



December 19, 2022

Dear Duchenne community,

Today 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 initiated this program as a proof-of-concept study with the goal of understanding if the next-generation chemistry in WVE-N531 would address the issues experienced with our first-generation DMD clinical candidate, suvodirsen.

### **Study Overview and Results**

Three boys participated in the study. 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 and leads to exon skipping, which would be expected to restore dystrophin protein.

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.

Given the early timepoint at which biopsies were taken, the study was not designed to understand if WVE-N531 changes dystrophin levels. Dystrophin levels observed in this study were below the lower limit of detection of the assay, which may be a result of the length of time required for dystrophin protein to be produced after exon skipping occurs.

### **Next steps**

We are encouraged by these early results and are evaluating next steps for the program, including the continuation of this initial cohort.

We are working with investigators to provide what they need to support the boys and families participating in this study, including the opportunity for each investigator to share individual

data with each boy and their family and complete their follow-up visits as part of the study design.

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

We will provide more information regarding the timing and next steps for this program in 2023.

**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 participated 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.

Sincerely,

Chelley Casey  
VP, Patient Advocacy