

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

Washington, DC 20549

**FORM 8-K**

**Current Report Pursuant  
to Section 13 or 15(d) of the  
Securities Exchange Act of 1934**

Date of Report (Date of earliest event Reported): **May 18, 2015**

**THERAVANCE, INC.**

(Exact Name of Registrant as Specified in its Charter)

**Delaware**

(State or Other Jurisdiction of  
Incorporation)

**000-30319**

(Commission File Number)

**94-3265960**

(I.R.S. Employer Identification  
Number)

**951 Gateway Boulevard  
South San Francisco, California 94080  
(650) 238-9600**

(Addresses, including zip code, and telephone numbers, including area code, of principal  
executive offices)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

**Item 7.01. Regulation FD Disclosure.**

On May 18, 2015, at the Annual Congress of the American Thoracic Society in Denver, Colorado, GlaxoSmithKline (GSK) held a mini symposium relating to the effect of reducing lung hyperinflation with fluticasone furoate/vilanterol (FF/VI) on cardiac structure, function and arterial stiffness. The presentation slides are furnished as Exhibit 99.1 to this Current Report on Form 8-K and are incorporated by reference herein. FF/VI has been developed under the LABA collaboration agreement between GSK and Theravance, Inc.

The information disclosed in this Item 7.01 is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities under that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act except as expressly set forth by specific reference in such filing.

**Item 9.01. Financial Statements and Exhibits.**

**(d) Exhibits**

99.1 Presentation Slides

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**SIGNATURE**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**THERAVANCE, INC.**

By: /s/ Eric d'Esparbes  
**Eric d'Esparbes**  
Vice President and Chief Financial Officer

Date: May 18, 2015



National Institute for Health Research Cardiovascular Biomedical Research Unit at Barts

## The Effect of Reducing Lung Hyperinflation with Fluticasone Furoate/ Vilanterol on Cardiac Structure, Function and Arterial Stiffness: A Cardiac Magnetic Resonance Study

Ian S Stone, Neil C Barnes, Wai-Yee James, Dawn Midwinter, Redha Boubertakh, Richard Follows,  
Leonette John, Steffen E Petersen

Monday 18<sup>th</sup> May 2015 , ATS Conference



### Faculty Disclosures *ATS 2015 - Denver*

**Ian S Stone**

#### ■ Relevant financial relationships with a commercial interest:

- GlaxoSmithKline, Research Support (previously)
- GlaxoSmithKline, Advisory Committee (previously)

# Overview

- Rationale of the study
- Study Design
- Results
- Conclusions and Implications

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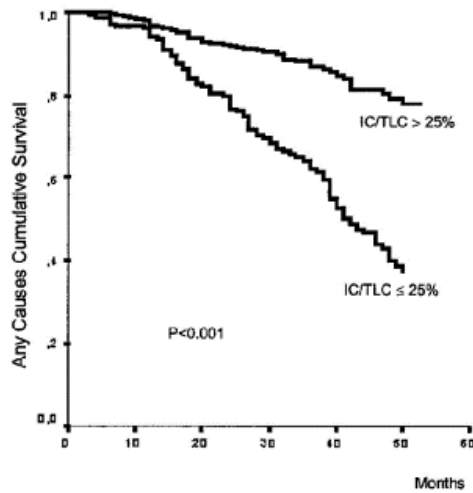
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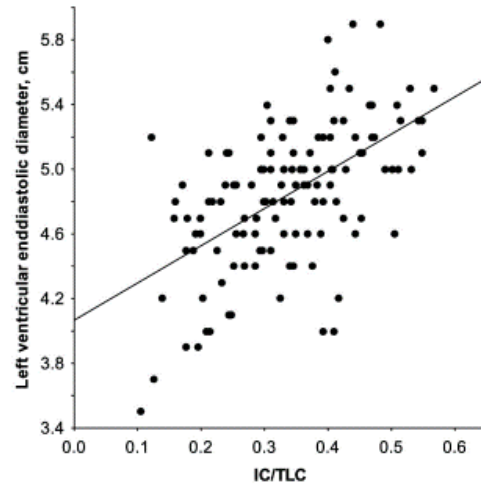
# Potential Mechanisms Linking COPD And Cardiac Disease

## Consequences of Hyperinflation

- 2x all cause mortality<sup>1</sup>



- Significantly reduced LV dimensions and diastolic filling pattern vs ratio of  $>0.25$ <sup>2</sup>



- 10% increase in CT defined emphysema associated with a reduction in RVEDV by 2.43 ml and 3.25 ml for current and ex-smokers respectively<sup>3</sup>

1. Casanova et al AJRCCM 2005
2. Watz et al Chest 2010
3. Grau et al, Chest 2013

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## Rationale Lung Deflation

- Respiratory benefits well described
  - improved exertional dyspnea and exercise tolerance<sup>1</sup>
    - reduced inspiratory muscle loading
    - Increase capacity to dynamically hyperinflate
- Benefits on cardiovascular function less clear
  - LVRS → improvement in  $O_2$  – pulse<sup>2</sup>

1. O'donnell et al Chest. 2006; **130**(3): 647-56.
2. Come et al Respir Med. 2012; **106**(1): 109-19.

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# Aims

Test the hypothesis that the cardiac structural and functional alterations seen in stable hyperinflated COPD are modifiable through pharmacological lung deflation.

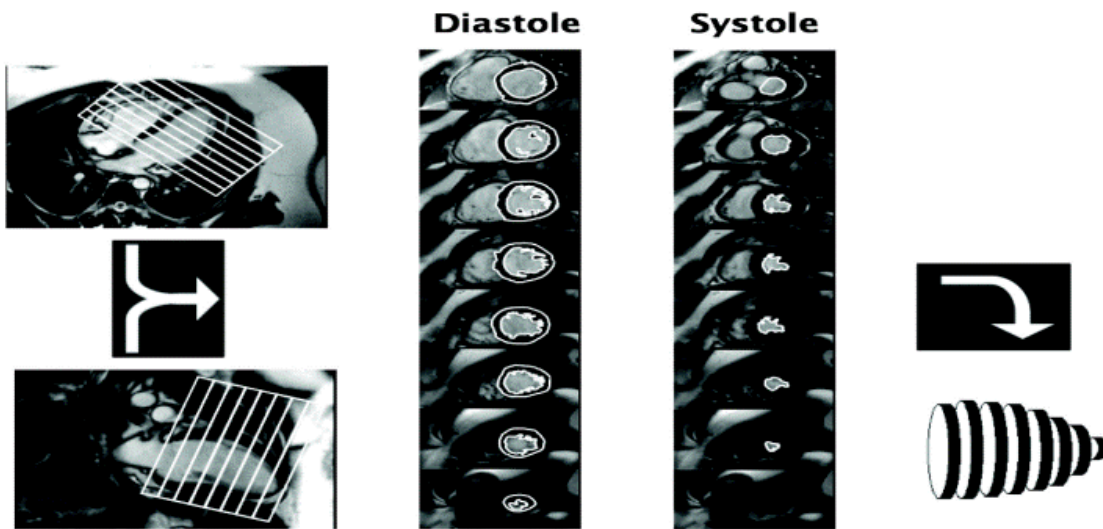
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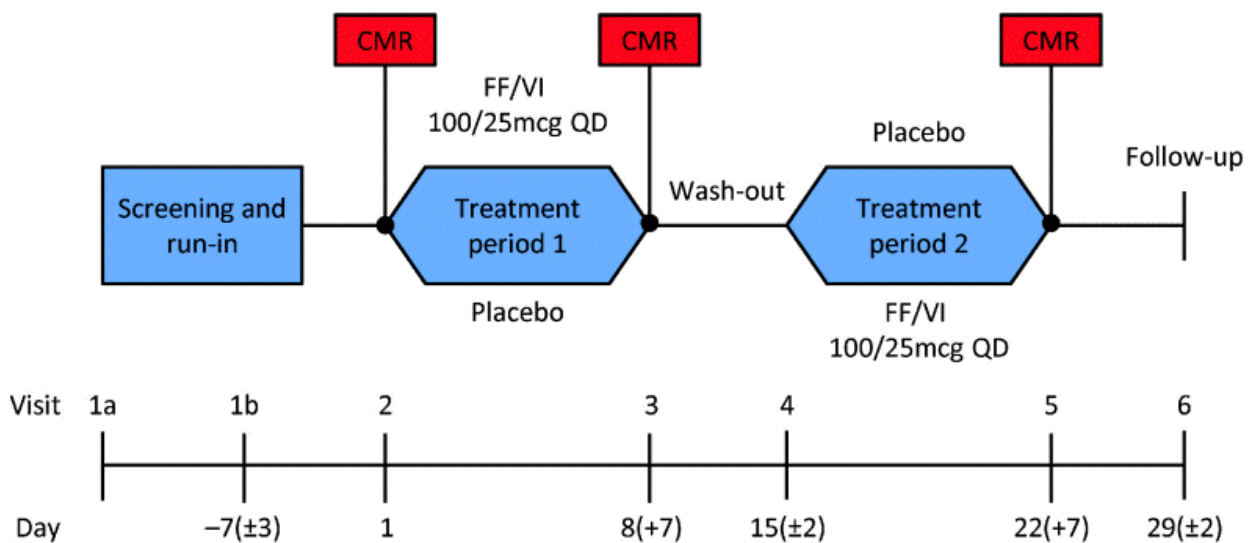
# Study Design: Cardiac Magnetic Resonance



- No geometric assumptions
- Highly accurate and reproducible
- Limitations with ECHO due to emphysema do not apply
- new advances intrinsic myocardial systolic and diastolic function.

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## Study Schematic



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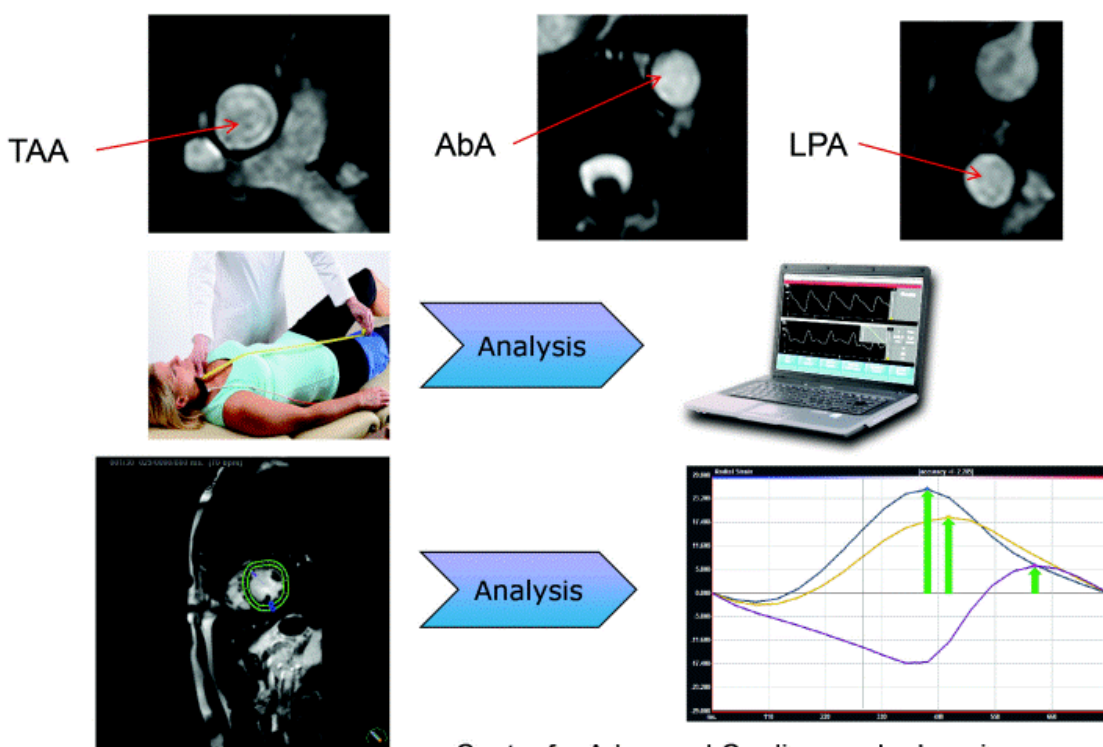


# Study Design: Primary Efficacy Endpoint

- Change in Right Ventricular End Diastolic Volume (indexed to body surface area) from baseline compared to placebo
  - thin-walled
  - most sensitive to the changes in pre-load conditions

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# Study Design: Other efficacy endpoints



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# Study Design : Inclusion Criteria

- > 40 yrs
- 15 PYH
- Established COPD diagnosis
- $FEV_1 < 70\%$  post-bronchodilator
- $FEV_1/FVC$  ratio after bronchodilator  $< 0.7$
- **Residual Lung Volume (RVol)  $\geq 120\%$**
- **RVol Reversibility post bronchodilator of  $\geq 7.5\%$  predicted**

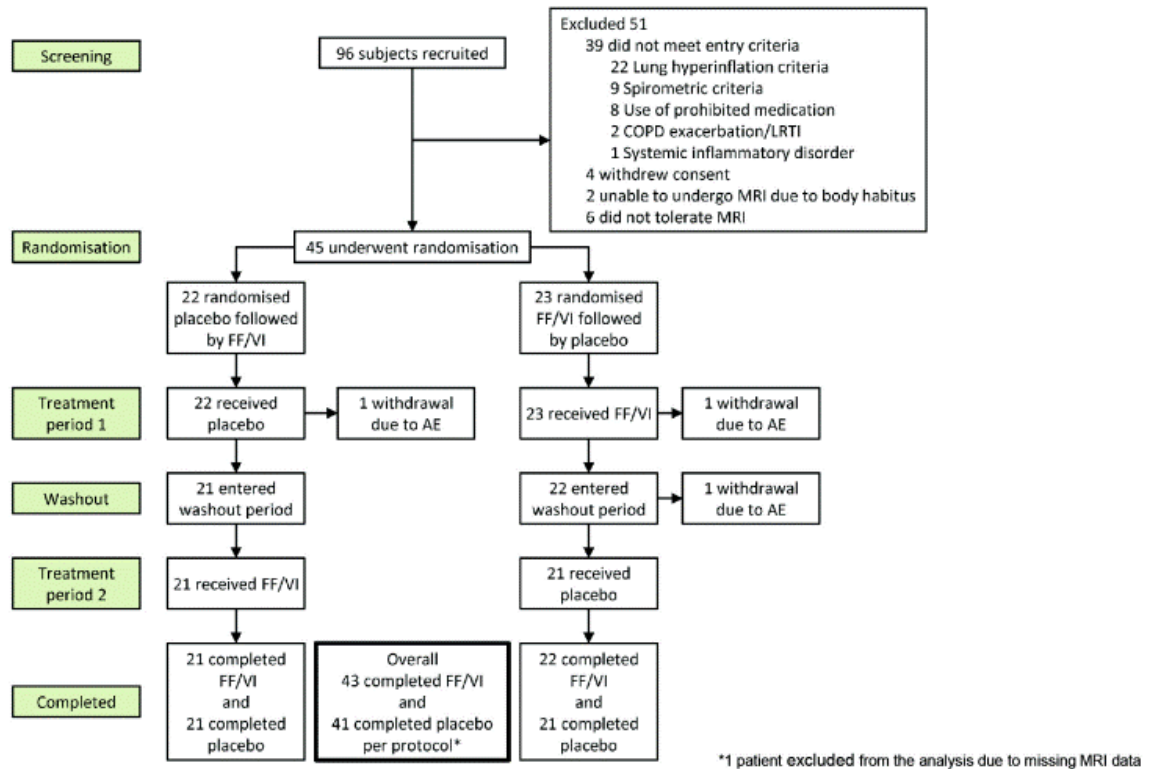
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# Results: Study Consort

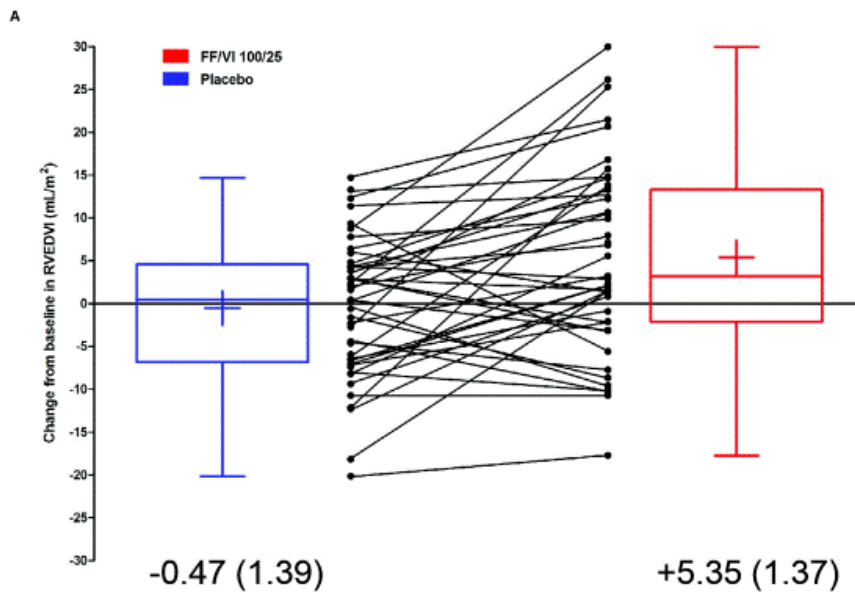


# Results: Demographics

- Age  $64.4 \pm 9$  yrs
  - 62% males, 87% caucasian
  - $48.5 \pm 30.9$  Pack years
  - Moderate to severe COPD\*
    - **FEV1%**  $52.5 \pm 12.2$
    - **FEV/FVC**  $45.3 \pm 10.3$
    - **RVol%**  $168.8 \pm 37.0$ 
      - -23.8% reversibility post bd
  - Comorbidity
    - Hypertension 36% / Statin 33%
- **CAT**  $18 \pm 8$
  - **Moderate or severe exacerbations in prior 3 years**
    - 47% > 2
    - 76% never hospitalised

\* Values Mean  $\pm$  SD

# Results: Primary Efficacy Endpoint RVEDVI



Difference	+5.83
95% CI	2.74, 8.91
P-value	<0.001

\* Statistical analysis performed using an ANCOVA model with covariates of treatment, baseline, period and subject as a random effect.

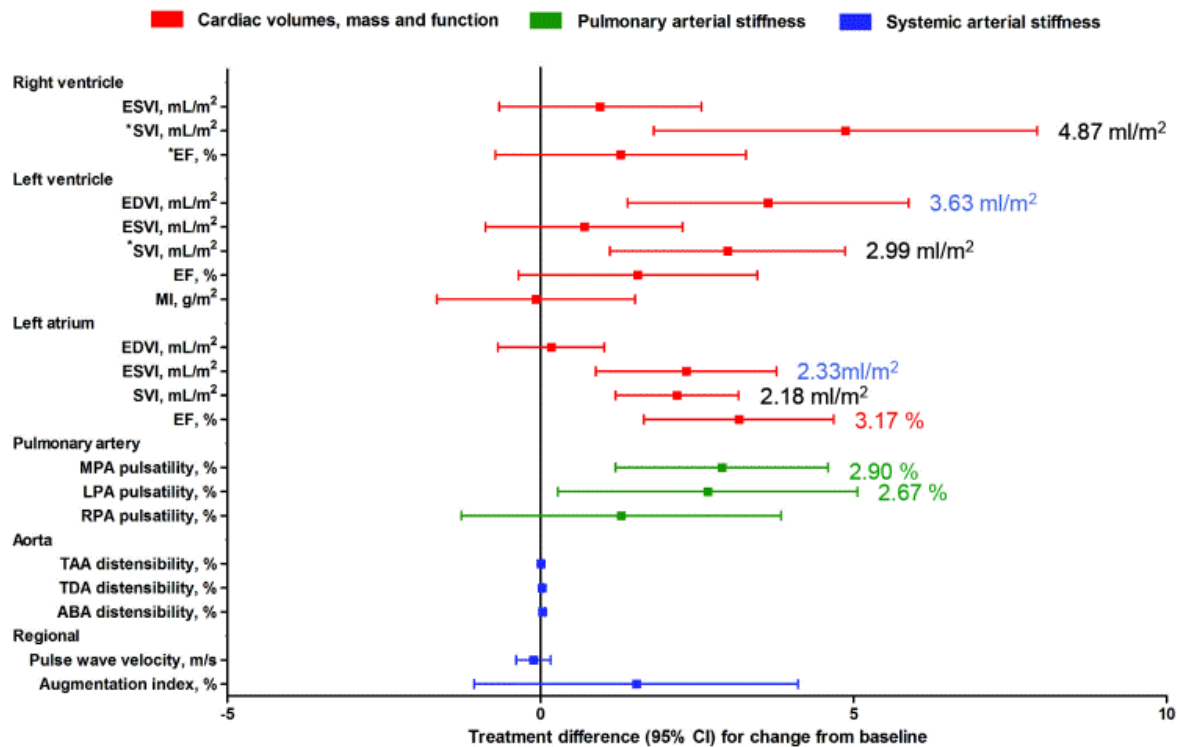
## Pulmonary Function

FF/VI 100/25 vs Placebo	FEV (l)	FVC (l)	FEV/FVC (%)	Residual Volume (l)
Difference	0.220	0.350	2.0	-0.429
95% CI	0.12, 0.31	0.21, 0.49	-0.3, 4.3	-0.59, -0.27
P-value	<0.001*	<0.001*	0.092	<0.001*

Analysis performed using an ANCOVA model with covariates of treatment, baseline, period and subject as a random effect.



# Other Efficacy Endpoints



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\*Analyses performed post hoc

# Safety

	FF/VI 100/25	Placebo
No. of subjects with on treatment AEs	6 (14%)	5 (12%)
Drug related on and post treatment	1 (2%)	1 (2%)
Withdrawals on and post treatment	2 (5%)	1 (2%)
SAE	0	0



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## Summary Of Findings

- Lung deflation with FF/VI 100/25 resulted in
  - Decompression of cardiac chambers and pulmonary vasculature
    - Increased End Diastolic Volumes
    - Improved atrial function
    - Alterations to pulmonary artery properties
  - No effects on systemic arterial stiffness or intrinsic myocardial function

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# Clinical Implications

- RV
  - Small RV associated with onset of dyspnoea (Kaufmann 2013 PLoS One)
- LAEF
  - Predicts atrial fibrillation in dyspnoeic patients independent of atrial size (Hsiao 2013 Circulation Journal)
- PA Pulsatility
  - Contributes to RV efficiency (Milnor 1966 Circulation Research)
  - May Attenuate RV adaptation (Stevens 2012 JACC Cardiovascular Imaging)

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## Conclusion

- First study to demonstrate that changes in cardiac structure and function can be achieved following the pharmacological treatment of lung hyperinflation
- Whether over the long term lung deflation treatment can impact on intrinsic myocardial function is as yet unverified

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# Acknowledgements

- Supervisors: Professor Steffen Petersen  
Professor Neil Barnes
- Funding GSK
- Research Nurse: Wai-Yee James
- Physicist and programming: Dr. Redha Boubertakh
- Statistics : Dawn Midwinter (GSK)



William Harvey  
Research Institute