Clinuvel communique
December 2016

CEO's Outlook

At the end of a calendar year we look back on plenty of activities and a solid financial performance by the CLINUVEL Group. Our teams will break over the season's holidays to reflect on a hectic year, but most of all to prepare ourselves physically and mentally for more exciting challenges ahead.

SCENESSE® EUROPEAN ACCESS

The primary emphasis of the Company in developing SCENESSE® (afamelanotide 16mg)[1] has long been on the safety of this new molecular entity, and hence we have established a pharmacovigilance system (PVS). The safety of a new therapy remains instrumental to successful distribution long term, and thus far we are content with the data and clinical feedback from expert centres, EPP patients and our own team leads. As the product enters more centres in various countries the workload increases, while the same intensity of clinical monitoring, analyses and periodic reports is expected.

Looking forward, we intend to expand the PVS to provide us the required tools to distribute SCENESSE® in the US when the Company obtains US Food and Drug Administration (FDA) marketing authorisation. A staged plan is being implemented to grow the systems as we expand access to SCENESSE®.

In serving European EPP patients, we fulfil part of the social mandate for an innovative company to make novel drugs available to orphan populations; we have addressed those (porphyria) patients who have spent their lives indoors deprived of light in confinement. We continue to be innovative as we press for the further development of a paediatric formulation to serve children suffering from EPP. Health care policy makers and insurers bear a great responsibility to EPP patients whose voices have become louder with time, and therefore we are confident that SCENESSE® will be made available sequentially in the European countries where the EPP patients are being seen by expert centres who will be trained and accredited to use the product.

As part of market access and reimbursement our task is to communicate to policy makers for them to be able to differentiate CLINUVEL from other pharmaceutical and biotech companies, in that we expend a minimum on R&D while maximising the clinical outcome. I foresee in the coming year that the cost effectiveness of a pharmaceutical development program will become a real factor for decision makers when assessing the payments and reimbursement for a pharmaceutical product. As stated previously, the firing salvo was made in 2013 by Sir Andrew Dillon, the Chief Executive of the English advisory body NICE, who stated publicly that the pharmaceutical sector needs to appraise themselves when spending a median £1.2 billion on one pharmaceutical program.[2] Implicitly, Sir Andrew pointed at returns on investment in pharmaceutical development and a new approach to pharmaceutical companies coming to market. In contrast, and well in anticipation of changing macro-economic conditions, CLINUVEL navigated through a myriad regulatory and clinical obstacles whilst utilising its available equity under US$125 million during 12 years of relentless focus on SCENESSE® in EPP. From this perspective CLINUVEL fulfils the modern criterion of underspending on innovation in a sector in dire need for new drugs for untreated patient populations.

The European distribution of SCENESSE® will continue to progress while discussions with advisory bodies and insurance groups dictate the speed available treatment to patients who are much in need. The drug is currently being

assessed in a number of European countries on its unique properties, effectiveness in EPP patients, lack of available alternative and patients' persistent demand.

To our surprise, and not reported before, the discontinuation of the SCENESSE® treatment following various Special Access Schemes has led to a number of EPP patients reporting psychiatric decompensation and mental illness. Our team, together with the treating physicians, is now required to assess the psychiatric distress as part of the long term follow up of the patients. The lifelong deprivation of light has long been an area of interest of the scientific community to gain knowledge on the detrimental effects on human biology. Yet the consequences of discontinuing an effective treatment in EPP – one which provides patients their first opportunity to expose to light without anxiety for anaphylactoid reactions and burns – is new. We are investigating the reports from these EPP patients to better understand the circumstances and urgency for further treatment.

US PLANNING

Following the pre-New Drug Application (NDA) meeting on 7 November with the FDA, our teams will progress in 2017 to sequentially file the scientific dossier on SCENESSE® per individual module, a process estimated to take eight months from the start of the filing. During this time an active exchange will take place between Company and agency, with the purpose of providing additional information on a novel melanocortin in a less characterised disorder. At the end of the filings, a dialogue with the FDA will take place on the expected regulatory review period to arrive at a timely decision on marketing authorisation.

Earlier this month, and perhaps overshadowed by the formation of President-elect Trump's team absorbing the majority of the US media attention and with bipartisan support, President Obama signed the 21st Century Cures Act. I view this as one of the most significant pieces of healthcare legislation to have been proposed.

I believe this act may well have an impact on the FDA's review process. Through this act the FDA is asked to evaluate the innovative nature of a proposed treatment while at the same time taking into account the real world experience of patients. With FDA Commissioner Califf's public assertion that patients' experiences would benefit the FDA's decision process, the pathway to align the FDA's review process with the European Medicines Agencies (EMA) novel decision process involving patients and scientific experts has now been paved. The 21st Century Cures Act will change the agency's approach to innovation in orphan diseases and the resulting review may well be beneficial for US EPP patients. We will update you in the course of 2017.

VALLAURIX PTE LTD SINGAPORE

With much excitement, I witness how the Singaporean team has become an integral part of the CLINUVEL family. With the VALLAURIX laboratory fully operational, we have added to the Group further chemical, analytical and pharmaceutical knowhow to support our competitive position.

It is obvious that the European marketing authorisation of SCENESSE® has led a number of groups and universities to progress their research in melanocortins. In this sense CLINUVEL is not only leading the field, but also providing the scientific justification for additional research funding to flow to these groups. The more reason for us not to rest on our laurels (if any) but to keep our heads down and deliver on the next generation and complementary product pipeline.

EVOLUTION OF CLINUVEL

Our Board is finalising a portfolio transformation which is aimed at enforcing the Group's competitive position. We have entered a phase of restructuring, with an emphasis to further invest our funds in innovation to create value short- and mid-term. We have a vision to establish a consolidated group of companies investing in R&D to be the global leader in:

I optical physics & photomedicine;

II use of melanocortins; and

III skin protection.

In expanding the Group with impressive individuals in all our regional offices, we are looking at the next generation of pharmaceutical staff taking the Company in diverse directions.

We will further expand on the evolution of the Company in the coming months.

OUTLOOK FOR 2017

In looking ahead to 2017, we realise that we have a number of parallel activities in different continents within the CLINUVEL Group. For all stakeholders to remain informed on the Company's progress, we will have bi-monthly newsletters and half-yearly management updates along with the necessary market announcements to be disclosed via the ASX.

Our commitment to vitiligo in 2017 will be largely dictated by the FDA's responsiveness to our proposed advanced clinical program together with the Vitiligo Expert Consilium (VEC) which overlooks the clinical need, treatment regimen and clinical trials. A meeting with VEC is scheduled in H1 2017.

In 2017, we will provide the outlines of VALLAURIX's strategy, while carefully preserving the technological knowhow residing with our teams. Fitting within CLINUVEL's diversified strategy our global teams work together to ensure the consolidated group of companies support the focus: to provide patient groups novel medicinal therapies now and in the future.

Time has proven to be our friend, no matter how frustrating regulatory and governmental delays are. Patients' and CLINUVEL's urgencies are not always shared by decision makers, but history has shown that our teams possess of a relentless persistence to overcome the hurdles in time. We are all guided and focused on a shining beacon to get SCENESSE® to EPP patients in Europe and the US.

The recent AGM in Melbourne exemplified how CLINUVEL's following is evolving into enthused shareholders who view our breakthrough technology as one with multiple applications for the future. Certainly the journey undertaken by US-based shareholders to attend the Australian meeting speaks volumes, and reflects the increasing attention the company is receiving from the US market. I thank these overseas shareholders for their zest to travel a long way to meet us.

I am confident that, in 2017, CLINUVEL will continue to build a reliable foundation for growth in an environment where patients need novel drugs and therapies.

Finally, we share our appreciation to all our patients, at whom we look with admiration for their endurance and energy to gain access to SCENESSE®, and to all expert physicians for the time they have made available to EPP patients and our teams.

I wish all shareholders, patients and physicians a Merry Christmas and healthy 2017.

Philippe Wolgen

[1] *SCENESSE® (afamelanotide 16mg) is approved in Europe as an orphan medicinal product for the prevention of phototoxicity (anaphylactoid reactions and second degree burns) in adult patients with EPP. The innovative nature of the therapy in an orphan disorder, the lack of available scientific instruments to adequately measure the therapy, ethical considerations and the drug's positive safety profile were some of the factors which led to the European marketing authorisation of SCENESSE®. Information on the product can be found on CLINUVEL's website at www.clinuvel.com. Information on EPP can be found at www.epp.care.*

[2] *NICE responds to article in The Times. 3 September 2013. https://www.nice.org.uk/news/article/nice-responds-to-article-in-the-times.*

US UPDATES

On 24 October the FDA held a scientific workshop on EPP, seeking perspective on EPP disease symptoms, its impact on daily life, experience with current treatment regimens for EPP, and aspects of clinical development of products intended to treat EPP. Transcripts from the workshop are available at http://www.fda.gov/Drugs/NewsEvents/ucm501389.htm.

CLINUVEL met with representatives of the FDA's Division of Dermatology and Dental Products (DDDP) on 7 November to discuss the content and format of a new drug application (NDA) submission as part of the US regulatory pathway for CLINUVEL's medicinal product SCENESSE® (afamelanotide 16mg). CLINUVEL will submit the modular dossier on SCENESSE® on a rolling basis during the first half of 2017. After the completion of the submission of the dossier the FDA will observe a validation period of two months. Further interactions between the DDDP and CLINUVEL will take place as the submission progresses.

More information can be found on the announcements section of CLINUVEL's website, www.clinuvel.com.

ANNUAL GENERAL MEETING

CLINUVEL held its Annual General Meeting (AGM) on 28 November in Melbourne. Copies of the CEO's AGM presentation, along with speaking notes, can be found on CLINUVEL's website, www.clinuvel.com.

HQ RELOCATION

Recent events

- FDA Scientific Workshop on Erythropoietic Protoporphyria (EPP) – Silver Spring (24 Oct)

Upcoming events

- 2017 American Academy of Dermatology Annual Meeting – Orlando (3 Mar)

CLINUVEL's Melbourne office has relocated to 6/15 Queen St Melbourne, Vic, 3000.

ASX: CUV

Shares on issue:	47,725,227
Net cash from operating activities (Jul-Sept '16)	A$3.562
Average daily volume (past 3 months):	**22,658**
Cash/Asset Balance at June 30 '16:	**A$17.265m**

CLINUVEL is also listed on XETRA (UR9) and issued a level 1 ADR with Nasdaq International Designation (CLVLY).