

Experience with Edasalonexent Demonstrates Ability of 4 to 7 Year-old Boys with Duchenne Muscular Dystrophy to Take Softgel Capsules in Clinical Trials

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Background

Background


Availability of easy to swallow formulations contributes to improved medication compliance in children

- Tablets and capsules are widely manufactured and prescribed and may provide a number of advantages over other dosage forms, including ease of administration, patient compliance, and accuracy in dosing
- However, inability to swallow tablets and capsules is a common issue in young children¹. In one study as few as 25-45% of patients aged 4 to 7 could swallow solid dosage forms, but the ability to do so improved at older ages².
- Nonetheless, patients as young as 4 to 5 years old can learn to swallow tablets, and in one study, learned more quickly than older children³.

Edasalonexent is in clinical development as a potential foundational therapy for Duchenne muscular dystrophy

- Supplied as 100 or 250 mg softgel capsules
- In adults, characteristics such as smoothness and "slipperiness" are associated with improved perception of a medications' ability to be swallowed.
- Edasalonexent softgel capsules are formulated with a special coating that minimizes friction and aids swallowing

Information on capsule swallowing is limited in children with Duchenne muscular dystrophy



¹ Terrick et al., 2017, Inter J Pharm
² Jones et al., 2018, Clin Ped
³ Garvie et al., 2007, Pediatrics

Study Design

Capsule size selection and ability to swallow assessed in edasalonexent clinical trials

- In the Phase 3 PolarisDMD randomized, double-blind, placebo-controlled trial evaluating the efficacy and safety of edasalonexent in boys with Duchenne ages 4 to 7 (up to 8th birthday)
 - This study has completed enrollment
- In the completed Phase 2 MoveDMD randomized, double-blind, placebo-controlled trial evaluating safety and tolerability in boys with Duchenne ages 4 to 7 (up to 8th birthday)

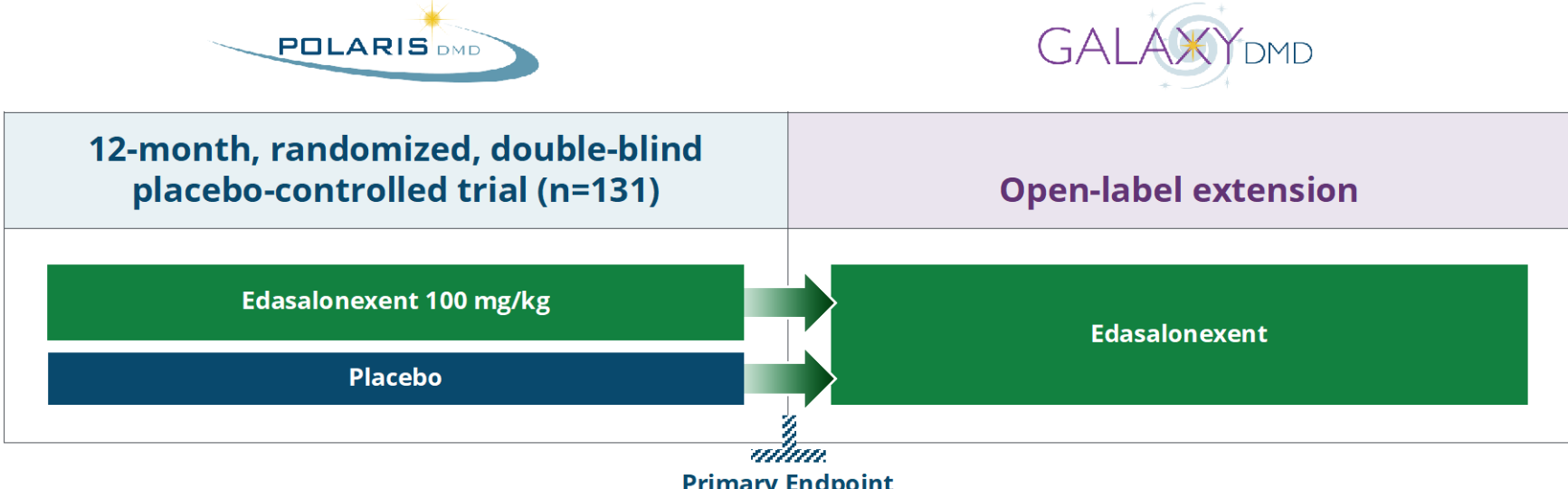


Global Phase 3 PolarisDMD trial



Phase 2 MoveDMD trial with Open-Label Extension

Fully Enrolled Edasalonexent Phase 3 PolarisDMD Trial Designed for Global Registration



Eligibility:

- All mutations
- Age 4 to 7 (up to 8th birthday); off steroids for ≥6 months
- Able to swallow placebo capsules at the Screening Visit

Endpoints: Consistent with regulatory guidance

- Primary: Change in North Star Ambulatory Assessment
- Key secondary: Age-appropriate timed function tests
- Additional assessments include growth, cardiac and bone measures

Study Design


MoveDMD®, a Phase 1/2 Trial with Open-Label Extension

Study Objectives

- Safety and PK in pediatric patients with DMD
- Proof of concept using MRI to assess changes in muscle health

Design


- Study population
 - Age 4 to 7 (up to 8th birthday); off steroids for ≥6 months
 - Able to swallow placebo capsules at the Screening Visit
- Phase 1:** 1-week open-label to assess safety and PK, with initial assessments of function and MRI
- Off-treatment period** of ~6 months prior to Phase 2
- Phase 2:** 12-week placebo-controlled period of 67 mg/kg and 100 mg/kg doses of edasalonexent
- Open-label extension up to 150 weeks



Edasalonexent is Taken as a Softgel Capsule

Capsules in both PolarisDMD and MoveDMD

- Available Capsule Sizes**
 - 100 mg capsules, similar to the size of a Tic Tac™
 - 250 mg capsules, similar to the size of a jellybean
- Edasalonexent 100 mg/kg/day** (administered as approx. 33 mg/kg TID) or placebo
 - For a 20 kg boy
 - 100 mg: total of 20 capsules per day or 6, 6, 8 given TID with food
 - 250 mg: total of 8 capsules per day or 2, 2, 4 given TID with food



Methods


Site Techniques to Support Ability to Swallow Capsules at Screening Visit

Study coordinators and Investigators identified techniques to enhance intact capsule swallowing since capsules must be kept whole when swallowed:

- Practice at home with Tic Tacs™, M&Ms™ or jellybeans
- Make postural adjustments (i.e., tilt head back when swallowing with the capsule at the back of tongue)
- Swallow the capsules with something thick, like jam or a milkshake
- Place the capsule inside soft foods like a ripe banana or in applesauce

Medi-straw

Utilize pill-swallowing aids such as the Medi-straw®, a straw with an internal shelf to position capsules on; drinking liquids then helps to decrease sensation of capsules in mouth



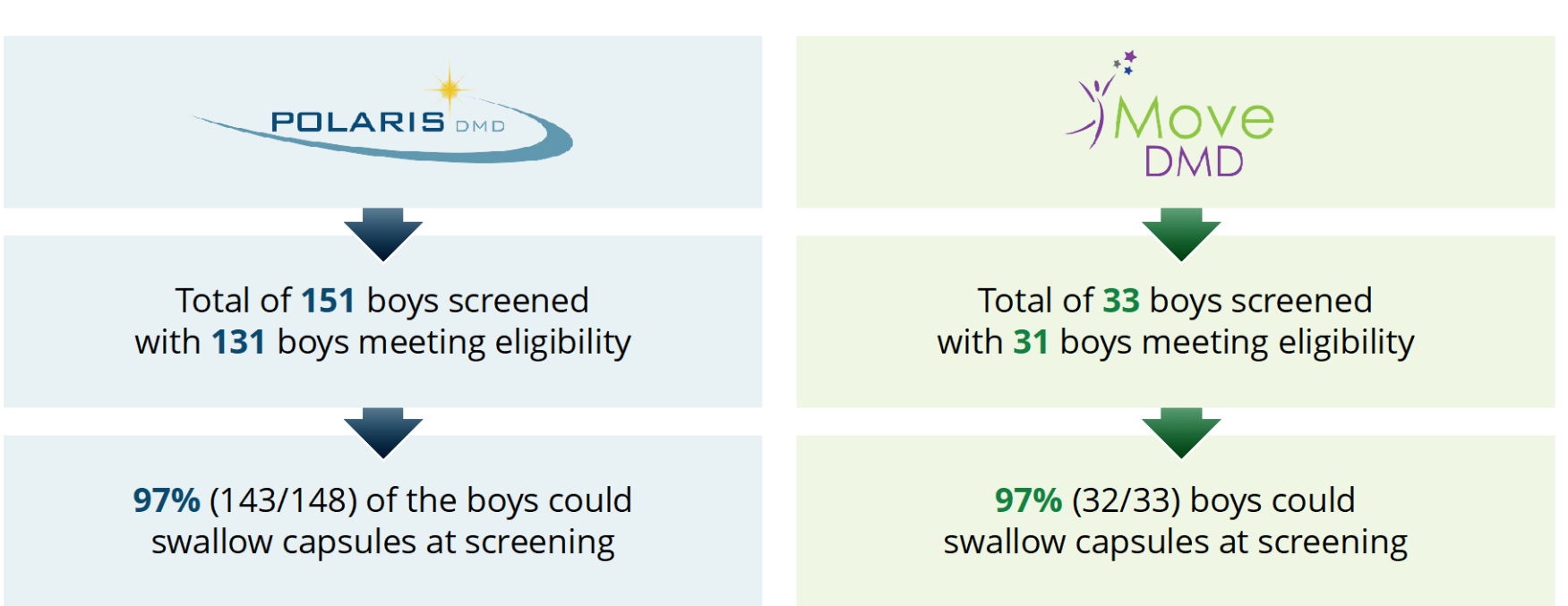
Typically, once boys practiced swallowing several times using these techniques, they were able to swallow capsules easily thereafter.

Results – Capsule Swallowing Ability at Screening

Most Young Boys Could Swallow Capsules at Study Screening

Ability to Swallow Capsules Assessed at Screening Visits

- Eligibility criteria in both the Phase 3 PolarisDMD and the Phase 2 MoveDMD required boys to demonstrate ability to swallow at least one capsule size to meet eligibility

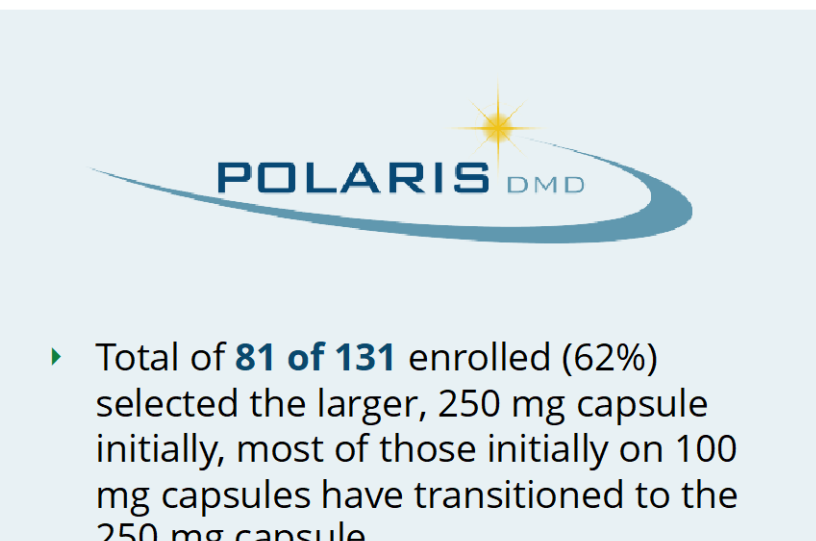


In boys aged 4 to 7 (up to 8th birthday), 97% of boys were able to swallow capsules for the clinical trial

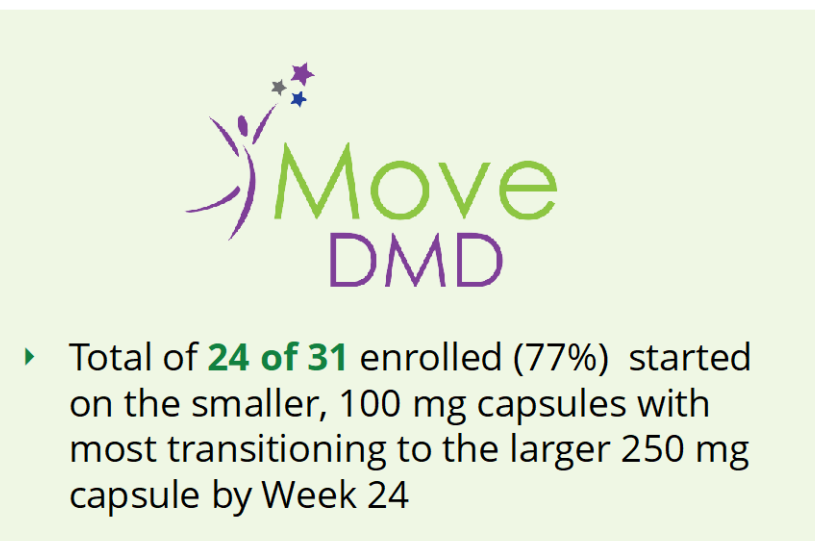
Results – Capsule Size and Swallowing Ability

Softgel Capsules Sizes Were Not a Barrier to Enrollment in Young Boys

Majority of boys in both the Phase 3 PolarisDMD and the Phase 2 MoveDMD, selected the larger (250mg) capsule for the duration of the studies.

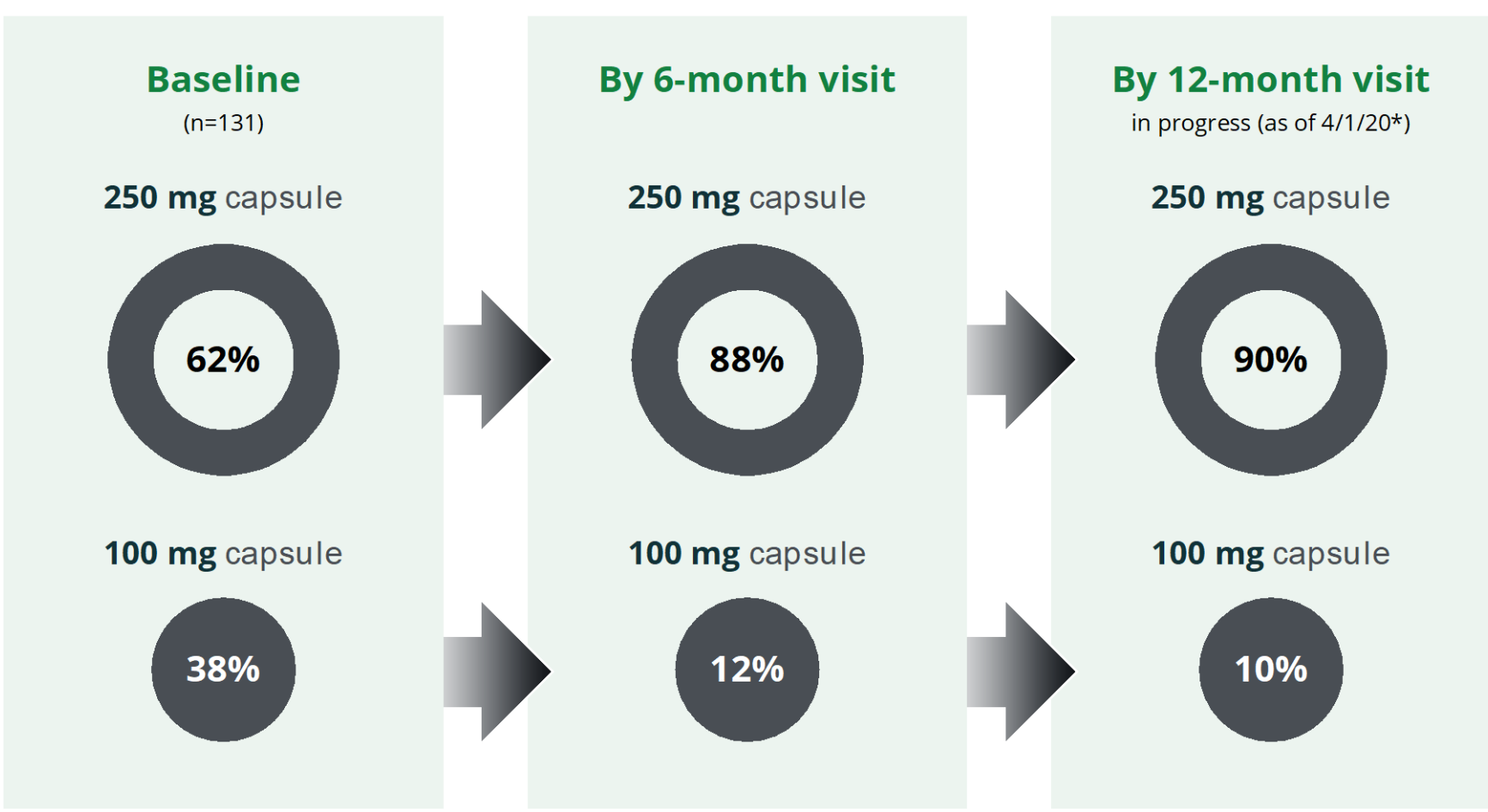


- Total of **81 of 131** enrolled (62%) selected the larger, 250 mg capsule initially, most of those initially on 100 mg capsules have transitioned to the 250 mg capsule
- Sites that only offered the larger size capsule found that all boys were able to take the larger capsule



- Total of **24 of 31** enrolled (77%) started on the smaller, 100 mg capsules with most transitioning to the larger 250 mg capsule by Week 24
- Compliance was high (~98%) with no discontinuations due to capsule burden

Most Boys in PolarisDMD Could Swallow Either Size Capsules

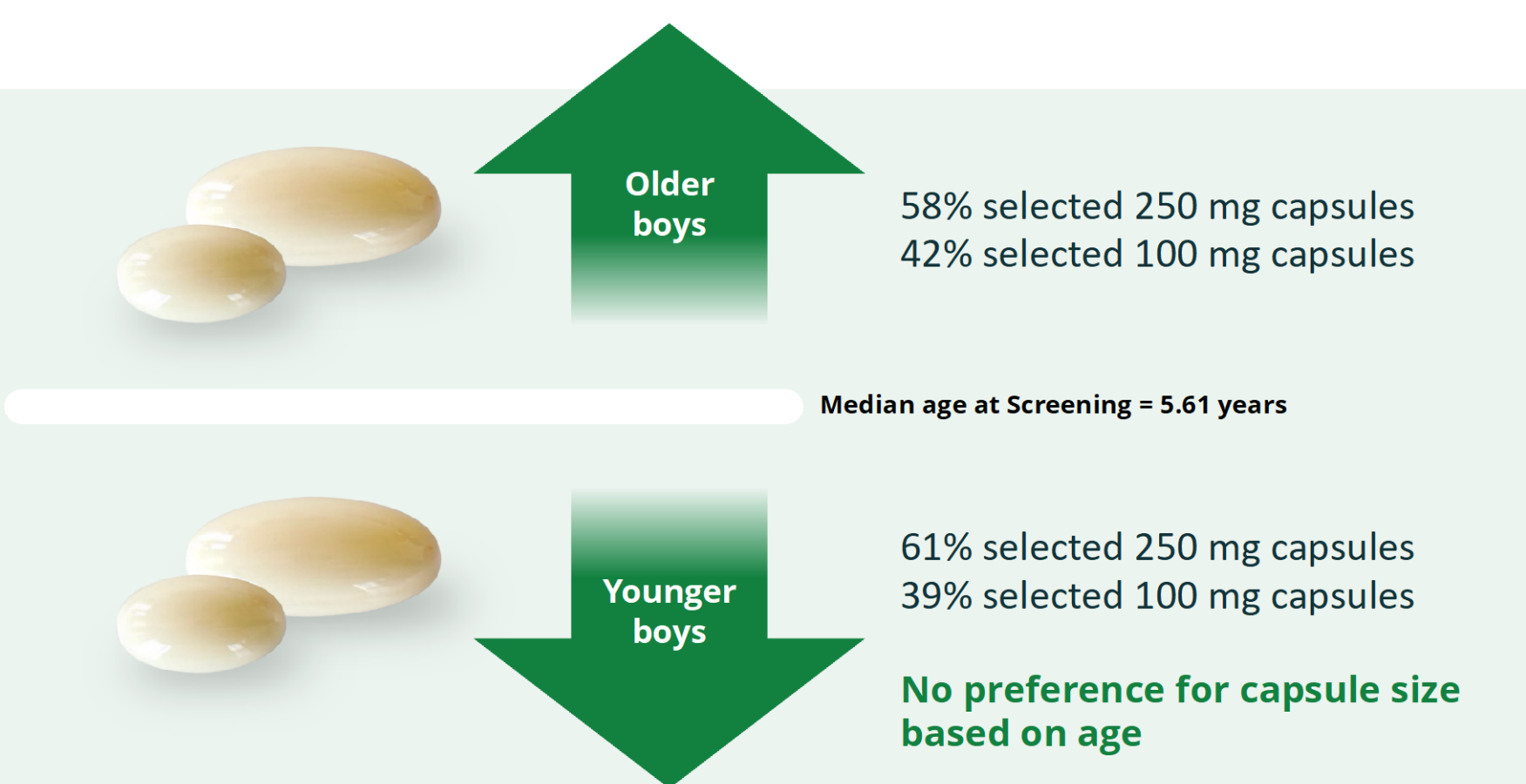


Results – Capsule Selection by Age and Geography

Selection of Capsule Size not Correlated with Age

Boys in the PolarisDMD trial were highly successful at swallowing capsules

- Of 4 year-olds, 90% could swallow capsules
- All boys 5 and older could swallow capsules

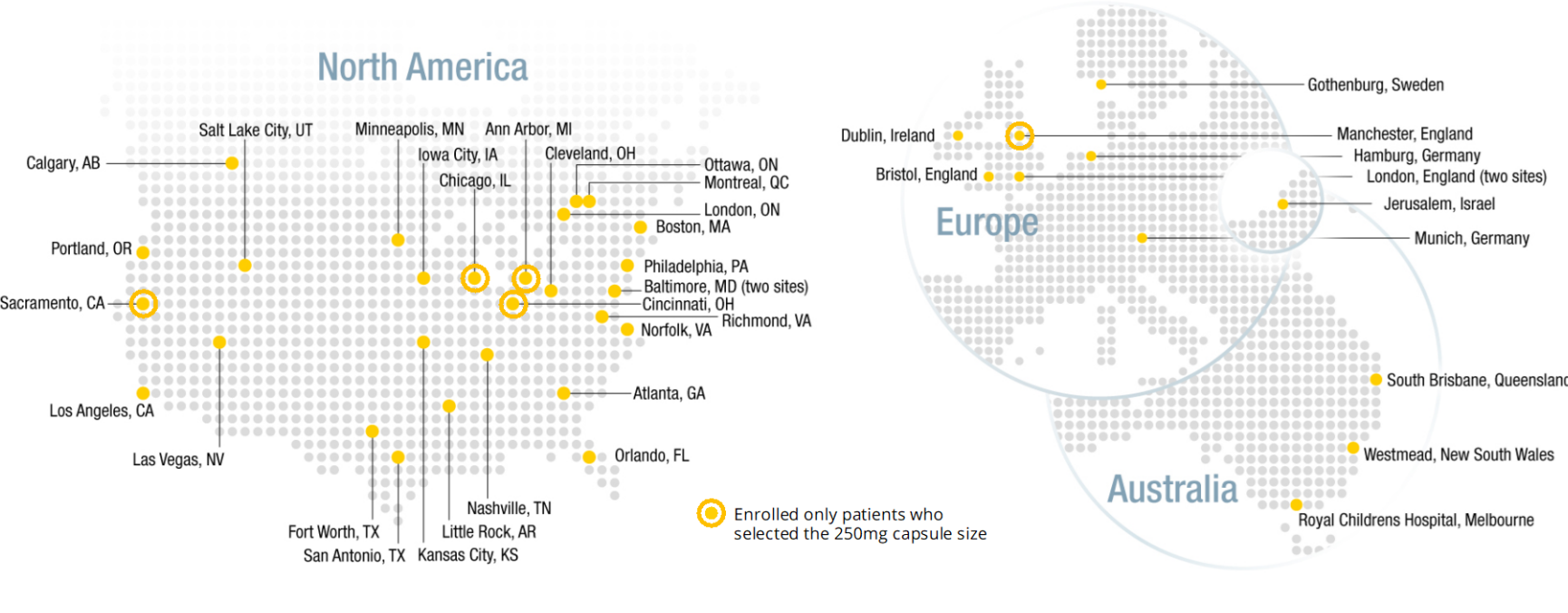


No preference for capsule size based on age

Selection of Capsule Size did not Differ by Geography

No obvious geographical differences in ability to swallow the larger capsules

- Phase 3 PolarisDMD Clinical Trial Sites shown as yellow circles
 - Total of 5 sites with 100% of patients that could swallow the larger 250 mg capsule at Screening shown by the larger yellow circles



In North America, 97% (103 /106) were able to swallow capsules

In Europe, Israel and Australia, 95% (40/42) were able to swallow capsules

Summary of Experience with Edasalonexent Capsules in Catabasis Clinical Trials

- Edasalonexent capsules were well-accepted in boys with DMD**
 - Almost all boys as young as 4 were able to take softgel capsules in a clinical trial setting
 - Capsule acceptance was similar across the global study
- Capsule size did not impede the boys' ability to swallow capsules**
 - Site personnel confidence and experience coupled with initial capsule size presentation significantly impacted the subjects' decisions for capsule size
- Capsules were well-accepted and successfully utilized in boys as young as 4 years**



Acknowledgements

- Patients and families
- Patient groups
- PolarisDMD Phase 3 Site staff
- MoveDMD Phase 2 Site staff
- Catabasis team
- Thanks to PPMD and MDA for generous grant support for patient travel in the MoveDMD Phase 2 trial

