CELLMID

ASX ANNOUNCEMENT

KEY MILESTONE COMPLETED: CELLMID LEAD ANTIBODY SELECTED FOR CLINICAL TRIALS

- **Key milestone towards clinical program: humanised anti-midkine antibodies successfully generated, tested and lead drug selected**
- **Significant reduction in chemotherapy resistance in preclinical models of lung cancer shown by lead antibody**

SYDNEY, 07 May 2014: Cellmid Limited (ASX:CDY) advises that is has completed humanisation, testing and selection of its lead anti-midkine (MK) antibody for its planned "first in class" clinical trials in oncology. This is a significant step in advancing towards clinical studies and on track with the development program outlined to the market earlier in 2014.

The lead antibody, designated CAB102, has been shown to significantly reduce chemotherapy resistance in a preclinical model of lung cancer in combination with carboplatin. In addition to its functional activity *in vivo,* it has produced strong *in vitro* functionality in specifically designed MK migration assays. Initial cell expression and stability data confirmed that it can be manufactured commercially, making it a feasible drug product.

"With the completion of lead selection, and after a well-planned and extensive testing program, our preparations for clinical trials are well on track," said Cellmid CEO Maria Halasz.

Selection of CAB102 is the result of a pre-clinical program in which dozens of Cellmid's proprietary and patent-protected murine anti-MK antibodies were assessed for efficacy and mechanism of action both *in vivo* and *in vitro*. The two most promising murine antibodies identified by this process were humanised by Cellmid's collaborators, Biotecnol Ltd.

Of the 78 humanised antibody (humAb) variants generated by Biotecnol the six most promising candidates were then assessed further for mechanism of action, *in vivo* anti-tumor efficacy, and 'manufacturability' (cell line expression, antibody purification, molecular stability and absence of aggregates).

All six humAb candidates demonstrated similar or improved affinity when compared to their murine precursors. Specificity for MK has been retained, with no evidence of binding to other proteins. A preliminary assessment showed all six candidates were secreted at commercially viable concentrations during cell culture, all six candidates were readily purified and have been confirmed as structurally stable and aggregate free.

The six humAb candidates were then tested for functional activity using an *in vitro* cell migration inhibition assay and an *in vivo* tumor xenograft model in combination with carboplatin. Carboplatin was selected as the chemotherapy of choice as it is standard therapy in lung cancer. The cancer xenograft studies were performed in the widely studied K-Ras mutant, highly refractory and difficult to treat human non-small cell lung carcinoma (NSCLC) cell line NCI-H460.

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As expected, and consistent with clinical experience, carboplatin did not significantly reduce tumor volume or mass when used alone compared to untreated controls in the NCI-H460 model. However, three of the six humAb candidates significantly reduced tumor growth when combined with carboplatin.

When combined with carboplatin CAB102 has shown the greatest efficacy, with mean tumor volumes at 21 days post treatment reduced by 50% (mean 1295.5mm3; $p<0.001$ vs untreated control; $p<0.01$ versus carboplatin-only treated group).

"Strong preclinical performance by reducing chemotherapy resistance is important to progress our "first in class" anti-MK antibody program to the clinic," said Head of Product Development Darren Jones.

"The results are consistent with the independent findings by other research groups confirming midkine's role in chemotherapy resistance in glioblastoma, and provide a strong commercial rational for our product development program in multiple cancer types," he added.

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Cellmid Limited (ASX: CDY)

Cellmid is an Australian biotechnology company with lead drug candidates in immuno-oncology. The Company is developing innovative novel therapies and diagnostic tests for a number of cancer indications, in particular solid tumours. Cellmid holds the largest and most comprehensive portfolio of intellectual property related to the novel oncology target midkine and midkine antagonists globally. The Company's most advanced development programmes involve using its anti-midkine antibodies in addition to commercialising midkine as a biomarker for the early diagnosis and prognosis of cancer. For further information, please see www.cellmid.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 part 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 present in a disease context, and targeting midkine is not expected to harm normal healthy tissues.