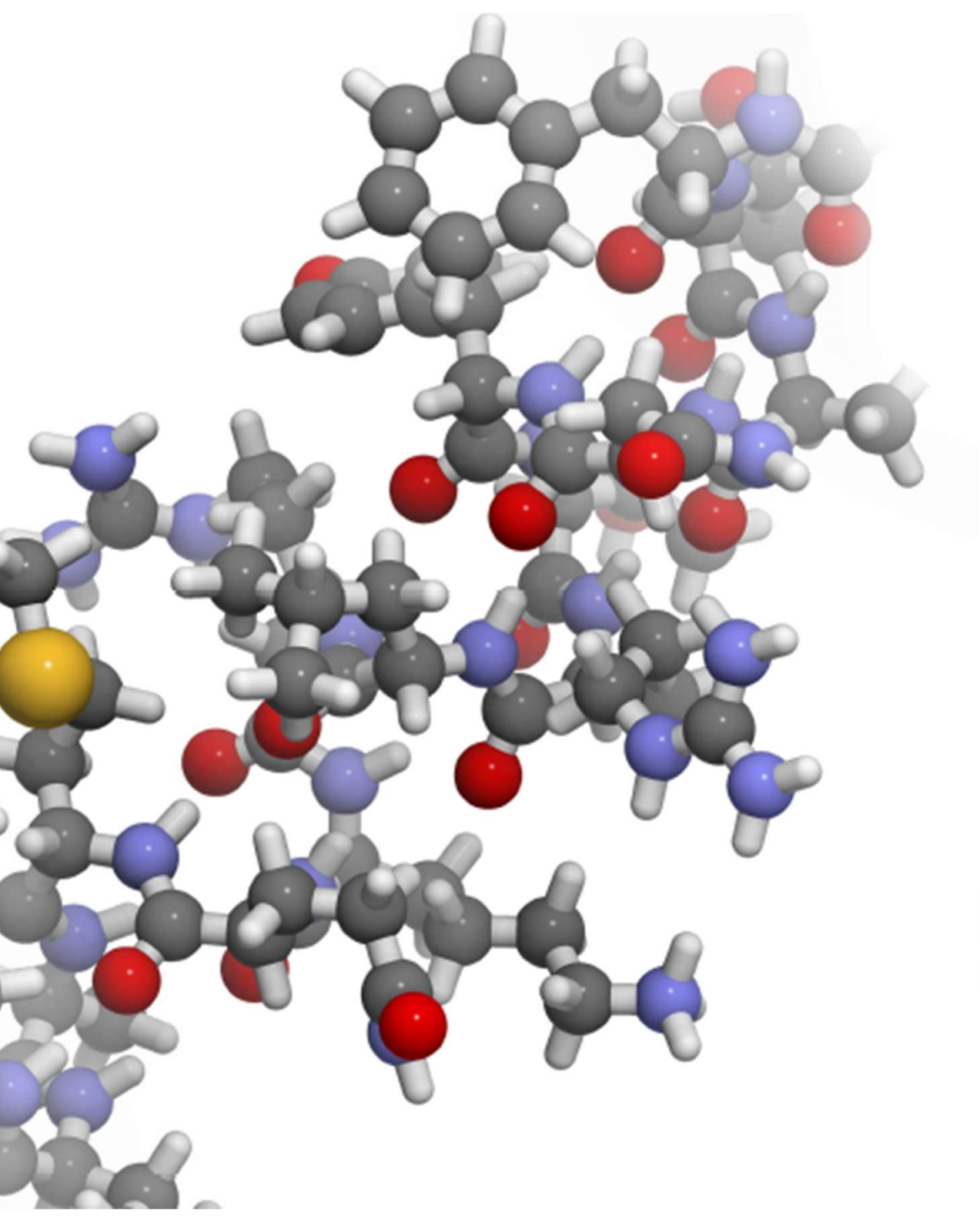


VIP Agonists – The Benchmark for Anti-Fibrotics

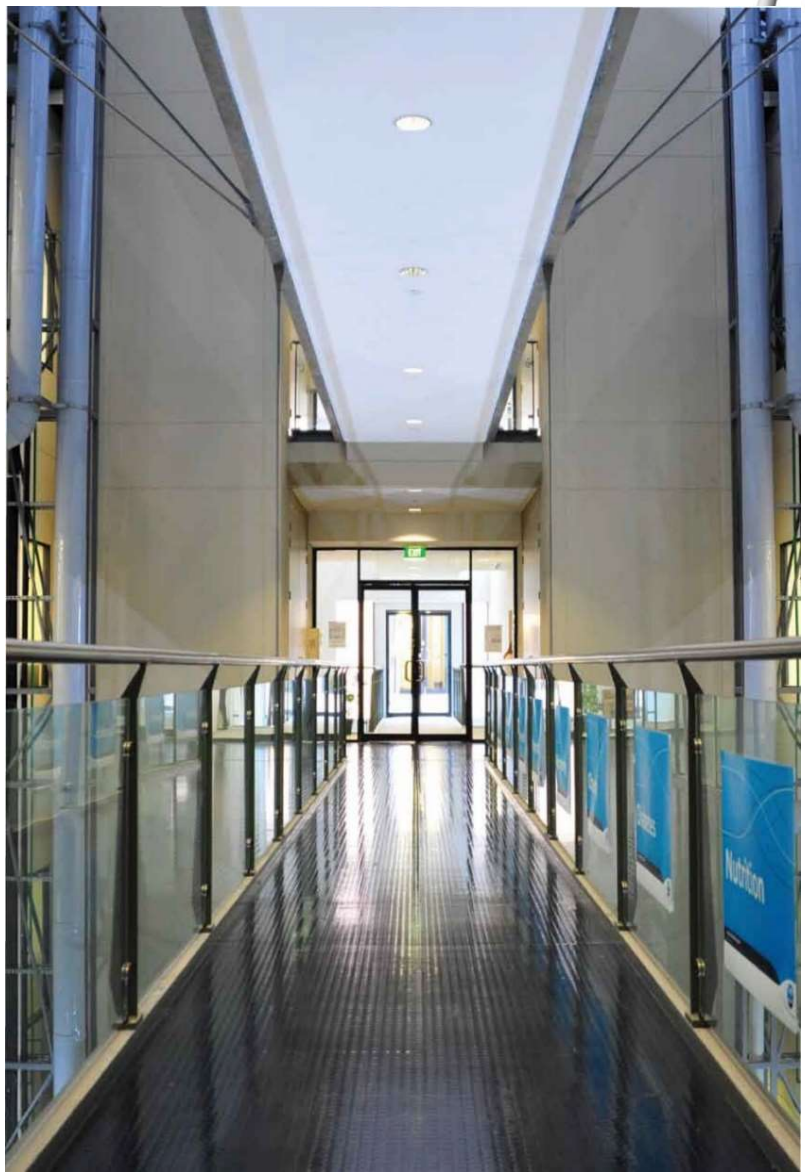
VECTUS BIOSYSTEMS

OVERVIEW

Fibrosis is the replacement of normal tissue (heart, lung, kidney etc) by scar tissue and can lead to organ failure

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)

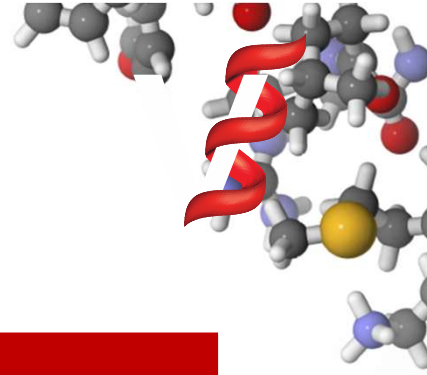


Fibrotic disease contributes to more than **40% of all deaths worldwide**

Fibrosis Reversal, a major unmet need

VECTUS BIOSYSTEMS

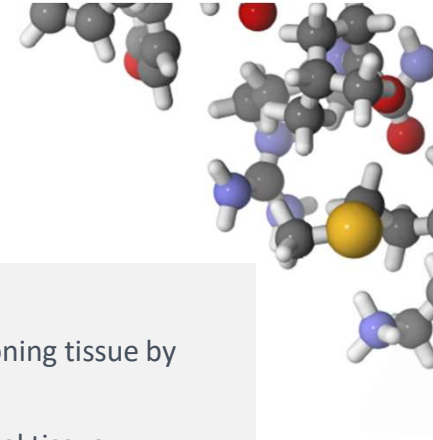
PATH TO THE CLINIC



Pharma criteria	Vectus
Platform Technology	✓
Transformational Agent	
Validated Target	
Demonstrated Efficacy in Animal Model	
Demonstrated Safety – IND toxicology	
IP Covers Composition of Matter	
Synthesis at Scale	
Cost of Good Competitive	
Sufficient Patent Life	
Phase I Safety Study	
Human pD (Efficacy) Data	

VECTUS BIOSYSTEMS

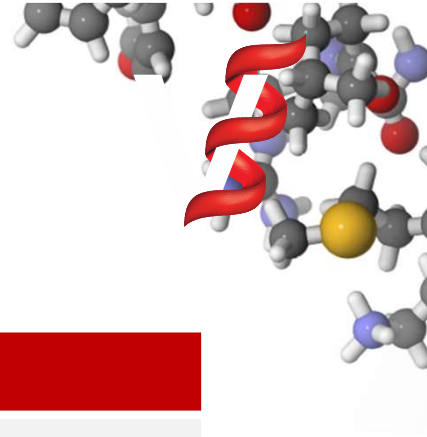
LEAD DRUGS IN 4 SIGNIFICANT AREAS



Cardiovascular - Renal	• Heart and kidney failure constitute the largest current imposts on healthcare budgets world-wide • Although there are many causative factors the underlying pathology is replacement of normal functioning tissue by fibrous (“scar”) tissue • VB0004 unlike current agents or those in development of which we are aware is able to restore normal tissue architecture
Liver Disease	• Hepatic cirrhosis (liver fibrosis) is an important and challenging health issue in many developing countries • Hepatic cirrhosis may be cryptogenic, genetic, infectious (Hepatitis B and C), alcohol related, diabetic or due to obesity in origin and it may result in liver failure and/or liver cancer • Vectus is unaware of any FDA approved therapeutics for liver fibrosis which can reduce the progression of fibrosis or cirrhosis nor for liver inflammation
Idiopathic Pulmonary Fibrosis	• Idiopathic Pulmonary Fibrosis (IPF) is a chronic condition characterized by damage to lungs, resulting from inflammation and scarring. More than 70,000 people in the US and the EU suffer from this condition, and the FDA has nominated that drugs targeting this disease would be considered for orphan drug status • Global data projected that the US and the EU markets would be worth over $1.1bn by 2017 due to lack of other options. There is also a significant opportunity in Asian markets, where lung disease is highly prevalent
Kidney Protection	• A side effect of some cancer therapies can be inadvertent destruction of kidney tubules leading to dialysis requiring kidney failure • Although it represents a small population there is no current therapy

VECTUS BIOSYSTEMS

PATH TO THE CLINIC



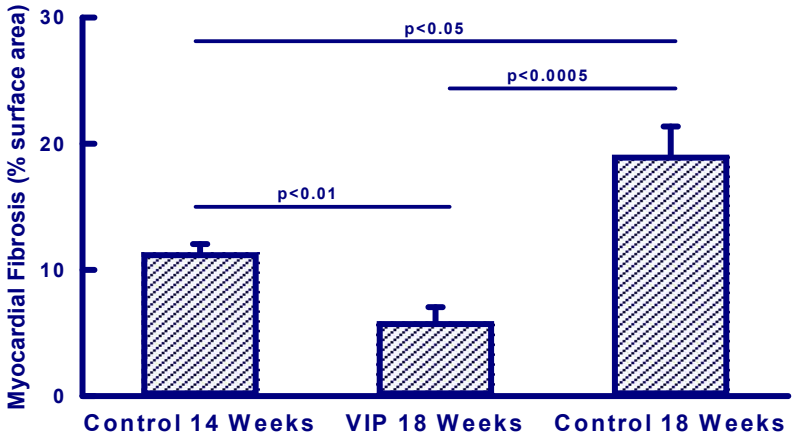
Pharma criteria	Vectus
Platform Technology	✓
Validated Target	✓
Transformational Agent	
Demonstrated Efficacy in Animal Model	
Demonstrated Safety – IND toxicology	
Synthesis at Scale	
Cost of Goods Competitive	
IP Covers Composition of Matter	
Sufficient Patent Life	
Phase I Safety Study	
Human pD (Efficacy) Data	

TARGET VALIDATION

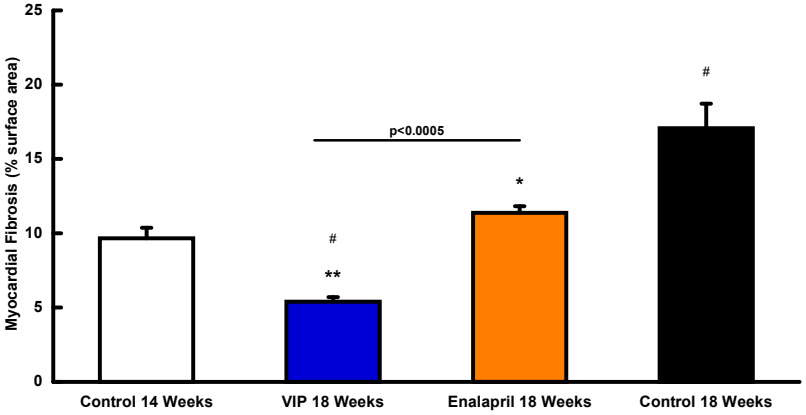
VB0004 is a non-peptide (small molecule) mimetic of Vasoactive Intestinal Peptide (VIP)

VIP reversed cardiac fibrosis in multiple animal models

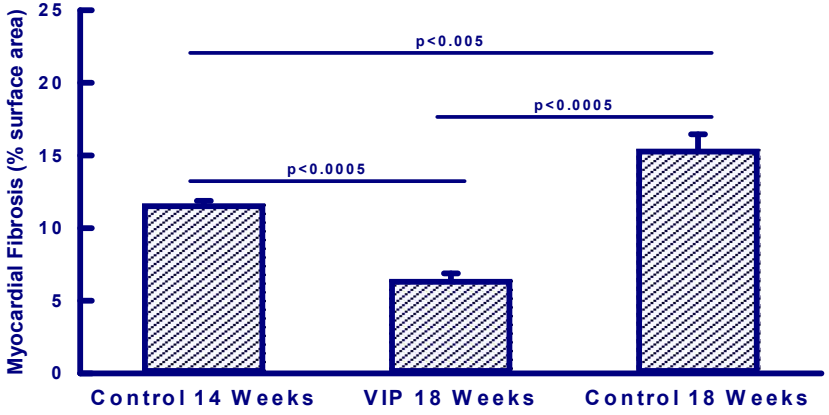
Normotensive rats on 4.4%



Hypertensive rats on 2.2% salt diet

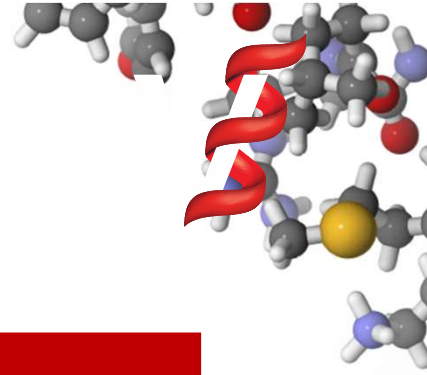


L-NAME Treated rats



VECTUS BIOSYSTEMS

PATH TO THE CLINIC



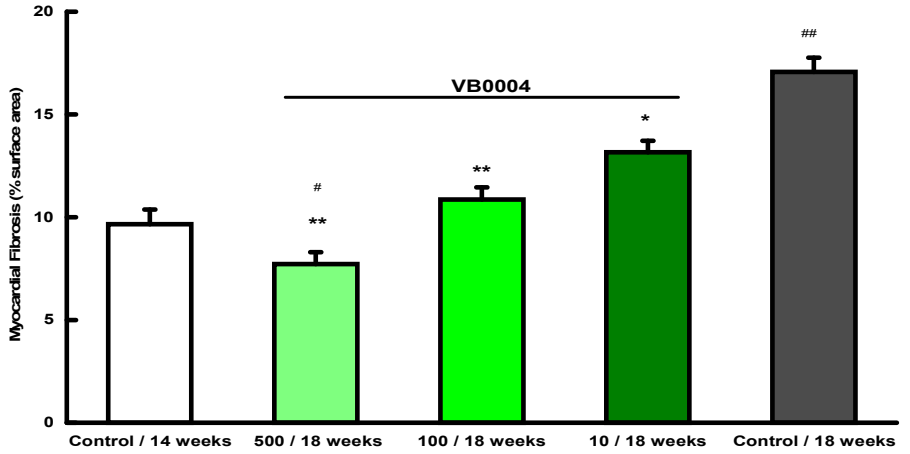
Pharma criteria	Vectus
Platform Technology	✓
Validated Target	✓
Transformational Agent	✓
Demonstrated Efficacy in Animal Model	✓
Demonstrated Safety – IND toxicology	
Synthesis at Scale	
Cost of Goods Competitive	
IP Covers Composition of Matter	
Sufficient Patent Life	
Phase I Safety Study	
Human pD (Efficacy) Data	

VB0004 & CARDIAC FIBROSIS

VB0004 has been shown to:

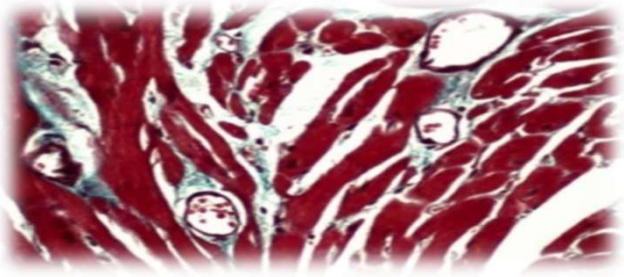
- Rescue cardiac tissue damaged by fibrosis
- Repair existing cardiac damage
  i.e. VB0004 is transformational
- Reduce systolic blood pressure

Treatment with VB0004 at 3 Doses



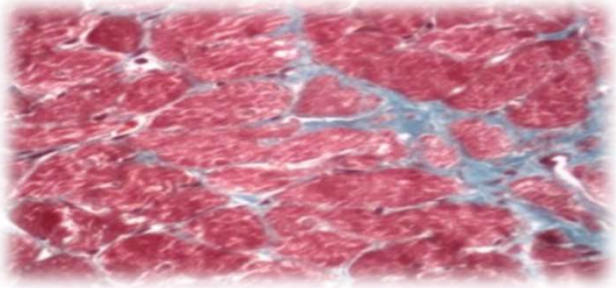
At the highest dose (500pmol/kg/min), VB0004 reversed pre-existing fibrosis, while a dose response effect on the level of fibrosis is apparent

14-Week Control



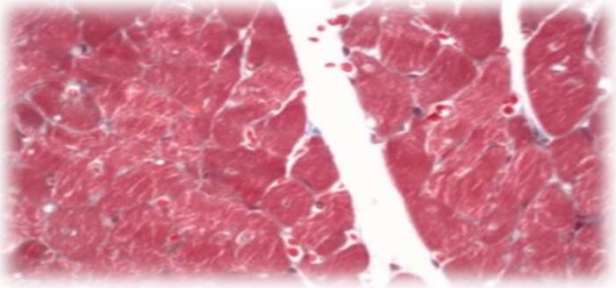
Fibrous tissue (blue staining) is visible around blood vessels and extending between muscle fibres

5% Ethanol 18-Week Control (Vehicle Control For VB0004)



Fibrosis visible as blue stained tissue is present throughout the section.

Heart At 18 Weeks After 4-week Treatment With VB0004 (500 Pmol/Kg/Min)



Minimal fibrosis is visible; normal architecture has been restored

VECTUS BIOSYSTEMS

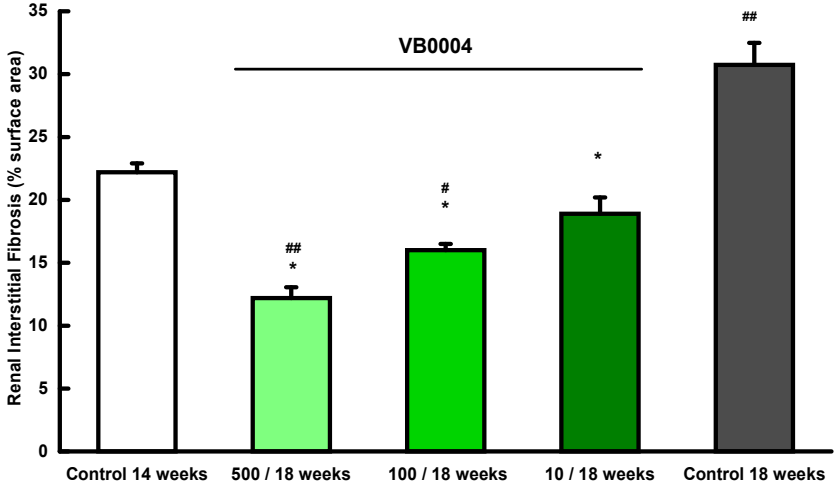
VB0004 & KIDNEY FIBROSIS

In the kidney VB0004 has been shown to:

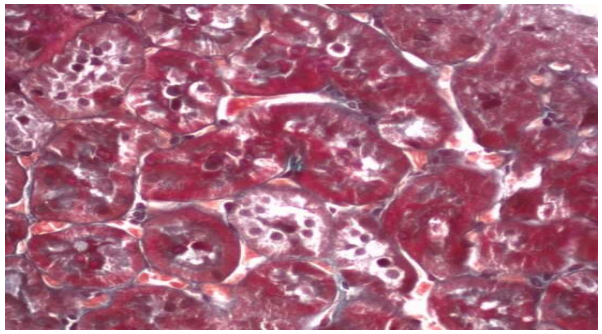
- Reverse renal interstitial fibrosis at all doses
- Restore normal architecture at all doses

  i.e. VB0004 is considered transformational

Treatment with VB0004 at 3 Doses

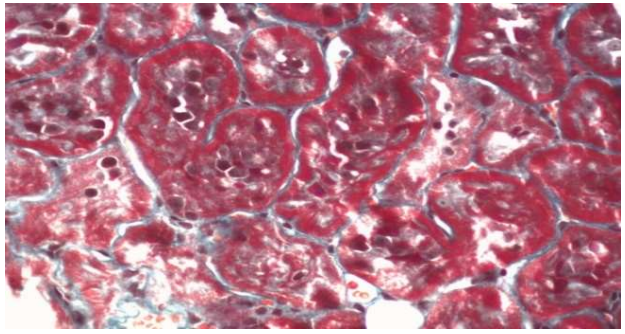


14-Week Control



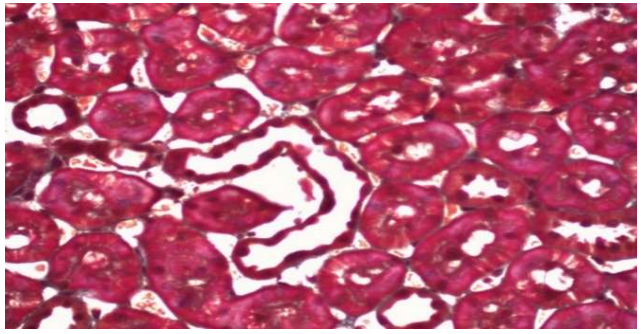
Fibrosis (blue) partially surrounds some but not all tubukes

5% Ethanol 18-Week Control (Vehicle Control For VB0004)



Fibrosis has progressed to surround most tubules

Kidney At 18 Weeks After 4-week Treatment With VB0004 (500 Pmol/Kg/Min)



No fibrosis visible

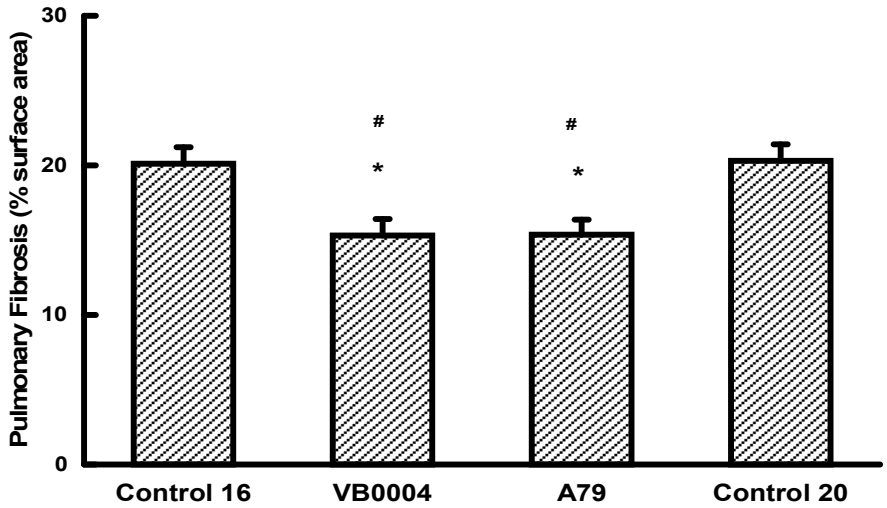
VECTUS BIOSYSTEMS

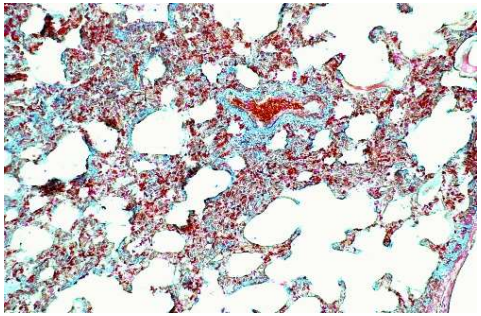
VB0004, VB4-A79 & PULMONARY FIBROSIS

In the lung:

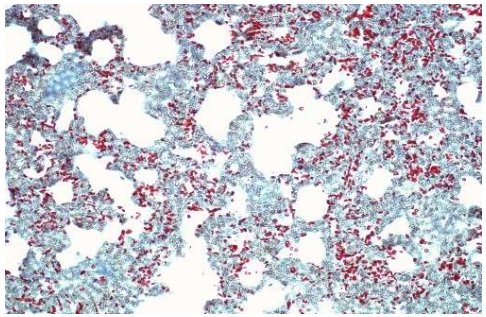
- VB4-A79 and VB0004 reversed fibrosis present 2 weeks after treatment with bleomycin (an anti-cancer drug)

i.e. both are considered transformational

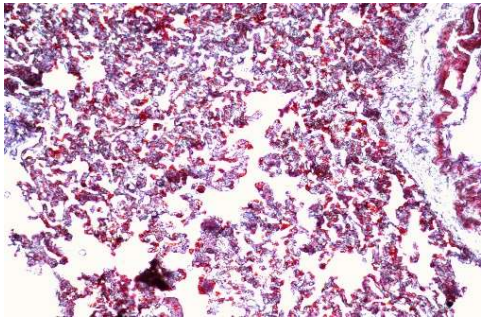




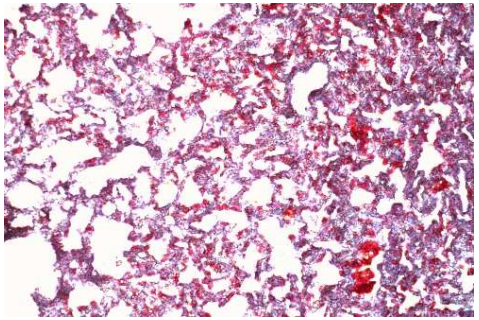
16 Week Control



20 Week Control



VB4-A79 at 20 weeks



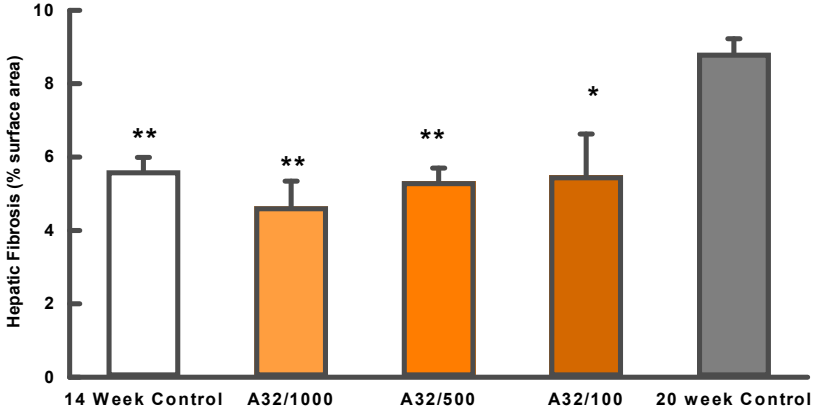
VB0004 at 20 weeks

VECTUS BIOSYSTEMS

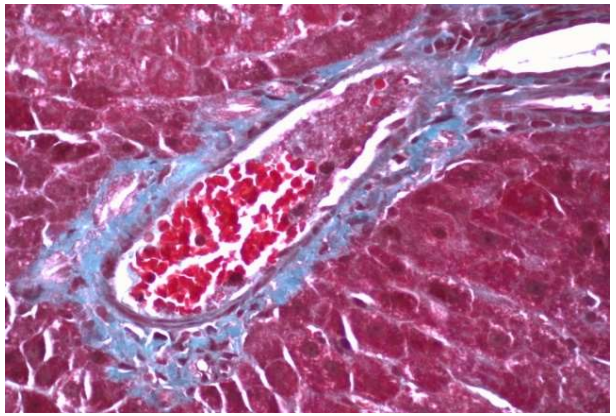
VB4-A32 & HEPATIC CIRRHOSIS

VB4-A32 demonstrated ability to

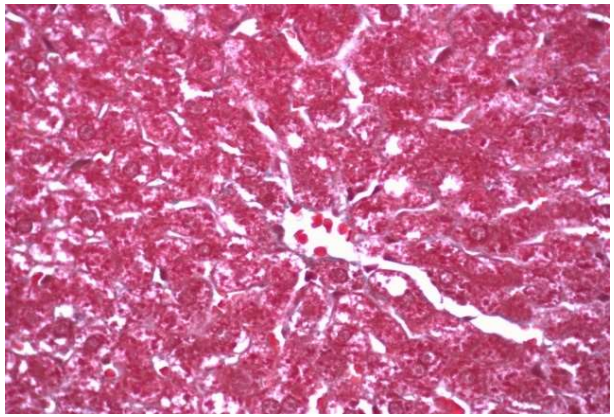
- reduce peri-portal fibrosis in the liver in a dose dependent manner (right and below)
- Improve liver function tests (below right)

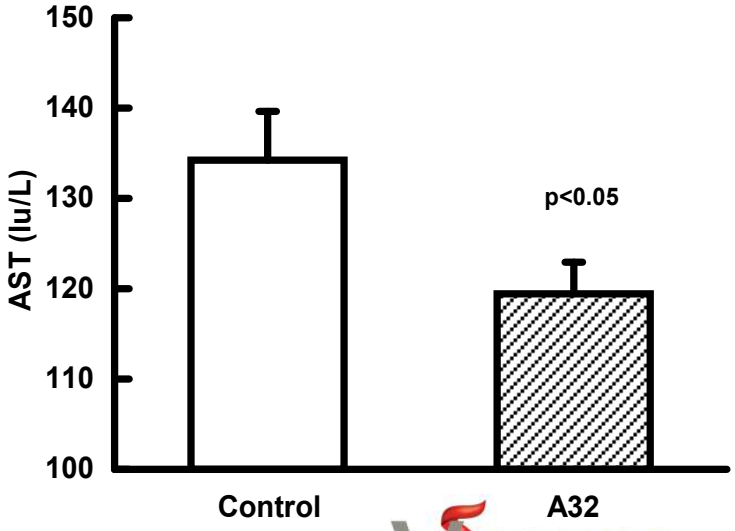


20 Week Control



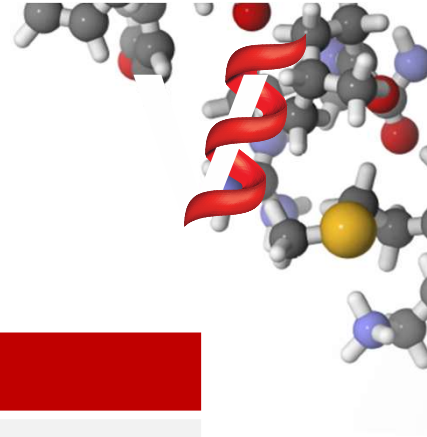
A32 20 Weeks





VECTUS BIOSYSTEMS

PATH TO THE CLINIC



Pharma criteria	Vectus
Platform Technology	✓
Validated Target	✓
Transformational Agent	✓
Demonstrated Efficacy in Animal Model	✓
Demonstrated Safety – IND toxicology	✓
Synthesis at Scale	
Cost of Goods Competitive	
IP Covers Composition of Matter	
Sufficient Patent Life	
Phase I Safety Study	
Human pD (Efficacy) Data	

DEMONSTRATED SAFETY

- SAD and MAD (2 species)
  - ➢ single ascending dose to 2,000mg/kg no adverse events
  - ➢ 7 day multiple ascending dose to 2,000mg/kg no adverse events
  - ➢ 28 day multiple ascending dose to 500mg/kg no adverse events
  - ➢ audited reports received for SAD and 7 and 28 day MAD,

- Cardiovascular safety
  - ➢ hERG studies
    - ❖ 2.6, 8.7 20.5uM
    - ❖ IC50 18.31uM
    - ❖ low arrhythmia potential
  - ➢ Dog cardiovascular safety –
    - ❖ Maximum dose 1,000mg/kg
    - ❖ No adverse events
    - ❖ No associated effects on cardiovascular function

- Respiratory Safety
  - ➢ rat study no adverse events

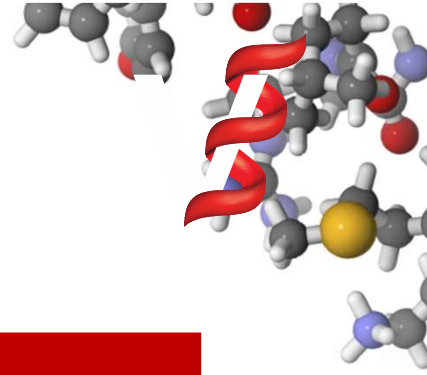
DEMONSTRATED SAFETY

- Mutagenic potential
  - Ames test doses 158, 50,15.8,5 and 1.58ug/plate
    - TA98, TA102 strains negative at all doses with and without S9
    - TA100, TA1535, TA1537 negative at all doses with S9
    - TA100, TA1535, TA1537 negative at doses to 50ug/plate without S9, positive only at 158ug/plate
  - CHO-K1 mutagenic test doses 10, 3.17 and 1ug/ml
    - No chromatid or chromosomal structural aberration after 6 hrs exposure with or without S9 at all concentrations
    - No chromatid or chromosomal aberrations at all concentrations after 18 hours exposre without S9
  - Mouse micronucleus test
    - 100, 300 and 1,000 mg/kg for 3 days
  - Bone marrow toxicity study completed
    - 28 day rat study maximum dose 1,000mg/kg
    - no *in vivo* no adverse events
    - Bone marrow macroscopically and microscopically normal

DEMONSTRATED SAFETY

- Metabolite profile same in human, rat and dog
- P-glycoprotein substrate
- CYP Inhibition Results
  - ➢ inhibitor
    - ❖ CYP1A2 (IC_{50} - 5.96±0.51 & 5.70±0.42 µM, n=7 each)
    - ❖ CYP2C19 (IC_{50} – 19.2±2.2 & 23.2±3.2 µM, n=7 each)
  - ➢ 20% inhibition of CYP2B6 and CYP2C8 at 25µM VB0004 concentration
  - ➢ No inhibition CYP2C9, CYP2D6, CYP3A4

PATH TO THE CLINIC



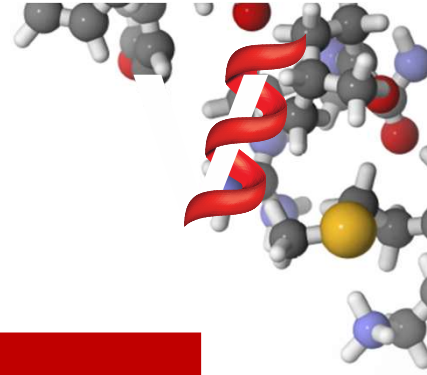
Pharma criteria	Vectus
Platform Technology	✓
Validated Target	✓
Transformational Agent	✓
Demonstrated Efficacy in Animal Model	✓
Demonstrated Safety – IND toxicology	✓
Synthesis at Scale	✓
Cost of Goods Competitive	✓
IP Covers Composition of Matter	
Sufficient Patent Life	
Phase I Safety Study	
Human pD (Efficacy) Data	

VECTUS BIOSYSTEMS

SYNTHESIS SCALE AND COST

- National phase entry patent covering GMP synthesis method
- 3 synthetic steps
- GMP synthesis by Glycosyn(www.glycosyn.com)
- Yield has increased as scale has increased
- VB0004 manufactured to 5kg scale
- Cost efficient at 5kg scale < $(US) 0.05 per mg
- Estimated dose 1-5mg
- Stability studies to 12 months

PATH TO THE CLINIC

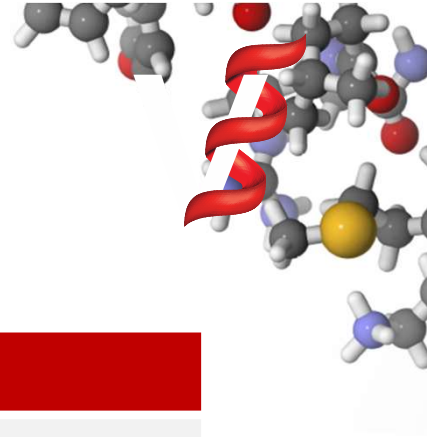


Pharma criteria	Vectus
Platform Technology	✓
Validated Target	✓
Transformational Agent	✓
Demonstrated Efficacy in Animal Model	✓
Demonstrated Safety – IND toxicology	✓
Synthesis at Scale	✓
Cost of Goods Competitive	✓
IP Covers Composition of Matter	✓
Sufficient Patent Life	✓
Phase I Safety Study	
Human pD (Efficacy) Data	

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, Russian Federation
  - as well as Australia, Israel, Phillipines, South Africa, Canada, ARIPO
- Patent life
  - Priority date September 2013
  - 16 years (+5 years on licensing)
- VB0004 Method of synthesis patent at National Phase entry stage

PATH TO THE CLINIC



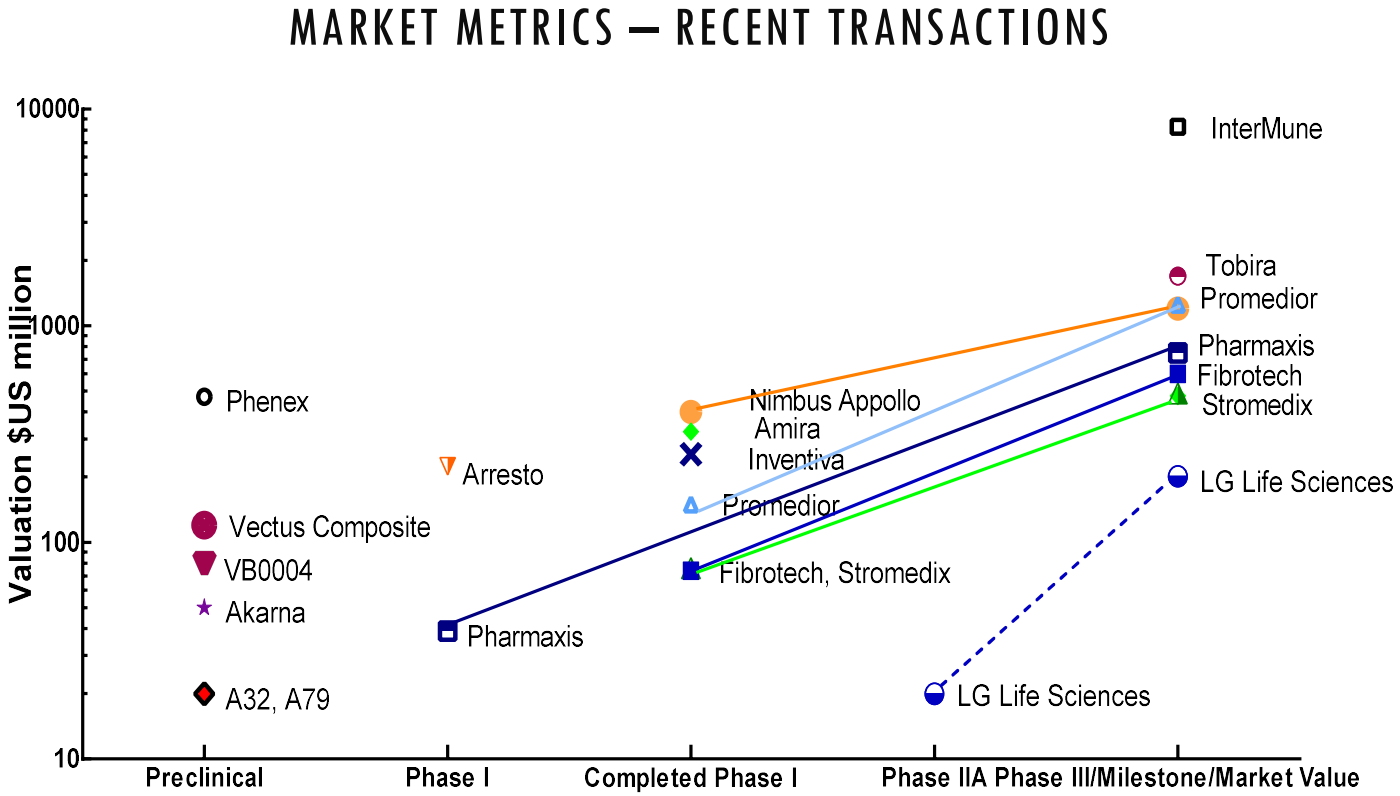
Pharma criteria	Vectus
Platform Technology	✓
Transformational Agent	✓
Validated Target	✓
Demonstrated Efficacy in Animal Model	✓
Demonstrated Safety – IND toxicology	✓
Synthesis at Scale	✓
Cost of Good Competitive	✓
IP Covers Composition of Matter	✓
Sufficient Patent Life	✓
Phase I Safety Study	
Human pD (Efficacy) Data	

PHASE 1

- Tendering process underway with selected providers
- Trial site identified
- Trial design conventional Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD)
- Healthy subjects 14 day MAD
- Affected individuals 2 groups 28 days 2 doses
- Biomarkers identified
- Includes pharmacokinetic and pharmacodynamic studies
- Expected outcomes – maximum tolerated dose, dose limiting toxicity (if present), pharmacokinetic data and pharmacodynamic data
- Time frame – pre-trial preparation and ethics 4 months, trial 9-12 months

COMPARABLE TRANSACTIONS

- **Vectus could see a substantial upside if Phase I and IIa trials for VB0004 drug candidates are successful**



- It is feasible that positive clinical data from the Phase IIa trial could see Vectus negotiate an agreement, with up to US$250M in upfront fees and US$400M in milestones
- Based on reinvestment of the upfront fee, and milestones paid over a seven-year period (clinic to market), the value of the license could add up to US$100–200M to Vectus' valuation

Source: Gleneagle Research

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, Russian Federation, Israel, Singapore, allowed in ARIPO, Canada, Philippines, South Africa*
- **VB0004 library of approx. 70 related compounds compositions and methods of use for treatment of hypertension, cardiac and renal fibrosis –** *granted US, Australia, Singapore allowed in Europe, Japan, South Africa*
- **A32 and library of related compounds compositions and methods of use for treatment of hepatic, cardiac and renal fibrosis –** *entering national phase*
- **P5 and library of related compounds compositions and methods of use for treatment of renal cell death, renal fibrosis and hepatic fibrosis -** *entering national phase*
- **GMP method of synthesis VB0004 –** *entering national phase*
- **A79 and related compounds compositions and use for treatment of pulmonary fibrosis –** *entering national phase*
- **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*

VECTUS BIOSYSTEMS