ASX/Media Release

19 June 2019

Botanix study identifies novel cannabinoid anti-inflammatory and immunomodulation effects in skin disease

Key highlights

- **Botanix has completed a world-first randomised clinical study to establish the mechanism of action of cannabidiol in skin disease**
- **Interim analysis confirms that BTX 1308 has significant anti-inflammatory and immune cell modulating activity, via previously undescribed pathways**
- **Study data also supports the anti-inflammatory mechanism of action relevant to acne and atopic dermatitis, which are well advanced in Phase 2 clinical studies**
- **Further analysis is underway with additional study data expected, along with new data on the antimicrobial performance of cannabidiol**

Philadelphia PA and Sydney Australia, 19 June 2019: Clinical stage cannabinoid company Botanix Pharmaceuticals Limited (ASX:BOT, "Botanix" or "The Company") is pleased to announce interim results from the BTX 1308 psoriasis Phase 1b mechanism of action study. The Phase 1b patient study was conducted in Australia in collaboration with BioSkin GmbH, a German-based clinical contract research organisation, and Professor Jim Krueger at Rockefeller University in New York.

The interim results confirm that BTX 1308 has significant anti-inflammatory and immune modulating activity in skin disease. This is the first time in global research that mechanism of action data outlining how cannabidiol (CBD) exerts its multiple beneficial effects in skin disease, has been generated in a randomised clinical study.

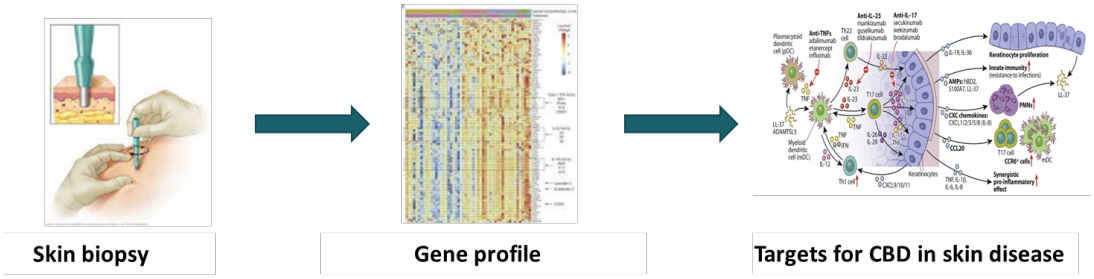
Professor Jim Krueger commented: "Our results show Permetrex™ effectively delivers CBD to the skin layers involved in the pathogenesis of skin disease and the drug triggers significant alterations in inflammatory and immune response pathways. Of particular interest is BTX 1308's ability to down-regulate the p38 MAP Kinase pathway, as pharmaceutical companies have tried unsuccessfully to target this pathway for many years. This anti-inflammatory and immune modulation activity potentially makes BTX 1308 a very important treatment option for patients, not only with psoriasis, but other skin diseases that have an inflammation and/or an immune response component."

Study overview

The study met its target enrolment of 15 patients and all patients completed the treatment phase of the study. Skin biopsies were collected from 10 of the 15 patients after they received treatment with BTX 1308, vehicle (or placebo) and an active comparator over a period of 19 days. Biopsies were collected from the untreated psoriatic and normal skin from the same patient to serve as controls. A comprehensive analysis of the expression of over 50,000 genes was then undertaken by Professor Jim

Krueger's laboratory to determine differences in gene expression between normal, treated and untreated psoriatic skin (refer to Figure 1).

Figure 1: Overview of BTX 1308 data capture, analysis and input into MOA identification

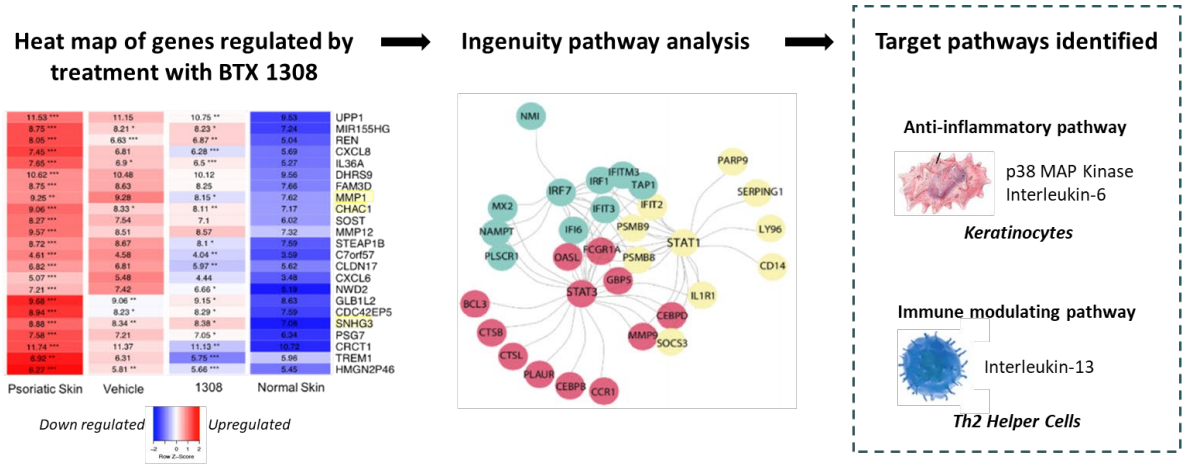


Study data / results

Data from the BTX 1308 study confirms for the first time that genes contributing to the key inflammatory disease pathways known to be involved in psoriasis, specifically the p38 MAP Kinase pathway and Interleukin-6 (IL-6), were significantly down-regulated in psoriatic skin biopsies that had been treated with BTX 1308, compared to placebo (vehicle) treated, or untreated psoriasis lesion biopsies. MAP kinases and IL-6 are both associated with the excessive growth, differentiation, immune responses and death of cells in the skin. In psoriasis, both molecular targets encourage excessive skin cell growth and inflammation.

The biopsy study data is therefore important, as it shows for the first time that BTX 1308 can work to influence these industry accepted targets and potentially modify psoriasis disease severity and progression. Figure 2 outlines the heat map which shows the regulation of target genes between normal skin, vehicle (placebo), treated psoriatic skin and BTX 1308 treated psoriatic skin.

Figure 2: Heat map of Gene Regulated by treatment (BTX 1308) and Ingenuity Pathway Analysis



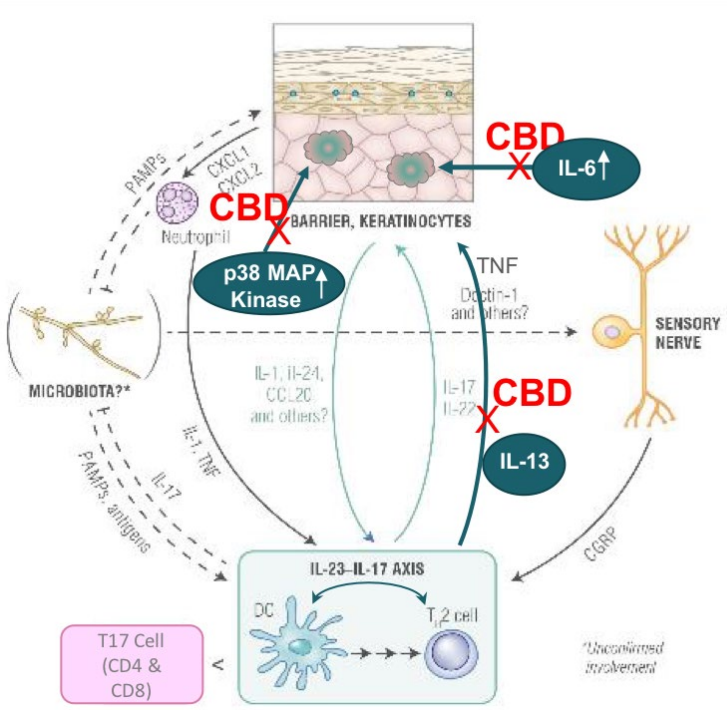
Regulated genes were uploaded and mapped algorithmically using the Ingenuity Pathways Knowledge Database to identify target pathways

Botanix Executive Director Matt Callahan said: "We are delighted with these positive results and the ability to collaborate with Professor Jim Krueger, a leading expert in the pathogenesis of skin diseases.

The new insights into the mechanism of action for CBD in BTX 1308 provides us with further excitement and justification for our lead programs currently in Phase 2 clinical development for acne (BTX 1503) and atopic dermatitis (BTX 1204), that both have significant inflammatory and immune components. These programs are well advanced with study completions approaching in 3Q and 4Q this year respectively."

Psoriasis and atopic dermatitis are diseases that are driven by 'T-cells' or 'T-helper cells', that play an important role in controlling and shaping the body's immune response to different allergic and other challenges. While psoriasis and atopic dermatitis are generally characterised by different subsets of these T-cells (Th17 and Th2 respectively), they share some common elements which contribute to inflammation, skin barrier disfunction, increasing susceptibility to infection and allergic sensitisation. Figure 3 highlights the newly identified mechanism of action for CBD in psoriasis based on the BTX 1308 biopsy study data.

Figure 3: Inflammatory loop in psoriasis



Further data from the BTX 1308 study will continue to be analysed and the Company plans to share some of these data with potential industry partners and key opinion leaders in the coming months.

Impact of study data on Botanix's broader pipeline

In addition to confirming the positive effect that BTX 1308 had on psoriasis relevant targets, the biopsy data also showed significant down-regulation of genes involved in the atopic dermatitis relevant Th2

immune response, primarily through the Interleukin-13 (IL-13) cytokine pathway. IL-13 is a well-accepted target in atopic dermatitis and many injectable biologics have been developed to block this cytokine pathway, but they typically act by lowering the overall immune system of the patient, which can cause serious safety issues if there is an infection. This new biopsy data therefore supports the positive clinical outcomes already seen in the recently completed BTX 1204 Phase 1b atopic dermatitis study, as well as provides increased confidence of success for the BTX 1204 Phase 2 atopic dermatitis study, currently underway.

The new biopsy data is also relevant to how BTX 1503 may benefit acne. Being an inflammatory disease, it is known that colonisation of *P. acnes* leads to an up regulation of the p38 MAP Kinase pathway in keratinocytes. As data from the fully enrolled BTX 1503 acne Phase 2 clinical study also becomes available after study completion in 3Q CY2019, the mechanism of action data from this BTX 1308 study will (in combination with the BTX 1503 clinical data), form the basis of a comprehensive clinical and scientific package for the Company's planned partnering and other corporate activities.

The Company also expects new data from its BTX 1801 development program to be available for release in the near term, which is expected to add to the understanding of the antimicrobial mechanism of action of CBD in skin disease, which complements the findings of the anti-inflammatory and immune modulating properties of the drug identified in this BTX 1308 study.

About Botanix Pharmaceuticals

Botanix Pharmaceuticals Limited (ASX:BOT) is a clinical stage cannabinoid company based in Perth (Australia) and Philadelphia (USA) committed to the development of pharmaceutical products that are underpinned by science and supported by well-controlled randomised clinical trials. The Company's focus is the development of safe and effective topical treatments for acne, psoriasis, atopic dermatitis and other skin conditions. The active ingredient contained in Botanix products is a synthetic form of cannabidiol. Treatment targets include inflammation, deterioration of the of the skin barrier, skin cell proliferation, pruritus (itch), excess sebum production and bacterial infection.

Botanix has an exclusive license to use a proprietary drug delivery system (Permetrex™) for direct skin delivery of active pharmaceuticals in all skin diseases. Botanix is working with multiple parties to test the application of Permetrex™ on both a fee-for-service and traditional license basis. Botanix pursues a rapid clinical development strategy aimed at accelerating product commercialisation.

The Company completed its first acne patient studies with BTX 1503 in January 2018 and has commenced a Phase 2 clinical study in June 2018 with study completion expected in 3Q CY2019. The BTX 1204 atopic dermatitis Phase 2 patient study is also underway with study completion expected on 4Q CY2019. Finally, Phase 1b BTX 1308 psoriasis mechanism of action study has recently completed, with positive interim data announced in June 2019. Pipeline development that leverages

the antimicrobial properties of cannabidiol are also moving forward and are planned to enter the clinic in 2H CY2019.

To learn more please visit: https://www.botanixpharma.com/

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