

Therapeutic products

for

respiratory and

autoimmune diseases

October-November 2005





# The Offering

#### US and Australian tranches

Issuer Pharmaxis, Ltd.

Exchanges PXSL (Nasdaq) / PXS (ASX)

US Offering 1,400,000 ADSs

Australian Offering 1,166,667 ADSs

ADSs Outstanding 11,565,473

Pricing Week of Oct. 31

Bookrunner (US) CIBC World Markets

Bookrunner (Aus.) Wilson HTM

Co-Manager (US) JMP Securities





# Forward Looking Statements

This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These statements are based on management's current expectations and beliefs and are subject to a number of factors and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. The forward-looking statements contained in this presentation include statements about future financial and operating results, and risks and uncertainties that could affect Pharmaxis' product and products under development. These statements are not guarantees of future performance, involve certain risks, uncertainties and assumptions that are difficult to predict, and are based upon assumptions as to future events that may not prove accurate. Therefore, actual outcomes and results may differ materially from what is expressed herein. In any forward-looking statement in which Pharmaxis expresses an expectation or belief as to future results, such expectation or belief is expressed in good faith and believed to have a reasonable basis, but there can be no assurance that the statement or expectation or belief will result or be achieved or accomplished.

The following factors, among others, could cause actual results to differ materially from those described in the forward-looking statements: risks associated with preclinical, clinical and sales and marketing developments in the biopharmaceutical industry in general and in particular including, without limitation, the potential failure to meet Aridol revenue goals, the potential failure of Bronchitol to prove safe and effective for treatment of COPD and/or Cystic Fibrosis, determinations by regulatory, patent and administrative governmental authorities, competitive factors, technological developments, costs of developing, producing and selling Aridol, Bronchitol and Pharmaxis' other products under development; and other economic, business, competitive, and/or regulatory factors affecting Pharmaxis' business generally, including those set forth in Pharmaxis' filings with the ASIC, including its Annual Report for its most recent fiscal year and its most recent Quarterly Report, especially in the "Factors Affecting Our Operating Results" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections, and its Current Reports. Pharmaxis is under no obligation to update or alter its forward-looking statements whether as a result of new information, future events, or otherwise.

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# Investment Highlights



**Aridol** 



Bronchitol



Autoimmune disease



Manufacturing

- Aridol: Asthma management tool
  - US Phase III to start late 2005
  - Filed for approval in EU, Australia (target 2006 launch)
- Bronchitol: Entering Phase III
  - Successful Phase II trial in cystic fibrosis
  - Successful proof of concept data in bronchiectasis
- Retained rights for all programs
- Experienced management
- Strong IP
- Near-term milestones





## Pulmonary and Autoimmune Focus

## -----Clinical Trials----research preclinical phase I phase II phase III registration market Respiratory diseases Aridol – asthma 2006 EU/Aus Aridol - COPD Bronchitol - bronchiectasis Bronchitol – cystic fibrosis Bronchitol - chronic bronchitis Autoimmune diseases PXS25/64 - multiple sclerosis PXS2076 – rheumatoid arthritis





CTO



# Management



Alan Robertson, PhD CEO Wellcome (GSK); Faulding; Amrad; Inventor of Zomig



David McGarvey, CA CFO, Memtec (NYSE); CFO, US Filter Filtration Group



Brett Charlton, PhD
Stanford: ANU



Gary Phillips, MBA Commercial CEO, Novartis Australia



John Crapper, MBA COO

Managing Director, Memcor; Syntex (Roche)



William Cowden, PhD

ANU; Co-inventor of TNF mAb's



lan McDonald, PhD

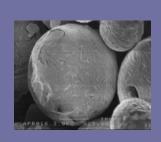
VP Discovery, SIBIA (Merck); VP Discovery, SGX



# Bronchitol



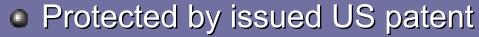
#### overview



 Dry powder mannitol formulation of discrete particle size



Manufactured by Pharmaxis at TGA-approved facility





Successful Phase II trials in CF, bronchiectasis

 Orphan Drug designation from the FDA for CF, bronchiectasis



## cystic fibrosis



## Background

- Genetic disorder affecting 30,000 in U.S.
- Poorly hydrated, tenacious, thick mucus
- Current life expectancy is 31 years

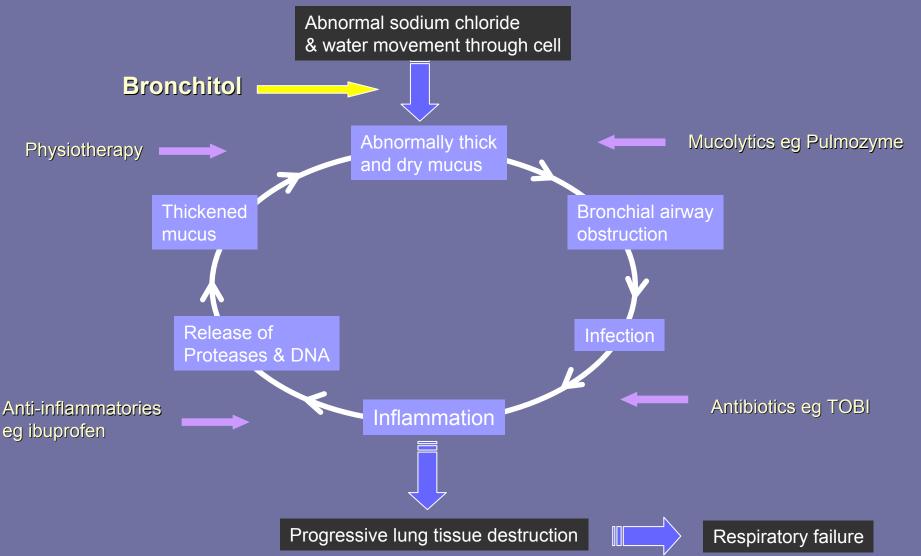


- Delivered by nebulizer (preparation, sterilization)
- Pulmozyme: \$265mm @ ~30% penetration





# Thickened mucus begins a vicious cycle....







# How Bronchitol works.....

osmotic clearance of abnormal mucus





# IN LAST LIND

#### Phase II CF trial



- Crossover, 8 site study in 39 CF patients
- Randomised two week treatment periods
- Double-blind, placebo controlled



- Primary Endpoint:
  - Change in FEV<sub>1</sub>
- Secondary Endpoints:
  - Effect on other lung function measures
  - Effect on symptoms/signs
  - Effect on QoL
  - Safety (including microbiology)







## CF Phase II Results: Change in Lung Function

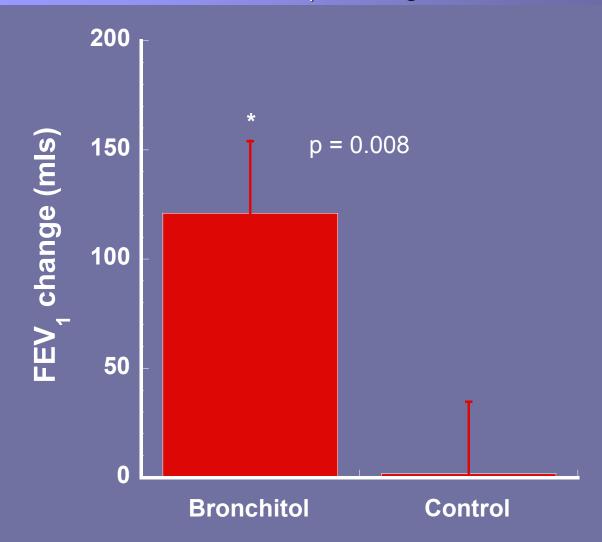
	Bronchitol*	Control*	p value
Change in FEV <sub>1</sub>	7 ± 2%	0 ± 2%	0.008
Change in FEF <sub>25-75</sub>	15.5 ± 5%	0.6 ± 5%	< 0.01

(FEF<sub>25-75</sub> or MMEF is considered a measure of small airway function)

<sup>\*</sup>includes patients being treated with pulmozyme



## CF Phase II Results: FEV<sub>1</sub> Change

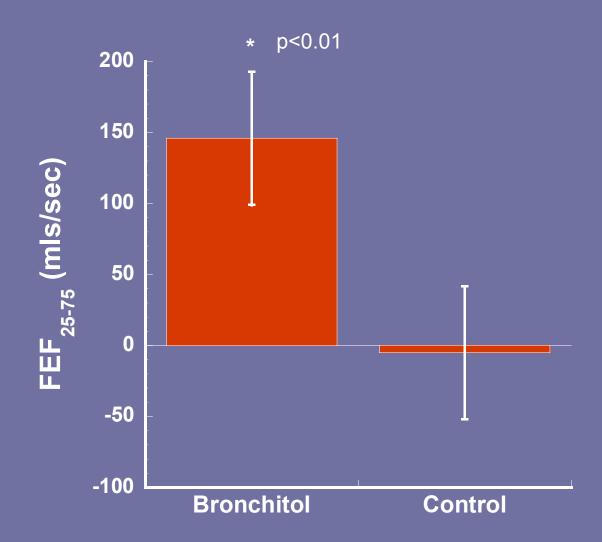






# **Bronchitol**

# CF Phase II Results: FEV<sub>25-75</sub> Change







### cystic fibrosis status



- Dose ranging study underway; data 1H2006
- Phase III trial (EU & Aus) to commence 1H2006



- Phase III trial (US) to commence 2006
- US Orphan Drug designation



Combination study with pulmozyme underway





#### bronchiectasis





- Abnormal, irreversible dilation of the lower airways
- Daily mucus production, constant coughing, breathlessness:
   major quality of life impact



- Normal lung clearance impaired
- 100,000 affected in the U.S.



- Current treatments: bronchodilators, antibiotics
  - No drugs effective to clear mucus







#### bronchiectasis

#### Phase II Trial results

- 60 patient, double-blind, crossover, placebo-controlled
- Promising results in QoL, symptom scores (p<0.05 versus placebo)</li>
- For all patients 4.5 unit improvement in St. George's impact score
- For the 75% of patients with unclear chests 6.9 unit improvement in St George's impact score
- Well tolerated, no adverse events

#### Phase III Trials

- Plan to commence 4Q05/1Q06 in Australia, EU
- Finalising protocol following FDA meeting
- Initiate US pivotal trial mid-2006
- Supplied on compassionate-use basis in Australia

# **Bronchitol**



### chronic bronchitis





- Chronic cough, breathlessness, tenacious sputum
- >30 million people affected in 7 major pharma markets
- No therapy halts disease progression
- Palliative treatments aimed at symptom relief / bronchodilation



- Acute pilot studies completed
- Phase II clinical protocol in development







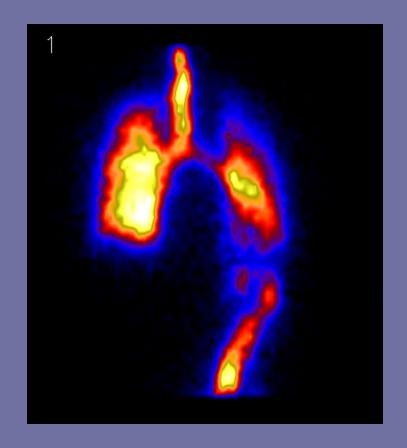


Study to commence 2006



# Bronchitol in the clinic......

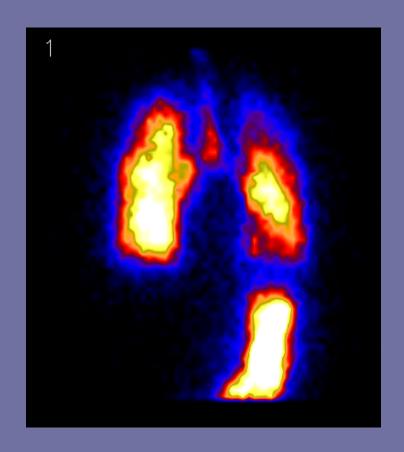
Chronic bronchitis – without bronchitol





# Bronchitol in the clinic......

Chronic bronchitis – with 400 mg bronchitol







A rapid and simple test for airways inflammation that facilitates diagnosis and management of asthma and COPD patients.





## Asthma and COPD Opportunity

#### Asthma

- 51mm patients in 7 major markets
- No simple test, many not diagnosed
- ~34% of people diagnosed with asthma do not have the disease
- Ongoing patient management difficult

#### COPD

- 30 million people affected in 7 major pharmaceutical markets
- Cost to US healthcare US\$30 billion pa
- 20-25% respond to inhaled steroids but no test to identify them
- methacholine (US), histamine (EU), saline (Aus) currently used



### potential advantages

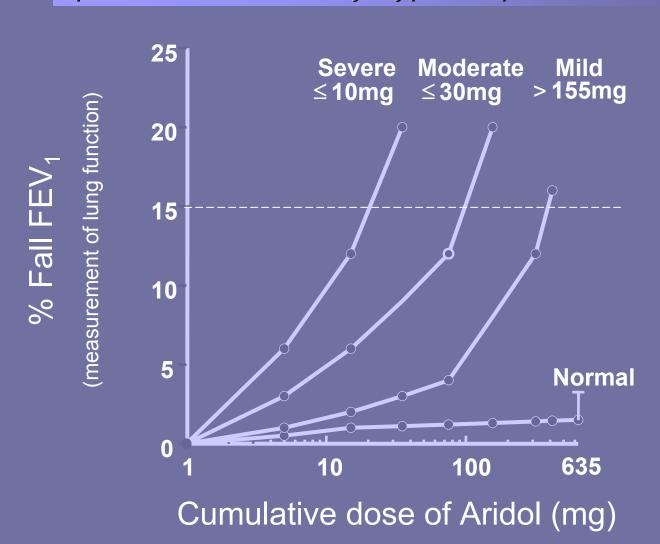


A simple, "point of care" test with a high degree of sensitivity and specificity for airway inflammation

- Useful in excluding and confirming asthma
- Useful for exercise asthma
- Assess disease severity, control
- Identifies COPD patients who respond to steroids (20-25%)



## quantitation of airway hyperresponsiveness







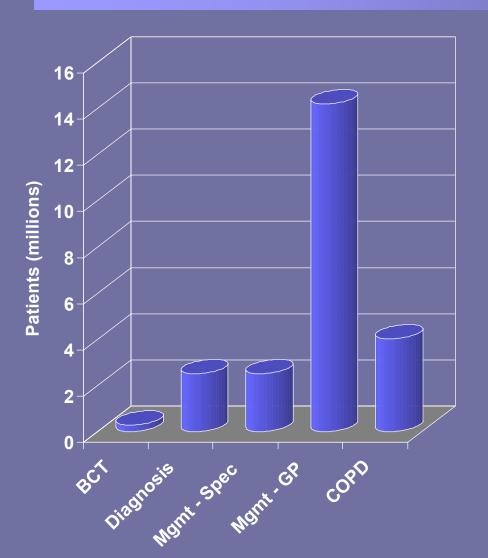


#### current status

- Phase III results (646 patient study)
  - Good agreement with hypertonic saline (p<0.01)</li>
  - Effective at identifying clinical mis-diagnosis (7%)
  - 20% of subjects over treated and over diagnosed
  - 25% of subjects not well controlled
- European and Australian marketing authorization submitted
  - Potential 2006 launch
- US Phase III
  - Comparison vs. methacholine in identifying exercise-induced bronchoconstriction
  - Commence 4Q05, data 1H06, NDA thereafter



#### addressable market



- Multiple trials in progress with key US/EU opinion leaders
- Reimbursable under existing codes in US
- Marketing partner for GP audience
- Publication of clinical results for ICH acceptance
- First revenue 2006 (subject to approval)



# Financial Overview





# Income Statement

## US GAAP at 30 June 2005

	Years ended June 30,								
	20	2003		2004		2005		2005	
	<b>A</b> \$		<b>A</b> \$		<b>A</b> \$		U.S.\$		
	(in thousands, except per share data)								
Revenue	\$		\$		\$		\$		
R&D		925		4,806		7,885		6,007	
G&A		981		2,182		3,105		2,365	
Commercial						807		615	
Amortization of intangibles		86		89		90		68	
Stock option expense		383		532		260		199	
Total operating expenses		2,375		7,609		12,147		9,254	
Loss from operations	(	2,375)	(	7,609)	(	12,147)		(9,254)	
Interest and other income		327		1,123		1,702		1,297	
Amortization of preference share issue expenses		(65)		(161)		-			
Net loss	(\$	2,113)	(\$	6,647)	(\$	10,445)	(	\$7,957)	
Basic and diluted net loss per share	(	\$0.19 <u>)</u>	(	\$0.09)		(\$0.08)		(\$0.06)	
Weighted average number of ordinary shares used in calculating basic and diluted net loss per share	1	1 200	7	5 744	1:	23 933	1	23 933	



# **Balance Sheet**

## US GAAP / US\$ at 30 June 2005

		Actual		As adj. for offering		As adj. for offering and Australian Placement	
Cash and cash equivalents Total assets Total shareholders' equity	\$	25,344 28,824 27,019	\$	65,886 69,366 67,561	\$	101,461 104,941 103,136	

Debt-free Balance Sheet







## Recent Milestones

#### Aridol

- Completed Phase III Aridol trial in asthmatics
- Filed for Aridol approval in Australia, EU

#### Bronchitol

- Announced positive Phase II CF results
- Announced positive Phase II bronchiectasis results
- Received Orphan Drug designation for CF, bronchiectasis
- In FDA discussions regarding pivotal program
- Discovered PXS64 for MS improved / oral form of PXS25
- Tripled manufacturing capacity
- A\$6 million Aus P3 government grant awarded

# IR LIRE LED



# Upcoming Milestones

#### Aridol

Potential Aridol approval in Australia & EU: 1H06

Data from Phase II COPD trial: 2H06

#### Bronchitol

Initiate bronchiectasis pivotal trial: 4Q05/1Q06

Initiate US bronchiectasis pivotal trials: mid-06

Initiate CF pivotal trials:
2006

Data from CF dosing study1H06

### Pipeline

US IND for PXS64 for multiple sclerosis: 1H06

Nominate IND candidate for PXS2076 for RA: 2006



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# Autoimmune diseases

multiple sclerosis rheumatoid arthritis

# Autoimmune Disease



Inflammation: the leukocyte activation cascade

Blood vessel wall Progressive activation Leukocyte **Blood flow** Capture Firm adhesion Rolling Slow rolling Transmigration Endothelium Enzymes digest basement PXS25 membrane blocks Attractants on enzyme endothelial cell surface Tissue function



# Autoimmune Disease

#### PXS64

- Selective inhibitor of T cell migration
- Novel mechanism
- Effective in animal models of multiple sclerosis
- Oral prodrug of PXS25, both discovered by Pharmaxis
- Current status: preclinical development, start human
   Phase I clinical trials 1H06