

# Verona Pharma plc

## **“First-in-Class” Drugs to Treat Unmet Needs in Respiratory Diseases**

*A UK-based drug development company*

*Preliminary Results 2012*

10<sup>th</sup> April 2013

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# Agenda

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- Dr Jan-Anders Karlsson, CEO Verona Pharma – biographical sketch
- 2012 Results overview
- Update on Company strategy
- RPL554 – a unique approach to COPD
- VRP700 – a unique approach to treat chronic, severe cough
- An accomplished Board of Directors and Management
- Shareholder analysis
- Newsflow
- Investment Highlights

# Jan-Anders Karlsson

*30 years in the pharmaceutical industry*

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- CEO since June 2012
- CEO; S\*BIO Pte Ltd (Singapore) from 2005
  - Oversaw discovery of 6 novel drug candidates
    - Brought the lead JAK2 inhibitor pacritinib to phase III
    - Brought HDAC inhibitor pracinostat to phase II
  - Established multiple international drug-development and commercial partnerships
- EVP Global Research; Bayer Pharma
  - Member of the Executive Management Committee with responsibility for global drug discovery organization
  - Bayer from 1996
- Numerous management positions; RPR, Astra AB

# 2012 Highlights

## *Strategic Focus, Clinical Progress and Financial Prudence*

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### Operational Highlights

- Dr. Jan-Anders Karlsson succeeded Professor Michael Walker as CEO (June)
  - Strategic review undertaken
- Anti-inflammatory, LPS challenge clinical trial on lead drug, RPL554 started
  - Medicines Evaluation Unit (MEU), Manchester, UK.
- New patent granted for RPL554 by the USPTO.
  - Fourth patent granted for RPL554 and related compounds in the U.S.
- Clinical data on bronchodilator effects of RPL554 presented:
  - In COPD patients at ERS
  - In Asthmatics at the International Severe Asthma Forum (ISAF)

### *Post-period*

- *RPL554 demonstrated substantial anti-inflammatory effect in COPD-like inflammation in challenge study (Mar 2013)*

### Financial Highlights


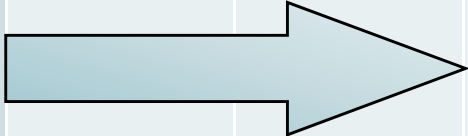
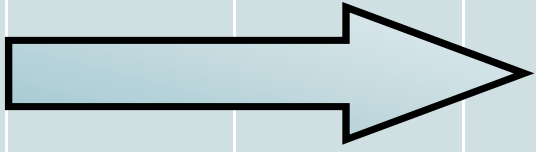
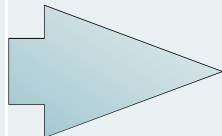
- Loss after tax of £2.52m (2011: £1.72m); Cash at 31 Dec. 2012 of £0.96m (2011: £2.53m)

### *Post-period*

- Completed a £1.1m share placing and entered into a £5m equity financing facility with Darwin Strategic Limited (Jan 2013)



# Promising pipeline of drugs with novel mechanisms of action

Project	Indication	Mechanism of Action	Pre-clinical	Phase I	Phase II	Phase III	Market
RPL554	Bronchodilator for COPD (asthma)	PDE3/4 inhibitor					
	Anti-inflammatory						
VRP700	Chronic, severe cough	Novel (undisclosed)					
NAIPs	Inflammation	undisclosed					

# Refining the strategy

*Fastest route to market to build shareholder value*

- RPL554: Focus on nearer-term value generation
  - Leveraging proven potent bronchodilator properties
  - Target high unmet need in COPD
    - Patients presenting at hospital with acute exacerbation
    - Different mechanism of action; complementary to existing bronchodilators
    - Allows commercial flexibility
- RPL554: Continue to broaden therapeutic use
  - Incrementally expand potential market positioning
  - Anti-inflammatory potential
    - Broader profile to be pursued with commercial partner at the right time
- VRP700: Focus on treating chronic, severe cough
  - Confirm significant activity already seen in investigator-run pilot study
  - True innovation in a large market lacking effective options



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# **RPL554 – a unique approach to treat COPD**



# RPL554: a novel bronchodilator to treat severe COPD

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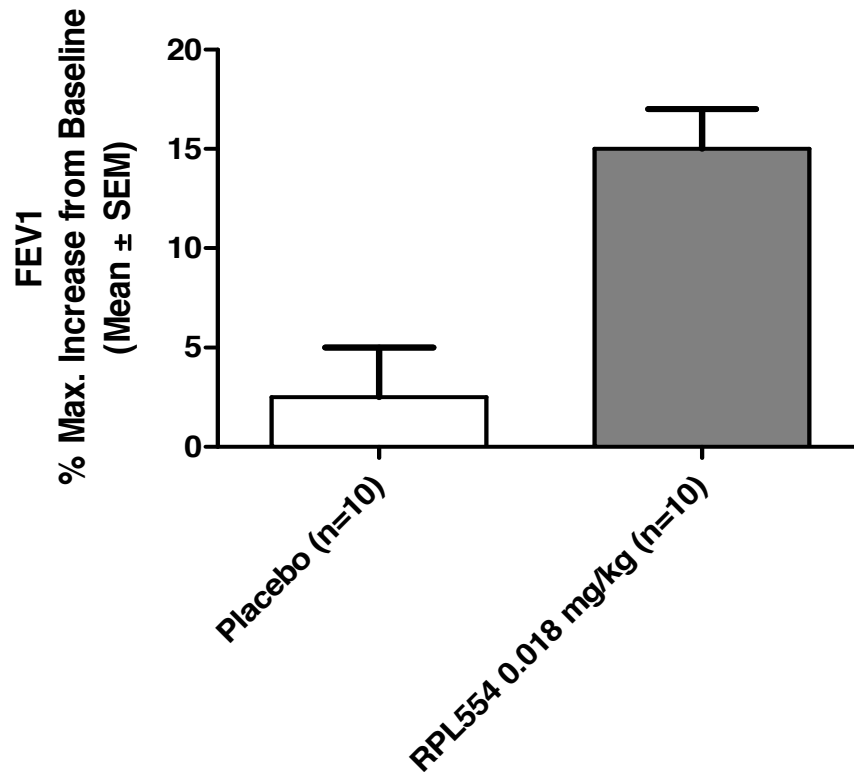
- Preliminary target product profile:
  - Nebulized RPL554 as a bronchodilator in patients with severe COPD
    - Hospitals and Specialist Care settings
- COPD expected to be third leading cause of death in the world by 2020
  - Up to 75% of sufferers do not receive treatment
  - In the US c.24 million people have mild to severe COPD
    - BOLD study says only 10 million know it!
- Strong pharmacoeconomic argument for proposed use
  - In one year in the US COPD causes:
    - 8 million primary care office visits
    - 1.5 million emergency room visits
    - 750,000 hospitalizations
    - 119,000 deaths

# RPL554 clinical studies – what has been achieved

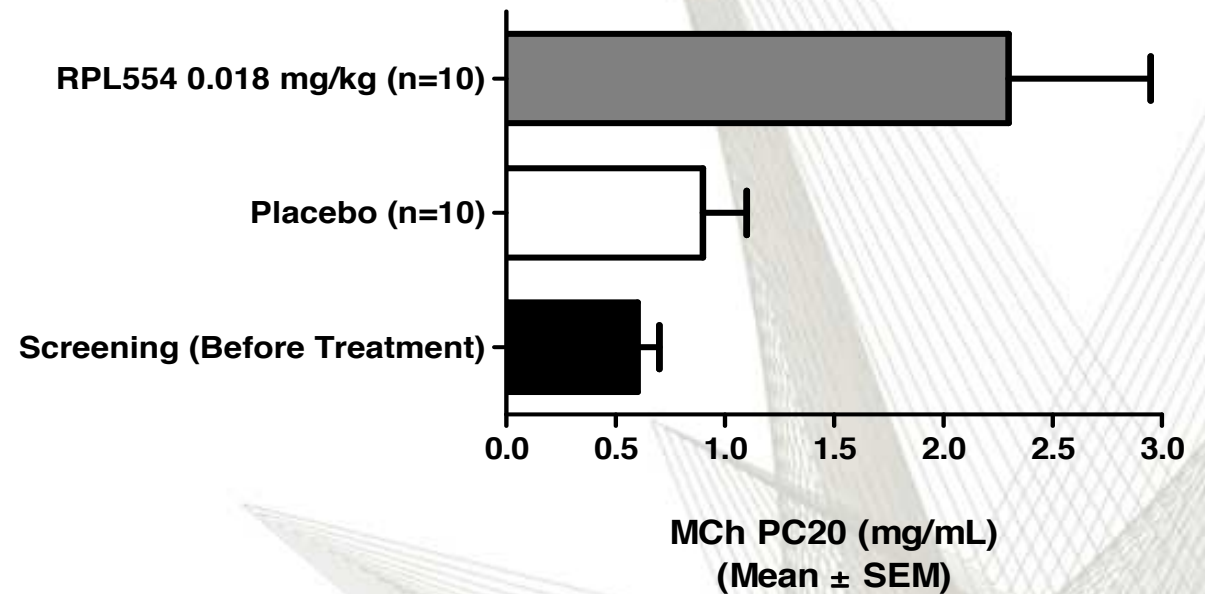
Development Stage	Subjects	Subjects treated with RPL554	Outcome of study
Phase I/II	Healthy subjects	12	RPL554 is well tolerated
	Mild Asthma / Rhinitis	26	Bronchodilator and possibly anti-inflammatory after single dose
Phase IIa	Mild to Moderate Asthma	26	Bronchodilator, reduces bronchial hyper-responsiveness and well tolerated for one week
Phase IIa	Mild to Moderate COPD	12	Well tolerated and bronchodilator
Phase I	Healthy subjects	21	Anti-inflammatory effect after one week treatment
	<b>Total number of treated subjects:</b>	<b>97</b>	

# RPL554 improves airway function in asthmatics

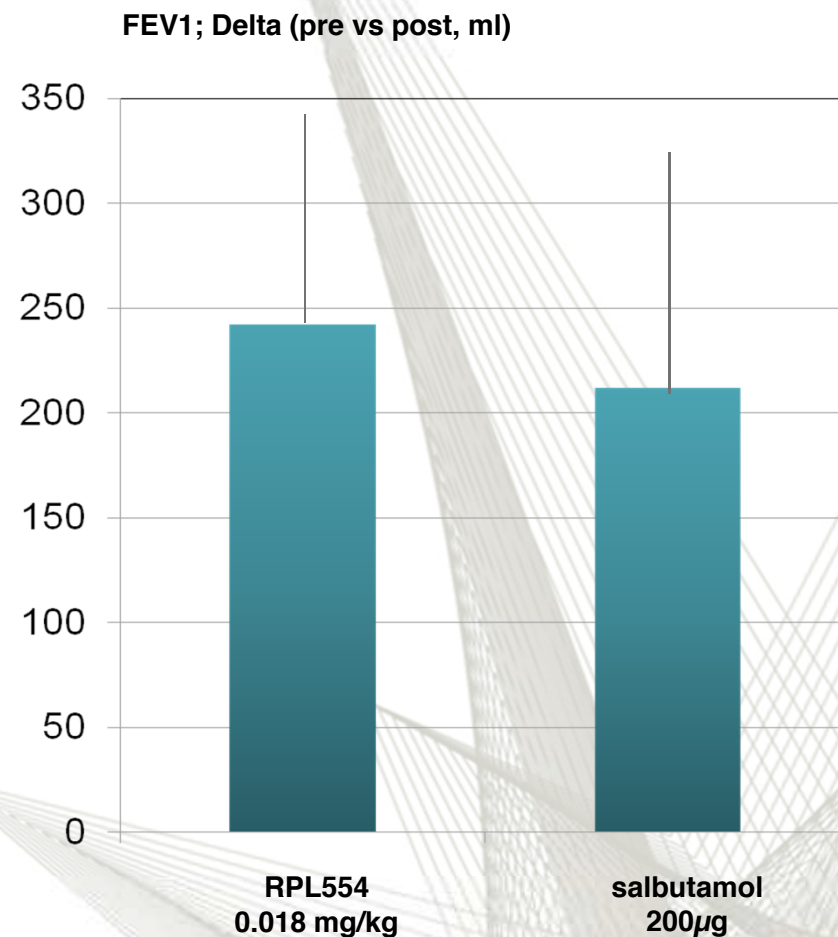
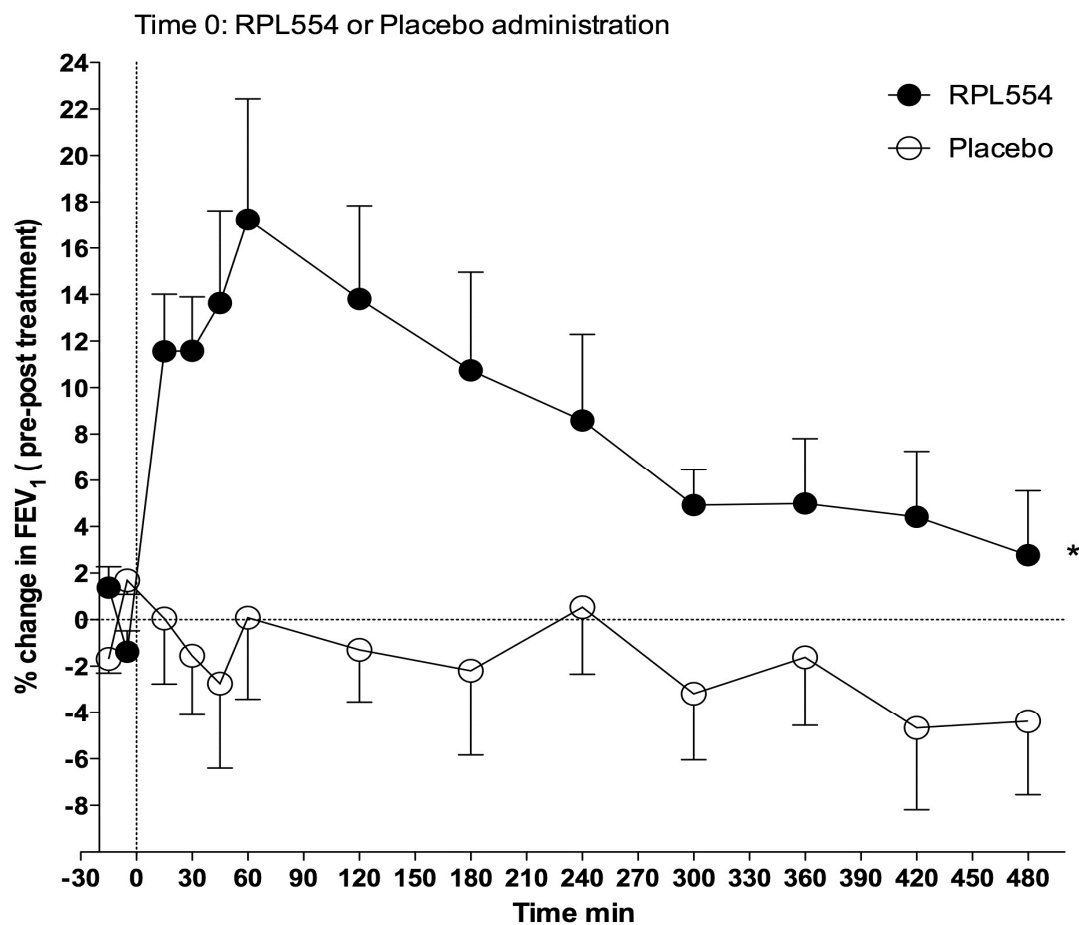
Produces Bronchodilation



Reduces airway sensitivity to metacholine challenge



# RPL 554 induces rapid and pronounced bronchodilation in COPD patients



Cazzola M, et al, ERS, 2012

# RPL554 demonstrated anti-inflammatory effect in clinical study

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- Placebo-controlled, double-blind clinical trial designed to specifically evaluate the anti-inflammatory properties of RPL554 in healthy subjects challenged with an inhaled irritant.
  - Relevant to inflammation seen in COPD patients.
- Statistically highly significant reduction in total cells and in various types of inflammatory cells in RPL554-treated, compared to placebo-treated, subjects
- RPL554 was well tolerated in these healthy subjects.
- No evidence of cardiovascular or gastrointestinal side effects.
- The primary end point was a reduction in the proportion of neutrophil cells, to total inflammatory cells in the sputum.
  - There was a strong trend in favour of the primary endpoint, but the study narrowly missed reaching statistical significance even though there was a highly significant reduction in the *absolute* number of neutrophils.



# Clinical Data supports profile & significantly de-risks programme

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- Clinically significant bronchodilation
  - Demonstrated in COPD, asthma, and allergic rhinitis patients
  - Rapid onset of action
  - Peak effect at *c.*1h
- Anti-inflammatory effect demonstrated in human subjects
- Complementary and unique mechanism of action
- Well tolerated
- No evidence of:
  - Dose-limiting beta2-agonist like side effects e.g. tremor or hypokalemia,
  - Anti-cholinergic like side-effects e.g. dry mouth
  - Dose-limiting PDE4 – like side effects e.g. nausea and vomiting

**Phase II efficacy and safety data significantly de-risks opportunity**

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## **VRP700 – a unique approach to treat chronic, severe cough**

# Chronic Severe Cough – The Opportunity and the Challenge

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- VRP700: Significant activity already seen in investigator-run pilot study
  - Novel mechanism of action
- Cough is the most common symptom for which medical advice is sought
- Chronic, severe cough is common in many conditions
  - Including, severe lung disorders such as interstitial lung diseases and idiopathic pulmonary fibrosis
- Current therapies are ineffective or have significant side effects
- Significant seasonal US cough/cold prescription market
  - c.35m prescriptions p.a. in the US alone
  - Generics/branded generics

# Verona Pharma's solution: VRP700

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VRP700 is

- A “first-in-class” drug with unique mechanism of action and administered via inhalation
- Significant antitussive activity in pre-clinical models

Development Stage *	Subjects	Subjects treated with VRP700	Outcome of study
Phase IIa	Lung disease with chronic severe cough	8	Significant anti-tussive activity measured objectively and via questionnaire Well tolerated
Phase IIa	Lung disease with chronic severe cough	About 20 planned	Confirm anti-tussive activity
	<b>Total number of treated subjects:</b>	<b>8 (28)</b>	

\* VRP700 was well tolerated in previous studies involving > 100 patients

Near-term strategy

- Confirm anti-cough activity in patients with severe lung disease

# Verona Pharma Management Team and Key Consultants

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## **Lui Franciosi, COO**

Experience of drug and medical device trials in academia and industry with post-doctoral research in COPD progression modelling at GSK, UK and CHDR, The Netherlands

## **Danny Lowe, CFO**

Part time: Previously CFO for several public companies in the drug discovery, alternative energy and mineral resources sector

## ***Advisors with substantial industry experience:***

### **Grahaem Brown, Clinical Development and Clinical Operations**

Formerly Glaxo, Novartis, Pharmacia, UCB/Celltech

### **Peter Spargo, CMC and Manufacturing**

Formerly Pfizer, Novexel

### **Lars-Goran Carlsson, Clinical Development**

Formerly AstraZeneca

### **Bengt Sarnstrand; Clinical Project Management and Clinical Development**

Formerly AstraZeneca

## ***Clinical and Scientific Advisory Board:***

KOLs to further guide development : *To be announced soon*



# Verona Pharma Board of Directors

*Extensive experience in the pharmaceutical and financial industries*

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## **Prof. Clive Page**, *Non-Executive Chairman*

Company co-founder. Recognised international authority on lung diseases and inflammation. Co-inventor of NAIPs technology. Joint Head of IPS King's College London

## **Dr. Jan-Anders Karlsson**, *Chief Executive Officer*

Former CEO of S\*Bio Pte Ltd, Singapore. Previously R&D roles in pharmaceutical industry, incl EVP Research Bayer Healthcare AG, Rhone Poulenc Rorer and Astra

## **Claire Poll**, *Corporate Director*

Legal & corporate executive. Previously Corporate Development Director Inmarsat Ventures plc (LSE: c. £2.5b market cap)

## **Prof. Trevor Jones**, *Non-Executive Director*

Former Director General, Association of the British Pharmaceutical Industry. Successfully led development of numerous drug treatments as R&D Director at The Wellcome Foundation

## **Dr. Patrick Humphrey**, *Non-Executive Director*

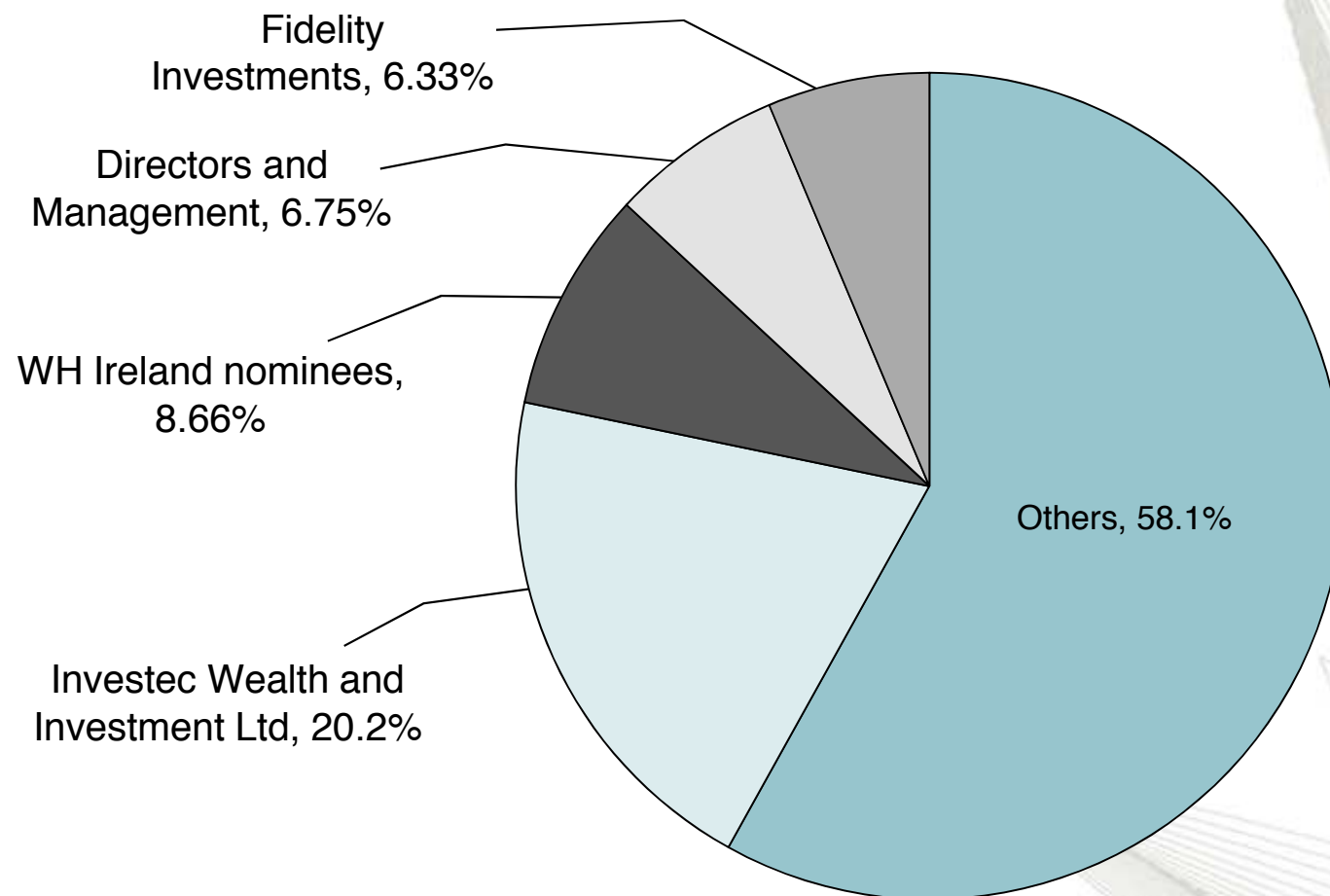
Former Director of GlaxoSmithKline's Division of Pharmacology. Instrumental in the discovery of numerous respiratory and CNS drugs on the market. Latterly the Executive Vice President and Head of Research at Theravance in South San Francisco from 2001 to January 2008.

## **Stuart Bottomley**, *Non-Executive Director*

Financier & former leading fund manager

# Shareholder Register Analysis

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Others: Retail, Private Client & Other Institutions

Source : Argus Vickers

Note: Ownership as at 31 March 2013

## Anticipated 18 Month Milestones – Focus on Data

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### 2013

- Q1 RPL554: Data from anti-inflammatory study conducted at MEU, Manchester ✓
- Q2 VRP700: First dosing confirmatory anti-cough study
- Q2 RPL554: ATS conference in USA, Asthma and COPD data
- Q3 RPL554: ERS conference in Europe, Asthma and COPD data

### 2014

- H1 VRP700: Data from confirmatory anti-cough study
- H2 RPL554: Data from bronchodilator dose-response study
- H2 RPL554: Data from phase IIa COPD 1-2 weeks dose finding study

# Investment Highlights

*Developing innovative medicines to treat unmet needs in respiratory diseases*

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- Accelerating value creation by focusing on high unmet medical need and a clear path to commercialization
  - Severe COPD – RPL554
  - Chronic, severe cough – VRP700
- Drug candidates with Novel Mechanisms of Action
  - Clearly differentiated from current treatments
  - Complementary or stand-alone therapy
  - De-risked assets – phase IIa studies successfully completed
- “Big Pharma” quality, but with biotech speed and cost-effectiveness
- Highly accomplished Board and Management teams
  - Access to network of industry experts and global Key Opinion Leaders