

# Australia's Medicinal Photoprotection

## Afamelanotide – First-In-Class



Clinuvel Pharmaceuticals Ltd

Dr Philippe Wolgen, CEO  
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ASX: CUV  
XETRA-DAX: UR9  
ADR: CLVLY



Australia's medicinal photoprotective drug, afamelanotide, is the world's first regulated photoprotective drug to undergo human testing in Phase III trials. The trials currently underway will evaluate safety and efficacy in reducing the effects of light/UV on skin.

15 years of research has led to optimised proprietary processes in chemistry, formulation and dosage to offer medicinal photoprotection.

Clinuvel is in the final stage of development and commercialisation of afamelanotide.

## Safe harbor statement

Clinuvel is an Australian biopharmaceutical company focused on developing its leading drug candidate, 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 program for afamelanotide can or will be achieved;

- no assurances can be given by Clinuvel that, even if its development program 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.



## Financials

- Shares on issue 303,148,665 c/s
- Fully diluted basis 320M c/s
- Market cap US\$78m\*
- OPEX (Dec '06-Jun '09) <US\$0.79m\*/month
- Reserves (Jun 30 '09) US\$30.6m\*
- Projected gross expenditures (Dec 31 '10) US\$24.2m\*



\* Based on exchange rate of A\$1:US\$0.79, as at 30/6/09



Clinuvel is funded to file for Marketing Authorisation for afamelanotide.

As the activities of Clinuvel increase over 3 continents, the (cash) burn rate will increase to US\$1.35m (A\$1.7m)/month by the end of 2009.

## Afamelanotide: a world's first

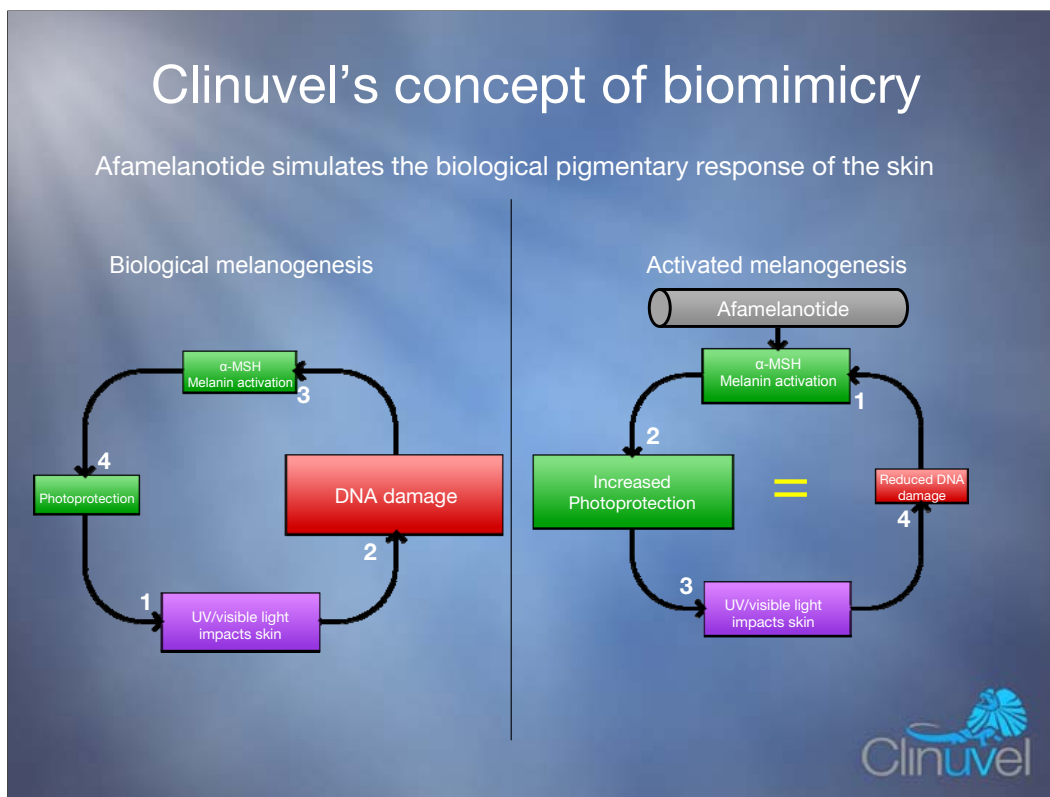
- First priority orphan diseases:
  - porphyria (EPP: absolute light intolerance)
  - solar urticaria (SU: acute immune response to light/UV)
- Registration strategy in 4 markets:  
EMEA, TGA, Swissmedic, FDA
- Phase III completion Q4/09 (CUV017)



In afamelanotide, a long process of development and optimisation of chemistry, dosage and formulation is nearing its end. The drug is first-in-class, meaning that no other company worldwide has previously developed a drug in this therapeutic area: **medicinal photoprotection to patients who are deficient in their pigmentary response to light and UV.**

Clinuvel has the funds to develop and register afamelanotide in all 4 global markets. The priorities are led by the acute clinical need in patients who suffer from porphyria and solar urticaria.

Lead Phase III trial completed in Australia and Europe Q4 2009 for porphyria.



Afamelanotide assists a natural pigmentary response of the skin known as melanogenesis, where a photoprotective layer of melanin is produced, protecting the skin from light and UV.

The concept of assisted melanogenesis is of benefit to those patients with an insufficient dermal physiological response to UV.

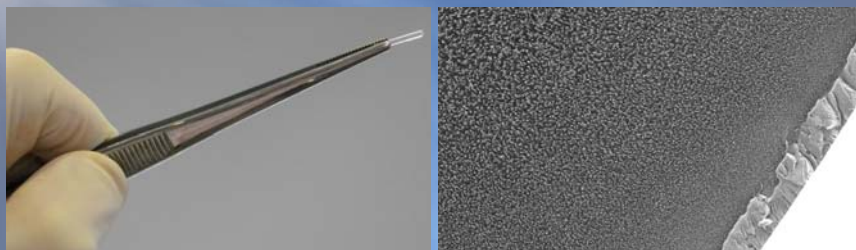
Afamelanotide intercepts the “**UV-impact loop**” at the point where the dermal cellular response is provoked by UV–damage [no. 3 on the physiological loop]: Clinuvel’s drug provides medicinal photoprotection **before** UV impacts the skin..

#### References:

Barnetson, R et al, (2006). “[Nle<sup>4</sup>-D-Phe<sup>7</sup>]-  $\alpha$ -Melanocyte-Stimulating Hormone Significantly Increased Pigmentation and Decreased UV Damage in Fair-Skinned Caucasian Volunteers”. *Journal of Investigative Dermatology*. 126: 1869-1878.

Dwyer, T et al, (2002). “Cutaneous Melanin Density of Caucasians Measured by Spectrophotometry and Risk of Malignant Melanoma, Basal Cell Carcinoma, and Squamous Cell Carcinoma of the Skin”. *American Journal of Epidemiology*. 155(7): 614-621.

## Afamelanotide 16mg implant

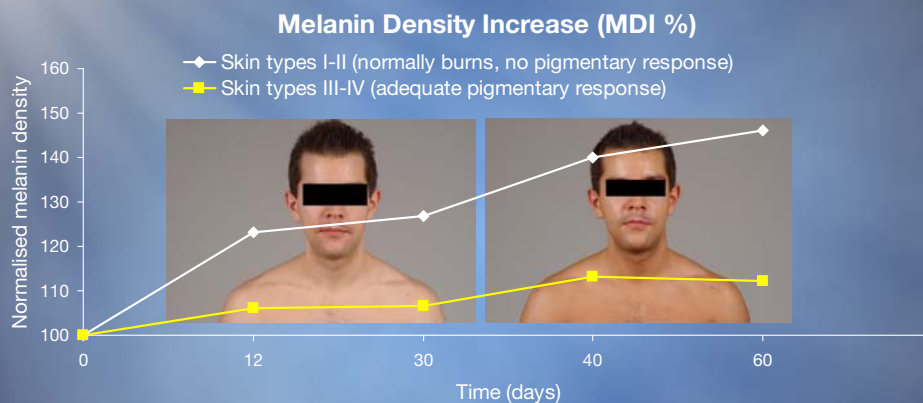


- Controlled release formulation
- Proprietary technology



Afamelanotide delivered by a novel implant technology, proprietary to Clinuvel.  
Developed over 10 years.

# Pharmacodynamics



- Drug released over 10 days
- Melanin density elevated for 60 days

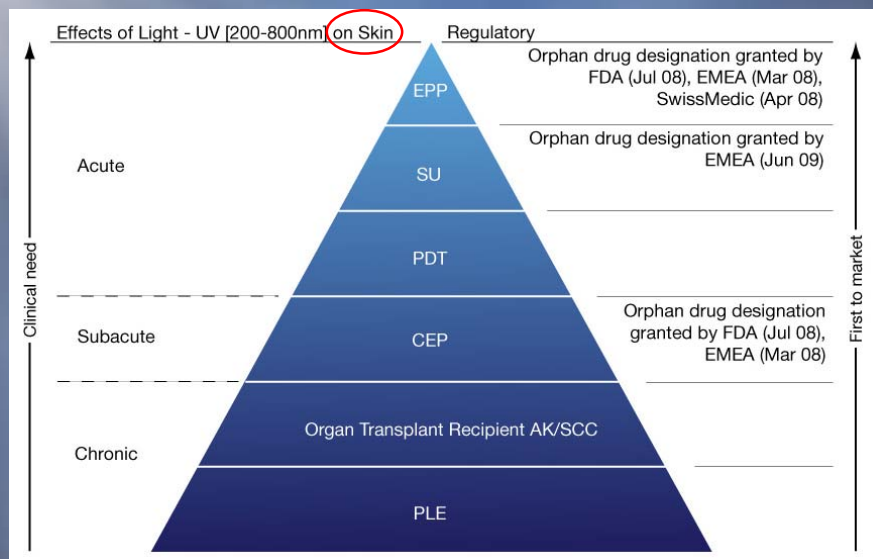
Source: Dwyer et al; 2002; Clinuvel trial EP002



Graph shows melanin density increase (pigmentary response) in two different skin type groups, following administration of afamelanotide.

Skin types I-II show a greater melanin density increase than skin types III-IV (Fitzpatrick scale).

## Afamelanotide: EPP and SU priorities



References:  
 Dunn, R et al (2009). "Afamelanotide, an  $\alpha$ -melanocyte stimulating hormone (MSH) agonist reduces phototoxicity in Erythropoietic Protoporphyrria (EPP), as tested under laboratory conditions." *Australasian Journal of Dermatology*. 50 Suppl. 1:A12-A13, 13 May.  
 Harms, J et al. (2009). "Mitigating Photosensitivity of Erythropoietic Protoporphyrria Patients by an Agonistic Analog of  $\alpha$ -Melanocyte-Stimulating Hormone". *Photocem and Photobiol*. ePub June 2009.



6 medical indications in the clinic for developing afamelanotide, with Congenital Erythropoietic Porphyria (CEP) studied under compassionate use.

With strong regulatory support globally (multiple Orphan Drug Designations) Clinuvel's strategy is to commercialise afamelanotide for those patients with the most acute clinical need: erythropoietic protoporphyria (absolute light/UV intolerance – EPP) and solar urticaria (acute anaphylactic reaction to light/UV – SU) are the first priorities.

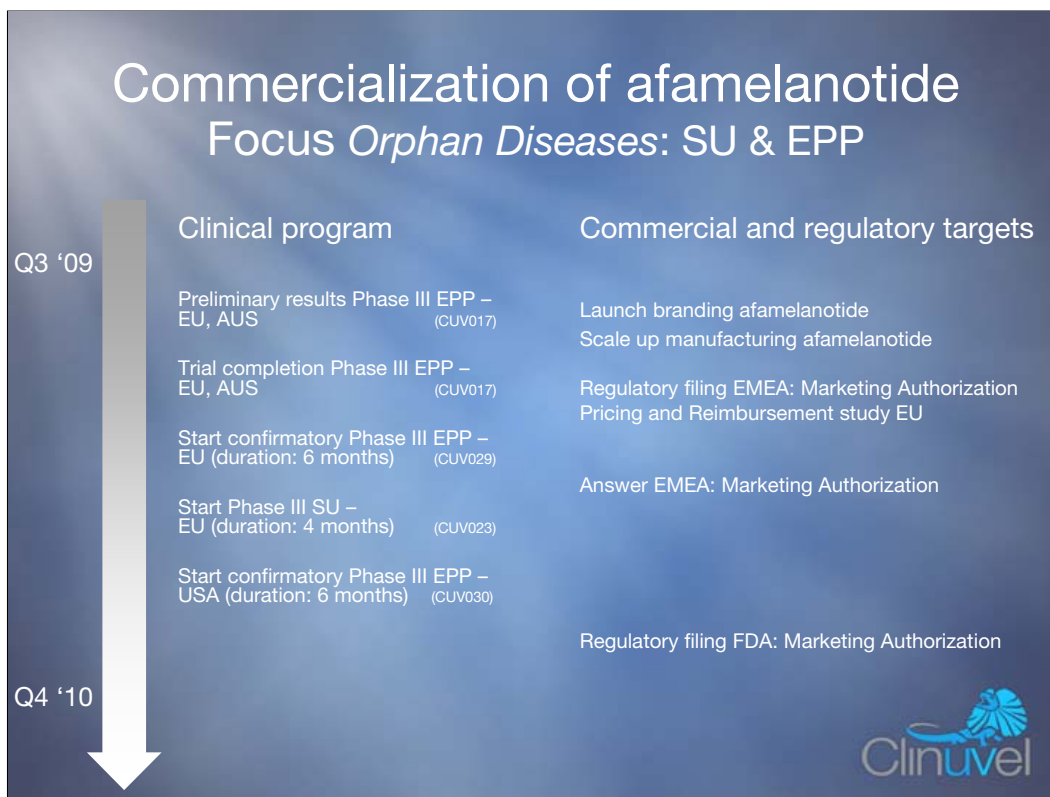
In EPP, afamelanotide has the potential to reduce maximum severity of phototoxic reactions and to reduce the total severity of phototoxic reactions during spring and summer months (Phase III Swiss 12-months results, January 2009).

In SU, the tolerance of the skin to light of various wavelengths and intensities was increased following administration of afamelanotide (Phase II results, July 2009).

References:

Dunn, R et al, (2009). "Afamelanotide, an  $\alpha$ -melanocyte stimulating hormone (MSH) agonist reduces phototoxicity in Erythropoietic Protoporphyrria (EPP), as tested under laboratory conditions." *Australasian Journal of Dermatology*. 50 Suppl. 1:A12-A13, 13 May.

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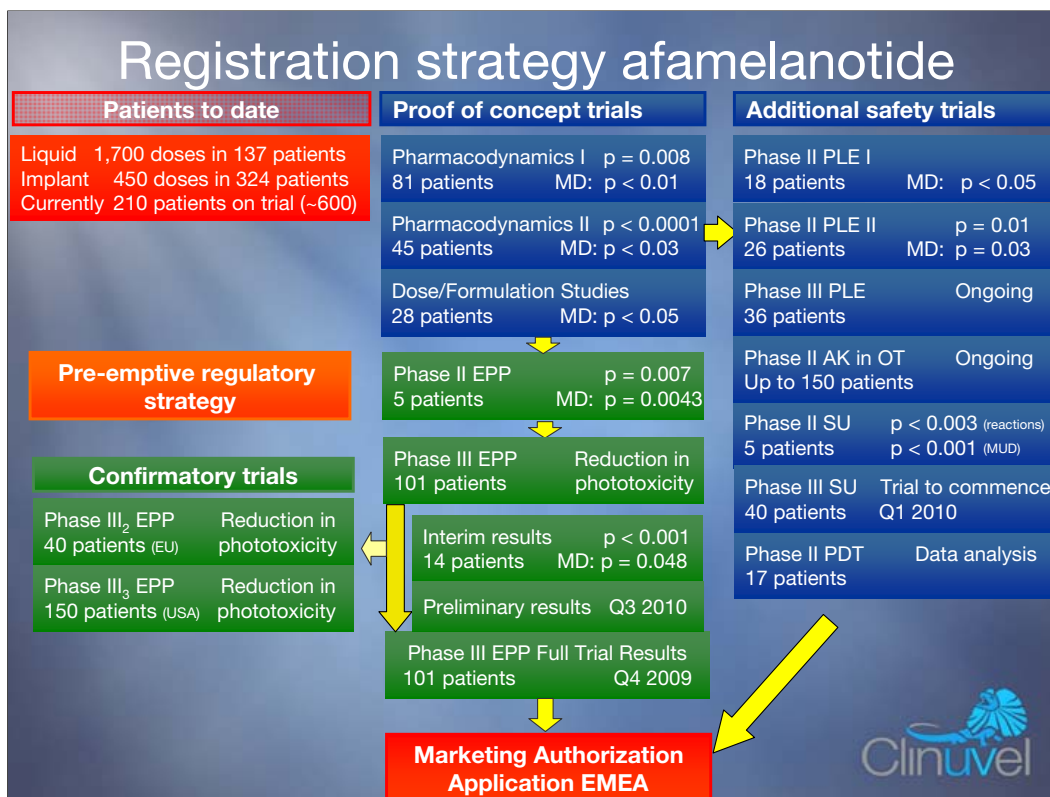


Clinical and commercial timeline for the two orphan indications.

While filing in Europe is under way, confirmatory Phase III EPP trials are planned in Europe and USA: additional safety data to maximise probability of approvals and speed to market in a tight regulatory environment.

By the completion of the program, the company will have administered 4000 doses in 800 patients, more than usually seen in the development of orphan drugs.

Management is now increasingly focused on branding, manufacturing and pricing.



Orphan drug strategy to develop afamelanotide for patients who have not yet received adequate medicinal therapy.

The middle column illustrates Clinuvel's main clinical program in porphyria (EPP) for which the company anticipates to file for registration upon successful completion of trial CUV017 where results are expected in Q4 2009.

The right column shows additional safety data.

The left column illustrates Clinuvel's pro-active regulatory strategy whereby, in anticipation of regulatory reviews, the company undertakes two more clinical trials for additional efficacy and safety. The pre-emptive strategy is unique to Clinuvel.

## Summary

- First-in-class, afamelanotide
- Strong cash reserves
- Proprietary technology
- Phase III porphyria (EPP) complete Q4/09
- MAA: EMEA first



Photoprotection in orphan diseases

