

## ASX/Media Release

13 September 2018

### Botanix presents at European Dermatology Conference

#### Key highlights

- Botanix will be presenting at the 27<sup>th</sup> EADV Congress in Paris, France
- Botanix to provide an update on its Phase 2 products and other pipeline products
- Botanix will have the opportunity to engage with market leading global pharmaceutical organisations and researchers

**Philadelphia PA and Sydney Australia, 13<sup>th</sup> September 2018:** Medical dermatology company Botanix Pharmaceuticals Limited (ASX: BOT, “Botanix” or the “Company”) is pleased to release an updated company presentation for the 27<sup>th</sup> Congress of the European Academy of Dermatology and Venerology (EADV Congress), held in Paris, France.

The EADV Congress provide Botanix an opportunity to showcase the novel use of cannabidiol in dermatology. The Company will provide an update on the progress of its key Phase 2 products, BTX 1204 for atopic dermatitis and BTX 1503 for acne. The Company will also provide the latest development for its other pipeline products: BTX 1308 for psoriasis which is expected to enter Phase 1b in the near term; and the key driving factors and recent results for BTX 1801 antimicrobial.

The EADV Congress offers Botanix a chance to engage with potential prospective partners, global market leading pharmaceutical companies, and market leading researchers that have an interest in the treatment of dermatological conditions. These potential opportunities will be explored in parallel with the ongoing execution of the Company’s clinical programs.

#### About Botanix Pharmaceuticals

Botanix Pharmaceuticals Limited (ASX:BOT) is a clinical stage medical dermatology company based in Perth, Australia and Philadelphia, PA. 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 a widely studied natural compound. 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 patient treatment duration of clinical studies is generally completed within a 4 to 12 week timeframe.

The Company completed its first acne patient studies with BTX 1503 in January 2018 and has commenced a Phase 2 clinical trial in June 2018 with completion expected in mid-2019. The Phase 1b BTX 1204 atopic dermatitis patient study concluded in June 2018 and preparation is underway for a Phase 2 clinical trial. A further Phase 1b BTX 1308 psoriasis patient study is also scheduled to commence in 3Q CY2018.

For more information on Botanix, please visit [www.botanixpharma.com](http://www.botanixpharma.com)

**For more information, please contact:**

**General enquiries**

Matt Callahan  
Botanix Pharmaceuticals  
Founder & Executive Director  
+1 215 767 4184

[mcallahan@botanixpharma.com](mailto:mcallahan@botanixpharma.com)

**Investor enquiries**

Joel Seah  
Vesparum Capital

P: +61 3 8582 4800

[botanixpharma@vesparum.com](mailto:botanixpharma@vesparum.com)

**Media enquiries**

Julia Maguire  
The Capital Network

P: +61 419 815 386

[julia@thecapitalnetwork.com.au](mailto:julia@thecapitalnetwork.com.au)



# EADV presentation

September 2018

# Agenda

1. Executive summary
2. Cannabidiol – target drug with significant potential
3. Phase 2 products – BTX 1204: atopic dermatitis and BTX 1503: acne
4. Pipeline products – BTX 1308: psoriasis and BTX 1801: antimicrobial
5. Outlook



# 1. Executive summary



# Key investment highlights

Botanix is an emerging global **dermatology company** with advanced clinical programs and an exciting pipeline



**Dermatology  
Focused**

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



**De-risked drug  
active**

Products use a synthetic form of an FDA approved natural product - **greatly enhances 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 system - **Permetrex™** - **greatly improves delivery of drug to the skin** compared to traditional 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

Rapidly advancing acne and atopic dermatitis programs, with deep pipeline in development and Permetrex™ collaborations to augment revenue and news flow

Product candidate	Indication	Pre-Clin	Ph 1	Ph 1b	Ph 2	Next milestones
Synthetic form of natural product extract – cannabidiol	BTX 1503	Moderate to Severe Acne				Phase 2 clinical trial underway Data available mid-2019
	BTX 1204	Atopic Dermatitis				Phase 2 clinical trial pending IND 3Q CY2018
	BTX 1308	Psoriasis				Phase 1b patient study pending Commence late 3Q CY2018
	BTX 1801	Antimicrobial				Phase 1b patient study Following pre-clin work 4Q CY2018
Permetrex™ programs	Internal/ External	Various	Collaborations			Ongoing

## 2. Cannabidiol

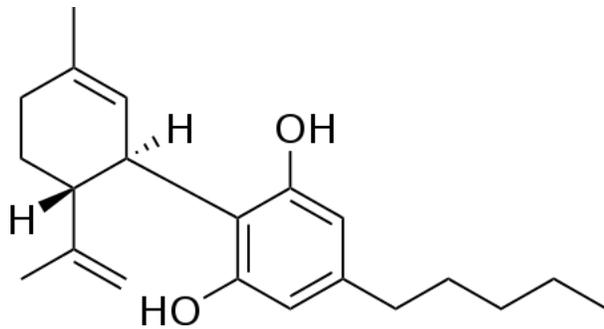
Target drug with significant potential



# Cannabinoids are emerging as a novel class

Cannabinoids are attracting strong interest as their efficacy and safety profiles are validated in clinical studies

## Cannabidiol (CBD)



- One of ~ 113 cannabinoids identified in the *cannabis sativa* plant
- Accounts for up to 40% of natural plant extract
- Not psychoactive, nor addictive – does not convert to THC *in vivo*
- Broad MOA including CB1/2, immune response and inflammatory pathways

## Significant clinical trial interest

The image is a screenshot of the ClinicalTrials.gov website. The header shows the NIH logo and the text "U.S. National Library of Medicine". The main title is "ClinicalTrials.gov". There are links for "Find Studies" and "About S". Below the header, there is a search bar and a "Search Results" link. The search results show "138 Studies found for: cannabidiol". The number "138" is circled in purple. There are also links for "Modify Search" and "Start Over". At the bottom, there are buttons for "By Topic", "On Map", and "Search Details".

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

**Only 1 trial in dermatology (Botanix)**

# Recent approval increasing focus on cannabidiol potential

First FDA approval for cannabidiol use in a form of paediatric epilepsy (Epidiolex® - GW Pharma) in Q2 2018 – helps establish safety profile of molecule and desirability of synthetic form (purity)

## First FDA approved cannabidiol product

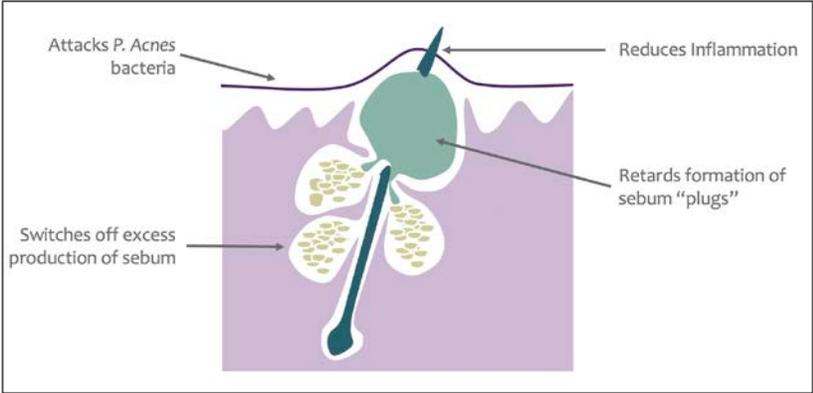
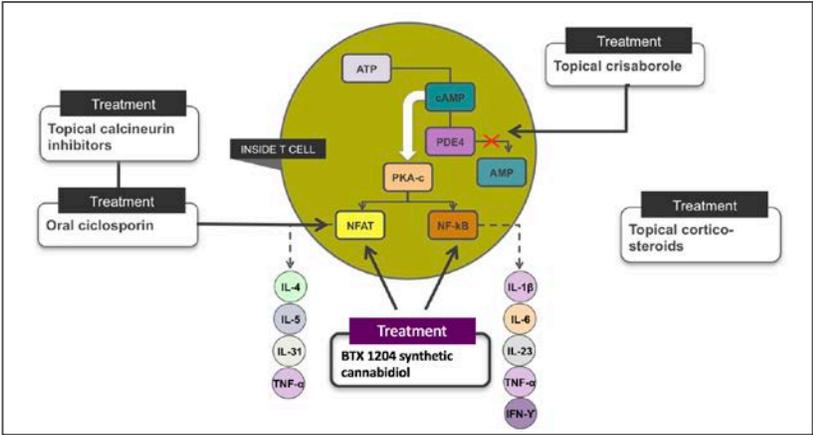


### Epidiolex® is GW's lead cannabidiol product

- Designed to treat two rare forms of childhood epilepsy
- First cannabidiol product to achieve FDA approval
- Analysts expect Epidiolex® to generate ~\$400-700M in annual sales
- GW Pharma's market cap ~ \$4B

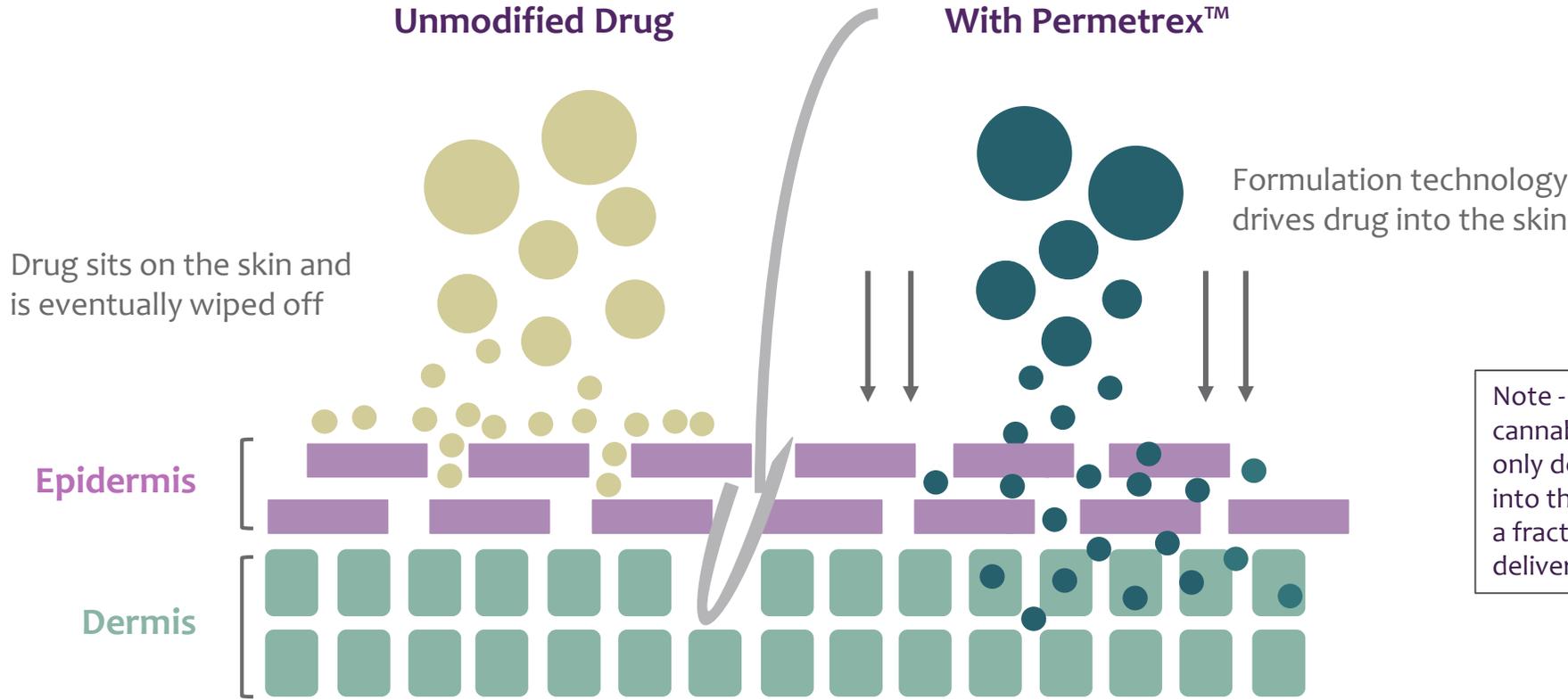


## Botanix is validating MOA in skin diseases



# Permetrex™ skin delivery technology

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



Note - oral administration of cannabidiol (oils and capsules) only delivers ~6% drug active into the blood stream and only a fraction of *that* amount is delivered into the skin

Botanix holds the **exclusive rights** to utilise Permetrex™ for all drugs that treat skin diseases

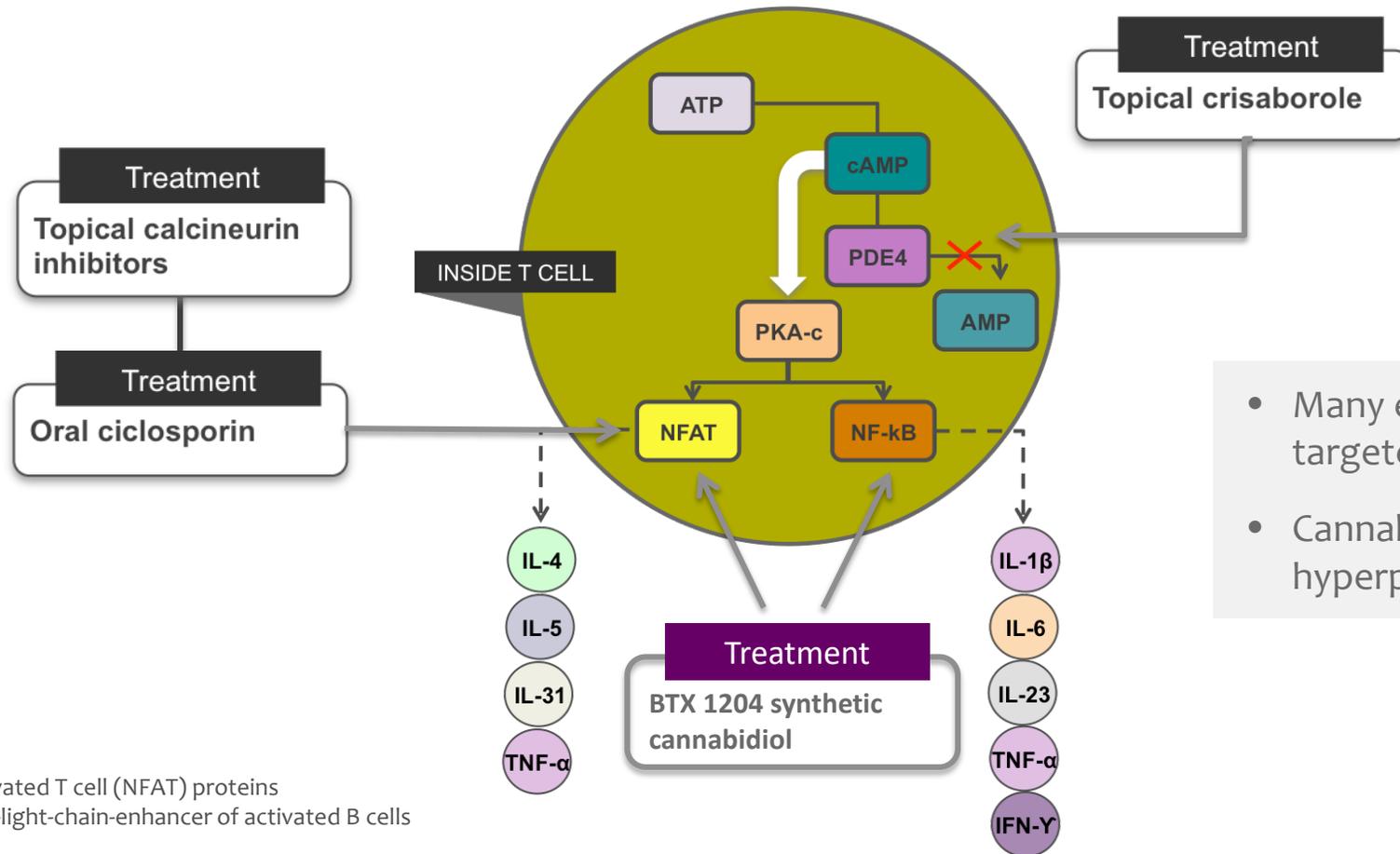
### 3. Phase 2 products

BTX 1204: atopic dermatitis

BTX 1503: acne

# BTX 1204: atopic dermatitis – cannabidiol mechanism of action (MOA)

Atopic dermatitis (AD) and psoriasis are both T-cell mediated inflammatory diseases of the skin. Cannabidiol has been shown to inhibit immune responses via T-helper cell populations (including Th17, Th1 and also Th2) and to a decrease of IFN- $\gamma$  amongst others

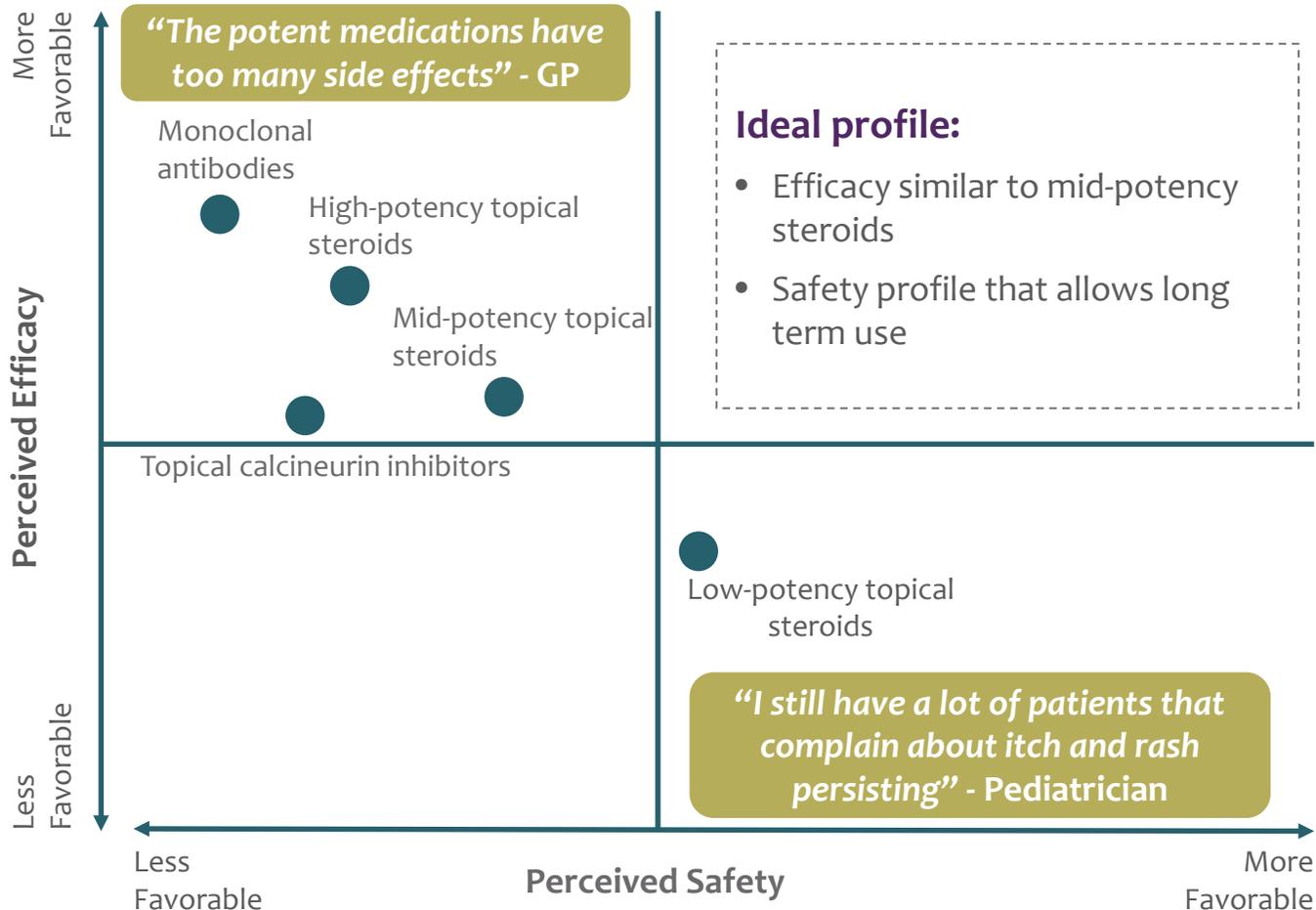


- Many existing AD treatments are targeted upstream of NFAT and NF-kB
- Cannabidiol also inhibits keratinocyte hyperproliferation

NFAT = Nuclear factor of activated T cell (NFAT) proteins  
 NF-kB = Nuclear factor kappa-light-chain-enhancer of activated B cells

# BTX 1204: atopic dermatitis – positioning and opportunity

Botanix is targeting efficacy improvements with an improved safety profile, with new benefits in inflammation and itch reduction



**BTX 1204 has shown potential to meet a number of unmet needs:**

- ✓ Non-steroidal treatment option
- ✓ Potential impact of itch
- ✓ Improved safety profile and elimination of severe adverse side effects
- ✓ Ability to use long term (>12 weeks)
- ✓ Address underlying inflammation
- ✓ Correct skin barrier dysfunction
- ✓ Greater cost effectiveness

# BTX 1204: atopic dermatitis – Phase 1b study design

Successful 4-week treatment period, double-blind, vehicle controlled patient study concluded in late May 2018

## 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 cm<sup>2</sup>), on the trunk upper or lower extremities
- Signs of AD score  $\geq 6$  and  $\leq 12$
- 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

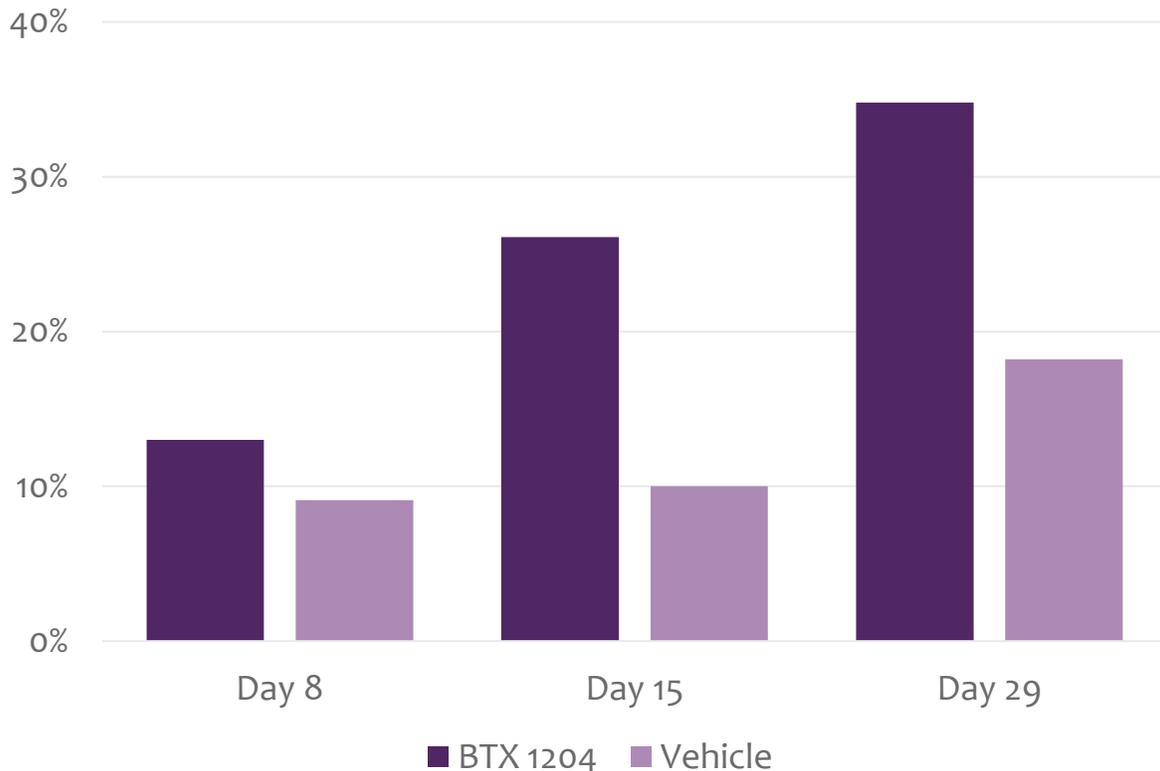


Study successfully completed in Q2 CY2018

# BTX 1204: atopic dermatitis – Phase 1b study results

After only 4 weeks of treatment, study data indicated BTX 1204 was twice as effective over the vehicle (with efficacy still increasing) and substantial improvement in the key signs of AD observed

Treatment success (%)<sup>1</sup>



## 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

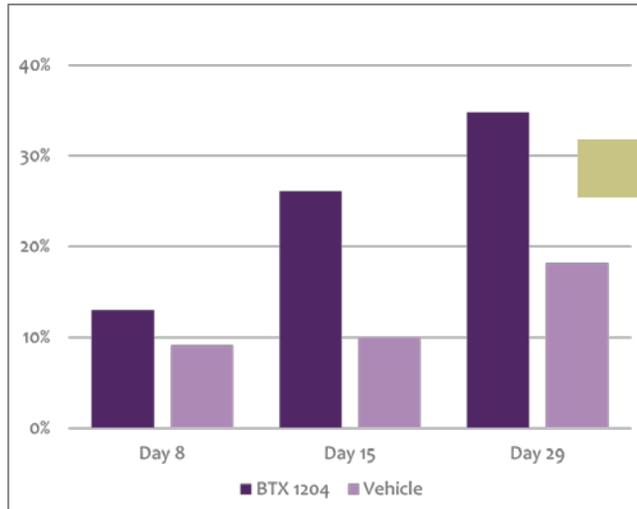
Notes: Results indicated substantial reduction in key signs of AD, providing confidence that unmet needs in AD can be addressed - more detailed results on slide 33

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

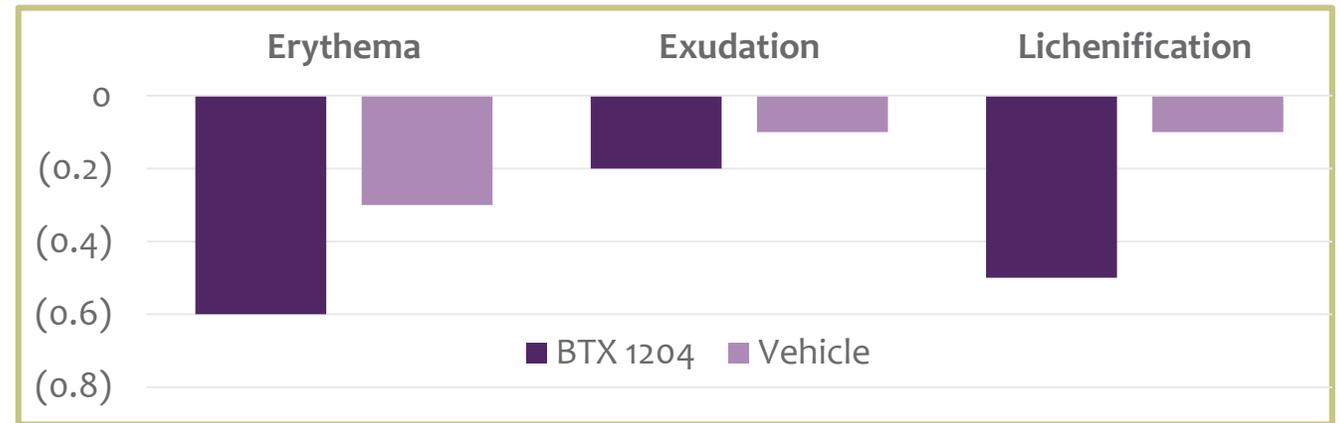
# BTX 1204: atopic dermatitis – Phase 1b study results

Substantial reduction in key signs of AD, provides confidence that unmet needs in AD (itch / inflammation) can be addressed

Treatment Success<sup>1</sup>



Substantial reduction in the key signs of AD<sup>2</sup>



**Erythema:** inflammation, common clinical manifestation of several skin diseases, including acne and rosacea

**Exudation:** ooze from lesion, associated with inflammation / infection

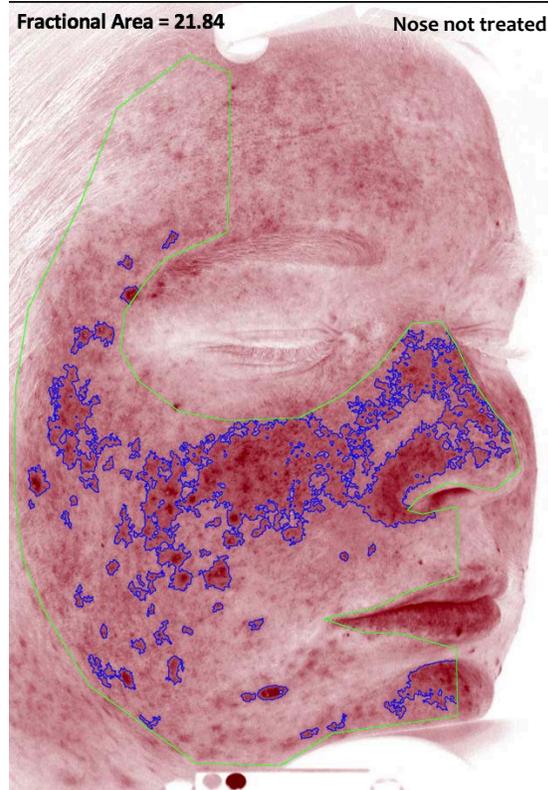
**Lichenification:** thickening of the skin in response to itching

1. Treatment success defined as a greater than, or equal to, a 4 point improvement in the signs and symptoms of AD  
2. Based on improvement in average score ratings from baseline to Day 29

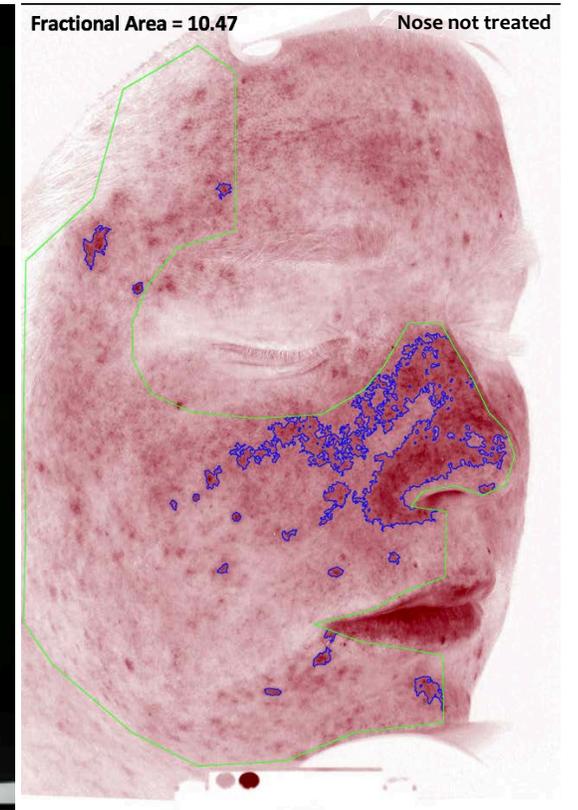
# New data supporting anti-inflammatory effects of cannabidiol

Newly processed images from the Phase 1b acne patient study, demonstrate deep penetration of cannabidiol into the skin and a clear anti-inflammatory effect and improvement over the treatment course (4 weeks)

Baseline (0 days)



Visit 4 (28 days)



# 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
- Adolescents and Adults
- Moderate AD patients

## 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
  - Eczema Area Severity Index (EASI) Score
  - % body surface area (BSA) affected by AD
  - time to achieve IGA success
- Safety
  - adverse events and local tolerability

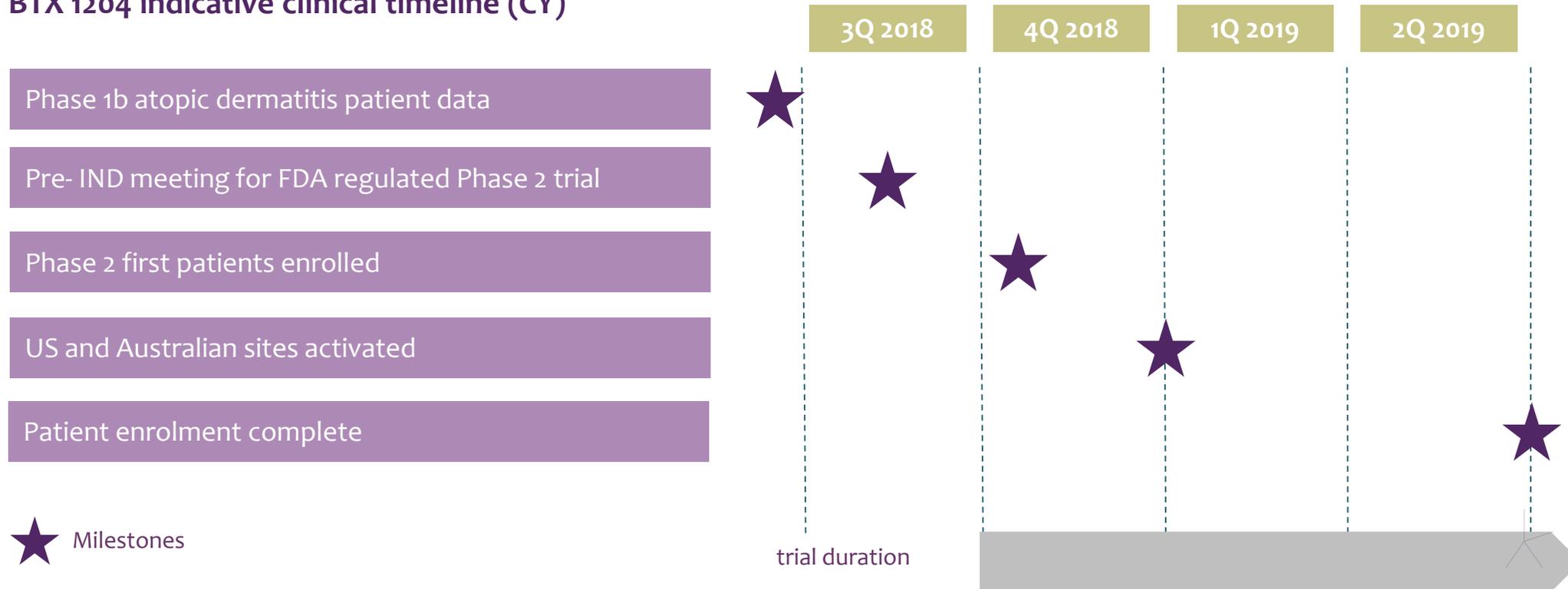
First patients in Q4 CY2018 – fully funded

# BTX 1204: atopic dermatitis – next steps

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

- Development program leverages existing data from BTX 1503 acne studies, so regulatory and safety risk is lowered
- Common usage of DEA licensed dermatology clinics in USA from BTX 1503 acne Phase 2 trial reduces cost and start-up timing

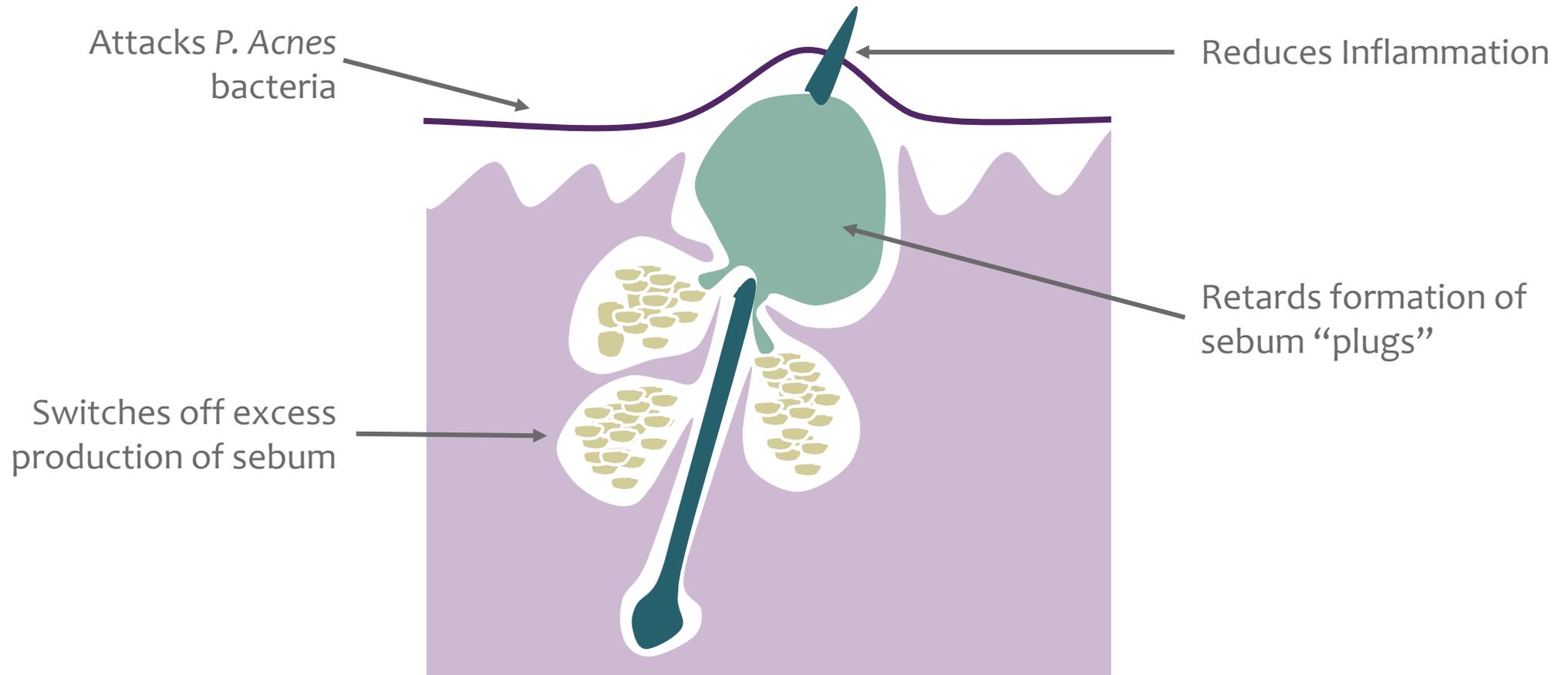
## BTX 1204 indicative clinical timeline (CY)



★ Milestones

# BTX 1503: acne – MOA for acne

BTX 1503 potentially address all 3 key pathologies of acne with a very safe side effect profile



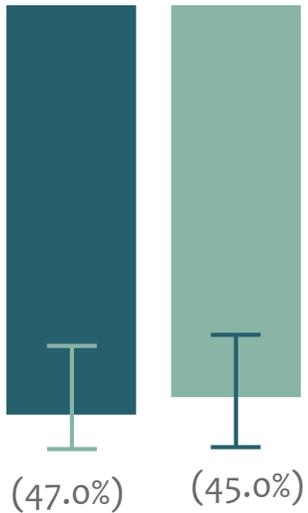
Source: Cannabidiol exerts sebostatic and anti inflammatory effects on human sebocytes (2014). *The Journal of Clinical Investigation*

# BTX 1503: acne – outperforms leading acne products

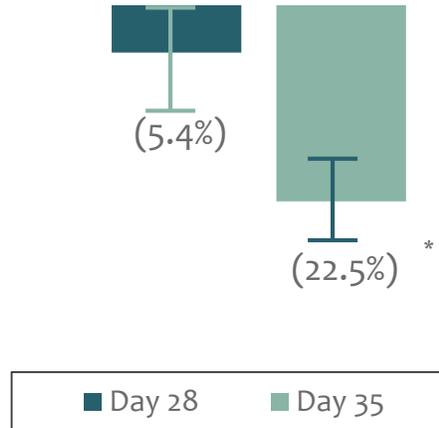
Study data resulted in a reduction in inflammatory lesions greater than any other FDA approved topical acne product after only 4 weeks

## Lesion count reduction (%)

### Inflammatory lesions



### Non-inflammatory lesions



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

## Comparison of other FDA approved products

Product	Owner	Lesion count reduction (%) <sup>1</sup>	2016 annual revenue <sup>2</sup>
 Epiduo®	Galderma	~42%	US\$494m
 Aczone®	Allergan	~38%	US\$456m
<b>BTX 1503</b>	<b>Botanix</b>	<b>~47%</b>	-

- 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

1. Lesion count reduction based on average inflammatory lesion reduction at 4 weeks  
 2. Based on 2016 annual revenue in the US  
 3. Patient demographics: 21 year old female

# BTX 1503: acne – Phase 2 study overview

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

## Design

- 5 dose groups: ~360 subjects
  - High Dose twice a day: ~90 subjects
  - High Dose once a day: ~90 subjects
  - Low Dose once a day: ~90 subjects
  - Vehicle/Control: ~90 subjects
- ~28 US and Australian dermatology sites
- Moderate to severe acne patients

## Endpoints

- Primary endpoints:
  - absolute change from Baseline to Week 12 in inflammatory lesions
- Secondary endpoints:
  - absolute change from Baseline to Week 12 in non-inflammatory lesions
  - % change from Baseline to Week 12 in inflammatory and non-inflammatory lesions
  - proportion of patients with at least 2 grade reduction from Baseline IGA at week 12
- Safety
  - adverse events and local tolerability

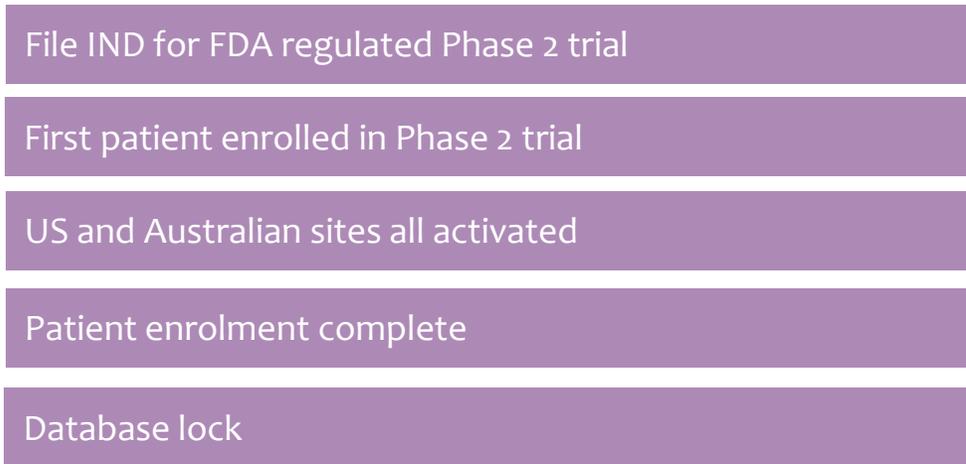
Commenced July 2018 (~12 months duration) – fully funded

# BTX 1503: acne – next steps

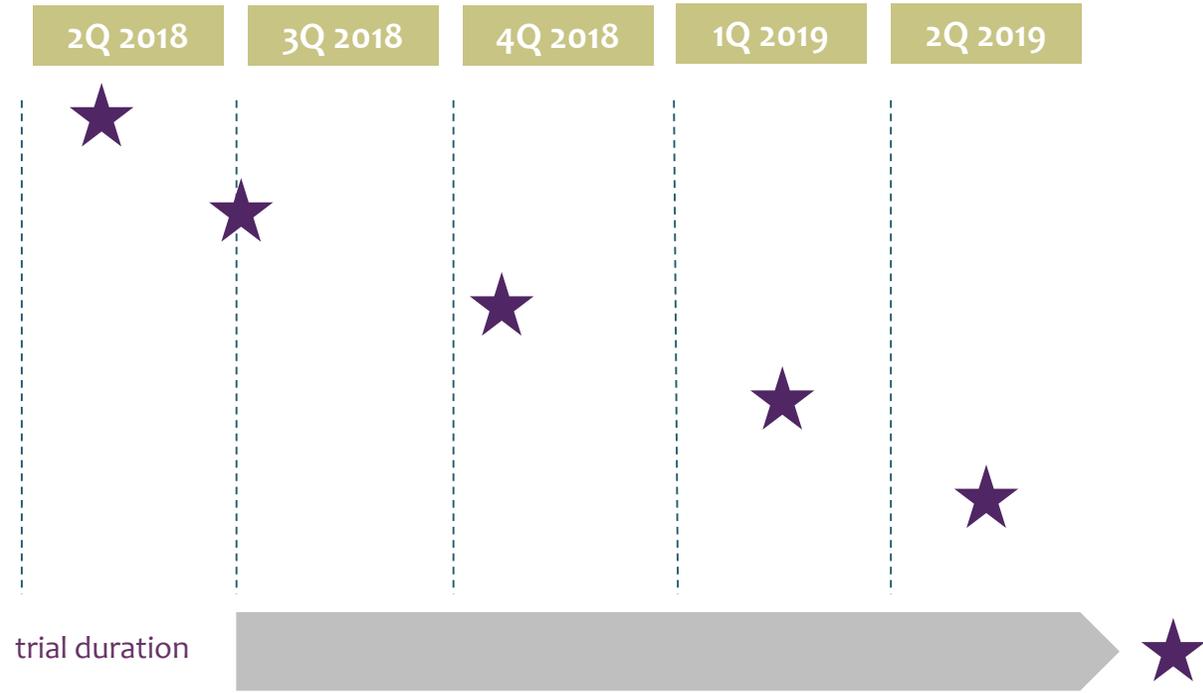
Botanix is pursuing a rapid clinical development strategy to accelerate product commercialisation and timing to first revenues

- Phase 2 clinical trial started mid-CY2018 and will take approximately 12 months to complete
- Trial designed to deliver data that allows licensing and other corporate opportunities

## BTX 1503 indicative clinical timeline (CY)



★ Milestones



## 4. Pipeline products

BTX 1308: psoriasis

BTX 1801: antimicrobial

# 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)
- **Market size:** estimated annual costs of injectable biologic treatments in the US is ~US\$20bn p.a.
- **Current issues:** biologic drugs are expensive and have serious side effect issues
- **Unmet needs:** safe and effective topical product for mild to moderate psoriasis



*Psoriasis*

**Botanix is planning a Phase 1b study to commence in late 3Q CY2018**



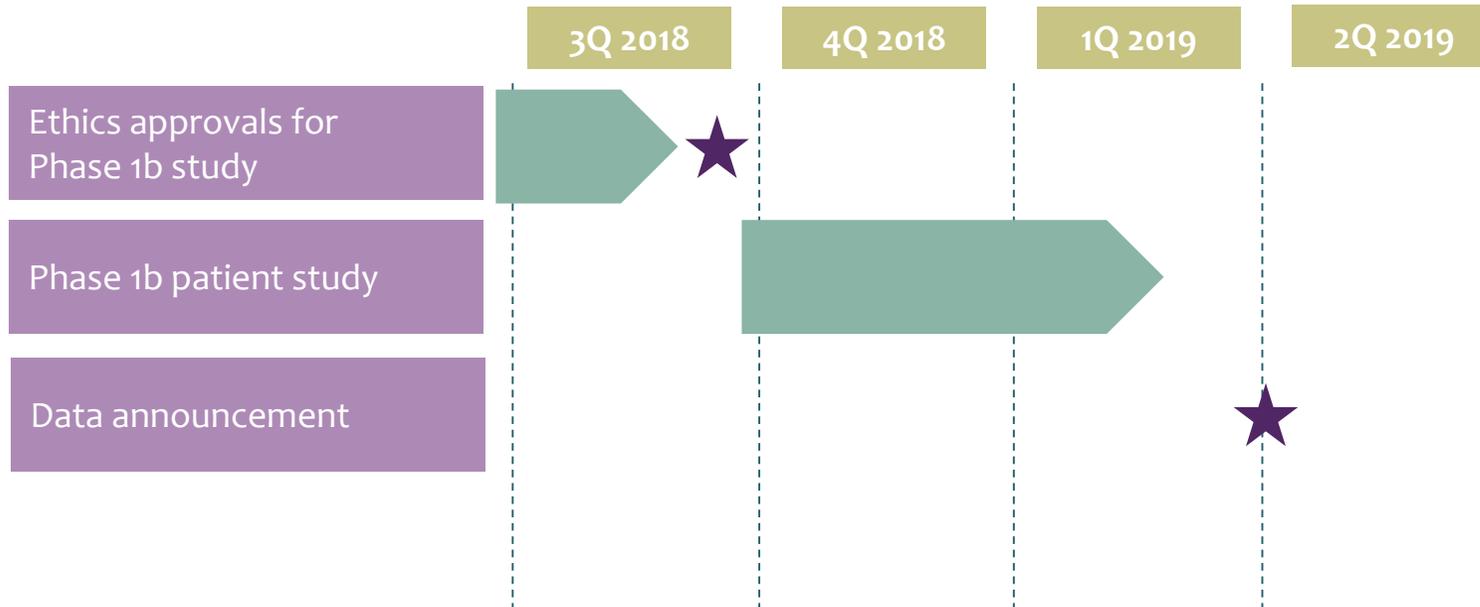
## BTX 1308 leverages prior data from:

- ✓ BTX 1503 acne clinical program
  - ✓ BTX 1204 AD clinical program
  - ✓ Permetrex™ technology clinical studies
- ➔ No need to repeat early studies

# BTX 1308: psoriasis – next steps

Botanix is preparing for a Phase 1b study to test BTX 1308 against placebo and another psoriasis drug in patients starting in late Q3 CY2018

## BTX 1801 indicative development timeline (CY)



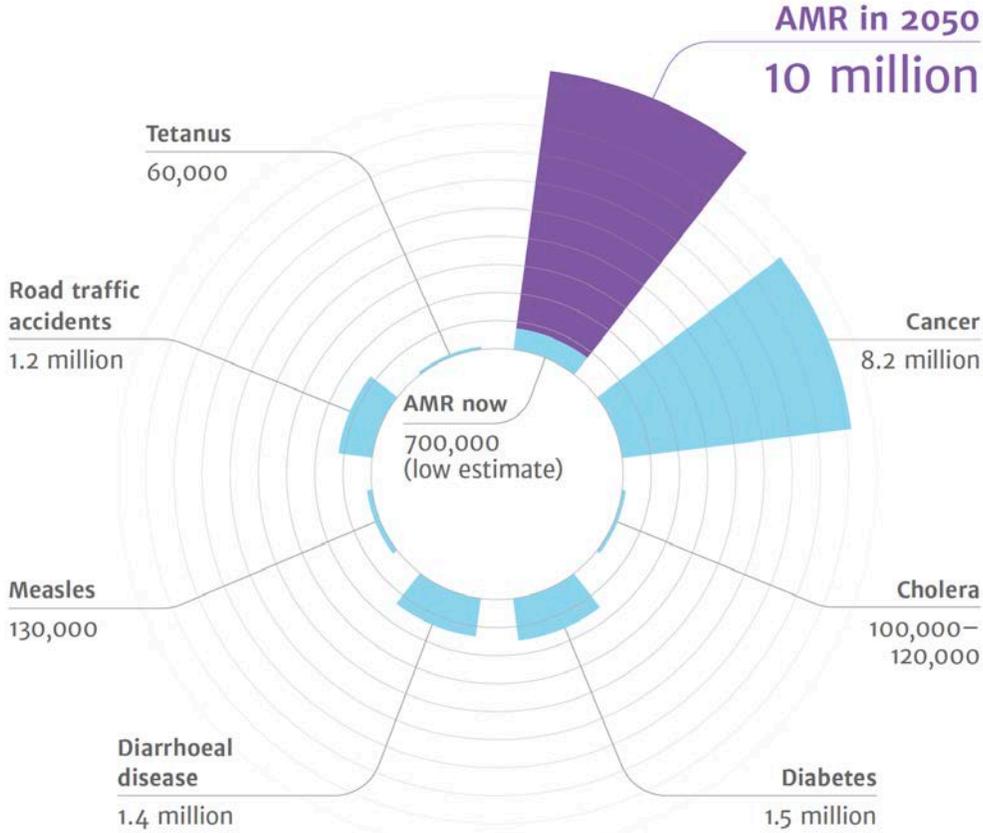
- Development program leverages existing data from BTX 1503 and BTX 1204 programs – no need to repeat early clinical studies and low regulatory risks
- Clinical studies are rapid and provide comparative data to demonstrate efficacy and safety benefits

★ Milestones

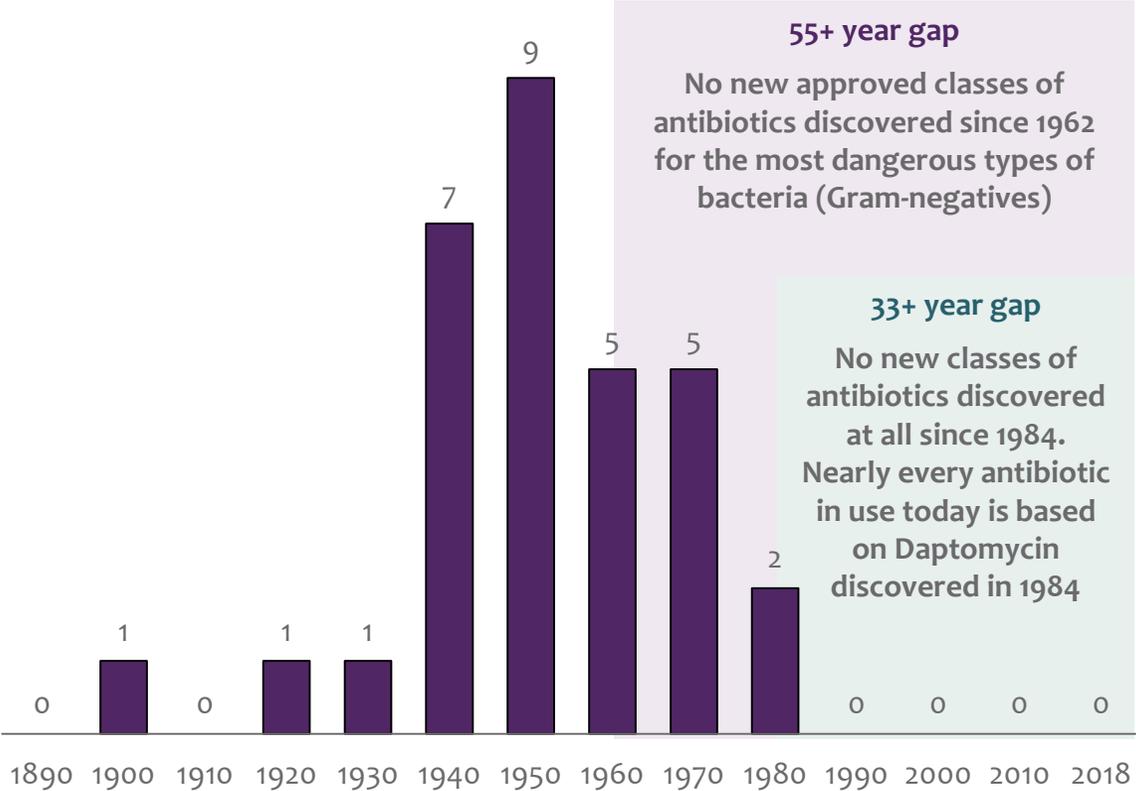
# BTX 1801: antimicrobial – the problem of antimicrobial resistance

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)<sup>1</sup>



Number of antibiotic classes discovered or patented<sup>2</sup>



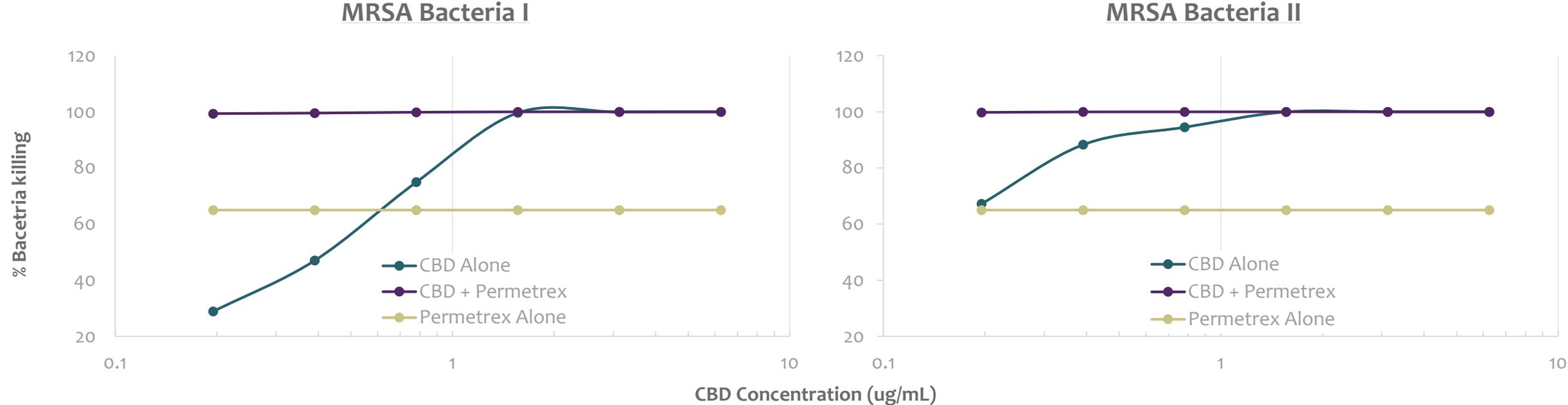
1. Tackling Drug Resistant Infections Globally Final Report and Recommendations (2016), The Review on Antimicrobial Resistance  
 2. Pew Charitable Trusts; Deak et al. Progress in the Fight Against Multidrug Resistant Bacteria?; A Review of FDA Approved Antibiotics 2010-2015. 31 May 2016. DOI: 10.7326/M16-0291



# BTX 1801: antimicrobial – Permetrex™ formulation of cannabidiol

In two of the common antibiotic resistant bacteria strains, Permetrex™ significantly improves the killing power of cannabidiol, to achieve close to 100% bacteria killing effect (at low concentrations)

### Summary of data

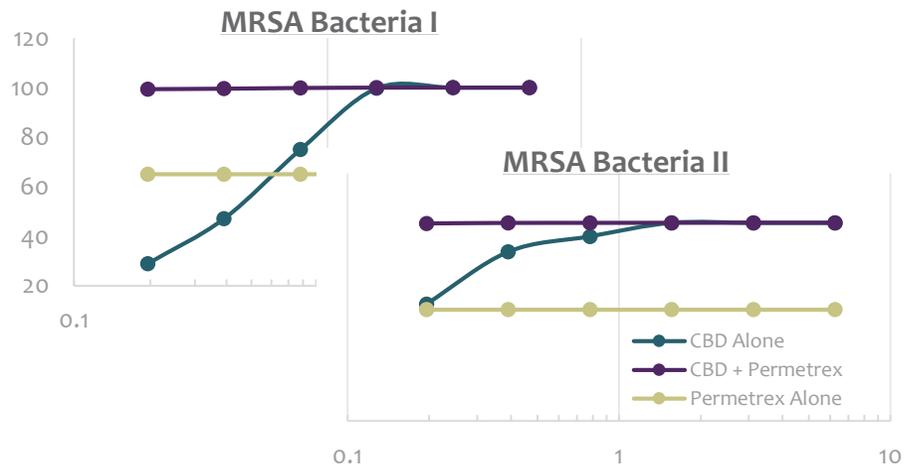


Combination of Permetrex™ and cannabidiol achieved high levels of bacteria killing (at low concentrations) by **allowing the active drug to permeate the biofilm / protective layer** often secreted by bacteria and **killing 99%+ bacteria to substantially reduce potential for resistance development**

# 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)

## Summary of data



***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***

## 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)



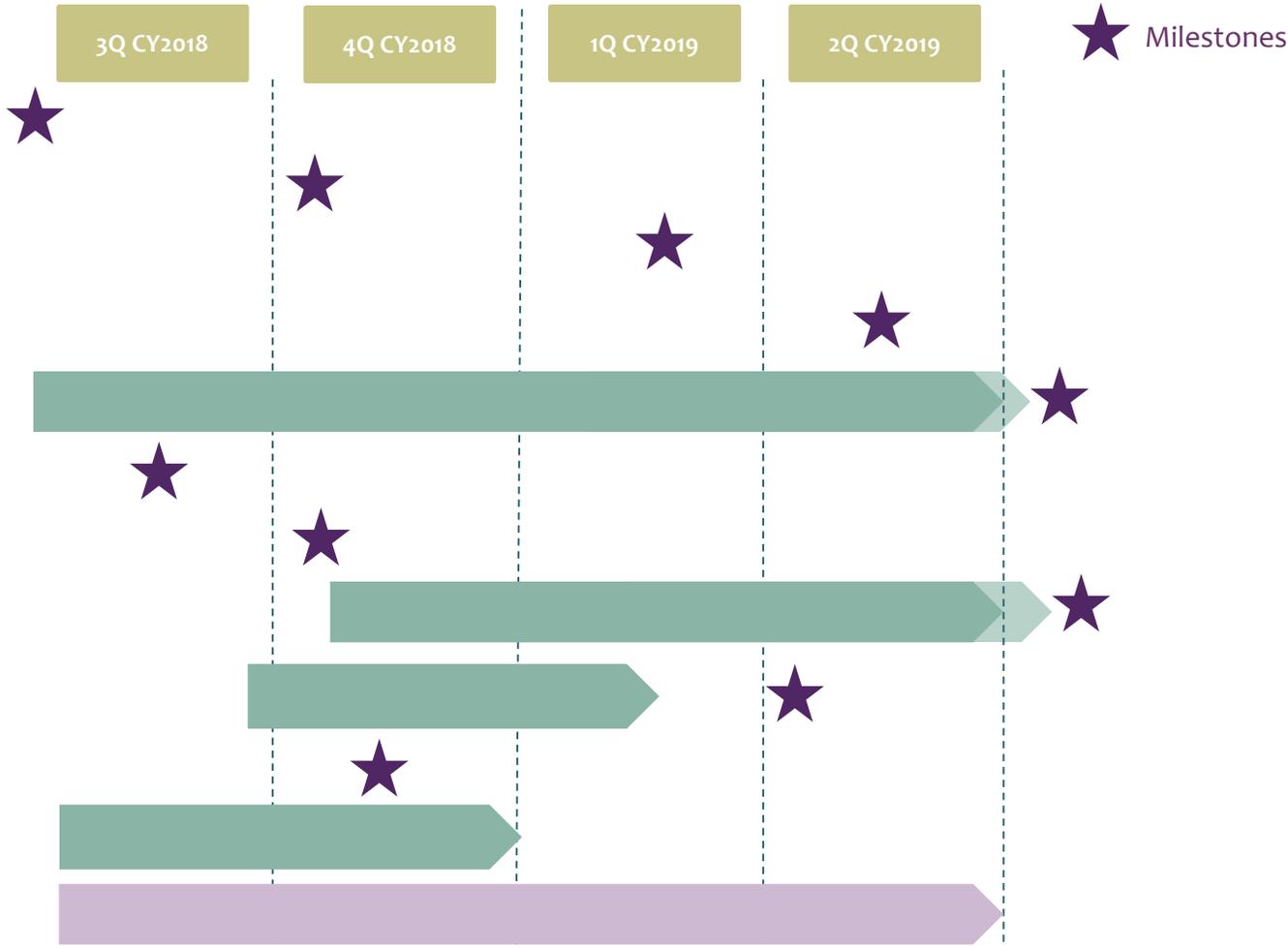
## 5. Outlook

# Key catalysts

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

## Indicative activities and milestones

Phase 2 BTX 1503 Acne	First patient enrolled in Phase 2 trial
	All US and Australian sites active
	Patient Enrolment Complete
	Database Lock
	Phase 2 multi-centre acne patient clinical trial
Phase 2 BTX 1204 Atopic Dermatitis	Pre-IND Meeting for Phase 2 Trial
	First Patients Phase 2 trial
	Phase 2 multi-centre AD patient clinical trial
BTX 1308 Psoriasis	Phase 1b study in psoriasis patients
BTX 1801 Antimicrobial	Identification of skin disease indication
	Collaboration with University of Queensland
Permetrex™	Research collaborations and partnership discussions



# Disclaimer

This presentation prepared by Botanix Pharmaceuticals Limited ("Company") does not constitute, or form part of, an offer to sell or the solicitation of an offer to subscribe for or buy any securities, nor the solicitation of any vote or approval in any jurisdiction, nor shall there be any sale, issue or transfer of the securities referred to in this presentation in any jurisdiction in contravention of applicable law. Persons needing advice should consult their stockbroker, bank manager, solicitor, accountant or other independent financial advisor.

This document is confidential and has been made available in confidence. It may not be reproduced, disclosed to third parties or made public in any way or used for any purpose other than in connection with the proposed investment opportunity without the express written permission of the Company.

This presentation should not be relied upon as a representation of any matter that an advisor or potential investor should consider in evaluating the Company. The Company and its related bodies corporate or any of its directors, agents, officers or employees do not make any representation or warranty, express or implied, as to the accuracy or completeness of any information, statements or representations contained in this presentation, and they do not accept any liability whatsoever (including in negligence) for any information, representation or statement made in or omitted from this presentation.

This document contains certain forward looking statements which involve known and unknown risks, delays and uncertainties not under the Company's control which may cause actual results, performance or achievements of the Company to be materially different from the results, performance or expectations implied by these forward looking statements. The Company makes no representation or warranty, express or implied, as to or endorsement of the accuracy or completeness of any information, statements or representations contained in this presentation with respect to the Company.

It is acknowledged that the Company will not undertake any obligation to release publicly any revisions or updates to these forward-looking statements to reflect events, circumstances or unanticipated events occurring after the date of this presentation except as required by law or by any appropriate regulatory authority.

# Contact us

**Matt Callahan**

Botanix Pharmaceuticals

Executive Director

P: +1 215 767 4184

E: [mcallahan@botanixpharma.com](mailto:mcallahan@botanixpharma.com)

**Visit us**

[www.botanixpharma.com](http://www.botanixpharma.com)

**Follow us on social media**



Botanix Pharmaceuticals Limited (ASX:BOT)

**botanix**  
PHARMACEUTICALS  
RESTORING HEALTHY SKIN