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ASX/Media Release

15 November 2018

Updated investor presentation

Philadelphia PA and Sydney Australia, 15 November 2018: Medical dermatology company Botanix Pharmaceuticals ("Botanix" or "the Company") is pleased to release an updated investor presentation. The presentation will be used to update shareholders, investors and strategic partners across Australia and North America in the coming weeks. The presentation outlines the progress across the Company's acne, atopic dermatitis, psoriasis and antimicrobial programs.

For more information, please contact:

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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. The Phase 1b BTX 1308 psoriasis patient study has commenced in September 2018.

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



Botanix Overview

November 2018

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RESTORING HEALTHY SKIN

Key investment highlights

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

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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

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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

Product candidate		Indication	Pre-clin	Ph 1	Ph 1b	Ph 2	Next milestones
Synthetic cannabidiol	BTX 1503	Moderate to severe acne	→	→	→	→	**Phase 2 clinical study underway**
	BTX 1204	Atopic dermatitis	→	→	→	→	**Phase 2 clinical study pending**
	BTX 1308	Psoriasis	→	→	→		**Phase 1b patient study underway**
	BTX 1801	Antimicrobial	→				**Phase 1b patient study**
Permetrex™ programs	**Internal/ external**	Various		Collaborations →	→	→	**Ongoing** Service fees and potential licenses

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Experienced team

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

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Mr Matthew Callahan — *Corporate + IP*

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 — *Operations + Regulatory*

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 — *Medical + Clinical*

Chief Medical Officer

- Ex-CMO of Almirall US operations and VP Sanofi and Novartis
- Broad commercial and clinical development experience



Ms Jillian Chapas Reed — *Clinical*

Snr 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 — *Regulatory*

VP Regulatory Affairs

- 30 years regulatory experience with multiple FDA approved dermatology products
- Ex-AVP Global Regulatory Affairs at Sanofi



Dr Bill Bosch — *Manufacturing + IP*

Executive Director

- **6 FDA approved products** and inventor of the iCeutica SoluMatrix Technology
- Founder of NanoSystems and co-inventor of drug delivery technology NanoCrystal

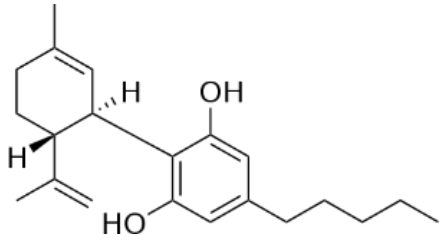
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Cannabinoid research interest is exploding

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)

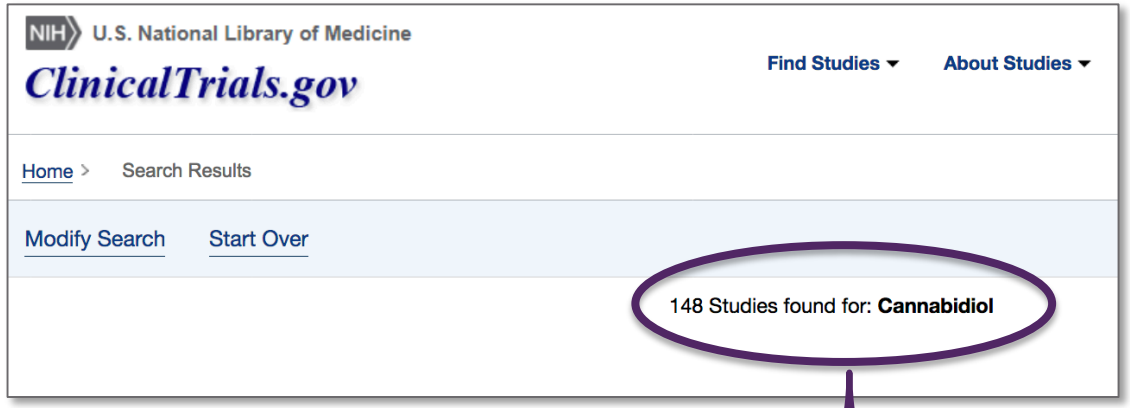
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Cannabidiol (CBD)



- 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**

Significant clinical trial interest



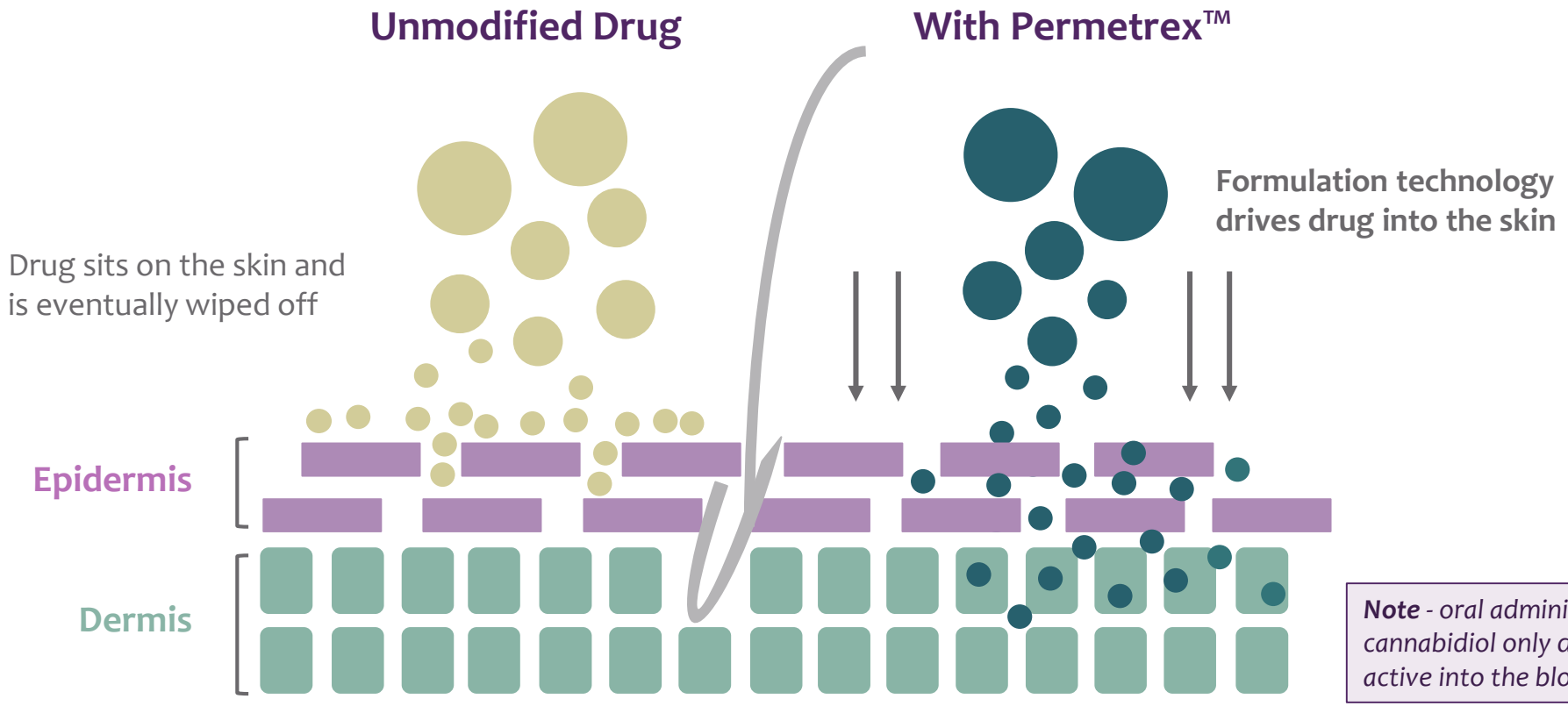
- 38 Epilepsy
- 15 Pain
- 6 Cancer
- 17 Multiple Sclerosis
- 9 Schizophrenia
- 63 Other

Only 1 trial in dermatology (Botanix)

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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



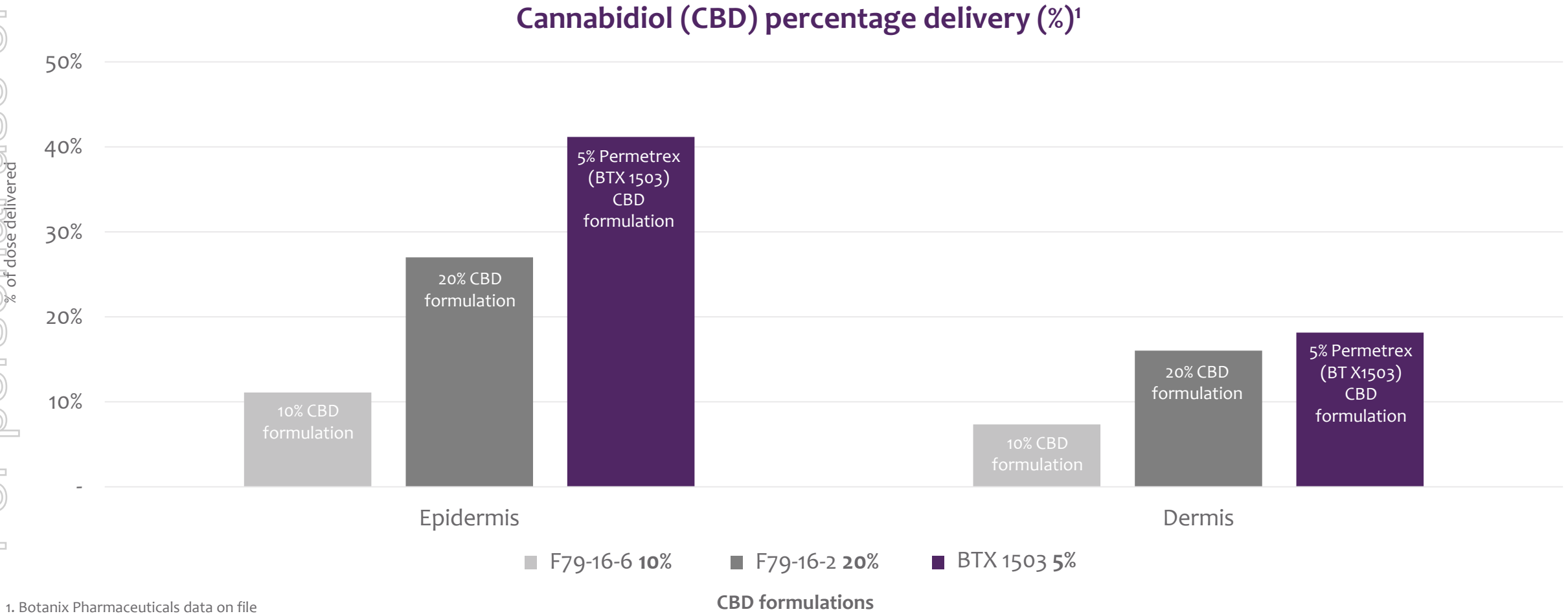
***Note** - oral administration of cannabidiol only delivers ~6% drug active into the blood stream*

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

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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



1. Botanix Pharmaceuticals data on file

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Development Pipeline

BTX 1503: acne

BTX 1204: atopic dermatitis

BTX 1308: psoriasis

BTX 1801: antimicrobial



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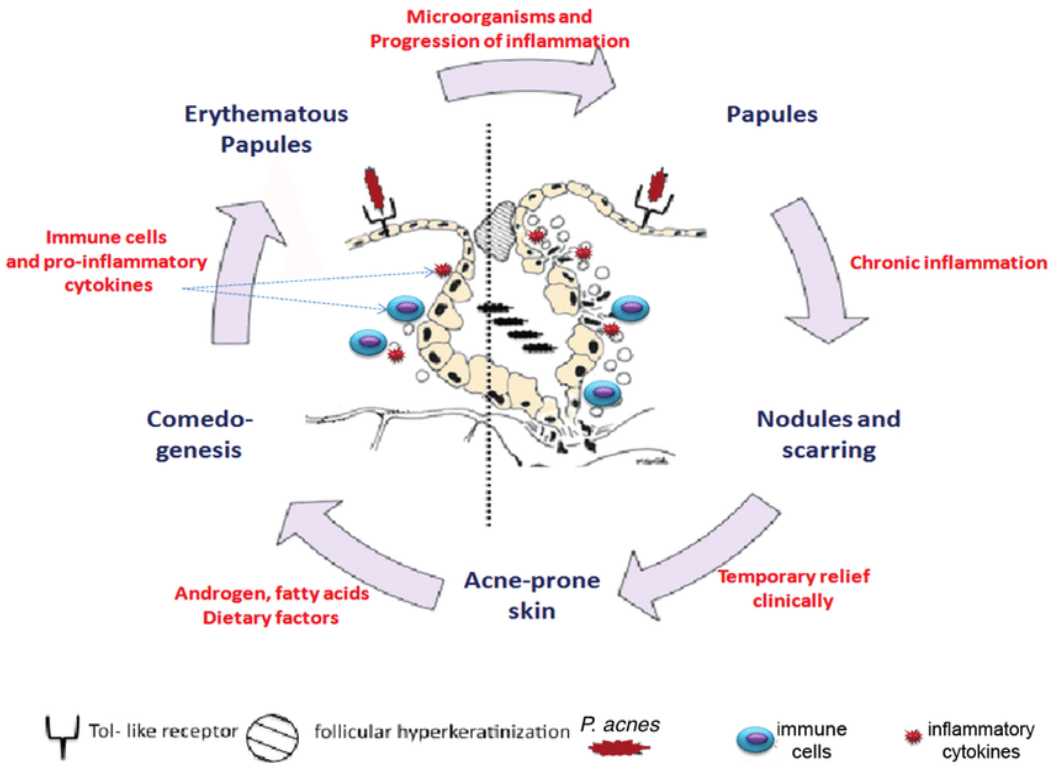
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BTX 1503: acne – mechanism of action for acne

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

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Inflammatory mechanisms involved in different stages of acne[1]



CBD has been shown to…

- Have **anti-inflammatory effects** on human **sebocytes** and to **suppress sebocyte proliferation**[2]
- **Have potent anti-microbial** activity against gram-positive bacteria[3]
- **Inhibit human keratinocyte proliferation,** through a non CB1/CB2 mechanism[4]

1. *Rocha & Bagatin Acne Vulgaris: an Inflammatory Disease Even Before the Onset of Clinical Lesions (2014). Inflammation and Allergy – Drug Targets June 13(3);* 2. Olah et al. *J Clin Invest*. 2014:124(9):3713-3724; 3. Appendino et al. *J Natl Prod*. 2008;71:1427-1430; 4. Wilkinson & Williamson. *J Derm Sci*. 2007;45:87-92.

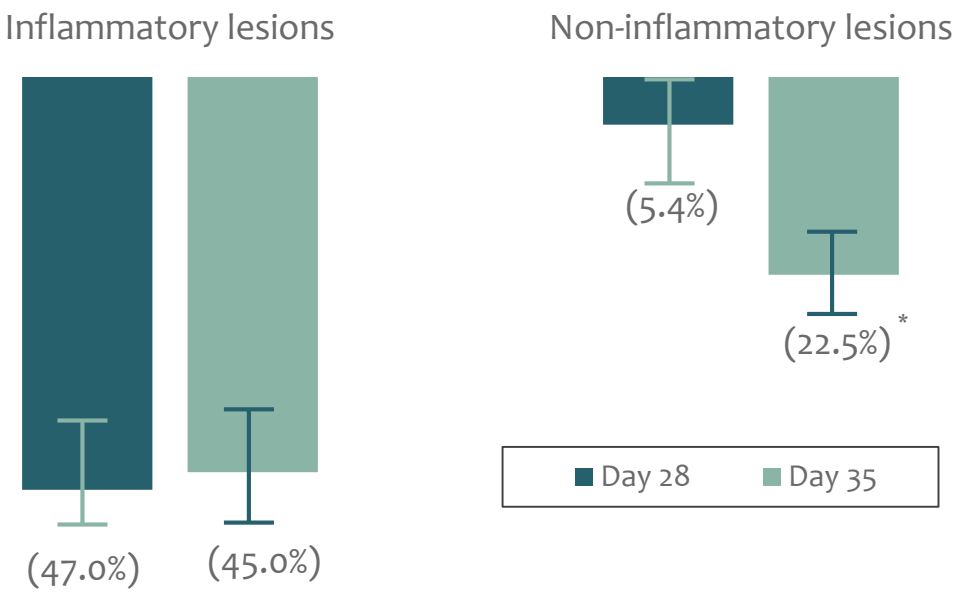
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BTX 1503: acne – outperforms leading acne products

4 week study data shows a marked reduction in inflammatory lesions, greater than any other FDA approved topical acne product [1]

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Lesion count reduction (%)



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

Comparison with other FDA approved products

Product	Owner	Lesion count reduction (%)[2]	2016 annual revenue[3]
Epiduo®	Galderma	~42%	US$494m
	• Combination of two drugs – benzoyl peroxide and adapalene × Common side effects include redness, skin peeling mild burning / stinging and dryness		
Aczone®	Allergan	~38%	US$456m
	✓ 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		
BTX 1503	**Botanix**	**~47%**	-

1. Botanix Pharmaceuticals data on file. 2. Lesion count reduction based on average inflammatory lesion reduction at 4 weeks. 3. Based on 2016 annual revenue in the US.

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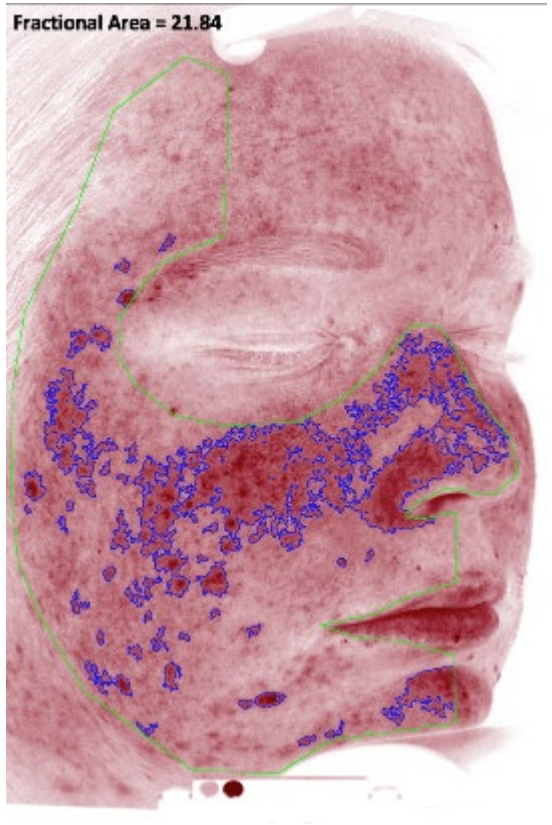
New data supporting anti-inflammatory effects of cannabidiol

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

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Baseline (Day 1)

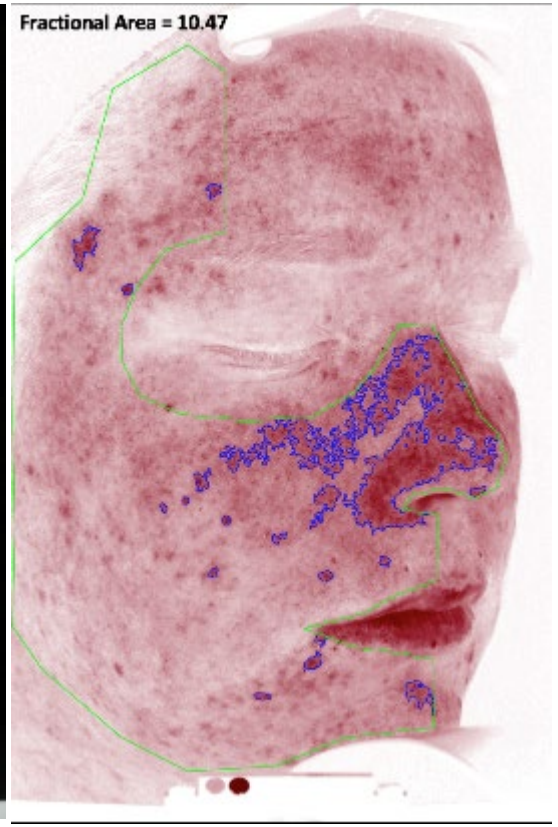




Nose not treated

Visit 4 (4 weeks)





Nose not treated

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

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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
- Children (> 12 years) and adults
- Moderate to severe acne patients
- Treatment Period 12 weeks

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

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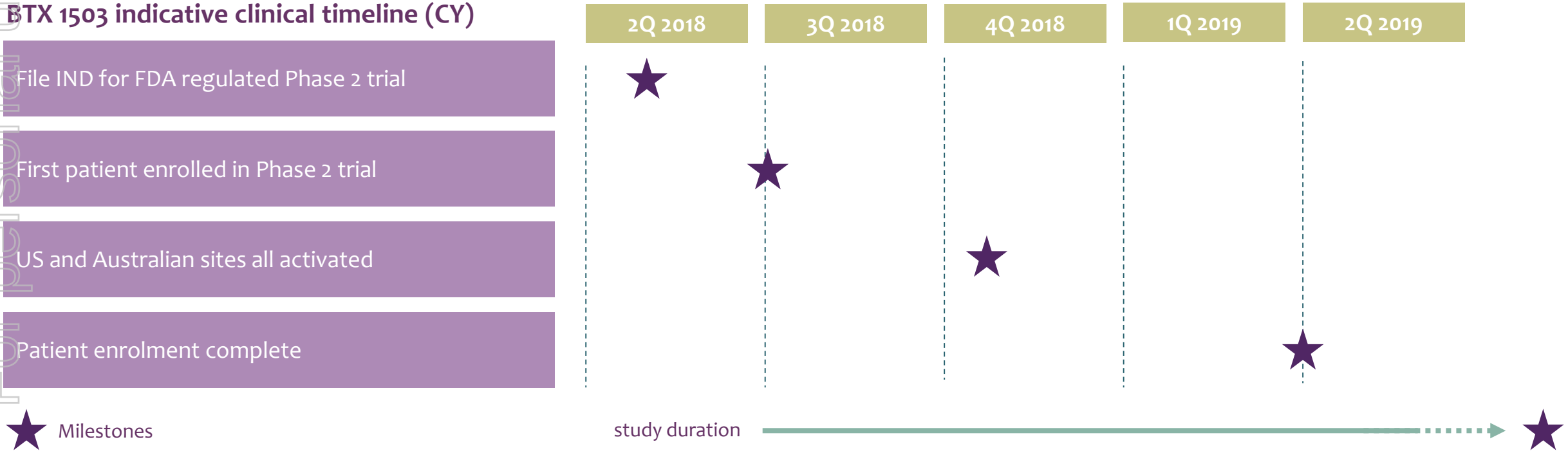
BTX 1503: acne – next steps

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

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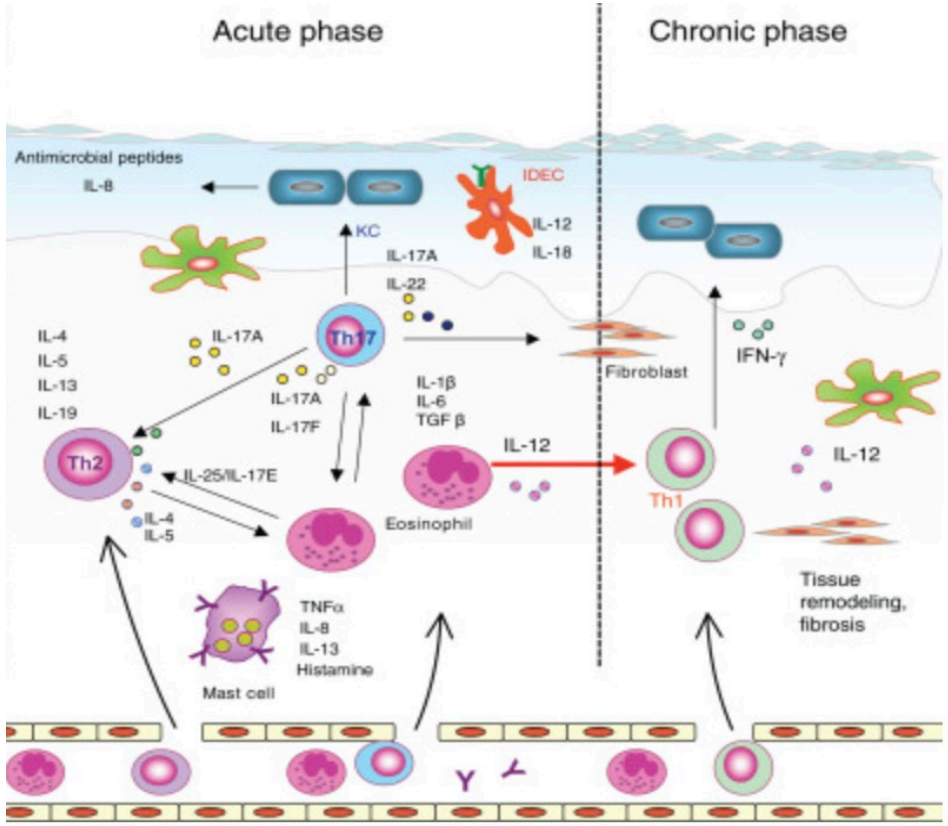
BTX 1503 indicative clinical timeline (CY)



BTX 1204: atopic dermatitis – mechanism of action

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

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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]

1. Harvey et al. *Cytokine*. 2014;65:236-244; 2. Kaplan et al. Biochem Pharmacol. 2008;76(6):726-737; 3. Gaffal et al. *Exp Derm*. 2014;23;401-406; 4. Kim et al. *Int J Derm*. 2015;54:e410-e408; 5. Lee et al. *Mol Med*. 2016;22:136-146.

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BTX 1204: atopic dermatitis – Phase 1b study design

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

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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



Study successfully completed end Q2 CY2018

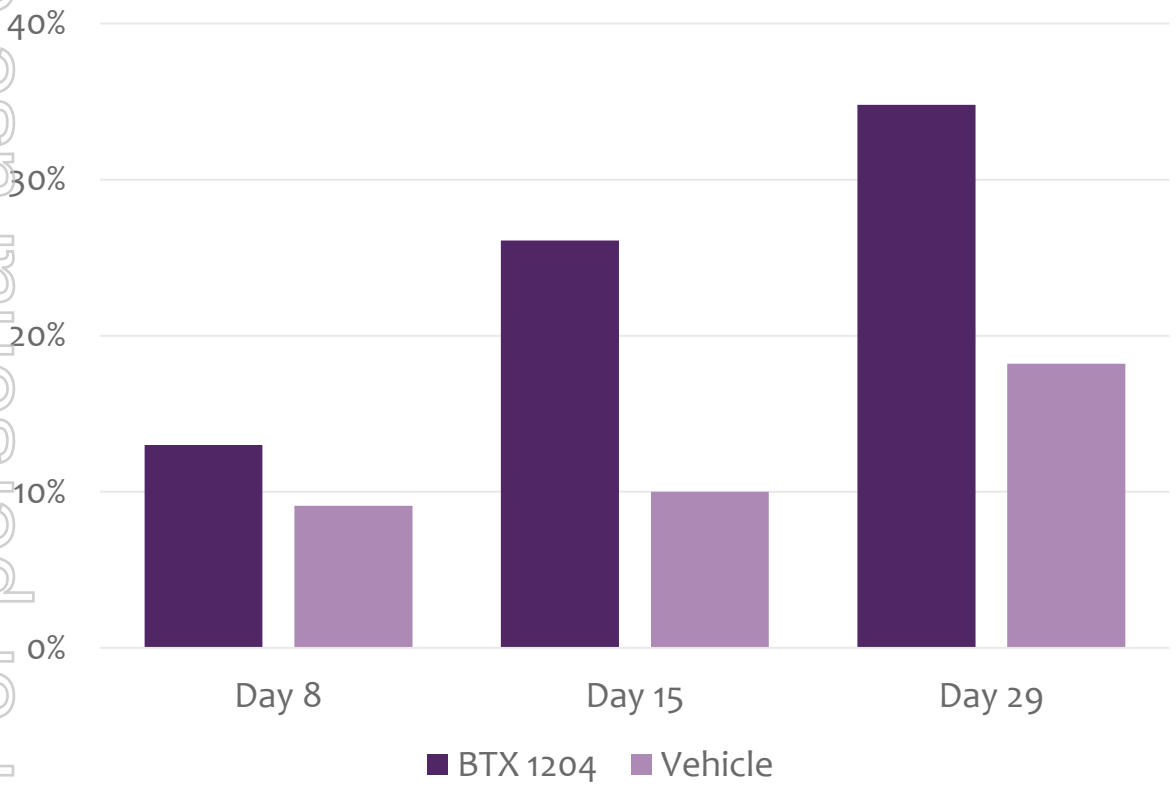
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BTX 1204: atopic dermatitis – Phase 1b study results

BTX 1204 was twice as effective as vehicle (with efficacy still increasing) and displayed a substantial improvement in the key signs of AD [1]

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Treatment success (%)[2]



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

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

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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

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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

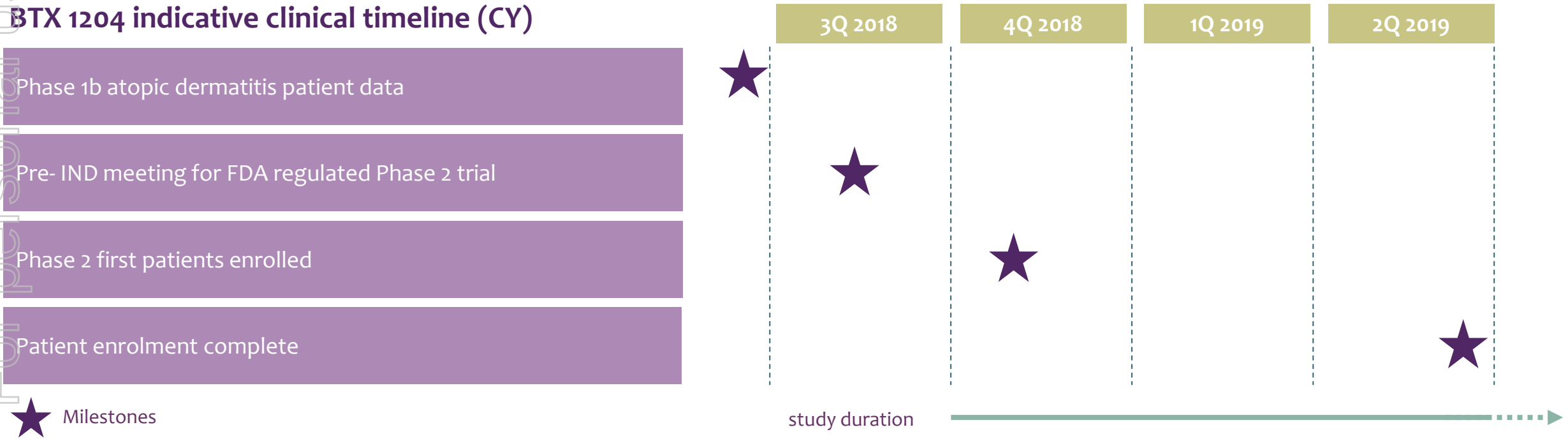
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BTX 1204: atopic dermatitis – next steps

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)



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BTX 1308: psoriasis – overview

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

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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

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

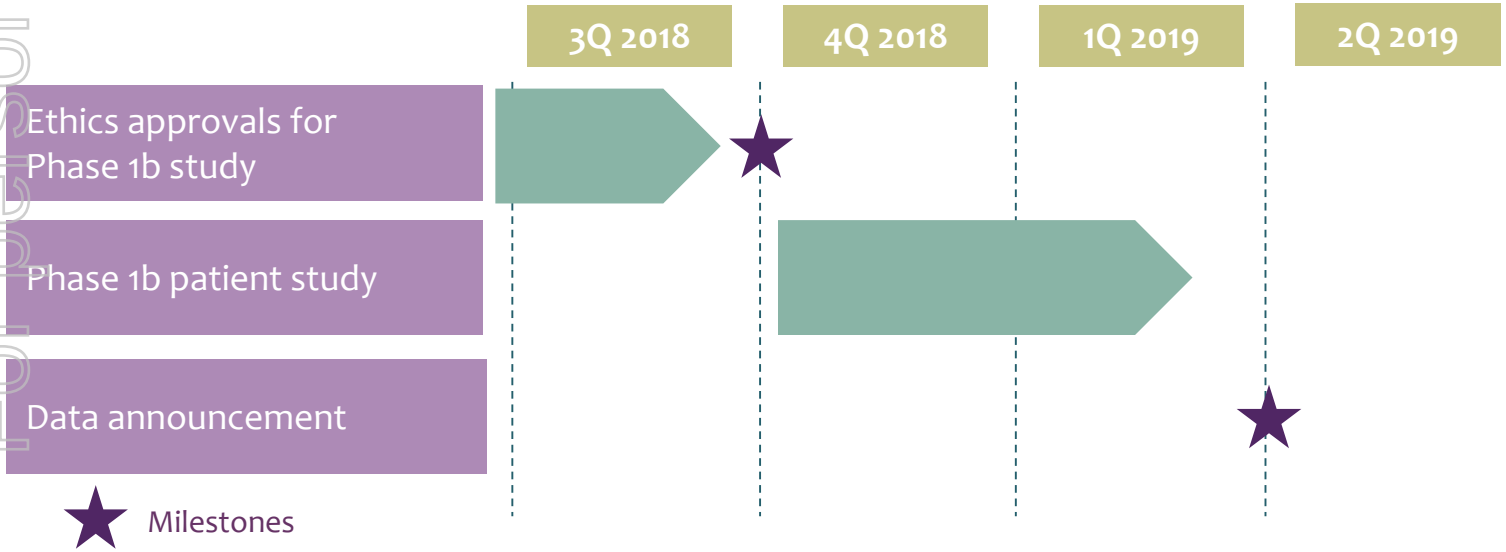
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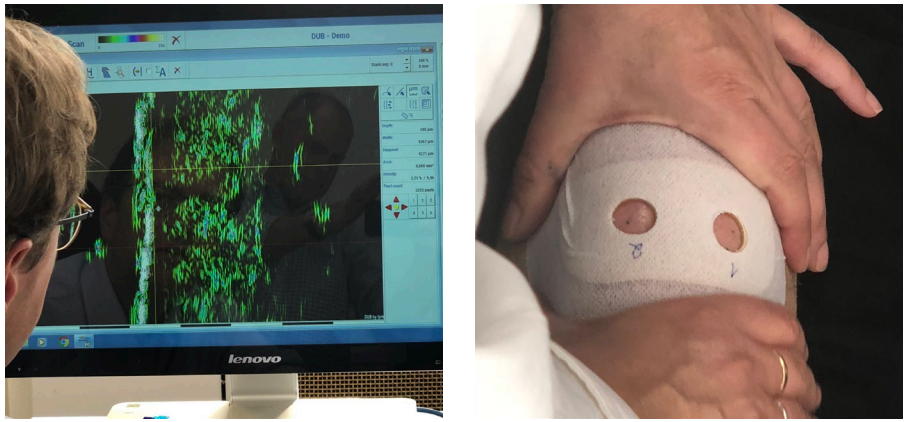
BTX 1308: psoriasis – next steps

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)





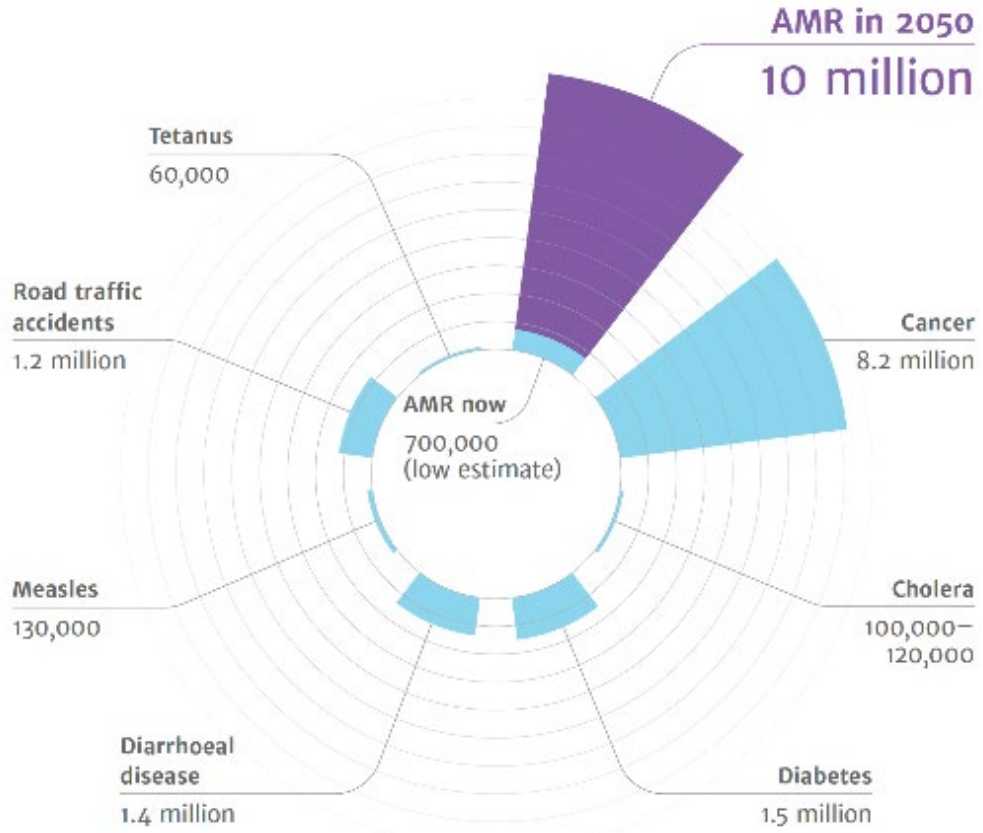
Bioskin GmbH psoriasis plaque test, including change in infiltrate thickness as measured by sonography

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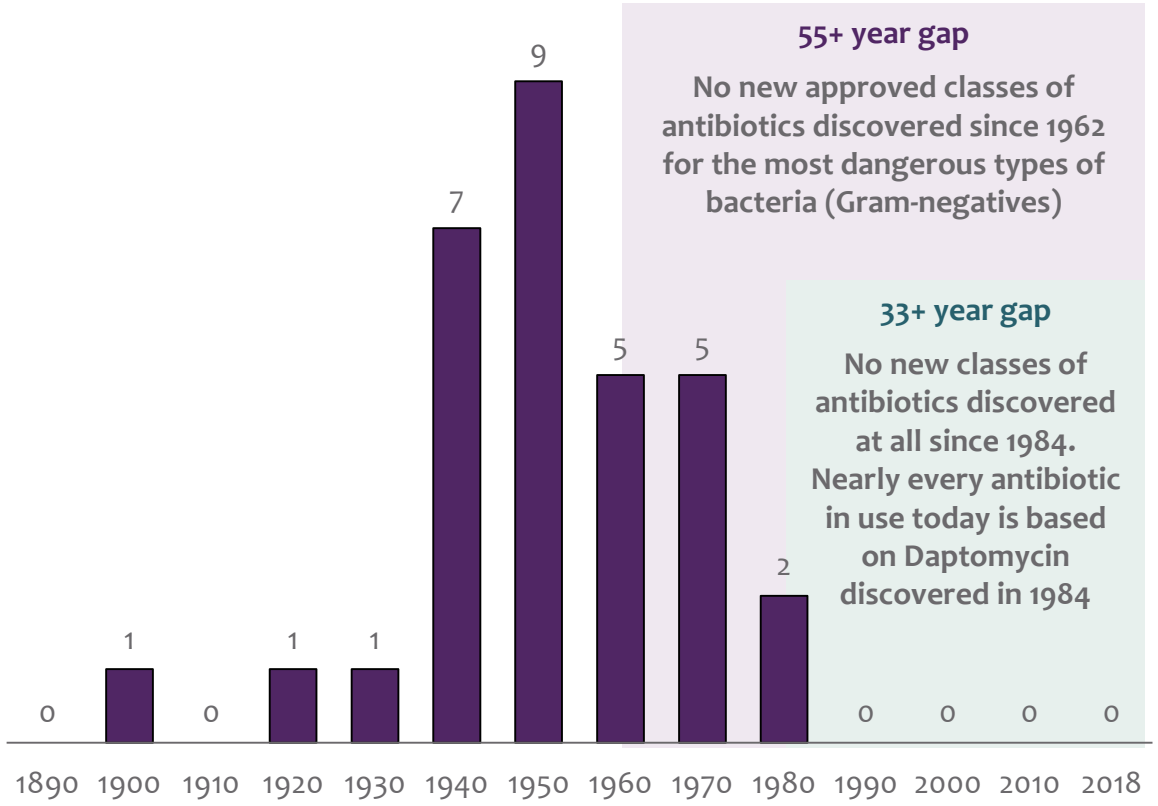
BTX 1801: antimicrobial – the problem of antimicrobial resistance

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 patented[2]



55+ year gap

No new approved classes of antibiotics discovered since 1962 for the most dangerous types of bacteria (Gram-negatives)

33+ year gap

No new classes of antibiotics discovered at all since 1984. Nearly every antibiotic in use today is based on Daptomycin discovered in 1984

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

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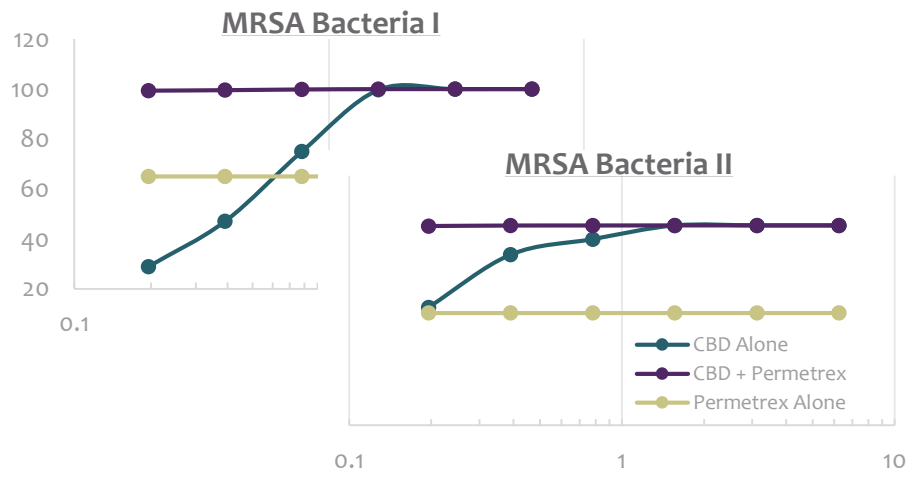
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BTX 1801: antimicrobial – results summary

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)

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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)

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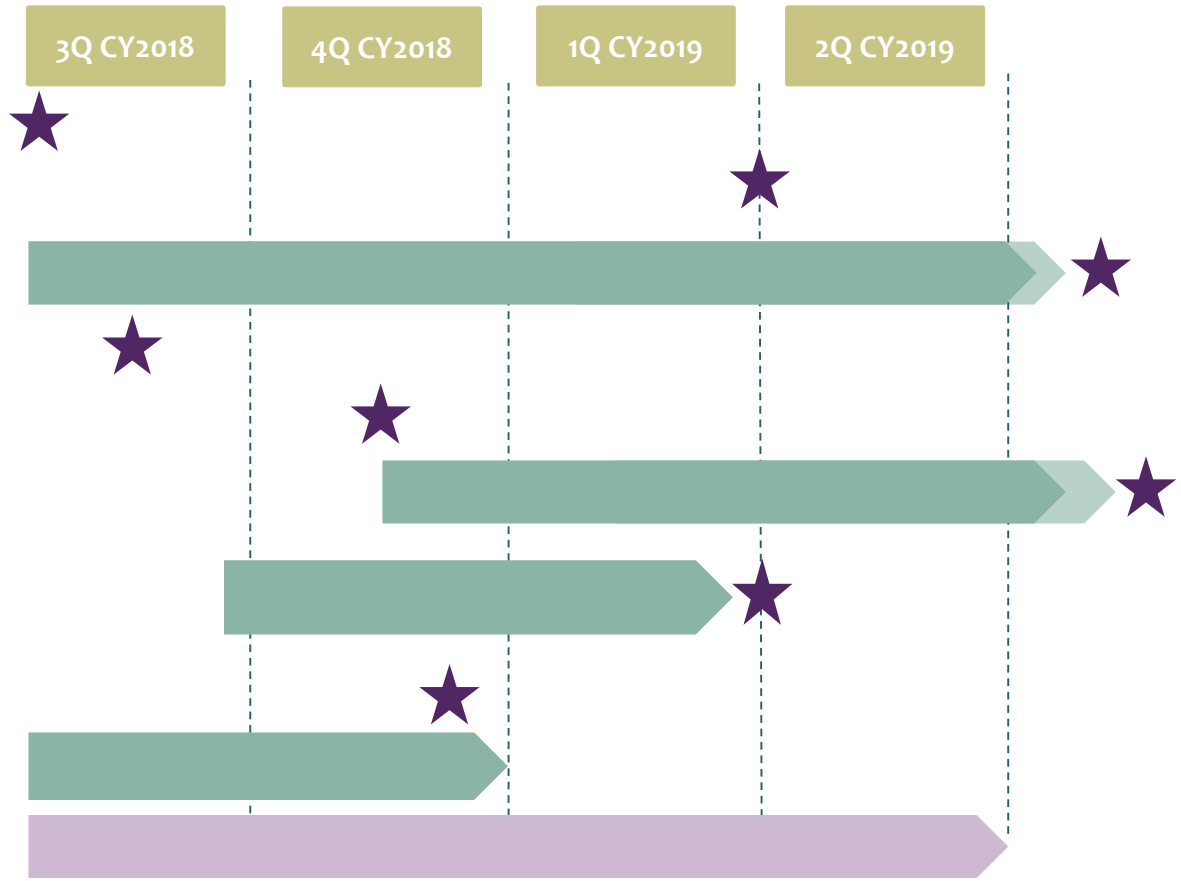
Key catalysts

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

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Indicative activities and milestones

BTX 1503 Acne Phase 2	First patient enrolled in Phase 2 study
	Patient enrolment complete
	Phase 2 multi-centre acne patient clinical study
BTX 1204 Atopic dermatitis Phase 2	Pre-IND Meeting for Phase 2 study
	First Patients Phase 2 study
	Phase 2 multi-centre AD patient clinical study
BX 1308 Psoriasis Phase 1b	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



★ Milestones

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