receptor in trials. In contrast, the Gb Sciences solution combines non-psychoactive ingredients from cannabis in Minimum Essential Mixtures that target TRP and CBR receptors in the pain response system through its terpene-driven mixtures. Gb Sciences' novel chronic pain formulations are designed to be a more effective treatment of chronic pain by targeting multiple parts of the pain pathway, without the psychoactivity (no THC) and with less potential for addiction (no opioids). As previously mentioned, Gb Sciences also uses the oral, time-released nanoparticles for delivery of

these effective formulations to allow patients to maintain their pain relief for a longer time between doses.

Conclusion E

Chronic pain plagues an estimated 60 million Americans, and the existing remedies- surgery, implantable devices, and potentially dangerous drugs-fall far short of providing a caring and effective solution.

Gb Sciences is bringing together hard science and plant-based medicine for a novel approach to chronic pain. Gb Sciences' drug discovery system isolates the most effective compounds from plants like cannabis and then uses data-driven processes to identify the most effective combinations of these ingredients to create potential medications that already show great promise for extended pain relief with less potential for addiction and side effects.

Gb Sciences' novel chronic pain formulations are designed to simultaneously target multiple parts of the pain pathway for increased efficacy using compounds derived from the cannabis plant, without the psychoactivity (no THC) and with less potential for addiction (no opioids).

Gb Sciences also uses an oral nanoparticle for delivery of these effective formulations to provide a time-released dosing for patients.

By combining traditional plant-based medicine approaches with modern data-driven drug discovery processes, Gb Sciences is creating the future of healing.

Learn More about GbSciences by



