Company Announcement
Wednesday 21 January 2009
Melbourne, Australia

Clinuvel announces positive Phase III interim results for EPP

Clinuvel Pharmaceuticals Limited (**ASX: CUV; XETRA-DAX: UR9; ADR: CLVLY**) today announces the results of the interim analysis of its Phase III trial studying the photoprotective drug afamelanotide in patients with erythropoietic protoporphyria (EPP). The interim analysis shows clinical benefits to patients suffering from this debilitating disease.

EPP is a rare genetic and metabolic disease characterized by severe phototoxicity of the skin resulting in intolerable pain, blistering and swelling typically of the hands and face. Patients experience aggravated symptoms of the skin following sun exposure, most commonly in spring and summer.

Interim analysis
The data from the first 14 Swiss patients to complete the 12 month study period were analyzed. These represent the first out of 101 EPP patients in Europe and Australia being treated with afamelanotide under the same treatment protocol, and the study is expected to be completed in the last quarter of 2009.

Study results
The severity of phototoxicity, determined as a primary endpoint to the study, was assessed by measuring the pain experienced during episodes of phototoxicity using a standard visual analogue pain scale. The maximum severity of phototoxic reactions was significantly reduced by afamelanotide treatment compared with placebo ($p<0.001$) and the total severity of phototoxic reactions was reduced during spring and summer by afamelanotide compared with placebo ($p=0.028$).

Skin melanin density, determined as secondary endpoint to the study, increased following afamelanotide treatment and then declined during the placebo treatment period as expected. There was a significant difference in the change from baseline in melanin density (skin darkening) for afamelanotide compared to placebo for the first two treatment periods, during spring and summer ($p=0.048$).

No significant differences between the afamelanotide and placebo treated patients were seen for the number of phototoxic reactions experienced, the amount of sunlight exposure or the quality of life measurements. This may have been due to the small numbers of patients ($n=14$).

Importantly, there were no afamelanotide-related serious adverse events or safety concerns identified during the study.

An independent Data and Safety Monitoring Board has reviewed the data on the safety and efficacy of afamelanotide in this clinical setting and consider it appropriate, and of benefit, to continue the study to its conclusion.

Compassionate program
On completion of the study by the Swiss cohort of patients, all 14 patients requested continuation of the drug for photoprotection for the next 12 months. This compassionate use request was granted by SwissMedic, the Swiss regulatory agency.

CSO Dr Helmer Agersborg commented: “In 2008, three regulatory agencies, the FDA, the EMEA and Swissmedic granted Clinuvel Orphan Drug Designation for the treatment of phototoxicity in EPP patients. The results of this trial are very encouraging. While this was an interim analysis involving data from only 14 patients, it was pleasing to see that afamelanotide reduced the severity of phototoxicity. If these results are repeated in the full study analysis, afamelanotide will be of clinical benefit in the reduction of the symptoms of EPP.”

CEO Dr Philippe Wolgen said today:"We are most happy with these results, but safety remains the most important aspect we are looking at when evaluating afamelanotide as a new class of drug in preparation for marketing authorization in various markets. It is a very positive sign that all Swiss patients requested further medication after completion of the trial. Today's results bode well, although we remain cautious in our predictions until the completion of the trials. We are on schedule in our development of afamelanotide and look modestly but confidently ahead to late 2009, when we anticipate the final Phase III results."

Appendix I (Following Code of Best Practice, ASX)

Name of trial
CUV0017. A Phase III, Multicentre, Randomised 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 phototesting (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 month period.

Number of trial subjects
Up to 101 patients in total (14 patients in the interim analysis).

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 (interim analysis on patients enrolled in Zürich).

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

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

About Afamelanotide
Afamelanotide stimulates the body's natural ability to produce eumelanin, the dark pigment of the skin which is known to have photoprotective properties, thus providing skin protection against UV radiation (UVR). Increased pigmentation of the skin appears a few days after administration of afamelanotide and lasts up to two months. Afamelanotide is administered underneath the skin as a biodegradable 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 mainly accumulation of porphyrin. They manifest with either skin problems or with neurological complications (or occasionally both).

EPP is a rare genetic disease found in people with fair skin. It is characterized by severe light-sensitivity or "phototoxicity" of the skin resulting in intolerable pain, swelling, and scarring, usually of the hands and face. The pain suffered by an EPP patient when their skin is exposed to light is comparable to scalding water on the skin. EPP patients are often forced to remain indoors, severely affecting their quality of life.

About Clinuvel Pharmaceuticals Limited
Clinuvel Pharmaceuticals Limited is an Australian biopharmaceutical company with offices in San Francisco and Zürich developing its photoprotective drug afamelanotide as a preventative treatment for a range of UV-related skin disorders as well as cancer related treatments.

Clinuvel's five UV-light related indications are:

Indication	Description	Clinical Trial Status
Erythropoietic Protoporphyria (EPP)	Absolute sun intolerance	Phase III trials started April 2007
Polymorphic Light Eruption (PLE / PMLE)	Severe sun poisoning	Phase III trials started May 2007
Actinic Keratosis (AK) and Squamous Cell Carcinoma (SCC) in Organ Transplant Recipients (OTR)	OTRs have an absolute dramatic risk to skin cancers	Phase II trials started October 2007
Solar Urticaria (SU)	Acute anaphylactic reaction to sun	Phase II trials started June 2008
Photodynamic Therapy (PDT) systemic	Phototoxicity associated with the use of a photosensitiser used with PDT in cancer treatment (esophagus, gall bladder)	Phase II trials started September 2008

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.

Following successful conclusion of the development program, Clinuvel will work closely with global regulators to facilitate marketing approval of afamelanotide.

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