Clinuvel demonstrates positive treatment effect of afamelanotide in US Phase II study

Analyses from US confirmatory study demonstrate a dramatic improvement in Quality of Life from SCENESSE® (afamelanotide 16mg) in the 'orphan' disease erythropoietic protoporphyria (EPP)

Melbourne, Australia and Baar, Switzerland, November 3, 2011

Executive summary

- EPP patients who received afamelanotide (active drug) were able to spend more time in direct sunlight between 10 AM and 3 PM and 10 AM and 8 PM (p=0.036, p=0.025).
- Photoprovocation on the back and hand in a subset of patients showed a significant treatment effect up to Day 60 (p=0.019 to p=0.045, depending on the study day and body site tested).
- Afamelanotide significantly improved patients' Quality of Life (QoL) as measured by an EPP-specific QoL questionnaire at Day 180 (p<0.001) and at Days 60 and 120 (p=0.001 and p=0.003). The generic DLQI was insensitive to changes in quality of life in EPP (non-significant).
- All treatment centres (6) reported positively on the trial and treatment effect and requested afamelanotide 16 mg for further use on behalf of their patients (FDA pending).
- Data Monitoring and Safety Board (DSMB) reviewed the analyses and deemed the drug safe for further use on the basis of the adverse event profile seen in this and other studies.

Clinuvel Pharmaceuticals Limited (**ASX: CUV; XETRA-DAX: UR9; ADR: CLVLY**) today announced that analyses of its Phase II US study in EPP (CUV030) had shown a clinically relevant positive prophylactic treatment effect for patients who had been administered SCENESSE® (afamelanotide 16mg controlled-release formulation).

SCENESSE® is the first photoprotective drug developed as an orphan product for the prevention of symptomatic EPP. Clinuvel is currently finalising a Marketing Authorisation Application (MAA) for SCENESSE® for submission to the European Medicines Agency (EMA) before the end of 2011.

STUDY DESIGN

CUV030 was a randomised placebo-controlled trial consisting of two parallel treatment arms conducted in six different US academic centres which recruited a total of 77 EPP patients. The drug was tested during six months of spring and summer under conditions of use. Patients recruited were evenly distributed over all six university centres.

This study and its objectives were designed in conjunction with the European Medicines Agency (EMA) following advice through the Protocol Assistance (PA) program obtained in 2009 and global experts in porphyria management.

CHARACTERISATION OF DISEASE AND STUDY OBJECTIVES

EPP is reported as a serious and heavily disabling disease, whereby patients have learned to avoid ('adapted behaviour') the sun and UV exposure under ambient conditions to avert the emergence of phototoxic pain and burns. Characteristic of EPP patients – and different from other photodermatoses – is that they experience prodromal symptoms upon light and UV exposure, meaning that they are able to feel their dermal symptoms developing. This phenomenon causes them to escape daylight upon experiencing these first symptoms. Significantly, EPP patients are conditioned to avoid light and UV from childhood and through adapted behaviour have learned to live indoors and lead nocturnal existences.

The primary objective of evaluating afamelanotide in EPP patients was to determine whether the prophylactic effect has clinical benefit. The clinical relevance of the proposed treatment with afamelanotide is expected to allow patients to lead a life which includes exposing themselves to ambient light and to engage in outdoor activities. A similar, secondary objective was to assess the effect of treatment on the impact on Quality of Life (QoL).

RESULTS AND ENDPOINTS

Seventy-seven patients started the study and 68 completed study medication and all clinical visits. In total 12,254 days were evaluated during the six month study. An adaptive and compound statistical analysis was performed. Results of the study showed that SCENESSE® was well tolerated, allowed EPP patients to expose their skin to sunlight during the middle of the day and improved their Quality of Life (QoL). Overall the study demonstrated a strong clinical benefit to patients, despite their deeply learned behaviour to avoid reactions caused by sun exposure.

Overall, EPP patients who received afamelanotide (active drug) were able to spend more time in direct sunlight between 10 AM and 3 PM and 10 AM and 8 PM ($p=0.036$, $p=0.025$) in comparison to placebo patients. The indicated times are the periods of the highest UV intensity, equating to the 'brightest' times of the day when EPP patients are most at risk of developing symptoms. Patients on drug reported a three-fold increase in the median amount of time in direct sunlight compared to placebo. Consequently many patients on drug reported no pain or only mild pain compared to their previous life of experiencing severe phototoxic reactions.

A subset of patients was subjected to photoprovocation (laboratory testing) on the surface of the hand and lower back to assess the time and dose to provoke to minimal symptoms (MSD). Of 15 patients who started the testing, only six completed the four month provocation (40%). Although a positive trend was found in the first 60 days ($p=0.019$ to $p=0.045$), no statistical significant result was found for Days 90 or 120 when fewer patients were retested. The substantial reduction in participants was attributed to the rigors of the phototesting protocol.

In analysing the impact of drug on the Quality of Life (QoL), a positive difference was found between mean (average) scores recorded at baseline (before start of treatment) and at day 60 ($p=0.001$). A positive impact of treatment was also found between mean scores recorded at baseline and at day 120 ($p=0.03$) and day 180 ($p<0.001$). Similar results were not found when the more generic Dermatology Life Quality Index (DLQI) was used.

Most common adverse events were associated with implant administration (such as pain or bruising following injection) and transient nausea and headache. After reviewing and confirming all analyses and the safety data, the independent Data Safety Monitoring Board (DSMB) deemed afamelanotide safe for further use in man.

All study centres reported positively on the afamelanotide 16mg treatment and requested the drug on behalf of their patients for compassionate use. The FDA will decide whether Clinuvel should supply the drug after reviewing the analyses of this trial.

COMMENTS

Clinuvel's Chief Scientific Officer, Dr Hank Agersborg, said: "I am very pleased by these results. EPP is a disorder requiring patients to adapt their lives by avoiding ambient light and conducting a life of isolation. It is the first time we observed and quantified how the drug changes behaviour and quality of life."

Dr Robert J Desnick, Dean for Genetic and Genomic Medicine and Professor and Chairman Emeritus of the Department of Genetics and Genomic Sciences at Mount Sinai School of Medicine, New York, and a lead investigator on the CUV030 study commented: "The results clearly indicate that afamelanotide increased patient exposure to light without severe pain. Patient demand for ongoing treatment following the study indicates that there is a clinical benefit to the drug."

Dr Hank Agersborg concluded: "We are fully aware that in today's regulatory climate meeting study objectives and endpoints in smaller populations of patients is as important as demonstrating treatment effect and clinical relevance of the new proposed drug to obtain marketing authorisation. We now await the final results from the European Phase III study. If similar findings emerge from this study, Clinuvel will have sufficient data to support a submission to the EMA for SCENESSE® as a first line therapy for EPP. This is meaningful for patients because it will allow them to undertake activities which were never possible before because of the risk and consequences of sun exposure. Clinuvel will now enter a discussion with the FDA to assess the final requirements for our US EPP program."

– End –

About SCENESSE® (afamelanotide)
SCENESSE® is a first-in-class therapeutic being developed by Clinuvel, with the generic name (or INN) afamelanotide. An analogue of α-MSH, afamelanotide is a linear peptide which activates eumelanin of the skin, the dark pigment which is known to provide photoprotective properties (offering skin protection against light and UV radiation). SCENESSE® is administered underneath the skin as a dissolvable implant approximately the size of a grain of rice. For more information on SCENESSE® go to http://www.clinuvel.com/scenesse.

SCENESSE® is a registered trademark of Clinuvel Pharmaceuticals Ltd.

About Clinuvel Pharmaceuticals Limited
Clinuvel Pharmaceuticals Ltd (ASX: CUV; XETRA-DAX: UR9; ADR: CLVLY) is a global biopharmaceutical company focused on developing drugs for the treatment of a range of severe skin disorders. With its unique expertise in understanding the interaction of light and human skin, the company has identified three groups of patients with a clinical need for photoprotection and another group with a need for repigmentation. These patient groups range in size from 10,000 to 45 million. Clinuvel's lead compound, SCENESSE® (afamelanotide), a first-in-class drug targeting erythropoietic protoporphyria (EPP), is in Phase II and III trials in the US and Europe, and is expected to be filed before the end of 2011 for review by the European Medicines Agency. Based in Melbourne, Australia, Clinuvel has operations in Europe and the US. For further information please visit www.clinuvel.com

About Erythropoietic Protoporphyria (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 main accumulation of porphyrin. They manifest with either skin problems, neurological complications or gastro-intestinal problems (occasionally all).

EPP is a rare genetic disease found mainly in people with fair skin. It is characterised by severe phototoxicity (or intolerance to light) of the skin resulting in intolerable pain, swelling, and scarring, usually of the exposed areas such as the face, hands and feet. The pain experienced and expressed by EPP patients when their skin is exposed to light is reported as intolerable. EPP patients are often forced to remain indoors, severely affecting their quality of life.

For more information go to http://www.clinuvel.com/erythropoietic-protoporphyria/

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Clinuvel is an Australian biopharmaceutical company focussed on developing its photoprotective drug, SCENESSE® (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 SCENESSE® can or will be achieved;
- no assurances can be given by Clinuvel that, even if its development programme for SCENESSE® 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