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ASX ANNOUNCEMENT

NEW MIDKINE RESULTS FOR HEART ATTACK TREATMENT

- **New study shows that sustained midkine treatment after heart attack improved heart function in rats**
- **These findings compliment Cellmid's current CAM103 trials and are consistent with previous study results by CDY's scientists**
- **Cellmid has broad patent protection for using midkine for the treatment of ischemia related diseases, including heart attack**

Sydney, 9 April 2010: Cellmid (ASX:CDY) is currently conducting trials (CAMI103 program) using midkine for the treatment of heart attack (AMI or acute myocardial infarction) in collaboration with Pharmahungary, as announced on 4 March 2010. The trials have been designed to advance midkine into the clinic for this indication.

A new study published in *Cardiovascular Research* adds further validation to these trials as it confirms that sustained midkine treatment ameliorates left ventricular dysfunction following heart attack in a rat model of the disease improving cardiac outputs.

The journal article, *Midkine gene transfer after myocardial infarction in rats prevents remodelling and ameliorates cardiac dysfunction,* provides details of the study which was conducted by using gene transfer technology and was to confirm previous positive results using midkine in pig and mouse models of heart attack.

The study adds important validation to results published by Cellmid's researchers demonstrating that midkine can prevent apoptosis, reduce remodelling of the cardiac tissue and increase revascularisation following heart attack. These studies showed that both short and long term survival rates were improved as a consequence of midkine treatment.

"This new study further reinforces the science behind our CAMI103 program for using midkine therapy for heart attack", said Maria Halasz, CEO of Cellmid.

"We now have extensive *in vivo* data that demonstrates midkine as a potent protector of the cardiac muscle acting simultaneously via several mechanisms of action. These mechanisms act to save the heart from both the immediate and the long term effects of AMI. Furthermore, these studies show that midkine can be effectively delivered either as the protein or by gene therapy" she added.

Cellmid holds the world's largest and most comprehensive patent portfolio concerning midkine, an embryonic cytokine implicated in a range of human diseases. The portfolio includes a patent for midkine manufacture and 11 patents worldwide for midkine therapy for heart attack.

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Outline of the publication

Acute myocardial infarction was surgically induced in rats. Thirty minutes after AMI the heart muscle was directly injected with a genetic vector encoding the midkine gene. Midkine protein expression, cardiac function, formation of new blood vessels and apoptotic cell death were assessed for up to ten weeks following AMI with the following results:

- Midkine gene therapy successfully induced midkine protein expression in the heart muscle for up to eight weeks
- Midkine treated animals showed increased new blood vessel growth
- Midkine treated animals showed reduced fibrosis of the heart tissue
- Midkine treatment enhanced anti-apoptotic pathways
- Echocardiograms showed that heart function of midkine treated rats was far superior to that of control animals for at least six weeks after AMI

The publication concludes that "overexpression of midkine prevents left ventricular remodelling and ameliorates left ventricular dysfunction by anti-apoptotic and pro-angiogenic effects".

Acute Myocardial Infarction (AMI)

Acute myocardial infarction is the term for damage to the heart muscle caused by heart attack. Such an attack occurs when a vessel supplying blood to the heart muscle is blocked suddenly by a blood clot or plaque. Heart attack usually strikes unexpectedly and is often fatal. Even when heart attack is not immediately lethal damage done to the heart muscle often results in chronic heart dysfunction that leads to death in the months following. Myocardial infarction is the leading cause of death in developed countries and in Australia around 28,000 people die from heart attack every year accounting for 22% of all deaths. In the US around 800,000 people are affected and 250,000 of them die annually. There are limited treatment options to prevent the death of myocardial cells during or even after a heart attack. Current therapies for heart attack are useful but all have significant and recognised side effects and they fail to directly address the fundamental issue of apoptosis.

Midkine's role in the treatment of heart attack

Administration of Cellmid's midkine, a validated cell protecting and anti-apoptotic agent, is expected to directly reduce cell death from myocardial injury, and therefore improve immediate and long terms survival of heart attack patients. Using midkine in previous animal studies showed significant improvement in mortality rates, reducing it from 33% to 10%. In addition, long term cardiac outputs and survival also improved significantly. Cellmid's CAMI103 program has been planned to confirm the results of these previous trials, to establish optimum dosing regimes and to confirm safety data in preparation for an IND application.

The Journal *Cardiovascular Research*

Cardiovascular Research is the International Basic Science Journal of the European Society of Cardiology. The Journal is concerned with basic and clinical research in the field of cardiovascular physiology and pathophysiology. *Cardiovascular Research* had an impact

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factor of 5.947 in 2008, and ranked 6th out of 78 journals publishing in cardiac & cardiovascular science worldwide [Citation Reports, Science Citation Index, ISI].

Cellmid's previous publications
Cellmid has the following related publications in peer-reviewed journals:

Takenaka, H., et al., *Midkine prevents ventricular remodelling and improves long-term survival after myocardial infarction.* Am J Physiol Heart Circ Physiol, 2009. **296**(2): p. H462-9.

Fukui, S., et al., *Therapeutic effect of midkine on cardiac remodeling in infarcted rat hearts.* Ann Thorac Surg, 2008. **85**(2): p. 562-70.

Horiba, M., et al., *Midkine plays a protective role against cardiac ischemia/reperfusion injury through a reduction of apoptotic reaction.* Circulation, 2006. **114**(16): p. 1713-20.

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About Cellmid Limited (ASX: CDY)
Cellmid Limited is a biotechnology company listed on the Australian Stock Exchange. The Company is the owner of the most comprehensive intellectual property portfolio around midkine globally. Midkine is a significant novel therapeutic and diagnostic target. It is a native protein expressed during early cancer formation as well as at the onset of a number of inflammatory processes. Cellmid is committed to the commercialisation of its portfolio of therapeutic and diagnostic products. In addition to its product development programs Cellmid is actively seeking partners for some of its non-core assets.

Investment in biotechnology companies
There are a number of inherent risks associated with the research, development and commercialisation of pharmaceutical products. Investment in companies specialising in these activities carry specific risks which are different to those associated with trading and manufacturing businesses. As such, these companies should be regarded as highly speculative. Medical Therapies recommends that investors seek professional advice before making an investment in its shares.