

ASX ANNOUNCEMENT

NEW PUBLICATION FOR CELLMID'S MIDKINE ANTIBODY

- **New research shows midkine antibody restores bone loss and improves fracture healing in osteoporosis model**
- **Results published in the journal Public Library of Science One**
- **Data adds to recent findings that midkine antibodies improve fracture healing**

SYDNEY, 9 August 2016: Cellmid Limited (ASX: CDY) is pleased to report on new research which indicates that its midkine antibodies (MK antibodies) improve bone quality and fracture healing in an animal model of osteoporosis.

In the study conducted and published by Cellmid collaborators at the University Medical Centre in Ulm, Germany, the therapeutic benefit of MK antibodies has been assessed in the important clinical setting of osteoporosis.

The study was again led by Dr Astrid Liedert at the Institute of Orthopaedic Research and Biomechanics, University Medical Center Ulm and the results were recently published in PLoS ONE. (*Haffner-Luntz M et al., Inhibition of Midkine Augments Osteoporotic Fracture Healing. PLoS One. 2016 Jul 13;11(7):e0159278. doi: 10.1371/journal.pone.0159278. PMID: 27410432*).

In a previous publication from the same group studies showed that treatment with Cellmid's MK antibody accelerated bone fracture healing in otherwise normal rodents (ASX announcement, 24 June 2016).

The current findings demonstrate that MK antibodies were effective in accelerating bone healing in osteoporotic settings, and therefore may benefit elderly patients with fragile bones that are prone to debilitating and sometime fatal fractures. Especially at risk are post-menopausal women with over 30% experiencing osteoporotic fractures after the age of 50.

Osteoporotic patients have reduced regeneration capacity and require considerably more time for successful fracture healing. Apart from the reduced quality of life and extra health care costs associated with recuperation following osteoporotic fractures, immobility due to fractures can cause severe, sometimes life-threatening, complications in the elderly.

Cellmid filed a patent application earlier this year covering its MK antibodies for fracture healing and restoring bone loss due to osteoporosis. Cellmid is keen to explore novel clinical opportunities afforded by its MK antibody assets, which are commercially exploited by Lyramid Limited, Cellmid's wholly owned subsidiary.

Details of the study and results

Dr Liedert used a validated model of osteoporosis in rodents to show that the amount of bone deposited in the fracture site is reduced and the healing bone is weaker in mice that lack estrogen. Treatment with an MK antibody improved the rate of fracture healing evidenced by mechanical strength and bone volume in both normal and osteoporotic animals ($p < 0.05$).

Dr Liedert then made the critical observation that the loss of bone mineral density and volume in otherwise intact but osteoporotic bones some distance away from the fracture site was reversed following MK antibody treatment ($p < 0.05$).

The experimental design involved examining bone within the fracture site in the femur as well as the corresponding site in the other leg which was undamaged. In addition to restoring bone quality in the femur, the MK antibodies improved bone parameters in osteoporotic vertebrae ($p < 0.05$). This result is relevant for many aged patients as weakened spines have a major impact on quality of life and mobility.

Detailed molecular analysis within the healing bone at the fracture site revealed that a key regulator of bone formation and integrity called beta-catenin was dramatically reduced in osteoporotic animals. After only 10 days of MK antibody treatment beta-catenin was restored to levels seen in normal animals ($p < 0.05$) showing the ability of MK to modulate the action of this critical factor involved in bone biology.

Therapeutically targeting this pathway forms the basis for other drugs being developed for bone health and demonstrated to be effective in late stage clinical trials (eg Amgen's Romosozumab). Therefore MK antibodies have considerable potential to be developed for a clinically validated therapeutic strategy.

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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, Lynamid, 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 Lynamid 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.