Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Analyst	Date	Price Target
Seth Lizee	**9th August 2021**	**$0.17/sh**

Initiation of Coverage

Investment case

Botanix Pharmaceuticals Ltd (BOT) is a clinical stage synthetic cannabinoid pharmaceutical company.

The company is looking to shake up big markets in dermatology and antimicrobials with its four clinical programs (target indications: acne, antimicrobial, rosacea and atopic dermatitis) which leverage the unique anti-inflammatory, immune modulating and antimicrobial properties of synthetic cannabinoid, in conjunction with an exclusively licensed proprietary drug delivery system Permetrex™.

The prize, should individual programs ultimately be clinically successful, is huge. We believe the market is pricing in failure, or very close to it, whereas our initial insights into the company's programs and respective clinical studies suggest the opposite.

We believe the stock will trade up as the market begins to better understand the potential of BOT's programs, we anticipate this will occur as we near the multiple catalyst due early to mid-next year. If BOT can deliver successful clinical outcomes, we believe the stock can trade above our price target, potentially multiples of it.

We initiate coverage on Botanix Pharmaceuticals Ltd with a Speculative Buy recommendation and 12-month Price Target of $0.17/sh, implying 127% upside from initiation.

Investment Thesis

- **New Treatments Wanted** – There has been no new mechanisms of action approved by the FDA in 20-30yrs across most of the targeted indications (acne, rosacea, antimicrobial), despite clear demand by sufferers for new products with similar efficacy; but without the risks or side effects of existing options.
- **Large Addressable Markets** – The company is going after multibillion-dollar markets, the acne market alone is worth an estimated US$5.1bn annually with other target markets ranging from hundreds of millions to billions per annum.
- **Advanced Development Pipeline** – BOT has a total of four clinical programmes in development, two of which have completed phase II clinical studies (Acne; Antimicrobial). The company recently kicked off a new clinical study (rosacea: phase 1b), with a further 2 human clinical studies (acne: phase 3, antimicrobial: phase 2b) and a canine study (atopic dermatitis) planned.
- **Excellent Safety Profile** – BOT's products leverage the properties of cannabidiol in a topical formulation, which has demonstrated excellent safety profiles across all clinical studies; an aspect which is foundational towards a successful product and ultimately commercialisation.

Botanix Pharmaceuticals Ltd	Year End 30 June	
Share Price	**0.075**	**A$/sh**
Price Target	**0.17**	**A$/sh**
Valuation	0.17	A$/sh
Shares on issue	1041.6m, diluted	
Market Capitalisation	78.1	A$m
Enterprise Value	49.5	A$m
Debt (Jun'21)	0.0	A$m
Cash (Jun'21)	21.6	A$m
Unpaid cap	7.1	A$m
Turnover	5.2m	sh/day
12 Mth Hi-Lo	0.045-0.19	A$/sh
Balance date	June 30th	

Directors & Management

Vince Ippolito	Exec Chair & Pres.
Matthew Callahan	Exec Dir
Dr William Bosch	Exec Dir / CSO
Dr Stewart Washer	Exec Dir
Dr Clarence Young	Chief Med Off
Anthony Robinson	VP of DevLynda
Berne	Head of Comm.

Company Details

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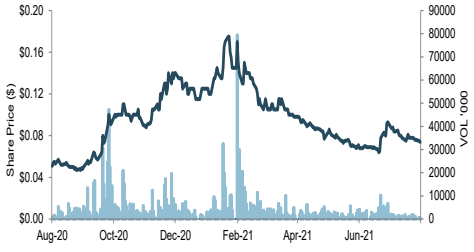
botanixpharma.com

Share Price Chart



Disclaimer

This analyst declares that he has a beneficial interest in Botanix Pharmaceuticals Ltd.

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

- **Platform Technology** – The company has exclusive license to use a proprietary drug delivery system, Permetrex™, which is utilised across all programs and is being explored with a number of other product opportunities.
- **Experienced Board and Management** – The management team and board of directors are highly experienced in the field of dermatology and antimicrobials; the combined leadership have developed ~30 FDA approved products;
- **Attractive Valuation** – BOT trades at a 56% discount to our $0.17/sh. Valuation. With an EV of $50m, we believe there is a highly attractive risk-to-reward case;
- **Near Term Programs Funded** – BOT is funded to undertake near-term development programs with $21.6m in cash as of the June Q;
- **Multiple Upcoming Catalyst** – We note a number of short to medium term catalysts lie ahead:

24 Month Timeline	CY'2021		CY'2022				CY'2023+	
	Sep'Q	Dec'Q	Mar'Q	Jun'Q	Sep'Q	Dec'Q	Mar'Q	Jun'Q+
BTX1503 (Acne)								
Phase 3 Study								
BTX1801 (Antimicrobial)								
Phase 2b Study								
Phase 3 Study								
BTX1702 (Rosacea)								
Phase 1b Study								
Phase 3 Study								
BTX1204A (Atopic Derm.)								
Canine Follow up Study								
INAD								
Commercial Partner (Cannine)								
Phase 2b Study								
Phase 3 Study								
Permetrex (Delivery Tech.)								
Licensing Agreements								

Source: EHL Estimates

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Table of Contents

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Risks

We highlight key investment risks below:

- **Development Risk** – As a biotech development company all products are in varying stages of clinical trial or development. There is considerable risk surrounding success. Clinical outcomes on face value are binary and will be seen by the market as such.
- **Domino Effect** – All current products in development utilise the same active ingredient, synthetic CBD, varying by dosage and delivery. Hence successes as well as failures will have an impact across the company's whole development portfolio. This is similarly applicable to BOTs delivery platform, Permetrex™.
- **Regulation** – Although essentially a moot point around CBD post de-regulation in recent years, there remains the risk surrounding regulatory changes across all aspects of the business, CBD or otherwise.
- **Over-The-Counter (OTC)** – There is a growing market for OTC CBD products; these pose the risk of competing with BOTs products. Previous studies by BOT have shown a number of these OTC products to be inferior.
- **Funding** – BOT is currently cashflow negative and will likely require additional capital to fund development, there remains the usual risks around timing of any future funding requirements.
- **Commercialisation** – Clearly a commercial outcome cannot be guaranteed; this risk will decline as the company completes development milestones.
- **Intellectual Property (IP)** - BOT maintains an extensive intellectual property portfolio, loss or issues surrounding these patents could impact the business.
- **Key Personnel** – The company has a number of experienced Key personnel, the loss of which could slow development process.
- **COVID-19** - There is a risk COVID-19 may disrupt timelines.

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Valuation and Price Target

We initiate coverage with a $0.17/sh. Valuation and Price Target.

Our valuation is derived through a sum of the parts (SOP) risked NPV (rNPV) of BOTs development programs. We believe this is the most appropriate method which defines individual programs successful value and respectively adjusts for clinical development milestones.

Further justifying our investment case, we have also considered listed peers and recent industry M&A transactions.

On balance, we believe there is a highly asymmetrical investment opportunity, whereby the downside to near cash backing (see: 'downside case') is significantly outweighed by the potential upside; both in terms of comparables and our 'fundamental risked' valuation.

rNPV – Risked Net Present Value

A summary of our sum of the parts (SOP) risked NPV (rNPV) is shown below.

We have calculated an equity value of $174.4m or 0.17/sh.

	Asset Value (NPV)	Risking (r)	Risked Valuation (rNPV)	
Program	**A$m**	**%**	**A$m**	**A$/sh**
BTX1503	337.4	27%	92.1	0.09
BTX1801	186.7	23%	42.4	0.04
BTX1702	94.2	6%	5.9	0.01
BTX1204A	82.8	6%	5.2	0.01
Net Cash	21.6	100%	21.6	0.02
Unapid Capital	7.1	100%	7.1	0.01
Total	729.8		174.4	0.17

Source: EHSL Forecasts

We model the successful asset value of each program using an NPV of free cashflows. We have forecasted free cashflows using the following assumptions:

- Peak market share & uptake curve;
- Pricing;
- Economic period;
- Margin; and
- Development capital required

We detail our individual assumptions and the forecasted free cashflows for each program further into this report.

These cashflows are then discounted to present value using **a conservative 30% discount rate to calculate an NPV, we note there is scope to reduce this as the company de-risks its development.**

We have then risked each asset value by the respective statistical likelihood of approval. We have specifically applied the clinical success rates as defined by the FDA. We note these success rates are among the most conservative, these shown below.

Phase	Primary Goal	Phase Success Rates*	Success Rate to Full Approval
Pre-Clin	Pre-human testing of efficacy, toxicity, and PK info.	na	6%
Phase 1	Safety and dosage	70%	9%
Phase 2	Efficacy and side effects	33%	27%
Phase 3	Efficacy and monitoring of adverse reactions	30%	90%
NDA	New Drug Approval	90%	100%

**Per FDA figures. Source: FDA*

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Sensitivity Analysis

We have gone further to include sensitivities on our valuation.

In the table below, we fix all other assumptions and explore the valuation (rNPV) of individual programs at different stages of clinical development.

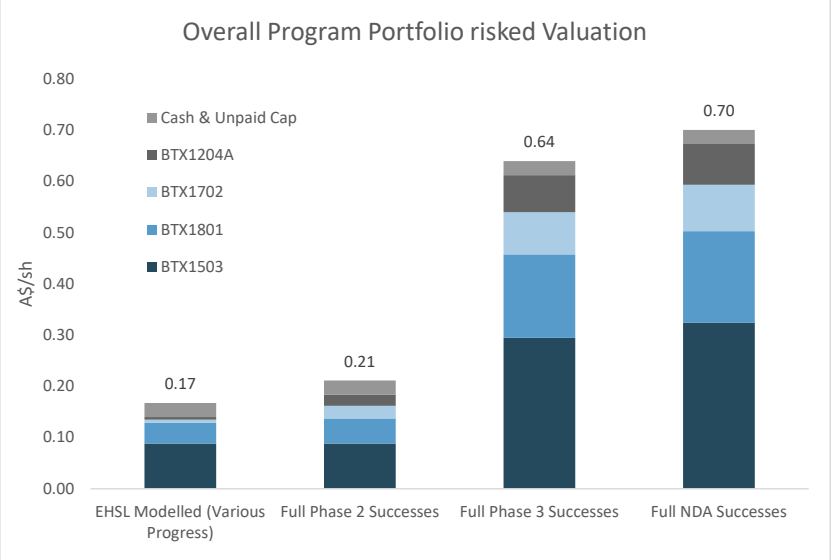
This demonstrates the huge value uplift possible through clinical trial success.

Program Stage	BTX1503	BTX1801	BTX1702	BTX1204A	Cash & Unpaid Cap	Total
Pre-Clin	0.09	0.04	0.01	0.01	0.03	0.17
Phase 1	0.09	0.04	0.01	0.01	0.03	0.17
Phase 2	0.09	0.05	0.02	0.02	0.03	0.21
Phase 3	0.29	0.16	0.08	0.07	0.03	0.64
NDA	0.32	0.18	0.09	0.08	0.03	0.70

Source: EHL Forecasts

Taking the total from the right-hand side, we can explore the valuation of the combined portfolio of programs at the point of each clinical stage (Successful stage) of development.

In reality, stages of clinical development for the programs will likely be staggered, however, this table is indicatively useful in showing the full value potential of BOT's portfolio.



Source: EHL Forecasts

As we can see in this indicative analysis, there is significant value upside beyond our defined price target if clinical developments are successful. Even under a mixed scenario, where only a portion of the programs are successful, there is still significant value potential.

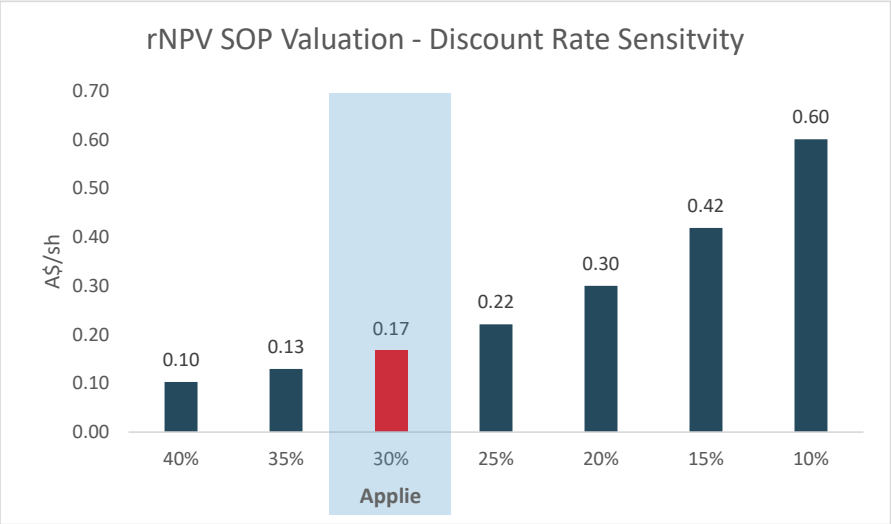
Each program on its own, if fully successful, is worth more than the current share price.

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

We have further included a sensitivity analysis of the discount rate used in our valuation (rNPV), this shown below.



Source: EHL Forecasts

The table highlights the value uplift possible as the program de-risks (through using lower discount rates).

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Dermatology Company Transactions

In the past few years there have been a number of transactions in the dermatology space, ranging from US$150m to upwards of US$8.4bn for single indications.

Target Company	Acquirer	Year	Country	Transaction value (US$m)*	Lead Indication (s)	Lead Indication Product Stage	Lead Product(s)
Medicis Pharmaceutical	Valeant	2012	US	2,600	Acne	Market	Solodyn; Zianna
Trius Therapeutics	Cubist	2013	US	812	Bacterial skin infections	NDA	Tedizolid
Galderma	Nestle	2014	Switzerland	3,600	Various	Market	Various
Durata Therapeutics	Actavis	2014	US	822	Bacterial skin infections	Market	Dalvance
PreCision Dermatology	Valeant	2014	US	500	Acne; Atopic Dermatitis	Market	Locoid; Hylatopic; Clindagel; BenzEFoam
Aqua Pharmaceuticals	Almirall	2014	US	403	Acne; Dermatitis; AK	Market	Monodox; Cordran; Fluoroplex; Xolegel
Cubist	Merck & Co.	2015	US	8,400	Bacterial skin infections	Market	Cubicin
Poli Group	Almirall	2015	Switzerland	386	Nail diseases; Rosacea	Market	Ciclopoli; Sililevo; Zeloglin
Anacor	Pfizer	2016	US	5,200	Atopic Dermatitis	NDA	Eucrisa
Astellas (division)	LEO Pharma	2016	Japan	725	Atopic Dermatitis	Market	Protopic
Vitae Pharmaceuticals	Allergan	2016	US	639	Psoriasis; Atopic Dermatitis	Ph 2	VTP-43742; VTP-38543
Creabilis	Sienna	2016	Italy	150	Psoriasis; Atopic Dermatitis; Pruritus	Ph 2	SNA-120; SNA-125
Bayer (Division)	Leo Pharma	2018	Germany	750	Various	Market	Various
Allergan (Porfolio)	Almirall	2018	Ireland	650	Acne; Atopic Dermatitis	Market	Aczone; Tazorac; Azelex; Cordran
Median				**738**			
Average				**1,831**			
**Total Transaction value*							

Source: Bloomberg LP, Company Announcements, EHL estimates

These transactions indicatively demonstrate the significantly large potential upside possible for BOT, every transaction listed would imply multiples of the company's current valuation.

The table highlights the significant valuations players in the market are willing to pay for companies possessing a single product or products with desirable indications, such as:

- Acne;
- Atopic Dermatitis; and
- Bacterial skin infections, among other conditions

We specifically note Pfizer's acquisition of Anacor, a company BOT executive chairman and President Vince Ippolito was involved in. Pfizer paid US$5.2bn (~A$7.2bn) for the company which had a product targeting Atopic Dermatitis. This demonstrates the market understands the demand for new products. A commercial outcome like this for BOT would value the company at over $7.00/sh.

These transactions also highlight the major value uplift possible as the company passes through clinical study phases, with increasing valuation paid for the later stage products.

Broadly speaking there is clearly interest in the sector, with the transactions listed above amounting to over US$25 billion. These transactions demonstrate a potential pathway for BOT whereby a takeover by a larger dermatology company or broader pharmaceutical company is possible.

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Listed Peers

We explore listed peers below:

Name	Ticker	Background	Lead Indication	Lead Product Stage	Mkt Cap	EV
Telix Pharmaceutical	TLX	TLX is developing diagnostic and therapeutic products using molecularly taregted radiation (MTR)	Oncology	Phase II	1,493	1,443
Imugene Limited	IMU	IMU is a immuno-oncology company developing immunotherapies that seek to activate the immune system of cancer patients.	Oncolgy	Phase II	1,447	1,244
Mesoblast Limited	MSB	MSB develops allogeneic cellular medicines for treatement of severe and life-threatening inflamatory conditions	Inflammatory Diseases	Registration	1,281	1,204
Immutep Ltd	IMM	IMM is developing LAG-3 related immunotherapeutic products for the treatment of cancer and autoimmune diseases.	Oncology	Phase II	434	373
Paradigm Bio.	PAR	PAR is looking to develop and commericalise Pentosan Polysulfate Sodium for the treatment of pain associated with musculoskeletal disorders	Osteoarthritis	Phase III	409	338
Next Science Limited	NXS	NXS is commercialising its proprietary Xbio technology to resolve the issues caused by biofilms	Antimicrobial	Market	294	281
Opthea Limited	OPT	OPT is developing therapies for treatment of highly prevalent and progressive retinal diseases.	Retinal Diseases	Phase II	439	236
Recce Pharmaceutical	RCE	RCE is developing and commercialising new classes of synthetic ani-infectives.	Anitbiotics	Pre-clinical	158	137
Actinogen Medical	ACW	ACW is developing treatments for cognitive impairement associated with neurologucal diseases amenable to modifications of raised cortisol levels inside brain cells	CNS Diseases	Phase II	138	124
Prescient Ltd	PTX	PTX is a oncology company developing personalised medicnes for cancer, including targeted and cellular therapies	Oncology	Phase II	116	100
Chimeric Therapeutic	CHM	CHM is a cell therapy company focused on bringing the cell therapy to more patients with cancer	Oncology	Phase I	111	88
Patrys Limited	PAB	PAB is developing its deoxymab platform of cell-penetrating antibodies as therapies for a range of different cancers	Oncology	Pre-clinical	71	64
				Median	**352**	**259**
				Mean	**532**	**469**
Botanix Pharma Ltd	BOT	BOT is a clinical stage synthetic cannabinoid pharmaceutical company developing a number of dermatology and antimicrobial products	Dermatology	Phase II	78	50

Source: Bloomberg LP, Company Announcements, EHL estimates

Peer comparisons are difficult as there are no domestic dermatology companies. As a broader analysis, we have compiled small-to-mid sized clinical stage biotechnology companies. These peers are indicatively useful in showing the huge potential possible for BOT.

There is a clear market disconnect between BOT and most of these listed peers. We note a number of these companies are targeting similarly large markets and are at similar or earlier stages of clinical development yet attract market valuation multiples higher than BOT. This is shown by the fact BOT trades at a 80% discount to the median enterprise value of the peer set, even the smallest company in the table, Patrys Ltd (PAB), trades at a 28% premium to BOT despite the company's lead product being in pre-clinical stage of development.

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Downside Valuation

Rounding off our analysis we can explore the worst-case scenario, this downside outcome would imply BOT's clinical programs do not succeed.

The company is backed by circa $0.03/sh. (Fully diluted) in cash & unpaid capital. This is significantly outweighed by the potential upside in our $0.17/sh. Price Target. This analysis highlights the asymmetrical nature of the investment opportunity present.

Price Target and Recommendation

Our $0.17/sh. Price Target per our analysis is based on the current portfolio of development programs.

The staged success of these programs should de-risk the assets and translate into progressively higher valuations, outlining the potential upside beyond our current price target.

The risks surrounding unsuccessful outcomes and outright failures of these programs further drive our **Speculative Buy Recommendation.**

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Company Background

Botanix Pharmaceuticals Ltd (BOT) is a clinical stage synthetic cannabinoid pharmaceutical company developing a number of dermatology and antimicrobial products. Founded in 2016 the company is headquartered out of Perth with most operations in Philadelphia (United States) and Phoenix (United States).

botanix PHARMACEUTICALS

Source: Company website

BOT has two separate CBD development platforms:

- Dermatology (target indications: acne; rosacea; and atopic dermatitis); and
- Antimicrobial (target indication: nasal decolonisation in haemodialysis patients)

The company leverages the unique anti-inflammatory, immune modulating and antimicrobial properties of synthetic cannabinoid, in conjunction with an exclusively licensed proprietary drug delivery system Permetrex™.

These various products are in varying stages of development:

	Pre-clinical	Phase 1	Phase 2	Phase 3	Status
BTX1503 Acne					Planning underway for Ph3 studies
BTX1801 Antimicrobial					Ph2b planned for early CY22
BTX1702 Rosacea					Patient enrolment for Ph1b has started
BTX1204A Atopic Dermatitis					Expanded Canine POC study planned for 2Q'2021
New Indications Assement					Activel targeting new canine indications for clinical Dev.
Permetrex Delivery Technology					Ongoing project work and internal development

Source: EHL Estimates, BOT Presentations

We discuss these in detail throughout this report.

Botanix Pharmaceuticals Ltd

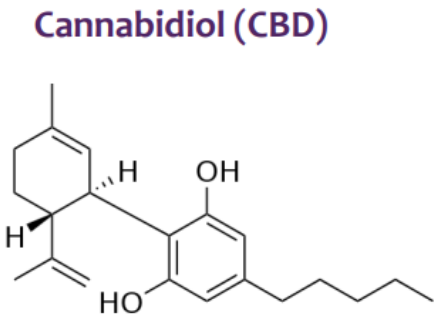
(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Cannabidiol (CBD)

Cannabidiol (CBD) is the base active ingredient across all products in development. Studies completed by BOT show synthetic CBD is well suited to treat a number of skin diseases and infections. We explore these exciting properties in detail below.

Cannabidiol or "CBD" is the second most active ingredient in cannabis, and is one of 114 identified cannabinoids. CBD itself was first isolated from hemp in 1940, its fine structure (shown below) was later defined in studies during the 1960s.



Source: BOT Presentation

Not to be confused with cannabis, CBD lacks intoxicating properties and is non-psychoactive.

The CBD market is large, currently estimated at US$3.5bn and is expected to grow to over US$13bn by 2028.

CBD is well known by most people, with the majority sold as supplements and health products. There is a gap in the market in terms of more formally regulated and clinically validated products. This is likely the result of regulation and connected bureaucracy of CBD through most of the 20th century, it is only in the last few years where deregulation has allowed research to be undertaken in a significantly simpler fashion. BOTs experience in CBD research leaves it well placed to take advantage of the growing market for CBD products.

Therapeutic Properties

The interest in CBD comes from its numerous ascribed therapeutic properties. Despite the long list, many remain anecdotal and under researched requiring further clinical studies to validate. Notwithstanding, the field of research is expanding. GW Pharmaceuticals made headlines in 2018 when it received FDA approval for the first CBD based drug, EPIDIOLEX, a prescription drug to treat seizures associated with: Lennox Gastaut syndrome, Dravet syndrome, or tuberous sclerosis complex. The significance of this new drug was shown in late 2020 when Jazz Pharmaceuticals acquired GW Pharmaceuticals for US$7.2bn (~A$9.9bn).

In this research we will focus on the several unique properties BOT has identified from synthetic CBD, shown across various pre-clinical and clinical studies completed by the company. We discuss these studies in detail throughout this report.

BOT intends to leverage these various properties through its development pipeline to treat a number of skin conditions and infections.

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Anti-inflammatory / Immune modulating Properties

Research has shown CBD has a number of anti-inflammatory and immune modulating effects. These include:

- **Interleukin 6 (IL-6)** – CBD inhibits a key cytokine which affects skin barrier disfunction;
- **Interleukin 13 (IL-13)** – CBD attenuates a well-known cytokine which drives the inflammatory response; and
- **P38 MAPK** – CBD inhibits a pathway which disrupts the signalling driving the body's response.

We discuss further throughout this report how BOT leverages these properties to address specific conditions.

Antimicrobial Properties

Research conducted by BOT has shown CBD possesses novel antimicrobial properties. This research has the potential to address issues in the increasingly concerning area of bacterial resistance.

Some of the properties identified by BOT include:

- CBD is active against all tested Gram-positive bacteria (including: Staphylococcus aureus, methicillin-resistant S. aureus), and possibly more significantly a subset of Gram-negative bacteria (including drug resistant neisseria gonorrhoeae);
- CBD has remarkable activity against bacteria without inducing resistance; and
- CBD disrupts the bacteria's biofilm protective cover

We discuss these properties as well as the mechanism of action in further detail in Appendix A.

Safety

In the dermatology world, safety is key – products that aren't safe or come with major side effects (redness, burning, stinging or any other inflammation) severely hinder the products ability to commercialise.

CBD has shown to be safe. This property is a key pillar in the investment thesis behind BOTs pipeline of products.

This high level of safety has been shown by BOT's clinical research and as well as in other published journals.

Examining literature on the only FDA approved CBD drug, EPIDIOLEX, we only see the emergence of some adverse effects relating to transaminase elevation and hepatic injury for 10 and 20 mg/kg/day (620mg/day, 1240mg/day). This however remains of dispute to whether it is the result of CBD. Looking at broader scientific literature, there is almost no described adverse effects to CBD with most studies describing CBD as being well tolerated – some of these studies having dose ranges as high as 6,000mg/day.

BOTs own clinical studies have demonstrated CBD possesses an excellent safety profile, of the minor adverse effects noted they remain both minimal and likely unrelated to CBD.

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Anecdotally, in GW Pharma's EPIDIOLEX new drug application (NDA) we see the FDA granted the company a number of exceptions around safety, this was highlighted by nearly five pages of post marketing requirements requesting basic safety studies – an indirect way of saying the FDA is quite confident that CBD is safe for humans.

In BOTs case, this safety is further strengthened on the basis all its products are topical. Significantly more topical drug is required to be absorbed into the body vs oral or injectable drugs.

Synthetic

BOT utilises synthetic CBD rather than naturally extracted. The benefits of this include:

- Higher quality / consistent quality;
- Easier to mass produce and scale production; and
- Likely more cost effective

BOT has supply agreements for synthetic CBD with a major manufacturer, Purisys. These agreements will allow BOT to meet its requirement for existing and future commercial supplies of synthetic CBD.

Regulation

CBD for most of recent history has been regulated the same way as cannabis despite lacking its psychoactive properties.

Up until 2018, the US Federal Government severely restricted research on CBD with tough regulation and bureaucracy. US Federal law further prohibited the importation of and intra- and interstate trade in cannabis.

The 2018 Farm Bill removed hemp and hemp extracts (including CBD) from the controlled substances act (CSA). The unaddressed grey area on synthetic CBD was also rectified by the DEA, where the agency outlined that synthetic CBD was also no longer a controlled substance.

These regulatory changes mean BOT is not burdened by any drug regulation relating to the manufacturing, distribution and eventual possible sale of its products in the US.

Botanix Pharmaceuticals Ltd

(BOT $0.075) Speculative Buy – Initiation of Coverage

EUROZ HARTLEYS

Permetrex – Delivery Platform

Permetrex™ is one of BOTs key assets, underpinning the company's pipeline of drug programs through a unique skin delivery technology.

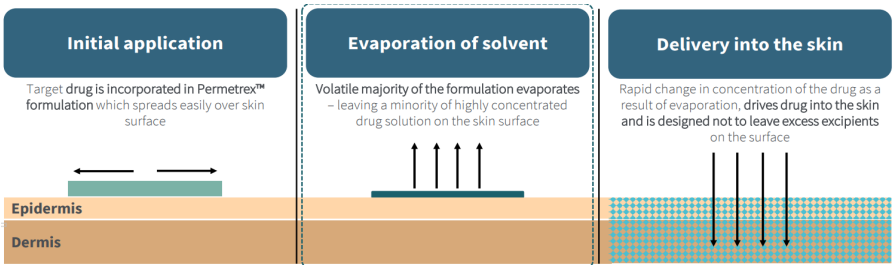
The whole concept with a drug delivery system is to get the drug across the skin barriers, first the epidermis then the dermis.

Typical topical drugs will use a permeation enhancer, a chemical the drug is dissolved into, this is designed to open up the pores of the skin and allow the drug to enter; although this sounds fine in theory, most enhancers use high levels of alcohol and/or petroleum derivatives, ingredients which irritate and dry out the skin.

The Permetrex™ technology enables the delivery of very high doses of drug into the layers of the skin without using permeation enhances, preservatives, or irritating levels of alcohol/petroleum derivatives.

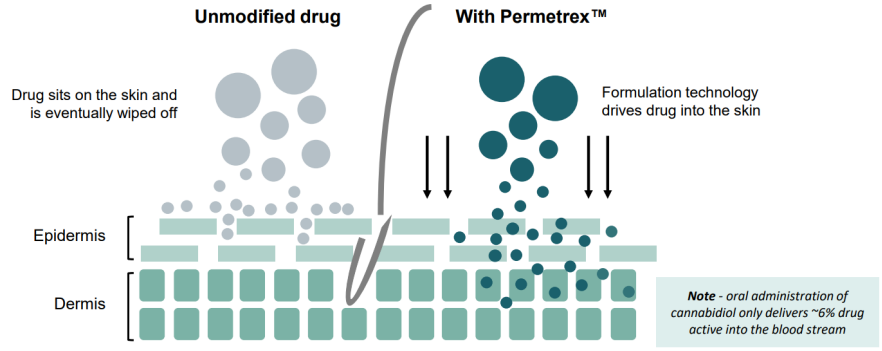
This more effective delivery system provides BOT a platform to administer drugs in a non-irritating fashion, one that does not use chemicals that dry out the skin or cause serious allergic reactions.

The mechanics of the technology is annotated below:



Source: BOT Presentation

The technology works by using a volatile formulation that enables the delivery of a high concentrations of active drug without leaving any residue behind.



Source: BOT Announcement

Botanix Pharmaceuticals Ltd

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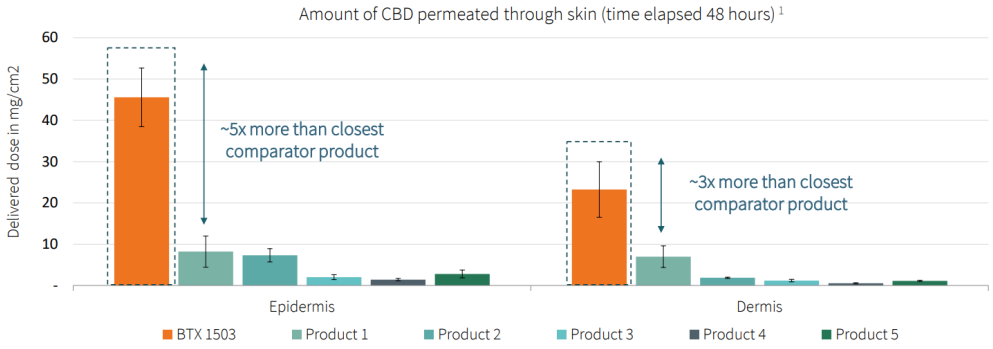
The key benefits beyond the 'gentle' properties of the formulation is the technology's incredible ability to hold and deliver high doses of drug into the skin – An extremely important property when dealing with CBD.

In 2019, BOT commissioned an independent comparative analysis of CBD products to test the effective dosage of active drug delivered. Leading US Skin testing laboratory, Tioga Research, showed BOTs product (BTX1503 in this case) delivered ~5x more drug into the epidermis and ~3x more into the dermis than its closest comparator product. This shown below.



Source: BOT presentation

Licensing

BOT has licensed full exclusivity of Permetrex™ over all dermatology and antimicrobial applications. The company initially only licensed the technology for CBD applications, this was later expanded in 2017.

Opportunities Beyond CBD

The comprehensive licensing arrangement BOT has over Permetrex™ opens up additional commercial avenues, the company could potentially partner, license or outright buy a drug (possibly unrelated to CBD) to port into the Permetrex™ platform.

The company stated in its recent June quarterly they are reviewing a number of opportunities to either:

- Rescue stranded assets that are currently unable to deliver enough active drug to the target site in the skin; or
- Which may benefit from the improved safety, efficacy and/or cosmetic elegance of the Permetrex™ technology

BOT further stated these opportunities are expected to be complimentary to the company's existing pipeline.

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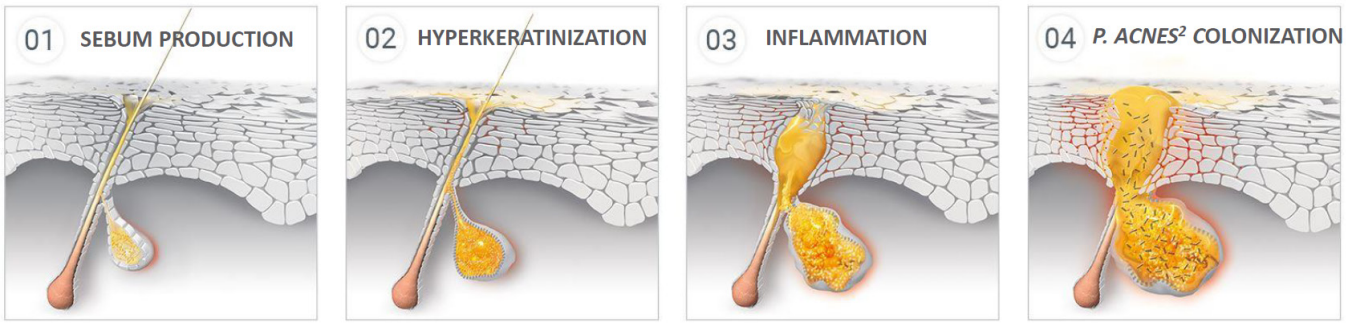
BTX1503 – Acne

The BTX1503 program is being developed by BOT for treatment of moderate to severe acne. Planning is currently underway for a phase 3 clinical study; the company is looking to optimize the study using results from the upcoming BTX1702 phase 1b clinical study which will utilize a higher dosage of CBD.

Acne

Acne is a prevalent skin condition affecting ~630 million people globally. Primarily affecting adolescents, acne occurs when dead skin cells and oil from the skin clog hair follicles, this is followed by bacteria proliferation and inflammation. This progression shown below:



Source: BOT presentation

The condition typically affects skin with a high number of oil glands, areas such as the face, upper chest and back.

Common symptoms of acne include:

- Whiteheads (close plugged pores);
- Blackheads (open plugged pores);
- Small red, tender bumps (papules);
- Pimples (Pustules);
- Large, solid, painful lumps under the skin (Nodules); and
- Painful, pus-filled lumps under the skin (cystic lesions)

BTX1503 Mechanism of Action in Acne

BTX1503 works against acne through four mechanisms, leveraging synthetic CBDs key properties. These being:

1. **Normalizes sebum product** – CBD inhibits lipogenesis and sebocyte proliferation in respond to "pro-acne" agenets (andorgents);
2. **Inhibits Keratinocyte Hyperproliferation** – CBD's antiproliferative effects mediate through PPAR agonism;
3. **Broad Anti-inflammatory effects** – CBD Inhibits P38 MAP kinase dependent inflammatory responses in addition to inhibiting: IL-1, IL-6, IL-8 and IL12; and
4. **Antimicrobial** – CBD possesses broad spectrum antimicrobial properties, killing gram-positive bacteria (including drug resistant strains such as MRSA), and a select number of gram-negative bacteria

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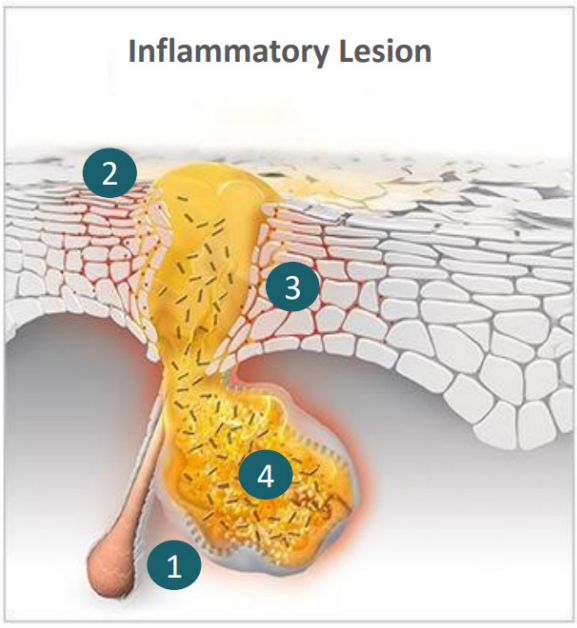
These points of action are annotated on the diagram below:



Source: BOT Presentation

Product landscape

There are a number of existing treatment options for sufferers of moderate to severe acne, out of the treatments available the more effective ones carry a greater number of side effects, some not suitable for long term use either. This highlights the clear demand for new solutions that delivery comparably strong results with minimal side effects.

Clinicians will typically look to prescribe topical medication as an initial treatment, topical drugs typically come with lower risks (vs oral or injectable treatments). Topical acne treatments include:

- **Retinoids and retinoid-like drugs** – Creams, gels, or lotion which contain retinoic acids or tretinoin. Effective for moderated acne, side effects include increasing skin sensitivity to sunlight (photosensitivity), skin irritation (peeling, stinging, redness, swelling), as well as not being suitable during pregnancy (Can cause birth deformities);
- **Topical Antibiotics** – Work by killing bacteria on the skin, reducing redness and inflammation. Topical antibiotics aren't usually recommended alone, and are typically combined with other treatments (such as benzoyl peroxide). Side effects are mild with the most common side effect being dryness. Topical antibiotics are not recommended for repeated or long term use due to growing issues around bacterial resistance; and
- **Azelaic acid and salicylic acid** – These work by removing the outer layer of the skin. These treatments are effective for mild to moderate acne. Side effects include skin irritation (tingling or stinging, itching, peeling skin, hives) as well as dryness.

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Should these treatments not work, clinicians will typically move to prescribe oral or injectable treatments. These include:

- **Oral antibiotics** – These are more powerful than topical antibiotics, they face the same issues around developing antibiotic resistance and hence aren't a suitable long-term treatment; and
- **Isotretinoin** – Commonly known by its commercial brand name 'Accutane', Isotretinoin is an oral drug used to treat severe acne. Although effective, the drug is usually only prescribed if other treatments don't work due to the number of side effects and connected risks. Possible side effects include IBS, depression, and severe birth defects. All people receiving isotretinoin must participate in an FDA-approved risk management program.

The existing product landscape highlights a clear gap in the market, a gap we believe BTX1503 can address. Existing effective solutions either have some degree of side effects and risks or are not suitable for long term use (in the case of antibiotics). This is visualized in the table below:

Methods of Action	BTX1503	Retinoids	Antibiotics	Azelaic/ Salicylic Acid	Isotretinoin
Reduces Excessive sebum (Skin oil) production	✓				✓
Anti-inflammatory	✓	✓			✓
Anti-Bacterial	✓		✓		✓
Topical	✓	✓	Varies	✓	
Suitable Long Term	✓	✓		✓	
Minimal Side Effects	✓	✓	✓	✓	

Source: EHL Estimates

Clinical Studies

The BTX1503 program is one of BOTs most advanced having completed a phase 2 clinical study in 2019. At the same time the journey has been a complicated one with a few bumps along the way, however, as we discuss below the devil is in the detail. We see a solid underlying program with significant potential – something we believe the market has completely discounted.

Phase 1a clinical trials done in early 2017 were successful in showing BTX1503 is tolerable and safe. A follow up phase 1b clinical study confirmed these findings, further showing encouraging early efficacy results.

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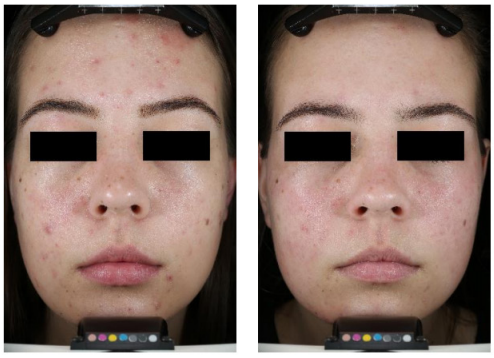
These early efficacy results shown below:

Phase 1b acne patient study data

Patient satisfaction high due to the rapid onset of improvement and significant effect on inflammatory lesions

Photographs of acne study patient before and after treatment[1]



Baseline Day 28

Patient result

57% reduction in inflammatory lesions

15% reduction in non-Inflammatory lesions

Patient satisfaction report was

"Much Better"

Source: BOT Presentation

The phase 2 clinical study is where we believe the devil lies in the detail. The study results were announced in late 2019, missing its headline primary endpoint, however, delivering excellent safety & efficacy data – the analysis of this data is key, as discussed below.

The design of the study was follows:

Study Design	Endpoints
• **5 dose groups: 368 subjects in total** – 5% twice a day (BID): 92 subjects – 5% once a day (QD): 92 subjects – 2.5% once a day (QD): 92 subjects – Vehicle once a day (QD): 46 subjects – Vehicle twice a day (BID): 46 subjects • **36 US and Australian dermatology sites** – 11 sites in Australia – 25 sites in USA • **Children (> 12 years) and adults** • **Moderate to severe acne patients** • **Treatment Period 12 weeks**	• **Primary endpoint** – Absolute change (by number) from Baseline to Week 12 in inflammatory lesion count • **Secondary endpoints** – Absolute change (by number) from Baseline to Week 12 in non-inflammatory lesion count – Change (by percentage) from Baseline to Week 12 in inflammatory and non-inflammatory lesions – Proportion of patients with clear/ almost clear and a 2 grade reduction from Baseline IGA at week 12 • **Safety** – Adverse events local tolerability

Source: BOT Presentation

Analyzing the results, we see the active arms in both regions (Australia and US) demonstrated solid efficacy in the primary endpoint, inflammatory lesions change from baseline, the results showing up to a 13.2 number reduction (43.1%) in inflammatory lesions – **this is a comparable reduction to other FDA approved products (Epiduo® ~42% reduction, Aczone® ~38% reduction).**

However, the study results failed to be statistically significant due to an abnormally high vehicle response. Specifically, the US vehicle arm of the study had almost twice the response of the Australian (45.9% vs 26.4%), significantly skewing overall results. This shown below.

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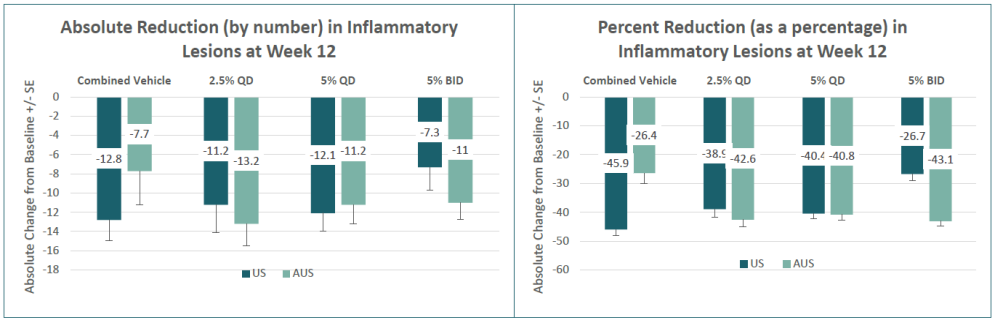


Source: BOT Presentation

The Australian clinical sites in solidarity showed statistically significant improvements in reduction of inflammatory lesions, a statistical success, whereby the BTX1503 BID showed a 43.11% reduction with a p-value <0.05.

Exploring deeper into the issue, BOT noted the execution of the study protocol was consistent across and within geographies, one of the only differences between geographies being the manufacturing process.

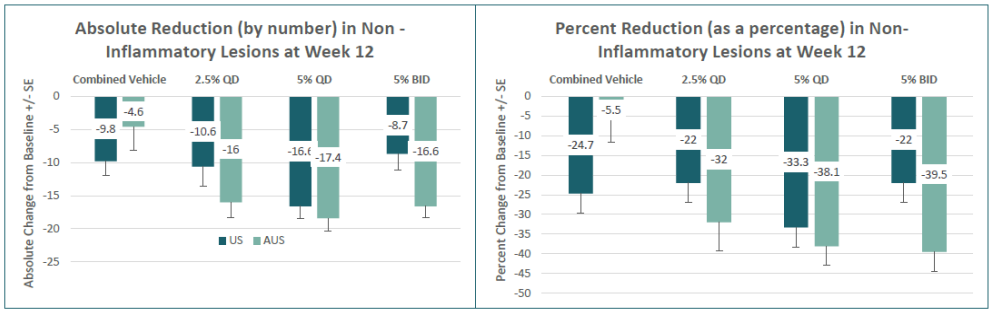
BOT notes these manufacturing issues were the result of three factors, all of which have since been rectified. This detailed below.

	Phase 2 Study Structure	Current Position / Solution
Regulatory	• DEA regulation previously restricted production, transport and manufacturing	• No longer applicable, DEA de-schedule CBD
Sourcing	• 3 CBD manufacturers	• Single CBD manufacturer (Purisys)
	• Multiple suppliers for Permetrex™ formulation inputs	• Permetrex™ key formulation inputs and manufacturing undertaken by global #2 chemicals manufacturer
Manufacturing	• 11 batches manufactured in two sites in Australia and US	• Large scale manufacturing at single site
	• Pilot scale manufacturing	• Commercial scale

Source: BOT Presentation

The studies secondary endpoint, reduction in non-inflammatory lesions, faced similar abnormal US vehicle response. Whereby the US vehicle was almost 4x more responsive than the Australian arm (24.7% vs 5.5% reduction in non-inflammatory lesions).

Although, the secondary endpoint did achieve statistical significance, with the BTX1503 5% QD group showing a 34.99% reduction in non-inflammatory lesions vs the vehicles 19.08% response (P-value=0.007). This separation is even greater when examining the Australian arm in solidarity, with the subset showing a 38.1% reduction vs a 5.5% vehicle response (p-value<0.002). These results shown below.



Source: BOT Presentation

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A further takeaway that was likely missed amongst the headline result was the extremely positive safety and tolerability data. The study showing all doses of BTX1503 were very safe. BOT noted there were:

- No 'Serious Adverse Events' reported; and
- Extremely low incidence of 'Adverse Events'

The most common adverse event was an upper respiratory infection (common cold) not related to the treatment. The company further notes, out of the 368 subjects, only 3 withdrew due to a treatment related adverse event – none of which were in the BTX1503 5% QD group.

Subsequent to all of this, in July of last year BOT successfully completed an End of Phase 2 meeting for BTX1503 with the FDA. The FDA's feedback highlighted BTX1503's excellent safety profile by allowing several safety waivers normally required for dermatology drug registration. The company further stated the two parties reached an agreement on the required co-primary efficacy endpoints for the planned phase 3 clinical studies, these being:

- Absolute change from baseline in inflammatory and absolute change from baseline in non-inflammatory lesions at week 12; and
- Proportion of patients with an Investigators Global Assessment (IGA) of "Clear" or "Almost Clear" and at least 2-grade improvement in IGA from baseline at week 12

BOT comments that the timeline of the BTX1503 phase 3 study is under review, pending results from BTX1702 which should provide the company with supporting information to help design its planned phase 3 study.

The significantly higher active drug dosage used in BTX1702 study may provide the company further data around optimizing its phase 3 dose ranges, we note the clinical success seen with similarly high doses in the recently completed BTX1801 phase 2a study.

We anticipate the phase 3 study will commence late next year and run for around 12 months, with a data read out likely occurring in late CY'2023.

Inline with our analysis above, we form opinion that should the vehicle response issue be resolved in this next study, that the results of this planned phase 3 look promising on the basis similar efficacy results are replicated.

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Market Opportunity / Forecasts

The US Acne market is worth an estimated US$5.1bn, making it one of BOTs largest target markets. The US is the centerpiece of the global pharmaceutical market, accounting for a large majority of global sales. As a result, throughout this research we remain focused on the US market.

BOT is targeting the prescription drug market for moderate to severe acne sufferers. There are an estimated 50 million people who suffer from acne in the US making it one of the most common skin conditions in the country; roughly 10 million of these are moderate-to-severe acne sufferers.

There are currently over 2 million active and diagnosed acne patients under health care professional care, with circa 22 million total prescriptions in 2019. Up to two thirds of prescriptions are for topical medications (the balance for oral).

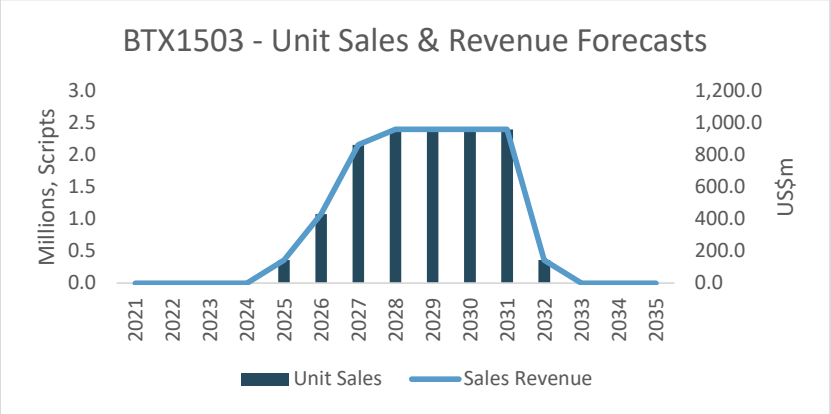
We have modelled potential sales and cashflows as part of our analysis, we assumed the following in building up our model for BTX1503:

- 8 Year economic period (5yrs defined exclusivity + 3 additional yrs.);
- 2 million patient prescribers base with 12 scripts per year;
- 10% Peak market Share;
- US$400/script, no price escalation;
- 60% peak gross margin (Inc. COGS, Marketing, etc); and
- Commercial launch in 2025

We further assume the following remaining development capital:

- Phase 3 clinical study: US$20m; and
- NDA: US$2m

We model unit sales through applying a adoption curve to our peak forecasted market share, adding unit pricing we model unit sales and revenues as follows:



Source: EHL Forecasts

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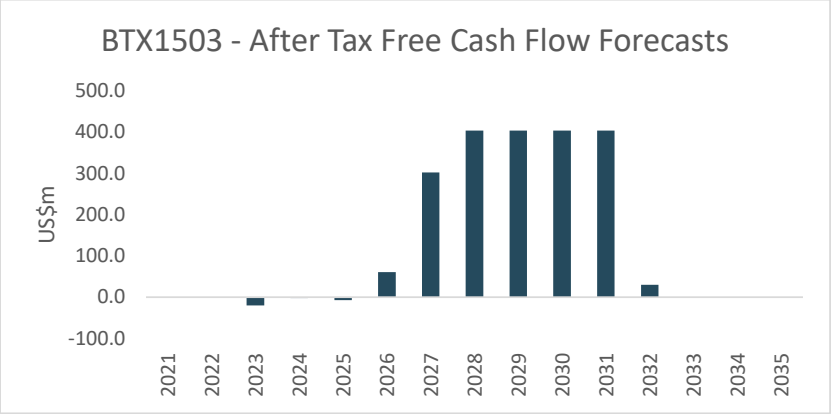
On our conservative assumptions we forecast BTX1503 could generate peak sales nearing US$1 billion per annum, there is clearly scope for higher sales if the product can achieve greater market share and pricing (such outcome would constitute a blockbuster drug).

We can model potential after tax free cash flow generation through applying our forecasted margin, taxes, and remaining development capital. As shown in the chart below, we anticipate BTX1503 could generate circa US$400 million in annual free cashflows.



Source: EHL Forecasts

This sort of analysis highlights the huge potential in the BTX1503 program if validated clinically and commercially successful.

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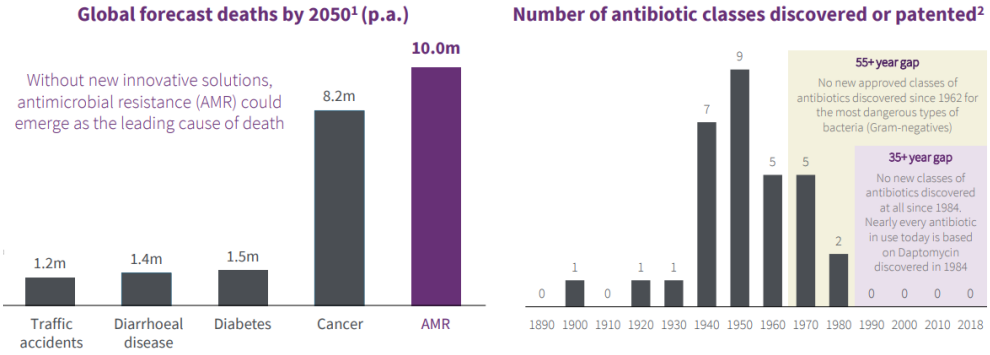
BTX1801 – Antimicrobial

The BTX1801 program is being developed by BOT as a novel antimicrobial drug. The company looks to leverage the unique properties of CBD to develop a new class of drugs that could potential address some of the emerging issues in antimicrobial resistance. The program recently completed a successful phase 2a clinical study, with an expanded phase 2b in planning.

Antimicrobial Resistance

There is growing concerns around overuse of antibiotics and the emergence of antimicrobial resistant bacteria.

The Review on Antimicrobial Resistance stated in a recent report that without new solutions, antimicrobial resistance could grow to become the leading cause of death in the world; killing an estimated 10 million people per year by 2050.



Source: BOT Presentation

The concern comes from both the increasing miss-use of antibiotics as well as the overall lack of new innovation in the space. There have been no new classes of antibiotics discovered in over 35 years (since 1984), and more worrisome, no new Gram-positive targeted antibiotic classes discovered in over 55 years (since 1962).

Target Indication

A product like BTX1801 could be applied to a wide variety of conditions, BOT has indicated they are initially targeting nasal decolonisation in haemodialysis patients.

We view this as an optimal initial market, one where there is a clear clinical demand, no existing or substitute products in the market, and a large commercial potential. A successful commercial launch could further act as a springboard for BOT to enter other indications and markets.

Haemodialysis (or simply, dialysis) is an ongoing therapy that takes over the key functions of the kidneys, removing waste materials from the blood. The process is required for sufferers of chronic kidney failure, a condition where a patient's kidneys aren't working properly.

To access the blood, about 80% of haemodialysis patients start out with a central venous catheter which is generally replaced after 12 months by a 'fistula' or graft access port in the arm. Patients will typically undergo dialysis 3 times per week.

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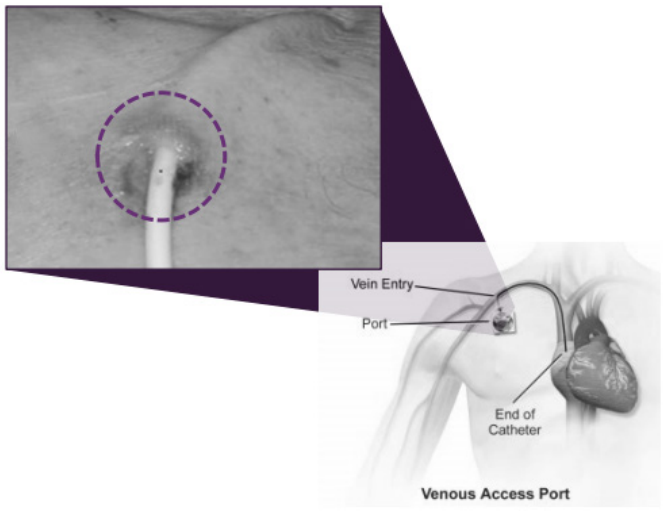

Source: BOT Presentation

Haemodialysis patients are at a high risk for bloodstream infections due to the frequent use of these catheters to access the blood stream. Studies have found that the risk for central venous catheter-related complications were as high as 30% and 38%, at years 1 and 2 respectively. In these patients, infection is a leading cause of death, with 20-40% of haemodialysis patients eventually dying from an infection.

In the US alone, there is more than 468,000 patients currently receiving dialysis, with more than 100,000 new patients added annually. The central venous catheter population numbers roughly 160,000 but is responsible for more than 70% of blood infections in the total dialysis population – these would form BTX1801's target user base.

These infections bare a massive burden on the US healthcare system, costing an estimated US$1 billion annual (treatment cost of bacteraemia in haemodialysis patients with central venous catheters).

The stats of the situation are:

- ~60% of staph aureus-related hospital admissions occur within the first year of initiating dialysis therapy;
- The average length of stay is 13 days, with 11.8% of patients being readmitted within 12 weeks of hospitalisation; and
- ~US32k mean cost (per episode) of treating staph aureus bloodstream infections, including re-admissions and outpatient costs.

Current preventative measures are limited, the CDC only recommends disinfecting the catheter hub with appropriate antiseptics prior to accessing it. The issues of this being:

- These anti-septics can degrade the plastic of catheters and are not widely used; and
- If antiseptics enters the lumen (opening) of the catheter, they can potentially cause toxicities to the patient

Further complicating the issue, concerns around antimicrobial resistance and fungal growth mean antibiotic creams or gels are not recommended for catheter sites.

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BOT believes this issue can be addressed with a BTX1801 based nasal decolonisation therapy. The practice of nasal decolonisation is underutilised, however multiple publications demonstrate the utility of nasal decolonisation to prevent bloodstream infections.

Previous studies using mupirocin (an antibiotic) supported this thesis but were never approved.

The antibiotic was evaluated in clinical studies in the 1990s as a potential nasal decolonisation therapy in haemodialysis patients. The studies indicated that mupirocin was able to reduce staph aureus (staph) bloodstream infections by as much as 60-70% among patients undergoing dialysis.

Despite these successful studies, mupirocin's developer GlaxoSmithKline never pursued FDA approval for its use in haemodialysis patients. Since then, the drug has become generic leaving little incentive to pursue approval.

Furthermore, mupirocin is not a suitable long-term solution as a result of the growing levels of bacterial resistance to the drug (As high as 95% in some hospitals).

The CDC even commented on the matter in 2011 saying:

> *"Several studies have demonstrated a reduced risk of [catheter related bloodstream infections] when mupirocin ointment was applied nasally... However, enthusiasm for this measure has been dampened by the rapid emergence of mupirocin resistance observed at some centres and the potential degrading effect that mupirocin has on polyurethane catheter."*

The takeaway:

- There is clearly an absence of solutions; and
- There is historical clinical precedence that a nasal decolonisation treatment reduces bloodstream infections in haemodialysis patients

We believe if BOT can demonstrate BTX1801 has efficacy in line with mupirocin (which it has done on comparable end-points in early studies to date), in combination with the drugs solid safety profile and its long-term suitability (does not develop bacterial resistance) that there is a genuine pathway to market.

The key benefits of using BTX1801 for nasal decolonisation are summarised:

- **Safe** – BTX1801 is safe and well tolerated in the body, a property of the underlying active ingredient, CBD;
- **Long lasting effect** – BOT's studies have shown the bacterial killing effect can be sustained in a proportion of patients without further treatment for up to 3 weeks;
- **Anti-resistance** – No bacteria analysed by BOT over a 28-day period developed resistance to BTX1801 (vs traditional antibiotics that did);
- **Prolonged use** – As a result of the above properties, there is potential for BTX1801 to be used for a prolonged period of time; and
- **Targeted and localised Effect** – BOT's studies have shown very low systemic blood levels of active drug

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We further note, there are a number of applications beyond nasal decolonisation in haemodialysis patients, including nasal decolonisation for the prevention of surgical site infections (SSI's). Some of these future applications could include:

- Skin infections: impetigo and bacterial folliculitis;
- Skin structure infections: diabetic ulcers and wounds;
- Systemic infections; and
- Ocular infections

Regulatory Benefits

There are a number of regulatory incentives provided by the FDA for this area of research. These incentives can possibly accelerate product development and increase the exclusivity period offered, these include:

- **Qualified Infectious Disease Product (QIPD) status** - Extra 5 years (total of 8 years) exclusivity from generic competition; creating attractive economic benefits from FDA approval;
- **Fast Track Status** – Following IND submission, the fast track status allows for increased consultation with the FDA, benefits which de-risk clinical trials and accelerate the development pathway; and
- **Limited Population Pathway for Antimicrobial and Antifungal Drugs (LPAD) status** – LPAD allows for smaller, fewer and / or shorter clinical trials for FDA approval

BOT received (April 2020) QIPD status for BTX1801 in prevention of post-surgical infections, and further intends to apply for the programs for the dialysis indication. These incentives if all granted should allow BOT to accelerate BTX1801's development, reduce its clinical costs and overall increase the product's exclusivity period.

Clinical Studies

BTX1801 is mid-stage in its development having recently completed a successful phase 2a clinical study.

The formulation was completed in late 2017, the drug demonstrated promising results in pre-clinical testing in the following year, showing high bacteria killing power in MRSA.

In 2018, BOT announced ground breaking data in its collaboration with the University of Queensland (UQ).

The study data presented showed CBD's potential to be a powerful broad-spectrum gram-positive antibiotic, confirming BTX1801 can rapidly kill gram-positive Staphylococcus Aureus (Staph) and Methicillin Resistance Staphylococcus Aureus (MRSA). Just as exciting was the low innate resistance frequency of CBD, showing that despite extensive exposure that bacteria did not develop resistance (vs the comparable antibiotic, Mupirocin, which did).

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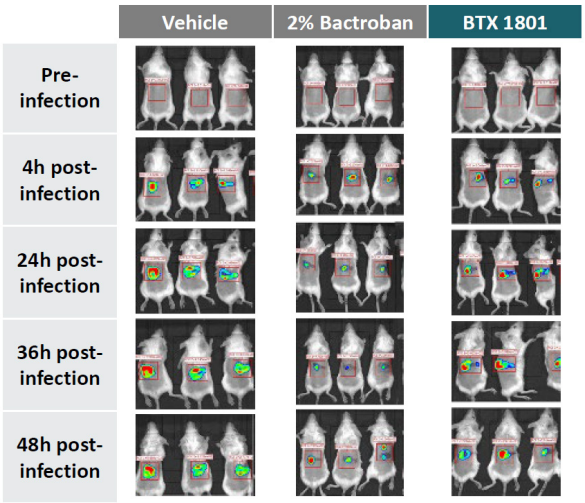
As part of the same research, BTX1801 was also shown to be successful in an animal proof of concept and a biofilm test. The independent testing showed the formulation to be effective in an animal wound model of skin infection (in-vivo mouse model), this shown below.

***In vivo* mouse model**[1]



Source: BOT Presentation

We discuss the data from this UQ collaboration in further detail in 'Appendix A'.

In late 2020, BOT kicked off its phase 2a study to examine nasal decolonization of Staph Aureus. The study design being:

- Double-blind, vehicle-controlled phase 2a clinical study
- 4 dose groups: 66 patients
  - BTX1801 formulation A
  - BTX1801 formulation B
  - Vehicle A
  - Vehicle B
- Sites: single Australia site
- Patients: Adults (+18yrs) with positive nasal staph aureus
- Treatment: Twice daily for a 5-day period

The primary endpoints were safety and tolerability assessments, in addition to the proportion of volunteers carrying Staph / MRSA at day 12. Secondary endpoints included:

- Proportion of volunteers carrying Staph / MRSA at day 8 and 28;
- Nasal recolonization rates of Staph at day 12 and/or 28; and
- Pharmacokinetics (PK) studies on formulation A and B

The study was successful in meeting the targeted endpoints.

The study showed excellent safety and tolerability at doses up to 20% active drug, this especially highlighted by all 66 participants completing the study with no severe adverse events reported.

Good efficacy was shown across all endpoints for both the gel and the ointment arms.

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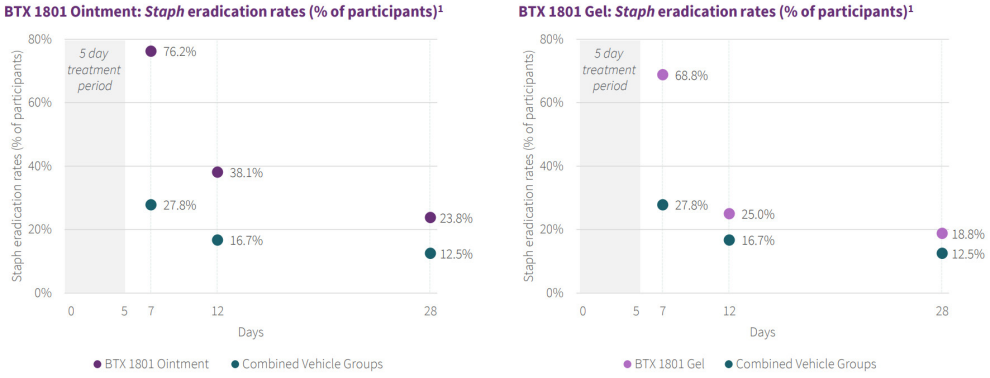


Source: BOT Presentation

Results showed significant eradication of S. Aureus 2 days after the treatment period, with 68.8%-76.2% eradication observed – a significant separation from the combined vehicle group which reported only 27.8%.

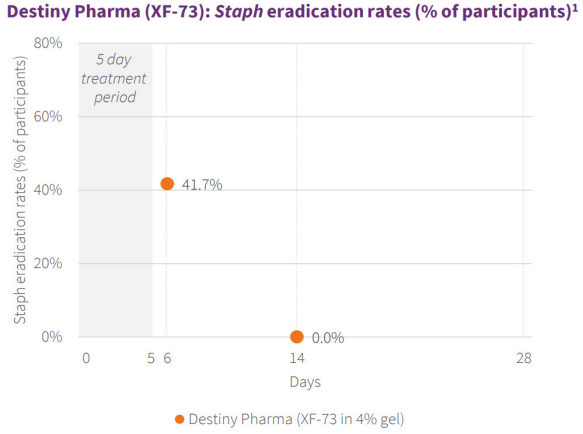
Just as captivating was the significant percentage of subjects who continued to maintain S. Aureus eradication 7 and 23 days after the treatment period, similarly showing wide separation from the vehicle.

It's also important to note that this study:

- Did not include a full body chlorhexidine wash, a procedure that has been used in other clinical studies to remove bacterial reservoirs in other parts of the body (these recolonise the nose); and
- BOT used highly accurate PCR testing to detect bacteria rather than the less accurate culture methods.

These results stack up very favourably against the only FDA approved product for nasal decolonisation, mupirocin (Bactroban), whereby using the exact same study design mupirocin showed efficacy rates around 65-70% vs BTX1801 69-76%. Mupirocin is the drug we explored previously that suffers from growing bacterial resistance concerns, whereas BTX1801 as shown in previous studies has a low innate resistance frequency.

We can go further and compare these results to another antimicrobial being developed for nasal decolonization, XF-73.



Source: BOT Presentation

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The results above show XF-73 has relatively poor efficacy when compared to BTX1801 and a very minimal lasting effect; the drug showing 0% eradication at day 14. Furthermore, this study included a favourable full body chlorhexidine body wash which as we stated above BTX1801 does not include.

These results show the solid clinical utility behind BTX1801.

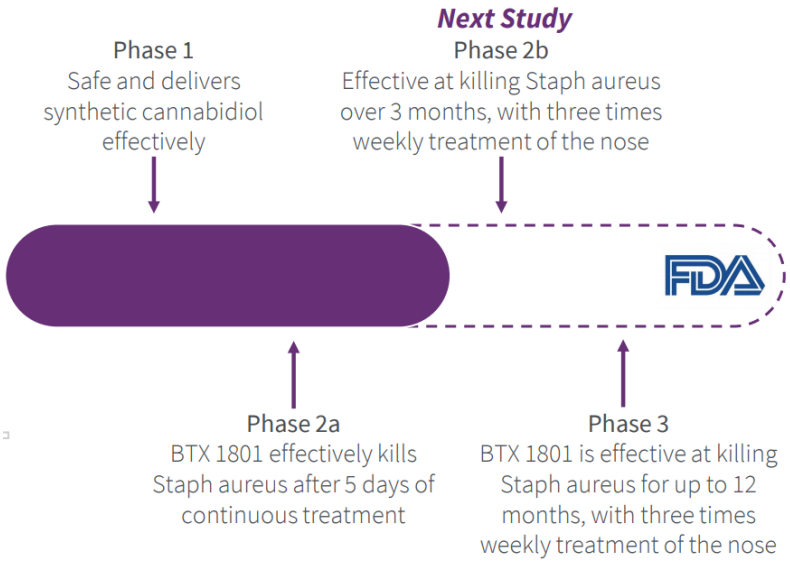
BOT is now intending to follow these results up with an expanded phase 2b clinical study. This study aims to assess how effective BTX1801 is at killing S. Aureus over a 3-month treatment period, with patients treating the nose 3 times per week.

We expect this phase 2b study to be more tailored to nasal decolonization in hemodialysis patients (BOTs target indication). We conservatively anticipate the company will initiate this study in early CY'22, as a result we would expect results in the 2H'CY22.

If successful we would expect the company to initiate a phase 3 study possibly later that year (CY'2022), this one likely larger and longer (at least 12 months).

In line with our analysis above, we have a positive outlook on future study results and the potential application of BTX1801 for its targeted indication. We note studies to date have been demonstrably good, in addition to past literature supporting the concept of the target indication.

We believe if BTX1801 can demonstrate efficacy inline with mupirocin (as it has to date on comaprable endpoints), in combination with the drugs excellent safety profile and no related AMR issues then there is solid grounds on having a sucessful product.



Source: BOT Presentation

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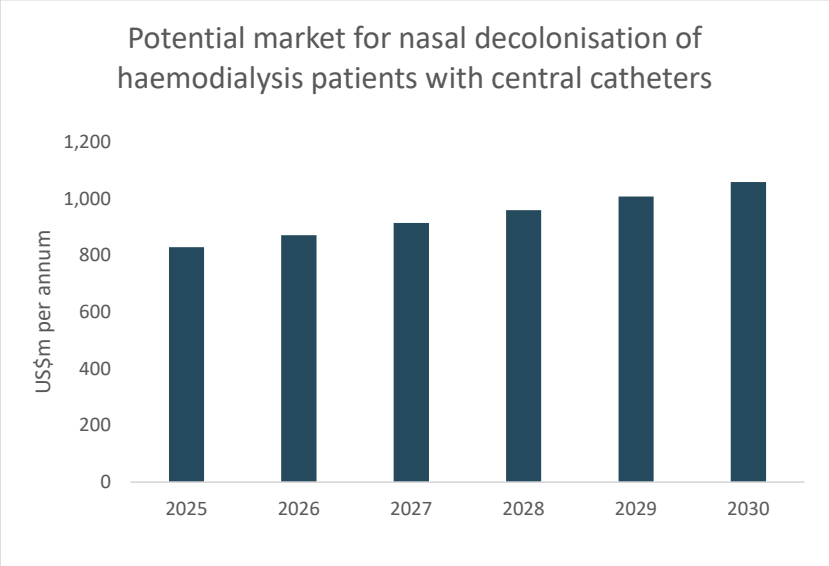
Market Opportunity

There is a significant market opportunity for BOT's initial indication (nasal decolonisation in haemodialysis patients with central venous catheters).

We consider the following:

- The central venous catheter population: ~160,000 patients; and
- A conservative benchmark unit market price, based on GlaxoSmithKline Bactroban (mupirocin) nasal drug: ~US$5,184/pa

Based on this we estimate the market could be worth in excess of US$830 million per annum, this possibly growing to be over a billion dollars when including price escalation. As shown below.



Source: EHL Forecasts, based on assumed 2025 product approval/launch

One could argue a higher unit pricing is feasible based on the significant clinical and economic benefits possible.

Furthermore, we note this is based only on the central venous catheter population, there is an even larger population of patients using other vascular access methods which BOT could expand into later on.

Finally, this market is purely for the current target indication, as noted previously there is a potentially large number of applications BTX1801 could eventually be used for.

We have further modelled sales and cashflows as part of our analysis, we assumed the following in building up our model for BTX1801:

- 11 Year economic period (extended to Include potential QIPD status);
- 160,000 patient prescribers base, 12 scripts per year;
- 40% Peak market Share (No other product options in the market);
- US$430/script (Mupirocin pricing, conservative), 5% pa escalation;
- 60% peak gross margin; and
- Commercial launch in 2025

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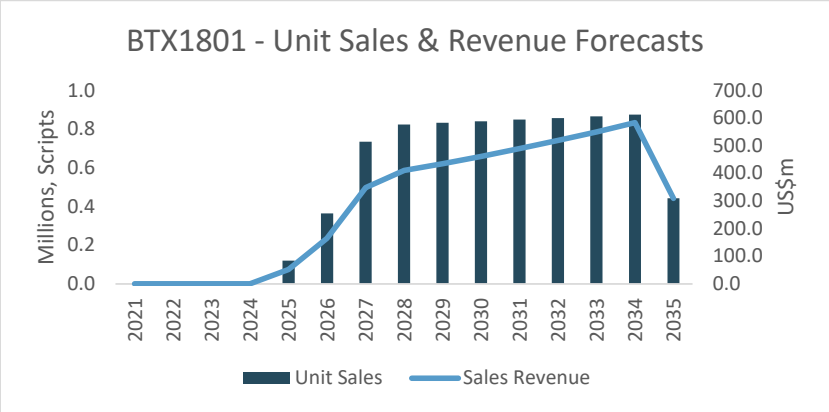
We further assume the following remaining development capital:

- Phase 2b clinical study: US$2.5m;
- Phase 3 clinical study: US$12m; and
- NDA: US$2m

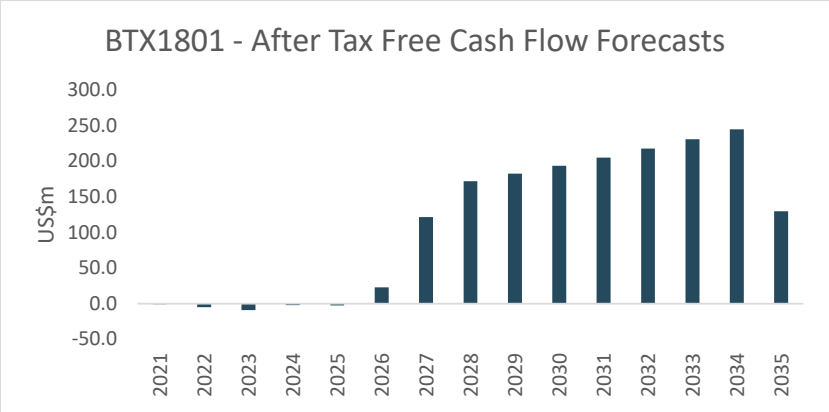
We model unit sales through applying an adoption curve to our peak forecasted market share, adding unit pricing we model unit sales and revenues as follows:



Source: EHL Forecasts

On our conservative assumptions we forecast BTX1801 could generate sales exceeding US$500 million per annum, as stated previously there is scope for higher sales under higher unit pricing. This once again, doesn't even consider other potential catheter populations or even other possible indications beyond this targeted subset.

We can model potential after tax free cash flow generation through applying our forecasted margin, taxes, and remaining development capital. As shown in the chart below, we anticipate BTX1801 could generate circa US$200 million in annual cashflows.



Source: EHL Forecasts

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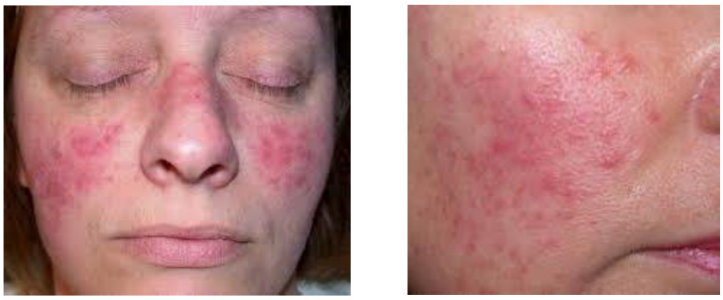
BTX1702 – Rosacea

The BTX1702 program is being developed by BOT as a new therapy for the treatment of Papulopustular Rosacea (or Rosacea for short). The company recently launched its phase 1b clinical study for BTX1702 in June, we anticipate results mid next year, which if successful should see the program roll into a phase 3 clinical study.

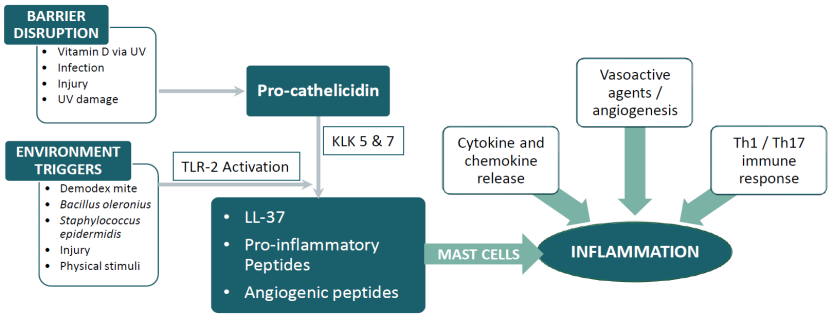
Papulopustular Rosacea (Rosacea)

Papulopustular rosacea or inflammatory rosacea is a chronic skin disease characterized by redness (inflammation) and visible blood vessels in the face. The condition sometimes also produces small, red, pus-filled bumps.



Source: BOT Presentation

The mechanism which drive the development of rosacea are shown below:



Source: BOT Presentation

Sometimes mistaken for acne, rosacea can flare up for weeks or months at a time and then go dormant.

The disease is relatively common, affecting about 5.5% of the population or ~430 million individuals globally. Although rosacea can affect anyone, it typically affects middle aged women, with about 85% of sufferers over the age of 30.

Rosacea is a burdensome condition, affecting the daily lives and overall quality of life of its sufferers. Surveys done by the National Rosacea Society (NRS), showed that:

- 90% of sufferers said rosacea had lowered their self-confidence and self-esteem; and
- 41% reported it had caused them to avoid public contact or cancel social engagements.

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The disease is notably worse among those suffering from severe rosacea, with those respondents saying:

- 88% saying the condition had adversely affected their professional interactions; and
- 51% said they had missed work because of their rosacea.

There is currently no cure for rosacea, only management of the symptoms.

The National Rosacea Society (NRS) estimates at least 16 million Americans are affected by the disease, with possibly millions more in temporary remission.

BTX1702 Mechanism of Action in Rosacea

BOT indicates the active CBD ingredient in BTX1702 has the potential to target multiple areas in the rosacea inflammatory cascade.

The company notes the following points of action as:

1. **Prevents Barrier Disruption** – CBD inhibits p38 MAP kinase activation and IL-6 production in keratinocytes responsible for triggering skin inflammation;
2. **Modulates Immune System** – CBD inhibits Th17 (IL-17) and Th2 responses (IL-13);
3. **Potent Gram-Positive Antimicrobial** – CBD reduces B. oleronius and S. epidermidis bioburden responsible for triggering skin inflammation; and
4. **Broad Anti-inflammatory Effects** – CBD inhibits inflammation mediated by proinflammatory cytokines TNFα, IL-1, IL-6, IL-8, and IL-12 as well as suppressing TLR-2 mediated inflammatory responses

Product Landscape

As there is no cure for rosacea, clinicians aim to manage and reduce symptoms. Treatment options may vary depending on the underlying severity of symptoms.

Products in the market are either targeted to reduce the redness in the skin or combat the acne-like breakouts.

Similar to acne treatments discussed earlier, there is a gap in the market for drugs that are effective at reducing the underlying symptoms that also aren't burdened by side effects or issues of antibiotic resistance (long term use limitations).

Topical medication used to reduce redness include:

- **Brimonidine** – A adrenergic agonist (α2 selective), the drug works by constricting blood vessels in the skin to reduce redness. Common side effects include redness, burning, and headaches, with more severe side effects including allergic reactions and low blood pressure; and
- **Oxymetazoline** – Also an adrenergic agonist (α1 selective), similarly works by constricting blood vessels in the skin to reduce redness. Common side effects include redness, burning, and headaches, with more severe side effects including allergic reactions and low blood pressure.

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Other topical and oral treatments available are used to manage the acne-like symptoms of rosacea. These medications are also used in the treatment of acne itself and include topical and oral antibiotics, retinoids and retinoid-like drugs, oral acne drugs (e.g. Isotretinoin), as well as a variety of other options. We discussed these drugs in detail in the previous sections.

As discussed earlier, although some of these options are effective at managing the acne-like symptoms they come with a myriad of side effects which can be quite severe in certain cases, or otherwise suffer from bacterial resistance issues in the case of antibiotics.

Recent studies and analyses have highlighted the dislike of current rosacea solutions, with:

- A 2019 FMX103 demand study showing: **73%** of patients indicate they are likely to seek a better solution than their current treatment; and
- A 2015-18 symphony Health analysis showing: over **70%** switch or discontinue Rosacea therapy after first diagnosis

As a result, we are of the opinion that if BOT can prove up the BTX1702 therapy to deliver similar or better efficacy without any of the adverse or side effects then there is potentially a solid pathway to market.

Clinical Studies

In late 2019 BOT announced the BTX1702 clinical program following the successful completion of the formulation development and pre-clinical studies.

This program follows on from the successful development of BTX1801 to date, in addition to the company's growing data set showing synthetic CBD's powerful antimicrobial and anti-inflammatory properties – the two-key mechanism for successful management of rosacea.

The company had originally planned to kick off the initial phase 1b clinical study in 2020, however as a result of COVID-19 and related restrictions, study enrollment and study start were put on hold.

Following on from this, BOT updated the original study design in 2021, expanding it to enable increased data capture and to provide valuable insights across its broader dermatology pipeline. This updated study design received ethics approval in march this year.

This phase 1b study will be used to investigate the safety and tolerability of BTX1702.

The study design:

- Four dose groups, ~120 patients:
  - High dose – twice daily: 40 patients
  - Low dose – twice daily: 40 patients
  - Vehicle – twice daily: 40 patients
- Sites: ~12 dermatology sites across Australia & NZ
- Patients: Adults (18-65 Yrs. old) with moderate to severe papulopustular rosacea
- Treatment period: 8 weeks

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The primary endpoint is a safety and tolerability assessment, in addition to exploratory endpoints which include:

- Absolute change and percentage change in inflammatory lesion counts (papules and pustules) from baseline to day 57;
- Change from baseline in the Investigator's Global Assessment (IGA-PP) scale at day 29 and 57; and
- Reduction of erythema (redness) severity assessments by each patient and investigator

As part of the study design update, BOT will centralize review of each investigators ratings and use a state-of-the-art advanced canfield imaging technology across all sites to support clinical assessment. These changes should significantly enhance the quality and consistency of the data collected.

We further note the highly desirable cohort being studied, highlighting the older mean age of rosacea sufferers, which in our view could imply a more compliant cohort that is more motivated to find a solution, and more disciplined to follow study protocols.

Although called a 'phase 1b', the study in reality is equivalent to a phase 2 as its dose ranging. The naming is purely the result of having ethics approved in Australia, where a study of this nature is required to be grouped as such. Whereas in the US, it would be called a phase 2 study because its dose ranging. As a result, BOT could take the data if successful to the FDA to get approval to undertake a follow up phase 3 study in the US.

On its primary safety and tolerability endpoints we believe the study is likely to be successful, following the excellent safety profile shown to date across all of BOT's development programs.

We have similar positive views on efficacy outcomes, rosacea as previously discussed is treated similarly to acne. If BTX1702 can deliver similar solid efficacy results as seen in BTX1503 then that is a successful outcome in our view and potentially creates a solid pathway to market.

BOT announced in its recent quarterly the study launched in June, without major changes to timelines we would expect results in Q2 of next calendar year (2022). If successful, we would anticipate a follow up phase 3 clinical study late next year (Q3/4 CY2022) which would likely run for about 12 months (implying data read out in late CY'23).

Market Opportunity

The rosacea market is worth an estimated US$1.9bn per annum as of 2020, and is forecasted to grow to US$2.6bn by 2025 (6.5% CAGR).

These sales are supported by ~5 million total annual prescriptions in the US. The market is fragmented and genericized following numerous patents expirees. Topical therapies dominate with ~60% of the market.

We have further modelled sales and cashflows as part of our analysis, we assumed the following in building up our model for BTX1702:

- 8 year economic period;
- 5 million annual scripts base;
- 10% peak market share;
- US$600/script;
- 60% peak gross margin; and
- Commercial launch in 2025

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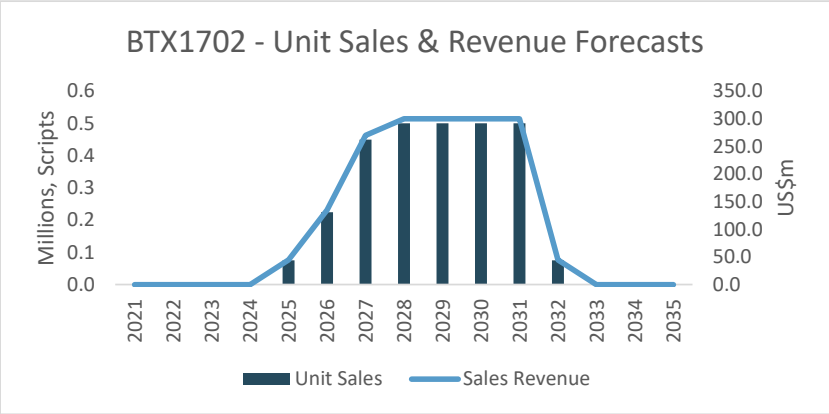
We further assume the following remaining development capital:

- Phase 1b clinical study: US$2.5m;
- Phase 3 clinical study: US$15m; and
- NDA: US$2m

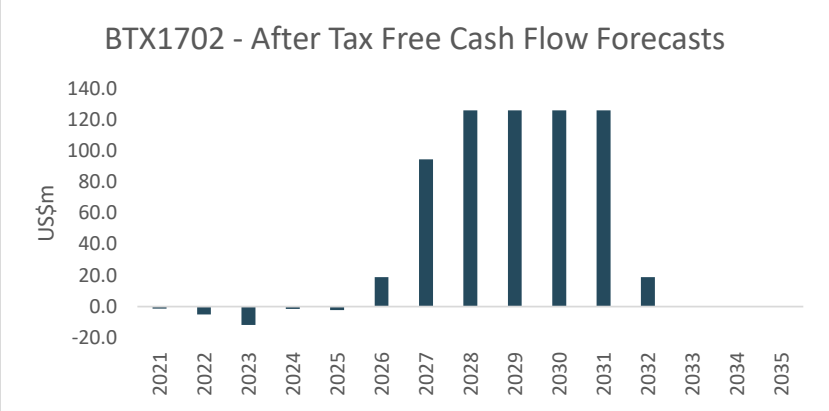
We model unit sales through applying an adoption curve to our peak forecasted market share, adding unit pricing we model unit sales and revenues as follows:



Source: EHL Forecasts

On our conservative assumptions we forecast BTX1702 could generate peak sales of US$300 million per annum.

We can model potential after tax free cash flow generation through applying our forecasted margin, taxes, and remaining development capital. As shown in the chart below, we anticipate BTX1702 could generate circa US$125 million in annual cashflows.



Source: EHL Forecasts

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BTX1204A – Atopic Dermatitis

The BTX1204A program intends to develop a treatment therapy for atopic dermatitis. BOT had previously undertaken clinical studies on the efficacy of synthetic CBD for treatment of atopic dermatitis, these initial works called BTX1204 didn't prove successful.

In May this year BOT re-engaged research on the skin condition in a new canine pilot study with a significantly higher formulation of active drug. This new study showed highly encouraging results, re-igniting the potential for treating AD with synthetic CBD. The company is currently looking to follow up this initial study with a larger canine study before going into human trials.

Atopic Dermatitis

Atopic dermatitis, also known as eczema is a chronic skin condition that results in itchy, red, swollen and cracked skin. These symptoms can lead sufferers to scratch their skin, aggravating the condition in vicious cycle.

About 20% of people are affected by atopic dermatitis at some point in their lives. Typically starting in childhood with severity changing over time, many people will go onto outgrow the skin condition.

The disease has significant negative impacts on patient's quality of life, these including:

- Itch and discomfort affect sleep;
- Sleep loss affects school/work performance; and
- Scratching often leads to secondary infections

The mechanism underlying the development of atopic dermatitis include:

- **Skin Barrier Dysfunction** – Filaggrin deficiencies and/or mutations, decreased terminal keratinocyte differentiation;
- **Pruritis (itch)** – Various cutaneous mediators of pruritus (e.g. histamine, proteases, neuropeptides, cytokines, leukotrienes) in atopic dermatitis;
- **S. aureus colonization** – Research has shown skin the barrier disfunction present in atopic dermatitis can be exploited by staphylococcus aureus (staph); the entry of this bacteria directly correlated with expression of IL4, IL13, IL22, TSLP and other cytokines associated with atopic dermatitis; and
- **Immune pathway activation** – Th2 cell adaptive immune response (acute: ↑IL-4, IL-5, IL-13) becoming mixed with Th1 (chronic: IL-12 and IFN-γ)

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BTX1204A Mechanism of Action in Atopic Dermatitis

BOT believes CBD is well suited for addressing the mechanism underlying atopic dermatitis outlined above.

CBD addresses these 4 key areas as follows:

1. **Inhibits itch** – CBD suppresses itch by interacting with VR/TRPV-1 receptor present on mast cells and keratinocytes;
2. **Repairs barrier dysfunction** – CBD inhibits p38 MAP Kinase activation and IL-6 production in keratinocytes which interrupts the signaling process to dendritic cells and Th2 helper cells;
3. **Potent antibiotic** – CBD reduces S. aureus and MRSA colonization responsible for triggering skin inflammation and secondary skin infections; and
4. **Modulates immune system** – CBD inhibits Th17 (IL-17) and Th2 responses (IL-13) responses limiting the release of pro-inflammatory cytokines (TNFα, IL-1, IL-6, IL-8, and IL-12)

The multiple points of action form a core strength of BTX1204A, such multi prong approach aligns well with current opinions in the field. This best described by Donald Leung in 2016 (a key opinion leader), who commented:

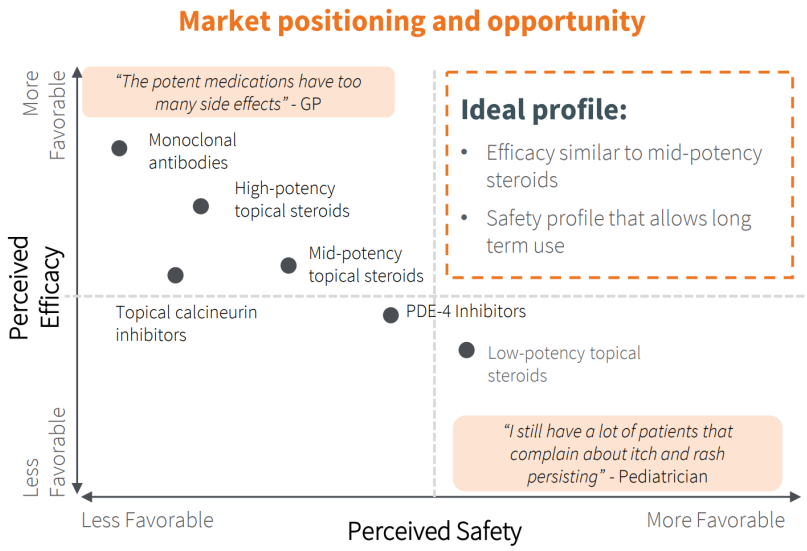
> *"Successful treatment of atopic dermatitis requires a multi-pronged approach eliminating atopic dermatitis triggers, improving skin barrier function, and a proactive anti-inflammatory approach."*

Product Landscape

Atopic dermatitis sufferers are lacking effective and safe long-term solutions. Although there exists a number of effective products, they all come with major side effects, cancer risks, or are not suitable for long term use.

Further to this, there is a graveyard of recent pipeline failures (e.g. Menlo Therapeutics; Vanda Pharmaceuticals) highlighting the lack of late-stage products with new mechanisms of action.

The current landscape is summarized below, highlighting the lack of ideal solutions.



Source: BOT Presentation

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The product landscape can be further broken into the following groups:

- **Monoclonal Antibodies** – Dupilumab is an approved monoclonal antibody therapy for the treatment of moderate to severe atopic dermatitis. The drug administered by injection works by inhibiting signaling of cytokines IL-4 and IL-13. Clinical trials have shown 36-39% of patients had clear or almost clear skin after 16 weeks of treatment. Although relatively effective, the drug comes with a number of side effects including injection site reactions (very common), allergic reactions, cold sores, and inflammation of the cornea. The drug is highly expensive, costing upwards of US$37,000 per year in the United States.
- **Topical Calcineurin Inhibitors** – Calcineurin inhibitors are a class of drugs with immune modulating properties, marketed drugs include Tacrolimus and Pimecrolimus. These drugs are applied topically and effective for treatment of moderate to severe atopic dermatitis. Calcineurin inhibitors come with a number of side effects, most common being burning and itching sensation as well as less common flue like symptoms, however, most significantly these drugs come with black-box warnings surrounding cancer risks.
- **Topical Steroids** – Applied topically, steroids work by reducing inflammation in the skin. The drug is available in various strengths for treating different severity atopic dermatitis. Steroids are not suitable for long term use and are only recommended for short term use in treating flare ups. Steroids come with numerous side effects if used long term or repeatedly which include, stinging/burning, skin thinning/discoloration/stretching, hair growth and allergic reactions. More severe systematic side effects include growth effects in children, high blood pressure, bone damage, and Cushing's syndrome.
- **PDE-4 Inhibitors** – phosphodiesterase 4 inhibitors are a class of drugs with anti-inflammatory properties. Crisaborole is a PDE-4 inhibitor approved by the FDA for treatment of mild to moderate atopic dermatitis. Although effective, the drug applied topically comes with the common side effects of burning or stinging with further risk of allergic reactions. These side effects are thought to have held back the commercial success of the drug.

We believe if BOT can demonstrate the effectiveness of BTX1204A in human studies, matching the efficacy of its recent canine studies, in combination with CBD's known solid safety profile that there is potentially a genuine pathway to market.

Clinical Studies

As stated earlier, BOT had previously conducted studies on the application of synthetic CBD for the treatment of atopic dermatitis. This initial program, BTX1204, proved unsuccessful in phase 2 studies.

The initial BTX1204 program used a very weak 4% active CBD formulation, the possible result of its failure.

Following the success seen in BTX1801 the company decided to revisit the atopic dermatitis program with a stronger formulation in a new pilot study. The new program, BTX1204A, is based on a significantly higher CBD dose in a novel Permetrex™ formulation (used in recent BTX1801 phase 2a study).

The company conducted a pilot study in canines with atopic dermatitis, treating the animals topically with BTX1204A over a 28-day period.

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The canine atopic dermatitis model used is highly relevant, with the condition being clinically and immunologically similar to the human version, as well as both suffering from similar skin barrier problems. These similarities are shown in the table below:

REVIEW

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

Rosanna Marsella[1] and Giampiero Girolomoni[2]

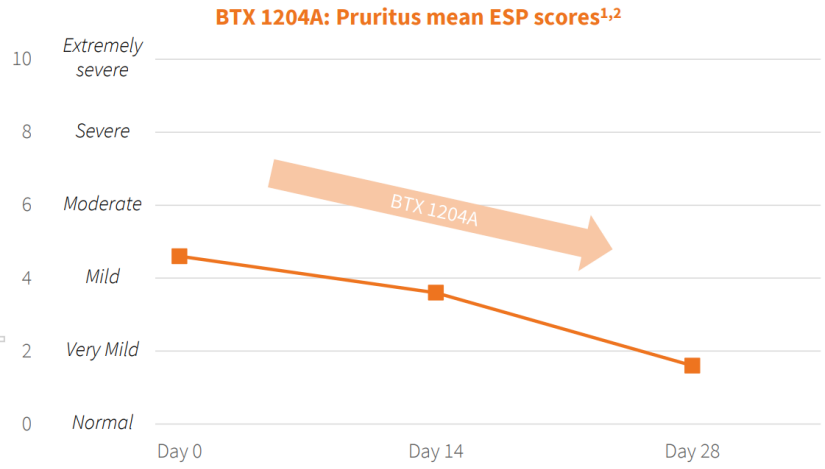
	Canine AD	Human AD
Prevalence in population	10-15%	5-20%
Age of onset	1-3	1-5
Skin affected	Face, folds	Face, folds
Infiltration eosinophils	+	+-
Infiltration igE and dendritic cells	+	+
Pruritus	Severe	Severe
Skin colonization Staph Aureus	+	+
Th-2 dominated immune response	+	+

Source: BOT Presentation

This model allows BOT to undertake studies faster and more cost effectively, allowing the company to de-risk later stage human studies.

Treatment efficacy in this pilot study was measured using the 'Enhance Pruritus Score' (EPS or 'itch scale') in addition to 'Canine Atopic Dermatitis Extent and Severity Index' (CADESI-04) measurements.

The Dogs started the study with a pre-treatment mean EPS of 'Moderate', the BTX1204A treatment reduced the mean ESP to 'Very Mild' over a 28-day period. This shown in the diagram below.



Source: BOT Presentation

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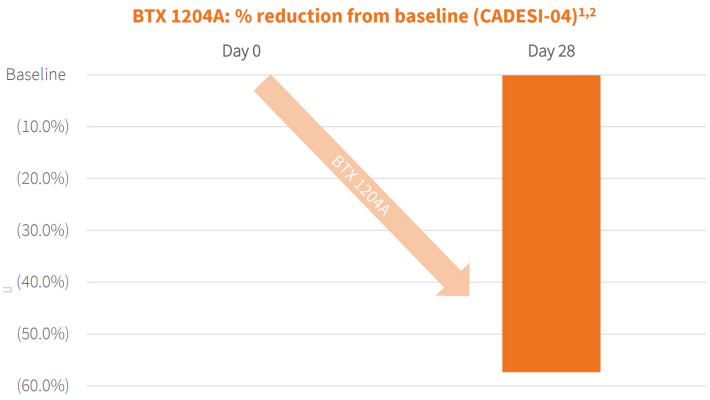
Similarly encouraging results were seen in the CADESI-04 assessment, with the dogs showing an improvement in skin lesions over the 28-day treatment period, resulting in a ~57.3% reduction from baseline severity.



Source: BOT Presentation

Put into context this essentially matches the 28-day CADESI-02 baseline reduction seen in Zoetis's highly successful canine oral dermatitis product Apoquel®, the US$550m annual revenue generator showed a comparable ~58.3% reduction in skin lesions.

The main caveat of this study is its small size, only done in 4 dogs in Australia. Clearly warranting further investigation in larger studies.

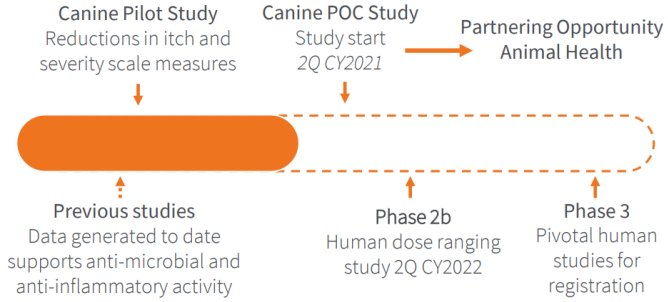
BOT intends to undertake a larger proof of concept canine study this quarter. The results of this study informing a potential licensing program for animals and relaunch of the later-stage human atopic dermatitis clinical programs.

The parameters of the larger canine POC study planned are:

- Four dose groups, ~40 dogs
  - High dose: 10 subjects
  - Medium dose: 10 subjects
  - Low dose: 10 subjects
  - Vehicle: 10 subjects
- Sites: 5 Australian Sites
- Treatment period: twice daily for 28 days
- Endpoints: EPS, CADESI-04 assessments

If successful, BOT has outlined a pathway which may include:

- Phase 2b: Human dose ranging study, 2Q'CY2022; and
- Phase 3: Pivotal human studies, likely CY2023+



Source: BOT Presentation

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Market Opportunity

The market for atopic dermatitis is very large with roughly 1 in 10 people developing the disease at some point in their lives. In the United States alone there is an estimated 31.6 million people with some form of atopic dermatitis.

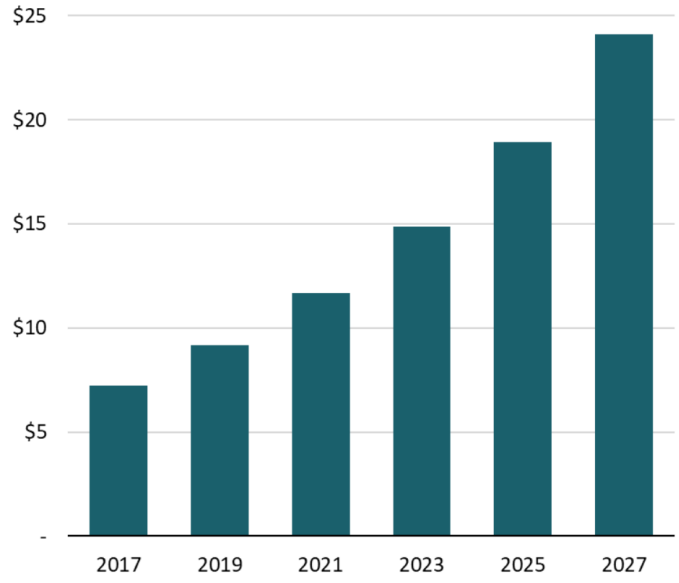
22 million are on treatments in the United States, broken up as follows:

- Mild: 10.5 million
- Moderate: 8.5 million; and
- Severe: 2.8 million

BOT is targeting mild-to-moderate sufferers which makes up an addressable market of around 19 million people in the US alone.

The market was worth over US$7 billion per annum in 2017 and is estimated to be worth over US$12 billion this year, this is further forecasted to grow to circa US$25 billion per annum by 2027. As shown below.

Projected atopic dermatitis market by revenue (US$bn)[4]



Source: BOT presentation

Beyond this, we note there is also the potential animal market. BOT's studies in canines could possibly provide a pathway for its use in animals.

The animal market is potentially lucrative. We note Zoetis, one of the world's largest animal health companies if not the largest, has two products in the canine dermatitis / dog itch space, these being:

- APOQUEL (oral drug); and
- CYTOPOINT (Injectable, Monoclonal antibody)

Together these two products are estimated to generate circa US$750 million in annual sales globally.

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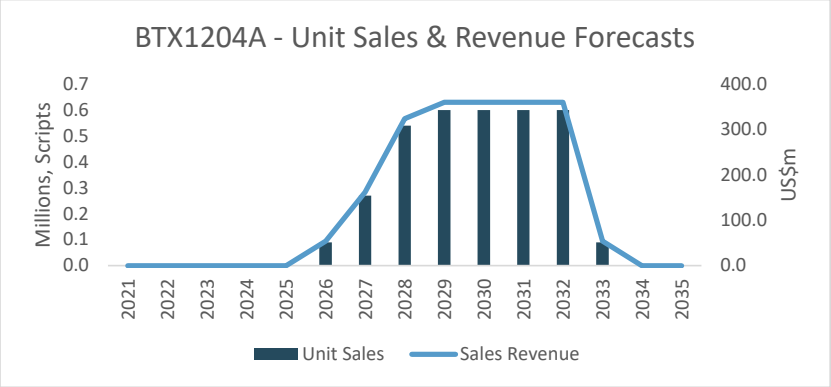
We have further modelled sales and cashflows as part of our analysis, we assumed the following in building up our model for BTX1204A in humans:

- 8-year economic period;
- 6 million annual scripts base;
- 10% peak market share;
- US$600/script;
- 60% peak gross margin; and
- Commercial launch in 2026

We further assume the following remaining development capital:

- Follow up canine study: US$0.2m;
- Phase 2b clinical study: US$5m;
- Phase 3 clinical study: US$20m; and
- NDA: US$2m

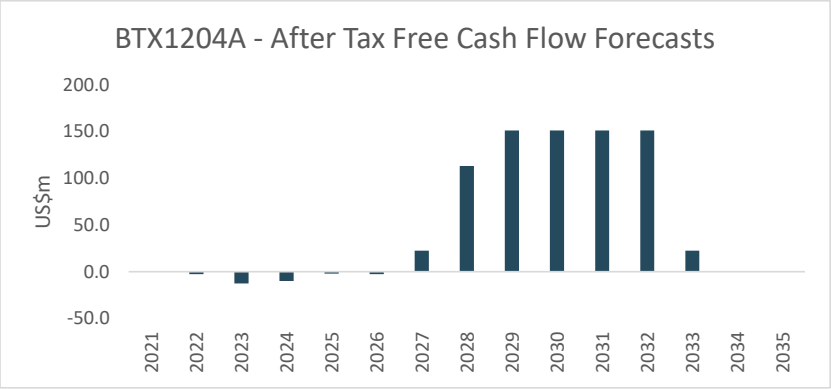
We model unit sales through applying an adoption curve to our peak forecasted market share, adding unit pricing we model unit sales and revenues as follows:



Source: EHL Forecasts

On our conservative assumptions we forecast BTX1204A could generate peak sales of US$360 million per annum, this as stated before does not include any potential sales from an animal formulation of the drug.

We can model potential after tax free cash flow generation through applying our forecasted margin, taxes, and remaining development capital. As shown in the chart below, we anticipate BTX1204A could generate circa US$150 million in annual cashflows.



Source: EHL Forecasts

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Commercialisation Strategy

There are a number of potential avenues for BOT to commercialise its pipeline of programs at their various stages of development. These include:

- **Sale / Acquisition** – The sale or acquisition of an individual program or the company (BOT) as a whole is a potential pathway, and the most rapid way to realise value. BOT as a mid-sized dermatology company with both a pipeline of products and platform technology could pose to be a lucrative acquisition target for dermatology specific or even broader pharmaceutical companies;
- **Licensing / Partnership** – If BOT proceeds through bringing its products to market, a licensing or partnership arrangement will be the most suitable avenue. Both reduce the upfront capital requirements to commercialise its products whilst maintaining the financial upside. Such deal could further realise a portion of value through upfronts payments; and
- **Independently Got-to-Market** – This is a potential outcome; however, we see it as the last avenue due to the increased resources and complexity required.

Balance Sheet

BOT finished the recent June quarter with ~$21.6m in cash at bank.

We forecast the company is well funded to undertake its near-term clinical development. We anticipate cash outflows over the next 12 months from the following programs:

- BTX1801 phase 2b study;
- BTX1702 phase 1b study;
- BTX1204A canine proof of concept study;
- BTX1204A phase 2b (partial); and
- Corporate overhead

We further forecast R&D tax credits received over this period for the relevant R&D expenditure.

We detail these forecasts in the table below, we anticipate BOT will finish FY'22 with circa $16-17m in cash at bank.

Quarter	Jun'Q 21	Sep'Q 21	Dec'Q 21	Mar'Q 22	Jun'Q 22
(-) BTX1503					
(-) BTX1801				-0.8	-0.8
(-) BTX1702		-0.6	-0.6	-0.6	-0.6
(-) BTX1204A		-0.2			-1.3
(-) Corp O/H		-0.4	-0.4	-0.4	-0.4
(+) R&D Tax Credit		0.4	0.3	0.6	1.2
Net Cash Burn		**-0.8**	**-0.7**	**-1.2**	**-1.9**
Cash Balace	**21.6**	**20.8**	**20.0**	**18.8**	**16.9**

Source: EHL Forecasts

Beyond FY22, if BOT's clinical development programs are successful we anticipate the company will require further funding to undertake more expensive later stage clinical studies. However, we note that under such scenarios the company's value will likely have appreciated to reflect these clinical successes.

BOT has no borrowings.

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Intellectual Property Portfolio

The company maintains an extensive intellectual property (IP) portfolio. The company has filed multiple patents in key jurisdictions covering each indication, the Permetrex™ technology, and the broader potential of CBD in different skin diseases.

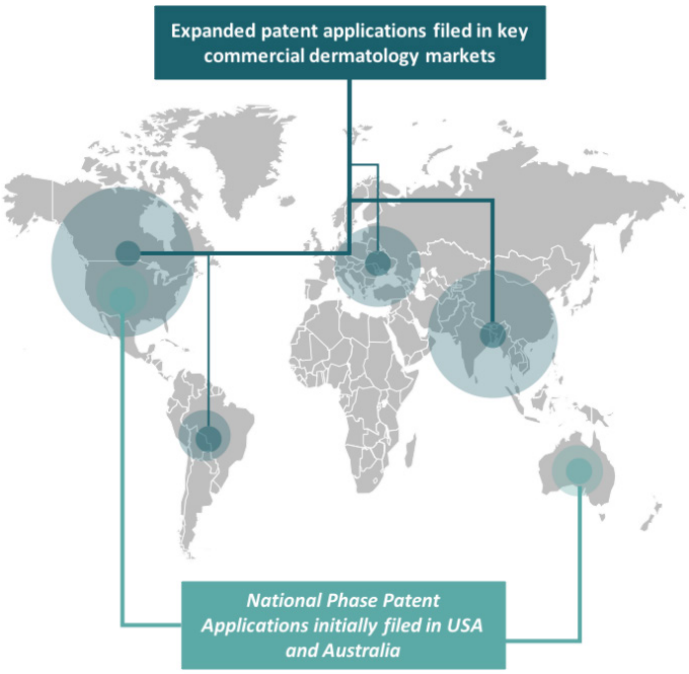
BOT current has 12 patent families that cover:

- Combination of Permetrex™ and CBD, as a unique composition of matter filling for each formulation used in each disease | (PCT/AU2018/050117, PCT/AU2018/050045, PCT/AU2018/050044, PCT/AU2018/050047);
- Specific doses of CBD that are effective (From BOT clinical data) to treat disease | (PCTAU2019/050050, PCT/AU2019/020051, PCT/AU2019/050052);
- Novel use of CBD (as well as CBD plus Permetrex™ and other excipients) to treat resistant bacteria and disrupt biofilms | (PCT/AU2018/051233, AU2018902331, PCT/AU2019/050626); and
- Novel use of CBD to target IL-6 and P38 MAPK and related cell stress pathways in selected diseases | (AU2019902123);

BOT has targeted patent protection in key regions including:

- United States;
- Europe;
- Japan;
- Australia;
- New Zealand;
- Korea;
- Singapore;
- China; and
- Brazil

We note most patent fillings have been done between 2016 and 2019, implying significant remaining patent life (circa 2036 to 2039 expiry).



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Board and Management

BOT's board of Directors, Key Management, and Advisors are listed below per the company's website.

Board of Directors

Mr Vince Ippolito - Executive Chairman and President

Shares: Nil shares, 33.0m Options

Description: Vince Ippolito is President and Executive Chairman of Botanix Pharmaceuticals and responsible for the Company's commercial operations worldwide. Mr Ippolito is based in Phoenix USA, where Botanix is building its commercial operations functions. Mr Ippolito also currently sits on the Board of Suneva Medical, a privately held regenerative aesthetics company. Mr Ippolito is a leading pharmaceutical expert who has over 30 years of experience in the industry, including more than 20 years in dermatology. Throughout his career, he has launched more than 20 brands in dermatology and aesthetic medicine and played a leading role in two of the largest dermatology acquisitions completed in the past decade with combined valuations of $7.8 billion. He served as the Chief Commercial Officer Executive Vice President of Anacor Pharmaceuticals, a dermatology-based biopharmaceutical company, until September 2017, where he was responsible for developing marketing and sales functions, as well as strategizing the company's product portfolio. Previously, Mr. Ippolito was Executive Vice President and Chief Commercial Officer at Medicis, an industry leading dermatology and aesthetic company.

Mr Matthew Callahan – Executive Director

Shares: 70.7m shares, Nil Options

Description: Mr Matt Callahan is the founding executive director of Botanix. Matt is an experienced life sciences and health tech executive based in Philadelphia, USA. He has been the founding CEO or Executive Director of a number of pharmaceutical and health tech companies including iCeutica Inc, Churchill Pharma Inc. Dimerix Biosciences, Emerald Clinics and Orthocell. He has led the development of four products that have received FDA approval and he has more than 25 years legal, IP and investment management experience. Mr Callahan has worked as an investment director for two venture capital firms investing in lifesciences, technology and other sectors, and was general manager of Australian listed technology and licensing company ipernica (now Nearmap ASX:NEA), where he was responsible for the licensing programs that generated more than $120M in revenue.

Dr William Bosch – Executive Director and Chief Scientific Officer

Shares: 16.0m shares, 4.9m Options

Description: Dr Bill Bosch is a seasoned pharmaceutical executive with more than 20 years of experience in the industry, focusing on applications of nanotechnology to drug product development. Dr Bosch worked with iCeutica Inc. as Chief Scientific Officer and is co-inventor of the SoluMatrix™ drug delivery technology, and has been instrumental in the development and scale up of the platform and development of three FDA approved products that use the SoluMatrix™ technology. Before iCeutica, he was Director of Pharmaceutical Research at Elan Corporation where he managed the development activities for four commercial products which incorporate nanotechnology. Dr Bosch was a co-founder of NanoSystems LLC in 1995 and a co-inventor of NanoCrystal® Technology.

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Dr Steward Washer – Executive Director

Shares: Nil shares, 8.9m Options

Description: Dr Stewart Washer is a respected senior executive with more than 20 years of experience at Board and senior executive levels across medical technology, biotechnology and agrifood companies. He has an established track record and has overseen acquisitions and strategic partnerships in the pharmaceutical and cannabinoid medicine sectors, with some of the world's leading companies. Dr Washer is currently active as an ASX board member with Orthocell (ASX:OCC), Zelda Therapeutics (ASX:ZLD) and Cynata Therapeutics (ASX:CYP). Previously, Dr Washer has been an Investment Director at Bioscience Managers, a leading life science investment firm and was a Venture Partner with the Swiss Inventages Fund, a €1.5bn life science fund, funded by Nestle. Dr Washer has held a number of Board positions previously including Chairman of Hatchtech which sold for A$279m in 2015 and as a Director of iCeutica, which was sold to US-based Iroko Pharmaceuticals in 2011.

Key Management

Dr Clarence Young – Chief Medical Officer

Description: Dr Young was recently Chief Medical Officer at Velicept Therapeutics and Senior Vice-President and Chief Medical Officer at Iroko Pharmaceuticals, where he provided clinical and medical leadership for three NDA filings and approvals. He also has held executive leadership positions for Novartis and one of its acquisitions, Protez Pharmaceuticals, where he served as Vice President, Drug Development and Chief Medical Officer. Dr Young began his pharmaceutical career at GlaxoSmithKline, where he was Vice President and Global Head, Anti-Infectives Clinical Development. Dr Young is a Fellow of the Infectious Diseases Society of America and served on the White House Working Group on Antimicrobial Resistance. He is a graduate of Williams College and Harvard Medical School and the author of numerous peer reviewed articles, reviews and scientific presentations.

Anthony Robinson – Vice President of Development

Description: Anthony Robinson was recently Vice President, Head of Clinical Operations, Program Management and Regulatory Affairs at Advicenne Inc and previously held similar positions at Aquestive Therapeutics and Intrommune Therapeutics, and developed extensive expertise in drug development, clinical operations and regulatory affairs at Shire (acquired by Takeda) and global contract research organization, Covance. Anthony holds multiple qualifications including Masters degrees in Science and Business Administration from Penn State and Drexel Universities and a Bachelor of Science from Cornell University.

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Lynda Berne – Head of Commercial

Description: Lynda Berne is a founder of BAL Pharma Consulting, LLC, a Princeton, NJ Management Consulting firm providing Commercial Advisory Services to Biotech and Specialty Pharma. Lynda has held several senior and executive roles in pharma encompassing broad commercial experience and including 13 years at Bristol-Myers Squibb where she held the roles of Vice President, Infectious Disease Marketing, managing a $600M business unit and Vice President, Managed Health Care Sales. Other senior commercial positions held include General Manager, Hospital/CV Portfolio, a $1B business unit, Abbott International, and Executive Director, Gastroenterology/Nephrology Marketing, a $200M business unit, Shire Pharmaceuticals. Lynda has a Bachelor of Science in Nursing from Indiana University, and Master of Science in Nursing from DePaul University and an MBA from Northwestern University, Kellogg Graduate School of Management.

Advisors

Dr Ron Dolle (CMC and Medicinal Chemistry)

Description: Dr Ron Dolle is an accomplished drug discovery executive with a record of innovation and success in drug design, team leadership, candidate selection, preclinical development, and registration. He also holds a Associate Professorship in the Department of Biochemistry and Molecular Biophysics at the Center for Drug discovery at the University of Washington in St Louis.

Dr Dolle is an expert in small molecule drug design, and has led cross-functional R&D teams at Cubist and Adolor in traditional and fully virtual research environments generating 16 development candidates including seven INDs. Dr Dolle's research and management experience, honed in the pharmaceutical and biotech industries, spans the therapeutic areas of infectious disease, inflammation, gastrointestinal disorders, and CNS conditions (pain, affective, neurology).

Dr Ira Lawrence (MD, FACP)

Description: Dr Lawrence has over 30 years of senior level leadership experience within the global pharmaceutical and medical device industries. He currently serves as a senior-level consultant, with numerous clients worldwide. Previously, he has served as the Chief Medical Officer of Alphaeon Corporation; Senior Vice President and Chief Medical Officer at Medicis Pharmaceutical Corporation; President and Chief Executive Officer and Member of the Board of Directors at SciClone Pharmaceuticals, Inc.; Senior Vice President of Research and Development at Astellas Pharmaceutical Company and Fujisawa Healthcare; and Senior Vice President of Research and Development at GenDerm Corporation. Dr Lawrence has had significant experience in the development and launch of numerous pharmaceuticals and devices and has played significant roles in over 75 INDs and IDEs, as well as, 17 NDAs, BLAs and PMAs. He is a Fellow of the American College of Physicians and has received numerous awards and honors. He is a member of several scientific and medical professional societies; the author of numerous scientific publications and textbooks; and has presented at several national and international scientific and medical meetings on a variety of subjects.

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Top Shareholders

We note the company's top shareholders below:

Top Shareholders		Shareholding*	
Rank	Shareholders	m	%
1	Matthew Callahan	70.7	7%
2	Gayle McGarry	59.6	6%
3	Kian Lim Ka	17.0	2%
4	Henry Bosch	16.0	2%
5	Yarraandoo Pty Ltd	10.0	1%
6	Sweet As Developments Pty Ltd	9.8	1%
7	Zenith Energy Ltd.	9.0	1%
8	T.T. Nicholls Proprietary Limited	7.0	1%
9	Michael Gaule	6.4	1%
10	Splendid Stuff Pty Ltd	6.2	1%
11	J & N Weston Investments Pty Ltd	5.7	1%
12	Stephane Fayd'herbe	5.6	1%
13	Brendan Cooper	5.4	1%
14	Argonaut Investments Pty Ltd, Asset Management Arm	5.0	1%
15	Michael Thurn	2.5	0%
16	Davy Global Fund Management Limited	1.2	0%
17	Dimensional Fund Advisors L.P.	0.7	0%
	Top 17 Total	237.8	24%
**As of June-30th 2021*			

Source: IRESS

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Appendix

Appendix A – Antimicrobial Properties of CBD

CBDs antimicrobial effect is among its various exciting properties.

The property has been known for some time, originally discussed in a 1976 publication (van Klingeren and ten Ham) that reported minimum inhibitory concentrations (MICs) for purified extracted CBD and THC, two of the most notable Cannabinoids in cannabis. Although there were earlier publications on the broader antimicrobial properties of cannabis extracts, this paper was the first on a purified compound.

MIC or minimum inhibitory concentration refers to the lowest concentration of drug which prevents visible growth of bacteria, often expressed in micrograms per millilitre (µg/mL).

Despite this early research, the antimicrobial effect was mostly ignored with the exception of research in 2008 assessing the potency of major Cannabinoids.

However, this changed with new research undertaken by BOT in conjunction with the University of Queensland (UQ). We explore the exciting findings below, which were published earlier this year in the Nature Research's Communication Biology, a leading peer-reviewed biological science journal.

The research article is entitled "The antimicrobial Potential of Cannabidiol"

The research demonstrated CBD has consistent activity against a wide range of Gram-positive bacteria, including a variety of drug-resistant strains (e.g. MRSA). Furthermore, for the first time and of much excitement, BOT showed this antimicrobial activity extended to a small subset of Gram-negative bacteria, which including bacteria responsible for:

- Gonorrhoea (Neisseria gonorrhoeae);
- Meningitis (Neisseria meningitides);
- Bronchitis and Pneumonia (Moraxella catarrhalis); and
- Legionnaires Disease (Legionella pneumophila)

Expanding further, the data showed a very consistent MIC (minimum inhibitory concentrations) of 1-4 µg/mL against a wide range of over 20 types of Gram-positive bacteria, including various strains of the key pathogens:

- Methicillin-resistant Staphylococcus aureus (MRSA);
- multidrug resistant (MDR) Streptococcus pneumoniae;
- Enterococcus faecalis;
- anaerobic bacteria Clostridioides difficile; and
- and Cutibacterium acne

Furthermore, as stated previously to much surprise, CBD possessed excellent potency against four Gram-negative bacteria, including:

- Neisseria gonorrhoeae (MIC: 1–2 µg/mL);
- Neisseria meningitides (MIC: 0.25 µg/mL);
- Moraxella catarrhalis (MIC: 1 µg/mL); and
- Legionella pneumophila (MIC: 1 µg/mL).

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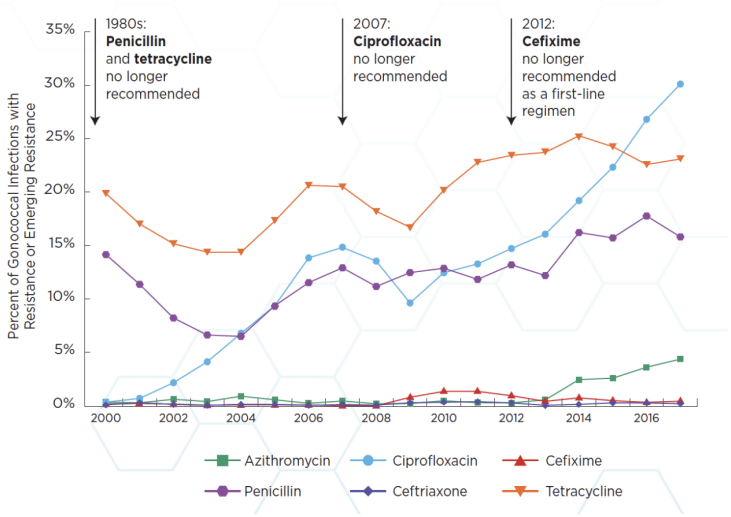
The Neisseria gonorrhoeae is a key pathogen listed by both the World Health Organisation (WHO) and the Centers for Disease Control and Prevention (CDC). There is growing concerns around increasing incidence rates in parallel to a demising ability to treat Neisseria gonorrhoeae due to rising antibiotic resistances – there is no longer a single reliable class oral antibiotic for treatment of Neisseria gonorrhoeae.

Figure 1 – Antibiotic resistance of Gonorrhea



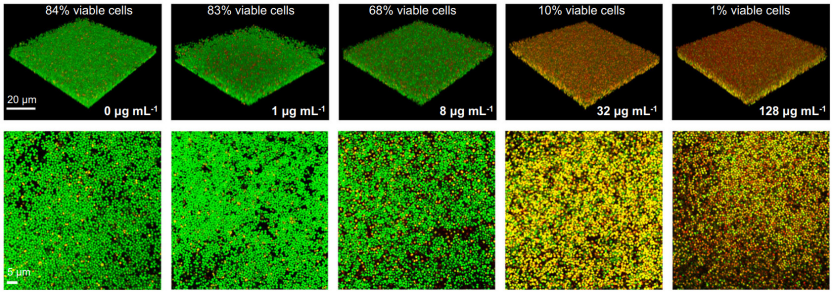
Source: BOT Announcement

Anti-biofilm activity

The research detailed the anti-biofilm activity of CBD.

For context, a biofilm is a community of bacteria and other micro-organisms contained in a layer of mucilage that adheres to a solid surface. It is estimated that roughly two-thirds of bacterial infections in the human body involve biofilms. Research shows that infection associated with biofilms are typically more challenging to eradicate, with a greater level of antibiotic resistance present versus non-biofilm bacteria.

The images below show confocal microscopy of CBD-treated biofilms, these demonstrate that CBD is capable of penetrating and killing the biofilm.



Source: The antimicrobial Potential of Cannabidiol

The implication of this property is major, as the ability to either inhibit this biofilm formation or outright eradicate already established biofilms should lead to improved treatment of infections.

CBD was active against both MSSA and MRSA biofilms.

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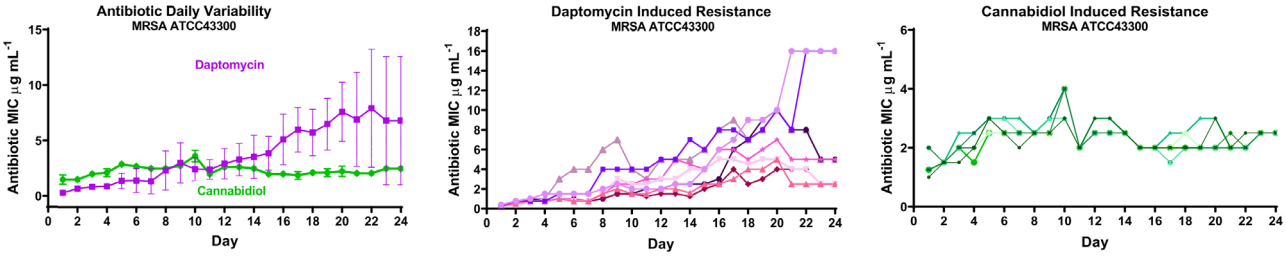
Low Innate Resistance Frequency

The research additionally showed CBD possesses a low innate resistance frequency value, in layman terms this means CBD doesn't easily develop bacterial resistance.

The publication specifically outlined CBD had a low propensity to induce resistance against MRSA ATCC 43300, whereby CBD has a 1.5-fold increase in MIC over 20 days of daily passage compared to a 26-fold increase seen with daptomycin (average 8 replicates each). This shown below:



Source: The antimicrobial Potential of Cannabidiol

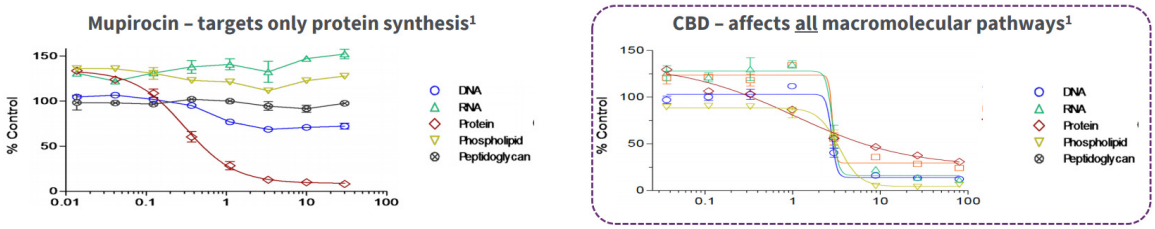
Novel Mechanism of Action

CBD was shown to have a novel mechanism of action, shown in the research to target all 5 macromolecular pathways. This compares against the single pathway (protein synthesis) target by the antibiotic mupirocin.

Specifically, a radiolabelled macromolecular synthesis assays of S. aureus RN42200 sharp inhibition of the pathways near the MIC (2–3 μg mL–1), the five pathways being:

- Protein;
- DNA;
- RNA;
- Phospholipid; and
- Peptidoglycan

This comparison against mupirocin is further shown below:



Source: BOT Presentation

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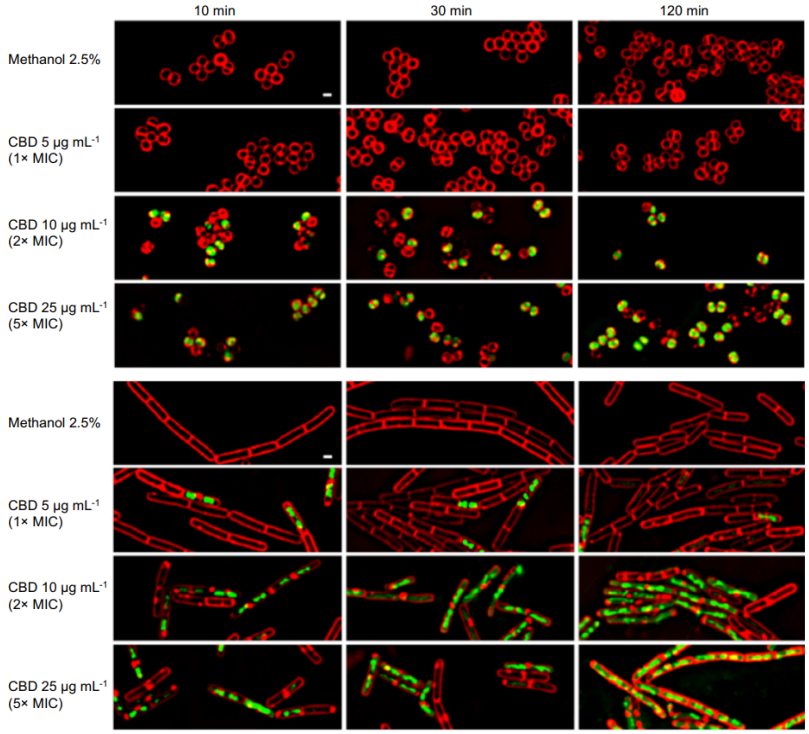
This is consistent with a rapid bactericidal action, we can further visualise this rapid killing activity as shown below: (Top: MRSA, Bottom: S. eueus ATCCC 2913).



Source: The antimicrobial Potential of Cannabidiol

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