pharmaxis

innovating for life

# Investor Presentation

**14th March 2016**

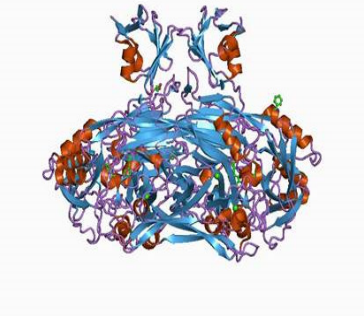
**Gary Phillips CEO**

# Forward looking statement

This document contains forward-looking statements, including statements concerning Pharmaxis' future financial position, plans, and the potential of its products and product candidates, which are based on information and assumptions available to Pharmaxis as of the date of this document. Actual results, performance or achievements could be significantly different from those expressed in, or implied by, these forward-looking statements. These forward-looking statements are not guarantees or predictions of future results, levels of performance, and involve known and unknown risks, uncertainties and other factors, many of which are beyond our control, and which may cause actual results to differ materially from those expressed in the statements contained in this document. Except as required by law we undertake no obligation to update these forward-looking statements as a result of new information, future events or otherwise.

# Pharmaxis today

new business focus creating value



## Drug developer

- ❑ Leading position in amine oxidase chemistry and mechanism based inhibitors
- ❑ Proven capability in delivering quality programs to achieve phase 2 ready compounds
- ❑ Exciting pipeline of drug candidates for valuable targets

## Management

- ❑ Management team and Board with global experience
- ❑ Extensive pharma industry network
- ❑ Proven capability of executing global BD transactions with major partners
- ❑ Preclinical, early and late phase clinical experience


## Drug manufacturer

- ❑ Supplies Bronchitol to global markets via experienced commercial partners
- ❑ Financial risks shared
- ❑ Financial upside from accessing new markets – US, Russia

## Financial strength

- ❑ A$46m cash balance at December 2015
- ❑ Significant value milestones from existing partner deals within reach
- ❑ Growing institutional presence on share register: >45%



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# What's new

recent progress at Pharmaxis

**Next cash milestone for partnered asset nears**

- Boehringer Ingelheim program update confirms timing for the start of phase 2 – Q1 2017. Related development milestone: ~A$25m

**Drug Discovery progresses valuable programs**

- Fibrosis program
  - On track to select a LOXL2 drug candidate for IPF and/or NASH and proceed into full preclinical evaluation in Q2 2016
  - Target phase 1 commencement H1 2017
  - Leading universities/academics now assessing utility of our LOXL2 inhibitors in kidney fibrosis, cancer and wound healing
- Neuro Inflammation program
  - SSAO/MAO-B program for Neuro inflammation: currently completing preclinical data package to assess pharma interest before proceeding to further development

**New opportunities for Bronchitol**

- US clinical trial passed 300 patients recruited – expect to complete recruitment mid 2016, complete and report H1 2017
- European clinical trial in paediatric patients (CF 204) reported:
  - Bronchitol provides significant improvements in lung function and sputum weight
  - Bronchitol was tolerated by most patients and reduced exacerbations by ~25%
  - Pharmaxis plans to submit an application to extend the existing label in EU to children with CF H2 2016
- New distributors appointed for Spain and Portugal – sales expected H2 2016
- Russian Orphan Drug Committee recommends Bronchitol for listing for paediatric and adult treatment of CF - final approval expected H1 2016, sales expected H2 2016

# Board and management

## experience that counts

**Board**

- Malcolm McComas – *Chair*
- Will Delaat
- Simon Buckingham
- Gary Phillips – *CEO*

- Broad network and experience in capital markets
- Biotech and Big Pharma commercial experience
- Extensive business development networks
- Experience of wide variety of partnering transactions

**Management**

- Gary Phillips – *CEO*
- David McGarvey – *CFO*
- Brett Charlton – *Medical*
- Wolfgang Jarolimek – *Drug Discovery*
- Kristen Morgan – *Alliance Management*

- Biotech and Big Pharma commercial experience
- Hands on experience across the whole of the Pharma value chain
- Proven track record in business negotiations and deal making
- Excellent industry and academic networks
- Australian and international capital markets
- Small cap companies

Refer to Pharmaxis website for further detail



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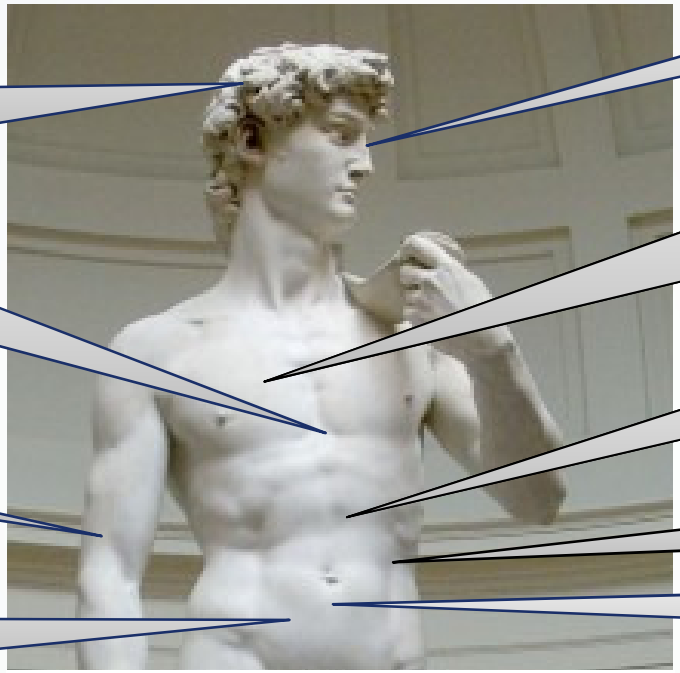
# Pharmaxis product portfolio

| Product | Indication | Status |
|---|---|---|
| *LOXL2 inhibitor* | *NASH (fatty liver disease), liver & kidney fibrosis* | *Lead optimisation* |
| *LOXL2 inhibitor* | *Idiopathic pulmonary fibrosis* | *Lead optimisation; collaboration with Synairgen* |
| LOX/LOXL2 inhibitor | Fibrosis, cancer | Exploratory |
| *SSAO inhibitor* | *NASH* | *Successful phase 1 study reported; sold to Boehringer* |
| SSAO/MAOB inhibitor | Neuro inflammation; Alzheimer's, MS, etc. | Lead candidate selected |
| SSAO/MPO inhibitor | Respiratory inflammation; Asthma, COPD | Lead optimisation |
| Orbital | Dry powder inhalation device | Phase 1 – seeking partner |
| ASM8 | Asthma | Phase 2 - seeking partner |
| Bronchitol US | Cystic Fibrosis | Partner: Chiesi, funding phase 3 study - currently underway |
| Bronchitol EU | Cystic Fibrosis | Partner: Chiesi (UK & Germany) - marketed |
| Bronchitol rest of world | Cystic Fibrosis | Marketed: Australia, CEE<br>Approval pending; Brazil, Russia |
| Aridol | Asthma diagnosis | Marketed: Australia, EU, Korea |

**amine oxidase chemistry platform**

# Our therapeutic focus

global leaders in amine oxidase enzyme chemistry



***Alzheimer's***
***Parkinson's***
***Stroke***

*Cardio-myopathy*
*Heart failure*
*Atherosclerosis*

***Scarring***

*Pancreatic cancer*
*Type 2 diabetes*

***Opthamology***

***COPD***
*Asthma*
***CF***
***Pulmonary***
***Fibrosis***

***NASH***
***Liver fibrosis***
*Liver cancer*

***Kidney fibrosis***

*Gastric cancer*
*IBD*

Amine oxidase enzymes are well validated as targets in diseases with a high unmet medical need

# Pharmaxis drug discovery strategy

building a biotech powerhouse in fibrosis and inflammation

## Strategy

Drug discovery:

- ❑ Improve drug discovery hit rate by:
  - ➢ Prioritise validated targets
  - ➢ Multiple small molecule drugs from in-house amine oxidase chemistry platform
  - ➢ Develop to phase 1 or 2

Partnering:

- ❑ Create value via:
  - ➢ Licence out to Big Pharma with attractive 1st in class drugs post phase 1 or 2
  - ➢ Collaborate to de-risk and accelerate PXS programs
  - ➢ Collaborate on in-licensing programs

## Achievements to date

Drug discovery:

- ❑ First in class NASH drug taken to phase 1
- ❑ *Two* further candidates in lead optimisation phase
- ❑ One lead candidate moving to preclinical

Partnering:

- ❑ In house BD expertise achieves valuable deal with Boehringer Ingelheim - A$39m upfront, total potential > A$750m
- ❑ Collaboration with Synairgen Research plc for early stage fibrosis program to widen spread of indications, enhance time to value inflection and spread risk

# SSAO for NASH

SSAO inhibitor PXS4728A sold to Boehringer Ingelheim in May 2015

## PXS 4728A

- Mechanism based inhibitor of SSAO
  - Small molecule inhibitor of semicarbazide-sensitive amine oxidase / vascular adhesion protein (VAP-1)
  - Important inflammatory pathway in several diseases including NASH and COPD
- Development status:
  - Pharmaxis discovery – patent filed 2012
  - Effective in pre clinical models of NASH and airway inflammation
  - Phase 1 study reported
    - orally bioavailable
    - long lasting inhibition after single dose
    - progressive dose response
- Competitors:
  - Genefit – GF505 Phase 2b NASH (reported)
  - Intercept - OCA (FXR agonist) Phase 2b NASH (reported)
  - Gilead – FXR agonist in pre clinical

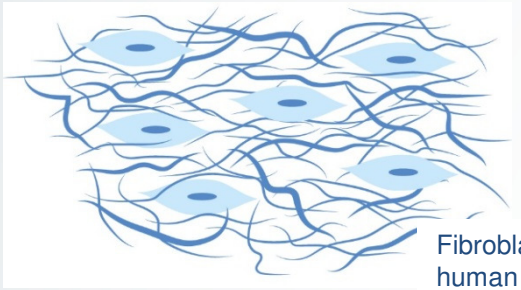
## Boehringer Ingelheim

- Excellent partner:
  - Boehringer leaders in metabolic disease
  - Industry leading development times
  - Boehringer responsible for all development, and commercialisation activities
- Competitive deal:
  - Total potential payments to approval for 2 indications: €418.5m (~A$600m),
    - acquisition (May 2015): €27.5m (~A$39m)
    - commencement of phase 2 and 3: up to total €55m (~A$80m)
    - filing, regulatory & pricing approvals: up to total €140m(~A$200m)
    - second indication: additional total milestone payments (€195m)
  - Earn-out payments on annual net sales
    - tiered percentages starting in high single digits
    - plus potential sales milestones
- External validation of PXS drug discovery and ability to negotiate valuable global deals

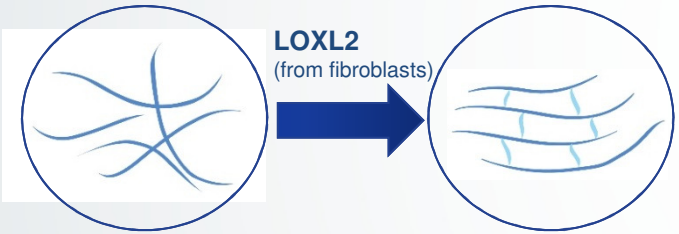
# LOXL2 inhibition for NASH & other fibrotic diseases

an attractive target and development program

Excessive production and linking of collagen fibres results in fibrosis



Fibroblast cells in human tissue




Collagen fibres

Excessive 'cross-linking' of collagen fibres, stiffens tissue, causing fibrosis

**Gilead – LOXL2 antibody**

- Acquired Arresto program $225m pre phase 1
- Now in broad phase 2b trial program
- Liver fibrosis; Idiopathic pulmonary fibrosis; Metastatic pancreatic cancer; Myelofibrosis; Solid tumours; Metastatic colorectal cancer

## ❑ Potential indications:

- ❑ NASH / Liver Fibrosis
- ❑ Pulmonary fibrosis (IPF)
- ❑ Cancer
- ❑ Wound healing

**Significant Market opportunity**

## ❑ Development status:

- ❑ Pharmaxis discovery – patent filed 2016
- ❑ Compounds with differentiated PK / PD profile identified
- ❑ Effective in pre clinical models of fibrosis and cancer

## ❑ Competitive profile:

- ❑ Novel target and mechanism of action
- ❑ Once daily oral drug
- ❑ Complete inhibition of LOXL2 versus partial inhibition by antibody
- ❑ Selective inhibition over other amine oxidases
- ❑ Low cost of goods



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# LOXL2 for pulmonary fibrosis

collaboration with Synairgen

## Idiopathic Pulmonary Fibrosis (IPF)

- IPF primarily affects people over the age of 50
- 5,000 patients have IPF in Australia
- 100,000 people with IPF in the US
- Prognosis is worse than that of many cancers
- Two drugs approved recently
  - Nintedanib (Boehringer Ingelheim)
  - Pirfenidone (Roche)
- Need for new therapies
- Current products expected to produce global revenues > $1.1 billion by 2017

## Synairgen collaboration

- Access to
  - Synairgen's strength in fibrosis biology and respiratory clinical development - BioBank human tissue models technology platform
  - expertise at University of Southampton
- Faster time to value appreciation and partnering points of phase 1 or 2a
- Synairgen to fund pre clinical tox and phase 1
- Shares risk and reward based on investment in program
- Allows PXS to pursue further indications in parallel

# Bronchitol for cystic fibrosis

CF, Bronchitol and clinical trial results to date

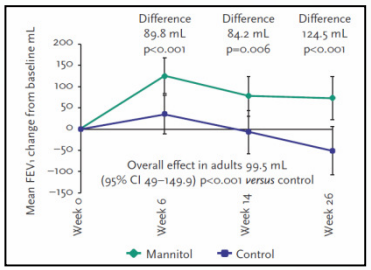

**Median $FEV_1$ % Predicted versus Age**

## Cystic fibrosis

- ❑ Patients
  - ❑ US: 30,000;
  - ❑ Europe: 37,000;
  - ❑ Rest of world: 21,000
- ❑ Disease characterised by poorly hydrated, tenacious, thick mucus
- ❑ Rapid decline in lung function
- ❑ Frequent infections


## Bronchitol

- ❑ Active ingredient mannitol delivered as an inhalable dry powder
- ❑ Restores airway surface liquid
- ❑ Mucus clearance enhanced
- ❑ Improves lung function
- ❑ Reduces incidence of lung infections




Pooled adult data from CF301 and CF302

## CF301/2 trial (adult) results

- ❑ Total 317 adults
- ❑ FEV1
  - ❑ CF301; p=0.001
  - ❑ CF302; p=0.038
  - ❑ Pooled; p=0.001
    rel % change = 4.7%
- ❑ Exacerbations
  - ❑ Pooled data
  - ❑ 26% reduction
  - ❑ 60% reduction in Bronchitol responders

## CF204 trial results

- ❑ Paediatric age 6-17
  - ❑ Placebo-controlled
  - ❑ 8 weeks crossover design
  - ❑ standard therapy continued
- ❑ Primary endpoint:
  - ❑ Absolute change in $FEV_1$: 3.42%; p=0.004
- ❑ Key secondaries
  - ❑ Absolute change in $FEF_{25-75}$: 5.75% (p=0.005)
- ❑ Acceptable safety profile
  - ❑ Well tolerated
  - ❑ Exacerbations and lung infection reduced by ~25%



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# Bronchitol for cystic fibrosis

partnering for success

## US market

- Largest CF market by value
- 28,103 CF patients
- 49.7% adults
- Bronchitol price target US$20k per patient / year
- 7 year post launch market exclusivity

Chiesi

People and ideas for innovation in healthcare

## US partner: Chiesi

- Fund CF303 up to US$22m
- ~A$13m milestone payment on launch, plus sales milestones
- High mid teens royalty % on in-market sales
- Mid teens % uplift on COGs
- Chiesi responsible for regulatory filing & commercialisation

## US trial: CF303

- Tie-breaker phase 3 trial commenced Q1 2015, managed by PXS
- 440 adult patients
  - 20+ countries
  - 130 sites
- Design
  - Full consultation with FDA
  - Similar design to CF301/2
- Fully recruited H1 2016
- Results H1 2017

## Rest of world

- Sold by Chiesi in UK & Germany
- Sold by PXS in Australia & Denmark
- Pending approval/distributor appointments in ten countries including Russia, Israel, Turkey, Brazil, Eastern Europe
- Additional distributors being appointed

# Pharmaxis short term opportunities

building a biotech powerhouse in fibrosis and inflammation

## SSAO program for NASH (fatty liver)

- NASH: US$35B market by 2025
- Acquired by BI at phase 1 for A$39m upfront, total >A$750m
- BI to develop for NASH and other inflammatory indications (eg. kidney fibrosis, COPD)
- Next milestone: ~A$25m at start of phase 2 – Q1 2017

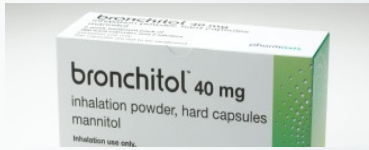
## LOXL2 program for pulmonary fibrosis

- Pulmonary fibrosis: market >$1B
- Collaborate to phase 1 or 2 then seek partner
- Revenue share for phase 1 partnering deal: 50/50
- Next milestone – commencement of formal preclinical program Q2 2016

## LOXL2 for NASH and other diseases

- Big pharma interest in NASH, LOXL2 and PXS chemistry
- Complimentary to SSAO program acquired by BI
- Next milestone – commencement of formal preclinical program H2 CY 2016

## Bronchitol for CF




- Access large US CF market with Chiesi
  - Chiesi funding CF303 to a cap of US$22m
  - ~A$13m milestone payments on launch
  - High teens % share of in-market sales
- Growth from existing markets
- New markets opening over next 24 months, including large Russian market

# Financials – key statistics

refer to December 2014 Half Year Report and Quarterly Shareholder Update for further financial disclosures

| A$'000 | Three months ended | | Six months ended | |
|---|---|---|---|---|
| (unaudited) | 31-Dec-15 | 31-Dec-14 | 31-Dec-15 | 31-Dec-14 |
| **Income statements** | | | | |
| Sales | 1,643 | 1,597 | 3,727 | 3,040 |
| Total revenue | 4,551 | 9,458 | 9,372 | 12,538 |
| Total expenses | (9,566) | (7,626) | (20,550) | (19,015) |
| Net profit (loss) after tax | (5,015) | 1,762 | (11,398) | (6,572) |
| Adjusted net profit (loss) after tax (for comparison purposes - see note below) | (6,233) | (8,146) | (10,085) | (14,913) |
| **Segment results – adjusted EBITDA** | | | | |
| Bronchitol & Aridol | (3,330) | 170 | (4,485) | (3,292) |
| New drug development | (866) | (1,408) | (1,847) | (1,733) |
| Corporate | (1,331) | (945) | (1,753) | (1,961) |
| Total | (5,527) | (2,183) | (8,085) | (6,986) |
| Adjusted Bronchitol & Aridol (for comparison purposes - see note below) | (3,330) | (4,196) | (4,484) | (8,588) |
| **Statement of cash flows** | | | | |
| Cash used in: | | | | |
| Operations | (2,994) | (4,653) | (6,426) | (13,456) |
| Investing activities | (646) | (37) | (1,092) | (107) |
| Financing activities | (430) | (467) | (872) | (913) |
| Total cash used | (4,070) | (5,157) | (8,390) | (14,476) |
| Foreign currency exchange rate changes impact on cash | (319) | 59 | 188 | 108 |
| **Cash at bank** | 45,936 | 19,814 | 45,936 | 19,814 |

**Adjusted comparatives:**

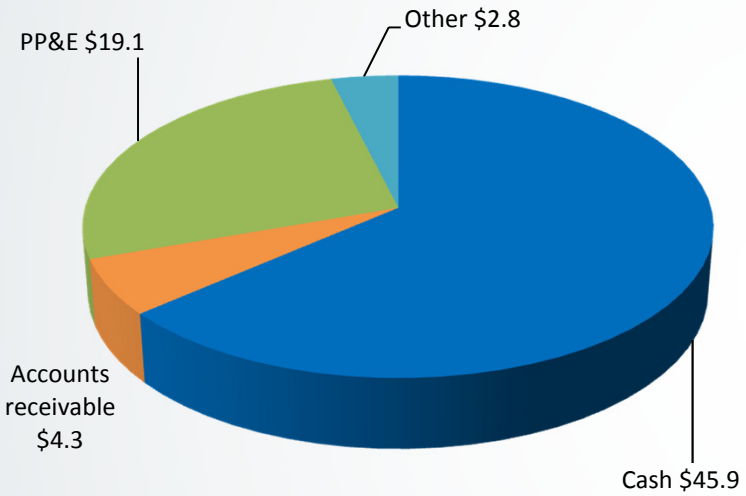
There were two significant transactions in the December quarter of 2014.

- Subsequent to completing an agreement with Chiesi in December 2014 the Company recorded an $8.5 million reimbursement for clinical trial costs of which approximately $4.1 million related to the period before the December 2014 quarter and $3.2 million related to the period before the December 2014 half.
- In the December 2014 quarter the Company completed an amended financing agreement which resulted in a negative finance expense of $5.5 million for the quarter, and a negative finance expense of $3.0 million for the six months.

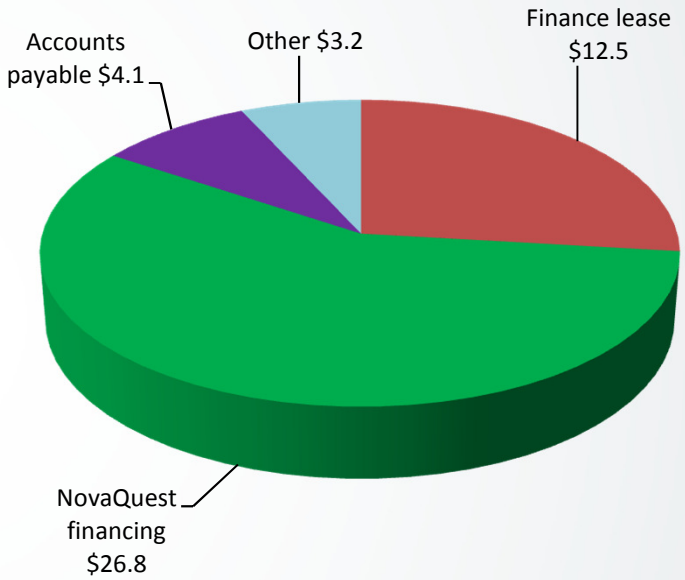
In addition, the Company recorded an unrealised foreign currency exchange gain of $1.2 million in the December quarter of 2015 and an unrealised foreign currency exchange loss of $1.3 million in the December half of 2015, both in relation to a US dollar denominated financing agreement.

# Balance sheet – 31 December 2015

## Assets (A$72m)



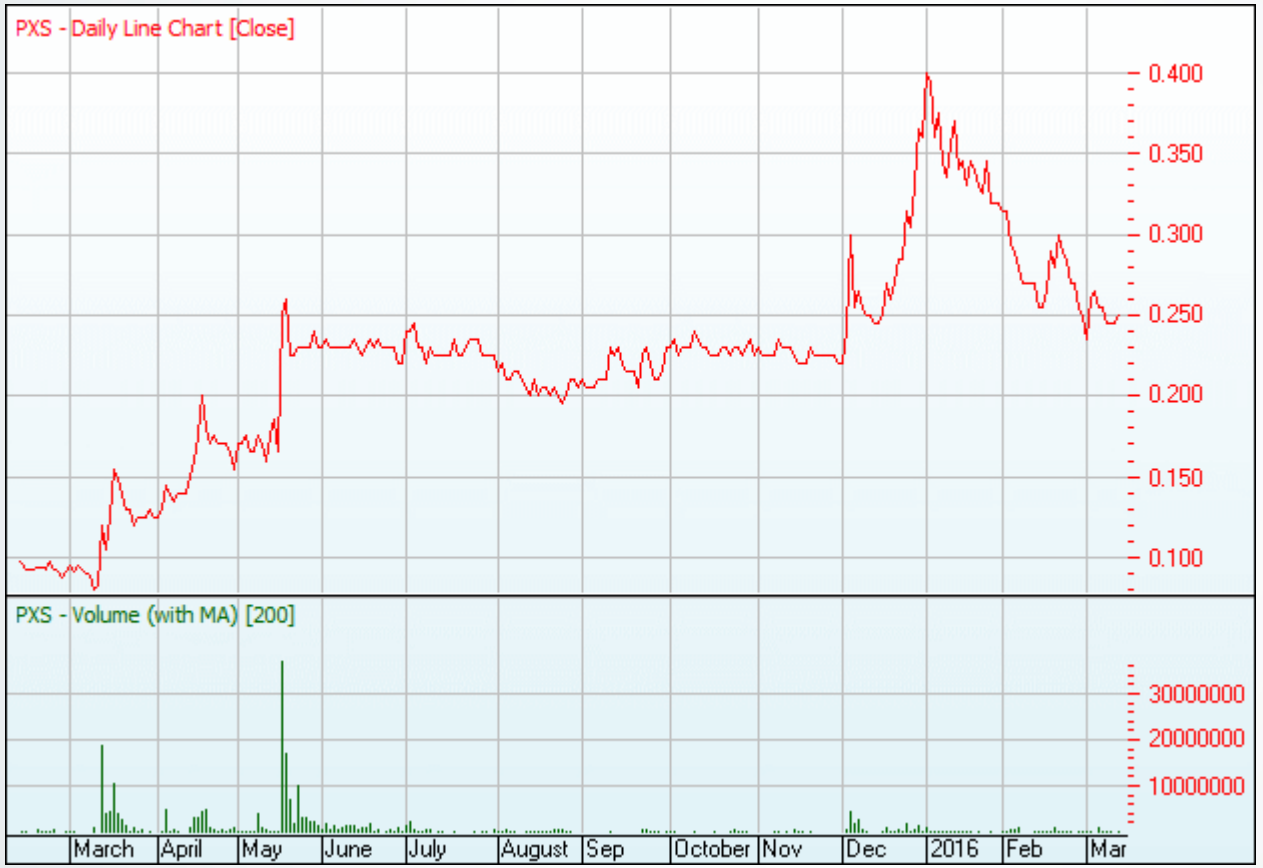

## Liabilities (A$47m)




- Finance lease over 20 Rodborough Rd (to 2024, break possible in 2019)
- NovaQuest financing – amount received plus accrued charge. Not repayable other than as % of Bronchitol revenue - average of mid-single digit % of net in-country sales by distributors in US (7 years from launch) and EU (to March 2020) and share of any sales milestones received from Chiesi

# PXS 12 month share trading

ASX code: PXS




## Shareholders

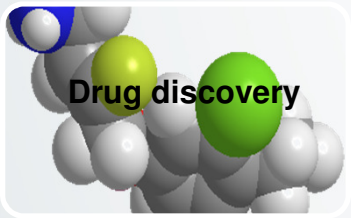
- Shares on issue: 317m (31 Dec 2015)
- Employee options: 7.5m (31 Dec 2015)
- Institutional shareholders (31 Dec 2015) ~48%:
  - Australia - Orbis (17%), Australian Ethical (5%)
  - US - BVF Partners (12%)
  - US – other (5%)
  - UK - Montoya Investments (6%)
  - UK – other (3%)

## Market capitalisation

- A$80m (11 March)

# Major upcoming milestones

Cash funds ($46m at 31 Dec) sufficient to reach near term valuable milestones

| Calendar years | 2016 | 2017 | 2018 |
|---|---|---|---|
| Boehringer Ingelheim | | ❑ ***PXS4728A Phase 2 commences – milestone payable*** | |
| Chiesi | ❑ CF303 fully recruited | ❑ CF303 – last patient completes trial<br>❑ CF303 – reports | ❑ FDA decision on Bronchitol approval in US |
| synairgen | ❑ Identify IPF lead candidate<br>❑ Complete pre clinical program | ❑ Commence IPF phase 1<br>❑ ***Partner asset*** | |
|  | ❑ Identify LOXL2 lead candidate for NASH<br>❑ Complete NASH pre clinical program | ❑ Commence NASH phase 1<br>❑ ***Partner LOXL2 Asset for NASH*** | |
| | ❑ Nominate SSAO combo disease indication<br>❑ Commence pre clinical program | ❑ *Commence SSAO combo phase 1*<br>❑ ***Partner Asset*** | |



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