For personal use only

27 April 2021

New publication and growing awareness of antimicrobial resistance boosts Botanix antimicrobial platform

Key highlights

- **Support for Botanix's ground-breaking research on the antimicrobial potential of cannabidiol (CBD) has been published by a leading South American academic group in BioRxiv**
- **The BioRxiv article supports Botanix's discovery that synthetic CBD can also kill a select group of Gram-negative bacteria, including the bacteria responsible for the sexually transmitted disease gonorrhoea and the increasingly challenging *Clostridioides difficile* (*C.Diff*) infections**
- **New data presented in the same week as the screening of the ABC TV's *Invisible Wars* segment, which highlighted the global threat of antimicrobial resistance (AMR) and specific challenges of *Staph Aureus*, *Neisseria Gonorrhoea* and *C.Diff* infections**
- **Botanix is poised to provide an update in relation to its BTX 1801 development program following recent success with its Phase 2a antimicrobial study**

Philadelphia PA and Perth Australia, 27 April 2021: Clinical stage dermatology and antimicrobial company Botanix Pharmaceuticals Limited (ASX:BOT, "Botanix" or "the Company") is pleased to announce that its ground-breaking research on the antimicrobial potential of cannabidiol (CBD) has been supported by the publication of research data from a leading South American academic group in online journal BioRxiv. The research article is entitled "Cannabidiol (CBD) repurposing as antibacterial: promising therapy of CBD plus polymyxin B against superbugs", by lead author Nathália Abichabki, has been released via open access (the 'BioRxiv Paper').

BioRxiv Paper

The BioRxiv paper abstract summarises the conclusions from the research as follows: "Our results show promising translational potential of the combination CBD plus [last resort antibiotic] polymyxin B against multi drug resistant and extensively drug resistant gram negative bacteria, including polymyxin B-resistant *K. pneumoniae*, highlighting its potential as a rescue treatment for life-threatening infections caused by these superbugs."

The BioRxiv Paper follows the publication of Botanix's ground-breaking research in Nature Research's peer-reviewed journal, *Communications Biology,* in January 2021. Lead authored by Botanix collaborator Dr Mark Blaskovich from the Centre for Superbug Solutions at The University of Queensland, the article entitled "The antimicrobial potential of cannabidiol" highlighted for the first time the activity of CBD against *Neisseria Gonorrhoea* and *C.Diff* infections and identified the potential of membrane disrupting antibiotics polymyxin B and colistin to enhance the effect of CBD against a range of problematic bacteria (the 'Botanix Paper').

Dr Blaskovich also appeared as a lead scientific commentator on ABC TV's *Invisible Wars* segment, which engaged top doctors and scientists from around the world to speak candidly about the alarming

For personal use only

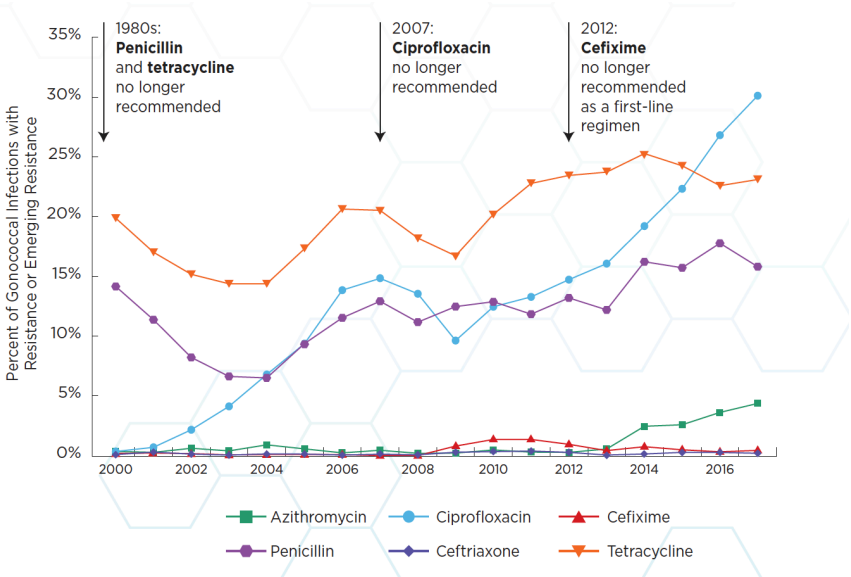
threat posed by superbugs and antimicrobial resistance (AMR). They compare AMR to the impact of climate change – an "unfolding disaster", getting worse every year. The *Invisible Wars* segment drew attention to a number of problematic bacteria such as *Neisseria Gonorrhoea* and *Clostridioides Difficile (C.Diff)* and highlighted the critical risks these infections pose to society and the significant costs they impose.

Gonorrhoea and *C.Diff*

The BioRxiv Paper supports the Botanix Paper discovery that CBD can kill the 'urgent threat' pathogen *Neisseria gonorrhoeae* which causes the sexually transmitted disease gonorrhea. *Neisseria gonorrhoeae* is a key pathogen on the World Health Organisation and US Centers for Disease Control and Prevention lists and is the second most commonly reported notifiable disease in the US, with almost 1m new infections each year in the US alone (~550k drug-resistant)[1], and ~78m cases globally[2].

In Australia, *Neisseria gonorrhoeae* is also the second most notified sexually transmitted infection, with infection rates increasing 63% between 2012 and 2016[3]. Despite rising incidence, the ability to treat *Neisseria gonorrhoeae* is diminishing due to the extraordinary capacity of the bacteria to develop resistance to clinically relevant antibiotics. Consequently, only Ceftriaxone remains as the only recommended treatment of *Neisseria gonorrhoeae* and a number of resistant strains have been identified around the world to this last antibiotic.[4]

Figure 1 – Antibiotic resistance of Gonorrhea[5]



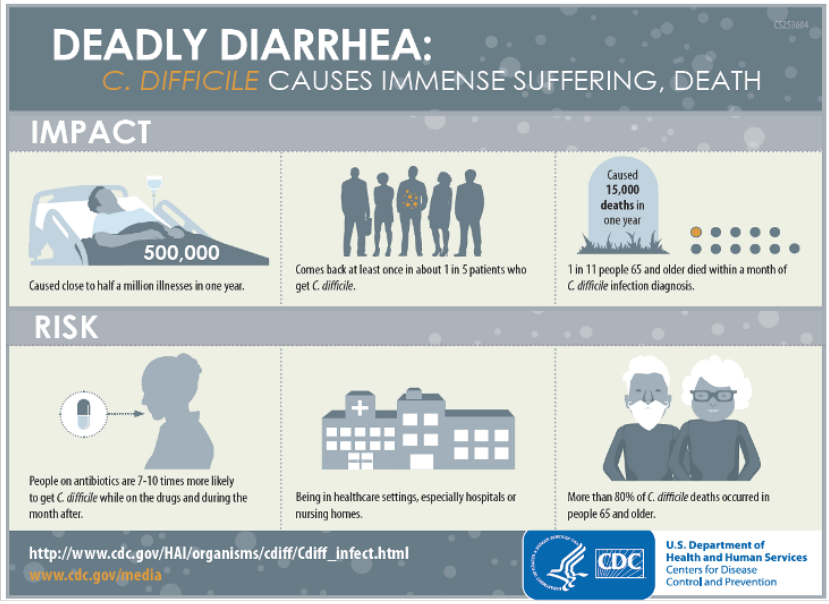
[1] American Academy of Pediatrics, "Adolescent Sexual Health" AAP Health Initiatives
[2] WHO: https://www.paho.org/hq/index.php?option=com_content&view=article&id=14872:sti-gonorrhea&Itemid=3670&lang=en
[3] Australian Government – Department of Health: https://www.health.gov.au/resources/pregnancy-care-guidelines/part-g-targeted-maternal-health-tests/gonorrhoea
[4] Emergence of ceftriaxone-resistant *Neisseria gonorrhoeae* strains harbouring a novel mosaic *penA* gene in China
Xiu L. et al (2020) Journal of Antimicrobial Chemotherapy
[5] CDC "Drug Resistant Neisseria Gonorrhoeae – Threat Level Urgent" available at https://www.cdc.gov/std/gonorrhea/arg/default.htm

For personal use only

The *Invisible Wars* segment also highlighted the challenge of *C.Diff* bacteria, which in the US is responsible for approximately US$5.4bn to US$6.3bn in costs each year[6]. *C.Diff* is a bacterium that can cause symptoms ranging from diarrhea to life-threatening inflammation of the colon which is estimated to reoccur among a considerable percentage of cases (~20% to ~30%). Although not exclusively, *C.Diff* infections are often associated with previous use of broad-spectrum antibiotics that disrupt the gut microbiota, leaving patients susceptible to infection by opportunistic pathogens.

In the US, *C.Diff* infections are the most frequent healthcare-associated infections (beyond MRSA infections), with an estimated 223,900 cases among hospitalised patients and 12,800 deaths in 2017, according to the US Centers for Disease Control and Prevention[7]. In recent years, *C.Diff* infections have become more frequent, severe and difficult to treat[8].

Figure 2 – US Centers for Disease Control and Prevention Risk assessment for *C. Diff*



Botanix has published data that shows synthetic CBD is effective against human and veterinary hypervirulent strains of *C.Diff* and was also effective against the super hypervirulent epidemic strains of ribotype 027 (responsible for severe outbreaks of disease in North America and Europe) and ribotype 078 (the strain generally associated with livestock which frequently spreads between animals and humans with no apparent geographic barrier).

Finalising BTX 1801 antimicrobial program development update

Botanix is currently finalising plans for the next steps in its BTX 1801 antimicrobial program, which includes analysis of positive data from the Phase 2a clinical study in February 2021, assessment of the optimal clinical development and expedited regulatory approval pathways, as well as reviewing the

[6] Zhang S, Palazuelos-Munoz S, Balsells EM, Harish N, Chit A, Kyaw MH. Cost of hospital management of Clostridium difficile infection in United States-a meta-analysis and modelling study. BMC Infect Dis. 2016; 16:447. Medline:27562241 doi:10.1186/s12879-016-1786-6

[7] ANTIBIOTIC RESISTANCE THREATS IN THE UNITED STATES. US Department of Health and Human Services. Centers for Disease Control and Prevention. 2019

[8] Mayo Clinic: https://www.mayoclinic.org/diseases-conditions/c-difficile/symptoms-causes/syc-20351691

For personal use only

commercial attractiveness of potential target indications. The double-blind, vehicle-controlled study was designed to evaluate the safety and local tolerability of two formulations of BTX 1801 to decolonise *Staph* and *MRSA* from the noses of healthy adults to reduce the risk of bacterial infections in surgical settings. Botanix will be providing an update on the development program in the near term.

Release authorised by

Vince Ippolito
President and Executive Chairman

About Botanix Pharmaceuticals

Botanix Pharmaceuticals Limited (ASX:BOT) is a dermatology and antimicrobial focused company based in Perth (Australia) and Philadelphia (USA) committed to the development of pharmaceutical products that are underpinned by science and supported by well-controlled randomised clinical trials. The Company has two separate development platforms, dermatology and antimicrobial products, both of which currently leverage the unique anti-inflammatory, immune modulating and antimicrobial properties of cannabinoids, particularly synthetic cannabidiol. Botanix has an exclusive license to use a proprietary drug delivery system (Permetrex™) for direct skin delivery of active pharmaceuticals in all skin diseases, which it utilises in its existing development programs and is being explored with a number of other product opportunities.

The Company is developing a pipeline of product candidates with recent positive data from its BTX 1801 Phase 2a antimicrobial study. For the dermatology platform, the Company has received ethics approval to commence its Phase 1b rosacea study and following a successful meeting with the FDA, the Company has confirmed a drug development plan for the BTX 1503 acne program to support registration. To learn more please visit: https://www.botanixpharma.com/

For more information, please contact:

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

Cautionary Note on Forward-Looking Statements

Any statements in this press release about future expectations, plans and prospects for the Company, the Company's strategy, future operations, and other statements containing the words "anticipate," "believe," "estimate, "expect," "intend," "may," "plan," "predict," "project," "target, "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the Company's ability to successfully develop its product candidates and timely complete its planned clinical programs and the Company's ability to obtain marketing approvals for is product candidates. In addition, the forward-looking

statements included in this press release represent the Company's views as of the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date hereof.

For personal use only