

# CELLMID (

**Newsletter 30 July 2012** 

#### Dear Shareholders,

As we are progressing with the distribution of our évolis hair growth products it is timely to provide you with an update. Our media launch in late March resulted in strong ongoing coverage from journalists, and interest from potential agents and distribution partners.

Terry White Chemists became the first pharmacy group selling the évolis products in June and we have since been able to sign up other groups. We expect to provide the market with an update on our distribution and sales in the near future.

Our midkine antibody program was boosted late last year with the humanisation of our drug candidate, hu91. Since then we have completed a preclinical development plan and started implementation with *in vitro* and *in vivo* testing. We continue to explore the opportunity to find a strategic development partner to fund this program through a non-dilutive arrangement.

The potential upside of this program has been aptly demonstrated by the recent preclinical antibody option and license deal between Celgene and Inhibrx, which is valued at \$500M including upfront and milestone payments, and royalties.

Our Midkine Conference at the end of June was a resounding success attracting almost twice the number of attendees than the last one in 2010. We expect a number of collaborations to result from the event.

Our patent strategy, especially in the area of ischemia, has received several boosts recently and we now have a complete US patent portfolio around using midkine, the protein, for the treatment of various forms of ischemic diseases. The claims include use and mechanism of action claims in conditions such as heart attack, stroke and kidney disease.

Independent validation of midkine as an early cancer diagnostic and prognostic marker continues. Since the beginning of 2012 five midkine diagnostic articles have been published in peer reviewed journals. With a strong intellectual property position in this space Cellmid's out-licensing program is enhanced by these publications and we have now extended it to the use of midkine as a prognostic marker.

We have recently raised funds to launch our évolis products to the pharmacy market and to continue with the partnering efforts in our other business units. To date we have received \$1.4 million of the \$1.5 million committed.

Thank you for your ongoing support.

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Maria Halasz

CEO and Managing Director





#### **Finance**

Cellmid has recently released its 4C quarterly cash flow statement showing a revenue of \$37,000, which was largely the result of Advangen and web based évolis sales in addition to receipts from our ELISA kit sales. This revenue does not include any pharmacy sales revenue.

Of the \$647,000 spent during the quarter we had one-off costs of some \$180,000 in relation to the out-licensing of the diagnostic and therapeutic assets. Smaller one-off costs included the biannual Midkine Conference.

At the Company's AGM on 28 April 2012 share-holders approved the issue of shares for up to \$1.5 million at a price of 1.65 cents per share. To date we have collected \$1.4 million.

With the dramatic downturn in market conditions between the time the commitments were made and the shareholders' approval was received, we believe this is a great result.

With a \$1,051,000 cash balance at the end of the quarter (not including the \$400,000 since received in new subscriptions), revenue from the Advangen and évolis sales, as well as a reduction in expenditure, the Company is sufficiently funded to proceed with its current, low cost business strategy.

In addition, we continue to actively pursue other funding opportunities, including non-dilutive grants and industry contributions, as well as strategic partnerships and licensing deals.

The Company has also been in discussions to secure corporate venture capital and/or strategic investments that would add not only the requisite funding but expertise, in particular for the antibody development program.

# évolis distribution growth well in advance of expectations

TGA listing of the évolis hair growth products has been a major milestone this year for Advangen International, Cellmid's subsidiary. Following the technology transfer from our Japanese research and development partner we successfully manufactured the first GMP run of the product in March 2012.

The media launch of the évolis products in late March has been a success with coverage in beauty and health publications nationally since. A full list of media articles is available at the <a href="https://www.evolisproducts.com.au">www.evolisproducts.com.au</a> website under the "évolis in the media" tab.

Terry White Chemists have made their first order in June and we have since received initial orders

from other groups through the Symbion wholesale channel. Our original distribution target was to open 400 pharmacy doors to the product during the first twelve months. We are well ahead of this target and expect to provide a further update to the market shortly.





#### Therapeutic midkine antibody program

Therapeutic antibodies continue to be the fastest growing area of drug development and can potentially provide a highly lucrative investment even in an early stage. Several preclinical stage deals have been done over the years, most recently an option and licensing deal between Celgene and Inhibrx valued at \$500 million including upfront, milestone and royalty payments.

Our midkine antibody program has been one of our most important assets. Midkine is implicated in a number of inflammatory and autoimmune disorders as well as in cancer. Previously preclinical studies have shown that inhibiting midkine in these conditions may be an effective way to control the disease.

Cellmid originally started with around 130 mouse monoclonal antibodies for midkine (MK). These antibodies were assessed for performance and those with the strongest MK binding were further tested in functional cell assays. Finally, a lead candidate was chosen and humanised in late 2011.

Preclinical testing aims to determine which specific diseases are most effectively treated with MK antibodies, and what should be the first clinical indication tested in human trials.

The models tested with Cellmid's anti-midkine antibodies include diseases of great unmet medical need with large potential markets, such as COPD<sup>1</sup>, kidney injury and disease, bone healing, cancer metastasis and surgical adhesion (see Table).

An extensive testing program was developed early this year with the firm objective to eventually enter into clinical development in the most promising indication. This program is now well underway in animal disease models with Cellmid's first in class humanized anti-midkine antibody.

A lead indication will be chosen based on a combination of factors, including efficacy in animal testing, Cellmid's patent position, the time needed to complete a trial, regulatory hurdles and access to specific patient populations.

**Table: Preclinical MK antibody testing** 

Indication	Animal model	Disease reduced in MK knockout	MK over- expressed in human disease?	Antibody testing result
Multiple sclerosis	ΕΛΕ	YES	Not tested	Modest disease reduction
Kidney Inflammation	Ischemia/Reperlusion	YES	YES Urine	Testing underway
	Diabetic nephro-pathy	YES	YES Renal biopsy	Testing planned
Surgical adhesion	Abdominal wall abrasion	YES	YES	Significant disease reduction
COPD	LPS/ clastase inhalation	Not lested	Not tested	No significant disease reduction
Cancer	Osleo sarcoma xenograft	YES	YES Serum Tumor	Significant tumor reduction Significant metastasis reduction
Bone healing (pilot study)	Femur fracture	Not lested	Not tested	Significant increase in flexural rigidity

Cellmid has to date pursued a low-cost strategy of collaborating with expert academic groups as well as using niche contract research companies worldwide to conduct these studies.

The Company has also been able to leverage its valuable midkine related inventory, including the MK protein, antibodies and its CE marked ELISA, to progress with these studies, which would otherwise have required significant capital investment.

In addition to this strategy, Cellmid has recently commenced discussions with corporate venture groups with the view to seek a strategic, non-dilutive investment into this potentially highly lucrative program. We will continue to pursue these funding and program strategies which not only contribute money but expertise.

1 Chronic obstructive pulmonary disease





## Midkine as early diagnostic and prognostic marker for cancer

Over the past year several diagnostic and pharma companies have expressed interest in midkine as an early cancer diagnostic marker.

The Company's strategy has previously been limited to out-licensing midkine on an indication basis for the early diagnosis of cancer. In early 2012 we added strong prognostic data to our licensing package and we are currently talking to a dozen groups, mostly as to the utility of midkine as a prognostic agent.

In addition to our out-licensing we have several collaborations with clinical and research groups in preparation for a regulatory meeting with the FDA.

Our Kumamoto University project is progressing well and we have now collected a progressive set of 470 control samples, of which 230 have already been tested (as previously announced) and the remaining samples will be tested by the end of 2012.

Our lab at the John Hunter Hospital in Newcastle has been testing samples from a variety of patients including COPD and kidney disease as well as in colorectal cancer. They are also conducting validation studies on our ELISA kit for plasma and urine. This is important data which adds to our regulatory package.

Our collaborators at the University of Istanbul have presented unpublished data on polycystic ovary syndrome (which corresponds strongly with infertility) during our midkine conference.

Finally, we have completed the second batch of GMP manufactured ELISA kits. We are not only using these kits in-house, but selling them to the research market in addition to utilising them as collateral in our collaborations.

# Ischemia program is boosted with US patents

With four new midkine patents granted in the USA for the treatment of ischemia Cellmid's intellectual property portfolio in this area is uniquely strong. Porcine and small animal studies have previously confirmed that MK is useful in the treatment of heart attack.

We are currently working on securing a manufacturing and development partner as this is essential to accelerate the progress of this program into the clinic.







#### **Excellence in Midkine Research Conference**

Cellmid sponsored the Second Excellence in Midkine Research Conference, hosted at the venerable University of Istanbul in Turkey by Cellmid's collaborators Prof Ayhan Bilir and Assoc Prof Mine Erguven. The meeting attracted 70 delegates from 15 countries (up from 42 at the inaugural Sydney meeting). The quality and breadth of science presented was outstanding and firmly establishes this event as a world-class showcase of research and development in a single target.

In addition to providing a forum to midkine researchers Cellmid established this unique conference in 2010 (held in Sydney at the time) to advance the company's commercial interests by building strong direct relationships with the scientific experts and key opinion leaders in MK, and to connect MK researchers from disparate fields with each other to help collectively solve questions of MK biology.

Historically, MK has emerged as a molecule of interest in a number of unrelated medical fields, and researchers have tended to work on MK within their own particular area of expertise. The conference has successfully broken down these barriers to help accelerate knowledge of underlying MK biology.

Like the Sydney meeting before it, the Istanbul meeting has already generated collaboration opportunities for Cellmid. Some highlights are included below.

Prof **Wei Han**, founder of General Regeneratives Inc, Shanghai, China, presented on his company's preclinical animal data on use of MK for treating osteoarthritis. His company expects to trial MK in Chinese patients in the near term, which could facilitate Cellmid's progress to the clinic through the utilization of safety and toxicity data generated.



Istanbul University



Dr. Rita Raisman-Vozari



Professor Ayhan Bilir, Darren Jones and Anna Nordin





## **Excellence in Midkine Research Conference (Cont.)**

Dr Guillermo Velasco, (Complutense University, Madrid, Spain) presented compelling data demonstrating that MK confers resistance to the drug Sativex in the deadly brain cancer glioblastoma. Cellmid is now working with Dr Velasco to trial the use of Cellmid's MK ELISA to stratify glioblastoma patients considered for Sativex treatment, as well as to test whether MK antibodies can kill glioblastoma cells when combined with Sativex.

Assoc Prof **Idit Shachar** (Weizmann Institute, Tel Aviv, Israel) recently discovered that MK is a key survival signal for B cells. The 'over survival' of B cells is a factor in a number of autoimmune diseases such as lupus and rheumatoid arthritis, as well as in B-cell cancers like chronic lymphcytic leukemia (CLL). Plans are underway to collaborate on the use of Cellmid's MK antibodies in animal models of these diseases.

Two presentations were given by current collaborators; Assoc Prof **Mine Erguven** (Yeni Yuzil University, Istanbul) and Dr **Astrid Liedert** (University of Ulm, Ulm). Both groups are making progress in the area of the potential commercial relevance using Cellmid's technologies;

Dr Erguven is using the MK ELISA to diagnose polycystic ovary syndrome, and Dr Liedert is using MK antibodies to improve bone healing in an *in vivo* fracture model.

Finally, Cellmid formed new connections with world -leading researchers including **Dr Rita Raisman-Vosari** (INSERM, Paris, France), **Dr Laurence Brill** (SBMRI, La Jolla, USA) and **Dr Ilyas Singec** (Group Leader at Pfizer, Boston, USA).

Professors Takashi Muramatsu and Kenji Kadomatsu offered to co-host the next midkine conference in Kyoto, Japan, in 2014.

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Dr Guillermo Velasco



Some of the conference attendees

