Innovative products for respiratory diseases

pharmaxis

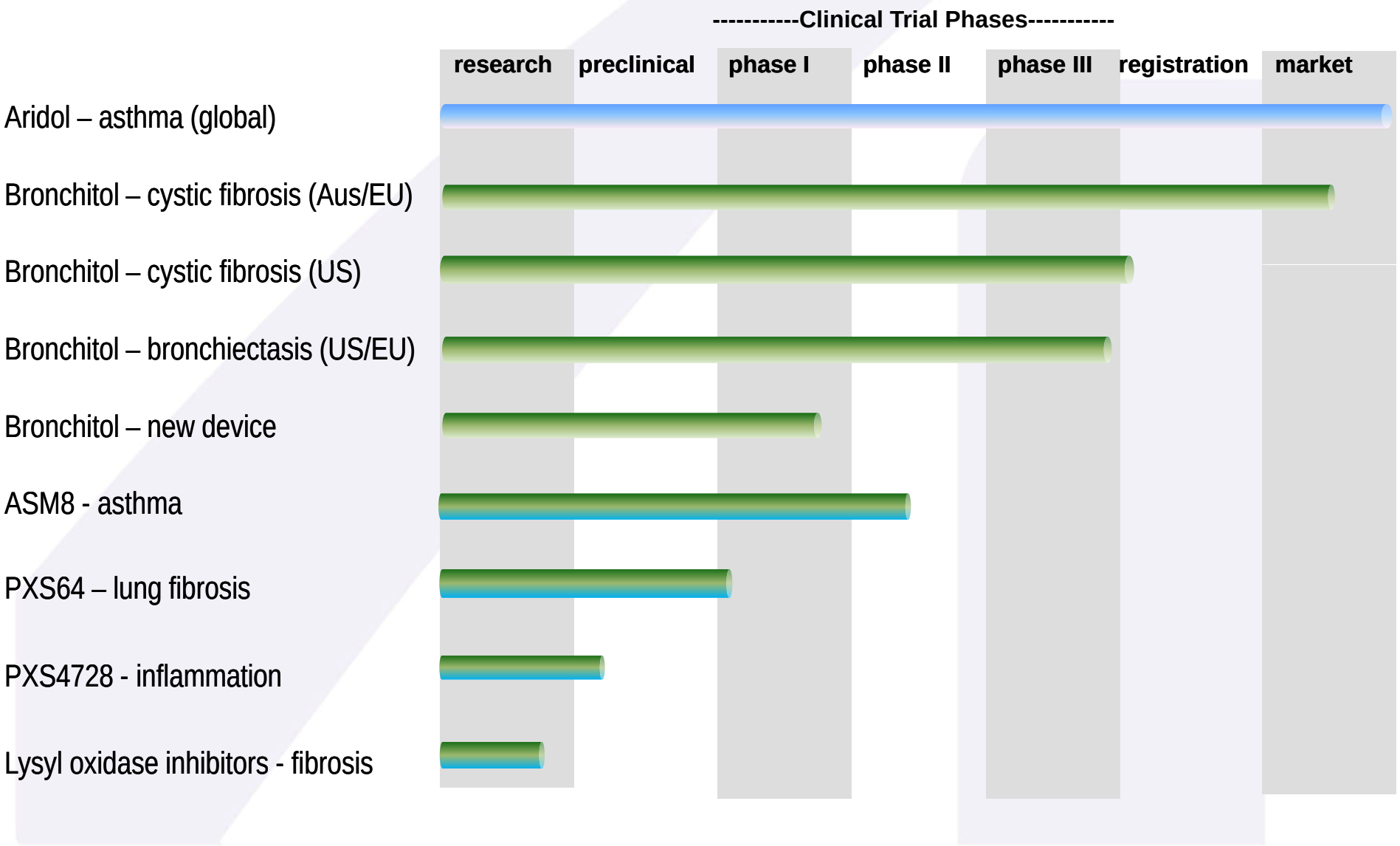
April 2012

Pharmaxis - company overview

Objectives	Development of products for respiratory diseases
Employees	153 involved in research and development, clinical trials, manufacturing and commercialization
Discovery	PXS25/64: Idiopathic pulmonary fibrosis PXS4728: Moderate-severe asthma
Lead products	Aridol®: Diagnosis of asthma and COPD Bronchitol®: Cystic fibrosis and bronchiectasis ASM8: Moderate-severe asthma
Locations	Australia, Europe, USA
Facility	GMP Manufacture of respirable dry powders

pharmaxis

Development pipeline



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			2008	2009	2010	2011	2012*
Sales (A$'000)							
Australia	Launched 2006	Direct	216	232	268	253	206
Europe	Staggered launch from 2006	Distributor model UK – direct	137	267	398	398	249
South Korea	Launched 2009	Distributor	-	32	162	205	239
Clinical trials		Direct	174	64	-	-	-
US	Launched Feb 2011	Direct	-	-	-	54	264
			527	595	828	910	958

* 9 months to March 2012

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

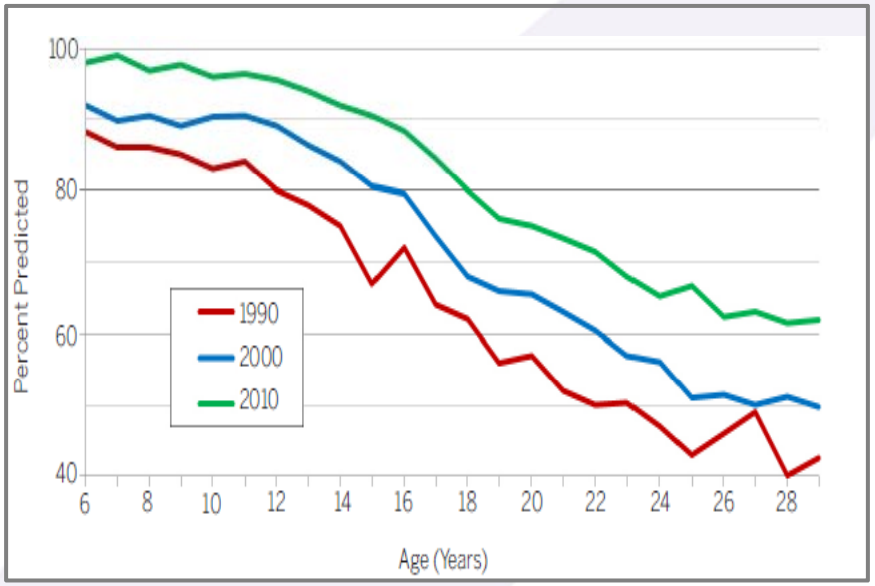
Bronchitol - Cystic Fibrosis

- **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)

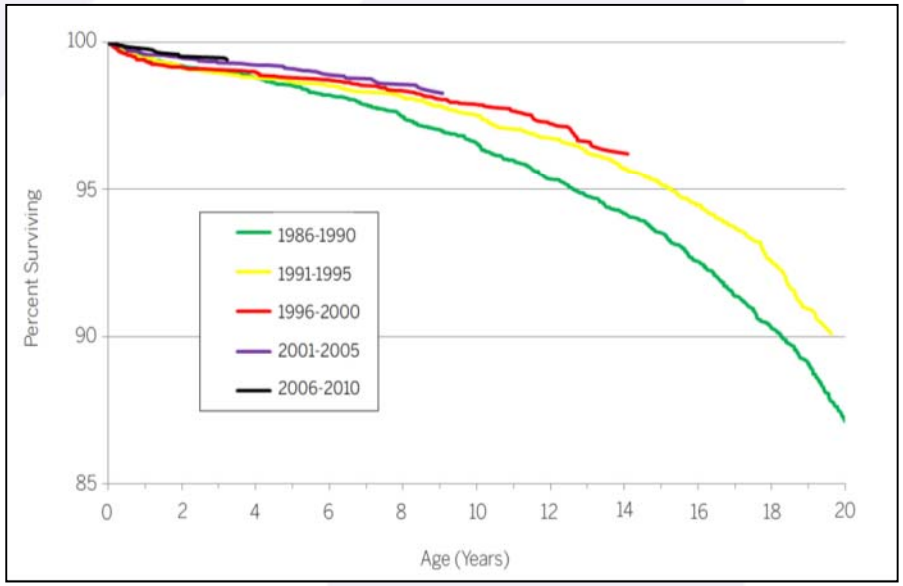
- **Main Therapeutics**
  - Mostly delivered by nebulizer (preparation, sterilization)
  - rhDNase (Pulmozyme®): global sales ~CHF 513m (2010)
  - Tobramycin (Tobi®): global sales ~US$ 279m (2010)
  - Aztreonam (Cayston®): approved EU: 09/09; US: 02/10

Lung function and life expectancy in CF patients

Median FEV_1 % Predicted versus Age



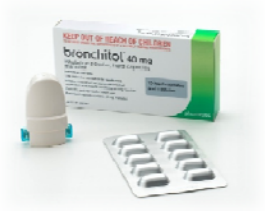
Survival by Birth Cohort



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 ← *Ivacaftor*

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

Impaired Mucociliary Clearance

Infection ← **rhDNase**, ← **Antibiotics**

Inflammation

Inadequate Lung Function ← **Transplantation**

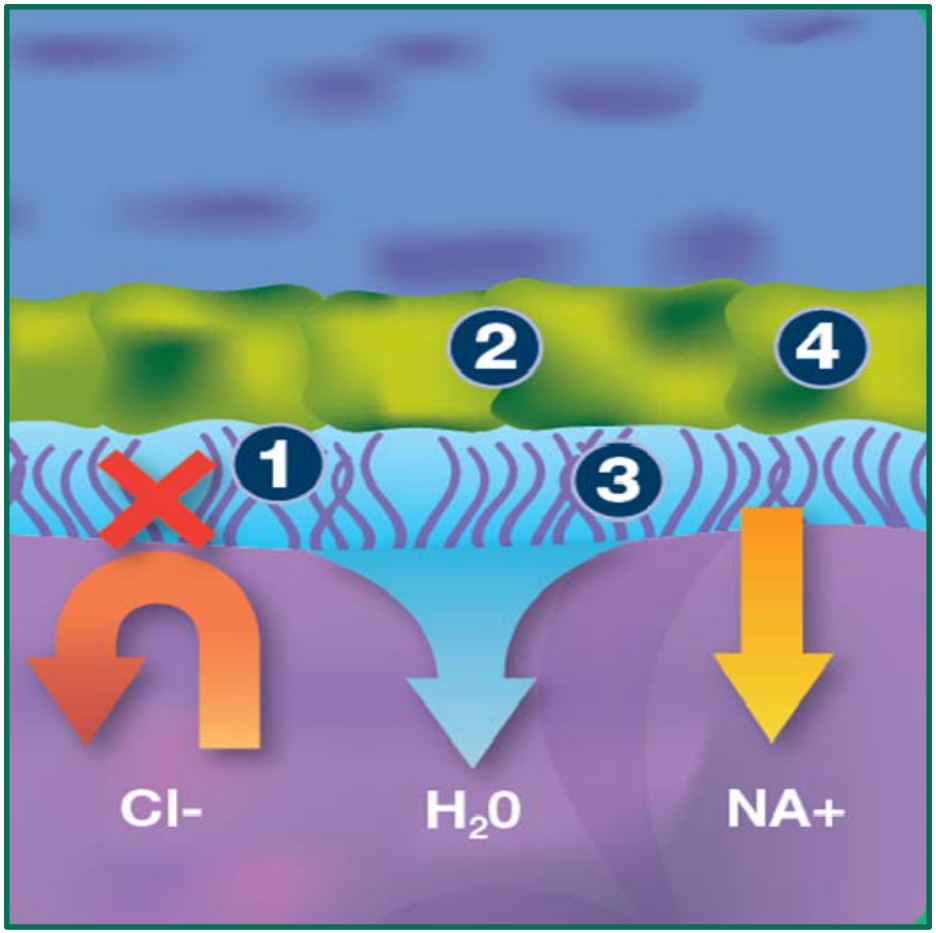
Death

Adapted from Davis 1996 Am J Respir Crit Care Med

Bronchitol - mode of action

Pre-Bronchitol

1. Dehydrated Airway Surface Liquid (ASL) caused by absent or reduced CFTR
2. Mucus becomes sticky and difficult to clear
3. Depleted ASL prevents cilia from functioning optimally
4. Creates a reservoir for infection and inflammation



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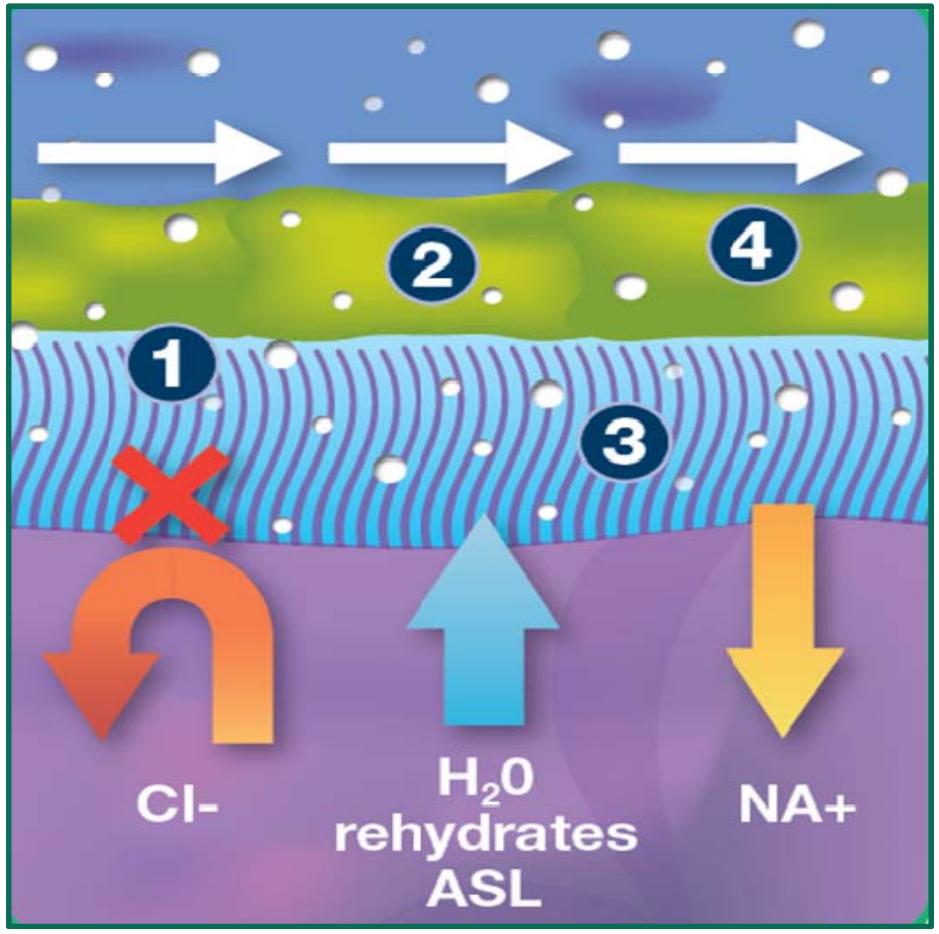
Bronchitol - mode of action

Post-Bronchitol

1. Inhaled dose of Bronchitol delivers a high osmolar load that persists, to drive water to ASL layer
2. Changes visco-elastic and flow properties of mucus, allowing for easier clearance
3. Rehydrated ASL allows the cilia to move freely facilitating easier movement of the mucus
4. Mucus is cleared through a productive cough



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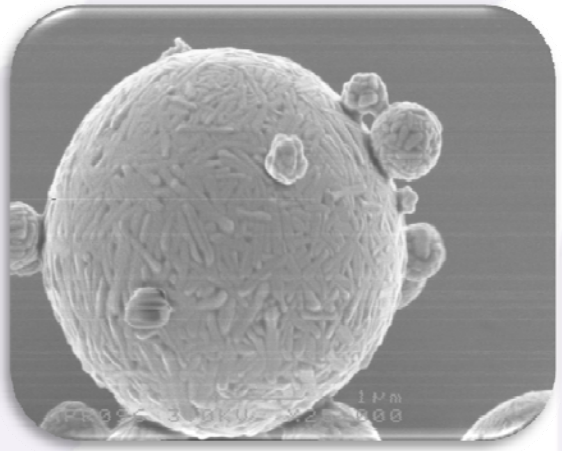
Bronchitol – formulation



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

Bronchitol development program

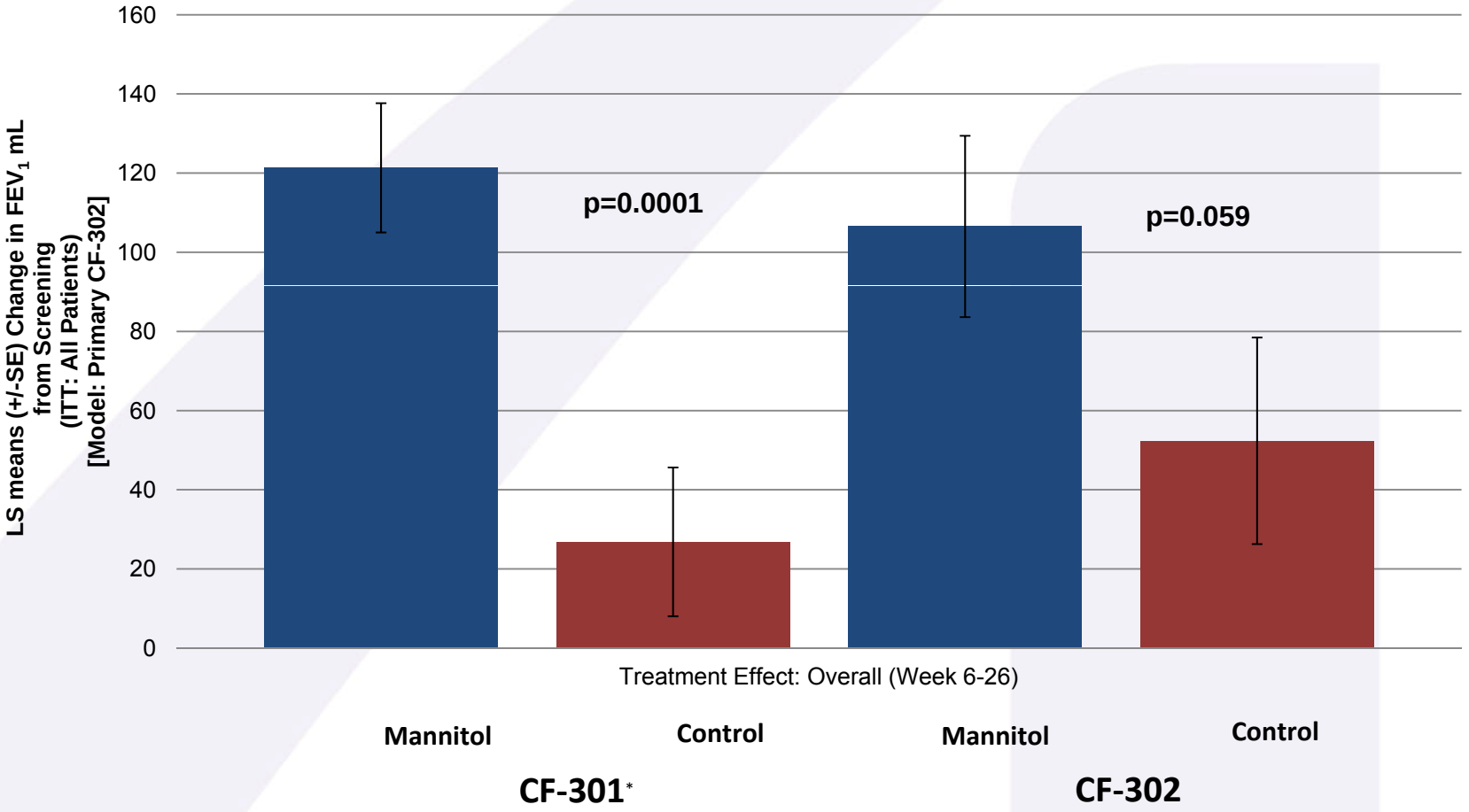
Study	Design	Population	Primary Endpoint	Treatment
CF-201 **Short term efficacy and safety**	Randomised Multicentre Double-blinded Placebo-controlled Cross-over	n=39: 18 adults 21 children CF patients with FEV_1 between 40 - 90% of predicted.	Effect of two weeks twice daily treatment on FEV_1.	420mg b.i.d. for 14 days.
CF-202 **Dose Response**	Randomised Multicentre Open label Cross-over	n=48; 19 adults 29 children CF patients with FEV_1 between 40 - 90% of predicted.	Dose required to obtain clinical improvement in lung function measured as FEV_1 and FVC.	400mg b.i.d., then 40, 120, 240mg b.i.d. for 14 days
CF-203 **Efficacy and Safety**	Three arm: rhDNase, Bronchitol Combined Open-label Crossover	n= 26 ; 26 children CF patients currently receiving rhDNase ,or having a FEV_1 <70% of predicted and eligible to receive rhDNase	Effect of 12 weeks treatment on FEV_1	400mg b.i.d. 2.5mg rhDNase daily.
CF-301 **Long term efficacy and Safety**	Randomised Multicentre Double-blinded Placebo controlled Parallel arm	n=325 (ITT=295); 105 (ITT) children CF patients with FEV_1 between 30 - 90% of predicted.	Effect of Bronchitol compared to control on FEV_1 over 26 weeks.	400mg or control b.i.d.
CF-302 **Long term efficacy and Safety**	Randomised Multicentre Double-blinded Placebo controlled Parallel arm	n=342 (ITT=305); 154 (ITT) children CF patients with FEV_1 between 40 - 90% of predicted.	Effect of Bronchitol compared to control on FEV_1 over 26 weeks.	400mg or control b.i.d.

Bronchitol - Cystic Fibrosis clinical program

Two Pivotal Phase III 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
  - Mucus clearance
  - 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 vs. CF302)
Overall effect (6-26 weeks)

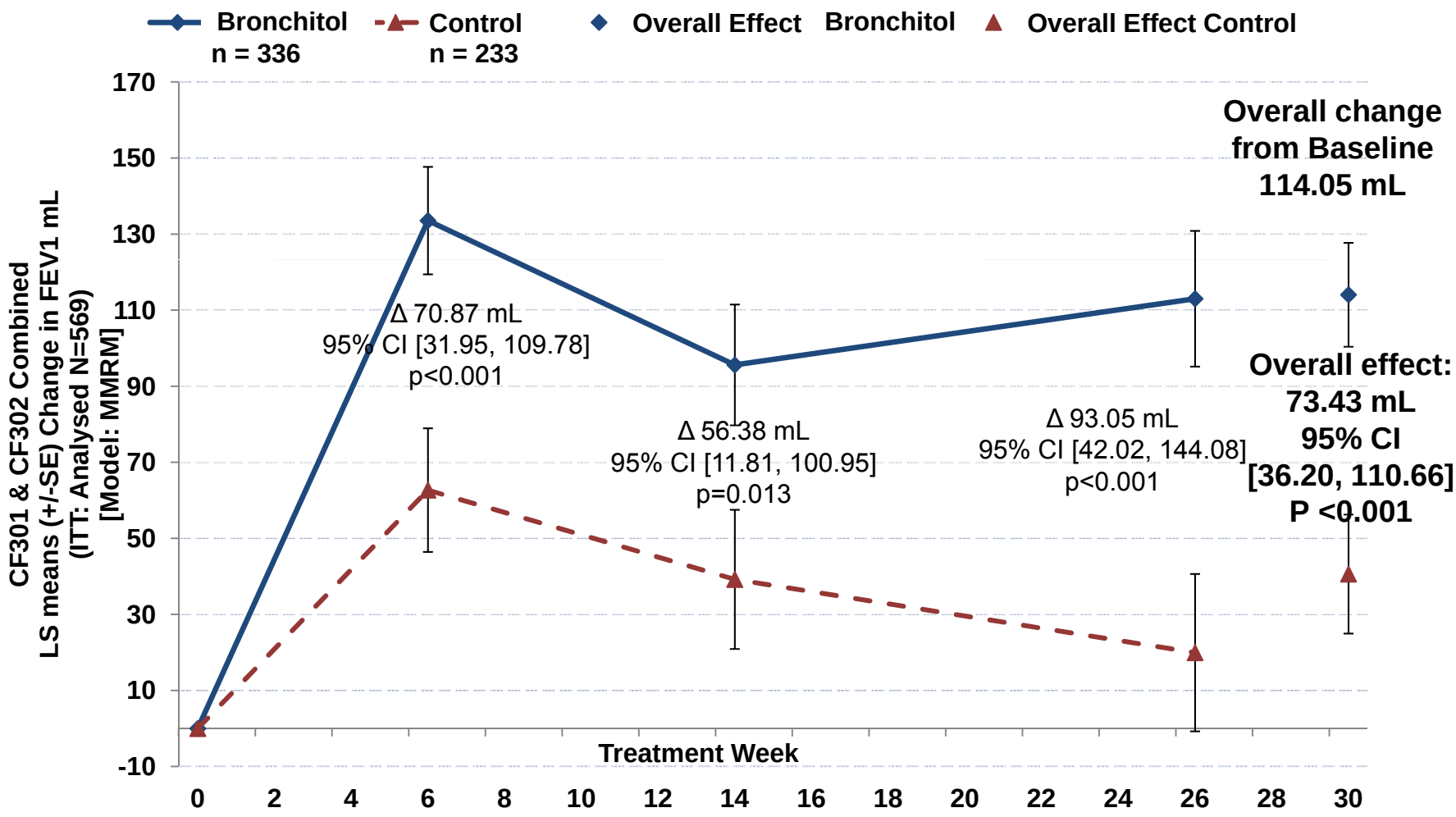


Source: CF302: fe01mma1_201, CF301: CF302 Post Hoc (6)

* Both CF-301 and CF-302 data has been modelled through the CF-302 Primary study model.

Pooled CF301 & CF302

FEV_1 (mL) significantly improved at each time-point

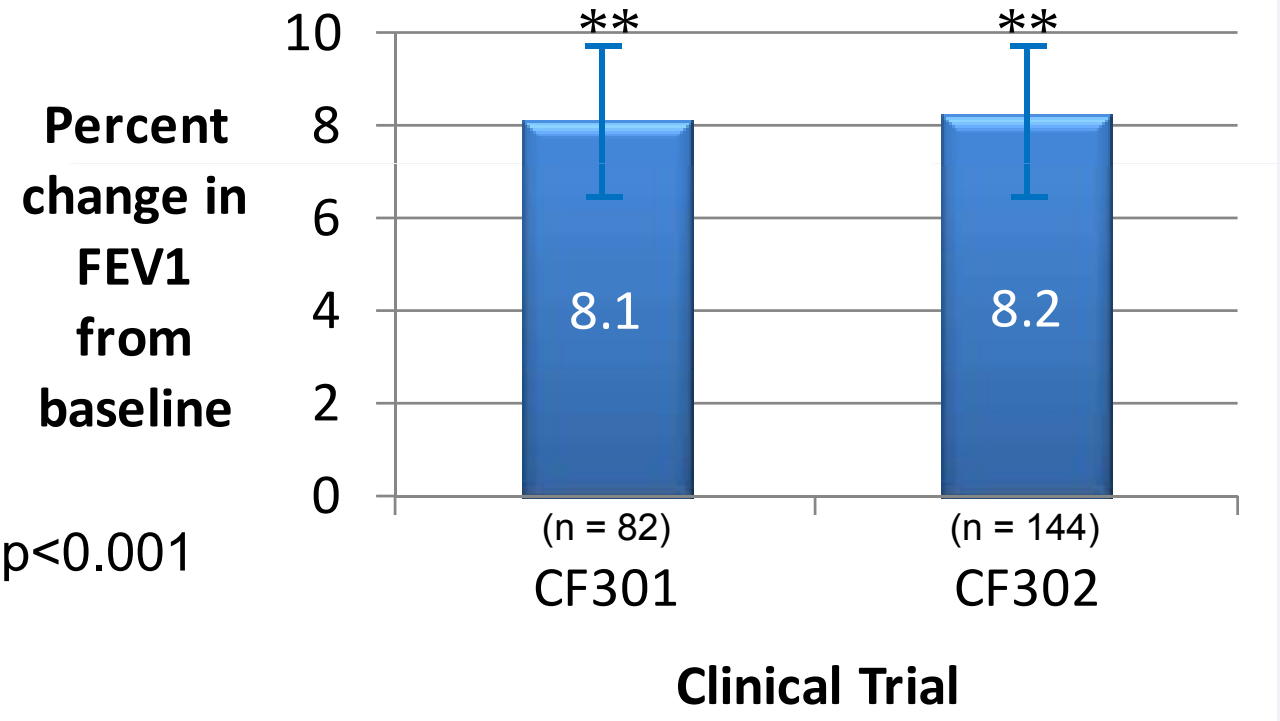


The difference between Bronchitol and Control was significant at each timepoint ($p<0.05$)

A priori covariates: age, baseline value, randomized treatment, rhDNase at screening, country, gender, disease severity, study project. The model included an interaction term for timepoint.

Bronchitol - sustained treatment effect

Change in lung function after 12 months Bronchitol treatment



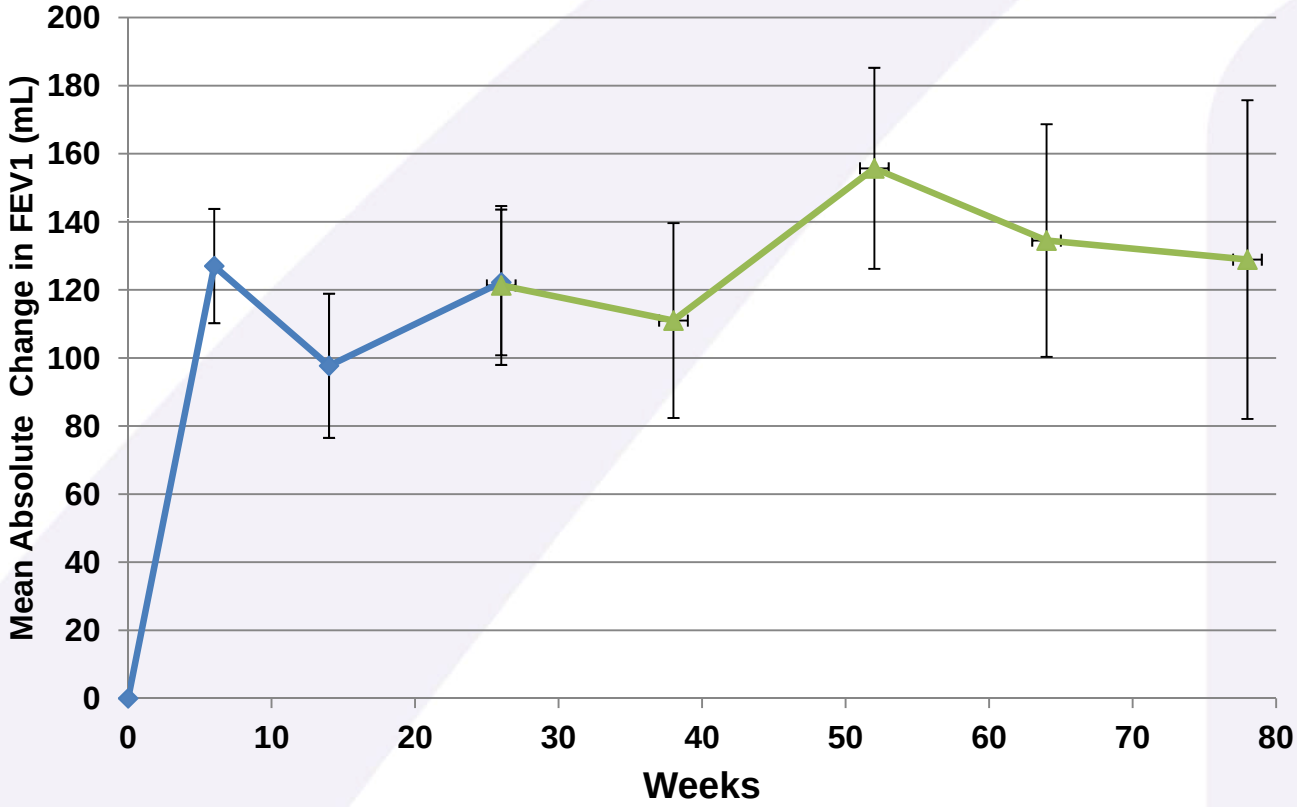
** denotes p<0.001

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

Effect sustained out to 18 months

CF301 Bronchitol arm (DB and OL for 18 months)

CF301 Change in FEV1 Summary Statistics for Bronchitol (DB patients only) over 18 months*



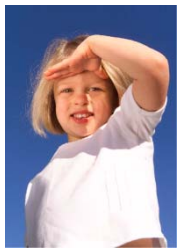
Week	Change	
26	6.5%	p<0.001
52	8.1%	p<0.001
78	7.9%	p<0.01

*** Patient numbers reduced over the 18 months of the study due to patient withdrawal, optional patient participation in OL weeks 27-52 and only 23 of 40 sites offered participation in OL weeks 53-78**

Bronchitol - exacerbation incidence reduced

Percentage reduction in exacerbation incidence after 6 months Bronchitol treatment		
CF301	35%	p=0.045
CF302	20%	p>0.05
CF301 +CF302 combined	29%	p=0.039

Bronchitol - US regulatory status



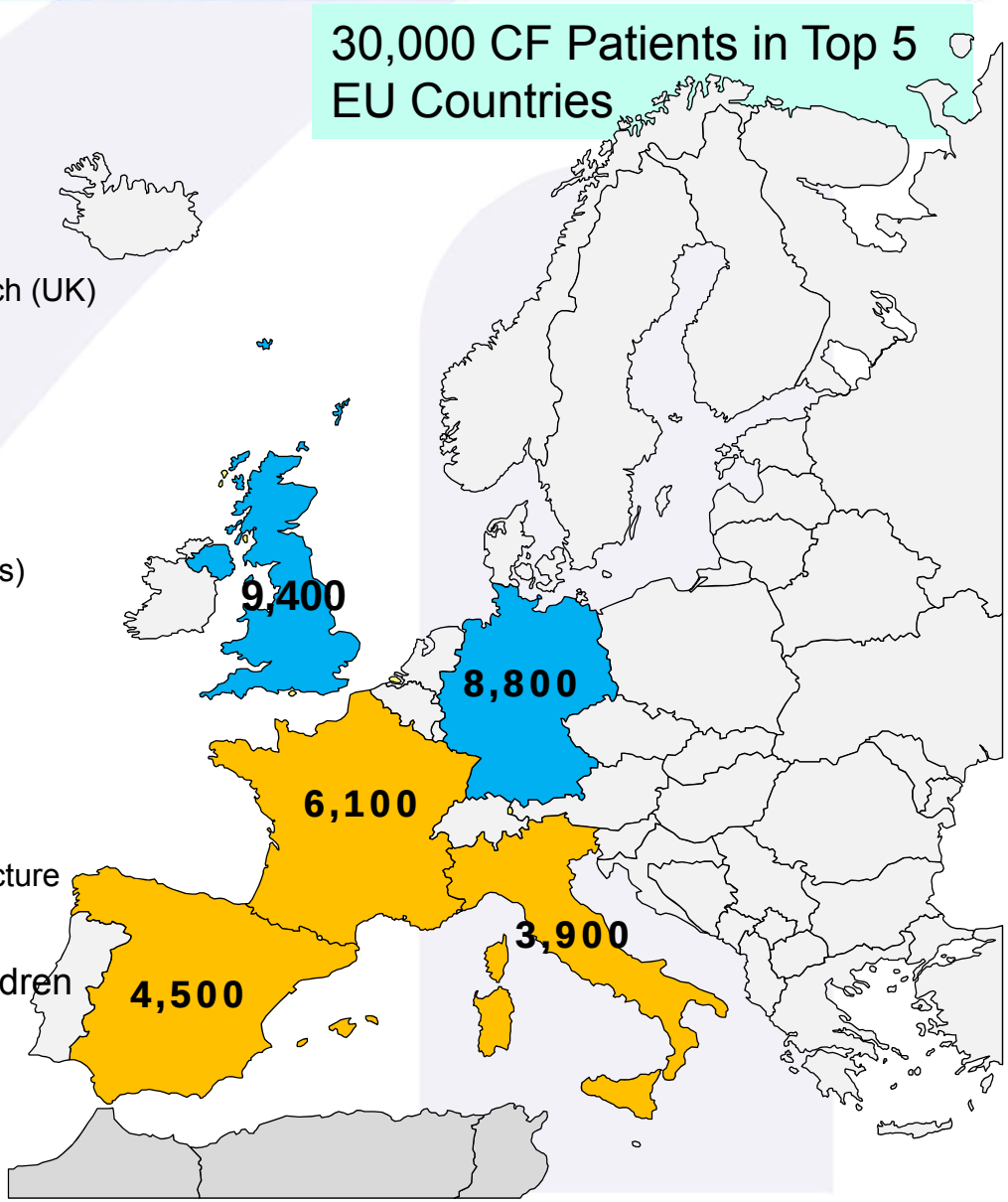
- End of Phase 3 Meeting completed
- NDA scheduled submission Q2 2012
- FDA review completed Q2 2013

- 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

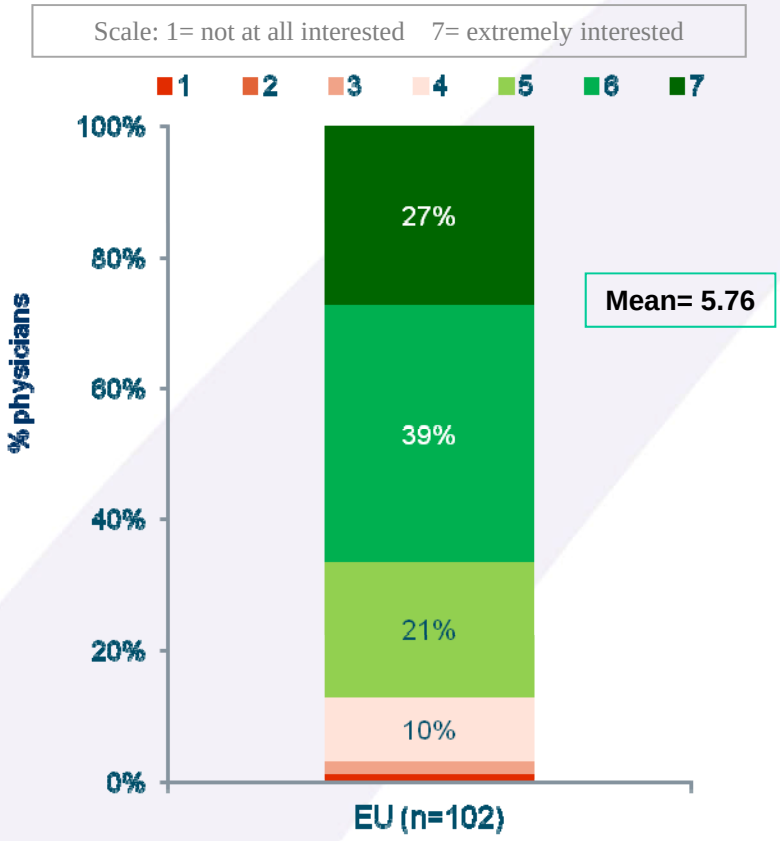
Bronchitol - Cystic Fibrosis (Europe)

- First two launch markets: UK and Germany
  - Revenues from Q2 2012
  - Free pricing on approval
  - NICE to review pricing / effectiveness post launch (UK)
  - 110 CF clinics in Germany and 50 in UK
  - Market access support from Quintiles
- Next three: France / Italy / Spain
  - To be launched after reimbursement (6-12 months)
  - 110 additional clinics
- Remaining EU countries (10,000 patients)
  - Subsequent rollout on country-by-country basis
  - Satellite model leveraging top 5 country infrastructure
- Label expansion to include adolescents and children
  - Adult CF population represents 50% of patients
  - Short clinical trial required
  - Represents one third of potentialmarket

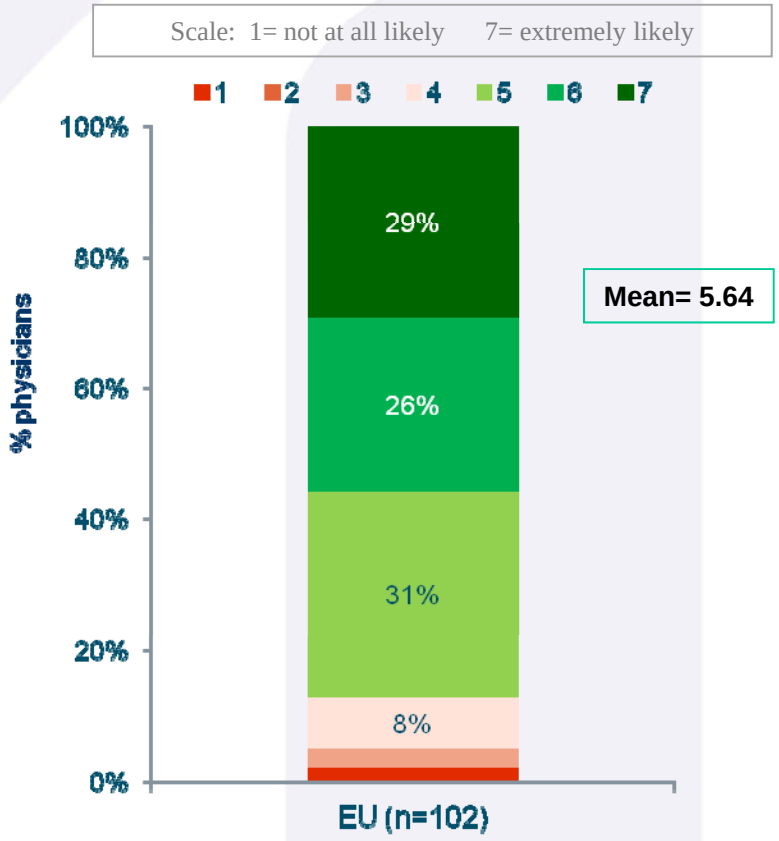


Very positive reaction to Bronchitol's product profile, with most EU[1] physicians stating they will probably prescribe it

Reaction to Bronchitol product profile



Likelihood of prescribing Bronchitol

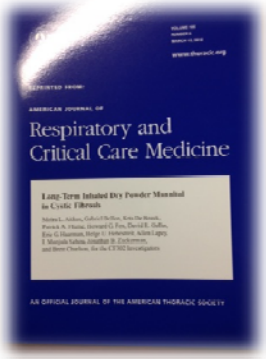


1. EU market research in the top 5 countries.

***Q9a**: Based on your overall reaction to the product profile, how interested would you say you are about Bronchitol on a scale of 1 to 7 where 1 = not at all interested and 7 = extremely interested.*

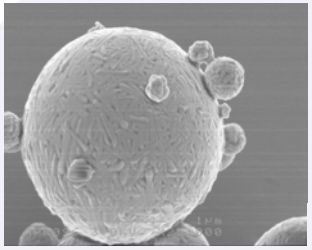
***Q9e**: If Bronchitol was available to you today, how likely would you be to prescribe it in your practice? Please rate the likelihood of prescription on a scale of 1 to 7 where 1 = not al all likely and 7= extremely likely.*

Bronchitol opportunity in the USA



- ~250 CF centres
- Anticipated requirement for 20 - 25 person field force
- ~30,000 people in the US with CF
- Pulmozyme price ~US$22,000 per patient per annum
- Market protection for 7 years

Bronchitol - bronchiectasis



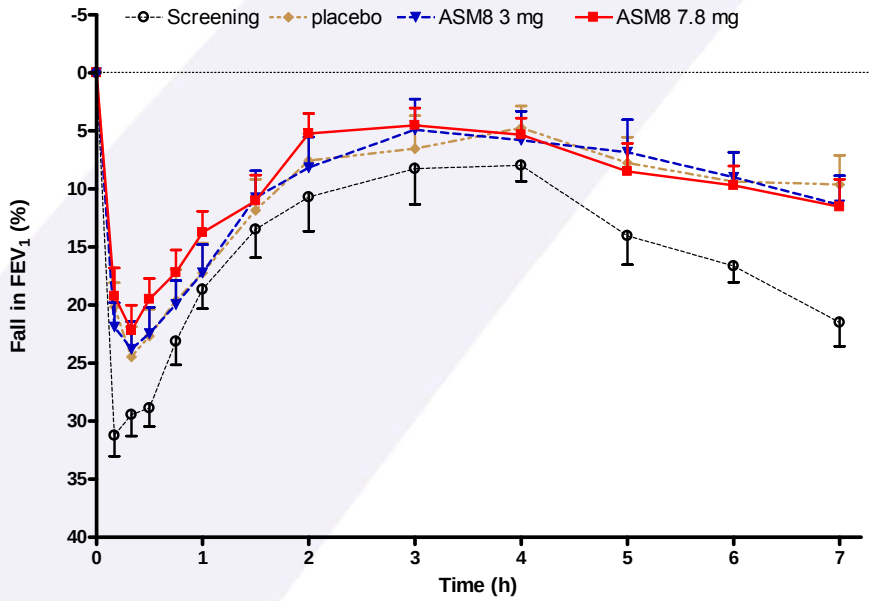
- Abnormal, irreversible dilation of the lower airways
- Daily mucus production, constant coughing, breathlessness, recurrent acute bronchitis with infective exacerbations : low quality of life
- In 30-50% of cases, the cause is unknown
- Normal lung clearance impaired
- Current treatments: bronchodilators, antibiotics
- **No** drugs proven effective to clear mucus
- Affects 600,000 people worldwide
- Orphan disease in the USA

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

ASM8 – Asthma

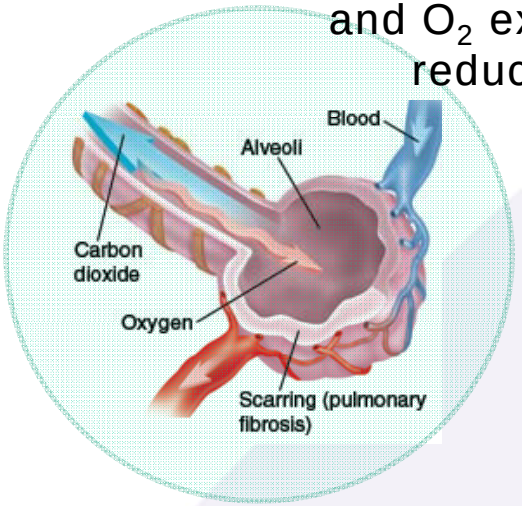
Phase IIa trial



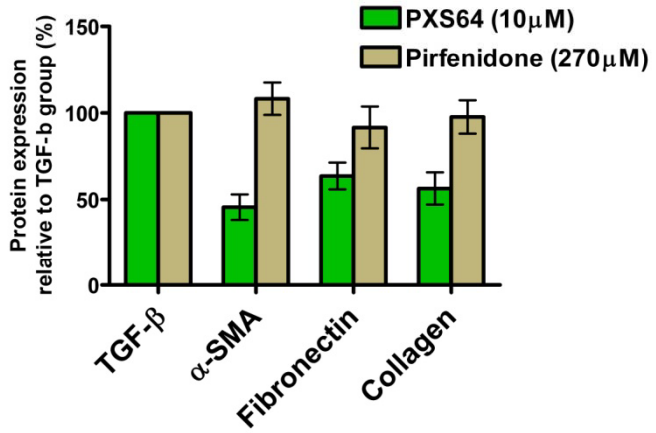
Indication	Moderate to severe asthma for patients who do not respond to inhaled steroids or cannot tolerate high doses
Target Product Profile	-Greater efficacy through multi-targeting -Better tolerability & convenience compared with current treatments -Once daily nebulisation
Market Size	Affects ~12 million people worldwide
Competitors	Xolair (US$369M, 2010)
Status	Phase IIa trial reported
Next Milestone	Publication of full trial results

PXS25 / PXS64 – Idiopathic Pulmonary Fibrosis

alveoli thickening and O_2 exchange reduction

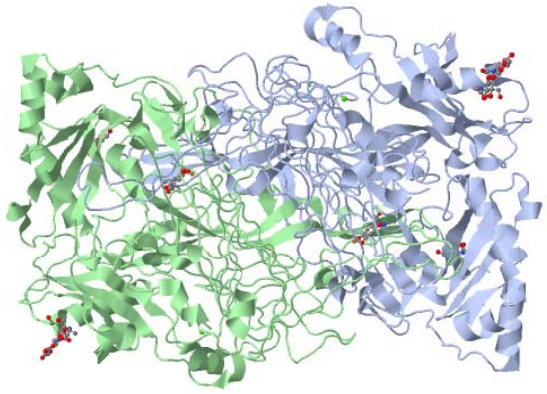


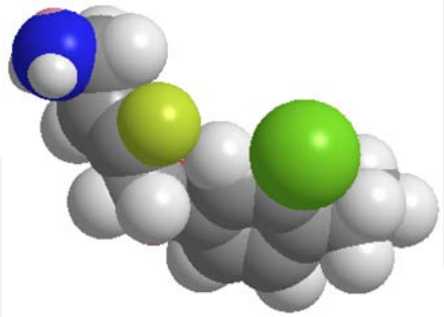
The effect of PXS64 *vs* pirfenidone in primary derived human lung fibroblasts



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		Nine months ended	
	31-Mar-12	31-Mar-11	31-Mar-12	31-Mar-11
	A$	A$	A$	A$
Revenue from sale of goods	298	318	958	677
Cost of sales	(110)	(148)	(365)	(266)
Gross profit	188	170	593	411
Interest	1,049	697	2,081	2,468
Other income	761	82	2,433	332
Expenses				
Research & development	(6,461)	(7,832)	(21,821)	(25,552)
Commercial	(2,971)	(2,668)	(7,358)	(6,329)
Administration	(1,383)	(1,206)	(3,998)	(3,999)
Finance expenses	(208)	(215)	(567)	(648)
Total expenses	(11,023)	(11,921)	(33,744)	(36,528)
Loss before income tax	(9,025)	(10,972)	(28,637)	(33,317)
Income tax expense	29	(58)	123	(65)
Loss for the period	(8,996)	(11,030)	(28,514)	(33,382)
Basic and diluted earnings (loss) per share - $	(0.029)	(0.048)	(0.109)	(0.147)
Depreciation & amortisation	1,164	1,167	3,511	3,573
Fair value of securities issued under employee plans	211	352	756	1,182

Financial Statements

Balance Sheet Data	As at	
	31-Mar-12	30-Jun-11
	A$	A$
Cash and cash equivalents	91,550	44,343
Property, plant & equipment	28,368	30,570
Intangible assets	14,585	15,954
Total assets	141,576	94,525
Total liabilities	(22,156)	(23,696)
Net assets	119,421	70,830

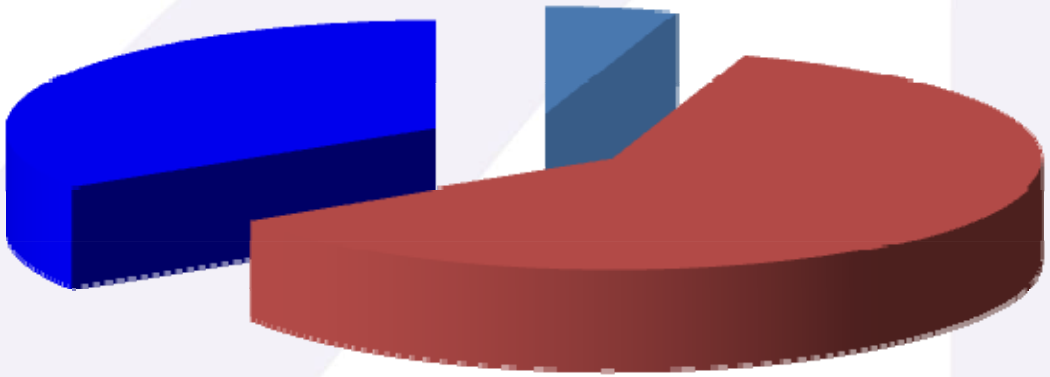
Cash Flow Data	Three months ended		Nine months ended	
	31-Mar-12	31-Mar-11	31-Mar-12	31-Mar-11
	A$	A$	A$	A$
Cash flows from operating activities	(9,086)	(10,174)	(28,164)	(27,395)
Cash flows from investing activities	(130)	(297)	(84)	(1,140)
Cash flows from financing activities	(423)	(304)	75,445	(563)
Impact of foreign exchange rate movements on cash	(13)	62	10	(405)
Net increase (decrease) in cash held	(9,652)	(10,713)	47,207	(29,503)

Share Capital
(including options)

Management – 4%

Other/retail – 33%

Institutions – 63%
(73 institutions)



31 March 2012: 306m shares; 11m options

Summary

- **Respiratory company with approved products and strong pipeline**
- **Aridol**
  - → Approved in Australia, South East Asia, Europe and USA
  - → Fully reimbursed in USA and South Korea
- **Bronchitol**
  - → Approved in Australia for cystic fibrosis
    - recommended for reimbursement
  - → Approved in Europe
    - commercial launch May 2012
  - → USA marketing application to be filed 1H 2012
  - → Clinical trials in progress to extend reach into Bronchiectasis
- **ASM 8 for asthma**
  - → Phase IIa trial results released April 2012
- **PXS 64 for Idiopathic Pulmonary Fibrosis**
  - → Phase I trial completed with IV formulation

The end

April 2012