pharmaxis

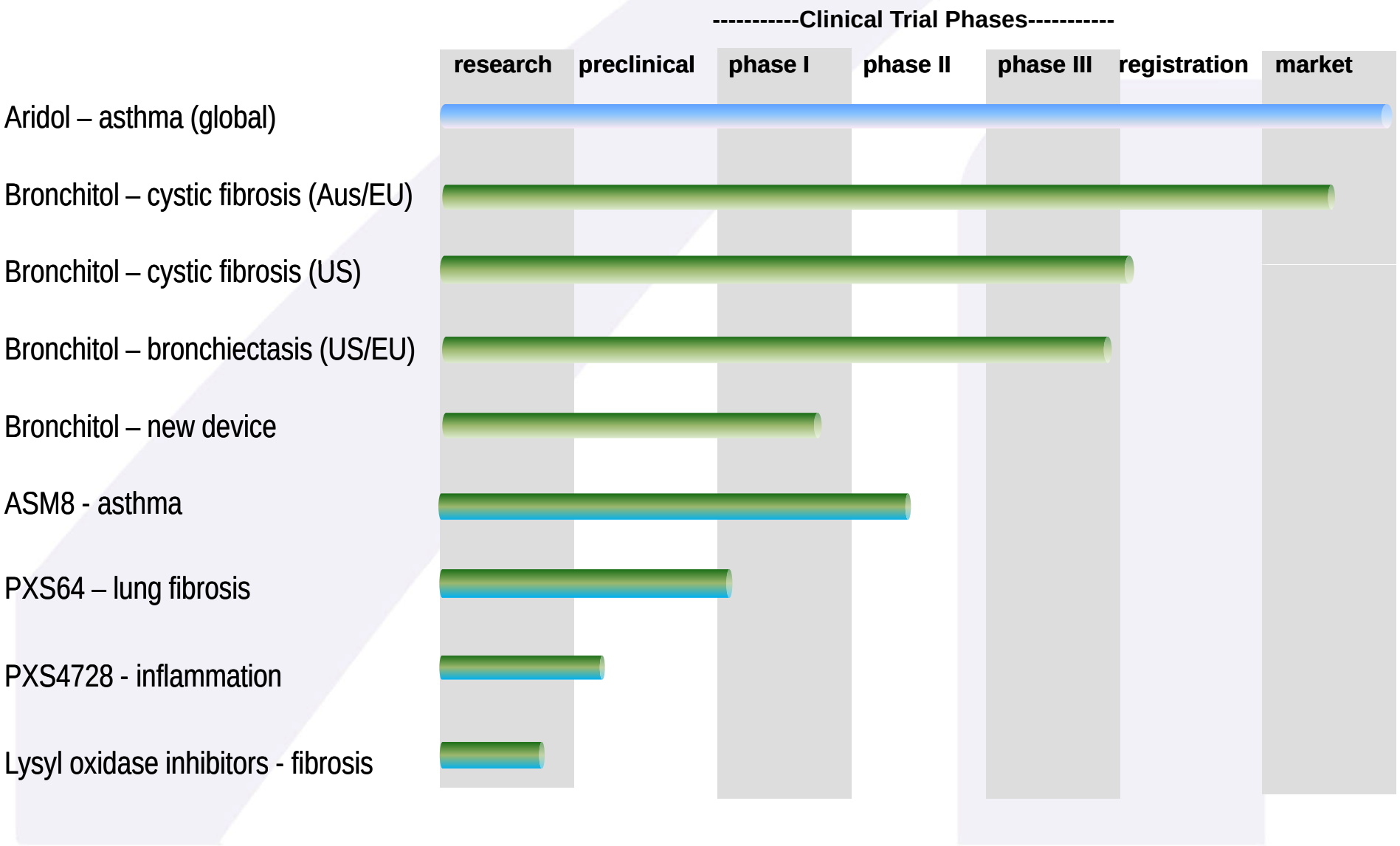
Innovative products for respiratory diseases

September 2012

Pharmaxis - company overview

Summary	• A pharmaceutical company which develops therapeutic products for human chronic respiratory diseases. • Headquartered in Australia with operations in the US and Europe	
Approved products	Bronchitol® for cystic fibrosis Aridol®: diagnosis of asthma	
Products in the clinic	Bronchitol® for bronchiectasis ASM8: moderate-severe asthma	
Products in development	PXS64: idiopathic pulmonary fibrosis PXS4728: anti-inflammatory LOXL2 inhibitor: fibrosis and cancer	
Employees	Australia	108
	Europe	33
	USA	17
Production	GMP manufacture of respirable dry powders	

Development pipeline



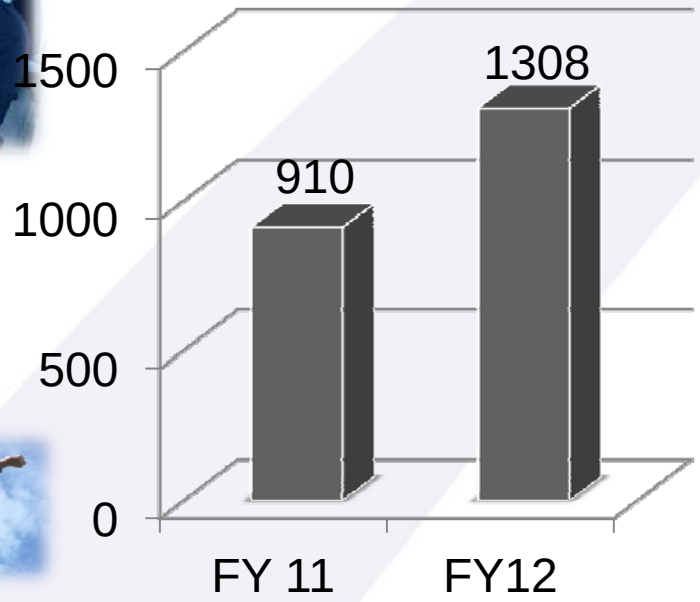
Aridol®

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

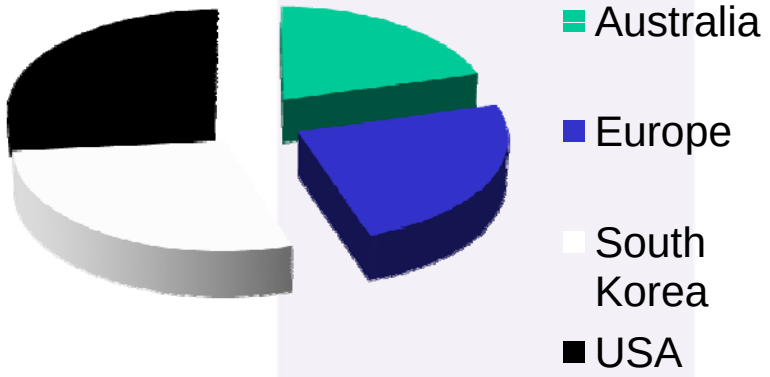
- An **easy-to-use test kit** provides rapid results and doesn't require specialized equipment

Aridol – approved and sold around the world

Sales ($000's)



Region contribution



Future growth

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

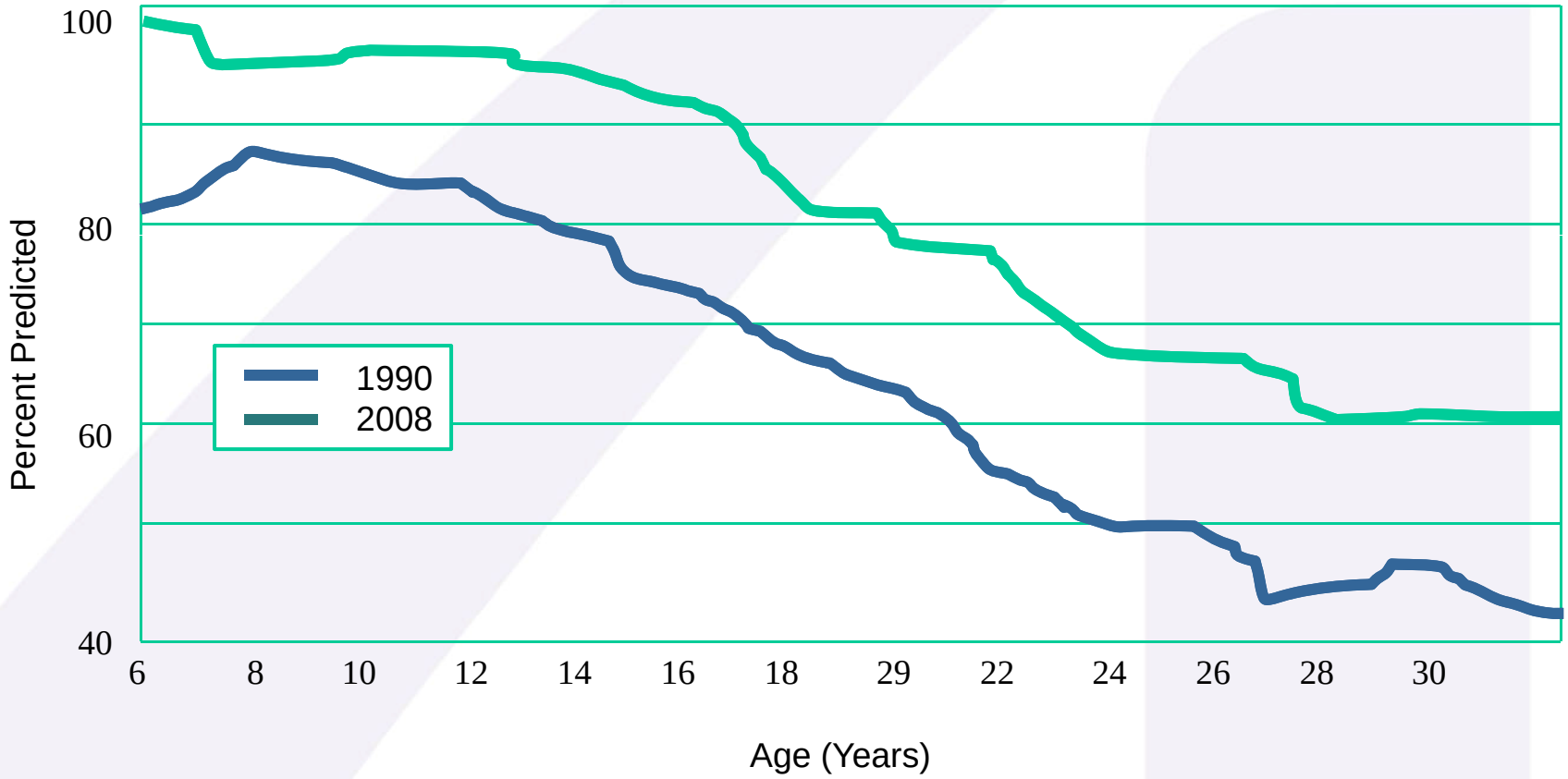
Bronchitol® - Cystic Fibrosis

- **Background**
  - Genetic disorder affecting ~40,000 in Western Europe, ~30,000 in US and ~3,000 in Australia
  - Poorly hydrated, tenacious, thick mucus
  - Median predi urvival approximately 35 years (2009 – US a

Aridol - approved and sold around the world

- **Main Therapeuti**
  - 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)

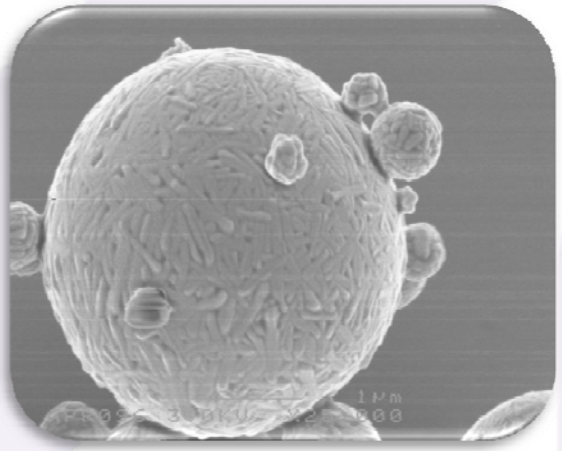
Median FEV_1 % predicted vs age 1990 - 2008

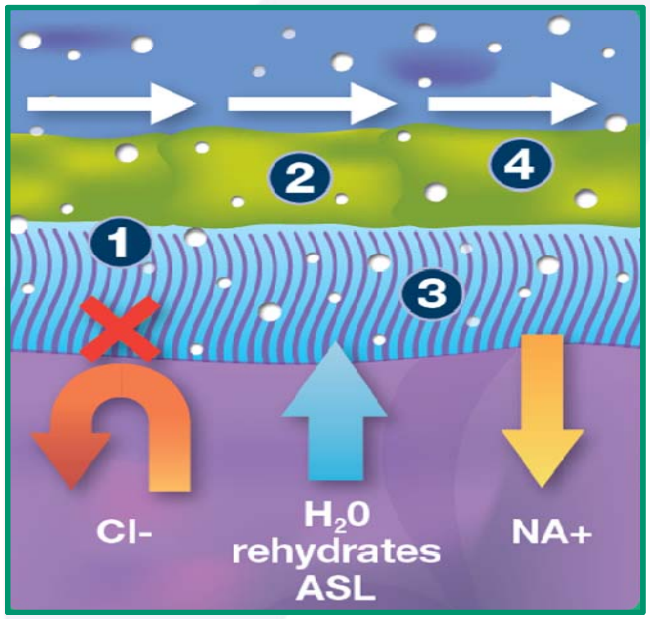


Median FEV_1 has improved more than 10 percentage points at all ages from 6 to 30 since 1990 however the rate of FEV_1 decline has not improved

2008 CFF Registry

Bronchitol





Bronchitol

- active ingredient mannitol
  - delivered as an inhalable dry powder
- restores airway surface liquid
- increases cilia beat frequency
- mucus flow properties improved
- mucus clearance enhanced

Pathophysiological cascade in CF

New therapeutic targets

Current therapeutic targets

Defective CF gene

Defective/deficient CFTR

Reduced airway surface liquid

Impaired mucociliary clearance

Infection

Inflammation

Inadequate lung function

Death

Bronchitol

rhDNase

Antibiotics

Transplantation

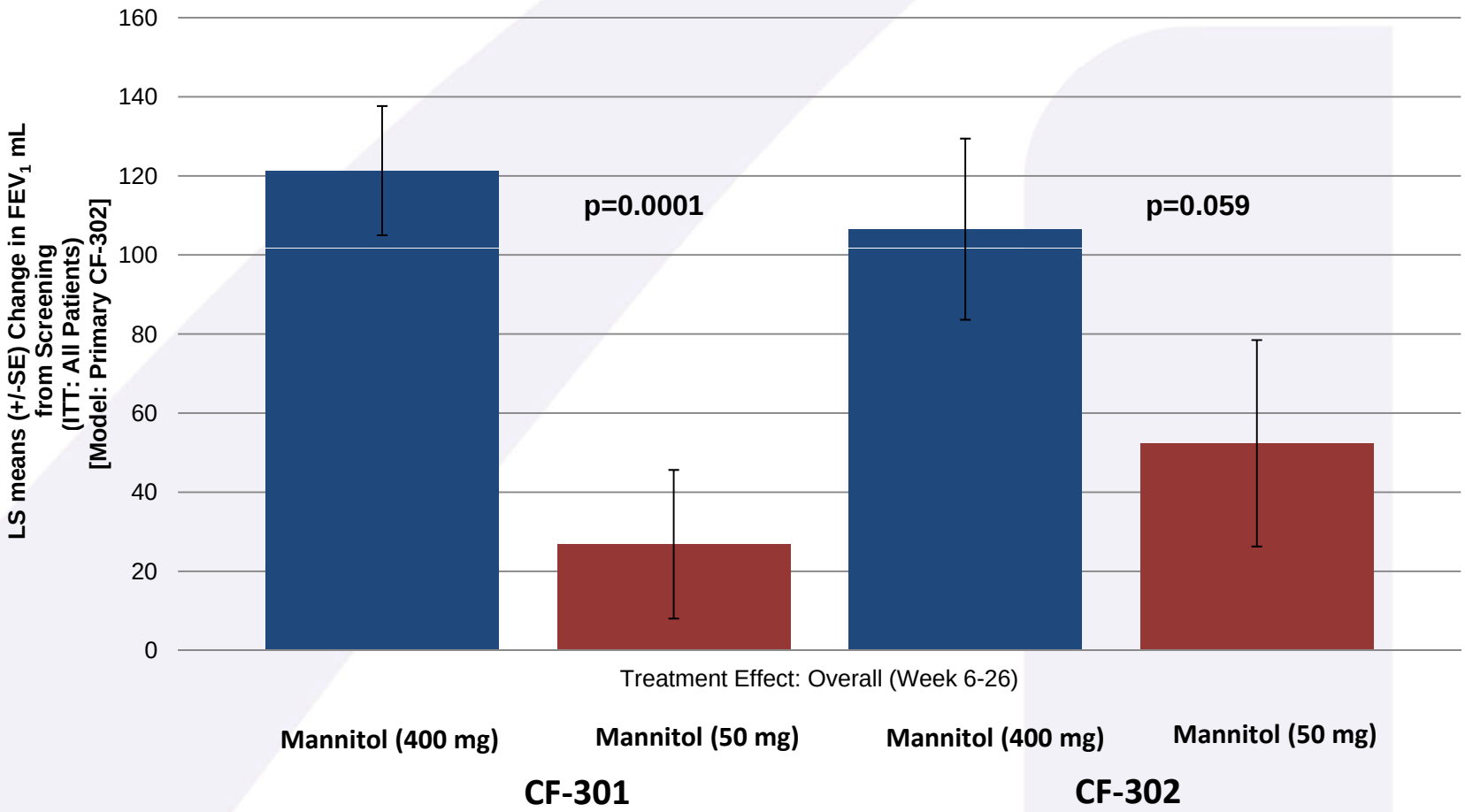
Adapted from Davis 1996 Am J Respir Crit Care Med

Bronchitol - Cystic Fibrosis Phase III clinical program

Two Pivotal trials – same design

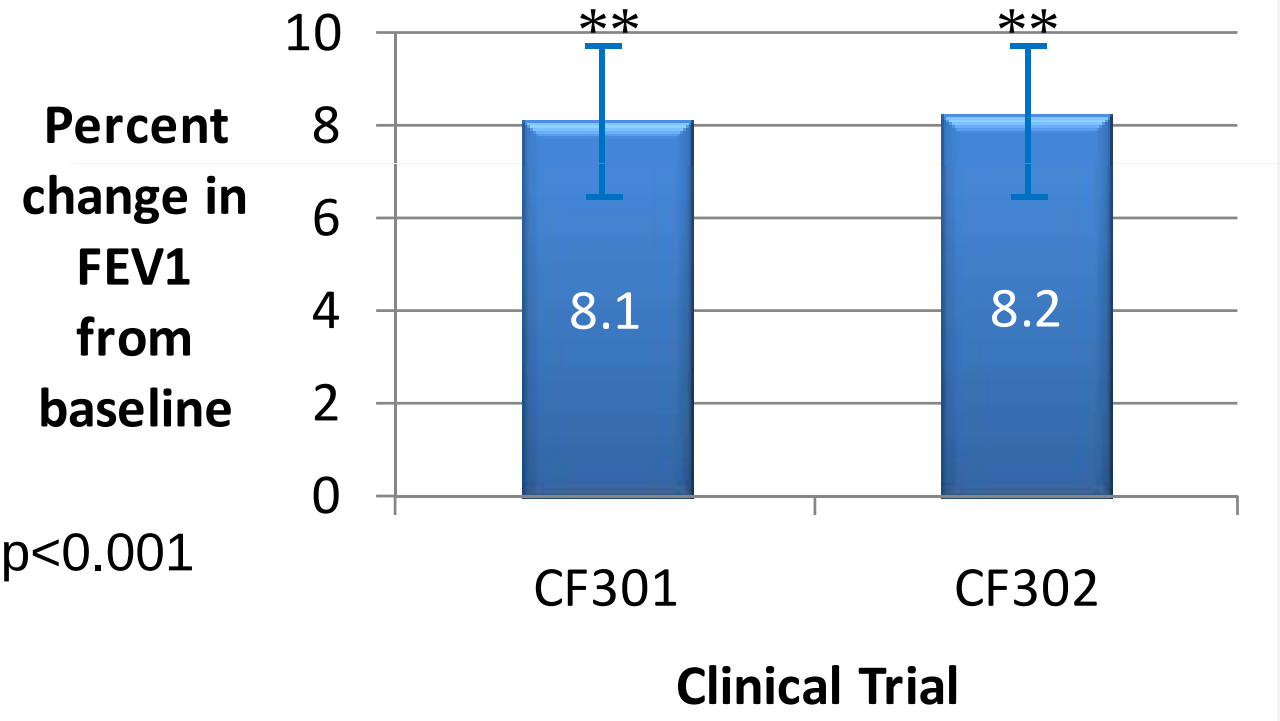
- Multicentre, double blind, controlled
- Approx 300 subjects per trial greater than 6 years old
- 6 month treatment, 400mg twice per day followed by 6 month open label
- Primary endpoint:
  - lung function (FEV_1)
- Secondary endpoints:
  - Other lung function measures
  - Cleared sputum weight
  - 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)



Sustained treatment effect

Change in lung function after 12 months Bronchitol treatment

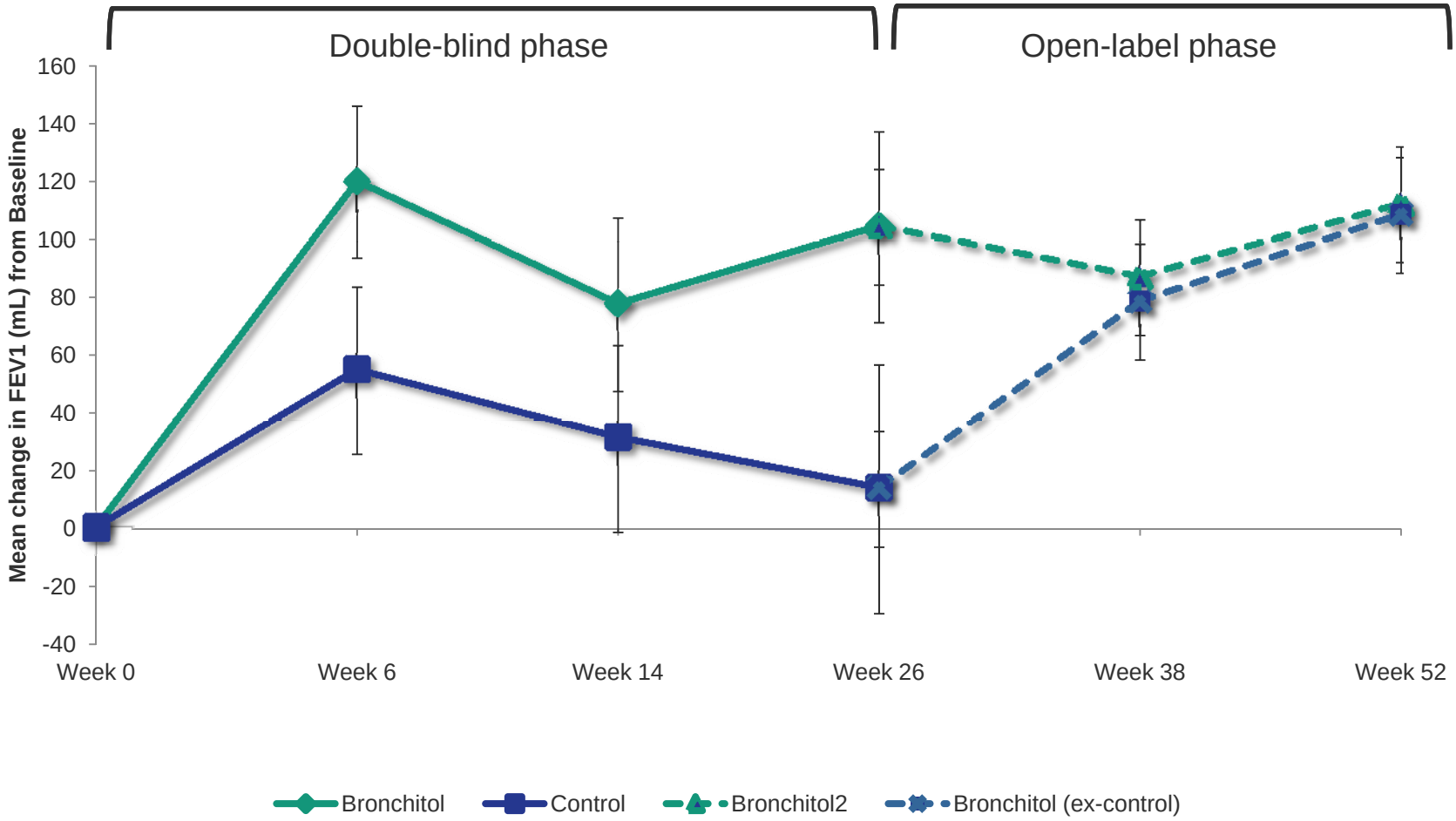


** denotes p<0.001

CF301 and CF302 – Double Blind for 6 months followed by Open Label for 6 months

CF301 & 302: 12-month FEV_1 data
Summary data of mean change (mL) over time

Control patients experience additional FEV_1 benefit when switched to Bronchitol



Analysis: Intent to Treat Population

Source: Pharmaxis data on file - fe01chg3_201

Bronchitol – Cystic Fibrosis

<u>European Union</u>

- Approved for patients >18 years
- Launched in first European countries June 2012

<u>Australia</u>

- Approved for patients >6 years
- Reimbursement effective August 2012
- Launched August 2012

<u>USA</u>

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

<u>Rest of world</u>

- distributor model by country

Bronchitol in Europe (I)

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

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

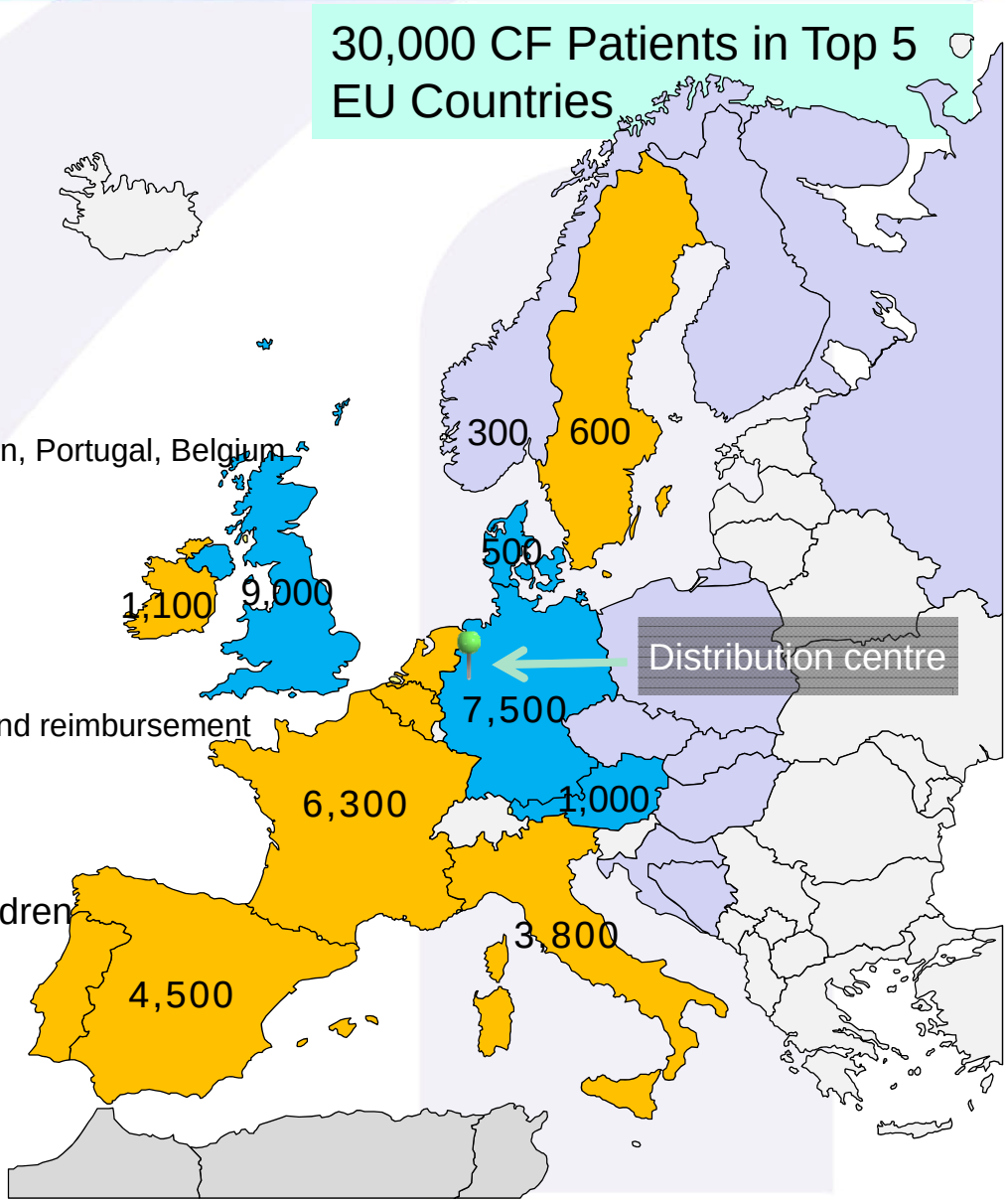
QUINTILES

Sales, marketing and market access

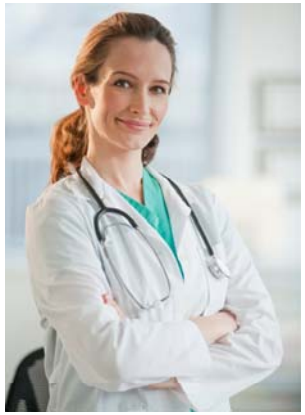
Germany	France
Italy	Spain
Austria	Ireland
Netherlands	Portugal
Sweden	

Bronchitol in Europe (II)

- 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



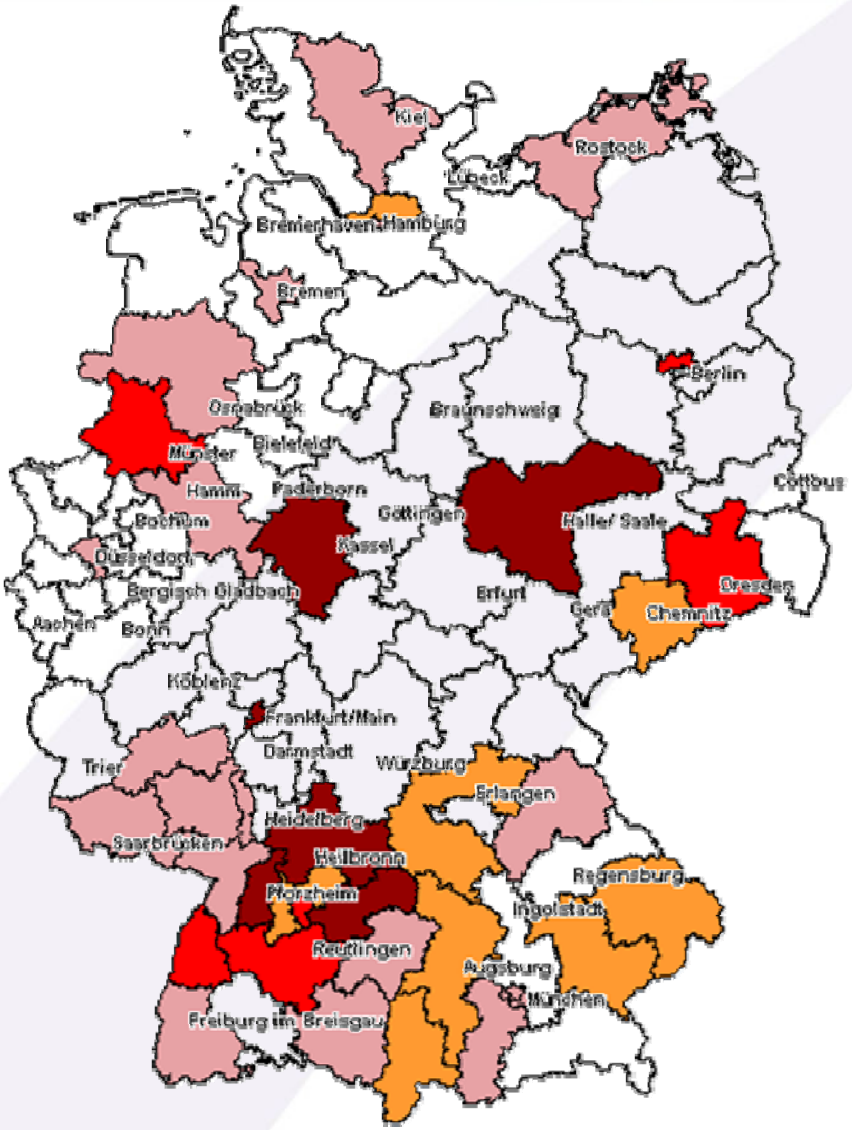
Commercialisation priorities - Europe



Market introduction

- Consistent ex-factory price throughout EU (€20-25 per day)
- National Institute for Health and Clinical Excellence (NICE - UK) – Q4 2012
- French reimbursement – Q1 2013
- Emphasis on training and education
  - Consistent messages to all CF centres
  - CF clinics trained in Bronchitol administration
  - Centres administer initiation dose first to patients
- Patients prescribed ongoing supply
- Additional country introductions
- Distributors for non EU countries

Progress in Germany



Initiation pack sales by region

- 134 CF Centres
  - 90% centres detailed on Bronchitol
  - 75% of centres trained on Bronchitol
  - Orders received from 182 pharmacies
- 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 dose logistics
  - 50% prescribed to a patient and then the patient brings the initiation dose to the clinic
  - 50% initiation dose are prescribed for next visit in 2 – 3 months

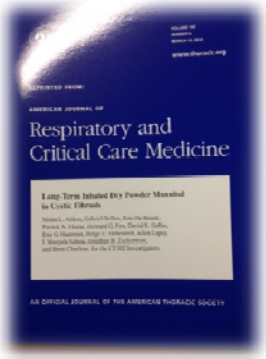
Bronchitol - Cystic Fibrosis (Australia)

- ~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

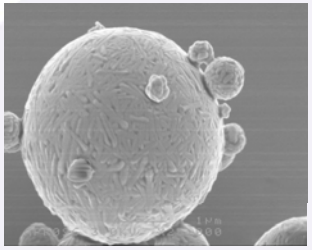
- Two key account managers, one marketing manager

Bronchitol – Cystic Fibrosis (USA)



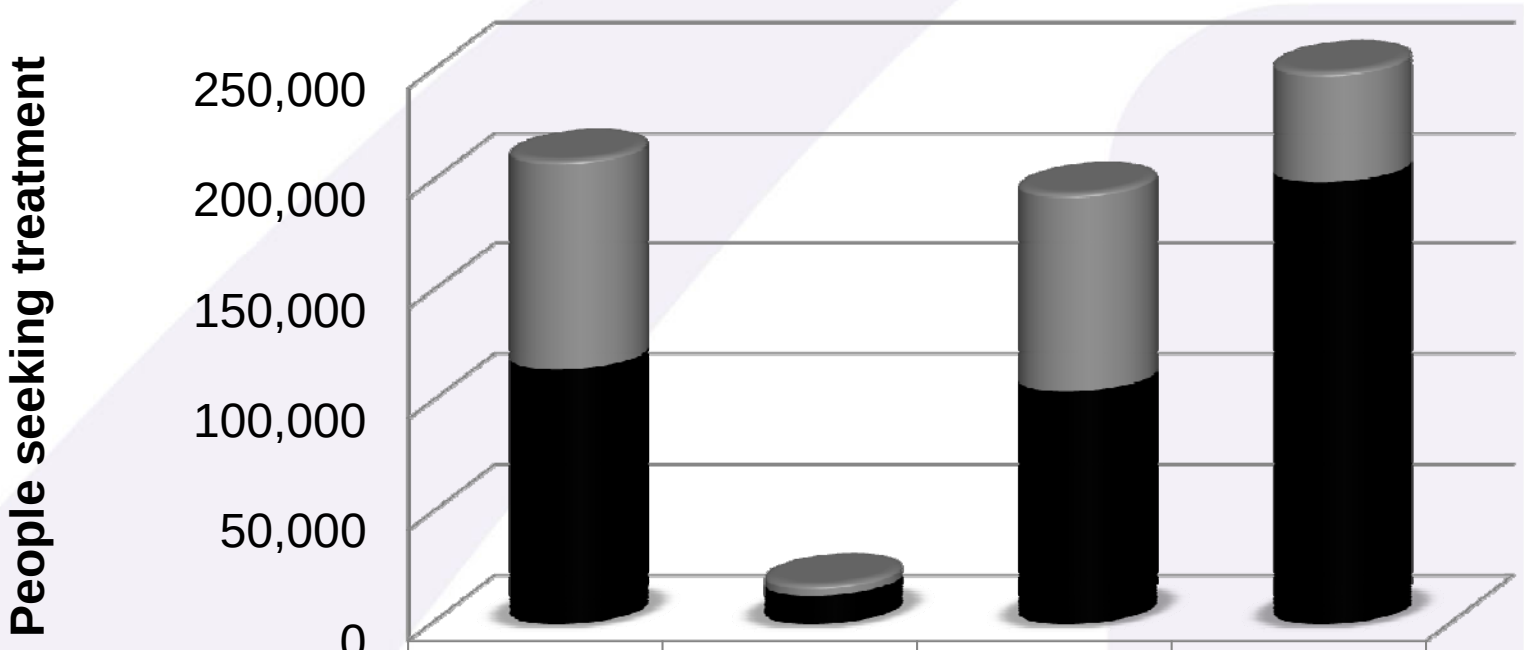
- NDA submitted May 2012
- FDA review scheduled for completion in March 2013
- Requested indication
  - Bronchitol is indicated for the management of cystic fibrosis patients 6 years of age or older to improve pulmonary function
- Orphan drug status provides 7 years market exclusivity from date of FDA 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
- In 30-50% of cases, the specific cause is unknown
- 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
- Increasing prevalence & diagnosis

Bronchiectasis - patients seeking treatment



	Europe	Australia	USA	Asia
Mild	95,000	5,000	90,000	50,000
Moderate / severe	115,000	13,000	105,000	200,000

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

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

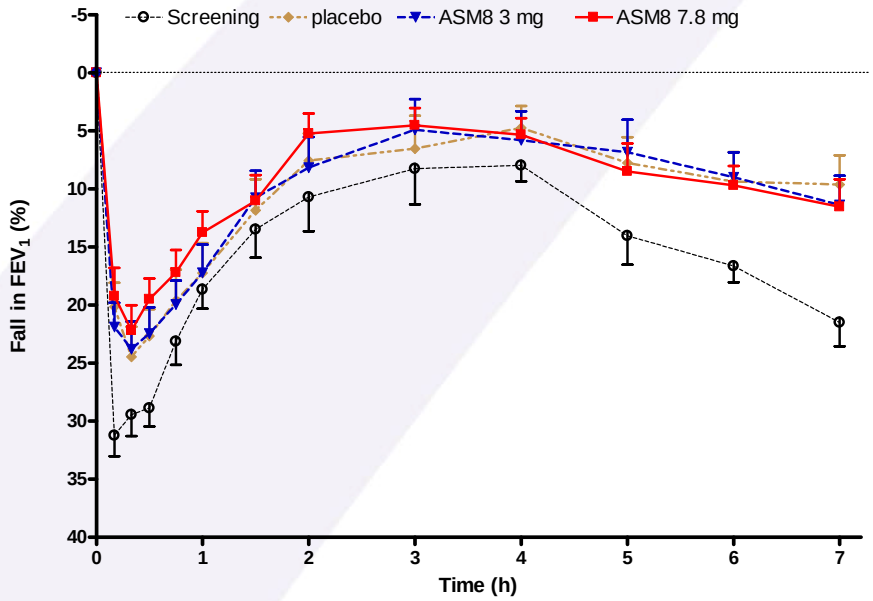
Bronchitol – bronchiectasis registration

- **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

ASM8 – asthma

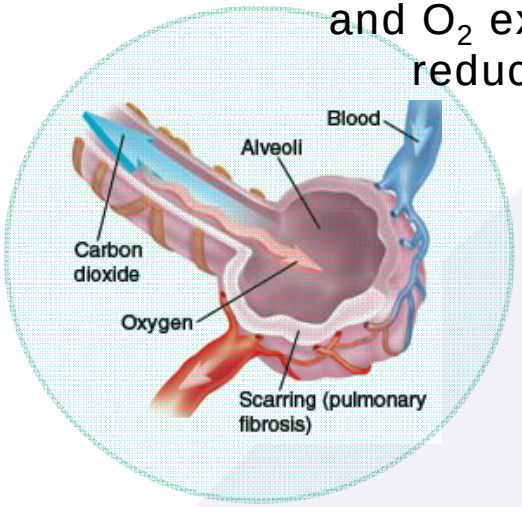
Phase IIa trial



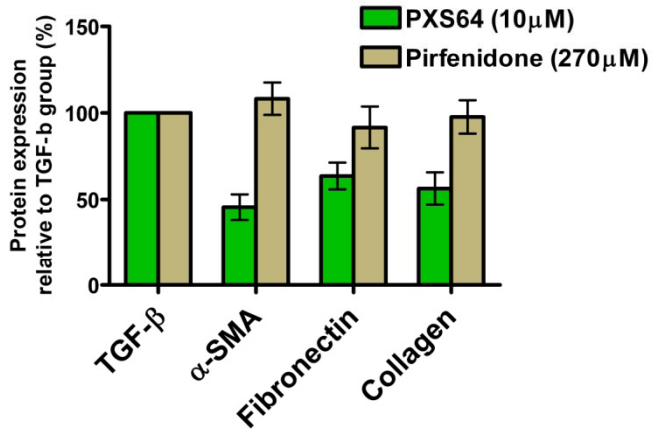
Indication	Moderate to severe asthma for patients who do not respond to inhaled steroids or cannot tolerate high doses
Target Product Profile	-Greater efficacy through multi-targeting -Better tolerability & convenience compared with current treatments -Once daily nebulisation
Market Size	Affects ~12 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

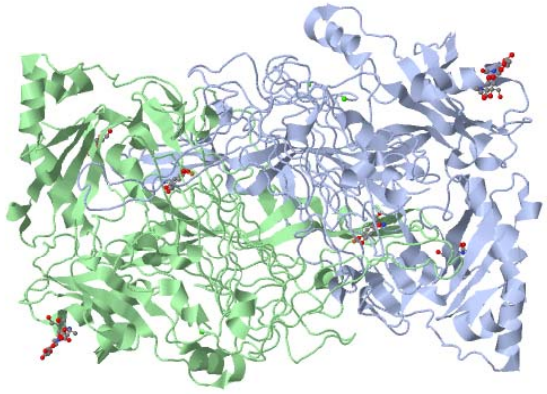


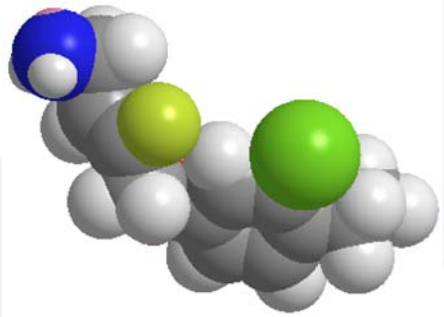
The effect of PXS64 *vs* pirfenidone in primary derived human lung fibroblasts



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



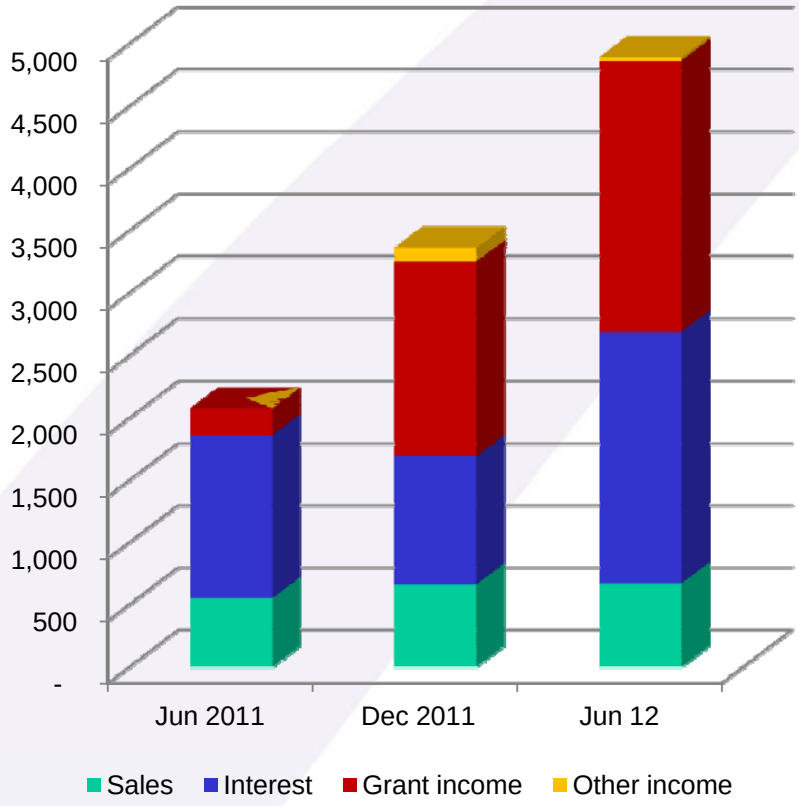


small molecule inhibitor of SSAO

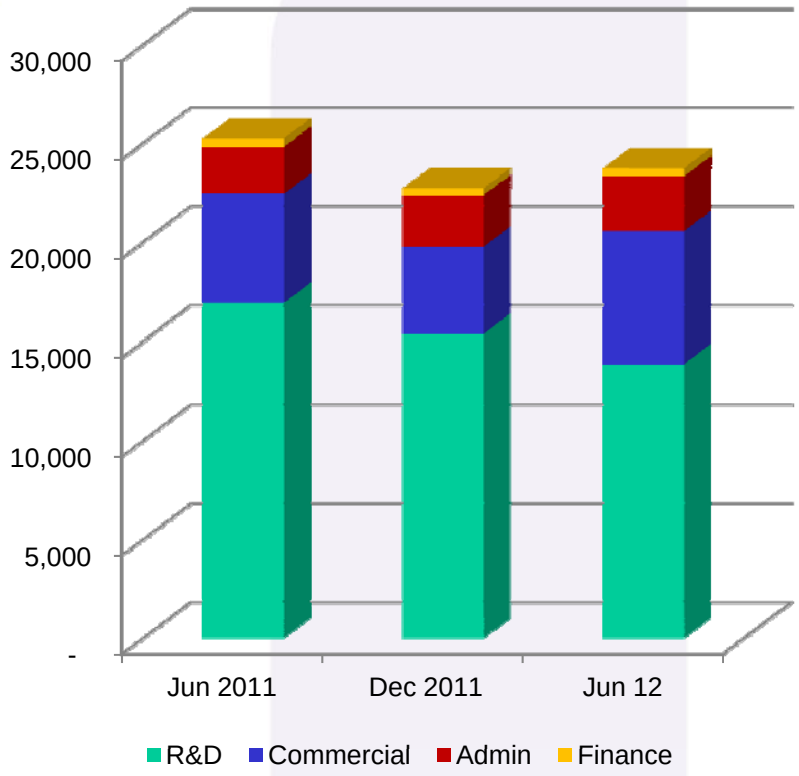
Indication	Anti-inflammatory agent with anti-fibrotic properties
Target	SSAO / VAP-1 inhibitor
Target Product Profile	-COPD / IPF -Once daily oral dosing
Market Size	Affects ~23 million people worldwide
Competitors	Significant clinical pre-clinical activity amongst pharmaceutical companies
Status	Pre-clinical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

Income Statement – Half Years

Revenue

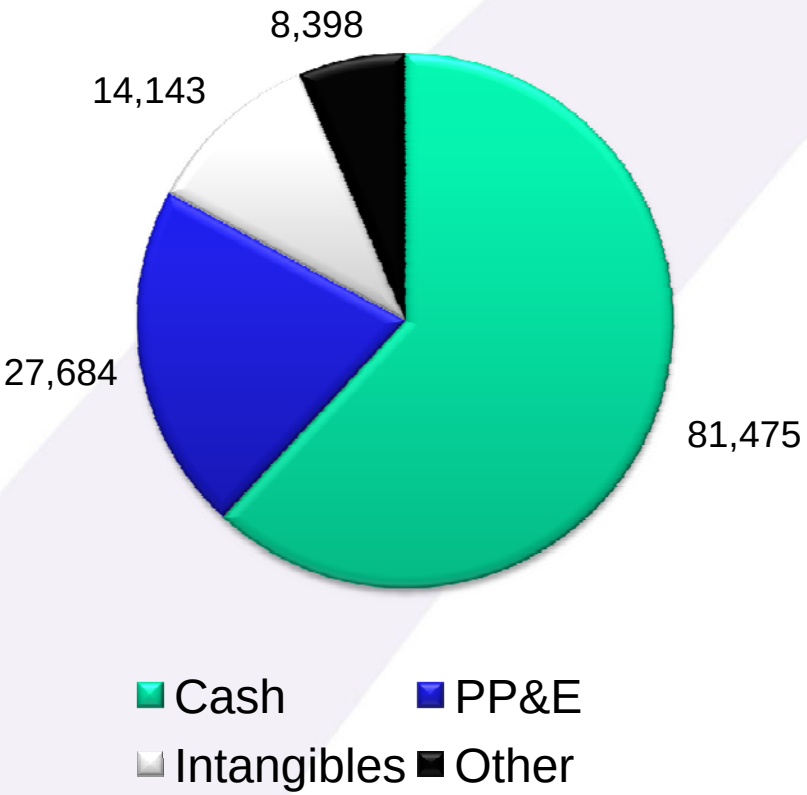


Expenses

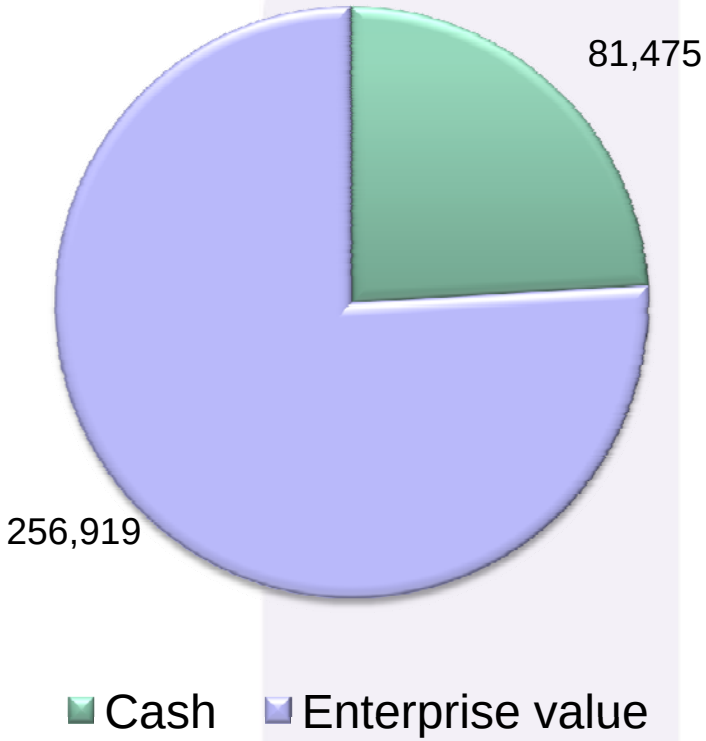


Balance Sheet

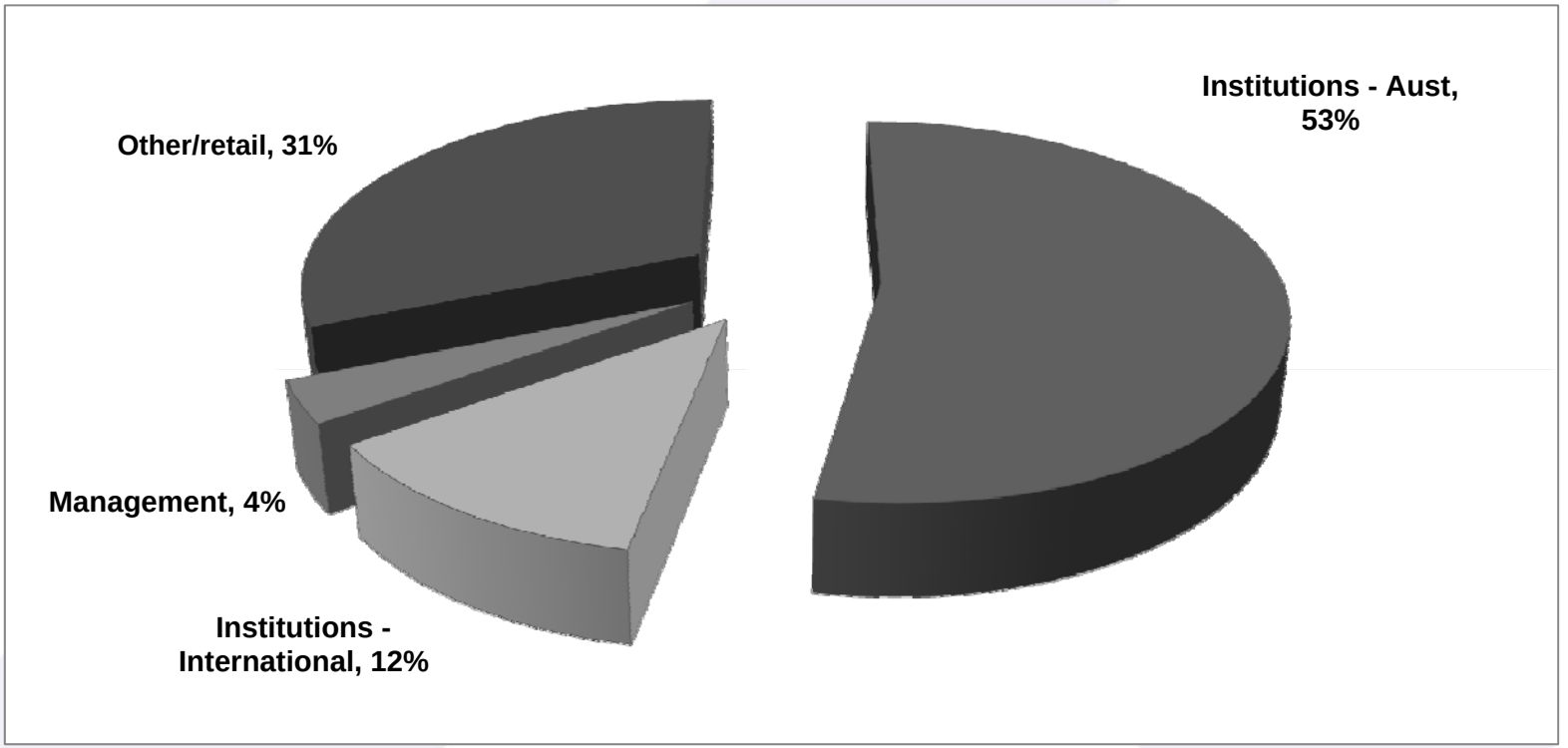
Assets (A$000's)



Market Capitalisation (A$000's)



Share Capital
(including options)



30 June 2012	
No of shareholders	7,100
Shares on issue	308 million
Options outstanding	12 million

Summary

Pharmaceutical company with approved products and strong pipeline

- **Bronchitol**
  - → Selling in Australia and Europe for cystic fibrosis
    - launched in Germany, UK, Austria, Denmark
  - → USA marketing application under review by FDA
  - → Bronchiectasis Phase III trial closed to recruitment and awaiting data
- **Aridol**
  - → Marketed in Australia, South Korea, Europe and USA
  - → Full reimbursement in USA and South Korea

- **ASM 8 for asthma**
  - → Phase IIa trials completed
- **PXS 64 for Idiopathic Pulmonary Fibrosis**
  - → Phase I trial completed with IV formulation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