Botanix Overview

November 2018
Key investment highlights

Botanix is a global dermatology company delivering synthetic cannabinoids topically for the treatment of skin diseases.

**Dermatology focused**
Advanced clinical programs targeting multi-billion dollar prescription markets for acne, atopic dermatitis and psoriasis.

**De-risked drug active**
Products use a synthetic form of cannabidiol with a proven safety profile (Epidiolex® recently approved by FDA) – increases the probability of success.

**Clinical stage**
Successful clinical data from acne and atopic dermatitis patient studies shows industry leading performance, after only 4 weeks of treatment.

**Novel approach**
Novel skin delivery technology, Permetrex™ - enhances delivery of cannabidiol into the skin compared to traditional formulation approaches.

**Experienced team**
Predominantly US based leadership team with 20+ FDA approvals between them and extensive dermatology industry experience.
Clinical programs with near term milestones

Phase 2 acne and atopic dermatitis programs supported by exciting development pipeline, with Permetrex™ collaborations to augment revenue and news flow

<table>
<thead>
<tr>
<th>Product candidate</th>
<th>Indication</th>
<th>Pre-clin</th>
<th>Ph 1</th>
<th>Ph 1b</th>
<th>Ph 2</th>
<th>Next milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthetic cannabidiol</td>
<td></td>
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<tr>
<td>BTX 1503</td>
<td>Moderate to severe acne</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase 2 clinical study underway</td>
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<tr>
<td>BTX 1204</td>
<td>Atopic dermatitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase 2 clinical study pending</td>
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<tr>
<td>BTX 1308</td>
<td>Psoriasis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase 1b patient study underway</td>
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<tr>
<td>BTX 1801</td>
<td>Antimicrobial</td>
<td></td>
<td></td>
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<td></td>
<td>Phase 1b patient study</td>
</tr>
</tbody>
</table>

Permetrex™ programs

<table>
<thead>
<tr>
<th>Internal/external</th>
<th>Various</th>
<th>Collaborations</th>
<th>Ongoing Service fees and potential licenses</th>
</tr>
</thead>
</table>

Botanix Overview – November 2018
**Experienced team**

Global team with proven experience in dermatology and a track record of securing drug approvals

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Background/Experience</th>
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</table>
| Mr Matthew Callahan   | Founder and Board Executive Director | Developed 3 products to date that have received FDA approval, 1 pending approval  
|                       |                                 | Ex-investment director of 2 venture capital firms in life sciences  
|                       |                                 | Serial entrepreneur with extensive produce development and launch experience  |
| Dr Michael Thurn      | Head Australian Operations      | Extensive start up life sciences experience across a range of technology platforms  
|                       |                                 | Previous MD of Spinifex Pharmaceutical, which sold to Novartis for A$700m  |
| Dr Stephane Levy      | Chief Medical Officer           | Ex-CMO of Almirall US operations and VP Sanofi and Novartis  
|                       |                                 | Broad commercial and clinical development experience  |
| Ms Jillian Chapas Reed| Sr Director Clinical Operations | 20 years clinical trial experience across dermatology and immunology  
|                       |                                 | Held senior director roles with CRO’s companies and hospital sponsors  |
| Dr Judith Plon        | VP Regulatory Affairs           | 30 years regulatory experience with multiple FDA approved dermatology products  
|                       |                                 | Ex-AVP Global Regulatory Affairs at Sanofi  |
| Dr Bill Bosch         | Executive Director              | 6 FDA approved products and inventor of the iCeutica SoluMatrix Technology  
|                       |                                 | Founder of NanoSystems and co-inventor of drug delivery technology NanoCrystal  |
Cannabinoid research interest is exploding

Cannabinoids are attracting strong interest as their efficacy and safety profiles are validated in clinical studies and the recent FDA approval of Epidiolex® (GW Pharma)

- One of ~113 cannabinoids identified in the cannabis sativa plant
- Accounts for up to 40% of natural plant extract
- Not psychoactive or addictive – does not convert to THC in vivo
- Broad mechanism of action - including immune modulation, anti-inflammatory effects and anti-microbial activity
- Substantial human safety database published

Cannabidiol (CBD)

Significant clinical trial interest

148 Studies found for: Cannabidiol

- 38 Epilepsy
- 15 Pain
- 6 Cancer
- 17 Multiple Sclerosis
- 9 Schizophrenia
- 63 Other

Only 1 trial in dermatology (Botanix)
Permetrex™ skin delivery technology

Proprietary Permetrex™ technology delivers high doses of drug into the layers of the skin without use of permeation enhancers, preservatives, or the use of irritating alcohol/petrolatum additives.

Unmodified Drug

Drug sits on the skin and is eventually wiped off

Epidermis

Dermis

With Permetrex™

Formulation technology drives drug into the skin

Note - oral administration of cannabidiol only delivers ~6% drug active into the blood stream

Botanix holds the exclusive rights to utilise Permetrex™ for all drugs that treat skin diseases
Permetrex™ technology enables superior delivery of cannabidiol

Permetrex™ delivers more much more cannabidiol (CBD) into the target layers of the skin, even though the CBD concentration of the BTX 1503 formulation is only ¼ to ½ the concentration of alternative formulations.

![Cannabidiol (CBD) percentage delivery (%)](chart.png)

1. Botanix Pharmaceuticals data on file
Development Pipeline
BTX 1503: acne
BTX 1204: atopic dermatitis
BTX 1308: psoriasis
BTX 1801: antimicrobial
BTX 1503: acne – mechanism of action for acne

BTX 1503 is a safe and well tolerated topical treatment that addresses all 3 key pathologies of acne

**CBD has been shown to…**

- **Have anti-inflammatory effects on human sebocytes and to suppress sebocyte proliferation**
- **Have potent anti-microbial activity against gram-positive bacteria**
- **Inhibit human keratinocyte proliferation**, through a non CB1/CB2 mechanism

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**BTX 1503: acne – outperforms leading acne products**

4 week study data shows a marked reduction in inflammatory lesions, greater than any other FDA approved topical acne product.

<table>
<thead>
<tr>
<th>Inflammatory lesions</th>
<th>Non-inflammatory lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 28: (47.0%)</td>
<td>Day 35: (45.0%)</td>
</tr>
<tr>
<td>Day 28: (5.4%)</td>
<td>Day 35: (22.5%)</td>
</tr>
</tbody>
</table>

* Day 35 results indicates the reduction effect persists 7 days after the last treatment

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**Comparison with other FDA approved products**

<table>
<thead>
<tr>
<th>Product</th>
<th>Owner</th>
<th>Lesion count reduction (%)</th>
<th>2016 annual revenue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epiduo®</td>
<td>Galderma</td>
<td>~42%</td>
<td>US$494m</td>
</tr>
<tr>
<td>Aczone®</td>
<td>Allergan</td>
<td>~38%</td>
<td>US$456m</td>
</tr>
<tr>
<td>BTX 1503</td>
<td>Botanix</td>
<td>~47%</td>
<td>-</td>
</tr>
</tbody>
</table>

- Combination of two drugs – benzoyl peroxide and adapalene
- Common side effects include redness, skin peeling, mild burning / stinging and dryness
- Few side effects
- Studies showed large placebo / vehicle effect – i.e. at 12 weeks Aczone reduced inflammatory lesions by 54% while vehicle achieved 48% reduction

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2. Lesion count reduction based on average inflammatory lesion reduction at 4 weeks.
3. Based on 2016 annual revenue in the US.
New data supporting anti-inflammatory effects of cannabidiol

Newly processed images from the Phase 1b acne patient study, demonstrate a clear anti-inflammatory effect over the 4 week treatment course.¹

Baseline (Day 1) vs. Visit 4 (4 weeks)

¹ Botanix Pharmaceuticals data on file
# BTX 1503: acne – Phase 2 study overview

12-week randomised, double-blind, vehicle controlled study to evaluate the safety and efficacy of BTX 1503 in patients with moderate to severe acne

<table>
<thead>
<tr>
<th>Design</th>
<th>Endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 5 dose groups: ~360 subjects</td>
<td>• Primary endpoints:</td>
</tr>
<tr>
<td>– High Dose twice a day: ~90 subjects</td>
<td>– absolute change from Baseline to Week 12 in inflammatory lesions</td>
</tr>
<tr>
<td>– High Dose once a day: ~90 subjects</td>
<td>– Secondary endpoints:</td>
</tr>
<tr>
<td>– Low Dose once a day: ~90 subjects</td>
<td>– absolute change from Baseline to Week 12 in non-inflammatory lesions</td>
</tr>
<tr>
<td>– Vehicle/Control: ~90 subjects</td>
<td>– % change from Baseline to Week 12 in inflammatory and non-inflammatory lesions</td>
</tr>
<tr>
<td>• ~28 US and Australian dermatology sites</td>
<td>– proportion of patients with at least 2 grade reduction from Baseline IGA at week 12</td>
</tr>
<tr>
<td>• Children (&gt; 12 years) and adults</td>
<td>• Safety</td>
</tr>
<tr>
<td>• Moderate to severe acne patients</td>
<td>– adverse events and local tolerability</td>
</tr>
<tr>
<td>• Treatment Period 12 weeks</td>
<td></td>
</tr>
</tbody>
</table>

Commenced July 2018 (~12 months duration) – fully funded
**BTX 1503: acne – next steps**

Botanix is pursuing a rapid clinical development strategy to accelerate product commercialisation and timing to first revenues

- Phase 2 clinical study started early 3Q CY2018 and will take approximately 12 months to complete
- Study designed to deliver data that allows licensing and other corporate opportunities

### BTX 1503 indicative clinical timeline (CY)

<table>
<thead>
<tr>
<th>Milestones</th>
<th>2Q 2018</th>
<th>3Q 2018</th>
<th>4Q 2018</th>
<th>1Q 2019</th>
<th>2Q 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>File IND for FDA regulated Phase 2 trial</td>
<td></td>
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</tr>
<tr>
<td>First patient enrolled in Phase 2 trial</td>
<td>⭐️</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>US and Australian sites all activated</td>
<td></td>
<td></td>
<td>⭐️</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient enrolment complete</td>
<td></td>
<td></td>
<td></td>
<td>⭐️</td>
<td></td>
</tr>
</tbody>
</table>

*study duration*
BTX 1204: atopic dermatitis – mechanism of action

Atopic dermatitis (and psoriasis) are both T-cell mediated inflammatory diseases of the skin.

1. During the “acute phase”, dendritic cells cause excessive Th2 and Th17 cell activation.
2. During the “chronic phase”, dendritic cells recruit Th1 cell populations that release Interferon-γ.

CBD inhibits Th17 responses (IL17), anti-inflammatory effect (in vitro model of IL-17A-induced mucosal inflammation using human cells)\(^1,2\).

CBD attenuates Th2 responses (IL4/IL13), anti-inflammatory effect (in mouse models of AD)\(^3,4\).

CBD inhibits Interferon-γ production which prevents deterioration of skin barrier function (in activated lymphocyte cultures)\(^1\) (mouse model of autoimmune myocarditis)\(^5\).

### Design

- ~36 subjects 18 years and older (24 active / 12 vehicle)
- 4 Australian dermatology sites
- BTX 1204 solution BID applied topically
- At least 1 lesion (25 to 200 cm²), on the trunk upper or lower extremities
- Signs of AD score ≥6 and ≤ 12
- Investigator’s Static Global Assessment (ISGA) of mild (2) or moderate (3)

### Endpoints

- Primary endpoints:
  - safety – AEs, labs, local tolerability and signs of atopic dermatitis
- Exploratory endpoints:
  - ISGA
  - target lesion size

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Study successfully completed end Q2 CY2018
BTX 1204: atopic dermatitis – Phase 1b study results

BTX 1204 was twice as effective as vehicle (with efficacy still increasing) and displayed a substantial improvement in the key signs of AD.

1. Botanix data on file. Results indicated substantial reduction in key signs of AD, providing confidence that unmet needs in AD can be addressed

2. Treatment success defined as a greater than, or equal to, a 4 point improvement in the signs and symptoms of AD

Key takeaways

Efficacy still increasing at 4 week timepoint

- Achieved treatment success similar to many competitive topical products at the end of their peak treatment period
- Data suggests longer treatment period for BTX 1204 possible for increased efficacy, potentially to exceed industry performance

Clear separation from vehicle (placebo)

- Despite being a small study, BTX 1204 shows superiority over vehicle, starting at early time points
- First vehicle-controlled study for Botanix, which also supports potential for other pipeline products

Excellent safety profile

- Safety and tolerability established with no burning, stinging or application site adverse events
- BTX 1204 profile allows extended dosing which remains a key challenge with most available therapies
BTX 1204: atopic dermatitis – Phase 2 study design

12 week randomised, double-blind, vehicle controlled study to evaluate the safety and efficacy of BTX 1204 in patients with moderate AD

**Design**
- 2 dose groups: ~200 subjects
  - BTX 1204: ~100 subjects
  - Vehicle/Control: ~100 subjects
- ~25 US and Australian dermatology sites
- Children (> 12 years) and adults
- Moderate AD patients
- Treatment period of 12 weeks

**Endpoints**
- Primary endpoint:
  - proportion of subjects with ISGA success defined as an ISGA score of “Clear” (0) or “Almost Clear” (1) with at least a 2 grade improvement from Baseline at Week 12
- Secondary endpoints:
  - change from Baseline in the Signs of AD
  - % body surface area (BSA) affected by AD
  - time to achieve IGA success
- Safety
  - adverse events and local tolerability

First patients in Q4 CY2018 – fully funded
BTX 1204: atopic dermatitis – next steps

BTX 1204 complements existing products in development, allowing faster development and transition times through key regulators (FDA and DEA)

- development program leverages existing data from BTX 1503 acne studies, lowering regulatory and safety hurdles
- common usage of DEA licensed dermatology clinics in US from BTX 1503 acne Phase 2 study, reduces cost and start-up timing

**BTX 1204 indicative clinical timeline (CY)**

- Phase 1b atopic dermatitis patient data
- Pre-IND meeting for FDA regulated Phase 2 trial
- Phase 2 first patients enrolled
- Patient enrolment complete

**Milestones**
- 3Q 2018
- 4Q 2018
- 1Q 2019
- 2Q 2019

**Study duration**
BTX 1308: psoriasis – overview

Development pipeline also includes other synthetic cannabidiol and Permetrex™ enabled products targeting key dermatology markets

BTX 1308: psoriasis

- Target market: ~7.5m Americans have psoriasis (note: most have plaque psoriasis)
- Current issues: biologic drugs are expensive and have serious side effect issues
- Unmet needs: safe and effective topical product for mild to moderate psoriasis

Phase 1b study commenced November CY2018 – fully funded

BTX 1308 leverages prior data from:

- BTX 1503 acne clinical program
- BTX 1204 AD clinical program
- Permetrex™ technology clinical studies

Minimal development pathway
BTX 1308: psoriasis – next steps

Botanix has commenced a Phase 1b study to test BTX 1308 against vehicle and a marketed psoriasis drug in patients

- Novel multi-drug comparison study format in the same patient, provides high quality data on BTX 1308 efficacy
- Biopsy data will elucidate MOA and (for the first time) confirm anti-inflammatory and immune modulation activity
- Study de-risks psoriasis indication, as well as provides scientific support to mechanisms for acne and atopic dermatitis

BTX 1801 indicative development timeline (CY)

Ethics approvals for Phase 1b study

Phase 1b patient study

Data announcement

**Milestones**

Bioskin GmbH psoriasis plaque test, including change in infiltrate thickness as measured by sonography
BTX 1801: antimicrobial – the problem of antimicrobial resistance

More than 700,000 people die as a result of antimicrobial resistance globally every year and estimates predict that by 2050, 10m lives p.a. will be at risk. However, no new classes of antibiotics have been approved in 33+ years.

Deaths attributable to antimicrobial resistance (AMR)¹

Number of antibiotic classes discovered or patented²

BTX 1801: antimicrobial – results summary

BTX 1801 data demonstrates potential for a new antimicrobial to treat unmet needs in skin infections together with additional benefits seen in prior Botanix studies (e.g. reduction in inflammation)

The study results demonstrate that the delivery of cannabidiol with Permetrex™ can reduce the concentration of the active drug required to achieve the highest levels of bacterial killing

Summary of data

BTX 1801 may have the following benefits

- Gram-positive bactericidal effect
- New mechanism of action
- Active against MRSA
- Topical application suited for skin infections
- Benign side effect profile based on previous clinical studies
- Ability to use long term
- Anti-inflammatory and skin barrier improvement properties
- Suitable for treatment of children (due to low toxicity)
- Prevent early use of IV antibiotics (significant side effects)
Key catalysts

Significant clinical and operational milestones across multiple programs expected over the next 12 months

**Indicative activities and milestones**

<table>
<thead>
<tr>
<th></th>
<th>3Q CY2018</th>
<th>4Q CY2018</th>
<th>1Q CY2019</th>
<th>2Q CY2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>BTX 1503 Acne Phase 2</td>
<td>First patient enrolled in Phase 2 study</td>
<td>Patient enrolment complete</td>
<td>Phase 2 multi-centre acne patient clinical study</td>
<td></td>
</tr>
<tr>
<td>BTX 1204 Atopic dermatitis Phase 2</td>
<td>Pre-IND Meeting for Phase 2 study</td>
<td>First Patients Phase 2 study</td>
<td>Phase 2 multi-centre AD patient clinical study</td>
<td></td>
</tr>
<tr>
<td>BX 1308 Psoriasis Phase 1b</td>
<td>Phase 1b study in psoriasis patients</td>
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<tr>
<td>BTX 1801 Antimicrobial</td>
<td>Identification of skin disease indication</td>
<td>Collaboration with University of Queensland</td>
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<tr>
<td>Permetrex™</td>
<td>Research collaborations and partnership discussions</td>
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**Milestones**

- BTX 1503 Acne Phase 2
- BTX 1204 Atopic dermatitis Phase 2
- BX 1308 Psoriasis Phase 1b
- BTX 1801 Antimicrobial
- Permetrex™
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Contact us

Matt Callahan
Botanix Pharmaceuticals
Founder and Board Executive Director
P: +1 215 767 4184
E: mcallahan@botanixpharma.com

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