pharmaxis

Therapeutic products for respiratory diseases

June 2011

Company Overview

Objective	The development of products for respiratory diseases	
Lead products	Aridol:	•assessment of asthma and COPD •approved & launched in major markets
	Bronchitol for cystic fibrosis:	•Completed two Phase III trials •Approved in Australia; in EU review •US NDA in preparation
	Bronchitol for bronchiectasis:	•Phase III trial in progress
	ASM8 for asthma:	•Phase II trial in progress
Discovery	PXS25 (M6P receptor blocker); VAP1 inhibitor	
Listing	ASX (Nov 2003): PXS	
Locations	Sydney, Australia • Exton, USA • Slough, UK	
Facility	GMP Manufacture of Aridol & Bronchitol	
Employees	139 (29/6/11)	
Cash	A$56 million (31/3/11)	
Shares & Options	Shares outstanding: 228m; Options outstanding: 13m (29/6/11)	
Analyst coverage	SHAW STOCKBROKING; Merrill Lynch A subsidiary of Bank of America Corporation; CREDIT SUISSE; RBS Morgans; BBY; Wilson HTM INVESTMENT GROUP	

bronchitol™

MANNITOL

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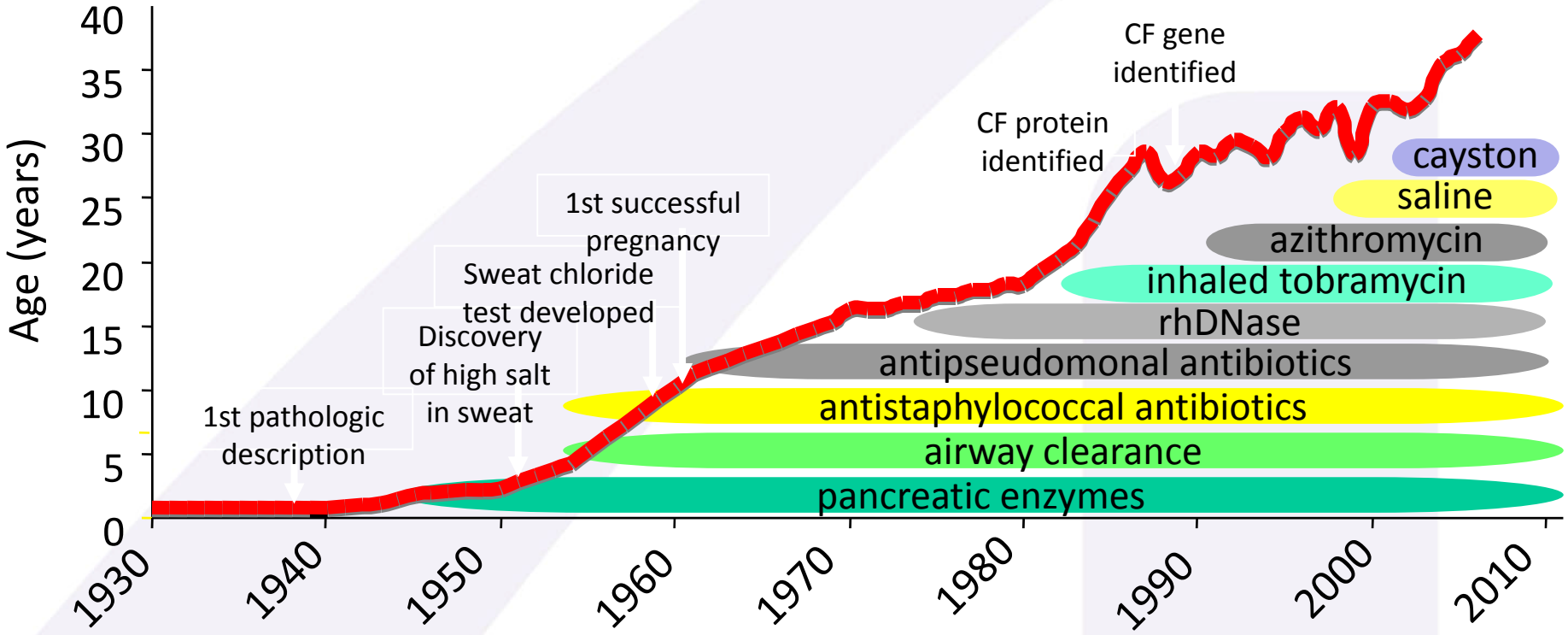
innovating for life

Cystic Fibrosis

bronchitol™ MANNITOL

- **Background**
  - Genetic disorder affecting 75,000 worldwide (30,000 in US)
  - Poorly hydrated, tenacious, thick mucus
  - Life expectancy is 37 years (US)
- **Current treatments**
  - Delivered by nebulizer (preparation, sterilization)
  - rhDNase (Pulmozyme®): global sales US$540m (2010)
  - Tobramycin (Tobi®): global sales US$300m (2009)
  - Aztreonam (Cayston®): approved EU: 9/09; US: 02/10

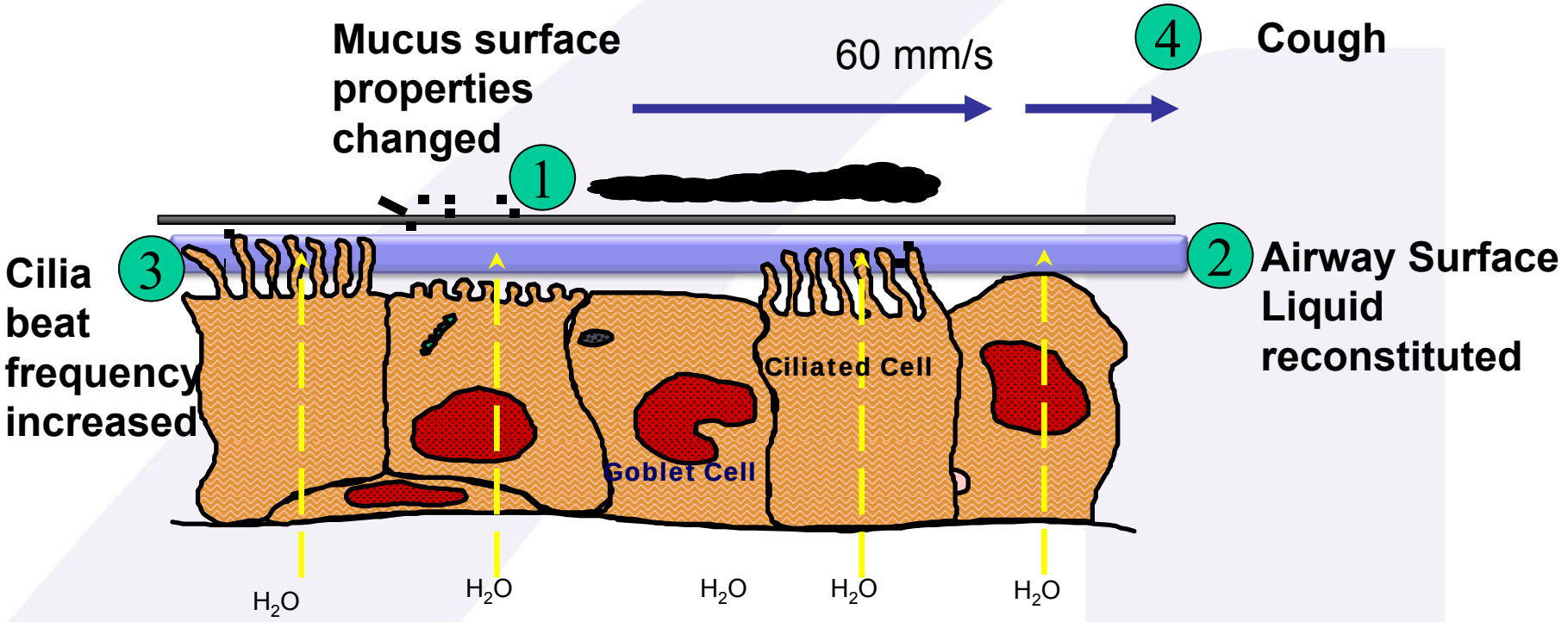
Improved Survival with Treatment Innovation



- Advances in therapy have been incremental
  - Life expectancy nevertheless increased
- Multiple therapies must be used in combination
  - "One size does not fit all"
- Restoring airway surface liquid and method of delivery now a key focus
- No approved treatment improves mucus clearance

Mode of action of Bronchitol

Lung defence (after Bronchitol)



Bronchitol

1. alters the rheological properties of mucus
2. increases the volume of airway surface liquid (ASL)
3. increases cilia beat frequency
4. promotes productive cough and assists in clearing mucus

bronchitol™
MANNITOL

- *2 - 5 minutes delivery time*
- *Convenient and portable*
- *No power source*
- *No cleaning / maintenance/ sterilisation*
- *No additives or preservatives*
- *Precision spray dried particles*
- *Twice a day dosing*
- *400mg dose*

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
  - QOL and safety
- CF301: 40 centres in UK, Ireland, Australia & New Zealand
- CF302: 53 centres in US, Canada, Argentina, Germany, France, Belgium & Netherlands
- Subjects remain on existing background therapies

Bronchitol - Clinical trial demographics

Wide range of patients on high standard of care

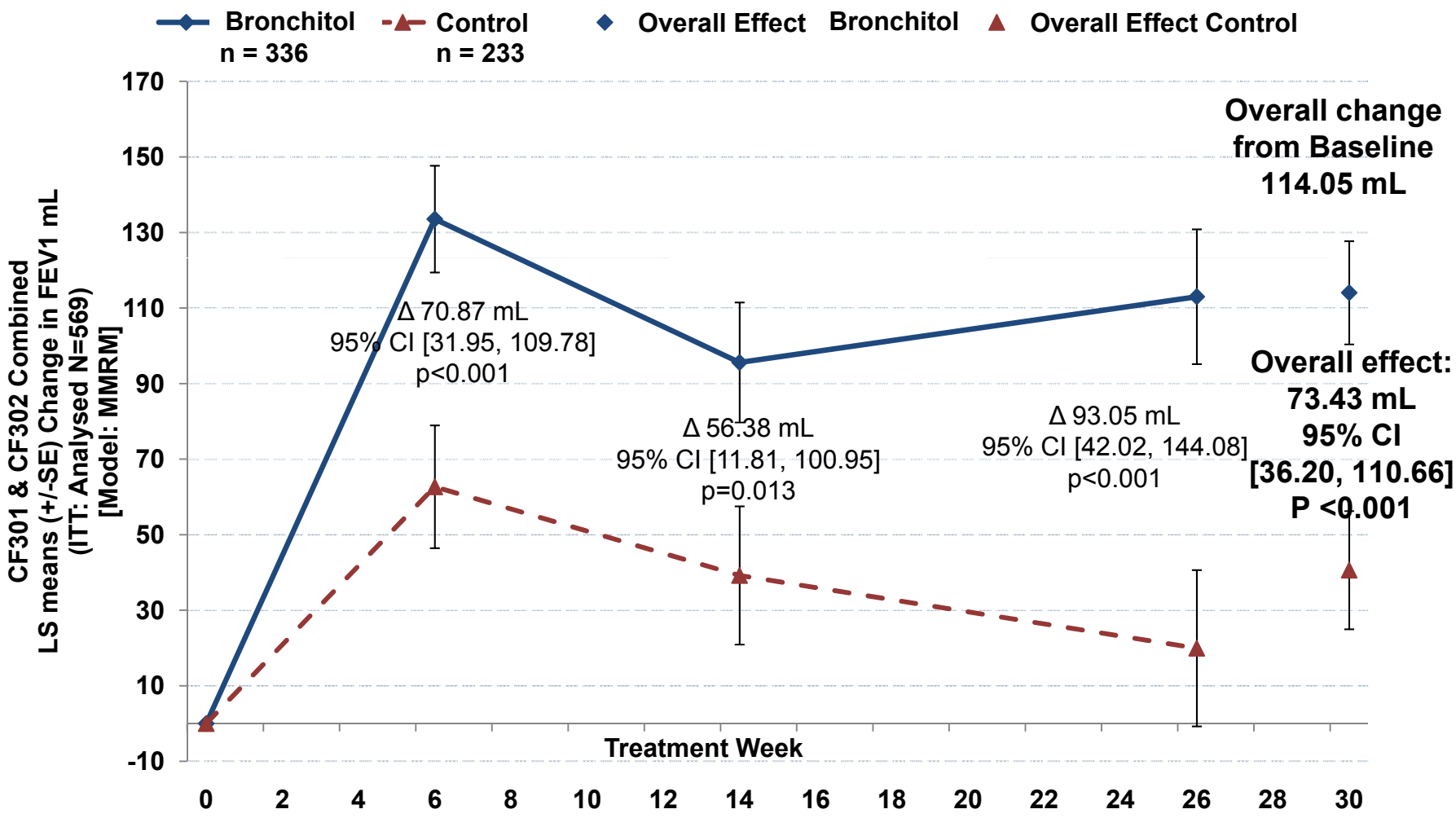
	CF301 N = 295	CF302 N = 305
Mean age years Range	23 6-56	20 6-53
Age Groups 6 – 11 years n (%) 12 – 17 years n (%) ≥18 years n (%)	 48 (16.3%) 57 (19.3%) 190 (64.4%)	 59 (19.3%) 95 (31.1%) 151 (49.55)
Gender Female n (%)	132 (44.7%)	148 (48.5%)
FEV_1 baseline mean (range) L % predicted	 2.02 (0.71-4.92) 62.0 (26-94)	 2.02 (0.61-4.12) 63.9 (25-105)
Regular medication n (%) rhDNase antibiotics^ drugs for obstructive airways disease (OAD)*	 163 (55%) 272 (92.2%) 249 (84.4%)	 229 (75%) 237 (77.7%) 279 (91.5%)

^ 3 most common antibiotic [301 vs 302]: Azithromcyin 53%vs.44%, Tobramycin 40%vs.42%, Colistin 44% vs.19%

* Medications classified as OAD include: ICS, LABA, β-agonists, LTA, anticholinergic bronchodilators, theophylline, aminophylline, nedocromil

Bronchitol - Pooled CF301 & CF302 – all subjects

FEV_1 (mL) significantly improved at each time-point

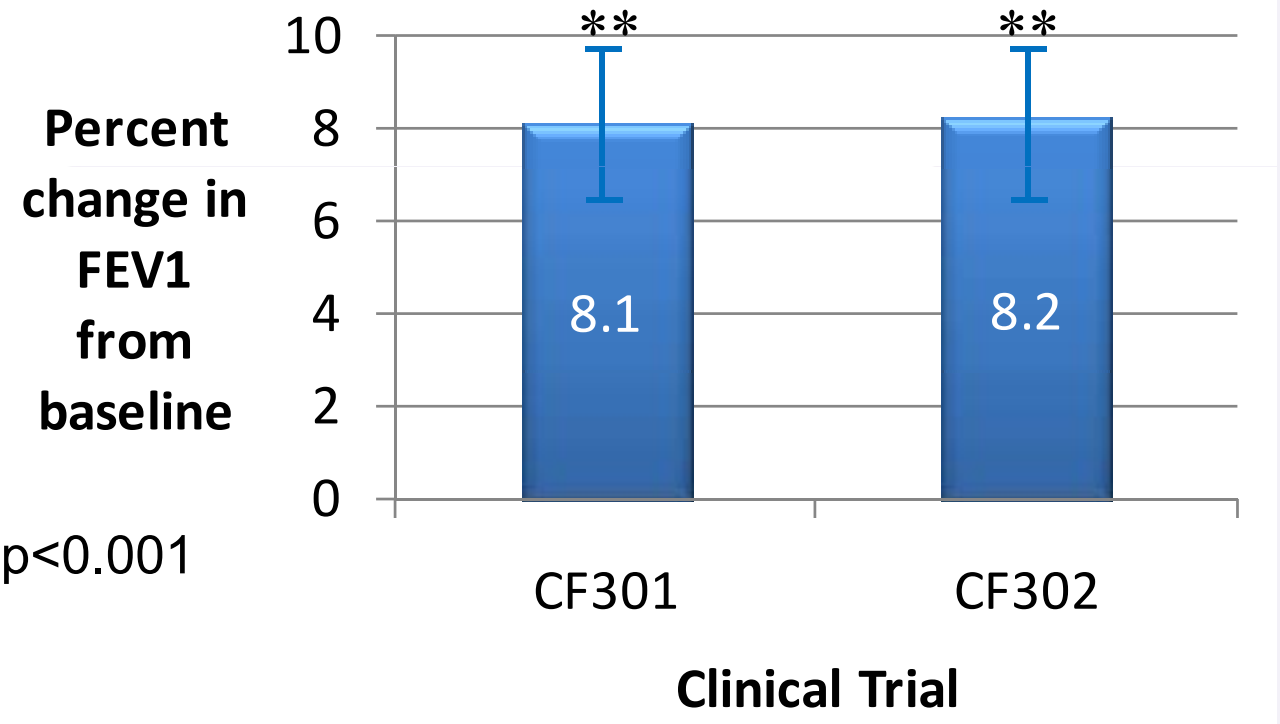


The difference between Bronchitol and Control was significant at each timepoint ($p<0.05$)

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



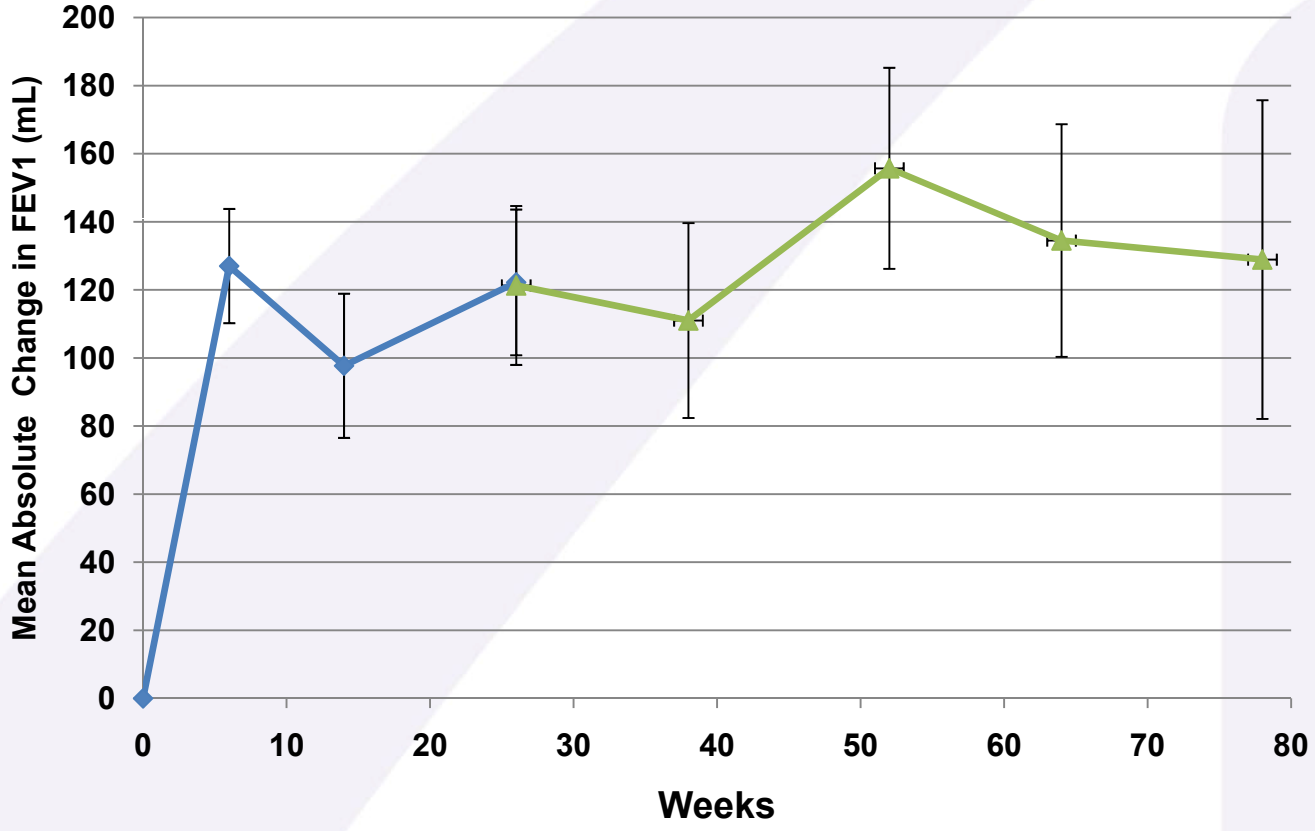
** denotes p<0.001

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

Bronchitol - effect maintained 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**

Clinically meaningful improvement in lung function

Overall treatment response (FEV_1) over 26-weeks – all age groups (Pooled Data)

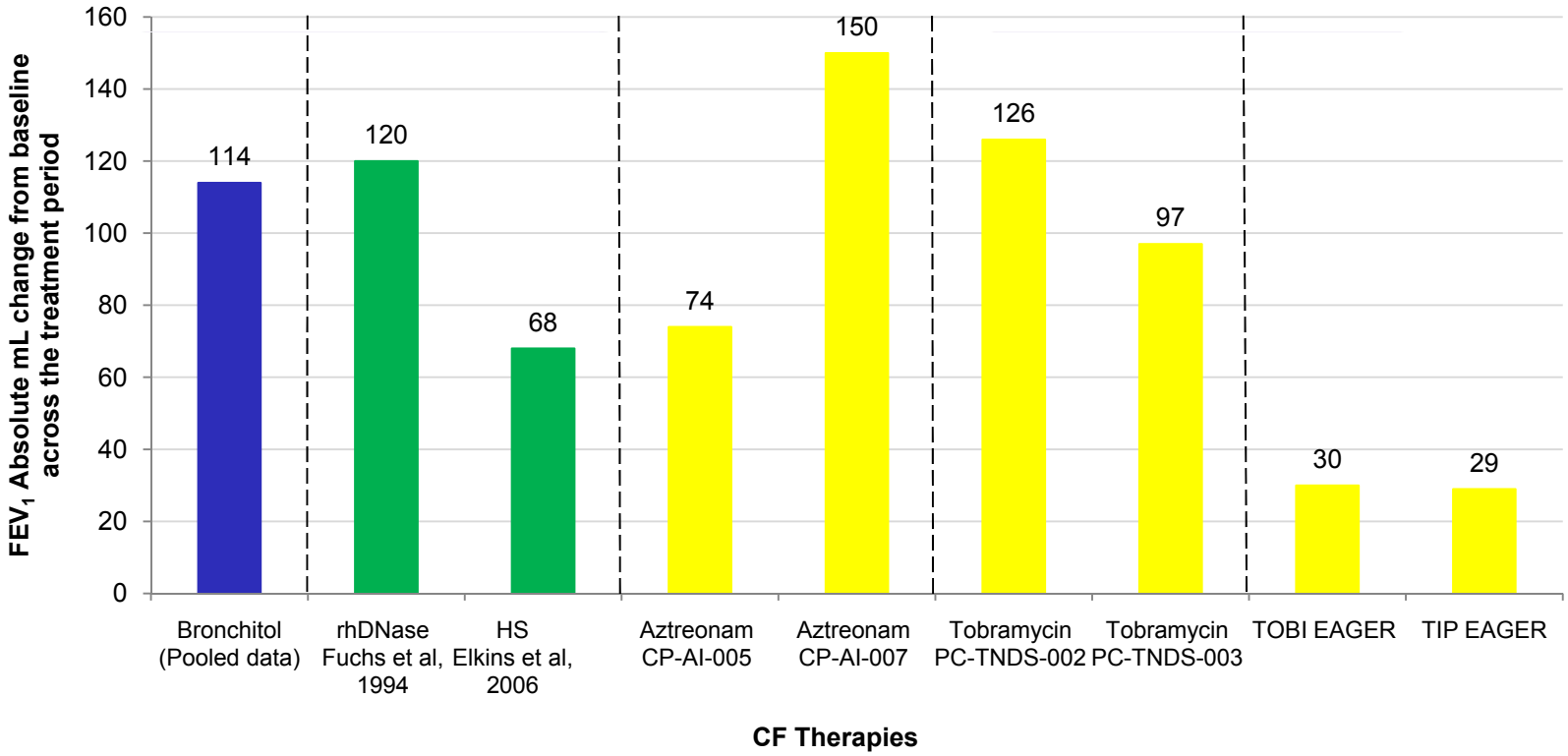
	Trials CF301 and CF302 combined				
	Paediatric (6-11yrs)	**Adolescents** (12-17 yrs)	**Adults** (≥18 yrs)	**Overall**	
	FEV_1	FEV_1	FEV_1	FEV_1	p value
difference versus control (mL)	**73.73**	**20.07**	**99.5**	**73.42**	**<0.001**
% difference versus control (mL)	**4.16**	**1.25**	**4.88**	**3.80**	**<0.001**
Bronchitol % change from baseline (mL)	**13.19**	**8.41**	**4.68**	**7.32**	**<0.001**

Note:
1: trial not powered for individual subgroups
2: FEV_1 will naturally increase as children and adolescents grow
3: trial powered for overall treatment response

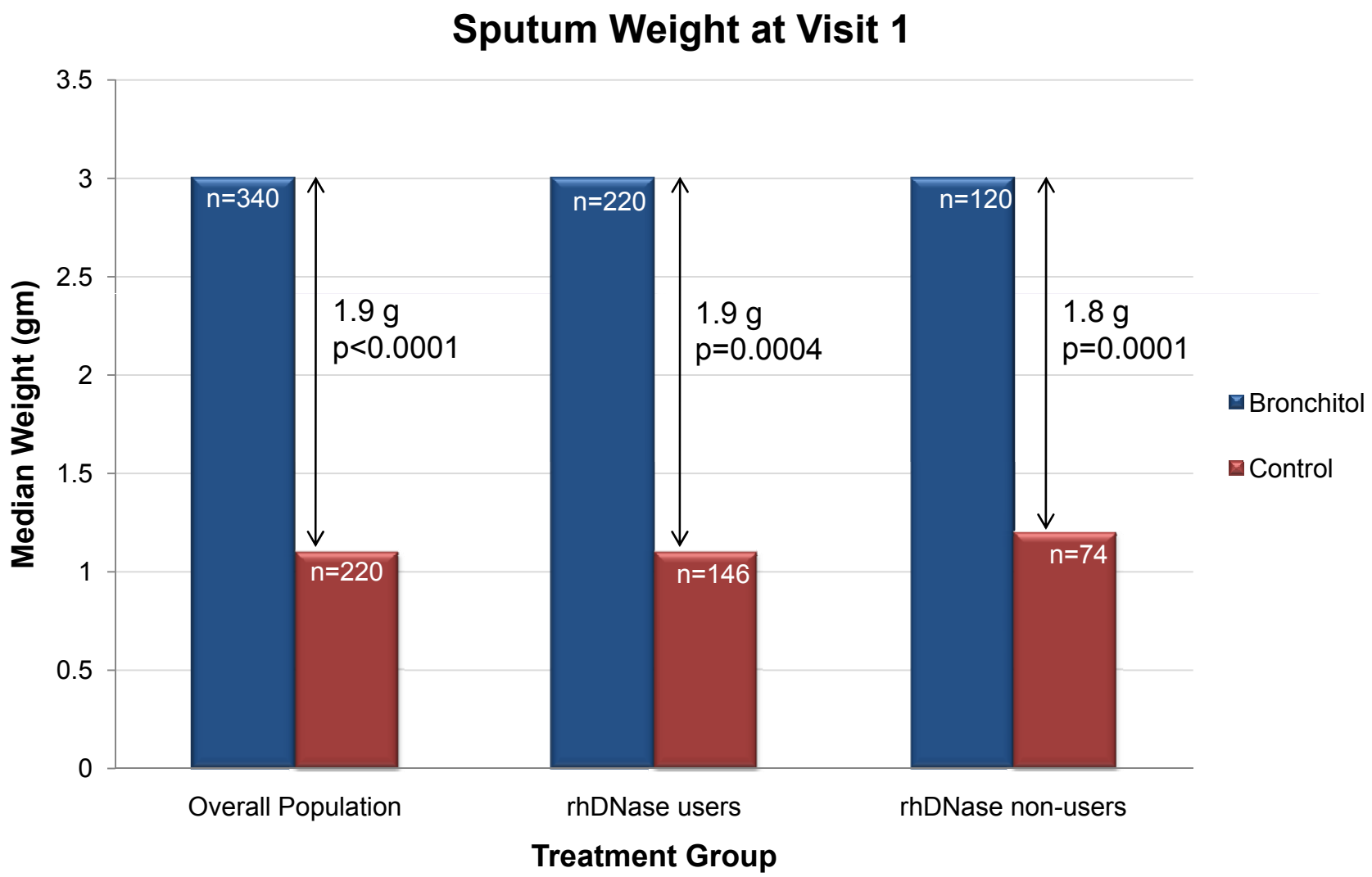
Bronchitol Comparable to Other CF Therapies

FEV_1 mL change from baseline across treatment period by CF therapy

Drug	Bronchitol	rhDNase	Hypertonic saline	Aztreonam		Tobramycin			
Source	Pharmaxis	Fuchs *et al*, 1994	Elkins *et al*, 2006	Cayston EPAR		US FDA NDA 50,753 review		Konstan *et al*, 2010	
FEV_1 mL change from baseline across the treatment period	114	120	68	74	150	126	97	30	29



Bronchitol - post-dose mucus clearance
(CF301 and CF302 combined)



Clinically important reductions in exacerbations

- 29% reduction in exacerbation incidence (Bronchitol vs control) - combined CF301 and CF302 (p=0.039)

- 46% reduction in exacerbation rate in patients who completed the study – CF301(p=0.055)

- Exacerbations associated with subsequent lung function decline in both adults and children with CF

Source: Sanders *et. al.,* Pediatric Pulmonology , 2011,**46**,393

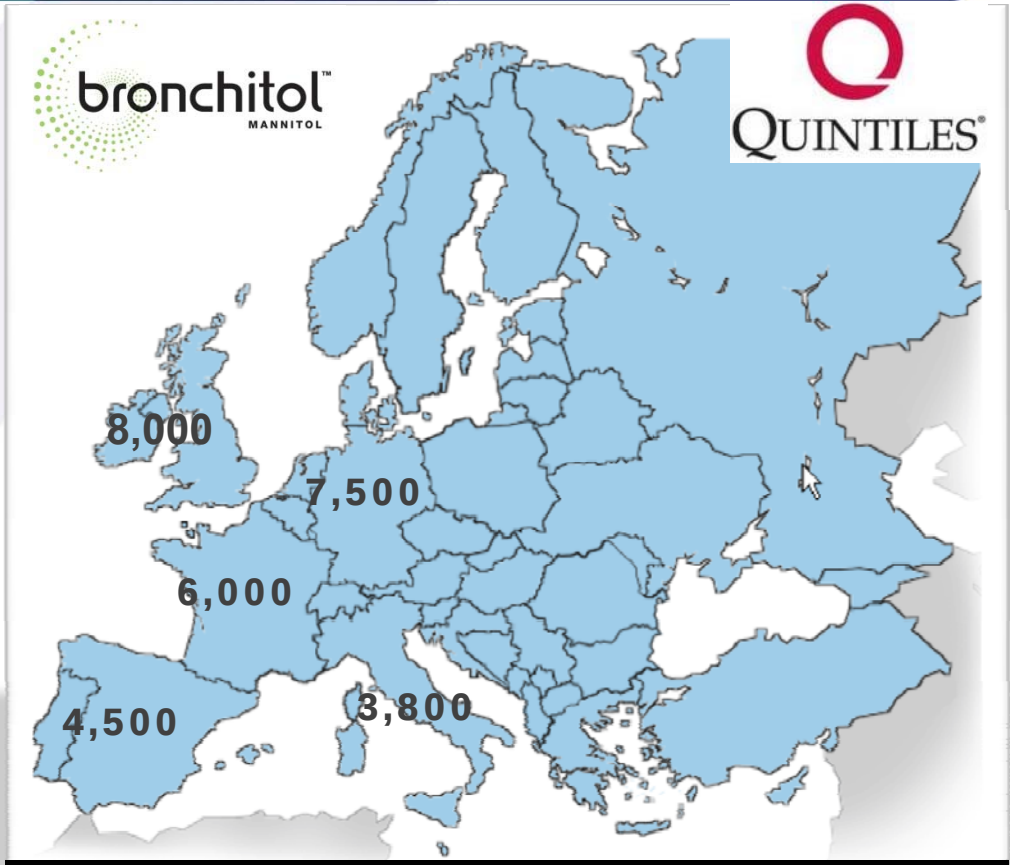
Favourable Safety of Bronchitol Compared to Other CF Therapies
(AEs of Interest) Incidence (%) Over 6 Months Except Aztreonam

Adverse Events %	Bronchitol (CF-301 +CF302) N=361	rhDNase (once daily) N=322	Aztreonam Pooled TID (4 week) N=146	Nebulised tobramycin (TOBI) N=209	Dry powder tobramycin (TIP) N=308
Dyspnoea	1	37	7	12	16
Wheeze	2	N/A	10	6	7
Chest Discomfort	3	18	6**	3	7
Bronchoconstriction	1	N/A	3**/***	5.3*	5.2*
Cough	20	40	36	31	48
Productive Cough	5	N/A	13	20	18
Pharyngolaryngeal Pain	12	36	10	11	14
Haemoptysis	9	17	5	12	13

*Clinically significant post dose bronchoconstriction FEV_1 fall ≥20%, not necessarily reported as AE; N/A – Not Available
** data available from one study – Not pooled *** Clinically significant post dose bronchoconstriction FEV_1 fall ≥15%,
Source: Data on file; Fuchs et al, 1994; Pulmozyme PI, 2005; McCoy et al 2008; Retsch-Bogart, 2009; Konstan et al, 2010

Commercialisation of Bronchitol in Europe

- **Orphan drug – 11 years exclusivity**
- **Marketing Approval Process**
  - **MAA review completed**
  - **Re-examination to be requested**
  - **Process to conclude Q4 2011**
- **Promotion by Pharmaxis in Western Europe (14 countries)**
- **Logistics infrastructure by 3rd party**
- **Distributor for Central / Eastern Europe**
- **Launch**
  - **Top 5 < 12 months of approval**
  - **UK/Germany – on approval**



CF Patients	
Top 5	30,000
Western EU - other	10,000
Central / Eastern EU	8,000
Total EU	**48,000**

US Cystic Fibrosis Opportunity for Bronchitol

Clinical

- Two pivotal Phase 3 trials completed in over 600 subjects

Regulatory

- NDA scheduled submission H1 2012
- Earliest FDA review completed H1 2013
- Orphan drug provides 7 years market exclusivity

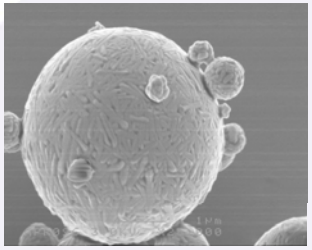
Marketing

- 150 CF centres require 15 - 25 person field force
- 30,000 people in the US with CF
- Pulmozyme price ~ USS$22,000 pa

Manufacturing Capacity

- Facility No 1 – Frenchs Forest Australia
  - GMP manufacture of Aridol for sale in EU, Asia & Australia
  - Manufacture of Bronchitol for clinical trials and compassionate use
  - Inspected by FDA in approval of Aridol
- Facility No 2 - Frenchs Forest Australia
  - TGA licence for clinical trials and compassionate use
  - Equipment installation & validation complete
  - Full TGA Commercial Licence - 2011
  - Capacity
    - Initial capacity - 1 spray drier: 40,000 patients p.a.
    - Expanded capacity – 2nd spray drier: 80,000 patients p.a.

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

Bronchitol – bronchiectasis registration

- **2nd Phase III trial**
  - 475 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**
  - Special Protocol Assessment concluded with US FDA
  - Orphan Drug designation — USA
  - First patient enrolment — October 2009
  - Complete recruitment — H2 2011
  - Data — 2012

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

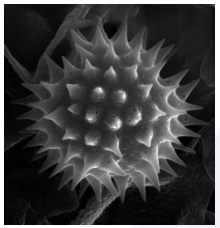
Aridol – commercialisation status

			2008	2009	2010	2011 (9 months)
Sales (A$'000)						
Australia	Launched 2006	Direct	216	232	268	186
Europe	Staggered launch from 2007	Distributors (7); UK – direct;	137	267	398	319
Korea	Launched Oct 09	Distributor	-	32	162	158
Clinical trials		Direct	174	64	-	-
US	Launched Feb 11	Direct	-	-	-	14
			527	595	828	677

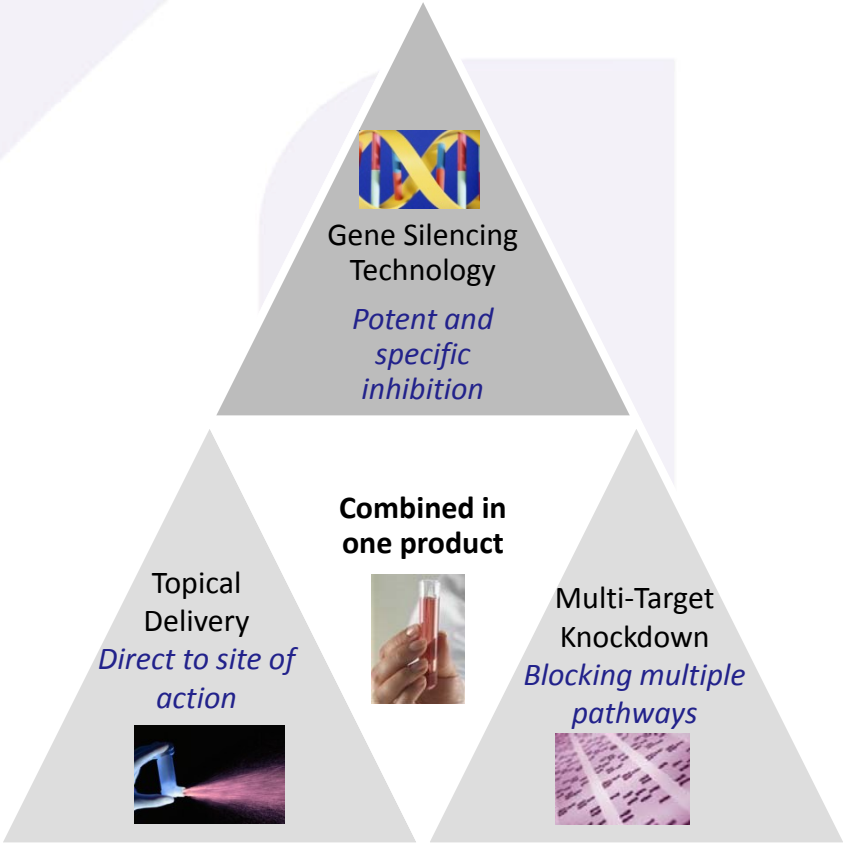
Marketing via education, key opinion leaders:

- Investigator initiated studies, > 70 peer reviewed articles
- US ACRN study: Aridol utility in asthma management
- UK investigator : steroid management in asthma using Aridol
- Swiss investigator: steroid management in COPD

ASM8 : A new approach for uncontrolled asthma



- Targeting severe asthma
  - affects ~6 million people
  - major cause of ER visits
  - limited treatment options
  - current treatment - Xolair
- Once daily by inhalation
- Improved side effect profile
  - low systemic exposure
- Improved effectiveness
  - targets multiple inflammatory proteins
- Inhibits protein synthesis

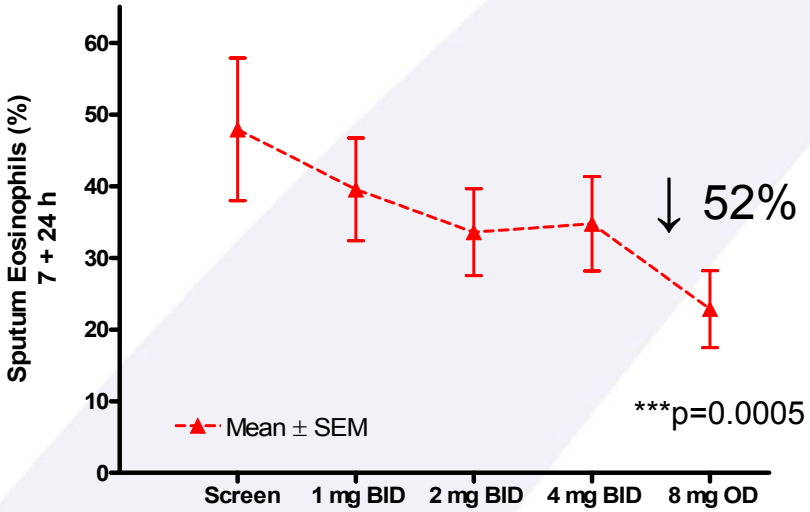


There exists an unmet medical need in patients with severe asthma

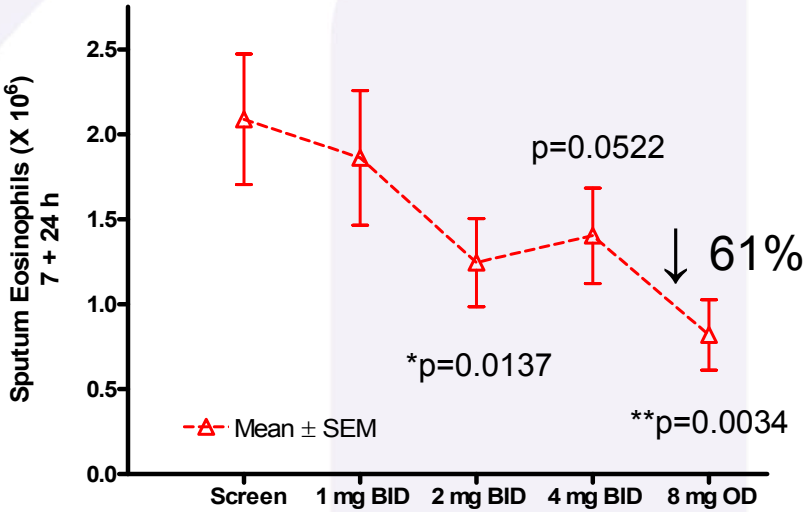
ASM8: results of Phase IIa dose profiling study

(Sputum Eosinophils (sum of 7h and 24h))

% Eosinophils



Absolute # Eosinophils

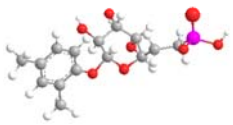


- 4 day treatment – sequential escalating dose
- 12 subjects – mild allergic asthma
- Primary endpoints – sputum eosinophils & safety
- Secondary endpoints – LAR, EAR, Target mRNA

Next study

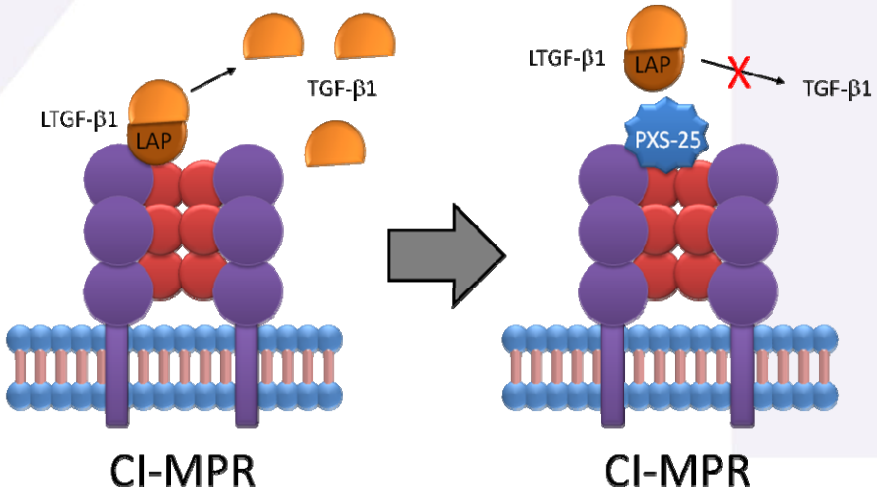
- 14 day allergen challenge
- commenced Q4 2010

PXS25 for fibrosis



- Inhibits cleavage of latent TGFβ to active TGFβ
  - Targeting Idiopathic Pulmonary Fibrosis
    - Affects >500,000 people worldwide
  - Small molecule with robust pharmaceutical profile

- Phase I trial completed - safety, pharmacokinetics in healthy subjects



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-11	31-Mar-10	31-Mar-11	31-Mar-10
	A$	A$	A$	A$
Revenue from sale of goods	318	282	677	636
Cost of sales	(148)	(125)	(266)	(232)
Gross profit	170	157	411	404
Interest	697	1,003	2,468	2,933
Other income	82	123	332	288
Expenses				
Research & development	(7,832)	(8,991)	(25,552)	(26,287)
Commercial	(2,668)	(1,261)	(6,329)	(3,725)
Administration	(1,206)	(4,631)	(3,999)	(8,165)
Finance expenses	(215)	(148)	(648)	(656)
Total expenses	(11,921)	(15,031)	(36,528)	(38,833)
Loss before income tax	(10,972)	(13,748)	(33,317)	(35,208)
Income tax expense	(58)	-	(65)	(42)
Loss for the period	(11,030)	(13,748)	(33,382)	(35,250)
Basic and diluted earnings (loss) per share - $	(0.048)	(0.063)	(0.147)	(0.162)
Depreciation & amortisation	1,167	689	3,573	1,836
Fair value of securities issued under employee plans	352	719	1,182	1,872

Financial Statements

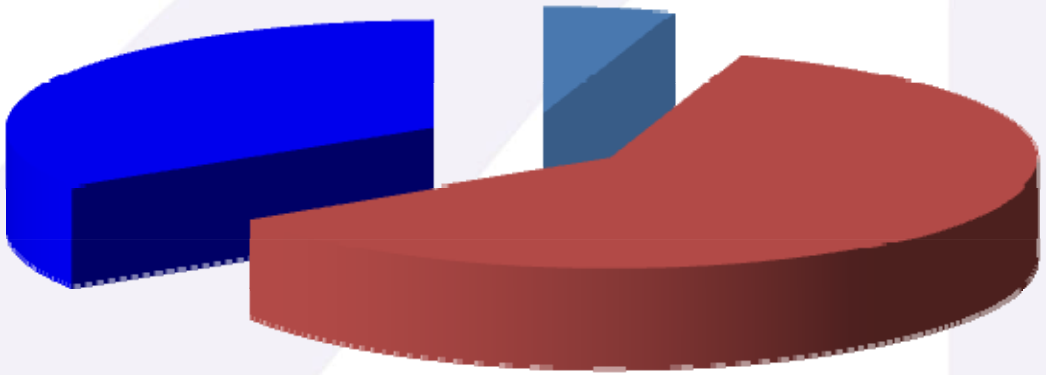
Financial Statement Data - Unaudited				
(International Financial Reporting Standards)				
('000 except per share data)				
Balance Sheet Data	As at			
	31-Mar-11	30-Jun-10		
	A$	A$		
Cash and cash equivalents	56,284	85,787		
Property, plant & equipment	31,244	32,537		
Intangible assets	16,401	17,702		
Total assets	107,420	140,767		
Total liabilities	(24,718)	(25,751)		
Net assets	82,702	115,016		
Cash Flow Data	Three months ended		Nine months ended	
	31-Mar-11	31-Mar-10	31-Mar-11	31-Mar-10
	A$	A$	A$	A$
Cash flows from operating activities	(10,174)	(11,543)	(27,395)	(31,863)
Cash flows from investing activities	(297)	5,515	(1,140)	3,282
Cash flows from financing activities	(304)	(181)	(563)	(492)
Impact of foreign exchange rate movements on cash	62	(11)	(405)	(35)
Net increase (decrease) in cash held	(10,713)	(6,220)	(29,503)	(29,108)
Share Data	Ordinary Shares as at			
	31-Mar-11	30-Jun-10		
Ordinary shares on issue	228,128	225,410		
Options over ordinary shares outstanding	12,882	13,155		

Share Capital
(including options)

Management – 5%

Other/retail – 35%

Institutions – 60%
(61 institutions)



31 May 2011: 228m shares; 13m options

End

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