CLINUVEL Communiqué VI

20 August 2019

CLINUVEL

Dear patients, shareholders, friends,

In this News Communiqué VI for the year we report further on CLINUVEL's regulatory progress in the US and the latest quarterly results for the period ending 30 June 2019.

US FDA REVIEW PROCESS SCENESSE®

Ongoing interactions between the US Food and Drug Administration (FDA) and our scientific teams continue to take place as the final outcome date of **October 6** approaches. In the latter half of the scientific review the FDA attempts to address substantive review issues which have not yet been covered by its committee members. The overall appraisal at this stage is not yet fully assessed by the signatory authority, the Division Director and the Cross-Discipline Team Leader (CDTL), to come to a final regulatory decision for the submission. The nature of the discussions is collaborative and there is frequent exchange of information and clarifications on data submitted, for example on specifications and on the meaningful benefit against the side effect profile of SCENESSE®. At this stage, it is apparent that the FDA uses its time to gain a broader insight of risks and benefits while it reserves its right - at any time - to identify new review issues that may trigger an extension of the Prescription Drug User Fee Act (PDUFA) goal date if the Division deems it is needed. There is no indication that the current PDUFA date cannot be met; it is our expectation that the 6 October will remain the current PDUFA goal date for an outcome to be provided. At this stage an Advisory Committee is not planned but again, the FDA reserves – at this late stage of the review – its right to call an Advisory Committee if it concludes that a further independent opinion is needed. Vague as this may sound, the review process is strictly dictated by the assessment of the Division of Dermatology and Dental Products (DDDP) to do all in its power to arrive at an appraisal regarding the innovative therapy proposed, according to the FDA's internal guidelines and rules laid down in the PDUFA.

All in all, our teams are working around the clock to ensure that this historic review comes to a positive conclusion. For now, the CLINUVEL teams are preparing documentation and internal processes for two possible outcomes.

The lengthy reviews by both EMA (in 2012-14) and FDA were not unexpected and have illustrated once again that the review of *a novel systemic photoprotective therapy*, the world's first injectable therapy, is far from a standard evaluation. I believe firmly that in many ways these thresholds of global regulatory reviews provide CLINUVEL its current advantage, a position emerging from the complexity posed to regulatory authorities.

The late shift in scientific approach by regulatory bodies was required from the realisation that hormonal expression by epidermis was of predominant importance. In contrast, for decades the classical endocrine beliefs of exclusive expression of proopiomelanocortin (POMC) hormones by central (read CNS) structures took hold of medical evaluations. A new dawn arose with the acknowledgement of the expression of melanocortins by peripheral tissues as contemporary scientists started to understand

its importance, while more traditional endocrinologists had viewed the pituitary-hypothalamic-adrenal axis as logical one with regard to POMCs. With the emergence of CLINUVEL's linearly configured hormone afamelanotide 16mg, the debate on the essence of reviewing old adages was promptly required.[1]

In News Communiqués VII and VIII we will delve deeper in the subject of 'first-in-class' and 'New Chemical Entity' from a regulatory perspective in order to differentiate the afamelanotide molecule from other peptides.

As published in News Communiqué V, a Complete Response Letter (CRL) – in common terms, a regulatory rejection – would come with a number of formal arguments which would require analyses and addressing. A Formal Dispute Resolution is restricted to a timeframe during which the Company is able to pose questions and argue the decision detailed in the CRL. On the other hand, a possible grant of marketing authorization in the US could come with a number of conditions and commitments which require our clinical and quality professionals to be involved. The simultaneous activities are targeting completion of standard operating procedures and expansion of quality management systems to ensure safe and effective market access for US EPP patients.

Hence, the interim period is being used to evaluate all European processes and pharmacovigilance to be implemented in the US, should the FDA decide that the benefit-risk assessment is in favour of SCENESSE®. As we had published in 2014, CLINUVEL aimed to harmonise the European pharmacovigilance systems with those required in the US early on, such that pooled clinical post-marketing data would become available in years to come for statistical analyses, and for efficiency of our global distribution.

Central to all these processes remain people, those in our offices who have built and implemented the quality and pharmacovigilance systems for product distribution in the European Union. Most of these professionals are being involved in preparing for US market access in the near or distant future. From these preparations, one can distil that CLINUVEL intends to distribute afamelanotide itself without appointing a licensee or US distributor. There have been numerous arguments over the years which have spoken in favour of this commercial and clinical approach.

FDA TIMELINE 2019 SCENESSE®

9 Jan	PDUFA date set	✔
Jan	FDA clinical inspections	✔
Mar	Quality assessments	✔
8 Apr	FDA communication on labelling, post-marketing authorisation	Postponed
May	Ongoing communication	✔
	Q&A clinical use post-MA	✔
31 May	FDA extends PDUFA date by three months	✔
6 Sept	FDA communication on product labelling, post-marketing authorisation requirements, CLINUVEL commitments	
6 Oct	PDUFA DATE	

FDA RISK-BENEFIT SCENESSE®:

1. Marketing Authorisation (Approval)

OR

2. Complete Response Letter (Rejection)
   - Appeal grounds, Formal Dispute Resolution (FDR)
   - Timeframe for FDR
   - Further communication with DDDP

QUARTERLY FINANCIAL RESULTS ENDING 30 JUNE 2019

The last quarter saw our team achieving an increase of Cash Receipts of 25% compared to the same quarter ending June 2018. Due to fluctuations in seasonal orders we will always expect quarters to differ, while a steady rise in clinical demand by EPP patients is seen year on year. As stated previously, in treating EPP patients we see an increase of light intensity and risk of phototoxic crises starting in February until November in the Northern

hemisphere, hence it is expected that clinical demand follows this pattern.

Overall the Cash Receipts for the year have increased by 36% in comparison to 2018.

At the same time, we incurred an increase of 25.6% in Net Operating Payments for the quarter, mainly due to increase in product manufacturing expenditures to meet the clinical demand for SCENESSE®. Here we aim to plan in advance to meet reasonably expected clinical demand.

One of our Board's principal objectives is to establish a group of companies which is able to independently operate and advance R&D activities in the continuation of building value through: a) our own pipeline, and b) strategic acquisitions. For the past quarter, the positive Net Cash from Operations was $8,618,000 assisting us in meeting the objectives outlined.

Due to management of foreign exchange we benefited from a positive impact of $718,000 to the total Cash Balance.

As can be read from our Communiqués, the financial management of the Group is a discipline which is continuously under review of Board and management and forms the foundation for CLINUVEL's past success. The same financial rigour as seen the past years is expected in the immediate future for us to attain all goals. *We refer to the quarterly report (Appendix 4C) published on 31 July 2019.*

INVESTOR AND PUBLIC RELATIONS

The vast majority of CLINUVEL's shareholders are patiently awaiting the US FDA outcome and are commended for their understanding of CLINUVEL's specific business model and the long-held belief that positive news will prevail. In my decades of market exposure, I am all too aware that SMEs are subject to market swings without being able to exert much influence on hausse or baisse. Against the recent decline in market valuations, our teams work diligently towards our business objectives, irrespective of the gyrations of the stock price.

Our Investor Relations Manager is handling an increasing number of queries from existing and potential shareholders, particularly from institutions. The interest of Australian and international institutions has been trending upwards during 2019 and has become more prevalent since we were included in the S&P / ASX 200 Index on 24 June 2019. Our management team acknowledges the privilege of being ranked amongst the largest public companies in Australia and is conscious that this is the result of the accumulation of a decade of work and a function of increasing demand for the CLINUVEL story. Depending on news flow and outcomes in the coming months, we may need to consider an increase in our IR resources to match the upswing in investor relations service.

The ongoing challenge in discussing CLINUVEL with potential investors is to attract new shareholders who share our vision and beliefs and who are willing to commit to the Company for the long haul.

Reflecting the focus of our teams to share CLINUVEL's story, several conference and investor presentations are being prepared. These do not necessarily feature on our public board since they are ad-hoc requests or annual roadshows, usually following the release of financial results. Each of the international markets in which we have a presence requires our acte de présence to explain the growth of the Company over the past year while our teams ensure that all stakeholders receive the same publicly released information.

(Continued next page)

We share with you as per usual, an updated table of the IR/PR activities for the 2019 year.

I end this Communiqué by sending my best wishes to all those who have been counting the hours to the US final outcome, mostly the EPP patients and their families.

Philippe Wolgen

[1] SCENESSE® (afamelanotide 16mg) is approved in Europe as an orphan medicinal product for the prevention of phototoxicity in adult patients with EPP. Information on the product can be found on CLINUVEL's website at www.clinuvel.com.

CLINUVEL PRESENCE 2019

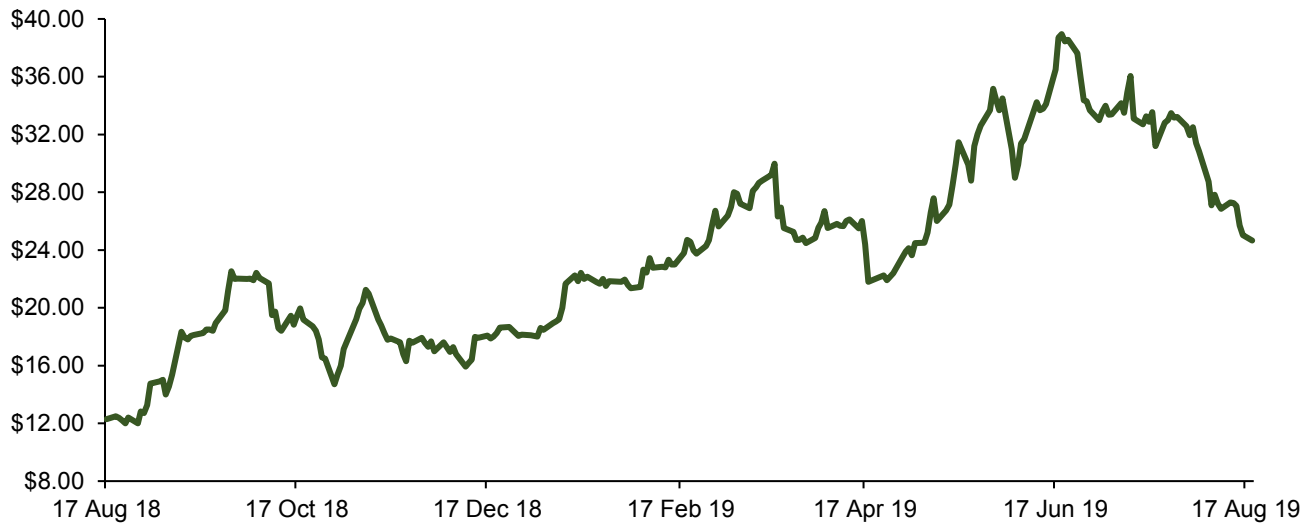
Mar	Global Vitiligo Foundation Annual Meeting	✔
	American Academy of Dermatology	✔
	German EPP Expert Meeting	✔
Apr	Goldman Sachs Emerging Leaders Conference	✔
	Italian EPP Expert Meeting	✔
	HC Wainwright Healthcare Conference	✔
	BioCentury Future Leaders	✔
May	UBS Global Healthcare Conference	✔
Jun	15th Sun Protection Conference	✔
	Jefferies Healthcare Conference	✔
	World Congress of Dermatology	✔
	British Porphyria Association meeting	✔
Aug	World Congress of Light and Life	
Sept	International Congress on Porphyrins and Porphyrias	
Oct	European Academy of Dermatology and Venereology	
Nov	German EPP patient association meeting	

ASX: CUV

Share price

(ASX: CUV 17 August 2018 - 19 August 2019)

Shares on issue	48,960,633
Fully diluted	49,608,546
Market cap (19 August 2019)	A$1.21B



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 2018 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.

Contact

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

+61 3 9660 4900
+61 3 9660 4909

www.clinuvel.com