**ASX/Media Release**

**22 October 2019**

# Botanix announces BTX 1503 data and progression to Phase 3

**Philadelphia PA and Sydney Australia, 22 October 2019:** Clinical stage cannabinoid company Botanix Pharmaceuticals Limited (ASX:BOT, "Botanix" or "the Company") is pleased to attach topline data from its Phase 2 BTX 1503 study evaluating the safety and efficacy in patients with moderate to severe acne and preparations for a Phase 3 clinical program.

Botanix is releasing this information at this time, to allow all Australian and US investors to have the opportunity to review the release, prior to the commencement of normal trading on Wednesday, 23 October 2019 (AEDT).

## About Botanix Pharmaceuticals

Botanix Pharmaceuticals Limited (ASX:BOT) is a clinical stage synthetic 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 serious skin diseases, leveraging the unique anti-inflammatory, immune modulating and antimicrobial properties of synthetic cannabidiol. Botanix has an exclusive license to use a proprietary drug delivery system (Permetrex™) for direct skin delivery of active pharmaceuticals in all skin diseases.

The Company has announced data from its Phase 2 clinical study and is moving forward with its clinical program with a Phase 2 FDA meeting. A Phase 2 patient study in atopic dermatitis is on target to complete enrolment in 4Q CY2019 with data in 1Q 2020. The Company has successfully completed a mechanism of action study for synthetic cannabidiol in skin disease, with positive data announced in June 2019 and is developing a pipeline of product candidates that leverages the antimicrobial properties of cannabidiol, with first products planned to enter the clinic in 2H CY2019.

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

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**Cautionary Note on Forward-Looking Statements**

Any statements in this press release about future expectations, plans and prospects for the Company, the Company's strategy, future operations, and other statements containing the words "anticipate," "believe," "estimate, "expect," "intend," "may," "plan," "predict," "project," "target, "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the Company's ability to successfully develop its product candidates and timely complete its planned clinical programs and the Company's ability to obtain marketing approvals for is product candidates. In addition, the forward-looking statements included in this press release represent the Company's views as of the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date hereof.

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# Botanix announces BTX 1503 data and progression to Phase 3

- **Botanix announces data from BTX 1503 Phase 2 randomised, double blind, vehicle-controlled acne patient study**
- **The 5% once a day (QD) BTX 1503 dose performed the best of all of the active doses tested on inflammatory and non-inflammatory lesions**
- **Study saw no serious adverse events and very low incidence of treatment-related adverse events**
- **Botanix is moving forward with its preparations for Phase 3 clinical program and planning an end-of-Phase 2 meeting with the US Food and Drug Administration**

**Philadelphia PA and Sydney Australia, 22 October 2019:** Clinical stage cannabinoid company Botanix Pharmaceuticals Limited (ASX:BOT, "Botanix" or "the Company") today announced topline data from its Phase 2 BTX 1503 study evaluating the safety and efficacy of BTX 1503 in patients with moderate to severe acne ("Phase 2 Study"). Based on the study results, Botanix is now moving forward with its preparations for Phase 3 clinical studies with the 5% BTX 1503 once a day dose and is planning an end-of-Phase 2 meeting with the US Food and Drug Administration (FDA).

**Study design and endpoints**

The Phase 2 study was a randomised, double blind, vehicle-controlled study that enrolled 368 patients with moderate to severe acne across 35 dermatology sites in Australia (n=118) and the USA (n=250). Patients were randomised into 5 separate treatment groups:

- **5% BTX 1503 QD**: 5% synthetic cannabidiol applied once daily (n=92);
- **5% BTX 1503 BID**: 5% synthetic cannabidiol applied twice daily (n=92);
- **2.5% BTX 1503 QD**: 2.5% synthetic cannabidiol applied once daily (n=92); or
- **Combined Vehicle**: vehicle applied once daily (n=46) or vehicle applied twice daily (n=46).

The treatment period was for 12 weeks in accordance with the FDA's guidance. In light of our established safety profile of synthetic cannabidiol, FDA allowed the enrolment of patients into the Phase 2 Study as young as 12 years of age. The median age of subjects was 18 years of age which is representative of the expected Phase 3 patient population.

The primary endpoint for the Phase 2 Study measured an absolute change from baseline in inflammatory lesions at week 12. Secondary endpoints included: percent change from baseline in inflammatory lesions; absolute and percent change from baseline in non-inflammatory lesions; and

the proportion of patients achieving at least clear or almost clear and a 2-grade improvement from baseline (IGA Success) on the 5-grade Investigator's Global Assessment (IGA) scale. Each endpoint was assessed at the end of the 12-week treatment period.

**Analysis of topline data**

For the primary endpoint, all dose groups of BTX 1503 reduced the number of inflammatory lesions from baseline with the highest efficacy obtained for the 5% BTX 1503 QD group (-11.8 lesions). This corresponds to an average percent reduction of 40.54%. The combined vehicle group result was -11.3 lesions or an average percent reduction of 40.15%.

For the non-inflammatory lesions, all dose groups of BTX 1503 reduced the number of non-inflammatory lesions from baseline with the highest efficacy observed again for the 5% BTX 1503 QD group. The number of non-inflammatory lesions with this dose of BTX 1503 was reduced by-17.3 compared to -8.3 lesions in patients in the combined vehicle group (p=0.006), or an average percent reduction of 34.99% compared to 19.08% (p=0.007). The primary endpoint of reduction in inflammatory lesions did not achieve statistical significance, but the secondary endpoint of reduction in non-inflammatory endpoints, was statistically significant.

Investigator's Global Assessment (IGA) of acne severity measure was also included as a secondary endpoint. This measure is not required by FDA to be included in Phase 2 acne studies, but provides guidance as to the proportion of patients who achieved clear or almost clear with at least a 2 grade reduction in the IGA scale measured from baseline to week 12. For IGA success, results were similar across all treatments groups with 15.2% of patients treated with 5% BTX 1503 QD achieving a successful improvement in IGA score compared to 14.1% of patients in the combined vehicle group. There was no significant difference between the active or combined vehicle groups.

A summary of primary and secondary endpoints for the Phase 2 Study is set out below in Table 1.

**Table 1 - Primary and Secondary Endpoints - Intent to Treat (ITT) Analysis – USA and Australia**

| | Combined Vehicle | 5% BTX 1503 QD | 5% BTX 1503 BID | 2.5% BTX 1503 QD |
|---|---|---|---|---|
| *Inflammatory* | -11.3 | -11.8 | -8.6 | -11.8 |
| *Non-Inflammatory* | -8.3 | -17.3* | -11.5 | -12.1 |
| *IGA Success* | 14.1% | 15.2% | 16.3% | 13.2% |

* statistically significant to combined vehicle (p= 0.006)

**Director of Dermatology, Clinical studies and Division Head of Dermatology at Henry Ford Health System in Michigan USA, Dr Linda Stein Gold commented:** "The safety and efficacy outcomes provide confidence that synthetic cannabidiol can represent an exciting new treatment option for acne patients.

"The effect on comedones (*inflammatory lesions*) is particularly pleasing, given BTX 1503's proposed mechanisms on the underlying causes of acne including inflammation and bacterial infection."

Consistent with previous clinical studies, BTX 1503 was very well-tolerated. Adverse events were low across all treatment groups with the most commonly reported adverse event being upper respiratory tract infection (2.2% - 6.5%). Adverse events commonly seen with the use of topical acne products, application site stinging/ burning, itching (pruritus), pain, dryness, peeling and erythema were either absent or only observed in one or two patients. There were no severe adverse events reported and no treatment related discontinuations in the 5% BTX 1503 QD group. The very low incidence of application site adverse events supports the positioning of the Permetrex™ delivery technology as a safe and cosmetically elegant new formulation option for patients.

The results were effected by an unusually high vehicle response that was limited to the USA clinical sites that participated in the Phase 2 Study. Because of the DEA licensing requirements around cannabidiol as a controlled substance, the supply chain for each of Australia and the USA was independent.

There were substantial differences in the vehicle responses recorded between Australian and USA clinical sites. Pooled analysis of all the Australian clinical sites showed statistically significant improvements in the absolute reduction in inflammatory (5% BTX 1503 BID group; -11.0 reduction) and non-inflammatory lesions (all BTX 1503 active groups; -16.0 to -17.4 reduction) were seen for the BTX 1503 active groups compared to the combined vehicle group, as set out in Table 2 below.

**Table 2 - Absolute reduction in lesions from baseline from baseline to week 12 - Intent to Treat (ITT) Analysis – Australia**

| | Combined Vehicle | 5% BTX 1503 QD | 5% BTX 1503 BID | 2.5% BTX 1503 QD |
|---|---|---|---|---|
| *Inflammatory* | -7.7 | -11.2 | -11.0* | -13.3 |
| *Non-Inflammatory* | -4.6 | -17.4** | -16.6** | -16.0** |

* statistically significant to vehicle ($p < 0.05$); ** statistically significant to vehicle ($p < 0.005$)

In the BTX 1503 QD group, efficacy outcomes in both Australia and the USA were in line with inflammatory lesion reduction (40.4% reduction in the USA versus a 40.8% reduction in Australia) and non-inflammatory lesion reduction (33.3% in the USA versus 38.1% in Australia). As outlined above, in contrast, vehicle responses in the USA were unexpectedly high, at almost twice the response for combined inflammatory lesion reduction (45.9% reduction in the USA versus a 26.4% reduction in

Australia) and more than four times the response for non-inflammatory lesion reduction (24.7% in the USA versus 5.5% in Australia).

For IGA, in Australia, 14.4% of combined active groups achieved a 2-grade reduction over the Phase 2 Study compared to only 7.4% of combined vehicle groups. In the USA, 15.2% of combined active groups achieving a 2-grade reduction over the Study compared to 16.9% of combined vehicle groups.

**Vince Ippolito, President and Executive Chairman of Botanix said:** "We are pleased with the overall efficacy outcomes, clean safety profile and highly significant Australian data."

"We are very thankful to all of the investigators and patients who helped Botanix rapidly complete this Phase 2 study."

Botanix is moving forward with its preparation for Phase 3 studies and reported cash of A$4.7m at the end of 2Q CY2019 and completed a capital raising of A$40m (before costs) in 3Q 2019. The Company is also expecting to receive approximately A$7m in R&D tax incentive in 4Q CY2019. Design of the Phase 3 program and timing will be reviewed by Botanix in consultation with the Company's key opinion leaders and clinical trial investigators.

**Australian investigator and Fellow of the Australasian College of Dermatologists, Dr Catherine Reid:** "Patients found Permetrex™ enabled BTX 1503 easy to apply, it was not sticky and didn't burn or sting."

"We are pleased to have contributed to this study and are excited by the potential of BTX 1503 and we look forward to participating in the Phase 3 study program."

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