



CLINUVEL

## CEO LETTER

02 December 2019, Melbourne

Dear shareholders,

On 8 October 2019, CLINUVEL obtained its first and historic US Food and Drug Administration (FDA) approval, some 39 years since the afamelanotide technology was first discovered in a university laboratory. On this day the intraday share price went up briefly to A\$45.88, valuing the Company at A\$2.2B; we have seen sell offs since that corporate event.

Apart from profit taking by long term investors, we observe that – at the time of writing – 6.91% of the CUV stock is shorted. This is equivalent to 18 days of ASX trading, at the current (5 day) average daily trading volume of 192,266 shares, to cover these positions. Although this percentage has gradually increased in the past weeks, we do not see this market phenomenon as exclusive to CLINUVEL.

Of far more interest is how CLINUVEL enters its final chapter: what are we aiming for and why?

As laid down in the Performance Rights Plan 2019, the stepwise approach to various programs will need to conflate in a portfolio of pharmaceutical and OTC products in the domain of photomedicine. Having obtained the regulatory approval from the FDA, we are now focussing on an R&D program to expand the use of melanocortins in – what we hold as the most exciting part of the melanocortin puzzle – ultraviolet (UV) radiation-induced DNA-repair. For further readings, we point to the various write ups on CLINUVEL's website, published over the years.

*Why is DNA-repair of clinical and commercial relevance? Why is CLINUVEL only now focussing on this domain?* These are two of the questions recently posed to us.

First, many have made claims through topical over the counter (“OTC”) and consumer products to enable regeneration or repair of single or double-strands defects in DNA. Unfortunately, little to no scientific proof can be demonstrated as to the effects of these low-concentration non-pharmaceutical products on cellular nuclear response. Our teams have always believed that the systemic route was the most prominent and effective way to induce DNA-reparative effects.

Over the long-term and following chronic exposure to the sun, UV-induced DNA damage leads to photoageing and higher risk of developing skin cancer(s). Certainly, in fair-skinned blue-eyed and blonde individuals with a deficient melanocortin-1 receptor (MC1R) the risk of contracting skin cancers is dramatically higher in their lifetime. A number of co-factors eventually determine whether or not one develops actinic damage, actinic keratoses and, subsequently, squamous cell carcinoma. Another cellular route is followed in the development of basal cell carcinoma, and significantly different in the genesis of melanoma. However, all three prevalent skin cancers mentioned share in common the underlying actinic and DNA damage incurred from UV-exposure and subsequent signature mutations caused.

Data generated by CLINUVEL, together with the scientific work undertaken by leading research institutes, has shown that alpha-melanocyte stimulating hormone (alpha-MSH, the natural hormone of which afamelanotide is a synthetic analogue) optimises MC1R binding, improves cellular signalling and influences UV-generated DNA defects. In the overall cascade of sun-induced erythema (sunburn), of DNA-damage through the formation of photoproducts, the physiologic response, and initiation of reparative processes, there is a strong indication as to a determinative role of alpha-MSH and its analogues for eliciting a beneficial effect in those individuals at risk.

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CLINUVEL has had this interest and focus from the start of its program in 2005, however a linear route to proving the thesis was impossible without overcoming FDA's resistance to the use of melanocortins as a systemic photoprotective.

It is somewhat ironic that the leading regulator had long been most concerned about a hypothesised carcinogenic potential of alpha-MSH analogues, while our teams always had held the opposite view based on scientific data. Diametrically opposing the regulators' view, we actually identified strong arguments in favour of alpha-MSH analogues in general, including SCENESSE® (afamelanotide 16mg)<sup>1</sup> potentially being an anti-carcinogenic agent able to slow down, mitigate actinic damage and assist in DNA-repair.

Now, 14 years later, we are finally executing the ultimate part of the *strategic trilogy*, having first shown chemically induced systemic repigmentation without UV radiation and followed by the benefits of systemic photoprotection. By evaluating the effects of SCENESSE® as a DNA-reparative agent we aim to complete the three-pronged plan. Although we are once again entering uncharted territory, the prospect is most exhilarating for all involved.

The clinical challenge and the commercial opportunity are both immense, and we are now preparing for two trials. The excitement led our teams to stay together to finalise this part of the strategic trilogy. Nobody at CUV thinks lightly about this endeavour, given some of our managers would have spent half of their professional existence in one company to see this ultimate objective of DNA abrogation being proven. While all of us have choices to leverage past professional performances to other employment opportunities, the CUV team recognises the magnitude and significance of the challenges ahead sufficiently so to undertake and proceed despite all the adversaries encountered along the way.

In seeing an ensemble of professionals who have proven to be resourceful, genuine and able to play along the rules of the game in the industry – yet have differentiated their approach – I have the utmost confidence that they will once again succeed in this final mission of illustrating the ability of SCENESSE® to affect DNA-repair in diseased and non-diseased individuals, those at high risk for actinic damage. The market for these prescriptive and non-prescriptive products should be sufficient to keep everyone around this Company excited and able to withstand momentary volatility in share price.

Philippe Wolgen

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<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 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).

#### **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 of 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, repigmentation and genetic defects. 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 by the Food and Drug Administration (FDA) 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 headquartered in Melbourne and has a number of operations in Europe, North America and Singapore. For more information 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 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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