BELL POTTER

Speculative
See Key Risks on Page 12 & Biotechnology Risk Warning on Page 14
Speculative securities may not be suitable for Retail clients

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Pharmaxis Ltd. (PXS)

Bronchitol gets positive recommendation from Adcom by a narrow majority

Recommendation
Buy (unchanged)
Price
$0.275
Valuation
$0.54 (previously $0.47)
Risk
Speculative

GICS Sector

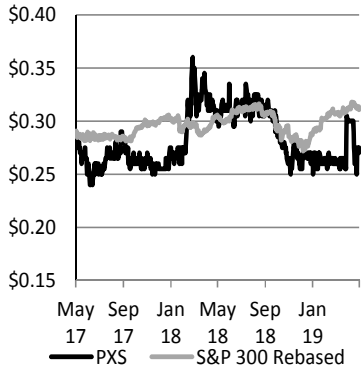
Pharmaceuticals & Biotechnology

Expected Return	
Capital growth	**96.4%**
Dividend yield	**0.0%**
Total expected return	**96.4%**
Company Data & Ratios	
Enterprise value	**$80.8m**
Market cap	**$108.4m**
Issued capital	**394.3m**
Free float	**98.7%**
Avg. daily val. (52wk)	**$68,858**
12 month price range	**$0.247- $0.347**

Price Performance

	(1m)	(3m)	(12m)
Price (A$)	0.26	0.26	0.31
Absolute (%)	7.84	5.77	-9.84
Rel market (%)	7.54	2.02	-11.96

Absolute Price



SOURCE: IRESS

FDA advisory committee backs approval of Bronchitol in US

The FDA Advisory Committee (Adcom) on Drugs for Pulmonary Allergies (PADAC) voted 9-7 in favour of approving bronchitol for adults with cystic fibrosis along with standard of care therapies. While the overall vote is in favour by a narrow margin, we note that the votes were in favour by a higher margin (10-6 in each case) on individual efficacy and safety questions supporting approval. Based on the outcome of the Adcom, strong support by the CF community, high unmet need, high morbidity and mortality with CF, bronchitol's potential to improve adherence and potentially benefit a subset of CF patients and its usage over the last 7 years in EX-US markets, the case for approving it in our view has become stronger. We now include the US opportunity for Bronchitol in our model and conservatively assign 85% probability of success to it.

Strong balance sheet with multiple catalysts in CY19

With its key assets approaching inflexion points and a strong balance sheet, we believe CY19 could be a transformational year for PXS. Net cash position of $27.7m provides ~1.5 years runway, ahead of boost expected through a licensing deal for LOXL-2 and milestone from Chiesi on launch of Bronchitol in US. Key Catalysts: a) Successful completion of commercial process for LOXL-2 asset, with a licensing deal expected to be finalised by end of FY19; b) FDA approval decision on Bronchitol by mid CY19, with potential launch and milestone from Chiesi in 2HCY19; c) Results from Phase 2A NASH trial run by partner Boehringer Ingelheim in Sep/Oct'19 (trial is fully recruited) and d) Results from Phase 1 trial with LOX (systemic) asset in 4QCY19.

Valuation lifted to $0.54, Retain Buy (speculative)

Revisions to our model have resulted in an increase in our Net loss forecast for FY19 by 15%, driven by lower Bronchitol revenue and higher opex. For FY20 we now expect a Net profit instead of a loss, which was driven by inclusion of Bronchitol related revenue from the US (milestone and sales) in our model. Changes to our Net loss forecast for FY21 was not material. Our valuation for PXS has lifted to $0.54/sh (was $0.47/sh), driven primarily by inclusion of the US Bronchitol sales from FY20 onwards and rolling forward of our DCF model. We retain Buy (Spec).

Earnings Forecast

Year end 30th June	2017A	2018A	2019E	2020E	2021E
Revenue (A$m)	17.3	50.2	18.0	28.9	10.7
EBITDA (A$m)	-15.2	11.5	-8.8	3.4	-14.2
NPAT (reported) (A$m)	-18.3	6.4	-13.3	-0.0	-17.8
NPAT (normalised) (A$m)	-17.4	7.6	-12.0	1.3	-16.4
EPS (reported) (cps)	-5.7	2.0	-3.5	-0.0	-4.5
EPS (adjusted) (cps)	-5.5	2.4	-3.2	0.3	-4.2
EPS growth (%)	N/A	NM	N/A	NM	N/A
PER (x)	N/A	11.5	N/A	83.3	N/A
EV/EBITDA (x)	-5.3	7.0	-9.2	23.7	-5.7
Dividend (¢ps)	0.0	0.0	0.0	0.0	0.0
Yield (%)	0.0%	0.0%	0.0%	0.0%	0.0%
Franking (%)	N/A	N/A	N/A	N/A	N/A
ROE (%)	NM	68.5%	NM	5.6%	NM

NOTE: REVENUE INCLUDES R&D TAX INCENTIVE, MILESTONES FROM BI DEAL AND CHIESI DEAL AND FY19 AND FY20 REVENUE INCLUDES RISK ADJUSTED UPFRONT AND MILESTONES FROM LICENSING DEAL FOR LOXL-2. SOURCE: BELL POTTER SECURITIES ESTIMATES

DISCLOSURE: BELL POTTER SECURITIES ACTED AS JOINT LEAD MANAGER FOR THE $24M PLACEMENT IN AUGUST 2018 AND RECEIVED FEES FOR THAT SERVICE.

Bronchitol receives narrow backing of FDA panel for approval

Background on Advisory Committees

The US Food and Drug Administration (FDA), as part of its pre-market review process for drugs, seeks unbiased advice/input from external experts who make up its advisory committees, to address areas of scientific or technical uncertainty. The FDA generally completes an initial review of a drug application during which it identifies questions on which it requires external input prior to making its decision.

The FDA then convenes an advisory committee meeting during which both the FDA representatives and the company seeking approval of the drug make presentations to the committee panel, then discuss the relevant questions on which FDA requires the committees input and then the committee members vote either in favour or not of approval of the drug. Importantly, there is an Open Public Hearing session to the meeting, during which interested community members/patients/clinicians can present relevant information/views in support of or against the product.

After the meeting, the FDA reviewers take into account the input of the Adcom when making an approval decision and assign a PDUFA date by which they are expected to communicate their approval decision. FDA in most cases follows the recommendations of the committee, however the recommendations are not binding.

FDA has 31 different advisory committees for different therapy areas. Pharmaxis/Chiesi's Bronchitol product for Cystic Fibrosis was discussed by PADAC (Pulmonary-Allergy Drugs Advisory Committee).

Bronchitol is in its second review cycle

In 2013, FDA had issued a complete response letter (CRL) at the back of the recommendation of the first advisory committee (PADAC) meeting who reviewed and voted unanimously (14-0) against recommending approval of the drug citing inadequate evidence of substantial efficacy as well as safety signals (hemoptysis) identified in the paediatric patients in two Phase 3 trials (Study 301 and Study 302). Study 301 demonstrated statistical significance on primary endpoint, however there were higher drop outs in the study among patients receiving Bronchitol and in Study 302 Bronchitol did not achieve statistical significance on the primary endpoint.

In the CRL, FDA requested that the sponsor (PXS) conduct an additional clinical trial to provide substantial evidence of efficacy and balance the safety findings specifically addressing hemoptysis (coughing up of bloody mucus).

PXS and its partner Chiesi then conducted a third Phase 3 trial Study 303 and narrowed the indication they would pursue to include only adults (i.e. patients 18 years and older), to address the hemoptysis seen in children.

Chiesi resubmitted the NDA (New Drug Application) with the US FDA for Bronchitol in Dec'18.

We understand that Study 303 is being considered by the FDA as being the most statistically robust out of the three pivotal trials. In this study, discontinuations were less of an issue, as patients who ceased treatment with Bronchitol were encouraged to continue to participate in the study rather than withdraw. FDA also believes the hemoptyis concern was largely addressed in the Study 303 by narrowing the proposed indication for Bronchitol to adults.

However, FDA wanted to convene a second PADAC meeting to obtain input from external experts due to primarily three issues as per its briefing documents:

- They believed that Bronchitol seems to have an effect on primary endpoint of change in FEV1 (a measure of lung function), however they consider the effect size as being modest and smaller than what they have observed for other marketed cystic fibrosis drugs in the US (such as Kalydeco). The question they wanted input from the Adcom is to understand if this modest effect size would represent a clinically meaningful benefit.
- Furthermore FDA's concern was that the efficacy of Bronchitol on the primary endpoint was not supported by secondary endpoints in any of the 3 trials. In Study 303, Bronchitol did not show statistical significance on any secondary endpoints including the Cystic Fibrosis Questionnaire which measures quality of life. Even though there was a numerical improvement in Bronchitol treated patients, the difference was not statistically or clinically meaningful. Lack of support from clinically meaningful secondary endpoints such as exacerbations when effect size on primary endpoint is modest, raises again the question around clinically meaningful benefit of the drug.
- On the safety side, there was a similar incidence of cystic fibrosis exacerbations among Bronchitol patients (32%) across the three pivotal trials vs. the control arm (33%). Investigator-reported adverse events of "condition aggravated" were considered CF exacerbations. In Study 303, the incidence of pulmonary exacerbations coded as SAEs (Serious Adverse Events) was consistent between the Bronchitol and control groups overall (13% and 11% respectively). However, in a subgroup analysis of CF exacerbations coded as SAEs, US Bronchitol treated patients had more exacerbations than control patients. 23 (21%) US Bronchitol-treated patients vs. 10 (11%) US control patients reported condition aggravated SAEs.

Based on the modest effect size in Study 303, we had chosen not to include Bronchitol's US opportunity in our model earlier leaving it as an upside should the Adcom decision be positive and FDA approval come through.

Bronchitol has received narrow backing of PADAC, with FDA decision expected in the next couple of months

In the May'19 meeting, PADAC voted 9-7 that the benefits of Bronchitol outweigh its risks and therefore its risk-benefit profile was adequate to support approval of the drug for its proposed indication (i.e. management of cystic fibrosis to improve pulmonary function in adults in conjunction with standard of care therapies). This is a vote in favour by a narrow margin and still leaves some uncertainty around what FDA's final decision may be vs. if we had a stronger endorsement from the panel.

However, we note that on the individual efficacy and safety questions i.e. whether the data provided substantial evidence of efficacy and whether the safety data was adequate to support approval for the proposed indication, the votes were in favour by a higher margin, 10-6 in each case. This in our view, improves likelihood of a positive decision by the FDA.

The discussion in the meeting focused on Bronchitol's safety, efficacy and use in clinical practice.

The drug found a huge support from the cystic fibrosis community (patients, clinicians and non-profit advocacy organisations) who strongly presented their case in support of its approval during the open public hearing.

KEY POINTS FROM THE MEETING DISCUSSION

- Overall the panel of committee members acknowledged that Bronchitol only demonstrated modest efficacy on the primary endpoint and did not have any support from secondary endpoints. However, the members who voted yes on efficacy (10-6 margin in favour) believed that there would still be a subset of patients that the drug

could benefit and potentially with a larger effect size than seen in the trials and clinicians who are specialists would be best positioned to figure out who these subset of patients are. We also understand that the clinicians who routinely treat CF patients argued that even a small improvement in lung function (which is main cause of morbidity and mortality in this patient population) as being the difference between a patient being able to perform a simple daily activity or not.

- On safety, the key issue was the numerically higher rate of 'condition aggravated' CF exacerbation seen in the US sub group treated with bronchitol. However, this difference appears to be driven by a higher rate of baseline Pseudomonas infections in the US population. It was noted that the US patients enrolled in the trial tended to be sicker and also had a history of more exacerbations than patients recruited in the trial outside of US and that potentially made them more vulnerable to additional exacerbations. We understand several panel members who supported approval on safety (10-6 margin in favour) were of the view that clinicians (who are not generalists but focused specialists) and CF patients who are very sophisticated should be left to assess the safety risk vis-à-vis the benefit. One was of the view, that any significant adverse effect would be quickly picked up and communicated within the CF community and its utility will accordingly be altered. They believed the option should be given to the clinicians and patients to choose to take the risk given the benefits.
- Clinicians routinely treating CF patients, CF patient advocacy organisations and CF patients themselves strongly highlighted the ease of use of Bronchitol being highly advantageous for adherence. During the open public hearing patients mentioned that hypertonic saline which they use through a nebuliser is very cumbersome and requires not only 20 minutes to complete but also requires washing, sterilising etc. which adds to time burden. This leads to patients avoiding taking them as often as they should (once daily vs. recommended twice daily). Bronchitol on the other hand is potable, inhaled powder, does not require a nebuliser and takes five minutes to complete treatment. Panel members in support of approval of Bronchitol agreed that the ease of use without adding time burden would improve patient adherence to the drug. We note there were some concerns among some clinicians whether the ease of use may lead to substitution of a less efficacious treatment by patients (hypertonic saline in favour of bronchitol). We also note however that though hypertonic saline is used in the majority of patients in the US, it is not an FDA approved-therapy.

OTHER FACTORS WHICH SUPPORT BRONCHITOL APPROVAL

- Cystic Fibrosis is a rare or orphan disease with very few therapy options. There are ~2000 mutations of the CFTR gene that cause cystic fibrosis and people even with the same mutations are known to have varied response to therapy. New treatments are urgently needed that can improve lung function.
- Bronchitol has a unique mechanism of action and provides an alternative treatment for improving lung function, especially in those patients whose mutations prevent them from using the current novel CFTR modulator drugs, which are tailored for specific gene mutations. Also, what may work for one CF patient in hydrating their airways (e.g. - nebulized hypertonic saline), may cause side effects such as bronchospasms in another patient. Hence, it addresses an unmet need by providing another option to patients which may not benefit all but benefit some CF patients greatly.
- Ease of use being a single dose inhaled dry powder could improve adherence and reduce time burden of treatment. Patients with CF have to follow a complex medical regimen on a daily basis and endure therapeutic interventions which require considerable time on a daily basis. Most patients also have co-morbidities which require further specialty interventions and affect quality of life. The time burden alone of routine patient self-care averages from 2-3 hours on a daily basis, if patient is adherent and compliant to all prescribed therapies and this increases if they have additional

treatment for co-morbidities. Some people partially follow the treatment regimen (once daily instead of twice daily) due to time burden.

- Bronchitol has been approved in 35 countries and as of Dec' 18, 8000 CF patients have been treated with the product primarily across Europe, Australia and Russia. This post market data should further support the safety case.

Based on the outcome of the advisory committee meeting, strong support for approval of the drug by the CF community (clinicians, advocacy organisations and patients), high unmet need for new CF treatments, the high morbidity and mortality associated with the CF disease, its potential to improve adherence and potentially benefit a subset of CF patients and the fact that it has been approved and used in several markets outside US over the last 7 years, the case for approving the product in our view has become stronger.

In our view, based on factors above FDA is likely to approve the product but would still have to focus on getting the label right to highlight risks and also deliberate on the need for post market approval studies etc. For example due to risk of bronchospasm, FDA can recommend that patients be asked to undergo a mannitol tolerance test (MTT) prior to introduction of Bronchitol (which would be consistent with the clinical trials).

Hence, in summary we believe the panel discussions and their backing albeit narrow for approving bronchitol, has greatly improved the likelihood of the product getting approved for the US market. We now include the US opportunity for Bronchitol in our model and conservatively assign an 85% probability of success to it of reaching the market.

Earnings and Valuation Changes

We have reviewed our assumptions for PXS and made adjustments to our forecasts based on the recent positive recommendation for Bronchitol from the FDA panel and quarterly update for 3QFY19 filed on the ASX, which have impacted earnings and valuation.

Key changes to our modelling assumptions

- We now include Bronchitol sales in the US market from FY20 onwards and also model the milestone of US$10m receivable on launch of the product in the US by partner Chiesi. At this stage we assign a risk adjustment to sales and the milestone of 85%.
- We have increased our manufacturing purchases cost for Bronchitol from FY20 onwards to reflect the US sales. We do not expect an increase in other operating costs for the Bronchitol/Aridol segment, given the core cost base is relatively fixed.
- We have also increased our forecasts for PXS' sales based payments to NovaQuest. As per the financing agreement (NovaQuest invested US$20m to support development, manufacturing and commercialisation of Bronchitol in 2013), NovaQuest is eligible to receive payments from PXS based on US sales revenue for Bronchitol for 7 years from launch of Bronchitol in US. We note that apart from sales based payments, PXS is not liable to make any other cash payment to service this liability.
- We have reduced our Bronchitol sales forecasts for FY19 driven primarily by lower than expected sales order from Chiesi for Western Europe in 3QFY19 and sales from Russia now expected to be recorded in 1QFY20 (vs. earlier estimate of 2HFY19). We do not expect another order from Chiesi for Western Europe in FY19. For Russia, the next order is now expected to be shipped in the June quarter and the sales will likely be recorded in September quarter.
- For FY19 we have reduced our clinical trial costs by ~$0.8m due to lower spend in 3QFY19 on the recently completed LOXL-2 program and our expectation now that the MAD (Multiple Ascending Dose) portion of the Phase 1 trial with the LOX systemic asset will only start in 1QFY20. We have also moved some of the clinical trial costs for FY20 into FY21 (where we had nil before) as we now understand that the topical asset from PXS' LOX program will move into the clinic only in 2HFY20 and PXS will potentially also start a Phase 1c/2 trial for the LOX systemic asset in 2HFY20. This was offset partially by cost moved from FY19 to FY20 related to the MAD portion of LOX systemic Phase 1 trial.
- For FY19 we have increased our drug development costs by ~$1.2m, which was driven primarily by the LOX program (systemic and topical), based on the higher spend on these in 3QFY19, partially offset by modestly lower spend than we expected on the LOXL-2 program during the quarter.
- We have increased our capex forecasts for FY19 based on spend in 3QFY19. PXS spent $212k to acquire new research equipment and software for drug discovery in the quarter and we expect similar expense in 4QFY19.
- We have reduced our forward D&A forecasts based on lower than expected depreciation expense in 3QFY19.
- We have slightly reduced our inventory forecast for FY19 based on the balance at end of 3QFY19.
- We have updated our model for the options and performance rights exercised and forfeited/expired over the last 3 months.
- We have rolled forward our DCF model for the quarter.

We value PXS at $0.54/sh

Revisions to our model resulted in an increase in our Net loss forecast for FY19 by 15% driven by lower Bronchitol revenue and higher opex. For FY20 we now expect a Net profit instead of a loss, which was driven by inclusion of Bronchitol related revenue from the US (milestone and sales) in our model. Changes to our Net loss forecast for FY21 was not material, with higher revenue being mostly offset by higher opex. Our valuation for PXS has lifted to A$0.54/sh (was A$0.47/sh), driven primarily by inclusion of the US opportunity for Bronchitol from FY20 onwards and rolling forward our DCF model for the quarter. **We retain our Buy (Speculative) recommendation.**

Table 1 - Key Changes to our FY19-21 Forecasts

	FY2019E			FY2020E			FY2021E		
	Old	New	Change (%)	Old	New	Change (%)	Old	New	Change (%)
Revenues	19.1	18.0	-6%	16.6	28.9	75%	8.6	10.7	24%
Interest Income	0.9	0.9	2%	0.9	1.0	16%	0.6	0.8	46%
Operating Costs	25.9	26.8	4%	25.6	25.5	0%	21.9	24.8	13%
EBITDA	-6.8	-8.8	29%	-9.1	3.4	-138%	-13.3	-14.2	6%
EBIT	-9.8	-11.5	17%	-12.1	0.7	-106%	-16.4	-17.0	4%
NPAT (adjusted)	-10.4	-12.0	15%	-11.6	1.3	-111%	-16.1	-16.4	2%
Adjusted Diluted EPS	-2.8	-3.2	15%	-2.9	0.3	-111%	-4.1	-4.2	2%
NPAT (reported)	-11.7	-13.3	13%	-12.9	0.0	-100%	-17.4	-17.8	2%
Reported Diluted EPS	-3.1	-3.5	13%	-3.3	0.0	-100%	-4.4	-4.5	2%

ALL AMOUNTS IN AUD IN MILLIONS EXCEPT EPS. SOURCE: BELL POTTER SECURITIES ESTIMATES

Our DCF valuation model is based on a WACC of 16.0% and a terminal growth rate of 1%.

Table 2 - Summary of Valuation

Forecasts	Base case
Enterprise value from DCF (AUDm)	194.7
Add: Reported Cash (AUDm)	35.1
Less: Current Debt	7.5
Equity value (AUDm)	222.3
Total diluted shares (million)	411.1
Value per share (AUD)	**$0.54**
Current Share price (AUD)	$0.28
Expected Capital Growth	96.4%

SOURCE: BELL POTTER SECURITIES ESTIMATES

Table 3 - PXS Sum-of-parts DCF Valuation Summary

Asset	Probability adjusted NPV (A$m)	Value per share (A$)	% Mix	Probability of success/Risk adjustment	Current Phase
Bronchitol and Aridol	$22	**$0.05**	10.0%	Aridol - Canada (80%), Bronchitol - US (85%)	Marketed (Ex-Canada) and for Bronchitol (Ex-US and Canada)
New Drug Development	$205	**$0.50**	92.3%	BI_1467335 (NASH, DR - 23.5%), LOXL-2 (NASH -22.0%)	BI_1467335 (Phase 2A) and LOXL-2 (Phase 1 complete)
Corporate/Non-Allocated	($33)	**-$0.08**	-14.7%	NA	NA
Reported Cash	$35	**$0.09**	15.8%	NA	NA
Reported Debt	($7)	**-$0.02**	-3.4%	NA	NA
Equity Value	**$222.3**	**$0.54**	**100.0%**		

SOURCE: BELL POTTER SECURITIES ESTIMATES

Table 4 – PXS- Key assumptions used in New Drug Development segment

Asset	Indication	Stage	Partnering Status	First Fiscal Year of sales (Est.)	Peak Market share	Peak Global Sales (US$m)	Probability of success
BI_1467335	NASH - F2/F3 fibrosis stage	Phase 2A	Boehringer Ingelheim	2027	5% (US), (3.5% ROW)	$1,962	23.5%
BI_1467335	Diabetic Retinopathy (DR)	Phase 2A	Boehringer Ingelheim	2027	10.0%	$813	23.5%
LOXL-2	NASH - F3/F4 fibrosis stage	Phase 1 complete	Will look to partner	2028	5% (US), (3.5% ROW)	$1,448	22.0%

GLOBAL PEAK SALES ARE PRE-RISK ADJUSTMENT AND ROYALTIES. SOURCE: BELL POTTER SECURITIES ESTIMATES

Table 5 – Deal Assumptions for Key Drug Development Pipeline Assets

Asset	Indication	Stage at Licensing	Licensee	Fiscal Year Timing of deal (Est.)	Total Deal Value in USDm (upfront plus milestones)	Upfront (USDm)	Other developmental & regulatory Milestones (USDm)	Commercial Milestones Est (USDm)	Royalty Rate (%)	PXS's share
BI_1467335	NASH and Diabetic Retinopathy	Phase 1	Boehringer Ingelheim	2015	645	33	462	150	11.0%	100.0%
LOXL-2	NASH and a second indication (potentially IPF)	Phase 1 complete	TBC	2019	700	50	470	180	11.0%	83.0%

NOTE: ROYALTIES ARE LIKELY TO BE TIERED. WE ASSUME A FLAT RATE FOR NOW. FOR LOXL-2 DEAL PXS AND ITS PARTNER SYNAIRGEN WILL SHARE THE DEAL VALUE IN 83:17 RATIO. THE BI DEAL VALUE INCLUDES OUR ESTIMATES ABOUT POTENTIAL UNDISCLOSED COMMERCIAL MILESTONES WHICH ARE PART OF THE DEAL AND HENCE MAY BE CONSERVATIVE. THE BI DEAL IS IN EUROS, WE HAVE CONVERTED IT TO USD AT CURRENT EXCHANGE RATES. SOURCE: BELL POTTER SECURITIES ESTIMATES

Upside Risk to our valuation

- **Clinical success will allow for increased probability of success:** We currently assign a 23.5% probability of success (of reaching the market) to BI_1467335, given that it's currently in a Phase 2A trial, for both NASH and DR. We envisage that completion of the trials with positive results and subsequent advancement of BI_1467335 into Phase 2B trials (BPe CY20) will allow us to assign a higher probability of success and therefore will lead to material upgrades in our numbers.

  Similarly, we currently assign a 22.0% probability of success (of reaching the market) to LOXL-2 in NASH, following the successful completion of its Phase 1 trial. We envisage that subsequent advancement of LOXL-2 into Phase 2A trials will allow us to assign a higher probability of success and therefore will lead to material upgrades in our numbers.

- **Conservative assumptions for BI_1467335 in absence of Phase 2 clinical data:** Our market penetration & pricing assumptions, are all based on the premise that BI_1467335 will be behind a few years to other NASH approaches such as Allergan's CCR2/CCR5 antagonist and Gilead's selonsertib. Our base assumption at this stage is that BI_1467335 shows at least equivalent efficacy to these assets, with a better safety profile, with the advantage potentially to be used both as a monotherapy and in combination, in the moderate-severe fibrosis stage NASH population, with one or more approved assets by that stage. In the absence of Phase 2 clinical data we are conservative in our assumptions at this stage.

- **Conservative assumptions for LOXL-2 to start with in absence of Phase 2 clinical data:** Our market penetration & pricing assumptions and deal size assumptions, are all based on the premise that LOXL-2 will be behind several years to other drugs targeting NASH to get to market. At that stage we expect the drug is more likely than not to be used as an add on therapy with existing standard of care by then to improve efficacy, likely in the more severe end of the fibrosis stage spectrum of NASH. However, given the scarcity of anti-fibrotic assets in development for NASH, we expect both partnering interest and deal size for the LOXL-2 asset with its novel mechanism of action (MoA) to be in line with other high value deals in this space recently. In the absence of Phase 2 clinical data from LOXL-2 we are conservative in our assumptions at this stage including our assumptions for the deal size. Following positive Phase 1 data and the fact that multiple pharma parties seem to be interested, there exists a potential for a deal to emerge with a value higher than our current forecast.

- **We do not model royalty revenue from a second indication (likely IPF) for LOXL-2 presently:** At this stage in our valuation, we do not include a market revenue model for LOXL-2 for Idiopathic Pulmonary Fibrosis (IPF) as a potential secondary indication and therefore do not model royalty revenue as a percentage of net sales from this indication to PXS. Confirmation of IPF as a second indication by PXS' future partner and progress of this into Phase 2 clinical trials is likely to considerably increase the market opportunity for this asset, in which case it's likely to be a source of considerable upside to our valuation in future.

- **No sales milestones from LOXL-2 deal included in our model:** At this stage we do not model PXS' share of the assumed US$180m sales milestones from a potential LOXL-2 deal in our model. We intend to include it in our model once a LOXL-2 deal is inked by PXS, in which case it's likely to be a source of upside to our valuation.
- **No value assigned for other early stage pipeline assets:** We also do not include any value for PXS' other early stage assets namely SSAO/MPO inhibitor and LOX inhibitor. PXS has initiated a Phase 1 trial in healthy volunteers with its LOX systemic asset in Feb'19.

  The LOX inhibitor program is developing a drug which broadly inhibits all the LOX family of enzymes, which has potential anti-fibrotic application in scarring (a topical formulation) and other severe fibrotic indications including some cancers (a systemic formulation). PXS has had positive results from its LOX systemic asset in myelofibrosis and pancreatic cancer and also intends to complete 3 month toxicology studies while running the currently ongoing Phase 1 trial in healthy volunteers. PXS intends to start a clinical study in pancreatic cancer patients in early CY20. Preclinical development is continuing for the topical asset, with PXS targeting early 2020 to start a Phase 1 trial in healthy volunteers with scarring.

  The SSAO/MPO program is developing a dual inhibitor of both SSAO and myeloperoxidase (MPO), which has potential anti-inflammatory application in both respiratory and cardiovascular disease. Preclinical development is continuing for this asset, however in has moved down the priority list behind the LOX topical asset.

  PXS believes that the above two assets may have higher potential and value add if developed to Phase 2A or 2B before partnering, vs. the strategy with its later stage assets targeting NASH which it looked to partner at or after Phase 1. Progress of these two assets into Phase 2 trials in future is likely to be a source of upside to our valuation.
- **We model limited markets for Bronchitol and risk adjust the US opportunity:** For Bronchitol, we model the existing markets of Australia, Western Europe including Italy, Eastern Europe and Russia and now also model US, following the recent positive recommendation in support of approval by the FDA advisory committee. PXS' US partner Chiesi is responsible for its commercialisation. Should Bronchitol get approved and launch in US, PXS will receive a US$10m milestone from Chiesi, additional US$15m sales milestones and a mid to high teen percentage of royalties on net sales. At this stage we assign US sales and the launch milestone from Chiesi an 85% probability of success, given FDA approval is yet to be granted. FDA approval and launch of Bronchitol in the US therefore will be an upside to our valuation for PXS. We also do not model the US$15m sales milestone receivable from Chiesi on meeting certain undisclosed sales thresholds at this stage, which would represent an upside to our valuation.
- **We model limited markets for Aridol:** For Aridol, we model the existing markets of Australia, Europe and South Korea and now also model US where the company relaunched Aridol in Dec'18 following FDA approval of its manufacturing facility. We also model revenue from Canada (assigning it an 80% probability of success), given Aridol is not approved in Canada as yet. Filing for approval in Canada was made in June 2018, with approval expected by mid-CY19. We assume an FY20 launch in Canada.
- **Small contribution from Bronchitol and Aridol segment in our valuation:** With the addition of the US opportunity for Bronchitol in our model, we now expect the Bronchitol and Aridol segment to transition to profitability over the next 1-2 years. Excluding the US opportunity, we believe Russia for Bronchitol and Canada for Aridol may surprise us on the upside, however at this stage we choose to be conservative till we see increasing traction in Russia for Bronchitol after obtaining wider reimbursement and launch in Canada for Aridol.

Pharmaxis Ltd. (PXS)

COMPANY DESCRIPTION

Pharmaxis, is a biopharmaceutical company focused on the development of drugs for inflammatory and fibrotic diseases. Its lead assets Phase 2 SSAO/VAP-1 inhibitor BI_1467335 partnered in a multi-million dollar deal with Boehringer Ingelheim and currently unpartnered Phase 1 LOXL-2 inhibitors are targeting Non-alcoholic Steatohepatitis (NASH), a multibillion dollar market, estimated to grow to be ~US$20bn-US$35bn. The drugs while not first-in-class, have the potential to be best-in-class and be useful in other fibrotic diseases and we forecast both to be blockbusters (i.e. have over US$1bn in peak sales). NASH market is expected to grow with rise in obesity and surpass HCV as the leading cause of liver transplant by 2020. There are currently no approved drugs which make the market largely untapped and underserved. The multifactorial aspect of NASH and future treatments likely to be a combination of therapies ensures that companies remain on the lookout for promising assets to license, which bodes well for licensing prospects for PXS' LOXL-2 inhibitors. PXS also has two marketed respiratory products Bronchitol and Aridol which we view as non-core, however they represent an existing albeit small revenue stream for PXS with potential upside should US approval come through.

INVESTMENT STRATEGY

We have a Buy (speculative) recommendation on Pharmaxis. Our investment thesis is based on:

$0.54 valuation: We value PXS using a risk adjusted DCF at $0.54. The valuation is approximately a 96.4% premium to the current share price of $0.275/sh.

Lead assets targeting NASH have blockbuster potential: Pharmaxis' lead assets Phase 2 SSAO/VAP-1 inhibitor BI_1467335 and Phase 1 LOXL-2 inhibitor are both targeting Non-alcoholic Steatohepatitis (NASH), a multibillion dollar market, estimated to grow to be ~US$20bn-US$35bn. We model US$1.96bn peak worldwide sales (pre risk adjustment) for BI_1467335 in NASH and US$1.45bn for LOXL-2 in NASH.

NASH represents significant commercial opportunity: NASH is a large market, growing rapidly with an increasing obese population. It is estimated that NASH will surpass Hepatitis C Virus (HCV) as the leading cause of liver transplants by 2020. There are currently no drugs approved for NASH, which makes this market largely untapped and underserved and a lucrative market opportunity for PXS to target. There are several drugs in development and interest and competition has both heated up. There have been a number of high value deals in this space recently and active companies are looking to license or acquire to build a portfolio of assets targeting different stages of NASH. Average deal sizes are around US$860m, however some deals recently have been over $1bn.

PXS emerging as a key player in NASH: Drugs targeting NASH in development fall under 3 groups based on their mechanism of action and stage of NASH they target – metabolic modifiers, anti-inflammatory agents and anti-fibrotic agents. It is expected that the future treatment for NASH is likely to be a cocktail of therapies as was seen earlier with HCV. Therefore we see drugs from each of the 3 categories to complement each other and competition likely to be restricted to drugs within the same category. Pharmaxis has two assets which fall under two different categories. BI_1467335 is an anti-inflammatory agent and LOXL-2 asset is an anti-fibrotic agent and therefore should complement each other and other drugs in advanced development. There are very few drugs in development in these 2 categories and as far as we are aware both these drugs are currently the only one in their class being actively developed for NASH.

Drugs not first-in-class but potentially best-in-class: PXS' SSAO/VAP-1 and LOXL-2 inhibitor are not the first in their class. However based on pre-clinical data for both and Phase 1 data for the SSAO drug, we believe the drugs possess a more favourable PK/PD

profile which could make them best-in-class. Data so far provides evidence of good safety profile, good oral bioavailability and potent, long lasting inhibition of targeted enzyme.

Potential exists to expand the use of lead drugs beyond NASH: Both the lead drugs have potential to be used across fibrotic diseases with the SSAO inhibitor in a phase 2 trial for Diabetic Retinopathy (DR) and LOXL-2 being explored in Pulmonary Fibrosis.

Partnership with Boehringer Ingelheim validates chemistry platform: PXS signed a multi-million dollar product acquisition deal with Boehringer Ingelheim (BI) in 2015, which marked the start of the turnaround for the company, strengthened its balance sheet and validated its amine oxidase chemistry platform and its ability to execute valuable deals.

Value inflexion points approaching: Results from phase 2A trials for the SSAO/VAP-1 drug partnered with BI in NASH is expected in 2HCY19 and in Diabetic Retinopathy in 1HCY20. LOXL-2 has successfully completed Phase 1 trials and longer term toxicology studies and PXS is now in discussions to potentially partner it, with a multi-million dollar licensing deal expected in 1HCY19.

Strong cash position: PXS' current cash reserves of A$35.1m, in our view, provides ~1.5 years cash runway, with flexibility to defer some expenses on other pipeline programs to further extend this runway. The company has a modest debt (related to finance lease) of $7.5m. PXS is unlikely to require any capital raisings in the medium term, given it has recently raised capital and strengthened its balance sheet. We believe the company is well placed to look at capital management initiatives such as a share buyback or special dividend to return some surplus capital to its shareholders after they finalise a deal for LOXL-2 later this year. PXS' strong cash position should also help its ongoing negotiations for the LOXL-2 asset. It will also allow it to pursue some asset acquisitions to further enrich its drug development pipeline and also allow the company to consider Phase 2A/2B development for some of its pipeline assets to add more value before partnering them out.

Risks

The key risks specific to Pharmaxis include, but are not limited to, the following:

- **Clinical risk:** There is a risk that PXS' clinical trials for its pipeline assets fail to reach their endpoints, which would in turn impact its commercial and partnering prospects.
- **Timing and clinical risk on partnered product:** For its partnered product BI_1467335, PXS is reliant on Boehringer Ingelheim (BI) for development timelines. The ability of PXS' product to finally reach the market and translate into royalty revenue streams for it depends on BI. Delays in timelines will affect near term milestone payments to PXS as well as its long-term revenue flow. Also if the product fails at any stage of clinical development or BI decides to discontinue the development of the product PXS' ability to generate revenue from that asset will diminish/or fail totally.
- **Reliance on partnerships to unlock value:** The success of PXS' business model is underpinned by its ability to ultimately attract valuable partnering deals for its assets, given PXS lacks the commercial infrastructure to support commercialisation. Our valuation in part is underpinned by PXS' ability to ultimately attract a valuable partnering deal for its LOXL-2 asset. Failure to attract partners for this asset or to negotiate attractive deal terms as we have postulated will impact our forecasts.
- **Bronchitol US approval decision will now affect our valuation:** While we look at Bronchitol and Aridol, PXS' currently marketed products as non-core assets and attribute minimal value to it, our inclusion of Bronchitol's US opportunity now makes our valuation vulnerable to FDA's decision on Bronchitol. We note that FDA's advisory committee has recently voted in support of approval of the product albeit only by a narrow majority. FDA does not have to follow the recommendation of the panel, but in most cases it does, however with such a narrow majority vote in favour, there still remains uncertainty around what the FDA's final decision may be. We currently assign an 85% probability of success to US sales of Bronchitol and risk adjust the potential US$10m milestone receivable from Chiesi on launch.
- **Regulatory risk:** Successful commercialisation of PXS' products is ultimately dependent on getting approval from the regulatory authorities to commercially launch the product. While PXS' partner with much more experience in navigating regulatory channels will be responsible for obtaining approvals, failure to satisfy regulatory requirements could mean that the product will fail to reach the market.
- **Commercial risk:** The pharmaceutical market is intensely competitive and in particular the NASH space which PXS is targeting has several companies engaged in drug development. PXS' products are unlikely to be the first to market and therefore would not have first mover advantage. There is no guarantee that mid-late stage clinical trial results of the BI drug or the LOXL-2 drug, even if they hit the endpoints of the studies, will be viewed as clinically meaningful by clinicians' vis-à-vis other approved NASH drugs by then on the market. Even if the drugs do get approved on successful pivotal studies, commercial adoption might still be hampered by the cost of the combination (especially in LOXL-2's case where we assume an add-on therapy positioning) or the competition in the NASH market having much larger impact than we have postulated.
- **Funding risk:** Delays in partnering of LOXL-2 may impact PXS' funding position in the long term. PXS has A$35.1m in cash and debt related to finance lease of A$7.5m, amounting to a net cash position of A$27.7m. Although PXS has a high cash balance currently, which should provide ~1.5 years cash runway, the company may need to raise additional capital for funding its requirements beyond that should there be delays in partnering its LOXL-2 asset. There is no guarantee that PXS will be able to secure additional financing if and when required.

Pharmaxis Ltd.
as at 15 May 2019

Recommendation	Buy, Speculative
Price	$0.275
Valuation	$0.54

Table 6 - Financial summary

Pharmaxis Ltd (PXS) — **Share price (A$) $0.275**
As at 14 May 2019 — **Market cap (A$m 108.4**

Profit and Loss

Y/e June 30 (A$m)	2017A	2018A	2019E	2020E	2021E
Product Sales Revenues	4.8	6.1	5.0	8.2	10.0
Other Revenue (commercial)	8.6	43.5	12.5	20.1	0.0
Other Income	3.9	0.7	0.5	0.7	0.7
Total Revenue	**17.3**	**50.2**	**18.0**	**28.9**	**10.7**
EBITDA	**-15.2**	**11.5**	**-8.8**	**3.4**	**-14.2**
Depreciation & Amortisation	-3.1	-3.1	-2.7	-2.7	-2.8
EBIT	**-18.3**	**8.4**	**-11.5**	**0.7**	**-17.0**
Net interest & Other Income/(Expense)	0.9	-0.8	-0.5	0.6	0.5
Pre-tax profit	**-17.4**	**7.6**	**-12.0**	**1.3**	**-16.4**
Tax	0.0	0.0	0.0	0.0	0.0
Net profit (loss) normalised	**-17.4**	**7.6**	**-12.0**	**1.3**	**-16.4**
Abnormal items	-0.9	-1.2	-1.3	-1.3	-1.3
Reported Net profit (loss)	**-18.3**	**6.4**	**-13.3**	**0.0**	**-17.8**

Cashflow

Y/e June 30 (A$m)	2017A	2018A	2019E	2020E	2021E
Reported NPAT	-18.3	6.4	-13.3	0.0	-17.8
Non-cash items	3.7	5.6	5.4	4.5	4.4
Net change in Working capital	-0.6	0.1	-1.1	0.0	0.0
Operating cashflow	**-15.3**	**12.2**	**-9.0**	**4.4**	**-13.3**
Capex	-0.3	-0.8	-0.8	-0.8	-0.8
Investments	0.0	0.0	0.0	0.0	0.0
Investments in intangible assets	-0.4	0.0	-0.4	-0.4	-0.4
Other investing cash flow	0.0	0.0	0.0	0.0	0.0
Investing cashflow	**-0.7**	**-0.9**	**-1.2**	**-1.2**	**-1.2**
Change in borrowings	-1.5	-1.5	-1.6	-1.7	-1.7
Equity issued	0.0	0.0	22.7	0.0	0.0
Dividends paid	0.0	0.0	0.0	0.0	0.0
Other financing cash flow	-0.2	-0.2	-0.2	-0.5	-0.8
Financing cashflow	**-1.7**	**-1.8**	**20.9**	**-2.2**	**-2.5**
Net change in cash	**-17.7**	**9.6**	**10.7**	**1.1**	**-17.0**
Cash at end of period*	21.5	31.1	41.8	42.9	25.9
* Includes effect of exchange rate fluctuations on cash balance					
Free cash flow (op. CF less capex and intangibles)	**-16.0**	**11.3**	**-10.2**	**3.3**	**-14.5**

Balance sheet

Y/e June 30 (A$m)	2017A	2018A	2019E	2020E	2021E
Cash	21.5	31.1	41.8	42.9	25.9
Current receivables	4.4	2.4	2.5	2.6	2.7
Inventories	2.6	2.4	2.5	2.6	2.7
Other current assets	0.1	0.1	0.1	0.1	0.1
Current assets	**28.6**	**36.0**	**46.9**	**48.2**	**31.4**
PPE	14.9	12.5	10.4	8.3	6.1
Non-current receivables	1.4	1.2	1.2	1.2	1.2
Intangible assets	0.5	0.4	0.7	1.0	1.3
Other non-current assets	0.0	0.0	0.0	0.0	0.0
Non-current assets	**16.8**	**14.1**	**12.4**	**10.5**	**8.7**
Total assets	**45.4**	**50.1**	**59.2**	**58.7**	**40.1**
Payables	6.8	5.6	4.6	4.7	4.8
Debt	9.3	8.3	7.2	5.9	4.5
Provisions	0.9	1.0	1.1	1.2	1.3
Financial liabilities (Novaquest financing agreement)	22.1	22.8	23.4	22.9	22.1
Deferred Lease Incentive	1.6	1.4	1.1	0.9	0.7
Other liabilities	1.1	0.0	0.0	0.0	0.0
Total liabilities	**41.9**	**39.0**	**37.4**	**35.6**	**33.4**
Net Assets	**3.5**	**11.1**	**21.8**	**23.1**	**6.7**
Shareholders' equity	344.6	344.6	367.3	367.3	367.3
Reserves	19.5	20.7	22.0	23.3	24.6
Retained earnings/(losses)	-360.6	-354.2	-367.5	-367.5	-385.3
Total shareholders equity	**3.5**	**11.1**	**21.8**	**23.1**	**6.7**

Valuation data

Y/e June 30	2017A	2018A	2019E	2020E	2021E
Net profit -normalised (A$m)	-17.4	7.6	-12.0	1.3	-16.4
EPS - normalised (c)	-5.5	2.4	-3.2	0.3	-4.2
EPS growth (%)	N/A	NM	N/A	NM	N/A
P/E ratio (x)	N/A	11.5	N/A	83.3	N/A
FCFPS (c)	-5.0	3.5	-2.6	0.8	-3.7
Price/FCF (x)	-5.5	7.8	-10.7	33.0	-7.5
DPS (c)	0.0	0.0	0.0	0.0	0.0
Yield (%)	0.0%	0.0%	0.0%	0.0%	0.0%
Franking (%)	N/A	N/A	N/A	N/A	N/A
EV/EBITDA	-5.3	7.0	-9.2	23.7	-5.7
EV/EBIT	-4.4	9.6	-7.0	118.1	-4.8

Share price now (A$)	$0.275
Valuation (A$):	$0.54
Premium (discount) to price	96.4%
Recommendation:	Buy
Risk Rating	Speculative

Profitability ratios

Y/e June 30	2017A	2018A	2019E	2020E	2021E
EBITDA margin (%)	N/A	22.9%	N/A	11.8%	N/A
EBIT margin (%)	N/A	16.7%	N/A	2.4%	N/A
Return on assets (%)	-38.3%	15.2%	-20.2%	2.2%	-41.0%
Return on equity (%)	NM	68.5%	NM	5.6%	NM
Dividend cover (x)	N/A	N/A	N/A	N/A	N/A
Effective tax rate (%)	0.0%	0.0%	0.0%	0.0%	0.0%

Liquidity and leverage ratios

Y/e June 30	2017A	2018A	2019E	2020E	2021E
Net debt (cash) (A$m)	-12.3	-22.8	-34.6	-37.0	-21.4
Net debt/equity (%)	N/A	N/A	N/A	N/A	N/A
Net interest cover (x)	N/A	NM	N/A	-1.7	N/A
Current ratio (x)	2.7	4.4	5.5	5.5	3.4

Segmentals

Y/e June 30	2017A	2018A	2019E	2020E	2021E
Bronchitol and Aridol					
Product Sales	4.8	6.1	5.0	8.2	10.0
Other revenue (Clinical trial cost reimbursement)	8.6	1.3	0.0	11.3	0.0
Other income	0.1	0.0	0.0	0.0	0.0
Total Revenues	**13.5**	**7.5**	**5.1**	**19.5**	**10.0**
EBITDA	**-7.1**	**-3.8**	**-5.3**	**8.1**	**-1.7**
New Drug Development					
Product Sales	0.0	0.0	0.0	0.0	0.0
Other revenue (Milestone+license+royalty)	0.0	42.1	12.5	8.8	0.0
Other income (R&D tax incentive etc.)	3.4	0.2	0.0	0.2	0.2
Total Revenues	**3.4**	**42.3**	**12.5**	**8.9**	**0.2**
EBITDA	**-4.1**	**28.8**	**0.6**	**-0.5**	**-8.3**
Corporate					
Other income	**0.3**	**0.5**	**0.5**	**0.5**	**0.5**
EBITDA	**-4.0**	**-13.5**	**-4.1**	**-4.1**	**-4.1**
Total Company					
Revenues	**17.3**	**50.2**	**18.0**	**28.9**	**10.7**
EBITDA	**-15.2**	**11.5**	**-8.8**	**3.4**	**-14.2**

Interims

Y/e June 30 (A$m)	2H17A	1H18A	2H18A	1H19A	2H19E
Revenue	10.8	31.1	19.1	2.5	15.5
EBITDA	-6.8	7.8	3.7	-9.8	1.0
Depreciation & Amortisation	-1.5	-1.6	-1.5	-1.3	-1.4
EBIT	**-8.3**	**6.2**	**2.2**	**-11.1**	**-0.4**
Net interest & Other Expense	1.5	0.3	-1.1	-0.8	0.3
Pre-tax profit	-6.8	6.5	1.1	-11.9	0.0
Tax	0.0	0.0	0.0	0.0	0.0
Net Profit (loss) - normalised	**-6.8**	**6.5**	**1.1**	**-11.9**	**0.0**
Net Profit (loss) - reported	-7.3	5.9	0.5	-12.6	-0.7

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.

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