CLINUVEL

COMPANY ANNOUNCEMENT

NEURACTHEL® manufacturing processes advance

Analytical method development completed for ACTH as part of CLINUVEL's melanocortin portfolio expansion.

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	BÖRSE FRANKFURT:	UR9
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Executive Summary

- **CLINUVEL advancing ACTH as part of portfolio of melanocortins**
- **ACTH manufacturing process and analytical method development complete**
- **cGMP manufacture of validation batches to commence**
- **Filing of DMF for ACTH expected in H2 2023**

CLINUVEL today announced an update on its commercial development of the analogue adrenocorticotropic hormone (ACTH), part of CLINUVEL's portfolio of melanocortin products. The Company will launch a range of ACTH products under the trade names *NEURACTHEL® Instant* and *NEURACTHEL® Modified-release* for patients with neurological, endocrinological, and degenerative disorders, with plans to file a regulatory drug master file (DMF) for ACTH in the second half of 2023. CLINUVEL is currently pursuing the development of three melanocortin-based pharmaceutical product lines globally: NEURACTHEL®, PRÉNUMBRA®, and SCENESSE®.

Critical manufacturing processes

Working closely with exclusive manufacturing partners, CLINUVEL completed method and process development work throughout H2 2022, including the establishment of critical process parameters serving the commercial product manufacturing. In the coming months work is planned for on production of the ACTH drug substance under current Good Manufacturing Practices (cGMP) standards at commercial scale, characterisation of the drug substance, and overall evaluation stability. Data from validation batches support the filing of a DMF with global regulatory authorities laying the foundation for the submission of marketing authorisation applications.
The development pathway for the NEURACTHEL® product range is outlined in *Figure 1*.

"Our development work continues apace, with an aggressive goal set for the team to deliver the ACTH DMF later this year, followed by completion of the NEURACTHEL® product development and marketing authorisation applications," CLINUVEL's Chief Scientific Officer, Dr Dennis Wright said. "Today, we have stablished a framework to support our next commercial steps in the form of drug batches which can be used as commercial product development. The pathway to file a dossier on the generic molecule ACTH is clear and is expected to result in a relatively fast regulatory review once filed.

"Our work is geared towards the objective of bringing treatments to patients with high unmet need, and who are unable to reliably access ACTH right now. There is a pool of other severely affected patients, whom we believe may benefit from ACTH treatment but, to date, have not been a focus for the industry." Dr Wright said

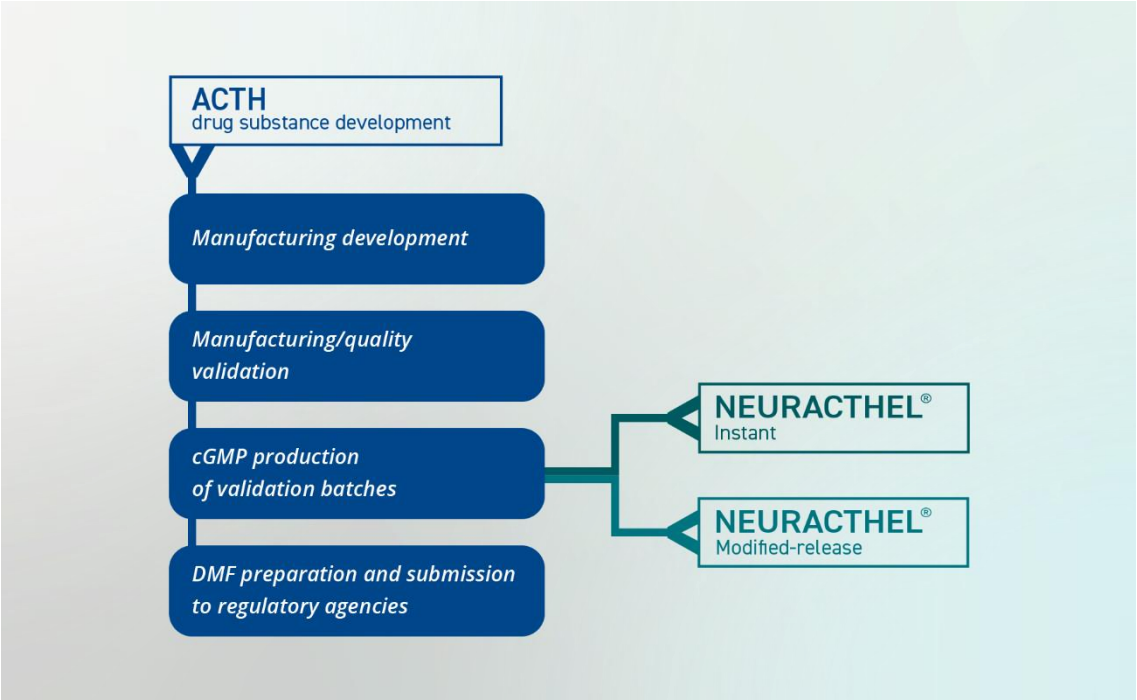

Figure 1: *Development pathway for the NEURACTHEL® (ACTH) product range*

CLINUVEL's portfolio of large melanocortin molecules

Melanocortins are a group of bioactive hormones derived from the precursor peptide proopiomelanocortin (POMC), which is produced both in the pituitary gland and in peripheral tissues and skin. These are responsible for the regulation of a wide range of biological functions including pigmentation, food intake regulation, and immune and reproductive systems.

Having successfully commercialised the melanocortin-based drug afamelanotide in a controlled-release injectable (SCENESSE®), CLINUVEL has established an expanded portfolio of melanocortins for therapeutic use. The Company's approach involves both developing new pharmaceutical products and formulations to market, as well as evaluating the potential of its established products in patient populations with high unmet need (no effective or alternative treatment).

Product	Active pharmaceutical ingredient	Formulation(s)	Patient populations	Indications	Manufacturing status
SCENESSE®	Afamelanotide	Controlled-release	Adults, adolescents	EPP, XP, vitiligo	cGMP scale, commercial
PRÉNUMBRA®	Afamelanotide	Instant & Modified-release	Adults, children	Stroke, undisclosed vascular disorders	cGMP scale, clinical trial
NEURACTHEL®	ACTH	Instant & Modified-release	Adults, children	Infantile spasms, multiple sclerosis, undisclosed	ACTH process & analytical method development complete

Figure 2: *CLINUVEL's melanocortin pharmaceutical portfolio*

"As our programs progressed the past two decades, the understanding of the role and potential of melanocortins to address severe disorders has grown considerably. Having led melanocortin drug development, CLINUVEL is very well placed to address medical challenges and, ultimately, commercialise new products for patients," Dr Wright said.

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About ACTH

ACTH is a naturally occurring hormone which plays an important role in the production of cortisol, enabling the combat of stress and regulation of immune responses, maintenance of blood pressure, moderation of blood sugar, and regulation of metabolism. Developed as a therapeutic agent in the 1950s, ACTH was first administered for human use as an animal derived hormone to influence the glucocorticoid secretion from the adrenal glands, and to treat a host of neurological and inflammatory diseases.

An injectable gel formulation of ACTH is approved by the US Food and Drug Administration (FDA) for the treatment of 19 different medical conditions, including infantile spasms, acute exacerbations of multiple sclerosis, and rheumatic disorders.

References

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

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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