CLINUVEL INITIATES VARIEGATE PORPHYRIA PROOF OF CONCEPT STUDY

SCENESSE® to be clinically evaluated in second cutaneous porphyria

Melbourne, Australia, 01 October 2018

EXECUTIVE SUMMARY

- *Proof of concept Phase IIa study in genetic metabolic disorder variegate porphyria (VP)*
- *Six patients evaluated following up to six doses of SCENESSE® in 2019*

CLINUVEL PHARMACEUTICALS LTD **(ASX: CUV; XETRA-DAX: UR9; NASDAQ INTERNATIONAL DESIGNATION: CLVLY)** today announced that it has reached agreement with two European porphyria expert centres on a clinical trial protocol to conduct a Phase IIa proof of concept study evaluating the safety and effectiveness of SCENESSE® (afamelanotide 16mg) in variegate porphyria (VP). The study (CUV040) will start patient treatment in the northern hemisphere spring of 2019.

Currently, SCENESSE® is being prescribed by porphyria experts centres in Europe for the treatment of erythropoietic protoporphyria (EPP), a genetic disorder which causes absolute light intolerance due to a deficiency of ferrochelatase, an enzyme critical in the synthesis of haem. SCENESSE® was granted European marketing authorisation in October 2014.[1]

VARIEGATE PORPHYRIA

The porphyrias are a group of nine genetic metabolic diseases, including VP and EPP, characterised by specific enzyme deficiencies along the biochemical pathway of haem synthesis.

VP is a rare autosomal dominant inherited disorder resulting from the deficiency of the mitochondrial enzyme protoporphyrinogen oxidase (PPOX), the sixth enzyme of the haem biosynthesis pathway.

A debilitating and burdensome disease for patients, VP is classified as both a cutaneous and acute porphyria. The cutaneous symptoms are characterised by adult-onset blistering lesions (bullous symptoms, subepidermal vesicles) and chronic fragility (hypotrophy and hypoplasia) of sun and light-exposed skin, especially the back of the hands and the face. The propensity of the dermis to form wounds (lesions and erosions which form crusts, heal slowly or not at all, and are prone to infection) following the mechanical use of hands and feet further restricts VP patients in their daily activities. Typically, patients experience scarring of the face, hands and feet. Patients diagnosed with VP experience phototoxicity and suffer episodes in spring and summer when the atmospheric intensity of light increases. The acute neurovisceral symptoms may present as severe episodes as early as adolescence, with women more affected than men. Psychiatric disturbances, autonomic neuropathy and muscle weakness have been reported in some patients.

The reported prevalence of VP varies from 0.3 to 2 cases per 100,000 inhabitants but has been reported as more common in the Caucasian South African population (up to 1 in 300 people) due to a founder effect.[2] European prevalence varies from 0.32 to 1 cases per 100,000 inhabitants, whereas the reported prevalence in the US is 0.5 cases per 100,000 inhabitants.

Currently, there is no standard of care or alternative therapy for cutaneous VP symptoms. Patients are forced to lead a life sheltered from light and to avoid any mechanical contact with their skin surface or risk of triggering wounds and long-lasting ulcerations (lesions).

PROOF OF CONCEPT PHASE IIA STUDY DESIGN

The CUV040 study will be the first time SCENESSE® is administered to VP patients. It is planned that up to six doses of SCENESSE® will be administered to six patients during the northern hemisphere spring and summer months of 2019. Patients will be treated for up to six months with a follow-up of one month. The study will evaluate the impact of intervention with afamelanotide on the severity of skin disease in VP patients, measured with physician assessment tools. The extent of VP lesions will also be assessed, along with patient reported outcomes, including impact on quality of life.

Commencement of the study is subject to regulatory and ethical approvals at both the national and local level of both expert centres involved.

COMMENTARY

"This is the first time SCENESSE® will be evaluated in patients with VP, extending our clinical understanding of the product in the porphyrias," CLINUVEL's Director of Clinical Affairs, Dr Emilie Rodenburger said. "This family of disorders is relatively unknown but cause a level of human suffering not recognised or discussed in public. It is our hope that we can make a difference to these patients' lives.

"The proof of concept study, to be conducted at two porphyria expert centres, will help us gauge the safety and efficacy of SCENESSE® in a small group of patients, after which we can evaluate further potential use of the product. It will also be the first experience of a 28-day dosing cycle in any porphyria, mirroring that used in our vitiligo program," Dr Rodenburger said.

– End –

[1] SCENESSE® (afamelanotide16mg) is approved in Europe as an orphan medicinal product for the prevention of phototoxicity in adult patients with EPP. Information on the product can be found on CLINUVEL's website at www.clinuvel.com.

[2] Elder et al (2012). The incidence of inherited porphyrias in Europe. *J Inherit Metab Dis*. Horner et al (2013). Cutaneous porphyrias part I: epidemiology, pathogenesis, presentation, diagnosis, and histopathology. *In J Dermatol*. Singal & Anderson (2013). Variegate Porphyria. *GeneReviews®*. Online at https://www.ncbi.nlm.nih.gov/books/NBK121283/

Annex I: Trial summary

Name of trial

A Proof of Concept, Phase II, Open Label Study to Evaluate the Safety and Efficacy of Afamelanotide in Patients with Variegate Porphyria (VP)-related skin disease (CUV040).

Primary objective

Evaluate the impact of afamelanotide on the severity of skin disease in patients with VP.

Secondary objectives

- Evaluate the safety and tolerability of afamelanotide in patients with VP.
- Evaluate the impact of afamelanotide on the quality of life of patients with VP.

Blinding status

Open label.

Product development status

Good Manufacturing Practice (GMP) Standard.

Treatment method, frequency, dose levels

One controlled-release injectable afamelanotide 16mg implant every 28 days (up to six treatments in total).

Number of trial subjects

Six adult patients with a documented medical history of variegate porphyria.

Subject selection criteria
The participant must fulfil the following criteria:

- Male or female patient with a biochemically and/or molecular-genetically confirmed diagnosis of VP;
- Patients with VP-related skin symptoms. Skin symptoms characterised by fragility and erosions, blisters, miliae and/or hirsutism which may be present in light exposed skin areas;
- Aged 18-70 years.

Further inclusion and exclusion criteria may apply.

Trial location
Two European porphyria expert centres (pending regulatory and ethics committee approvals).

Duration of trial
Six months treatment with a one month screening period and a one month follow-up (eight months total).

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

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 and delivering treatments for patients with a range of severe genetic and skin disorders. As pioneers in photomedicine and understanding the interaction of light and human biology, CLINUVEL's research and development has led to innovative treatments for patient populations with a clinical need for photoprotection and repigmentation. These patient groups range in size from 5,000 to 45 million worldwide. 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, with the UK acting as the EU distribution centre.
For more information go to http://www.clinuvel.com.

SCENESSE® is a registered trademark of CLINUVEL PHARMACEUTICALS LTD.

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Forward-Looking Statements
This release to the Australian Securities Exchange and to press may contain forward-looking statements, including statements regarding future results, performance or achievements. These statements involve known and unknown risks, uncertainties and other factors which may cause CLINUVEL's actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Some of the factors that could affect the forward-looking statements contained herein include: that the FDA may require additional studies beyond the studies planned for product candidates or

may not provide regulatory clearances, including for SCENESSE®; that the FDA may not provide regulatory approval for any use of SCENESSE® or that the approval may be limited; that CLINUVEL may never file an NDA for SCENESSE® regulatory approval in the US; that the Company may not be able to access adequate capital to advance its vitiligo programs; that the Company may not be able to retain its current pharmaceutical and biotechnology key personnel and knowhow for further development of its product candidates or may not reach favourable agreements with potential pricing and reimbursement agencies in Europe and the US; that the Company may incur unexpected delays in the outsourced manufacturing of SCENESSE® which may lead to it being unable to supply its commercial markets and/or clinical trial programs.

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