



Company Announcement

CLINUVEL

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

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# PRÉNUMBRA® - NEW LIQUID AFAMELANOTIDE PRESENTATION

*Second afamelanotide product to be evaluated in acute diseases*

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## EXECUTIVE SUMMARY

- PRÉNUMBRA® non-solid dosage form of afamelanotide
  - Active life-cycle management of melanocortin-based therapy
  - Second formulation of afamelanotide to be used in acute disorders
  - Product to be used for haemodynamic, vasoactive, and anti-oncotic potency
  - CLINUVEL holds proprietary rights for formulation, identified indications & trademark for PRÉNUMBRA®
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Melbourne, Australia and Singapore, 13 July 2020

CLINUVEL PHARMACEUTICALS LTD today announced its expeditious development of PRÉNUMBRA®, a new non-solid (liquid) presentation of its drug afamelanotide.

PRÉNUMBRA® follows the development of SCENESSE® (afamelanotide 16mg) aimed at allowing dosing flexibility as part of the active life-cycle management of afamelanotide and to address clinical needs in critical disorders.<sup>1</sup> CLINUVEL will be evaluating PRÉNUMBRA® in to-be-announced clinical indications. The Company has been able to secure both the intellectual property rights for the dosage form in the identified indications as well as the international registered trademarks for PRÉNUMBRA®.

## LIFE-CYCLE MANAGEMENT OF AFAMELANOTIDE

Afamelanotide is an analogue of alpha-melanocyte stimulating hormone ( $\alpha$ -MSH) and belongs to the family of proopiomelanocortins (POMCs). There are five identified melanocortin receptors expressed in various tissues and organs, with afamelanotide exerting a clinical effect through binding to four of these receptors. Among the multitude of pharmacological properties of afamelanotide, it can serve clinically as a non-steroidogenic hormone. Variation in the dose frequency and strength provides clinical potential in the treatment of acute disorders.

PRÉNUMBRA® is the second formulation of afamelanotide to be progressed through an expedited clinical development program by CLINUVEL. The Company has made available SCENESSE®, a novel controlled-release injectable implant formulation of afamelanotide, in the USA, Europe and China for adult patients with the rare genetic disorder erythropoietic protoporphyria (EPP). SCENESSE® is also being evaluated as a therapy for systemic photoprotection, systemic repigmentation and DNA repair in further clinical indications.

From the pharmacological mode of action of afamelanotide a positive safety profile and clinical effectiveness have been established over more than 15 years of clinical development and use under real-world conditions; in total, in excess of 10,000 afamelanotide doses have been administered in more than 1,400 individuals, with a cohort of EPP patients in Europe receiving annual treatment for over 10 years.

## PHARMACEUTICS OF AFAMELANOTIDE

In managing the life cycle of afamelanotide, a synchronous strategy has been followed to generate pharmacological data in pre-clinical models and human subjects, analysing dose intervals, dose levels, formulations, and biological effects (the body's response to the drug). In total four formulations, three dose intervals, and four dose strengths

had been evaluated over more than a decade, which resulted in the first product SCENESSE®, now distributed as a solid dosage form administered to EPP patients every two months.

Originating from CLINUVEL’s evaluation of scientific data, PRÉNUMBRA® is a liquid presentation delivering afamelanotide systemically, allowing flexible drug loading in a number of patient populations where benefit is expected from a different dose and dose frequency than is currently seen from the SCENESSE® injectable implant formulation. The addition of PRÉNUMBRA® is part of the organic expansion of CLINUVEL’s product pipeline.

### APPLICABILITY OF THE NEW FORMULATION

CLINUVEL is advancing PRÉNUMBRA® as a potent haemodynamic, vasoactive (acting on blood vessels) and anti-oncotic (counteracting fluid formation in tissues) therapeutic agent, initially in adult patients. PRÉNUMBRA® will be evaluated in a number of critical disorders with vascular anomalies and oedema (fluid formation) – where corticosteroids and other anti-inflammatory drugs have not been successful, cause drug dependency or severe side effects.

The new medical applications will be disclosed when the respective ethics committees and regulatory authorities have agreed to the expanded use of afamelanotide.

As an overview, the various indications for both dosage forms of afamelanotide are illustrated below.

AFAMELANOTIDE INDICATIONS					
SCENESSE® [solid dose form]			PRÉNUMBRA® [liquid dosage form]		
1. SYSTEMIC PHOTOPROTECTION	ERYTHROPOIETIC PROTOPORPHYRIA (EPP)	EU USA CN AUS JP	1. ACUTE DISORDERS	TO BE ANNOUNCED	EU AUS USA
2. SYSTEMIC REPIGMENTATION	VITILIGO	USA CAN	2. VASCULAR ANOMALIES	TO BE ANNOUNCED	EU AUS USA
3. DNA REPAIR	TO BE ANNOUNCED	USA EU			

### COMMENTARY

*“The foundation of our enterprise has been, and will also always be, our approach to the toxicology and safety of SCENESSE® and the way we make new products clinically available,”* CLINUVEL’s Chief Scientific Officer, Dr Dennis Wright said.

*“In developing SCENESSE® we kept our focus on new formulations and we saw the advent of an exciting phase with the development of PRÉNUMBRA®. This first of the new formulations provides us with flexible treatment options for identified patient groups beyond and quite distinct from those we are already addressing with SCENESSE®. The two products will complement each other and address various acute and life-threatening diseases.*

*“We had earmarked the use of afamelanotide as an anti-oedematous drug since the molecular properties and pharmacology lend themselves to the intended uses. However, we first needed to safely progress afamelanotide as a systemic photoprotective and repigmentation agent in Europe and North America before taking the regulatory authorities along to the wider use of the molecule. We have a growing body of data on the long-term use and safety profile of SCENESSE® and this gives comfort as we engage regulatory authorities on the use of PRÉNUMBRA® in the clinic.*

*“We have, for some time, prepared to commence clinical studies this calendar year, engaging with regulatory authorities and through an accelerated pathway will seek authorisation for PRÉNUMBRA® in global markets. The first non-solid dose product will be made available for adult patients and, with the collection of sufficient safety data, a presentation suitable for paediatric patients will then follow.*

*“Our overall aim of expanding the use of melanocortins will turn to reality by providing clinicians with more than one therapeutic option to treat critical conditions. There is strong global regulatory support to address unmet clinical needs with novel formulations, and CLINUVEL’s team is well placed to pursue these opportunities,” Dr Wright said.*

**- END -**

<sup>1</sup> SCENESSE® (afamelanotide 16mg) is approved in the European Union as an orphan medicinal product for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP). SCENESSE® is approved in the USA to increase “pain-free” light exposure in adult EPP patients with a history of phototoxicity. Information on the product can be found on CLINUVEL’s website at [www.clinuvel.com](http://www.clinuvel.com).

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

#### **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, skin and vascular disorders. As pioneers in photomedicine and understanding the interaction of light and human biology, CLINUVEL’s research and development initially 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>.

CLINUVEL is advancing its portfolio of melanocortins, among which is PRÉNUMBRA® for the treatment of several critical disorders. Headquartered in Melbourne, Australia, CLINUVEL has operations in Europe, Singapore and the USA. For more information please go to <http://www.clinuvel.com>.

SCENESSE® and PRÉNUMBRA® are registered trademarks 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 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); 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, 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® 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 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 the forecasts and estimates is available on request. Past performance is not an indicator of future performance.

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