VISION-DMD

Vamorolone Development Program

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Medical and Regulatory Director

Duchenne UK Information Day for Parents and Caregivers

Manchester, England

September 28, 2019

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CINRG Cooperative International Neuromuscular Research Group

Steroids help boys with Duchenne muscular dystrophy stay stronger longer

- But with serious side effects
  - Loss of bone density resulting in fractures
  - Weight gain
  - Suppressed immunity
  - Mood and behavior changes
  - Stunting of growth

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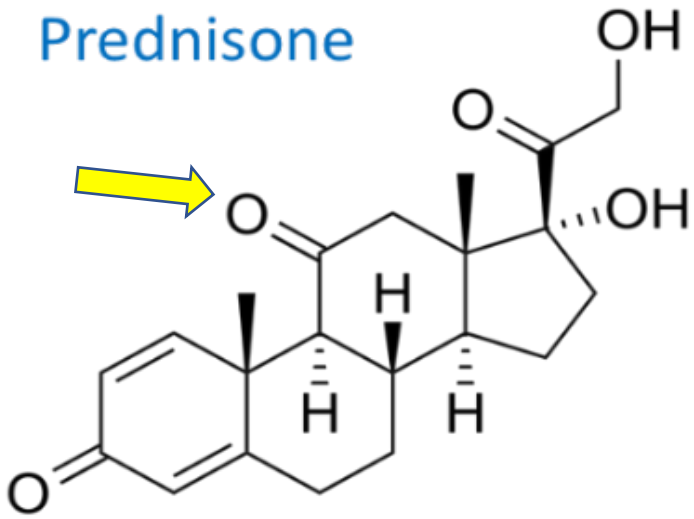
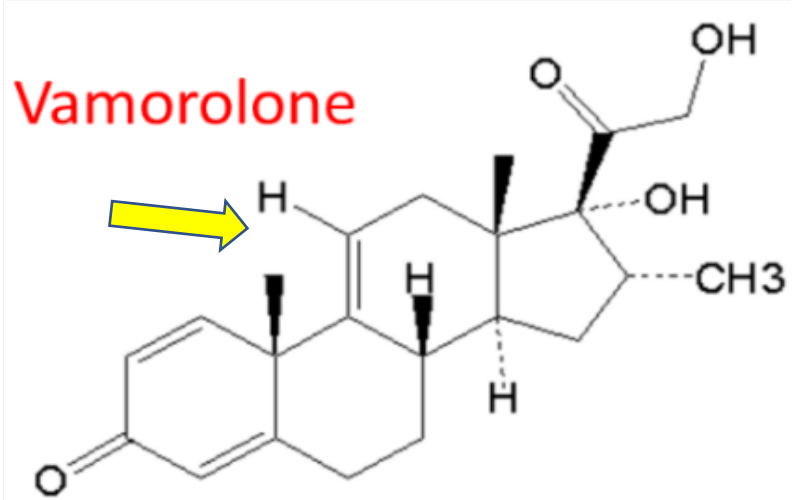
Vamorolone – Novel Anti-inflammatory Drug

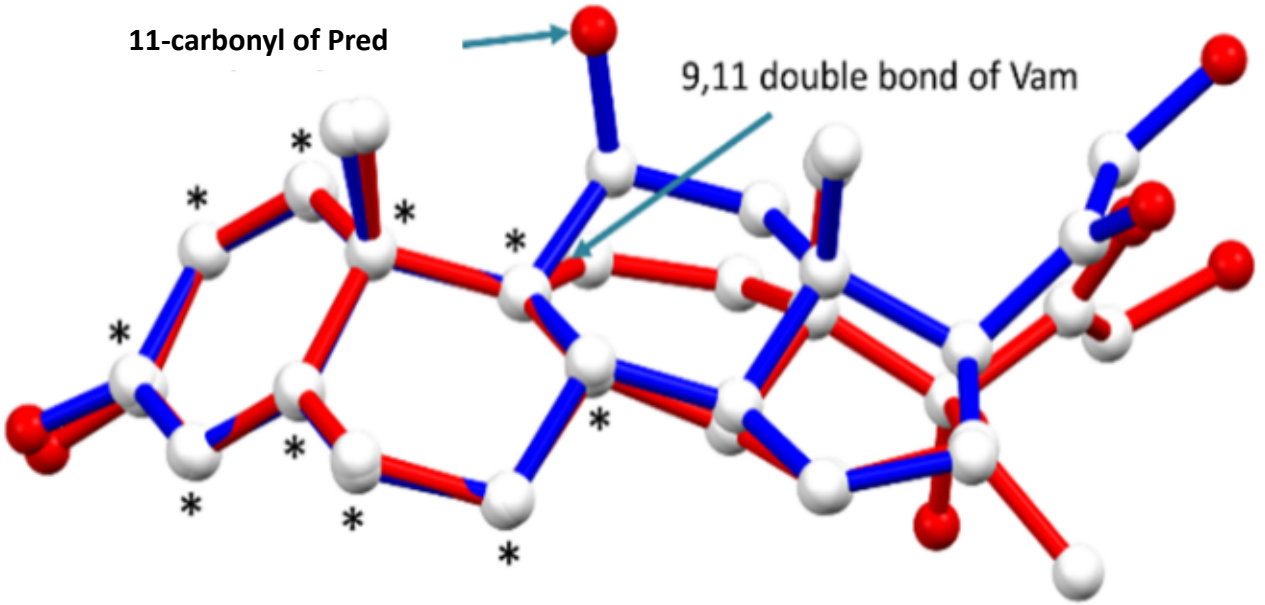
Prednisone



Vamorolone



Prednisone Vamorolone



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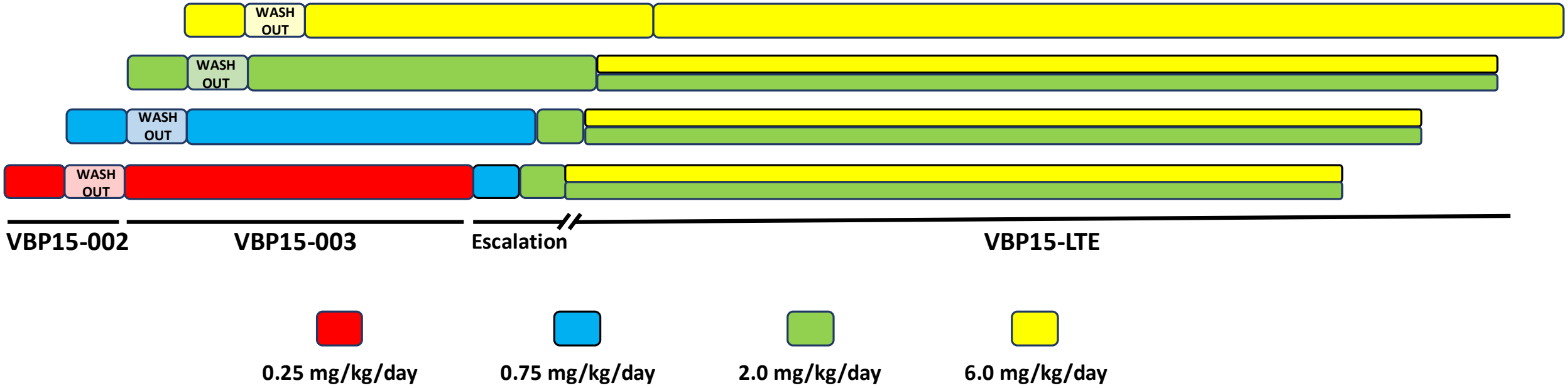
VAMOROLONE TRIALS IN BOYS WITH DUCHENNE MUSCULAR DYSTROPHY



- Segment 1 (VBP15-002): 2 wk treatment followed by 2 wk washout
- Segment 2 (VBP15-003): 24 wk treatment - same dose as Segment 1
- Long-term extension (VBP15-LTE): 24 months treatment with an opportunity for dose escalation

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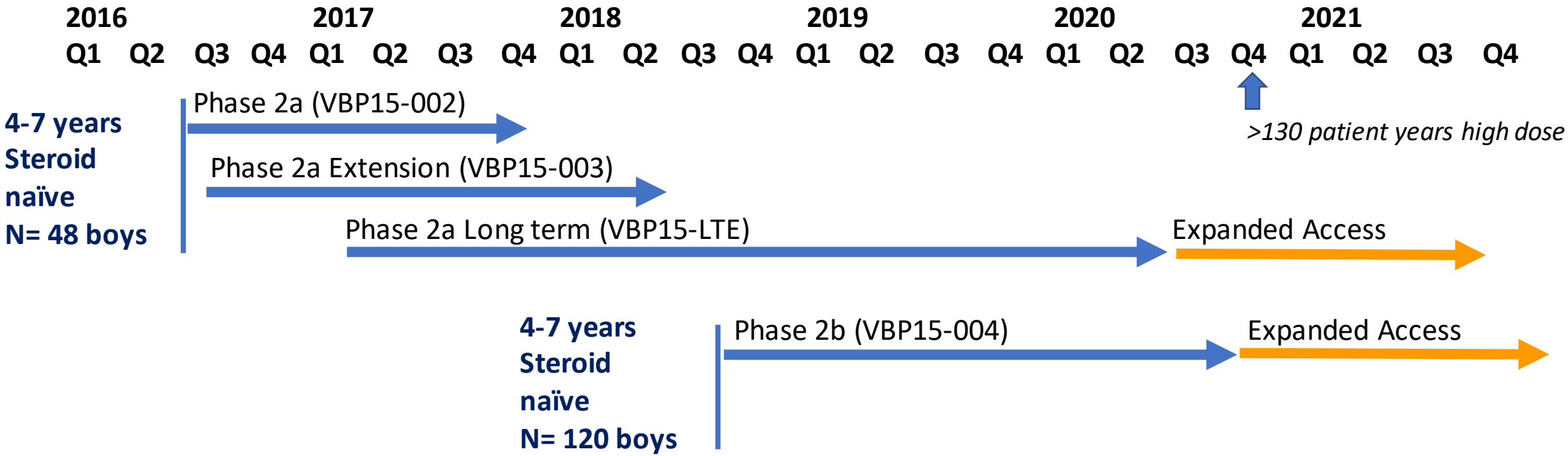

VBP15-006: Safety and Dosing in boys ages 2-4 years, and 7-17 years (N=40 boys)

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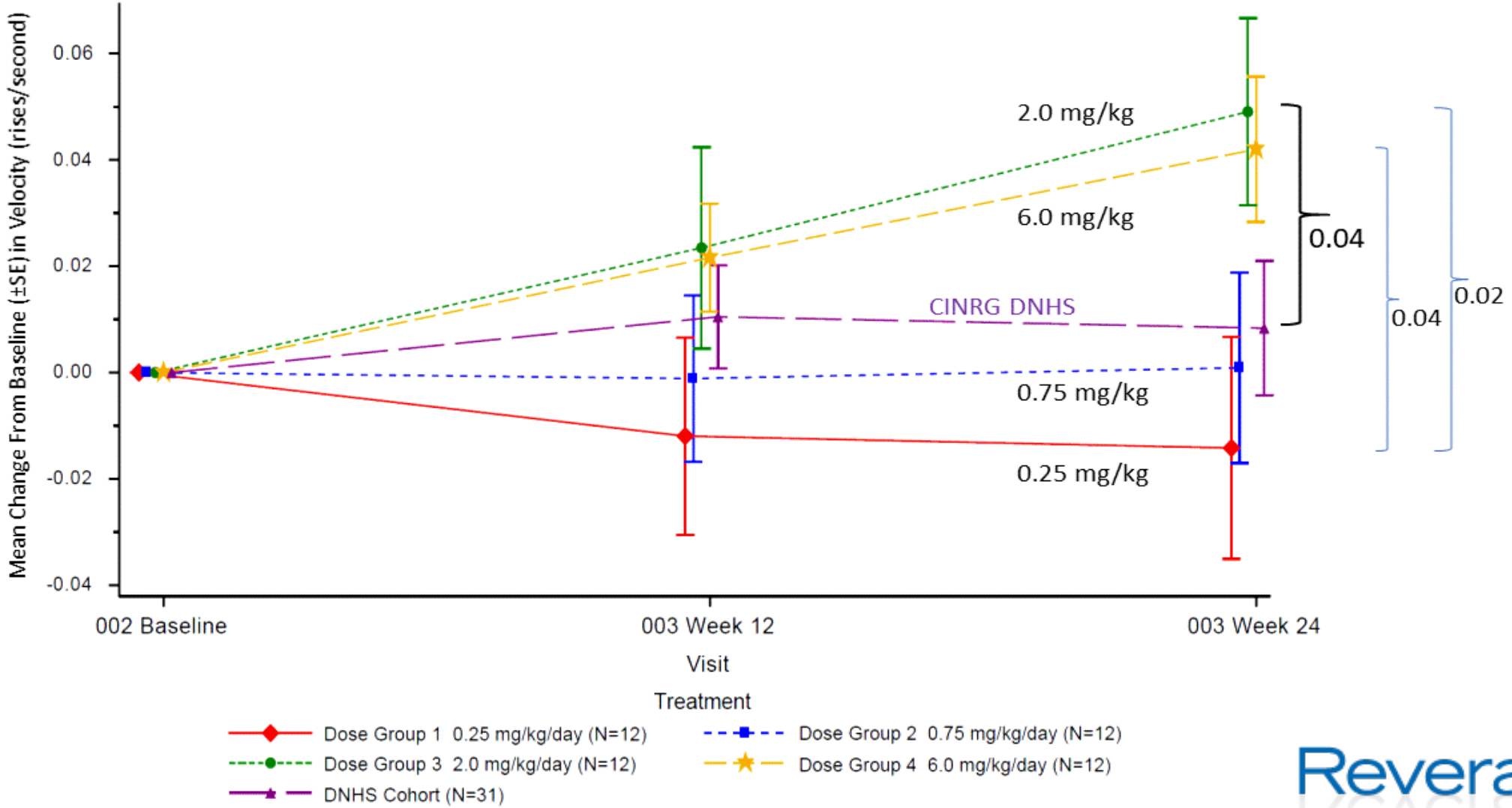
Time to Stand Velocity (6 months)



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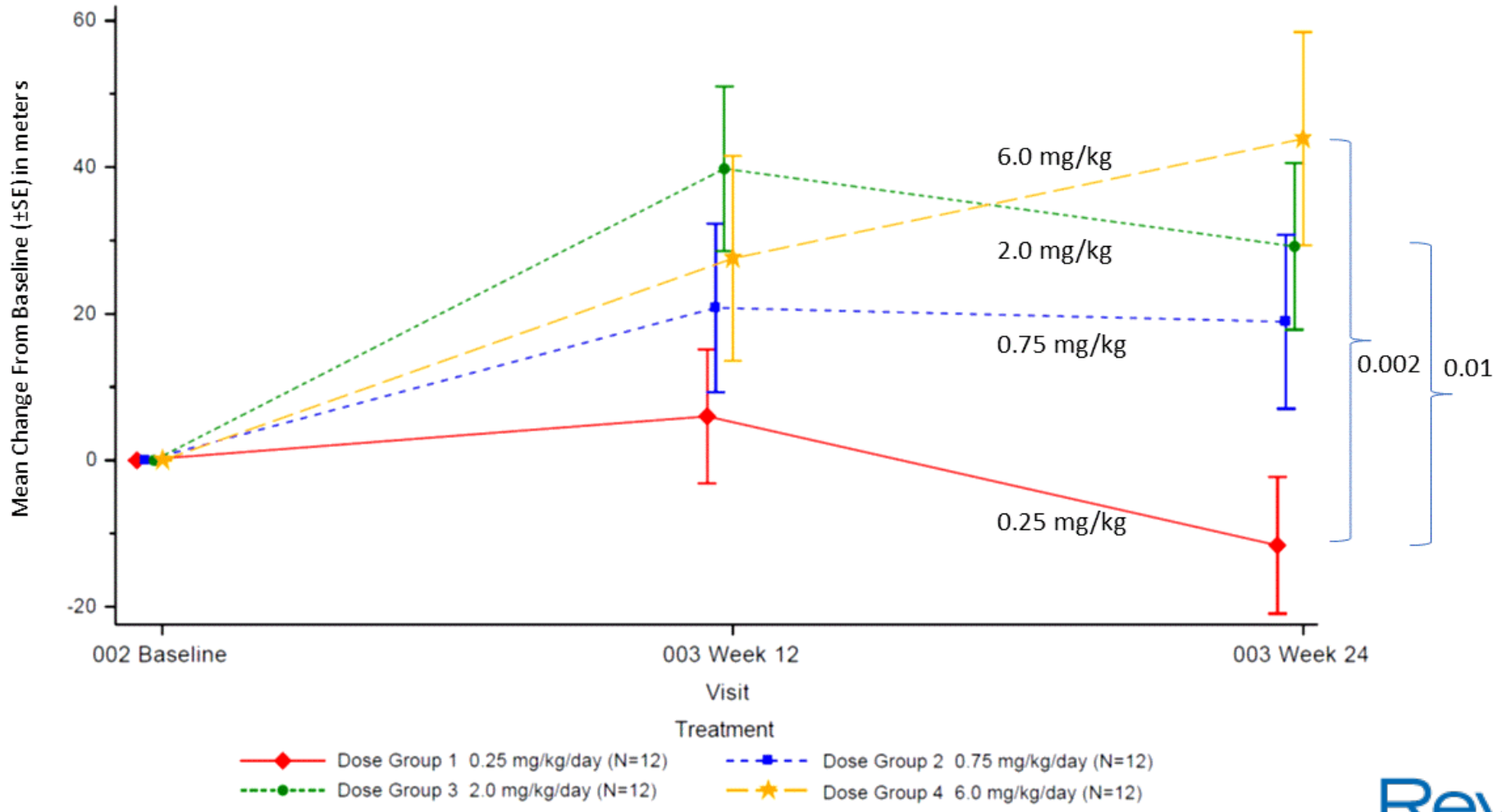
6-Minute Walk Test (6 months)



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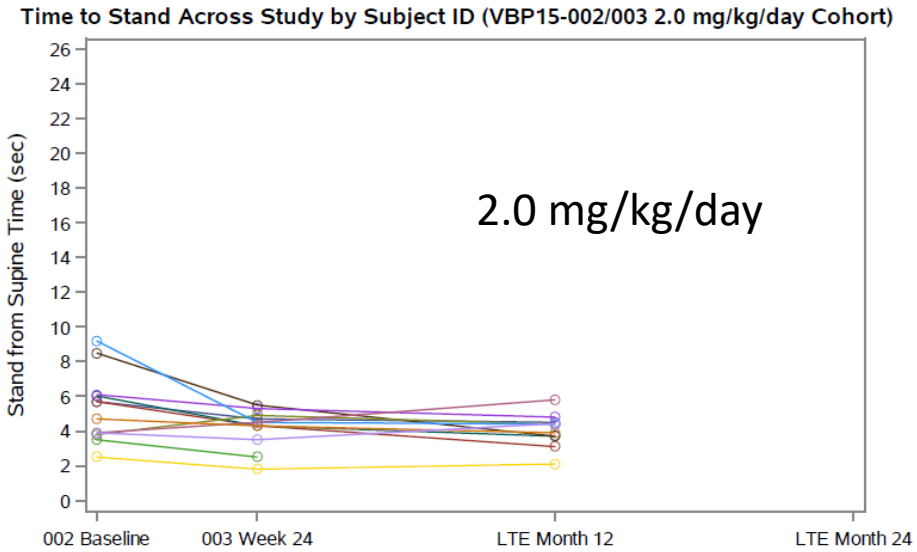
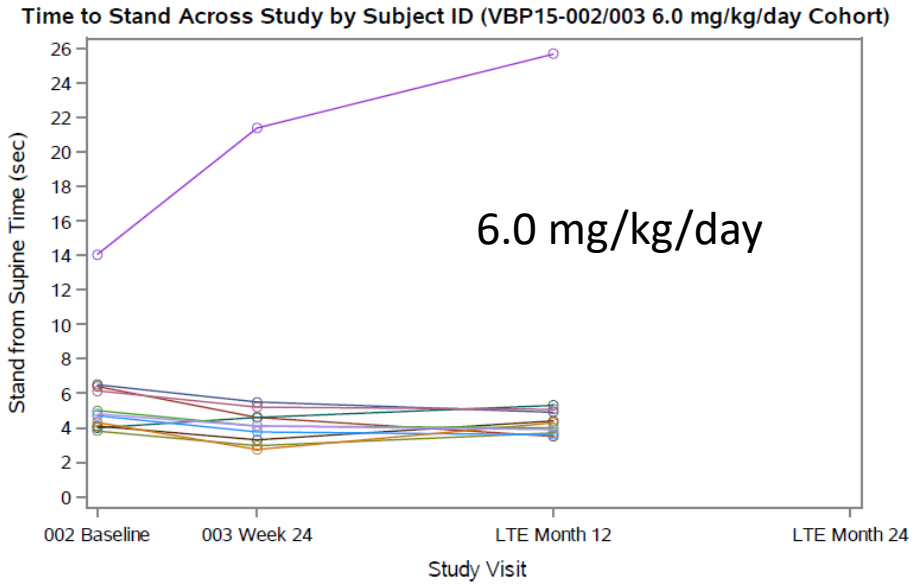
Longitudinal Time to Stand (TTSTAND) (in seconds) for 2 mg/kg and 6 mg/kg Dose Groups (18 months of treatment)





Milestone group 1: Time to stand <5 seconds

- Are likely to show stability or improvement versus those who are likely to decline

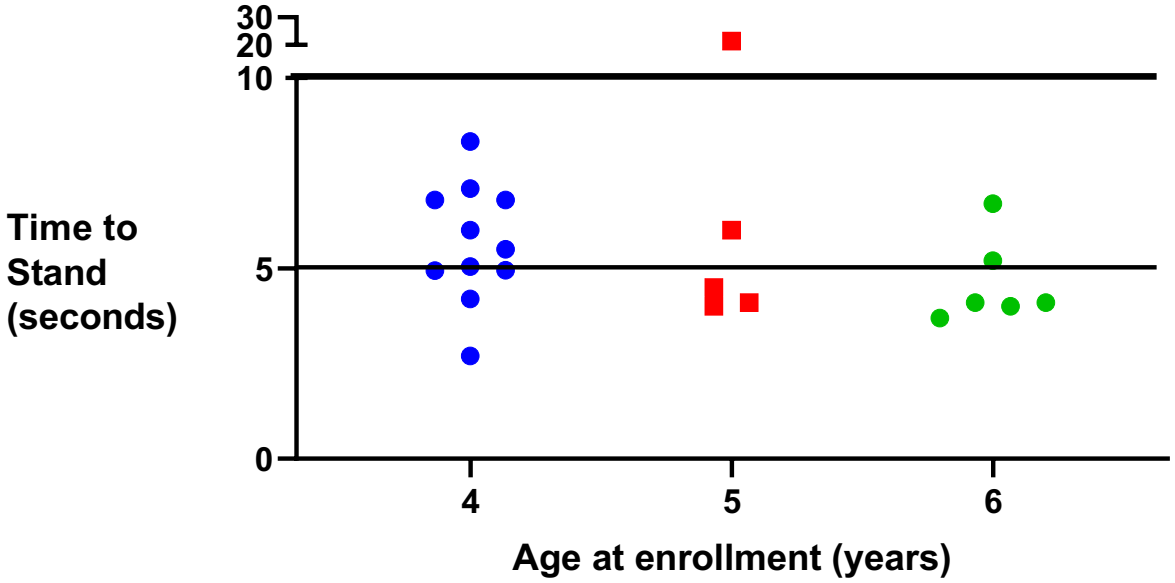
Milestone group 2: Time to stand >5 and <10 seconds

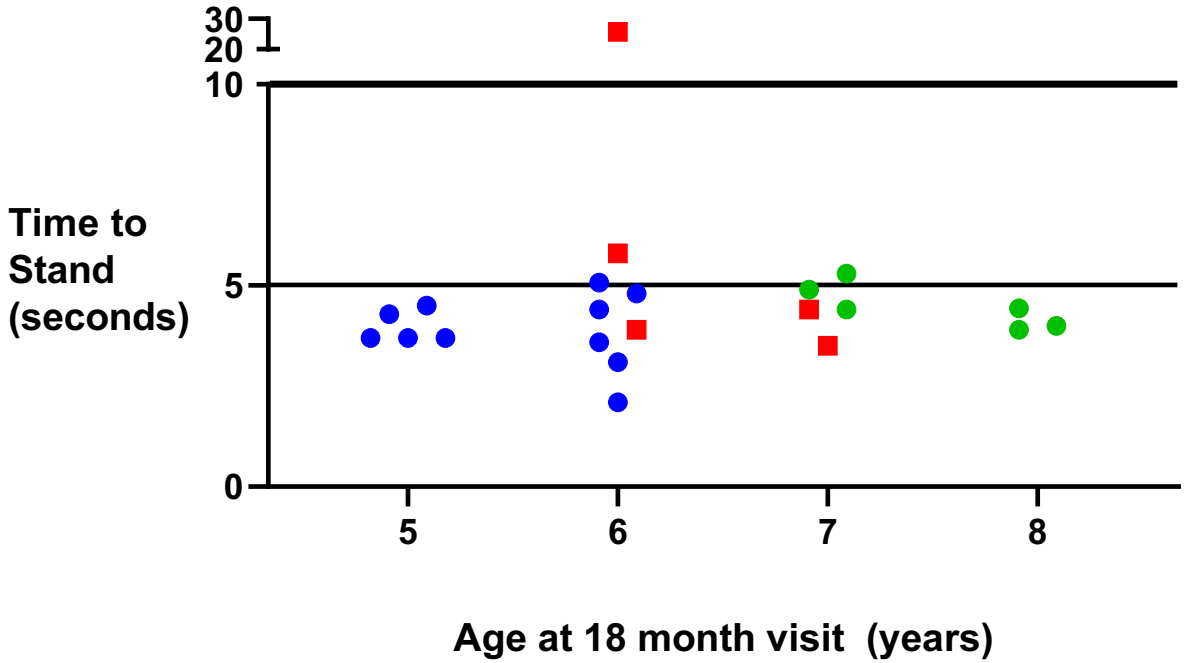
- Are likely to experience decline in function and possibly loss of standing ability

Long-term effects of glucocorticoids on function, quality of life, and survival in patients with Duchenne muscular dystrophy: a prospective cohort study

*Craig M McDonald, Erik K Henricson, Richard T Abresch, Tina Duong, Nanette C Joyce, Fengming Hu, Paula R Clemens, Eric P Hoffman, Avital Cnaan, Heather Gordish-Dressman, and the CINRG Investigators**

www.thelancet.com Vol 391 February 3, 2018





Time to Stand (seconds) Before and After 18 Months of Vamorolone Treatment

2 and 6 mg/kg/day groups

n=22

Most patients improve from Milestone Group 2 to Milestone Group 1

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

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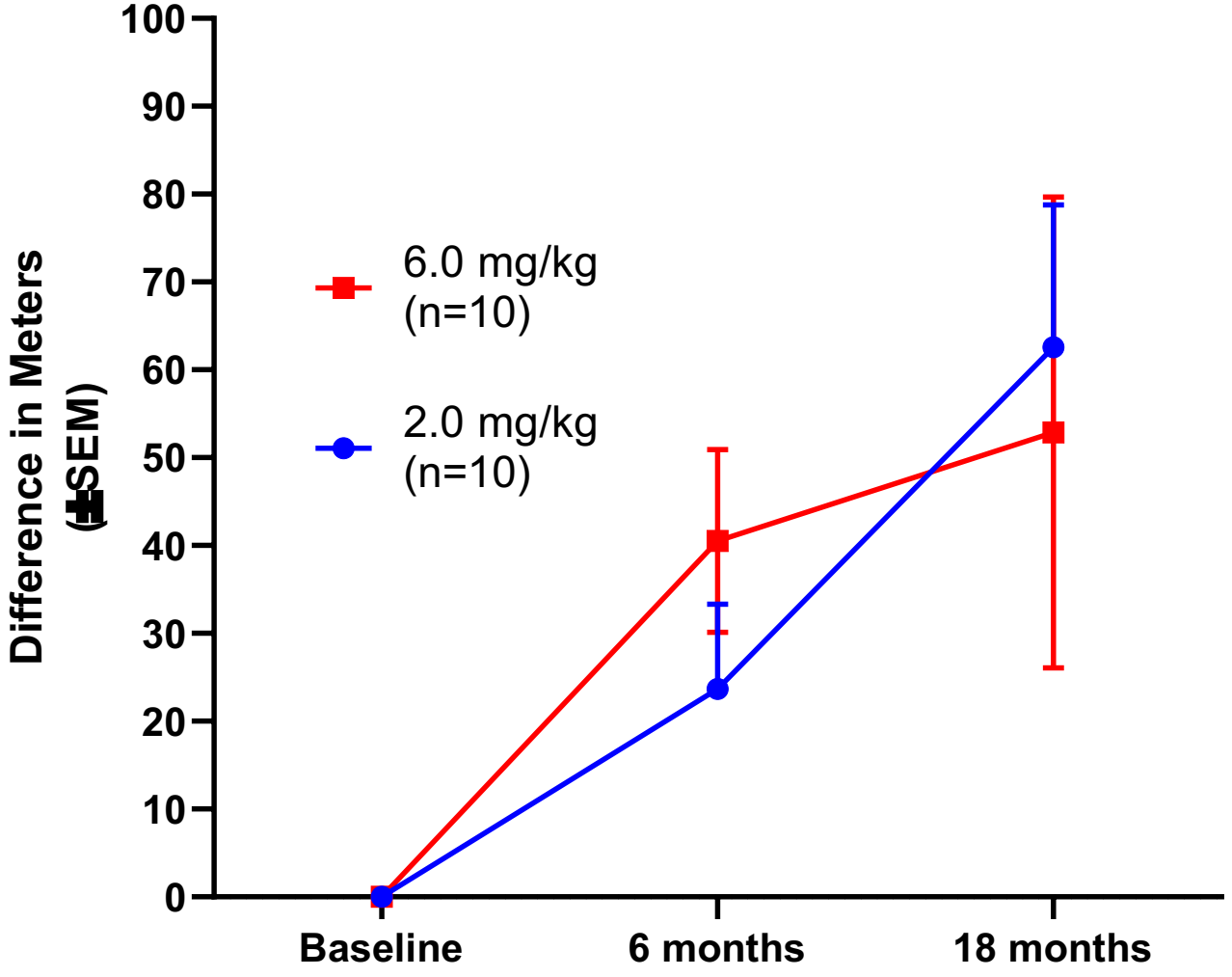
Change in 6 Minute Walk Distance over 18 months of Vamorolone Treatment



About 50% of 2 mg/kg patients escalated to 6 mg/kg for a year

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- What about side effects seen with corticosteroids (prednisone, deflazacort)?

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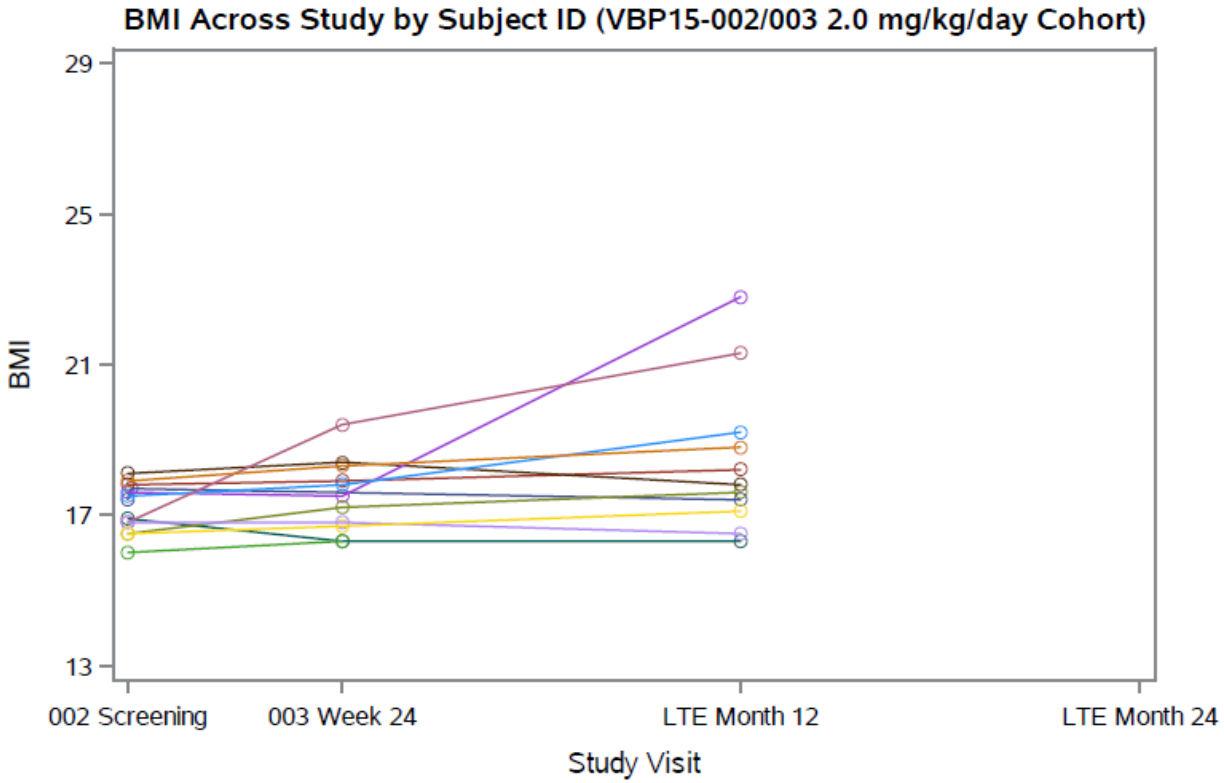
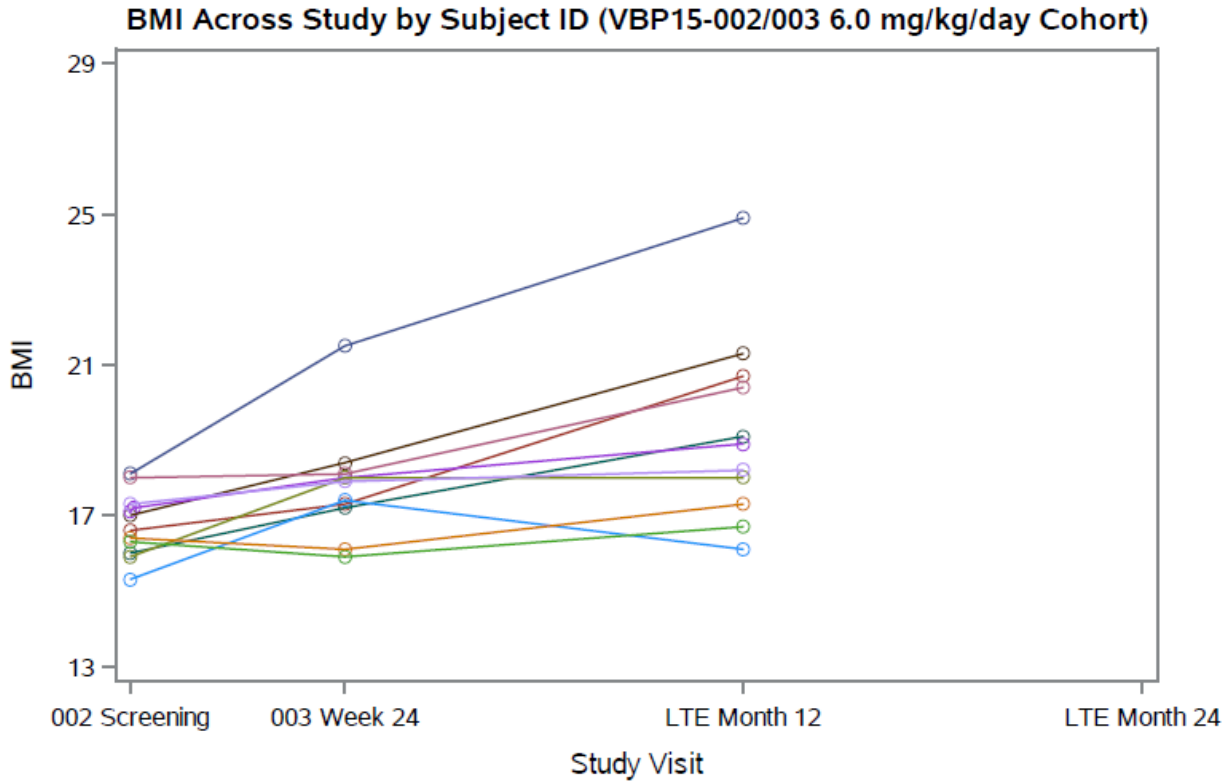
Longitudinal Body Mass Index (BMI) for 2 mg/kg and 6 mg/kg Dose Groups





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Vamorolone shows loss of Cushingoid, Weight Gain Relative to Corticosteroids

Physician Reported Adverse Events (% patients)

Vamorolone LTE data from Signal Detection Report March 13, 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%

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Vamorolone shows Loss of Stunting of Growth and Osteocalcin Decrease Relative to Corticosteroids

		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)

Bone biomarker data:
Osteocalcin significantly decreased by corticosteroids
Osteocalcin significantly increased by vamorolone

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Vamorolone data to date

- DMD boys treated with vamorolone improve over 18 months
- Time to stand for most patients treated for 18 months changes from Group 2 (declines expected) to Group 1 (improvement or stabilization expected)
- Bone side effects of corticosteroids not seen with vamorolone
  - No stunting of growth
  - Bone formation biomarker osteocalcin improves

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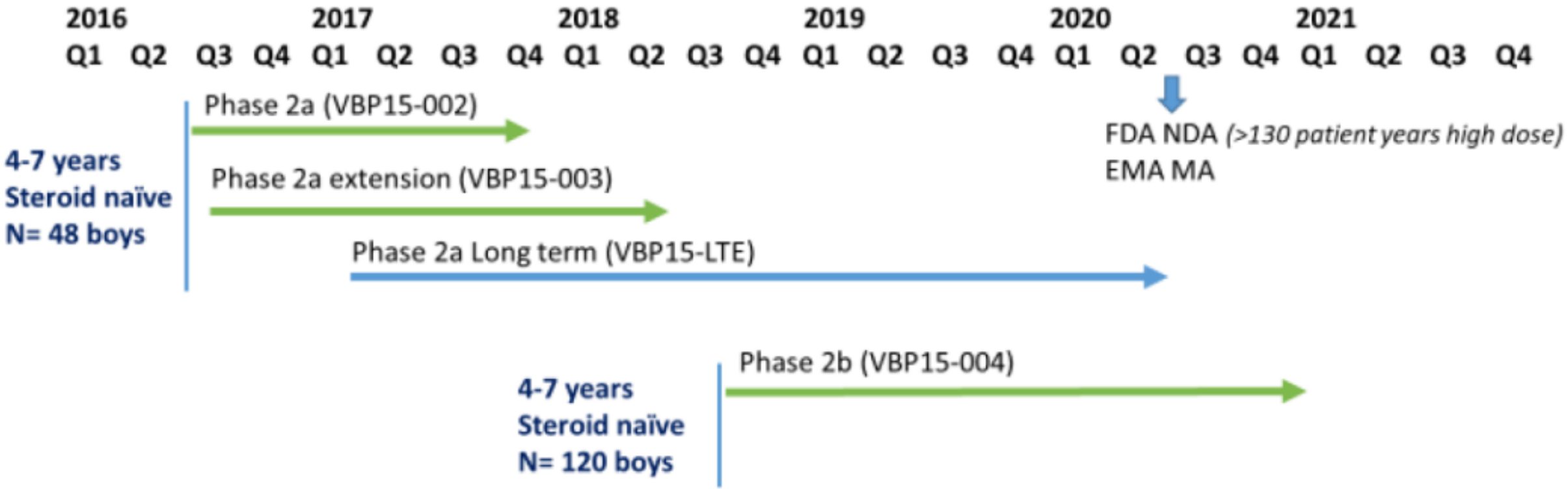

VBP15-006: Study Evaluating Dosing/Safety in boys ages 2-4 years and 7-17 years (n=44)

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Target:

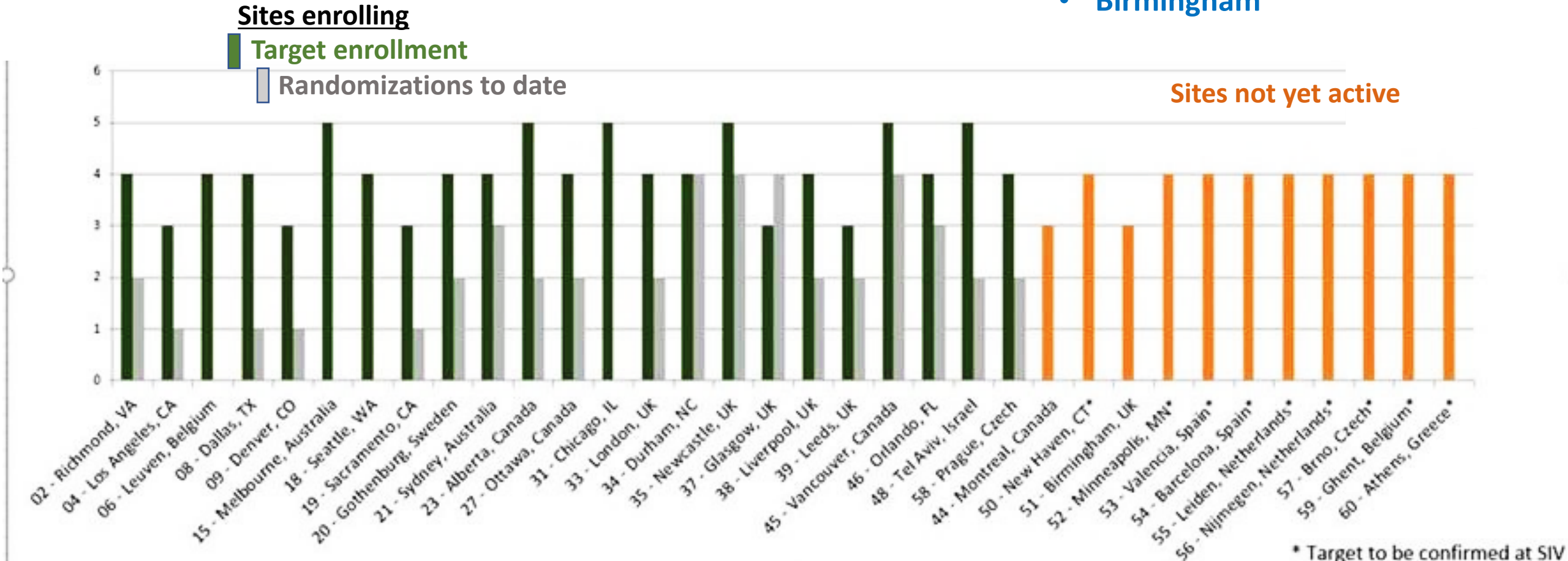
Full enrollment next 4 months

Countries enrolling:

- UK
- Canada
- Belgium
- Sweden
- Israel
- Spain
- Netherlands
- Czech Republic
- Greece
- Australia

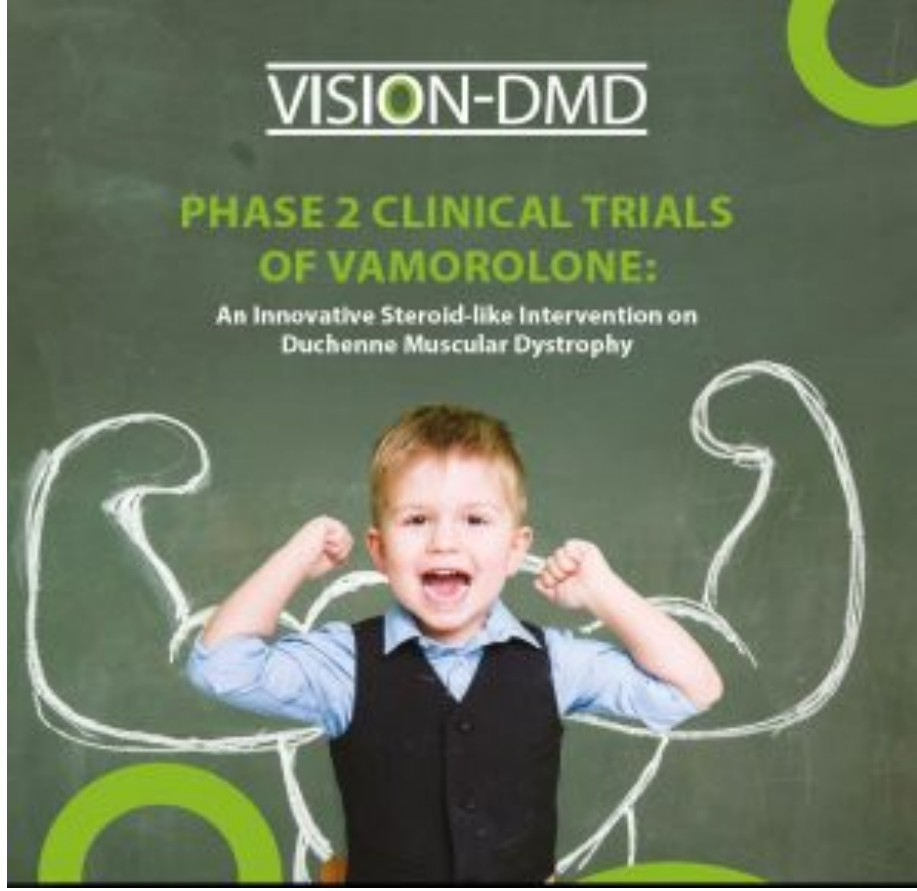
Sites enrolling in UK:

- **London**
- **Newcastle**
- **Glasgow**
- **Liverpool**
- **Leeds**
- **Birmingham**



Enrolling Phase 2b

- 120 boys, 4-<7 years old
- Never used steroids
- Daily dosing by mouth at home
- 24 weeks randomized: 50% vamorolone, 25% prednisone, 25% placebo
- 24 weeks: all participants on 1 of 2 doses of vamorolone (2 or 6mg/kg)
- Visits approximately monthly
- Expanded access after the trial is available
- ReveraGen covers most travel costs



www.clinicaltrials.gov NCT03439670

Contact:

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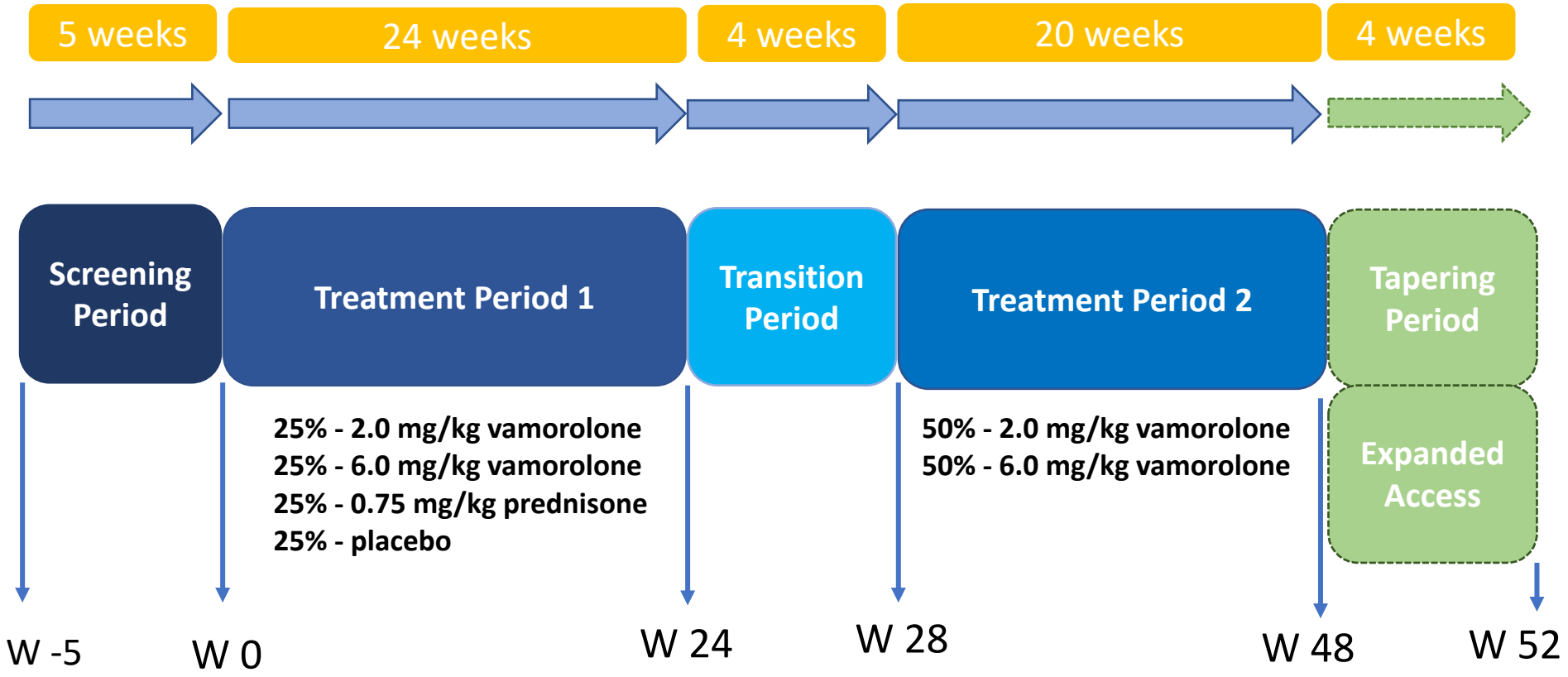
Vamorolone Pivotal Study Design VBP15-004 (Enrolling)



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

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US NATIONAL INSTITUTES OF HEALTH GRANT AWARDED TO REVERAGEN

ESTABLISHING A COST-EFFECTIVE RETURN OF RESULTS TO PARENTS OF BOYS IN VISION-DMD CLINICAL TRIALS

Administrative Supplement for Research on Bioethical Issues

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Problem:

- Patients/families participate in clinical trials at substantial commitment (time off school, work, travel, disruption)
- They typically do not know how their son did in the trial
- Lack of knowledge causes additional anxiety above/beyond disease
- Return of data typically requires extensive work at over-burdened academic trials sites

Possible solution?

- Recruitment of families through stake holder foundations
- Central IRB, consent, re-identification at ReveraGen; information firewall within ReveraGen

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Thanks DuchenneUK

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http://vision-dmd.info/