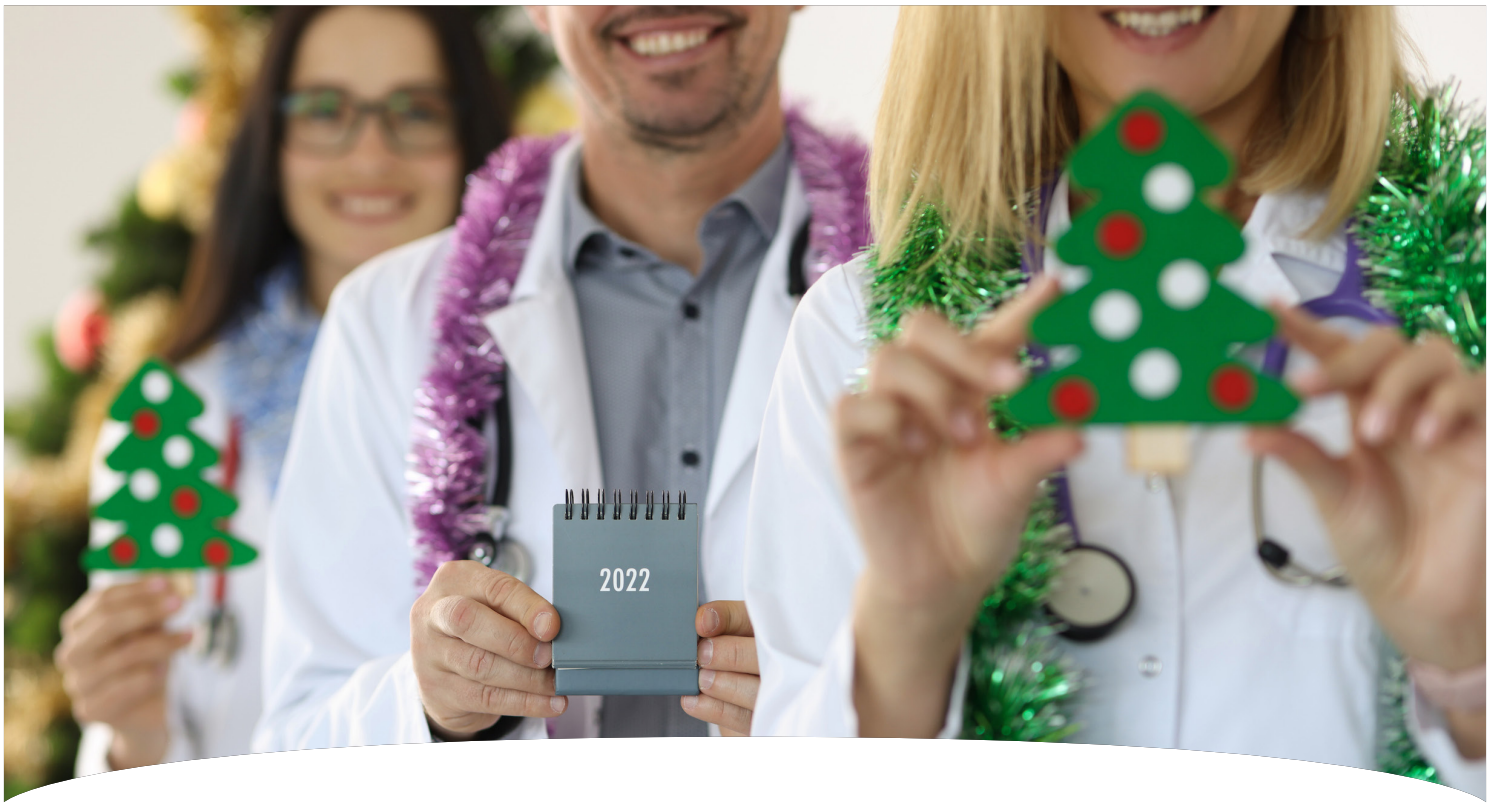
ABLIVA Delivering mitochondrial health



Newsletter

December 2021

Celebrating our successes as we say goodbye to 2021

In November, we received approval of our Investigational New Drug (IND) application for KL1333 by the U.S. Regulatory Authorities, the FDA. This is important news on many fronts. First, the FDA performs a detailed and rigorous review of all of the data supporting the program. Their approval indicates the KL1333 nonclinical, clinical and CMC (Chemistry, Manufacturing and Controls) data is sufficient to justify putting the drug in healthy volunteers, and, given our Phase 1 data, into seriously ill patients with Primary Mitochondrial Diseases. The IND approval means that the FDA will allow us to move forward with the planned study in the US, important not only given the large number of mitochondrial disease patients residing there, but also a critical geography when it comes to pricing and access. The comments provided by the FDA will be instrumental as we finalize the protocol and submit it for consideration by the competent authorities in other countries.

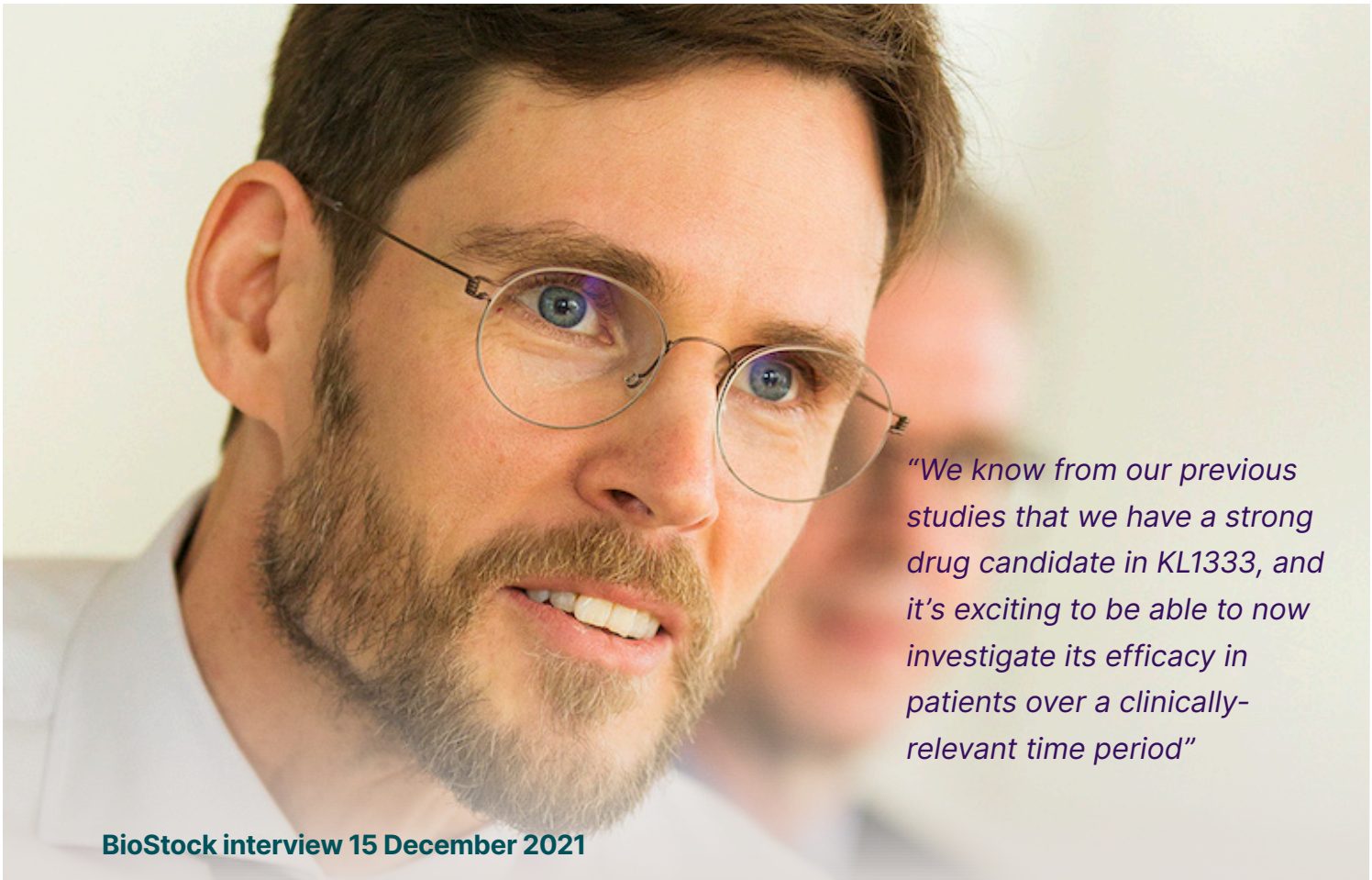
Our upcoming Phase 2/3 study, recently named FALCON, will be a groundbreaking study in many regards. In the study we will test KL1333, a novel compound and a 'first-in-class' molecule (the first molecule with this mechanism of action to be tested in patients). We will evaluate the efficacy of KL1333 with two primary endpoints, a functional endpoint as well as a fatigue endpoint. During the year we completed a study validating the method of measuring mitochondrial fatigue, and this work resulted in a specific and tailored questionnaire for the patients who will participate in the study. Read more in the interview with our Chief Medical Officer Magnus Hansson.

In this issue, we also highlight our second program in the portfolio, NV354, and the devastating pediatric disease Leigh syndrome.

The team at Abliva gathered together last week to celebrate a successful year and the upcoming holiday with a Christmas fika. We also had the chance to celebrate Matilda Hugerth, our Director of Clinical and Regulatory Affairs, who will be leaving us at the end of the year. Matilda's impact at Abliva over the past six years stretched across many disciplines, therapeutics areas and projects, and we are extremely grateful for her dedication, her passion and her friendship. I hope you will join me in wishing Matilda the best of luck in her new role.

Now onto the holidays! Merry Christmas and Happy New Year!

Ellen Donnelly
CEO



"We know from our previous studies that we have a strong drug candidate in KL1333, and it's exciting to be able to now investigate its efficacy in patients over a clinically-relevant time period"

BioStock interview 15 December 2021

Abliva on the IND-approval from FDA

A few weeks ago, the US Food and Drug Administration approved Abliva's Investigational New Drug (IND) application for KL1333, enabling the start of a registrational Phase 2/3 study with first patients due to be recruited in 2022. BioStock reached out to Magnus Hansson, CMO & VP Preclinical and Clinical Development, for a comment.

Lund-based Abliva develops treatments for rare primary mitochondrial diseases. The company currently has two ongoing, clinical-Phase projects within the field: NV354 and KL1333. NV354, the earlier program, is being developed as a chronic oral treatment of Leigh syndrome, a severe mitochondrial disease that mainly affects young children.

KL1333, the company's latest-stage asset, targets a subset of adult primary mitochondrial disease patients suffering from multiple debilitating symptoms, including chronic fatigue and myopathy. The candidate has been evaluated in both healthy volunteers and in patients and has been granted orphan drug designation in both the United States and Europe.

The CMO comments on the positive FDA ruling

During 2021 the company has achieved several milestones within the project and recently reached perhaps the most important milestone in the KL1333-project. This was when the US Food and Drug Administration (FDA) approved Abliva's Investigational New Drug (IND) application for KL1333, enabling the start of a registrational Phase 2/3 study with first patients due to be recruited in 2022. Read more here.

BioStock has spoken with Magnus Hansson, CMO & VP Preclinical and Clinical Development, to get his view on the FDA ruling, and what to expect in the coming months as the company initiates the Phase 2/3 study.

Magnus, can you start by telling us why the IND approval is so important to Abliva?

"The IND is a quality stamp for the KL1333 program, validating not only the hard work that the team has done but also the intellectual scholarship and decision making that went into designing the full nonclinical and clinical program. We know from our previous studies that we have a strong drug candidate in KL1333, and it's exciting to be able to now investigate its efficacy in patients over a clinically-relevant time period. The IND means we have a 'go' to start the study in the US and we plan to expand to other countries as soon as we can."

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Your team has chosen two primary endpoints for KL1333 in the upcoming trial, which will allow you to assess the impact of KL1333 on multiple aspects of the disease including fatigue and muscle weakness. Can you elaborate on this?
"Fatigue is the most common and debilitating symptom amongst patients with mitochondrial diseases with muscle weakness, or myopathy, coming in a close second. These symptoms severely obstruct the patient's ability to live a normal life. The two disease expressions are measured in different ways, and, by including both as primary endpoints, we have optimized the chance of catching potential improvements in either fatigue or myopathy following dosing with our drug candidate KL1333."

What can you tell us about the upcoming global registrational study itself, in terms of timelines, number of patients and location?
"The study will be a randomized, double-blind, and placebo-controlled trial in up to 180 patients with primary mitochondrial diseases. Patients included will have a mutation in the mitochondria's own DNA (mtDNA) and suffer from chronic fatigue and muscle weakness. Sixty percent of the patients will receive tablets containing KL1333 and forty percent will receive visually indistinguishable placebo tablets, twice daily for twelve months. As discussed earlier, we will evaluate two separate primary endpoints, as well as a number of complementary secondary endpoints. Now that we have the approval to start the study in the US, we will start to submit the study for approval in other geographies with the goal to dose our first patient in 2022. "

More on KL1333 and 2021 highlights

Magnus Hansson, CMO

You often speak about validating a fatigue endpoint. What does this mean and why is it important?
"Fatigue is often evaluated as an endpoint in clinical studies using one of a number of recognized scales, NeuroQol or PROMIS being the ones most favorably looked upon by regulatory authorities. The scales that are used, however, are general scales that were designed to be relevant across many disease areas. Conceptually this is a nice idea but may lead to a negative outcome if the questions are not relevant to the specific patient population being evaluated. We discussed this topic with the FDA during our pre-IND meeting and agreed that it would be beneficial to actually test and 'validate' the commonly used fatigue questions with actual mitochondrial disease patients."

"This validation study tested the relevance of specific questions with mitochondrial disease patients and, in the end, selected a short set of fatigue questions that are the most relevant to the burdensome fatigue experienced by them. We are hopeful that the increased specificity of our fatigue short form will increase our likelihood of getting good data from this endpoint in our upcoming study."

Ellen Donnelly, CEO

As we come to the end of 2021, what do you see as the highlights?
"It is hard for me to talk about the highlights of 2021 because it will be a one–dimensional response in a year that is better depicted in three dimensions. The highlights for the KL1333 program were clearly the readout of the PMD patient cohort in May and the IND approval last month. And we were all thrilled with the favorable feedback from the MHRA on the NV354 program, allowing this asset, one that was discovered and developed by team members at Abliva, to move into the clinic in 2022. These three milestones were all instrumental for the company as we derisked our Phase 2/3 program, confirmed the quality of our KL1333 data package, and brought a second asset into the portfolio."

"But when I look at 2021, I am most proud of how the team worked together to deliver these milestones – and all of the other 'foundational' studies and preclinical experiments that are viewed as supportive in nature and often don't feature in our communication. What you don't see when we talk about the milestones is the brilliant solutions to those hard questions, the hours spent writing FDA briefing documents when you had intended to be on holiday, and the consultants who are "consultants" on paper but put their heart and souls into these programs, just like the full-time employees at Abliva. This tiny team in Lund, Sweden delivered as much in 2021 as biotech teams in the U.S. with 5 times as many employees and 10 times as much money. If this team can deliver like this in the midst of COVID with a new AMERICAN CEO, I can't wait to see what the Abliva team will deliver in 2022."

BioStock article 27 October 2021

Abliva's NV354 targets fatal paediatric disease

Earlier this autumn, Abliva announced that NV354, the company's second candidate within the primary mitochondrial disease space, will progress to clinical phase. NV354 is initially being developed for the fatal Leigh syndrome, a disease that usually debuts before the age of 2 and patients often die before the age of 5. With NV354 about to join Abliva's leading candidate against primary mitochondrial disease, KL1333, in clinical development, BioStock takes a closer look at the candidate.

Primary mitochondrial diseases may be rare, but their impact on patients is profound. Lund-based Abliva has made it their mission to develop treatments that can improve the lives of these patients and are currently developing two candidates, KL1333 and NV354.

Primary mitochondrial diseases

Starting with the basics, what is a primary mitochondrial disease? In short, the term encompasses a group of diseases caused by genetic mutations leading to poorly functioning mitochondria, which leads to a range of debilitating symptoms. As the mitochondria are responsible for the body's energy production, some of these symptoms can be very severe, such as difficulties breathing and moving.

Leigh syndrome – a neurological syndrome

One mitochondrial disease that causes severe symptoms leading to early death in children is Leigh syndrome, named after British neuropsychiatrist Archibald Denis Leigh, the first to describe the syndrome in the early 1950s. This neurological syndrome is characterised by changes in the brain and early symptoms include recurrent vomiting and movement disorders. Later, symptoms such as breathing difficulties can emerge.

Poor prognosis and no treatment

Whilst Leigh syndrome is very rare, according to the Swedish National Board of Health and Welfare it affects 2-3 children in Sweden per year, it takes a heavy toll on mainly young children. In most cases the disease debuts early, already before the age of 2, and, for the majority of sufferers, sadly, the prognosis is extremely poor. Most of the affected children die before the age of 5 and there are currently no treatments available.

NV354 restores energy production

With NV354, Abliva is aiming to fix a fundamental problem in Leigh syndrome and other mitochondrial diseases – energy conversion. Leigh syndrome is typically caused by what is known as Complex I dysfunction – a malfunctioning of the first of five protein complexes in the mitochondria that leads to poor energy conversion. Abliva's NV354 is aimed at restoring energy production by functioning as an energy replacement, through succinate, an energy substrate already present in the human body.

NV354 shows promise

Abliva has several reasons to feel satisfied about the ongoing development of NV354. Not only is NV354 and its mechanism of action a product of research conducted by members of Abliva's own research team, it has also shown promising preclinical results. In September, Abliva presented the preclinical documentation regarding NV354 to the British regulatory authority, the MHRA, who confirmed with Abliva that the preclinical package supports dosing in human subjects. Following this meeting, Abliva will now advance NV354 to clinical studies with the aim of initiating a phase I study in 2022.

Finally, it is worth noting that the company believes that NV354 has potential beyond Leigh syndrome. Abliva has mentioned two other mitochondrial diseases, MELAS and LHON, as indications where NV354 could be used and potentially help make a difference to patients who today lack treatment options.

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. Our recent events have included:

Mitocon's Mitochondrial Diseases Conference 2021
15 – 16 October 2021.
https://youtu.be/5V3ubCOKqn8?t=1201

Aktiespararna's Kvinnokvällen (Women's night) Malmö
19 October 2021.
https://youtu.be/YdRNEbHjae4

BioStock Life Science Summit
20 - 21 October 2021.
https://youtu.be/OOFFrwnPj2w

Mitochondrial Medicine – Therapeutic Development
30 Nov - 2 December 2021.

Abliva attended this virtual conference, organized by the Wellcome Connecting Science located at the Wellcome Genome Campus in the UK. Abliva's CMO, Magnus Hansson, was invited to give a presentation on the topic Academia-pharma interplay in drug development, during Session 1: Mitochondrial Medicine – pharma and funding perspectives.

Upcoming events in 2022

22 - 24 Feb

Mitochondria-Targeted Drug Development Summit

20 - 21 Apr

Nordic Life Science Days