CLINUVEL

COMPANY ANNOUNCEMENT

PRÉNUMBRA® formulation completed for clinical trial use

Expansion of melanocortin portfolio, third drug in production

Melbourne, Australia, 15 February 2023	ASX:	CUV
	Börse Frankfurt:	UR9
	ADR Level 1:	CLVLY

Executive summary

- cGMP manufacture of PRÉNUMBRA® Instant (afamelanotide)
- new flexible dosage form of afamelanotide: immediate-release liquid injectable
- defined regulatory pathway (EMA, FDA)
- comprehensive and diversified portfolio of melanocortins

CLINUVEL today announced the completion of manufacture of the first cGMP batch of PRÉNUMBRA® Instant, an immediate-release liquid injectable presentation of afamelanotide. The product will first be evaluated in patients who have suffered arterial ischaemic stroke (AIS).

Pathway to market

The next stage is for manufacturing processes to be scaled up, followed by manufacturing validation work generating data for the regulatory dossiers to be submitted in the United States and European Union. Since data from preclinical studies and long-term clinical use of the SCENESSE® (afamelanotide 16mg) implant are available, a full development of PRÉNUMBRA® Instant is not required. Rapid validation of the specifications and batch release testing of PRÉNUMBRA® Instant is possible due to the extensive existing SCENESSE® dossier.

The American and European pathway to marketing approval for PRÉNUMBRA Instant is summarised in figure 1.

PRÉNUMBRA® Instant, new dosage form

CLINUVEL has completed the manufacture of clinical trial supplies of PRÉNUMBRA® Instant under Good Manufacturing Practice (cGMP) via an exclusive arrangement with a contract manufacturing organization.

The use of the fast-releasing formulation of afamelanotide provides flexibility in acute care, allowing physicians to adapt the patient's dose according to individual needs.

Specialized neurology centres have been selected and engaged as clinical trial sites for CLINUVEL's second study of afamelanotide in stroke patients (CUV803), which will be the first to prescribe the PRÉNUMBRA® Instant formulation. CUV803 will commence following regulatory and ethics consent.

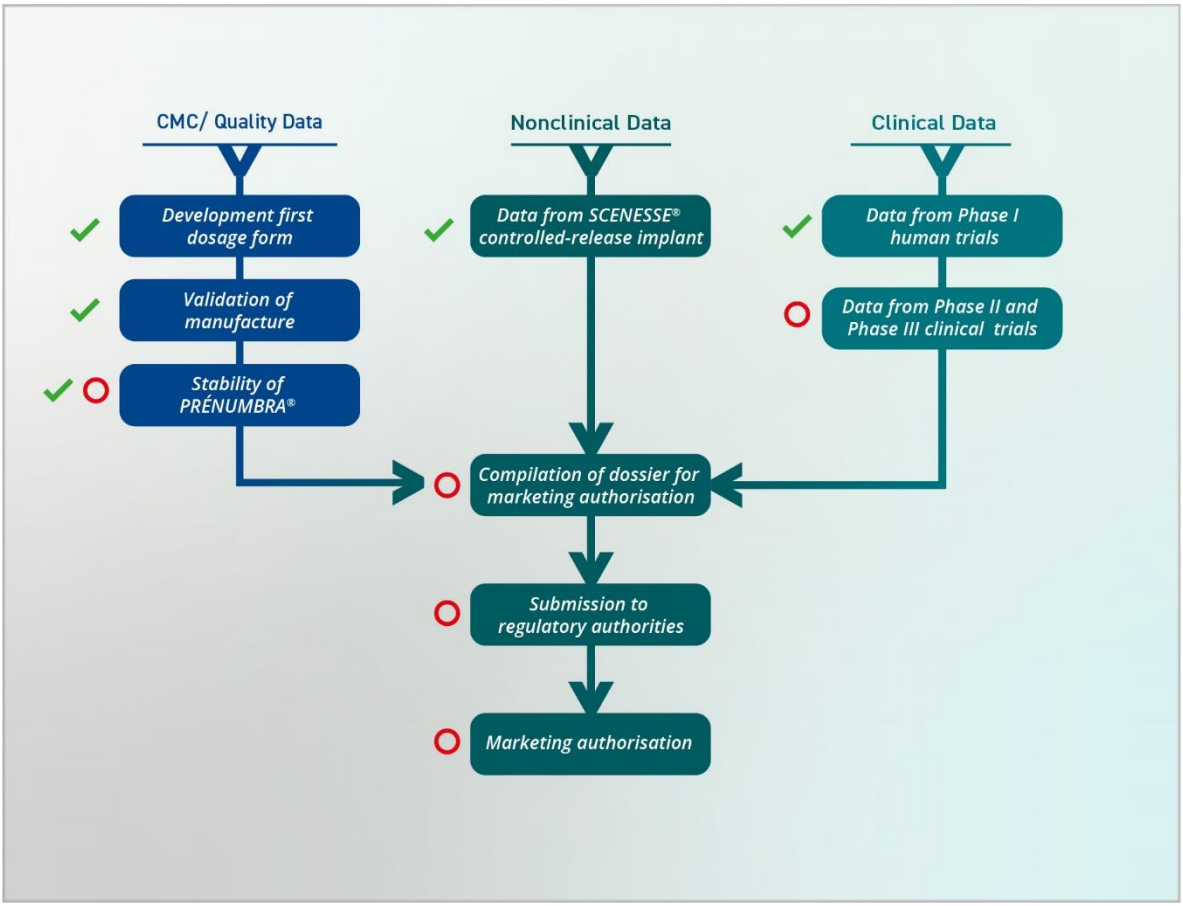

Figure 1 *Pathway to market for PRÉNUMBRA® Instant*

CLINUVEL's melanocortin portfolio

Having commercialised the first afamelanotide formulation – the 16mg SCENESSE® controlled-release implant – CLINUVEL has retained extensive expertise on the therapeutic potential of the drug, plus the broader melanocortin family.

The development of melanocortins and their various formulations is part of the Company's strong focus, risk management, and diversification. Thereby, the red line running through R&D is to lead clinical development based on populations in highest need of treatment or care.

Product name	Active pharmaceutical ingredient	Formulation(s)	Patient populations	Indications	Manufacturing status
SCENESSE®	Afamelanotide	Controlled-release	Adults, adolescents	EPP, XP, vitiligo	cGMP grade, commercial
PRÉNUMBRA®	Afamelanotide	Instant & Modified-release	Adults, children	Stroke, undisclosed CNS, vascular disorders	cGMP grade
NEURACTHEL®	ACTH	Instant & Modified-release	Adults, children	Infantile spasms, multiple sclerosis, undisclosed	ACTH process & analytical method development complete
Undisclosed	Parvys-/Phi-melanotide, CUV9900	Topical	Adults, adolescents	Skin care, skin conditions	Ongoing

Commentary

"CLINUVEL has been shoring up a targeted portfolio, setting itself apart as the only pharmaceutical company entirely focussed on melanocortins," CLINUVEL's Chief Scientific Officer, Dr Dennis Wright said. "In plain terms, our team is building on the Company's knowhow of potent human hormones and optimum delivery methods.

"In the approach to reformulating known and effective melanocortin molecules, we take the most critical risks out of the drug development model. In three decades of use, we have generated an abundance of data on afamelanotide, making our regulatory dossier for PRÉNUMBRA® Instant much easier and faster than having to start from a blank sheet. As part of life cycle management, it is really a matter of execution to bring PRÉNUMBRA® Instant to market for patients affected by acute conditions, such as stroke," Dr Wright concluded.

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About CLINUVEL PHARMACEUTICALS LIMITED
CLINUVEL (ASX: CUV; ADR LEVEL 1: CLVLY; Börse Frankfurt: 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 specialised 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®, and NEURACTHEL® are registered trademarks of CLINUVEL.

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

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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), 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®, 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.

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