



## Company Announcement

Wednesday 9<sup>th</sup> December 2009  
Melbourne, Australia

### **Afamelanotide improved quality of life in cancer patients**

*Pilot study evaluating afamelanotide as adjunct therapy in systemic photodynamic therapy (PDT)*

Clinuvel Pharmaceuticals Limited (**ASX: CUV; XETRA-DAX: UR9; ADR: CLVLY**) today announced that it had obtained positive results from an experimental randomised placebo-controlled Phase II trial (CUV025) evaluating the photoprotective effect of afamelanotide in 16 patients.

#### **Objectives and results**

The objective of this exploratory trial was to determine the effect of a single 16mg dose of afamelanotide on the quality of life and phototoxicity in patients undergoing PDT. The trial was conducted by 4 French academic departments of gastro-enterology. Patients were followed up during 90 days.

In total 16 Caucasian patients were included, 9 patients were administered afamelanotide and 7 patients placebo treatment as a subcutaneous implant at the same time as the photosensitising agent Photofrin<sup>TM</sup>.

Post-operative analysis at 7 and 12 days revealed a positive trend to tolerate ambient light at standardised exposure by 7 out of 9 patients receiving afamelanotide. In patients on active drug, a significant improvement in quality of life assessment was demonstrated at 60 days of treatment (p=0.02). Clinical observations from all physicians and reports from patients supported and encouraged further use of afamelanotide in PDT cancer trials. No significant drug-related adverse events were reported.

#### **Background**

In oncology, treatment of cholangiocarcinoma (bile duct cancer) and esophageal cancer remains clinically challenging. Recently, with systemic photodynamic therapy (PDT) remarkable progress has been made in the palliative treatment of advanced stage cholangiocarcinoma, where a median time survival of 498 days has been reported in PDT as opposed to 98 days with conventional therapy.<sup>1</sup>

In PDT, a photosensitising drug (Photofrin<sup>TM</sup>) is administered intravenously to enhance and accelerate tumour treatment by LASER illumination. This photosensitisation restricts patients to an indoor life for up to 90 days after treatment, or they risk phototoxic reactions and second degree burns. Phototoxicity of the skin is the dominant and clinically significant side effect of PDT and precludes wider use of the therapy in these patients.<sup>1,2</sup>

Clinuvel's Chief Scientific Officer, Dr Hank Agersborg said:

"These results are meaningful as they statistically confirmed the benefits of the adjunctive use of afamelanotide in a small group of oncology and terminally ill patients. In the next few weeks we will decide on a further Phase III trial in PDT. The particular choice for afamelanotide as an adjuvant photoprotective drug in gastro-intestinal cancer stems from the common biochemical pathways seen in both PDT and erythropoietic protoporphyria (EPP), a disease in which we are using afamelanotide in parallel advanced Phase III trials."

"Today's results are of particular relevance because we have learned from regulatory agencies that data from PDT studies may be used as supporting evidence when we file for EPP registration. Therefore, the confirmation of safety and the improvement in quality of life in these light intolerant patients provides a substantial step toward the registration of afamelanotide for EPP,"<sup>3,4</sup> Dr Agersborg said.

- End -

## Appendix I: References

1. Ortner M-A., (2009). "Photodynamic therapy for cholangiocarcinoma: overview and new developments." *Curr Opin Gastroenterol.* 25 (5): 472-476.
2. Jong C.T., et al., (2008). "The quality of life of 790 patients with photodermatoses." *Brit J Derm.* 159 (1): 192-197.
3. Millward L.M., et al., (2001). "Self-rated psychosocial consequences and quality of life in acute porphyrias." *J Inherit Metab Dis.* 24 (7): 733-747.
4. Lecluse A.L.Y., et al., (2007). "Erythropoietic protoporphyria without skin symptoms-you do not always see what they feel." *EU J Pediat.* 167 (6): 703-706.

## Appendix II (Following Code of Best Practice, ASX)

### Name of trial

CUV025. A Phase II, multicentre, double blind, placebo-controlled pilot study to evaluate the safety and efficacy of afamelanotide as adjunctive therapy in patients undergoing Photodynamic Therapy (PDT) utilizing porfimer sodium.

### Endpoints

- a) To determine whether afamelanotide implants can reduce the period of phototoxicity experienced by patients who have undergone Photodynamic Therapy with porfimer sodium;
- b) To evaluate the effect of afamelanotide on quality of life;
- c) To evaluate the safety and tolerability of afamelanotide by measuring treatment-emergent adverse events.

### Blinding status

Double blind.

### Product Development Status

Good Manufacturing Practice (GMP) Standard.

### Treatment method, frequency, dose levels

A single implant (16 mg afamelanotide or placebo) administered subcutaneously.

### Number of trial subjects

16 patients.

### Subject selection criteria

- a) Male or female Caucasian subjects undergoing PDT with porfimer sodium;
- b) Aged greater than 18 years.

### Trial location

Multicentre trial in France including Amiens, Angers, Brest and Paris Hospitals.

### Duration of the trial

Approximately 6-12 months.

### 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  $\alpha$ -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 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
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Erythropoietic Protoporphyrin (EPP)	Absolute sun/UV intolerance	Phase III trial preliminary results due Confirmatory Phase III trial approved August 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
Polymorphic Light Eruption (PLE / PMLE)	Severe sun/UV poisoning	Phase III trial preliminary results due
Actinic Keratosis (AK) and Squamous Cell Carcinoma (SCC) in Organ Transplant Recipients (OTRs)	Skin cancer in transplant patients	Phase II trial started October 2007

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.

#### **About Photodynamic Therapy (PDT)**

In PDT, a photosensitising drug (Photofrin™) is administered intravenously to enhance and accelerate tumour treatment by LASER illumination. The photosensitiser in the tumour absorbs the light and produces an active form of oxygen that destroys nearby cancer cells.

Photosensitising agents such as porfimer sodium (Photofrin™) make skin and eyes ultra sensitive to light for up to 90 days following treatment. Patients suffer intense pain and second degree burns associated with this phototoxicity and are forced to avoid sunlight/artificial light for up to 90 days following treatment.

The main advantages of PDT over other cancer therapies include the significant degree of selectivity of drug accumulation in the tumour tissue, and the ability to retreat a recurrent tumour. PDT has proven valuable as a treatment option in cancers such as esophageal cancer, gastric, endobronchial, papillary bladder and gliomas. Phototoxicity of the skin is the dominant and clinically significant side effect of PDT and precludes wider use of the therapy in these patients.

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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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