TAYLOR COLLISON

Sharebrokers and Investment Advisers
www.taylorcollison.com.au

June 14, 2017

Pharmaxis (PXS)

Outperform

Accumulate for Fibrosis Pipeline Following Lukewarm Ph3 Bronchitol Data

$0.35

Elyse Shapiro
eshapiro@taylorcollison.com.au
+61 4 9126 7142

Summary (AUD)

Market Capitalisation	**$79.8**
Share Price	**$0.25**
52 week low	$0.23
52 week high	$0.34
Ave Monthly Vol (year rolling)	523K

Key Financials (A$ million)

Year End	FY16 Act.	FY17 Est.	FY18 Est.
Revenue ($m)	**19.0**	**31.1**	**18.6**
EBITDA ($m)	17.8	24.1	29.9
NPAT ($m)	**9.0**	**13.5**	**18.0**
EPS (c)	-5	-3	-4
EPS Growth (%)	-188%	39%	-32%
PE (x)	**-5**	**-8**	**-6**
DPS (c)	7.0	10.0	13.3
Div Yield	1.7%	2.4%	3.2%
EV ($M)	53.4	53.4	53.4
EV/EBITDA (x)	**16.2x**	**11.9x**	**9.6x**
ROE	na	na	na
EBITDA Margin	-71%	-11%	-44%

Share Price Graph (AUD)

The Taylor Collison Insight

PXS announced top-line data from the Phase 3 Bronchitol trial which is being conducted in collaboration with Italian pharma Chiesi. We were unimpressed by the 2.2% effect size, which, albeit statistically significant, is unlikely to have a real clinical effect. We would see current weakness in the stock as a buying opportunity for the robust fibrosis pipeline, especially since we did not factor bronchitol sales into our price target. We maintain our $0.35 price target.

Mediocre effect size, inconsistent secondary endpoints are red flags. The Phase 3 study evaluated Bronchitol in adults with CF. The study met its primary endpoint, achieving a 2.2% relative improvement over placebo (p=0.025), with FEV1 change from baseline over 26 weeks of 54mL. While the study met statistical significance, we were not impressed by the effect size, especially since it was lower than the 4.72% delta seen in adults in the other two Phase 3s. We do not like that there was no improvements in secondary endpoints, as we like to see consistency across primary and secondary endpoints, especially with data that already shows a small effect size. One potential explanation the lack of effect on secondary endpoints is that the study was not sufficiently powered to show such an effect.

Regulatory steps going forward: PXS plans to file another NDA. Management indicates that Chiesi plans to file an NDA for Bronchitol with FDA in 2018 and expects a potential outcome about 6 months following submission. We anticipate an extended process, in-line with the 2013 FDA interactions, although we do not anticipate another AdComm because PXS addressed the FDA's concerns with the trials in the most recent Phase 3. We are ambivalent around potential approval, and do not attribute value to the stock for Bronchitol, but we do consider an approval as free upside to the stock, since it is not currently priced in, and we would not anticipate significant impact to the stock should Bronchitol not be approved. We also note that as a part of the partnership, in addition to mostly funding the Phase 3, Chiesi also has responsibility to prepare the NDA submission. On that basis, there should be minimal resource allocation from PXS for the potential US Bronchitol approval from now.

We see real value in the fibrosis opportunity. In our previous reports, we discussed the significant value opportunity with the company's pipeline in the fibrosis space. PXS partnered with big-pharma Boeringer Ingelheim (BI) for PXS-4782A, an SSAO inhibitor. BI will soon initiate a Phase 2 trial for the compound in NASH (non-alcoholic liver steatohepatitis), which will trigger a ~$25M milestone payment for the PXS imminently (we think within the next month). BI also expressed interest in developing the compound for a second, respiratory indication, which would trigger an estimated $18M milestone. PXS's second pipeline candidate, a LOXL2 inhibitor, is being developed for NASH and potentially other fibrotic indications, and one month toxicology studies are underway. We foresee Ph1 being completed by the middle of 2018, and think that positive data could attract big pharma interest for a potential partnership. We think that following a positive Phase 1, an upfront payment in the $50-75M range would be extremely conservative, considering most deal-sizes for NASH are much larger (post Ph1 asset acquisitions are normally well above the US$100M range), but an upfront payment in the $50-75 range would have a significant impact on the stock at current levels.

Bronchitol Overview

DPM (dry powder manitol) was investigated for the management of cystic fibrosis (CF) in patients age 6 or older to improve pulmonary function, and is currently marketed in the EU and Australia for Adults with CF. Mannitol is a naturally occurring sugar alcohol, an osmotic agent which was optimized as a 3-micron-sphere dry powder which can be delivered via a disposable inhaler for the treatment of CF. Inhaling mannitol changes the viscoelastic properties of airway phlegm, increases the hydration of airway surface liquid, and contributes to the increased clearance of the retained secretions through mucociliary activity and productive cough action.

Phase 2

Study 202, a Phase 2 trial, provided dose ranging data for Bronchitol in 48 patients. 44 patients completed the study (they did not demonstrate airway hyperresponsiveness). The cross-over design (2 week treatment period followed by a 1 week washout period) was problematic because all patients began treatments sequences with 2 weeks at the highest dose (400mg) twice daily, and were then randomized to the other 2-week dosing treatments. We think the value generated from this Phase 2 study was limited. The primary endpoint was change in FEV1 and FVC from baseline. Improvements in % change in FEV1 from baseline were -1.6%, 3.6%, 3.9%, and 8.7% for the 40, 120, 240, and 400 mg twice daily doses, respectively. Results for FVC were similar.

Phase 3

Studies 301 and 302, the two Phase 3 studies, were randomized, double blind, placebo controlled, parallel group trials designed to assess the efficacy and safety of 26 weeks of treatment with DPM 400 mg twice daily in patients ages 6 years and older. The double-blind phase was followed by an open-label phase of up to 52 weeks and 26 weeks duration for trials 301 and 302, respectively. Inclusion criteria required patients to have an FEV1 between 30-90% predicted for trial 301 and between 40-90% predicted for trial 302. Patients were excluded if they had lung transplants or listed for lung transplant, or a history of significant hemoptysis (> 60 mL within 3 months of enrolment). Patients were allowed to continue their chronic medication regimens, but were not allowed to continue treatment with hypertonic saline, a commonly used but not FDA-approved mucolytic/expectorant, was excluded.

Patients were initially screened for airway hyper-responsiveness by receiving a MTT under medical supervision. Eligible patients were randomized 3:2 to receive either DPM 400 mg (contents of ten 40 mg capsules) or control (50 mg inhaled mannitol as ten 5 mg capsules. A true placebo couldn't be used to control for the sweet taste associated with mannitol, so a 50mg dose was chosen given the lack of response at 40mg in the Phase 2). Prior to dosing patients were to self-administer a short-acting bronchodilator in order to minimize acute bronchoconstriction. Because patients with CF typically use several inhaled therapies, the following standardized order of treatment was recommended: 1. Short acting bronchodilator 2. Study drug 3. Chest physiotherapy 4. rhDNase (if used) 5. inhaled antibiotics (if used) 6. inhaled corticosteroids (if used) Evaluations were made at screening to assess for eligibility and, once randomized, at baseline, week 6, week 14, and week 26. For the openlabel extension periods, additional evaluations were made at weeks 38, 52, 64, and 78 in study 301 and at weeks 38 and 52 only for study 302. The primary efficacy endpoint was absolute change from baseline (mL) in FEV1 at week 26.

Baseline FEV1 was obtained at week 0 (visit 1). Other efficacy endpoints included: Additional respiratory assessments (FVC, FEF25- 75), pulmonary exacerbations (PE) based on adverse events entered into the eCRF, protocol defined pulmonary exacerbation (PDPE) defined as occurring when patients were treated with IV antibiotics and experienced at least four of the following 12 signs or symptoms: change in sputum production (volume, color, consistency), dyspnea, new or increased hemoptysis, malaise, fatigue or

lethargy, fever (> 38°C), anorexia or weight loss, sinus pain or tenderness, change in sinus discharge, FVC or FEV1 decreased by ≥ 10% from previous recorded value, radiographic signs indicative of pulmonary infection, increased cough, changes in physical examination of the chest), quality of life using Cystic Fibrosis Questionnaire-R (CFQ-R) (completed at weeks 0, 14, and 26, rescue antibiotic use (recorded in the study diary), and days in hospital due to pulmonary exacerbation.

Study personnel in study 302 received superior training, which may have led to fewer dropouts (a decrease from around 30% to around 15% in study DPM-CF-302). Another key difference between the two studies was the percentage of patients under 18. The proportion of under-18 patients was around 50% in study 302 vs 36% in study 301.

Results

Study	**301**	**302**	**303**
Difference in FEV1 over 26 weeks between treated and control	**94.45 mL**	**54.14 mL**	**54 mL**
p-value	**p<0.001**	**p=0.059**	**p=0.020**

Study 301: 340 patients were enrolled, and the study was designed with the assumption that about two thirds of patients were using rhDNAse, with a 20% withdrawal rate. There was no plan for imputation of missing data. The overall treatment effect was 54.17ml (p100ml, or >5% relative to baseline, or >5% relative change in % predicted). Among patients who completed the study and received 400mg BD treatment, 41.4% (or 27% of the ITT population) had >5% increase in FEV1%PP.

Patients treated with Bronchitol had a statistically significant 6.6% improvement in lung function from baseline (p=0.001 vs placebo). Lung function improved at week 6 and was sustained through to week 26. Secondary endpoints were also consistent, with treated patients receiving Pulmozyme and Bronchitol showing FEV1 improvement of 5.2% from baseline

Study 302: Failed to meet its primary endpoint of FEV1 vs control at 26 weeks (p=0.059, narrowly statistical significance). While the % improvement was similar to that in study 302 which did meet stat sig, we note differences in patient baseline characteristics between the trials. Patients treated with DPM had an 8.2% (107ml) improvement in FEV1 vs baseline (p<0.001), and similar to the 6.3% improvement in study 301. Improvements were seen as early as 6 weeks, and were sustained at weeks 14 and 26. Secondary endpoints showed improvement in FVC (p=0.022), and FEV1%PP (p=0.024).

A pooled analysis of the results from both Phase 3 studies included data from 643 patients across 11 countries. Over the 26 weeks of treatment, DPM treated patients experienced an average of 7.3% improvement in FEV1 (p<0.001), and a significant improvement compared to patients in the control group (p<0.001) A subgroup analysis of DPM+rhDNase patients showed a 5.3% improvement from baseline (p<0.001), and an improvement over control (p=0.02). DPM Patients not on rhDNase showed a 9.44% improvement over baseline (p<0.001), also also superior to control (p=0.009). Overall, the rate of exacerbations from Bronchitol patients vs control was 25% (NS), and the number of patients experiencing an exacerbation was 29% lower for those taking Bronchitol. The pooled analysis showed the highest (and most stat sig) effect size in % predicted FEV1 for adults treated with Bronchitol. Adolescent data and child data did not meet stat sig. However, we caution against relying on the pooled analysis data given the child-adolescent subgroup analysis was not pre-specified, the protocols were different between both trials (staff at sites in study 302 received more training), and the weighting of under-18s was much higher in the '301 study.)

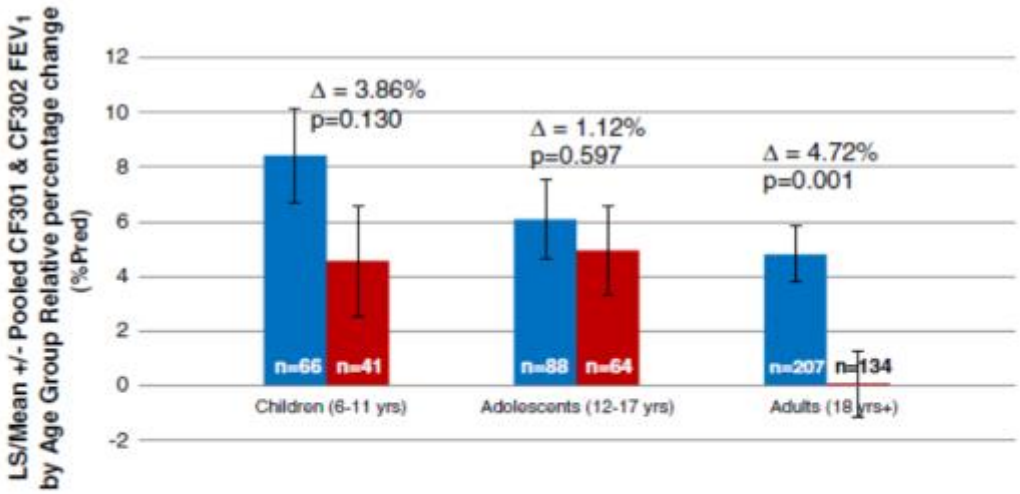

Fig. 3. % Change from baseline in % FEV_1 predicted by age — ITT population.

Source: D. Bilton et al. / Journal of Cystic Fibrosis 12 (2013) 367–376

Study 303 protocol

The Phase 3 trial is a 26 week, randomized, double-blind, parallel group investigation of Bronchitol in 423 CF patients over 18. The primary endpoint was the mean change in FEV1 from baseline to week 26. Secondary endpoints are mean change from baseline FVC, time to first pulmonary exacerbation, number of days in hospital due to pulmonary exacerbations, incidence of pulmonary exacerbations, number of days on antibiotics due to pulmonary exacerbations, ease of expectoration, and CFQ-R respiratory domain scale.

Study 303 Data

The study showed a statistically significant 2.2% improvement over placebo (54 ml treatment effect on FEV1, p=0.020). The effect size was smaller than that seen in studies 302 and 301, and smaller than the effect sizes seen in cystic fibrosis in previously approved therapies. We note that Chiesi's NDA package will likely include all three Ph3 trials. The full dataset will be presented at the North American Cystic Fibrosis Conference, which takes place November 2-4, 2017. There was no effect on secondary endpoints. Management indicated that the patient numbers made it hard to evaluate secondary endpoints, but we think that there could have been a trend, with 423 patients enrolled in the trial.

Safety data was encouraging, with similar withdrawal rates in the treatment and control arms (12.4% vs 11.2%), and only 6.6% of patients failing the mannitol tolerance test.

Partnership with Chiesi As a reminder, Pharmaxis is partnered with Chiesi, and Chiesi will fund up to US$22M of the cost of the trial (the total cost is estimated at ~US$26M), US$10M for the launch of Bronchitol in the US, and another US$15M in milestone payments, as well as high-teens % share on in-market sales. Chiesi is also responsible for completing the Bronchitol NDA with the FDA. We think the partnership represents a good way for PXS to retain some upside if Bronchitol receives approval from the FDA while minimizing capital risk. We see a US Bronchitol approval as upside to the current valuation, rather than being priced into the stock at current levels.

Disclaimer

The following Warning, Disclaimer and Disclosure relate to all material presented in this document and should be read before making any investment decision.

Warning (General Advice Only): Past performance is not a reliable indicator of future performance. This report is a private communication to clients and intending clients and is not intended for public circulation or publication or for the use of any third party, without the approval of Taylor Collison Limited ABN 53 008 172 450 ("Taylor Collison"), an Australian Financial Services Licensee and Participant of the ASX Group. TC Corporate Pty Ltd ABN 31 075 963 352 (“TC Corporate”) is a wholly owned subsidiary of Taylor Collison Limited. While the report is based on information from sources that Taylor Collison considers reliable, its accuracy and completeness cannot be guaranteed. This report does not take into account specific investment needs or other considerations, which may be pertinent to individual investors, and for this reason clients should contact Taylor Collison to discuss their individual needs before acting on this report. Those acting upon such information and recommendations without contacting one of our advisors do so entirely at their own risk.

This report may contain “forward-looking statements". The words "expect", "should", "could", "may", "predict", "plan" and other similar expressions are intended to identify forward-looking statements. Indications of and guidance on, future earnings and financial position and performance are also forward looking statements. Forward-looking statements, opinions and estimates provided in this report are based on assumptions and contingencies which are subject to change without notice, as are statements about market and industry trends, which are based on interpretations of current market conditions.

Any opinions, conclusions, forecasts or recommendations are reasonably held at the time of compilation but are subject to change without notice and Taylor Collison assumes no obligation to update this document after it has been issued. Except for any liability which by law cannot be excluded, Taylor Collison, its directors, employees and agents disclaim all liability (whether in negligence or otherwise) for any error, inaccuracy in, or omission from the information contained in this document or any loss or damage suffered by the recipient or any other person directly or indirectly through relying upon the information.

Disclosure: Analyst remuneration is not linked to the rating outcome. Taylor Collison may solicit business from any company mentioned in this report. For the securities discussed in this report, Taylor Collison may make a market and may sell or buy on a principal basis. Taylor Collison, or any individuals preparing this report, may at any time have a position in any securities or options of any of the issuers in this report and holdings may change during the life of this document.

The preparation of this report was funded by ASX in accordance with the ASX Equity Research Scheme. This report was prepared by Taylor Collison and not by ASX. ASX does not provide financial product advice. The views expressed in this report do not necessarily reflect the views of ASX. No responsibility or liability is accepted by ASX in relation to this report.”

Analyst Interests: The Analyst(s) may hold the product(s) referred to in this document, but Taylor Collison Limited considers such holdings not to be sufficiently material to compromise the rating or advice. Analyst(s)’ holdings may change during the life of this document.

Analyst Certification: The Analyst(s) certify that the views expressed in this document accurately reflect their personal, professional opinion about the financial product(s) to which this document refers.

Date Prepared: June 2017
Analyst: Elyse Shapiro
Release Authorised by: Campbell Taylor

Taylor Collison Limited
Sharebrokers and Investment Advisers
A.B.N. 53 008 172 450 AFSL No. 247083

Participant of the Australian Stock Exchange Group
www.taylorcollison.com.au

ESTABLISHED 1928

Level 16, 211 Victoria Square
Adelaide, South Australia, 5000
G.P.O. Box 2046, Adelaide, South Australia, 5001
Telephone: 08 8217 3900 Facsimile: 08 8231 3506
Email: broker@taylorcollison.com.au

Level 10, 167 Macquarie Street
Sydney, New South Wales, 2000
G.P.O. Box 4261, Sydney, New South Wales, 2001
Telephone: 02 9232 1688 Facsimile: 02 9232 1677
Email: sydney1@taylorcollison.com.au