

Circadian granted key strategic VEGF-D patent in Europe for angiogenic applications

- **Patent grants exclusive rights to the use of VEGF-D protein and VEGF-D antibodies in a broad spectrum of therapeutic indications**
- **Now have granted VEGF-D patents in Europe and the US – the world's largest markets**

Circadian Technologies Limited (ASX:CIR) announced today that its subsidiary company, Vegenics Limited, has been granted European Patent 1749836 covering the use of VEGF-D protein and antibodies to VEGF-D in a broad spectrum of therapeutic indications, including the treatment of cancer.

VEGF-D, a major novel target for cancer and other diseases, is closely related to VEGF-A, the target of Genentech's Avastin[®], a leading cancer therapy with worldwide sales in excess of US\$6 billion.

This European patent together with the VEGF-D patent granted in the United States last year provides Circadian with a major commercial advantage and access to the world's two largest markets.

Circadian is currently developing its VGX-200 series of humanised VEGF-D antibodies as anti-cancer agents.

"Stemming from the enormous success of Avastin[®], the development of antibody drugs targeting angiogenic molecules such as VEGF-D is widely considered one of the most promising strategies in the pharmaceutical industry," commented Circadian CEO, Mr Robert Klupacs. "This patent adds to our considerable estate of intellectual property covering VEGF family members, in particular building on the US patent granted to us last year covering VEGF-D antibodies. It is an important protection for our internal therapeutics development programs and represents a major asset for commercial partnerships with other companies seeking to pursue this approach."

Vegenics owns worldwide rights to an extensive intellectual property portfolio covering angiogenesis targets VEGF-D, VEGF-C and the receptor protein VEGFR-3.

Mr Klupacs added, "The grant of this patent is another successful step in Circadian's execution to become a leading developer of therapeutic antibody drugs for cancer."

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About Circadian Technologies Limited

Circadian (ASX:CIR) is a biologics drug developer utilising the significant intellectual property portfolio around Vascular Endothelial Growth Factor (VEGF) C and D that it has accumulated in its unlisted wholly owned subsidiary Vegenics. The applications for the VEGF technology, which functions in regulating blood supply, are substantial and broad. Circadian's internal product development programs are focussed on novel anti-cancer therapeutics for large unmet needs. Circadian has also licensed rights to some parts of its intellectual property portfolio for the development of other products to UK company Ark Therapeutics Group plc (LSE: AKT) and ImClone Systems (a wholly owned subsidiary of Eli Lilly & Company - NYSE: LLY). Ark is developing Trinam®, a treatment for vascular grafts associated with renal dialysis based upon Circadian intellectual property which has commenced Phase 3 clinical trials. ImClone Systems is currently developing an antibody-based drug targeting VEGFR-3 for the treatment of solid tumours.

The VEGF patent portfolio developed by LICR and Licentia has been assigned to Vegenics. Vegenics also has rights to CoGenesys Inc/Human Genome Sciences Inc's VEGF-C intellectual property.

About VEGF Technology and angiogenesis

In Cancer

The clinical and outstanding commercial success of Avastin®, an antibody that blocks the activity of VEGF-A, clinically validated anti-angiogenic drugs as an effective means of inhibiting solid tumour growth. By blocking the interaction of VEGF-A with its receptors, primarily VEGFR-2, the multi-billion dollar cancer therapeutic slows tumour growth by inhibiting blood vessel recruitment into the tumour, effectively starving tumours of essential nutrients and oxygen required for growth. Avastin, which is sold by Genentech, now part of Roche, and Hoffman-La Roche, had U.S. sales in 2007 of US\$2.3 billion and worldwide sales in excess of US\$6 billion.

VEGF-C and VEGF-D inhibitors, key therapeutics in the portfolio of Circadian's unlisted subsidiary Vegenics, blocks the alternative ligands for VEGFR-2. As such, they have the potential to block blood vessel growth in tumours resistant to anti-VEGF-A therapy and, when used in combination with drugs like Avastin, may completely shut down angiogenesis (the growth of blood vessels) mediated by VEGFR-2, resulting in greater clinical efficacy.

VEGF-C and VEGF-D also bind and activate VEGFR-3 which drives lymphatic vessel and tumour-associated blood vessel growth. Inhibitors of VEGF-C, VEGF-D and VEGFR-3 thus have therapeutic potential to inhibit not only primary tumour growth through their anti-angiogenic activities, but to also inhibit tumour spread or metastasis via the lymphatic vessels - a mechanism of tumour dissemination that is often the deadliest aspect of many tumour types and a mechanism that is not effectively blocked by anti-VEGF-A or anti-VEGFR-2 therapeutics.

Other Disease Applications

VEGF Technology also has applications in other diseases, where shutting down angiogenesis and/or lymphatic vessel growth is important, such as eye diseases including age related macular degeneration and diabetic retinopathy.