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Exonate—Global R&D Effort in Drug Discovery Leads to Collaboration With Big Pharma

John Kurek, Peter Devine

Abstract: Exonate, a Sydney-based ophthalmology start-up biotech company, has developed an eye-drop treatment for Diabetic Macular Oedema and wet Age-Related Macular Degeneration in a strategic collaboration agreement with Janssen Pharmaceuticals, Inc.

Keywords: Exonate, diabetic macular oedema, macular degeneration, retinal disease.

1. The success story—Exonate

Diabetic Macular Edema (DME) and wet Age-Related Macular Degeneration (wAMD) are some of the leading causes of vision loss in people aged 60 and older. VEGF signalling has been identified as an underlying molecular mechanistic driver of these ophthalmic diseases. Drugs that inhibit VEGF and its receptors are already the standard of care for several diseases, including wAMD and DME. These drugs are administered by an injection into the eye and are also a mainstay of cancer therapy. Exonate—an early-stage biotech company built on an IP from the University of New South Wales, the University of Nottingham, and the University of Bristol—is focused on alternative splicing of Vascular Endothelial Growth Factor (VEGF) in ophthalmology. Exonate has developed small molecules that inhibit the production of pro-angiogenic VEGF through selective inhibition of serine/threonine-protein kinase 1 (SRPK1)-mediated VEGF splicing. These inhibitors have demonstrated superior efficacy as topical agents in preclinical models of wet AMD.

2. Where did it start and the motivation?

Exonate was established in 2013, from early collaborative work between the Universities of NSW, Bristol, and Nottingham, with a mutually owned IP. Professor Jonathan Morris at UNSW, Sydney pioneered the small molecule SRPK1 inhibitors' work, and Professor David Bates at the University of Nottingham specialised in the biology and biochemical pathways of VEGF splice variants. The collaboration allowed Exonate to develop small molecules that inhibit the production of pro-angiogenic VEGF through the selective inhibition of

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serine/threonine-protein kinase (SRPK1)-mediated VEGF splicing. VEGF is alternatively spliced into two classes of proteins—pro-angiogenic VEGF-Axxx_a isoforms, which are responsible for disease progression, and anti-angiogenic VEGF-Axxx_b isoforms, which mitigate these effects through competitive binding [1]. By exploiting the alternative splicing of VEGF, Exonate is developing an eye drop that can penetrate the back of the eye, reach the retina, and stop blood vessel growth to treat wet AMD and DME. With many patients not responding to existing treatments, Exonate's lead program has the potential to become the patient's treatment of choice in these retinal eye diseases, which remain an area of high unmet medical need.



Figure 1. Exonate team: Professor Steven Harper (Medical Director), Sunil Shah (Chairman), John Kurek (Biotechnology investment manager, Uniseed), Dr. Catherine Beech OBE (Chief executive officer), Professor David Bates (Chief Scientific Officer), Dr. Andrew Naylor (CEO, Nottingham Technology Ventures Ltd), Dr. Chris Torrance (Chief Executive Officer, PhoreMost Ltd).

3. The journey so far

Uniseed first invested in Exonate in November 2016—one of the first investments from its most recent commercialisation fund (Fund-3). Uniseed is a partnership between The University of Queensland, The University of Sydney, The University of New South Wales (UNSW Sydney), The University of Melbourne, and the CSIRO. In 2018, Uniseed participated in a follow-on investment round, with just over \$836,000 invested by Uniseed over both rounds. Exonate is domiciled in Cambridge UK, though with the investment rounds supported by Uniseed, Exonate has funded a significant amount of contract R&D in the laboratory of Professor Morris at Uniseed's partner research organisation, UNSW. In 2017, Exonate also received a £4.9m Wellcome Trust Seeding Drug Discovery Award (one of the largest awarded). The funding allowed Exonate to complete a lead optimisation programme, nominate a preclinical candidate drug with optimal characteristics, and complete regulatory toxicology and safety pharmacology studies that would support an application to the

regulatory authorities for clinical evaluation. Exonate expects to reach this milestone and enter the clinic in 2020.

4. Look into the future

In January 2020, Exonate announced that it had entered into a strategic collaboration agreement with Janssen Pharmaceuticals, Inc. The collaboration facilitated by Johnson & Johnson (J&J) Innovation, allows Exonate to work with Janssen R&D scientists to develop an eye drop treatment for retinal vascular diseases, such as wet AMD and DME based on Exonate's small molecules. These collaborations are of mutual benefit for both parties. While it can be tempting for VC's such as Uniseed to continue funding the development program and complete clinical trials before entering into a deal, small biotech companies also need to be nimble and continually review their strategy. In this case, the partnership with J&J was the best strategic decision for Exonate. Janssen Pharmaceuticals is one of the largest pharmaceutical companies in the world and tapping into their expertise, and global resources are invaluable at the preclinical and clinical stages of development. For a start-up company, the risk-reward analysis and probability of success (or failure) are never static, it is on a continuum, and you need to continually look at commercial opportunities as they arise because in some cases, it may make more financial sense to do a deal early.

The Company

The logo for Exonate, featuring the word "Exonate" in a bold, sans-serif font. The letter 'E' is blue, 'x' is green, 'o' is yellow, 'n' is blue, 'a' is blue, 't' is blue, and 'e' is blue.

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References

[1] Stevens M., Oltean S., Modulation of Receptor Tyrosine Kinase Activity through Alternative Splicing of Ligands and Receptors in the VEGF-A/VEGFR Axis. *Cells* 2019, 8, 288.

John Kurek is the Biotechnology Investment Manager at Uniseed, Australia's longest-running venture fund, operating at the Universities of Melbourne, Queensland, Sydney & New South Wales, and the CSIRO, with investment capital provided by these research organisations. At Uniseed, John is responsible for identifying new investment opportunities from the five research partners, and also covers



Uniseed's overall biotechnology and life sciences portfolio. Uniseed has returned significant capital to its investors, including Novartis acquisition of Spinifex for US\$700m; Shire plc acquisition of Fibrotech Therapeutics for US\$557m; and Hatchtech sale to Dr Reddy's Laboratories for ~US\$200m.

John brings 20 years of industry experience as a Biotechnology Manager with a focus on the strategic design and implementation of drug development programs. John's previous roles have been with ASX listed biotech companies BioDiem Ltd and Amrad Corporation Ltd., where he was responsible for the management of preclinical and early clinical stage drug development projects. His experience extends from late drug discovery to the phase I-II clinical phases of drug development. John's experience covers a range of areas, including 1) Acting as Director on investee company boards, 2) Biotechnology project management, 3) Investment analysis and due diligence, 4) Financial modelling, 5) Intellectual property management, 6) Business development, 7) Risk management, and 8) Relationship management.

John has a PhD in Neuroscience and a Post Graduate Diploma in Drug Evaluation & Pharmaceutical Science, both from the University of Melbourne, and is a graduate of the Australian Institute of Company Directors.

Peter Devine is CEO of Uniseed and has extensive experience at board and executive management levels in the commercialisation of early-stage technologies, having held senior R&D, business development and commercialisation positions in several Australian companies and Australian universities. Has served on the Board of numerous start-ups which have collectively raised over AU\$300m, with a number of these being successfully sold to large multi-nationals in deals collectively worth over AU\$1.75b.



Peter holds a PhD from the University of Queensland and received the Dean's Prize for his MBA studies at the Australian Graduate School of Management. He is a Graduate and Fellow of the Australian Institute of Company Directors and holds a Diploma of Financial Services (Financial Markets) and a Graduate Diploma in Applied Finance from Kaplan Professional. Peter was previously VP of Business Development at ASX-listed Progen Industries Ltd. He was Research, Development and Commercialisation Manager at Brisbane-based PanBio Pty Ltd from 1996 to 2000, which ultimately was sold to Inverness Medical. He received a Federal Government Centenary Medal in 2003 for outstanding contribution to the business of biotechnology.

Recent Uniseed successes include Fibrotech Therapeutics' sale to Shire in 2014; the Spinifex Pharmaceuticals sale to Novartis in 2015; the Hatchtech sale to Dr Reddy's in 2015 and FDA approval in 2020; the Smart Sparrow sale to Pearson on 2020 and Exonate's collaborative agreement with Janssen in 2020.