



Clinuvel communications

Live on Clinuvel.com today: Podcast - CSO Dr H Agersborg discusses the regulatory strategy at Clinuvel

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ASX: CUV | XETRA-DAX: UR9 | ADR: CLVLY

Company Announcement

Monday 31st August 2009
Melbourne, Australia

Confirmatory Phase III EPP trial receives approval

Regulatory strategy to optimise chances of marketing approval

Clinuvel Pharmaceutical Limited (**ASX: CUV; XETRA-DAX: UR9; ADR: CLVLY**) today announced that it received European regulatory approvals to begin a confirmatory Phase III clinical trial of afamelanotide, its photoprotective drug, in Erythropoietic Protoporphyrria (EPP). EPP is a rare metabolic disorder causing severe phototoxicity.

The multicentre trial is Clinuvel's second Phase III clinical trial (CUV029) to test afamelanotide in EPP and will further evaluate the reduction in the severity of phototoxic reactions. In line with planning, Clinuvel expects to complete its first European and Australian Phase III trial (CUV017) in EPP patients by the last quarter of 2009. Pending results, the regulatory submission for marketing authorisation in Europe will follow shortly after.

In 2008, afamelanotide was granted orphan drug status for the treatment of EPP by the European Medicines Agency (EMA), Swissmedic and FDA.

Clinuvel's Chief Scientific Officer Dr Hank Agersborg said:

"Part of Clinuvel's business management is to anticipate regulatory requirements for further data by planning and organising an additional trial ahead of the results in our first Phase III trial. This strategy also meets our broader clinical objectives to subject as many EPP patients as feasible to afamelanotide during the testing phase to collect optimum safety data. The six month trial CUV029 will start in five centres across Europe shortly, and it is anticipated that approximately 40 patients will be included in this trial."

"Our clinical and regulatory team has been proactive in trying to anticipate the most stringent of regulatory requirements. We are not prepared to wait for a possible equivocal review panel, but anticipate what might come. The parallel planning of an additional trial – while not being requested – is the most cost-efficient way and forward management I have been involved in. It stands in contrast to traditional waiting for the regulatory verdict when being asked to generate more clinical data after regulatory review. Our approach translates to a potential 12 month gain in development."

- End -

Appendix I (Following Code of Best Practice, ASX)

Name of trial

CUV029: A Phase III, Multicentre, Double-Blind, Randomised, Placebo-Controlled Study to Confirm the Safety and Efficacy of Subcutaneous Bioresorbable Afamelanotide Implants in Patients with Erythropoietic Protoporphyrin (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 Dermatology Life Quality Index (DLQI) questionnaire and supplementary EPP specific questions);
 - 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 70 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 70 patients

Subject selection criteria

The participants have to fulfill all of the following criteria for study participation:

- a) Male or female subjects with a diagnosis of EPP (confirmed by elevated free protoporphyrin in peripheral erythrocytes) 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

Multiple trial sites in Europe.

Expected duration of the trial

6 month treatment for an individual patient.

Trial standard

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

Appendix II

About afamelanotide

Afamelanotide is an analogue of α -MSH, a peptide which activates 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 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.

Clinuvel is currently testing afamelanotide in five clinical indications:

Indication	Description	Clinical Trial Status
Erythropoietic Protoporphyrin (EPP)	Absolute sun/UV intolerance	Phase III trials started April 2007
Polymorphic Light Eruption (PLE / PMLE)	Severe sun/UV poisoning	Phase III trials started May 2007
Actinic Keratosis (AK) and Squamous Cell Carcinoma (SCC) in Organ Transplant Recipients (OTRs)	Skin cancer in transplant patients	Phase II trials started October 2007
Solar Urticaria (SU)	Acute anaphylactic reaction to sun/UV	Phase II trials reported July 2009
Photodynamic Therapy (PDT) - systemic	Phototoxicity following cancer treatment	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.

About Erythropoietic Protoporphyrin (EPP)

Porphyrias are a group of inherited disorders with enzymatic deficiency in the heme synthesis pathway (also called porphyrin pathway). They are broadly classified as 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, which causes protoporphyrin IX to accumulate in the skin. It is characterised 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.

In 2008, afamelanotide was designated orphan drug status for the treatment of EPP by the European Medicines Agency (EMA), SwissMedic and FDA. Orphan status provides greater regulatory and financial support for drug development, as these drugs have the potential to treat rare, severe disorders, for which there is no current effective therapy.

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Clinuvel is an Australian biopharmaceutical company focussed on developing its photoprotective drug, 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 afamelanotide can or will be achieved;
- no assurances can be given by Clinuvel that, even if its development programme for afamelanotide 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

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