
FDA accepts SCENESSE® clinical data package for NDA submission

Clinuvel prepares New Drug Application (NDA) for the treatment of erythropoietic protoporphyria (EPP)

Melbourne, Australia and New York, USA, July 18 2016

EXECUTIVE SUMMARY

- *FDA concludes initial review of datasets on SCENESSE® in EPP*
 - *FDA deems datasets satisfactory for submission of New Drug Application*
 - *Pre-NDA meeting with FDA to be scheduled to discuss timelines and procedure*
 - *Clinuvel will request rolling review of NDA under Fast Track designation*
 - *Clinuvel to request Priority Review to shorten review from 10 to 6 months*
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Clinuvel Pharmaceuticals [ASX: CUV; Nasdaq International Designation ADR: CLVLY; Xetra-DAX: UR9] today announced that the US Food and Drug Administration (FDA) has concluded an initial review of Clinuvel's clinical data package for its drug SCENESSE® (afamelanotide 16mg) in patients with the orphan (rare) genetic disorder erythropoietic protoporphyria (EPP). The FDA has deemed Clinuvel's clinical data package satisfactory for submitting a New Drug Application (NDA).

FDA SUBMISSION PROCESS

In January 2016 the FDA requested that Clinuvel submit clinical datasets generated from trials of SCENESSE® in EPP conducted between 2006 and 2013. The need to understand the severity of EPP symptoms and clinical effectiveness of SCENESSE® were the basis of FDA's request.

After a four month review the FDA concluded that the data generated is both satisfactory and sufficient for Clinuvel to submit its NDA dossier. In accordance with 21 CFR Section 314.5 the dossier comprises seven technical sections (chemistry, manufacturing and controls, nonclinical pharmacology and toxicology, human pharmacokinetics and bioavailability, clinical data, statistics) and other pertinent information, including labelling, patents and company financials.¹ A pre-NDA meeting will now be organised between the FDA and Clinuvel.

Clinuvel will request a rolling review of its NDA dossier under its designation of Fast Track to SCENESSE®, announced to the Australian Securities Exchange (ASX) on July 6, 2016. Clinuvel will request a Priority Review from the FDA to shorten the dossier review time from 10 months to 6 months. Data from 352 patients who participated in five trials in EPP between 2006 and 2013, as well as data from over 200 patients who received the drug during compassionate use and special access programs, will be submitted. Additional data from other patient populations who have been exposed to SCENESSE® will be part of the scientific dossier.

The FDA has initiated an EPP workshop on October 24 to learn more about the disease and the effectiveness and safety of the proposed treatment.

SCENESSE® was granted orphan drug designation by the FDA in 2008. As a result, the FDA will waive all PDUFA user fees usually required during the submission process.

COMMENTARY

"Since 2008 Clinuvel has regularly consulted with the FDA throughout Phase I, II and III of its clinical program, and we have since submitted annual reports to update the Agency on our progress," Clinuvel's Director of Regulatory Affairs, Nicoletta Muner said. "Today's FDA outcome is a direct result of a decade of our team's consistency, dedication and transparency in negotiating the best pathway with the Agency."

“I am very much looking forward to achieving the milestone of presenting the FDA with a quality dossier. Our submission will serve for years to come as a basis for further development and new indications with SCENESSE®,” Dr Muner said.

“The FDA Division seems to justly balance scientific data and patients’ experiences with SCENESSE®,” Clinuvel’s Chair, Stan McLiesh said. “The NDA filing will be the next significant step towards making SCENESSE® available in North America, where patients have been vocal in requesting the drug for some time.

“After a complex and difficult journey spanning more than a decade I am proud and delighted that Clinuvel’s teams continue to meet longstanding company objectives in the development of SCENESSE®. I thank our active investors for the confidence they place in Clinuvel. Most importantly, the patients are to be commended for their participation in the US trials.”

PUBLICATIONS OF SCENESSE® IN EPP

A first-in-class drug, SCENESSE® activates the pigment melanin in skin, providing a barrier which protects skin cells from light (photoprotection). The drug also acts as an anti-oxidant. SCENESSE® is delivered via a subcutaneous dissolving implant approximately the size of a grain of rice. Increased pigmentation of the skin appears after two days and lasts up to two months.

Results from three clinical trials of SCENESSE® in EPP have been peer-review published. Results from the Phase II CUV010 study were published in both the *New England Journal of Medicine* and *Photochemistry and Photobiology* in 2009. Results from the Phase III studies CUV029 (Europe) and CUV039 (USA) were published in the *New England Journal of Medicine* in 2015.²

Data from ongoing use of the drug – up to eight years in some patients – from compassionate use and expanded access programs were published in the *British Journal of Dermatology* in 2015.³

EUROPEAN DISTRIBUTION OF SCENESSE®

SCENESSE® was approved by the European Medicines Agency in 2014 under EC2004/726 article 14(8) and is now commercially available for the prevention of phototoxicity in adult EPP patients.⁴ The drug has a positive safety profile which continues to be monitored through a strict European post-authorisation pharmacovigilance program comprising an EPP Disease Registry.

- End -

References & Notes

¹ 21 CFR Section 314.5

² Harms J, Minder CE, Minder EI, (2009). An alpha-melanocyte-stimulating hormone analogue in erythropoietic protoporphyria. *NEJM*, 360(3):306-307.

Harms J et al (2009). Mitigating photosensitivity of erythropoietic protoporphyria patients by an agonistic analog of alpha-melanocyte stimulating hormone. *Photochem Photobiol* 85(6):1434-9.

Langendonk J et al (2015). Afamelanotide for Erythropoietic Protoporphyria. *NEJM*. 373(1):48-59.

³ Biolcati G et al (2015). Long-term observational study of afamelanotide in 115 patients with erythropoietic protoporphyria. *BJD*. 172(6):1601-1612.

⁴ SCENESSE® (afamelanotide 16mg) is approved in Europe as an orphan medicinal product for the prevention of phototoxicity (anaphylactoid reactions and burns) in adult patients with EPP. The innovative nature of the therapy in the orphan disorder, the lack of available scientific instruments to adequately measure the therapy, ethical considerations and the drug’s positive safety profile were some of the factors which led to the European marketing authorisation of SCENESSE®. Information on the product can be found on Clinuvel’s website at www.clinuvel.com.

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 drugs for the treatment of a range of severe

disorders. With its unique expertise in understanding the interaction of light and human skin, the Clinuvel has identified patient populations with a clinical need for photoprotection and for repigmentation. The worldwide prevalence of these patient groups range from 5,000 to 45 million. 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).

Headquartered in Melbourne, Australia, Clinuvel has operations in Europe, Switzerland, the US and Singapore. 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.

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