Clinuvel communique

December 2017

CEO's Outlook

In the last communiqué of the calendar year, we take a breath and contemplate CLINUVEL's status, a holding position for our teams over Christmas in the run up to a full 2018. In looking back, I thank all of you who are working and who have collaborated with CLINUVEL, wishing you the best of health and spirit. Every day I am aware that it is a privilege to work with many gifted and specialised talents, who offer their sincere dedication to the execution of their tasks in hand and always with an eye to attaining the team's objectives. I appreciate all of you who keep supporting us by emails and letters, and those who stay with us along this epic journey.

The results from the year 2017 has exceeded our internal expectations on drug supply to EPP patients within the European Economic Area. While it is no surprise that payors and insurers are mandated to curb drug prices in Europe and US, trying to find an appropriate way to evaluate innovative technologies can pose challenges for the authorities. Ultra-orphan disorders definitely require a different analytical approach from both regulators and advisory bodies, and I am certain this will require attention as the national healthcare systems evolve and mature. Our teams, health economists, consultants and scientists are engaging with the European payment agencies one by one to introduce SCENESSE® to each individual European country. While we are shifting a number of long established beliefs by launching a hormonal treatment for systemic photoprotection, our team is steadfast in achieving the objective for the sake of EPP patients who - in an historical sense - have been waiting for an effective therapy since 1961[1] [first publication on EPP].

CLINUVEL's scientists derive principles of clinically effective treatment from data and clinical observations combined. All reports and observational phenomena from European patients provide increasing strength to the notion of systemic photoprotection. In the meantime, our teams continue their work on technology, methodology, and applicability of melanocortins. We deepen the subjects of photomedicine to intensify the attention on light absorption, the prismatic effects incurred by human tissues. This specialised knowledge serves us in the expansion of product offerings.

CLINUVEL had tested a new theory residing in optical physics, and one whereby EPP patients have been gradually been able to be exposed to light emitted along the visible spectrum, to be precise, wavelengths 408 nanometres and above. In 2017, we have seen how EPP patients continue to report a positive response to the drug under real life circumstances. The notion that *blue light* causes deep dermal reactions is known and published, as our teams had tested SCENESSE® in the early days in a pilot trial in patients that underwent photodynamic therapy.

In EPP the genetic defect on chromosome 18q21.3 causes a disturbance in energy transfer at cellular level, and for which SCENESSE now offers the first therapy. The kinetic and thermal energy dissipated causes significant tissue injuries and anxiety, a lifelong incapacitation for these patients. CLINUVEL has pioneered research in this area of pharmacology and our continued efforts are progressing well.

Patients and physicians have a free choice to prescribe and request SCENESSE® and therefore the significance of their independent feedback is a motivating factor for our teams. On behalf of physicians and patients I thank all of you who supported our work during 2017.

ERYTHROPOIETIC PROTOPORPHYRIA IN THE US

Akin to CLINUVEL's approach to the European regulatory review, we have put thought into how best to optimise the chances of a successful US FDA outcome and mitigate the risk of rejection or further delay of review of afamelanotide 16mg. By writing a dossier consisting of both relevant clinical trial data and securing fresh data from real-world use of the product we introduce a new chemical entity, a 'Novum Organum'. This step has enabled CLINUVEL to overcome the FDA's earlier (2003/04) position against a molecule once proposed such that we are now able to address questions on long term safety and clinical benefit and response. We carefully weigh up the cost of a comprehensive US submission aiming for an optimised outcome versus the cost of an unthinkable FDA rejection, and look forward to months of scientific dialogue with the FDA.

For EPP patients it is about time that SCENESSE® becomes available, or to cite one of the patients during the US FDA EPP Workshop in October 2016:

"I was fortunate enough to receive the drug during CUV039, since then I had to go back into hiding, now I want to gain a life I had a glimpse of".

DISTRIBUTION UPDATE EUROPE

Over the past four years, CLINUVEL has been in a lengthy exchange with the English National Institute of Health and Care Excellence (NICE). NICE acts as the advisory body to the English National Health Service (NHS), which eventually is responsible for offering SCENESSE® to English patients under full state reimbursement. It is foreseen that the formal review and discussions with NICE will continue throughout 2018, whereby further processes are led by the agency. In the meantime, this very process deprives British EPP patients from long awaited treatment, having first participated in clinical trials in the UK in 2008. The queue of pharmaceutical products awaiting reimbursement is carefully managed by NICE providing arguments towards value for money for each individual treatment proposed.

Overnight, Melbourne time, NICE published a draft not to recommend reimbursement for SCENESSE® by the NHS in England. However, further exchanges with NICE are scheduled until May 2018, after which a final recommendation for reimbursement to NHS England will follow. A number of meetings are scheduled in early 2018 where our teams are expected to discuss the cost-effectiveness of SCENESSE® leading to the final recommendation by NICE.

As this document goes to print the second Annual Report to the European Medicines Agency (EMA) is being finalised. This document contains safety and effectiveness data from the EPP European Disease Registry and will be submitted as per agreement with the EMA. The report concludes a full year of safety data accumulated from physicians and medical staff who have monitored the well-being of patients on and off treatment.

As stated on 28 November, CLINUVEL's European EPP analyses will be supplied in the next months to the US Food and Drug Administration as part of the New Drug Application. Drug safety is the one criterion which will continue to be reviewed and analysed for years to come and an expected feature of novel therapeutic modalities. I wish all our readers a happy and safe festive season and I look forward to 2018.

Philippe Wolgen

[1] Magnus 1966

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; any failures to comply with any government payment system (i.e. Medicare, NHS) 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 2017 Annual Report and Annual General Meeting. 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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