

**Vectus Biosystems Limited**  
**Chairman's Address to the 23 November 2022 Annual General Meeting**

The 2022 year was very productive for Vectus as it continued with progress in its Phase Ia human trials of its proprietary **VB0004** that addresses a significant unmet need for anti-fibrotic agents for patients with cardiovascular and/or kidney disease. The previous toxicology work completed to-date indicated that there would be a good result from the Phase Ia trials and this was validated when the Company announced to ASX on 14 September 2022 the completion of the final segments of its first-in-human trial that had been reviewed by the Trial Safety Review Committee, which further enhanced the impressive safety record of VB0004. While there were challenges in recruiting patients for the Phase Ia trial due to COVID-19, the results achieved made the wait worthwhile.

Vectus continues to advance work on its library of over 1,000 compounds, derived from the platform underpinning VB0004. These emerging lead compounds address some of the most significant unmet needs in medicine today and include:

- VB4-A32 (liver fibrosis, including NASH and ASH);
- VB4-A79 (pulmonary fibrosis, including idiopathic fibrosis, asbestosis and coal dust pneumoconiosis (Black Lung Disease)); and
- VB4-P5 (renal tubular cell death consequent on cytotoxic therapy).

As a Radiologist and Clinical Physician, I emphasise the real need for this new class of drugs, providing significant social, patient and health economic outcomes. Fibrosis, or scar tissue, is the end point of a whole host of diseases, including high blood pressure, injury, post infections (such as COVID-19), radiotherapy and silicosis. To have potential drugs, like those in the Company's stable, that can not only stop the growth of scar tissue, but also reverse the fibrosis, is a major development in medicine. To take the drug orally, in tablet form, also decreases the cost of production and, more importantly, increases the ease of use by patients. The use of Vectus' compounds to reduce blood pressure is also very significant.

#### Finance

This morning Vectus announced to the market a \$4.5 million capital raising, to be carried out in two tranches, being a Placement of \$3.5 million and a Share Purchase Plan (SPP) of \$1 million. The Placement of 4.375 million shares at \$0.80 per share will raise \$3.5 million and the SPP will enable each Vectus shareholder to invest up to \$30,000 each at a share price of \$0.80. The SPP will be capped at \$1 million. The funds raised will be used to fund the human Phase Ib clinical trials for VB0004, to fast-track work on the Company's additional compounds towards lead status and human trials, for the commercialisation of the Accugen technology, and for working capital.

It is pleasing to note that shareholder value remained relatively strong during the last year even though the biotech market segment suffered on the share market. The share price encouraged all the remaining convertible note holders to convert their notes into ordinary shares at \$0.50 and Vectus is now debt free.

#### Commercialisation Process

Vectus continues its dialogue with a cross-section of some of the world's leading pharmaceutical companies and regional mid-sized firms, and feedback from these industry leaders remains very positive. The Company's objective is to partner with one or more companies via a licencing programme focusing initially on VB0004 now that its Phase Ia trials have been completed successfully. The additional compounds also present an attractive commercial opportunity for Vectus, and the

success with VB0004 is likely to generate increased attention by pharmaceutical companies with particular interest in the franchises and disease states that Vectus addresses.

#### Accugen

Since the previous AGM, Vectus has worked to enhance its technology aimed at improving the speed and accuracy of measuring the amount of DNA and RNA in samples tested in laboratories. The technology, consisting of AccuCal™ and RealCount™ software, offers a time, cost and accuracy benefit compared with currently available systems. Activities in the commercialisation programme, consisting of a combination of direct sales, distribution partnerships and licensing opportunities, result in a broad potential market for the Accugen product. Opportunities are being worked on for applications related to food safety, which is a large and growing market. The Accugen reagent (AccuCal-D™) and software evaluation continue by internationally renowned research groups for possible utility in diagnostic tests.

#### The Vectus Team

I thank Dr Karen Duggan and the Vectus team, for the success getting VB0004 through the important Phase Ia human trials during a period of very significant challenges. I appreciate the very relevant expertise of the Company's Board, with the experience of Dr Susan Pond in medical research and in large pharmaceutical companies being critical. Mr Peter Bush has resigned from the Board and we thank him for his service.

Vectus' shareholders have been very active in their support during the last year. We continue to believe that the Company's unique library of assets, its activities and its growth potential will contribute in a meaningful way to society, patients, our stakeholders and the delivery of improved healthcare worldwide.

#### **Vectus Biosystems Limited**

**Ron Shnier**

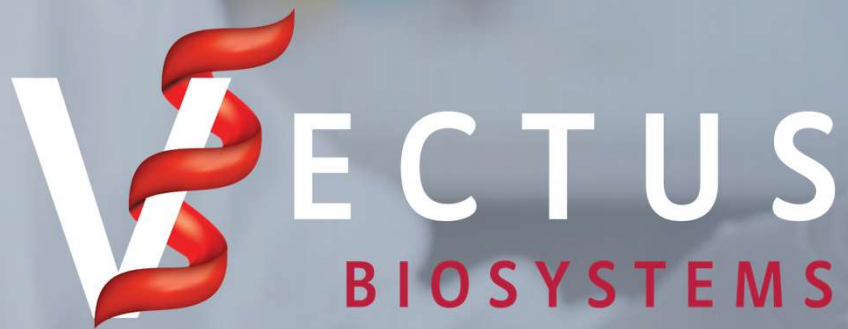
Chairman



# **Vectus Biosystems Limited**

**ABN 54 117 526 137**

## **Annual General Meeting**



**BIOSYSTEMS**

AGM - 2022

[vectusbiosystems.com.au/](http://vectusbiosystems.com.au/)

# INVESTMENT HIGHLIGHTS



**3 FIRST IN CLASS ASSETS ADDRESSING MAJOR UNMET THERAPEUTIC NEEDS**

VB0004 – 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



**LEAD PROGRAM VB0004 CONTINUES POSITIVE PROGRESS THROUGH PHASE 1**

Completion of Single Ascending Dose (S.A.D) study with no adverse events observed

Completion of 14 day Multiple Ascending Dose (M.A.D) study with no significant adverse events

Interim data shows potential for single daily dose of VB0004 to treat various chronic conditions



**EXCEPTIONAL PATENT PORTFOLIO ENCOMPASSING A LIBRARY OF > 1,000 COMPOUNDS**

VB0004 Patent granted in all major jurisdictions including USA, Europe, Japan, Peoples Republic of China, Republic of South Korea, Russian Federation, as well as Australia, Israel, Philippines, South Africa, Canada, ARIPO



**MANUFACTURING SECURED ADDING TO COMMERCIAL POTENTIAL**

GMP manufacturing and scale up fully validated at two international centres

Broad pharmaceutical engagement established with both tier-1 and mid-size potential licensees

Targeting first-in-class reimbursement for large franchise indications

# CORPORATE SNAPSHOT



## KEY METRICS

ASX	VBS
Shares on issue	47.25m
Market Capitalisation	\$45.4m
Share Price (22/11/22)	\$0.96
52-week trading range	\$0.90 - \$1.70

## HIGHLY EXPERIENCED BOARD & MANAGEMENT

**Dr Ronald Shnier**  
Non-Executive Director and Chairman

**Mr Maurie Stang**  
Non-Executive Director and Deputy Chairman

**Dr Karen Duggan**  
Executive Director and Chief Executive Officer

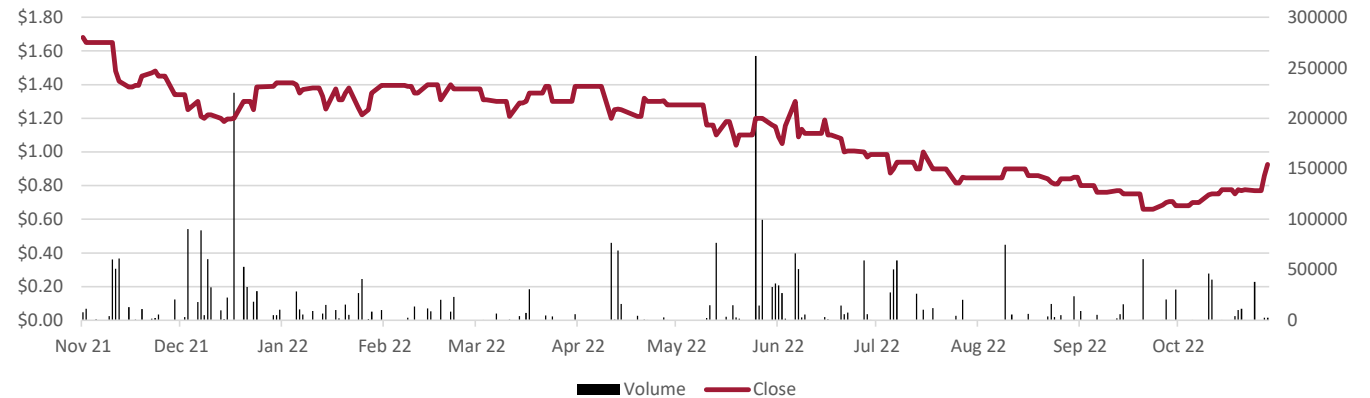
**Mr Peter Bush**  
Non-Executive Director

**Dr Susan Pond**  
Non-Executive Director

## SHAREHOLDER BREAKDOWN

19.04%	Board of Directors
39.94%	Top 20
41.23%	Other

## SHARE PRICE PERFORMANCE – LAST 12 MONTHS



## TARGETING LARGE MARKETS WITH SIGNIFICANT UNMET NEEDS

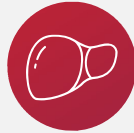


Fibrosis is the replacement of functional tissue by scar tissue, usually as a result of injury, and is the pathology which underlies:



### HEART FAILURE

(largest single item on US health care budget \$US32b in 2013)



### LIVER FAILURE

(40% of population of China, India and South East Asia are affected)



### KIDNEY FAILURE

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



### RESPIRATORY FAILURE

(pulmonary fibrosis)

FIBROSIS REVERSAL,  
A MAJOR UNMET NEED

Fibrotic disease  
contributes to more than

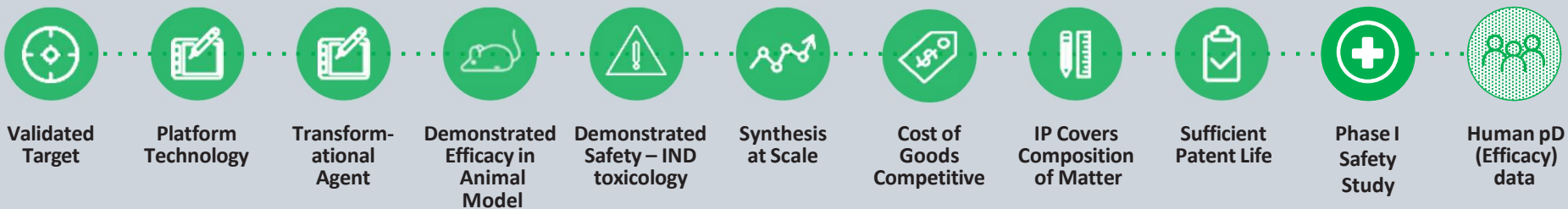
40%

of all deaths worldwide

# PATH TO CLINIC – VB0004



## PHARMA LICENSING CRITERIA



 COMPLETED    IN PROGRESS



# VIP - 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”

European Journal of Pharmacology 862 (2019) 172629

Contents lists available at ScienceDirect

European Journal of Pharmacology

journal homepage: [www.elsevier.com/locate/ejphar](http://www.elsevier.com/locate/ejphar)

Full length article

**Vasoactive intestinal peptide infusion reverses existing myocardial fibrosis in the rat**

Karen A. Duggan<sup>a</sup>, George Hodge, Juchuan Chen, Tegan Hunter<sup>1</sup>

<sup>a</sup> *Vetvet Australia, North Ryde, Australia*

**ARTICLE INFO**

**Keywords:**  
Heart failure  
Myocardial fibrosis  
Vasoactive intestinal peptide

**ABSTRACT**

Chronic 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 replacement of myocardial VIP might treat myocardial fibrosis and therefore represent a new therapeutic target.

Male 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

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”

European Journal of Pharmacology 873 (2020) 172879

Contents lists available at ScienceDirect

European Journal of Pharmacology

journal homepage: [www.elsevier.com/locate/ejphar](http://www.elsevier.com/locate/ejphar)

Full length article

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

Karen A. Duggan<sup>a</sup>, George Hodge, Juchuan Chen, Sofie Trajanovska<sup>1</sup>, Tegan Hunter<sup>2</sup>

<sup>a</sup> *Vetvet Australia, 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 (cAMP) response to histamine with VIP. Tubulointerstitial fibrosis in the VIP treated

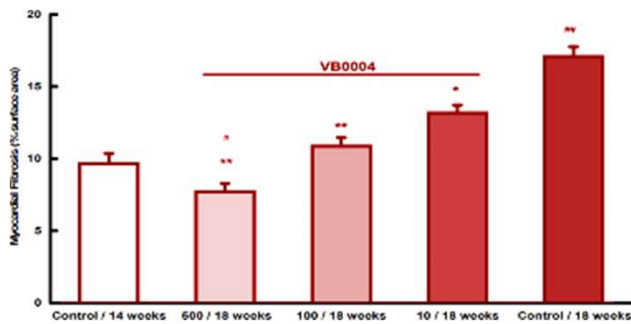
# VB0004 & CARDIAC FIBROSIS



## VB0004 has been shown to:

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

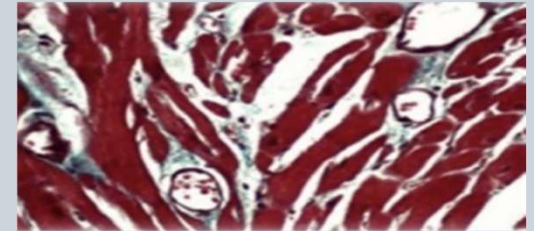
## Treatment with VB0004 at 3 Doses



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

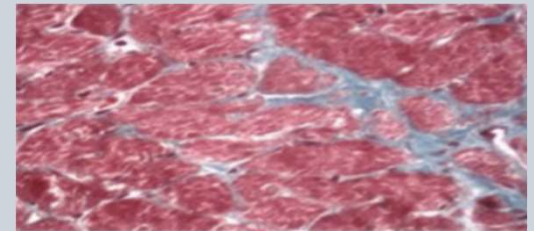
## 14-Week Control

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



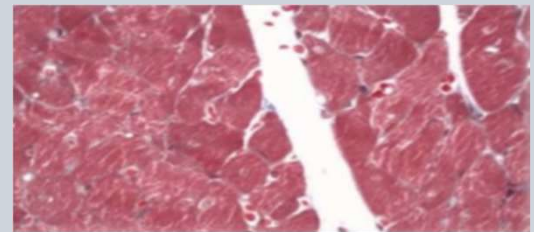
## 5% Ethanol 18-Week Control (Vehicle Control For VB0004)

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



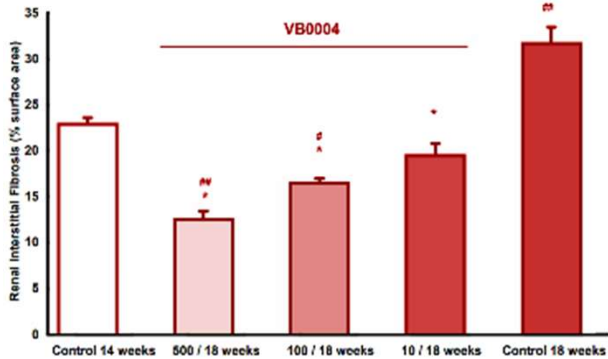
# VB0004 & KIDNEY FIBROSIS



In the kidney VB0004 has been shown to:

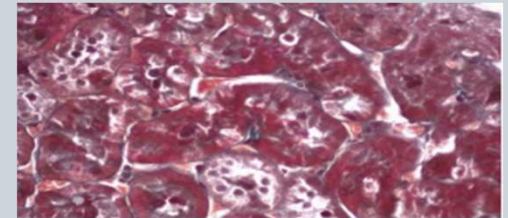
- Reverse renal interstitial fibrosis at all doses
- Restore normal architecture at all doses (i.e. VB0004 is considered transformational)

## Treatment with VB0004 at 3 Doses



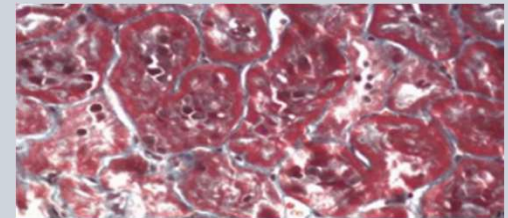
## 14-Week Control

Fibrosis (blue) partially surrounds some but not all tubules



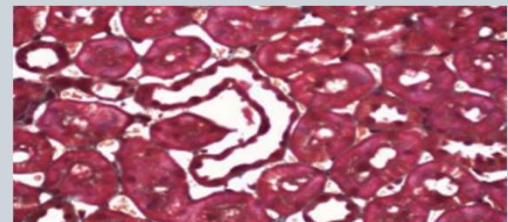
## 5% Ethanol 18-Week Control (Vehicle Control For VB0004)

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

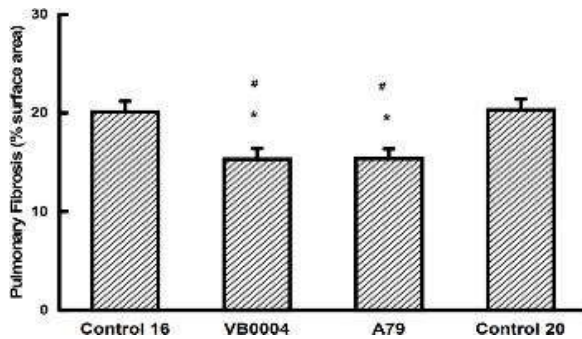


## In the lung:

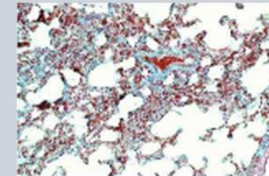
- VB0004 reversed fibrosis present 2 weeks after treatment with bleomycin (an anticancer drug)

(i.e. VB0004 also transformational in the lung)

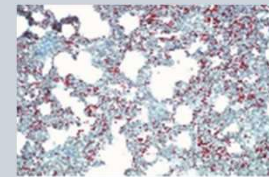
## Treatment with VB0004 and VB4-A79



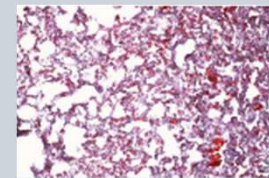
16-Week Control



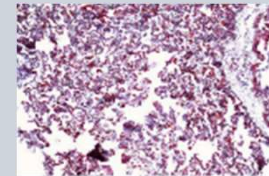
20-Week Control



VB4-A79 at 20 weeks



VB0004 at 20 weeks



## SYNTHESIS AT SCALE & COST



# 01

### 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)



# 02

### SECOND GMP SYNTHESIS BY ASSYCHEM

- 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



## PHASE 1



**Trial design – conventional Single Ascending Dose (SAD) & Multiple Ascending Dose (MAD)**

**Includes pharmacokinetic and pharmacodynamic studies**

**Expected outcomes – maximum tolerated dose, dose limiting toxicity (if present), pharmacokinetic (PK) and pharmacodynamic (PD) data**

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

**SAD completed with no significant adverse events, max tolerated dose 300mg**

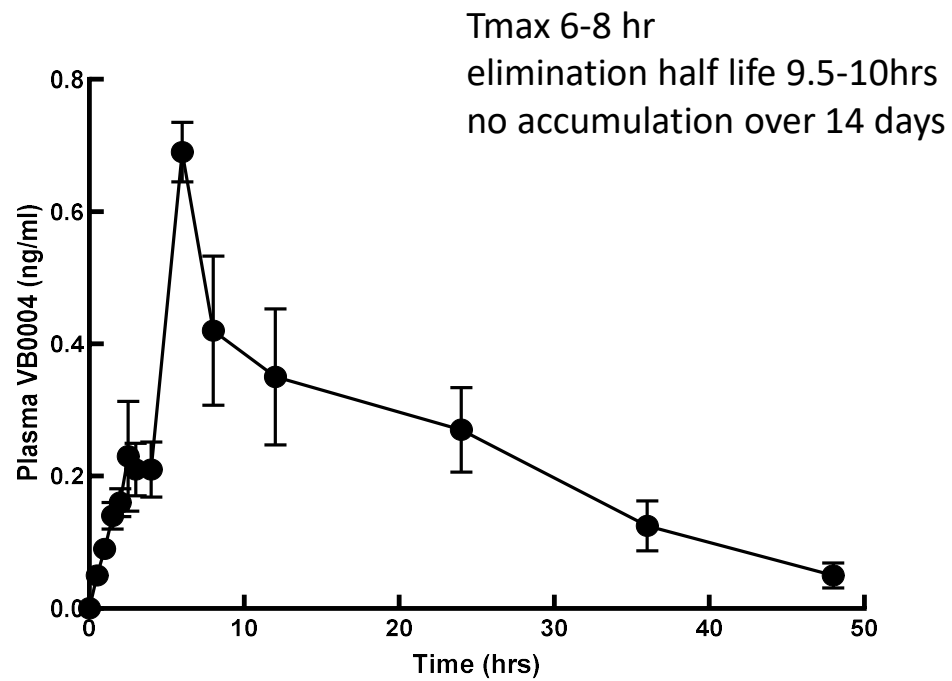
**Healthy subjects 14 day MAD completed, no significant adverse events, max tolerated dose 100mg daily**

**PK – Tmax at 6-8hrs, half life 10-15hrs, no accumulation over 14 days**

**Affected individuals 2 groups 28 days 2 doses biomarkers identified - recruiting**



# Phase 1 - Pharmacokinetics



## Phase 1a - Outcomes



VB0004 a very safe drug:

SAD – maximum planned dose 300mg  
– maximum tolerated dose 300mg

MAD – maximum planned dose 100mg / day for 14 days  
– maximum tolerated dose 100mg /day for 14 days

PK – consistent with once daily dosing  
– T<sub>max</sub> 6-8 hr  
– elimination half life 9.5-10hrs  
– no accumulation over 14 days





## VB0004 IN SUMMARY



### Fist in class therapeutic

- VIP agonist

### Transformational agent

- reverses existing fibrotic disease
- effective in multiple organs

### Synthesis

- 3 steps
- cost competitive (\$0.05 /mg)

### Stability

exceeds 2 years

### Efficacy

- significantly greater reductions in SBP, cardiac and renal fibrosis at lower doses than current agents.

### Potential role

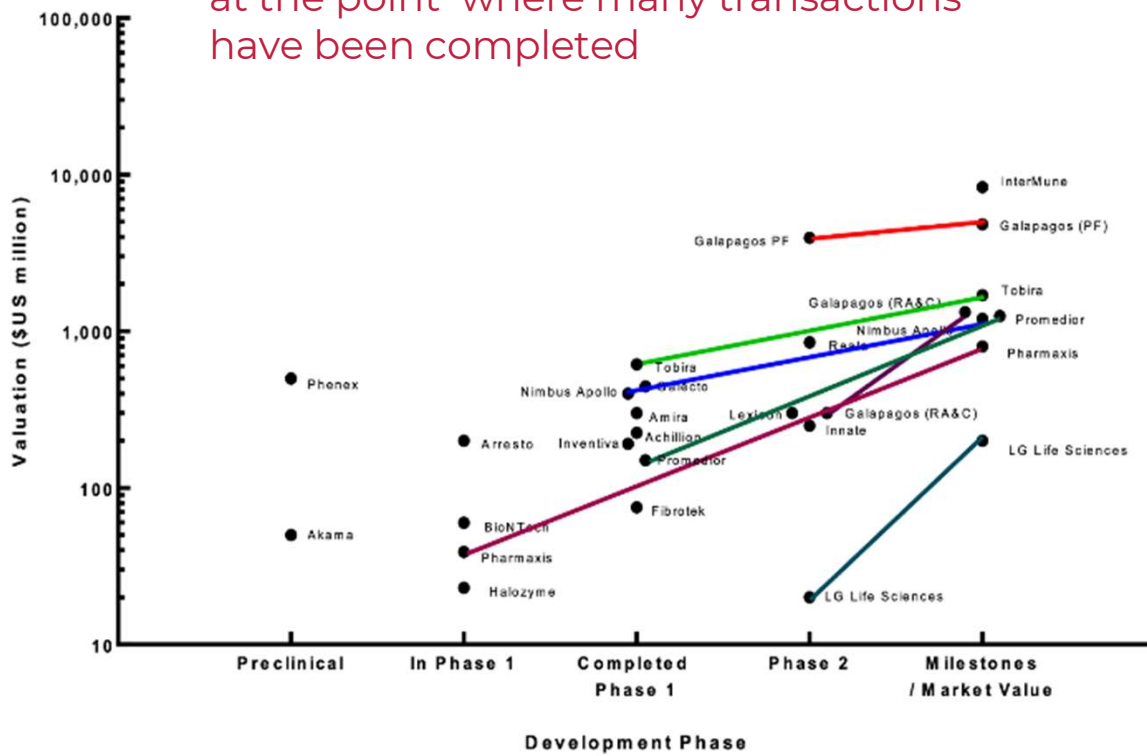
- given significantly greater efficacy at lower doses than current agents may replace RAS blockers as the foundational agent for therapeutic regimens in cardiovascular and renal disease

# COMPARABLE TRANSACTIONS



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

MWO

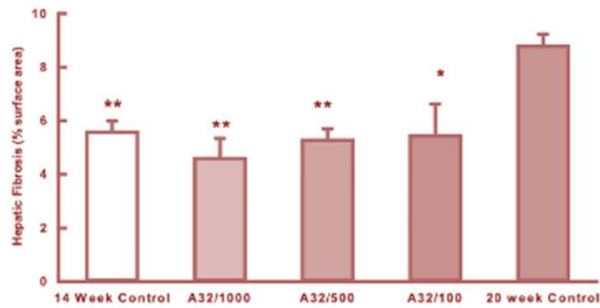


## 2023 CATALYSTS



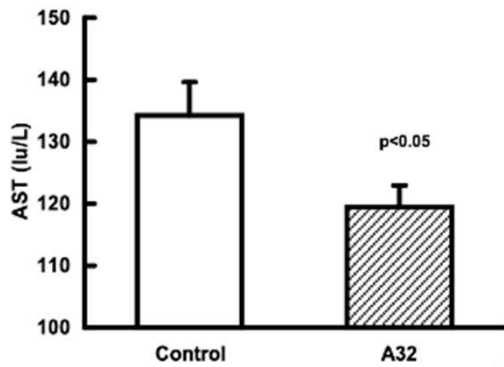
VB0004	<ul style="list-style-type: none"><li>• Completed Phase 1a Human Safety Trials</li><li>• Phase 1B Human Trial in progress</li><li>• Leverage engagement with global pharmaceutical companies</li></ul>
VB4-A32	Undertake GMP synthesis (Assymchem), with IND toxicology studies to follow
NEW EMERGING LEADS	Accelerate work on detailed mechanisms of action for VB4-A32, VB4-A79
EXPAND	Facilities and resources to undertake a broader drug development program
INVESTIGATE	Candidates from Vectus' extensive patented library for roles in other fibrotic / protein accumulative diseases such as osteoarthritis, retinal fibrosis, Alzheimer's disease
COMMERCIALISE	Broaden Accugen commercial roll out with Vectus' breakthrough qPCR platform

# VB4-A32 & HEPATIC CIRRHOSIS

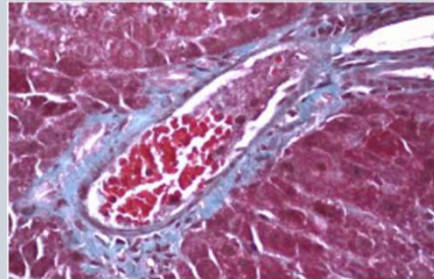


VB4-A32 demonstrated ability to:

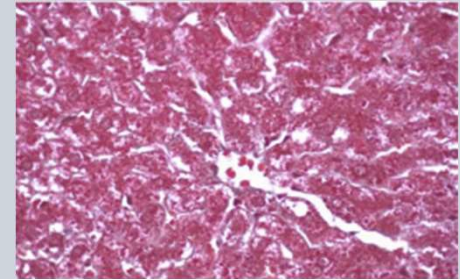
- Reduce peri-portal fibrosis in the liver in a dose dependent manner (above left)
- Improve liver function tests (below left)



20-Week Control



A32 20 Weeks

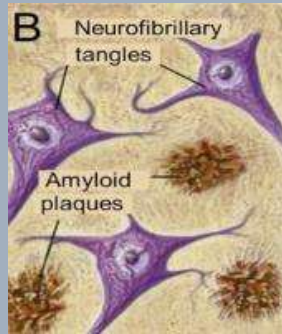
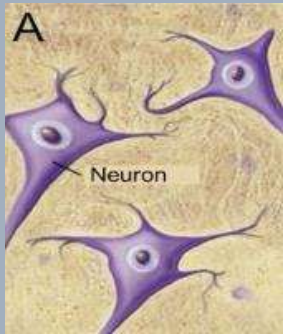


# NEW INDICATIONS ALZHEIMERS & LONG COVID



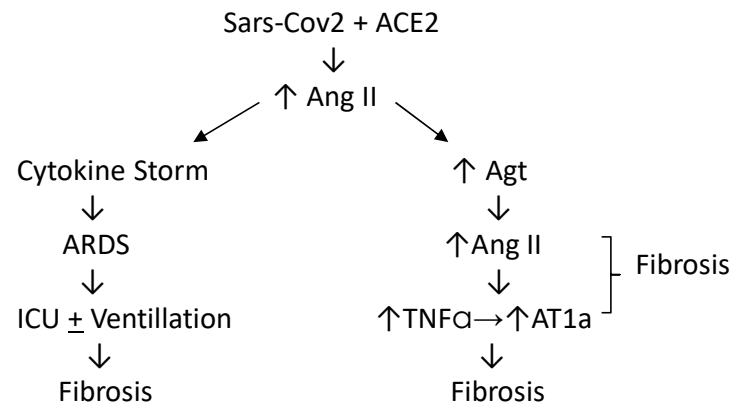
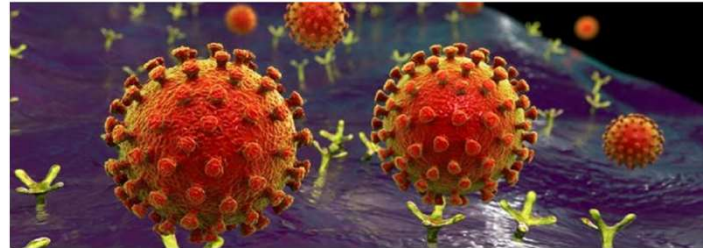
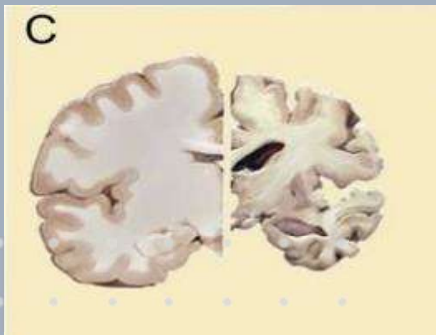
NORMAL

ALZHEIMER'S DISEASE

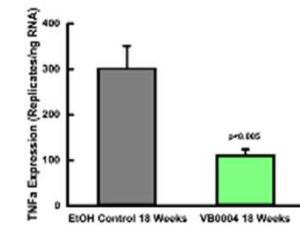
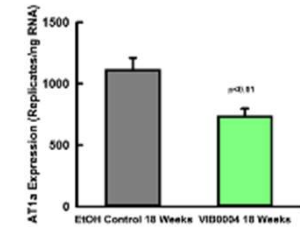
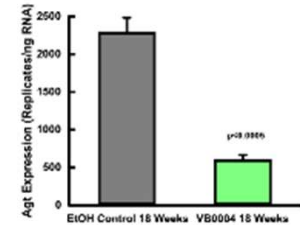


HEALTHY BRAIN

SEVERE ALZHEIMER'S



Ang II = Angiotensin II  
 ARDS = Acute Respiratory Distress Syndrome  
 Agt = Angiotensinogen, the Ang II precursor  
 TNFα = Tumour Necrosis Factor alpha



## PATENT PORFOLIO – LONG PATENT LIFE



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



# IN THE MEDIA – VECTUS INCREASING MARKET RECOGNITION



## Why medtech veteran Maurie Stang says the time is right for Vectus

Almost 15 years after the company was founded, medical technology veteran Maurie Stang is convinced 2022 is the tipping point for long-discovery company Vectus Biosystems.

The ASX-listed small cap, which surged more than 8 percent on Wednesday, is developing a series of oral drugs based on a peptide in the intestine to treat cardiovascular, pulmonary and liver fibrosis, as well as systemic blood pressure.

**RELATED QUOTES**

VBS \$1.45 ▲ 4.1%

1 Year 2 Day

1.00  
0.50  
0.00

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October 3, 2022 | Tim Boreham

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May 25, 2022 | Eddy Sumarto

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TECHNOLOGY COVERING A RANGE OF HEALTH GAPS

**SMALL CAPS**

**MAURIE STANG**  
VECTUS BIOSYSTEMS (ASX: VBS)

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0:10 / 29:52

Vectus Biosystems progresses its human trials with lead cardiovascular drug candidate VB0004

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