ASX ANNOUNCEMENT

NEW PUBLICATION AND PATENT APPLICATION FOR CELLMID'S MIDKINE ANTIBODY

- **Cellmid's midkine antibody accelerates bone healing and bone formation**
- **Results published in the British Journal of Pharmacology**
- **Cellmid filed patent to secure IP for the application of its midkine antibodies in bone therapy**

SYDNEY, 24 June 2016: Cellmid Limited (ASX: CDY), in collaboration with a leading bone research group in Germany, has completed the first ever study showing that treatment with a midkine (MK) antibody accelerated bone fracture healing in an aged rodent model of the condition.

The study was led by Dr Astrid Liedert at the Institute of Orthopedic Research and Biomechanics, University Medical Center Ulm, Germany and the results were recently published in the British Journal of Pharmacology. *(Haffner-Luntzer M et al, Antagonizing Midkine Accelerates Fracture Healing in Mice by Enhanced Bone Formation in the Fractured Callus. Br J Pharmacol. doi: 10.1111/bph.13503. PMID: 27111560)*

Demonstrating the beneficial effects of a MK antibody in bone fracture healing has considerable clinical significance. The rate of delayed bone healing and even non-union formation can be as high as 10% of all long bone fractures. The incidence of bone complications following fractures increases markedly amongst the older population. Such complications of bone healing involve higher cost to the health care system as well as a burden to patients, with longer recuperation times together with potential ongoing defects in the affected bone, highlighting the need for better therapies such as Cellmid's MK antibodies.

The data generated adds substantial commercial value to Cellmid's antibody assets and the new intellectual property is now the subject of a patent application by the Company. Commercialisation of Cellmid's MK antibody assets are carried out by wholly owned subsidiary Lyramid, a company dedicated to developing drugs in various conditions by targeting MK *(ASX announcement, 8 April 2016)*.

Cellmid already has promising data using its antibodies to antagonize MK in chronic kidney disease models. Together with the new information from Dr Liedert's study, the Company will have a strong impetus to further investigate whether MK antibodies would also be useful in preventing vascular calcification, a common complication and major cause of death in patients with Type 2 diabetes and chronic kidney disease.

The collaboration with Dr Liedert's group is the direct outcome from the Company's biennial Midkine Symposia, where Dr Liedert first presented preliminary results on MK levels following bone fracture in Kyoto in 2014. The current study was designed in partnership between Cellmid and Dr Liedert's group. The results were shared with the

wider MK community in April 2016 in the most recent Midkine Symposium held in Budapest, Hungary.

"While considerable preclinical and clinical development is still required to assess MK antibodies as treatments for bone disorders, the current study by Dr Liedert demonstrates the potential of this approach" said Cellmid's Head of Research and Development, Associate Professor Graham Robertson.

"The data generated greatly contributes to Cellmid's plans to successfully commercialise its MK antibody assets" said CEO Maria Halasz. "Together with our promising results in the treatment of chronic kidney disease, we are encouraged to investigate complex and unexplored major complications of diabetic nephropathy, such as vascular calcification leading to serious cardiovascular events" she added.

Details of the study and results

Dr Liedert and her team used Cellmid's therapeutic MK antibody to treat experimental bone fractures in aged rodents. Prior to starting treatment Dr Liedert made the important discovery that the levels of MK protein in the blood increase dramatically following bone fractures.

Together with previous studies that showed how MK controls normal bone growth, this finding implicated MK in bone damage conditions. After only 10 days treatment with the MK antibody, the amount of bone deposited within the fracture site was increased significantly ($p< 0.05$), while the mechanical strength of the bone and bone repair were markedly improved after 28 days of treatment ($p<0.05$).

Detailed analysis of the bone fracture showed that the MK protein accumulates within the healing bone and acts to slow the repair process. The MK antibody treatment not only reduced the amount of MK in the bone fracture site but also diminished the amount circulating in the blood. By reducing the availability of MK in both healing bone and blood, the MK antibody treatment 'takes the brakes' off bone formation, leading to faster bone replacement and better quality, stronger bone within the fracture.

Even broader clinical relevance is an additional discovery that Dr Liedert has made using Cellmid's MK antibody. She found that it impacts on the *Wnt* signaling system that regulates bone formation, the target of drugs that are currently being developed for the treatment of osteoporosis. The sclerostin targeting drug Romosozumab developed by Amgen, for example, highlights the opportunities for bone-modulating therapeutic antibodies to be block-buster treatments for osteoporosis.

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Cellmid Limited (ASX: CDY)
Cellmid is an Australian life sciences accelerator with lead programs in multiple disease indications. The Company, through its wholly owned subsidiaries, Lyramid, Kinera and Advangen, develops and markets innovative novel therapies and diagnostic tests for fibrotic diseases, cancer, ischemic diseases of the heart and hair loss. Cellmid holds the largest and most comprehensive portfolio of intellectual property relating to the novel targets midkine (MK) and FGF5 globally. Intellectual property pertaining to this novel target is being exploited through wholly owned subsidiaries Lyramid and Kinera. Advangen, Cellmid's consumer health business, sells its FGF5 inhibitor hair growth products in Australia and Japan, and currently expanding distribution in other territories. For further information, please see www.cellmid.com.au and www.evolisproducts.com.au.

Midkine (MK)
Midkine is a growth factor that is highly expressed during embryonic development. Midkine modulates many important biological interactions such as cell growth, cell migration and cellular adherence. These functions are relevant to cancer, inflammation, autoimmunity, ischemia, nerve growth/repair and wound healing. Midkine is barely detectable in healthy adults and only occurs as a consequence of the pathogenesis of a number of different disorders. Midkine expression is often evident very early in disease onset, even before any apparent physical symptoms. Accordingly, midkine is an important early marker for diagnosing cancers and autoimmune diseases. Finally, midkine is only evident in a disease context, and targeting midkine is not expected to harm normal healthy tissues.

Investment in life sciences 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. Cellmid recommends that investors seek professional advice before making an investment in its shares.

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