Company Announcement

CLINUVEL

ASX: CUV
Nasdaq International Designation: CLVLY
XETRA-DAX: UR9

FDA GRANTS MARKETING APPROVAL FOR SCENESSE®

CLINUVEL is granted approval to supply treatment for adult patients with the rare metabolic disorder erythropoietic protoporphyria (EPP) in the USA

An investor teleconference will be held at 16:30 AEDT today; see details below

Melbourne, Australia, 09 October 2019

It is a privilege for CLINUVEL PHARMACEUTICALS LTD to announce the US Food & Drug Administration (FDA) has granted marketing approval to use SCENESSE® (afamelanotide 16mg) for the treatment of EPP patients in the United States.

With the approved New Drug Application (NDA), SCENESSE® is the first global systemic photoprotective drug for the treatment of patients with EPP. SCENESSE® acts as a potent anti-oxidative and melanogenic agent providing pandermal (total surface) photoprotection. This genetic disorder causes absolute light intolerance and forces patients to lead an indoor or nocturnal existence. Due to a defect in heme biosynthesis, EPP patients accumulate and store the compound protoporphyrin IX (PPIX) in the blood and tissues. When exposed to visible light and near-visible ultraviolet radiation, PPIX is photoactivated, causing damage to surrounding tissue and resulting in intolerable pain. SCENESSE® was approved for the prevention of phototoxicity in adult EPP patients in Europe in December 2014.[1]

FDA approval
The regulatory path to approval has taken over a decade, starting with clinical trials of SCENESSE® in EPP patients in Europe in 2006. The FDA granted SCENESSE® Orphan Drug Designation in 2008, recognising the rarity, severity and unmet need in EPP. A Phase II US clinical trial (CUV030) commenced in 2010, with a Phase III US clinical trial (CUV039) completed in 2013, subsequently published in the New England Journal of Medicine.[2]

In January 2016, the FDA requested the full data sets of CLINUVEL's clinical trials in EPP. In October 2016, the FDA organized a Workshop on EPP in Silver Spring to which 150 patients and families were invited to share their experiences living with EPP. The FDA then awarded SCENESSE® Fast Track Status in May 2017 and Priority Review in January 2019.

The NDA was made under a 505(b)(1) application containing integrated reports on safety and benefits, manufacturing processes and adequacy of proposed labelling, as well as CLINUVEL's post-marketing proposals to clinically follow-up EPP patients over the long-term. As part of this review, the real-world evidence from the European distribution of SCENESSE® was reviewed by the Agency.

On 8 October 2019, the FDA's Center for Drug Evaluation and Research approved the NDA for SCENESSE®, following a three-month extension of its review on 31 May 2019.

Under the Orphan Drug Act of 1983, the FDA granted SCENESSE® seven years of market exclusivity from competitors for the designated use in EPP whereby a further extension of two years can be granted once a paediatric product has been approved. Post-approval the novel pharmaceutical therapy will be monitored by the Office of Surveillance and Epidemiology which is charged with the responsibility to oversee the safe use of SCENESSE® during commercial

distribution. The FDA agreed with the intention to harmonize the US EPP Disease Registry with one established in Europe by CLINUVEL to monitor long-term use of SCENESSE®.

SCENESSE® for treatment of EPP

Under the approved labelling of SCENESSE®, the drug is indicated to "*increase pain free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria (EPP)*".

The approved labelling covers all written material about the drug, including, for example, packaging, prescribing information for physicians, and patient information leaflets. The approved frequency and strength of dosing of SCENESSE® is 16 mg once every two months.

Commentary

"I cannot start to describe what it means to dedicate a large portion of one's professional life to a single molecule and for one group of patients, while not knowing the regulatory outcome," CLINUVEL's Chief Scientific Officer, Dr Dennis Wright said. "However, we kept our awareness of the regulatory risks with a first-in-class melanocortin agonist as we faced the subsequent regulatory challenges. The team kept going.

"The outcome today is greatest for the patients and their families who kept asking us to continue the R&D of SCENESSE® despite the obstacles we faced. The approval of SCENESSE® today is deserved and based on its safety and medical benefits to patients," Dr Wright said.

"This is one day on which all interests converge and history is written both for the US EPP patient community and investors who have actively supported our mission for the last 14 years," CLINUVEL's Chief Executive Officer, Dr Philippe Wolgen said.

"The FDA approval of SCENESSE® as a new molecular entity and medical innovation is memorable for this Company and for the Australian life science sector.

"At this time, it is most appropriate to express my gratitude to the Board of Directors and CLINUVEL staff who never hesitated or lost the belief in a strategy that was devised in 2005 and which was religiously pursued by all. Despite numerous setbacks, resistance and delays, the commitment of my staff is quite unique, and I publicly wish to thank them all. In curtailing costs and maximising data required, we stressed throughout the safety aspects of the novel pharmaceutical technology. In working together with select scientific and clinical experts we gained understanding and feedback on our chosen course.

"This event is transformational in that we are now accelerating our exchange with the FDA and European Medicines Agency to expand the use of SCENESSE® in additional indications, as the passing of time has unveiled that our breakthrough technology deserves wider application in modern medicine. I am confident that our teams will understand going forward that art and skills will be required to execute against due dates while containing the costs. If the past had been arduous, the hard labour is just about to start," Dr Wolgen said.

CLINUVEL briefings

CLINUVEL will host an investor and analyst teleconference at 16:30 AEDT today to discuss the decision and its implications. Participants can register using the link below and dial-in with the number received. Additional briefings will be held to advise investors, other stakeholders and the media in the coming days.

Investor Teleconference 16:30 AEDT Today

You are invited to participate

To register link here

Registered participants will then receive the dial in number

If you have a question, please enter it in the text box; selections will be answered during the call

– End –

[1] SCENESSE® (afamelanotide16mg) is approved in the European Union and the USA 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] Langendonk et al (2015). Afamelanotide for erythropoietic protoporphyria. *NEJM*. 373(1):48-59.

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 and the US Food and Drug Administration in 2019 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, Singapore and the USA. For more information please go to http://www.clinuvel.com.

SCENESSE® is a registered trademark 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, including our ability to develop, manufacture, market and sell biopharmaceutical products; competition for our products, especially SCENESSE® (afamelanotide 16mg); our ability to achieve expected safety and efficacy results 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 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® 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 based products; decisions by regulatory authorities regarding approval of our products as well as their decisions regarding label claims; any failure 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 2019 Preliminary Financial 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 the forecasts and estimates is available on request. Past performance is not an indicator of future performance.

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