Clinuvel communique

CLINUVEL 2020

For those who have followed the Company over the years, the journey of our teams has most often been counter-current to arrive at the present point. Rather than traversing along the fastest imaginable and plotted route to success, we have frequently been impelled to take tortuous avenues to achieve our objectives. I do not believe that dead reckoning is applicable to pharmaceutical innovators, and in building CLINUVEL to a long-term establishment we will need to navigate through a contorted path to ensure ongoing success. In this third periodical of 2017, the future will be laid down themed as "**CLINUVEL 2020**". The Board of Directors had, for years, revisited the possibilities to grow the Group on offerings beyond SCENESSE® (afamelanotide 16mg).[1] Today I have the pleasure of sharing with you some of the background, while the unveiling of the exact process will follow at a later stage. In any event we plan to erect a monolithic Australian architecture in which all stakeholders can take pride in years to come.

Prerequisite to any discussion on further expansion was the successful release of SCENESSE® through European EPP Expert Centres (EEECs) and advancing the regulatory pathway in the US (FDA).

A number of factors had dominated the Board's deliberations. First had been the quest to diversify the Company's offerings beyond SCENESSE® and SCENESSE® ENFANCE®, the product in development for paediatric erythropoietic protoporphyria (EPP) patients. The timing of diversification had been a most critical consideration. Persistent focus on execution is a hallmark of the Company and had led to our success, thus we did not want our teams to divert attention from SCENESSE®.

Therefore, only once our team have completed the US regulatory pathway for SCENESSE® would the time to channel the attention of our managers to other domains be most opportune. Since our staff had remained with the Company – many for more than eight years – their intrinsic understanding of the Company's functioning and objectives would offer the foundation for our growth. I firmly believe that successful companies are made up of a blend of unique existing talents and added new skills, all held together by one common and clearly defined objective to establish and grow a going concern.

The foundation of growth was to expand on our core competencies and the skills of CLINUVEL's current teams. Unique capabilities usually distinguish a specialised entity from its peers, and we had determined that staying close to our acquired expertise would lead to the highest probability of success. To name a few, our managers' biomedical understanding of the use of melanocortins, G-protein coupled receptors, photoprotection, skin and biological interaction with light, biochemical signalling pathways, and, importantly, our proficiency in project finance and financial management are some of the identified main skills. There is plenty more knowhow residing with our managers, but it goes outside the realm of this communiqué to list them all. The Board of Directors had concluded in our pursuit of growth that each stage would require evaluation of minimal risk – borne out of operational and financial execution.

A further factor was the vision to reinvest in ongoing research, and to go long on innovation. Where established large pharmaceutical companies expend a median 8 to 12% of their earnings on R&D, we believe that for small and midsize companies this number ought to be consistently higher to spur growth.

Gradually, our joint venture VALLAURIX PTE LTD is becoming central, an innovation centre to assist in long term growth of the Company.

In general, my view is that corporate objectives should strive for a going concern to become resistant to

macroeconomic and regulatory risks, one which can navigate through market fluctuations and, preferably, one comprising multiple business units to spread uncalculated systemic risk. In doing so, it is mandatory that we maintain the same financial discipline as the past 12 years which brought us where we are today.

The research and development in our laboratories in Singapore aim to provide diversity in product categories, markets, and target groups. Together with our quest for diversification, leveraging core values, skills and emphasis on longevity of managerial talent the challenge has been to gradually introduce R&D risk – albeit keeping it minimal – for CLINUVEL's next steps towards independence and growth.

In the coming months, a number of publications will centre on the restructuring and repositioning of CLINUVEL, illustrating how we aim to take the Group to gradual growth while providing more visibility in US, ASEAN countries, and the EU.

An important factor in our decisions has been the next generation of human talent identified in Asia-Pacific and macroeconomic conditions in the region. Key to our success is horizontal integration of all staff across our offices, free exchange of information and transfer of historical data. While this seems logical and obvious, the practical implementation across four continents is far from easy. Yet it is the only way to guarantee long term success and we are well under way.

EUROPEAN DISTRIBUTION

The first two quarters we have seen growth in the use of SCENESSE® and importantly we have also seen repetitive use of SCENESSE® by EPP patients treated in accredited EEECs; over 98% of patients treated in the first annual cycle are seeking a second year of photoprotection. The analyses of conditions of use provide some insight in patients' behaviour and physicians' attitudes towards the novel therapy.

As CLINUVEL UK has already been subjected to two laborious regulatory inspections this year, I had great satisfaction in seeing how our European – and Australian – team passed the most recent tests. After six months of preparation and work, the UK team, led by General Manager Lachlan Hay, withstood the regulatory investigations in pharmacovigilance and good distribution practices. It is not unexpected for a company not long after entering its post-marketing phase of a novel compound to receive regulatory inspectors onsite. This probing seeks to learn whether all quality systems, (such as pharmacovigilance and European distribution standards) are in place and functioning. The frequency and number of planned visits the past two years has kept our European and Australian teams well occupied.

For over a decade we had frequently pledged publicly not to allow off-label use of SCENESSE® for a variety of reasons. Despite our proclamations European regulators still seek evidence and confirmation of our exclusive 'on-label' supply to EPP patients. At times I have been surprised by the lack of realisation of leading regulatory authorities as to the significance of public statements made by listed companies, including CLINUVEL. In many ways our professional teams wish to stand out, not only in the way we conduct ourselves in relation to the management of SCENESSE® but also how we follow up our commitments to safe distribution to EPP patients.

While European insurers and payors publicly announce they will impose greater scrutiny on novel therapies for rare disorders, our teams continue to push for treatment access for EPP patients. In a common market where uniformity in pricing and access are to become the mainstay of pharmaceutical products, we demand that our teams persist for a worthy clinical cause for those who have no other means of therapy and live an isolated existence. The never-let-go-attitude has become the code of the Group, a pride we take with us.

A recent presentation made by a well-known physician diagnosed with EPP in one of the European countries will remain with us forever. His 53 years of trying to find a life 'out of darkness' was offset and compensated by eight years during which he had received SCENESSE®. In his summary he stated that as a general physician he had been in a position to feel more compassion for his patients, since he had learned through his own suffering that one cannot express the intensity of his internal ordeal and lack of energy to enjoy the simplest things in life. Using one's own experience with porphyria as a patient to assist one's own patients deepens the notion of compassion on more

than one level. During five decades his immediate family, wife and children had never understood the intensity of his internal "inferno" and "pain" (expressed thus due to lack of appropriate terminology) until the day he had received afamelanotide. The treatment has changed his life forever and provided a vital energy that he had never experienced, freed from any inhibition and physical handicap. His emotive gratitude for the work of CLINUVEL's teams was heartfelt and priceless, it motivates our teams to continue the fight.

US FILING, MARKET ACCESS AND PRESENCE

The rolling submission of the SCENESSE® dossier to the FDA is ongoing. Exchanges with the FDA are taking place to ensure that the scientific package on SCENESSE® satisfies the regulatory criteria for a new drug application (NDA). The data from the commercial distribution in Europe assist our work towards the NDA dossier, whereby the real-time safety data from European patients provide our dossier on the assessment of long term safety of the drug, since European patients have continuously received the product without significant concerns of safety. Once the final of the five modules are submitted, and the FDA has validated the dossier, our teams will announce the start of the FDA's review clock.

In the meantime US EPP patients request information on the availability of the drug in the US, undoubtedly due to the seasonal intensity of symptomatology. Knowing that there is a treatment available while not being able to obtain it must be an unspeakable frustration of many diseased patients in the US. I stress to all of the American – but also to the European – patients that the regulatory hurdles to make a novel drug available for a poorly characterised disease are increasingly high, and the administrative processes after drug approval have become complex and time consuming.

The preparation to make SCENESSE® available as a prescriptive drug in the US is under way. We recognise that there is much demand for the innovative therapy and we also recognise a demand for the Company's presence in the US. In careful analyses of other Australian companies who have pursued a US presence – either having substantial operations and/or a listing – we are progressing towards a decision to base part of the Company in the world's largest and most knowledgeable pharmaceutical market. As stated before, a number of internal, systemic, and financial factors dictate our considerations towards basing CLINUVEL in the US. In the coming weeks, we shall make our decisions public regarding the repositioning of the Group.

As a continuum of CLINUVEL's International Designation granted by Nasdaq, we monitor the growth of our Level 1 American Depository Receipt (ADR) program. CLINUVEL established its Level 1 ADR program (OTC: CLVLY) in July 2004 primarily to facilitate US investors to invest in the Company and there has been a consistent growth witnessed over time in both the number of issued ADRs and in their trading volumes. The support of the ADR program is reflected in 11.6% of the total outstanding shares in CLINUVEL held in sponsored ADRs, and this support exists without the Company actively promoting the program.

In viewing the liquidity of CLINUVEL shares in comparison to the liquidity of the ADR program since our International Designation on Nasdaq on 2 June 2016, it appears that the daily trading of CLINUVEL's ordinary shares on ASX (ASX: CUV) averaged 0.044% of its total issued shares. This compares to an average daily volume of ADRs traded of 0.156%. In relative terms, the average daily traded volumes as a measure of total issues is higher for the ADR program than the CLINUVEL shares publicly traded on the ASX.

A careful first comparative conclusion is that the Level 1 ADR program appears more liquid to the ASX for the 12 months since the Company joined the International Designation. However, it is by far still trailing the monetary turnover on the ASX. Naturally one needs to account for buoyant US equity markets since the new administration against a reasonably stable ASX All Ordinaries.

Together with the percentage of US institutional investors in CLINUVEL's stock we cautiously consider the attraction of CLINUVEL's story to US investors and future steps. One can make a case that US investors have been attracted to the CLINUVEL story the past few years since European approval of SCENESSE®, but that more US demand is likely

when CLINUVEL starts distributing its lead drug in the US, should SCENESSE® obtain marketing license from the FDA.

BREXIT

The topic of the recent UK election was centred around the prime minister's wish to have a firm mandate from the electorate prior to entering the BREXIT negotiations. While the decision to call elections backfired on Theresa May, as reflected in the unexpected resurgence of the Labour Party, Article 50 had been invoked and a point of no return has been reached for the UK. Whereas the mechanistic execution of BREXIT is a daily political topic in press, the UK's departure is expected to have some impact on CLINUVEL's post-marketing program and distribution of SCENESSE®.

In the coming months, we will form a definitive view on how to guide our recently established UK team through the uncertainty arising from BREXIT. Whether the UK remains part of a common market or customs union will determine our ability to continue the physical distribution of SCENESSE® from the UK. From a regulatory viewpoint, the European Medicines Agency (EMA; our collective regulator at present) must leave London to redomicile in one of the European countries. Restructuring of EMA's committees and possible reappointment of new national rapporteurs will impact CLINUVEL one way or another. The European rapporteurs overseeing the post authorisation program for SCENESSE® may well change. In addition, one may conclude that the role of the UK's regulator (MHRA) within the EMA is to diminish – despite Jeremy's Hunt plea to keep MHRA part of the European regulatory framework – therefore continuity of knowledge and familiarity of the SCENESSE® dossier may be lost once the BREXIT becomes reality. There will be more to report on progress during the remainder of 2017 and throughout 2018.

INTERNATIONAL PORPHYRIA CONGRESS, BORDEAUX 25-29 JUNE

Fresh in our minds is the International Congress of Porphyrins and Porphyrias (ICPP), held last month in Bordeaux, France. This is the sixth time CLINUVEL has been represented at this biennial event, and our development programme has featured heavily throughout the years.

For those perhaps less familiar with the disease, EPP is one of a 'family' of genetic disorders grouped together due to a common underlying mechanism: defects in the haem synthesis pathway, resulting in the accumulation and storage of compounds, porphyrins, in various organs. Despite this common heritage the various forms of porphyria present very differently in the clinic. Even for expert physicians this common grouping may cause confusion, hence our need to reiterate at every opportunity the mechanism and impact of EPP.

The variety of clinical presentations in porphyrias inevitably makes the ICPP a diverse conference, as well as one of the few medical conferences where patients are thoroughly integrated in the discussion. Since a great number of individual physicians and specialties treat EPP patients there is a need to secure multi-disciplinary care, which is currently being offered through the European post authorisation and special access programmes.

The ICPP provided the CLINUVEL team with the opportunity to interact with patient association representatives and expert physicians from across the globe. During the patient day Dr Emilie Rodenburger, CLINUVEL's Director of Clinical Affairs, provided an overview of the post authorisation safety study, and other risk minimisation measures which have been outlined in previous editions of this newsletter. Throughout the Congress these measures were raised a number of times by patient representatives and physicians. It is clear that there is great interest in how they are being implemented, and whether they remain the most appropriate methods of tracking long term use of a novel drug in EPP.

Dr Janneke Langendonk[2] of Erasmus Medical Center Rotterdam presented the first observational results from 12 months of the use of SCENESSE® in EPP. We continue to monitor ongoing use of the drug. Prof Elisabeth Minder of Triemli Hospital in Zurich presented on the broader theme of market access for novel medicinal products, using the SCENESSE® experience in Switzerland as a case study. In particular Prof Minder emphasised the value of special access programs – such as compassionate use programs – in rare diseases, for allowing clinicians to accelerate access in cases of severe unmet need.

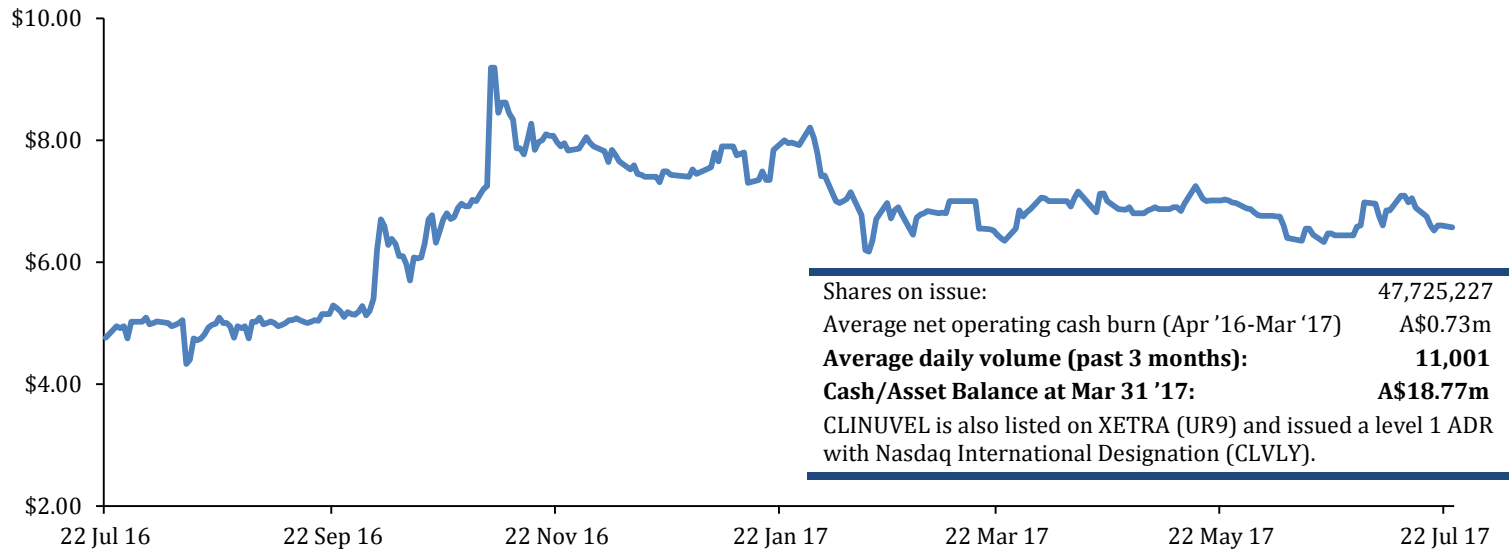
Having seen some of our first clinical results presented at this Congress in 2007, it is now even more satisfying to witness the ongoing expert discussions on the use of afamelanotide as an established EPP treatment.

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.

[2] CLINUVEL does not sponsor, reimburse or incentivise expert physicians to present clinical results from the clinical administration of SCENESSE®.

ASX: CUV



Shares on issue:	47,725,227
Average net operating cash burn (Apr '16-Mar '17)	A$0.73m
Average daily volume (past 3 months):	**11,001**
Cash/Asset Balance at Mar 31 '17:	**A$18.77m**

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