Vectus Biosystems Limited

Chairman's Address to 16 November 2017 Annual General Meeting

The year 2017 has seen a major consolidation and development of the position of Vectus Biosystems Limited in the growing franchise for drugs that inhibit the process of fibrosis in organs damaged by disease. Fibrosis, a process whereby healthy tissues are replaced by non-functioning collagen fibres, is the main cause of organ failure in the hearts and kidneys of people with high blood pressure or diabetes, in the livers of people with cirrhosis and in a wide range of lung diseases. The benefits of our drugs in development are not only improvements in wellbeing for patients, but also economic gains for Australia's health system. Heart and kidney failure represent costs to economies around the world of many billions of dollars annually.

Among our significant achievements were:

- Further expansion of the Vectus proprietary drug library to in excess of 1,000 compounds, and the granting of full patent status for our lead compound in the cardiovascular fibrosis franchise, VB0004, in the USA, Europe, China, Japan, Australia and New Zealand.
- Scaled-up production of VB0004 to GMP standards and the completion of the 28-day animal toxicity studies, the final step on the critical pathway to Phase 1 human studies, which are scheduled to commence in early-to-mid 2018.
- Validation of the efficacy of lead compounds A39 and A79 in liver and lung fibrosis models respectively.
- Detailed understanding of the mechanisms of action of VB0004 and other lead compounds, essential information for due diligence by pharmaceutical industry partners, and ongoing research planning.
- High levels of interest from human and animal health companies, which are continuing, with discussions under confidentiality agreements in progress with 12 companies.
- Commercialisation of our Accugen platform technology for quantitative polymerase chain reaction (qPCR). This is a fundamental laboratory procedure for which Accugen provides a leap in quantitative precision at lower cost than current technologies.

Vectus Research and Development (R&D)

From Dr Karen Duggan's original research into vasoactive intestinal peptide (VIP), Vectus has progressed to the development of small molecule compounds that retain VIP's therapeutic benefits of reversing fibrosis and are ideally placed for investment by pharmaceutical companies. Since the Company's last Annual General Meeting, we have focussed on building value in Vectus by:

- developing complete data packages on mechanisms of action and efficacy to support therapeutic and patent claims, and to define avenues for the future R&D of our compound library;
- actively expanding franchises into fibrosis of the liver and lungs; and
- exploring, with animal health companies, the potential for the veterinary use of Vectus' products. Such partnerships have the additional advantages of allowing us to study our compounds in animal models, prior to beginning studies in human subjects.

Vectus is still at the forefront of the development of drugs that reverse fibrosis, rather than merely slowing its progress, in spite of a rapidly increasing number of companies entering the franchise. Building the market for Accugen will provide further funds for development. The Company qualifies for the Federal Government's R&D Tax Incentive cash-back programme. We continue to satisfy all auditing standards.

The composition of the Board is unchanged since our last AGM. The skills represented by its members cover well the needs and goals of the Company. I thank all Board members for their high level of commitment during the past year, and our Company Secretary, Mr Robert Waring, for his unfailing attention to the Company's conduct and compliance with ASX and regulatory requirements. Dr Karen Duggan, as Chief Executive Officer, Medical and Scientific Director, and Board member, is unifying the Company's scientific and business management.

My final acknowledgment is of our outstandingly-competent and dedicated laboratory staff, whose commitment and hard work underpin our success. Dr Nicholas Sigglekow, formerly a senior research scientist, has joined our team as a highly-regarded laboratory manager. We have also appointed new managers for the Accugen business and for Vectus' commercial development.

Vectus remains strongly positioned to become a global leader in anti-fibrotic drug development. My sincere thanks go to our shareholders, whose continuing support inspires and motivates the whole Company.

Vectus Biosystems Limited

Graham Macdonald
Non-Executive Chairman

VECTUS BIOSYSTEMS

Annual General Meeting 2017

Achievements 2017

- **VB0004**
  - GMP synthesis completed at scale
  - IND toxicology almost complete
  - VB0004 patent granted in major jurisdictions
  - Selected to present at Biotech Showcase (JP Morgan San Francisco)
  - Invited to present at Bioshares 2017 in Queenstown
  - Pharma engagement
- **VB4-A32 – Hepatic Fibrosis**
  - Further pre-clinical work completed
  - In house toxicology in progress
  - Pharma engagement
- **VB4-A79**
  - PCT lodged
  - In house toxicology in progress
  - Pharma engagement
- **Compound Library**
  - PCT lodged
- **Accugen**
  - Manufacturing contact in tendering
  - KOL's selected

VECTUS BIOSYSTEMS

Oral Vasoactive Intestinal Peptide (VIP) Agonists

The Transformational Platform To Manage Fibrotic Disease

Why is Fibrosis Important ?

- **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.

Pharma Check List for Potential Therapeutics

- Platform technology
- Transformational agent
- Validated target
- Demonstrated efficacy in appropriate animal model

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Pharma Check List for Potential Therapeutics

Demonstrated safety – IND toxicology

IP covers compositions of matter

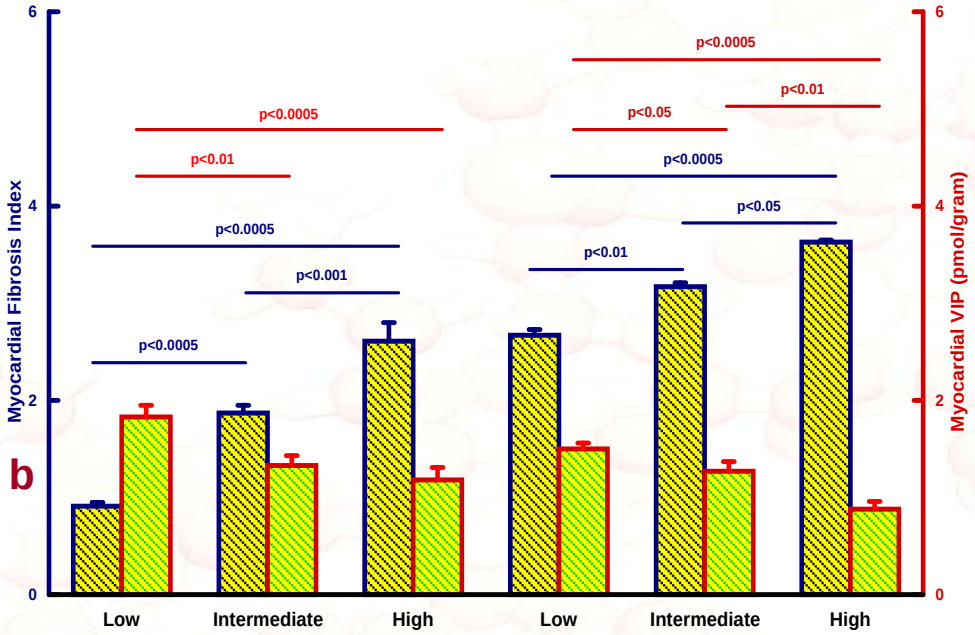
Synthesis at scale

Cost of goods competitive

Long patent life

VECTUS BIOSYSTEMS

Defining VIP as the Therapeutic Target

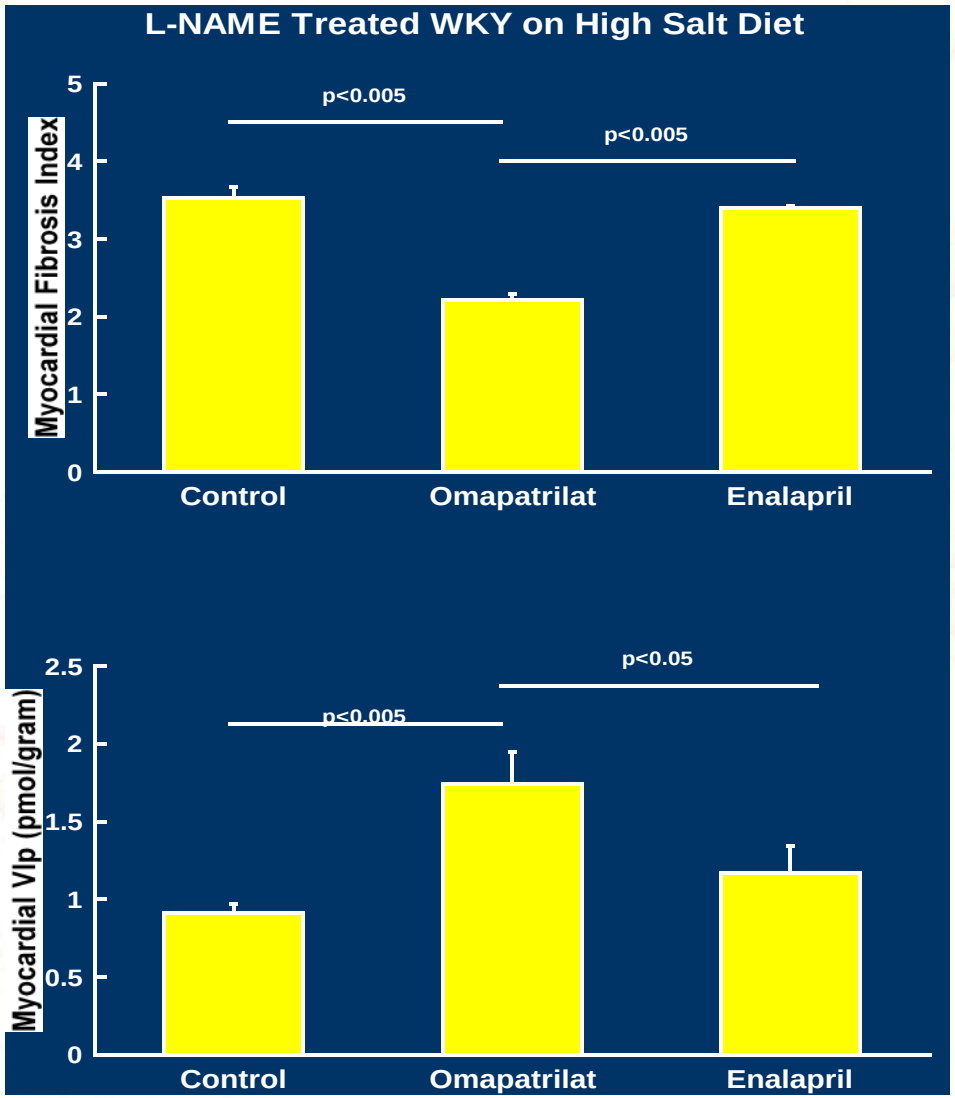


- Myocardial fibrosis (blue) and VIP concentrations (red) in WKY and SHR rats on varying salt diets
- The degree of fibrosis increased across the spectrum from WKY on low salt diet to SHR on high salt diet
- The concentration of VIP decreased from WKY on low salt diet to SHR on high salt diet
- i.e. the degree of fibrosis in the heart was inversely related to VIP concentration in the heart
- ? Decreased VIP caused fibrosis
- ? VIP replenishment a therapeutic option

Ye, VZC Hodge, G Yong, JLC & Duggan, KA Exp. Physiol. 2002; 87:539-546
Ye, VZC Hodge, G Yong, JLC & Duggan, KA Acta Physiol. Scand. 2003; 179:353-360.

VECTUS BIOSYSTEMS

Defining VIP as the Therapeutic Target



- E24.11, (Neprolysin) is the metabolising enzyme for VIP
- Does increasing myocardial VIP by inhibiting VIP metabolism decrease fibrosis?

- Comparison fibrosis and VIP levels in the heart after 4 weeks treAtment with either a combined neprolysisn ACE inhibitor (ommapatrilat) with Ace inhibitor (enalapril)

- Omipatrilat increased VIP and decreased fibrosis while at the same level of BP reduction enalapril had no effect on either.

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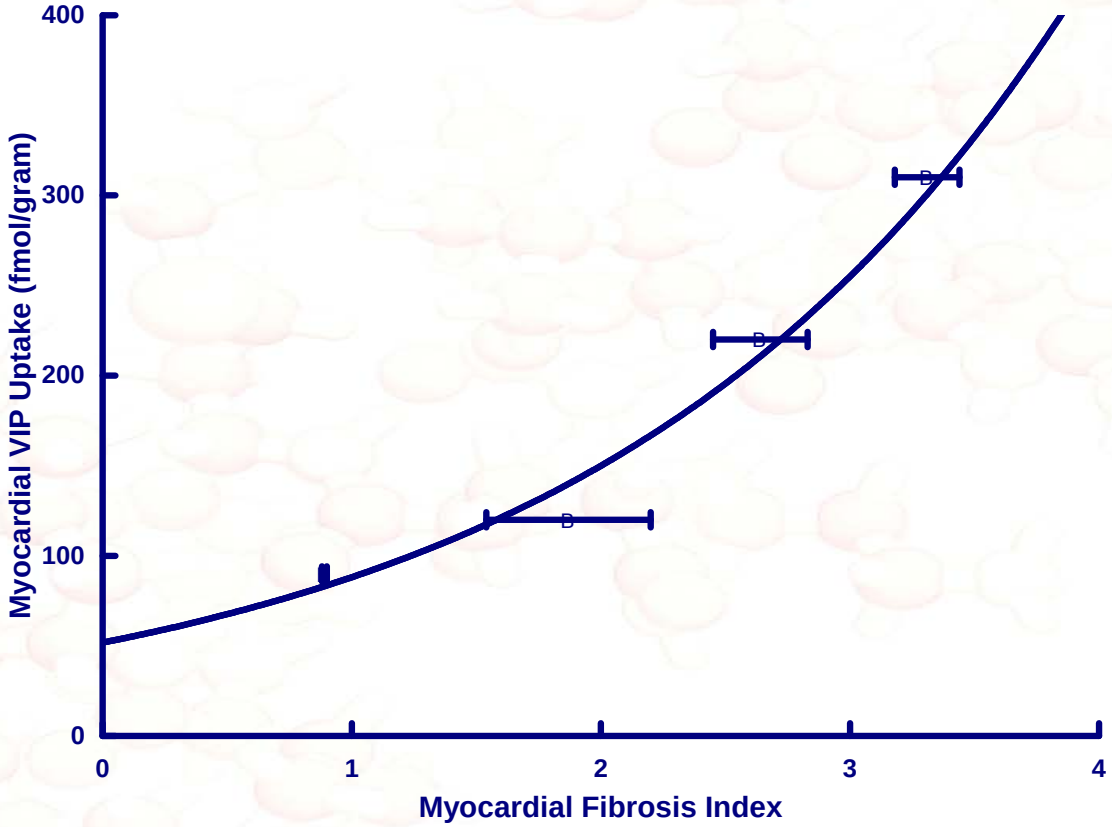
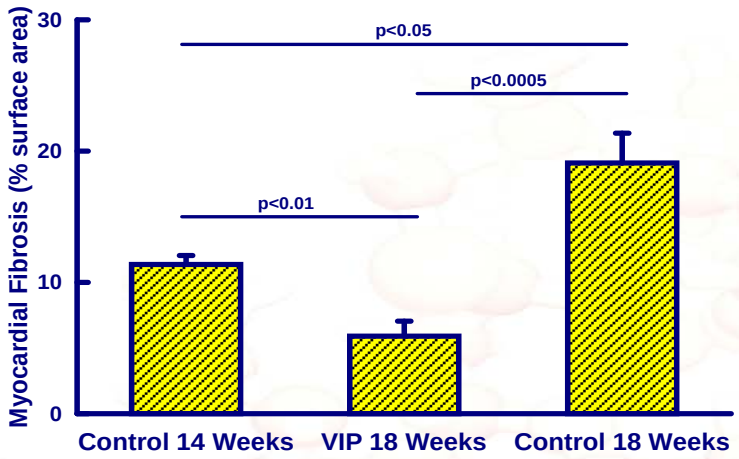
Defining VIP as the Therapeutic Target



Myocardial VIP uptake as a function of the degree of fibrosis in 4 models (from left to right WKY low salt, WKY low salt L-NAME, WKY high salt, WKY high salt L-NAME). Exponential increase in uptake as disease level increases R2=0.9655

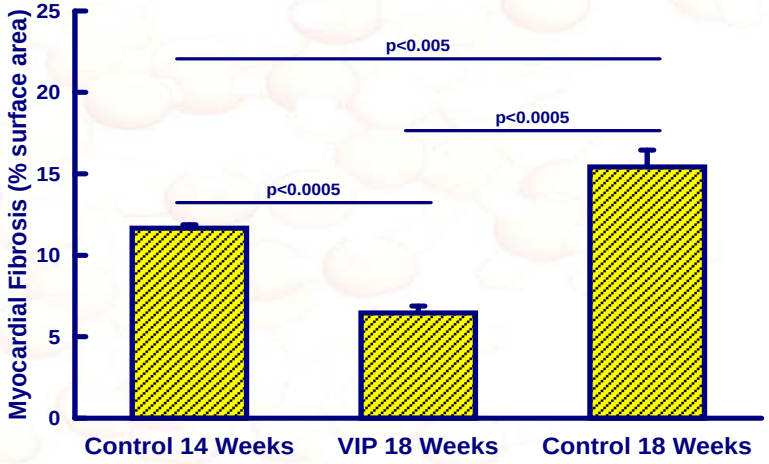
Defining VIP as the Therapeutic Target

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



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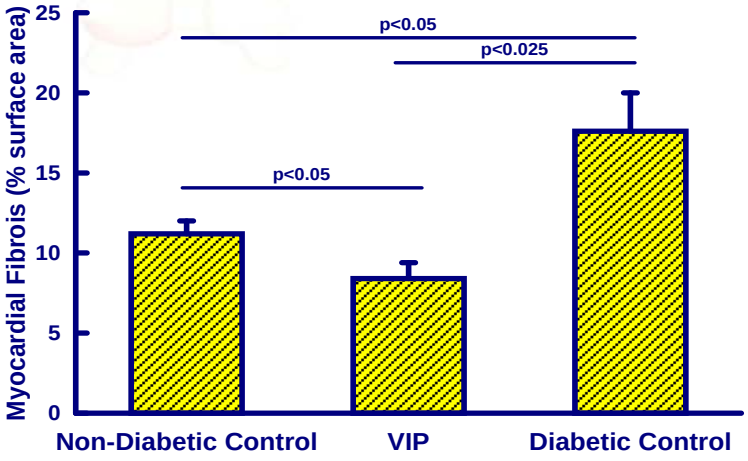
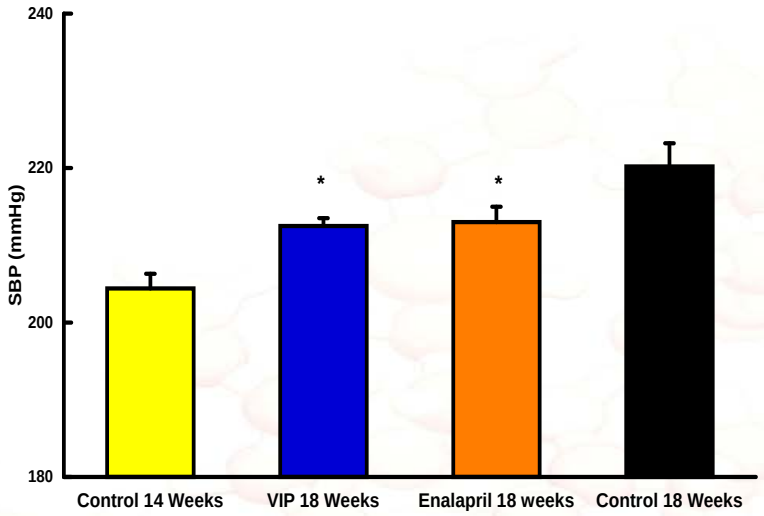


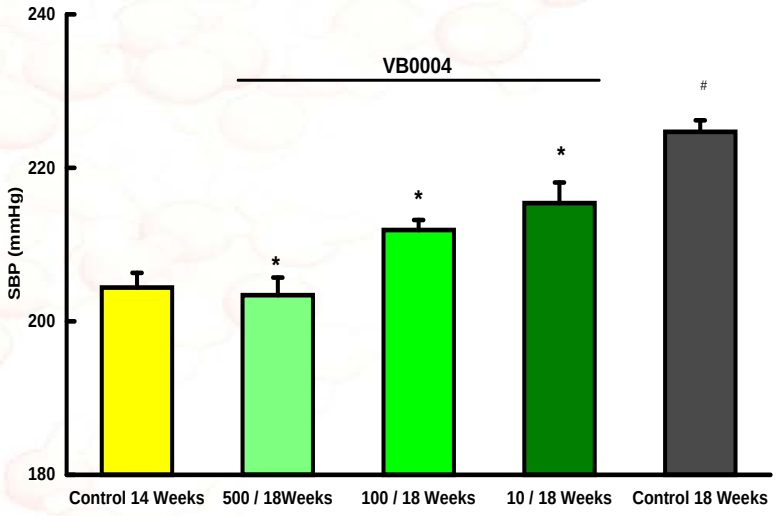
VECTUS BIOSYSTEMS

VECTUS BIOSYSTEMS

HYPERTENSION, CARDIOVASCULAR AND RENAL DISEASE

Systolic Blood Pressure

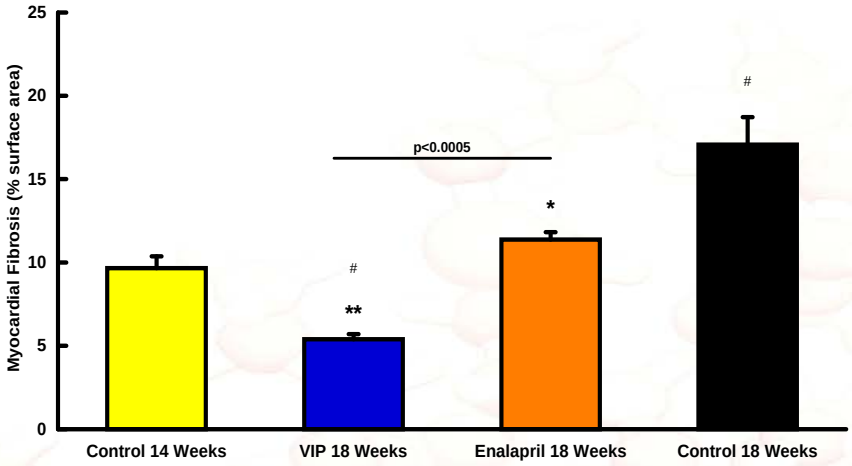


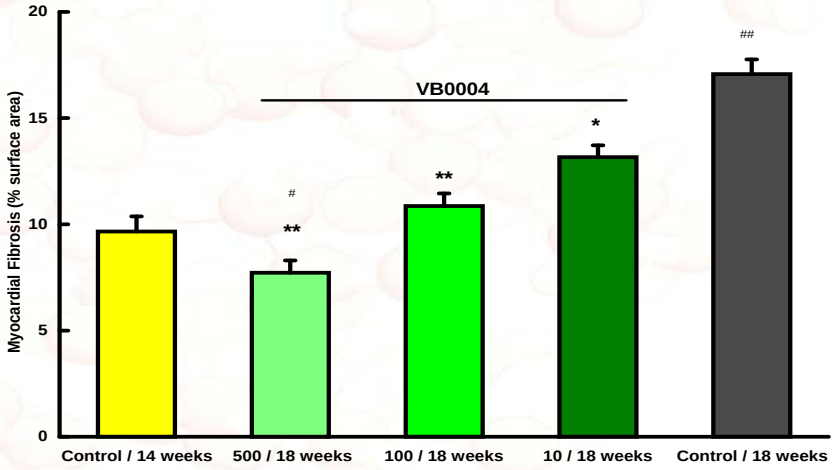


Left Panel: SBP in SHR after 4 weeks' treatment with VIP (5 pmol/kg/min) or enalapril (dose adjusted), compared with 14 and 18 week controls. * $p<0.05$ vs 18 week controls.

Right Panel: SBP in SHR after 4 weeks treatment with VB0004 at 10 (dark green), 100 (mid green) and 500 (light green) pmol/kg/min, compared with 14 and 18 week controls. * $p<0.0005$ vs 18 week controls.

Myocardial Fibrosis



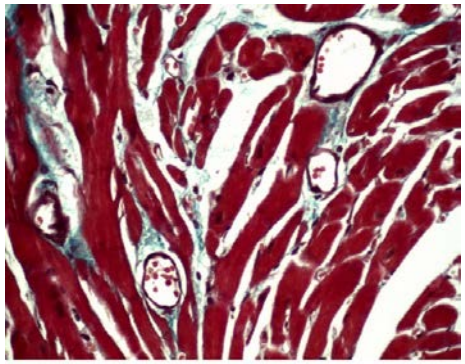


- **Upper Panel:** Myocardial fibrosis after 4 weeks treatment with VIP (5pmol/kg/min) or enalapril (dose adjusted to maintain the same BP reduction as VIP average dose 705 pmol/kg/min). * p<0.005, ** p<0.001, *** p<0.0005 vs 18 week control and ## p<0.0005 vs 14 week control
- **VIP (5pmol/kg/min) reversed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

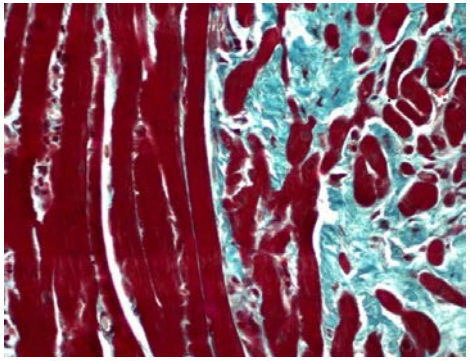
VECTUS BIOSYSTEMS

Cardiac Histology

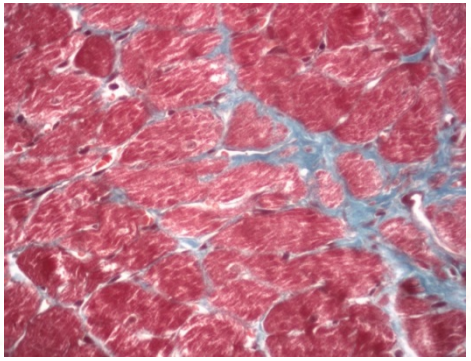
Control 14 weeks

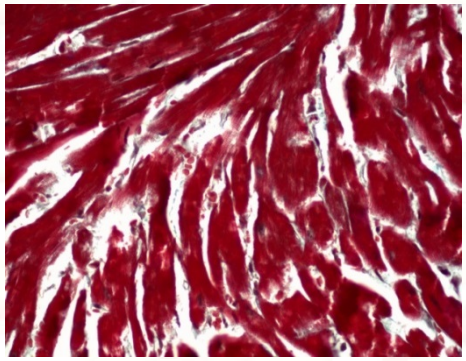


Control 18 Weeks

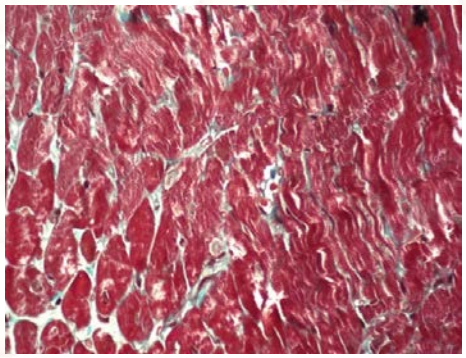


18 Weeks 5% EtOH

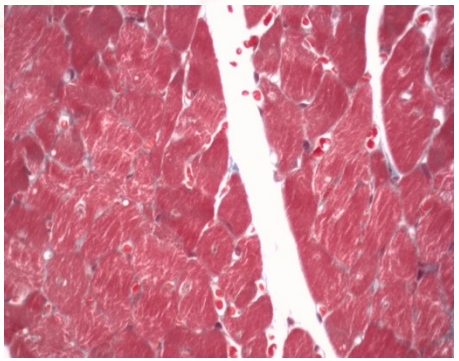




VIP 18 Weeks



Enalapril 18 Weeks



VB0004 18 Weeks

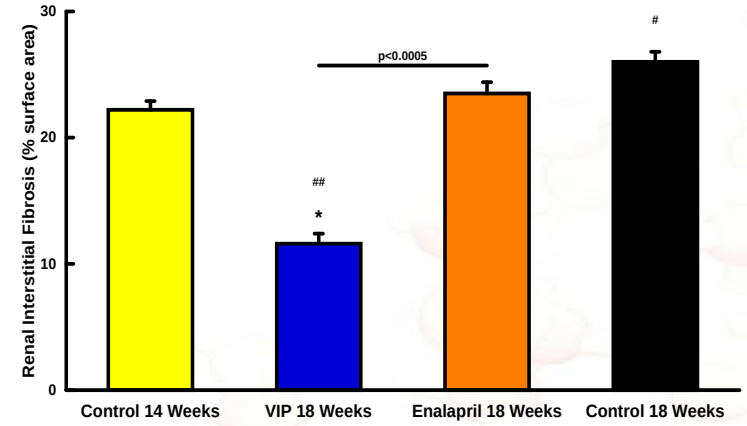
Heart sections stained with Masson trichrome, fibrous tissue appears blue-cyano in colour

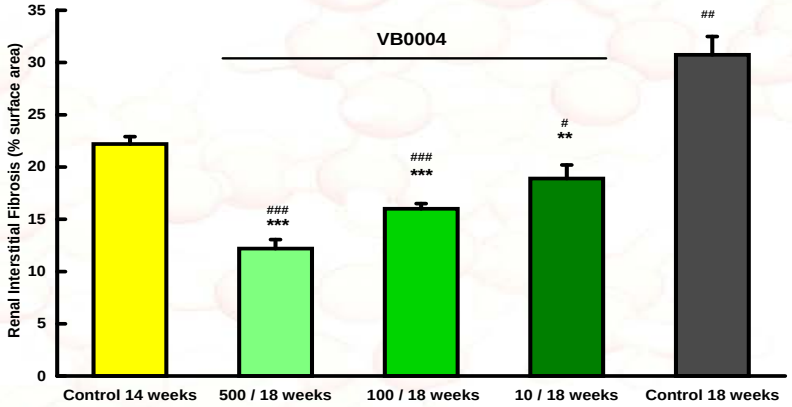
Upper Panels: 14 week control fibrosis is predominantly around blood vessels with some interstitial extension 18 week vehicle control marked increase in interstitial fibrosis surrounding muscle fibres and loss of muscle fibres 18 week 5% ethanol drinking solution. Fibrosis is visible as blue stained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

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

VECTUS BIOSYSTEMS

Renal Fibrosis



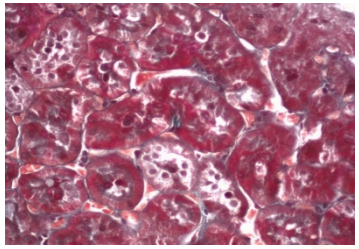


- In humans increasing interstitial fibrosis in the kidney parallels the decline in renal function leading to dialysis
- Upper panel shows results from 14 week old SHR on 2.2% salt diet which were randomised to
  - 14 week control (open bar)VIP (5pmol/kg/min) infusion for 4 weeks (solid blue bar)
  - 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.

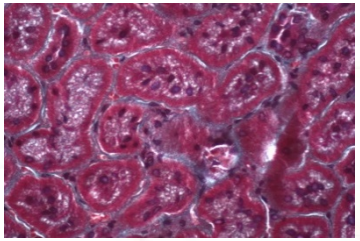
VECTUS BIOSYSTEMS

Renal Histology

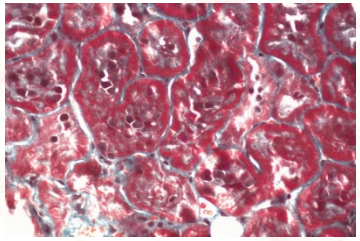
Control 14 weeks

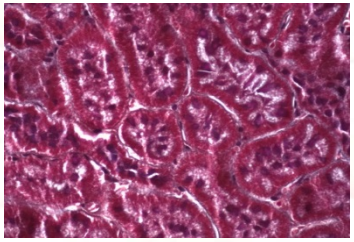


Control 18 Weeks

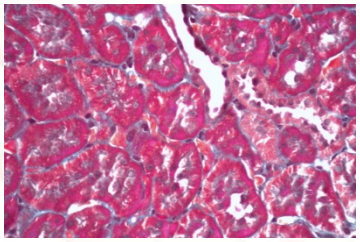


18 Weeks 5% EtOH

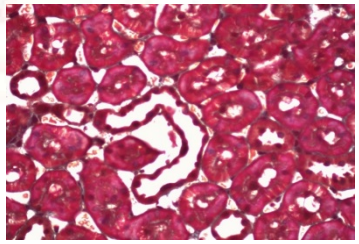




VIP 18 Weeks



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

VECTUS BIOSYSTEMS


The Path To The Clinic

GMP Synthesis

- PCT lodged covering GMP synthesis method
- VB0004 manufactured to 5kg scale
- Yield increased as scale increased
- Cost efficient
- Cost of goods at current scale < $(US) 0.05 per mg
- Estimated dose 1-5mg
- Stability studies to 6 months completed

VECTUS BIOSYSTEMS

IND Enabling Toxicology

- SAD and MAD
  - Single ascending dose to 2,000mg/kg no adverse event
  - 7 day multiple ascending dose to 1,000mg/kg no adverse events
  - 28 day multiple ascending dose to 600mg/kg no adverse events
- Cardiovascular safety
  - hERG studies low arrhythmia potential
  - Dog study no adverse events
- Respiratory Safety study no adverse events
- Mutagenic potential
  - Ames test negative
  - Bone marrow toxicity study in progress
- **NO** inhibition of major drug metabolising enzymes
- Acceptable pharmacokinetic profile

VECTUS BIOSYSTEMS

Intellectual Property

- VB0004 patent covers
- compositions of matter
- methods of use
- VB0004 Patent granted in all major jurisdictions
  - USA, Europe, Japan, Peoples Republic of China, Republic of South Korea
  - as well as Australia, Israel, Phillipines
- VB0004 Patent has been accepted for grant in
  - ARIPO, Canada, Russian Federation, South Africa
- Patent life
  - Priority date September 2013
  - 17 years (+5 years on licensing)
- VB0004 Method of synthesis patent at PCT stage

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VB0004 Check List

Pharma Criteria	Vectus
Platform technology	√
Transformational agent	√
Validated target	√
Demonstrated efficacy in appropriate animal model	√

VECTUS BIOSYSTEMS

VB0004 Check List

Pharma Criteria	Vectus
Demonstrated safety – IND toxicology	√
IP covers compositions of matter	√
Cost of goods competitive	√
Long patent life	√

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Fibrotic Lung Disease

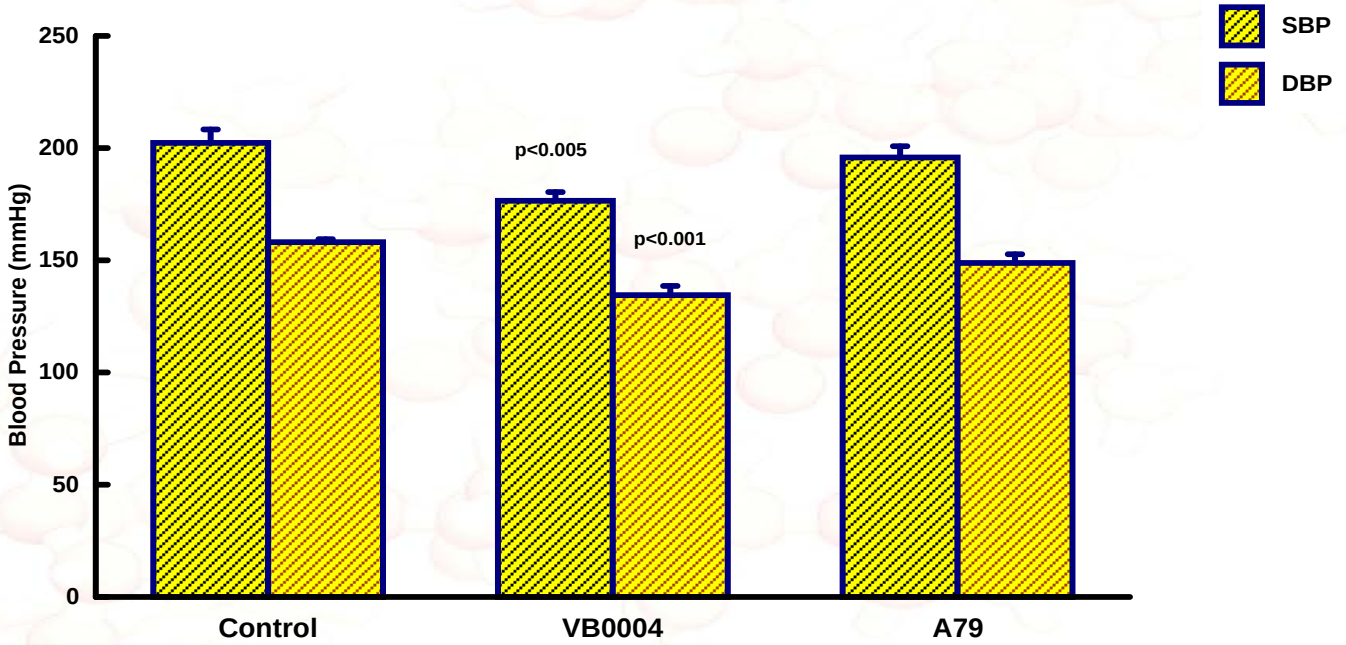
Pulmonary Fibrosis

Causes

- Environnemental (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.

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.

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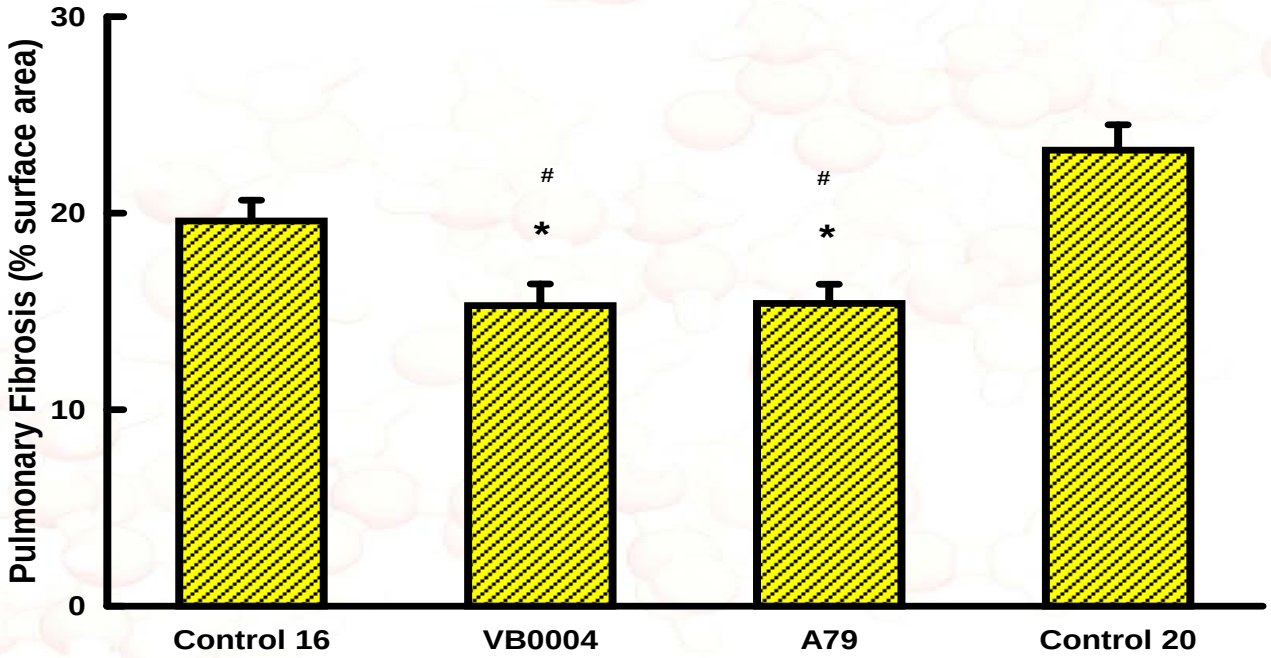
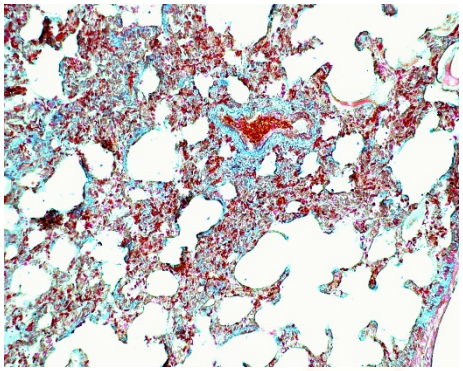
Pulmonary Fibrosis



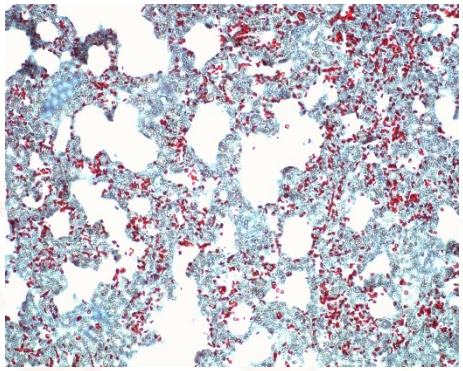
Pulmonary fibrosis in 16 week controls (two weeks after Bleomycin administration) and at 20 weeks after 4 weeks treatment in VB0004, A79 and vehicle control rats. VB0004 and A79 were administered at 500pmol/kg/min in the drinking solution (5% ethanol) vehicle control is drinking solution alone.
* $p<0.001$ vs 20 week control, # $p<0.01$ vs 16 week control.

VECTUS BIOSYSTEMS

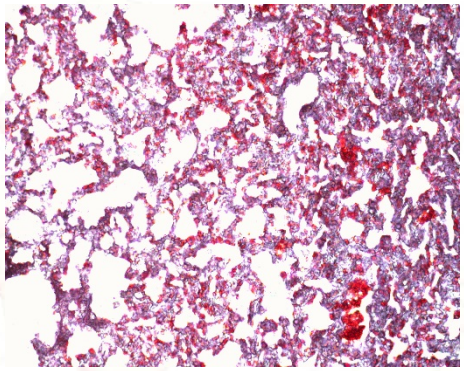
Histology



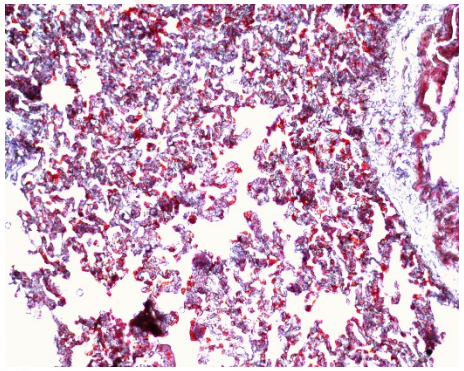
16 Week Control



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 (500pmolkg/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.

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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 an orphan disease which causes multiple organ fibrosis as well as severe hypertension

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

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Fibrotic Liver Disease

Hepatic Cirrhosis (Liver Fibrosis)

Causes

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

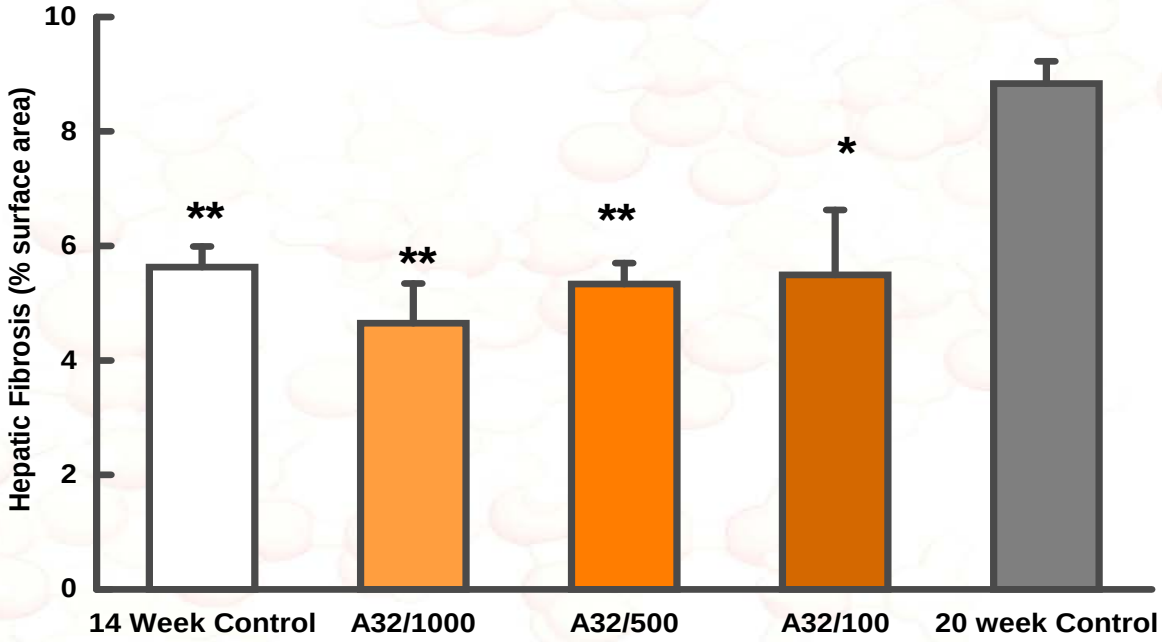
Prevalence

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

Hepatic (Peri-Portal) Fibrosis



Hepatic fibrosis in the SHR on a high fat diet and 10% ethanol treated with varying doses of A32 or drinking solution alone for 6 weeks commencing at 14 weeks of age. A32 at all doses was able to prevent development and progression of fibrosis in this model. * $p<0.01$, ** $p<0.005$ vs 20 week control.

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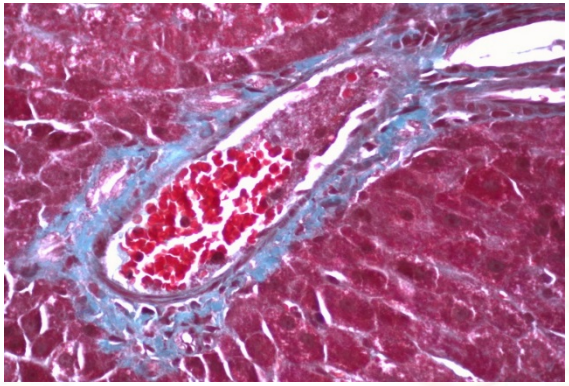
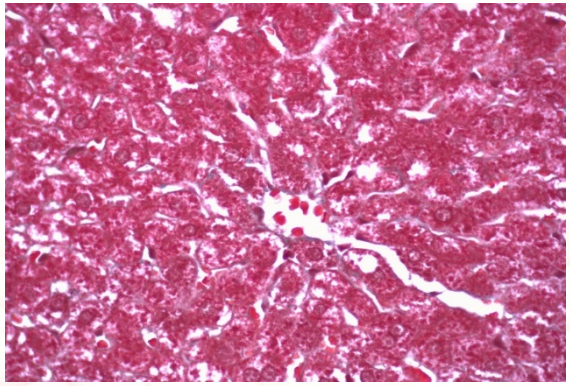
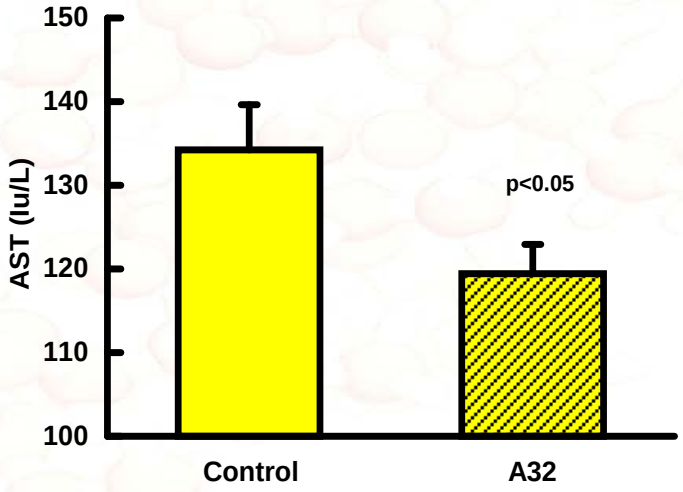
A32 – Liver

20 Week Control



A32 20 Weeks





Treatment with oral A32 (500 pmol/kg/min) for 6 weeks in a rat model of liver cirrhosis resulted in:

Upper Left: restoration of sinusoidal architecture (right) and removal of fibrosis compared with 20 week control (left)

Lower Left: significant improvement in liver function as estimated by plasma AST activity

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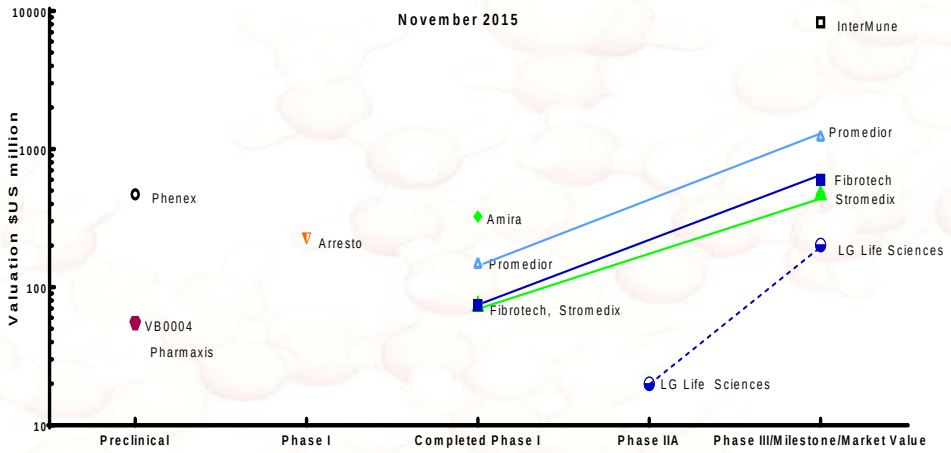
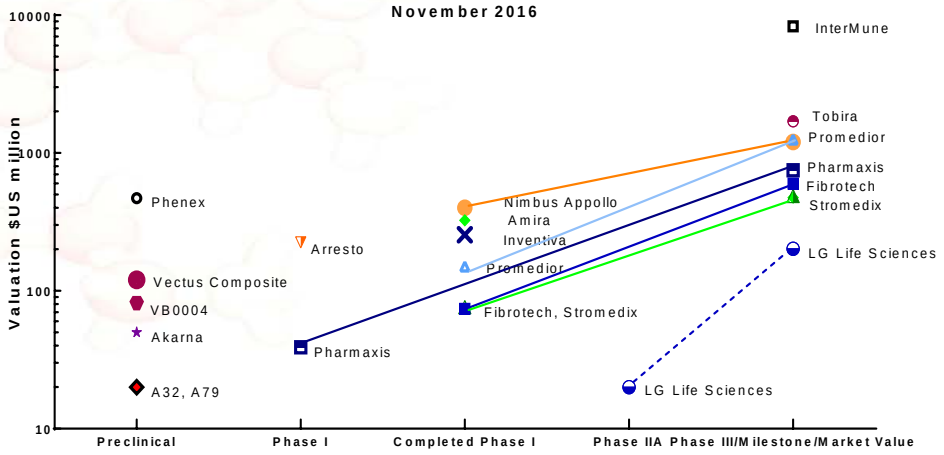
Market Metrics Summary





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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, Japan, China, South Korea, Europe, Australia allowed in ARIPO, Canada, Russian Federation, South Africa*

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*

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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 - *PCT application*

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

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

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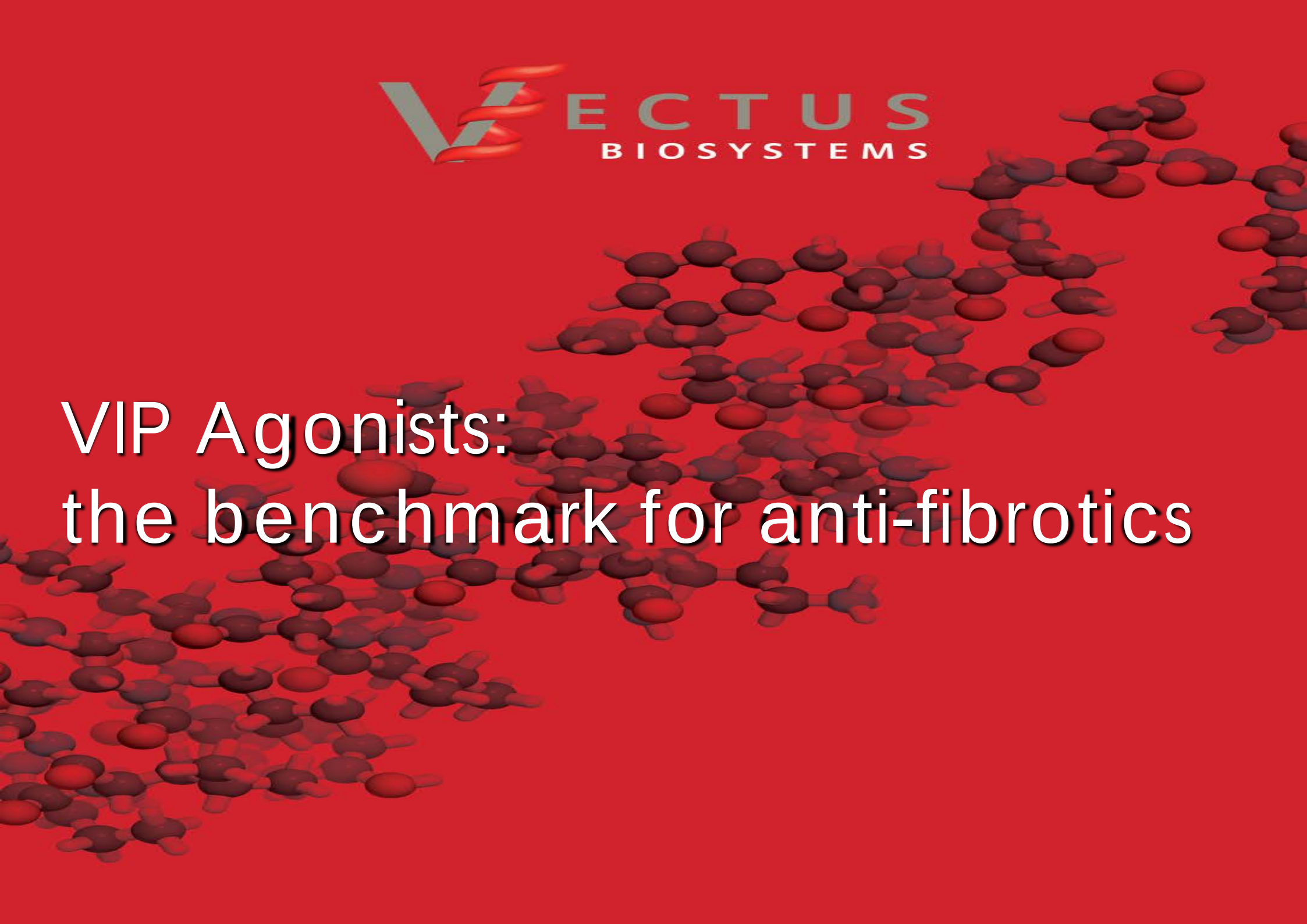
Advantages

- Transformational technology – Reverses fibrotic disease
  - Unique selling point
  - Large market(s) – unmet need
  - Strong argument for re-imbursement
- 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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the benchmark for anti-fibrotics