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Message from the CEO



It has been a busy start to 2015 with another midkine patent grant in the USA for the treatment of heart failure and with the allowance on our Australian midkine patent for hair growth. In December the Japanese Patent Office also granted our oncology antibody patent, strengthening our asset portfolio and reinforcing our position as leaders in midkine intellectual property.

In January we reported a 60% increase in sales for the December 2014 quarter in Advangen, a fantastic achievement by our teams considering that they worked with a reduced product range and distribution due to the ongoing rebranding in Australia. This, by the way, is expected to result in substantial sales growth in the 2015 calendar year.

We are broadening our Australian pharmacy distribution and working to increase our footprint in this channel manifold. Our salon sales force is also expected to double by the end of 2015 with commensurate increase in sales.

These major changes will be implemented by our already capable team and with the leadership of our new VP of Consumer Health Division, Evan Rees. With fifteen years in pharmacy sales and brand management Evan brings to us an invaluable depth of skills and experience, as well as his extensive contacts. A big welcome to Evan, we are very excited to have him on the Advangen team.

Our consumer health products have enormous market potential and our 2015 plans have been developed to turbocharge the business towards the market; all our Australian products, pharmacy and salon, will be brought under the single évolis brand, our pharmacy product range will increase from two to six and our salon offerings from six to fifteen products. As ever, our scientists are working hard in the background to continue the product innovation.

Even though we have only raised a fraction of the planned \$5 million in December for our phase I oncology trials, the money we have will allow us to progress to the next value inflection point in our CAB102 program. As an outstanding achievement by our team we have recently completed the first ever production of our humanised anti-midkine antibody, CAB102. We now have sufficient quantities of the drug product to complete tissue cross reactivity and single dose toxicology studies leading us to a pre-IND meeting.

For a 'first in class' antibody, such as our CAB102, these data sets will add substantial value to the programme. Not only they will enable us to reach a pre-IND meeting, but they will also facilitate our partnering discussions in relation to our other antibody assets.

We are all looking forward to a productive 2015.

Maria Halasz, CEO

 @mariahalasz

Welcoming Advangen's VP Consumer Health Division, Evan Rees

We are delighted to welcome Evan Rees as Advangen's new Vice President of the Consumer Health Division.

Evan has over 15 years healthcare industry experience across retail pharmacies, multinational pharmaceutical companies and contract manufacturing with Roche, PharmaCare, Sanofi, Pharmacia, Sphere and Frostbland.

Evan's key areas of expertise are in skin care, hair care, OTC, vitamins, supplements and ethical products where he has launched and re-launched brands with great success such as Somac, Caverject, MS Contin, Pharmacists Formula, KP24, Bondi Sands, Indeed Labs, Ardell, Batiste, Milk, Transformulas and Iluka.

Evan has recruited and nurtured successful sales and marketing teams nationally. His extensive knowledge of the industry resulted in significant sales and profit growth across multiple channels, including key retail partnerships in Australia and New Zealand.



"The company has great products and technology ideal for long term success in a multichannel consumer health business. I'm very excited to join the Advangen team and looking forward to making an immediate impact" said Evan.

Our Head of Research, Dr Masakuni Yamamoto, provides an insight into the exciting new developments in our Japanese laboratories

Our Advangen research team has started the year having secured Japanese Government funding for new equipment. Under the "Monozukuri" grant program Advangen Inc. may receive up to JPY 23 million (\$240,000) in funding for research equipment. The grant comes in the form of reimbursement for equipment purchased during the qualifying period.

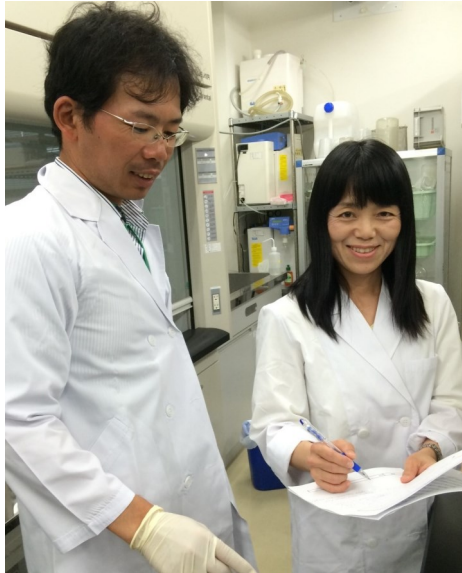
Our research focus is to continue the discovery of novel hair-growth actives by using our highly accurate and reproducible bio-assays. In this process we are participating in several academic and commercial research collaborations. The outcomes support the company's intellectual property strategy and help maintain our position at the cutting edge of hair research.

In recent months we have had exciting results including data from our highly predictive whole hair assay, which we have fine-tuned for the accurate assessment of hair growth potential for our new compounds. The recent data on our novel, patented compounds are encouraging, showing FGF5 inhibition and strong hair growth promotion.

In the hair follicle assay we use the tissue culture of hair follicles that are isolated from murine whiskers. This ex-vivo assay is ideal to demonstrate the elongation of early anagen hair from the follicle as well as the morphological changes of the hair root. The follicles are extremely delicate and even slight damage would decrease the survival rate and the uniformity. Because of these technical difficulties, not only companies but academic researchers in hair science are also interested in our work. It is certainly a very attractive resource for strategic collaborations.

Our academic collaboration with Professor Matsuzaki's team at Shimane University was key to the development of our ex-vivo whole follicle assay. As Chairman of the Japanese Society for Hair Research, Professor Matsuzaki is one of the leaders in the field of hair science and hair regeneration and remains very supportive of the work by our scientific team.





In an exciting development that could mean new, patented products our Chiba University collaboration with Professor Taiichi Sakamoto is expected to deliver aptamers designed to bind specifically to and inhibit FGF5. These will be the first nucleic acid based compounds for hair-growth in the world.

Our novel products are also being tested in a collaboration with leading Tokyo University surgeon Dr. Kotaro Yoshimura. He is a specialist in plastic and reconstructive surgery and runs a hair growth research team using in-vivo, in-vitro and ex-vivo systems. His laboratory is working on testing the hair growth activity of our novel, proprietary compounds and is expected to publish some of the results in the coming months.

In a boost to our intellectual property Kikkoman, the number one soy sauce producer in the world, has agreed to use their proprietary recombinant protein production system for the production of FGF5S, at their cost. FGF5S is a truncated peptide of FGF5, which has previously been reported by AIST, the National Institute of Advanced Industrial Science and Technology, to inhibit biological functions of FGF5. As one of our intellectual property assets, we have an exclusive license to use FGF5S in our products. Kikkoman will be the first group able to produce biologically active and stable FGF5S.

We are fortunate that our in-house capabilities and collaborations position Advangen at the cutting edge of hair research. Due to the decade long research into hair biology and FGF5 we have the tools, systems and proprietary assays to develop and discover new active ingredients from natural sources or which are “drug like” in their efficacy. In addition, our background as a biotechnology company also means that we have the capabilities to run the type of clinical trials that show quantitatively that our products work. Our structural flexibility allows us to rapidly formulate new products.

Cellmid bolsters its comprehensive midkine intellectual property assets

Since our August 2014 update Cellmid has had three significant patents granted in key geographical regions over the use of midkine (MK) and anti-MK agents in the treatment of several diseases and conditions. The granted patents are yet another important piece of our already comprehensive IP protection over Cellmid's MK based therapeutics and MK antibodies, including our lead oncology candidate CAB102. The key patents include:

Patent application 2008-544071 entitled "*Antibody recognising C-domain of midkine*" was granted by the Japanese Patent Office in December 2014. The granted claims cover antibodies and antibody fragments, including Cellmid's lead clinical candidate CAB102, which binds to a critical functional site in the C-domain of MK. The granted claims strategically cover the use of any such antibodies for the prevention and treatment of cancer, autoimmune disease, and inflammatory diseases. Equivalent patents have already been granted in Europe and Australia.

Patent application 2011220326 entitled "*Method of treatment or prevention of hair loss or for the enhancement of hair growth*" was allowed by IP Australia in January 2015. This patent protects the use of MK and the closely related protein pleiotrophin for use as hair loss and/or hair growth treatments. The granted claims cover topical formulations of all kinds, including shampoos, conditioners, creams and lotions with protection until 2031.

This patent is the second member of the extensive midkine patent family for hair growth to be accepted, following the July 2014 granting of the UK patent member.

Patent application 11/720,983 entitled "*Composition for treating or preventing myocardial disorder or heart failure*" was granted by the USA Patent Office in January 2015. The granted claims cover the use of MK as a treatment for heart failure which commonly follows non-fatal heart attacks. It is estimated that more than five million people in the United States have heart failure and arising complications making the USA a key geographic region for future MK based therapeutics.



Darren Jones, our Head of Product Development at Cellmid, provides an update on recent advances in midkine research

Around the world research groups continue to publish on midkine (MK) and not only advance our understanding of this interesting molecule, but add to the data set supporting our intellectual property.

The MK literature now stands at approximately 680 papers, and since June 2014 MK has been the subject of 20 new papers. Some of the recent highlights in MK research include:

Cancer: Yet more clinical evidence that higher MK levels correlate with more deadly disease. Five recent studies affirm this to be true for stomach cancer (2 studies), thyroid cancer (1 study), plus brain tumours (gliomas and glioblastomas; 2 studies). These studies further reinforce the central role that MK plays in the progression of many tumor types, highlighting the opportunity that MK offers as both a biomarker and a target in oncology.

Kidney injury and disease: Three studies in very different renal disease settings concluded that MK expression correlated strongly with kidney damage. Last November, researchers from the Nagoya University School of Medicine in Japan presented results at the world's pre-eminent nephrology conference (American Society for Nephrology annual meeting) to show that MK levels closely mirrored severity and activity of kidney damage in patients with lupus nephritis (LN). Lupus is an autoimmune disease; around 60% of lupus sufferers develop chronic kidney inflammation (nephritis) as a consequence. Importantly, the researchers found that kidney damage was greatly reduced in a MK-knockout mouse model of LN, thereby showing that MK is not merely a marker of LN kidney damage- it is a key driver of damage.

Meanwhile last month, a different group of investigators in Europe showed MK is also elevated in patients suffering acute kidney injury (KI). In this study, serum biomarkers were monitored after the use of toxic imaging dyes. These dyes are necessary for cardiologists to visualise the heart during coronary interventions, but a common consequence is renal toxicity which results in serious KI. The researchers found that MK elevation occurred within two hours of dye administration, indicating KI early and accurately. Midkine out-performed the other known markers for KI in this setting.

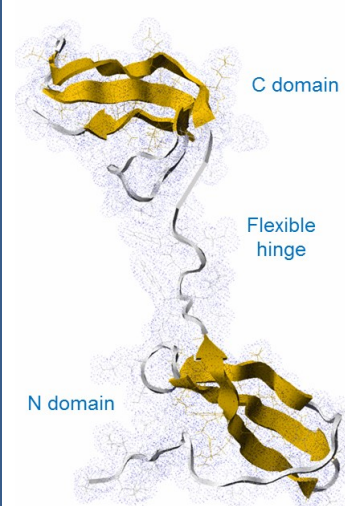
Lastly another Japanese study by the group of our scientific adviser Professor Kenji Kadomatsu, also MK co-discoverer, used mouse models to show that MK elevates blood pressure (BP) in animals with compromised renal function- and this BP rise can be blocked using anti-MK antibodies. High BP is another mechanism which contributes to kidney damage; this paper suggests that elevated MK from kidney damage in turn contributes to high BP, leading to a feedback loop. Breaking this loop with anti-MK therapy represents another opportunity by which a MK antibody could treat KI.

Midkine as a treatment for osteoarthritis (OA): Cellmid's collaborator Professor Wei Han of Regeneron (Shanghai, China) published a study of OA induced in a mouse model. Injections of MK into joints affected by OA were able to prevent cartilage degradation. Importantly, the group also reported that the treatment was apparently safe; no toxicological effects were seen during dosing, and *post mortem* pathology on the major organs showed no evidence of abnormality.

Midkine as a treatment for congestive heart failure (CHF): It is already well known that MK can alleviate cardiac damage due to ischemia (blockage of the coronary artery, which is crucial to keeping the heart beating). A recent study has now also found that treatment with MK can treat heart failure due to non-ischemic origins. In rabbits with tachycardia-induced CHF, MK dosing after heart attack had two beneficial effects; it reduced cardiomyopathy and also strengthened the ventricle. In turn these effects lead to better cardiac function and greater survival post-CHF.



The structure of midkine



The recent option agreement with Zoetis means opportunities in animal health

Zoetis is the world's largest animal health company and firmly holds its position as the global industry leader. Formerly the animal health unit of Pfizer, the company was spun out in 2013 and is currently capitalised at US\$23 billion. Zoetis builds on over 60 years of experience in animal health and aims to discover, develop, manufacture and commercialise a diverse portfolio of animal health medicines and vaccines designed to meet the real-world needs of veterinarians, and the livestock farmers and companion animal owners they support.

In November 2014, Cellmid signed an agreement with Zoetis for the evaluation and option to license of one



of Cellmid's anti-midkine antibodies for therapeutic use in companion animals. Companion animals are a growing market opportunity and have generated much of the growth in the animal health market in recent years.

Zoetis' diverse and strong product portfolio and an exceptionally capable and experienced sales team led it to generate US\$4.6 billion annual revenue in 2013, 36 percent of which was generated from Zoetis' companion animal product portfolio. Cellmid is pleased to be collaborating on such an exciting project with the industry leader in animal health.

Zoetis at a glance

60+ years of experience in animal health

\$4.6 Billion in annual revenues (2013)

120+ Countries in which Zoetis products are sold

64% Revenue from farm animal products

9,800+ Number of Zoetis employees

36% Revenue from companion animal products

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Cellmid - Fast Facts

Listings

Australian Securities Exchange (ASX)

ASX Code: CDY

Issued Capital - Ordinary Shares

792,911,791

(Listed) Options

290,542,770 (exercise price \$0.034 exp. 23 October 2016)

Market Capitalisation

A\$19.8M (10 February 2015)

Cash Position

A\$2.684M (last reported 31 December 2014)

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