Clinuvel communique
August 2016

# CEO's Outlook

In the arduous journey from explorative concept to development to commercial availability of the novel molecular entity – SCENESSE® (afamelanotide 16mg)[1] – one may become engrossed in the processes leading to the desired outcome. The ultimate goal of changing people's lives is what drives us at Clinuvel and our team is constantly surprised by the dramatic feedback from patients stating that they are now to able to lead a life they never could imagine. It is one thing to understand the impairment endured by erythropoietic protoporphyria (EPP) patients but it is another thing to actually live with the restriction. Our teams have genuinely understood over the years what EPP patients go through daily, and we wholeheartedly revel in the choice to treat these patients. Most certainly, it has been my aspiration and the ultimate goal of the Clinuvel team to commercially release SCENESSE® to the entire EPP patient population.

Over the last months we have finally been able to distribute the photoprotective product under the European Risk Management Plan, including the long term post-authorisation safety study. The product is commercially available in two European countries, the Netherlands and Austria and non-commercial special access schemes are ongoing in Italy and Switzerland. We have initiated the roll out methodically to establish complex pathways to obtain full reimbursement for the product in each country. Each of the European countries has its own rules and regulations surrounding market access. It falls outside the remit of this bulletin to expand on the progress in each individual country. These processes require time and lengthy communication through conviction on the safety and effectiveness of the drug, while the pressure from the end users is felt.

I do sympathise with the need to curb healthcare costs in Europe and the scrutiny to which each novel therapy is subjected. Yet, in my twelfth year of leading a global program – fully funded by active investors – the need for treatment of EPP patients should no longer be a topic for debate, nor should be the necessity to reimburse at a state level the only available therapy.

Here we do not differ from our peers in seeking full reimbursement for a new therapy. I do believe, however, that Clinuvel differs from others in that it has gone through the most demanding procedures to see the drug come to market. The porphyria medical community has been very patient in its quest to obtain treatment with SCENESSE®. With the novelty of the product, new mode of action and a '*somewhat misunderstood disorder*', national authorities and insurers have been faced with a conundrum as to how to evaluate the drug. Yet, I hold that the novelty of this specific therapy and lack of comparator can never be a reason to defer or even deny payment, and most payors centrally or regionally to date have agreed to cover the patients.

EPP is a specific and unique disorder. The health economic impact of light deprivation and the various handicaps posed by EPP fall outside the usual economic modelling. As discussed over the years, including the explanation during the 2015 Annual General Meeting, one can mirror EPP to a number of 'disease comparators', but such an exercise does not adequately reflect the patients' impairment and inability to expose themselves to outdoor conditions and live a *normal* life. In our recent experiences most insurers, governmental and advisory bodies are coming to understand and accept the novel approach required to rank EPP amongst a new class of treatable diseases.

Payors are asked to gain knowledge and appreciation of the specific impairment in a short space of time, but then to also acknowledge the medical solution offered by SCENESSE®. It is not easy for these panels and decision makers to learn new pathology, innovative science, and quantify the therapeutic solution proposed.

I have always seen our drug as one which would facilitate a previously unattainable quality of life for our patients. In clinical terms I believe we have delivered a drug which provides freedom compared to a baseline existence of a lifelong avoidance to sun and light due to continuous fear and anxiety of burning. This message is slowly being acknowledged in the EU at national level.

Naturally, over the years we foresaw that payors would seek to quantify the added benefit that SCENESSE® provides to patients and society. In modern days, the ***ongoing*** *value added* by a newly introduced therapy is a crucial question. Our team had an advantage of time to prepare for the health economic questions and evidence required to ultimately satisfy national advisors and insurers. In many European countries the process of evaluating the benefit of SCENESSE® has already started or is in its final stages. For instance, in the UK SCENESSE® is currently being evaluated as a Highly Specialised Technology, where the decision process for reimbursement takes more than one year.

The specialised community of medical experts in Europe and the patient associations have engaged in an ongoing communication on the availability of new treatment. Since patients freely move across national borders to seek treatment, it was logical for us to adopt a uniform European pricing policy for SCENESSE®. While this may be uncommon for our peers in the industry, in the case of SCENESSE® we do not support price differentiation as a justifiable option in today's open market.

Initially some of the national insurers were sceptical about the treatment value. Indeed, some suspected that each country would be paying more than its neighbour. As we progress, however, there is growing recognition of the transparent, fair approach Clinuvel has followed. A fixed price across the EU implies that Clinuvel is bearing the currency fluctuation in an economic zone where eleven different currencies prevail next to the Euro currency.

Each quarter we will report on the European progress in EPP. We expect seasonal influences due to the highest medical need expected from February to November. We receive clinical feedback that some countries require the treatment all year round, while others expect drug administration at times of highest light intensity and therefore increased risk of anaphylactoid reactions and burns.

Once the uniform pricing is introduced in the countries of reference and the majority of centres are actually dispensing the drug, Clinuvel will make the outcome of ongoing negotiations on pricing and reimbursement available. Our expectations and targets are being met, and for now we are reasonably content with the response we obtain from most national agencies and payors.

Of all the years I have managed Clinuvel it is easy to say that this year is one in which the excitement and enthusiasm of all our members of staff and Board is at the highest I have ever witnessed. Our staff are displaying an indelible appetite to overcome each hurdle, perhaps motivated by the ultimate goal of seeing the patients' responses. The distribution under the European PASS protocol is demanding and requires many processes to be followed; the real time demand for the drug is driven by patients and physicians and these factors seem to spur our people. The senior staff, supporting staff and finance team are going the extra mile to progress the company, and I am frankly impressed by the workload our relatively small team is able to handle.

## FDA

I also see that Clinuvel's progress in the US is providing extra impetus to our teams. It is a privilege to lead the company as it tackles a number of complex issues to be solved with the FDA. While details can be shared, I believe that most shareholders understand the progress Clinuvel is making.

The process of introducing SCENESSE® in the US has been far from easy. The EPP and vitiligo programs are related and both contribute data to a safety profile which is being accepted by the FDA reviewers. We long aimed at timing the interconnectedness of the programs, such that an in-depth dialogue would evolve around one drug at different dosing regimens in two targeted disorders. While one indication (vitiligo) is further away from regulatory approval than the other (EPP), by emphasising safety we overcame the expected threshold of maximum safety from regulators. We started from the premise that each novel molecular entity is potentially seen by regulators as a health hazard. Since the safety issues faced with thalidomide, the safety systems concerning an introduced drug – otherwise known as 'pharmacovigilance' - became the main focus of attention of regulatory authorities. We addressed this theme systematically over the years of development.

The recent Fast Track designation and the FDA's green light to compose a New Drug Application – scientific dossier – are two of the most significant pieces towards full acknowledgement of safety of SCENESSE®. Later this year we expect to hold further discussions with the FDA, details of which will be made public as the agency allows. For now it suffices to say that SCENESSE® is moving closer to being available to all EPP patients who need it.

Philippe Wolgen

## US PROGRAMS PROGRESS

Clinuvel announced key updates to both its US development programs for SCENESSE® (afamelanotide 16mg) in recent weeks.

On July 6 the company announced that the FDA had granted SCENESSE® Fast Track designation for the treatment of erythropoietic protoporphyria (EPP). This designation recognises both the severity of EPP and the *unmet medical need* of the disorder.

On July 18 the company announced that the FDA had concluded an initial review of Clinuvel's clinical data package for SCENESSE® in EPP and deemed it satisfactory for NDA submission. This now enables the company to file a New Drug Application (NDA) on a rolling basis for US regulatory assessment.

On August 3 the company released results from an important pre-clinical study of SCENESSE® for the pigmentation disorder vitiligo, modelling the use of the drug as a combination therapy with narrowband UVB (NB-UVB) light. The pre-clinical study, requested by the FDA prior to advanced clinical trials, confirmed the safety of the combination therapy over a 24 week period, adding to the long-standing pre-clinical safety profile of SCENESSE®. Clinuvel will now seek a guidance meeting (Type C) with the FDA to discuss the final clinical trial program in vitiligo required to submit a second NDA.

Details on these announcements can be found on Clinuvel's website, www.clinuvel.com.

## NASDAQ INTERNATIONAL DESIGNATION

Clinuvel's sponsored level 1 American Depository Receipt (ADR) program has been included in Nasdaq's International Designation, a new visibility offering available to non-US companies. Clinuvel is the first life science company to be selected for this initiative, first launched by Nasdaq on 9 December 2015.

Nasdaq is one of the world's leading electronic stock markets, attracting many companies who focus on innovation. The International Designation provides Clinuvel with access to Nasdaq's visibility assets. Nasdaq will distribute the company's news through its press release distribution service, reaching both investor and financial news and online services.

## Upcoming events

- 24th European Academy of Dermatology and Venereology Congress – Copenhagen (Oct 7-11)
- FDA Scientific Workshop on Erythropoietic Protoporphyria (EPP), *invitees only* – Silver Spring (Oct 24)

## ASX: CUV

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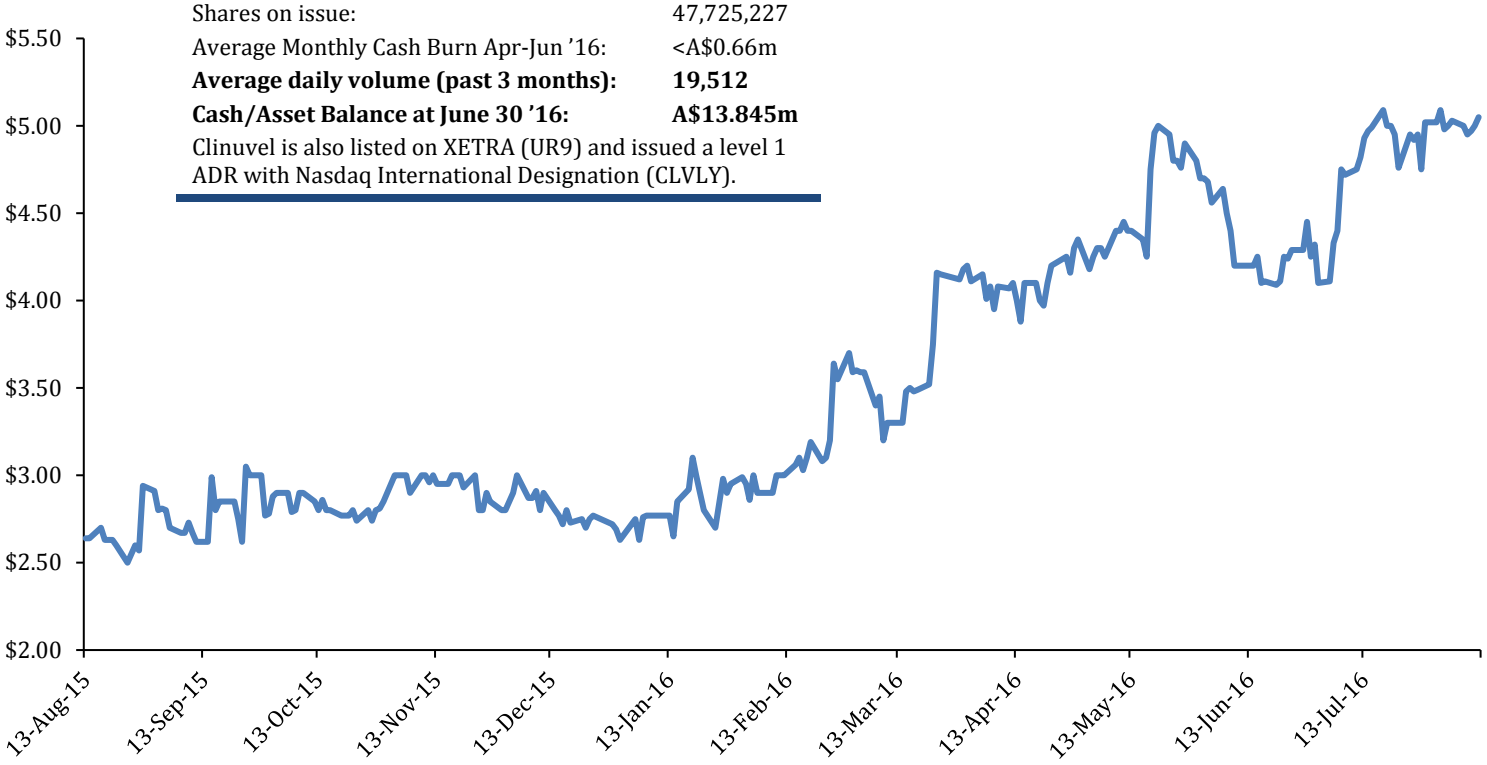
| Shares on issue: | 47,725,227 |
| Average Monthly Cash Burn Apr-Jun '16: | <A$0.66m |
| **Average daily volume (past 3 months):** | **19,512** |
| **Cash/Asset Balance at June 30 '16:** | **A$13.845m** |

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




[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. Information on EPP can be found at www.epp.care.