

# Targeting Premium DSO Bauxite



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## **ASX ANNOUNCEMENT**

Queensland Bauxite Limited (ASX:QBL)

announces

## **A WORLD FIRST FOR MCL IN AUTOIMMUNE DISEASE RESEARCH**

Medical Cannabis Research and Multiple Sclerosis

## A World First for MCL in Autoimmune Disease Research

### Cannabis as a Potential Therapy for Multiple Sclerosis

The Board of Queensland Bauxite Limited (ASX:QBL) is pleased to announce that its subsidiary company Medical Cannabis Limited (MCL) through its wholly owned subsidiary Medical Cannabis Research Group Pty Ltd (MCRG), has signed a Research Funding Agreement with the Research & Development Foundation at the Technion Institute, Haifa, Israel. The agreement revolves around the research of Prof. David (Dedi) Meiri, from the Faculty of Biology at the Technion Institute.

According to the agreement MCRG will sponsor the continued Research of how the cannabis plant can be used for the treatment of Multiple Sclerosis (MS). Prof. Meiri has identified the synergistic relationship between the Cannabis plant and the human genome that will form the basis for this research.

### Highlights

- Medical Cannabis Ltd (MCL) a subsidiary of Queensland Bauxite Limited (ASX: QBL), completes an arrangement to sponsor research into medical cannabis treatments for Multiple Sclerosis (MS).
- MCL through its Medical Cannabis Research Group Pty Ltd (MCRG) has signed an agreement with the Technion Research & Development Foundation for the performance of research by Prof. David (Dedi) Meiri, from the Faculty of Biology at the Technion - Israel Institute of Technology in Haifa, Israel. Prof. Meiri is Head of the Technion's Cannabis research team. According to the agreement, MCRG will sponsor research into how the cannabis plant can be used in the treatment of symptoms and halting the progression of autoimmune diseases with special emphasis on Multiple Sclerosis (MS).
- Long-standing and approved MS treatments can reduce relapses, but current solutions may slow down, but ultimately do not arrest the progression of the disease.
- The overall objective of Prof. Meiri's study is to identify specific cannabis compounds that can be used in clinical trials as a potential treatment for Multiple Sclerosis (MS).
- MCL through its Medical Cannabis Research Group (MCRG) will agree to fund Research into Prof. Meiri's study **in return for an exclusive license for any product derived** from the Research.
- Should a successful product eventuate, the Board believes, in time, this Research has the potential to be a global medical 'game changer' for MS sufferers, and a material revenue stream for MCL.
- MCRG has committed to fund USD\$3M over a 3-year period, towards the research budget, in return for an exclusive license of any product to be developed from this research for MS, or potentially for any product that could alleviate or treat any other auto immune disease that could be developed from this research.



**Prina Feldman, Executive Chairperson of QBL** says: *"The Boards of QBL and MCL feel privileged to be working with Prof. Meiri and his team of medical cannabis researchers at the Technion-Israel Institute of Technology, not only for the opportunity to be in with top researchers who are one of the leaders in the world with this research, and not only to commercialise the products that may result from this research, but for this unique and ground-breaking opportunity to work diligently towards the betterment of health worldwide. Everyone knows someone with an- autoimmune disease in one form or another, and there could be no more satisfying outcome, or more important work, than making the lives of these people not only easier, but hopefully enabling respite from symptoms and cures for disease. The benefits of the age-old cannabis plant, combined with state of the art medical technology, is opening new horizons, and we are both proud and humbled to be amongst the pioneers supporting and being a part of this amazing research."*

## Background - Dr. David (Dedi) Meiri PhD



Assistant Professor, Heads the "Laboratory of Cancer Biology and Cannabinoid Research", Technion, Israel Institute of Technology, Israel.

**David (Dedi) Meiri, PhD**, is an Assistant Professor at the Faculty of Biology at the Technion Israel Institute of Technology and a member of the Technion Integrated Cancer Center (TICC). Dr. Meiri's scientific background is highly diverse. He holds a M.Sc. in biochemistry and a Ph.D. in plant biotechnology from Tel Aviv University. Dr. Meiri conducted his post-doctoral fellowship at the Ontario Cancer Institute where he expanded his knowledge in human biology and cancer pathogenesis and focused on the role of the GEF-H1 protein in tumor invasion and metastasis. Upon completion of his post-doctoral fellowship, Dr. Meiri took a position at the Technion Israel Institute of Technology, where he heads the "Laboratory of Cancer Biology and Cannabinoid Research".

Presently, his lab investigates the therapeutic potential of phytocannabinoids, the unique active compounds of the *Cannabis sativa* plant. On top of other research being conducted in the lab, the main focus of his research is to determine the antitumor effects of cannabinoids, including the anti-metastatic and pro-apoptotic effects of phytocannabinoids.

From the establishment of his lab it has grown significantly and it is now comprised of 38 scientists; a highly trained team of skilled plant biologists, chemists, cancer experts and neuroscientists who work together in synergy to complement one another in order to achieve the highest level of results. Dr. Meiri's lab, is one of the leading laboratories in the world that is exceptionally equipped with the capabilities and resources to ask and answer almost any question in the field of medical cannabis.

Dr. Meiri operates the "Cannabis Database Project" and his lab is currently involved in eight clinical trials covering diverse aspects of cannabis treatment, such as: colon disease, pain prevention, cancer treatment and epilepsy. He collaborates with cannabis growers, clinicians and major manufacturers and distributors of medical cannabis, including Andrew Kavasilas from QBL: MCL in the purpose of revolutionizing cannabis treatment.

Dr. Meiri is also highly involved in governmental regulations and is a residing member in several Israeli Ministry of Health committees which seek to advance the fundamental understanding of optimal cannabis usage and minimization of adverse side effects.

## Background - Technion Israel Institute of Technology

Technion - Israel Institute of Technology was founded in 1912 in Haifa and is the oldest university in Israel. The Institute is currently rated **#93** in the World's Top 500 Universities and is the **only Israeli university in the top 100 of the list.** ([2017 - Shanghai Ranking World Leading Universities](#))



Technion researchers, including **three Nobel laureates in chemistry**, have won many International awards for their research in the fields of Microbiology, Microbial Diagnostics, Genomics, Antibiotics to name just a few. Technion people, ideas and inventions make immeasurable contributions to the world including life-saving medicine, sustainable energy, computer science, water conservation and nanotechnology.

Technion is widely recognized as a global leader in Medical Cannabis Research. Israel has been leading the world since the early 1960's in Medical Cannabis research.

In November 2017, Times Higher Education ranked Technion as the **world's leading academic institution** in teaching digital skills to students, ahead of the prestigious American M.I.T. University.

## Background - Autoimmune disease

The Australian Society of Clinical Immunology and Allergy (ASCIA) states that autoimmune diseases affect around 5% of people and are one of the most important health issues in Australia and New Zealand.

**An autoimmune disease** is a disease in which the body's immune system attacks healthy cells. The most common types of autoimmune diseases include:

- **Rheumatoid Arthritis:** A chronic inflammatory disorder affecting many joints, including those in the hands and feet.
- **Lupus:** An inflammatory disease caused when the immune system attacks its own tissues.
- **Celiac Disease:** An immune reaction to eating gluten, a protein found in wheat, barley and rye.
- **Multiple Sclerosis:** A disease in which the immune system eats away at the protective covering of nerves. This condition can last for years or be lifelong. In MS resulting nerve damage disrupts communication between the brain and the body.
- **Type 1 Diabetes:** A chronic condition in which the pancreas produces little or no insulin.
- Other diseases include: Sjogren's syndrome, Polymyalgia rheumatica, Ankylosing spondylitis, Alopecia areata, Vasculitis, Temporal arteritis, Crohn's disease, Graves disease (thyroid) etc. In all, there are 80 known autoimmune diseases, with an estimated 50 million Americans suffering these diseases in increasing numbers. The disorders range in severity from mild to disabling, depending on which system of the body is under attack and to what degree.

The causes of autoimmune diseases are unknown. In many cases it appears that there is some hereditary tendency. However, other factors such as infections and some drugs may play a role in triggering autoimmune diseases.

## No Known Cure

Autoimmune disorders in general have no known cure, but the conditions can be somewhat controlled and managed in many cases.

## Treatments

Historically, treatments include:

- **Anti-inflammatory drugs** - to reduce inflammation and pain.
- **Corticosteroids** - to reduce inflammation. They are sometimes used to treat an acute flare of symptoms.
- **Pain-killing medication** - such as paracetamol and codeine.
- **Immunosuppressant drugs** - to inhibit the activity of the immune system.
- **Physical therapy** - to encourage mobility.
- **Treatment for deficiency** - for example insulin injections in the case of diabetes.
- **Surgery** - for example to treat bowel blockage in the case of Crohn's disease.
- **High dose immunosuppressants** - the use of immune system suppressing drugs (in the doses needed to treat cancer or to prevent the rejection of transplanted organs), have been tried recently, with promising results. Particularly when intervention is early, the chance of a cure with some of these conditions seems possible.

## Background - Autoimmune disease continued

- **Stem cell Research** - Recent experimentation in Israel with stem cell implanting to treat impaired bodily functions is being trialled and although very invasive is showing some progress.

The goal of the cannabis research in the field of auto immune disease is to find a treatment and possible cure that does not have the serious side effects of other treatments being researched or used to date.

## The Role of Cannabis in Autoimmune Diseases

So far, the approved and available treatment for autoimmune diseases with medicinal cannabis, has been in the area of pain relief, the cannabis formula replacing morphine and its derivatives, with morphine in high and frequent doses being serviceable mainly in palliative care. The medicinal cannabis pain relief available for (MS) for example, is most effective in relieving pain, enabling sufferers to function better without the side effects of pain relieving drugs such as morphine. The danger of morphine has been recognized by the Australian authorities, who as of February 1, 2018 requires codeine to be a prescription only drug.

**Andrew Kavasilas, Technical Director of MCL**, said: *"This is a very logical avenue of research, especially when the only semi-legal Cannabis medicine in the world was developed for the treatment of MS. That was a first wave cannabinoid medicine and a vast amount of knowledge has been gained since then. There's an incredible amount of work being done in Israel which has capitalised on many opportunities due to their government's willingness to allow medical Cannabis use by well over 100 000 people, while the profession scientific research catches up to break down all this valuable evidence".*



## Dr David (Dedi) Meiri - Cannabis as a Potential Therapy for Multiple Sclerosis

Due to the legal access to medical researchers and doctors of high and low THC Cannabis plants under the auspices of the Israeli Health Department, Israel is currently **at the forefront** of medicinal cannabis research, and the world-renowned Dr Meiri is arguably today's leading medicinal cannabis researcher in Israel, if not in the world.

Dr Meiri is head of the Technion's Cannabis Research team and will be the principal investigator in research to be funded by MCRG (the research and wholly owned subsidiary company of MCL). Dr Meiri lectures and teaches about the latest developments in cannabis research throughout the world, and has recently been on a lecture tour to Australia, speaking in Sydney at a function organized at Wolper hospital for doctors interested in Dr Meiri's new and exciting research insights.

Assisting Dr Meiri's team of close to 30 researchers, will be supporting investigators Dr Igal Louria-Hayon PhD and Dr Gil Lewitus PhD.



### Overall Objective

The overall objective of Dr Meiri's study is to match effective cannabis extracts and specific cannabinoids composition that regulate/modulate immune function, specifically, autoimmunity in MS in order to optimize treatment for MS patients.

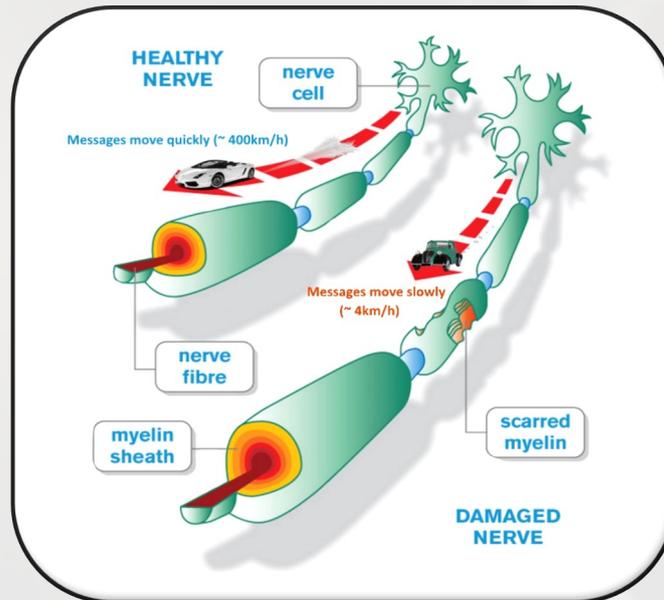
It is hoped that achieving a successful outcome of the overall objective could lead to a possible cure for MS through the strengthening of the immune system, which in turn will assist the research into other autoimmune diseases and diseases in general.

### Dr Meiri Comments:

“Although current treatment of MS with broad-spectrum immunomodulatory drugs reduces immune cell activity and entry into the central nervous system (CNS) and decreases relapse frequency, they are often associated with side effects, ranging from flu-like symptoms to the development of other auto-immune disorders; fatal opportunistic infections such as progressive multifocal leukoencephalopathy; and other malignancies.

## Dr Meiri Comments continued:

“These side effects highlight the need to identify more specific therapeutic targets that can be effectively modulated without inducing such adverse reactions. In addition, it is increasingly acknowledged that although the long-standing and approved MS treatments can reduce relapses, they do not ultimately halt the disease. Therefore, neuroaxonal damage, which results in progressive physical disability, continues to accumulate and becomes permanent throughout the disease progression.



“Recently, the therapeutic potential of phytocannabinoids, the unique active compounds of the cannabis plant, has been discovered in the area of immunology; More than 140 phytocannabinoids have been identified within the cannabis plant. A few specific natural and synthetic cannabinoids have been proposed to have therapeutic potential for various diseases. The U.S. Food and Drug Administration (FDA) recently approved the use of several synthetic cannabinoids to be available by prescription for pain relief treatment.

“Cannabinoids have been largely characterized for their action in the immune system and were tested in several *in vitro* and *in vivo* disease models for inflammation (a common symptom of numerous autoimmune diseases). Recent research showed that administration of tetrahydrocannabinol (THC) with mice triggered significant caspase mediated cell death in T cells and dendritic cells, resulting in immunosuppression. In addition, other research demonstrated that cannabinoids downregulate cytokine and chemokine production and at times upregulate T regulatory cells as a mechanism to suppress inflammatory responses. The targeted actions of cannabinoids in the endocannabinoid system is also involved in immunoregulation.

“CBD another abundant cannabinoid was found to exhibit a suppressive effect on T cell functional activities via reducing IL-17 cytokine secretion, a key autoimmune factor which was also shown to be involved in multiple sclerosis (MS). In this context, its additional neuroprotective effects, which included the upregulated of a number of anti-oxidative genes (e.g. those of glutathione synthesis) in CBD exposed microglial cells from inflammation-induced apoptosis may significantly enhance its anti-inflammatory beneficial properties and account for alleviation of MS pathology.

## Dr Meiri Comments continued:

“As of now, there are several different cannabinoid medications approved for patients with MS, including cannabis in its natural form. Cannabis is primarily used to reduce muscle stiffness and pain. However, chemical trials to date done with specific cannabinoids showed small or no effect on disease progression from the above current cannabinoid medications.

“Other compounds in Cannabis have been poorly studied regarding their potential immunosuppressive effects. For example, it has been shown that terpenoids are key components of cannabis activity as they are known to participate in making the plant extract more potent than synthetic cannabinoids. Overall, Cannabis’s multiple inflammatory effects on various immune cell types, together with the vast number of phytocannabinoids and different ratios of cannabinoids in different strains makes the Cannabis plant a complex matrix with great therapeutic potential.

“Cannabis chemical composition analyses currently focus on identifying and qualifying and quantifying several major Cannabinoid types including THC, CBD, and in some recent studies also cannabichromene (CBC), cannabinol (CBN), and cannabigerol (CBG). Other Cannabis compounds which may be important for their therapeutic effects, have predominantly been neglected.

“In order to identify more cannabinoid types, we developed, in our lab, a novel ability to analyze the metabolomics and the specific chemical composition of cannabis plants.

“As far as we know, ‘WE ARE THE ONLY LAB IN THE WORLD TODAY THAT HAVE THESE ABILITIES OF COMPREHENSIVELY PROFILING THE CANNABINOID COMPOSITION FOR A VARIETY OF CANNABIS STRAINS AND ALSO TO BE ABLE TO PURIFY SINGLE PHYTO-CANNABINOIDS AND CREATE “SUSPECT PROFILES” FOR EXAMINATION IN DIFFERENT TYPES OF STUDIES.’

## Dr Meiri Comments continued:

### Research Plan

“In the last year, we established the novel ability to analyze the metabolomics and the specific chemical composition of Cannabis plants (principally of phytocannabinoids and terpenes). We intend to identify the effects of different cannabinoids and terpenes both individually and in combination on the function of immune cells, specifically on MS-derived autoimmune and regulatory cells in vitro. We intend to evaluate the immunomodulatory properties of specific cannabinoid extracts in in vivo rodent models of MS. This will enable us to detect the most effective extracts in in vivo rodent models of MS. This will enable us to detect the most effective Cannabis extract and cannabinoid profiles for regulating immunopathology in MS.

### Specific Aims

- **Characterize clinically-used *Cannabis* strains using comprehensive mass-spectrometry based metabolomics.**
- **Screen for the immunoregulatory properties of different *Cannabis* extracts on immune cell function and MS immunopathology.**
- **Demonstrate the immunomodulatory properties of specific *Cannabis* extracts on various MS rodent models and identify specific compounds that can then be used in clinical trials as potential treatment for MS.**

### Significance

“Affecting millions of people worldwide, Multiple Sclerosis (MS) is the most common autoimmune disorder affecting the central nervous system. Therapies for MS are only partially effective and there is no known cure. Therefore, there exists a great and unmet clinical need for the development of neuroprotective treatments. Today, MS patients are treated with medical Cannabis primarily for the palliative purposes. Furthermore, the specific Cannabis strain for palliative treatment is chosen arbitrarily. Consequently, evaluating the immunomodulatory properties of Cannabis in MS and tailoring the best combination of phytocannabinoids may open new treatment possibilities for MS patients with the intention of finding a cure.”

### Summary

“In this work we aim to elucidate the immunoregulatory properties of phytocannabinoids and terpenes in MS, as well as further investigate Cannabis’s mechanisms of action in these areas. This research not only has the ability to advance the identification of new drug candidates, but also advance our abilities to optimize Cannabis treatment options and efforts towards the creation of personalized medicine for MS patients.”



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**Pnina Feldman, Executive Chairperson and Director of Business Development of QBL stated:** *“Having had the pleasure of meeting Dr David Meiri at the Wolper Doctors Conference, in Australia, in June 2017, I was very happy for the opportunity to open a dialogue with Dr Meiri, which was the beginning of this current deal. We are very excited about the work being carried out by Dr Meiri, and his team at Technion, and we believe that this research will hopefully be of major benefit worldwide, and in particular to QBL shareholders who support our ground-breaking work.”*

Pnina Feldman

Executive Chairperson,

Director of Business Development,

Queensland Bauxite Limited

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## About Queensland Bauxite

Queensland Bauxite Ltd is an Australian listed company focused on the exploration and development of its bauxite tenements in Queensland and New South Wales. The Company's lead project is the South Johnstone Bauxite Deposit in northern Queensland which has rail running through the project area and is approximately 15-24 kilometres from the nearest deep water port. The Company intends to become a bauxite producer with a focus on commencing production at South Johnstone as early as possible. The Company also pursues additional investment opportunities, and has acquired a 55% shareholding in Medical Cannabis Limited, an Australian