CLINUVEL Communiqué

7 February 2019

CLINUVEL

Dear patients, shareholders, friends,

In this second Communiqué for the year we will delve deeper in the ongoing treatment of erythropoietic protoporphyria (EPP) patients in Europe and look ahead at the expected news flow from the US Food and Drug Administration (FDA) in the coming months.

Gradually, we are sharing the contours of the Company (see the notes to "AGM 2018": CUV by 2021) and discussing our progress towards expanding the Company.

EUROPEAN DISTRIBUTION

As of June 2018, 98.5% of the European EPP patients who had received treatment during the previous two years were continuing to receive SCENESSE® (afamelanotide 16mg)[1] in the third annual cycle. This percentage had slightly changed to a 95% rate of continuation and positive feedback on treatment of 99.3%. The results are significant in light that CLINUVEL does not actively promote the drug treatment but enables clinical demand and purchase orders to occur "as is". This commercial approach can be open to much critique but reflects our belief in an open system where patients and physicians can decide together whether a treatment should be received and prescribed without the pharmaceutical company intervening. We are fully aware that not all would opt for this commercial path, but our attitude to date has been proven correct, is defendable and has received some acclaim from insurers and other payor groups. As said, this *laissez-faire* attitude to specialty product distribution has suited our teams.

While the orders for SCENESSE® have increased monthly, our quality department, pharmacovigilance team and regulatory professionals have been working incessantly with National Competent Authorities, the European Commission and independent consultants to ensure continuation of drug supply in the midst of the introduction of the Falsified Medicines Directive[2] – 8 February 2019 – and the rapidly-approaching Brexit[3] – 29 March 2019. Both events have left the pharmaceutical sector in a frantic state to mitigate against supply disruptions in Europe and the UK.

CLINUVEL has established a subsidiary in Ireland to streamline the import into Europe of SCENESSE® and allow for ongoing European distribution while our second manufacturing facilities in Europe are assigned to test and release the product within the customs union. As stated before, CLINUVEL only supplies accredited European centres of porphyria expertise. This ensures:

1. absolute control on distribution,
2. selective use by experts working in a multi-disciplinary setting, and
3. avoidance of off-label use of SCENESSE®.

We are therefore pleased to see that thus far only one "off-label use" has been allowed by our teams, for a terminally ill CEP (congenital erythropoietic porphyria) patient. We are all moved by the healthcare misfortunes patients

endure, exceptionally and occasionally we are able to provide SCENESSE® on a compassionate basis.

As the third Annual Report was submitted to the European Medicines Agency (EMA) in December 2018, we aim to continue the stringent pharmacovigilance program overseeing the use of the drug in EPP patients in Europe, with a planned harmonisation of the program in the future for US patients.

In terms of reporting obligations, now in the third year of European supply we have received EMA notification that the frequency of the Periodic Safety Update Reports (PSURs) is continuing with two reports due per annum. The burden on our teams is considerable and takes much valuable time away to perform other pressing matters and pharmacovigilance tasks.

BREXIT

As 29 March 2019 approaches and a significant historic event will befall Westminster, the preparations to ensure orderly transfer of medicinal product licenses are under way. Specifically, our teams are working around the clock to see that our European dossier is being transferred from the UK to Ireland, while some of the functions of our pharmacovigilance and quality assurance will be split between the European Union and the UK.

Our primary obligation is to ensure that the various National Competent Authorities as well as the overarching EMA are satisfied that CLINUVEL has taken all precautions to ensure that no counterfeit products can enter the supply chain. In CLINUVEL's case this hypothetical risk is zero, since we control the product distribution to selected university centres, accredited to prescribe SCENESSE®. In addition, the chosen implant formulation is unique and set to CLINUVEL's specifications which has precluded the commercial development of any other biosimilar product thus far. Therefore, in the case of SCENESSE® the risk of falsified medicines entering the supply chain is not even theoretically imaginable. Since our pharmacovigilance teams follow up any EPP patients on treatment and no off-label use is permitted, the risk of counterfeits is nil. Our systems were deliberately constructed to pre-empt any of these counterfeit discussions to be held on potential risk.

As to the regulatory side, as reported last year the EMA decided to move its headquarters from the prime location of Canary Wharf in London to the newly built high rise in the Vivaldi district of the Zuidas in Amsterdam. It is expected that more than 25% of the EMA staff will seek employment elsewhere. Regrettably this will likely cause a lack of continuity – as every business would face with such a significant percentage of its work force leaving. The physical relocation will take place between 11 February and 25 March, during which time the EMA will suspend many of its activities and an overall slowdown is expected to last until July.

In the meantime, CLINUVEL has seen the appointment of a new rapporteur, while the MHRA will abandon its role as co-rapporteur to be replaced by France. A rapporteur and co-rapporteur act as supervisory national competent authorities within the EU and are the first points of contact for the Company when it comes to discussing product related matters. Our challenge is to carefully manoeuvre through a European system which finds itself in a state of flux.

FDA REVIEW OF SCENESSE®

Our regulatory teams are currently working with the FDA's Division of Dermatology and Dental Products to supply all further information requested. In a series of correspondence, the Division poses questions on all detailed aspects of the dossier and drug product. For instance, the conditions under which the drug would be prescribed in the US and by whom, the status of the expert centres, the training materials, the accreditation process of expert centres and more details related to supply chain. As said in the January News Communiqué, around **8 April 2019** we expect to receive further questions from the FDA on the labelling conditions of the product as well as comments on our proposed post-marketing strategies. CLINUVEL will pursue controlled-distribution of the product in the United States to mitigate all possible 'product risks' in the new market while appeasing the concerns of the pharmaceutical regulator. The same approach to safety of patients will apply as we have taken in other parts of the world.

Held in great uncertainty, the industry witnessed the possible impact of the US government shutdown on the activities of the US FDA. The FDA's commissioner Dr Gottlieb stated in January that a shutdown would pose operational challenges to the agency and put user fee programs in peril. Although the filing of the 'orphan product' SCENESSE® had been completed prior to the US shutdown, it is not to say that the FDA is not scrambling for available manpower in each Division. The FDA reviewers do deserve our utmost sympathy for working throughout the existing submissions without knowing if and when they would be paid. Now that the pay freeze has been lifted, we hope for the sake of the reviewers, patients and all involved that the second threat of a renewed moratorium will not take place. Our experience thus far has been positive as the FDA is progressing its scientific review of SCENESSE® without having communicated a shortage in available personnel. We will keep all informed as and when material events related to the US administration unfold.

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
MAY	Final communication, Q&A clinical use post-MA

8 JULY 2019: PDUFA DATE

FDA RISK-BENEFIT SCENESSE®:

1. Marketing Authorisation (Approval)
   OR
2. Complete Response Letter (Rejection)

With much interest we watched the State of the Union address, with President Trump referring to drug pricing as a point of attention for the current administration. After just an hour in the oration, he asked the Congress for more transparency and an end to price differentiation for foreign drugs coming to America. We will deliberate on our pricing strategy later this year, however I pause a moment to recall our decision in 2014 to set an example for the industry by introducing the concept of uniform pricing of SCENESSE®, treating all nations equitably. We foresaw a global movement of curtailing pharmaceutical prices and believed fair treatment of all nations, hospitals and end

users, prescribers, was in the best interests of patients and payors, and we stuck to our plan. Trump concluded by stating that this administration (and probably with the consent of Democrats across the aisles), will succeed in putting a halt to higher drug prices in America. As we have been in discussions with the US distributors and pharmacy chains the reception to CLINUVEL's attitude was embraced and seen as 'refreshingly novel'. Without any claim on ownership of concept here, as a Board we think this health-economic approach is socially responsible and fair. I will comment more on this topic later this year.

At a time when Google has been fined €50 million for failing to be transparent on how it uses data, although at much smaller scale, the risks of managing clinical and patients' data are increasingly being scrutinised in the sector. CLINUVEL is establishing global systems to ensure it not only complies with General Data Protection Regulation (GDPR) but also circumvents any future discussion on personal and clinical being managed.

As reported, in 2014 CLINUVEL established a specific European EPP Disease Registry and intends to convert this now into a Global Disease Registry to ensure that longitudinal data are stored and managed for the exclusive purpose of safety monitoring and reporting to the EMA and FDA. In the anticipation of possible future concerns or complaints on data handling and distribution, the Company uses a so-called pseudonymised approach to data, whereby the identification and personal details of each patient are stripped for our staff to remain blinded at all times. This correct and cautious approach proves relevant in a world where GDPR has become the subject of political debate. We pre-empted the complexity surrounding data management in the hope to be able to provide waterproof answers to possible FDA questions the coming months on this topic. In establishing a regulatory and pharmacovigilance team in the US, we intend to coordinate the European and US activities, preparing ourselves for a possible launch of the product in the US.

CLINUVEL EXPANSION

In the past year we organised ourselves by laying a foundation for growth. First, we aligned all staff and stakeholders on the basic values of CLINUVEL by explicitly stating our approach and value system for years to come. One may find the 'rules' of our playbook on CLINUVEL's website. This corporate guidance – so to speak – serve as a basis for expansion, be it organically and inorganically. All new staff are inducted in a set of values which connect us all.

Second, we strived for all open-ended projects to be completed such that we could free up managerial capacity to allow greater focus on other items, preparing the next phase of growth. Foremost, the regulatory progress in the United States gave us gradually more time as the dossier came to a completion.

Third, we have invested in a new and comprehensive financial reporting system. The training of all finance staff and alignment of timelines across all offices are some of the factors which provide the basis for further growth.

Foremost, in continuing to financially manage the Company with an eye on the changing macroeconomic and geopolitical climate we analyse the quarterly global indices and financial data as part of our business to understand which way relevant economies are heading. Naturally, we watch the Eurozone and United States as our addressable markets. We take into account the decisions made by central banks to keep the rates unchanged or impose small hikes while we revisit our foreign currency exposure. As we track the growth forecast to be around 3% GDP mark globally

and 2.4% for the US, the yield curves and monetary policies in general require us to remain vigilant of market fluctuations and possible impact on the Company's stock market performance. Having gone through various cycles, we deliberate daily on how to manoeuvre the Company through times of contractions and tightening, a healthy debate prompting us to seek ways to reduce the effects of systemic risk to our business. We live by the lines 'be prepared at all times, see as far as one can'.

Expansion and risk are closely connected, and we see our duty at CLINUVEL as managing the duration risk of the Group. Operationally we do this by focusing on research & development of follow-on products (both prescriptive and over-the-counter), the continuous search and discussions about compatible product categories offered to us, complementary services, and integration of technology.

As exemplified previously, we have seen the need for us to change our infrastructure to be able to compete in years to come, this requires investments in technology and, at opportune times, in further expansion of the Group through acquisitions.

As to the prescriptive category of our follow-on products, CLINUVEL intends to be the first company to launch topical melanocortins for a range of diseases and conditions. Our teams are building the framework to commercial success by addressing each part of the supply chain of this novel category. Whereas SCENESSE® is a specialty pharmaceutical for the use by select academic centres, the follow-on topical products may have a much wider user and prescribers' base. Therefore, starting from the targeted product profile to supply chain we are investing in systems to increase probability of success.

In all our approaches, risk minimisation dominates the decision processes.

[1] SCENESSE® (afamelanotide16mg) 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] Directive 2011/62/EU, amends to Directive 2001/83/EC.

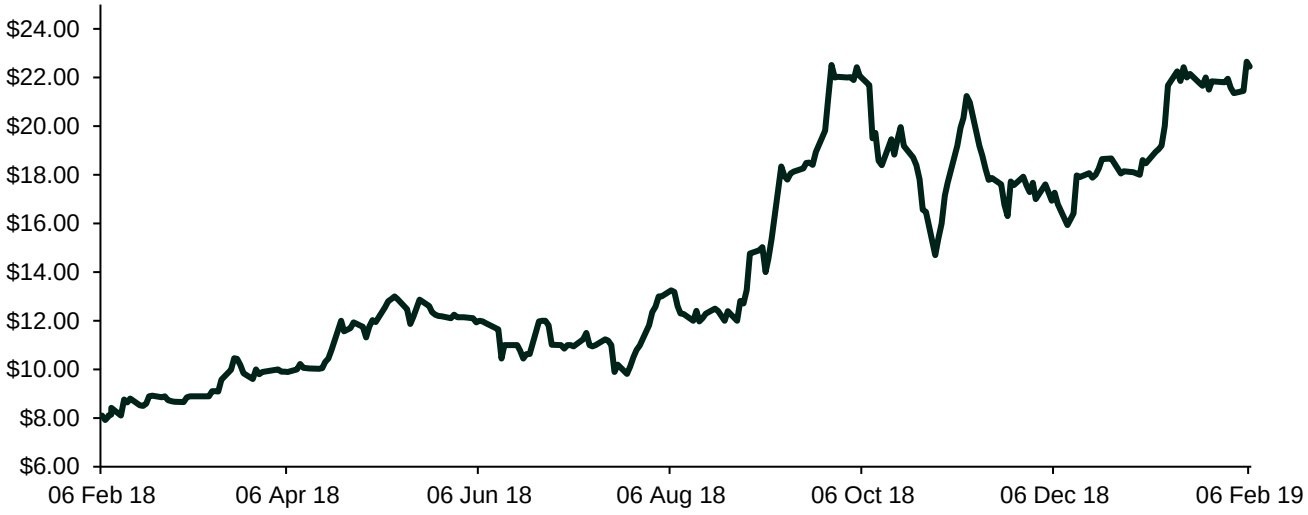
[3] Two years from the invocation of Article 50 of the Treaty of the European Union by the United Kingdom.

ASX: CUV

Share price

(ASX: CUV 6 Feb 2018-6 Feb 2019)

Shares on issue	47,857,986
Fully diluted	49,608,546
Market cap (6 February 2019)	A$1.07b



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 6, 15 Queen St
Melbourne, 300 Vic, Australia

+61 3 9660 4900
+61 3 9660 4909

www.clinuvel.com