ASX/Media Release

2 July 2018

Botanix update on development pipeline products

Key highlights

- **Completed pre-clinical testing of BTX 1801 - a novel antimicrobial with the potential to address unmet needs in serious skin infections with significant market opportunities**
- **Pre-clinical testing indicated the BTX 1801 formulation achieved high levels of bacteria killing effect compared with cannabidiol or Permetrex™ alone**
- **Target indications for BTX 1801 antimicrobial skin treatment being reviewed and accelerated development pathway currently underway**
- **In addition, BTX 1308 pre-clinical study achieved primary objectives, and Botanix remains on track to commence Phase 1b psoriasis patient study in 3Q CY2018**

Philadelphia PA and Sydney Australia, 2 July 2018: Medical dermatology company Botanix Pharmaceuticals Limited (ASX: BOT, "Botanix" or the "Company") is pleased to provide an update on the progress of key development pipeline products (BTX 1801 and BTX 1308) and has released a presentation outlining the data and market opportunity for its new BTX 1801 antimicrobial product.

Matt Callahan, Executive Director of Botanix said: "With two Phase 2 ready programs moving into the clinic, we are very excited by the significant potential of our pipeline products. BTX 1801 has the potential to address the significant global public health issue of antimicrobial resistance. In addition, we are pleased to be able to bring on our third program into a Phase 1b patient study. BTX 1308 has the potential to provide a new topical solution to sufferers of psoriasis which is safe and effective."

Botanix's newest pipeline product (BTX 1801), is a novel antimicrobial with the potential to address unmet needs in serious skin infections, with significant market opportunities. Data from the pre-clinical testing recently completed by the Company indicates that Permetrex™ significantly improves the antimicrobial killing power of cannabidiol, achieving close to 100% bacterial killing effect (at low concentrations) of antibiotic resistant strains of the most common skin infection bacteria – Methicillin-resistant Staphylococcus aureus (known as MRSA). The development of new and novel antimicrobials is now the subject of a globally coordinated effort and the market opportunity for new antimicrobials is significant and many unmet patient needs remain.

Botanix is now focused on completing, in conjunction with key opinion leaders, a market review with a view to identifying the ideal skin infection to target initially for BTX 1801, with the intention to execute a rapid development pathway. The BTX 1801 presentation attached outlines unmet market needs, favourable market dynamics, potential value upside, BTX 1801 pre-clinical data and the BTX 1801 development pathway.

Botanix has also completed its BTX 1308 psoriasis pre-clinical formulation and testing work which supports the mechanism of action for the drug in addressing inflammation, bacterial infection and

immune system modulation. With this data in hand, Botanix is now advancing a psoriasis patient study which will compare a number of BTX 1308 formulations against placebo, with a study planned to commence in Europe in late 3Q CY2018. More details on the study design for BTX 1308 will be provided at a later date.

About Botanix Pharmaceuticals

Botanix Pharmaceuticals Limited (ASX:BOT) is a clinical stage medical dermatology company based in Perth, Australia and Philadelphia, PA. The Company's focus is the development of safe and effective topical treatments for acne, psoriasis, atopic dermatitis and other skin conditions. The active ingredient contained in Botanix products is a synthetic form of a widely studied natural compound. Treatment targets include inflammation, deterioration of the of the skin barrier, skin cell proliferation, pruritus (itch), excess sebum production and bacterial infection.

Botanix has an exclusive license to use a proprietary drug delivery system (Permetrex™) for direct skin delivery of active pharmaceuticals in all skin diseases. Botanix is working with multiple parties to test the application of Permetrex™ on both a fee-for-service and traditional license basis.

Botanix pursues a rapid clinical development strategy aimed at accelerating product commercialisation. The patient treatment duration of clinical studies is generally completed within a 4 to 12 week timeframe.

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

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

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BTX 1801 antimicrobial

Pre-clinical data and additional information

July 2018

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RESTORING HEALTHY SKIN

Botanix investment highlights

Botanix is an emerging global dermatology company with two advanced clinical programs and a well developed pipeline

Dermatology Focused	Advanced clinical programs targeting multi-billion dollar prescription markets for **acne and atopic dermatitis**, with pipeline products targeting **psoriasis and now skin infections**
Clinical Stage	**Successful clinical data** from acne and atopic dermatitis patient studies shows industry leading performance, after only 4 weeks of treatment
Novel Approach	Products use a synthetic form of a widely studied natural product, **which greatly enhances the probability of clinical and regulatory success,** combined with the Permetrex™ delivery system
Experienced Team	Predominantly US based leadership team with **20+ FDA approvals** between them and extensive dermatology industry experience

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Executive summary: BTX 1801

BTX 1801 is a novel antimicrobial with the potential to address unmet needs in serious skin infections, with significant market opportunities

Unmet market needs *Slide 4-6*	Antimicrobial resistance is a significant issue, **with no new classes of antibiotics approved in more than 33 years**
Favourable dynamics *Slide 7-8*	**Significant market opportunity** underpinned by **increasing global focus** and **coordination of research, regulatory and funding efforts**
Potential value upside *Slide 9*	**Major pharmaceutical players are pursuing aggressive acquisition strategies** to secure emerging antibiotic development opportunities
Exciting initial data *Slide 10-11*	Pre-clinical data indicates the **combination of CBD and Permetrex™ significantly improves killing effect** and demonstrates the **potential to treat unmet needs in skin infections**
Clear pathway *Slide 12*	**Complete evaluation of opportunities** in the near term to **identify high priority indication(s),** with the objective to move the lead indication into **patient study in 4Q CY2018**

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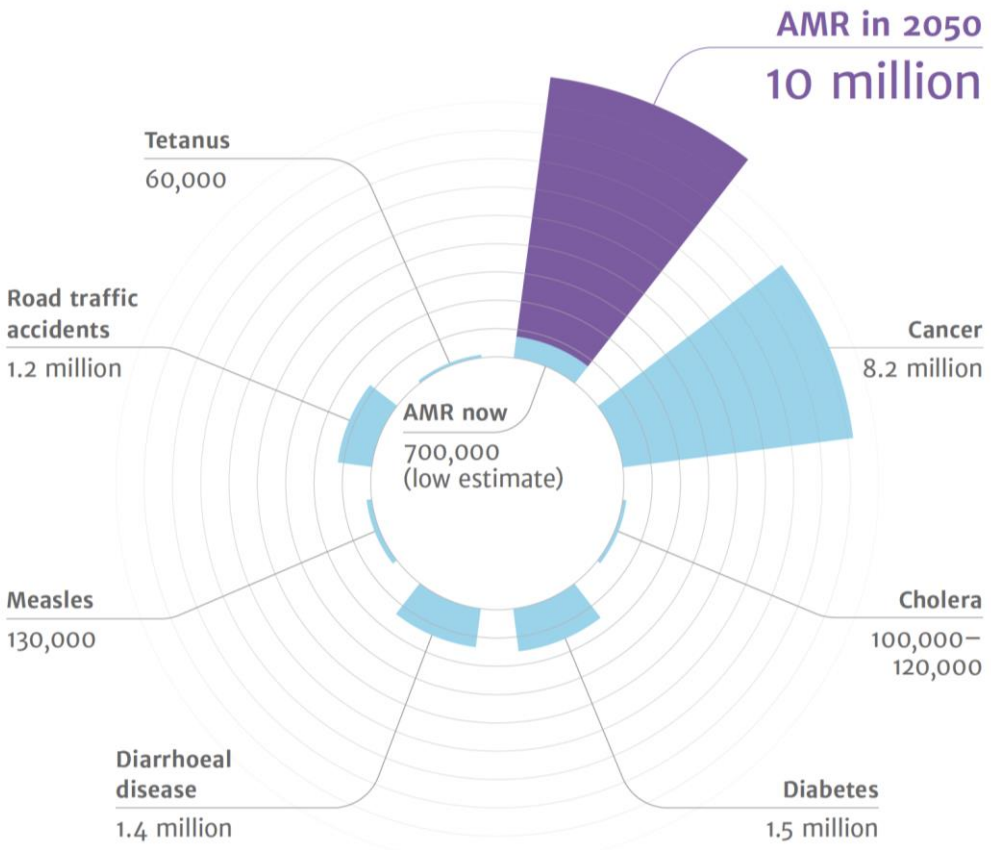
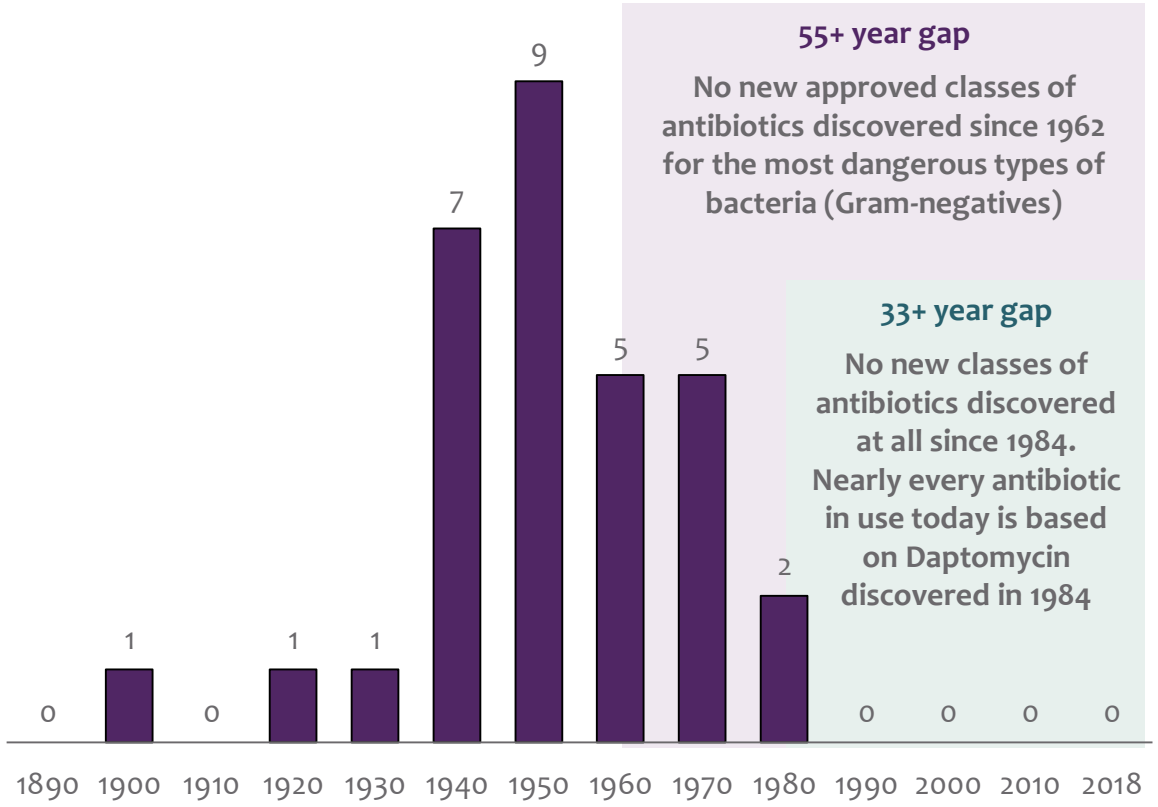
The problem of antimicrobial resistance

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

Deaths attributable to antimicrobial resistance (AMR)[1]



Number of antibiotic classes discovered or patented[2]



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

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How antibiotic resistance is developed

When bacteria survive exposure to drugs that would normally eliminate them, these surviving bacteria strains grow and spread resistance, which leads to the emergence of "superbugs"

Overview

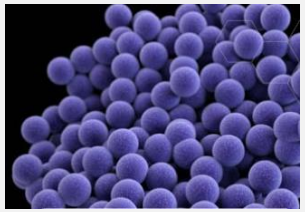
- Strains of bacteria that avoid being eliminated by antibiotics lead to the emergence of "superbugs" (such as MRSA)
- Resistant infections cause severe illnesses which may increase recovery time, increase medical treatment expenses and/or kill patients
- **Failure of "first-line" antibiotics requires physicians to use stronger, more toxic alternatives, which in turn enhances the likelihood of developing further resistance and the exhaustion of limited treatment options available**
- Increased use of antibiotics in food and animals has contributed significantly to human antibiotic resistance with ~400k people suffering from food-borne antibiotic resistance in the US each year

Antibiotic resistance

1. Only a few bacteria are drug resistant
2. Antibiotics kill bacteria causing illness, along with good bacteria that protect the body
3. Drug-resistant bacteria are able to grow and overtake
4. Some bacteria give their drug-resistance to other bacteria, causing more problems

Methicillin-resistant staphylococcus aureus (MRSA)[1]

MRSA is a serious public health concern and requires prompt and sustained action to ensure the problem does not grow



80,461
severe MRSA infections per year

11,285
deaths from MRSA per year

1. Centers for Disease Control and Prevention - https://www.cdc.gov/mrsa/index.html

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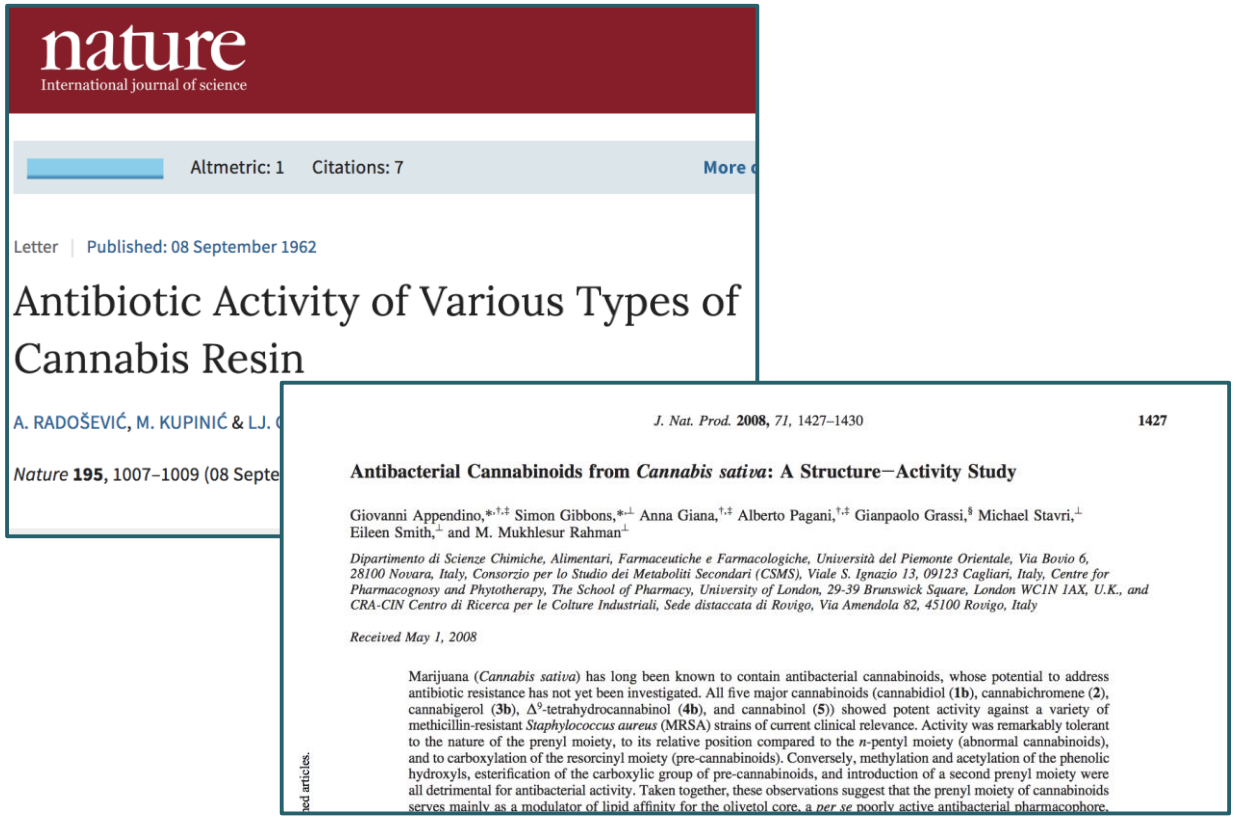
Cannabidiol as a prospective new antimicrobial

The limited scientific research that is available has indicated a potential role for cannabidiol in the treatment of antibiotic resistant bacterial infections

Literature support



nature
International journal of science

Altmetric: 1 Citations: 7 More

Letter | Published: 08 September 1962

Antibiotic Activity of Various Types of Cannabis Resin

A. RADOŠEVIĆ, M. KUPINIĆ & LJ.

Nature **195**, 1007–1009 (08 Septe

J. Nat. Prod. **2008,** *71,* 1427–1430 **1427**

Antibacterial Cannabinoids from *Cannabis sativa*: A Structure−Activity Study

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Received May 1, 2008

Marijuana (*Cannabis sativa*) has long been known to contain antibacterial cannabinoids, whose potential to address antibiotic resistance has not yet been investigated. All five major cannabinoids (cannabidiol (**1b**), cannabichromene (**2**), cannabigerol (**3b**), Δ^9-tetrahydrocannabinol (**4b**), and cannabinol (**5**)) showed potent activity against a variety of methicillin-resistant *Staphylococcus aureus* (MRSA) strains of current clinical relevance. Activity was remarkably tolerant to the nature of the prenyl moiety, to its relative position compared to the *n*-pentyl moiety (abnormal cannabinoids), and to carboxylation of the resorcinyl moiety (pre-cannabinoids). Conversely, methylation and acetylation of the phenolic hydroxyls, esterification of the carboxylic group of pre-cannabinoids, and introduction of a second prenyl moiety were all detrimental for antibacterial activity. Taken together, these observations suggest that the prenyl moiety of cannabinoids serves mainly as a modulator of lipid affinity for the olivetol core, a *per se* poorly active antibacterial pharmacophore.

ed articles.

Research suggests potential, but questions remain…

- What is the mechanism of action?
- What is the effective dose?
- Is there a broad spectrum effect?
- What is the optimal delivery mechanism to target lesion?
- Implication of long term use?
- Will bacteria develop resistance to cannabidiol?

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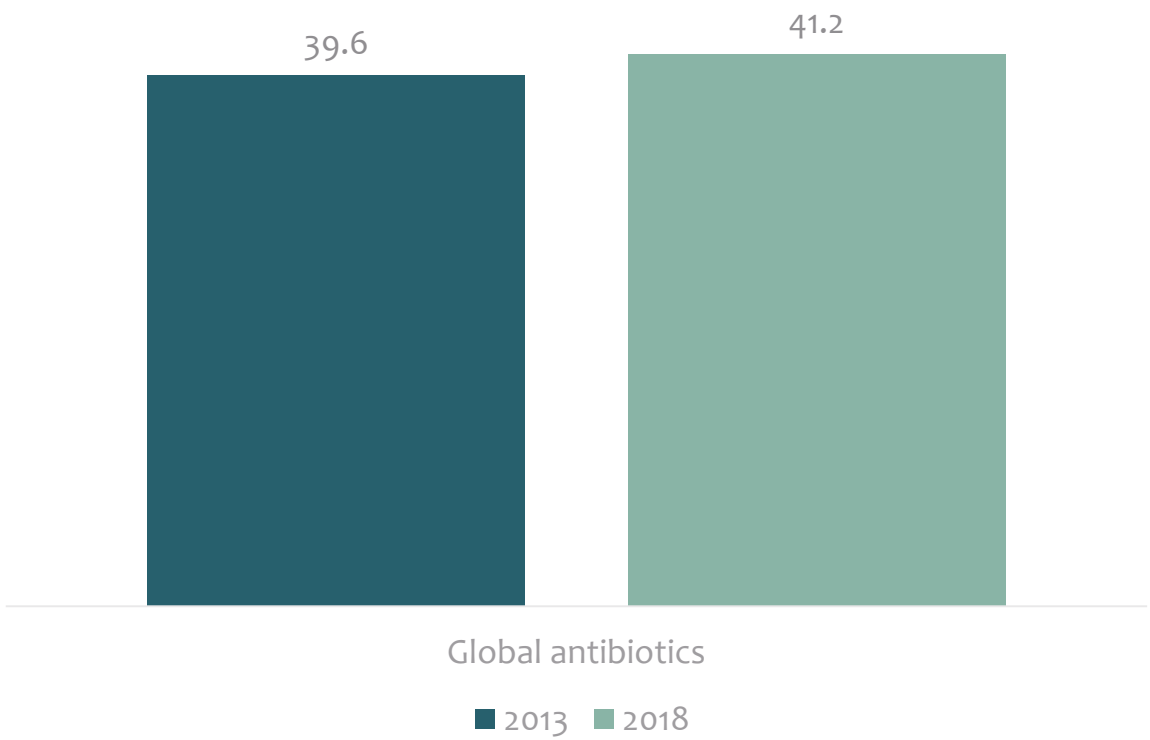
Large antimicrobials market with numerous opportunities

There is a substantial global market for antimicrobials. Botanix is currently assessing the market potential of multiple target indications

Global market size of antimicrobials (US$bn)



Potential target indications

- ✓ Skin and soft tissue infections
- ✓ Acute bacterial skin and skin structure infections
- ✓ Diabetic foot ulcers
- ✓ Bite related infections
- ✓ Decubitous ulcer infections
- ✓ Necrotising skin infections

Source: Visiongain

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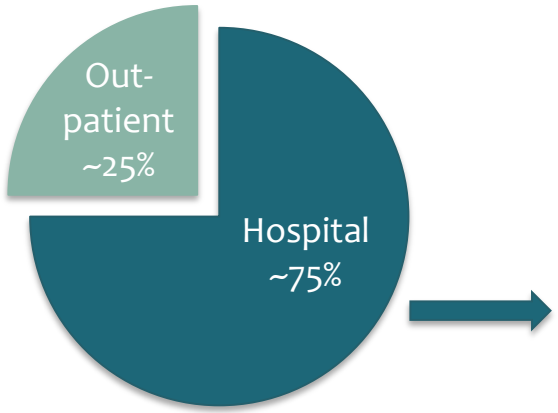
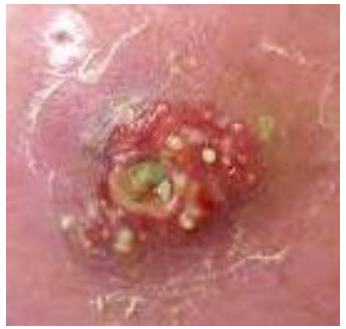
Example market opportunities - ABSSSI

Acute bacterial skin and skin structure infections (ABSSSI) is only one target market – 3m+ patients hospitalised each year, which in combination with outpatients, comprises an estimated 30m days of treatment worth ~US$10bn[1]

ABSSSI annual days of treatment (DOT)





Product	DOT (m)
Vancomycin	7.2
Cefazolin	3.4
Piperacillin	3.4
Clindamycin	2.5
Ampicillin	1.6
Ceftriaxone	1.3
Levofloxacin	1.1
Gentamicin	0.7
Daptomycin	0.6
Tigecycline	0.4

- Acute bacterial skin and skin structure infections (ABSSSI) includes cellulitis, erysipelas, major skin abscesses and wound infections with a minimum lesion surface area of 75 cm^2
- In the US alone, there more more than 11m out-patient visits for ABSSSI annually, but if hospitalised, the average hospitalisation stay is 6.2 days
- There is an ~22.8% failure rate with initial antibiotic, which leads to a 3-fold increase in mortality risk
- 82% of pathogens identified in ABSSSI patients comprise methicillin resistant staph aureus (MRSA) or methicillin sensitive staph aureus (MSSA)
- Hospitals face significant financial penalties for readmissions and misdiagnoses, even though testing takes 48-72 hours and treatment needs to occur prior

Source: Stanford Group June 2017; Tackling Drug Resistant Infections Globally Final Report and Recommendations 2016; Hersh AL et al *Arch Internal Med* 2008 168: 1585-91; Edelsberg J et al. Infect Control Hosp Epidemiol. 2008; 29(2):160-69,

1. AMR conversion generic units to branded pricing

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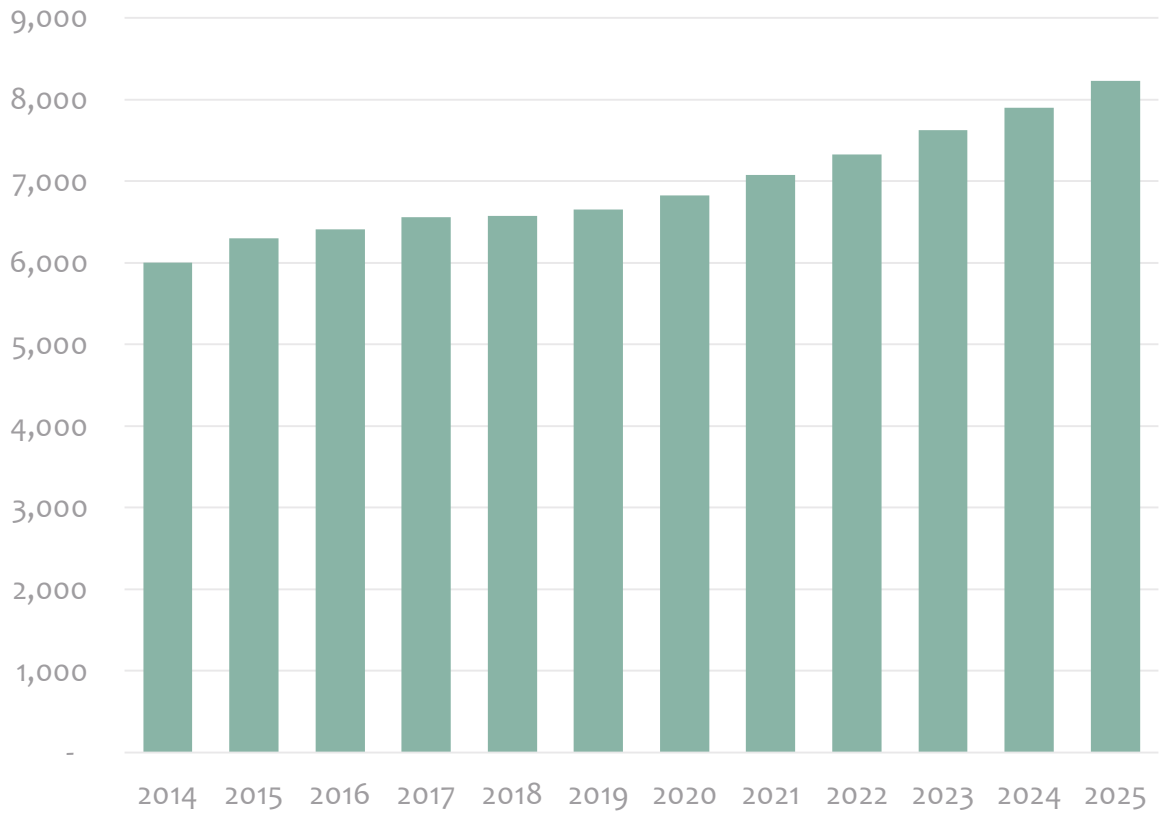
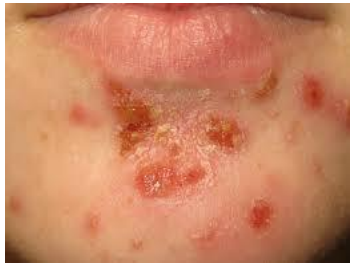
Other example market opportunities - SSTIs

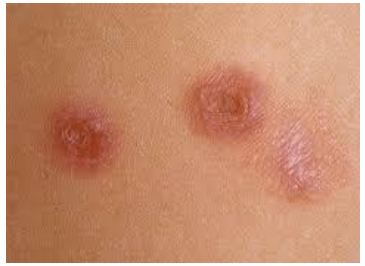
Skin and Soft Tissue Infections (SSTIs) is a separate potential target market – it generates more than US$6bn in annual revenue with a rapidly growing incidence and no new treatment options

Skin Infection Drugs Market Forecast 2014-2025 (US$m)



- Skin and Sift Tissue Infections (SSTIs) include infections of skin, subcutaneous tissue, fascia and muscle and range from simple cellulitis to rapidly progressive necrotizing fasciitis
- SSIs are also the most common healthcare-associated infection (HAIs) accounting for 31% of all HAIs among hospitalized patients
- MRSA accounts for ~59% of SSTIs presenting to the emergency department
- It is estimated that patients with a diagnosis of SSTI face prolonged hospital stays, treatment-associated risks, and potential long-term adverse outcomes, as well as a 2–11-fold increase in mortality risks





Source: Visiongain 2015 Dermatological Drugs Market Forecast 2014-2025, Kalyanakrishnan Ramakrishnan, MD et al, Skin and Soft Tissue Infections (2015) American Academy of Family Physicians.

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Increasing global focus on drug resistance

Favourable market dynamics underpinned by increasing focus on drug resistance globally and numerous regulatory initiatives and funding efforts available

Increased global focus recently

- Antimicrobial resistance (AMR) is a **significant global public heath issue** currently
- Many countries have developed a **dedicated and comprehensive plan** to deal with AMR

Key regulatory incentives

- Potential for **additional regulatory exclusivity** (extra 5 years – total of 10 years exclusivity) makes economic benefits from achieving FDA approval very attractive
- FDA's priority review potentially leads to **faster development pathway**
- Potential for **increased pricing** for resistant patient populations (in certain jurisdictions)
- Key legislation: GAIN Act; 21st Century Cures Act

Other funding sources

- **Non-dilutive funding** potentially available in various regions
- Potential sources: BARDA (US); IMI (EU); NARS (AU); CARB-X[1]

Source: Antimicrobial Resistance. Library of National Action Plans. World Health Organisation (WHO), 2017

1. BARDA (US): Biomedical Advanced Research and Development Authority; IMI (EU): Innovative Medicines Initiative, National Antimicrobial Resistance Strategy (AU)

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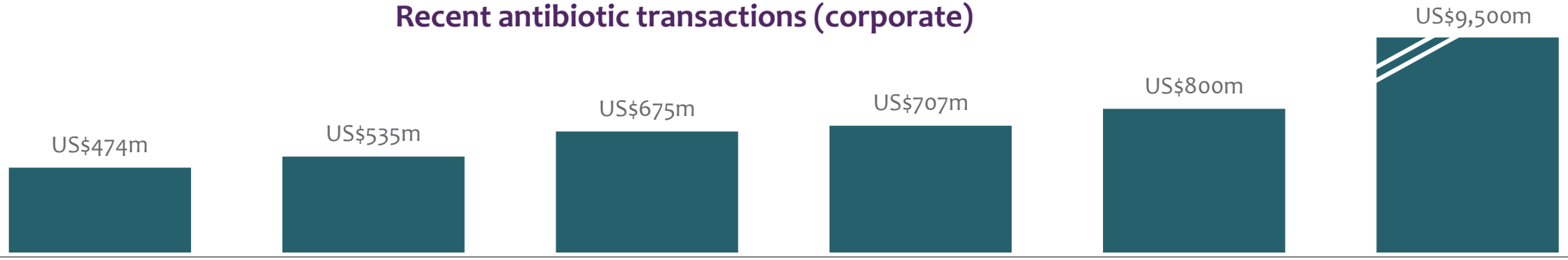
Potential value upside

Significant recent M&A interest in antibiotics development companies

Recent antibiotic transactions (corporate)



Deal date	Dec 2013	Jul 2013	Oct 2014	Jul 2013	Oct 2016	Dec 2014
Acquirer	The Medicines Company	Cubist Pharmaceuticals	Actavis	Cubist Pharmaceuticals	Horizon Pharma	Merck
Target	Rempex Pharmaceuticals	Optimer Pharmaceuticals, Inc.	Durata Therapeutics	Trius Therapeutics	raptor pharmaceuticals	Cubist Pharmaceuticals
Lead product	Carbavance™	DIFICID®	DALVANCE™	TR-701	PROCYSBI® QUINSAIR™	Multiple
Indication	Intravenous bacterial infections (gram negative)	Diarrhoea	ABSSSI	ABSSSI; pneumonia	Metabolic disorder; chronic pulmonary infection	Multiple
Phase	Completed Phase I	FDA Approved	FDA Approved	In Phase III	Commercially available	Commercially available

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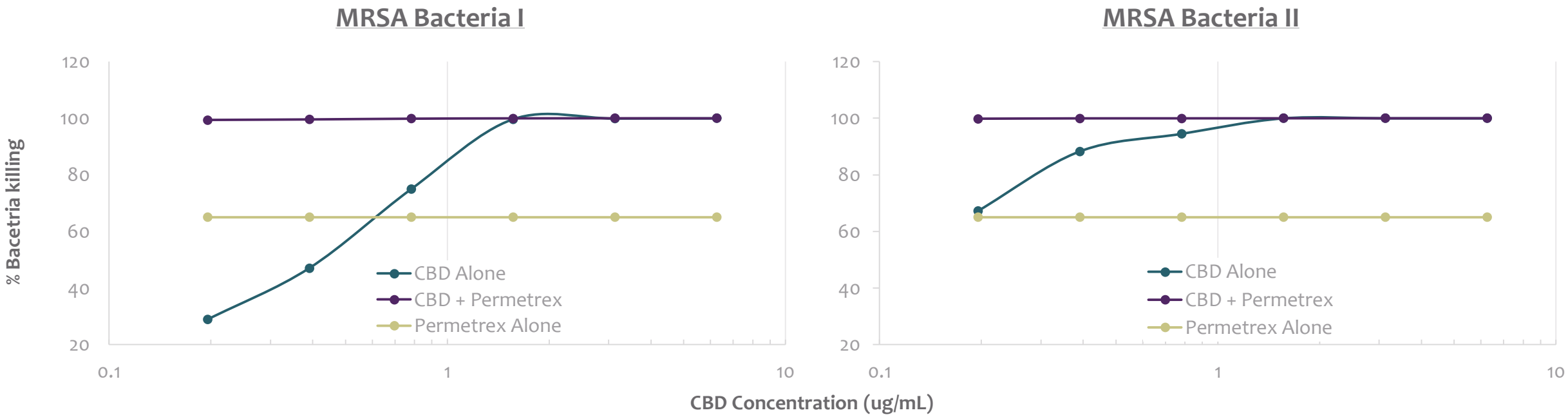
BTX 1801: Permetrex™ formulation of cannabidiol

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

Summary of data



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

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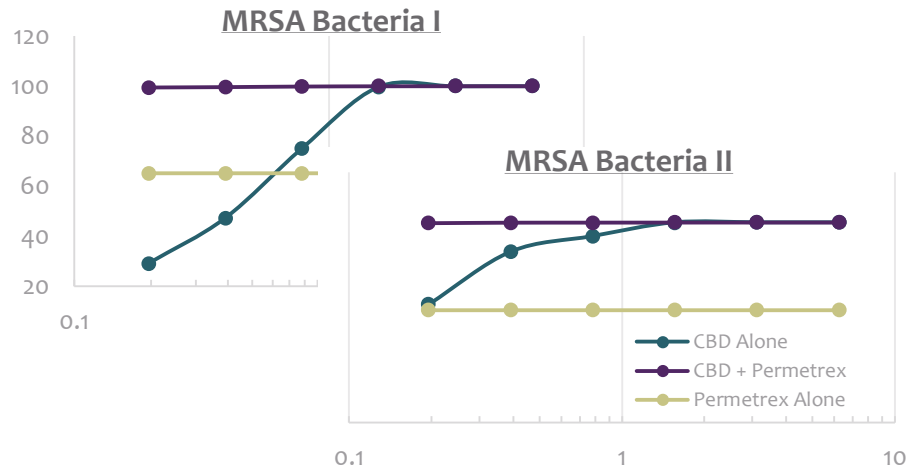
BTX 1801: key takeaways

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

Summary of data



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

BTX 1801 may have the following benefits

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

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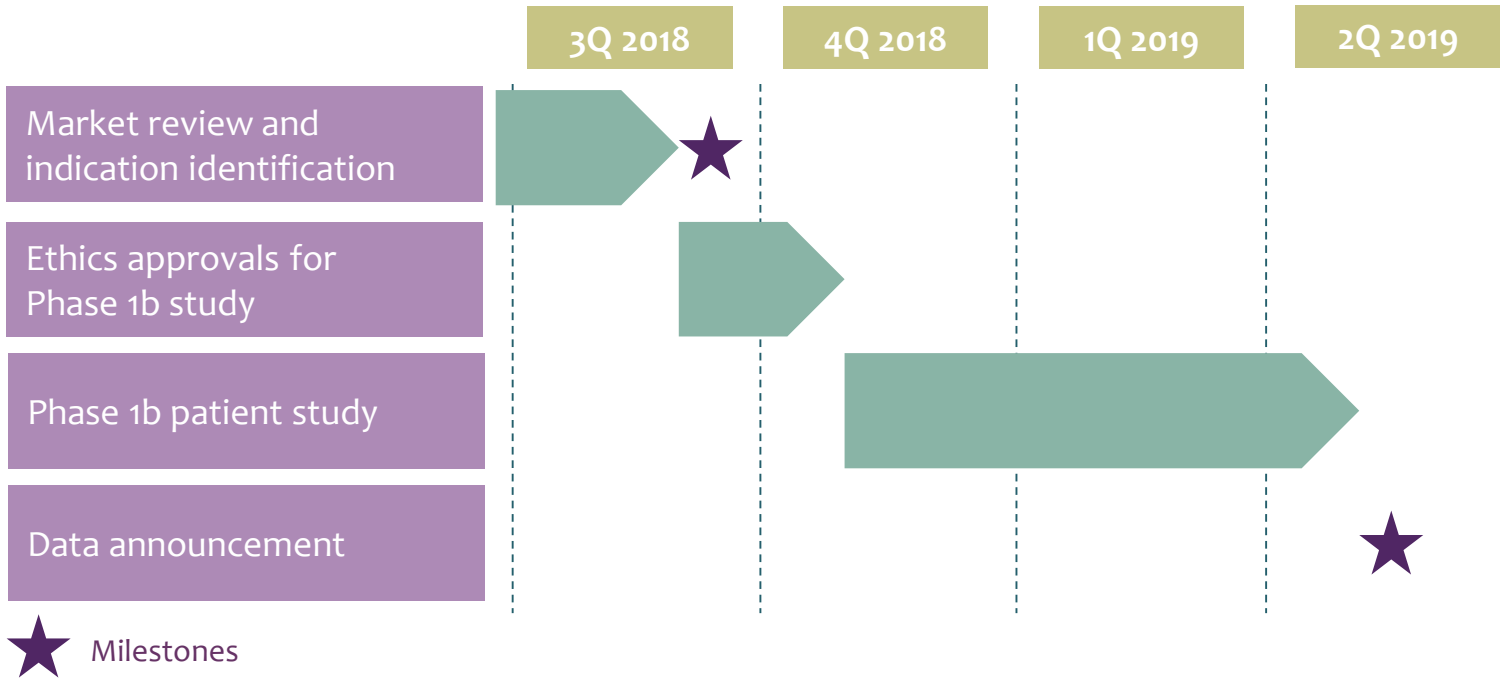
BTX 1801: next steps

Botanix is currently finalising the identification of the preferred type of skin infection to target and intends to follow a rapid development pathway to generate early clinical data and accelerate commercialisation

BTX 1801 indicative development timeline (CY)



- Development program leverages existing data from BTX 1503 and BTX 1204 programs – no need to repeat early clinical studies and low regulatory risks
- Assessment of indication ranging from simple skin infections to more challenging skin structure infections (incl diabetic foot ulcers)
- Clinical studies are rapid and provide comparative data to demonstrate efficacy and safety benefits

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