CLINUVEL

ASX ANNOUNCEMENT

Melbourne, Australia, 04 March 2024

ASX: CUV | **Börse Frankfurt**: UR9 | **ADR Level 1**: CLVLY

SCENESSE® provides photoprotection, improves QoL in variegate porphyria

Results from CUV040 study show clinical benefit over six months of treatment

EXECUTIVE SUMMARY

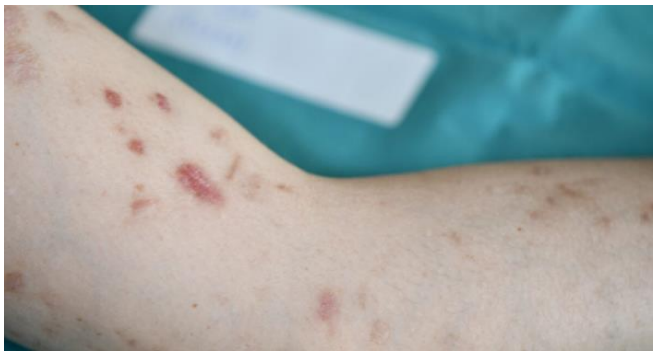
SCENESSE® provides clinical benefit to variegate porphyria (VP) patients (CUV040, n=6)

- primary endpoint (CGIC)[1] shows positive change in disease severity (6 months)
- patients increased time spent outdoors in direct light
- reduction in skin symptoms (dermal symptoms, new lesions and skin fragility)
- improvement in patient quality of life
- positive safety profile over six months

CLINUVEL today announced positive results from its first Phase II study evaluating SCENESSE® (afamelanotide 16mg) as a treatment for variegate porphyria (VP) patients. Analyses from the CUV040 study showed that SCENESSE® provides systemic photoprotection to VP patients, reducing disease severity and clinical symptoms, and improving patients' quality of life.

UNMET NEED IN VARIEGATE PORPHYRIA

VP is a metabolic disorder which leads to the accumulation and storage of excessive porphyrin intermediates in the skin and liver. As a result, sun and light exposure cause severe dermatological symptoms for VP patients: dermal lesions, ulcers, and blistering, as well as skin fragility which delays healing. There are no approved treatments to prevent or address the dermatological symptoms in VP.



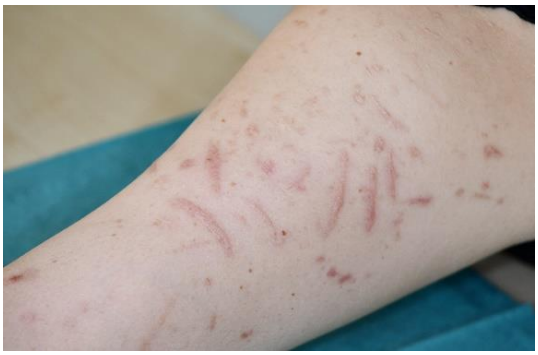


***Figure 1 (previous page)**: Sun and light exposure cause severe dermatological symptoms in VP patients. Wounds, lesions, and scars on the upper arms of a variegate porphyria patient in the CUV040 study **prior** to treatment. Images courtesy of the investigator.*

SCENESSE® IN VP: REDUCED DERMATOLOGICAL SYMPTOMS, IMPROVED QOL

SCENESSE® provides systemic (full body) photoprotection and acts as a strong antioxidant.[2] The six-month CUV040 study evaluated whether the drug could offer systemic photoprotection to VP patients and reduce the impact of dermatological symptoms. Six adult VP patients with active dermal symptoms enrolled and commenced treatment in the spring and summer months, receiving six SCENESSE® doses and completing all study visits.

The validated Clinical Global Impression of Change (CGIC[1]) tool was used as the primary endpoint to assess changes in disease severity compared to baseline. All six patients experienced a positive change – improvement up to three times baseline scores – in disease severity after treatment. The average CGIC change was rated as "much improved", first changes observed as early as four weeks after the first treatment.

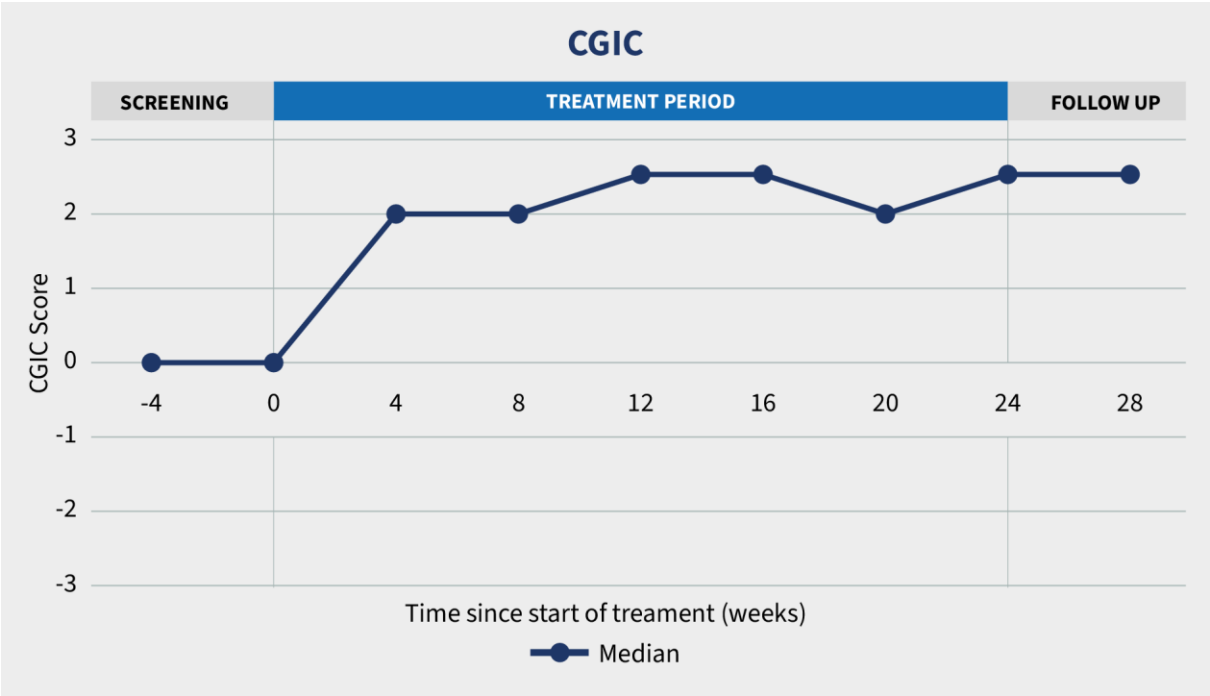


***Figure 2**: Median Clinical Global Impression of Change (CGIC) data from the CUV040 study. Patients' disease severity change is assessed on a 7-point scale ranging from positive (+3) to negative (-3). Assessments were made at each visit compared to baseline (week 0).*

Secondary endpoints measured the impact of SCENESSE® treatment on clinical symptoms, patients' ability to expose to light, and quality of life. Two physician assessment tools – the Investigator Global Assessment Visual Analogue Scale (VAS IGA) and 5-point Investigator Global Assessment (5-point IGA)[3] – determined the degree of skin dysfunction and disease at a given timepoint, with a median decline in disease severity compared to baseline.

Counts of new skin lesions (wounds, blisters and/or ulcers) on light-exposed skin revealed a decrease over time with the median lesion count decreased from 10.5 to 3 across the treatment period. All patients also experienced decreased fragility of sun exposed skin following treatment.

Through daily diaries, patients reported an increase in direct sunlight exposure over the treatment period compared to baseline, with up to a 24% median increase in the number of days spent outdoors.

Patients' quality of life and their ability to perform daily activities improved over the study. Analyses from the VP-derived QOLEB tool[4] – measuring the impact of disease on a scale of 0-60, where a lower score equates to a better quality of life – showed a median improvement from 30 at baseline to 20.5 four weeks after final treatment.

Treatment with SCENESSE® was well tolerated. All treatment-related adverse events were reported as mild or moderate in severity and generally consistent with its use in other patient groups.[1]

Commentary

"Today's results show a further indication of the potential of SCENESSE® to offer photoprotection for those patients affected by light and UV, providing patients a new life," CLINUVEL's Head of Clinical Operations, Dr Pilar Bilbao said.

"As a pilot study in VP, we have looked at a range of endpoints to understand the impact of the disease, how it presents in the clinic, and how we may be able to evaluate the photoprotective effect of novel treatment.

"These results give us the momentum to continue the development program for VP, establishing a larger clinical trial program and subsequently preparing and filing a marketing authorisation application," Dr Bilbao said.

– END –

[1] The CGIC uses a 7-point ordinal scale to assess outcomes relative to a baseline (pre-treatment) measure. The tool encompasses questions to assess patients' symptoms, signs, and functioning (work, school, family, friends), and treatment side effects. A zero (0) means no improvement from baseline, with scores to a maximum (+3) or minimum (-3) indicating that symptoms and/or functional status have improved or worsened, respectively. Higher scores therefore represent symptomatic improvement over time.

[2] SCENESSE® (afamelanotide 16mg), is approved for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP) in Europe, the USA, Israel, and Australia. EPP is a similar metabolic disorder to VP, part of a family of conditions known as porphyrias. The summary of product characteristics is available at www.clinuvel.com.

[3] Both the VAS IGA and 5-point IGA use Likert-like point scales – 11-point and 5-point, respectively – to determine the overall severity of skin disease. Lower scores on these tools equate to less severe disease.

[4] VP-QOL, 15 questions derived from validated QoL in Epidermolysis Bullosa questionnaire (VP-derived QOLEB) and the Work Productivity and Activity Impairment Questionnaire: General Health V2.0.

References

Bonkovsky, H. L., Dixon, N., & Rudnick, S. (2019). Pathogenesis and clinical features of the acute hepatic porphyrias (AHPs). Molecular Genetics and Metabolism, 128(3), 213–218.

Busner, J., & Targum, S. D. (2007). The Clinical Global Impressions Scale. Psychiatry (Edgmont), 4(7), 28–37.

Ramanujam, V.-M. S., & Anderson, K. E. (2015). Porphyria Diagnostics-Part 1: A Brief Overview of the Porphyrias. Current Protocols in Human Genetics, 86, 17.20.1-17.20.26.

About CLINUVEL PHARMACEUTICALS LIMITED

CLINUVEL (ASX: CUV; ADR LEVEL 1: CLVLY; Börse Frankfurt: UR9) is a global specialty pharmaceutical group focused on developing and commercialising treatments for patients with genetic, metabolic, systemic, and life-threatening, acute disorders, as well as healthcare solutions for specialised populations. As pioneers in photomedicine and the family of melanocortin peptides, CLINUVEL's research and development has led to innovative treatments for patient populations with a clinical need for systemic photoprotection, assisted DNA repair, repigmentation and acute or life-threatening conditions who lack alternatives.

CLINUVEL's lead therapy, SCENESSE® (afamelanotide 16mg), is approved for commercial distribution in Europe, the USA, Israel, and Australia as the world's first systemic photoprotective drug for the prevention of phototoxicity (anaphylactoid reactions and burns) in adult patients with erythropoietic protoporphyria (EPP). Headquartered in Melbourne, Australia, CLINUVEL has operations in Europe, Singapore, and the USA. For more information, please go to https://www.clinuvel.com.

Authorised for ASX release by the Board of Directors of CLINUVEL PHARMACEUTICALS LTD.

Head of Investor Relations

Mr Malcolm Bull, CLINUVEL PHARMACEUTICALS LTD

Investor Enquiries

https://www.clinuvel.com/investors/contact-us

Forward-Looking Statements

This release contains forward-looking statements, which reflect the current beliefs and expectations of CLINUVEL's management. Statements may involve a number of known and unknown risks that could cause our future results, performance, or achievements to differ significantly from those expressed or implied by such forward-looking statements. Important factors that could cause or contribute to such differences include risks relating to: our ability to develop and commercialise pharmaceutical products; the COVID-19 pandemic and/or other world, regional or national events affecting the supply chain for a protracted period of time, including our ability to develop, manufacture, market and sell biopharmaceutical products; competition for our products, especially SCENESSE® (afamelanotide 16mg), PRÉNUMBRA® or NEURACTHEL®; our ability to achieve expected safety and efficacy results in a timely manner through our innovative R&D efforts; the effectiveness of our patents and other protections for innovative products, particularly in view of national and regional variations in patent laws; our potential exposure to product liability claims to the extent not covered by insurance; increased government scrutiny in either Australia, the U.S., Europe, Israel, China and Japan of our agreements with third parties and suppliers; our exposure to currency fluctuations and restrictions as well as credit risks; the effects of reforms in healthcare regulation and pharmaceutical pricing and reimbursement; that the Company may incur unexpected delays in the outsourced manufacturing of SCENESSE®, PRÉNUMBRA® or NEURACTHEL® which may lead to it being unable to supply its commercial markets and/or clinical trial programs; any failures to comply with any government payment system (i.e. Medicare) reporting and payment obligations; uncertainties surrounding the legislative and regulatory pathways for the registration and approval of biotechnology and consumer based products; decisions by regulatory authorities regarding approval of our products as well as their decisions regarding label claims; our ability to retain or attract key personnel and managerial talent; the impact of broader change within the pharmaceutical industry and related industries; potential changes to tax liabilities or legislation; environmental risks; and other factors that have been discussed in our 2023 Annual Report. Forward-looking statements speak only as of the date on which they are made, and the Company undertakes no obligation, outside of those required under applicable laws or relevant listing rules of the Australian Securities Exchange, to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise. More information on preliminary and uncertain forecasts and estimates is available on request, whereby it is stated that past performance is not an indicator of future performance.

Contact:

Tel: +61 3 9660 4900
Fax: +61 3 9660 4909
Email: mail@clinuvel.com
Australia (Head Office), Level 22, 535 Bourke Street, Melbourne, Victoria, 3000, Australia