VISION-DMD

Vamorolone Drug Development Program

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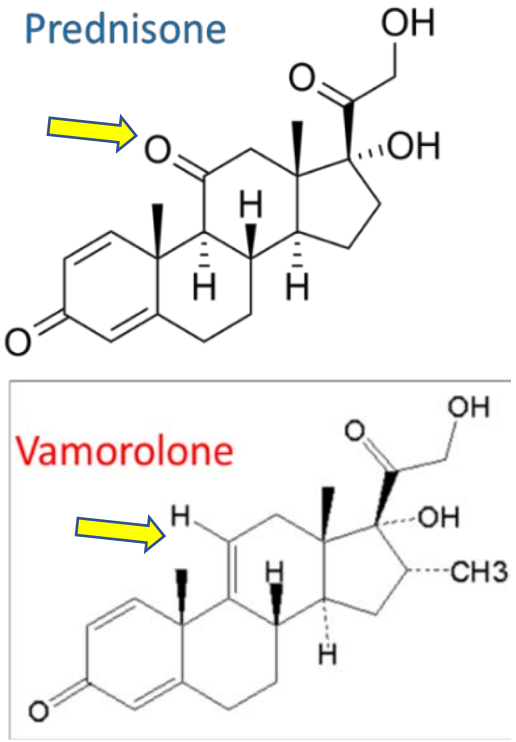
CINRG Cooperative International Neuromuscular Research Group

Vamorolone – Novel Anti-inflammatory Drug

A



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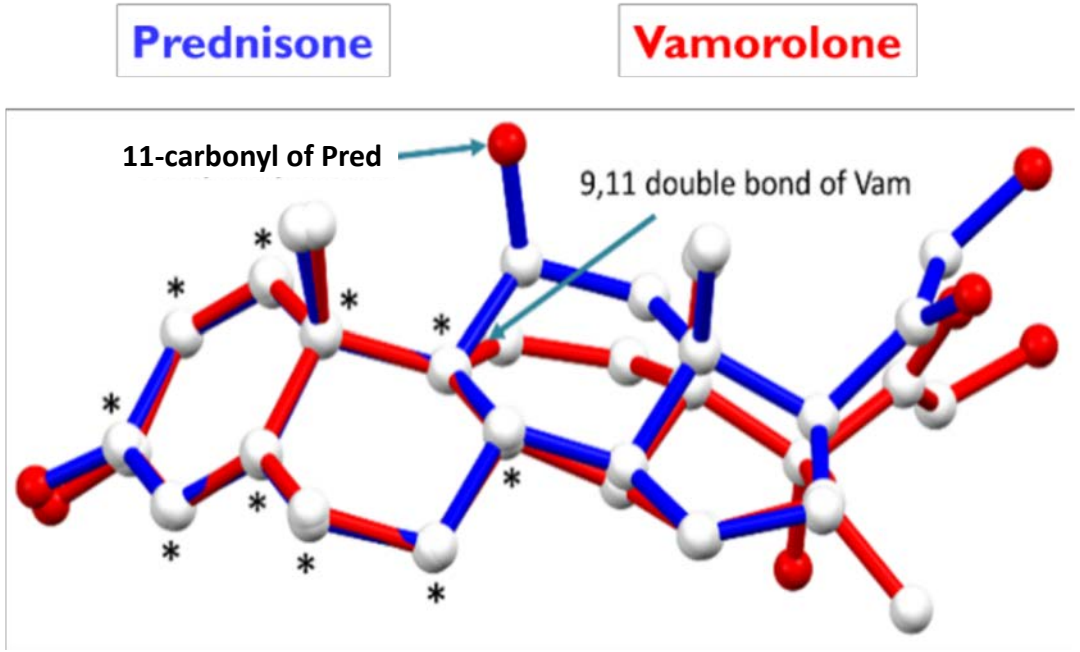


Vamorolone Clinical Trials in DMD

- **Phase 2a**
- **Open label**
- **Dose escalation**
- **18 months**
- **N=48 4 to <7 years**
- **Steroid naïve**

VBP15-002
Phase 2a
1 month

VBP15-003
Phase 2a extension
6 months

VBP15-LTE
Long term extension
2 years

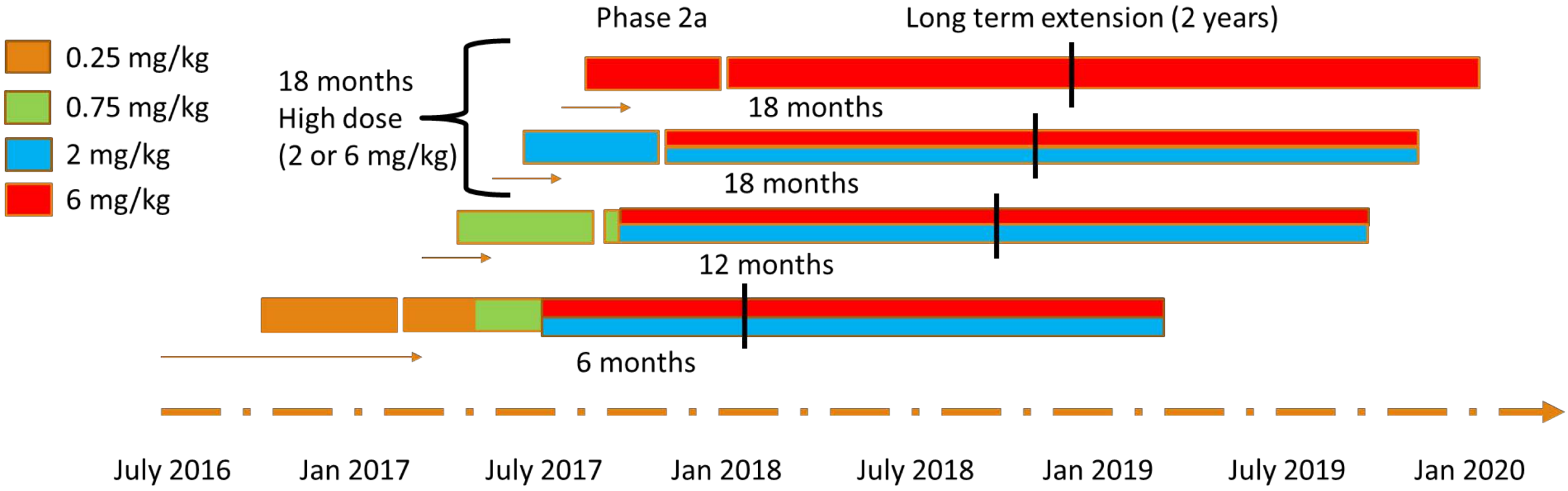
Expanded
Access
Program

N=48
0.25, 0.75, 2.0, 6.0 mg/kg/day

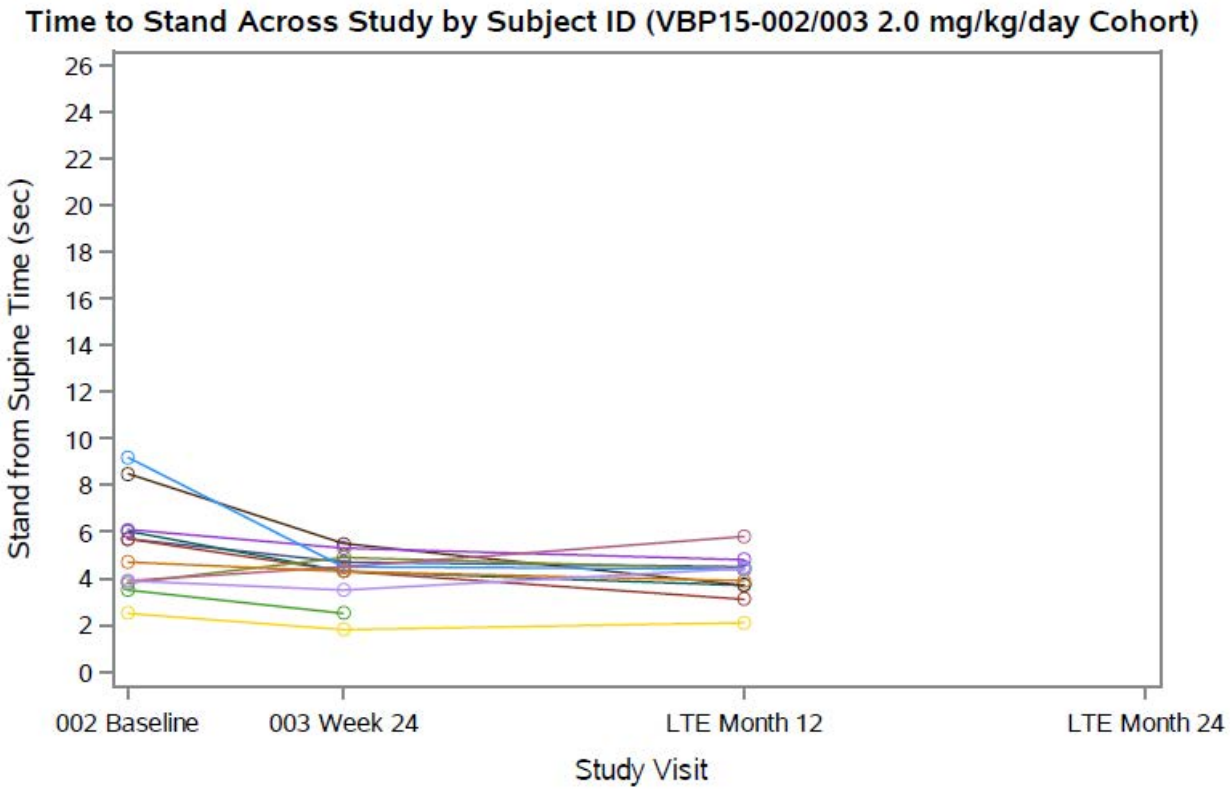
N=43
2.0, 6.0 mg/kg/day

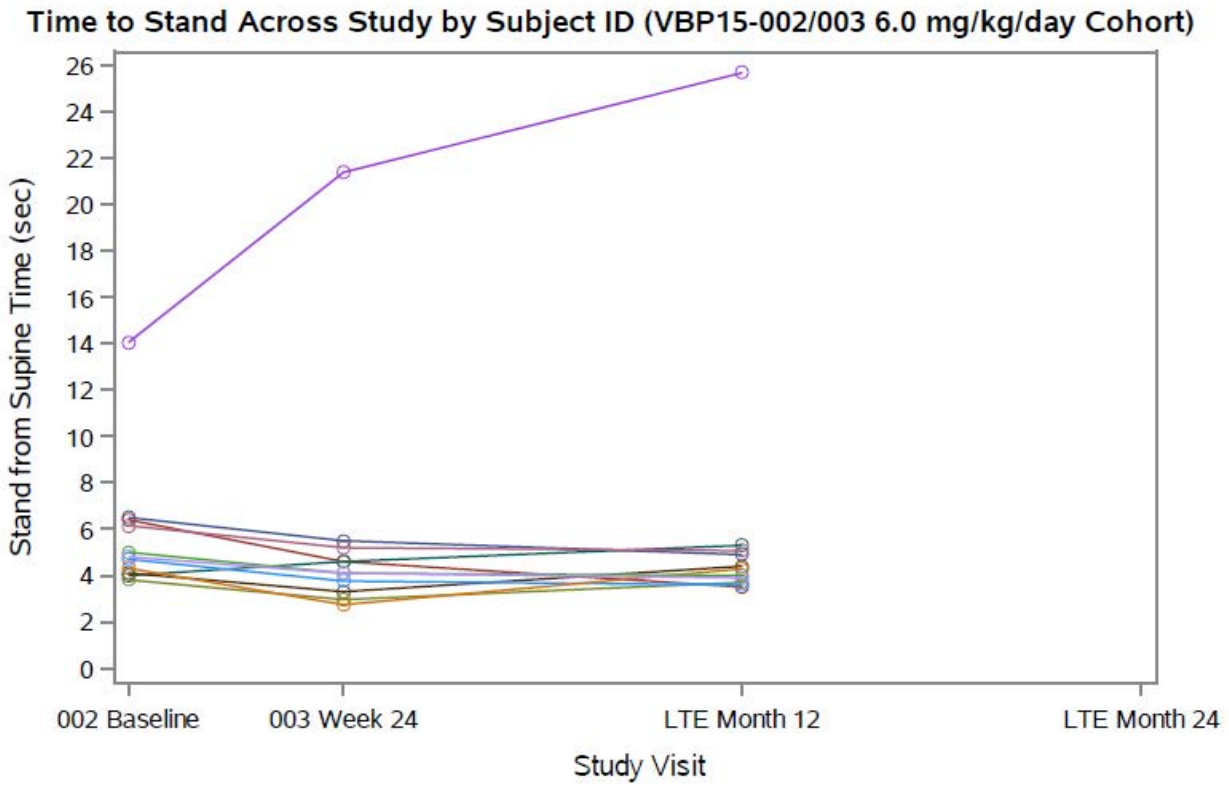
18 months treatment

Longitudinal Dose Assignment Across Original Dose Groups



Longitudinal Time to Stand (TTSTAND) for 2 mg/kg and 6 mg/kg Dose Groups

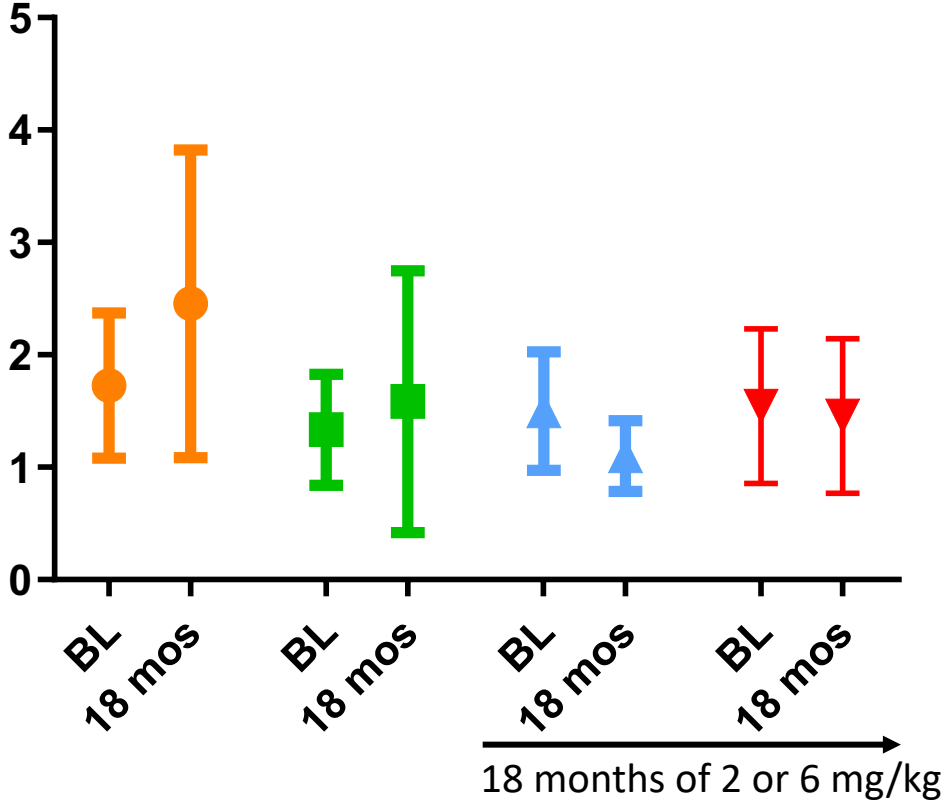




Mapping Vamorolone Dose Groups on DMD Milestone Groups After 18 Months Treatment

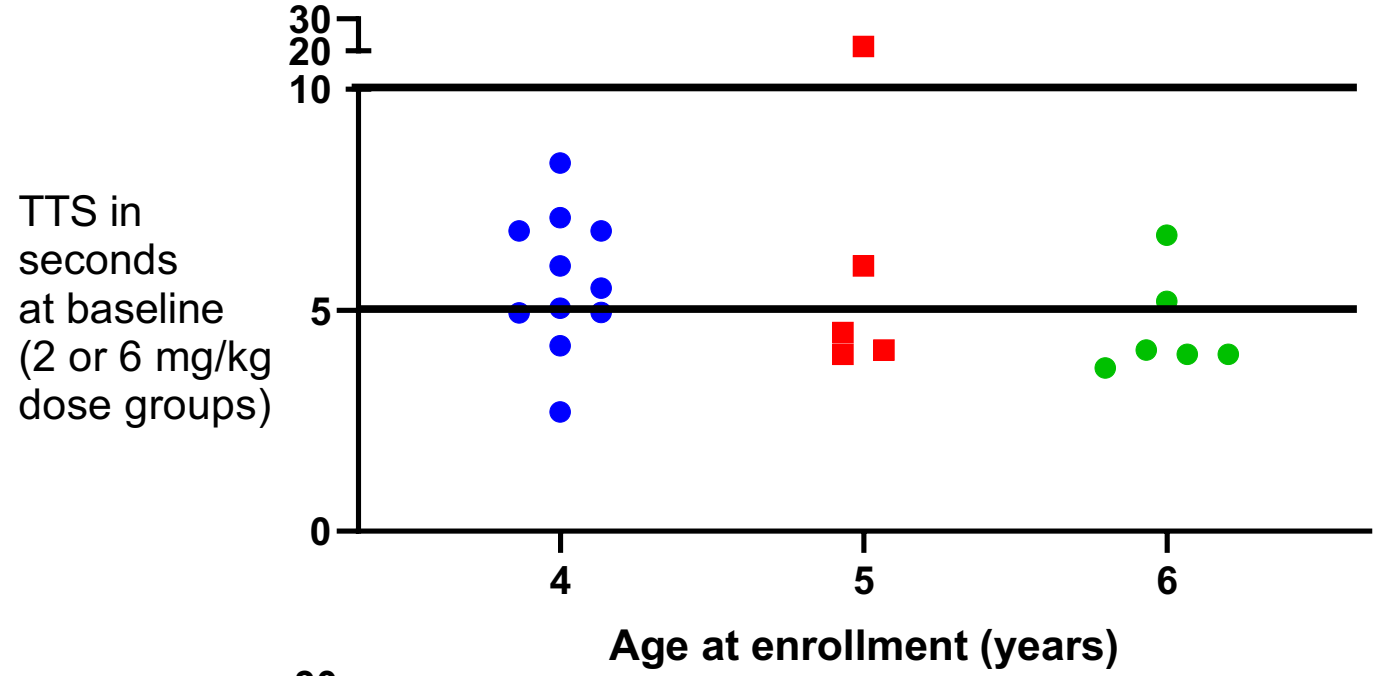
Dose group 1
Dose group 2
Dose group 3
Dose group 4

Milestone Group (mean ± SD)

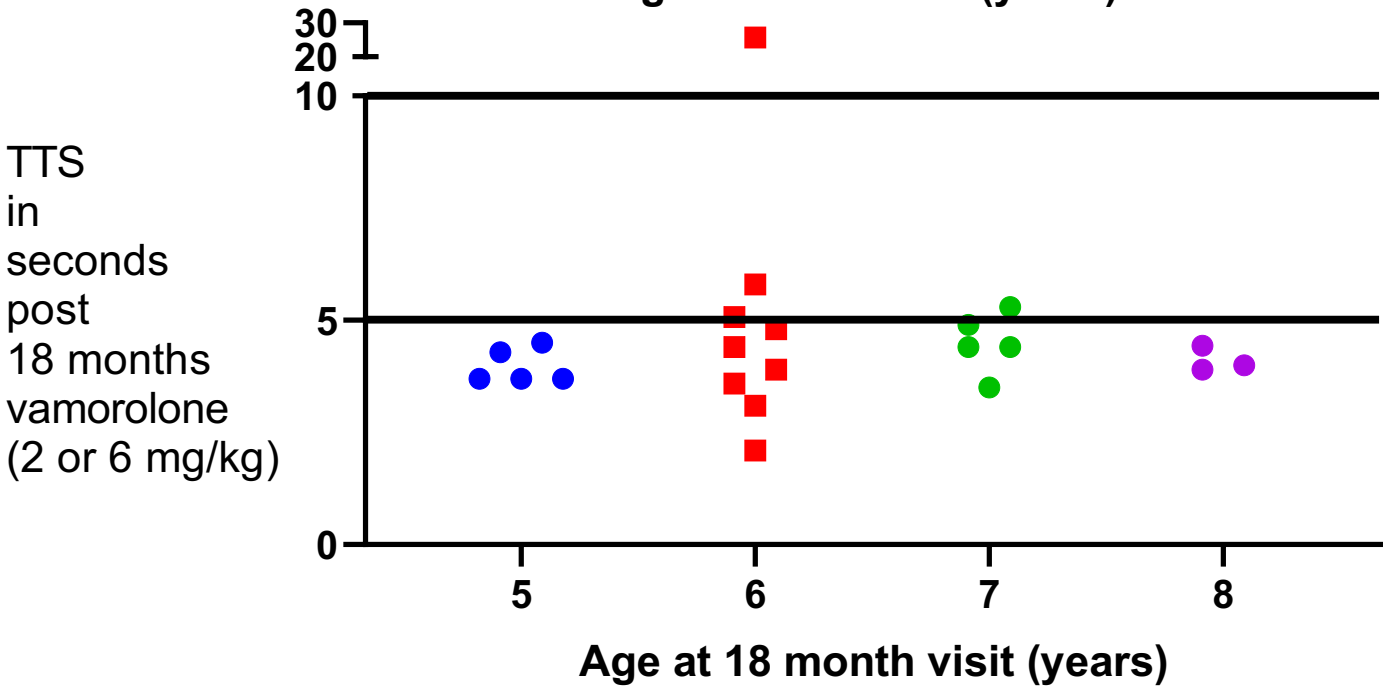


Duchenne Functional Milestone Groups
- Group 1: TTSTAND <5 sec
- Group 2: TTSTAND ≥5 and <10 sec
- Group 3: TTSTAND ≥10 sec

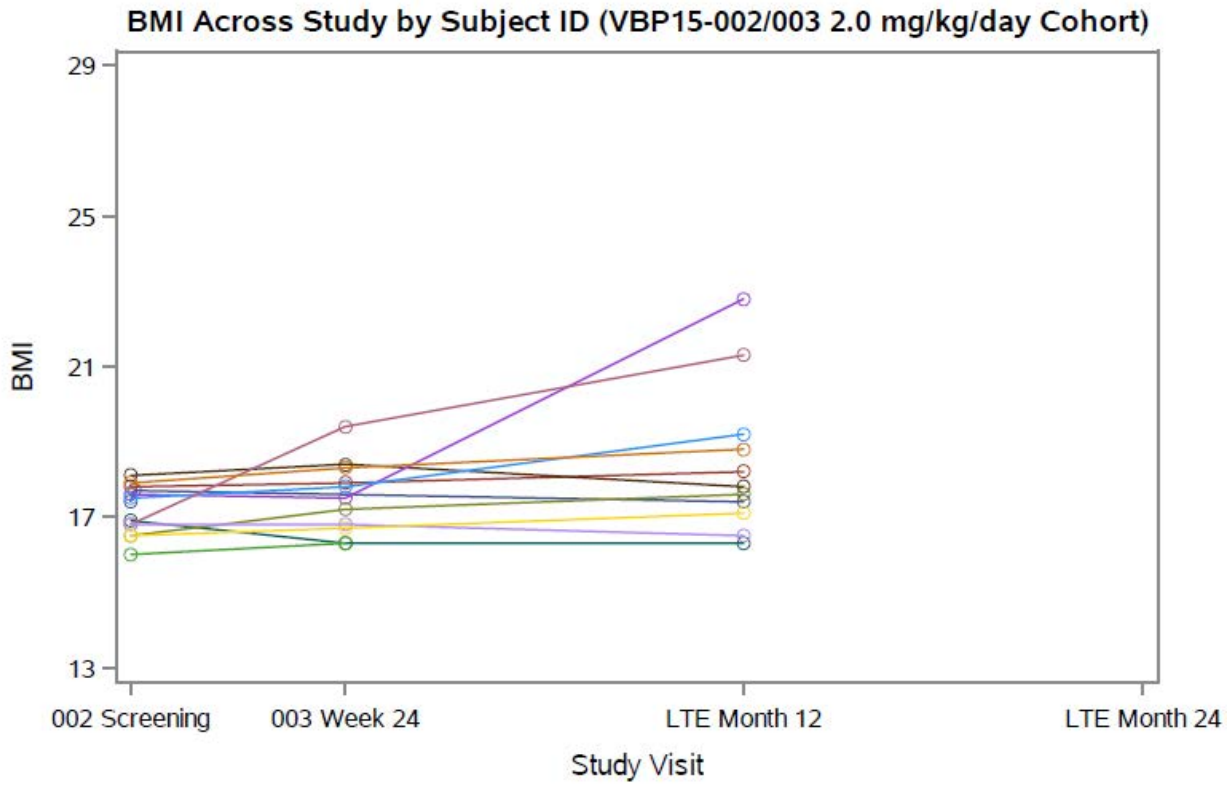
McDonald et al. Lancet 2018; 391:451-61

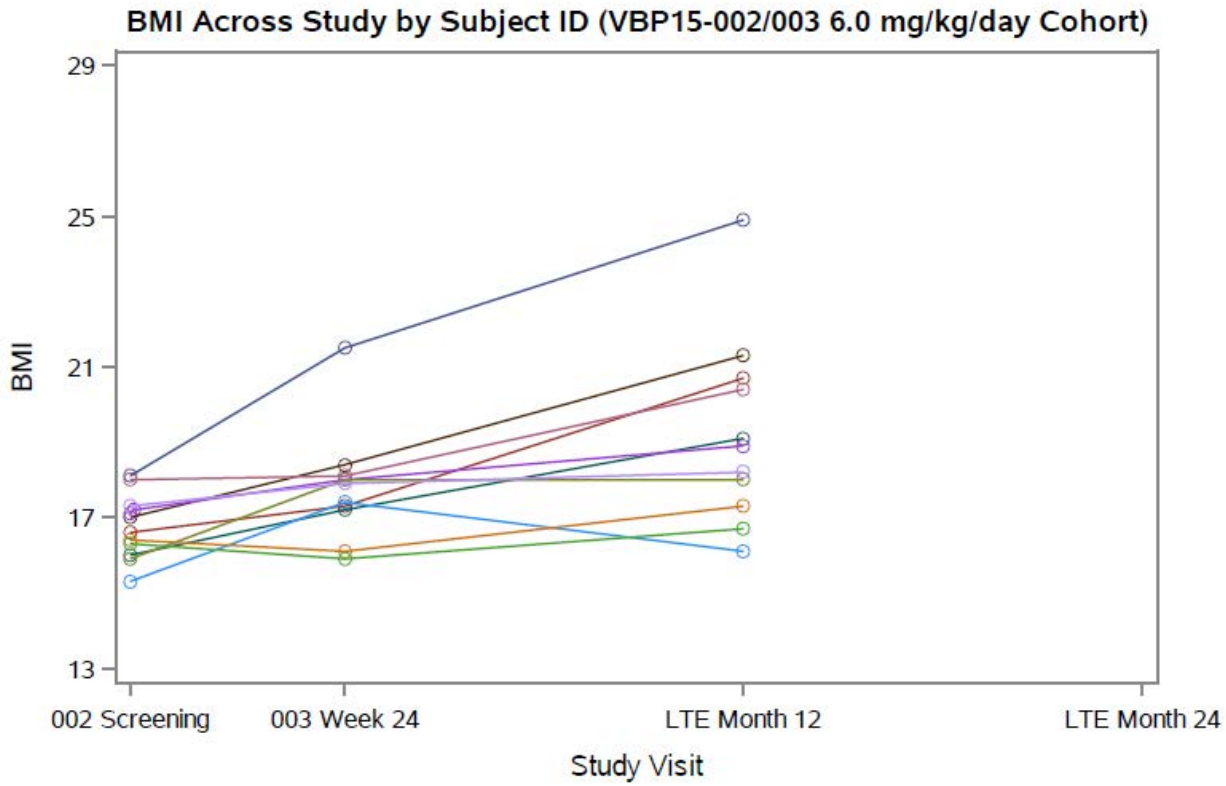


Log transformed Paired t-test (baseline vs 18 months)
p = 0.0075



Longitudinal Body Mass Index (BMI) for 2 mg/kg and 6 mg/kg Dose Groups





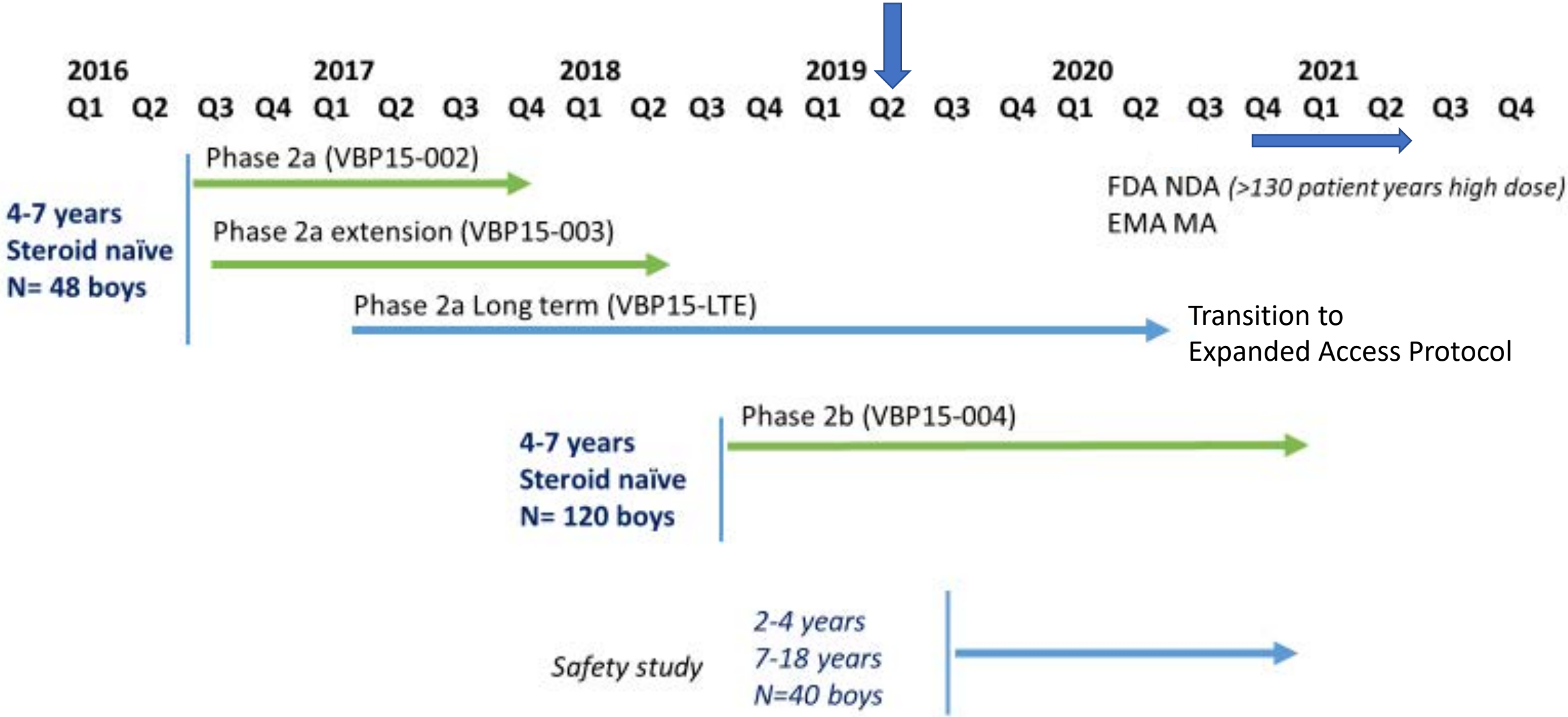
Physician Reports of Cushingoid Appearance and Weight Gain in Vamorolone Long Term Extension Study (highest dose, as of March 2019)

		N Age (SD)	Cushingoid	Weight increased
Vamorolone Long term extension	6.0 mg/kg/day	**N=38** **4.9 (0.9)**	**2.6%**	**13.2%**
**these drugs were not compared head to head and cross study comparisons have limitations in their interpretation				
Griggs 2016	**Placebo**	N=50 8.5 (3.1)	12%	6.0%
	0.9 mg/kg/day **Deflazacort**	N=68 8.8 (2.5)	60.3%	27.9%
	0.75 mg/kg/day **Prednisone**	N=63 8.9 (2.9)	77.8%	34.9%

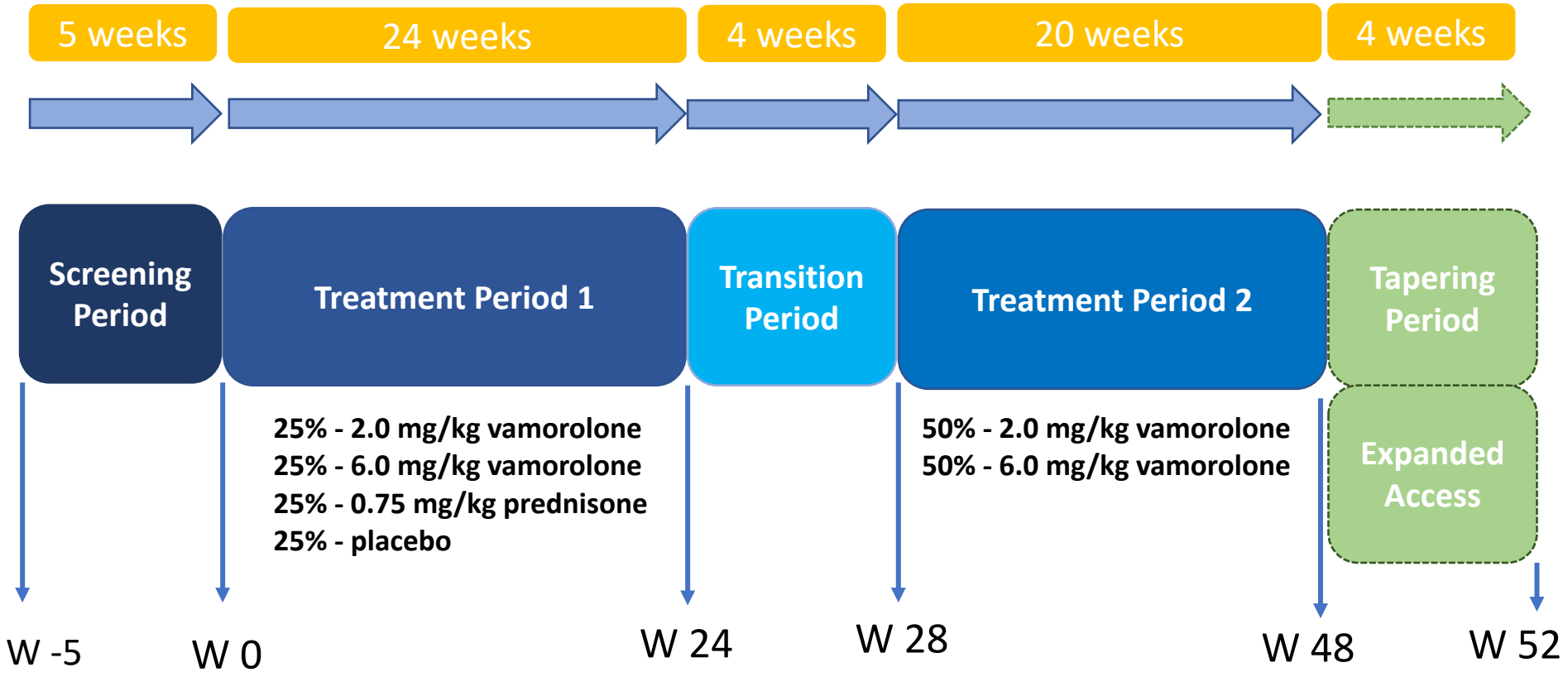
Change in height among patients receiving higher doses of vamorolone for a year in the long-term extension study

		N Age (SD)	Change in height percentile for age, baseline to week 52
Vamorolone Long term extension	2.0-6.0 mg/kg/day for a year	**N=27** **4.9 (0.9)**	**+2.69** **(+0.03, +5.34)**
**these drugs were not compared head to head and cross study comparisons have limitations in their interpretation			
Griggs 2016	**Placebo**	N=50 8.5 (3.1)	0
	0.9 mg/kg/day **Deflazacort**	N=68 8.8 (2.5)	**-11.43** (-15.46, -7.41)
	0.75 mg/kg/day **Prednisone**	N=63 8.9 (2.9)	**-7.04** (-11.32, -2.76)

Vamorolone Human Clinical Study Program – VISION-DMD



Vamorolone Pivotal Study Design VBP15-004



Study Participants: age 4 - <7 years; steroid-naïve; DMD

Sites Phase 2b: North America

Country	Institution	City, State	Site Principal Investigator
USA	**Duke University**	**Durham, North Carolina**	**Edward Smith**
	University of Texas Southwestern Medical Center	**Dallas, Texas**	**Diana Castro**
	University of California Davis	**Sacramento, California**	**Craig McDonald**
	Ann & Robert H. Lurie Children's Hospital	**Chicago, Illinois**	**Nancy Kuntz**
	Seattle Children's Hospital	Seattle, Washington	Susan Apkon
	UCLA	Los Angeles, California	Perry Shieh
	Children's Hospital Colorado	Denver, Colorado	Michele Yang
	Nemours Children's Hospital	**Orlando, Florida**	**Richard Finkel**
	Richmond Children's Hospital	Richmond, Virginia	Amy Harper
	Yale University	New Haven, Connecticut	Cristian Ionita
	Gillette Children's	St. Paul, Minnesota	Carla Grossman
CANADA	**Alberta Children's Hospital**	**Calgary, Alberta**	**Jean Mah**
	Children's Hospital of Eastern Ontario (CHEO)	Ottawa, Ontario	Hugh McMillan
	BC Children's Hospital	Vancouver, British Columbia	Kathy Selby
	Montreal Children's Hospital	Montreal, Quebec	Anne Marie Sbrocchi

PHASE 2A SITES

Study management by:

TRiNDS

Sites Phase 2b: Europe, Israel, Australia

Country	Institution	City	Principal Investigator
UNITED KINGDOM	Royal Hospital for Children	Glasgow	Iain Horrocks
	Alder Hey Children's Hospital	Liverpool	Stefan Spinty
	University College London	London	Giovanni Baranello
	Newcastle University	**Newcastle**	**Michela Guglieri**
	Leeds Teaching Hospitals Trust	Leeds	Anne-Marie Childs
ISRAEL	**Schneider Children's Medical Center**	**Tel Aviv**	**Yoram Nevo**
AUSTRALIA	**Royal Children's Hospital**	**Melbourne**	**Monique Ryan**
	The Children's Hospital at Westmead	**Sydney**	**Richard Webster**
SWEDEN	**Queen Silvia Children's Hospital**	**Gothenburg**	**Mar Tulinius**
NETHERLANDS	Leiden University Medical Center	Leiden	Erik Niks
	Radboud University	Nijmegen	Imelda de Groot
CZECH REPUBLIC	University Hospital Brno	Brno	Lenka Mrazova
	Charles University	Prague	Jana Haberlová
BELGIUM	Ghent University Hospital	Ghent	Nicolas Deconinck
	University Hospitals Leuven	Leuven	Nathalie Goemans
SPAIN	Hospital Universitario y Politécnico La Fe	València	Juan Vilchez
	Sant Joan de Deu Hospital	Barcelona	Andres Osorio
GREECE	Agia Sofia Children's Hospital	Athens	Maria Katsoulakis

PHASE 2A SITES

Study management by:

Acknowledgements

- **Study participants and their families**
- **Study Chairs:** Paula Clemens (Pittsburgh), Michela Guglieri (Newcastle)
- **Recruitment sites:** CINRG network (plus new sites in 004 blinded study)
- **Trial management:** TRiNDS LLC; Camden medical and clinical monitoring (Ben Schwartz, Laurel Mengle-Gaw); CINRG Data Safety Monitoring Board
- **ReveraGen development team:** John McCall, Jesse Damsker, Kanneboyina Nagaraju, Laurie Conklin, Suzanne Gaglianone, John van den Anker, Eric Hoffman
- **Financial support:** US government and European Commission, 12 non-profit foundations, including MDA and PPMD

VISION-DMD

http://vision-dmd.info/

VISION-DMD

- **An investigational drug, vamorolone, shows dose-dependent efficacy in DMD in open label study**
  - Preliminary evidence shows improvements in gross motor function tests significant within trial (between dose groups)
- **No patients exiting the trial due to safety concerns in 48 DMD boys**
  - ~50 patient years of high dose drug exposure in DMD
- **Currently enrolling patients in a trial for a double-blind comparison to placebo and prednisone**
  - At 6 months, placebo and prednisone arms change to vamorolone only
  - 4 to <7 years of age, steroid naïve
  - All travel/stay to one of 34 sites in 11 countries covered; visits ~1/month; dosing at home
  - Enrolling 120 boys total; currently ~25% enrolled