SCENESSE® successful in Phase IIa vitiligo study

Combination of novel drug with NB-UVB achieves better, faster repigmentation in vitiligo patients

- The primary study objective achieved: extent of repigmentation (VASI/VETF scores: p=0.025/p=0.023)
- Patients with darker skin types (Fitzpatrick IV-VI) responded best to the SCENESSE® combination treatment (VASI scores: p=0.037)
- The time to first repigmentation showed a strong favourable trend towards SCENESSE® treatment (p=0.086)
- The secondary study objective was met: no significant safety issues were reported.

Baar, Switzerland and Melbourne, Australia, December 19 2012

Clinuvel Pharmaceuticals Limited (**ASX: CUV; XETRA-DAX: UR9; ADR: CLVLY**) today announced successful, statistically significant results from its US Phase IIa pilot study (CUV102) of the novel drug SCENESSE® (afamelanotide 16mg implant) in the common pigmentation disorder vitiligo. These results show that SCENESSE® in combination with narrowband UVB (NB-UVB) therapy significantly improves repigmentation of depigmented lesions in vitiligo patients compared to NB-UVB as a monotherapy.

VITILIGO

Vitiligo is a common skin disorder, affecting approximately 45 million people, in which particular pigment producing cells of the skin (melanocytes) appear to become dysfunctional. As a result, lighter depigmented patches of skin (lesions) appear in different parts of the body due the loss of melanin (pigment). Vitiligo therapy is primarily intended to arrest depigmentation and to stimulate repigmentation of affected skin as a secondary action. There is no known cure for vitiligo. The current standard of care is treatment with NB-UVB, a controlled light therapy given in 2 to 3 sessions per week over the course of 12 to 18 months. The response rate to NB-UVB is low and repigmentation is incomplete, with combination therapies often employed in an attempt to enhance repigmentation.

CUV102 - STUDY OBJECTIVES AND DESIGN

SCENESSE® is a first-in-class drug which activates melanin in skin by mimicking the body's natural melanin production process. Developments in Clinuvel's clinical program, and broader progress in the field of human pigmentation over the past three years, have led to widespread support from the medical and patient communities to trial SCENESSE® as a repigmentary agent in vitiligo. CUV102, an open-label Phase IIa study conducted in three US expert centres (The Vitiligo & Pigmentation Institute of Southern California in Los Angeles, The Henry Ford Hospital in Detroit and Mount Sinai Hospital in New York), was designed as the first study to explore the potential of SCENESSE® to repigment depigmented skin in vitiligo.

The primary endpoint of the CUV102 study was to compare the efficacy – as expressed in VASI and VETF scores[1] – of SCENESSE® with NB-UVB in comparison to NB-UVB as a monotherapy in the treatment of generalised vitiligo. In this study the speed of repigmentation after drug administration and depth (degree) of repigmentation was evaluated. The secondary endpoint was to determine the safety of the combination treatment as well as comparing the stability of pigmentation.

Fifty-four patients were enrolled across the three study sites and randomly assigned to one of the two treatment groups. Group A (active) received one month of NB-UVB monotherapy, followed by monthly doses of SCENESSE® and combination NB-UVB for four months, then a final month of NB-UVB monotherapy. Group B received NB-UVB monotherapy for six months. The inclusion criteria sought to evaluate patients with a minimum of 15% to 50% of total body depigmentation with Fitzpatrick skin phototypes III-VI (dark skin).

CLINICAL TRIAL RESULTS

Forty-one (75.9%, n=41) patients completed the treatment. Thirteen patients withdrew due to their inability to comply with the demanding treatment protocol, or, in the case of five patients, due to the intensity of pigmentation

experienced. Overall the combined treatment was well tolerated and no serious drug-related adverse events were reported.

The primary endpoint was the extent of repigmentation between Day 0 and Day 168 as measured by the VASI and VETF scores (standard scoring methods for vitiligo). The extent of repigmentation in the SCENESSE®/NB-UVB group was significantly greater than observed in the NB-UVB-alone group (VASI, p=0.025; VETF p=0.023; 95% CI).

As a subset analysis reflected by the VASI scores, significantly better, more complete and deeper repigmentation was observed for those patients with the darkest skin complexion (phototype IV-VI, n=24) who had received the combination therapy compared to in comparison to those on monotherapy (p=0.046; 95% CI).

The time needed to observe the first signs of repigmentation in patients was also evaluated. The VASI scores showed that those patients who had received the combination therapy achieved earlier repigmentation than those on monotherapy (median time 43 days versus 68 days, p=0.086; 95% CI).

The quality of life (QoL) of patients was measured with the DLQI[2]. The impact of the treatment on QoL was found to be inconclusive. This is likely to have been due to the inadequacy of the questionnaire to measure the impact of repigmentation in vitiligo patients.

After six months follow-up of all patients, stability of the treatments will be evaluated.

DISCUSSION

"I think this is an exciting, major advancement for vitiligo, a disease for which we do not have adequate effective treatments," Dr Mark Lebwohl, Professor and Chair of Dermatology at Mount Sinai Hospital in New York and an investigator on the CUV102 study, said. "We were thrilled with the speed at which the pigment returned."

"Until now all treatments had taken many years to achieve repigmentation in vitiligo and patients had great difficulty complying with the rigours of light treatment regimes. We finally have a treatment that allows us to repigment patients much more quickly."

"The clinical significance of these observations from CUV102 is most promising. The proposed combination therapy with SCENESSE® enables a faster and more complete repigmentation for people with vitiligo," Clinuvel's acting Chief Scientific Officer, Dr Dennis Wright said. "This has the potential to substantially reduce the current regimen of 18 months of NB-UVB treatment thrice per week, while the new treatment achieves a better outcome for patients, enabling them a life without being stigmatised".

"Encouragingly, patients with skin phototype IV and above respond very well to treatment. These are patients for whom vitiligo can be the most visible and have the most devastating impact on quality of life. Overall, the feedback from patients and physicians has been extremely positive as to the potential of SCENESSE® becoming the standard of care in the treatment of vitiligo."

Pending regulatory filings and approvals, Clinuvel considers advancing its clinical program for vitiligo to a Phase IIb study, likely to be conducted first in Europe and Asia, with the goal of making SCENESSE® available to vitiligo patients as a repigmentation therapy.

Clinuvel is currently awaiting the outcome of a submission to the European Medicines Agency to obtain marketing authorisation for SCENESSE® for the treatment of the rare light intolerance disorder erythropoietic protoporphyria (EPP).

- End -

[1] The Vitiligo Area Scoring Index is a validated measure to assess the extent of vitiligo involvement in patients; the Vitiligo European Task Force score equally measures skin surface to assess the areas affected by vitiligo.
[2] The validated Dermatology Life Quality Index provides a measure of impact of disease in a number of skin disorders.

<u>A presentation outlining the CUV102 study and results has been released to accompany this announcement.</u>

Appendix 1 (Following Code of Best Practice, ASX)
Name of trial
A Proof of Concept Study to Compare the Efficacy and Safety of Subcutaneous, Bioresorbable Afamelanotide Implants and Narrow-Band Ultraviolet B (NB-UVB) Light versus Narrow-Band Ultraviolet B (NB-UVB) Light Alone in the Treatment of Nonsegmental Vitiligo* (CUV102).

Primary objective
To compare the efficacy of afamelanotide implants and NB-UVB light in the treatment of vitiligo.

Secondary objectives
1. To determine the short-term safety of both treatments in patients with vitiligo;
2. To compare the maintenance of pigmentation achieved with both treatments in patients with vitiligo.

Blinding status
Open label proof of concept.

Product development status
Good Manufacturing Practice (GMP) Standard.

Treatment method, frequency, dose levels
Patients randomised in equal numbers into two treatment groups:
- Group A received both afamelanotide implants (one implant administered on Days 28, 56, 84 and 112; 4 implants in total) and NB-UVB light (administered thrice weekly for 6 months, 72 treatments in total);
- Group B received NB-UVB light only (administered thrice weekly for 6 months, 72 treatments in total).

Number of trial subjects
54 enrolled, 41 completed

Subject selection criteria
Adult subjects with Fitzpatrick skin types III-VI diagnosed with stable or slowly progressive vitiligo of 15-50% body involvement. Patients must have been diagnosed with vitiligo within the past five years of study commencement and not received NB-UVB treatment within six months of the screening visit.

Trial location
Three sites across the United States of America.

Trial duration
Six month treatment phase with six month follow-up period.

Trial standard
In compliance with Good Clinical Practices (GCP) and ICH guidelines.

* Since the commencement of study CUV102 it has been agreed by the international medical community that 'nonsegmental vitiligo' no longer be used to describe the most common form of the disease, which is now referred to as 'vitiligo'. This instance has been maintained to correspond to international clinical trial databases.

Appendix II: 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/en/scenesse.

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), has completed Phase II and III trials in the US and Europe.

In February 2012 SCENESSE® was filed for review by the European Medicines Agency for EPP. A confirmatory six month Phase III US EPP trial started in May 2012. Presently, there is no known effective treatment for EPP and SCENESSE® has been granted orphan drug status. Based in Melbourne, Australia, Clinuvel has operations in Europe and the US. For further information please visit www.clinuvel.com

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About Vitiligo
Vitiligo is a common skin disorder in which the pigment producing cells of the skin (melanocytes) are absent or demonstrate lack of activity. As a result, lighter depigmented patches of skin (target lesions) appear in different parts of the body due the lack of melanin (pigment). The exact cause of vitiligo is unknown, but it is generally recognised that an autoimmune component plays a role in this disease. Between 0.1-2% of the global population is affected by vitiligo, affecting all races. Vitiligo causes significant psychological and emotional distress.

For more information go to http://www.clinuvel.com/en/vitiligo/

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