10 March 2020

Publication that Demonstrates Reversal of Established Kidney Fibrotic Damage by VIP in a Preclinical Model

Vectus Biosystems Limited (Vectus) is pleased to announce the publication of preclinical data in a model of tubulo-interstitial fibrotic damage to the kidney. The publication entitled: "*Vasoactive intestinal peptide infusion reverses existing renal interstitial fibrosis via a blood pressure independent mechanism in the rat*" (https://doi.org/10.1016/j.ejphar.2020.172979) appeared in the European Journal of Pharmacology, the official journal of The Federation of European Pharmacological Societies, published by Elsevier.

In this foundational, peer-reviewed publication, researchers from Vectus demonstrated that infusion of the naturally-occurring peptide molecule Vasoactive Intestinal Peptide (VIP) for four weeks had the unique ability to reverse fibrotic damage already present at the time VIP therapy was commenced. This feature provides a distinct therapeutic advantage compared with currently-available anti-fibrotic agents (see Appendix A).

This paper focused on the treatment of tubulo-interstitial fibrosis in the kidney. This form of kidney damage is present regardless of the initial form of kidney disease and the progression of tubulo-interstitial fibrosis is predominantly responsible for continuing loss of kidney function in all forms of kidney disease. In fact, the rate of progression of tubulo-interstitial fibrosis determines the time course until patients require kidney dialysis or transplantation. Currently available drugs do not adequately treat this form of kidney fibrosis and the Vectus data in this publication represent a major advance for the management of kidney disease. Kidney failure affects 10-14% of the general population, but its prevalence increases with age so that 30-50% of those aged over 75 years are affected. Further, data on end-stage kidney disease that requires renal replacement therapy (dialysis and/or transplantation) are indicative of a silent epidemic. In the USA and Europe the dialysis population continues to increase at 1-4% per annum, while in Australia the dialysis population has tripled over the past two decades.

In the heart, earlier work by Dr Duggan (Vectus' CEO) and other researchers had demonstrated that VIP levels decreased as the amount of fibrosis increased, becoming absent in end-stage experimental cardiomyopathy and in the hearts of patients with end-stage cardiomyopathy that were removed at transplantation. These combined data suggested that depletion of VIP in the heart plays a role in the development and progression of fibrosis. The demonstration that increasing cardiac VIP concentrations reversed pre-existing disease provides evidence for a pivotal role for the depletion of VIP in the heart in the development and progression of fibrotic disease. The current data expand this anti-fibrotic ability of VIP to include the kidney and further establish VIP as a new therapeutic target.

Vectus is completing toxicology and pharmacokinetic studies on an orally-available VIP analogue (VB0004), which displays similar capacity to reverse pre-existing fibrosis, to enable VB0004 to enter a Phase 1 clinical trial in 2020.

This announcement was authorised for release to ASX by Vectus' Board.

Vectus Biosystems Limited

Karen Duggan
Chief Executive Officer and Executive Director

About Vectus Biosystems Limited

Vectus Biosystems Limited (Vectus or the Company) is developing a treatment for fibrosis and high blood pressure, which includes the treatment for three of the largest diseases in the fibrotic market, namely heart, kidney and liver disease. Vectus successfully completed its Initial Public Offering (IPO) on the Australian Securities Exchange (ASX:VBS) and commenced trading on ASX on 23 February 2016, after raising A$5.1 million. Funds from the IPO were used to develop the Company's lead compound VB0004, which aims to treat the hardening of functional tissue and high blood pressure. Vectus has conducted a range of successful pre-clinical trials, which have shown that VB0004 slows down the advances of fibrosis, potentially repairs damaged cell tissue and reduces high blood pressure. VB0004 has progressed through a number of important milestones, including pharmaceutical scale-up and additional toxicity studies. Successful results have provided the Company with a clear path to Human Phase I and IIa Clinical Trials. Vectus' strategy is to develop and perform early validation of its drug candidates to the point where they may become commercially attractive to potential pharmaceutical partners.

The Company has also developed technology aimed at improving the speed and accuracy of measuring the amount of DNA and RNA in samples tested in laboratories. The technology, called Accugen, is owned by Vectus' wholly-owned subsidiary, Accugen Pty Limited. The technology offers a time, cost and accuracy benefit compared to currently-available systems. The Company's current stage of investment in Accugen is a commercialisation programme, where a combination of direct sales, distribution partnerships and licensing opportunities are being evaluated.

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Appendix A

This study was conducted in the spontaneous hypertensive rat (SHR). The kidney in the SHR is a model of interstitial fibrosis without glomerulosclerosis (Leh etal 2011) and, as such, provides a unique opportunity to evaluate the efficacy of interventions directed to treating tubulointerstitial fibrosis. Four groups of rats (n=5 per group) were studied, a 14-week control group, a VIP treated group, an enalapril treated group and a vehicle treated or 18-week control group. VIP, enalapril or the vehicle were given for a four-week period. The enalapril group provided the level of anti-fibrotic activity that would be obtained by current agents for the same amount of blood pressure reduction as was achieved in the VIP treated rats.

The amount of tubulointerstitial fibrosis in the kidney of the two control groups increased over the four-week experimental period from 22.2$\pm$0.7 % surface area at 14 weeks to 26.0$\pm$0.8 % surface area at 18 weeks ($P<0.01$). Enalapril treatment did not significantly decrease fibrosis compared with the 18-week or vehicle control (E=23.5$\pm$0.9 % surface area). In contrast, VIP infusion for four weeks decreased tubulointerstitial fibrosis to 11.6$\pm$0.8 % surface area, which was significantly less than both the 18-week controls ($P<0.0005$) and 14-week controls ($P<0.0005$) as well as fibrosis in the enalapril treated rats ($P<0.01$).

The study clearly demonstrated the superiority of VIP treatment to reduce tubulointerstitial fibrosis compared with current therapies as represented by the enalapril treated group. More significantly, the study demonstrated that VIP could reverse fibrotic disease that was present before VIP was commenced. The latter represents a unique feature of VIP treatment and has the potential to provide the basis for a major breakthrough in the treatment of chronic kidney disease.

Leh S, Hultström M, Rosenberger C and Iversen BM. 2011 Afferent arteriolopathy and glomerular collapse but not segmental sclerosis induce tubular atrophy in old spontaneously hypertensive rats. *Virchows Arch*. 459:99-108. doi: 10.1007/s00428-011-1100-3.

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