ABLIVA Delivering mitochondrial health

# Newsletter

December 2020

## The power of today's medical science is impressive

Soon we will be putting the strange year of 2020 behind us. The year has been marked by the covid-19 pandemic that periodically crippled the world and led us to change our behaviors and habits both privately and as professionals. As we enter a new year, we are doing so with greater optimism than we did just a few months ago. The rapid development of new vaccines means that there are good reasons to believe that life will be able to return to a more normal situation. The vaccine development that has taken place in 2020 shows the power and opportunities of today's medical science.

At Abliva, we are proud to be a certainly small yet part of the collective of academia and industry that works to make the world better. We too have had significant success during the year, especially in our KL1333 project developed for the treatment of primary mitochondrial diseases. After positive contacts with the FDA, we are now planning to initiate a pivotal Phase II/III study in the second half of 2021, which means that the development of this project during the year has taken a decisive leap towards the market.

With this I would like to wish everyone a merry Christmas and Happy New Year!

Also, take the opportunity to take a look at our new website abliva.com, launched just now.

**Erik Kinnman**, CEO

# KL1333 - development with the patient in focus

**There is a flurry of activity at Abliva right now. During the autumn, the company announced that the plan for the drug candidate KL1333 will be converted to significantly accelerate the development towards a treatment for patients with primary mitochondrial disease. In the second half of 2021, Abliva expects to be able to start a pivotal clinical efficacy study in patients, which may directly form the basis for market approval if it falls out well. This study will be a combined Phase II/III study.**

**Matilda Hugerth** is head of clinical development and regulatory affairs at Abliva and one of the key figures in the KL1333 project.

The most common is to first conduct a Phase II study involving a limited number of patients to learn more about the effects and doses of the drug, and then to conduct two Phase III studies in a larger number of patients to confirm the efficacy of the drug. The decision to carry out a combined Phase II/III efficacy study instead of several separate efficacy studies may at best shorten the time to market approval by up to two years.

Before the efficacy study can get started, a number of important preparatory activities will be carried out. Matilda Hugerth is a key person in this work at Abliva. She works as Director of Clinical and Regulatory Affairs, and has her office at the company's premises in Lund, Sweden. We met her for an interview.

**The news that Abliva plans to conduct a pivotal combined Phase II/III study in the second half of 2021 came as a very pleasant surprise to many who follow the company. Can you give us some background to this decision?**

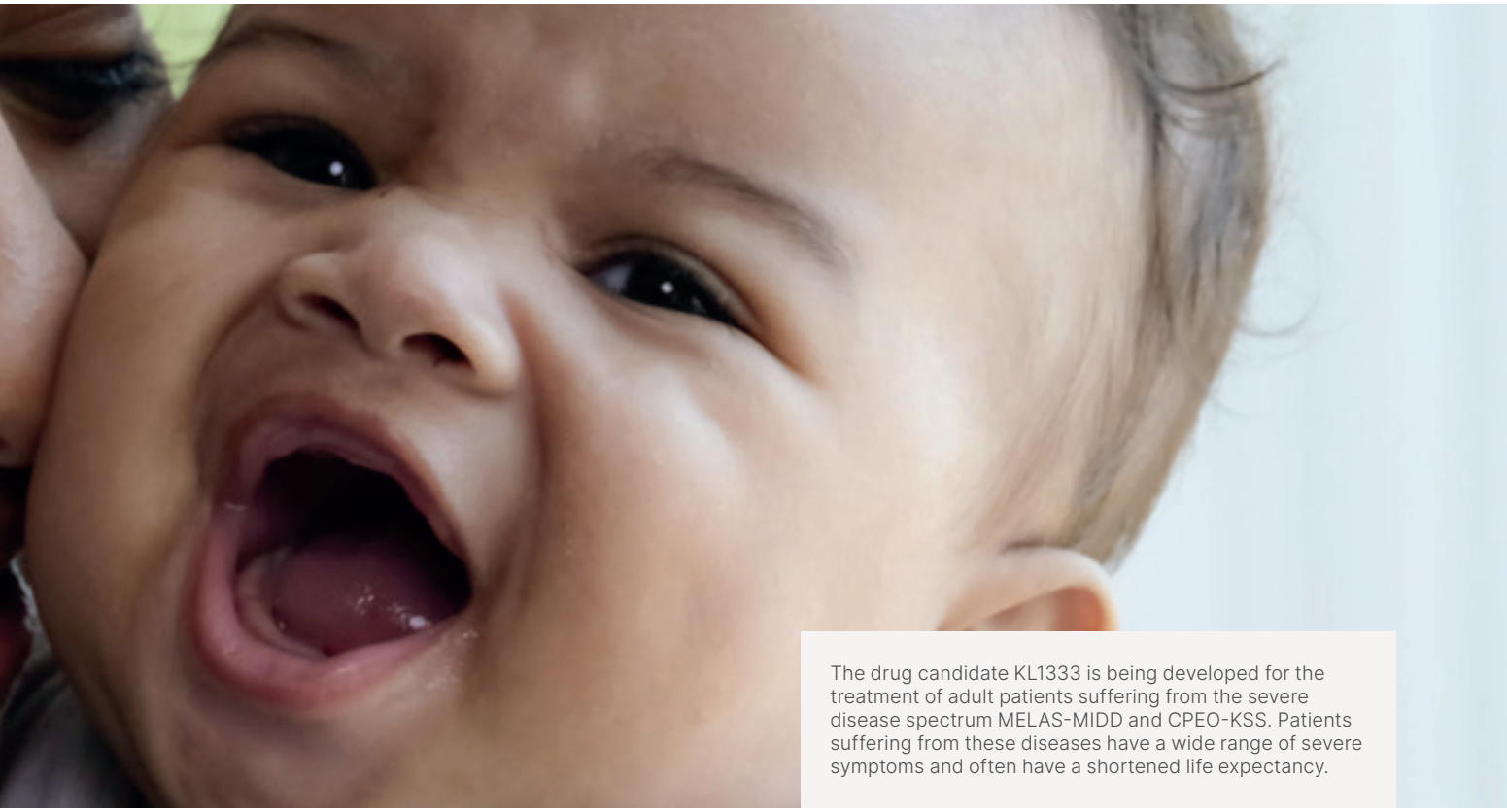
"It has emerged as a result of interactions with the US Food and Drug Administration, FDA. In terms of size, our study will resemble a Phase II study for a drug that is developed for a common disease. The fact that we are moving within the orphan drug space and intend to treat patients with severe diseases that currently lack treatment options, enables a compressed development plan".

**You have said that you are working according to a so-called patient-centric approach. What does it mean and why is it important in drug development?**

"The patients are our future recipients – it's for them we work, so we think it goes without saying that it is their needs that should form the basis of our operations. We are actively working to put patients at the centre of all aspects of what we do".

**How does it affect your work in more concrete terms?**

"As I said, it affects everything, from the overall strategy when choosing endpoints and small details in the study protocols, to making the structure of the studies facilitate as much as possible for the patients participating in



The drug candidate KL1333 is being developed for the treatment of adult patients suffering from the severe disease spectrum MELAS-MIDD and CPEO-KSS. Patients suffering from these diseases have a wide range of severe symptoms and often have a shortened life expectancy.

our studies. By working with patient organizations, we get information that enables us to have this approach".

**You have also told us that you plan to use a patient-reported outcome measure to measure the efficacy in the pivotal study, and that you now will do a study to validate it. Can you tell us more about it?**
"We want to ensure that we include all dimensions of de disease expressions that are most limiting and troublesome for patients. We therefore want to be able to measure the effect of KL1333 in the way that is most relevant. In the study, patients with mitochondrial disease will be in-depth interviewed about their disease and the scales we plan to use, according to an established methodology for this type of study. We are in the process of discussing the details of our proposed design with the FDA right now, to ensure that all regulatory aspects are covered before we start the interview study early next year".

**A drug-drug interaction study is now also underway. Why is that study being done?**
"Patients with mitochondrial disease are unfortunately often multimorbid and receive many different drugs at the same time to relieve the symptoms. By conducting a study in healthy volunteers where we investigate how concomitant dosing of KL1333 and a variety of representative drugs affects the turnover in the body of these drugs, we can facilitate for patients in our upcoming Phase II/III study. It is a regulatory requirement to have investigated this before entering the pivotal phase of clinical development".

**Right now, the patient portion of your Phase Ia/b study is ongoing. What is the goal of this part of the study?**
"This approach is in place to create early experience of how KL1333 behaves in the body in patients with mitochondrial diseases. The idea is to gather as much information as possible that we can use for the design of the Phase II/III study in the best way".

**How is this study affected by the ongoing pandemic?**
"First of all, I am very grateful to all these patients who, despite covid-19-pandemic and their own severe disease, agree to participate in this intensive study where they undergo lots of examinations and sampling. They receive KL1333 or placebo for ten days and are tested before, during and after that period, which is mostly spent in a hospital. We try to facilitate participation in the study as much as possible, including by offering alternatives to public transport now during the pandemic. So far, more than half of the patients have gone through the study".

**Finally, what does the support from the US and UK regulatory authorities mean?**
"Both the US and UK regulatory authorities support our accelerated plan for KL1333, which creates opportunities to carry out the combined efficacy study in both the US and Europe. This allows us to reach more patients and at the same time deepen our cooperation with the specialist centers that coordinate the care of patients with mitochondrial disease".

# Eventful Q3 paves way for Abliva's main candidate KL1333

**The third quarter of the year has been eventful for biopharma company Abliva, which released its report at the end of last week. The quarter began with the FDA giving the thumbs up to an accelerated development plan for the main candidate KL1333 and now the British Medicines and Healthcare products Regulatory Agency (MHRA) has also taken a positive view of the plan. At the same time, a drug interaction study is being initiated as a first part of the preparations for the important phase II / III study that is planned for the second half of 2021. BioStock has talked to CEO Erik Kinnman about the past quarter.**

Lund-based Abliva develops drugs for the treatment of primary mitochondrial diseases. During the past quarter, their main candidate KL1333, which is aimed at MELAS and similar conditions, has achieved important milestones.

### Positive feedback from FDA and MHRA

KL1333 has already obtained orphan drug classification in both Europe and the USA, and this summer the FDA recommended that Abliva conduct a cohesive phase II/III study that will form the basis for registration. This means that Abliva does not have to carry out separate phase II and phase III studies, which would have been both more expensive and more time-consuming. According to the company, a combined phase II/III study like this is estimated to cost 30-40 million USD until the application for market approval – approximately 10-15 million USD less compared to a plan with separate phase II and phase III studies. The FDA guidance also points towards a reduction in the time to potential market approval.

Last week, British MHRA also gave positive feedback on Abliva's accelerated development plan. This positions KL1333 for a trial approval also in the UK for the planned phase II/III study that will form the basis for registration.

### Increased activity since feedback from the FDA

Since receiving the FDA's positive feedback during summer, the company has worked intensively to prepare for the next step in development. The final clinical program has been redesigned and the goal is to be able to start the phase II/III study that will form the basis for registration during the second half of 2021. Abliva plans to carry out the required toxicological studies in parallel with the phase II/III study, and this plan has been approved by both the FDA and the MHRA.

In the ongoing phase Ia / b study with KL1333, the part of the study involving patients is currently under way and half the patients have been dosed.

### Several studies planned

Prior to the phase II/III study, Abliva has planned a number of other studies. The company announced last week that it has initiated a drug interaction study (DDI study) in order to be able to assess the potential impact of KL1333 on other drugs that are sometimes used in the symptomatic treatment of patients. Here, the first healthy volunteers have been dosed and a total of 14 healthy volunteers will for 12 days receive a daily dose of KL1333 together with a mix of other drugs.

Furthermore, the company is also planning a qualitative validation study of specific patient-reported outcome measures, a clinical dosing study, as well as a patient register study.

### NV354 – towards clinical studies during 2021

With regards to Abliva's second main project, NV354, for the treatment of Leigh's syndrome, work on the project has progressed during the quarter and the company aims to be able to complete preclinical pharmacology and safety studies during the first half of 2021. At the same time the company aims to produce test materials to then begin clinical studies during second half of 2021.

### Commenced the process to ensure financing

Abliva strengthened its finances in two stages during summer in order to be able to carry out the accelerated development work, primarily with KL1333. In May, a rights issue raised 54 MSEK and shortly thereafter, investment company Hadean Ventures showed its confidence in the project by investing 20 MSEK in a directed rights issue. At the end of the third quarter, the company's cash balance stood at just over 73 MSEK.

In light of the investment need that comes with the phase II/III study next year, the company's board has begun the process of securing additional financing. In the quarterly report, Abliva states that they are investigating various possibilities, including attempting to attract international capital to the company.

We contacted CEO Erik Kinnman for a comment.

This article was originally published on BioStock, 25 November 2020.

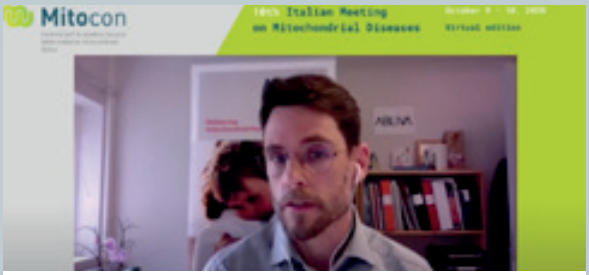
**Erik, first of all, how would you describe the past quarter?**
– It has been a successful and exciting quarter where we are now rapidly approaching the phase II/III study with KL1333 that will form the basis for registration. Soon after the end of the quarter, we dosed patients with KL1333 for the first time and we are now looking forward to the possibility of delivering a treatment option for patients with primary mitochondrial disease for whom there is currently no treatment. This is an area with ”blockbuster” potential.

**British MHRA is following in the path of the FDA and giving you positive feedback regarding the accelerated development plan for KL1333. What does this mean for the development of KL1333?**
– Not only does it pave the way for the planned study that will form the basis for registration, but the feedback from both authorities also validates the documentation and thus the project. This is also important when we are now discussing various possibilities for future financing of the business.

**There appears to be a lot going on right now, especially in the development of KL1333. What activities do you see as the most important in the near future?**
– The activities that need to be completed before the start of the study that will form the basis for registration, i.e., the drug interaction study and the validation study of the patient-reported outcome measures are the most important ones. We expect to have results from these studies well in advance of the application for the start of the study that will form the basis for registration.

# Spreading the (virtual) word

**Part of the work at Abliva consists of making the company's activities visible in different public contexts, partly to increase understanding of the enormous medical needs of people with primary mitochondrial disease, but also to increase interest in the company among potential investors or partners. Since the covid-19 pandemic struck in earnest, everyone has had to change. However, this has not prevented the possibility of virtual networking and dissemination of knowledge. Abliva has recently participated in the following events:**




**10th Italian Meeting on Mitochondrial Diseases**
*9 – 10 October 2020*

Magnus Hansson, Abliva's CMO, presented the company's innovative drug development programs for primary mitochondrial diseases and gave an update on the status and goals. The meeting was arranged by the Italian patient organization Mitocon.
https://youtu.be/oKa1xLUHgGI

**Aktiespararna – Women's night**
*12 October 2020*

Catharina Johansson, CFO, and Eleonor Åsander Frostner, R&D and Communications, presented the company during the evening. The event was arranged by Aktiespararna.
https://youtu.be/Vuwyc48oWu0


**BioStock Life Science Summit**
*17 – 18 November 2020*

CEO Erik Kinnman presented the company. The event is usually held in front of an audience at Medicon Village in Lund, but was held virtually this year.
https://youtu.be/2L7z3rwu3UQ

**Redeye Life Science Day**
*26 November 2020*

CEO Erik Kinnman gave an update on the company's activities during the day.
https://www.redeye.se/video/event-presentation/800122/abliva-ceo-erik-kinnman-presents-at-redeye-lifescience-day-2020

**Mitochondrial Medicine 2020**
*30 November – 2 December 2020*

The conference is gathers academic researchers and pharmaceutical companies from around the world. Abliva's Chief Medical Officer Magnus Hansson presented a poster entitled Targeting $NAD^+$:NADH ratio in primary mitochondrial disease with KL1333.
https://youtu.be/FUi_PcvoXhI

Take a look at our new website abliva.com