17 May 2021

New canine pilot study supports further investigation of synthetic cannabidiol in atopic dermatitis

Key highlights

- **BTX 1204A is a new higher dose formulation of synthetic CBD for atopic dermatitis, that leverages the Permetrex™ formulation used in the recent successful BTX 1801 Phase 2a study**
- **Results from a pilot study of canines with atopic dermatitis provides encouraging data to support further investigation**
- **Canine atopic dermatitis is clinically and immunologically similar to human AD, providing a clinically efficient approach to inform progression of further human studies**
- **Botanix plans to advance BTX 1204A to a fully funded proof of concept canine study in 2Q CY2021 which, if successful, provides opportunities for partnering for animal health markets and supports progression to Phase 2b study in humans in 1H 2022**

Philadelphia PA and Perth Australia, 17 May 2021: Clinical dermatology and antimicrobial company, Botanix Pharmaceuticals Limited (ASX:BOT, "Botanix" or "the Company"), is pleased to announce encouraging results from a small pilot study of BTX 1204A in canines with atopic dermatitis ('the BTX 1204A Pilot Study'). A presentation providing an overview of the BTX 1204 Pilot Study, an introduction to atopic dermatitis, and next step for development is attached to this release.

Vince Ippolito, President and Executive Chairman, commented: *"We are very encouraged that we are seeing early positive efficacy signals for BTX 1204A in canines with atopic dermatitis. These results, provide further support for our conclusion that drug dose and formulation design is critically important for synthetic cannabidiol – higher doses and the redesigned formulation successfully used in the BTX 1801 supports further exploration in atopic dermatitis.*

We are now in advance stages in planning to complete a larger BTX 1204A proof of concept canine study in Australia, with the primary objective to confirm and expand our data for safety and efficacy."

Summary of BTX 1204A Pilot Study design and endpoints

The BTX 1204A Pilot Study was conducted in canines with atopic dermatitis which were treated topically with BTX 1204A over a 28-day period. The study objective was to evaluate treatment effectiveness, using the Enhanced Pruritus Score (ESP) and Canine Atopic Dermatitis Extent and Severity Index (CADESI-04). BTX 1204A is based on a new higher dose formulation of synthetic cannabidiol (CBD) in a novel Permetrex™ formulation. This new formulation was utilised in the recent successful BTX 1801 Phase 2a study, which showed excellent efficacy in killing bacteria and separation between drug active and vehicle arms.

Effectiveness of the BTX 1204A treatment was evaluated at Day 0, Day 14 and Day 28 (for ESP) and Day 0 and Day 28 (for CADESI-04). The study was conducted in 4 dogs in Australia who were screened for moderate to severe dermatitis with visible lesions.

Summary of BTX 1204A Pilot Study results

Data generated in the BTX 1204A Pilot Study, undertaken by Botanix, demonstrated that a new higher dose formulation of synthetic CBD showed significant reductions on average in both the ESP and CADESI-04 scores over the 28-day treatment period.

BTX 1204A showed a decrease in pruritus over a 28-day treatment period, resulting in an average pruritus rating on the Enhanced Pruritus Score (ESP) system of Very Mild post-treatment (from pre-treatment rating of Moderate). In addition, BTX 1204A had a positive effect and showed a decrease in pruritus over a 28-day treatment period, resulting in a 57.3% reduction from baseline in the Canine Atopic Dermatitis Extent and Severity Index (CADESI-04) scale.

The results achieved in the BTX 1204A Pilot Study are encouraging and given the limited subjects enrolled, supports further exploration and investigation of the atopic dermatitis indication.

Disease overview and similarities between canine and human AD

Atopic dermatitis is the chronic inflammation of the skin resulting in itchy, red, swollen and cracked skin. Symptoms of the disease are made worse by scratching the affected area, and those affected have an increased risk of skin infections[i].

Dr Ira Lawrence, a clinical immunologist and allergist and former Senior Vice President of Research and Development and Chief Medical Officer for Medicis commented**:** *"*Atopic dermatitis in canines and humans is clinically and immunologically quite similar[ii], with both species sharing similar triggers and itch symptomology which cause longer term skin structure challenges.

Canine models are increasingly being used as valuable and effective screening tools for new therapeutic development, including dose ranging and safety assessments*."*

The potential benefit of BTX 1204A in canines and humans is supported by studies that indicate synthetic CBD addresses multiple factors of disease pathology, inhibits itch[iii] and repairs skin barrier dysfunction[iv,v], is a potent antimicrobial against Staph Aureus bacteria[vi] and broad anti-inflammatory properties.

A significant unmet need remains for a safe, topically applied therapeutic to treat atopic dermatitis. In the US, 31.6m people have a form of the disease with 1 in 10 people developing symptoms during their lifetime[vii,viii].

Next steps

While a relatively small study, the results of the BTX 1204 Pilot Study are encouraging and warrant expansion of the program into a larger proof of concept canine study planned to commence in 2Q CY2021.

Successful outcomes from this larger BTX 1204A proof of concept canine study will support both partnering opportunities for the animal health application of the product and also progression of BTX 1204A into a Phase 2b clinical study in humans with atopic dermatitis which could commence as early as 2Q 2022.

Release authorised by

Vince Ippolito
President and Executive Chairman

About Botanix Pharmaceuticals

Botanix Pharmaceuticals Limited (ASX:BOT) is a dermatology focused 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 has two separate development platforms, dermatology and antimicrobial products, both of which currently leverage the unique anti-inflammatory, immune modulating and antimicrobial properties of cannabinoids, particularly 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, which it utilises in its existing development programs and is being explored with a number of other product opportunities.

The Company is developing a pipeline of product candidates with recent positive data from its BTX 1801 Phase 2a antimicrobial study and plans for an upcoming Phase 2b study. For the dermatology platform, the Company has received ethics approval to commence its Phase 1b rosacea study and following a successful meeting with the FDA, the Company has confirmed a drug development plan for the BTX 1503 acne program to support registration. In addition, Botanix plans to advance its BTX 1204A atop dermatitis program to a proof of concept canine study following encouraging early data from a pilot study. To learn more please visit: https://www.botanixpharma.com/

For more information, please contact:

General enquiries	**Investor enquiries**	**Media enquiries**
Corporate Communications	Joel Seah	Haley Chartres
Botanix Pharmaceuticals	Vesparum Capital	H^CK
P: +61 8 6555 2945	P: +61 3 8582 4800	P: +61 423 139 163
investors@botanixpharma.com	botanixpharma@vesparum.com	haley@hck.digital

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.

---

[i] Simpson EL. Comorbidity in Atopic Dermatitis. Curr Dermatol Rep. 2012;1(1):29-38

[ii] Canine Models of Atopic Dermatitis: A Useful Tool with Untapped Potential (2009) Marsella R. et al Journal of Investigative Dermatology Volume 129, Issue 110 PP 2351-2357

[iii] Eagelston et al. Dermatol Online J. 2018 Jun 15; 24 (6);

[iv] BTX 1308 Phase 1b clinical study – BOT data on file

[v] Tan et al. Mal Med Rep 2017: 16(6) 8883-8867

[vi] BTX 1801 Phase 2a clinical study – BOT data on file

[vii] Hanifin JM, Reed ML, Eczema Prevalence and Impact Working Group. A population-based survey of eczema prevalence in the United States. Dermatitis. 2007;18(2):82-91

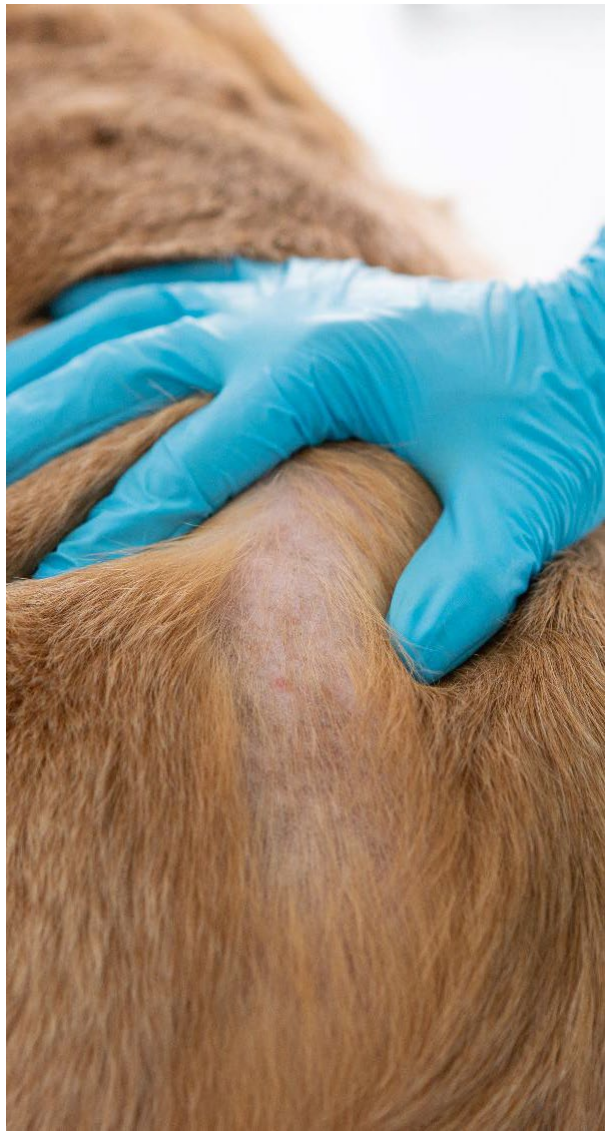
[viii] Silverberg JI, Hanifin JM. Adult eczema prevalence and associations with asthma and other health and demographic factors: a US population-based study. J Allergy Clin Immunol. 2013;132(5):1132-1138

botanix PHARMACEUTICALS

Unlocking the potential of synthetic cannabinoids

Atopic Dermatitis – Update

May 2021



BTX 1204A animal pilot study summary: Encouraging early data

Pilot study

- Canines with atopic dermatitis (AD) were treated topically with BTX 1204A over a 28-day period[1]
- Effectiveness of the treatment was measured using Enhanced Pruritus Score ("ESP" or "itch scale") and Canine Atopic Dermatitis Extent and Severity Index[2] ("CADESI-04") measurements

New formulation

- BTX1204A is a new higher dose formulation of synthetic cannabidiol (CBD) in a different Permetrex™ formulation for AD
- This new formulation was also used in the recent BTX 1801 Phase 2a study which showed excellent efficacy in killing bacteria and good separation between drug active (CBD) and vehicle (placebo) arms

Early signals

- In the canine pilot study, BTX1204A showed improvement in observed ESP and CADESI-04 scales over the 28-day treatment period[3]
- Data warrants further exploration of synthetic CBD in canine model of atopic dermatitis and potentially further human Phase 2b study

botanix PHARMACEUTICALS

1. Pilot study based on 4 dogs with moderate atopic dermatitis
2. Simplified scale for assessing skin lesions of atopic dermatitis in dogs
3. BTX 1204A clinical study data announced 17 May 2021

Atopic dermatitis: overview

Disease

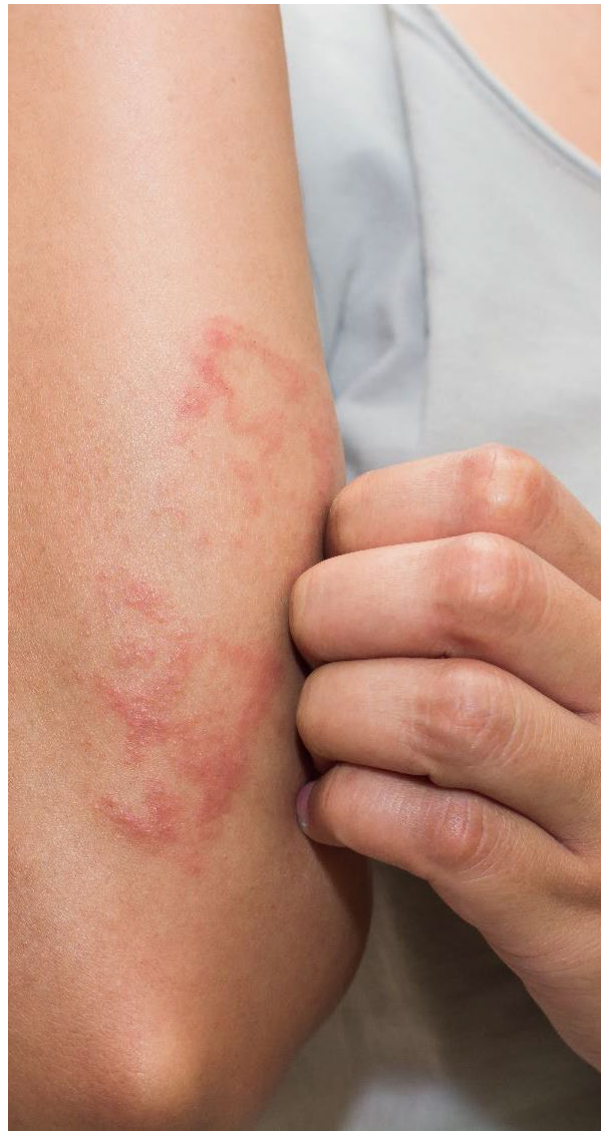
- Chronic inflammation of the skin resulting in itchy, red, swollen and cracked skin
- Scratching the affected area worsens the symptoms, and those affected have an increased risk of skin infections[1]
- Safety and tolerability concerns with use of steroids and non-steroidal options – biologic drugs targeting the immune system, are reserved for severe cases

Rationale

- Botanix studies indicate synthetic CBD can address multiple factors of disease pathology:
  - inhibits itch[2] and repairs barrier dysfunction[3,4]
  - potent antimicrobial against Staph Aureus bacteria[5]
  - broad anti-inflammatory properties

Market opportunity

- 31.6m people in America have a form of AD with 1 in 10 people developing the disease during their lifetime[6,7]
- The AD market by revenue is projected to grow to ~US$25bn by 2027[8]



botanix PHARMACEUTICALS

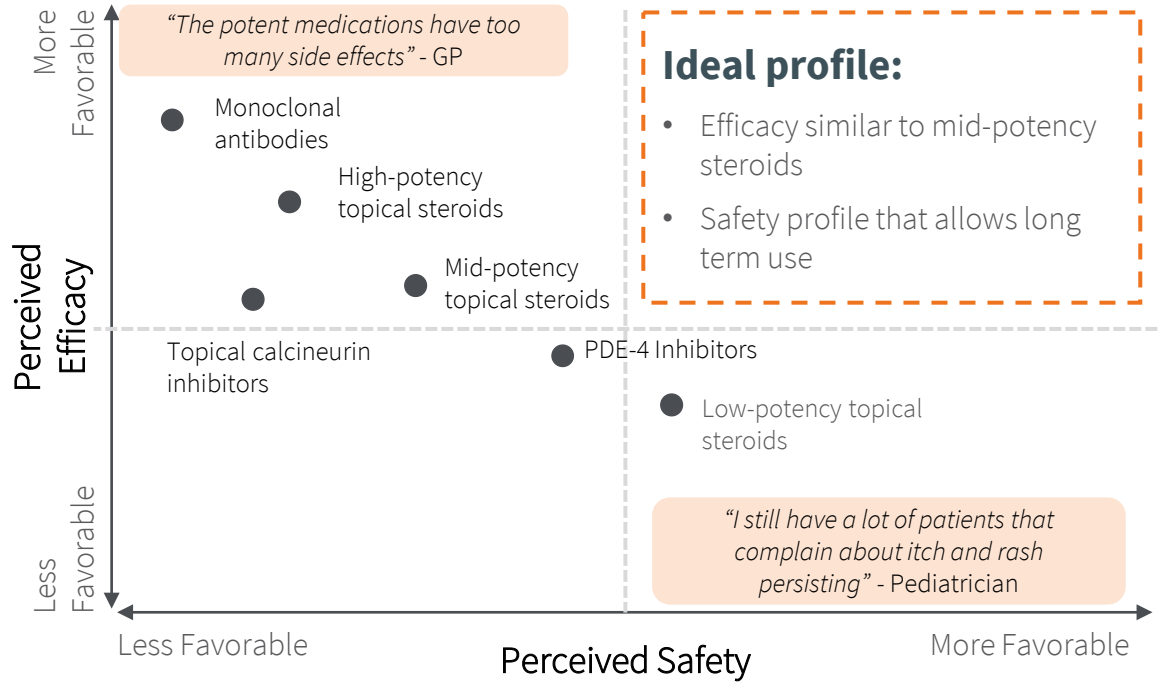
1. Simpson EL. Comorbidity in Atopic Dermatitis. Curr Dermatol Rep. 2012;1(1):29-38; 2. Eagelston et al. Dermatol Online J. 2018 Jun 15; 24 (6); 3. BTX 1308 Phase 1b clinical study – BOT data on file; 4. Tan et al. Mal Med Rep 2017: 16(6) 8883-8867; 5. BTX 1801 Phase 2a clinical study – BOT data on file; 6. Hanifin JM, Reed ML, Eczema Prevalence and Impact Working Group. A population-based survey of eczema prevalence in the United States. Dermatitis. 2007;18(2):82-91; 7. Silverberg JI, Hanifin JM. Adult eczema prevalence and associations with asthma and other health and demographic factors: a US population-based study. J Allergy Clin Immunol. 2013;132(5):1132-1138; 8. Symphony Health Services (PHAST) 2017

Atopic dermatitis competitive landscape

There still exists a significant unmet need for AD patients, despite recent FDA approval[1] of Eucrisa®

- Despite gaining FDA approval in 2016, lack of sales indicates that Eucrisa® has not been widely accepted – primarily due to the early on **reported burning and stinging**[2]
- Other topical AD products with moderate efficacy **carry boxed warning for cancer risks** (e.g. Elidel®; Protopic®)
- Recent pipeline failures (e.g. Menlo Therapeutics; Vanda Pharmaceuticals) highlight the **lack of late-stage atopic dermatitis products with novel mechanisms of action**
- **Long term use of the topical steroids is not recommended** and should not used on the face and sensitive skin areas[3]
- **A significant unmet need remains for a safe, topically applied therapeutic with a novel mechanism of action**

Market positioning and opportunity



Minimal innovation in topical atopic dermatitis products in the 15 years prior to Eucrisa® approval

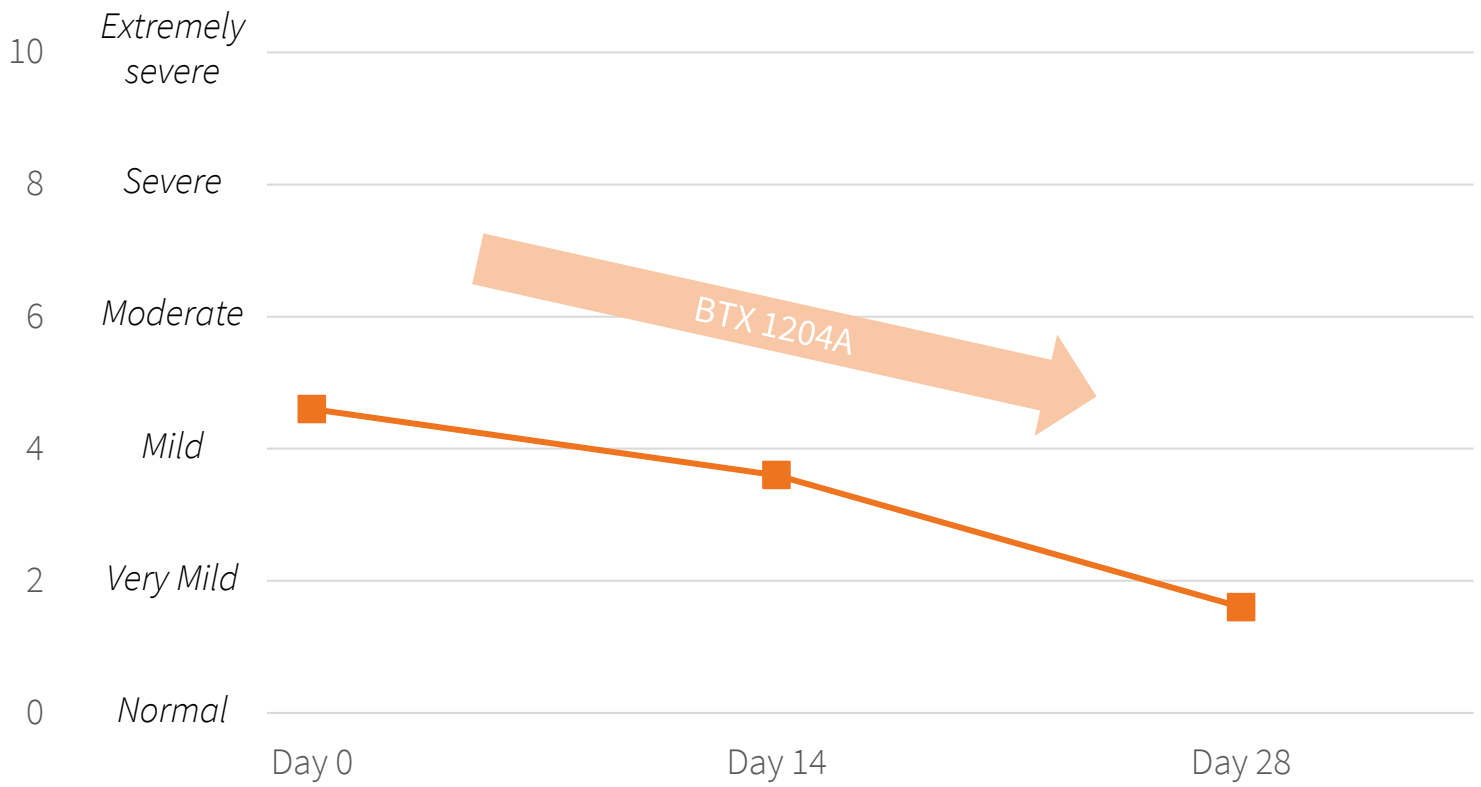
botanix PHARMACEUTICALS

1. Eucrisa was developed by Anacor which was sold to Pfizer for US$5.2bn in May 2016
2. Pfizer 2020 Annual Review https://annualreview.pfizer.com/
3. https://www.mayoclinic.org/steroids/art-20045692

BTX 1204A data

New animal data supports further investigation of dermatitis for animals and humans

BTX 1204A: Pruritus mean ESP scores[1,2]



- BTX 1204A canine study included dogs with **average pruritus rating of Moderate (pre-treatment)** and were treated for 28 days
- The study was focused on pruritus-relief via **topical administration of the new formulation BTX 1204A**
- BTX 1204A showed a decrease in pruritus over a 28-day period, **resulting in an average pruritus rating of Very Mild (post-treatment)**
- Limited subjects in study warrants further investigation in larger study

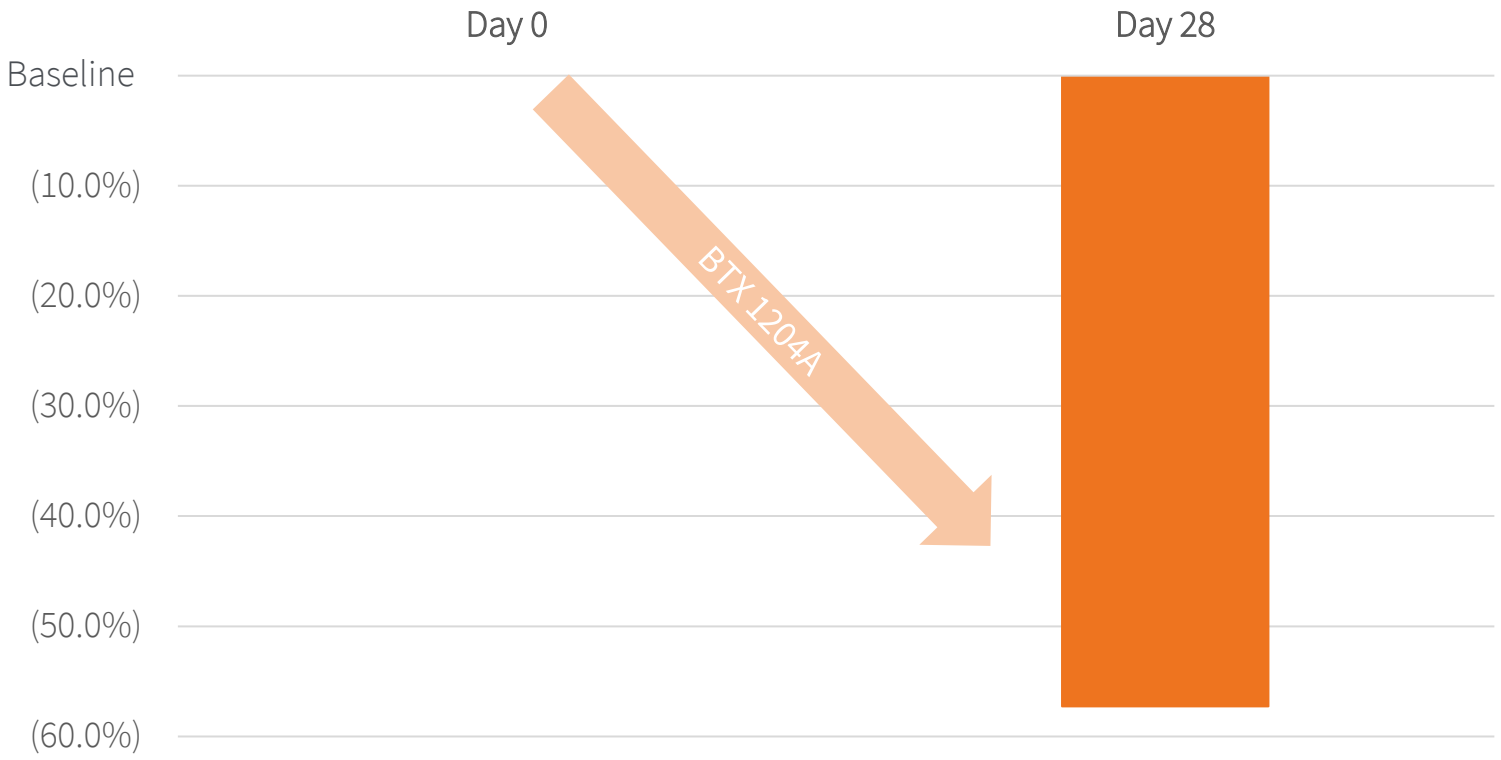
botanix PHARMACEUTICALS

1. BTX 1204A clinical study data announced 17 May 2021
2. Enhanced Pruritus Score– designed to measure the severity of itching in dogs

BTX 1204A data

New animal data supports further development of AD indication

BTX 1204A: % reduction from baseline (CADESI-04)[1,2]

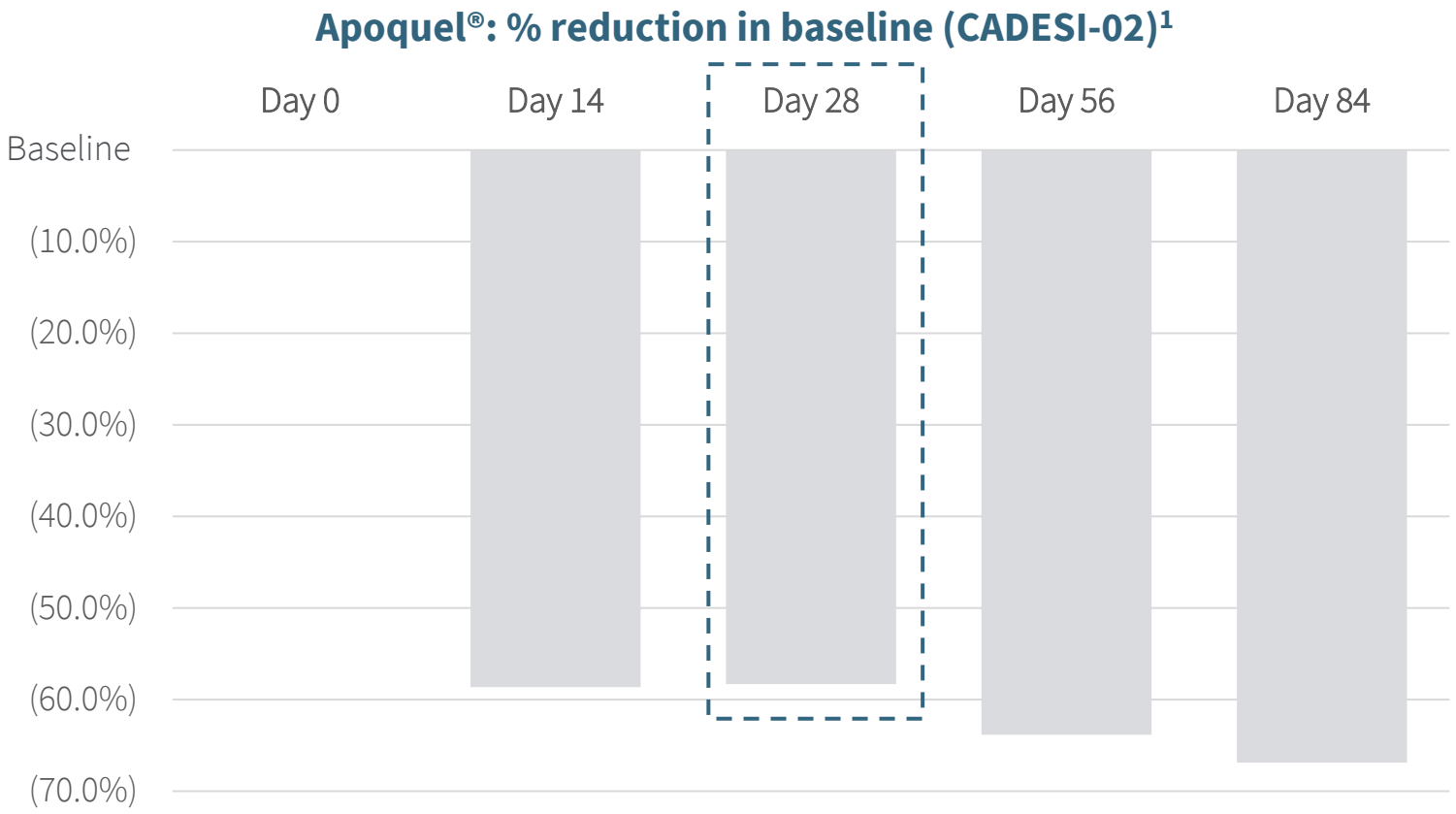


- BTX 1204A canine study also included a CADESI-04 assessment (*Canine Atopic Dermatitis Extent and Severity Index*)
- BTX 1204A had a positive effect and showed an improvement in skin lesions over a 28- day period, resulting in a ~57.3% reduction from baseline severity
- Limited subjects in study warrants further investigation in larger study

botanix PHARMACEUTICALS

1. BTX 1204A clinical study data announced 17 May 2021 (n=4)

Context: Currently approved animal treatment data



- Apoquel®, produced by Zoetis, is an oral animal dermatitis product prescribed for canines
- In the Australian run study, Apoquel® achieved ~58.3% reduction in skin lesion severity from baseline at Day 28 assessed using the CADESI-02 scale (an earlier version of CADESI-04)
- In CY2019, Apoquel® **generated >US$550m in revenue**[2] (comprising out of pocket payments by owners)
- Topically applied products are generally preferred over systemically available (orally delivered) products due to side effect concerns

botanix PHARMACEUTICALS

1. Apoquel: US Technical Monograph - https://www.zoetisus.com/products/dogs/apoquel/assets/pdf/apoqueltechnicalmonograph.pdf
2. Zoetis Annual Report 2019 – https://www.annualreports.com/HostedData/AnnualReports/PDF/NYSE_ZTS_2019.pdf

Canine atopic dermatitis:
close proxy for human atopic dermatitis

- Canines naturally and commonly develop a pruritic dermatitis that is **clinically and immunologically extremely similar to human AD**[1]
- Dogs and humans with AD also have **similar problems with skin barrier function** – these problems cause the skin to be very dry and prone to Staph Aureus infections[2]
- Canine models are **increasingly used as screening tools for new therapeutic development**, including dose ranging and safety assessments
- Canine studies are **faster and more cost effective** than human studies and help **de-risk later stage studies**

REVIEW

Canine Models of Atopic Dermatitis: A Useful Tool with Untapped Potential

Rosanna Marsella[1] and Giampiero Girolomoni[2]

	Canine AD	Human AD
Prevalence in population	10-15%	5-20%
Age of onset	1-3	1-5
Skin affected	Face, folds	Face, folds
Infiltration eosinophils	+	+-
Infiltration igE and dendritic cells	+	+
Pruritus	Severe	Severe
Skin colonization Staph Aureus	+	+
Th-2 dominated immune response	+	+

botanix PHARMACEUTICALS

1. Canine Models of Atopic Dermatitis: A Useful Tool with Untapped Potential (2009) Marsella R. et al Journal of Investigative Dermatology Volume 129, Issue 110 PP 2351-2357 - https://core.ac.uk/download/pdf/82218135.pdf
2. National Eczema Association - https://nationaleczema.org/dogs-shows-us-how-to-atopic-dermatitis/

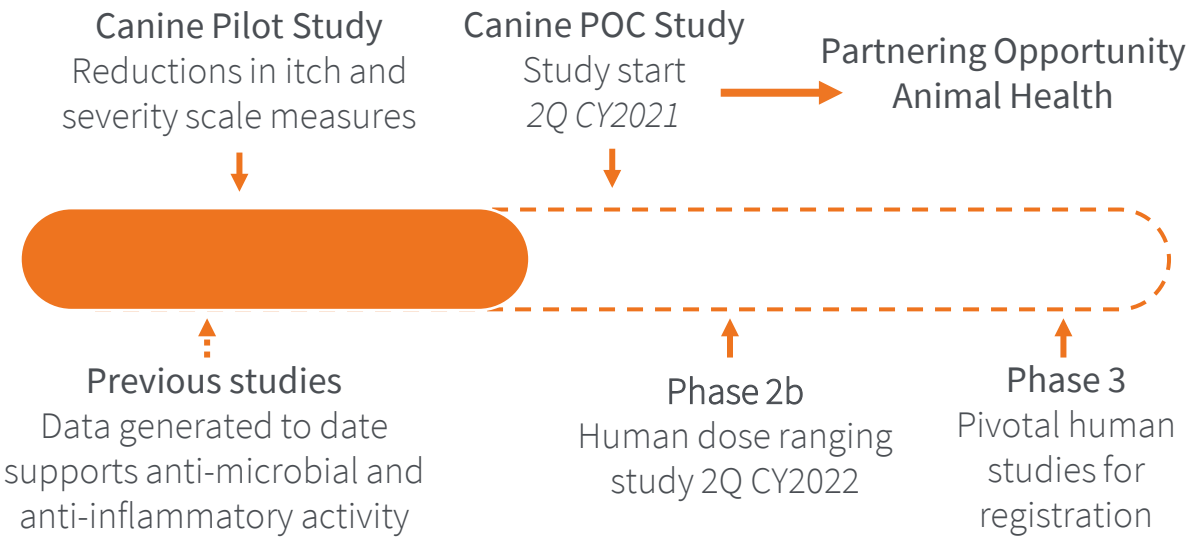
BTX 1204A development strategy:

Larger POC canine study in 2Q CY2021 - informs licensing program for animal use and potential relaunch of late-stage atopic dermatitis clinical program

Proposed canine study parameters

- **Four dose groups, ~40 dogs:**
  - BTX 1204A high dose: 10 subjects
  - BTX 1204A medium dose: 10 subjects
  - BTX 1204A low dose: 10 subjects
  - Vehicle: 10 subjects
- **Sites:** 5 Australian sites
- **Treatment period:** twice daily treatment for 28 days
- **Endpoints:** Enhanced Pruritus Score; Canine Atopic Dermatitis Extent and Severity Scale Index

Planned pathway to approval



Successful outcome from planned POC canine study opens up partnering opportunity and supports progression to Phase 2b human study in atopic dermatitis

botanix PHARMACEUTICALS

General enquiries

Botanix Pharmaceuticals
Corporate communications
+61 8 6555 2945
investors@botanixpharma.com

botanix
PHARMACEUTICALS