



## Media Release

Wednesday 21 January 2009  
Melbourne, Australia

# Clinuvel: positive interim Phase III results for unique skin protection drug

*Photoprotective drug afamelanotide moves a step closer to market*

Melbourne-based Clinuvel Pharmaceuticals Limited (ASX: CUV) achieved positive interim results of its photoprotective drug, afamelanotide, in a Phase III trial conducted in Switzerland. The trial investigated the medical benefits of afamelanotide in the orphan disease erythropoietic protoporphyria (EPP), a severe genetic disorder causing absolute ultraviolet radiation (UV) and light intolerance in the skin. This is the company's first Phase III test result.

People with EPP, a rare disease, suffer phototoxicity, painful symptoms from sunlight and UV exposure. Phototoxicity usually starts in early childhood with patients experiencing severe burning pain and blistering of the skin, typically on the face and hands. Severe symptoms may last for several days and may be accompanied by swelling and redness on sun exposed areas. EPP is exacerbated in the spring and summer months.

The drug afamelanotide stimulates the body's own natural melanin production. Melanin is known for its photoprotection as it absorbs ultraviolet radiation, shielding the skin from the effects of UV. This offers EPP patients the possibility of a better quality of life where they don't have to avoid the sun or live in the shadows.

The interim results are based on the trial's first 14 Swiss patients, with a 12 month study period analysed. A further 87 patients will complete the trial in Europe and Australia. The European and Australian Phase III EPP trial is expected to be completed in the second half of 2009.

The results showed that the maximum severity of phototoxic reactions for patients on the drug was significantly reduced compared to patients on the placebo ( $p < 0.001$ ). Further, the total severity of phototoxic reactions was reduced during spring and summer by afamelanotide, compared with placebo ( $p = 0.028$ ). Potentially, the drug offers EPP patients the possibility of an existence where exposure to light and UV become tolerable, and where patients are not confined to life indoors.

The patients were tested at higher altitude where ultraviolet radiation is more intense. The result showed a statistically significant reduction in the severity of phototoxic reactions in EPP patients and increased melanin density in the skin.

Exceptionally, at the end of the study all 14 Swiss 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.

An independent Data and Safety Monitoring Board has reviewed the data on the safety and efficacy of afamelanotide in this clinical setting and considered it appropriate, and of benefit to patients, to continue the study to its conclusion. Clinuvel hopes to file for the drug's approval in Europe in the next 18 months

"Afamelanotide is an Australian drug with many applications, and we are determined to show that this drug serves the most severe sufferers of UV-related skin diseases," said Clinuvel CEO Dr Philippe Wolgen.

"Photodermatoses or UV-sensitive skin is a global problem, most pronounced in fair-skinned patients. Over 15 years we have built knowledge at Australian-base Clinuvel, surrounded by a UV intensive environment and we are moving closer to solving a global problem. Clinuvel is a world leader as a photoprotection pharmaceutical company," Dr Wolgen said.

"These results validate the clinical path laid out by Clinuvel over the last four years," said Chief Scientific Officer Dr Helmer Agersborg. "The continued focus for the company is on proving the safety and efficacy of afamelanotide, and this is a positive step. We now look forward to full results from this study by the end of this year."

"To date no drug related serious adverse events have been reported following the use of afamelanotide. This supports the strong safety record of Clinuvel's development of afamelanotide through fifteen trials (including five ongoing) over eight years across five indications," Dr Agersborg said.

Clinuvel has identified five UV and light related disorders where clinical use of afamelanotide serves the needs of patients who suffer severe and chronic symptoms. One of the most severe categories is organ transplant recipients who endure high incidence of skin cancers, due to their life-long reliance on immune suppressing drugs in combination with UV daily exposure.

Clinuvel anticipates commencing trials in the US in early 2009, pending the US Food and Drug Administration's (FDA) approval of its first Investigational New Drug (IND) application, lodged in December 2008. A successful outcome will be important progress in ultimately marketing afamelanotide in the US as well as the rest of the world.

"The emerging field of photoprotection is becoming increasingly recognised by dermatologists and a range of physicians including haematologists, oncologists and transplant surgeons," Dr Wolgen said. "The behavioural response to photoprotection is one we all know through the Sunsmart programs. A pharmaceutical response to photoprotection is closer to reality on today's news of Clinuvel's progress."

--End--

Available for interview: Dr Philippe Wolgen, CEO

For more information or interview requests, contact:

Colin Mackie

Clinuvel Pharmaceuticals

+61 3 9660 4900

[investorrelations@clinuvel.com](mailto:investorrelations@clinuvel.com)

[www.clinuvel.com](http://www.clinuvel.com)

#### **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 Protoporphyrin (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:

<b>Indication</b>	<b>Description</b>	<b>Clinical Trial Status</b>
Erythropoietic Protoporphyrin (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.

Clinuvel is an Australian biopharmaceutical company focussed on developing its photoprotective drug, afamelanotide (CUV1647), 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.

**Level 11 / 330 Collins Street T +61 3 9660 4900      [www.clinuvel.com](http://www.clinuvel.com)**  
**Melbourne, Victoria 3000 F +61 3 9660 4999**  
**Australia**