



## Overview from CEO

Dear patients, physicians, shareholders,

The complexity of Clinuvel's regulatory operations has increased this year. Regulatory engagement with the various authorities worldwide has become more and more common as we near the filing for our first marketing authorisation. Much effort is required by our global clinical team to coordinate the comprehensive program in 3 continents and more than 40 clinical sites. We work intensely with our manufacturers to ensure an in-time supply of our exclusive drug formulation, while compiling the necessary manufacturing records in aid of our filings. In April 2008, we reached a breakthrough when EMEA, FDA and Swissmedic – after thorough review of our dossier – granted Clinuvel orphan drug designation (ODD) for the use of afamelanotide in EPP.

In the past four weeks, Clinuvel joined a select group of global companies with a **doubly designated orphan drug** in development. We now have an ODD to treat solar urticaria (SU), a rare and severe skin disorder characterized by acute edema formation of the skin as well as for protoporphyria (EPP). There is no adequate therapy currently available for either disease.

This month our team received the all-clear from the Data Safety Monitoring Board (DSMB) for the **release of results of the pilot study (CUV016) in SU**. To be able to arrive at conclusive results, 5 therapy resistant patients in Manchester were subjected to thorough clinical tests. One important tool was photoprovocation, a test used in diseases such as SU to reach conclusive diagnosis. All patients were exposed to 8 differing wavelengths of light with and without the drug. Statistical evaluation showed significant efficacy after administration of afamelanotide.

It should be mentioned that the assistance of the leading experts in photodermatology and photobiology over the past 2 years has been crucial in arriving at these results. I express my gratitude to all who have been involved in any stage of this unique trial. It is due to their perseverance that we achieved these positive results. This outstanding clinical result has prompted the decision to progress the development of afamelanotide for this second orphan disease.

The commercial relevance of these results may be even more significant when looking at **the biofysical provocation** data from both the erythropoietic protoporphyria (see results January 2009) and SU trials. Both diseases symptoms are evoked by exposure of the skin to light of wavelengths ranging from 300 to 600 nanometers, in simpler terms, the effects of UV and visible light.

Although these data are promising, Clinuvel's principal objective – and a prerequisite for long-term regulatory

success - remains drug safety. Continuous development and vigilance on drug safety overrides any other corporate goal to successfully developing this novel drug to market.

In the first quarter, Clinuvel joined the **ASX-300**; one of a handful of biopharmaceuticals to do so in Australia. Trading volumes stabilized shortly around Australian financial year end in June. Overall, we have seen a modest recovery on the ASX, which positively affected Clinuvel's enterprise value. The share register has shown stability among the top 50 holdings, who represent approximately 70% of outstanding equity. Another positive sign was the addition of a new international institution to our register. With A\$37.5M currently in reserves, the company is funded to file afamelanotide for marketing authorization (MAA).

In May, we hosted a successful **global scientific meeting in Vienna**, Austria, where several leading, independent physicians and international heads of departments participated in a symposium on afamelanotide. The overall objective was to gauge the academic opinions and provoke an active discussion on the use of our drug in the elected photodermatoses (UV and light related diseases). Universal scientific progress on skin pigmentation, related pharmacology and disease states were reviewed. It was concluded and confirmed by the attendees that the current afamelanotide formulation holds firm promise as a medicinal drug. Clinuvel will continue to seek peer review by organising these academic meetings annually.

Looking internally, the worldwide Clinuvel team continues to evolve as more specialized knowledge is required in the final stages of filing. From my position, it is a privilege to witness the caliber of talent in Clinuvel. Special thanks go towards Drs Agersborg and Wright who both successfully drive Clinuvel's scientific program.

We announced earlier this year that we expect the PDT Phase II results, PLE Phase III results and completion of the EPP Phase III trials to be accomplished during the course of this year. Clinuvel's objective to obtain final results from the global study in EPP, a prerequisite to make our first regulatory filing in Europe remains on the critical path.

Various clinical, regulatory corporate milestones are pending and I invite you to look out for the remainder of 2009.

**Philippe Wolgen, MBA MD**

### Inside:

Establishing a Phase III trial for Solar Urticaria (SU)  
Events where Clinuvel is represented

### Important date:

Clinuvel's AGM, November 13, 2009

## Share Price

### Shares on issue

303,148,665

Clinuvel is listed on XETRA (UR9) and has a level 1 ADR (CLVLY)

### Average Daily Volume:

(Past 6 months)

ASX: 280,751

**Cash/Asset Balance:** A\$37.5million

**Average Monthly Cash Burn Apr-Jun '09**

<A\$1.3m



## Solar Urticaria

### About Solar Urticaria (SU)

SU is a skin disorder marked by an acute allergic response following UV or sun exposure. Symptoms can be systemic, such as anaphylaxis, breathing difficulty, nausea and headaches. Immediate localized reactions vary from characteristic 'wheal' formation and erupting flares on exposed skin sites, to swelling of soft tissues. Current available treatment is only partially effective and consists of anti-histamines, immunotherapy and plasmapheresis (blood purification). It is estimated that 3-4 people per 100,000 suffer from SU worldwide.

### Afamelanotide and Solar Urticaria – establishing a Phase III trial

Clinuvel's Phase II trial of afamelanotide in SU has shown that the drug has potential to reduce the risk of incapacitating reactions to UV and sunlight in SU patients (company announcement July 15). The company is now accelerating its clinical program for SU to Phase III; a study to determine afamelanotide's safety and efficacy in a larger group of SU patients.

For the Clinuvel team, a new study involves a number of steps before the first patient can be recruited. Firstly, a new study protocol is designed. The protocol provides framework for the study, establishing the scientific questions that the study seeks to answer, the length of the study and the size of the patient population to be recruited. The study protocol will provide inclusion and exclusion criteria for patients to participate.

Protocols are usually designed with assistance from leading physicians in the field to ensure that the study's objectives can be met. Clinuvel's recent Orphan Drug Designation for afamelanotide to treat SU entitles the company to scientific assistance from the EMEA for the Phase III study in Europe.

Once all regulatory approvals have been received, the study can formally start. Clinuvel anticipates the start of the study in the spring of the Northern Hemisphere 2010.

## Events where Clinuvel is represented

### Recent

- SCOPE (Skin Care in Organ Transplant Patients Europe) Annual Meeting – Thessaloniki (May)
- 7<sup>th</sup> World Congress on Melanoma & 5<sup>th</sup> Congress of the European Association of Dermato-Oncology (EADO) – Vienna (May)
- Clinuvel's Global Scientific meeting – Vienna (May)
- 10<sup>th</sup> International Congress of Dermatology – Prague (May)
- International Porphyria meeting "Porphyrins and Porphyrins 2009" – Stockholm (June)
- Skin & Cancer Foundation & RACGP Dermatology conference for general practitioners – Melbourne (July)

### Upcoming

- Thredbo Biotech Summit – Thredbo, Australia (August)
- 13<sup>th</sup> Congress of the European Society for Photobiology – Wroclaw, Poland (September)
- Rodman & Renshaw Annual Global Investment Conference – New York (September)
- Sachs Biotech in Europe Investor Forum – Zürich (September)
- 15<sup>th</sup> meeting of the European Society for Pigment Cell Research (ESPCR) – Munster, Germany (September)
- 18<sup>th</sup> Congress of the European Academy of Dermatology and Venereology – Berlin (October)
- Gastro 2009 – London (November)

## Online communications

Clinuvel recently launched its own Twitter feed, providing news and views on the company and our field. To follow Clinuvel on Twitter, log onto [www.twitter.com/ClinuvelNews](http://www.twitter.com/ClinuvelNews).

To coincide with the release of the SU results, Clinuvel released a new podcast featuring Chief Scientific Officer Dr Hank Agersborg discussing the results and the year ahead for Clinuvel. To hear this podcast, and to view the company's other webcasts, log onto [www.clinuvel.com](http://www.clinuvel.com).

### Clinuvel on Twitter



Join us as Australia's afamelanotide goes global.

## Next value drivers

- PDT Phase II results
- PLE Phase III interim results

### About afamelanotide

Afamelanotide is an analogue of  $\alpha$ -MSH, a peptide which activates the body's natural ability to produce eumelanin, the dark pigment of the skin which is known to offer 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.



Clinuvel's 16mg afamelanotide implant

### 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 Protoporphyrria (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.

Contact Us:	Head Office Australia:	Swiss Office:	US Office:
If you have a question related to investor relations, please email us at <a href="mailto:investorrelations@clinuve.com">investorrelations@clinuve.com</a> <a href="http://www.clinuve.com">www.clinuve.com</a> Twitter: @ClinuvelNews	Clinuvel Pharmaceuticals Ltd 11/330 Collins St Melbourne, Victoria 3000 Tel: +61 3 9660 4900 Fax: +61 3 9660 4999	Hauserstrasse 14 8032 Zürich Switzerland Tel: +41 44 253 750 0 Fax: +41 44 253 750 1	Our US office is relocating shortly. More information will be available soon. Please contact the Head Office for all enquiries.

Clinuvel is an Australian biopharmaceutical company focused 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