ABLIVA Delivering mitochondrial health

Newsletter

June 2021

Positive safety results and signs of efficacy

The Abliva team had a strong start of the year with the completion of the Phase 1a/b study, the drug-drug interaction study, and the important round of financing. These activities provide the foundation for the more substantial milestones that are to come – from the determination of NV354 as a clinical candidate, to the filing of regulatory documentation to support the next KL1333 study, to the first patient dosed in our registrational study.

We are extremely pleased with the positive Phase 1a/b data and look forward to presenting more details during the United Mitochondrial Disease Foundation (UMDF) Mitochondrial Medicine Symposium in late June.

On top of that, we welcomed our Clinical Project Manager, Fia, to the team. She will be working closely with Magnus, our Chief Medical Officer, and Matilda, our Director Clinical and Regulatory Affairs, to drive current and future clinical projects forward towards a much-needed treatment for primary mitochondrial diseases.

It continues to be an exciting year for Abliva and I am thankful to be working with this team which is passionately invested in our work. Have a great midsommar and I hope to meet you face to face in the fall.

Ellen Donnelly
CEO

Published by BioStock 24 May, 2021.

Abliva on the positive study results

In May, Abliva announced positive safety and pharmacokinetic data from its phase 1a/b study with KL1333, as well as signals of efficacy in relevant clinical outcome measures in patients with primary mitochondrial diseases. BioStock reached out to the company CEO, Ellen Donnelly, for a comment.

On March 16, Swedish biotech Abliva announced the completion of its clinical phase Ia/b study with KL1333, the company's drug candidate for chronic oral treatment of primary mitochondrial diseases (PMD). No serious adverse events were reported, and the company said study data would be evaluated during the spring and early summer. Last week, the final outcome of the data analysis was published.

Positive phase Ia/b study results

The primary aim of the double-blind, randomised, placebo-controlled phase Ia/b study was to assess the safety and pharmacokinetics of KL1333, both in healthy volunteers and in patients.

Data from the study confirms single ascending dose data from a prior phase I study, and showed, for the first time, multiple-ascending dose data from healthy volunteers and multiple-day dosing in patients. The study included an analysis on the food effect and split dosing of KL1333 in healthy volunteers as well as a full characterisation of pharmacokinetic parameters in both healthy volunteers and patients with primary mitochondrial diseases.

The CEO comments

BioStock reached out to Abliva´s CEO Ellen Donnelly for a comment on the study results, their importance moving forward, and her take on the future for the candidate.

Ellen, first of all, congratulations on the study results. The study was conducted in collaboration with neurologists at the University College London and the Welcome Trust Centre for Mitochondrial Research at Newcastle University. What were the research group's reactions to the study results, given that there are currently no treatments targeting primary mitochondrial diseases?

– We spoke with the investigators this week and they were, of course, very pleased that the study met its primary objectives, to demonstrate safety and characterise the pharmacokinetic profile in primary mitochondrial disease patients. With these results in place, KL1333 can move forward in clinical development towards regulatory approval of an innovative treatment opportunity to patients which currently lack any proven efficacious and disease-specific therapies. The investigators, as well as we, are aware of the limitations to drawing firm conclusion from such a small and short study, but the positive changes seen in disease-relevant outcome measures provide important data for us as we finalize the phase 2/3 study design and are of course encouraging for the overall objectives of the program.

Despite the fact that the study was not primarily designed to evaluate efficacy and the duration of dosing was only 10 days, you could still see promising signs in the cohort that included PMD patients. Can you briefly walk us through the results that you saw in the PMD patients?

– We saw some exciting early signs of efficacy in the PMD patients in our study. First, the patients treated with KL1333 performed better than placebo patients on two independent fatigue scales and a functional scale called 30 Second Sit-to-Stand. In addition, the patients with the highest exposure of drug in their blood performed the best on the clinical efficacy measures. All of this data will be considered as we work to finalize our clinical design for the Phase 2/3 study.

Does the outcome embolden Abliva moving forward, preparing for the phase II/III study?

– Absolutely. This study provided us with important information about safety, efficacy and dosing of KL1333 and this information strengthens our program as we move towards regulatory submission and study start later this year. A wise mentor of mine once told me that "good drugs declare themselves early" and I hope that this data, in eight patients over 10 days of dosing, is our first sign that KL1333 has the characteristics to go all the way to market, into the hands of the patients who desperately need treatments for their disease.

Also, a second pharmacology study evaluating the interaction of KL1333 with seven enzymes (CYPs) that metabolise other drugs has just been completed. What have you learned from this study?

– The study was a comprehensive drug-drug interaction trial including seven of the most important drug metabolising enzymes in the body. Any strong inhibition of induction of these enzymes could pose issues to combining KL1333 with other medicines and limit which patients could be included in upcoming clinical trials. Even though there is no proven 'disease-specific' drug approved for multisystemic PMD, these patients are often on multiple symptomatic therapies so strong interactions would have posed a problem. The study results only show a mild inhibition of one of the less common CYPs, CYP1A2, so we are very pleased to see that there were no concerning interactions.

Finally, what remains to be done before you can submit an IND application later this year, and when do you anticipate the phase II/III study can be initiated?

– We have a busy period ahead of us as we work to prepare the package for IND submission. First, we will use the data from the Phase 1a/b study (population, dosing, efficacy endpoints, etc) to test our early assumptions on the study design and finalize our clinical protocol. At the same time, the team is working to finalize the clinical study reports for the Phase 1a/b study and the DDI study and we are busy running the fatigue validation study. The team has already started the process of writing the IND, though, so we hope to have everything prepared so that the IND can be submitted as soon as we have all of the supporting data. We remain on track to have the IND submitted and Phase 2/3 study start in the second half of this year but I will be the first to admit that it will be a busy time and everything needs to proceed as planned for us to achieve these ambitious goals!

New at Work

Interview with Fia Ence

In early May 2021, Abliva was happy to welcome Fia Ence to the team in Lund. Fia took on the new position as Clinical Project Manager during an eventful spring, just a few weeks prior to the the company's reporting of positive data from the Phase 1a/b study with KL1333. We took the opportunity to have a chat.

Hello Fia! And welcome to Abliva. You've been with the company for about a month now. What is your impression of the job so far, and what exactly does a Clinical Project Manager do?
-My impression is that I have joined a company fully engaged in developing a much needed treatment for a patient population that has few to none treatment options available. I believe the role as a project manager will be busy, rewarding and fun. As a project manager I will manage study progress regarding time, quality, risk and cost. I will coordinate the creation and maintenance of clinical development plans, as well as select and ensure oversight and collaboration with vendors.

How about your background – could you tell us a little bit about what you've done prior to joining Abliva?
-I have a master's degree in Biomedicine during which I focused on clinical drug development. After finishing my studies, I started working on clinical trials and have done so for the past seven years. Most recently I worked as a Clinical Research Associate, being the primary contact between the study sites and the study management. I have worked within several areas including cardiovascular disease, liver disease, endocrine systems, and metabolic disorders. I have mostly been employed at Clinical Research Organisations (CRO), which I believe can be helpful in my position here at Abliva as collaborations with CROs will be one of my main responsibilities.

What was it that attracted you to Abliva and the position?
-I have been interested in project management for a while and what attracted me specifically to Abliva is their interesting portfolio and the important work towards finding treatment for a group of patients who currently do not have available treatment options. It feels fantastic to be part of a company that works so hard trying to develop a treatment for these patients, and that takes into account symptoms that the patients themselves find the most bothersome, when conducting the upcoming study. I am really looking forward to interact with this patient community in our search for a successful treatment.

In your mind, what will be your major challenges as Abliva's Clinical Project Manager during the next twelve months?
-For the upcoming study I believe a challenge will be balancing the number of study assessments with a patient-friendly approach, since these patients usually suffer from severe fatigue.

Name: Fia Ence
Title: Clinical Project Manager
Dream trip would go to: Inca Trail and Machu Picchu
Rather do while not at work: Spend time with family and friends
Rather eat: Strawberries
Rather drink at a party: Margarita
In bookshelf: Anything between *Pride and Prejudice* and *Sapiens: A Brief History of Humankind*
On tv: Grey's Anatomy

Abliva has raised SEK 80m through directed share issue

(Modified from BioStock, published on 6 April 2021.)

In March, Abliva announced the completion of a directed share issue, later approved by the company's EGM on April 29. The more than 100 million shares were directed at several Swedish and international qualified investors, including Hadean Ventures*. At 0.75 SEK an issue, Abliva raised a total of SEK 80 million, before transaction costs, over two tranches, and the net proceeds will go towards further advancement of the company's clinical assets, mainly KL1333. CEO Ellen Donnelly joined BioStock for a comment on the financing round.

Why was it important to focus on this directed share issue now?

– The feedback Abliva received from the FDA in September last year changed the game plan in a very positive way when the FDA encouraged us to run a single study to support approval of KL1333. This recommendation was monumental for the company and will allow us to get KL1333 to the market approximately 2-3 years earlier than we would have with our proposed sequential Phase 2 followed by Phase 3 design.

– Our registrational Phase 2/3 study is planned to start in the second half of this year, so we are now working hard to de-risk the development program to ensure KL1333 has the best chance of success. Preparing for the registrational study is meticulous work and the directed issue provides the funds to build the evidence necessary to support our Phase 2/3 study – everything from reading out our ongoing studies, confirming our Phase 2/3 study design, to validating our primary endpoint and building our clinical site network.

Can you say anything about the participating investors in this financing round?

– All of the participating investors are qualified investors, both Swedish and international. The group is split between current shareholders and new shareholders. Our largest shareholder, Hadean Ventures, participated in the round with a significant contribution, a signal of the confidence they have in our program.

What comes next for you as CEO of Abliva?

– I am of course extremely happy about the positive results from our Phase 1a/b study and the DDI (drug-drug interaction) study. The results of these studies will inform the final design of our clinical protocol. The final study design as well as the development and commercialization strategy for KL1333 will be important as we communicate the Abliva story across Sweden, Europe and the U.S. As CEO, I pledge to be transparent as to the strengths and opportunities of our programs, and accurately set expectations as to what to expect from the company during this pivotal year for Abliva.

***Hadean Ventures - Investing in the Future of Healthcare**
Hadean Ventures is a European life science fund manager that invests in life science companies across Europe with a particular focus on the Nordic region. Hadean Ventures is managing funds backed by leading European and US-based private and institutional. Hadean Ventures has offices in Oslo and Stockholm and collaborates with world-class academic institutions and start-up hubs across the region.

Spreading the (virtual) word

Communicating our mission, our strategy and our data to the external community (patients, physicians, investors) is critical as we work to build the premier company in mitochondrial medicine. Primary mitochondrial disease is an area unknown to many, so we aim to educate and inform as we work to develop therapeutics to treat these patients. The best way to do this is to meet you all face-to-face, but the COVID-19 pandemic has moved us online. Our recent events have included:

European Biotech Investor Days 2021
7 – 8 April 2021.
https://troutaccess.com/investor.php/c/EUBiotechInvestorDays2021

Redeye Orphan Drugs
28 April 2021.
https://www.redeye.se/video/event-presentation/810274/abliva-ceoellen-donnelly-presents-at-redeye-orphan-seminar-2021?embed

Redeye Investor Forum Online
20 May 2021.
https://www.redeye.se/video/event-presentation/812654/abliva-ceo-ellen-donnelly-presents-at-redeye-investor-forum-may-20th?embed

UMDF Mitochondrial Medicine Symposium
US patient organization United Mitochondrial Disease Foundation (UMDF) is hosting its annual Mitochondrial Medicine Symposium, this year virtual, in late June. Abliva will participate in the scientific sessions:

- Chief Medical Officer, Magnus Hansson, will constitute one of the panelists, on Friday 25 June, at 1:50 p.m. EST, in the Clinical Trials Panel #2 Discussion, together with representatives from Baylor College of Medicine, Cyclerion Therapeutics, and Khondrion.
- Data from Abliva's Phase 1a/b study with KL1333 will be presented on an e-Poster, available to registered participants throughout the event.

Read the latest equity research on Abliva, including:
- KL1333 ready for pivotal Phase II/III trial, by Edison.
- Promising initial data in patients, by Analysguiden.

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