CEO PRESENTATION

VECTUS BIOSYSTEMS

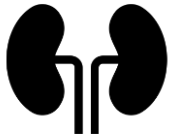
OVERVIEW

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)

LIVER FAILURE
(liver cirrhosis affects 40% of South Asians and East Asians)



KIDNEY FAILURE
(Dialysis and renal transplant costs in the US reached $49.2b in 2011)

RESPIRATORY FAILURE
(pulmonary fibrosis)

PATH TO THE CLINIC – VB0004

PHARMA CRITERIA	VECTUS
Validated Target	✓
Platform Technology	
Transformational Agent	
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	

TARGET VALIDATION

Treatment with VIP reversed cardiac fibrosis in multiple animal models data from one was published in the paper entitled “Vasoactive intestinal peptide reverses existing myocardial fibrosis in the rat” (see right)

https://doi.org/10.1016/j.ejphar.2019.172629

European Journal of Pharmacology 862 (2019) 172629

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journal homepage: www.elsevier.com/locate/ejphar

Full length article

Vasoactive intestinal peptide infusion reverses existing myocardial fibrosis in the rat

Karen A. Duggan*, George Hodge, Juchuan Chen, Tegan Hunter[1]

Vectus Biosystems, North Ryde, Australia

ARTICLE INFO

Keywords:
Heart failure
Myocardial fibrosis
Vasoactive intestinal peptide

ABSTRACT

Congestive cardiac failure has become one of the major health challenges of the 21st century and new therapies are needed to address this problem. The concentration of vasoactive intestinal peptide (VIP) in the heart has been shown to decrease as fibrosis (the pathology leading to heart failure) increases and to become undetectable in end stage cardiomyopathy. We sought to determine whether replenishment of myocardial VIP might treat myocardial fibrosis and therefore represent a new therapeutic target.

Wistar Kyoto rats on a high (4.4%) salt diet were randomised to zero time control, 4 week infusion of VIP (5 pmol/kg/min) or vehicle control infusion. Myocardial VIP concentration was measured by radioimmunoassay, fibrosis was quantitated by computerised histomorphometry and changes in pro-fibrotic mediators were measured by quantitative rt-PCR.

Myocardial VIP increased significantly in VIP treated rats compared with vehicle treated controls ($P < 0.01$) while fibrosis in the VIP treated rats was significantly lower than in both the zero time control ($P < 0.05$) and the vehicle infused control ($P < 0.0005$). Although all six profibrotic mediators which were measured increased over the 4 week experimental period VIP infusion only affected angiotensinogen (Agt) and angiotensin receptor type 1a (AT_{1a}) expression. In both instances VIP caused a significant decrease in messenger rna expression (Agt $P < 0.01$ and At_{1a} $P < 0.01$) compared with vehicle infused controls.

We conclude that VIP infusion increased myocardial VIP concentration and was able to reverse existing myocardial fibrosis suggesting a possible therapeutic role for a VIP based therapy in cardiac failure.

1. Introduction

The aging demographic in the developed world and rapid increase in obesity in developed and developing countries (Friedrich, 2017; The GBD 2015 Obesity Collaborators, 2017) has amplified the incidence of chronic diseases such as high blood pressure (hypertension) and diabetes (WHOa, b). Individually, hypertension and diabetes are significant risk factors for the development of congestive heart failure, while in combination, the risk is increased further. Consequent upon these demographic changes and their sequelae heart failure has become one of the major health challenges of the 21st century (Bleumink et al., 2004; Savarese and Lund, 2017).

Heart failure displays an age related prevalence affecting 1% of 50 year olds, increasing to affect 10–25% of those aged 80 and over (Aronow and Ahn, 1999; Gomez-Soto et al., 2011; Rich, 2006; Zannad et al., 1999). The prognosis for heart failure is worse than for most cancers with a 5 year mortality of 50–60% and a one year mortality exceeding 50% in those with NYHA class IV disease (Gomez-Soto et al., 2011; Zannad et al., 1999). Heart failure is the commonest cause for hospital admission in adult medicine and the most expensive health care item costing 1–2% of total health budgets in the US ($30.7 billion), UK, Sweden, and Australia (Agvall et al., 2005; Cowie, 2017; Mozzafarian et al., 2016; Sahle et al., 2016), despite newer therapeutic strategies (John et al., 2014).

The pathology underlying heart failure is replacement of normal functioning tissue by fibrosis, which begins around blood vessels (perivascular fibrosis) diminishing nutrient and oxygen delivery to heart muscle. Later, fibrosis extends between muscle fibres (interstitial fibrosis) limiting their ability to relax during diastole, decreasing ventricular filling and causing diastolic dysfunction. Later still, muscle fibres become encircled and their alignment disrupted reducing effective contraction, causing symptomatic heart failure, or systolic dysfunction. Currently available anti-fibrotic agents ameliorate progression of fibrosis but do not reverse it, so more effective anti-fibrotic agents are

* Corresponding author. Vectus Biosystems, Level 3, 11 Julius Ave, North Ryde, NSW, 2113, Australia.
E-mail address: kduggan@vectusbiosystems.com.au (K.A. Duggan).
[1] Current address: School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia.

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TARGET VALIDATION

Treatment with VIP was also found to reverse interstitial fibrosis in the kidney in multiple animal models data from one was published in the paper entitled “Vasoactive intestinal peptide infusion reverses existing renal interstitial fibrosis via a blood pressure independent mechanism in the rat” (see right)

https://doi.org/10.1016/j.ejphar.2020.172979

European Journal of Pharmacology 873 (2020) 172979

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Full length article

Vasoactive intestinal peptide infusion reverses existing renal interstitial fibrosis via a blood pressure independent mechanism in the rat

Karen A. Duggan*, George Hodge, Juchuan Chen, Sofie Trajanovska[1], Tegan Hunter[2]

Vectus Biosystems, North Ryde, Australia

ARTICLE INFO

Keywords:
Renal failure
Tubulointerstitial fibrosis
Vasoactive intestinal peptide

ABSTRACT

Dialysis requiring renal failure is a silent epidemic. Despite an annual mortality of 24% the dialysis population has increased by 1–4% per annum. Regardless of the initial injury, tubulointerstitial fibrosis is a feature of the renal pathology and it inversely correlates with declining renal function. Current agents display little efficacy against tubulointerstitial fibrosis. Clearly, therapies effective against tubulointerstitial fibrosis and able to preserve kidney function are needed. Vasoactive intestinal peptide (VIP) has been shown to reverse pre-existing cardiac fibrosis. We sought to determine whether VIP is effective in tubulointerstitial fibrosis. Spontaneous hypertensive rats (SHR) on a 2.2% salt diet were randomised to zero time control, 4 week infusion of VIP (5 pmol/kg/min) or vehicle control infusion. A fourth group, to match the blood pressure reduction achieved in the VIP infused group was included. Fibrosis was quantitated by computerised histomorphometry, changes in pro-fibrotic mediators were measured by quantitative rt-PCR and macrophage activation assessed by cyclic adenosine monophosphate (c-AMP) response to incubation with VIP. Tubulointerstitial fibrosis in the VIP treated rats was significantly lower than the zero time control ($P < 0.0005$), the vehicle infused control ($P < 0.0005$) and the blood pressure matched group ($P < 0.01$). Although all six profibrotic mediators increased over the 4 week experimental period VIP infusion only decreased tumour necrosis alpha (TNFα) expression significantly ($P < 0.001$). Incubation of RAW264 macrophages with VIP significantly increased c-AMP ($P < 0.01$).

We conclude that VIP infusion reversed existing tubulointerstitial fibrosis suggesting a possible therapeutic role for a VIP based therapy in chronic kidney disease.

1. Introduction

Kidney failure affects 10–14% of the general population, and displays an age related prevalence, with some studies suggesting that 30–50% of those aged over 75 years are affected (Stengel, 2011; Stenvinkel, 2010; Paraskevas et al., 2010). Other studies suggest that this is an overestimation due to inaccuracies in methods for estimating glomerular filtration rate in this age group (Hsu, 2010; Mangione and Dal Canton, 2010). However, data on end stage kidney disease that requires renal replacement therapy (dialysis and/or transplantation) are indicative of a silent epidemic. In the US and Europe the dialysis population continues to increase at 1–4% per annum despite an annual mortality of 18–24% (USRDS, 2019; Hsu, 2010; Stengel, 2011; Breyer and Susztak, 2016) while in Australia the dialysis population has tripled over the past two decades (AIHW, 2018).

The pathological lesion which underlies kidney failure is the replacement of normal functioning tissue by scar tissue (fibrosis). In the kidney, regardless of the nature of the initial injury tubulointerstitial fibrosis occurs. Declining renal function correlates with progression of tubulointerstitial fibrosis rather than glomerular damage *per se* (Nath, 1992, Klein et al., 2011; Breyer and Susztak, 2016; Bonventre, 2012; Schelling, 2016). Experimentally, currently available anti-fibrotic agents (ACE inhibitors, angiotensin receptor blockers, renin inhibitors and aldosterone antagonists) have been shown to ameliorate glomerular pathology but are much less effective in relation to tubulointerstitial fibrosis (Lahmer et al., 2012; Watanabe et al., 2009) prompting calls for the development of new agents directed to remediating this pathology (Stenvinkel, 2010; Stengel, 2011; Bonventre, 2012).

Vasoactive intestinal peptide (VIP) is a 28 amino acid peptide first isolated by Said and Mutt (1970), and its amino acid sequence is highly conserved across all mammalian species except the guinea pig where

* Corresponding author. Vectus Biosystems, Level 3, 11 Julius Ave, North Ryde, NSW, 2113, Australia.
E-mail address: kduggan@vectusbiosystems.com.au (K.A. Duggan).
[1] Current address: Sydney Imaging, The University of Sydney, Australia.
[2] Current address: School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia.

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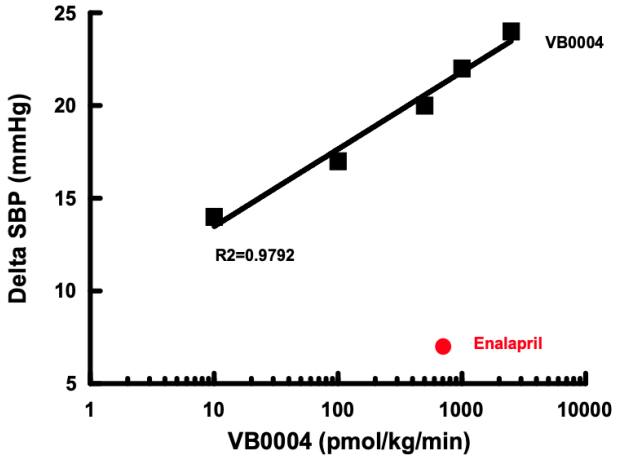
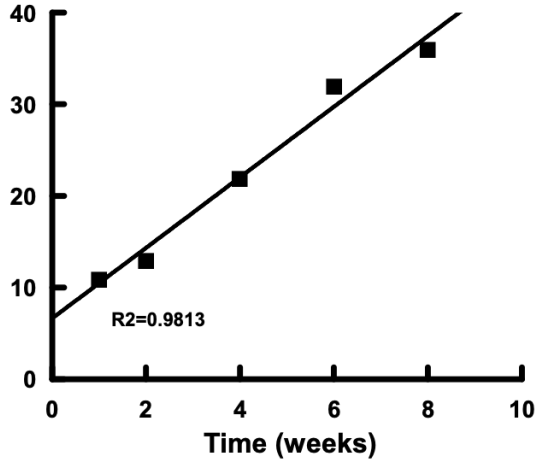
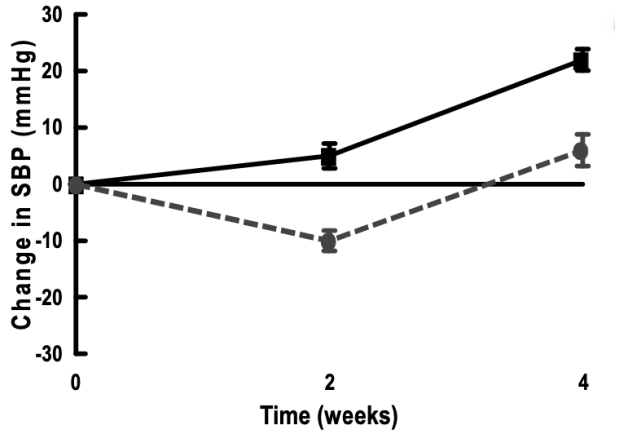
PATH TO THE CLINIC – VB0004

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

VB0004 & 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

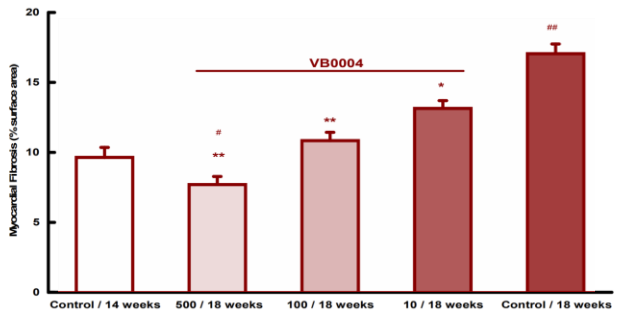
Right: Change in SBP from levels at the commencement of the experiment in Vehicle control for 4 weeks (solid line) SHR treated with VB0004 2,500pmol/kg/min for 2 weeks then vehicle for 2 weeks (dotted line) SBP in increased in parallel with vehicle control after cessation of VB0004

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

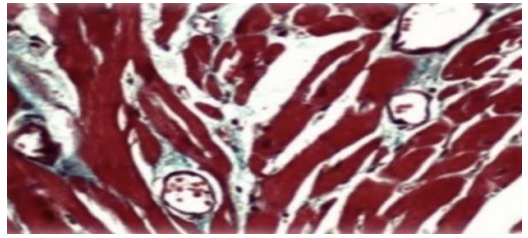
Treatment with VB0004 at 3 Doses



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

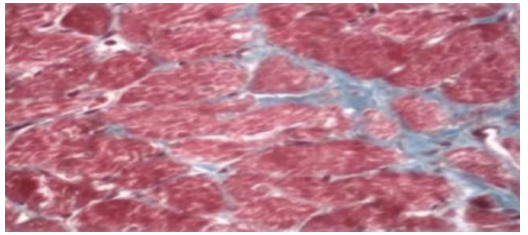
14-Week Control

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



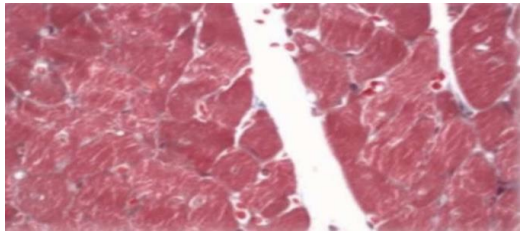
5% Ethanol 18-Week Control (Vehicle Control For VB0004)

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.

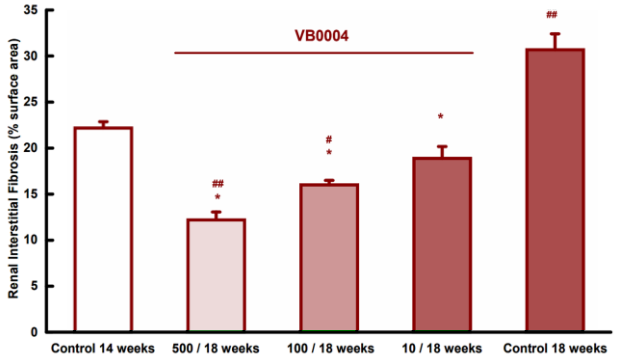


VB0004 & KIDNEY FIBROSIS

In the kidney VB0004 has been shown to:

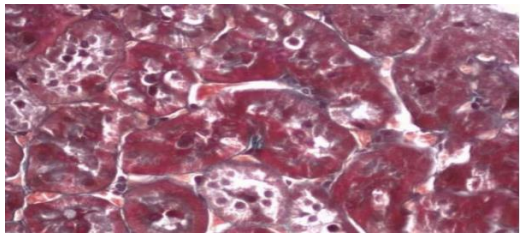
- Reverse renal interstitial fibrosis at all doses
- Restore normal architecture at all doses
  (i.e. VB0004 is considered transformational)

Treatment with VB0004 at 3 Doses



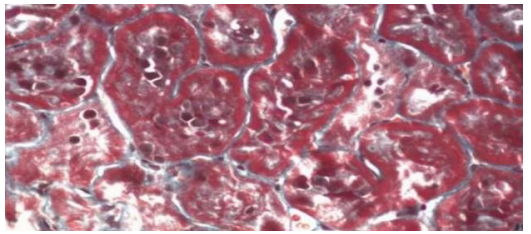
14-Week Control

Fibrosis (blue) partially surrounds some but not all tubules



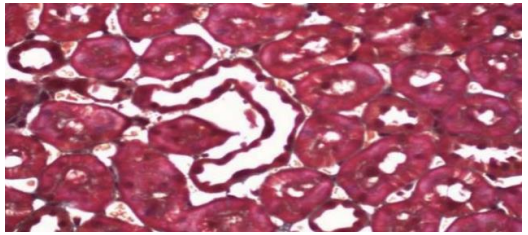
5% Ethanol 18-Week Control (Vehicle Control For VB0004)

Fibrosis has progressed to surround most tubules



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

No fibrosis visible

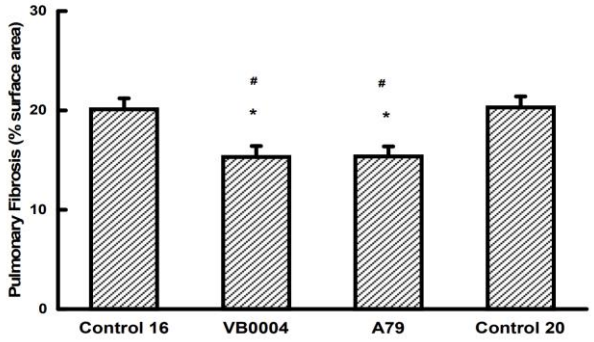


VB0004 & PULMONARY FIBROSIS

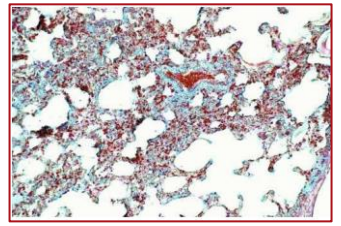
In the lung:

- VB0004 reversed fibrosis present 2 weeks after treatment with bleomycin (an anticancer drug)
- i.e. VB0004 also transformational in the lung

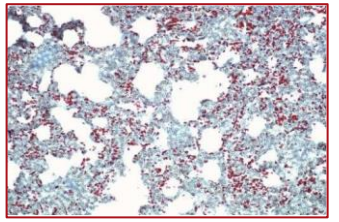
Treatment with VB0004 at 3 Doses



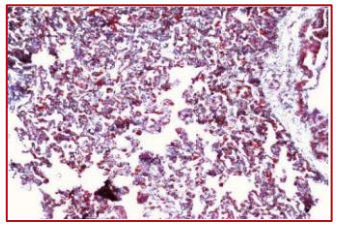
16-Week Control



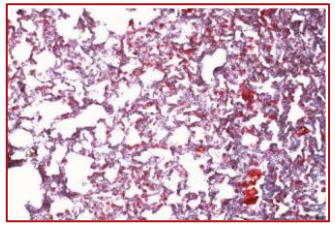
20-Week Control



VB4-A79 at 20 weeks



VB0004 at 20 weeks



SUMMARY

VB0004 THE FIRST NON-PEPTIDE, ORALLY DOSED VIP MIMETIC:

- Decreased systolic blood pressure in a dose dependent manner
- Reversed pre-existing cardiac fibrosis and restored normal cardiac architecture
- Reversed pre-existing renal interstitial fibrosis and restored normal renal architecture
- Reversed pre-existing pulmonary fibrosis secondary to bleomycin

PATH TO THE CLINIC – VB0004

PHARMA CRITERIA	VECTUS
Validated Target	✓
Platform Technology	✓
Transformational Agent	✓
Demonstrated Efficacy in Animal Model(s)	✓
Demonstrated Safety – IND toxicology	✓
IP Covers Composition of Matter	
Synthesis at Scale	
Cost of Good 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 (SAD) to 2,000mg/kg no adverse events
- 7 day Multiple Ascending Dose (MAD) to 2,000mg/kg no adverse events
- 28 day MAD to 500mg/kg no adverse events

Cardiovascular Safety

- hERG studies - low arrhythmia potential
- Dog cardiovascular safety – No effects on cardiovascular function at maximum dose of 10 grams/day

Respiratory Safety

- rat study no adverse events

Mutagenic potential

- In vivo and in vitro tests low to no mutagenic potential

Metabolism

- Metabolites are the same in human, rat and dog

Drug Interactions

- No Inhibition of major drug metabolising enzymes (drug interactions less likely)

PATH TO THE CLINIC – VB0004

PHARMA CRITERIA	VECTUS
Validated Target	✓
Platform Technology	✓
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Demonstrated Efficacy in Animal Model(s)	✓
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	

SYNTHESIS SCALE AND COST

FIRST GMP SYNTHESIS BY GLYCOSYN

- Yield increased as scale increased
- VB0004 manufactured to 5kg scale
- Cost efficient at 5kg scale < $(US) 0.05 per mg
- Estimated dose 1-5mg
- Stability studies – stable at 2 yrs (long shelf-life)

Second GMP synthesis Assymchem

- Campaign planned to provide 3 validation batches
- Confirm consistency of the synthesis process
- Samples of all 3 will undergo 2 yr stability testing
- Meets FDA requirements for GMP manufacture for Phase 1 and 2 clinical trials

PATH TO THE CLINIC – VB0004

PHARMA CRITERIA	VECTUS
Validated Target	✓
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Cost of Good 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 2014
- 13 years (+5 years on licensing)

VB0004 Method of synthesis patent at National Phase entry stage

PATH TO THE CLINIC – VB0004

PHARMA CRITERIA	VECTUS
Validated Target	✓
Platform Technology	✓
Transformational Agent	✓
Demonstrated Efficacy in Animal Model(s)	✓
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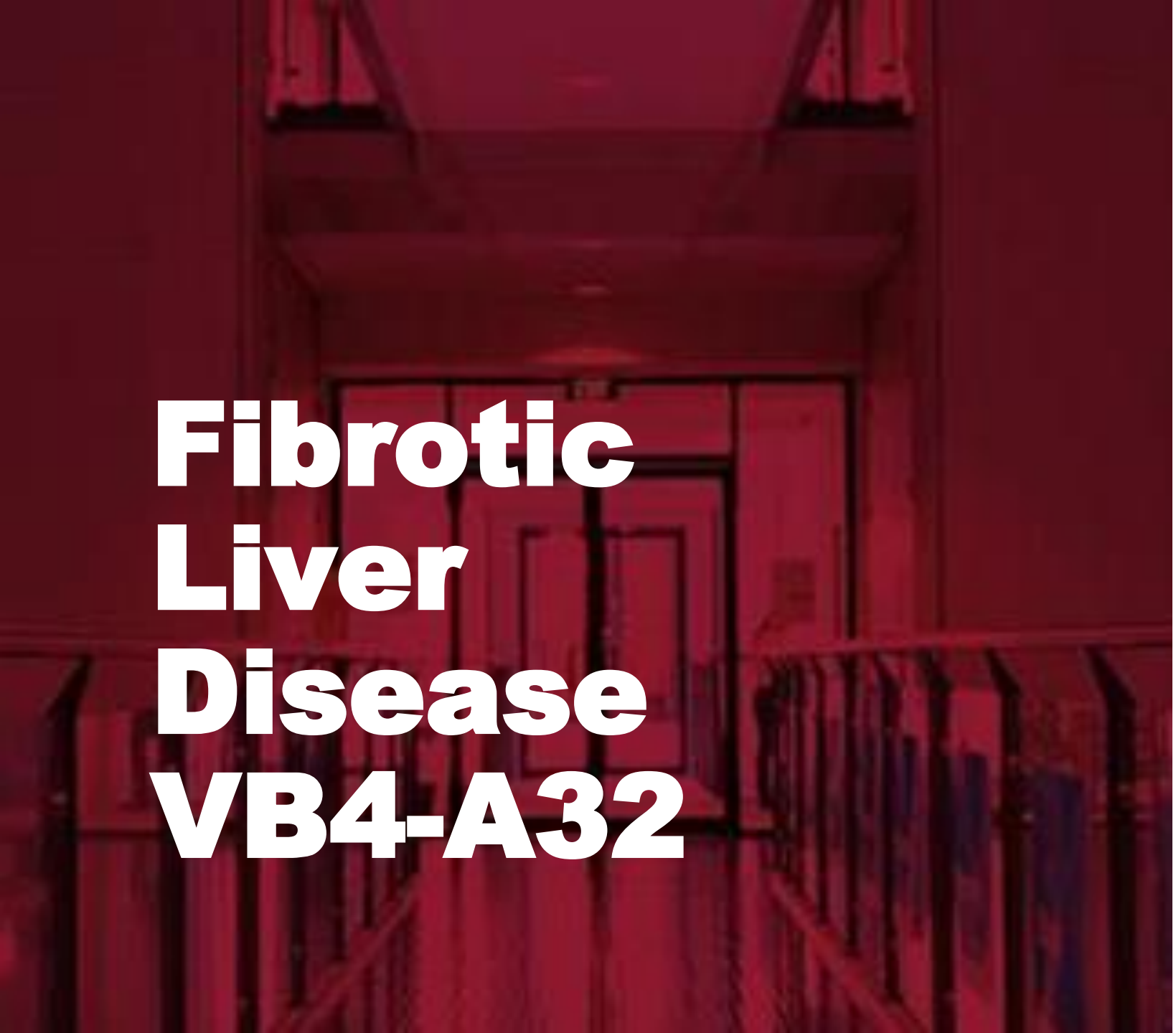
Synthesis at Scale	✓
Cost of Good Competitive	✓
IP Covers Composition of Matter	✓
Sufficient Patent Life	✓
Phase I Safety Study	
Human pD (Efficacy) Data	

PHASE 1

- Syneos Health (Nasdaq SYNH) retained to write Investigator Brochure (IB), trial protocol and monitor Phase 1 trial
- 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



Fibrotic Liver Disease VB4-A32

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

POTENTIAL THERAPIES

- FXR agonists – Phase 2 reduced liver fat at 6 months, Phase 3 no change in liver fat, decreased fibrosis at 18 months in 18-23% of patients, none achieved resolution of fibrosis. Side effects - itching moderate to severe in intensity in up to 50%
- PPAR-α/δ agonists – Phase 2 decrease in fat and no progression in 19% at 6 months but a reversible loss in renal function. Phase 3 no progression in 20% at 12 months
- Insulin sensitisers – Phase 2b no effect on liver disease, but improved insulin sensitivity
- FGF19 analogues – decrease in liver fat in 74-79% at 12 weeks. High incidence of side effects (93%) including injection site reaction, abdominal pain, diarrhoea, nausea
- PPAR α & γ agonists Phase 2 decrease in ALT at 16 weeks and reduced fat at the highest dose vs placebo. Well tolerated
- THR β agonist Phase 2 decreased ALT, AST and liver fat vs placebo at 12 weeks. SCDI inhibitor- Phase 2b no effect at 12 weeks
- ASK1 antagonists – Phase 2 open label decreased fibrosis at 6 months. Phase 3 discontinued as no decrease in fibrosis without worsening NASH at 12 months

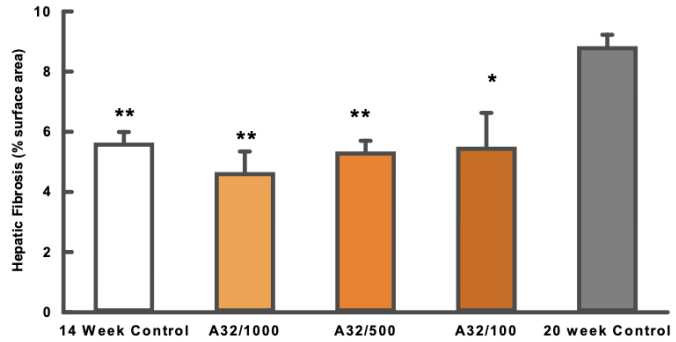
SUMMARY – LIVER FIBROSIS

- No current approved therapy
- Potential therapies – ineffective and/or high incidence of side effects
- Liver Fibrosis continues to represent an unmet therapeutic need

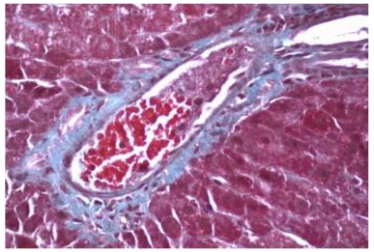
VB4-A32 & HEPATIC CIRRHOSIS

VB4-A32 demonstrated ability to:

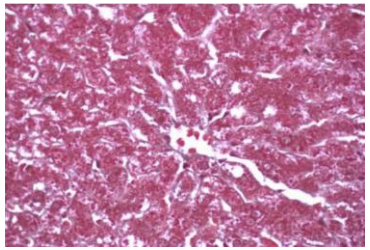
- reduce peri-portal fibrosis in the liver in a dose dependent manner (right and below)
- Improve liver function tests (below right)

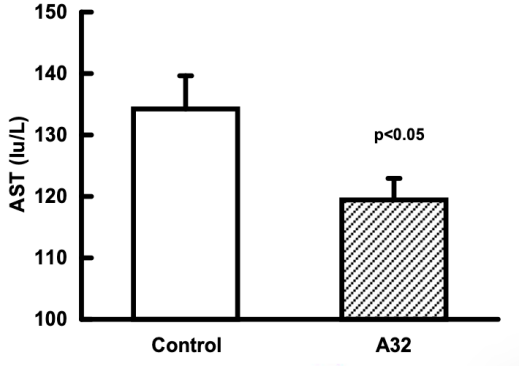


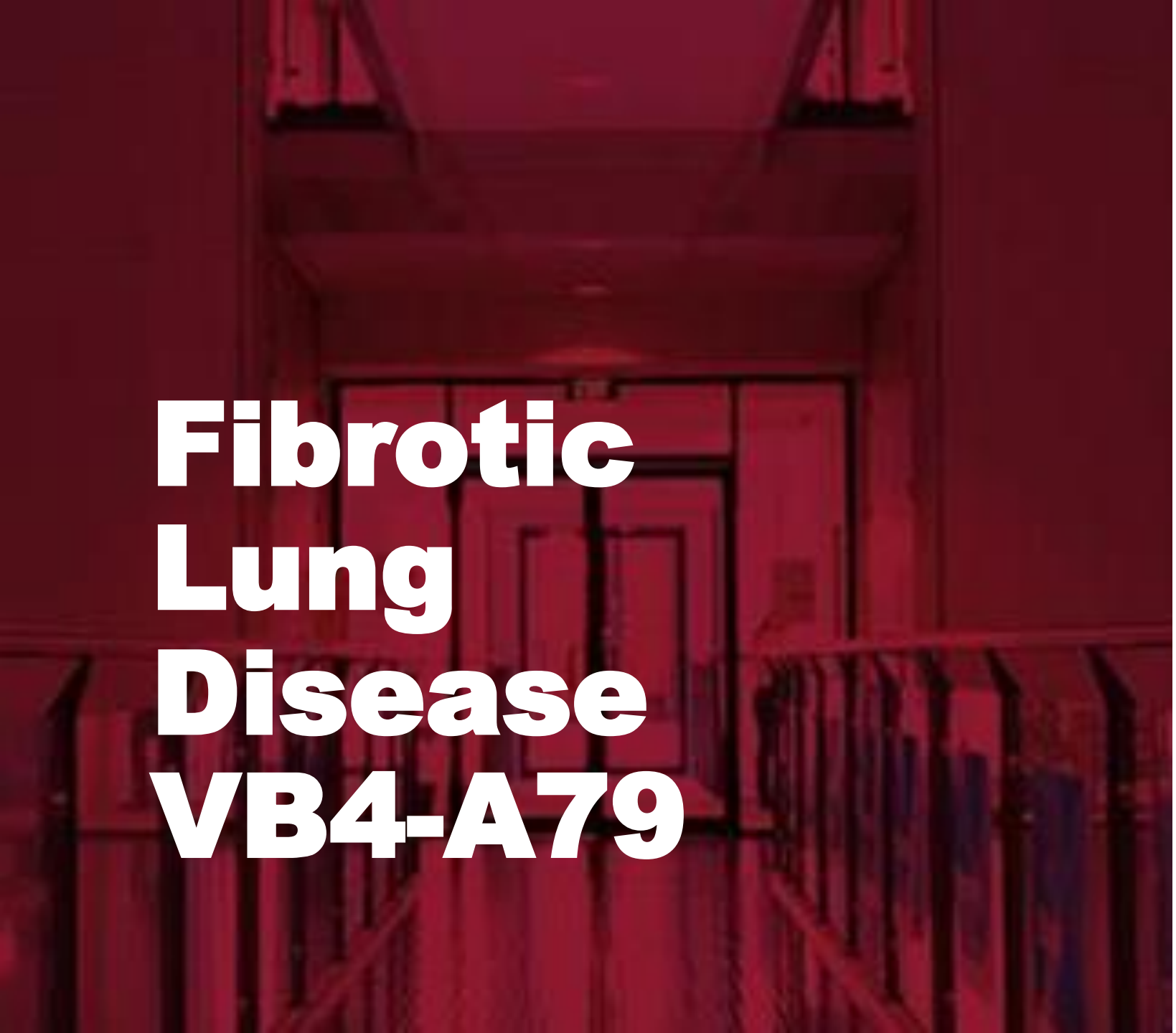
20-Week Control



A32 20 Weeks







Fibrotic Lung Disease VB4-A79

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, Spanish flu, COVID-19)
- 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 or silica 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.

CURRENT THERAPIES

Two current therapies:

Pirfenidone

regulatory approval approximately 5 years ago. Slows lung function (FVC and 6MWD) decline. Approximately 50% discontinued or reduced dose due to side effects.

Nintedanib

regulatory approval approximately 5 years ago also slows rate of lung function decline. High discontinuation rate due to side effects.

POTENTIAL THERAPIES

- Pentraxin 2 analogue – Phase 2 showed significant slowing of the decline in FVC and stabilisation of 6MWD at 6 months
- Anti-CTGF antibodies – Phase 2 slowed decline in FVC and 6MWD (awaiting review)
- Medium Chain Fatty Acid Analogue (PBI4050) – Phase 2 PBI4050, alone or combined with Nintedanib slowed decline or stabilised FVC at 12 weeks. However, in combination with Pirfenidone the rate of decline increased
- Autoxin-LPA Inhibitors – Phase 2a ? Halted FVC decline at 12 weeks. Phase 3 underway
- Anti-LOXL.2 Antibodies – No beneficial effect at Phase 2
- Anti-interleukin Antibodies – No efficacy
- Leukotriene Antagonists – Phase 2, no interim results
- Anti-Integrin Antibodies – Phase 2 completed, awaiting data

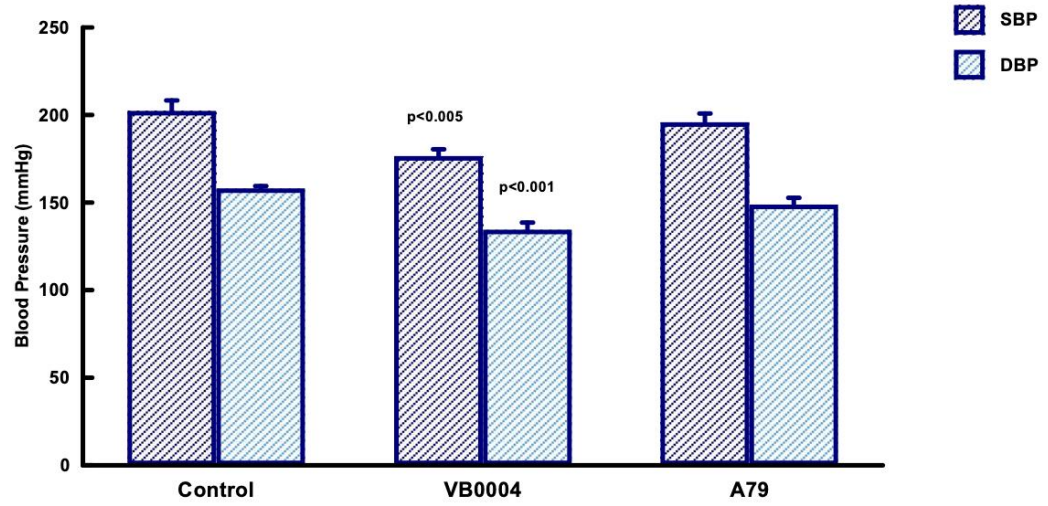
VB4-A79: BLOOD PRESSURE

Current therapies – slow the decline in lung function compared with placebo, but have a high incidence of unacceptable side effects

Potential therapies – slow decline or at best stabilise lung function

Pulmonary Fibrosis continues to represent an unmet therapeutic need

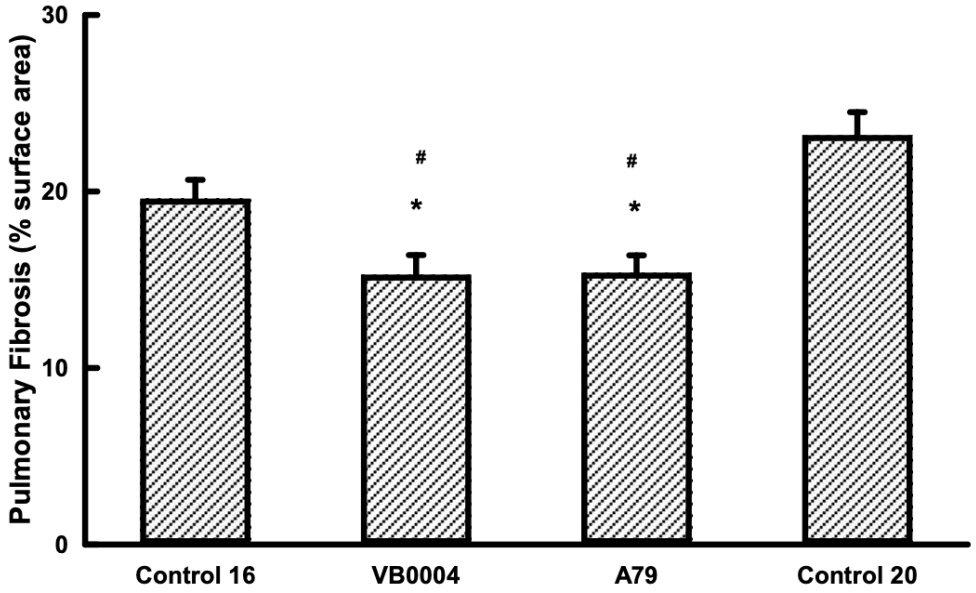
VB4-A79: BLOOD PRESSURE



Systolic and diastolic blood pressure in 20-week SHR following treatment with bleomycin at 14 weeks and randomisation to control, VB0004 or VB4-A79 at 16 weeks.

As previously VB0004 significantly decreases both systolic and diastolic pressure while VB4-A79 had no effect.

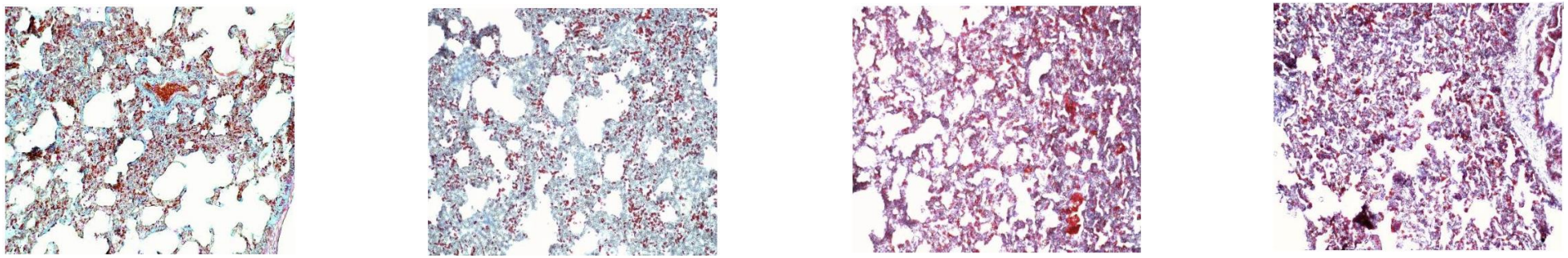
VB4-A79 PULMONARY FIBROSIS



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 VB4-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.

VB4-A79 HISTOLOGY



16-Week Control | 20-Week Control | VB4-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 VB4-A79 treated rats alveoli walls are thinner and capillaries are more numerous.

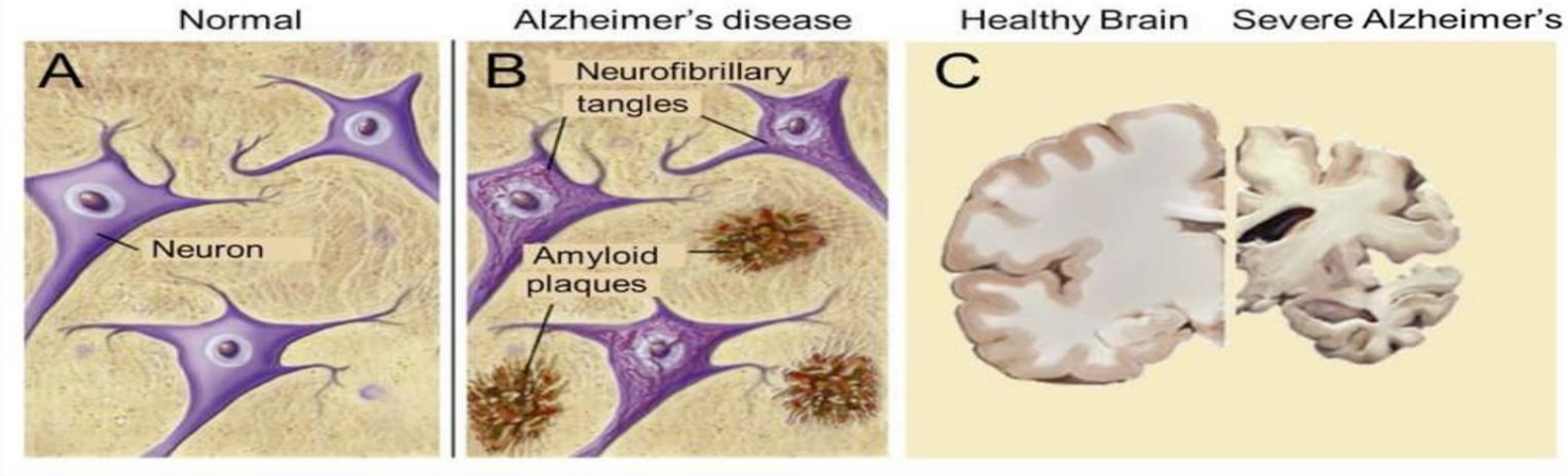
VECTUS IN SUMMARY

- **3 first in class** assets addressing major unmet therapeutic needs
- **VB0004** – entering Phase1, addressing Systolic Hypertension, cardiac, renal and pulmonary fibrosis, possible orphan indication for scleroderma
- **VB4-A32** – addresses liver fibrosis, restored normal liver architecture in NASH/ASH models
- **VB4-A79** – addresses pulmonary fibrosis from all causes except scleroderma where BP lowering probably required, revered existing fibrosis due to bleomycin
- Exceptional patent portfolio encompassing a library of > 1,000 compounds
- Successful raising of $7 million by Gleneagle and Morgans (Scone)

USE OF FUNDS

- **VB0004** – Phase 1
- **VB4-A32** – undertake GMP synthesis (Assymchem), with IND toxicology studies to follow
- **Laboratory** – further work on detailed mechanisms of action for VB4-A32, VB4-A79
- **Diversify** to encompass other areas of unmet therapeutic need and investigate therapies from Vectus extensive library e.g. develop cellular models for Alzheimer's disease and investigate efficacy of potential candidates

WHY ALZHEIMERS



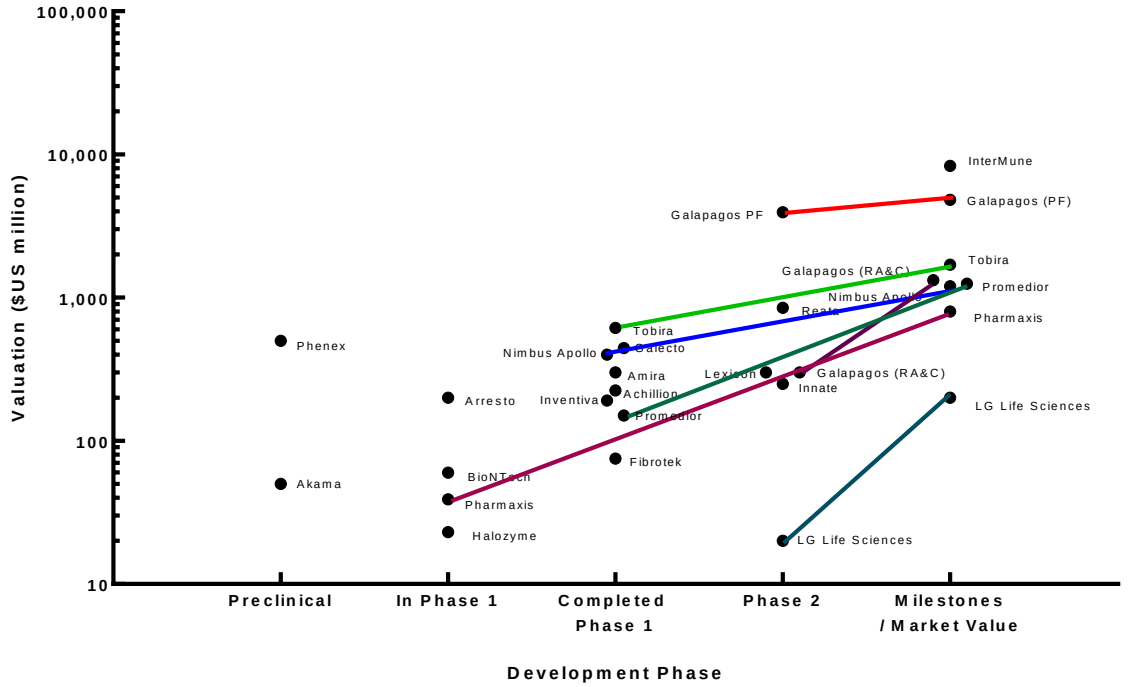
Accumulation of B-amyloid in the brain causes formation of plaques, which disrupt neuronal connections and cause accumulation of Tau proteins, which are dissociated from microtubules within neurones causing tangle formation, a precursor to neuronal cell death.

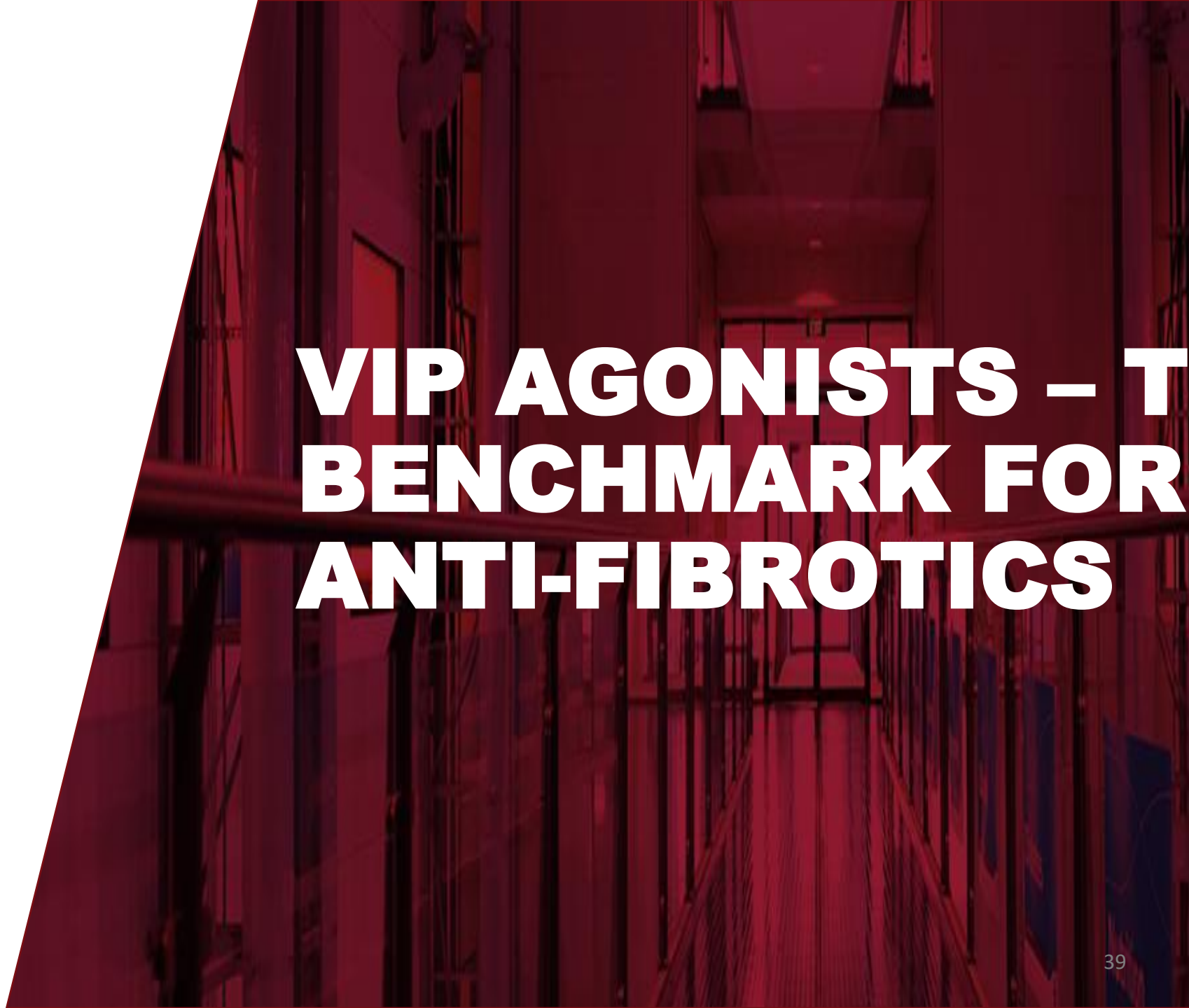
PATENT PORTFOLIO

- **VIP patents for heart, kidney and aortic fibrosis** – granted all 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 Russian Federation, Israel, Singapore, ARIPO, Canada, Philippines, South Africa, Ukraine, Vietnam, Nigeria, Mexico, accepted in Indonesia
- **VB0004 library of approx. 70 related compounds compositions and methods of use for treatment of hypertension, cardiac and renal fibrosis** – granted US, Australia, China, Europe, Japan, Korea, Russia, Ukraine, Hong Kong, Vietnam, Singapore, accepted in South Africa, ARIPO, Brazil, accepted Mexico
- **VB4-A32 and library of related compounds compositions and methods of use for treatment of hepatic, cardiac and renal fibrosis** – granted US, Europe, Australia, South Africa
- **VB4-P5 and library of related compounds compositions and methods of use for treatment of renal cell death, renal fibrosis and hepatic fibrosis** – granted US, China, Australia, South Africa, accepted Europe, Japan, Russia, Israel
- **GMP method of synthesis VB0004** – granted USA, Australia, India, accepted Europe, China
- **VB4-A79 and related compounds compositions and use for treatment of pulmonary fibrosis** – granted Australia, China, accepted USA, Europe, Mexico
- **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** – national phase

Comparable Transactions

- Successful Phase 1/1b would place Vectus at the point where many transactions have been completed





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