For release: 30 September

Metabolic acquires commercial rights to high potential analgesic compound

In-licensed for development

Metabolic today announced the in-licensing of an exciting new analgesic\(^1\) compound called ACV1, which was discovered by Associate Professor Bruce Livett and fellow scientists associated with the University of Melbourne.

Owing to the success and advanced stage of efficacy testing already performed on the compound, Metabolic will accelerate the commencement of a pre-clinical toxicity program.

Metabolic has acquired from the inventors the exclusive worldwide license to commercialise ACV1, in return for milestone and royalty payments.

ACV1 is a peptide\(^2\) compound discovered in the venom of the Australian marine cone snail, *Conus Victoriae*, which has been found to have profound analgesic properties.

Background

Cone snails have evolved a rich cocktail of peptides in their venom, which together act by a variety of mechanisms in the nervous system to quickly immobilize or kill their prey. The potential of cone snail venoms as a source of new therapies has been recognized for many years, and the first such compound to be commercialised is the analgesic Ziconotide being developed by Elan Pharmaceuticals\(^3\). Ziconotide acts by blocking a component of the central nervous system called the N-type calcium channel and must be injected into the spine (directly into the central nervous system) so as to avoid adverse reductions in blood pressure which would otherwise occur.

ACV1 acts by an entirely novel mechanism, specifically blocking a subtype of a broad class of receptors in the peripheral nervous system called neuronal nicotinic acetylcholine receptors (nAChR). Unlike other cone snail venoms, ACV1 is effective and without apparent adverse effects when administered by convenient routes such as subcutaneous injection\(^4\), providing substantial pain relief in models of nerve pain. Nerve (neuropathic) pain is the category of pain having the greatest need for improved drugs, as discussed below.

An additional unique feature is that ACV1 also appears from the animal data to accelerate the functional recovery of injured nerves.

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\(^1\) An analgesic is a drug that alleviates pain
\(^2\) A peptide is a molecule made up of a short string of amino-acid building blocks. Proteins are long strings of amino acids.
\(^3\) It is uncertain whether Ziconotide will obtain marketing approval from the regulatory authorities.
\(^4\) A subcutaneous injection is an injection under the skin, as opposed to in the muscle.
Current therapies for neuropathic pain
In contrast to acute pain resulting from tissue injury, neuropathic pain results from aberrant activity of damaged nerves. Neuropathic pain typically responds poorly to conventional analgesics such as morphine or aspirin. Current therapy for neuropathic pain relies largely on the ‘off-label’ use of anticonvulsants, antidepressants and local anaesthetics, which have well-documented side-effects and only limited efficacy for this indication.

ACV1 to be progressed immediately into preclinical toxicity study program
The inventors of ACV1 have amassed a large amount of efficacy data on the compound in animal models, and independent tests are consistent with their findings. Metabolic has therefore decided that the results are sufficiently conclusive to progress the compound immediately into preclinical toxicity studies. This pushes ACV1 ahead of Metabolic’s other three projects, and becomes the second most advanced project in the Company's development pipeline, behind its AOD9604 obesity drug.

Manufacturing of batches of ACV1 and preliminary testing is already underway. Formal preclinical toxicity studies are expected to commence in early-2004.

The first clinical indication for which ACV1 is likely to be targeted is neuropathic pain associated with diabetes, a market with billion dollar annual sales potential.

Metabolic’s expenditures on ACV1 over the next year have previously been budgeted for and the Company has sufficient cash on hand to advance all of its development projects this financial year.

Market projections
Analysts predict that a safe and effective therapy for neuropathic pain would gain immediate acceptance by doctors. With the market for analgesics to treat neuropathic pain estimated at several billion dollars, an effective therapy could potentially reap similar rewards to the blockbuster COX-2-selective anti-inflammatory analgesics - such as Celebrex - which are currently serving the arthritis pain market.

Publications
A paper detailing ACV1 has recently been published:


Patents
International Patent Application No. PCT/AU02/00411 filed in 2002 covers the ACV1 compound and the analgesic uses of a broad class of compounds blocking neuronal nAChRs, and has been exclusively licensed to Metabolic. The application has completed the international phase and is entering national phase in key markets. When granted, protection will last until at least 2022.
About Metabolic

Metabolic Pharmaceuticals Limited is a biotechnology company based in Melbourne, Australia, and listed on the Australian Stock Exchange (ASX: MBP). The Company’s mission is to develop a pipeline of new pharmaceuticals for world markets, and currently has active programs aimed at treating obesity, pain, type 2 diabetes, osteoporosis and iron overload.

AOD9604 for obesity is the company’s most advanced project, currently in Phase 2 human clinical trials. It is a peptide analogue of a fragment of human growth hormone which Metabolic believes has the potential to provide a safer and more effective pharmaceutical treatment for obesity. The drug, discovered by scientists at Monash University, reduces body fat by mimicking natural hormonal regulation of fat metabolism.

Further details are available from the Company's website - www.metabolic.com.au.

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