UNITE-CNM COMMUNITY UPDATE – DECEMBER 2021

Dear CNM Community,

Following please find an update regarding our work in myotubular and centronuclear myopathies, including our UNITE-CNM program, a Phase 1/2 clinical trial designed to evaluate the safety and tolerability of DYN101. We have also included a brief Q&A at the end of this document to address questions we have received from you. We will do our best to keep you informed and answer questions as appropriate in the months ahead.

We share your goal to have a therapy available for as many patients as possible, and as quickly as possible, and we are grateful for your engagement with us. Should you have additional questions or feedback, please submit them to patients@dynacure.com.

- In 2020, Dynacure began the clinical development of our investigational product candidate DYN101 with a Phase 1/2 clinical trial called UNITE-CNM. The goal of the trial is to learn about the safety and tolerability of DYN101 in patients aged 16 or older, with X-linked myotubular myopathy, or XLMTM, or autosomal dominant CNM, or ADCNM (*DNM2 gene mutation*). In a "Phase 1/2" trial, patients diagnosed with the disease are able to be dosed, which differs from a "Phase 1" trial in which only healthy volunteers receive an investigational drug.

- UNITE-CNM is currently running in the following countries: Belgium, Denmark, France, Germany, United Kingdom and The Netherlands.

- Our goal is ultimately to study DYN101 in all age groups. Should the results of the phase 1/2 clinical trial be encouraging, we plan to explore further clinical trials, including a pediatric study. We expect to have initial data from Unite-CNM in the second half of 2022 at the earliest. Should this data look promising, we will look to initiate a study in pediatric patients.

- Until we have more data around DYN101 and have a clinical plan with regulatory agencies, we cannot begin a pediatric study. There are no additional details available, including potential locations of study sites.

- We must follow the strict guidelines established in this research phase and we are obligated to follow reporting regulations as part of the study process. Therefore, we cannot share incremental updates on patients or our progress with you. If there is a major event that happens during the trial, we will share with the community when we are able.

Frequently Asked Questions Regarding DYN101 and the UNITE-CNM Study

What is DYN101?
DYN101 is an antisense oligonucleotide (ASO). It is designed to decrease the expression of a protein named dynamin-2, which is elevated in patients with MTM1 mutations and thought to be overly active in patients with DNM2 mutations (ADCNM). Preclinical studies of DYN101 have indicated that this may be a promising treatment approach, which is why we are developing the product candidate in patients with these mutations. There are patients with other CNM mutations that are not included in our clinical development program at this time.

A more extensive explanation of ASO technology is contained later in this document.

What is the UNITE-CNM Study?
The UNITE-CNM study is a multicenter, ascending dose study Phase 1/2 clinical trial to evaluate our investigational product candidate DYN101. We plan to study the safety, tolerability, pharmacokinetics (how the body distributes and eliminates the drug) and preliminary efficacy of DYN101. The trial is expected to enroll approximately 18 patients aged 16 years or older with X-linked myotubular myopathy (XLCNM) or autosomal dominant CNM (ADCNM) and who are mild-moderately affected. Enrolled patients will have a run-in period or be rolled over from an ongoing natural history study, which included 60 patients that have XLMTM or ADCNM. The Phase 1/2 clinical trial will primarily focus on safety and tolerability to find the dose of DYN101 to use for more advanced clinical trials. We will also explore other assessments such as muscular function, respiratory function, and muscle strength.

Will you be enrolling patients in the United States?

Our goal has been to enroll and complete this study as rapidly as we can regardless of geography, and with the safety of patient participants as our first priority. While the study is still ongoing, we have now identified enough patient participants already in Europe to eventually complete this study – including possible screening failures. While we would like to accommodate patients who are waiting in the U.S., if we delay recruitment to ensure that even one US patient can join, we could indeed delay our clinical development by several months. Therefore, at this time, trial recruitment for patients in the U.S. is not expected for this first study. We expect to have initial data from UNITE-CNM in the second half of 2022 at the earliest. Once we have this interim data, we will be able to comment on next steps for this program.

How far along is the UNITE-CNM study?

We must follow protocols that are in place for studies regarding communications, so there are limits on what we can share. If there is an important milestone to share, we will be proactive in our communication by issuing a press release and reaching out to leaders of patient advocacy organizations.

What, if any, impact have the patient deaths and clinical hold for the gene therapy study had on the UNITE-CNM study?

The passing away of the four children in the gene therapy study is absolutely tragic and has touched all of us. It is our collective responsibility to learn as much as we can from these experiences to improve our work and enhance safety for our patients. DYN101 is not a gene therapy. It is an antisense oligonucleotide (ASO). ASO aims to bind a synthetic drug to a specific messenger RNA that is involved in a particular disease and to stop unwanted proteins from being produced. While our approach is different from the replacement of a gene, we have still taken the steps to increase the monitoring of liver parameters of patients after being dosed. In addition, we are progressing dose increases very slowly and have added experts on liver function to our advisors. If a study participant has additional questions, they should contact their study investigator.

What happens after this initial study is complete?

After completing the UNITE-CNM trial, we will assess the data. Assuming the data are supportive, subject to regulatory approval, we plan to initiate Phase 2/3 clinical trials for all ages.

Why is Dynacure including mild-moderately affected patients only in their first trials?

We understand that even a "mild" classification of disability can be considered as a very important disability for the patient and/or their caregiver. The term "mild to moderate" is a term used by the medical profession today to classify the degree of disability in patients with neuromuscular disease. We have opted to use the medical terminology and to include "mild-moderately affected" patients of 16 years or above in the first trial for the following reasons:

- Severe patients are medically defined as requiring 24 hours of invasive respiratory support and not able to walk. Their medical status is often extremely fragile, and it would be challenging to have them participate in early trials where there are a lot of tests being carried out that could be a risk for them.

- There are many more, and different, types of tests to evaluate the benefit of a therapy for mild to moderate patients, than there are for more severely affected patients.

- There is a need for trial participants to have enough residual muscle to allow for repeated muscle biopsies that are required in the trial.

- Patients who are still able to walk a few steps have potentially some muscle that can still be recovered more quickly with treatment. This is an assumption that still needs to be confirmed by our clinical development program.

What are the goals of the Phase 1/2 (UNITE-CNM) clinical trial?

We will study:

- the pharmacokinetics of DYN101: how the body distributes and eliminates the drug.
- the extent to which DYN101 is available in muscle tissue.
- the right dose for further development that is both well tolerated and is expected to show benefit to patients.
- If the correct dose is found, to demonstrate whether and how strongly a positive effect is seen on signs and symptoms of the disease.
- Assess potential efficacy in terms of muscle strength and function, improvements in breathing, swallowing, ability to speak, and other day to day issues that impact patients' lives.

If we see positive results, the data we collect would help us to design a Phase 3 or pivotal trial that is intended to show benefit, which is the next step in then potential approval of the treatment.

If there is no enrolling trial site in my country, could I leave my country and enroll in a participating trial site?

Patients may contact their treating physician to discuss the criteria for Unite-CNM. Participants will be selected by the clinical trial investigators according to strict criteria, not by Dynacure nor by patient advocacy organizations. The participating sites are published on www.clinicaltrials.gov and https://www.clinicaltrialsregister.eu. The Phase 1/2 clinical trial will require that patients visit the trial site every week for at least 6 months and Dynacure will not be able to cover the costs related to moving to participate.

How many patients will be included and how do patients qualify for participation?

The trial is planned to include approximately 18 patients aged 16 or older. Patients must be symptomatic, preferably be able to walk a few steps, and have mild to moderate disease. The trial will require weekly visits, and travel and expense costs will be covered by Dynacure. However, we would not be able to cover moving/relocation expenses. All the eligibility criteria are on the clinical trial register: https://www.clinicaltrials.gov/ct2/show/NCT04033159?term=Unite-CNM&draw=2&rank=1

If I/my family member is not accepted into the UNITE-CNM trial, might there be additional trials in the future?

Yes, there may be additional opportunities to participate in a clinical trial – both for pediatric and for more severely affected adult patients – but we are focused first on the UNITE-CNM trial. If data are encouraging, we plan to work as quickly as we can to undertake additional trials for children of all ages, as well as adults.

What is the CNM Natural History Study?

The Natural History Study (NHS) is a study that began in 2016 and is a crucial element of the world's understanding and study of CNM. The goal of the study is to understand the trajectory of patients (how they are performing over time with regards to walking, muscle strength, breathing, as well as how their lives and those of their caretakers are impacted). This is important as every child or adult has a different trajectory over time: some patients have rapid progression of muscle weakness, breathing difficulties etc. and we believe knowing the course of these over a long period of time, will help to show whether or not DYN101 (or any other therapeutics in development) can improve the course of the disease in clinical trials.

Why is Dynacure starting their trials in adults?

Our goal is to develop DYN101 to treat infants, children and adults with XLMTM as well as ADCNM of all ages. In principle, new therapies should be tested first in adults for safety and potential efficacy prior to going into children/infants. Exceptions are made if the disease is only seen in children, or if results in adults would not be useful for the pediatric population. Once safety is established and a possibly effective dose is selected, and subject to regulatory approval, Dynacure intends to start clinical trials in infants and children of all ages as quickly as we are able to do so, as well as in parallel to progress clinical development program in adults.

Who determines which patients are accepted into UNITE-CNM?

Patients are selected by the physicians at participating clinical trial sites, not by Dynacure nor by patient advocacy organizations. If you believe you or your child may qualify, the most appropriate next step is to have your treating physician contact a clinical trial site.

What do I need to do if I or my family member want to be included in a clinical trial?

First, you will need to discuss with your treating physician whether or not you or your family member appear to meet the requirements for inclusion into the trial. DYN101 is administered as a weekly infusion at a hospital. Blood tests are carried out every week at the hospital, and more extensive tests (muscle function and strength, etc.) less frequently. Going to the hospital every week can be a challenge for many patients, and Dynacure is doing its utmost to minimize the inconvenience.

What is ASO technology?

Antisense technology aims to bind a synthetic drug to a specific messenger RNA that is involved in a particular disease and to stop unwanted proteins from being produced. For XLMTM or ADCNM, the ASO is created to decrease the amount of dynamin-2 protein which is too high or too active. Antisense oligonucleotides are short chemically modified strands of nucleotides (parts of DNA). They bind to parts of the messenger RNA that produce proteins, that lead to a particular disease. In many cases, when the ASO or antisense drug binds to the specific mRNA, it results in degradation of the mRNA, which means the targeted or unwanted protein cannot be produced. Therefore, the overall amount of the targeted protein in the cell will be reduced.

DYN101 is an ASO and treatments with these types of drugs have been associated with some side effects. What will Dynacure do to prevent this?
There are already several approved therapies using ASOs, particularly for rare genetic diseases. Our collaborator, Ionis Pharmaceuticals, is a leading developer of ASOs and has had a lot of experience and improved the technology to mitigate (lessen) these safety issues. Side effects have been seen with previous versions of ASOs, and Dynacure has been working with Ionis to mitigate the side effects observed. In addition, patients in the clinical trials will be carefully monitored for any side effects, including blood draws for lab testing with particular attention to the side effects that have been seen with other ASOs.

These safety precautions will include monitoring closely of any effect on liver tests, kidney tests, as well as any untoward effects on platelets that are important for blood coagulation (to form blood clots and stop bleeding). The experience with other ASOs has allowed for the development of good methods to manage patients with these side effects and have been included in Dynacure's clinical trial protocols with the assistance of Ionis, a leader in the development of therapies using ASOs.

Can Dynacure begin a pediatric study faster?
We understand the urgent need to have a safe and effective therapy available for as many patients and as soon as possible. We have evaluated many different scenarios to come up with what we believe is the safest, fastest route for all patients, including infants and children. Once safety is established and a possibly effective dose selected, subject to regulatory approval, we intend to start clinical trials in infants and children of all ages, both for XLMTM and ADCNM.

Will there be an expanded access program?
Expanded access is a potential pathway for a patient with an immediately life-threatening condition or serious disease to gain access to an investigational therapy for treatment outside of clinical trials. Having only just begun our first Phase 1/2 clinical trial, we still have much to learn about the safety and efficacy of DYN101 and the best way to do this is through clinical trials. We cannot begin an expanded access program at this time, particularly as no evidence exists yet, that the product candidate is effective.

When will we hear more from Dynacure?
We plan to publicly announce major milestones or events.

GLOSSARY

XLCNM: X-Linked Centronuclear Myopathy, or Myotubular Myopathy, or MTM1 mutation

ADCNM: Autosomal Dominant Centronuclear Myopathy, or DNM2 mutation

ASO: Antisense oligonucleotide. It is a synthetic molecule that looks like DNA or RNA that binds to the mRNA to stop it producing an abnormal protein. Diseases that are currently approved with ASO technology include familial hypercholesterolemia (an inherited disease with extremely high cholesterol

levels), severe viral infections of the eye, macular degeneration (which leads to blindness) amongst others.

CNM: Centronuclear Myopathies

DNA: Deoxyribonucleic acid. DNA is present in every cell of the body and is responsible for all the functions of the cells that make up a body. Changes in the DNA or mutations, can lead to abnormalities in the proteins that are involved in the normal function of a cell.

In vitro: Investigation done in a test tube instead of in a live animal or human.

Mutation: Change in structure of a gene which is a part of DNA. A mutation can be inherited from a parent or it can occur spontaneously.

Pharmacokinetics: The uptake of a substance into the body and the subsequent elimination of it. During the study of a drug, the pharmacokinetics include how much or the drug is absorbed by the body, what are its concentrations in blood or other tissues, and how long it takes to be eliminated from the body.

Messenger RNA or mRNA: Messenger Ribonucleic Acid that translates information from DNA into a protein. For example, the MTM-1 gene has a mutation of its DNA. mRNA then translates the change in the MTM gene into an abnormal protein (an abnormal enzyme) which then leads to the X-linked form of CNM.

Degradation of mRNA: Change in structure of the mRNA so that it no longer functions properly. This usually means that the mRNA will not produce a protein.

IV infusions: Injection into a vein of a liquid substance