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# Evaluation of Total Binding Antibodies Against rAAVrh74 in Patients With Duchenne Muscular Dystrophy

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## Objective

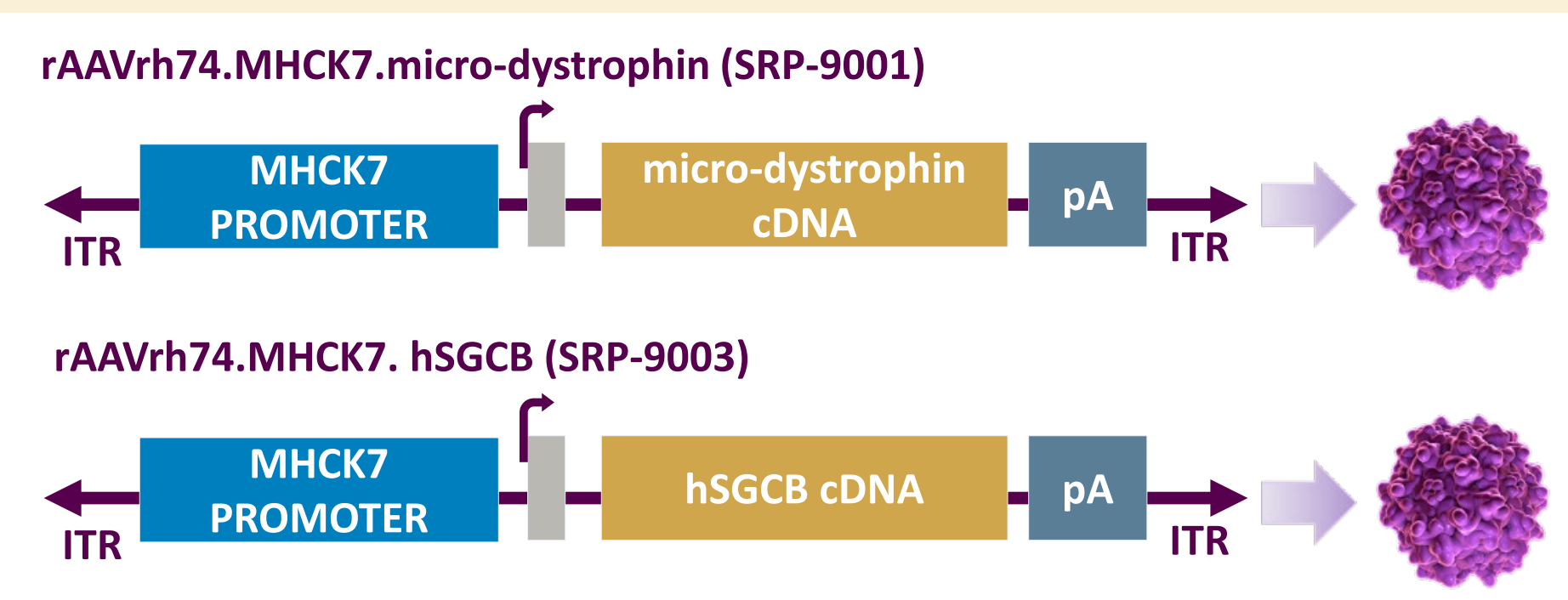
To evaluate total binding antibodies against rAAVrh74 in patients with Duchenne muscular dystrophy (DMD)

## Key Takeaway

Low seroprevalence of antibodies against rAAVrh74 support the broad applicability of rAAVrh74-based gene transfer therapy to patients with DMD

## BACKGROUND

- Adeno-associated virus (AAV) vectors have emerged as the vehicle of choice for gene transfer therapy for DMD and limb-girdle muscular dystrophy (LGMD), as they can be delivered systemically, are nonpathogenic, and exhibit broad tissue tropism<sup>1</sup>
- rAAVrh74 serotype efficiently transduces skeletal and cardiac muscle, following intravenous administration<sup>2</sup>
- Because pre-existing antibodies against AAV vectors can hamper therapeutic efficacy and pose a safety concern,<sup>3,4</sup> successful gene transfer requires patient pre-screening; those seropositive for total anti-rAAVrh74 binding antibodies may not be eligible for gene therapy
- Two investigational gene transfer therapies using rAAVrh74 vector are currently in clinical trials: SRP-9001 for gene transfer of microdystrophin for patients with DMD, and SRP-9003 for gene transfer of  $\beta$ -sarcoglycan for patients with LGMD type 2E/R4



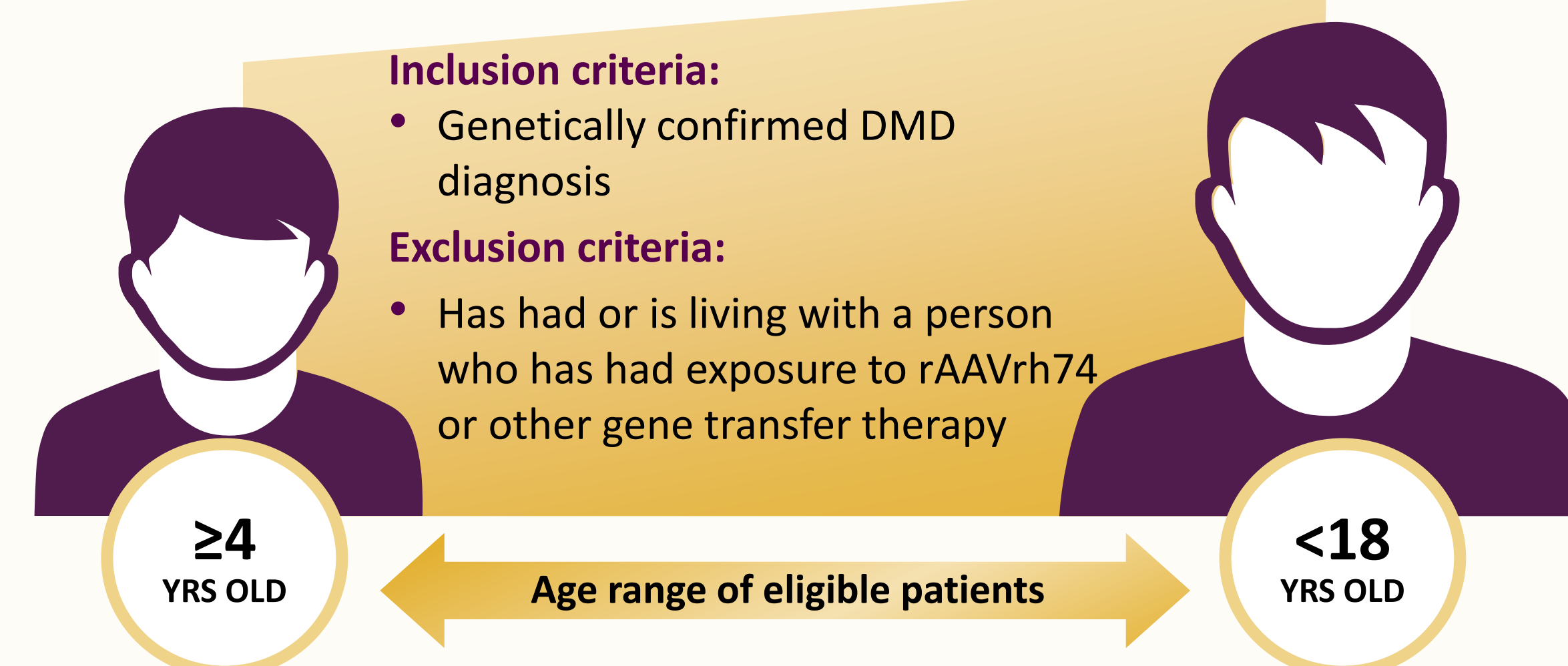
- Here we present interim results (as of July 19, 2021) of a study evaluating total binding antibodies against rAAVrh74 in patients with DMD for the first 53 participants enrolled (out of 100 planned)

## CONCLUSIONS

- The comprehensive approach of measuring total binding antibodies (both neutralizing and non-neutralizing) demonstrates that the majority of patients (84.9%) with DMD in this interim data set were seronegative (<1:400) for anti-rAAVrh74 total binding antibodies
- This interim analysis did not show an association between seroprevalence and age ( $\geq 4$  to <18 years old) in patients with DMD

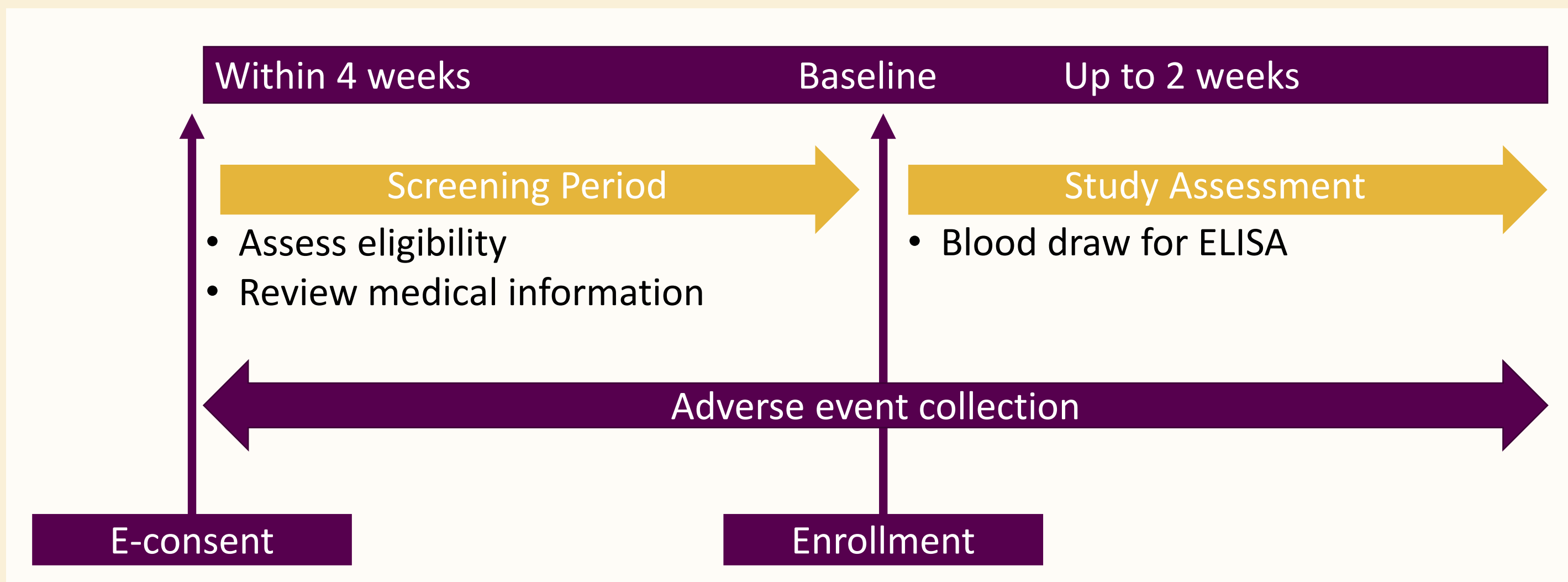
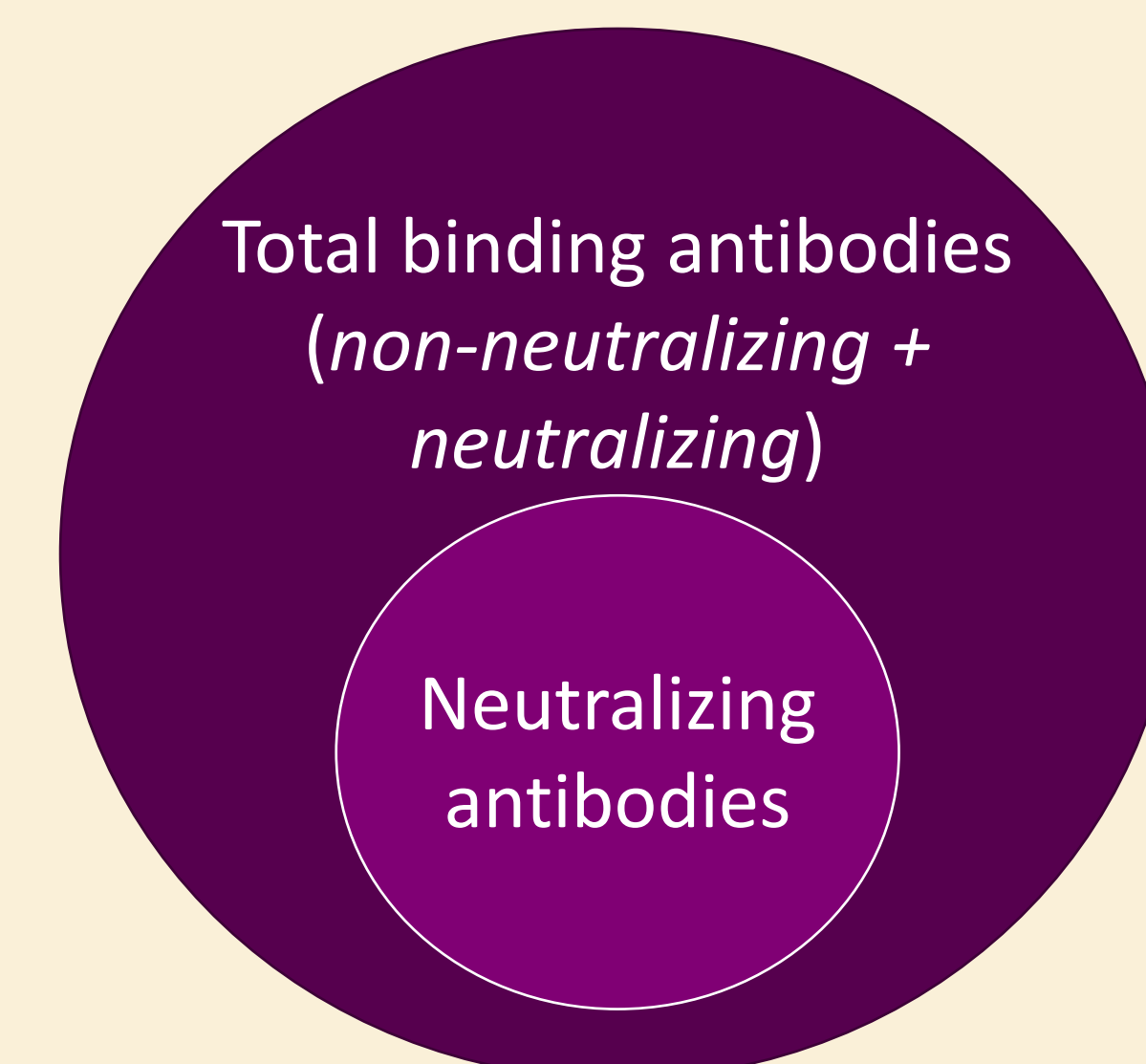
## STUDY DESIGN

Planned sample size: N=100



## Procedures

- A single blood sample was obtained from each patient and total anti-rAAVrh74 binding antibodies were measured by enzyme-linked immunosorbent assay (ELISA)
  - Total anti-AAV antibodies include both neutralizing antibodies, which prevent transduction of the vector, and non-neutralizing antibodies, which recognize the vector and may cause immune-mediated effects



## Endpoints

- Primary: Percentage of subjects with elevated ( $\geq 1:400$ ) total antibody titers to rAAVrh74
  - Total binding antibody level <1:400 was defined as “not elevated”
  - Cutoff was selected based on a previous study showing that antibody titers at 1:800 promoted loss of transgene expression<sup>5</sup>

## INTERIM RESULTS FOR THE FIRST 53 PATIENTS ENROLLED (as of 19 July 2021)

### Patients

- All 53 patients enrolled in the study with at least 1 sample evaluated with valid result for immunogenicity (full analysis set) completed the study

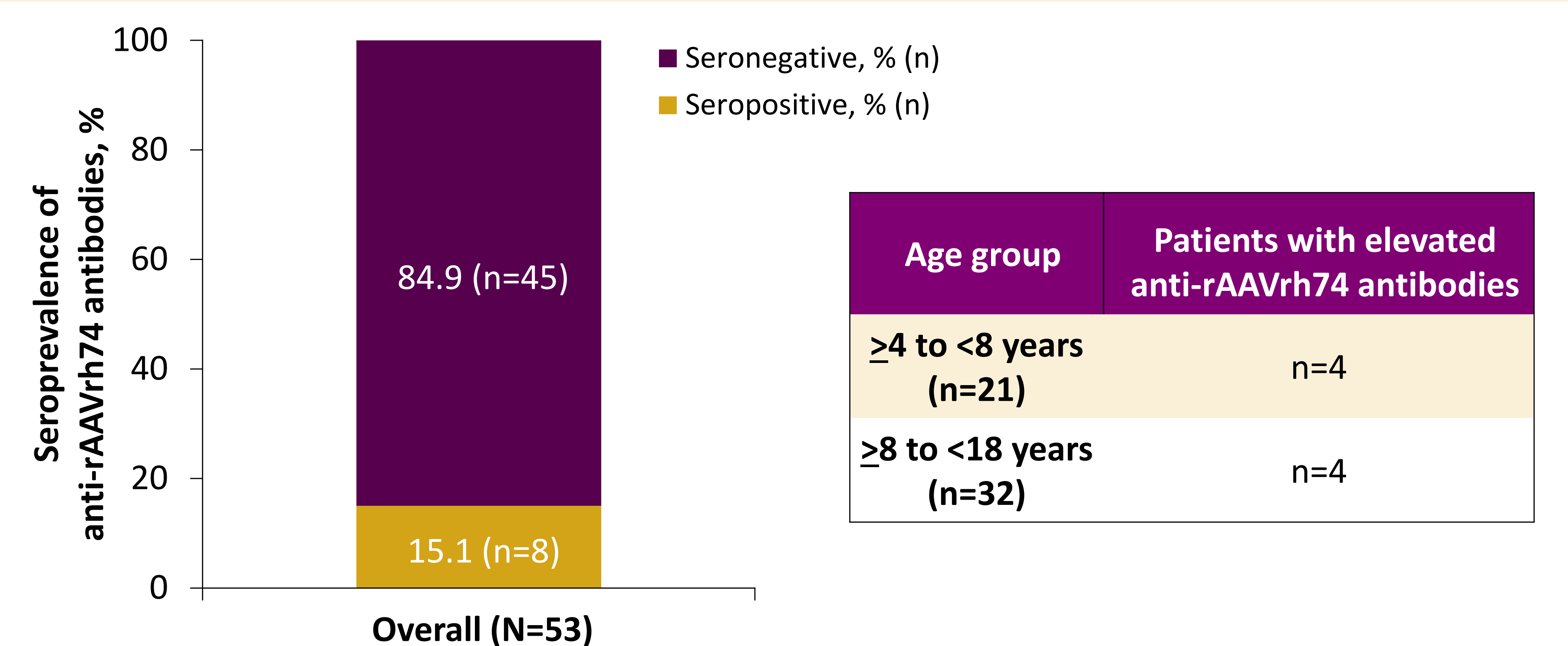
### Baseline characteristics

Parameter	Total (N=53)
Age, years	8.8 (3.4)
Race, n (%)	
White	44 (83)
Other	9 (17)
Years Since 1st motor symptom of DMD to study enrollment	6.2 (3.5)
Years since diagnosis of DMD to study enrollment	5.7 (3.5)
Years since the confirmatory genetic testing for DMD to study enrollment	5.6 (3.6)

Values are mean (SD) unless otherwise noted

### Total antibody titers to rAAVrh74

- Overall, 15.1% of patients had pre-existing elevated ( $\geq 1:400$ ) total antibody titers to rAAVrh74
  - In this interim data set, no association was observed between seroprevalence and age in patients with DMD aged  $\geq 4$  to <18 years



### Range of total antibody titers to rAAVrh74

- In the 8 patients with elevated anti-rAAVrh74 antibodies, titers ranged from 1:400 to 1:3200

### ACKNOWLEDGMENTS & DISCLOSURES