Company Announcement

Tuesday 30th March 2010
Melbourne, Australia

FDA allows US clinical trials of afamelanotide in EPP

Phase II trial of novel drug in erythropoietic protoporphyria (EPP) to commence immediately

Clinuvel Pharmaceuticals Limited (**ASX: CUV; XETRA-DAX: UR9; ADR: CLVLY**) today announced that the US Food and Drug Administration (FDA) has agreed for Clinuvel to proceed under its current Investigational New Drug (IND) to conduct a Phase II clinical trial (CUV030) to evaluate afamelanotide as a first-in-class photoprotective drug in patients diagnosed with erythropoietic protoporphyria (EPP). This outcome is a breakthrough in Clinuvel's global clinical program and will be the first therapeutic clinical trial of afamelanotide in the US. Afamelanotide was granted orphan drug designations (ODD) for EPP by the FDA and the European Medicines Agency (EMA) in 2008.

EPP is a metabolic disorder characterised by absolute intolerance to light (blue spectrum), caused by the accumulation of protoporphyrin IX. EPP symptoms are most severe during spring and summer months, when light levels are the most intense. The current estimates from existing databases indicate that there are approximately 3,000 known adult patients with EPP in the US. There is currently no effective drug therapy available in EPP.

In accordance with the provisions of Code of Federal Regulations (CFR) Title 21 Part 312 (21 CFR 312), the FDA has allowed Clinuvel to proceed with its clinical evaluation of afamelanotide in EPP.

CUV030 is a randomised placebo-controlled trial to analyse the safety and efficacy of afamelanotide in EPP. The trial will be conducted in six centres (Alabama, California, New York, North Carolina, Texas and Utah) with a total of 60 patients to be included. It is anticipated that patient recruitment will be finalised in the following weeks. The objectives of the trial are to further evaluate afamelanotide's effect on the severity of phototoxic reactions.

Currently, the final data from the European and Australian EPP Phase III trial (CUV017) are being evaluated and results are expected in the following weeks. A second European Phase III trial (CUV029), to confirm the safety and efficacy of afamelanotide in an additional number of EPP patients is in the final stages of preparation in Europe. The protocol used under CUV030 will be identical to the one used in the European EPP trial.

Clinuvel's Chief Scientific Officer, Dr Hank Agersborg said: "CUV030 will be the first therapeutic clinical trial of afamelanotide in the United States since the development and reformulation of the drug by the Clinuvel team. In the US we are reproducing the EPP program currently conducted in Europe. Today's major achievement has only been possible following close collaboration with the Office of Orphan Products Development (OOPD) and the Centre for Drug Evaluation and Research (CDER). Clinuvel intends to make its first regulatory filing to obtain marketing authorisation (MAA) in Europe, subject to all safety and efficacy data being reviewed."

Clinuvel's CEO, Dr Philippe Wolgen said: "This is a quantum leap in Clinuvel's existence. It took years of development to arrive at this stage and it certainly bodes well for our plans to commercialise afamelanotide for EPP patients in the US.

"We much desired and anticipated this FDA outcome, and started well ahead of time to obtain approval from ethics committees in the various US states. We just received our first approval from the Institutional Review Board (IRB) in North Carolina to start the trial, and more approvals in the other five states are expected in days to come."

Dr Wolgen concluded: "This US news certainly aligns the interests of both our patients and global investors."

- End -

Appendix I Explanatory Notes:
Upon successful completion of the program in EPP, the Division of Dermatology and Dental Products (DDDP) of the FDA will be responsible for the evaluation of the efficacy and safety data of patients who have been administered afamelanotide.

Investigational new drug means a new drug or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms “investigational drug” and “investigational new drug” are deemed to be synonymous.

Phase II includes the controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug. Phase II studies are typically well controlled, closely monitored, and conducted in a relatively small number of patients.

Human research ethics committee (HREC) means a review panel that is responsible for ensuring the protection of the rights, safety, and well-being of human subjects involved in a clinical investigation and is adequately constituted to provide assurance of that protection. An institutional review board (IRB), is one type of HREC.

Appendix II (Following Code of Best Practice, ASX)
Name of trial
CUV030: A Phase II, Multicentre, Double-Blind, Randomised, Placebo-Controlled Study to Confirm the Safety and Efficacy of Subcutaneous Bioresorbable Afamelanotide Implants in Patients With Erythropoietic Protoporphyria (EPP)

Primary endpoints
a) Determine whether afamelanotide implants can reduce the severity of phototoxic reactions in patients with EPP.

Secondary endpoints
1. Determine whether afamelanotide implant:
   a) reduces the number of phototoxic reactions in patients with EPP;
   b) improves the quality of life of EPP patients (measured with specific quality of life measurement tools);
   c) has an effect on free protoporphyrin IX levels.
2. Evaluate the safety and tolerability of afamelanotide by measuring treatment-emergent adverse events (AEs).

Blinding status
Double blind.

Product Development Status
Good Manufacturing Practice (GMP) Standard.

Treatment method, frequency, dose levels
This is a randomized placebo-controlled study to be conducted in two parallel study arms for a six month period (three doses) in spring and summer. Up to 60 eligible patients will be enrolled and will receive afamelanotide (16 mg implants) or placebo according to the following dosing regime:
- ***Group A*** will be administered afamelanotide implants on Days 0, 60 and 120
- ***Group B*** will be administered placebo implants on Days 0, 60 and 120

Number of trial subjects
Up to 60 patients

Subject selection criteria
The participants have to fulfill all of the following criteria for study participation:
a) Male or female subjects with a clinical diagnosis of EPP of sufficient severity that they have requested treatment to alleviate their symptoms
b) Aged 18 – 70 years (inclusive)
c) Written informed consent prior to the performance of any study-specific procedures.

Trial location
Six trial sites across the United States of America.

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

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

Appendix III
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 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 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 indication porphyria (EPP).

Clinuvel is currently testing afamelanotide in five clinical indications:

Indication	Description	Clinical Trial Status
Erythropoietic Protoporphyria (EPP)	Absolute sun/UV intolerance	Phase III trial full results due 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 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.

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 mainly 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 exposed areas as face, hands and feet. 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.

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