# Clinuvel Communiqué

## APRIL 2012 US BULLETIN



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### CEO OVERVIEW: US PROGRAM UPDATE

Dear shareholders,

Given the positive news flow from the US, I am compelled to summarise the activities of the past weeks and put these in context of the overall development of SCENESSE® (afamelanotide 16mg).

Longevity in pharmaceutical development is necessary to generate and evaluate long-term data providing evidence of safety, certainly when it comes to new drugs (so called new molecular entities). Safety has been at the forefront of Clinuvel's mind since starting the program in erythropoietic protoporphyria (EPP) in 2006, and this topic is the main one when regulatory agencies review a novel dossier. Our decision to focus on drug safety over the years is now starting to reap regulatory rewards. By optimising and modifying the chemistry of the afamelanotide molecule in 2006 and innovating the formulation, and deeper research in biological response, we adopted a company-wide approach to focus on drug safety and pharmacovigilance.

The outcome of the FDA meeting on 12th March therefore was lent more significance since safety has well been demonstrated in the EPP populations globally. Yet we must also bear in mind that continuous use in patients in years to come will provide the ultimate proof of safety. So far so good, with five years of clinical use data in EPP and more than 10 years in total in all populations tested. We have a fair indication of the pattern of safety data seen. These data give us reason to be optimistic yet we will continue to monitor the continuous use in all our patients, even after marketing authorisation.

The FDA discussion was conducted in a most professional and pleasant fashion, whereby I was surprised on the day by the level of acceptance of SCENESSE®, the support from the Agency to finalise the development in US EPP patients as well as the appraisal expressed to have developed a remedy for these patients.

The results of CUV029 and CUV030 were decisive factors, although we suspect that patients – individually and through formal patient associations – have also played a large role in the changed attitude of the FDA. In the fall of last year the FDA invited a prominent physician and two patients to record their testimonies of the disease and lack of available treatment. A positive "End-of-Phase II meeting" is a tremendous outcome for any company, but specifically for Clinuvel's teams who have never ceased to work towards this goal despite the challenges along the way. I congratulate our team in overcoming the major US hurdle of obtaining a positive "End-of-Phase II meeting".

Philippe Wolgen

## US PHASE III ERYTHROPOIETIC PROTOPORPHYRIA (EPP) PROTOCOL

We now have reached an in principle agreement with the FDA to accelerate the final Phase III study of SCENESSE® (afamelanotide 16mg implant) in the orphan disease EPP. The company is working diligently to finalise details of this study (CUV039) with an expected start date in May 2012. CUV039 will be a randomised, double blind, placebo-controlled study of SCENESSE® in adult EPP patients. Patients will receive three SCENESSE® or placebo implants during the study, which will last six months.

Up to seven centres will be involved in CUV039, with the aim of recruiting approximately 75 patients. The study's planned primary endpoint is to determine whether SCENESSE® enables patients to expose their skin to sunlight without experiencing pain, in particular at the most light (UV) intense periods of the days between 10am-6pm. Pending final approval from the FDA and local ethics boards (IRBs) Clinuvel expects results from the study in Q1 2013.

In the meantime the response from US patients has been phenomenal and much appreciation is being expressed by this community to finalise the development of SCENESSE® in the US.

## FDA RELEASES EPP PATIENT INTERVIEWS FOOTAGE

Following the finalisation of the US Phase II EPP study (CUV030) in 2011, the FDA had invited – independent of Clinuvel – two patients involved in the clinical study, along with the Principle Investigator, Dr Robert Desnick of Mt Sinai Medical School, New York, to discuss the study, EPP, and the impact of the disease on their lives. The two patients – Mike and Mat – spoke at length about growing up and living with EPP with Dr Tim Cote – then head of the FDA's Office of Orphan Products Development (OOPD) – and other members of the FDA. Dr Desnick provided his professional view of EPP and how the understanding of the field has developed. The FDA has since released footage from the meeting which can be viewed on its website. Following the FDA meeting, Mike also posted about his experiences on the American Porphyria Foundation's blog.

The FDA's initiative is to be commended and enhances the understanding of disease, need to find a pharmaceutical treatment and provides insight in the use of SCENESSE® in EPP.

To view the FDA's site, logon to: http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/VideosPatientswithRareDiseasesandConditions/ucm266593.htm

To viw Mike's blog post, logon to http://porphyriafoundation.blogspot.com/2011/05/day-at-fda.html

## VITILIGO PROGRAM PRESENTATION AWARDED

Data on repigmentation and further clinical observations from the open label Phase II US pilot trial of SCENESSE® in patients with vitiligo (CUV102) were presented at both the Meeting of the Vitiligo Working group and the Skin of Color Society Symposium in San Diego on March 15. Both meetings were held to coincide with the 70th Annual Meeting of the American Academy of Dermatology, the world's largest dermatology meeting which attracted over 16,500 delegates in 2011.

Dr Oma Agbai, co-investigator for the CUV102 study at Henry Ford Hospital in Detroit, Michigan, presented observations from the CUV102 study at both events and received the Best Resident/Fellow Presentation Award for her presentation to the Skin of Color Society meeting. We recognise the significance of this award and congratulate Dr Agbai and her colleagues in Detroit for this prize of excellence!

SCENESSE® is being tested as a repigmentation therapy in combination with narrowband UVB light therapy in vitiligo, a pigmentary disorder affecting more than 45 million individuals. The first observations are very positive and further results from the treatment phase of the CUV102 study are expected later this year.