## Company Announcement

Tuesday 13 July 2010
Melbourne, Australia

# Webcast transcript: Clinuvel CEO Dr Philippe Wolgen discusses results from the CUV017 trial

Attached is a transcript of a webcast interview to be released shortly to Clinuvel's website at clinuvel.com featuring Clinuvel's CEO, Dr Philippe Wolgen discussing the results of the company's Phase III study of SCENESSE® in erythropoietic protoporphyria (CUV017) released to the ASX today.

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***Interviewer:*** **Dr Wolgen, following today's results of the European and Australian trial in Porphyria, could you please explain in understandable terms what this means for the company?**

*Dr Wolgen:* Today's final results of the European and Australian trial in erythropoietic protoporphyria (EPP), or a disease best characterised by absolute light intolerance are significant for a number of reasons.
Perhaps it is best to put in perspective Clinuvel's trail of obtaining worldwide approval for SCENESSE®.
So today's study results needed to meet 3 objectives to successfully present to leading regulators a pharmaceutical dossier, in order to obtain marketing authorisation or the right to market SCENESSE so first of all:

(i) SCENESSE® needs to demonstrate a **TREATMENT EFFECT**
(ii) the results need to be **CLINICALLY RELEVANT**: and here, statistical analyses alone are not sufficient, regulators also wish to hear how the proposed drug or therapy assists these patients day to day and enable them to engage in activities they were not able to do before. We call this a baseline analysis, a challenging but relevant demonstration of the drug's effect. In comparison to the paitents state before the treatment started.
(iii) SCENESSE® needs to demonstrate a **positive balance on what we call the risk-benefit** axis, in clear terminology: by introducing a first-in-line therapy, one needs to demonstrate that there is a beneficial effect in relation to the side-effects that any pharmaceutical drug brings with it and here the crucial criteria of safety comes into place. Regulators want to know the long-term safety of administering a systemic drug for human use.

So to summarise, the results of this large-scale EPP trial in Europe and Australia needed to demonstrate a positive treatment effect, it needed demonstrate clinical relevance in administering the drug to these patients and it needed demonstrate a favourable risk-benefit analysis.
Today's trial results by and large have met these criteria for the first time.

***Interviewer:*** **Question 2: What do you mean or imply by first time?**

*Dr Wolgen:* Well, the choice of Clinuvel's management is to firstly develop SCENESSE® for skin diseases which are affected by UV and light. And here we chose a disease which is characterised and described by academic experts and patients themselves as severe, serious and totally incapacitating.
From the company's point of view, we have made the choice to test the drug SCENESSE® under the most extreme conditions which we could identify.
And the thought or hypothesis underlying our choices is that a successful testing program under – so to speak – extreme conditions, such as one finds in EPP, gives us the confidence and knowledge to develop the drug for other conditions which are affected by light and UV. And in this manner there is a structural development plan and approach. In commercial terms, this means that Clinuvel will be able to expand the medical utility of the drug in its market.
Now, to come back to your question, SCENESSE is a first pharmaceutical drug which attempts to address these extreme conditions to further the novel medical concept of providing photoprotection in these diseases.

And I stress that no other company or research group has conducted large-scale trials in light-affected patient populations, hence my mentioning of "first". So to, summarise, first equals the introduction of innovative technology.

***Interviewer:*** **Question 3: Could you also explain what these results mean in simple terms?**
With pleasure, I shall try to make the observations and analyses as simple as I am able to.
First, our teams set out to conduct a human trial which would demonstrate whether patients would record less, more or equal phototoxicity or pain of their skin after receiving the drug during one year. We dosed the patients every two months, whereby each patient received the drug alternated with placebo treatment. In this fashion a patient would receive 3 active and 3 placebo treatments.
We also collected how frequent the patients would record their pain or phototoxicity, which is indicative of their EPP symptoms.
And thirdly, we recorded the quantum or number of minutes or hours per day which time patients were able to expose themselves to daylight. Patients were also asked every day of the year to record how they felt, satisfied, unhappy, affected etc as seen in quality of life measures and these quality of life measures have become very important in medicine nowadays. Curing, preventing but also improving the quality of a patients' existence is paramount.
The separate statistical analyses, be it in a relative small population of 100 patients divided in 2 treatment arms, demonstrated significant findings to illustrate what happens in this disease EPP, in which patients are described as absolute light intolerant or nocturnal existents.
We found that the average pain severity (in 4 categories: severe, moderate, mild and none) were significantly lower among those who received treatment compared to those who received placebo. Also, the frequency of pain episodes, meaning the number of days on which pain was recorded, was significantly lower in those patients who were on SCENESSE treatment.
Then we went further, and asked ourselves and all the statisticians the question: can we determine a difference in daylight exposure in patients who received active treatment compared to those who received placebo treatment? And this particular analysis needed to give us an indication whether patients were receiving sufficient treatment effect to enable them to expose themselves to UV and sun light and that's activity which is not known in EPP patients as these patients literally get burnt and never lose the memory of the intense pain associated with their disease. So in simpler terms, EPP patients have altered, have changed their behaviour since childhood by staying indoors, and the association of pain and exposure time needed to help us understand the willingness of patients their risk propensity) to go outside as they were able to withstand the sun and UV in spring and summer months.
And here we were pleasantly surprised by the results, where we found that these patients who were exposing themselves increasingly and continuously received more benefit from the drug in the seasons spring and summer.
So perhaps to summarise, the various statistical analyses and approaches of data generated by 100 patients gave us the first time indication of how the drug could positively affect the severity, the frequency of pain, and enable these patients to challenge themselves to sun if they were prepared to change their behaviour.
**Question 4: Perhaps as a last question, what does this mean for Clinuvel's shareholders and return they can expect from this company?**
The best way to describe the significance of today's results for our shareholders is in the following manner.
At the end of the chain and development one meets the regulatory bodies FDA and EMA. They are the so-called regulatory leaders to which other countries look to agree the introduction of a new drug.
These positive results give us the foundation to discuss with these agencies the treatment effect of SCENESSE®, the clinical relevance and the risk-benefit profile of this newly proposed drug, and I stress, as a first-line therapy.
So we know that regulators worldwide are following the final development of our product as we are active in more than 10 countries, 3 continents. And don't forget that these same regulators had to review Clinuvel's dossier when we filed the past 5 years in each individual country to obtain approval for clinical trials:
So Clinuvel is well known to the agencies.
Against all this positive news, I make realistic comments and express my caution, as drug development remains a risky business and activity. One needs to anticipate many of these regulatory questions ahead and reviews and I call it almost overcompensating – doing more than is expected from a company. Fore instance we are doubling up on most activities, we've have conducted numerous animal studies and these are still ongoing, we engage in multiple trials in the same disease, we use various protocols to arrive at different approaches and much which we execute at Clinuvel needs to serve as the ultimate proof of risk management.

Perhaps, as a final comment, to reduce the risk of failure which equals regulatory rejection, we are targeting more than 2 regulatory agencies to obtain approval in more than one disease, and involving most academic experts in the world, leading scientists, and patients worldwide.
This strategy was rewarded in May earlier this year when the Italian Regulatory Agency AIFA included SCENESSE® as a first reimbursable drug while it was in the process to obtain marketing authorisation in Europe. Also here we also obtained a first.
So my final comment is that Clinuvel shareholders will see revenues posted by us which will translate in value creation.

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**About SCENESSE® (afamelanotide)**
SCENESSE® is a first-in-class therapeutic being developed by Clinuvel, with the generic name (or INN) afamelanotide. An analogue of α-MSH, SCENESSE® is a linear peptide which activates the skin to release eumelanin, the dark pigment which is known to have photoprotective properties (providing skin protection against light and UV radiation). SCENESSE® is administered underneath the skin as a dissolvable implant approximately the size of a grain of rice.
SCENESSE® is a registered trademark of Clinuvel Pharmaceuticals Ltd. For more information see scenesse.com.

**About Erythropoietic Protoporphyria (EPP)**
Porphyrias are a group of inherited disorders with enzymatic deficiency in the blood synthesis pathway (also called porphyrin pathway). They are broadly classified as erythropoietic porphyrias based on the site of the overproduction and main accumulation of porphyrin. They manifest with either skin problems, neurological complications or gastro-intestinal problems (occasionally all).

EPP is a rare genetic disease found in people with fair skin. It is characterised by severe phototoxicity (or intolerance to light) of the skin resulting in intolerable pain, swelling, and scarring, usually of the hands and face. The pain experienced and expressed by EPP patients when their skin is exposed to light is reported as intolerable. EPP patients are often forced to remain indoors, severely affecting their quality of life.

**About Clinuvel Pharmaceuticals Limited**
Clinuvel Pharmaceuticals Ltd is a leading and innovative Australian company focused on the development of SCENESSE® (afamelanotide), its proprietary first-in-class photoprotective drug. Clinuvel has identified five groups of patients with a clinical need for photoprotection. Currently, Clinuvel is in its final stages to complete testing of SCENESSE® in Phase II and III trials in Australia, Europe and the United States. Clinuvel's ongoing focus is to demonstrate the safety and efficacy of SCENESSE®. Pending positive clinical results, Clinuvel aims to file SCENESSE® for its first market approval for the orphan indication porphyria (EPP).

Clinuvel is currently testing SCENESSE® in five clinical indications:

| Indication | Description | Clinical Trial Status |
|---|---|---|
| Erythropoietic Protoporphyria (EPP) | Absolute sun/UV intolerance | Phase III trial full results reported July 2010<br>Confirmatory Phase III trial approved August 2009 |
| Actinic Keratosis (AK) and Squamous Cell Carcinoma (SCC) in Organ Transplant Recipients (OTRs) | Skin cancer in transplant patients | Phase II trial started October 2007 |
| Polymorphic Light Eruption (PLE / PMLE) | Severe sun/UV poisoning | Phase III trial preliminary results reported December 2009 |
| Solar Urticaria (SU) | Acute anaphylactic reaction to sun/UV | Phase II trial results reported July 2009* |
| Photodynamic Therapy (PDT) - systemic | Phototoxicity following cancer treatment | Phase II trial results reported December 2009* |

*Program deferred February 2010.

Phase I and II human clinical trials using SCENESSE® have demonstrated that the drug is well tolerated and no significant safety concerns have been identified to date. Following successful conclusion of the development program, Clinuvel will work closely with global regulators to facilitate marketing approval of SCENESSE®. For more information see clinuvel.com.

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Clinuvel is an Australian biopharmaceutical company focussed on developing its photoprotective drug, SCENESSE (afamelanotide) for a range of UV-related skin disorders resulting from exposure of the skin to harmful UV radiation. Pharmaceutical research and development involves long lead times and significant risks. Therefore, while all reasonable efforts have been made by Clinuvel to ensure that there is a reasonable basis for all statements made in this document that relate to prospective events or developments (forward-looking statements), investors should note the following:

- actual results may and often will differ materially from these forward-looking statements;
- no assurances can be given by Clinuvel that any stated objectives, outcomes or timeframes in respect of its development programme for SCENESSE can or will be achieved;
- no assurances can be given by Clinuvel that, even if its development programme for SCENESSE is successful, it will obtain regulatory approval for its pharmaceutical products or that such products, if approved for use, will be successful in the market place