Company Announcement

Monday 21st December 2009
Melbourne, Australia

Preliminary results in Clinuvel's Phase III porphyria trial

Significant pain reduction is demonstrated in light-intolerant patients with erythropoietic protoporphyria (EPP)

Clinuvel Pharmaceuticals Limited (**ASX: CUV; XETRA-DAX: UR9; ADR: CLVLY**) today announced that it has obtained promising 4-months results in testing afamelanotide in a multicentre randomised double-blind placebo controlled Phase III study in EPP (CUV017). In 2008, afamelanotide was awarded orphan drug designation (ODD) in the treatment of EPP by the FDA and EMEA.

EPP patients are known to be absolutely intolerant to visible and UV light. This genetic disorder leads to an accumulation of protoporphyrin IX in the skin and an increased risk of incapacitating phototoxic reactions manifesting as pain and severe ulceration of the skin. As expected, the quality of life of EPP patients is much reduced by the significant restriction of activities that involve exposure to sunlight such as outdoor activities.

Recent worldwide specialty meetings (haematology, dermatology, gastro-enterology) have confirmed the strong need for an effective preventative treatment for EPP. No effective symptomatic treatment currently exists.

Preliminary Results

An interim analysis of data from the first 4 months of treatment (March-October) in this 12 month trial was undertaken. The study employed a crossover comparison of afamelanotide (3 doses) and placebo (3 doses) in 100 patients. At dose intervals of 2 months, each patient received a single dose of either treatment.

Analysis of 2 treatment arms showed an overall reduction in the average number of phototoxic reactions. Thirty five patients with severe and/or moderate pain reported the greatest reduction in mean number of reactions ($p=0.03$, 95% CI). Analysis of pain severity was positively correlated with treatment, indicating that patient pain scores differed significantly between treatment groups ($p=0.006$, 95% CI).

Although the analysis of quality of life data is not yet complete, all 8 physicians involved in this trial reported a dramatic improvement in the patients' ability to engage in outdoors activities. Safety reports from all academic centres are excellent to date.
This study will be completed by the end of December 2009, after which a full analysis of data will follow.

Clinuvel's Chief Scientific Officer, Dr Hank Agersborg said: "The impact of this life-long disease is seen and reported in our trials by the adult patients who have been unable to lead a normal pain-free existence since early childhood."

"These first statistical analyses confirm the overwhelmingly positive anecdotal reports during the trial. The patients' response to our novel therapy and the physicians' assessment will play a significant role in the regulatory review process."

Managing Director, Dr Philippe Wolgen said: "I am excited by the positive response stated by the physicians and patients during this therapy. Part of the clinical benefit seen in EPP is attributable to our choice of a unique controlled release delivery formulation."

"We will obtain the full EPP analyses and incorporate these data in our next regulatory filing. Clinuvel plans to start confirmatory EPP trials (CUV029) in several European countries in the spring and summer, while we prepare continuation of our US program in 2010."

- End -

Appendix I (Following Code of Best Practice, ASX)

Name of trial
CUV017. A Phase III, Multicentre, Randomized Placebo Controlled Study to Evaluate the Safety and Efficacy of Subcutaneous Bioresorbable Afamelanotide (CUV1647) Implants in Patients with Erythropoietic Protoporphyria (EPP). Protocol No. CUV017.

Primary endpoints
a) The mean number of phototoxic reactions that occur whilst patients are on active compared with placebo implants.
b) The mean severity score for phototoxic reactions that occur whilst patients are on active compared with placebo implants.

Secondary endpoints
Difference in the mean between active and placebo:
a) Changes in melanin density (measured by spectrophotometry)
b) Amount of sunlight exposure, as recorded in diary card
c) Change in quality of life (measured with SF36 questionnaire)
d) The mean "time taken to develop provoked symptoms" following photo testing (in a subset of patients only)

Blinding status
Double-blind.

Product Development Status
Good Manufacturing Practice (GMP) Standard.

Treatment method, frequency, dose levels
Multiple crossover design in which patients received alternating 16 mg afamelanotide or placebo implants once every 2 months for a total of 6 implants administered subcutaneously over a 12 months period.

Number of trial subjects
Up to 101 patients in total.

Subject selection criteria
a) Male or female subjects with a positive diagnosis of EPP (confirmed by elevated free protoporphyrin in peripheral erythrocytes)
b) Aged 18-70 years

Trial location
Multiple trial sites in Australia and Europe

Expected duration of the trial
12 months treatment for an individual patient.

Trial standard
In compliance with Good Clinical Practices (GCP) and ICH guidelines.

Appendix II: About Afamelanotide
Afamelanotide is a first-in-line therapeutic being developed by Clinuvel. An analogue of α-MSH, afamelanotide is a linear peptide which activates the skin to activate and produce eumelanin, the dark pigment which is known to have photoprotective properties (providing skin protection against light and UV radiation). Increased pigmentation of the skin appears a few days after administration of afamelanotide and lasts up to 60 days. Afamelanotide is administered underneath the skin as a dissolvable implant approximately the size of a grain of rice.

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 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 afamelanotide in Phase II and III trials in Australia and Europe. Clinuvel's ongoing focus is to demonstrate the safety and efficacy of afamelanotide. Pending positive clinical results, Clinuvel aims to file afamelanotide for its first market approval for the orphan indications porphyria (EPP) and solar urticaria (SU).

Clinuvel is currently testing afamelanotide in five clinical indications:

Indication	Description	Clinical Trial Status
Erythropoietic Protoporphyria (EPP)	Absolute sun/UV intolerance	Phase III trial preliminary results reported December 2009 Confirmatory Phase III trial approved August 2009
Polymorphic Light Eruption (PLE / PMLE)	Severe sun/UV poisoning	Phase III trial preliminary results reported December 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
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

Phase I and II human clinical trials using afamelanotide have demonstrated that the drug is well tolerated and no significant safety concerns have been identified to date.

During the development program, Clinuvel is working closely with global regulators to facilitate marketing approval of afamelanotide.

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