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15 July 2003

Company Announcements Office
Australian Stock Exchange Ltd (ASX)
4th Floor, 20 Bridge Street
Sydney NSW 2000

Dear Sir/Madam

Please find herewith a commercially sensitive announcement “**US tests confirm Australian drug effective against severe pain**” to be distributed to the market immediately.

Yours sincerely

NICHOLAS MATHIOU
Finance Director



Media Release
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US tests confirm Australian drug effective against severe pain

Medica Holdings today announced that researchers at the University of California have confirmed the effectiveness of a new drug in the treatment of chronic pain.

The drug (Xen2174), based on the venom of a cone shell found on the Great Barrier Reef, has been developed by Medica's investee, Xenome, and could be a major breakthrough for cancer patients.

The research, conducted at the University of California showed that Xen2174 was highly effective in treating severe pain in animal models.

Dr Kevin Healey, a director of Xenome and Managing Director of Medica, said the new drug could revolutionise the way chronic pain is treated.

"Currently morphine dominates this market, but many patients develop tolerance with long-term use, and there is also reluctance by patients and clinicians to use morphine because of the fear of addiction and side effects. Up to 15% of cancer patients currently have no effective form of pain relief.

"Xenome's new drug promises to change this," Dr Healey said.

The intraspinal drug market for the treatment of chronic pain is currently valued at between US\$300–US\$500 million. Dr Healey said that Xenome was well placed to play a major role as the drug is expected to enter human trials early in 2004.

Xenome's release is attached.

About Medica Holdings Limited

Medica, an ASX-listed Pooled Development Fund, specialises in investing in the biotechnology sector. As well as its Xenome shareholding (25%), Medica facilitated the establishment of subsidiary Cytopia (79% owned), which is developing a range of drug candidates against immune diseases and cancer. Medica also owns around 21% of Alchemia, which is developing carbohydrate-based drugs and nutraceuticals.

Under the PDF Scheme, Medica's shareholders are exempt from tax on capital gains or profits from the sale of shares. For further information, please visit www.medica.com.au, email info@medica.com.au or contact:

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Tuesday, 15th July 2003

Media Release

Source: XENOME LIMITED

Xen2174 IS EFFECTIVE IN THE TREATMENT OF NEUROPATHIC PAIN

In a recently finalised report, Xenome announced that researchers from the University of California, San Diego had confirmed the therapeutic potential of Xenome's lead drug candidate Xen2174 in an animal model of neuropathic pain.

The researchers, led by spinal analgesic expert Professor Tony Yaksh, found that Xen2174 relieved the pain associated with nerve damage known as neuropathic pain, as commonly found in patients with shingles, diabetic neuropathy, chronic back pain, HIV/AIDS and cancer.

Professor Yaksh said "the analgesic activity produced by the intraspinal delivery of Xen2174 in the Chung model of neuropathic pain at doses which are without evident side effects is an important preclinical indicator as to the potential efficacy of this agent in humans."

Xenome's Head of Research, Dr Roger Drinkwater, believes Xen2174 represents a major breakthrough for cancer patients with debilitating pain and may revolutionise the way we treat chronic pain. "The results generated by Professor Yaksh are extremely encouraging and add to other successful Xen2174 pain efficacy studies completed by Associate Professor Maree Smith at the University of Queensland using an alternative neuropathic pain animal model."

"To observe efficacy in these different models of nerve injury, represents a very significant milestone in the development of Xen2174 for the treatment of chronic pain and further substantiates the drug's potential value in a number of clinical applications," Dr Drinkwater added.

Xen2174 is currently under development for the treatment of chronic cancer pain using intraspinal delivery methods. Xen2174 is a lead development candidate arising from Xenome's earlier research on a class of molecules called chi-conopeptides that target the norepinephrine transporter in the nervous system.

Dr Tony Evans, Xenome's CEO and Company Director commented on the emergence of intraspinal drug therapy over conventional pain therapies for the management of chronic cancer pain.

"There are a number of clinical studies that have quite clearly shown that intraspinal drug administration was superior over standard treatments used to control pain in cancer patients. The most influential of these clinical studies was published in 2002 in the Journal of Clinical Oncology by Dr Thomas Smith and colleagues. In this landmark study cancer patients receiving intraspinal drug therapy experienced significantly less pain, had far fewer side effects, and showed a marked improvement in survival time and quality of life," Dr Evans said.

"Intraspinal administration delivers the drug directly to the spinal fluid to block pain signals before they reach the brain," explained Dr Evans. "The immediate advantage here is that less drug is required which generally equates to fewer side effects. It is not surprising that intraspinal drug therapy is rapidly gaining wider acceptance in pain clinics."

The intraspinal drug market for the treatment of chronic pain is currently valued at between US\$300–US\$500 million. Morphine dominates this market but patients may be refractory to morphine or develop tolerance with long-term use. There is also reluctance by patients and clinicians to use morphine because of the fear of addiction and side effects.



Under US law, a new drug cannot be tested in human volunteers until an Investigational New Drug (IND) application is submitted and approved by the Food and Drug Administration (FDA). The IND application documents the results of the preclinical studies which should demonstrate that the drug is safe to administer to humans.

Xenome's Drug Development Manager, Dr Michael Thurn indicated that "the preclinical studies on Xen2174 were on track and human clinical trials were likely to begin early in 2004 following FDA approval."

"The preclinical efficacy and toxicity studies completed to date have shown that Xen2174 has a high therapeutic index, indicating that there is a broad margin between doses of Xen2174 that result in pain relief and doses at which mild side effects begin to emerge. The high therapeutic index, the ease of manufacture and the high stability of the drug product should ensure a rapid transition from the preclinical phase to the first human trials," Dr Thurn added.

The development program for Xen2174 at Xenome recently received a major boost through the investment of AUD\$6m by the Queensland BioCapital Fund (QBF).

About Xen2174

Xen2174 is a synthetic drug modelled on a peptide from the venom of a cone shell found on Australia's Great Barrier Reef. Xen2174 represents a new class of molecules, called the chi conopeptides that selectively inhibit the Norepinephrine Transporter (NET). NET is the primary mechanism regulating the biological effects of norepinephrine (NE) on the body. In episodes of pain, inhibition of NET by Xen2174 elevates the levels of NE leading to the activation of inhibitory pathways preventing pain signals from reaching the brain. The initial development of the chi conopeptides was supported by a two-year \$1.65m START grant to Xenome from AusIndustry.

About Chronic Cancer Pain

Chronic cancer pain of moderate to severe intensity is typically associated with advanced stages of cancer and may be due to tumour invasion of surrounding tissues, or to chemotherapy or radiotherapy. In up to 15% of cancer patients, the pain may be intractable or refractory to management with oral opioids and adjunctive, nonopioid medication. Further, while opioids may relieve pain, they often have serious side effects, including sedation, respiratory depression, clouded thinking, constipation, nausea and fatigue. These symptoms can prevent adequate pain treatment and there is a general reluctance by both patients and clinicians to use opioids because of addiction.

About Xenome

Xenome is a world leader in the discovery of novel peptides from animal venoms. Working from modern laboratories based in Brisbane, Australia, Xenome has generated a unique expertise in peptide chemistry to enable the production of a library of molecules from venoms that is now in demand by biotechnology and pharmaceutical companies in the USA and Europe. Peptides with unique chemistry and pharmacology are being used in Xenome's drug development activities that are focused on pain management, urological disorders, airway disorders and diseases of the central nervous system. Current major shareholders of the company are Queensland BioCapital Fund (QBF), a wholly owned subsidiary of the Queensland Investment Corporation, Medica Holdings Limited, an ASX listed biotechnology investment company, BioTech Capital Limited, an ASX listed biotechnology investment fund managed by Challenger International Limited and UniQuest Pty Ltd, the commercialisation company of the University of Queensland.

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