



ASX and Media release

27 June 2012

Healthscope to commercially launch Circadian's Cancers of Unknown Primary Diagnostic Test

- **Commercial launch to occur on July 16 in Australia, New Zealand, Malaysia and Singapore**
- **The test will be marketed under the tradename CUPGUIDE™**
- **Circadian to receive royalties on Healthscope sales**

Circadian Technologies Limited (ASX:CIR, OTCQX:CKDXY) announces that it has been advised by its development partner, Healthscope Advanced Pathology, that it will commercially launch Circadian's novel technology for aid in the diagnosis of "Cancers of Unknown Primary" (CUP), on Monday July 16 2012 in Australia, New Zealand, Singapore and Malaysia under the brand CUPGUIDE™.

The diagnostic test method has been developed in collaboration between Circadian, Healthscope, the Peter MacCallum Cancer Centre, a leading specialty cancer centre, and scientists at NICTA, Australia's Information and Communications Technology (ICT) Research Centre of Excellence.

A publication in March 2012 from Healthscope reported that the CUP test was able to detect actual primary source of tumour type with 93% accuracy within the first three predictions and had 98.5% specificity across 15 different tumour types.

Healthscope, through its subsidiary Clinical Laboratories Pty Ltd, has rights to develop, clinically validate and market the test throughout Australia, New Zealand, Malaysia and Singapore. Circadian retains rights to market the test in the remainder of the world. Healthscope has paid Circadian an upfront fee, and will pay a royalty on sales of the test. Circadian, through its wholly owned subsidiary Cancer Therapeutics Pty Ltd, owns exclusive worldwide rights to the test through a licensing arrangement with the Peter MacCallum Cancer Centre and NICTA.

The CUP diagnostic methodology identifies a patient's tumour type by comparing its pattern of gene expression to a database of known tumours. It is hoped that by correctly identifying a patient's tumour type, clinicians can choose the most effective treatment strategy for the cancer. CUP is generally less well known and publicised than other cancer types. However, it is actually more common than leukaemia and is the fifth most common cause of death due to cancer in Australia. In 2007, Cancer Council Australia estimated the incidence of CUP to be around 2900 case per annum; American Cancer Society estimated USA incidence at around 32,000 per annum and Cancer Research UK estimated UK incidence at 14,000 per annum.

Robert Klupacs, Circadian Managing Director and CEO stated, "We are absolutely delighted that after all of the efforts of the collaborative partners that CUPGUIDE™ will now be available to oncologists and pathologists. We are extremely hopeful that CUPGUIDE™ will have a major impact in significantly improving the clinical diagnosis of CUP".

Dr Keith Byron, Scientific Director of Healthscope's Advanced Pathology Division said, "Healthscope is proud and excited that after the extensive development program we have undertaken with our partners that we will now be able to provide this ground breaking diagnostic technology on a commercial basis. The test is an important addition to our existing business of providing diagnostic tools for doctors throughout our 43 hospitals and the health care industry in general".

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Prof David Bowtell, Head of the Cancer Genomics Program at the Peter MacCallum Cancer Centre and a co-inventor of the diagnostic methodology added, "The approach was initially developed in our lab several years ago but the assay needed to be made more generally available. Circadian and Healthscope have been critical to taking the work forward and it is very gratifying that this product of our translational research efforts will be made available to clinicians throughout the region. The concept of personalising treatments for patients based on highly specialised diagnostics is now very well accepted in oncology and has been shown to have significant patient benefit. We believe that the assay will lead to earlier diagnosis, improved treatment outcomes and enhanced quality of life for patients".

Dr Adam Kowalczyk, Leader of Diagnostic Genomics Team in NICTA's Victorian Research Laboratory, and a co-inventor of the diagnostic methodology added, "It is very satisfying that formal techniques for signal detection and pattern recognition can be utilised in practical medical applications. This diagnostic test heralds imminent arrival of many new developments bringing promises of personalised medicine and genomics, in particular, to everyday usage that benefits patients".

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About Circadian Technologies Limited

Circadian (ASX:CIR; OTCQX:CKDXY) is a biologics drug developer focusing on cancer and 'front of the eye' disease therapies. It controls exclusive worldwide rights to a significant intellectual property portfolio around Vascular Endothelial Growth Factor (VEGF)-C and -D. The applications for the VEGF technology, which functions in regulating blood and lymphatic vessel growth, are substantial and broad. Circadian's internal product development programs are primarily focussed on developing VGX-100 (a human antibody against VEGF-C) as a treatment for solid tumours, in particular glioblastoma and colorectal cancer, as well as for 'front of the eye' disease such as corneal neovascularisation and/or dry eye disease applications. Circadian has also licensed rights to some parts of its intellectual property portfolio for the development of other products to ImClone Systems, a wholly-owned subsidiary of Eli Lilly and Company, including the antilymphatic antibody-based drug IMC-3C5 targeting VEGFR-3.

About Cancers of Unknown Primaries

In spite of the increasing sophistication in the diagnostic workup for malignancies, detailed investigations fail to reveal a primary site of origin for a subset of patients with metastatic cancer. This is often referred to as Carcinoma of Unknown Primary (CUP) origin or occult primary malignancy. Usually, when cancer spreads, the secondary cancer cells look like abnormal versions of the primary cancer cells (in the tissue where the cancer began). For example, if breast cancer spreads to the lungs, the metastatic tumour in the lung is made up of cancerous breast cells (not lung cells) and is then described as metastatic breast cancer (not lung cancer). If it is not possible to identify the type of cancer cells, the diagnosis is CUP. The inability to identify a primary site of cancer poses many challenges. The primary site of cancer usually dictates the treatment, expected outcome and overall prognosis. The diagnosis of carcinoma of unknown primary thus generates anxiety among patients and caregivers, who may feel that the evaluation has been incomplete.

About Healthscope

Healthscope is a leading private health care provider within Australia that uniquely operates in every State and Territory, as well as in Asia. Our reach of facilities around the country firmly places Healthscope as the second largest private hospital provider operating 44 private hospitals. The company includes a leading pathology business with facilities in Australia, New Zealand, Singapore and Malaysia and a growing medical centres division with over 45 clinics.

Healthscope's Advanced Pathology division develops new clinical diagnostics and actively collaborates with pre-eminent research groups by validating their translational research for clinical application.

As well as providing specialised molecular pathology services, Healthscope Advanced Pathology has a strong research and development commitment. Current research programs focus on the clinical utility of pharmacogenomics, an area of great promise for improving individualised drug selection and dosing. Our other development program centres on the clinical application of genomics, with reference to cancer diagnosis.

About Peter MacCallum Cancer Centre

The Peter MacCallum Cancer Centre is Australia's only public hospital solely dedicated to cancer and one of an elite group of hospitals worldwide to have its own integrated cancer research program and laboratories. It treats more cancer patients each year than any other hospital in Australia and its highly skilled medical, nursing and allied health team is backed by Australia's largest cancer research group.

Peter MacCallum Cancer Centre's Cancer Genomics Program is led by Professor David Bowtell and seeks to use sophisticated high throughput genomic technologies to improve understanding of the biology of cancer and to progress the clinical management of cancer patients through the development of individualised approaches to treatment. Research in the program focuses primarily on breast, upper gastrointestinal and ovarian cancers and sarcomas, as well as Cancers of Unknown Primary and involves some of the largest familial and population-based cancer cohorts in the world. These studies address questions of general importance to solid cancers, including inherited susceptibility to cancer and genome-wide changes in gene expression, as well as more specific questions such as prediction of response to therapy and the use of gene expression profiling to inform more accurate cancer diagnosis. Professor Bowtell is Principal Investigator for the Australian Ovarian Cancer Study, a national molecular epidemiological study of ovarian cancer, creating the largest linked biospecimen/clinical database in the world for ovarian cancer. He also leads the Cancer Genetics and Genomics Laboratory, which interfaces with the recently formed Asia-Pacific Gastric Cancer Consortium, comprising participants from China, Japan, Korea, Singapore, Hong Kong and Australia.

About NICTA

NICTA (National ICT Australia Ltd) is Australia's Information and Communications Technology Research Centre of Excellence. NICTA develops technologies that generate economic, social and environmental benefits for Australia. NICTA collaborates with industry on joint projects, creates new companies, and provides new talent to

the ICT sector through a NICTA-enhanced PhD program. With five laboratories around Australia and over 700 people, NICTA is the largest organisation in Australia dedicated to ICT research.

NICTA is funded by the Australian Government through the Department of Broadband, Communications and the Digital Economy and the Australian Research Council through the ICT Centre of Excellence Program. NICTA is also funded and supported by the Australian Capital Territory, the New South Wales, Queensland and Victorian Governments, the Australian National University, the University of New South Wales, the University of Melbourne, the University of Queensland, the University of Sydney, Griffith University, Queensland University of Technology and Monash University.

The Diagnostic Genomics team at NICTA contributed expertise in Signal Processing and Pattern Recognition to the development of the CUP diagnostic methodology.

About Circadian's pipeline of treatments for cancer

The clinical and 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. However after a short period of time tumors can begin to grow again in the presence of Avastin®. Avastin® is approved by the US FDA in the following indications: metastatic colorectal cancer, non-squamous-cell lung cancer, metastatic breast cancer, glioblastoma, and metastatic renal cell carcinoma.

The angiogenic receptor VEGFR-2 can also be stimulated by VEGF-C and hence an inhibitor such as VGX-100, a key therapeutic in Circadian's portfolio, can produce greater blockade of this receptor pathway. As such, VGX-100 has the potential to block blood vessel growth in tumours which grow in the presence of Avastin® therapy and hence may completely shut down angiogenesis (the growth of blood vessels) mediated by VEGFR-2.

VEGF-C along with the molecule VEGF-D are also the only known proteins to bind and activate VEGFR-3 which drives lymphatic vessel and tumour-associated blood vessel growth. Inhibitors of VEGF-C 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.

Inherent risks of Investment in Biotechnology Companies

There are a number of inherent risks associated with the development of pharmaceutical products to a marketable stage. The lengthy clinical trial process is designed to assess the safety and efficacy of a drug prior to commercialisation and a significant proportion of drugs fail one or both of these criteria. Other risks include uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Companies such as Circadian are dependent on the success of their research and development projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Thus investment in companies specialising in drug development must be regarded as highly speculative. Circadian strongly recommends that professional investment advice be sought prior to such investments.

Forward-looking statements

Certain statements in this ASX announcement may contain forward-looking statements regarding Company business and the therapeutic and commercial potential of its technologies and products in development. Any statement describing Company goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those risks or uncertainties inherent in the process of developing technology and in the process of discovering, developing and commercialising drugs that can be proven to be safe and effective for use as human therapeutics, and in the endeavour of building a business around such products and services. Circadian undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise. Actual results could differ materially from those discussed in this ASX announcement.