

**Vectus Biosystems Limited**  
**Chairman's Address to 17 November 2016 Annual General Meeting**

The 2015-16 financial year has seen a continued series of milestones achieved by the Company, together with the successful Initial Public Offering (IPO) of Vectus in February this year. Most recently we have become the inaugural winner of the Medtech and Pharma category of the Australian Technologies Competition, and I congratulate our team on this. Companies were judged on various criteria, including market potential, business model, technology validation and protection, and their leadership teams. Ultimately, the winner was the company that was deemed to have the greatest potential to have a global impact.

The Company's key achievements during the year were:

- a significant expansion of Vectus' proprietary drug library and related patent activity, increasing from 70 compounds in late 2015 to over 1,000 compounds now, covered by your company's Intellectual Property (IP);
- the granting of a US patent, covering both the Company's lead compound, VB0004, and a number of other potential orphan candidates;
- the successful scale-up and Good Manufacturing Practice (GMP) synthesis of VB0004;
- the commencement of the VB0004 pre-clinical toxicology programme, ahead of schedule and in line with the Company's budget outlined in the IPO Prospectus; and
- the expanded and detailed engagement with a spectrum of human and animal health pharmaceutical companies.

**Vectus' Research and Development (R&D) Programme**

Built on an initial insight into the role of our synthesised Vasoactive Intestinal Peptide (VIP) mimetics, Vectus has successfully broadened its capability, covering not only applications to heart and kidney conditions, but growing into a transformational platform technology encompassing all solid organ fibrosis. Central to the Company's position is not only the arresting of disease progression, but the singular capability to reverse organ damage, thereby opening a spectrum of opportunities for 'first in class' applications.

To-date, Vectus is not aware of any other drug development programmes that can make a credible claim to reverse existing fibrosis. In our IPO Prospectus we featured the opportunity for applications to rarer diseases and these orphan indications, reaching smaller patient numbers, but able to command premium prices, are now a major focus for the pharmaceutical industry.

As announced to the market, Vectus is engaged with a cross-section of leading human and animal health pharmaceutical companies, which have shown interest in leveraging various compounds in our library to address disease states against which, to-date, conventional drugs have had little or no measurable clinical success.

Several of the important achievements on the Company's 'path to the clinic' have now been accomplished, including demonstrating a successful and cost-effective scale-up of synthesis of our lead compound. Further, an initial one kilogram batch of the compound has now been produced, providing a strong validation of the process, and enabling the important next steps in toxicology and pre-clinical activities to continue on time and on budget.



The size of the Company's Board was expanded during the last financial year, with Dr Ron Shnier, an eminent Radiologist with an enviable track record in both the clinical and research arenas, becoming a Director in September 2015, and Dr Susan Pond becoming a Director in May 2016, bringing with her a wealth of scientific and commercial knowledge, as well as extensive experience in the biotechnology industry. With their addition, four of the Board members now bring a wealth of clinical medical and pharmaceutical expertise, helping support your company's growth. Directors Messrs Maurie Stang and Peter Bush are experienced executives, with enviable track records of building multiple successful life science companies. We wish to thank outgoing Director Mr Bernard Stang for his efforts during his time on the Board. Following the changes to the Vectus Board, the increase in the number of the Company's independent Directors significantly improves its corporate governance.

Vectus is a powerful example of an emerging biotechnology company, which has not only been supported by its shareholders, but continues to be a recipient of the ATO R&D rebate. The Company has no net debt, cash reserves of \$2.85 million and a promising level of engagement with the global pharmaceutical industry.

The Accugen laboratory instrument platform is now in its broad pre-marketing programme. Significant international interest has been generated by the publication of a paper describing the Accugen method as, "A simple, accurate and universal method for quantification of PCR" in the peer-reviewed journal BMC Biotechnology. Accugen represents not only a near-term market entry opportunity, but has the potential to deliver a new reference standard in quantitative polymerase chain reaction (PCR) for both research and diagnostic applications, addressing an unmet need in a global market.

I recognise and thank our hardworking Board members, who share a strong belief and conviction in Vectus' potential to create growing shareholder value, whilst achieving an important and positive social outcome. Our laboratory R&D team has achieved remarkable outcomes in terms of speed of development, innovation and an ever-expanding drug library and IP portfolio.

## **Vectus Biosystems Limited**

**Graham Macdonald**

Non-Executive Chairman



Annual General Meeting 2016

# Achievements 2016

- Successful IPO
- ASX listing Feb 2016
- GMP synthesis almost complete (edd Dec 2016)
- Toxicology commenced (2 species)
- Major expansion in IP
  - Granting US patent for VB0004 (compositions and methods of use)
  - PCT applications for A32 and P5 libraries (compositions and methods of use hepatic cirrhosis and orphan renal diseases)
  - Provisional patent application A79 (compositions and methods of use pulmonary fibrosis)
  - Provisional patents extending library to ~1,000 compounds (compounds and methods of use CV & renal)
- Engagement with multiple pharmaceutical and animal health companies
- Selected to present at Biotech Invest
- Winner of Australian Technologies Competition - Medtech & Pharma



# Oral Vasoactive Intestinal Peptide (VIP) Agonists

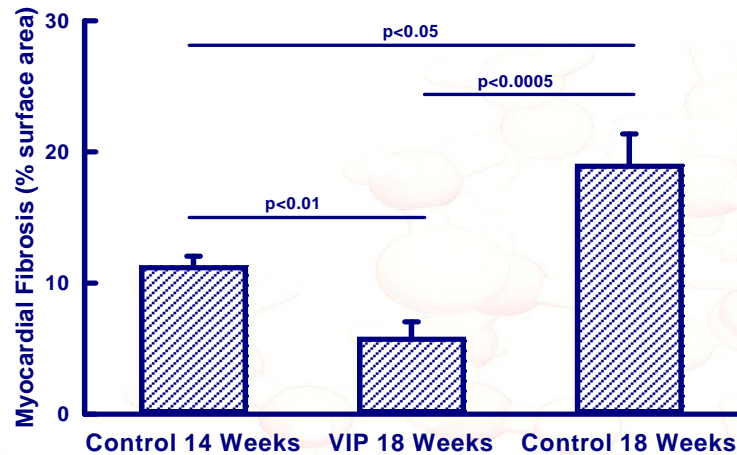
The Transformational Platform To  
Manage Fibrotic Disease

# Why Fibrosis?

- **Fibrosis is the pathology which underlies**
  - **Heart failure** (largest single item on US health care budget (\$US32b in 2013))
  - **Kidney failure** (Dialysis and renal transplant costs in the US reached \$49.2b in 2011)
  - **Liver failure** (also precursor to liver cancer)
  - **Respiratory failure** (pulmonary fibrosis)
- **Fibrotic disease** contributes to more than **40%** of all deaths worldwide
- **Few** anti-fibrotic drugs available: major **unmet** clinical need.

# Why VIP?

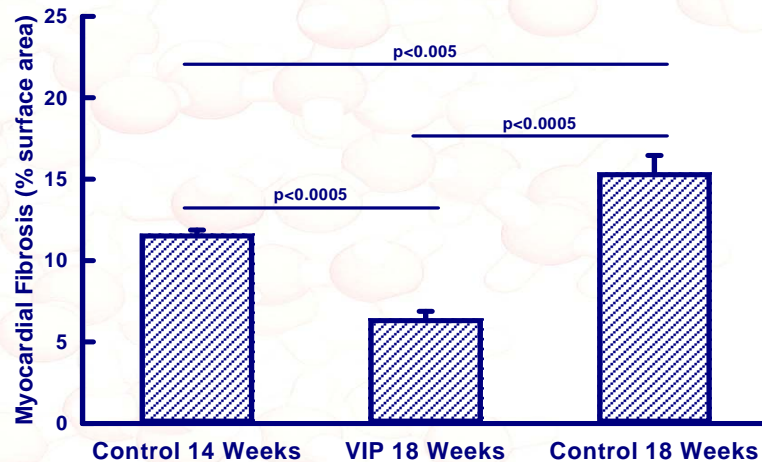
**a**



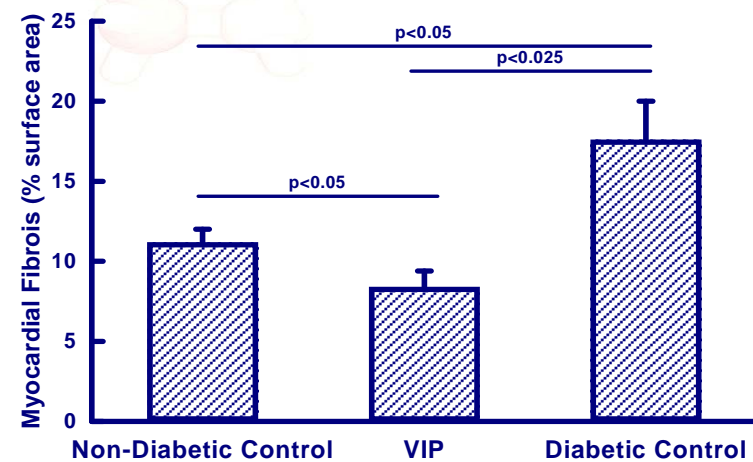
## VIP reversed fibrosis in multiple models

- **a** normotensive rats on 4.4% salt diet treated with VIP (5pmol/kg/min) or control vehicle infusion for 4 weeks
- **b** rats on 4.4% salt diet plus L-NAME (10mg/kg/day) treated with VIP (5 pmol/kg/min) or vehicle control infusion for 4 weeks
- **c** fibrosis in rats streptozotocin (60mg/kg) induced diabetes at 14 weeks. After 8 weeks diabetes (i.e. 22 weeks of age) VIP (5 pmol/kg/min) or vehicle commenced and continued for 4 weeks

**b**



**c**



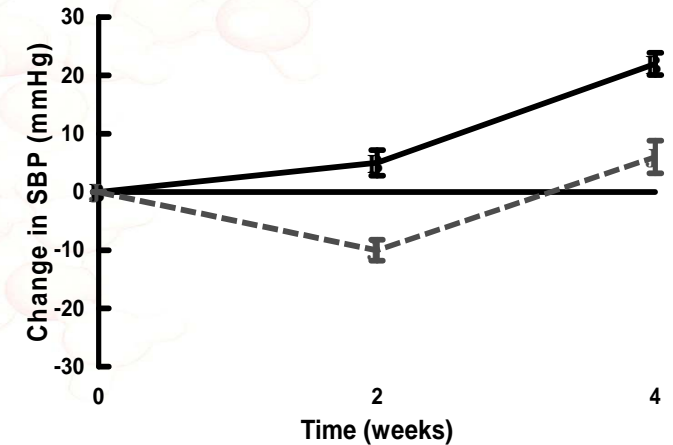
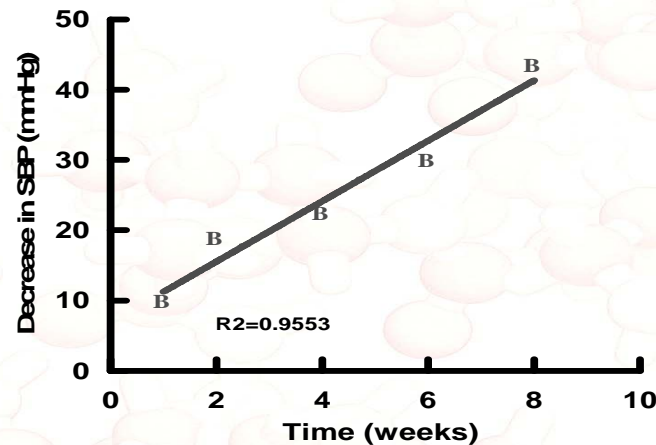
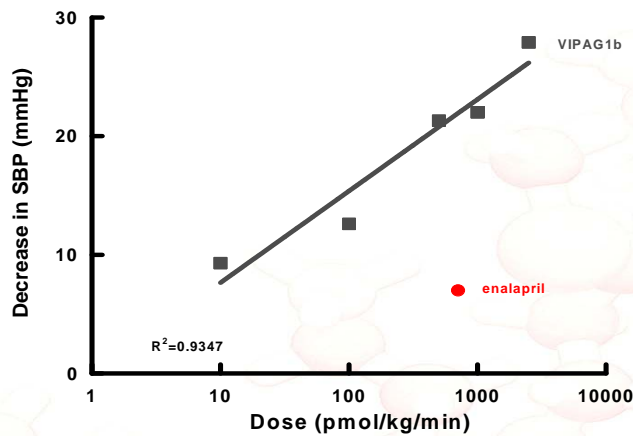


# *HYPERTENSION, CARDIOVASCULAR AND RENAL DISEASE*

# Why Include Hypertension?

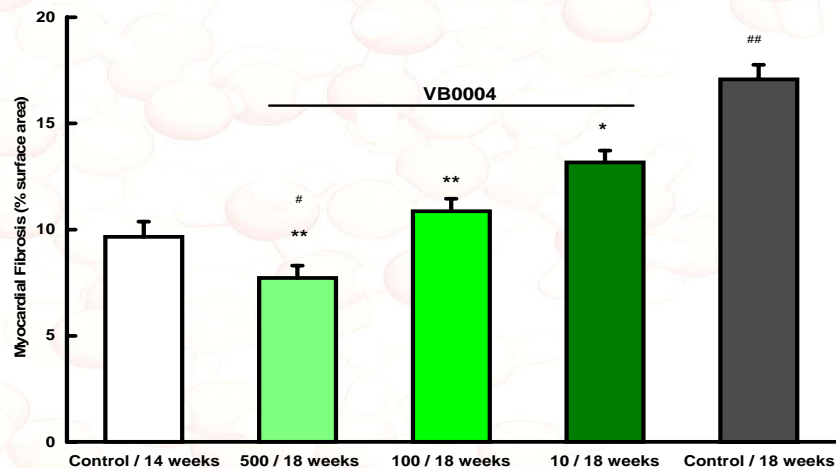
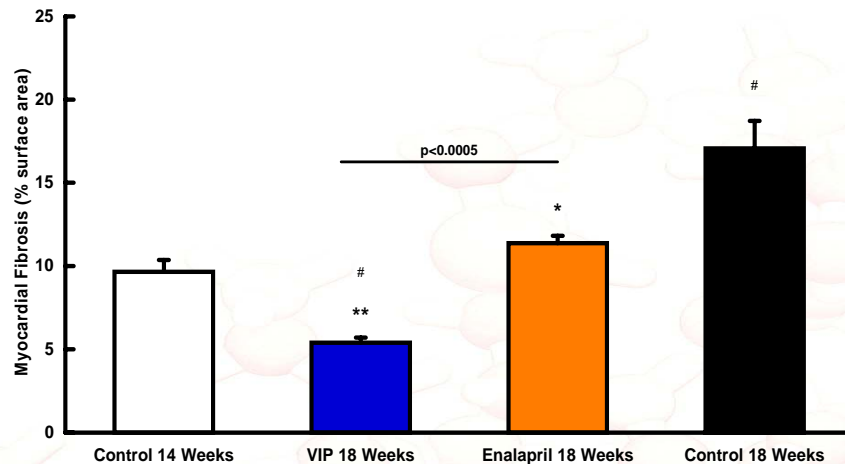
- Hypertension affects 40% of the adult population worldwide (exceeding the predicted 30% in 2025)
- less than 25% of patients achieve target blood pressure
- it is the major risk factor for
  - heart failure
  - kidney failure
  - stroke
  - dementia
- No current therapy effective for systolic hypertension

# Systolic Blood Pressure



- Left: Decrease in SBP from controls in 18 week old SHR treated with VB0004 at 10, 100, 500, 1,000 and 2,500 pmol/kg/min for 4 weeks. Enalapril dose to achieve 7mmHg was 705 pmol/kg/min. SBP continued to decrease with increasing dose to 2,500 pmol/kg/min
- Middle: Difference in SBP from control for SHR treated with VB0004 at 2,500 pmol/kg/min at 1, 2, 4, 6 and 8 weeks. The maximal effect of VB0004 in lowering SBP was not reached after 8 weeks treatment
- Right: Change in SBP from levels at the commencement of the experiment in Vehicle control for 4 weeks (solid line) SHR treated with VB0004 2,500pmol/kg/min for 2 weeks then vehicle for 2 weeks (dotted line) SBP in increased in parallel with vehicle control after cessation of VB0004

# Myocardial Fibrosis



■ **Upper Panel:** Myocardial fibrosis after 4 weeks treatment with VIP (5pmol/kg/min) or enalapril (dose adjusted to maintain the same BP reduction as VIP average dose 705 pmol/kg/min). \*  $p < 0.005$ , \*\*  $p < 0.001$ , \*\*\*  $p < 0.0005$  vs 18 week control and ##  $p < 0.0005$  vs 14 week control

■ **VIP (5pmol/kg/min) reversed fibrosis** present at commencement of infusion while enalapril (705pmol/kg/min) could only attenuate the amount of progression over the 4 weeks

■ **Lower panel:** fibrosis in the heart in from left :

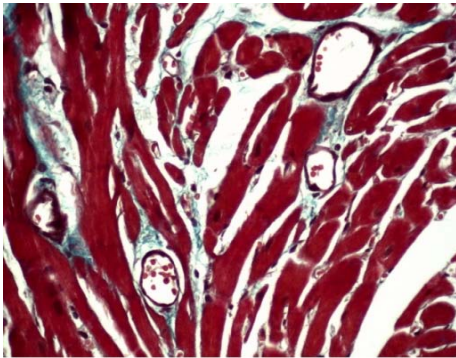
- 14 week old controls,
- 18 week old SHR treated with:
  - VB0004 500 pmol/kg/min for 4 weeks,
  - VB0004 100 pmol/kg/min for 4 weeks
  - VB0004 at 10 pmol/kg/min 4 weeks
- 18 week old vehicle controls

■ The amount of fibrosis present decreased with increasing dose of VB0004

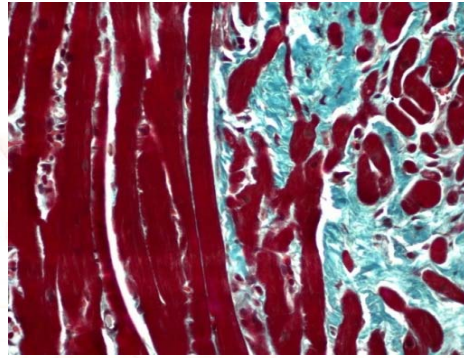
■ At the highest dose, fibrosis was significantly less than in rats studied at the beginning of the infusions at 14 weeks i.e. VB0004 reversed existing fibrosis

# Cardiac Histology

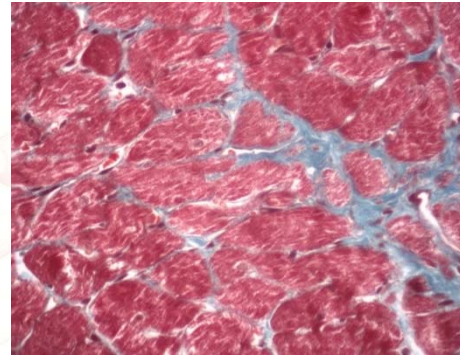
Control 14 weeks



Control 18 Weeks

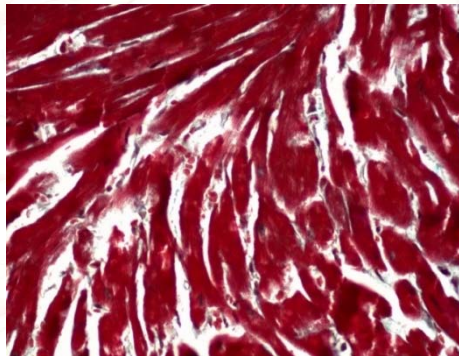


18 Weeks 5% EtOH

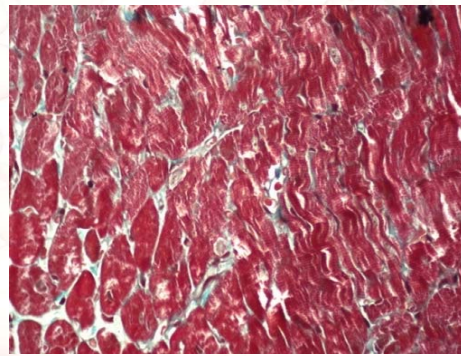


Heart sections stained with Masson trichrome, fibrous tissue appears blue-cyano in colour

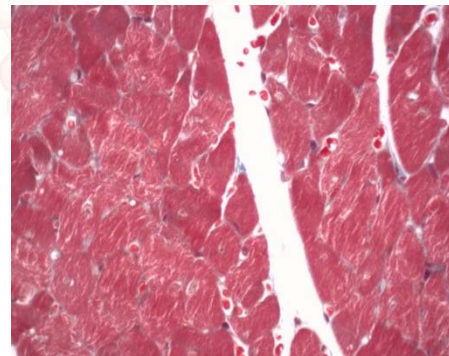
**Upper Panels:** 14 week control fibrosis is predominantly around blood vessels with some interstitial extension 18 week vehicle control marked increase in interstitial fibrosis surrounding muscle fibres and loss of muscle fibres 18 week 5% ethanol drinking solution. Fibrosis is visible as blue stained tissue and is present throughout the section.



VIP 18 Weeks



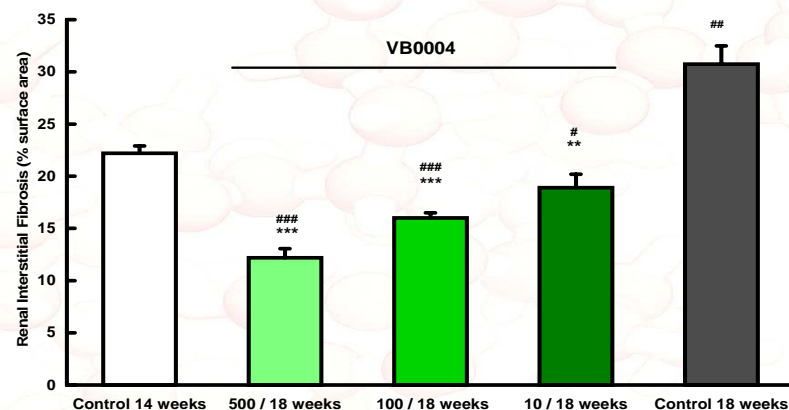
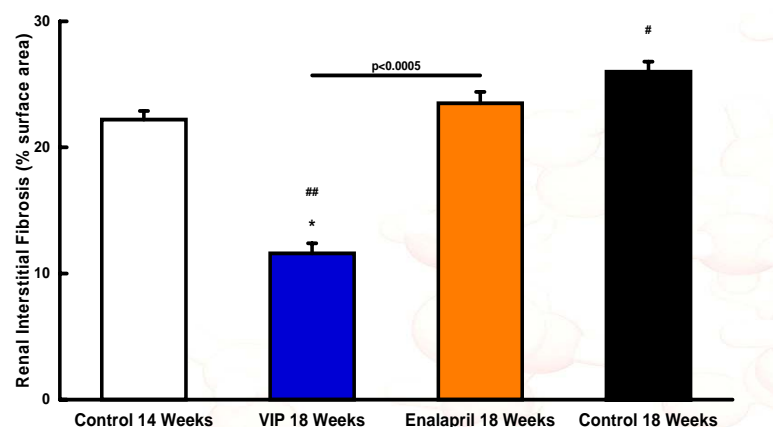
Enalapril 18 Weeks



VB0004 18 Weeks

**Lower Panels:** VIP infusion show restoration of normal tissue architecture after 4 weeks treatment. Enalapril treated - fibrosis is visible between most muscle fibres. 18 week old SHR after 4 weeks treatment with VB0004 delivered in the drinking solution (5% ethanol) for 4 weeks at a dose of 500pmol/kg/min. As with VIP treatment normal tissue architecture is restored by treatment

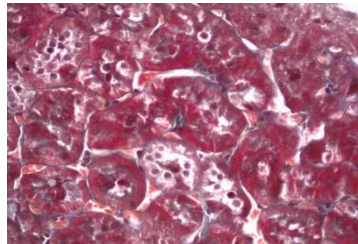
# Renal Fibrosis



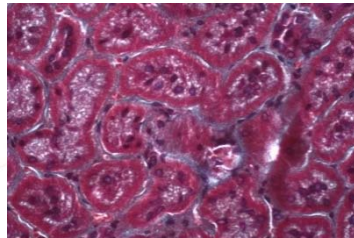
- In humans increasing interstitial fibrosis in the kidney parallels the decline in renal function leading to dialysis
- Upper panel shows results from 14 week old SHR on 2.2% salt diet which were randomised to
  - 14 week control (open bar) VIP (5pmol/kg/min) infusion for 4 weeks (solid blue bar)
  - enalapril dose adjusted to match BP reduction of VIP for 4 weeks (cross hatched bar)
  - 18 week control vehicle (Hartman's Solution) infusion for 4 weeks (hatched bar)
- Lower panel fibrosis in the kidney in from left
  - 14 week old controls (open bar)
  - 18 week old SHR treated with
    - VB0004 10 pmol/kg/min for 4 weeks
    - VB0004 100 pmol/kg/min for 4 weeks
    - VB0004 500 pmol/kg/min 4 weeks (hatched bars)
    - 18 weeks old vehicle controls (cross hatched bars)
- There is progression of fibrosis from 14 to 18 weeks
- VIP and VB0004 reversed the fibrosis which was present at the start of treatment.

# Renal Histology

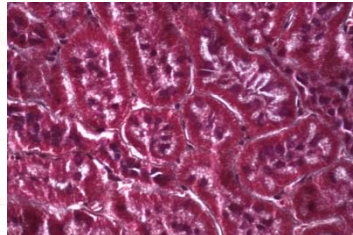
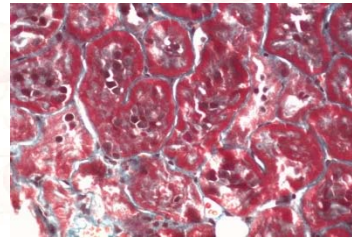
Control 14 weeks



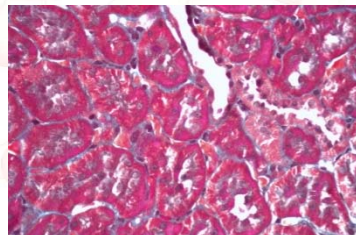
Control 18 Weeks



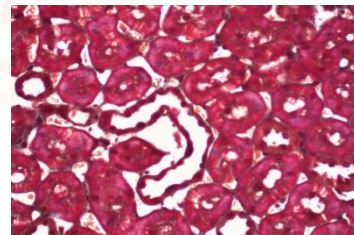
18 Weeks 5% EtOH



VIP 18 Weeks



Enalapril 18 Weeks



VB0004 18 Weeks

Kidney sections stained with Masson trichrome, fibrous tissue appears blue in colour

**Upper Panels:** 14 week control: fibrosis surrounds some but not all tubules 18 week vehicle control: marked increase in interstitial fibrosis surrounding all renal tubules 18 week 5% ethanol drinking solution. Fibrosis is present surrounding tubules throughout the section

**Lower Panels:** VIP: restoration of normal tissue architecture – tubules are “back to back”. Enalapril: fibrosis is visible around virtually all renal tubules 18 week old SHR after 4 weeks treatment with VB0004 delivered in the drinking solution (5% ethanol) at a dose of 500pmol/kg/min. As with VIP treatment normal tissue architecture is restored by treatment with tubules showing no surrounding fibrosis

# Market Metrics

The background of the slide features a complex, three-dimensional molecular model. It consists of numerous dark red spheres, likely representing carbon atoms, interconnected by a network of lighter red rods, which represent chemical bonds. The structure is dense and branching, filling the upper and right portions of the frame, and creating a textured, scientific backdrop for the text.

- Fibrotec – Shire
  - FT011
  - Phase I
  - renal only \$75m upfront
  - up to \$600m milestone payments
- Reata – Abbott
  - bardoxolone
  - renal only
  - \$850m plus royalties

# Current Status

- GMP synthesis almost complete
  - 1kg engineering batch manufactured
  - main 5kg batch edd Dec 2016
- toxicology and pharmacokinetic studies have commenced
- tendering process for Phase1 underway
- engagement with most of the major pharmaceutical firms with an interest in fibrosis
- engagement with animal health care companies



# *Fibrotic Lung Disease*



# Pulmonary Fibrosis

## Causes

- Environmental (e.g. air pollution, diesel particles)
- Occupational (e.g. dusts such as silica, **coal**, asbestos, cotton dust)
- Infections (e.g. TB, psittacosis)
- Drugs (e.g. bleomycin, methotrexate),
- Radiation
- Autoimmune diseases (e.g. sarcoid, SLE, **scleroderma**, Wegener Granulomatosis)
- Idiopathic (no discernible cause) termed **IPF**

Essentially, a triggering factor such as coal dust accumulates in the lung which initiates a scarring (fibrotic) reaction to wall off the irritant. However, instead of then turning off once this is achieved the process becomes autonomous and continues to damage the lung even in the absence of continuing exposure. This results in a reduction in the area available for oxygen to exchange across the lungs and manifests as increasing breathlessness.

# Aims

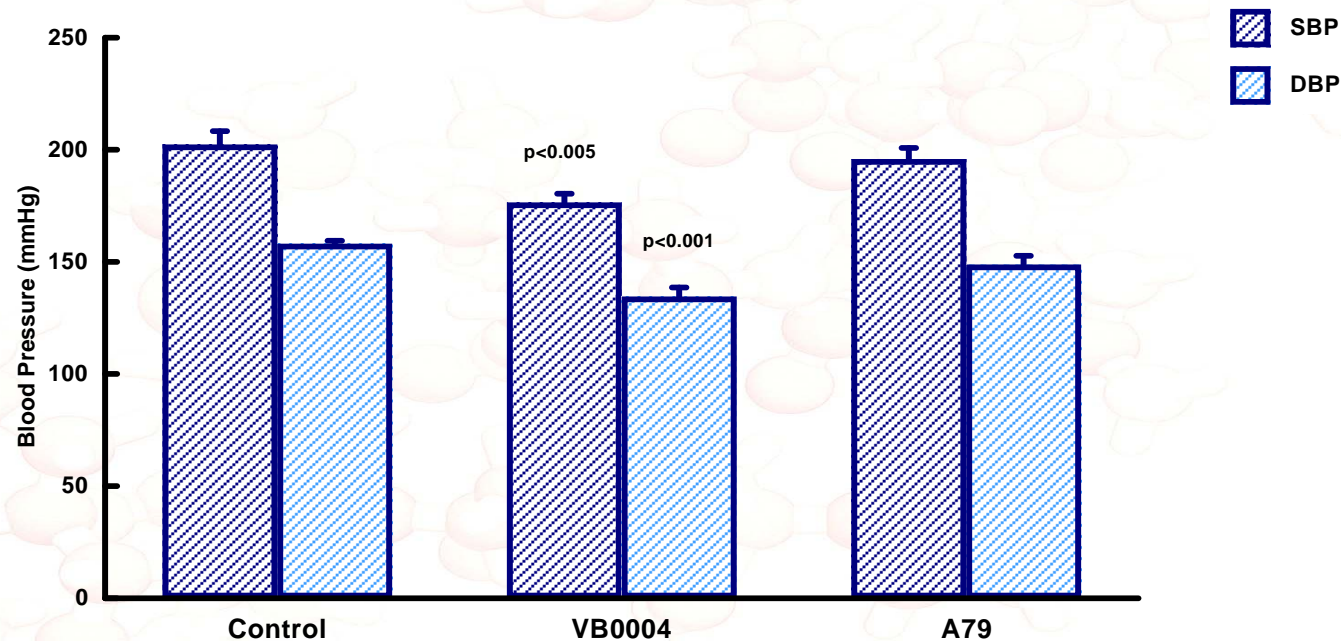
The aim was to evaluate VB0004 as a treatment for conditions such as scleroderma where severe hypertension and pulmonary fibrosis co-exist. Cardiac and renal fibrosis may also be present in this disease.

A second aim was to develop a non-blood pressure lowering analogue of VB0004 to treat conditions such as IPF where blood pressure lowering is not required and in fact may be contra-indicated.

# Why Scleroderma and IPF?

- Scleroderma and IPF have been declared orphan diseases by the FDA
- Affect
  - <200,000 people or if >200,000 no prospect of recovery in US
  - <1 in 2,000 people in Europe no current therapy
- Grants available for clinical trials in US
- Restricted market access for competitors in Europe

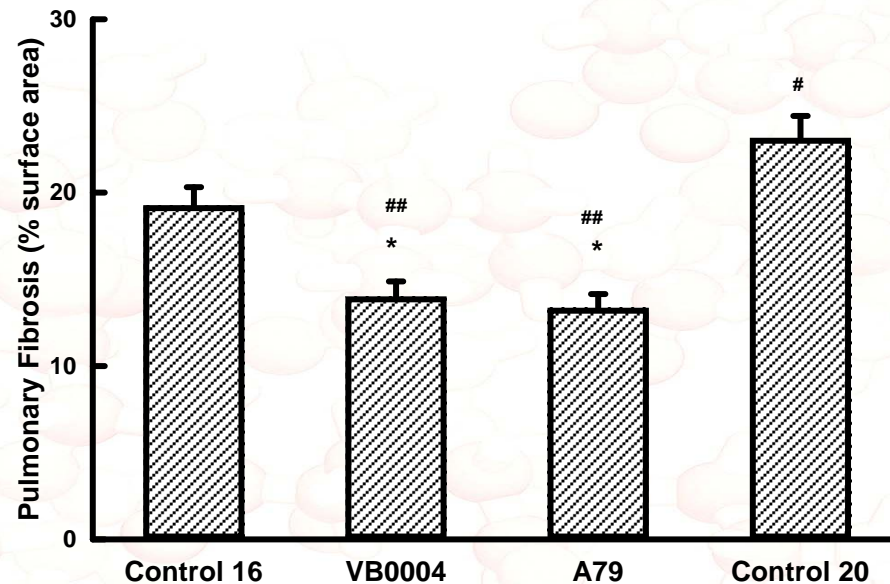
# Blood Pressure



Systolic and diastolic blood pressure in 20 week SHR following treatment with bleomycin at 14 weeks and randomisation to control, VB0004 or A79 at 16 weeks.

As previously VB0004 significantly decreases both systolic and diastolic pressure while A79 has no effect.

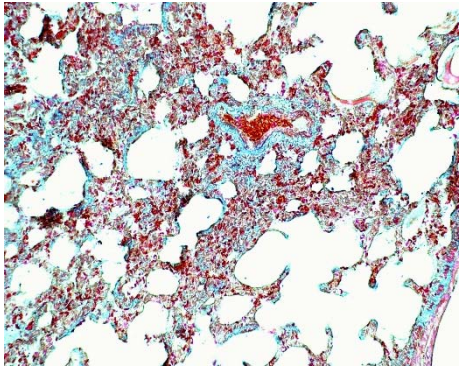
# Pulmonary Fibrosis



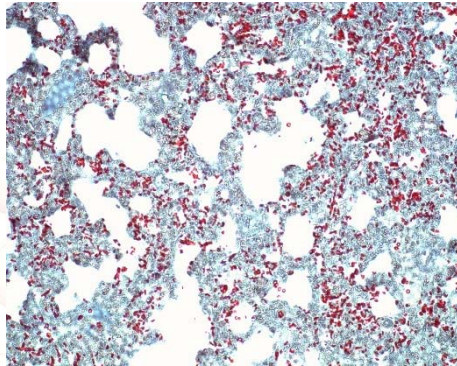
Pulmonary fibrosis in 16 week controls (two weeks after Bleomycin administration) and at 20 weeks after 4 weeks treatment in VB0004, A79 and vehicle control rats. VB0004 and A79 were administered at 500pmol/kg/min in the drinking solution (5% ethanol) vehicle control is drinking solution alone.

\*  $p < 0.001$  vs 20 week control, #  $p < 0.025$ , ##  $p < 0.001$  vs 16 week control.

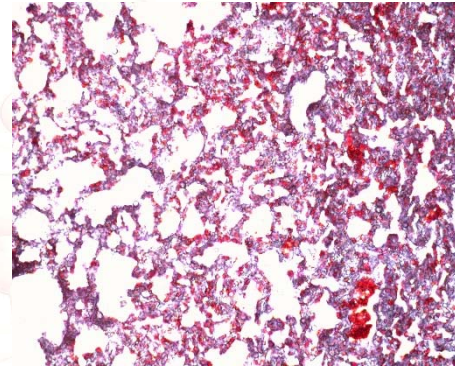
# Histology



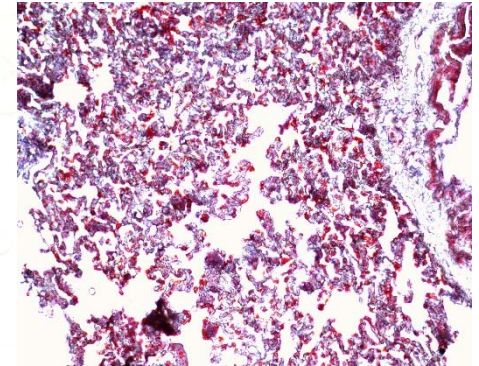
16 Week Control



20 Week Control



A79 at 20 Weeks



VB0004 at 20 Weeks

Lung sections in bleomycin treated rats after 2 weeks of control drinking solution (left), after 6 weeks of control drinking solution (centre) and after 2 weeks of control drinking solution followed by 4 weeks treatment with A79 or VB0004 (500pmol/kg/min). Scar or fibrous tissue appears blue / cyano in these sections. In the controls 2 weeks after bleomycin administration fibrous tissue has thickened many alveoli (air sac) walls but not yet obliterated small blood vessels (capillaries), which appear as red dots which are individual red blood cells. By 6 weeks in the control rats fibrous tissue is evident causing thickening of all of the alveoli walls and replacing many of the thin walled blood vessels (capillaries) which would normally surround the alveoli allowing gas exchange. In A79 treated rats alveoli walls are thinner and capillaries are more numerous.

# Summary

VB0004 reverses fibrosis in lung as well as in heart and kidney in addition to lowering BP making it a suitable agent for treatment of scleroderma

A79 reverses pulmonary fibrosis but does not affect blood pressure making it suitable for treatment of other causes of pulmonary fibrosis including IPF where BP reduction is not required or is contra-indicated

# Market Metrics

- InterMune – Roche
  - Pirfenidone
  - IPF
  - FDA approved
  - \$8.3bn acquisition
- Promedior – BMS
  - PRM-151
  - Phase IIA
  - IPF
  - \$125m plus \$1.1bn milestones
- Inventiva – Boehringer Ingelheim
  - IVA-337
  - Phase I
  - IPF & scleroderma
  - €170m plus royalties
- Galecto – BMS
  - TD139
  - Phase I
  - IPF
  - \$444m



# *Fibrotic Liver Disease*



# Hepatic Cirrhosis (Liver Fibrosis)

## Causes

- genetic,
- infectious (Hep A, B, C)
- alcohol related,
- diabetic
- due to obesity
- cryptogenic (no discernible cause)

## Prevalence

varies to >40% of the population in countries such as India, Cambodia, Vietnam and China due to endemic Hep B & C.

# Current Therapies

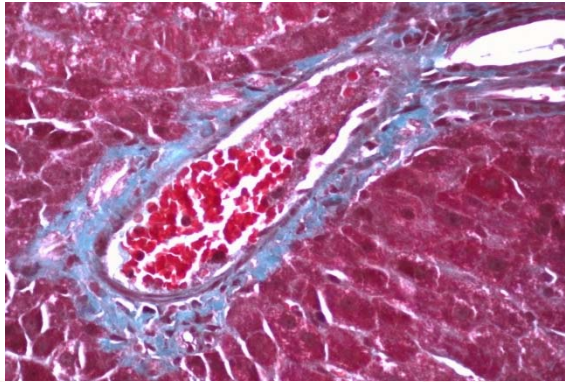
- vaccination Hep A, Hep B for prevention
- abstinence to prevent further damage (EtOH)
- weight loss,
- diabetes management,
- symptom relief (albumin infusion, ascites removal)
- sofosbuvir and related agents for Hep C  
(note this treats the infection but does not prevent progression of the established fibrosis for which lifetime monitoring is required)
- transplantation



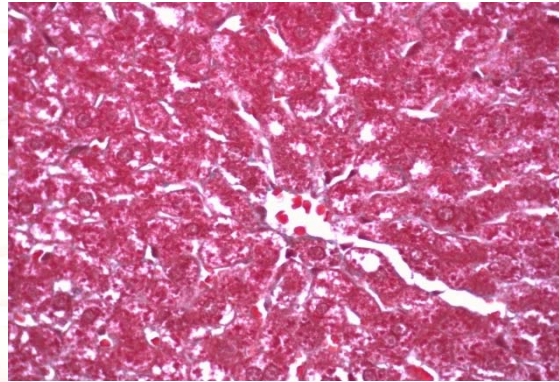
*NASH Video*

# A32 – Liver

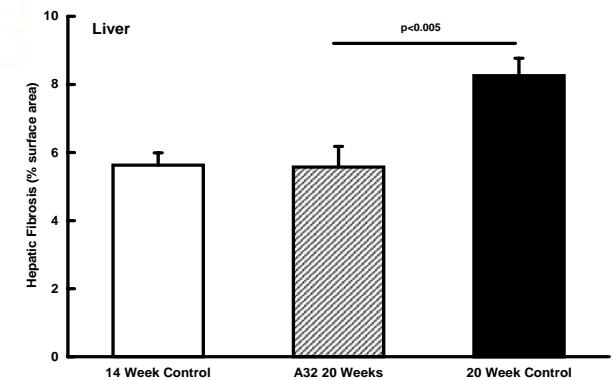
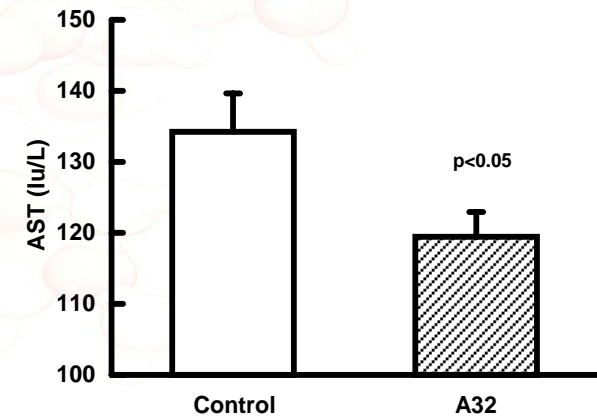
20 Week Control



A32 20 Weeks



Treatment with A32 for 6 weeks in a rat model of liver cirrhosis resulted in significant improvement in liver function (above right) and decreased fibrosis (above and lower right ).

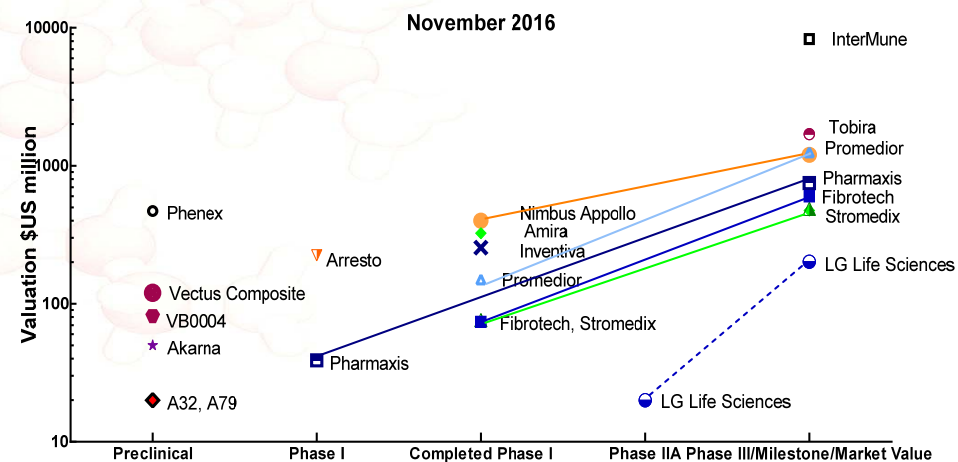
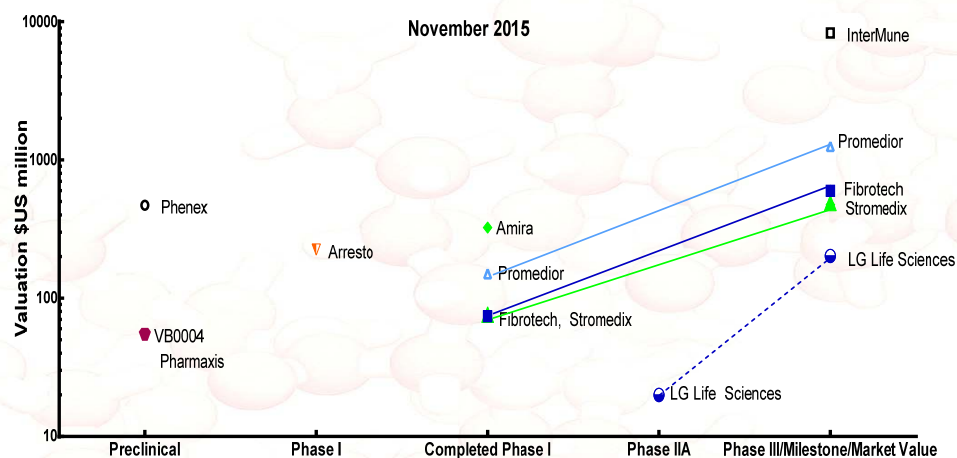


# Market Metrics



- Nimbus Apollo – Gilead
  - NDI-010976
  - NASH
  - \$400m upfront & \$800m milestones
- Pharmaxis – Boehringer Ingelheim
  - PXS4728A
  - NASH
  - \$39m upfront & \$711 milestones
- Tobira – Allergan
  - DPP-4
  - NASH
  - \$615m upfront & \$1.08bn milestones

# Market Metrics Summary



# External Recognition

## AusBiotech Updates

### Australian biotech wins technology award for global potential

8 November 2016: Australian biotechnology company [Vectus Biosystems](#) has won the 'Medtech & Pharma' category in the [Australian Technologies Competition](#) (ATC), which was announced last week at a gala dinner in Sydney.

The Competition looks to recognise Australia's best technology companies with global potential, and provide assessment, mentoring, profile and promotion for winners via a bespoke accelerator program. AusBiotech member, Vectus Biosystems, is a research-based drug discovery company.....



# Patent Portfolio

**VIP patents for heart, kidney and aortic fibrosis - *granted most jurisdictions***

**VIP fragment patents compositions and methods of use for hypertension, cardiac, renal and aortic fibrosis – *granted most jurisdictions***

**VB0004 compositions and methods of use for hypertension, cardiac and renal fibrosis - *granted US patent***

**VB0004 library of approx 70 related compounds compositions and methods of use for treatment of hypertension, cardiac and renal fibrosis - *entering national phase***

**A32 and library of related compounds compositions and methods of use for treatment of hepatic, cardiac and renal fibrosis - *PCT application***

# Patent Portfolio (cont)

**P5 and library of related compounds compositions and methods of use for treatment of renal cell death, renal fibrosis and hepatic fibrosis**

- *PCT application*

**GMP method of synthesis VB0004 - *PCT application***

**A79 and related compounds compositions and use for treatment of pulmonary fibrosis - *Provisional application***

**VB0001 and related compounds compositions and use for management of hypertension and fibrotic disease - *Provisional application***

**VB0002, VB0003 and VB0005 and related compounds compositions and use for management of hypertension and fibrotic disease - *Provisional application***



# Advantages

- Transformational technology – Reverses fibrotic disease
  - Unique selling point
  - Large market(s) – unmet need
  - Strong argument for re-imburement
- Strategic area(s) of interest: Pfizer, GSK, Roche, Merck, Sanofi, Novartis, BMS, Boehringer Ingelheim
- Validated global potential
- Carefully developed IP strategy
- A clear business model and pipeline of compounds to fund company growth.
- Leadership team with a strong track record of success



VIP Agonists:  
the benchmark for anti-fibrotics



**AccuCal™ and RealCount™: a new standard in qPCR**

Vectus Biosystems Limited - Annual General Meeting  
November 17, 2016

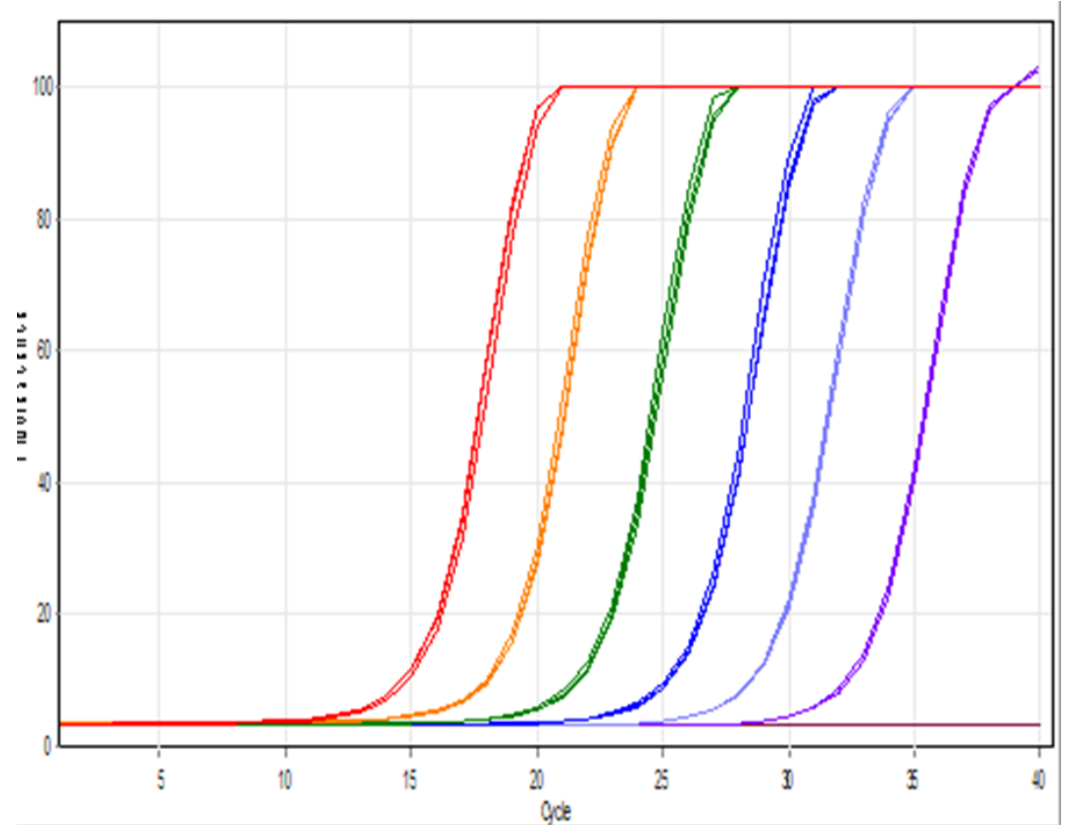
# What is qPCR?

- Quantitative real-time polymerase chain reaction.
- Gene expression analysis, genotyping, pathogen detection, food safety and drug target validation.
- Research, pharmaceutical development, clinical diagnostics.



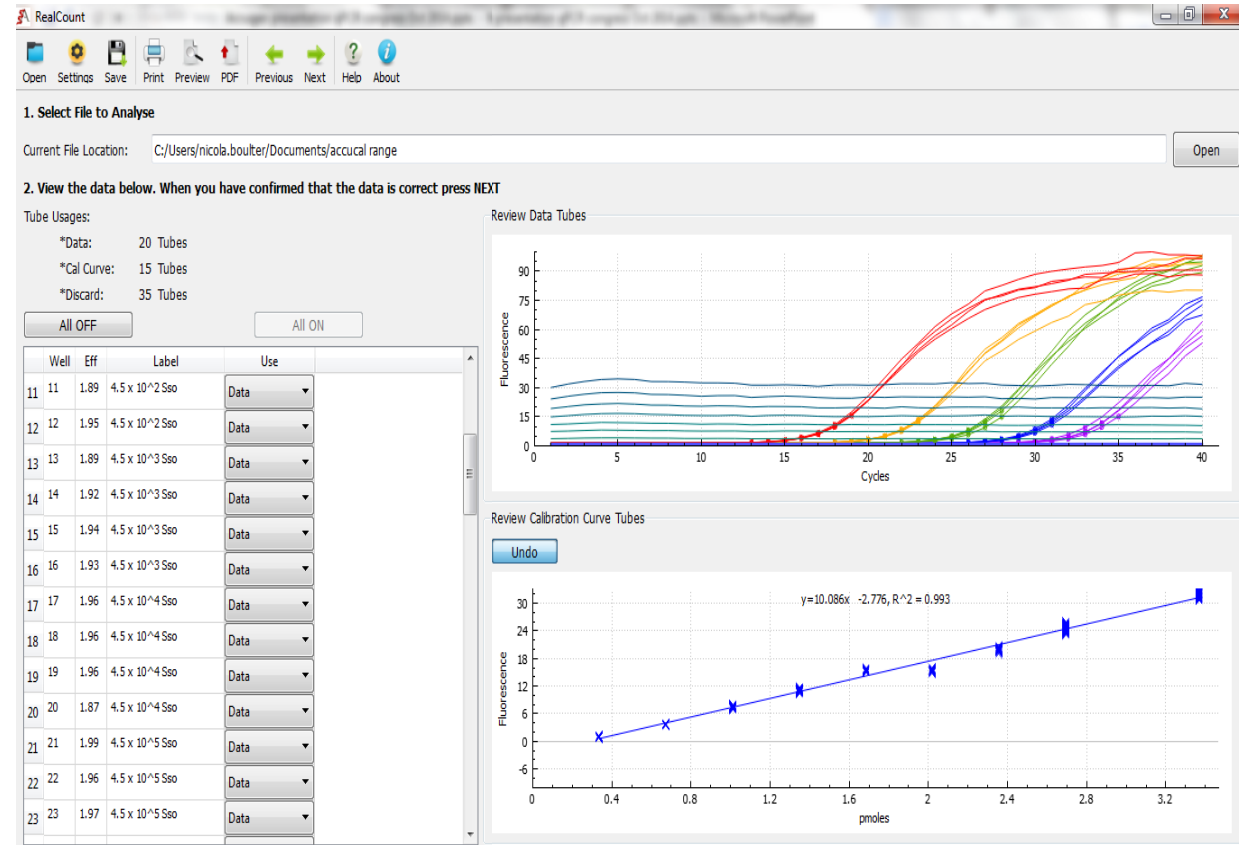
# The problem:

- Relative quantification: requires reference (or “housekeeping”) genes – sometimes these just don’t exist.
- Absolute quantification: requires construction of a standard curve – time-consuming, expensive, only valid for a single gene.



# The solution:

- Patented method (AU 2009904258)
- **AccuCal™** - a consumable DNA calibrator.
- **RealCount™** - a software package that processes raw qPCR data and performs the quantitation calculation.



# The solution:

- Reference genes no longer needed – opens up new experimental possibilities.
- Accuracy of standard curve method – applicable to all genes.
- Fast, simple, cheap, universally applicable.



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**AccuCal™ and RealCount™: a new standard in qPCR**



# Market potential

- Worldwide qPCR market: US\$500 million by 2018 - no market leader
- 35% instrumentation, 65% consumables (master mix: premade reagent mix for performing qPCR)
- Accugen total addressable market:
  - Australia: ~\$6 million
  - World: ~\$100 million



# Commercialisation

- Ongoing: product trial in labs across Sydney.
- Market research survey pre and post-use: usability and pricing information.
- Publication of paper in BMC Biotechnology has generated international interest.



# Commercialisation

- Business model: licensing deal with an established, multinational molecular biology consumables supplier.
- With no market leader, a licensing partner gets increased market share.
- Leverages established sales team, contacts and infrastructure.



# Summary

- Accugen solves a recognised problem in a sizable market.
- Using AccuCal™ and RealCount™ can save the user time and money and deliver increased confidence in the accuracy of results.
- We have identified a business model that can provide a revenue stream to your company, and is attractive to a potential partner.

