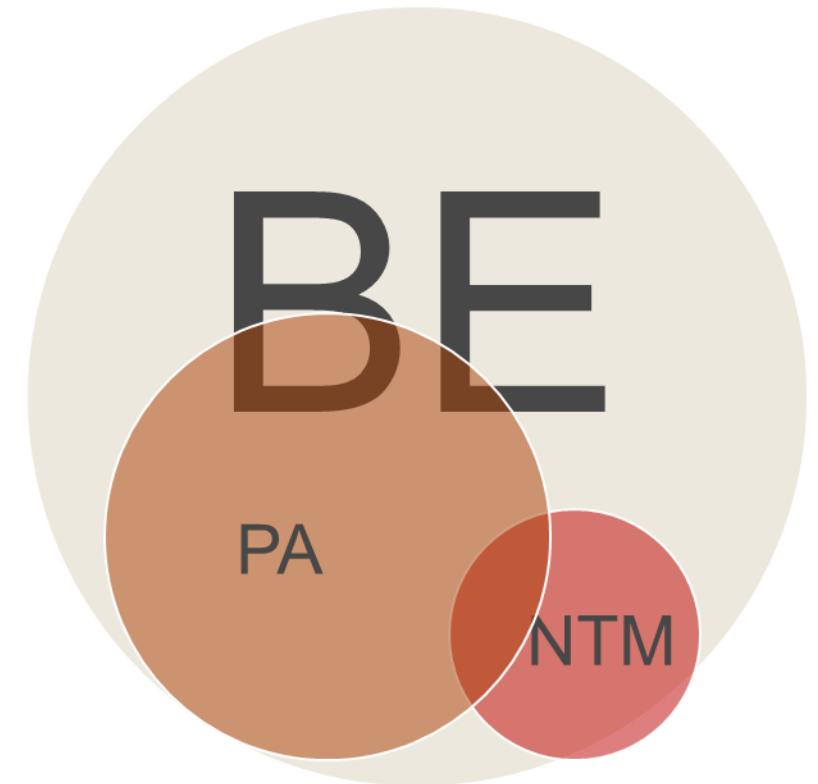


The unmet need for an inhaled antibiotic in the treatment of non-cystic fibrosis bronchiectasis (NCFB)

Professor James D Chalmers, MD PhD
British Lung Foundation Chair of Respiratory Research
University of Dundee, Scotland, UK

What is Bronchiectasis?

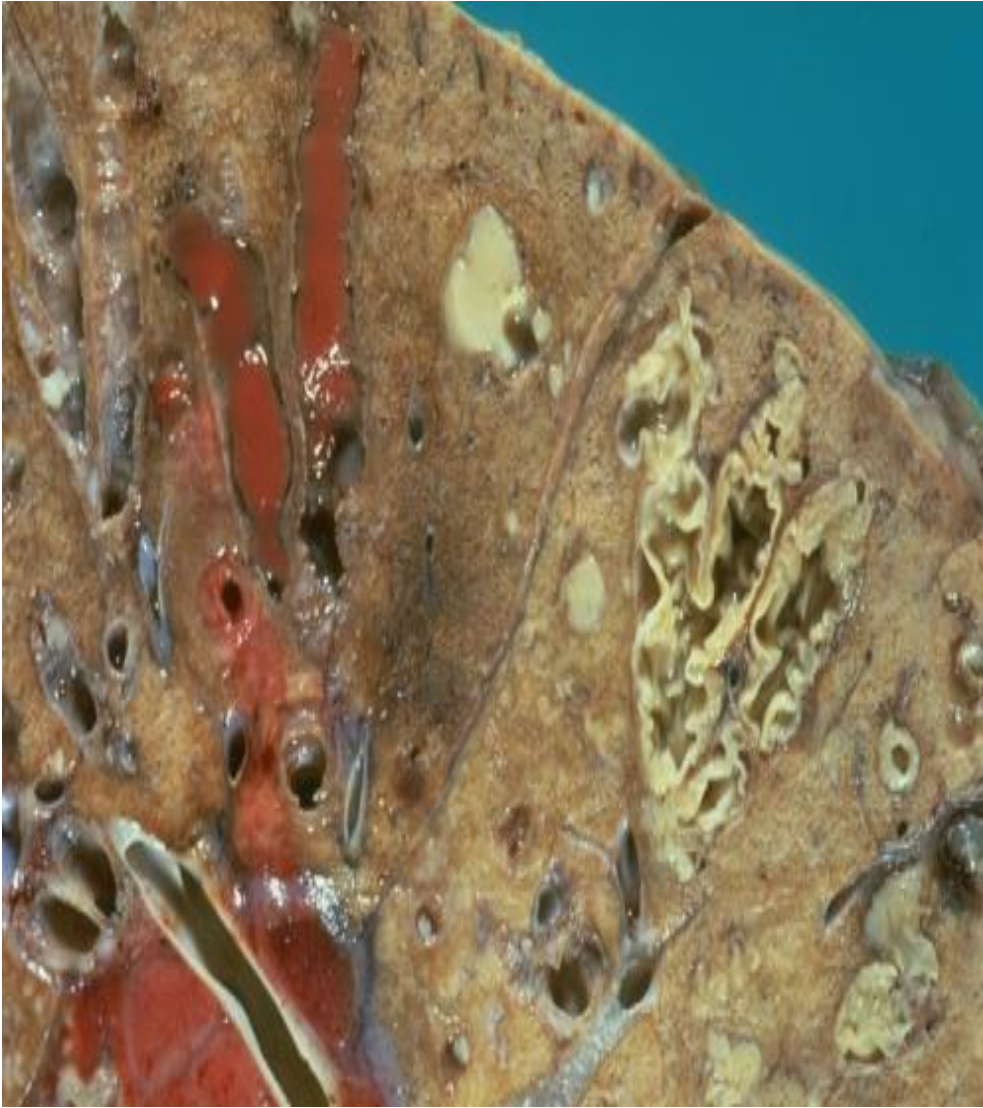
- ◆ Characterized pathologically by airway inflammation and permanent bronchial dilatation, and clinically by productive cough and recurrent respiratory infections
- ◆ Etiology
 - Idiopathic
 - Post-infectious
 - Endobronchial obstruction
 - Congenital syndromes
 - Immunodeficiency states
 - Immune mediated diseases
 - Non-tuberculous Mycobacterial infection



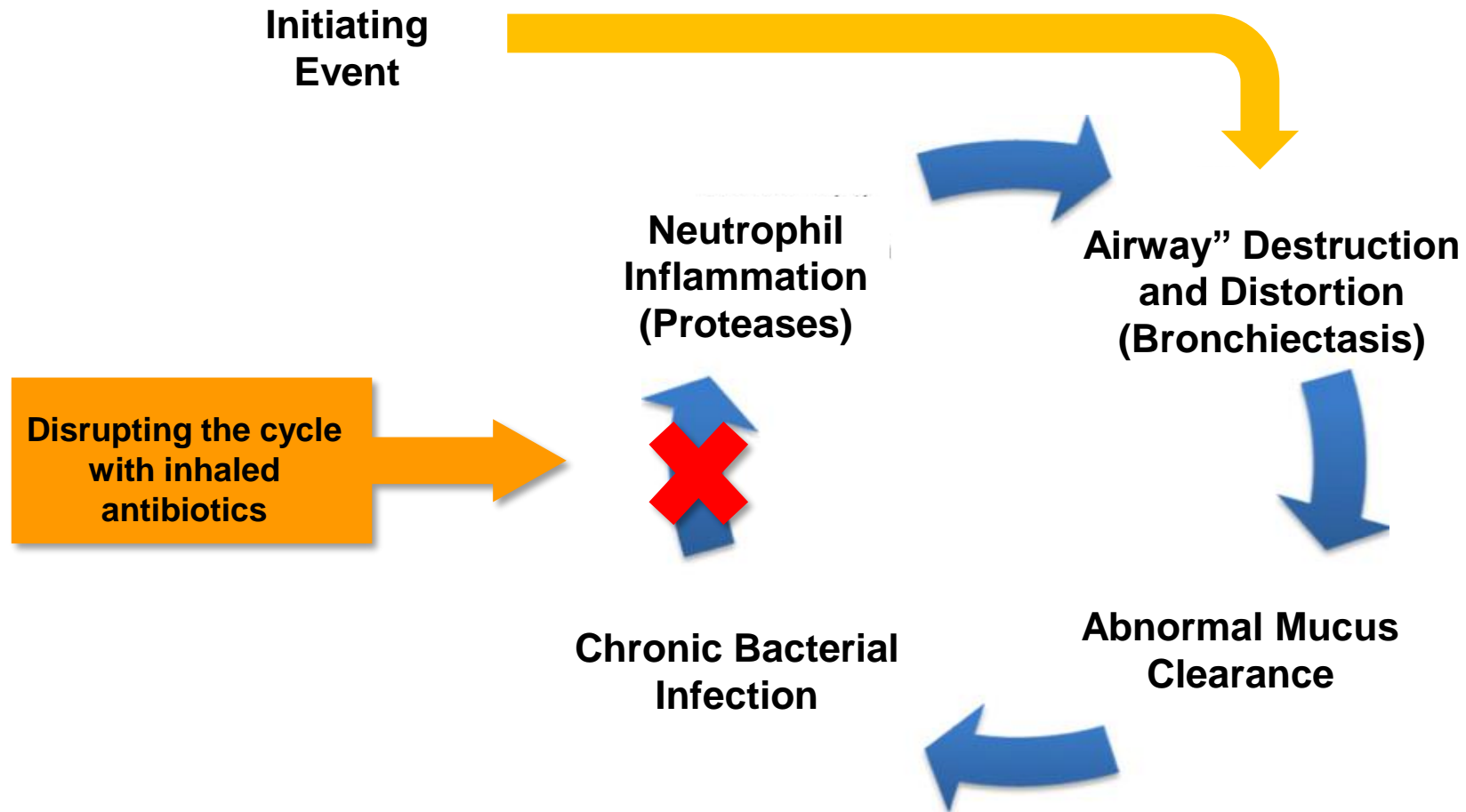
Barker AF. *N Engl J Med*. 2002;346:1383-1393.

Mysliwiec V, Pina JS. *Postgrad Med*. 1999; 106:123-131.

Pasteur MC, et al. *Am J Respir Crit Care Med*. 2000; 162:1277-1284.



Pathogenesis of Bronchiectasis is a Vicious Cycle



Adapted from McShane PJ, et al. *Am J Resp Crit Care Med*. 2013.

NCFBE Rates are Increasing

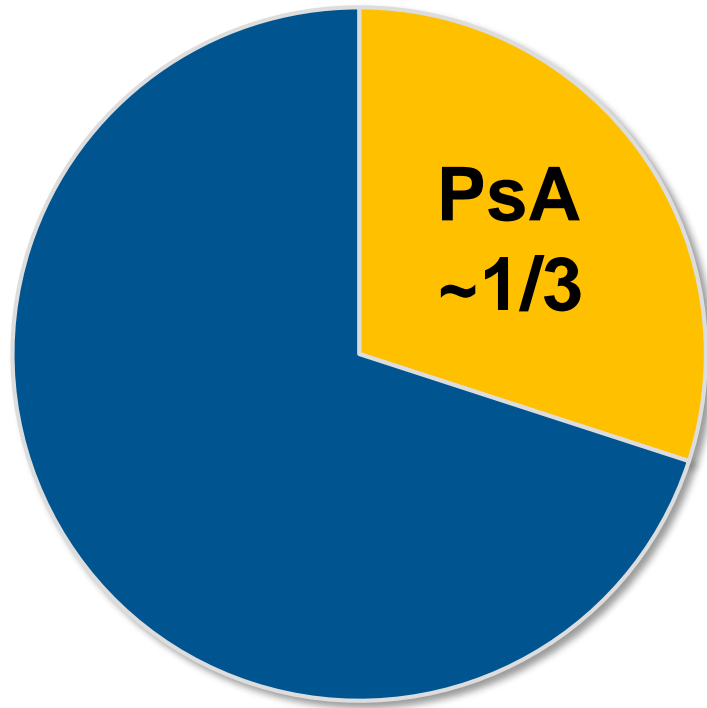
- ◆ **Prevalence is unclear**
 - **>110,000 patients in the United States¹**
- ◆ **Increasing at a rate of ~9% annually²**
- ◆ **Potential reasons for increases include**
 - **Increased use of chest CT scans as a diagnostic tool**
 - **Changes in the prevalence of diseases causing bronchiectasis**
 - **Increasing awareness that asthma and COPD may be closely linked with bronchiectasis**

1. Weycker 2005

2. Seitz 2012

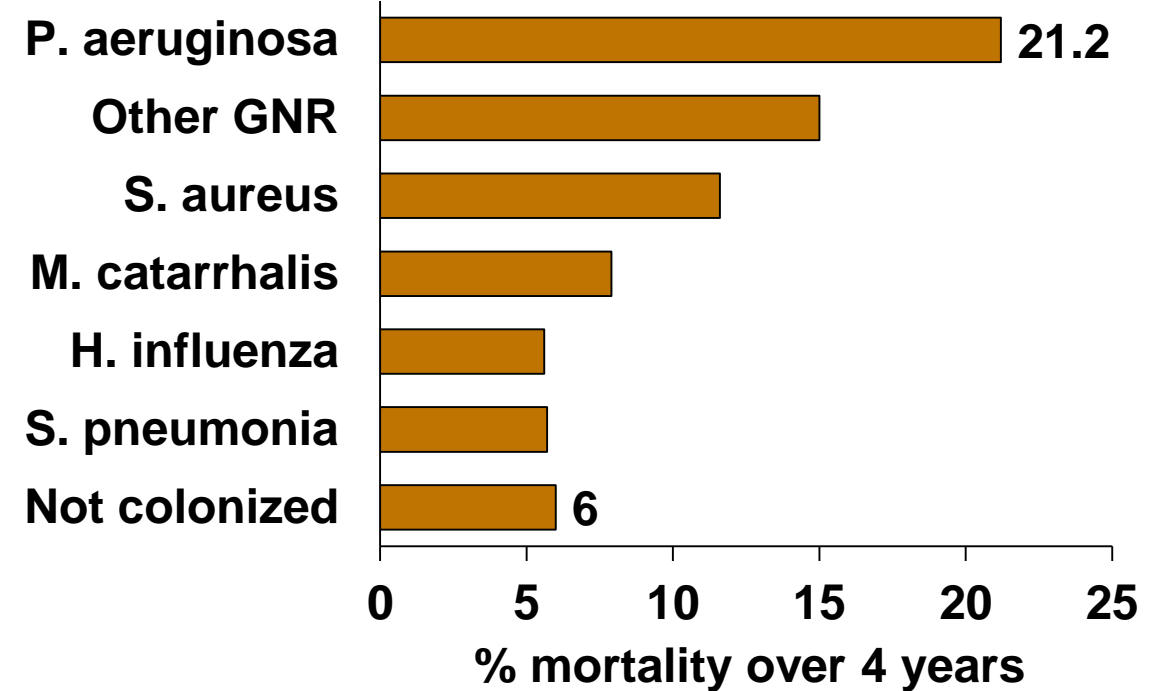
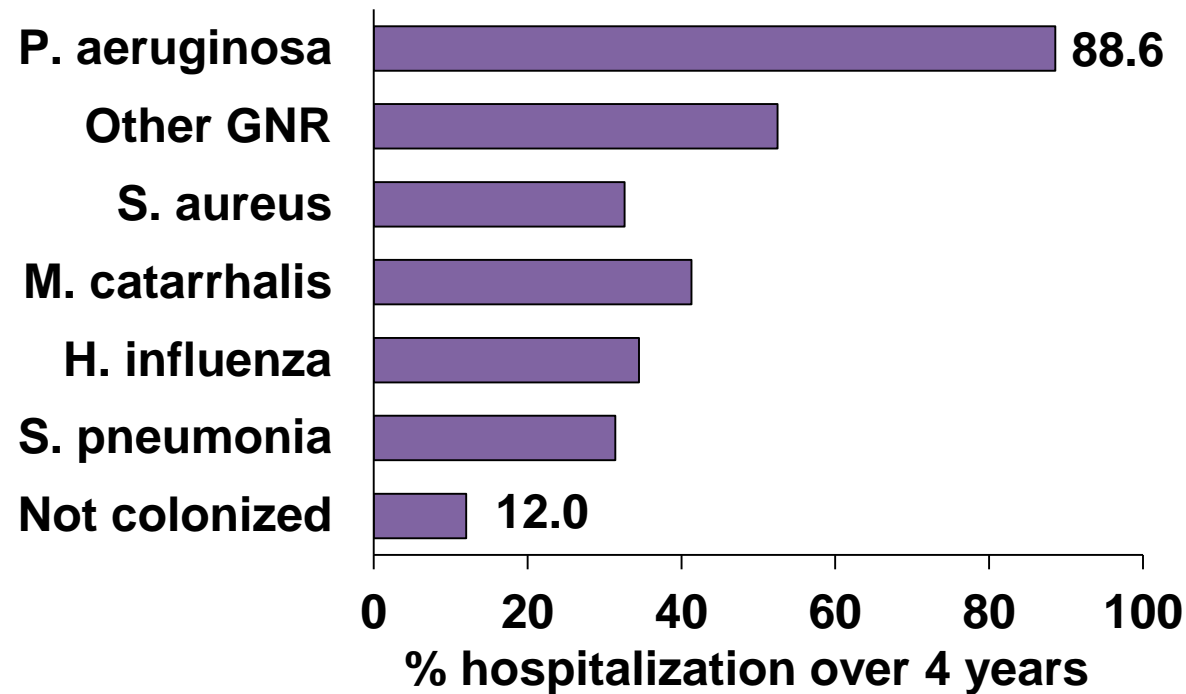
3. Quint 2016

NCFBE: Impact of *Pseudomonas Aeruginosa* (PsA)



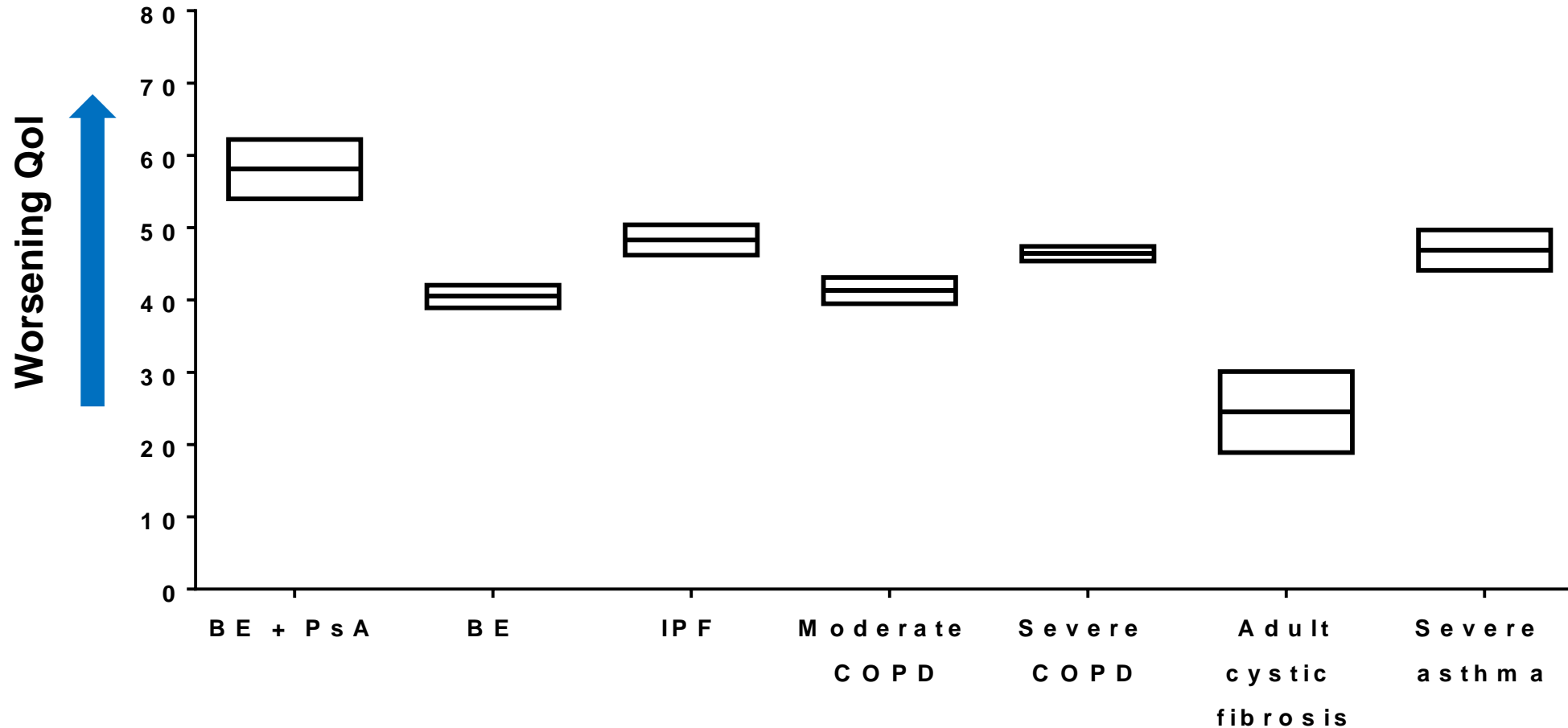
- ◆ 3× higher mortality
- ◆ 7× higher risk of hospitalization
- ◆ Average of 1 additional exacerbation per patient per year

PsA Results In More Hospitalizations and Higher Mortality Rates Than Other Infections



BE with PsA Results in Worse Quality of Life than Patients with Other Severe Respiratory Diseases

SGRQ total score



1. Kreuter, et al. *Respir Res.* 2017. 2. Kerwin, et al. *Intl J COPD.* 2017. 3. Magnussen, et al. *NEJM.* (Oct) 2014. 4. Padilla, et al. *Arch Bronconeumol.* 2007. 5. Ortega, et al. *NEJM.* (Sept) 2014.

Acute Pulmonary Exacerbations

- ◆ Increased cough and sputum volume
- ◆ Increased sputum purulence and viscosity
- ◆ Worsened dyspnea
- ◆ Fever
- ◆ Malaise
- ◆ Pleuritic chest pain
- ◆ Wheezing
- ◆ Hemoptysis

Why are Pulmonary Exacerbations Important?

- ◆ Median duration is 16 days
- ◆ Symptoms can persist for weeks; 16% had not recovered by 35 days
- ◆ Some patients may not return to baseline – “irreversible morbidity”
- ◆ Breathlessness is the second most common symptom of exacerbation (after cough)
- ◆ Functional ability is an independent predictor of long term mortality and exacerbation frequency

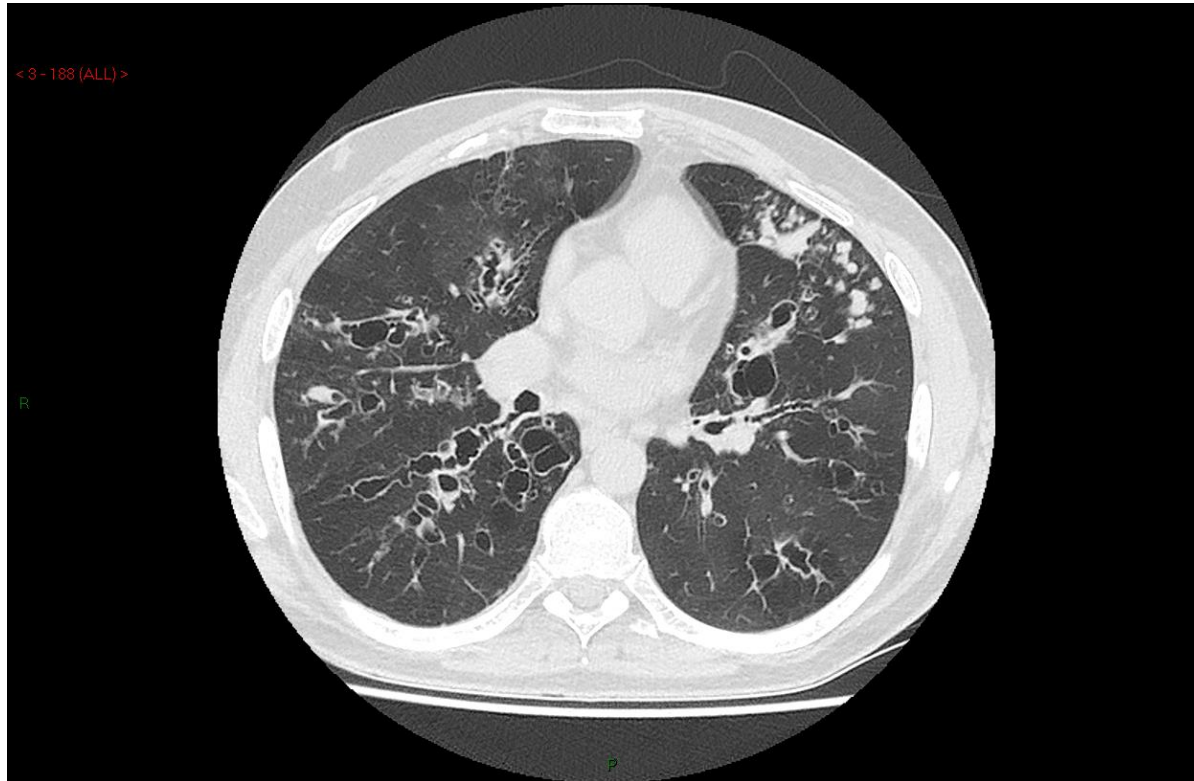
Current Clinical Practice

- ◆ **No approved treatments, including for prevention of PEs**
- ◆ **Variability and limitations of treatment**
 - **Use of antibiotics for exacerbation only - 41%**
 - **Suppressive antibiotics - 39%: 10% aerosol, 7% rotating regimen**
 - **Inhaled bronchodilators - 61%**
 - **Inhaled steroids - 39%, systemic steroids -13%**
 - **Airway clearance - 56%**

Case Study

◆ 57 y.o. man:

- Diagnosed with bronchiectasis at age 8 after a respiratory tract infection (negative tests for CF and primary ciliary dyskinesia)



- Excellent health during his 20's and 30's (ran 10k races and rowed at a high level).
- Presented just over 5 years ago with worsening symptoms
- *P. aeruginosa* acquired in sputum for the first time

Clinical Course

- ◆ Initially treated with sequential oral ciprofloxacin, intravenous ceftazidime and tobramycin.
- ◆ *P. aeruginosa* failed to clear from sputum
- ◆ Frequent exacerbations (up to 8 per year) requiring antibiotics
- ◆ Trialed on long-term macrolide but exacerbations persisted
- ◆ Various off-label long term inhaled antibiotics trialed. Unable to tolerate due to worsening of respiratory symptoms when on inhaled therapy.
- ◆ Very poor quality of life
- ◆ Ultimately managed with 6-8 weekly intravenous antibiotic courses

Target Population for Linhaliq

- ◆ The new European Guidelines recommend the use of inhaled antibiotics for bronchiectasis patients with frequent exacerbations and chronic infections with *Pseudomonas aeruginosa*
 - Aradigm's clinical development program focused on this patient population



TASK FORCE REPORT
ERS GUIDELINES



European Respiratory Society guidelines for the management of adult bronchiectasis

Eva Polverino¹, Pieter C. Goeminne^{2,3}, Melissa J. McDonnell^{4,5,6}, Stefano Aliberti⁷, Sara E. Marshall⁸, Michael R. Loebinger⁹, Marlene Murris¹⁰, Rafael Cantón¹¹, Antoni Torres¹², Katerina Dimakou¹³, Anthony De Soyza^{14,15}, Adam T. Hill¹⁶, Charles S. Haworth¹⁷, Montserrat Vendrell¹⁸, Felix C. Ringshausen¹⁹, Dragan Subotic²⁰, Robert Wilson⁹, Jordi Vilaró²¹, Bjorn Stallberg²², Tobias Welte¹⁹, Gernot Rohde²³, Francesco Blasi⁷, Stuart Elborn^{9,24}, Marta Almagro²⁵, Alan Timothy²⁵, Thomas Ruddy²⁵, Thomy Tonia²⁶, David Rigau²⁷ and James D. Chalmers²⁸

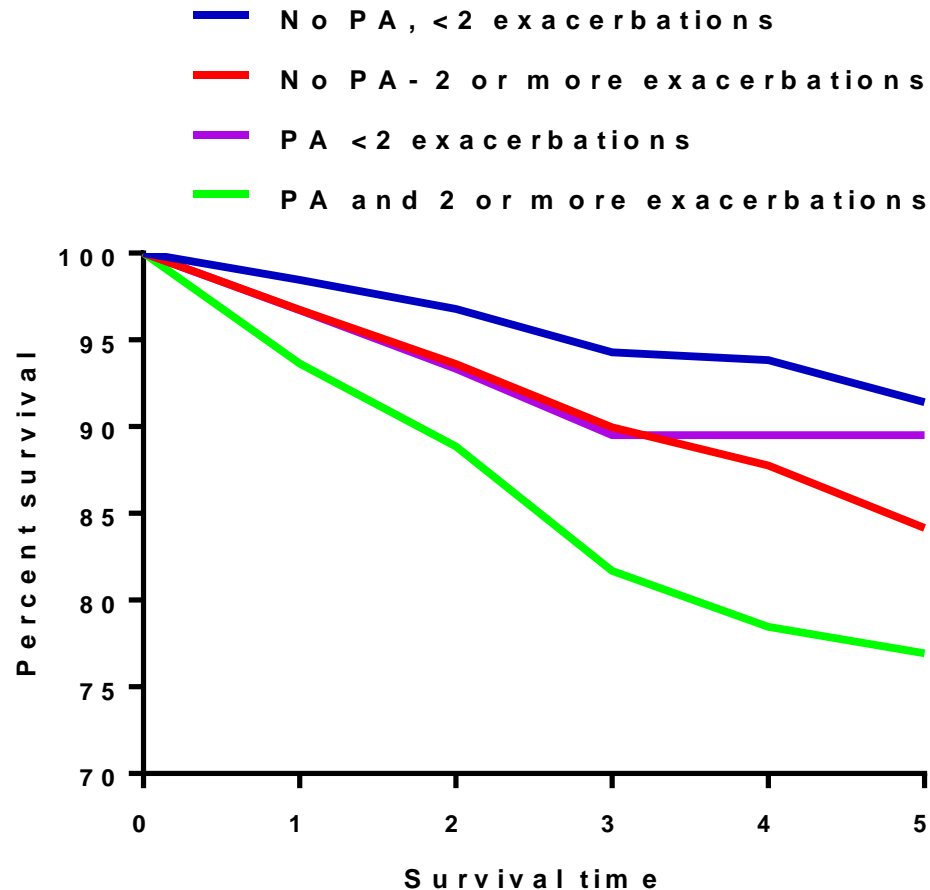
@ERSpublications

The publication of the first ERS guidelines for bronchiectasis <http://ow.ly/wQSO30dU0nE>

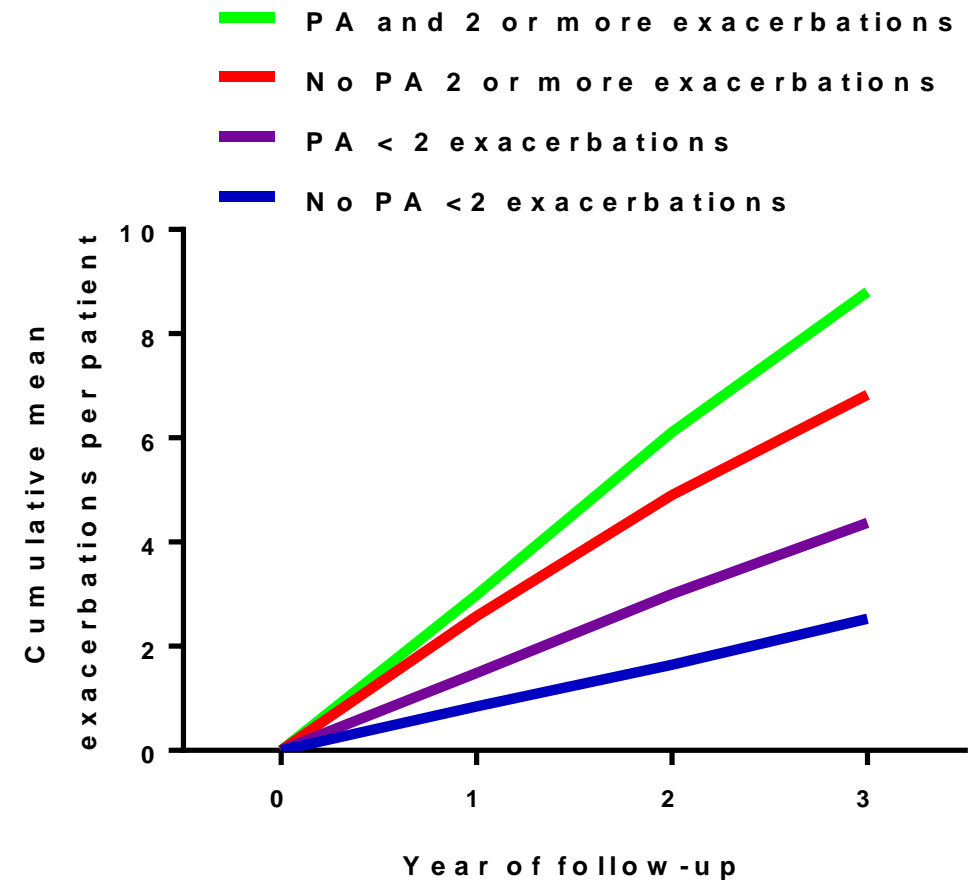
Cite this article as: Polverino E, Goeminne PC, McDonnell MJ, et al. European Respiratory Society guidelines for the management of adult bronchiectasis. *Eur Respir J* 2017; 0: 1700629 [https://doi.org/10.1183/13993003.00629-2017].

Bronchiectasis Patients with Chronic Lung Infections with *P. aeruginosa* and >1 Pulmonary Exacerbation per Year Have Strikingly Higher Mortality and Morbidity

Mortality



Exacerbations

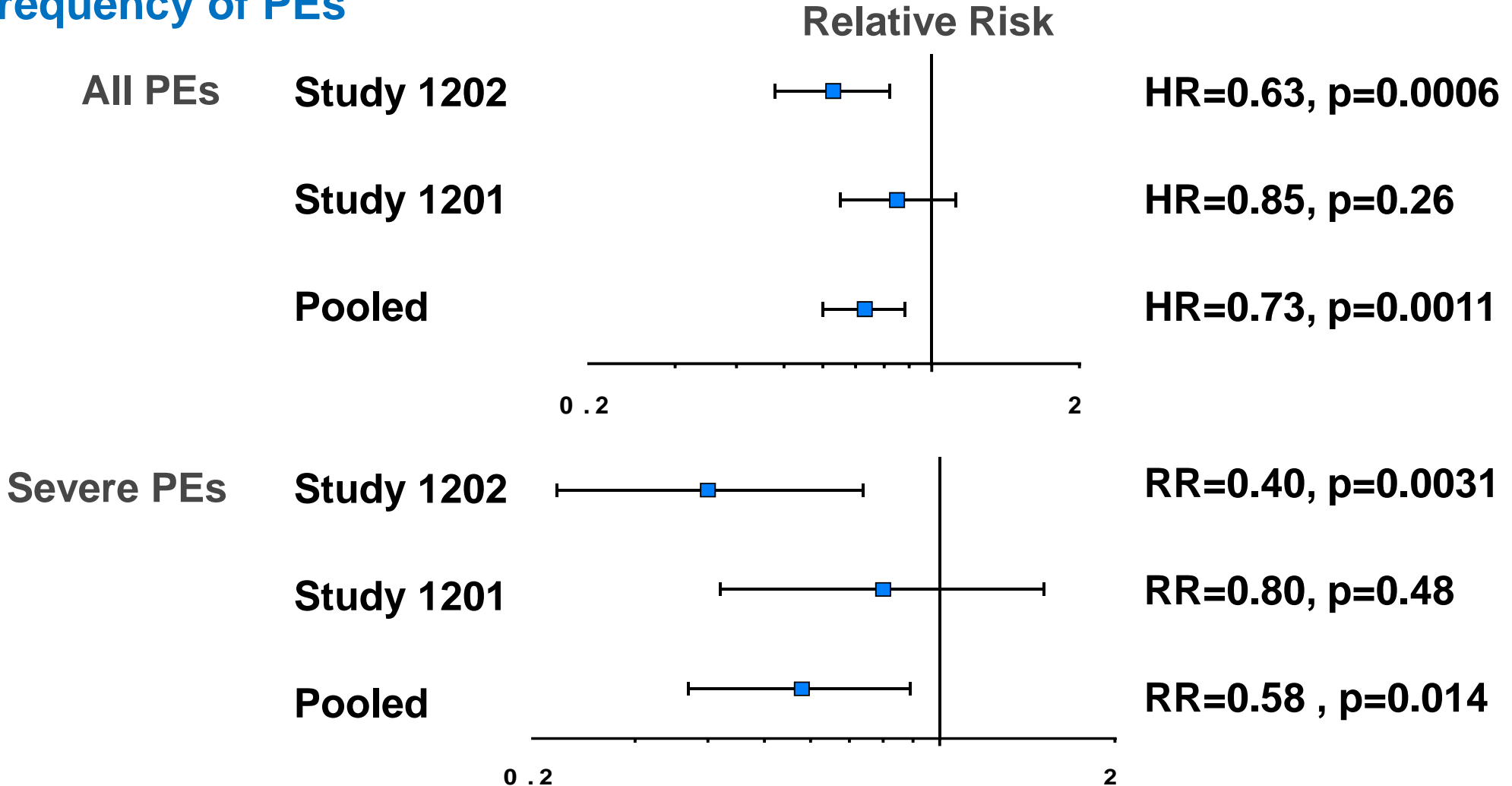


Reducing the frequency of pulmonary exacerbations is the key objective of bronchiectasis therapy

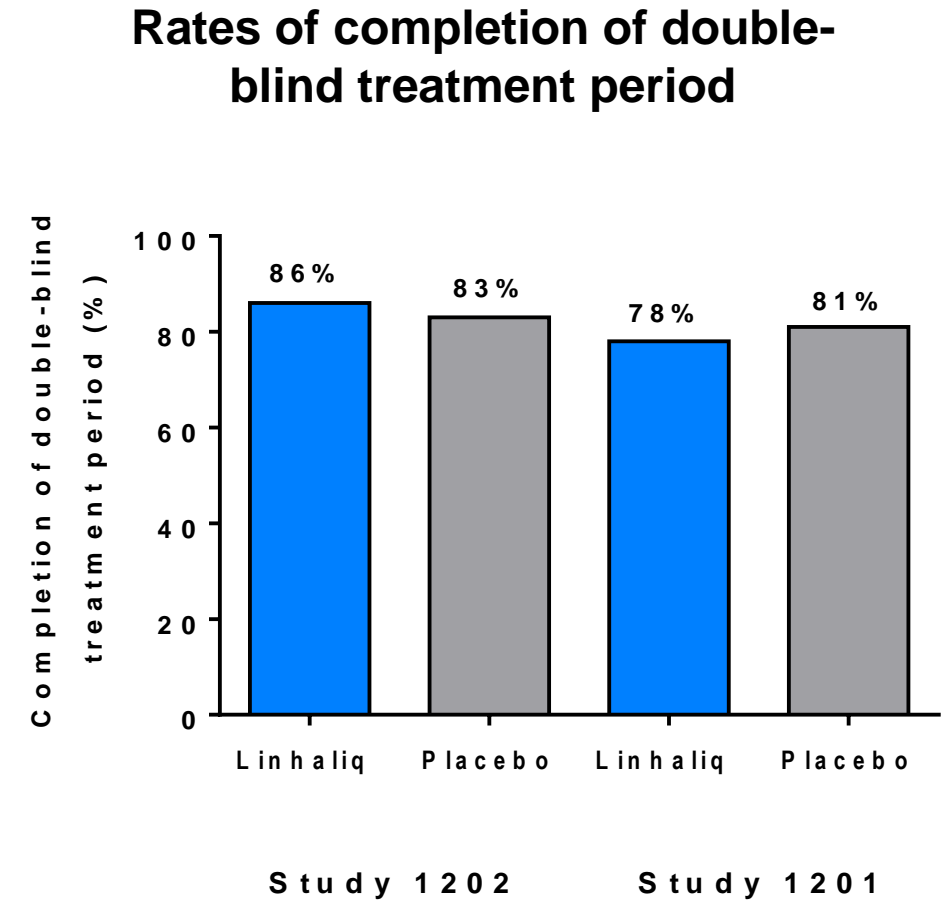
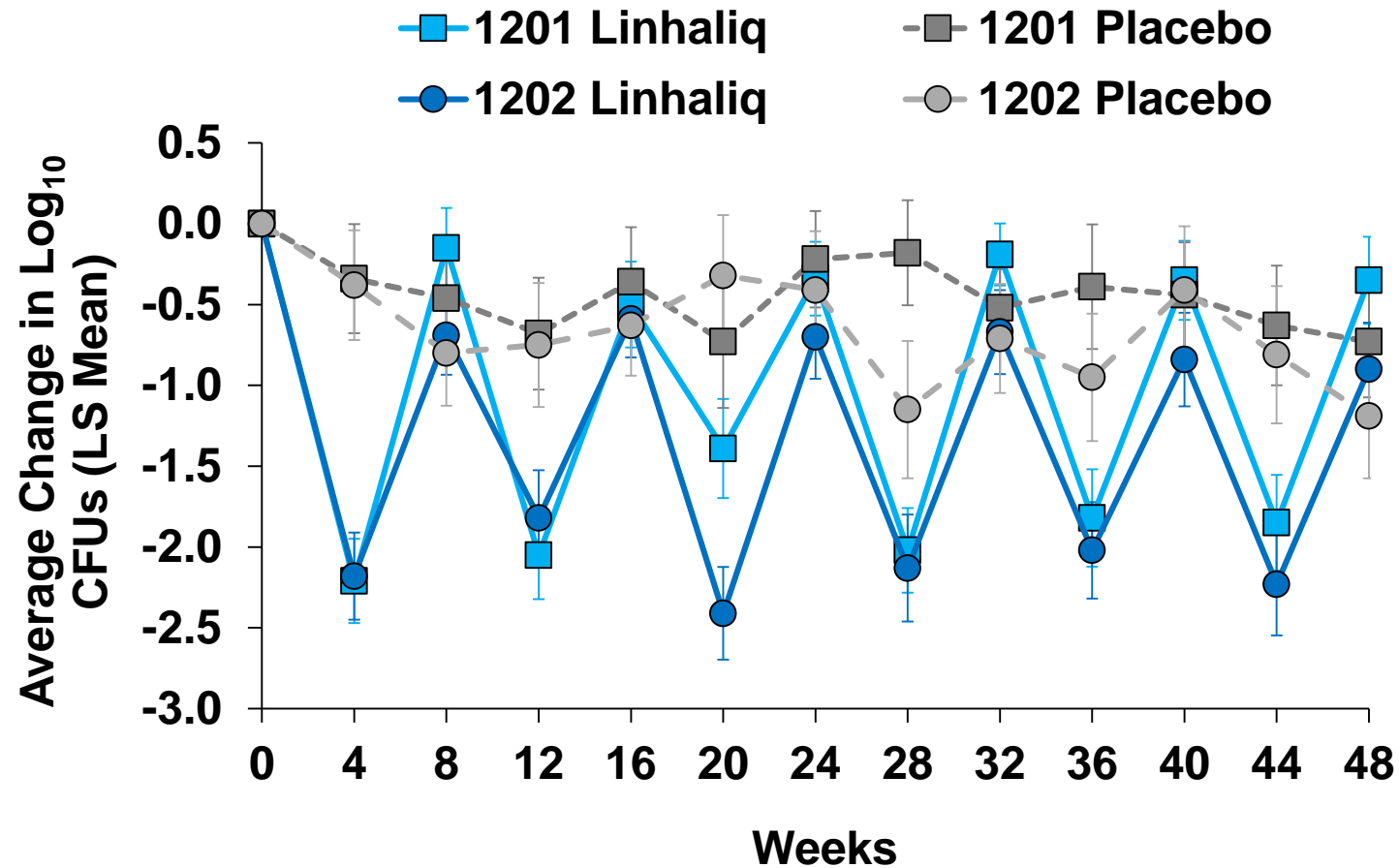
- ◆ Pulmonary exacerbations have a key role in disease progression and morbidity
- ◆ Some patients may never recover from exacerbations – “irreversible morbidity”
- ◆ The major driver in clinical guidelines and clinical practice for the use of prophylactic antibiotic therapies is annual frequency of exacerbations and severity of exacerbations
- ◆ Time to first exacerbation is not used for clinical decision making, but is regarded as a surrogate of annual exacerbation frequency
- ◆ The unmet medical need in bronchiectasis is to identify a safe therapy that can reduce exacerbation frequency and severe exacerbations

PE Endpoints in 1202 (ORBIT-4) and 1201 (ORBIT-3)

Frequency of PEs



Sustained antipseudomonal activity over 48 weeks and high rates of treatment completion



What are the alternatives to Linhaliq?

- ◆ **There is no inhaled antibiotic available on the US market for non-CF Bronchiectasis Patients**
- ◆ **Off label inhaled antibiotic use (10% of patients in the United States bronchiectasis registry)**
 - **Lack of proven efficacy**
 - **Poor tolerability**
 - **Lack of approval means many patients cannot access to therapy**
 - **Compliance is poor (estimated that only 41% of patients adhere to treatment, many discontinue due to side-effects)**

High Rates of Bronchospasm and other Respiratory Adverse Effects with Off-label Inhaled Antibiotics

Inhaled Tobramycin (TSI, TOBI) (Rubin, 2008)

- ◆ Barker et al. (2000): Respiratory AEs by 70% TSI vs. 51% placebo patients
- ◆ Drobnic, et al.(2005): 10% of subjects had bronchospasm while on TSI
- ◆ Bilton et al.(2006): 50% on TSI “wheeze” vs. 15% on placebo

Inhaled Gentamicin

- ◆ Murray et al. (2011):
 - 7 of the original 32 patients subsequently developed bronchospasm during the trial

Inhaled Aztreonam (Cayston, AZLI)

- ◆ Barker et al. (2014):
 - AZLI treatment did not provide significant clinical benefit
 - Adverse events leading to study drug discontinuation 22% vs 6% in AIR-BX1, 10% vs 5% in AIR-BX2

Linhaliq shows very good respiratory tolerability: Pre-specified Adverse Effects of Special Interest (AESI) <5%

**Bronchospasm reported in a very small number of patients in the Phase 3
Linhaliq clinical trials:**

1.3% in the Linhaliq group and 1.0% in the placebo group

Pre-specified Adverse Events of Special Interest $\geq 5\%$: Similar Rates in Placebo and Linhaliq Groups

Events	Linhaliq, %	Placebo, %
Cough	64.5	65.3
Dyspnea	54.2	53.4
Wheezing	39.3	43.5
Chest pain	5.9	4.7
Oropharyngeal pain	4.9	10.4
Chest discomfort	4.9	5.2

Efficacy and Safety Conclusions for Linhaliq

- ◆ The benefits demonstrated in the ORBIT trials are clinically meaningful to physicians and patients
- ◆ Good safety and tolerability profile, high compliance

Linhaliq could have a transformative effect on the field of bronchiectasis

NCFBE PATIENT POPULATION AND MARKET ANALYSIS

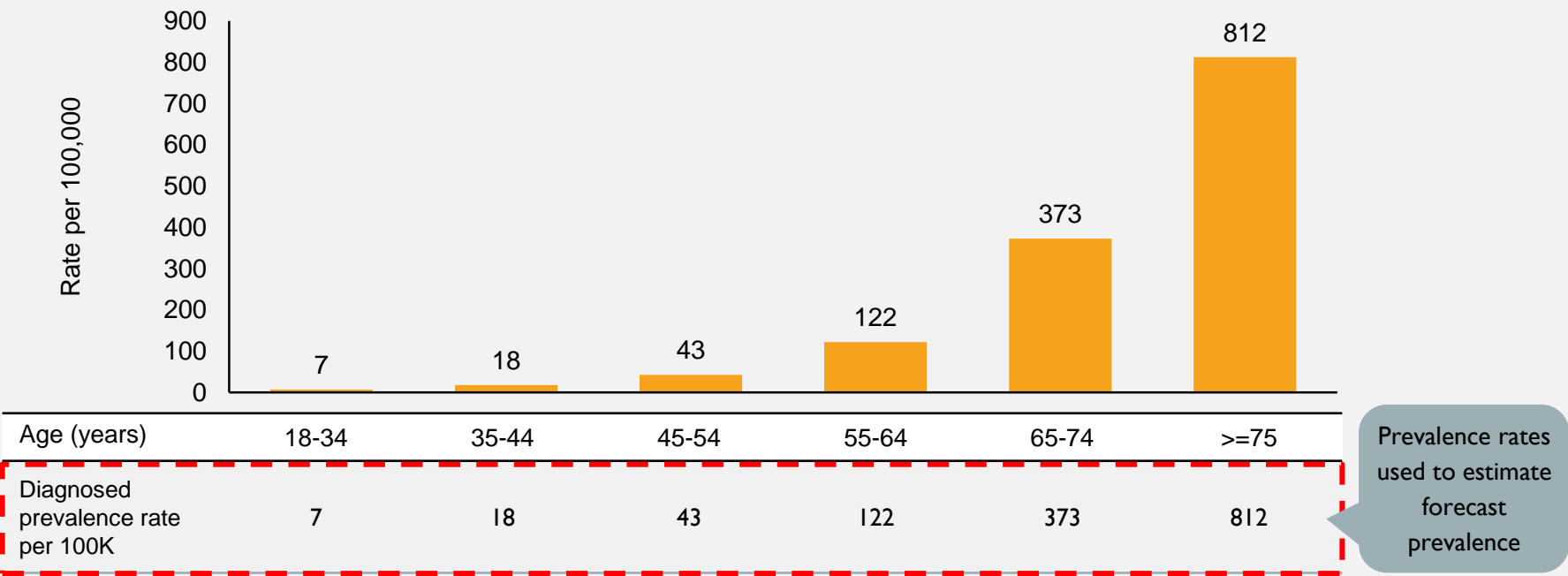
TREVOR SELL

NOVEMBER 9TH, 2017

PREVALENCE OF NCFBE

The Weycker study is the most commonly cited source for NCFBE patient population estimates⁽¹⁾

NCFBE Diagnosed Prevalence Rate by Age Group (31,122 patients with NCFBE identified in study database)⁽¹⁾



- Source based on claims data from Truven Health Analytics database covering a total of ~33.2M lives⁽¹⁾
- Academic studies have estimated prevalence growth rates between 2.0 – 8.7%^(1,2,3,4)
- Studies indicate the historical prevalence rate increased significantly (~8% p.a.) from 2000 – 2013^(1,2) driven by increased HRCT scan utilization, but may be moderated going forward as growth in HRCT usage slows⁽³⁾
- Based on these estimates, 5.0% p.a. overall prevalence growth rate is projected through 2021, tapering to 2.5% by 2025, in line with demographics

(1) Weycker D et al. *Chronic Respiratory Disease*, 2017, Vol. 14(4) 377–384

(2) Seitz et al. *Chest*. 2012 Aug;142(2):432-9.

(3) Quint et al. *Eur Respir J*. 2016 January; 47(1): 186–193.

(4) Sanchez-Munoz et al. *PLOS ONE* 2016; DOI:10.1371.

PREVALENCE OF NCFBE

Prevalence of NCFBE increases substantially with age and with an aging population

US Prevalence (2017 est.)

Age group	Pop. ⁽¹⁾	X	Prevalence Rate ⁽²⁾	=	Prevalence
18 – 34	66M		7 / 100K		4,648
35 – 44	41M		18 / 100K		7,354
45 – 54	43M		43 / 100K		18,670
55 – 64	42M		122 / 100K		50,713
65 – 74	29M		373 / 100K		108,349
>=75	21M		812 / 100K		174,453
Total	243M		150 / 100K		364,187

EU Prevalence (2017 est.)

Age group	Pop. ⁽¹⁾	X	Prevalence Rate ⁽²⁾	=	Prevalence
18 – 34	95M		7 / 100K		6,634
35 – 44	72M		18 / 100K		12,963
45 – 54	75M		43 / 100K		32,415
55 – 64	67M		122 / 100K		81,693
65 – 74	52M		373 / 100K		193,853
>=75	48M		812 / 100K		388,561
Total	409M		150 / 100K		716,120

Asia⁽³⁾ (non-Japan) Prevalence (2017 est.)

Age group	Pop. ⁽¹⁾	X	Prevalence Rate ⁽²⁾	=	Prevalence
18 – 34	457M		7 / 100K		31,964
35 – 44	288M		18 / 100K		51,918
45 – 54	301M		43 / 100K		129,545
55 – 64	210M		122 / 100K		255,867
65 – 74	123M		373 / 100K		459,613
>=75	72M		812 / 100K		587,877
Total	1,452M		150 / 100K		1,516,784

Japan (2017 est.)

Age group	Pop. ⁽¹⁾	X	Prevalence Rate ⁽²⁾	=	Prevalence
18 – 34	18M		7 / 100K		1,294
35 – 44	15M		18 / 100K		2,712
45 – 54	18M		43 / 100K		7,702
55 – 64	15M		122 / 100K		18,888
65 – 74	18M		373 / 100K		66,996
>=75	25M		812 / 100K		202,195
Total	110M		150 / 100K		299,787

(1) US Census Bureau, International Data Base.

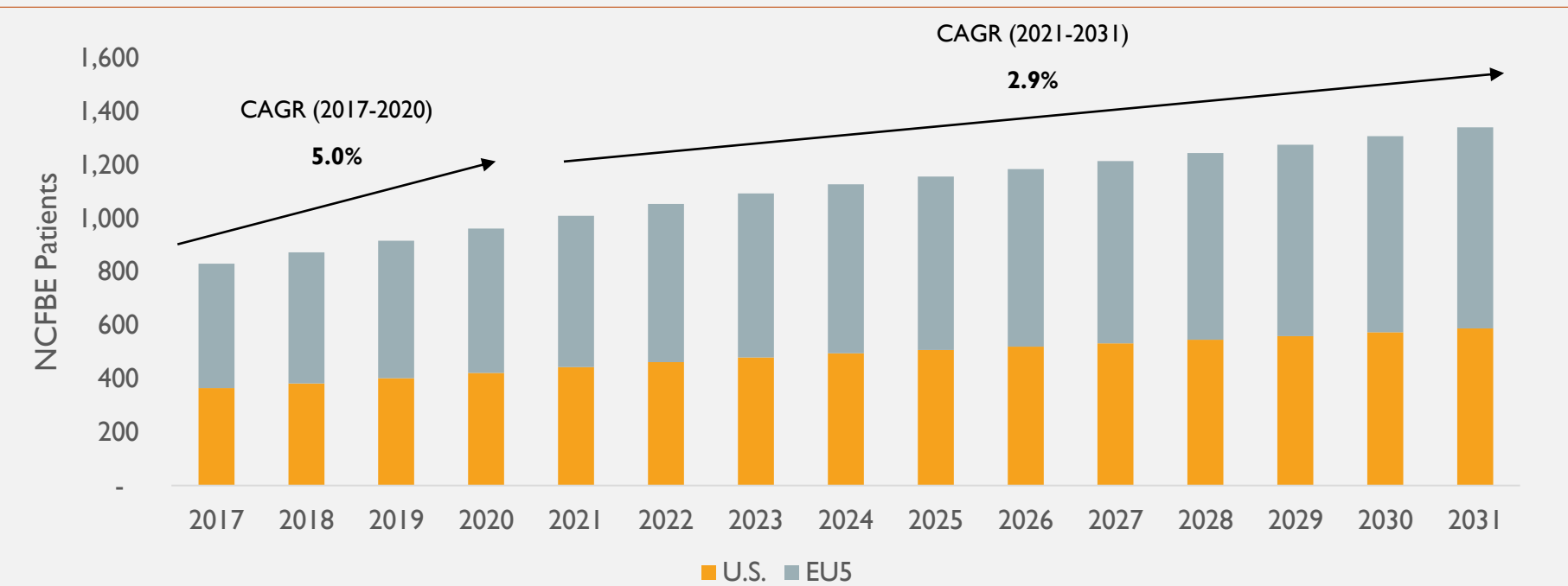
(2) Weycker D et al. Chronic Respiratory Disease, 2017, Vol. 14(4) 377–384

(3) Includes: Australia, China, Hong Kong, Indonesia, Malaysia, New Zealand, Philippines, Singapore, South Korea, Taiwan, Thailand.

PREVALENCE OF NCFBE

The NCFBE patient population is expected to grow ~5.0% p.a. in the coming years as growth in diagnosis rates slows

Total Diagnosed NCFBE Patients (US and EU5) (in thousands)



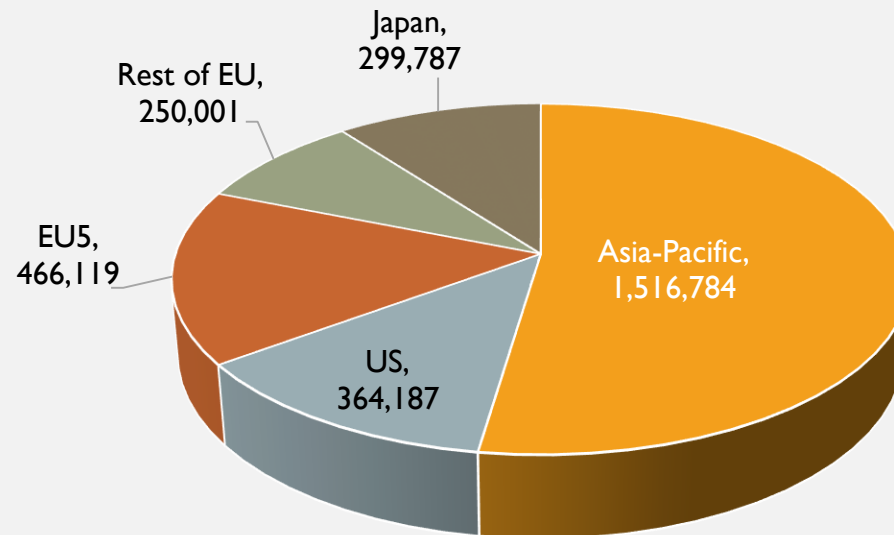
- Growth in the prevalent population is estimated at 5.0% p.a., tapering to 2.5% post-2024⁽²⁾, and is driven by:
 - Growth in the underlying diagnosed prevalence rate per 100,000 people
 - Population growth, particularly in the elderly population, given >75% of patients are >65 years old

(1) Quint et al. Eur Respir J. 2016 January; 47(1): 186–193.

ADDITIONAL MARKET OPPORTUNITIES

Asia-Pacific markets offer very large upside potential to US and EU market forecasts

Prevalence of NCFBE

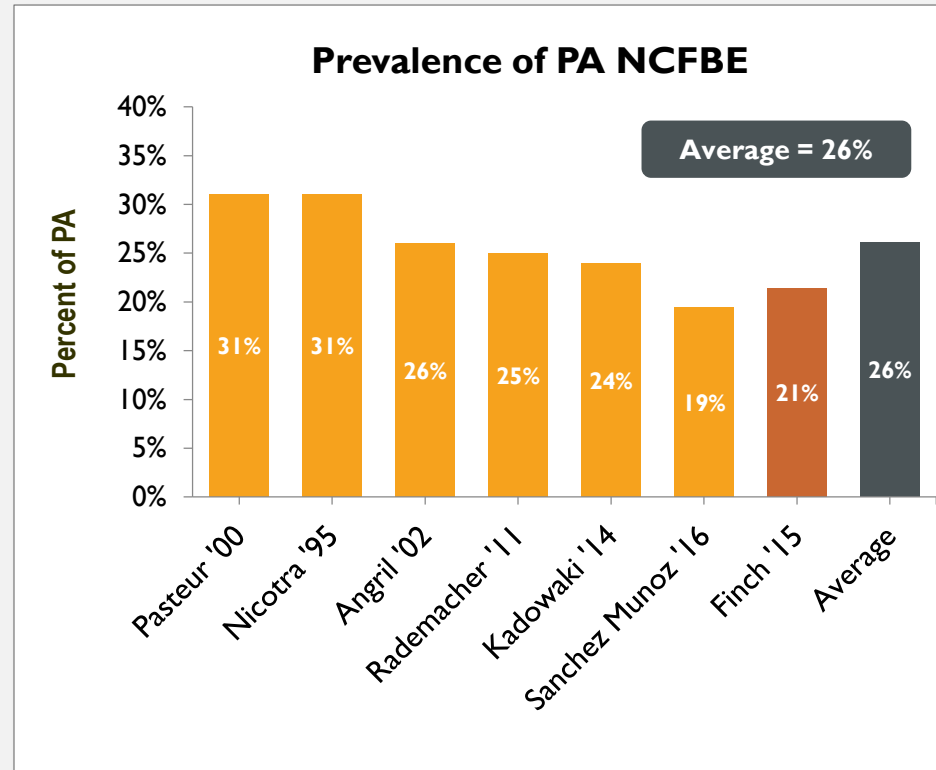


- Asia-Pacific markets present a large additional revenue opportunity
- ORBIT-3 and ORBIT-4 Phase 3 Studies included clinical sites in key target Asian geographies including South Korea, Taiwan, Australia and New Zealand

PREVALENCE OF CHRONIC PA INFECTION IN NCFBE PATIENTS

The prevalence of PA infection among NCFBE patients is not well defined; however, a number of studies suggest it may range between 15 – 58%

Academic literature^(1-6,8)



- Various studies have been conducted to determine the prevalence of PA infection among NCFBE patients
- The true prevalence remains unclear, and may differ regionally driven by climate, diagnostic techniques and other factors
- Blanchette et al. (2017) suggests a range from 15 – 58%⁽⁷⁾ of NCFBE patients may be chronically infected with PA
- Finch et al. (2015) performed an extensive meta-analysis of key studies and estimated a prevalence rate of 21.4%⁽⁸⁾ of NCFBE patients PA infected across all studies

- Authors of academic studies note a number of potential limitations
- Differences in classification of NCFBE as a primary vs. secondary diagnosis across studies
- Data sets limited to local or regional populations
- Lack of radiologic (CT) data to confirm true NCFBE diagnoses

(1) Pasteur et al. *Am J Respir Crit Care Med* 2000; Vol 162. pp 1277–1284.

(2) Nicotra et al. *Chest* 1995;108:955-961.

(3) Angril et al. *Thorax* 2002;57:15–19.

(4) Rademacher et al. *Dtsch Arztebl Int* 2011; 108(48): 809–15.

(5) Kadowaki T et al. *Japanese Resp Soc* 2014; 2212-5345.

(6) Sanchez-Munoz et al. *PLOS ONE* 2016; DOI:10.1371.

(7) Blanchette et al. *Med. Sci.* 2017, 5, 20; doi:10.3390/medsci5040020

(8) Finch et al. *Ann Am Thorac Soc* Vol 12, No 11, pp 1602–1611, Nov 2015

PATIENT COMPLIANCE

Forecast conservatively assumes 70% patient compliance, even though compliance rates of >80% were seen in Phase 3 trials

ORBIT-3/4 Linhaliq Patient Compliance⁽¹⁾

	ORBIT-3	ORBIT-4
% of patients with >= 90% compliance to dosing regimen	80%	86%
% of patients with >= 80% compliance to dosing regimen	89%	92%

- Based on a study of inhaled medication usage in 55,076 COPD patients, Toy et al found that patient compliance was “strongly correlated with dosing frequency”⁽²⁾
- Patient compliance in CF patients using TOBI (2x daily) and Cayston (3x daily) is estimated at around 50%
 - Studies confirm long-term compliance of inhaled medications (including home nebulizers⁽³⁾) may range from 40 – 80%^(3,4)
- Studies suggest that 1x daily dosing has a significant impact on patient compliance⁽⁵⁾:
 - 13 – 26% higher compliance compared to 2x daily dosing
 - 22 – 41% higher compliance compared to 3x daily dosing
- Linhaliq forecast assumes 70% patient compliance, given improved dosing relative to comparable inhaled antibiotics

(1) ORBIT-3 / ORBIT-4 Phase 3 Study Results.

(2) Toy et al. *Respir Med*. 2011 Mar;105(3):435-41.

(3) Bosley et al. *European Respiratory Journal*, 1996, 9, 2346–2350.

(4) Bryant et al. *Respiratory Research* 2013, 14:109.

(5) Saini et al. *American Journal of Managed Care*. 2009 Jun 1;15(6):e22-33.

PRICING COMPS ANALYSIS

Currently there are no approved agents for NCFBE, but as a reference point, inhaled antibiotics TOBI Podhaler and Cayston (approved for cystic fibrosis) were priced at an average \$8,427 (WAC) per cycle, equating to \$35,396 for annual treatment

Product	Company	U.S. Approval (Patent Expiry)	Indication	Dosing Regimen	Cycle Price (Trend) ⁽¹⁾	Estimated Annual Treatment Cost ⁽²⁾	2015 WW Revenue ^(3,4)
Cayston (aztreonam)	Gilead	2010 (Dec'21)	PA in cystic fibrosis	75mg TID; 28 days on + 28 off	\$7,992 (10% CAGR)	\$33,566 / year	\$174M (WW sales 2015)
TOBI Podhaler (tobramycin dry powder for inhalation)	Novartis	2013 (Sep'24)	PA in cystic fibrosis	112mg BID, 28 days on + 28 off	\$8,863 (10% CAGR)	\$37,225 / year	\$167M (WW sales 2015)
				Average:	\$8,427	\$35,396	

TOBI Podhaler and Cayston generated >\$340M in combined global sales in 2015 in cystic fibrosis, a much smaller indication compared to NCFBE

(1) Wolters Kluwer Clinical Drug Information, July 2016.

(2) Net cost, assumes discounts of 30% from ASP accounting for rebates and contracting.

(3) EvaluatePharma.

(4) Company 10Ks (Gilead and Novartis).

PRICING FORECAST ESTIMATES

Current modeled pricing assumption is to price Linhaliq at parity with the currently available branded nebulized and dry powder antibiotics, although premium pricing remains an option depending on payer and marketing partner negotiations

- Currently available branded nebulized and dry powder antibiotics (Cayston and TOBI Podhaler) are priced at an average of \$8,427.41 (per cycle) in US⁽¹⁾
 - Ex-US geographies modeled to assume pricing set 25% below US (\$6,320.56 per cycle) based on EU orphan drug price comps⁽³⁾
 - Modeled forecast assumes price increases of 10% p.a. in US through 2021, in-line with historical Cayston and TOBI Podhaler price increases⁽¹⁾; post-2021 prices increase in-line with inflation (2% p.a.)⁽²⁾
 - No price growth (0% p.a.) assumed in EU territories based on historical Cayston price growth in EU⁽³⁾
 - Asia and Japan price growth modeled in-line with inflation (2% p.a.)⁽²⁾
 - Modeled forecast assumes additional 30% discounts in all geographies to allow for rebates/contracting based on average 2015 gross-to-net discounts across select comparable biopharma companies⁽⁴⁾

(1) Wolters Kluwer Clinical Drug Information, July 2016.

(2) OECD Long-term Forecast Inflation.

(3) Mycka J et al. 2015; ISPOR Orphan Drug Pricing Study.

(4) Company 10Ks (Grifols S.A., Gilead, BioMarin and Novartis).

HEALTH ECONOMIC IMPACT

Acute pulmonary exacerbations impact quality of life and drive expensive hospital admissions

Exacerbations Drive the Health and Economic Impacts of NCFBE



No specific treatment is currently approved for chronic treatment to prevent or reduce the number of pulmonary exacerbations

- ~40% of patients experience 2+ exacerbations per year and these patients have >15% 4-year mortality⁽¹⁾
- Pulmonary exacerbations are a key reason for the high morbidity and mortality of the disease, and a high rate of hospitalizations
- Average cost: \$30-40K+ per hospitalized event^(2,3,4)
 - Most exacerbations due to respiratory infections result in admission to ICU⁽²⁾
 - Average ICU costs estimated between \$4K - \$5K per day with an average stay of 8 – 14 days⁽³⁾
- Agency for Healthcare Research and Quality (AHQR)⁽⁴⁾:
 - Annual age-adjusted hospitalization rate: 16.5 per 100,000 population
 - Rate increased from 1993 to 2006: 2.45% for men, 3.0% for women
 - Women >60 had highest admission rates
- When comparing all-cause healthcare costs between PA and non-PA NCFBE patients, Blanchette et al. estimated PA-infected patients cost 87% or \$31,551 more on average compared to non-PA patients⁽⁵⁾

(1) American Journal of Respiratory and Critical Care Medicine Volume 189 Number 5 | March 1 2014.

(2) Alizaman et al. Chest, Oct 2016; 150#4S.

(3) Dasta et al. Crit Care Med. 2005 Jun;33(6):1266-71.

(4) Seitz et al. Chest 2012.

(5) Blanchette et al. Med. Sci. 2017, 5, 20; doi:10.3390/medsci5040020



ARADIGM

MANAGEMENT PRESENTATION

NOVEMBER 2017

NASDAQ: ARDM

Safe-Harbor Statement

This presentation contains forward-looking statements that are based on Aradigm's current expectations and beliefs and are subject to a number of risks, uncertainties, and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, the extent of cash needs and the sufficiency of cash resources, other financial metrics, expected legal, arbitration, political, regulatory, or clinical results, and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Aradigm (Nasdaq: ARDM), including Aradigm's most recent annual report on Form 10-K and most recent periodic reports on Form 10-Q and Form 8-K. Please refer to Aradigm's most recent Forms 10-K, 10-Q, and 8-K for additional information on the uncertainties and risk factors related to our business. Unless otherwise noted, Aradigm is providing this information as of 3 November 2017 and expressly disclaims any duty to update information contained in this presentation.

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Investment Inflection Points

Linhalig™ is a first in class/best in class product candidate. Linhalig received Orphan Drug and Qualified Infectious Disease Product (QIDP) designations with Fast Track Review for the treatment of a severe respiratory disease with unmet medical need: Non-Cystic Fibrosis Bronchiectasis (NCFBE)

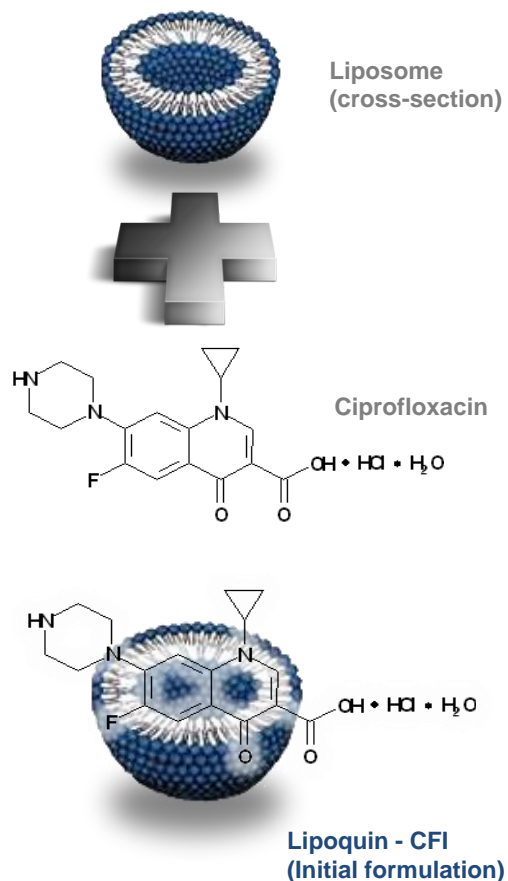
Accomplished and Near-term Milestones

Date	Milestone
Sept 2017	■ NDA accepted for filing with Priority Review (PDUFA date Jan 26 2018)
Q4'17/Q1'18	■ Advisory Committee possible
Q1/Q2'18	■ Anticipated US approval, commercial launch in US
Q1'18	■ Planned submission to EMA for regulatory approval
Q4'18/Q1'19	■ Anticipated EU approval, commercial launch in EU

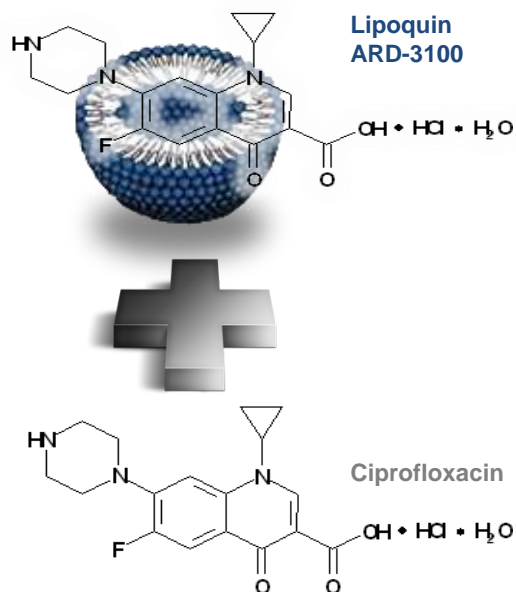
Linhaliq - Superior antibacterial activity in sputum plus anti-inflammatory effect

Linhaliq is a proprietary combined formulation of encapsulated and un-encapsulated ciprofloxacin that is designed to be inhaled once daily using a common and easy to use nebulizer that even patients with severely impaired lung function can use

Lipoquin ARD-3100



Linhaliq - ARD-3150



Pari LC Sprint Nebulizer

Inhaled once daily using
FDA-cleared Pari LC
Sprint Nebulizer



Key Goals for Linhaliq

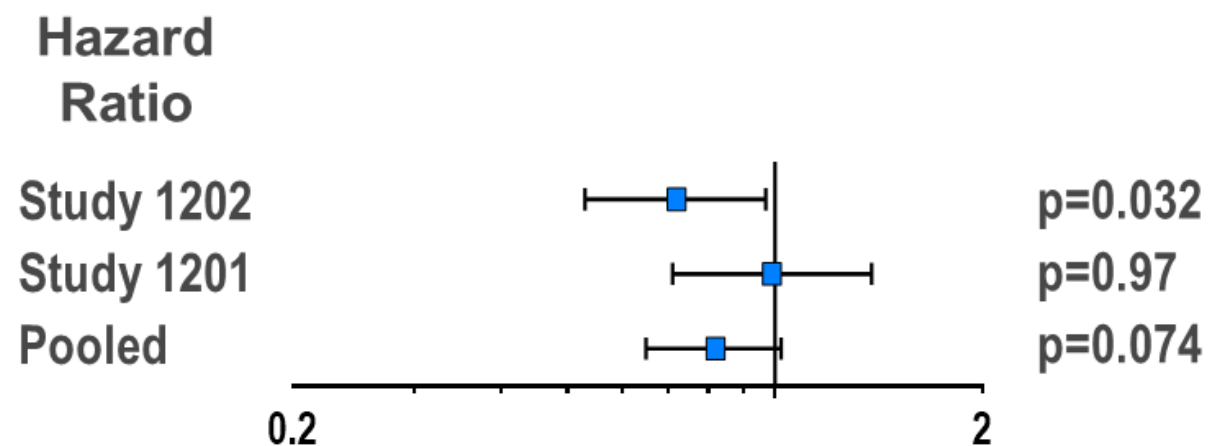
- **Linhaliq was designed to treat NCFBE patients with chronic lung infections with *Pseudomonas aeruginosa* (PA) and at least 2 pulmonary exacerbations (PEs) in the prior year treated with antibiotics**
 - These are the patients at the highest risk, with much higher morbidity, mortality and healthcare costs.
- **The primary and secondary endpoints focused on the ability of Linhaliq to prevent and reduce the number of PEs – the key goals of treatment of these patients**
- **Safety, tolerability, convenience**
 - Use liposomes to minimize irritation of airways and facilitate once daily dosing

Regulatory Paths

- **US: FDA MODERNIZATION ACT**
 - **ORBIT- 4 (ARD-3150-1202) provides substantial evidence of efficacy, met the primary and key secondary endpoints**
 - ORBIT- 3 (ARD-3150-1201) and ORBIT- 2 provide supporting evidence
 - Integrated safety supports Linhaliq's positive risk/benefit
- **EU: Totality of evidence including assessment of benefits of Linhaliq to reduce and prevent pulmonary exacerbations**
 - Focus on PEs requiring intervention with antibiotics

Time to First PE prolongation similar between 1202 and 1201

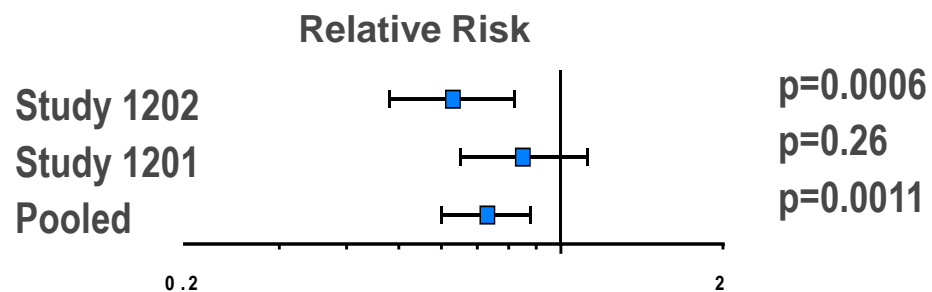
Stratified Unweighted Log rank Test



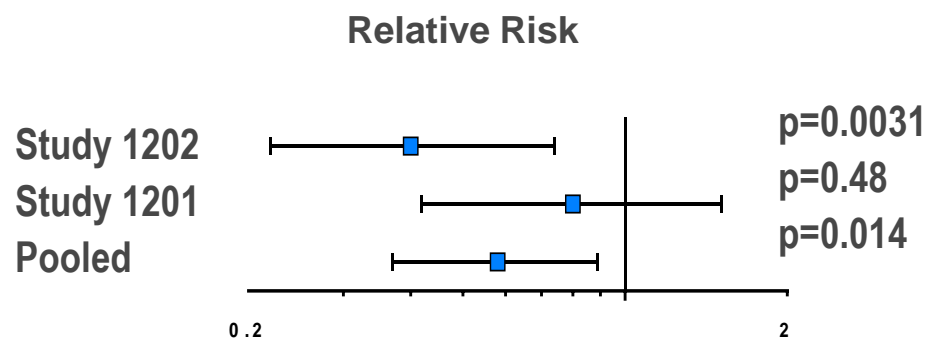
Frequency of all and severe PEs

Stratified Negative Binomial Regression

All
PEs

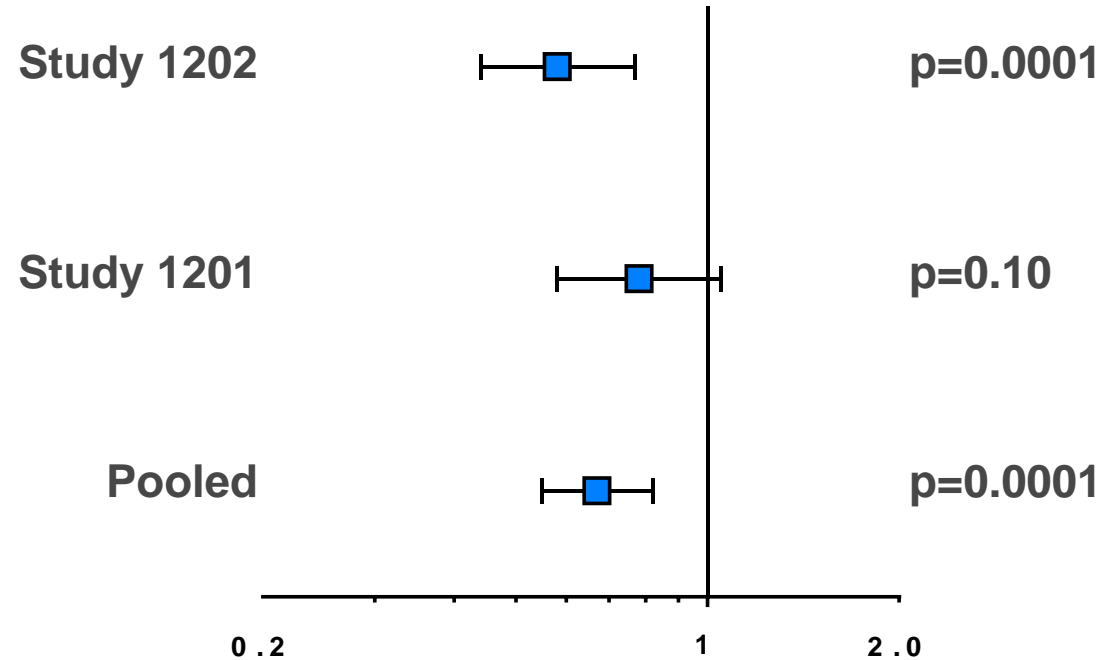


Severe
PEs



Reduced Risk of PEs Requiring Intervention with Antibacterials (Moderate or Severe PEs)

Stratified Negative Binomial Regression

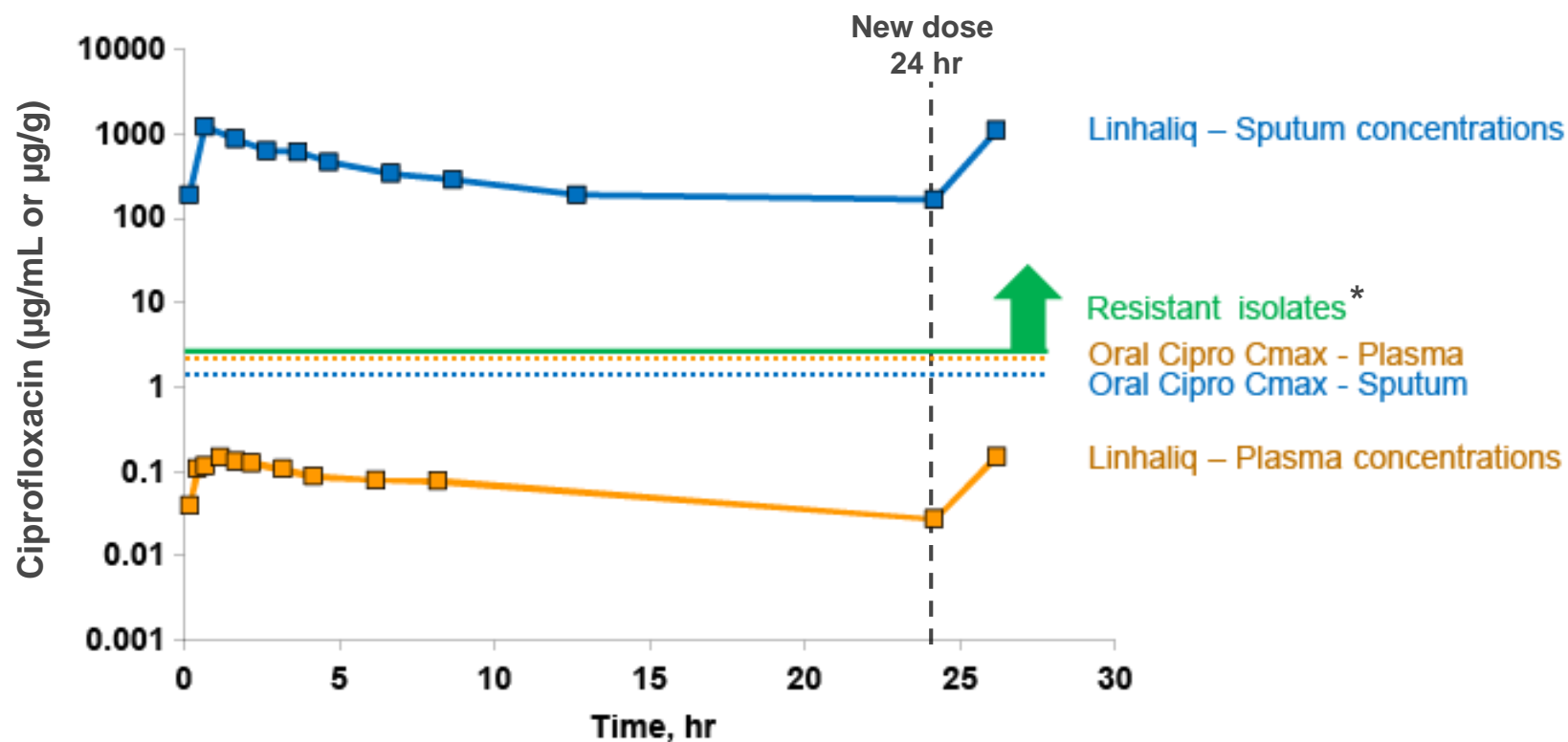


Risk Ratio for PEs Requiring Intervention

Did resistance to ciprofloxacin at study entry impact the efficacy of Linhaliq?

- **Patients with NCFBE are often chronically infected with *Pseudomonas aeruginosa* (PA), requiring multiple courses of oral and IV antibiotics including quinolones for treatment of pulmonary exacerbations (PEs)**
 - Repeated antibiotic treatment of PEs often results in ciprofloxacin resistant PA isolates from sputum
- **Linhaliq produces high concentrations of ciprofloxacin within the airway and minimizes systemic exposure**
 - Expected to be effective even against PA that are deemed to be resistant to oral and IV ciprofloxacin

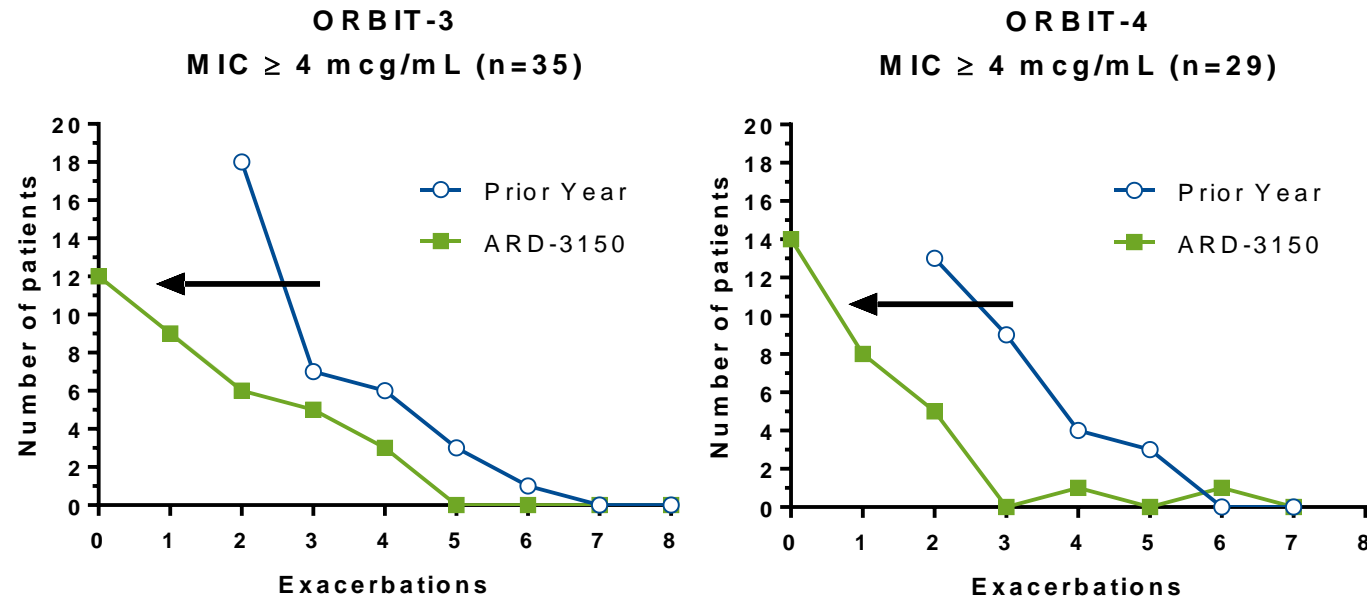
1202 and 1201: Sputum and Plasma Ciprofloxacin Exposures



* MIC \geq 4mcg/mL is deemed to be resistant to oral and IV ciprofloxacin

Reduction in Exacerbations in Patients With Resistant Isolates of PA at Study Entry

Treatment with Linhaliq reduced the number of PEs compared with the prior year in patients with resistant isolates at baseline ($\text{MIC} \geq 4 \text{ mcg/mL}$), shifting the exacerbation profile (ORBIT-3 = 1201, ORBIT 4 = 1202)



Partnership with Grifols, S.A.

GRIFOLS

Grifols (BME:GRF) is a biopharmaceutical company that develops, manufactures and distributes plasma derivative and respiratory products in the US and internationally

Key Statistics

Founded	1940
Headquarters	Barcelona, Spain
Employees	~ 15,000
Strengths	<ul style="list-style-type: none"> ▪ Significant specialty respiratory salesforce in place in both US and Europe ▪ Prolastin (for α-1 antitrypsin deficiency respiratory orphan disease) has 67% global market share and leading market share in the US ▪ 10 plus years detailing Prolastin to pulmonologists

Key financials in the licensing agreement:

- The royalty rate is 12.5% on the first \$300 million of annual sales for all territories and all indications, and 20% for annual sales in excess of \$300 million
- \$15 million in pre-approval and approval milestones remaining
- Aradigm responsible for the product supply
 - Sale to Grifols at “Cost of goods + mark-up”
 - Use US-based contract manufacturer Exelead who produced Phase 3 supplies at commercial scale

Key Investment Highlights:

NDA accepted for filing with Priority Review – PDUFA date Jan 26 2018

Aradigm is well-positioned to start generating in 2018 double digit royalty revenues from sales of Linhaliq in Non-Cystic Fibrosis Bronchiectasis (NCFBE), with potential upside from other indications



Aradigm believes the NCFBE indication for Linhaliq will exceed \$500MM of sales by 2021

- Ladenburg analysts project \$1B sales by 2022, Nektar projected \$750 million for their NCFBE product with Bayer



Important objectives achieved in Phase 3

- Prevention and reduction in frequency of pulmonary exacerbations
- High persistent drug concentrations in sputum, low in blood
- Sustained powerful antipseudomonal activity even for patients with resistant isolates
- Good safety and tolerability



US Orphan Drug Designation with no existing approved therapies



Commercial Launch in US expected in Q2'18

EU approval expected Q4'18/Q1'19



QIDP Designation and Fast Track received

- FDA priority review accompanies QIDP designation



Sole competitor: Bayer's twice daily, dry powder inhaled ciprofloxacin

- "Unencapsulated" inhaled antibiotics TOBI, Cayston and colistin have failed in all NCFBE trials
- Bayer's first Phase 3 showed efficacy with 14 day BID cycles and failed with 28 day cycles; second Phase 3 trial failed criteria agreed with FDA



Strong IP protection to 2031

- 8 patents issued in US; 41 issued patents in 37 countries outside the US



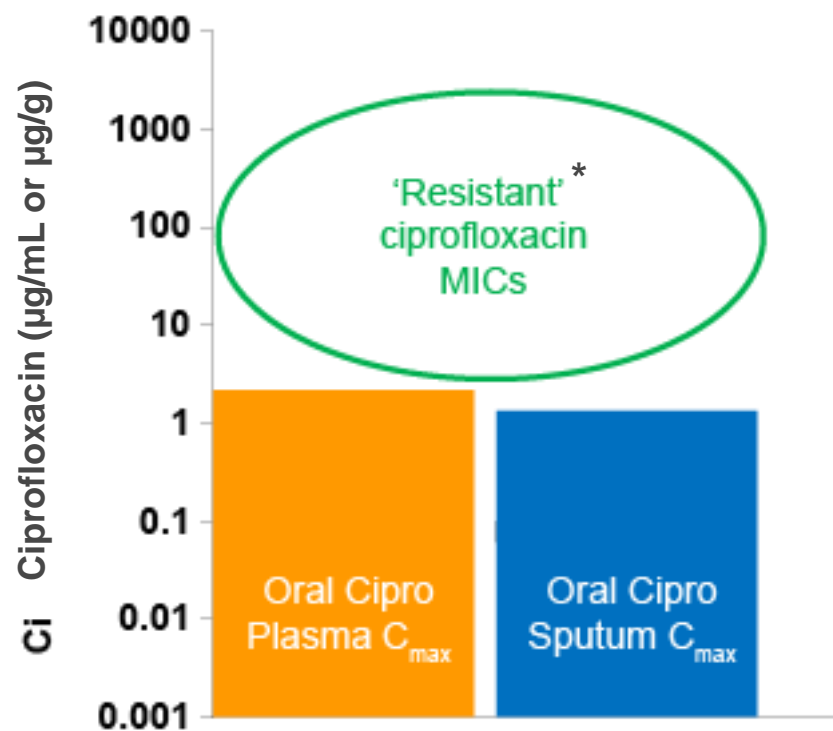
Linhaliq is administered once daily:

- Active in biofilms, uptake by macrophages

THANK YOU!

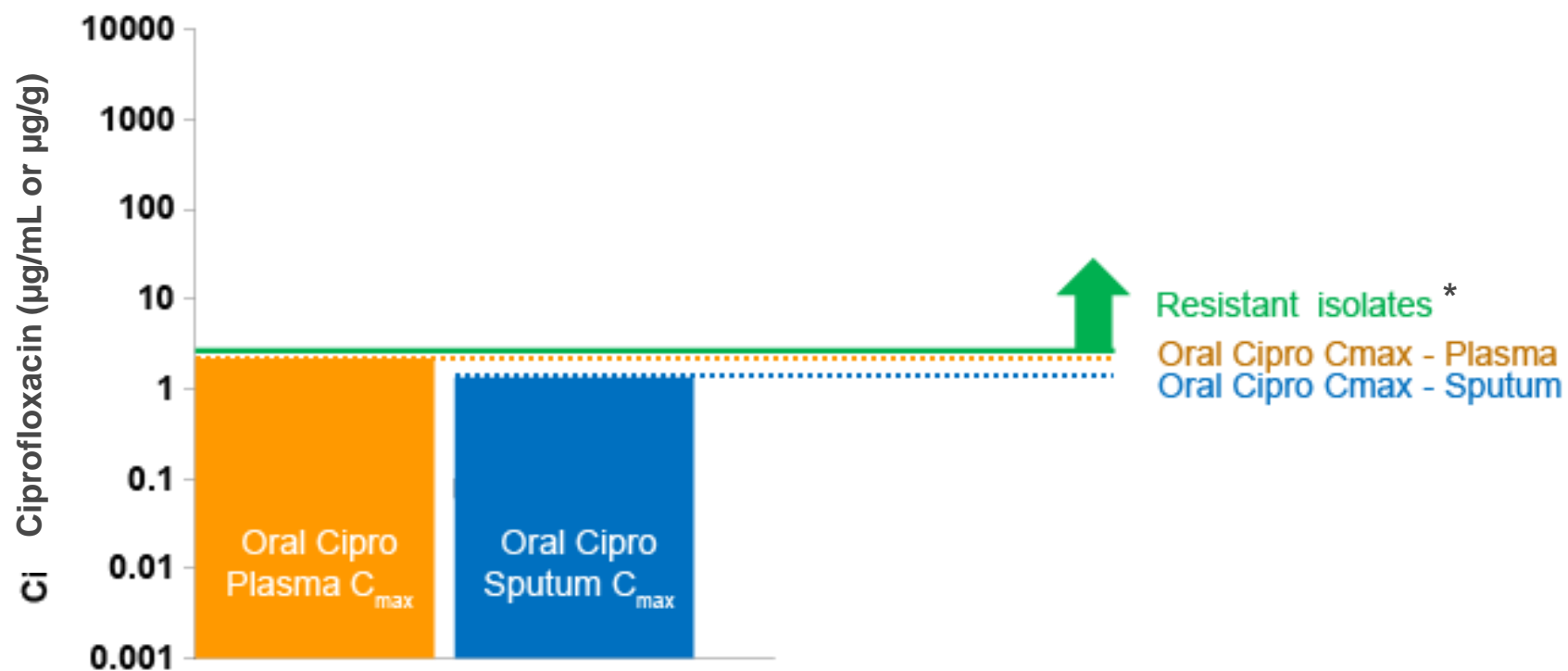
Any questions?

Oral Ciprofloxacin PK and *In Vitro* Susceptibility Breakpoint



* MIC \geq 4mcg/mL is deemed to be resistant to oral and IV ciprofloxacin

Oral Ciprofloxacin PK and *In Vitro* Susceptibility Breakpoint



* MIC ≥ 4 mcg/mL is deemed to be resistant to oral and IV ciprofloxacin