ASX ANNOUNCEMENT

5th MIDKINE SYMPOSIUM REINFORCES CLINICAL POTENTIAL FOR CELLMID'S BIOTECHNOLOGY ASSETS

- **Clinicians and scientists from 13 countries presented data on Cellmid's midkine; its biology and role in disease**
- **Novel findings confirmed strategy for subsidiary Lyramid to progress midkine inhibitors into the clinic**
- **Research and commercial collaborations arising are expected to accelerate clinical development path**

SYDNEY, Wednesday, 30 May 2018: Cellmid Limited (ASX: CDY) is pleased to report on its **5th Midkine Symposium** which was held in Munich, Germany on 3-5 May 2018. Exciting new research findings on midkine (MK) and MK inhibitors were revealed across 38 presentations by scientists from 13 countries.

Cellmid holds the most comprehensive intellectual property surrounding MK and anti-MK therapies, developing these assets as treatments for several life-threatening and chronic diseases. It has two wholly owned subsidiaries focussed on MK; Lyramid, a MK antibody company developing treatments for cancer, fibrosis and chronic kidney diseases; and Kinera, a company developing MK protein for the treatment of heart failure, chronic heart conditions and other ischemic diseases.

The biennial MK symposia provide critical support for these efforts, bringing together Cellmid's collaborators and other members of the MK community to present novel findings and discuss new research ideas through networking opportunities.

The symposia are also critical for developing new intellectual property, forging new research and commercial collaborations and gaining insight into the broader midkine research community. Speakers at the 5th Midkine Symposium contributed to a significant increase in the understanding of MK's role in many disease mechanisms. The meeting has been critical in fostering new and existing collaborations, enabling clear pathways for clinical validation of Lyramid's therapeutic antibodies and accelerating the clinical path for midkine in heart disease.

Highlights of the Symposium included themed sessions on the role of MK (and its related protein pleiotrophin) in cancer (12 talks), cardiovascular biology (6 talks), tissue injury responses (7 talks), as well as neural development and CNS disorders (6 talks). Many speakers highlighted and expanded upon research recently published in top ranking and prestigious journals including *Nature*, *Cell*, *Cell Reports*, *Science Signalling* and *Science Reports*, which contributed to an extremely high quality scientific meeting.

The quality of recent publications is reflective of the increase in understanding of the importance of MK in many disease processes. Significantly, the Symposium revealed new evidence around MK's role as a critical mediator of cell communication and inter-organ signalling in important diseases.

Amongst the novel and recent advances in the MK field, several speakers also presented new, promising data on the therapeutic potential of Cellmid's own drug candidates in different disease scenarios. The data presented in the Symposium supported and reinforced Cellmid's strategy of targeting MK as one of the few novel approaches of true disease modification, as opposed to management of symptoms, in areas of significant unmet need such as chronic heart failure and cardiovascular diseases.

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The MK Symposium encourages the open presentation of unpublished and potentially commercially sensitive data, with presentations and discussions held under confidential conditions. It is anticipated that most of the work will be published following the standard scientific peer review process and/or intellectual property protection. Due to the confidentiality undertakings, PowerPoint presentations and posters forming the scientific component of the conference will not be made public at this stage.

Key highlights included:

- Keynote address from Professor Marisol Soengas and Dr David Olmeda (CNIO, Madrid) detailing their work demonstrating that MK is responsible for metastatic spread of melanomas via the lymphatic system (See CDY ASX announcement 3 July 2017, comment on Olmeda D. et al *Nature* 2017). These exciting findings demonstrate that targeting MK blocks development of metastases, the ultimate cause of death for most melanoma patients. The novel discoveries reinforce the value of targeting MK with Lyramid's antibodies in melanoma and many other tumour types for which metastasis frequently leads to dismal outcomes for patients. Another example of this is a rarer form of melanoma, uveal melanoma that forms in the eye, for which Dr Jacobus Bosch (Erlangen, Germany) presented intriguing data showings MK's involvement in the disease and its associated metastases.
- Insights into the potential of MK as an immune modulator were delivered by Professor Rolf Brekken (UTSW, Dallas), who outlined the ability of MK and pleiotrophin to alter immune cells that are critical for tumour immune surveillance and evasion. These processes have recently been exploited with the very successful new cancer drugs based on immune checkpoint inhibition, suggesting that MK treatment could be an alternative or combination therapy target as a tumour immune modulator.
- Symposium co-host, Dr Ludwig Weckbach from Ludwig Maximillian's University in Munich, presented data on Lyramid's C- and N-domain binding MK antibodies in a mouse model of chronic heart failure. Promising results from this collaboration are the subject of a provisional patent application filed recently by Cellmid. With considerable mortality but limited available treatment options, this is a priority clinical area for Cellmid. Further collaboration is expected with Dr Weckbach's group and will be carried out at the state-of-the art research facility at the Biomedical Centre Munich, one of the largest research institutions to be recently built in Germany.
- Further evidence for the ability of Lyramid's MK antibodies to suppress glioblastoma resistance to cannabinoid treatment was presented by Professor Guillermo Velasco (Complutense University, Madrid). Lyramid's C- and N-domain MK binding antibodies inhibited glioma tumour growth in animals when combined with therapeutic cannabinoids. The relative efficacy of the antibodies indicated that targeting the N-domain of MK is the most promising strategy and will guide subsequent development of MK antibodies for this devastating form of brain cancer. Additional relevance for MK in glioma was given by Professor Michelle Monje (Stanford) whose recent *Cell* paper demonstrated that the closely related protein pleiotrophin drives the spread of gliomas in the brain, while Associate Professor Anna Dimberg (Rudbeck Lab, Sweden) showed that it promotes aberrant blood vessel formation in glioblastomas.
- In the most comprehensive clinical studies exploring MK as a tumour biomarker to date, Dr Anna Nordin (Gothenburg University, Sweden) presented her extensive analyses of MK levels in prostate cancer patients, using Cellmid's MK ELISA. She demonstrated that MK plays an important role at all stages of prostate tumour progression and is an important contributor to treatment resistance and poor patient outcomes.

- Cellmid collaborators Associate Professor Vincent Lee and Jeffrey Wang of Westmead Institute/University of Sydney presented further confirmation that Lyramid's MK antibodies protect the kidney from injury following "in live" testing in a mouse model of the rare disease Focal Segmental Glomerulo-Sclerosis, FSGS, (see ASX announcement 18 January 2017). This work, funded by an Australian Government's DIIS grant, showed that CAB102, Lyramid's humanised drug candidate, reduced renal damage in a murine model of FSGS with potential for orphan disease designation.
- The role of MK in other tissue injury settings associated with chronic inflammation were discussed, including the development of atherosclerosis (Professors Kenji Kadomatsu and Kaichiro Kamiya of Nagoya University) and the fatal lung disorder idiopathic pulmonary fibrosis (Associate Professor Yoshi Tanino of Fukushima Medical University). Further evidence for the role of MK in autoimmune diseases was given by Professor Kadomatsu who showed that lupus nephritis has reduced severity in the absence of MK.
- Additional insights into the molecular mechanisms of MK's interactions with glycosaminoglycans (GAGs) in various scenarios were presented and contribute to the understanding of how they affect biological function. This area of study is critical for understanding MK's biology, molecular interactions and pharmacodynamics of treatments. The findings were presented by Professor Xu Wang from Arizona State University, Dr Pedro Nieto from the University of Seville, Professor Heikki Rauvala from Finland and Professor Masaharu Noda from Okazaki in Japan.
- To close out the Symposium, the prospects and challenges critical for clinical development plans involving MK targeting therapies were explored, with agreement from the community surrounding key milestones and areas where research should be focussed, including uncovering specific details of mechanism of action in various disease states, developing additional academic and commercial collaborations and engaging with key opinion leaders in each of the major therapeutic areas internationally.

End

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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, is developing 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. For further information, please see www.cellmid.com.au and www.myevolis.com.au.

Midkine (MK)

MK 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. Midkine is thought to be a non-redundant, key inter-organ signalling molecule with functions relevant to cancer, inflammation, autoimmunity, ischemia, nerve growth/repair and wound healing.