

CLINUVEL Communiqué VII

17 October 2019



Dear patients, shareholders, friends,

In this [News Communiqué VII](#), we pause to reflect on the outstanding US regulatory outcome and look back one last time at all the events which led to the long-desired outcome on **8 October, the Food and Drug Administration's (FDA's) approval of SCENESSE® (afamelanotide 16mg)**.¹

AN HISTORIC ACHIEVEMENT

The FDA approval is a marvellous result for US erythropoietic protoporphyria (EPP) patients, their families and our investors, and a most exciting achievement for CLINUVEL's team. In the past days we have noticed what the impact of the US regulatory approval has been in the Asia-Pacific life sciences sector.

To put the FDA's approval in context of frequency, a prominent healthcare analyst in Australia pointed out that **SCENESSE®** is the first New Chemical Entity to have been developed out of Australia and to have reached both the EU and US markets, executed by one team. We hope that CLINUVEL's achievement will provide motivation for all the aspiring ventures working on new scientific technology to pursue their ambitions.

In my view the achievement is the result of a sequence of the decisions we took as part of the overall strategy spanning nearly a decade and half, whereby patients' clinical feedback was put at the core of our plans. Although this could be a claim made by all who develop pharmaceutical products, at CLINUVEL we incorporated the frequent and abundant feedback of patients during our trials and program development, and as part of our documentation in both the European and US regulatory submissions. The patient and

physician feedback formed the qualitative background for the quantitative data submitted. As the regulatory environment was changing, new terminology (such as "clinical advocacy", "clinical input", "real-world data", "real-world evidence") started to percolate the thinking of decision makers in London (UK) and Silver Spring (MA, US). Our anticipation of changing environments was very much part of a strategy to maintain situational awareness in our professional advancement.

FDA TIMELINE SCENESSE®

29 Jul '08	FDA orphan drug designation, EPP
29 Jan '09	Investigational New Drug application allowed
3 Nov '11	Positive results CUV030 study, Phase II EPP
15 Mar '12	FDA, CLINUVEL agree protocol for Phase III study CUV039
11 Nov '13	Positive results CUV039 study
24 Oct '16	FDA hosts EPP Scientific Workshop, Silver Spring MA
7 Nov '16	Pre-NDA meeting
22 Jun '18	New Drug Application filing under "rolling review" complete
9 Jan '19	PDUFA date set, "Priority Review" granted
Jan '19	FDA clinical inspections
Mar '19	FDA quality assessments
31 May '19	FDA extends PDUFA date by three months
8 Oct '19	FDA approves SCENESSE®

TURNING A RESEARCH PROJECT INTO A BUSINESS

In many cases, discoveries originating from institutions, universities and research facilities are important additions to progressive science, but often remain just a foundation for providing hope that ideas will one day be translated into commerce. In my interactions with most successful scientists, industry leaders and fund managers, I often come away with the notion that the gap between promising science and its translation into commercial products remains too large to be bridged. There are a multitude of factors which need to be addressed before one can conclusively state that a scientific idea, project and development is viable to reach commercial ground, and often the originators are understandably unable to escape their – inevitable – biases. For the past 14 years the CLINUVEL team have gone a long way to address our biases and render our decision making as objective as one could, in all areas of our projects and business.

The most satisfying part of the journey is very much being able to overcome the Company's unfortunate history which led to three negative opinions by the world's largest and most influential regulator, US FDA.

While the afamelanotide dossier was well known by the Center for Drug Evaluation and

Research and Division of Dermatology and Dental Products (DDDP), the challenge to overcome the objections issued in 1995, 1999 and 2004 required quite a strategy and effort. As one fund manager had asked management during the AGM of 2007, "*is CLINUVEL set on pursuing a Nobel Prize in medicine or building shareholder value?*" The answer then and now is that we deploy strategies to overcome and negate perceptions from decision makers, part of the value chain. Our conviction is that enterprise value is being built along that trajectory and based on the integrity of our decisions. On the 8 October the CLINUVEL's strategy was proven correct in all its details.

In aviation terms, one is obligated to check their instruments mid-air and downwind at regular times, and match these with acute awareness of aptitude, altitude and (humble) attitude. The same is applicable in more complex project finance: one needs to constantly adapt one's course to be able to reach the next airstrip for refuelling. Constant reading and addressing all conceivable risks in one's airspace is mandatory to safe and adequate navigation. This, unquestionably, is our *modus operandi*.

HOMAGE TO HANK AGERSBORG († September 2012) AND JACK WOOD († July 2014)

The FDA's approval of SCENESSE® is an homage to two great men who had worked passionately for CLINUVEL: Dr Hank Agersborg and Mr. Jack Wood. We should not forget how privileged we have all been to have benefited from their expertise. Hank and Jack's strongest wishes had been to see SCENESSE® coming through the FDA, a long-awaited dream and one they had never had any doubt that our team would actually be able to achieve. Jack's words were recorded and echo to date: "*As a Board, we will bet the entire farm (pharma) on this one outcome which will transform the company and have an impact in pharmland.*"

We dedicate the FDA's outcome to two unforgettable human beings and seasoned executives in the pharmaceutical business; without their passion for CLINUVEL's business we would not be where we are today. They have been an inspiration to persevere a road full of obstacles.

Among many others in the Company, the torch was kept burning by Dr Dennis Wright who oversaw the US regulatory aspects of our dossier and Nicoletta Muner, who is now one of the rare professionals in the Asia-Pacific life sciences industry to have become a CMC expert along the way.

With a high level of confidence, I am able to state that without the intellectual input of the prime woman in Australian finance Brenda Shanahan, the tenacity and entrepreneurship of Willem Blijdorp, the guidance of Stan

McLiesh, and the pragmatism of former Board member Eli Ishag, CLINUVEL would not be here today. The guardian of finance has been CFO Darren Keamy, who has agreed to remain in this position for another term.

FDA APPROVAL OF SCENESSE®

As part of the marketing authorisation, CLINUVEL has committed to a number of activities to be observed with certain due dates.

In the first place, as anticipated and requested by CLINUVEL, in order to follow up patients for a minimum of eight years (in reality for life), CLINUVEL is establishing the **EPP Global Disease Registry (EGDR)** such that pseudonymised data are pooled for annual analyses. These analyses will provide harmonised data for assessment of safety and behavioural changes by EPP patients who receive SCENESSE® treatment, both in the US and Europe. As per 21 CFR 314.80 and 314.81, the obligation to report to the FDA will remain after approval.

The EGDR is one of the measures we put in place to minimise present and future risks. Although the safety profile of our linear configured melanocortin is excellent, we will implement US pharmacovigilance and quality management systems for all possible eventualities in the future, a fire drill to be rehearsed periodically without the likelihood for blaze ever to occur. It is part of our attitude to risk, as mentioned above.

We also committed to conduct another electrocardiography (ECG) study in EPP patients to monitor the long-term effects of the drug product on the cardiovascular system. While there are no data indicating any adverse effects, in introducing a novel molecule the generation of these data are expected and will subject a small number of patients to electrophysiology tests.

An important part of our overall strategy and embedded in Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) is our post-marketing commitment to treat patients

under protocol. This means that porphyria expert physicians have a set order of clinical work-up activities to follow to render the treatment uniform across the globe. We very much profess standardisation of the SCENESSE® treatment to eliminate variability and uncertainty of follow-up data.

Reporting to the FDA will occur periodically and annually, as per section 506B, 505(o)(3) and 21 CFR 314.81(b)(2)(vii), as is the case in Europe. Our US pharmacovigilance program is, as much as possible, being harmonised with the ongoing European one in place, as we had always envisaged and proposed to the FDA at the time of dossier submission. Harmonisation provides significant cost efficiencies and ensures knowledge is being shared within the organisation.

Most importantly, CLINUVEL will train and accredit the US expert centres prior to allowing the prescription of SCENESSE® treatment to EPP patients. The training is multifaceted, including incorporating patient care, data monitoring and collection, the implant administration procedure, documentation, and management of the registry.

The ultimate objective of the processes is to ensure CLINUVEL is able to maintain controlled distribution as part of the overall approach to safety.

Finally, and important both for the FDA and our teams, **an FDA post-approval feedback meeting** will be conducted between the two parties to evaluate the communication process during the development stage and the agency's scientific review.

In light of CLINUVEL's forthcoming continuation with the vitiligo program and third

indication for SCENESSE[®], the more frequent contact there is between our teams and the Division for Dermatology and Dental Products, the better it will bode for the future.

VITILIGO PROGRAM

From here onwards, our teams are accelerating the US vitiligo program. While the final protocol has been agreed by the Global Vitiligo Expert Consortium, it is now up to our regulatory team to finalise the scientific data to be presented to the FDA's DDDP. This is the same Division which has scientifically reviewed and approved SCENESSE[®] on 8 October 2019. One can imagine that there is considerable advantage of the same reviewers having seen and voted on the drug's benefit-risk assessment now being presented the vitiligo dossier.

CLINUVEL's proposal will be to advance to a US-UK trial evaluating afamelanotide as a

combination therapy with narrowband UVB (NB-UVB) in vitiligo. It is best to conduct an in-depth discussion on the expected benefits and impact the treatment is expected to have in vitiligo patients.

It is perhaps inessential to stress how excited the medical community is about the prospect of SCENESSE[®] coming to the US market, and EPP paving the way for a vitiligo treatment.

We shall report on vitiligo shortly. Our approach to the relatively uncharted medical indication vitiligo will be similar to how our teams approached EPP in 2006.

INVESTOR AND PUBLIC RELATIONS

Investor presentations are being given by our finance and IR team since the demand to hear the CUV story has increased the past months, and certainly since the most recent FDA news. We will continue to provide information on the FDA's significance for the sector and the Company.

To the German Speaking Shareholders

We thank all of the German speaking shareholders who responded to the [German](#)

[News Communiqué I](#) we issued in May 2019. Our intent is to continue the German postings to reach our growing shareholder base in Austria, Germany and Switzerland. We now have a database of German speaking shareholders that can be used for specific parts of the Company's communication plans in the future. We encourage those who have not yet responded with their information to do so to our Investor Relations Manager, Mr Malcolm Bull.

I end this [News Communiqué VII](#) with our appreciation of the US patients who have been contacting us since the last US trials; your patience is commendable and beyond any reasonable imagination.

Philippe Wolgen

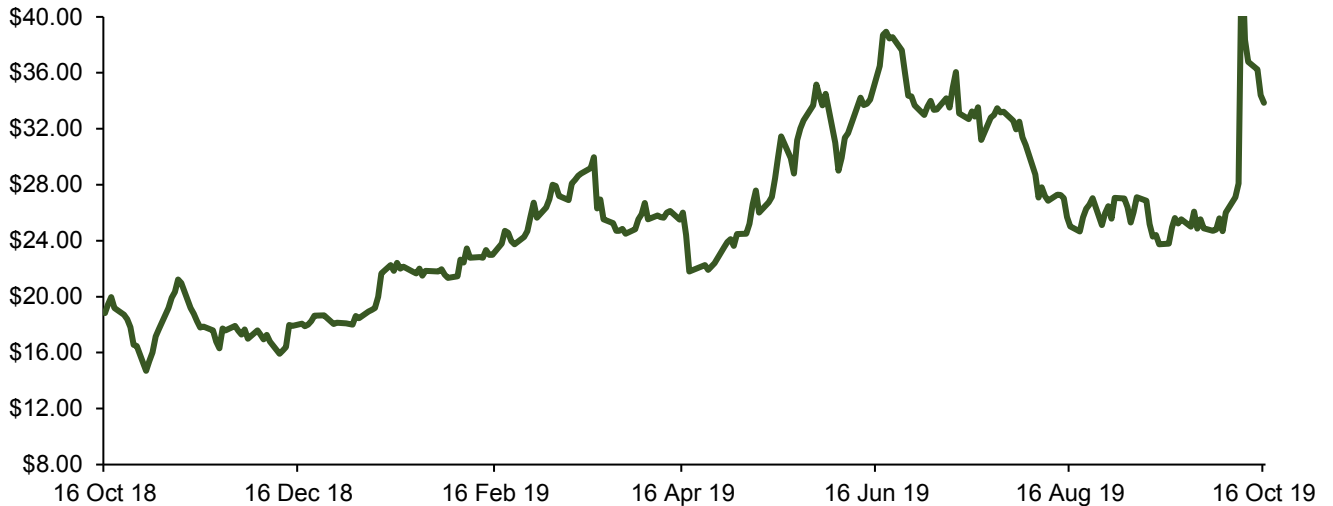
¹ SCENESSE[®] (afamelanotide 16mg) was approved in the European Union on 24 October 2014 as an orphan medicinal product for the prevention of phototoxicity in adult patients with EPP. SCENESSE[®] was approved on 8 October 2019 in the USA to increase pain free light exposure in adult EPP patients with a history of phototoxicity. Information on the product can be found on CLINUVEL's website at www.clinuvel.com.

ASX: CUV

Share Price

(ASX: CUV 16 Oct 2018 – 16 Oct 2019)

Shares on issue	48,960,633
Fully diluted	49,608,546
Market cap (16 October 2019)	A\$1.64b



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 Preliminary Final 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.

Contact



Level 11, 535 Bourke St
Melbourne, 300 Vic, Australia



+61 3 9660 4900
+61 3 9660 4909



www.clinuvel.com