



March 22, 2023

Dear Duchenne community,

In December 2022, we announced a positive update from the initial cohort of the Phase 1b/2a study of WVE-N531 in three boys with Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping. We were encouraged by these early results and what they may mean for WVE-N531's potential to restore meaningful levels of dystrophin with continued dosing. Today, we are providing an update regarding next steps for the WVE-N531 program.

### **Study Overview and Results**

Three boys participated in the initial cohort. After receiving escalating single doses of 1, 3, 6 and 10 mg/kg of WVE-N531, 10 mg/kg was selected as the dose to evaluate in a multidose portion of the study. The boys then received three biweekly doses of 10 mg/kg and a muscle biopsy was performed two weeks following the third and last dose (which was a total of six weeks after the first multidose). The objectives of the study were to evaluate safety and tolerability and understand if WVE-N531 gets into muscle tissue. Whether the treatment led to exon skipping or restored dystrophin protein were secondary objectives.

The data showed that WVE-N531:

- Appeared to be safe and well tolerated.
- Was present in high concentrations in muscle tissue.
- Resulted in 53% mean exon skipping. Exon skipping activity ranged from 48-62%, meaning all boys experienced substantial exon skipping.

After the boys received three biweekly doses of 10mg/kg of WVE-N531, mean dystrophin levels observed were 0.27% of normal (below the lower limit of the test to quantify), which may be a result of the length of time required for dystrophin protein to be produced after exon skipping occurs. The next phase of development is designed to measure dystrophin after a longer duration of treatment.

### **Next steps**

We have been working with DMD experts, study investigators and members of the community to determine next steps for our WVE-N531 program, which include:

- Continuing dosing of participants: pending regulatory approval, the boys who participated in the WVE-N531 study will have the option to continue receiving WVE-N531 bi-weekly at 10mg/kg for 12 months.
- Expansion of the study to include up to 10 boys. We plan to open additional sites to recruit these new participants.
- We will assess dystrophin after a longer treatment duration approximately 6 and 12 months.
- We will also assess functional endpoints such as NSAA and others.

Should we observe positive dystrophin data for WVE-N531, we would also plan to pursue treatments targeting other exons to expand the number of boys who have access to our next-generation exon skipping technology (or therapeutics).

We anticipate data on this next phase of development in 2024.

### **Gratitude**

Over the past few years, many of us at Wave have been privileged to meet families living with Duchenne and to work with the advocacy organizations that support you. All of us at Wave are enormously grateful to you and especially to the boys, their families and investigators who are participating in our study. We recognize the personal sacrifices made by each and every family involved in these studies. Their participation, along with the support of the entire DMD community, is critical to advancing the scientific and medical understanding required to defeat this devastating disease.

We are committed to the DMD community, to advancing the understanding of exon-skipping therapeutics, and supporting the needs of people living with DMD.

Sincerely,

Chelley Casey  
VP, Patient Advocacy