Analyst
John Hester 612 8224 2871
Tanushree Jain 612 8224 2849

Authorisation
David Coates 612 8224 2887

Botanix Pharmaceuticals (BOT)

Anti Microbial Trial

Speculative

See key risks on Page 7 and Biotechnology Risk Warning on Page 9. Speculative securities may not be suitable for Retail Clients.

Recommendation
Buy (unchanged)
Price
$0.07
Target (12 months)
$0.25 (unchanged)
Risk
Speculative

GICS Sector

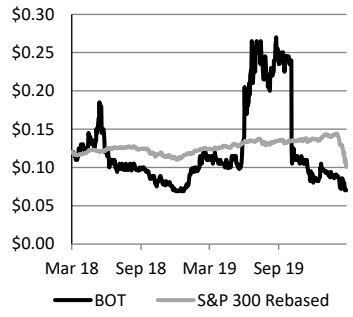
Pharmaceuticals & Biotechnology

Expected Return	
Capital growth	**257%**
Dividend yield	**0.0%**
Total expected return	**257%**
Company Data & Ratios	
Enterprise value	**$33.1m**
Market cap	**$68.1m**
Issued capital	**972.7m**
Free float	**91%**
Avg. daily val. (52wk)	**$930,000**
12 month price range	**$0.065 - $0.29**

Price Performance

	(1m)	(3m)	(12m)
Price (A$)	0.09	0.09	0.11
Absolute (%)	-19.5	-22.2	-36.4
Rel market (%)	9.7	3.4	-17.3

Absolute Price



SOURCE: IRESS

New Phase 2 Trial For Anti-Bacterial Platform

Calendar year 2020 will have significant news flow for Botanix with two separate Phase II trials reporting in the coming months. The first of these is for BTX1204 treating atopic dermatitis which is due 1Q CY2020. The second study reporting later this year is BTX1702 in Rosacea.

The company has now announced a third Phase II study. BTX1801 is a new formulation from its synthetic cannabinoid platform for use as an antimicrobial. The company had previously released data showing that the compound was effective in killing 132 different gram positive bacteria including staphylococcus aureus (s. aureus) and methicillin resistant staphylococcus aureus MRSA (aka golden staph). The formulation of BTX1801 is a tightly held trade secret with patents pending.

The use of the synthetic cannabinoids in clinical trials is in no way effected by any of the FDA's announcements regarding use of CBD products as a food or dietary supplement. BOT is seeking to have its products registered as drugs and is following the traditional clinical pathway towards registration.

The indiscriminant use of antibacterial medications including mupirocin over decades has resulted in the emergence and growing prevalence of anti-bacterial strains of s.aureus and MRSA. BOT has now released new data to demonstrate the potent antibacterial activity of BTX1801 against mupirocin resistant strains of s.aureus and MRSA. As a result BOT will now invest in a phase 2 study to investigate the potential of this drug to nasal colonisation of these bacteria. We expect this trial will be a stepping stone to a pivotal study in the US.

Maintain Buy Rating

Short term catalyst this month is the headline data from the Atopic Dermatitis trial. The valuation is maintain at $0.25 and we retain our Buy (Speculative) rating.

Earnings Forecast

June Year End	FY19	FY20e	FY21e	FY22e
Revenues	4.8	7.6	20.2	51.1
EBITDA $m	-17.0	-18.4	-7.7	33.1
NPAT (underlying) $m	-17.0	-18.4	-7.7	33.1
NPAT (reported) $m	-17.0	-18.4	-7.7	33.1
EPS underlying (cps)	-2.2	-1.8	-0.8	3.3
EPS growth %	1%	nm	nm	nm
PER (x)	nm	nm	nm	2.1
FCF yield (%)	nm	nm	-13%	45%
EV/EBITDA (x)	(2.0)	(1.8)	(4.3)	1.0
Dividend (cps)	-	-	-	-
Franking	0%	0%	0%	0%
Yield %	0%	0%	0%	0%
ROE %	-2549%	-83%	-53%	70%

SOURCE: BELL POTTER SECURITIES ESTIMATES

Antimicrobial Market Is Large and Underserved

Hospital acquired infections are a large cause of hospital readmissions following surgery in the US and around the world. In recent decades many of the bacteria responsible for causing these infections have become resistant to anti-bacterial treatments and have evolved into the so called "superbugs" that are increasingly challenging to treat.

MARKET DRIVER

There has not been a new class of antibiotic for the treatment of gram negative bacteria since the 1960's and no new class of antibiotic of any description since 1984. As a result serious infections including the well know staphylococcus Aureus (s.aureus) and Golden Staph (MRSA) have become very difficult to treat. MRSA is a subtype of s.aureus.

The new preclinical data from BTX appears highly encouraging. BTX1801 displays potent antibacterial activity against staphylococcus aureus strains resistant the standard of care (Mupirocin). Mupirocin is the generic name for this popular topical treatment used for the treatment of bacterial skin infections.

References to anti-bacterial resistant strains of both MRSA and s. aureus are readily available with numerous studies conducted in various hospitals. In a 2014 study, out of 82 non duplicate MRSA isolates (collected from inpatients and outpatient specimens), mupirocin resistance were in 15 (18.3%) isolates. Of these 8 were high level resistance[1].

In a separate study from 2015 nasal swabs were collected from 200 health care workers (HCWs) who were screened for MRSA. Approximately 14% of HCWs showed nasal carriage of MRSA. Nursing orderlies were the predominant carriers. E-test showed four mupirocin resistant isolates[2].

The widespread use of mupirocin has led to the rapid emergence of mupirocin resistance such that some hospitals in the US have abandoned its use. As consequence, there is a dire need for a new treatment.

Published research quoted by BOT now estimates the global mupirocin resistant s.aureus prevalence has now increased to 7.6% and MRSA 13.8%.

In US hospitals, hospital acquired infection rates are a major problem for surgical patients. US guidelines for peri-operative care in cardiac surgery required intranasal decolonisation prior to surgery with topical therapy applied universally to all cardiac surgical patients.

A further US Government funded study published in the New England Journal of Medicine showed that across >2000 surgical patients who underwent MRSA decolonisation for 6 months after discharge, there was a 44% reduction in MRSA infections.

FIRST MARKET – SURGICAL SITE INFECTION

Hospital acquired infections represent the nearest short term opportunity for commercialisation of a CBD based topical product. Ironically the data suggests that 80% of wound infections can be traced by DNA to bacteria in the patients' own nose. This data gave rise to the guideline for intra nasal decolonisation prior to surgery as noted above. Currently hospitals use Mupirocin for this function, however, resistance levels are now so high that hospitals are seeking alternatives – hence the opportunity for a new class of antibacterial.

[1] North American Jnl Science Medicine 2014 Aug, 6(8) 403 - 407

[2] Jnl Res Pharm Pract. 2015 Oct – Dec 182 – 186.

The preclinical work by Botanix concentrated on three mupirocin resistant strains of s. aureus. Mupirocin resistant strains are grouped into low level resistance and high level resistance phenotypes. Minimum inhibitory concentrations (MICs) are defined as the lowest concentration of antimicrobial that will inhibit the visible growth of a microorganism after overnight incubation. MIC's are commonly used in research to determine the in-vitro activity of new antimicrobials.

The results are shown in figure 1 below:

Figure 1 - Antibiotic MIC comparison

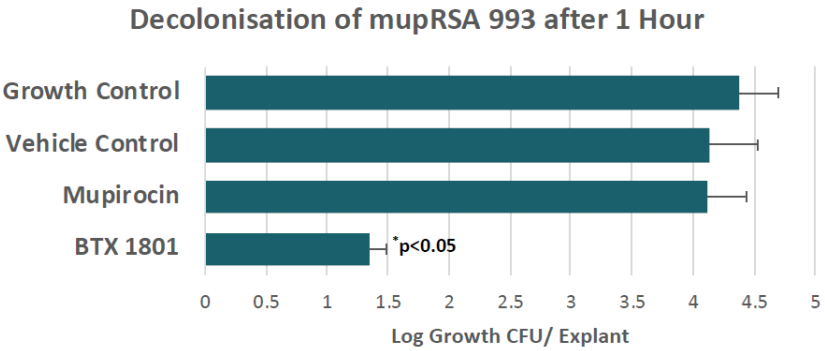
S. aureus Strain	Mupirocin Resistance Level	Cannabidiol MIC Range (µg/mL)	Mupirocin MIC Range (µg/mL)
mupRSA 815	Low level	3.125	16 - 32
mupRSA 329	High Level	3.125	>1,024
mupRSA 993	High Level	1.56 – 3.125	256 – 1,024

SOURCE: COMPANY DATA

Across all three phenotypes the concentration of the CBD compound was far less than Mupirocin. For the two high level Mupirocin resistant strains (329 and 993), the required use of cannabidiol is small fraction of the Mupirocin.

The results were confirmed in Ex-vivo pig skin (porcine) studies for decolonisation of mupRSA993.

Figure 2 - Ex vivo porcine skin model comparison



SOURCE: COMPANY DATA

In this experiment Mupirocin was virtually ineffective after 1 hour of treatment showing little to no improvement relative to the control. Conversely BTX1801 demonstrated a vastly superior rate of decolonisation.

These results were sustained for at least 24 hours. BTX 1801 was clearly superior to mupirocin in decolonisation of the bacteria with the added advantages that it has a rapid effect and is showing no signs of developing resistance.

BOT will target surgical sight infections in an upcoming study to be run in Australia. The study will target nasal colonisation of s. aureus which is thought to be responsible for up to 80% of wound infections (i.e. patients infecting themselves).

CLINICAL TRIAL TO CONFIRM ANTIMICROBIAL EFFICACY

The encouraging results from this preclinical work has led to the inception of a new clinical trial to confirm safety and efficacy in humans.

BOT will run a phase 2a trial targeting nasal decolonisation. The trial will be run at a single Australian site with the trial design described in figure 3 below.

Figure 3 - BTX1801 Trial design for nasal decolonisation

	n
BTX1801 Formulation A	20
BTX1801 Formulation B	20
Vehicle A	10
Vehicle B	10
	60
Patients randomly allocated to each arm	
Double blinded	
Participants treated twice daily for 5 days	
Primary endpoints	
Safety and tolerability	
Proportion of volunteers carrying s.aureus at day 8 and 28	
Proportion of volunteers carrying MRSA at days 8, 12, and 28	
Nasal recolonisation rates of s.aureus at days 12 or 28	
Pharmacokinetic studies on Formulations A & B	

SOURCE: COMPANY DATA

Pending the results from this study, the company plans to submit an IND application with the FDA in 3Q CY2020. The submission will almost certainly include the data from this study. If all goes to plan we would expect BOT to commence enrolment of an approval study in the US in early to mid 2021.

The nature of any future US study will depend on future discussions with the FDA. We would hope to see some measure of reduction in hospital acquired infection rates to support commercial adoption.

BTX1801 will be a prescription product (as are most antimicrobial products). If approved it will be highly differentiated from other antimicrobial products and is likely to have a long period of exclusivity. While it is early to be considering pricing discussions, the economic benefit to hospitals through the avoidance of hospital acquired infections could be enormous. The ultimate pricing of the product will depend on its efficacy (effect size) amongst other factors. In comparison, there are no branded mupirocin products i.e. the entire market is generic and it is quite inexpensive.

Pending the outcome from the study in nasal decolonisation, we expect to see further studies in the treatment of bacterial infection at the sight of surgical wounds and other wounds.

INTELLECTUAL PROPERTY

All BOT products including BTX1801 are synthetic cannabinoids, rather than plant derived. BOT is one of only a handful of companies pursuing clinical trials for the development of medicinal cannabis products globally. The synthetic product is available from API manufacturers. It is 100% pure and generally cheaper and more reliable to manufacture than the biological product.

BOT is focused on developing products for topical applications. All BOT products utilise the Permetrex topical delivery technology for which BOT has the exclusive global right to all drugs that treat skin disease.

The key patents on BTX1801 cover the formulation which is the combination of the synthetic drug with the permetrex technology and the dose.

BOT will pursue a qualified infectious disease product (QIDP) designation(s) with the US FDA for each new drug. This designation allows for an additional 5 years of marketing exclusivity following drug approval. In the addition, this designation allows for fast track designation and priority review.

The additional 5 years of exclusivity on marketing becomes redundant if the patents are held to be valid (i.e. patent life is 20 years), nevertheless, the QIDP designation is worthwhile for the fast track and priority review designation.

BTX1801 is being developed as a prescription medicine. Being a prescription only product, if approved, it will have a significant advantage compared to over the counter CBD products. For starters, label claims will have been proved by an extensive clinical trial program, hence the quality of the product can be assured as compared to OTC products. OTC products are largely unregulated and accordingly there may be significant variations in product quality and outcomes.

Figure 4 summarises the progress of the company's clinical program. Results from the Atopic Dermatitis trial are due in March 2020.

Figure 4 - Summary of clinical program

Indication	Development phase	Patients	Design	Primary endpoint	Bell Potter Comment
BTX1503 - Moderate to severe acne in children >12 ys	Phase 2	360	4 way, randomised, double blind, controlled	Change from baseline to week 12 vs non active placebo	Headline results reported that primary endpoints in the Australian arm of the study were met. End of Phase 2 meeting with the FDA expected in 2Q2020. Outcomes to inform the study design for a pivotal study.
BTX1204 Moderate atopic dermatitis	Phase 2	211	2 way, randomised, double blind, controlled study	ISGA score of "clear " or " almost clear" with at least a 2 grade improvement from baseline at week 12	Recruitment is complete. Headline results due in 1Q CY2020.
BTX1702 Papulopustular rosacea	Phase 1b	120	6 week double blind study in patients with moderate and severe disease	Safety and efficacy	Currently recruiting, headline results due 3Q CY2020
BTX1801 Antimicrobial resistance	Phase 2a	60	2 dosing groups each with a control. Separate formulations for each active group.	Safety, proportion of volunteers carry s. aureus at day 12. Nasal recoloniston rate at day12 and or day 28	Pts treated twice daily for five days. Study conducted in Australia. Company to apply for IND with the FDA later this year for a likely pivotal study in 2021.
Completed Studies					
BTX1308 Psoriasis	POC study	15	Gene regulation study only	Safety	Phase 1b study completed in 2Q 2019

SOURCE: COMPANY DATA AND BELL POTTER SECURITIES ESTIMATES

Figure 5 - Summary of changes to earnings

	2020			2021			2022		
	New	Old	% change	New	Old	% change	New	Old	% change
Revenues	7.6	5.0	51%	20.2	14.0	45%	51.1	40.0	28%
EBIT	-18.4	-13.6	-36%	-7.7	-6.5	-19%	33.1	29.3	-13%
NPAT	-18.4	-13.6	-36%	-7.7	-6.5	-19%	33.1	29.3	-13%
EPS	-1.8	-1.4	-31%	-0.8	-0.6	-28%	3.3	2.9	-14%

SOURCE: BELL POTTER SECURITIES

For 1H20, the only revenues were the R&D tax refund which was $2.5m higher than anticipated. Operating expenses were also higher than anticipated due mainly to the inclusion of non cash equity based remunerations.

For the 6 month ended 31 December 2019 the company reported a net loss of $7.0m with a net cash outflow from operations of $14.6m. The company had not received the $7.6 R&D cheque from the ATO before the end of the period, hence the separation between reported earnings and cash flow.

As at 31 December than company had notional cash of $35m (inclusive of the $7.6m receivable from the ATO). The cash will go a long way towards funding the entire clinical program noted above including the phase 3 study in acne.

The requirement for further capital from shareholders will depend primarily on the timing and quality of pending clinical outcomes. In the short term a good result in the atopic dermatitis trial is crucial the restoring market confidence in the product platform following the inconsistent results in the acne study from 2019.

We had previously taken into account revenue projections for the antimicrobial indication. Our valuation remains unchanged at $0.25 and we retain our Buy (speculative) recommendation.

Botanix Pharmaceuticals

Botanix Pharmaceuticals is an Australian biotech company engaged in the development of novel compounds for the treatment of a range of dermatological conditions. All products utilise synthetic cannabidiol (CBD) in conjunction with Permetrex™ skin delivery technology. The company has exclusive rights to this technology for all drugs that treat dermatology conditions. The first two indications are for chronic acne and atopic dermatitis (AD).

Key Risk Areas

Over the counter competition: The burgeoning market for nutraceutical CBD products presents a potential risk. These over the counter (OTC) formulations of plant derived CBD are gaining in popularity every quarter. OTC products are widely available throughout the US (by mail order) and in retail outlets and are relatively cheap, particularly for US patients without health insurance cover. It is likely there will be markets for both OTC products and pharmaceutical grade products. Competition may also emerge from other drug developers seeking to develop products involving synthetic CBD.

Efficacy remains unproven: Plant derived CBD products consist of well over 100 different types of CBD in a single product. Industry literature indicates the presence of an entourage effect whereby each of these compounds work together to generate the general healing effect whereas the Botanix products consist of a single synthetic cannabinoid. While the safety and efficacy data from clinical trials is encouraging, the long term efficacy and safety from BOT's products are yet to be studied in a large randomised trial.

Intellectual Property: The strength of the patents and other instruments protecting the intellectual property of Botanix are yet to be tested in the court. If Botanix's registered intellectual property is invalidated or removed from intellectual property registers this will adversely impact the long term earnings capacity of the company

Clinical Risk: BTX1503, BTX1204 and BTX1308 are a variation in dosage of the same active compound (CBD). Hence, if the company's leading asset BTX1503 is unsuccessful in phase II, this may increase the likelihood of further clinical failure in BTX1204, BTX1308 the other indications.

Financing Risk: The company is likely to require further capital from shareholders in order to progress its clinical program. The need for additional capital depends on numerous factors including the results from clinical studies and the willingness of development partners to engage in discussion for the commercialisation of BOT's various assets.

Regulatory Risk: The use of CBD for medicinal purposes remains at the fringe of mainstream medicine, hence there is no certainty that even with appropriate evidence from clinical trials that the company will secure a deal to commercialise these drugs.

DEA: Synthetic cannabidiol is a "Schedule 1" drug substance under the Controlled Substances Act (US) and is subject to strict control and regulation by the US DEA (Drug Enforcement Agency). The manufacture and handling of controlled substances is subject to strict limitations. Should any 3rd party be involved in the manufacture, handling or clinical trials involving the Botanix drugs lose their accreditation, these many hamper or halt entirely the development and commercialisation process.

Commercialisation: The company will almost certainly require a distribution partner in each market around the world. In the United States the ability of a distribution partner to sell these drugs will depend upon inclusion on various private payer formulary lists. Ultimately the distribution partner and the payers will determine the net price for each sale and this process is generally outside of the control of drug developers like Botanix.

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Botanix Pharmaceuticals

as at 16 March 2020

Recommendation	Buy, Speculative
Price	$0.07
Valuation (12 months)	$0.25

Table 1 - Financial summary

Profit & Loss (A$m)	FY18	FY19	FY20e	FY21e	FY22e
Year Ending June					
BTX1503 - Acne	-	-	-	-	29.4
BTX1204 - AD	-	-	-	13.2	4.4
BTX1308 - Psoriasis	-	-	-	-	5.9
R&D incentive	1.8	4.6	7.6	7.0	7.0
Total Revenue	1.8	4.8	7.6	20.2	51.1
COGS	-	-	-	-	-
Gross profit	1.8	4.8	7.6	20.2	51.1
GP margin	100%	100%	100%	100%	100%
Expenses Net of R&D	1.9	5.2	10.7	10.0	10.0
Total Clinical R&D Expense	11.0	16.6	15.3	18.0	8.0
Total Expenses	12.9	21.8	26.0	28.0	18.0
EBITDA	(11.1)	(17.0)	(18.4)	(7.7)	33.1
Depreciation	-	-	-	-	-
Amortisation	-	-	-	-	-
EBIT	-11.1	-17.0	-18.4	-7.7	33.1
Interest expense	0.0	0.0	0.0	0.0	0.0
Pre tax profit	(11.0)	(17.0)	(18.4)	(7.7)	33.1
Tax expense	-	-	-	-	-
NPAT- normalised	(11.0)	(17.0)	(18.4)	(7.7)	33.1
Reported NPAT	(11.0)	(17.0)	(18.4)	(7.7)	33.1

Cashflow (A$m)	FY18	FY19	FY20e	FY21e	FY22e
Gross cashflow	-10.1	-13.1	-18.6	-8.8	30.5
Net interest	0.1	0.0	0.0	0.0	0.0
Operating cash flow	-9.9	-13.1	-18.6	-8.8	30.5
Proceeds from asset sales	0.0	0.0	0.0	0.0	0.0
Free cash flow	-9.9	-13.1	-18.6	-8.8	30.5
Business acquistions	0.0	0.0	0.0	0.0	0.0
Proceeds from issuance	21.6	0.6	40.0	0.0	0.0
Movement in borrowings	0.0	0.0	0.0	0.0	0.0
Other	0.0	0.0	0.0	0.0	0.0
Change in cash held	11.6	-12.5	21.4	-8.8	30.5
Cash at beginning of period	5.7	17.3	4.8	25.5	16.8
FX adjustment	0.0	0.0	0.0	0.0	0.0
Cash at year end	**17.3**	**4.8**	**25.5**	**16.8**	**47.3**

Balance Sheet (A$m)	FY18	FY19	FY20e	FY21e	FY22e
Cash	17.3	4.8	25.5	16.8	47.3
Receivables	0.4	0.5	0.6	1.7	4.3
Short term investments	0.0	0.0	0.0	0.0	0.0
Other current assets	-	-	-	-	-
Property, Plant and Equipment	-	-	-	-	-
Other non current assets	-	-	0.6	0.6	0.6
Total assets	17.7	5.3	26.8	19.1	52.2
Trade payables	1.4	4.5	4.5	4.5	4.5
Debt	-	-	-	-	-
Other provisions	-	0.1	0.1	0.1	0.1
Total Liabilities	1.4	4.6	4.6	4.6	4.6
Net Assets	16.3	0.7	22.2	14.5	47.6
Share capital	33.3	33.9	73.9	73.9	73.9
Retained earnings	(17.5)	(34.5)	(52.9)	(60.6)	(27.5)
Reserves	0.4	1.3	1.3	1.3	1.3
Shareholders Equity	16.3	0.7	22.2	14.5	47.6

Valuation Ratios (A$m)	FY18	FY19	FY20e	FY21e	FY22e
Reported EPS (cps)	-2.3	-2.2	-1.8	-0.8	3.3
Normalised EPS (cps)	-2.3	-2.2	-1.8	-0.8	3.3
EPS growth (%)	-108%	1%	nm	nm	nm
PE(x)	**nm**	**nm**	**nm**	**nm**	**2.1**
EV/EBITDA (x)	nm	-2.0	-1.8	-4.3	1.0
EV/EBIT (x)	nm	-2.0	-1.8	-4.3	1.0
P/NTA (x)	3.3	81.5	3.0	4.7	1.4
Book Value Per Share (cps)	2.1	0.1	2.3	1.5	4.9
Price/Book (x)	3.3	81.5	3.0	4.7	1.4
DPS (cps)	-	-	-	-	-
Payout ratio %	0%	0%	0%	0%	0%
Dividend Yield %	0.0%	0.0%	0.0%	0.0%	0.0%
Franking %	0%	0%	0%	0%	0%
FCF yield %	nm	nm	nm	-13%	45%
Net debt/Equity	0%	0%	0%	0%	0%
Net debt/Assets	0%	0%	0%	0%	0%
Gearing	net cash	net cash	net cash	net cash	net cash
Net debt/EBITDA (x)	n/a	n/a	n/a	n/a	n/a
Interest cover (x)	n/a	n/a	n/a	n/a	n/a

SOURCE: BELL POTTER SECURITIES ESTIMATES

Recommendation structure

Buy: Expect >15% total return on a 12 month view. For stocks regarded as 'Speculative' a return of >30% is expected.

Hold: Expect total return between -5% and 15% on a 12 month view

Sell: Expect <-5% total return on a 12 month view

Speculative Investments are either start-up enterprises with nil or only prospective operations or recently commenced operations with only forecast cash flows, or companies that have commenced operations or have been in operation for some time but have only forecast cash flows and/or a stressed balance sheet.

Such investments may carry an exceptionally high level of capital risk and volatility of returns.

Research Team

Staff Member	Title/Sector	Phone	@bellpotter.com.au
TS Lim	Head of Research	612 8224 2810	tslim
Industrials			
Steven Anastasiou	Industrials	613 9235 1952	sanastasiou
James Filius	Industrials	613 9235 1612	jfilius
Sam Haddad	Industrials	612 8224 2819	shaddad
Alex McLean	Industrials	612 8224 2886	amclean
Hamish Murray	Industrials	613 9235 1813	hmurray
Chris Savage	Industrials	612 8224 2835	csavage
Jonathan Snape	Industrials	613 9235 1601	jsnape
Damien Williamson	Industrials	613 9235 1958	dwilliamson
Healthcare/Biotech			
John Hester	Healthcare	612 8224 2871	jhester
Tanushree Jain	Healthcare/Biotech	612 8224 2849	tnjain
Financials			
TS Lim	Banks/Regionals	612 8224 2810	tslim
Lafitani Sotiriou	Diversified Financials/Fintech	613 9235 1668	lsotiriou
Resources			
Peter Arden	Resources	613 9235 1833	parden
David Coates	Resources	612 8224 2887	dcoates
Stuart Howe	Resources	613 9235 1856	showe
Associate			
jJoseph House	Associate Analyst	+61 3 9235 1624	jhouse

Bell Potter Securities Limited
ACN 25 006 390 7721
Level 29, 101 Collins Street
Melbourne, Victoria, 3000
Telephone +61 3 9256 8700
www.bellpotter.com.au

Bell Potter Securities (HK) Limited
Room 1701, 17/F
Posperity Tower, 39 Queens Road
Central, Hong Kong, 0000
Telephone +852 3750 8400

Bell Potter Securities (US) LLC
Floor 39
444 Madison Avenue, New York
NY 10022, U.S.A
Telephone +1 917 819 1410

Bell Potter Securities (UK) Limited
16 Berkeley Street
London, England
W1J 8DZ, United Kingdom
Telephone +44 7734 2929