Innovative products for respiratory diseases

pharmaxis

August 2012

Pharmaxis - company overview

Objective	Development of products for respiratory diseases
Lead products	Bronchitol®: Cystic fibrosis and bronchiectasis Aridol®: Diagnosis of asthma and COPD ASM8: Moderate-severe asthma
Discovery	PXS64: Idiopathic pulmonary fibrosis PXS4728: Anti-inflamatory LOXL2 inhibitor for fibrosis and cancer
Employees	160 involved in research and development, clinical trials, manufacturing and commercialization
Locations	Australia, Europe, USA
Facility	GMP Manufacture of respirable dry powders

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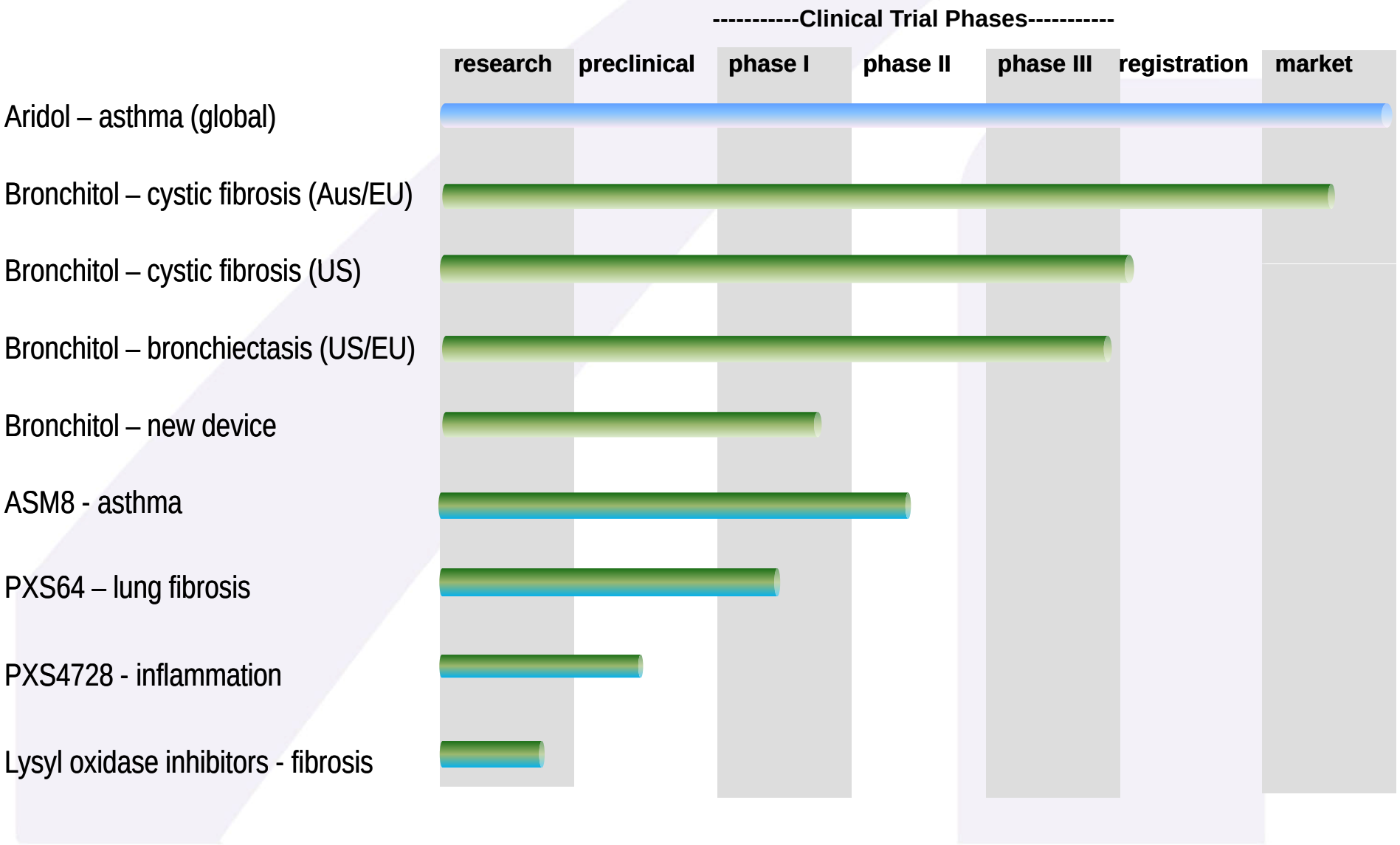
Development pipeline



Bronchitol – Cystic Fibrosis

- Approved
- Launched in first European countries June 2012

- Approved
- Reimbursement effective August 2012
- Launched August 2012

- NDA accepted by FDA – July 2012
- FDA review completion target - Q1 2013

- Rest of world - country by country basis

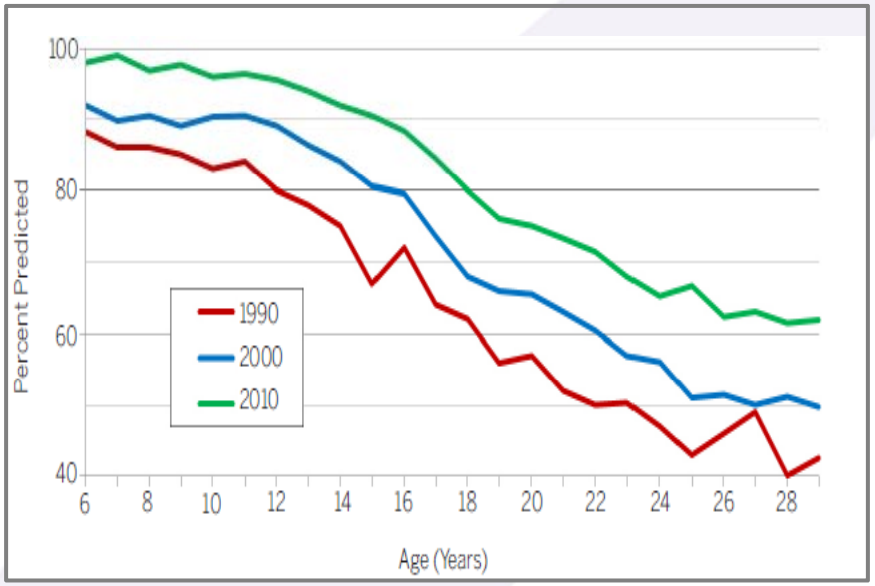
Bronchitol - Cystic Fibrosis

- **Background**
  - Genetic disorder affecting ~40,000 in Western Europe, ~30,000 in US and ~3,000 in Australia
  - Poorly hydrated, tenacious, thick mucus
  - Median predicted age of survival approximately 35 years (2009 – US and UK)

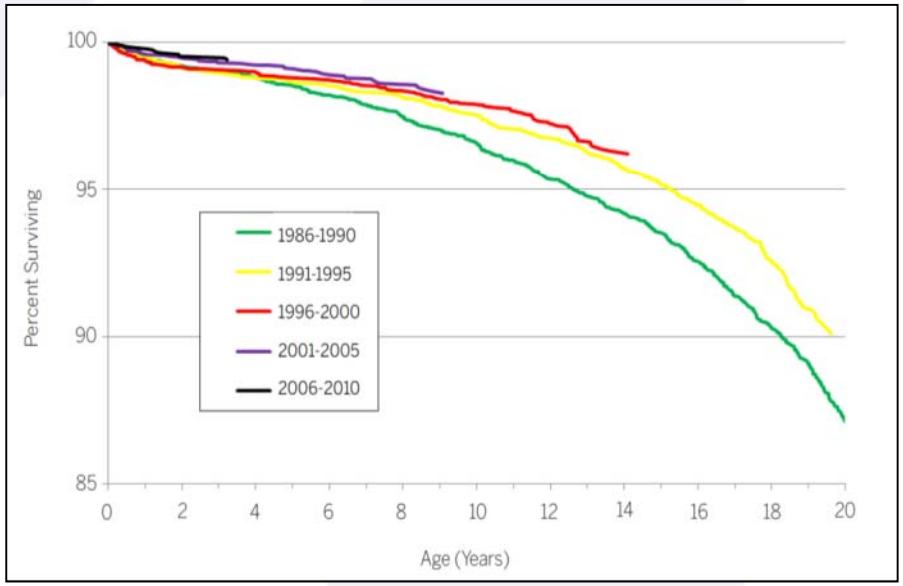
- **Main Therapeutics**
  - Mostly delivered by nebulizer (preparation, sterilization)
  - rhDNase (Pulmozyme®): global sales ~CHF 492m (2011)
  - Tobramycin (Tobi®): global sales ~US$ 279m (2010)
  - Aztreonam (Cayston®): approved EU: 09/09; US: 02/10; US sales $78m in US (2011)

Lung function and life expectancy in CF patients

Median FEV_1 % Predicted versus Age



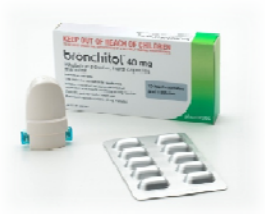
Survival by Birth Cohort



The outlook for CF patients has improved over the last 20 years but there remains a high unmet clinical need

Source: Cystic Fibrosis Foundation Patient registry report, 2010

Pathophysiological cascade in CF



New Therapies

Current Therapies

Defective CF gene

Defective/Deficient CFTR ← *Kalydeco ® (Ivacaftor)*

Reduced Airway Surface Liquid ← ***Bronchitol***

Impaired Mucociliary Clearance

Infection ← Pulmozyme ® (rhDNase)

Infection ← Antibiotics

Inflammation

Inadequate Lung Function ← Transplantation

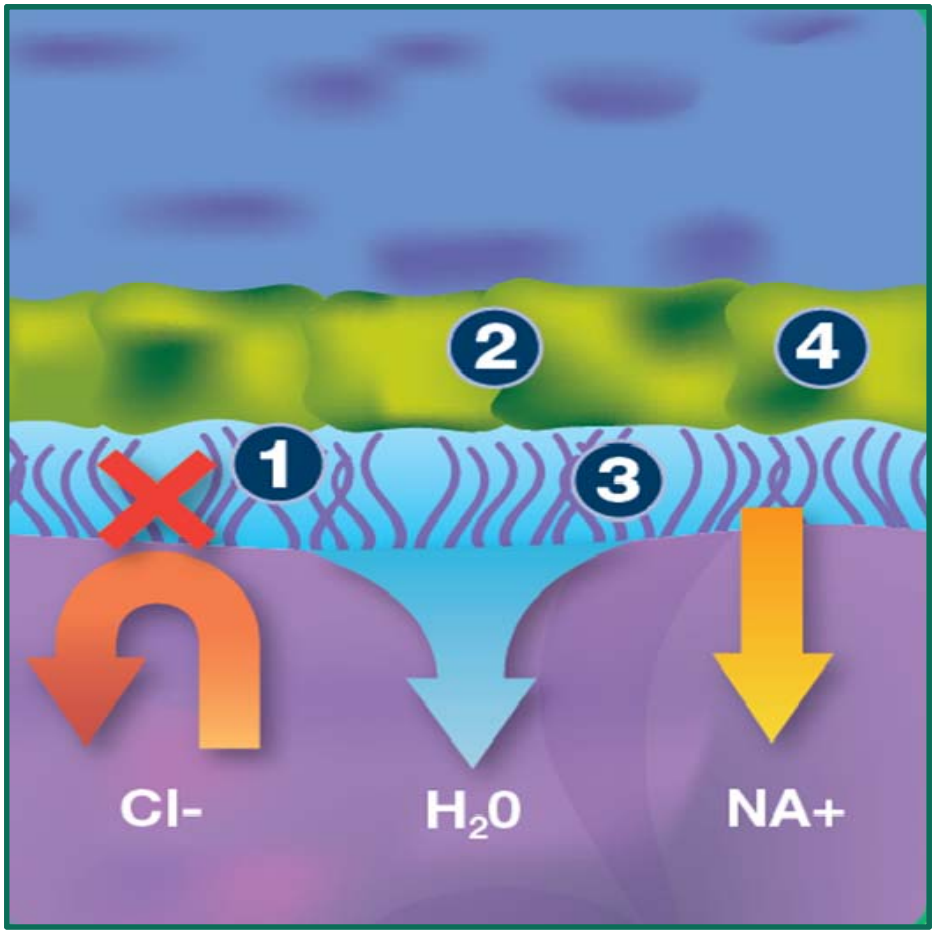
Death

Adapted from Davis 1996 Am J Respir Crit Care Med

Bronchitol - mode of action

For patients with CF

1. Dehydrated Airway Surface Liquid (ASL) caused by non-functioning CFTR
2. Mucus sticky and difficult to clear
3. Cilia not functioning
4. Reservoir for infection and inflammation

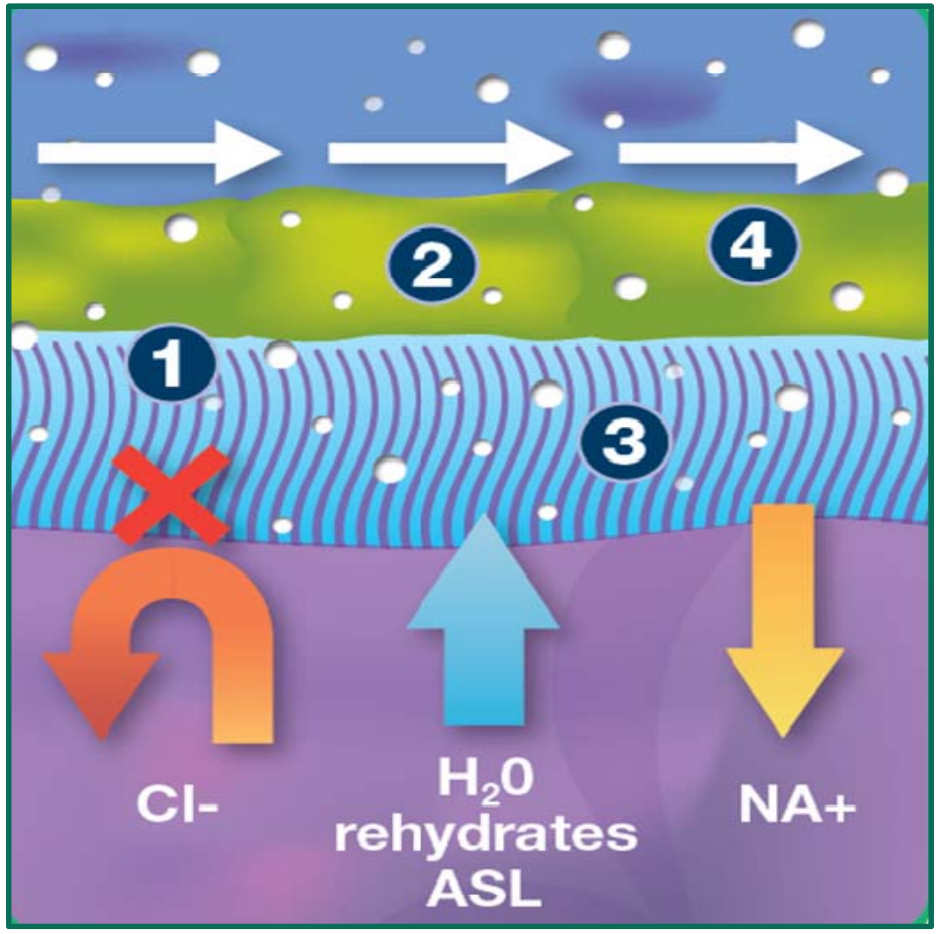


Daviskas & Anderson 2006, Daviskas 1999, Robinson 1999, Daviskas et al Respirology 2006; 10:46-56, Henke and Ratjen. Paed Resp Review 2007; 8:24-29, Yahgi A et al. Jour Aero Med Pulm, 2012; Vol 25:1-8

Bronchitol - mode of action

Following Bronchitol inhalation

1. Water driven to airway surface
2. Flow properties of mucus improved
3. Cilia beat frequency increased
4. Mucus is cleared through cilia and cough



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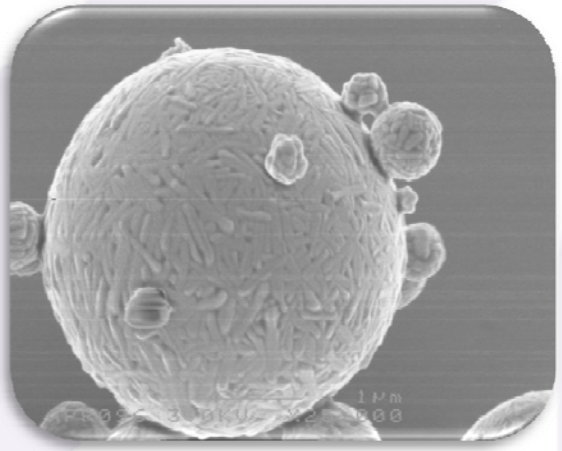
Bronchitol – formulation



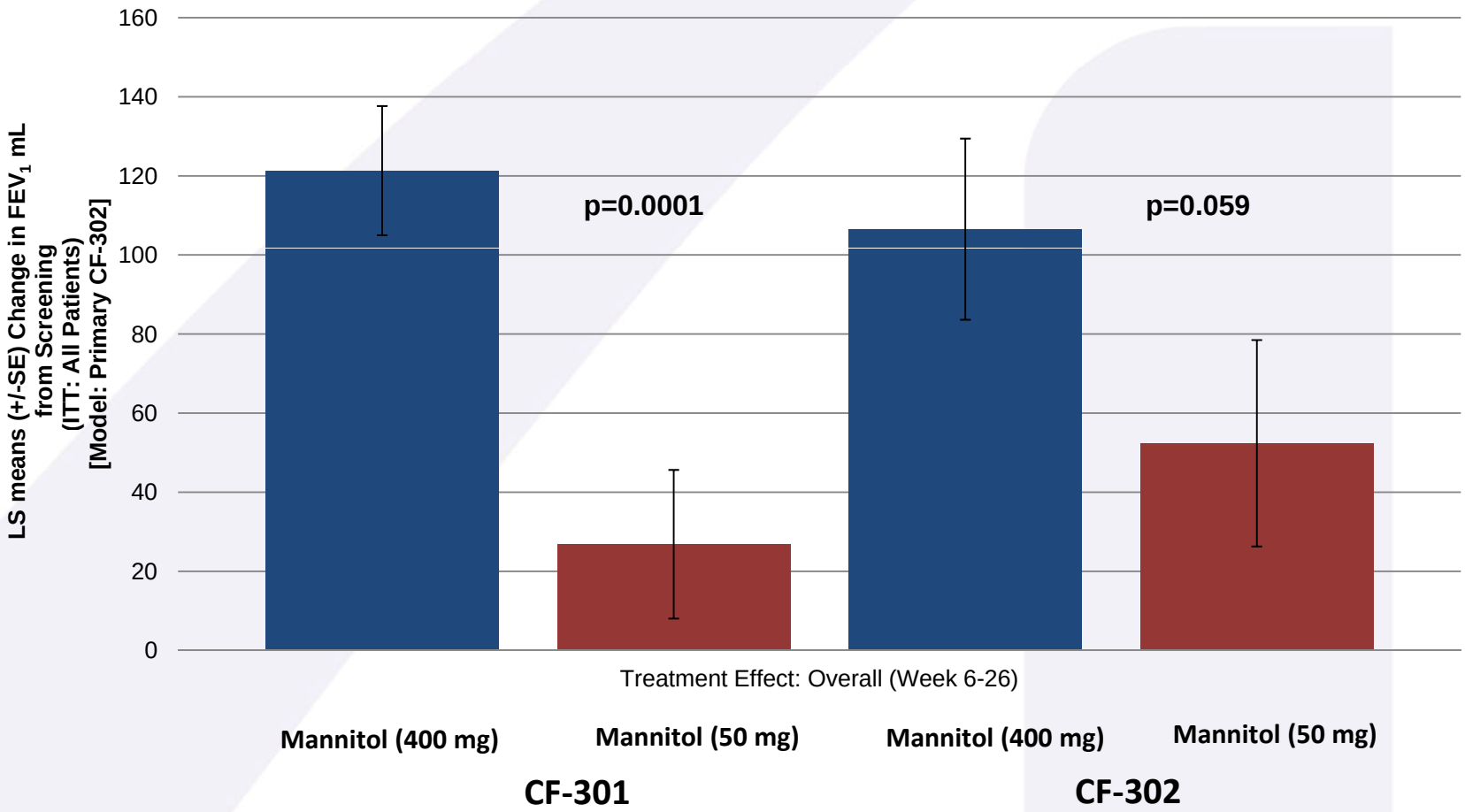
- **100% mannitol**
- **Precision spray dried**
- **3 micron particles – hollow spheres**
- **Capsule based dry powder inhaler**
- **400mg dose (10x 40mg caps)**

Bronchitol - Cystic Fibrosis Phase III clinical program

Two Pivotal trials – same design

- Multicentre, double blind, controlled
- Approx 300 subjects greater than 6 years old per trial
- 6 month treatment, 400mg twice per day followed by 6 month open label
- Primary endpoint:
  - lung function (FEV_1)
- Secondary endpoints:
  - Other lung function measures
  - Sputum weight
  - Exacerbations
  - Antibiotic use
  - Quality of life
- CF301: 40 centres in UK, Ireland, Australia & New Zealand
- CF302: 53 centres in US, Canada, Argentina, Germany, France, Belgium, & Netherlands
- Subjects remain on existing best standard of care

FEV_1 change from baseline (CF301 and CF302)

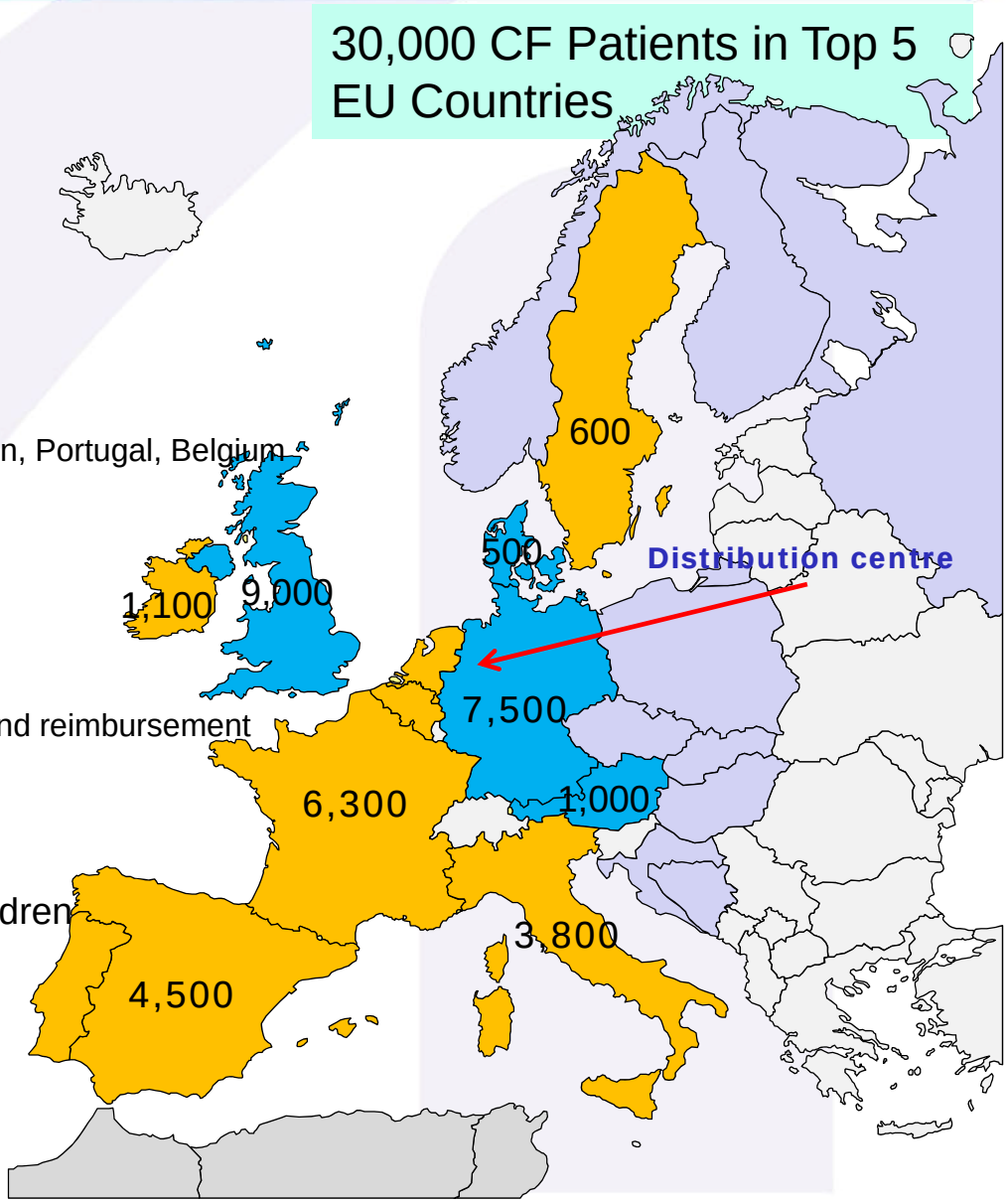


Bronchitol - exacerbation incidence reduced

Percentage reduction in exacerbation incidence after 6 months Bronchitol treatment (400mg *versus* 50mg)		
CF301	35%	p=0.045
CF302	20%	p>0.05
CF301 +CF302 combined	29%	p=0.039

Bronchitol - Cystic Fibrosis (Europe)

- First countries: 18,000 patients – H2 2012
  - Germany (134 CF clinics) - June 2012
  - UK (50 CF clinics) – June 2012
  - Austria – July 2012
  - Denmark – August 2012
- Second countries: 20,000 patients – H1 2013
  - France, Italy, Sweden, Netherlands, Ireland, Spain, Portugal, Belgium
  - To be launched after reimbursement
- Launch via distributors (~17,000 patients)
  - EU (~7,000 patients) – reimbursement key
  - Non EU (~10,000 patients) - separate approval and reimbursement
  - Country-by-country basis
- Label expansion to include adolescents and children
  - Adult CF population represents >50% of patients
  - Clinical trial required – in review with regulator
  - Represents one third potential market



Commercial & Manufacturing Infrastructure

Australia

- Installed capacity of 40,000 patients pa (1 spray drier)
- Ability to expand capacity to 80,000 patients pa (2nd spray drier) when required

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- UK office
- European sales & marketing management
- European pricing
- European support – medical info, PV
- Key account managers - UK and Denmark

QUINTILES

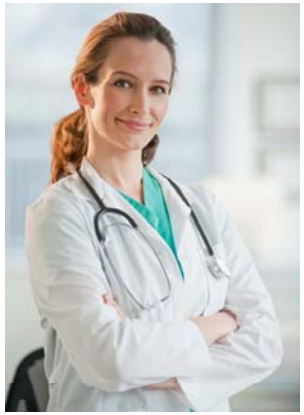
Sales, marketing and market access

Germany	France
Italy	Spain
Austria	Ireland
Netherlands	Portugal
Sweden	

arvato »HEALTHCARE BERTELSMANN

- Centralised European inventory management - Harsewinkel Germany
- Importation
- Distribution/consignment direct to pharmacy
- Invoicing and receivables

Commercialisation priorities



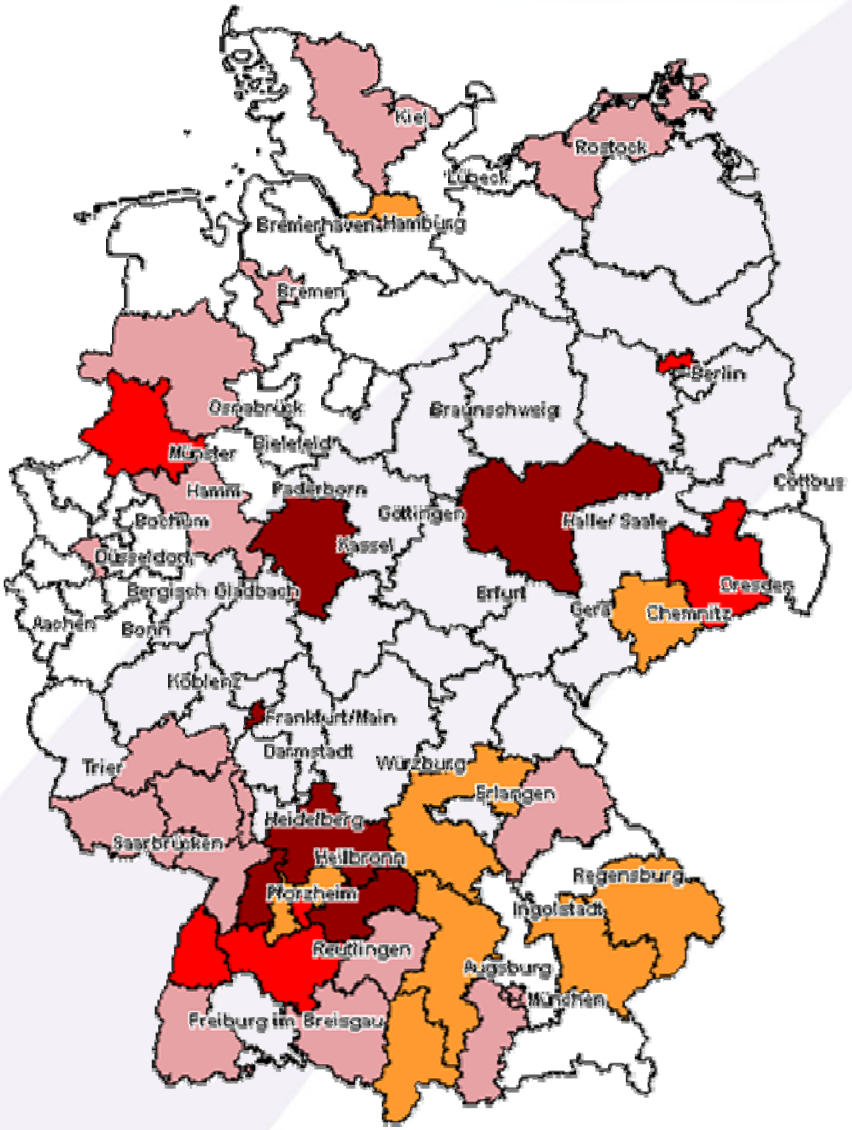
Pricing & Reimbursement

- Germany – introduced and reimbursed
- National Institute for Health and Clinical Excellence (NICE - UK) – Q4 2012
- Austria – introduced on named patient basis
- Scottish Medicines Commission – H1 2013
- French reimbursement – Q1 2013
- Consistent ex-factory price throughout EU (€20-25 per day)

Market introduction

- Emphasis on training and education
  - Consistent messages to all CF centres
  - CF clinics trained in Bronchitol administration
  - Centres administer initiation test first to patients
- Patients prescribed ongoing supply
- Additional country introductions
- Distributors for non EU countries

Early progress in Germany



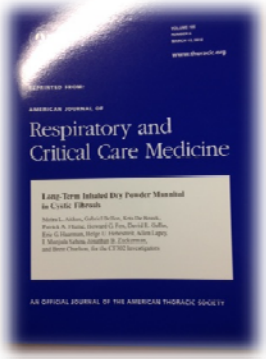
Initiation tests by region (end July 2012)

- 134 CF Centres
- Emphasis on initiation training
- Interest level is high
  - Early adopters; consider patients, logistics and plan for an initiation test
  - No significant objections to the product profile
  - Pricing acceptable
- Initiation test logistics
  - 50% prescribed to a patient and then the patient brings the initiation test to the clinic
  - 50% initiation test are prescribed for next visit in 2 – 3 months

Bronchitol - Cystic Fibrosis (Australia)

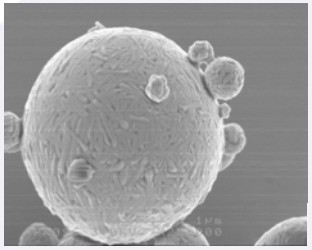
- ~3,000 people with CF in Australia
- Approved for patients aged 6 and over
- Reimbursement from 01 August 2012
- 22 CF centres in Australia
- Bronchitol included on all formularies
- >100 patients in PXS subsidised Physician Familiarisation Program – transitioning to PBS
- Two key account managers, one marketing manager

Bronchitol opportunity in the USA



- NDA submitted May 2012
- FDA review scheduled for completion in March 2013
- Requested indication
  - Bronchitol is indicated for the management of cystic fibrosis patients 6 years of age or older to improve pulmonary function
- Orphan drug status provides 7 years market exclusivity from date of FDA approval
- ~250 CF centres
- Anticipated requirement for 20 - 25 person field force
- ~30,000 people in the US with CF
- Pricing finalised after NDA complete

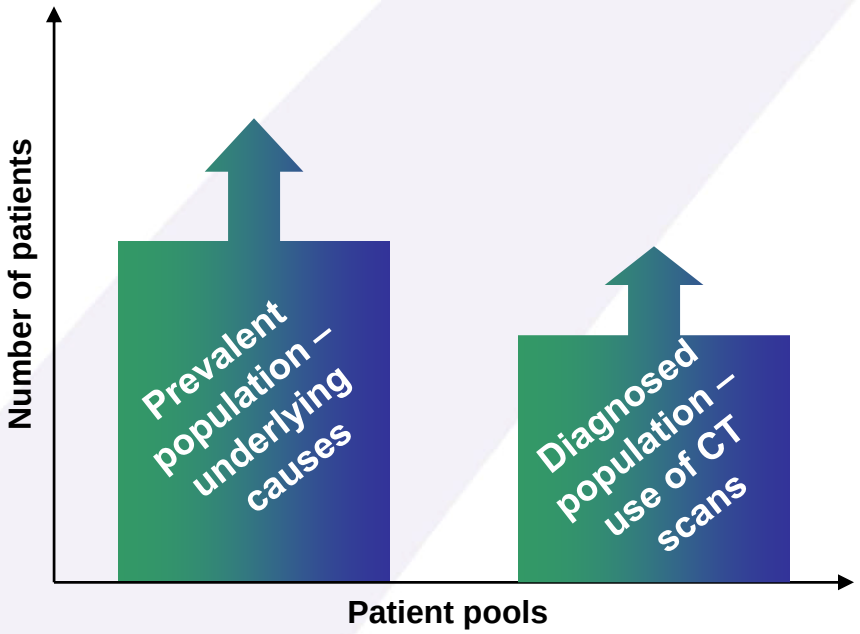
Bronchitol - Bronchiectasis



- Abnormal, irreversible dilation of the lower airways
- Daily mucus production, constant coughing, breathlessness, recurrent acute bronchitis with infective exacerbations : low quality of life
- Normal lung clearance impaired
- Current treatments: bronchodilators, antibiotics
- **No** drugs proven effective to clear mucus
- Orphan disease in the USA

Bronchiectasis – future prevalence to grow

In 30-50% of cases, the specific cause is unknown



Known causes include:

- Respiratory infections
  - TB, flu, pseudomonas, measles, whooping cough
- Bronchial obstruction
  - Lung tumour, mucus plug
- Inhalation injuries
  - Noxious fumes, stomach acid
- Hereditary conditions
  - CF, ciliary dyskinesia
- Immunological abnormalities
  - Autoimmune diseases, white cell dysfunction.
- HIV

Bronchiectasis - patients seeking treatment

	EU	Australia	USA	Asia	Total
% of pt pool seen by respiratory specialists	14%	9%	N/A	5%	
Trend	Stable or increasing	Stable	Increasing	Stable or decreasing	
Mod/Severe	55%	70%	55%	75%	
Patients seeking treatment	210,000	18,000	190,000*	250,000 ++	680,000

Note: Data from Datamonitor research and from Frost & Sullivan research (2007)

**CHEST*, August 2012;142(2):432-439. doi:10.1378/chest.11-2209

Bronchitol – bronchiectasis registration

- **2nd Phase III trial**
  - 485 patient, controlled, double blind, randomised, 52 week treatment, 89 sites in US, Europe, South America, Australia
  - 400mg twice a day
- **Primary endpoint**
  - Reduction in number of exacerbations
- **Secondary endpoints**
  - Exercise, mucus clearance, antibiotic use
  - Quality of life
- **Status**
  - Orphan Drug designation — USA
  - Completed recruitment — Dec 2011
  - Data — 1H 2013

Aridol®

- Identifies airway hyperresponsiveness which helps physicians in the overall assessment of **asthma**

- An **easy-to-use test kit** provides rapid results and doesn't require specialized equipment

Aridol – commercialisation status

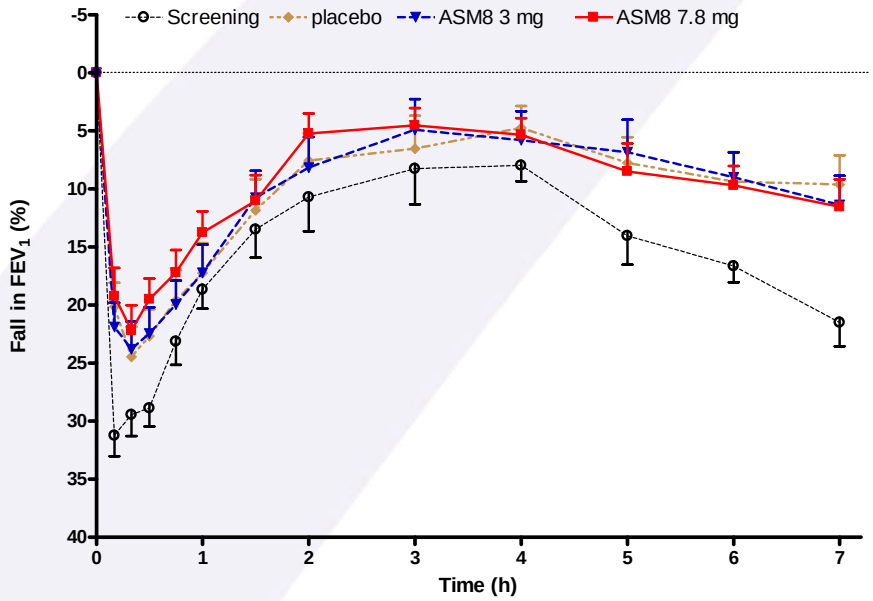
Financial years ending 30 June		2011	2012
Sales (A$'000)			
Australia	Direct	253	270
Europe	Distributor model UK – direct	398	319
South Korea	Distributor	205	372
Clinical trials	Direct	-	-
US	Direct	54	347
		910	1,308

Potential growth

- US and South Korea – full reimbursement for procedure and product
- Asthma management – recent investigator initiated trial published
- COPD – recent investigator initiated trial published

ASM8 – asthma

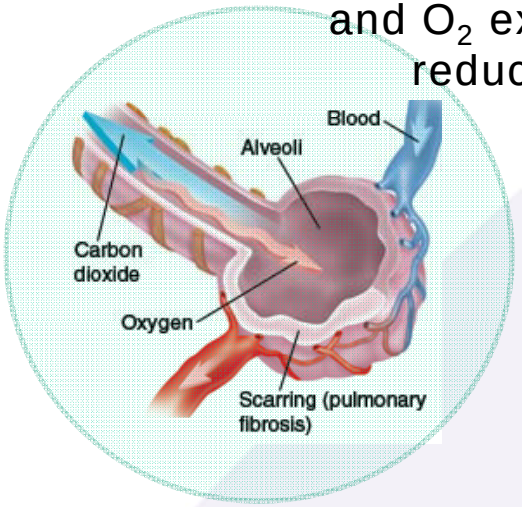
Phase IIa trial



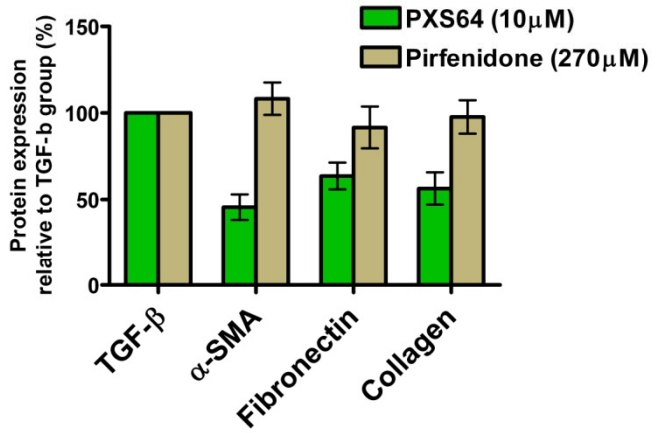
Indication	Moderate to severe asthma for patients who do not respond to inhaled steroids or cannot tolerate high doses
Target Product Profile	-Greater efficacy through multi-targeting -Better tolerability & convenience compared with current treatments -Once daily nebulisation
Market Size	Affects ~12 million people worldwide
Competitors	Xolair (2011: US: US$ 478m & RoW: CHF 603m)
Status	Phase IIa trial reported
Next Milestone	Publication of full trial results

PXS25 / PXS64 – Idiopathic Pulmonary Fibrosis

alveoli thickening and O_2 exchange reduction

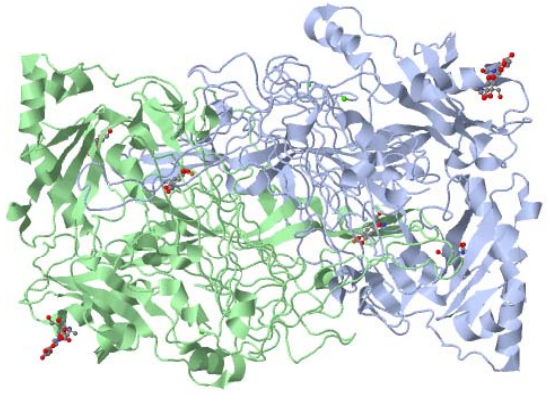


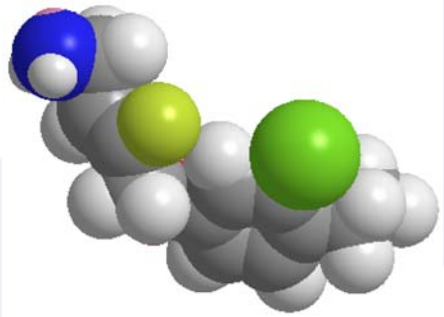
The effect of PXS64 *vs* pirfenidone in primary derived human lung fibroblasts



Indication	Idiopathic Pulmonary Fibrosis (IPF)
Target	M6P receptor blocker
Target Product Profile	-Inhibition of fibrosis and inflammation to lung tissue -Local administration to the lung -Safe & well tolerated in humans
Market Size	Affects ~200,000 people in the USA
Competitors	Pirfenidone (just launched in EU), immunosuppressives & steroids
Status	Initial Phase I trial (intravenous) completed
Next Milestone	Confirmatory in-vivo data Clinical plan in development

PXS4728A – Lung inflammation





small molecule inhibitor of SSAO

Indication	Anti-inflammatory agent with anti-fibrotic properties
Target	SSAO / VAP-1 inhibitor
Target Product Profile	-COPD / IPF / -Once daily oral dosing
Market Size	Affects ~23 million people worldwide
Competitors	Significant clinical pre-clinical activity amongst pharmaceutical companies
Status	Pre-clinical development
Next Milestone	Phase 1 clinical trials – Q1 2013

Financial Statements

Financial Statement Data - Unaudited				
(International Financial Reporting Standards)				
('000 except per share data)				
Income Statement Data	Three months ended		Twelve months ended	
	30-Jun-12	30-Jun-11	30-Jun-12	30-Jun-11
	A$	A$	A$	A$
Revenue from sale of goods	373	233	1,331	910
Cost of sales	(159)	(65)	(538)	(342)
Gross profit	214	168	793	568
Interest	968	615	3,049	3,083
Other income	1,441	134	3,874	465
Expenses				
Research & development	(7,400)	(9,096)	(29,207)	(34,632)
Commercial	(3,716)	(2,834)	(11,073)	(9,163)
Administration	(1,389)	(1,167)	(5,387)	(5,171)
Finance expenses	(201)	(212)	(768)	(859)
Total expenses	(12,706)	(13,309)	(46,435)	(49,825)
Loss before income tax	(10,083)	(12,392)	(38,719)	(45,709)
Income tax expense	(50)	16	74	(49)
Loss for the period	(10,133)	(12,376)	(38,645)	(45,758)
Basic and diluted earnings (loss) per share - $	(0.033)	(0.054)	(0.142)	(20.200)
Depreciation & amortisation	1,155	1,453	4,665	5,026
Fair value of securities issued under employee plans	201	385	957	1,567

Financial Statements

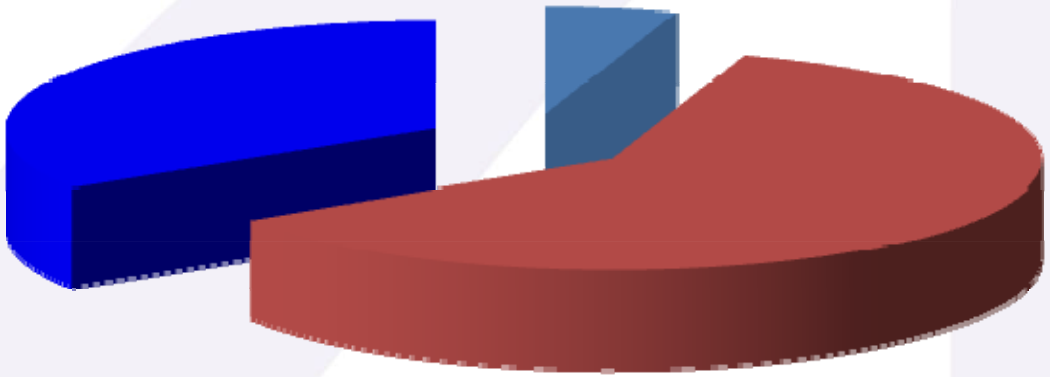
Balance Sheet Data	As at			
	30-Jun-12	30-Jun-11		
	A$	A$		
Cash and cash equivalents	81,475	44,343		
Property, plant & equipment	27,684	30,570		
Intangible assets	14,143	15,954		
Total assets	131,700	94,525		
Total liabilities	(21,897)	(23,742)		
Net assets	109,803	70,830		
Cash Flow Data	Three months ended		Twelve months ended	
	30-Jun-12	30-Jun-11	30-Jun-12	30-Jun-11
	A$	A$	A$	A$
Cash flows from operating activities	(9,979)	(9,971)	(38,143)	(37,366)
Cash flows from investing activities	(85)	(1,743)	(169)	(2,883)
Cash flows from financing activities	(18)	(195)	75,427	(758)
Impact of foreign exchange rate movements on cash	7	(32)	17	(437)
Net increase (decrease) in cash held	(10,075)	(11,941)	37,132	(41,444)

Share Capital
(including options)

Management – 4%

Other/retail – 31%

Institutions – 65%
(73 institutions)



30 June 2012:

- **7,100 shareholders**
- **308m shares**
- **12m options**

Summary

- **Pharmaceutical company with approved products and strong pipeline**
- **Bronchitol**
  - → Approved and reimbursed in Australia for cystic fibrosis
  - → Approved and launched in Europe
    - launch continues
  - → USA marketing application under review by FDA
  - → Clinical trials in progress to extend reach into Bronchiectasis
- **Aridol**
  - → Approved in Australia, South East Asia, Europe and USA
  - → Fully reimbursed in USA and South Korea
- **ASM 8 for asthma**
  - → Phase IIa trial results released April 2012
- **PXS 64 for Idiopathic Pulmonary Fibrosis**
  - → Phase I trial completed with IV formulation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August 2012