Clinuvel completes pre-clinical study of SCENESSE® as combination therapy

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EXECUTIVE SUMMARY

- FDA requirement for combination therapy model replicating clinical studies protocol in vitiligo fulfilled
- Safety of the combination therapy confirms observations in clinical trials CUV102 and CUV103
- Clinuvel will request a guidance meeting with the FDA to discuss the upcoming vitiligo trial in North America
- Safety data add to the New Drug Application package to be submitted to the FDA for erythropoietic protoporphyria (EPP)
- Global experts agree on the lack of current satisfactory treatment in vitiligo

Clinuvel Pharmaceuticals **[ASX: CUV; Nasdaq International Designation ADR: CLVLY; Xetra-DAX: UR9]** today announced that that it has fulfilled the FDA requirement to demonstrate safety in a pre-clinical model prior to progressing further with the clinical development of the combination therapy of its drug SCENESSE® (afamelanotide 16mg) and narrowband UVB (NB-UVB) light in the pigmentation disorder vitiligo.

FDA REQUIREMENT

Clinuvel has completed one US Phase II clinical trial of SCENESSE® in vitiligo patients (CUV102), with a second study (CUV103) underway in Singapore. In both studies the drug has been used in combination with NB-UVB light to evaluate its safety profile and ability to repigment skin in vitiligo patients.

The results of CUV102 and preliminary results in CUV103 show that SCENESSE® in combination with NB-UVB light administered twice or thrice weekly had a good safety profile, and the optimal effectiveness of the combination was identified in patients of darker skin complexion (Fitzpatrick skin types IV, V and VI).[1]

The FDA communicated to Clinuvel that – prior to pursuing later stage clinical trials and seeking marketing authorisation for SCENESSE® in vitiligo in the US – the company would need to demonstrate the safety of the drug in combination with NB-UVB light, simulating the proposed human dose regimen in a pre-clinical model.

Now that the requirement has been completed, Clinuvel will request a guidance meeting (Type C) with the FDA to discuss the next clinical trial in vitiligo patients in North America.

RESULTS

While the main purpose of the pre-clinical study was to evaluate the combination therapy, with SCENESSE® administered at 28 days intervals and NB-UVB light given thrice weekly for the duration of 24 weeks, the effect of SCENESSE® administered at 28 days intervals alone for the duration of 24 weeks was also assessed. Safety of the combination therapy was confirmed, whereby the No Observed Adverse Effect level (NOAEL) of SCENESSE® was found to be higher than the current clinical dose level of 16mg monthly.

These results add further support to the long-standing pre-clinical safety profile of SCENESSE®. Over the past two decades, SCENESSE® has been thoroughly evaluated in an extensive toxicology programme to support EU and US marketing authorisations for the treatment of erythropoietic protoporphyria (EPP) as a mono-therapy, administered every 60 days. The non-clinical safety evaluation encompassed genetic toxicology at maximum concentrations/dose levels, reproductive and developmental toxicity studies at doses far in excess of the human dose, and single, repeat-dose and chronic toxicity studies.

Importantly, these safety data add further supporting data to the New Drug Application package to be submitted to the FDA for erythropoietic protoporphyria (EPP).[2]

VITILIGO

Vitiligo is a depigmentation disorder most conspicuous in patients of darker skin complexion (Fitzpatrick skin types IV, V and VI). Progression of vitiligo over large body surfaces is distressing and often leads to patients reporting a loss of identity.

The current standard of care in vitiligo consists of NB-UVB light with often disappointing clinical results and no or incomplete repigmentation. The global experts in vitiligo agree that no satisfactory treatment modality exists for vitiligo.

Results in the use of SCENESSE® to date from the CUV102 and CUV103 studies have shown that monthly doses of SCENESSE® for 4 to 6 months in combination with twice or thrice weekly administered NB-UVB light provides optimum repigmentation in patients with darker skin complexion. Results from the CUV102 study have been published in the *Journal of the American Medical Association - Dermatology*.[3]

COMMENTARY

"In evaluating SCENESSE® in combination with NB-UVB light, we needed to comply with a regulatory requirement to demonstrate the safety of our proposed treatment regimen in a pre-clinical combination therapy model," Clinuvel's Director of Clinical Affairs, Dr Emilie Rodenburger said.

"The results of the repeated administration of SCENESSE® show its lack of toxicity when given alone at 28 day intervals over a 24-week period, but also that safety is upheld when the drug is combined with NB-UVB light dosed thrice weekly.

"Safety of SCENESSE® supplied to our patients will always be our primary focus, and I am thrilled with these results. Our team will now engage the FDA to establish the pathways forward for the upcoming vitiligo trials," Dr Rodenburger said.

- End -

[1] See Clinuvel announcements "SCENESSE® successful in Phase IIa vitiligo study", December 19, 2012 and "Positive preliminary results in Singaporean vitiligo study", December 3, 2015.
[2] See Clinuvel announcement "FDA accepts SCENESSE® clinical data package for NDA submission", July 18, 2016.
[3] Lim et al (2015). Afamelanotide and narrowband UV-B phototherapy for the treatment of vitiligo: a randomized multicenter trial. *JAMA Dermatol*. 151(1):42-50. E-pub September 2014. Abstract online at http://www.ncbi.nlm.nih.gov/pubmed/25230094.

SCENESSE® (afamelanotide 16mg) is approved in Europe as an orphan medicinal product for the prevention of phototoxicity (anaphylactoid reactions and burns) in adult patients with EPP. The innovative nature of the therapy in the orphan disorder, the lack of available scientific instruments to adequately measure the therapy, ethical considerations and the drug's positive safety profile were some of the factors which led to the European marketing authorisation of SCENESSE®. Information on the product can be found on Clinuvel's website at www.clinuvel.com.

About Clinuvel Pharmaceuticals Limited

Clinuvel Pharmaceuticals Ltd (ASX: CUV; NASDAQ INTERNATIONAL DESIGNATION ADR: CLVLY; XETRA-DAX: UR9) is a global biopharmaceutical company focused on developing drugs for the treatment of a range of severe disorders. With its unique expertise in understanding the interaction of light and human skin, the Clinuvel has identified patient populations with a clinical need for photoprotection and for repigmentation. The worldwide prevalence of these patient groups range from 5,000 to 45 million. Clinuvel's lead compound, SCENESSE® (afamelanotide 16mg), was approved by the European Commission in 2014 for the prevention of phototoxicity

(anaphylactoid reactions and burns) in adult patients with erythropoietic protoporphyria (EPP). More information on EPP can be found at http://www.epp.care.
Headquartered in Melbourne, Australia, Clinuvel has operations in Europe, Switzerland, the US and Singapore.
For more information go to http://www.clinuvel.com.

SCENESSE® is a registered trademark of Clinuvel Pharmaceuticals Ltd.

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