CLINUVEL

COMPANY ANNOUNCEMENT

Expansion of CLINUVEL's global porphyria programs

Variegate porphyria study starts, first Canadian EPP patient treated

Melbourne, Australia, 01 May 2023	ASX:	CUV
	Börse Frankfurt:	UR9
	ADR Level 1:	CLVLY

Executive Summary

- CLINUVEL expanding access for phototoxic porphyria
- CUV040 study of SCENESSE® expands to variegate porphyria (VP)
- First Canadian erythropoietic protoporphyria (EPP) patient treated
- Discussions ongoing with EMA on label expansion for adolescent EPP patients (12-17 years)

CLINUVEL today released an update on the use its drug SCENESSE® (afamelanotide 16mg) to treat patients diagnosed with EPP and VP, two distinct rare metabolic disorders.

Addressing unmet need in phototoxic porphyrias

Due to varying inborn errors of the haem biosynthesis pathway, EPP and VP patients incur debilitating reactions to light – phototoxic reactions – which have a considerable impact. Exposure to visible light causes anaphylactoid reactions and skin burns in EPP patients. VP reactions present as severe blistering and skin fragility, most commonly on the upper arms, hands, and face.

SCENESSE® is the only approved treatment for EPP and has been shown to prevent and reduce phototoxic reactions, both by acting as a strong anti-oxidant and offering systemic photoprotection. Over 12,000 doses of SCENESSE® have been administered globally across clinical, special access, and commercial programs since 2006. In VP, no treatment is available to prevent or reduce phototoxicity.

Variegate porphyria study CUV040 starts

CLINUVEL has commenced a new clinical study evaluating the safety and efficacy of SCENESSE® in VP patients (CUV040), with all six patients already enrolled to receive treatment. The patients will be administered SCENESSE® every four weeks for six months, with a one-month follow-up. The study focuses on the frequency and severity of phototoxic and dermatological symptoms, including regular observations of changes in the severity of skin disease.

"Long-term follow up of patients has shown a consistent safety profile of SCENESSE®, this is the basis for expansion into variegate porphyria and other disorders; the long term approach to patients is a key advantage CLINUVEL holds over most of its peers," CLINUVEL's Head of Clinical Operations, Dr Pilar Bilbao said. *"Given clinical similarities between VP and EPP, we see a good reason for extending the label of SCENESSE® to VP patients.*

"During the course of 2024, we will expect results from the study. In the meantime, we engage with authorities to learn their views on how best to extend the use of SCENESSE® to VP, since no treatment exists for this disease."

First Canadian EPP patient treated with SCENESSE®

As part of CLINUVEL's mission to make SCENESSE® available to wider populations, the first Canadian EPP patient has received treatment. Health Canada provided the approval to proceed under a Special Access Program (SAP). The patient is eligible to receive treatment all year round (up to six doses of SCENESSE®), with coverage provided by a first health insurer. Consistent with its global controlled-access program, CLINUVEL has trained and accredited a Canadian Specialty Center to administer SCENESSE®.

"We set out to make the novel therapy available in Canada and are delighted that the first patient has received treatment," CLINUVEL's Director of North American Operations, Dr Linda Teng said. *"The next step is to file a New Drug Submission with Health Canada. In the interim, the SAP allows Canadian patients to receive treatment."*

European label expansion

In 2022, CLINUVEL submitted a request to the European Medicines Agency (EMA) to expand the approved indication for SCENESSE® to adolescent EPP patients; already a number of adolescent patients are receiving treatment within the European Union. Discussions continue with the EMA on the avenue to broaden therapy to patients aged 12-17.

"It is really the data and feedback from the use of SCENESSE® in adolescents that have formed the foundation for the EMA application, " CLINUVEL's Chief Scientific Officer, Dr Dennis Wright said.

Porphyria	Erythropoietic protoporphyria (EPP)	Variegate porphyria (VP)
Genetic error leads to	Deficiency of ferrochelatase (FECH)	Deficiency of protoporphyrinogen oxidase (PPOX)
Phototoxic symptoms	Debilitating anaphylactoid reactions and burns following visible light exposure. Affects all EPP patients.	Blistering, skin fragility following light exposure. Transient but can be chronic. Affects some VP patients.
Approved treatments	SCENESSE® (afamelanotide 16mg) for adults (EU-USA-Australia)	None for phototoxicity
Patients	Estimated 10,000 worldwide	3,000-4,000 in USA & Europe

Figure 1 *Phototoxic porphyrias, EPP and VP*

– END –

References:

Elder G., et. al. (2013). The incidence of inherited porphyrias in Europe. *Journal of Inherited Metabolic Disease*, 36(5), 849–857.

Langendonk, J. G., et. al., (2015). Afamelanotide for Erythropoietic Protoporphyria. *The New England Journal of Medicine*, 373(1), 48–59.

Annex I: Following ASX Best Practice for Clinical Trials

Name of trial

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

Primary endpoint

To evaluate the efficacy of afamelanotide in severity of skin disease.

Secondary endpoints

To evaluate the safety and tolerability of afamelanotide in patients with VP.
To 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 and dose levels
SCENESSE® (afamelanotide) 16mg implant dosing.

Number of trial subjects
Six variegate porphyria patients.

Subject selection criteria
- Male or female patients with a confirmed diagnosis of VP.
- Patients with VP-related skin symptoms.
- Aged 18-70 years.
- Providing written Informed Consent prior to the performance of any study-specific procedure.
- Willing and able to comply with the conditions specified in the protocol and study procedures, in the opinion of the Investigator.

Further safety related exclusion criteria apply.

Trial location
Specialist European porphyria treatment centres.

Duration of trial
Six-month treatment phase with one-month follow up.

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

Annex II: About CLINUVEL PHARMACEUTICALS LIMITED

CLINUVEL (ASX: CUV; ADR LEVEL 1: CLVLY; Frankfurt Börse: 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 specialized 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.

SCENESSE®, PRÉNUMBRA®, NEURACTHEL®, and CYACÊLLE® are registered trademarks of CLINUVEL.

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), CYACÊLLE®, 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®, CYACÊLLE®, 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 2022 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

+61 3 9660 4900
+61 3 9660 4909

www.clinuvel.com

Level 11, 535 Bourke St
Melbourne, 3000 Vic, Australia