ABLIVA Delivering mitochondrial health

Newsletter

October 2020

Growing understanding of the importance of finding drugs for primary mitochondrial diseases

Mitochondrial diseases are classified as rare diseases. However, there are a large number of different mito diseases that cause severe symptoms and the total number of patients in the United States and Europe is estimated at around 135,000. The patients' association **International Mito Patients** is doing a fantastic job of raising awareness of mitochondrial diseases, including through the annually recurring World Mitochondrial Disease Week. This year Abliva drew attention to this important initiative by arranging a virtual Mitochondrial Day.

The great need for mitochondrial disease drugs is also demonstrated by the FDA's recommendation that Abliva should accelerate the development of its KL1333 project by conducting a coherent Phase II/III registration study, which will accelerate the clinical program significantly.

You can in this issue of our newsletter read more about all this.

Erik Kinnman
CEO

FDA recommendations lift the KL1333 project to pivotal clinical study

Registration study planned for the second half of 2021

Primary mitochondrial diseases cause a number of severe symptoms such as fatigue, developmental disorders, heart failure, diabetes, and reduced mobility. Primary mitochondrial diseases also often lead to premature death. Although primary mitochondrial diseases are classified as rare, the total number of patients is high. In Europe and the US, the number of patients is estimated to at least 135,000[1]. Apart from a drug for the mitochondrial eye disease LHON, there are currently no approved medical treatments for primary mitochondrial disease. This is the background to the FDA's recommendation that Abliva should accelerate the development of the drug candidate KL1333 by turning the planned Phase II proof of concept study and subsequent Phase III pivotal study into a coherent pivotal registration[2] Phase II/III study.

A unique opportunity to accelerate development

The FDA's recommendations have been received with great enthusiasm by Abliva. By being able to turn the two planned studies into a coherent study and to be allowed to do the mandatory long-term toxicological studies in parallel with this, the development time can at best be shortened by up to two years. Abliva has now started work to simplify and accelerate the clinical program for KL1333 with the ambition to start the pivotal Phase II/III study in the second half of 2021. Ahead of the Phase II/II study, Abliva will initiate two preparatory studies in the second half of 2020: a study for the validation of patient-reported outcome measures and a drug-interaction study, which Abliva recently received approval from the UK Medicines Agency MHRA to start.

Significant commercial potential

The commercial potential of an orphan drug such as KL1333 is significant. An indication of the business opportunities can be seen in the average price of an

"I am very pleased that in this way we will have an opportunity to reach our patients much earlier. The FDA has demonstrated that they understand the vulnerable position of patients with mitochondrial diseases and how important it is that we develop drugs as quickly as possible that can significantly improve the quality of life," said Abliva's CEO Erik Kinnman in a comment.

"The announcement from the FDA is extremely positive for Abliva. By the fact that the path to the market for the KL1333 project has now become so much shorter, I believe that Abliva's attractiveness on the capital market has been greatly strengthened. The fact that we are about to conduct a pivotal Phase II/III study provides the conditions for increased international interest in the company," comments Abliva's Chief Financial Officer Catharina Johansson.

orphan drug in the United States of USD 150,000 per patient per year. The world market for orphan medicinal products was USD 128 billion in 2019 and is estimated to have an annual growth rate of 11.2% between 2019-2024 to reach USD 217 billion by 2024.[3] KL1333 has been estimated by Edison Group to reach sales of USD 574 million per year.[4]

International capital raising

Conducting a Phase II/III study is relatively cost-intensive, although the KL1333 orphan drug designation limits costs compared to Phase III studies for common medicines. Given the very good news, Abliva will actively seek funding for the KL1333 program, also focusing on international capital markets.

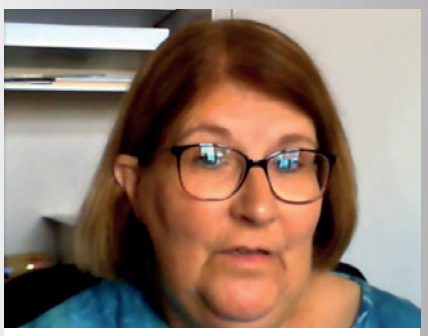
1 Gorman et al., Prevalence of Nuclear and Mitochondrial DNA Mutations Related to Adult Mitochondrial Disease, 2015
2 The most important study for the registration of a new medicine.
3 EvaluatePharma, Orphan Drug Report 2020
4 Analysis by Edison Group paid by the Company, 26 June 2020

"KL1333 is a very exciting drug candidate and with the recommendations of the FDA it shows additional strength. Our ambition is to significantly improve the lives of the patients we target who are heavily affected by their illness. With the announcement from the FDA, we are better placed than ever to make a difference," says Abliva's Chief Medical Officer Magnus Hansson.

KL1333 - PATIENTS/INDICATIONS
KL1333 is being developed for the treatment of adult patients in disease spectra MELAS-MIDD and CPEO-KSS. These diseases cause a wide range of severe symptoms and a poor quality of life.

The drug candidate is intended for long-term oral treatment.

INTERVIEWS AND FILMS FROM ABLIVA'S MITOCHONDRIAL DAY (click on the pictures)



Elja van der Veer from the Netherlands is founder and chair of the patient organization International Mito Patients (IMP).

Frank J. Sasinowski is an advisor on regulatory matters and a proponent of patient involvement in drug development.

Rebecca is five years old. She suffers from a primary mitochondrial disease and must be under constant supervision.

Abliva raises awareness of mitochondrial diseases

From 13-19 September, the World Mitochondrial Disease Week took place with events around the world aimed at raising awareness and knowledge about mitochondrial diseases. These diseases are rare and treatment options are scarce, which complicates the already difficult situation for these patients. Swedish Abliva, a leading company active in developing drugs for primary mitochondrial diseases (PMD), organised a virtual Mitochondrial Day on September 16 to highlight the extensive medical need in PMD.

Mitochondrial diseases are a group of rare diseases characterised by malfunctioning energy production in the mitochondria. This, in turn, often leads to a range of difficult and complex symptoms such as difficulty to move and breath, and in many cases to a shortened life expectancy.

These diseases affect about 1 in 5,000 people and, as with many rare diseases, knowledge about mitochondrial diseases is limited and there are no effective treatments available.

World Mitochondrial Disease Week – a global event

Therefore, World Mitochondrial Disease Week is organised in September each year with the aim of putting mitochondrial diseases under the spotlight. Behind this initiative is a network of national patient organisations that go by the name International Mito Patients. During the last week, a number of such events was organised, including one where you could participate in a Kiltwalk in Edinburgh to raise money for research on mitochondrial diseases, and several well-known buildings, such as the Colosseum in Rome, were lit up in the event's official green colour.

Abliva organised virtual Mitochondrial Day

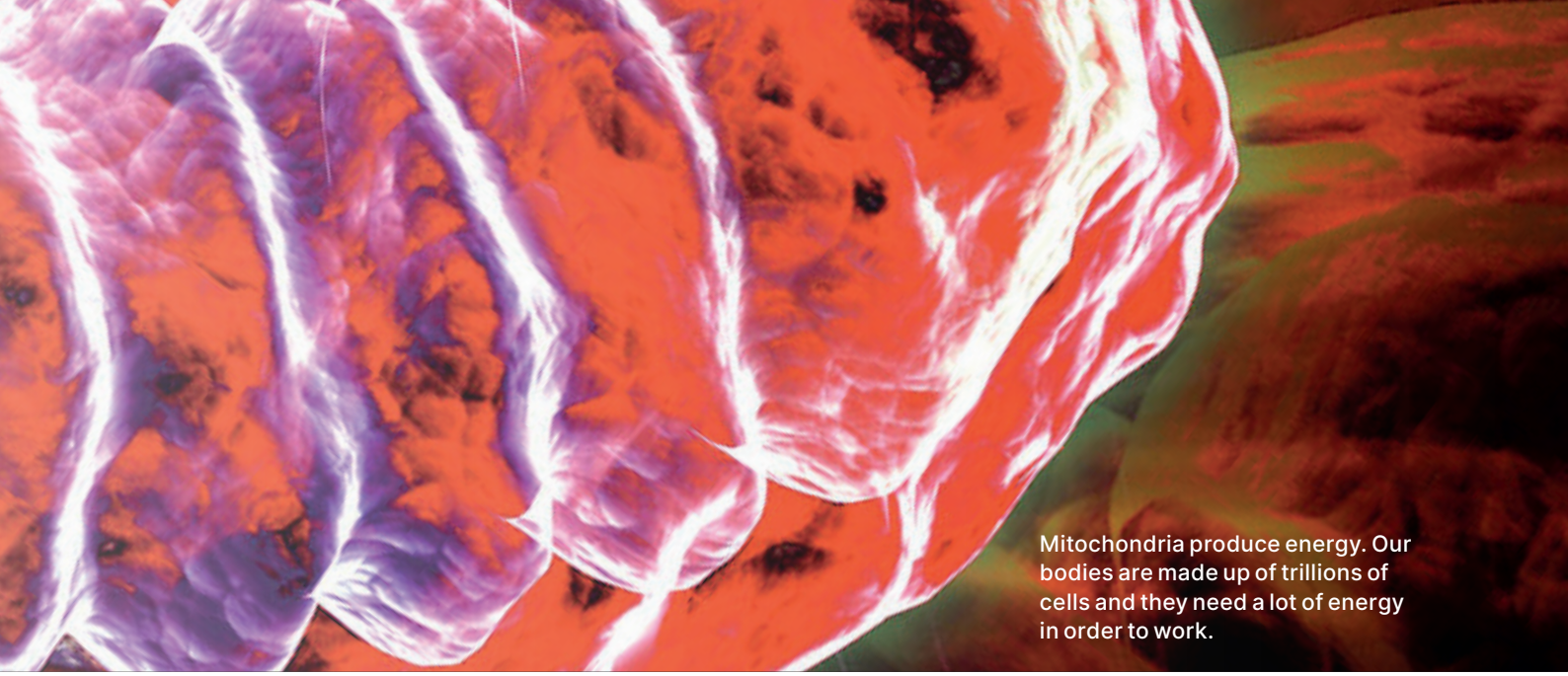
As in previous years, Swedish Abliva, a leading company in primary mitochondrial diseases (PMD), participated in World Mitochondrial Disease Week by organising a Mitochondrial Day – this time in a virtual setting. The company develops two candidates in the primary mitochondrial space, KL1333, which already has orphan drug designation in both the US and in Europe, and NV354.

The agenda of Abliva´s Mitochondrial Day included presentations and discussions that spanned over all aspects of mitochondrial diseases; from what it is like to live with these diseases, to how the US Food and Drug Administration (FDA) and investors view investments in rare diseases such as PMD. The event can be seen in retrospect here.

The company's team also showed their support for the global initiative by running the LHON Eye Society's 5.4 km race. The race took place in Hagaparken, Stockholm, but Abliva's team instead ran the remote version of the race at the company's headquarters in Lund.

Patient focus

For Abliva, it is especially important to highlight the patient and next-of-kin's perspectives perspectives in order to increase the understanding of the great medical need that prevails in mitochondrial diseases. The company works closely with a number of patient organisations and will, as part of the development of KL1333, conduct in-depth patient interviews.



Mitochondria produce energy. Our bodies are made up of trillions of cells and they need a lot of energy in order to work.

During the Mitochondrial Day programme, Elja van der Veer, founder and chairman of International Mito Patients, shared her experiences of living with a mitochondrial disease. She particularly emphasised the importance of strong patient organisations and explained that International Mito Patients' goal is to connect patients, researchers and clinics in order to pave the way for new treatments and possible cures.

For patients, and thus their next-of-kin, PMDs often involve lifelong physical and mental suffering. This fact was underlined in an interview and short film with Adrian Horvath, whose daughter suffers from a mitochondrial disease.

Abliva aims to develop effective treatment

Abliva develops PMD treatments with the aim of increasing the quality of life for patients, with two ongoing projects within the PMD space in its pipeline: the main project KL1333 against MELAS and similar conditions, and NV354 against Leigh's syndrome.

During the event, Matilda Hugerth, director of Clinical and Regulatory Affairs, offered an update regarding the KL1333 project, which has advanced significantly during the year. In early September, the company presented good news, as it was announced that it was accelerating the project development following supportive and positive feedback from the FDA. The agency recommended Abliva to conduct a phase II/III study with KL1333 – more specifically, a pivotal placebo-controlled study to advance the project to market.

The study is expected to begin in 2021 and will be preceded by a qualitative study for the validation of the specific patient-reported efficacy endpoints as well as a drug interaction study in healthy volunteers. A long-term pre-clinical safety study will be carried out in parallel with the phase II/III study, in agreement with the FDA. The new, accelerated plan means that Abliva now has the opportunity to take KL1333 to market and patients much faster than previously expected.

Abliva can shape the treatment of PMD

The virtual Mitochondrial Day ended with a panel discussion between **Erik Kinnman**, CEO of Abliva, **Roger Franklin**, partner at Hadean Ventures – that announced in April its intention to invest 20 million SEK in the company and now holds a Board of Directors seat in the company, and **Annika Espander**, CEO of Asperion and advisor in the life science sector.

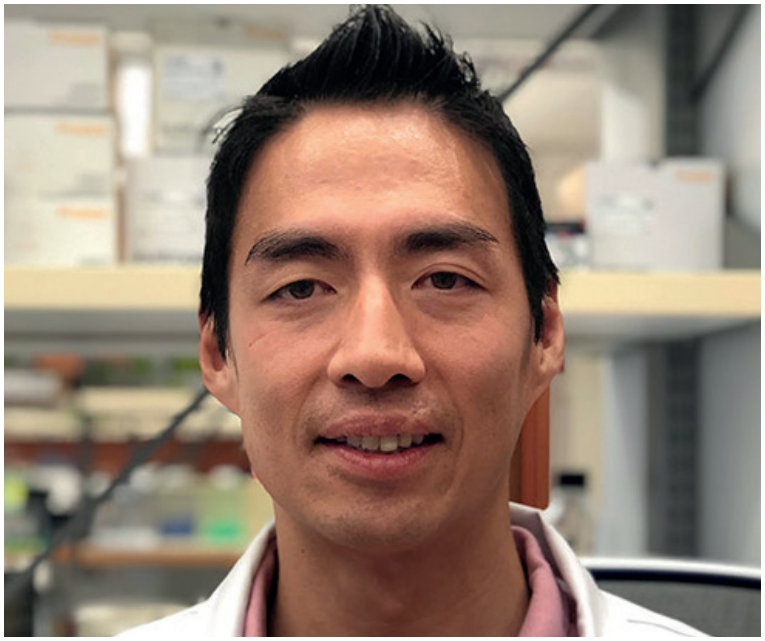
The discussion focused on the growing investor interest in companies active in rare diseases, something that can be exemplified by Hadean's investment in Abliva. Franklin and Espander agreed that companies, such as Abliva, which are active in the rare diseases space, as well as the orphan drug space, constitute an attractive invest-ment. This is mainly due to two of the benefits that come with orphan drug status: market exclusivity for seven years in the US and ten years in Europe, as well as con-tinuous support and guidance from regulatory authori-ties on the path to market.

The FDA's recommendation regarding Abliva's forthcoming phase II/III trial is an excellent example of how orphan drug designation can accelerate the pace of development, which according to the panel is attractive to investors and beneficial to patients.

Espander particularly emphasised that Abliva is in a favourable position where the company can have ongoing dialogues with patient organisations as well as regulatory authorities like the FDA. As there is currently a lack of effective treatments for PMD, there is, accord-ing to Espander, an attractive opportunity for Abliva to help shape a new treatment paradigm within PMD and improve the lives of patients who are currently without treatment options.

This article was made by BioStock and has previously been published on their website www.biostock.se

Mito News in Brief



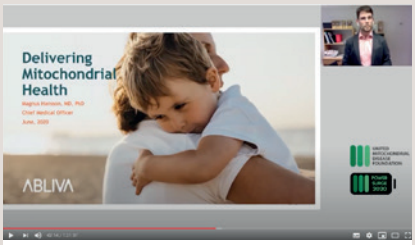
Research with Abliva's succinate prodrugs receives NIH grant

In May earlier this year, BioStock managed to get an interview with David H. Jang, Assistant Professor at the University of Pennsylvania Perelman School of Medicine in Philadelphia, USA, on the occasion of his then recently published research on how to use Abliva's cell-permeable succinate prodrug, NV118, to improve mitochondrial function in cells from patients with carbon monoxide poisoning. See the full article here. The overall project continued and has just received a USD 480 000 grant from the US National Institutes of Health's (NIH) National Institute of Environmental Health Science (NIEHS) for an R21 (R21ES1243). The awarded funding will support the study, entitled *Mitochondrial-directed therapy in carbon monoxide poisoning*, for two years. The long-term goals of the awarded research are to define specific mitochondrial defects in carbon monoxide poisoning and evaluate Abliva's preclinical phase cell-permeable succinate prodrug, NV354, as a novel therapy in an advanced experimental model, with Dr. David Jang as the PI, Dr. Todd Kilbaugh as the Co-I and Dr. Johannes Ehinger as a consultant. Abliva has long had a very successful collaboration with the team in Philadelphia, including Todd Kilbaugh and Sarah Piel.

Additional attention

On 1 September, the research paper *In vitro comparison of hydroxocobalamin (B12a) and the mitochondrial directed therapy by a succinate prodrug in a cellular model of cyanide poisoning* was published in the Open Access journal Toxicology Reports. Based on the findings in this study, David Jang and his co-authors suggest a new possible use for Abliva's succinate prodrugs, as treatment of a condition where there are today limited effective treatment options. Cyanide poisoning can occur from smoke inhalation, as an occupational hazard or as an agent of terrorism. Treatment consists primarily of supportive care and select use of antidotal therapy, e.g. hydroxocobalamin (B12a). David and team show that Abliva's NV118, but not B12a, improves the mitochondrial respiration and decreases the production of harmful free radicals inflicted in an in vitro model of cyanide poisoning.

CEO interview
In light of the positive news about Abliva's accelerated clinical development plan for KL1333, CEO Erik Kinnman gave an interview at Redeye. Watch the interview here.



UMDF Power Surge 2020
On 26 June, 2020, the United Mitochondrial Disease Foundation (UMDF) organized the virtual symposium UMDF Power Surge 2020. Abliva's Magnus Hansson, CMO, was invited to present the company's clinical program for KL1333 and to participate in a subsequent panel discussion.

See Magnus' presentation here.

Abliva's team showed their support for the global initiative by running the LHON Eye Society's 5.4 km race.