VISION-DMD Study

Top Line Results

PPMD Congress June 2021

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ReveraGen BioPharma

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Can the benefits of steroids be “uncoupled” from the side effects?

- Improves strength & mobility
- Prolongs ambulation
- Prolongs arm function
- Delays ventilator use
- Delays scoliosis

- Weight Gain
- Bone Fragility
- Growth stunting
- Cushingoid features
- Suppressed immunity
- Mood/behavior changes

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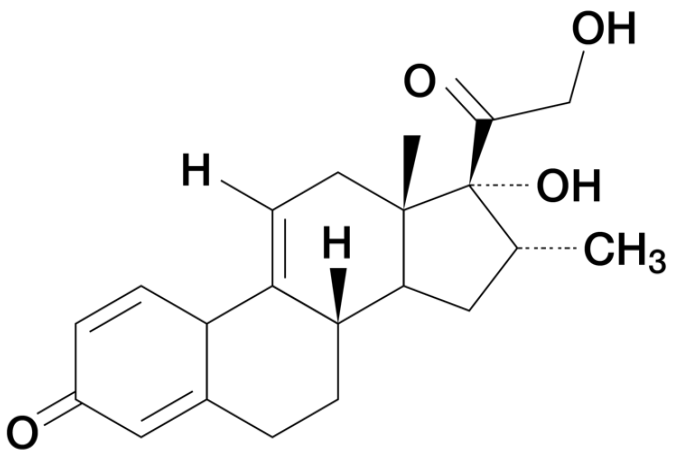
Vamorolone is a new class of corticosteroid, engineered to retain the benefits of steroids with fewer adverse events

Vamorolone Molecular Structure



Vamorolone is a first-in-class dissociative steroid

Like corticosteroids,
inhibits NF-κB activity

Retained efficacy due to potent anti-inflammatory action

Unlike corticosteroids,
- reduced activation of GREs
- mineralocorticoid antagonist (eplerenone-like)
- not a substrate for HSD enzymes

Potential for significant reduction of steroid-associated side effects

GREs, glucocorticoid-response elements; HSD, hydroxysteroid dehydrogenase; NF-κB=nuclear factor kappa B.
Heier CR, et al. *EMBO Mol Med*. 2013;5:1569-1585.

Phase 2a: long term study outcomes

46/48 patients with DMD enrolling in open label extension for up to 30 months with vamorolone

2 Weeks treatment (Conklin et al. 2018)

First dissociative steroid demonstrating anti-inflammatory action with decrease in steroid-associated safety biomarkers

6 Months treatment (Hoffman et al. 2019)

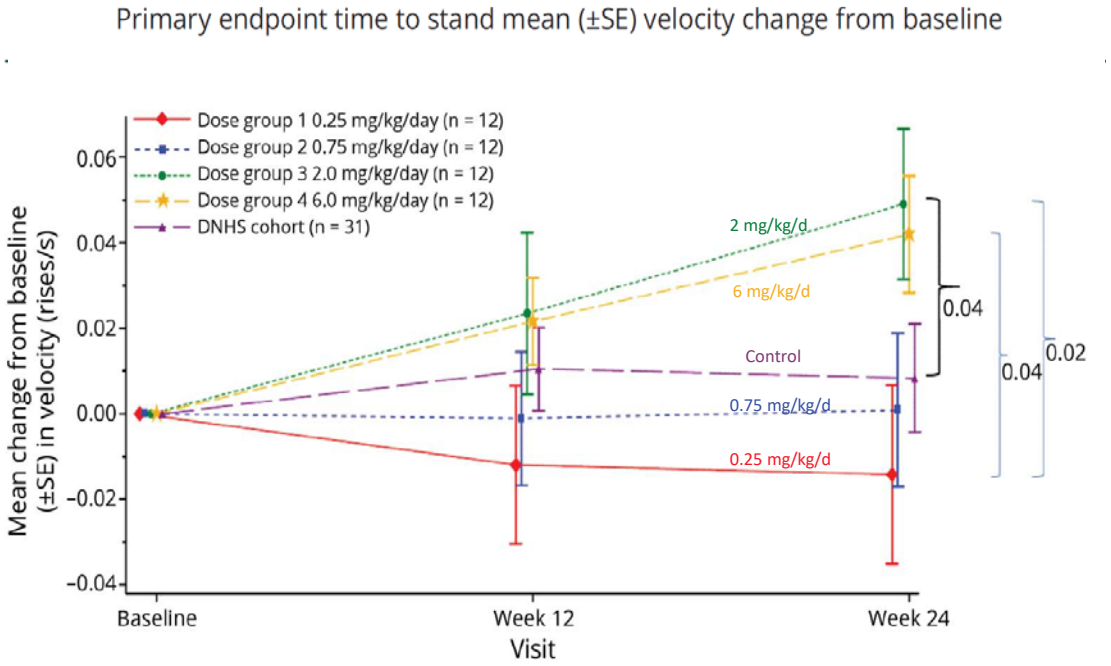
Dose related improvements in muscle function and compared to external control, treatment well tolerated

18 Months treatment (Smith et al. 2020)

Interim analysis of 24-month extension study showed improvement or stabilization of motor function compared to baseline, treatment well tolerated with fewer physician reported AEs typical of steroids

30 Months treatment (MDA conference March 18, 2021)

Long term treatment with vamorolone showed maintenance of treatment effect and disease modification over 30 months, treatment well tolerated with differentiated safety profile.



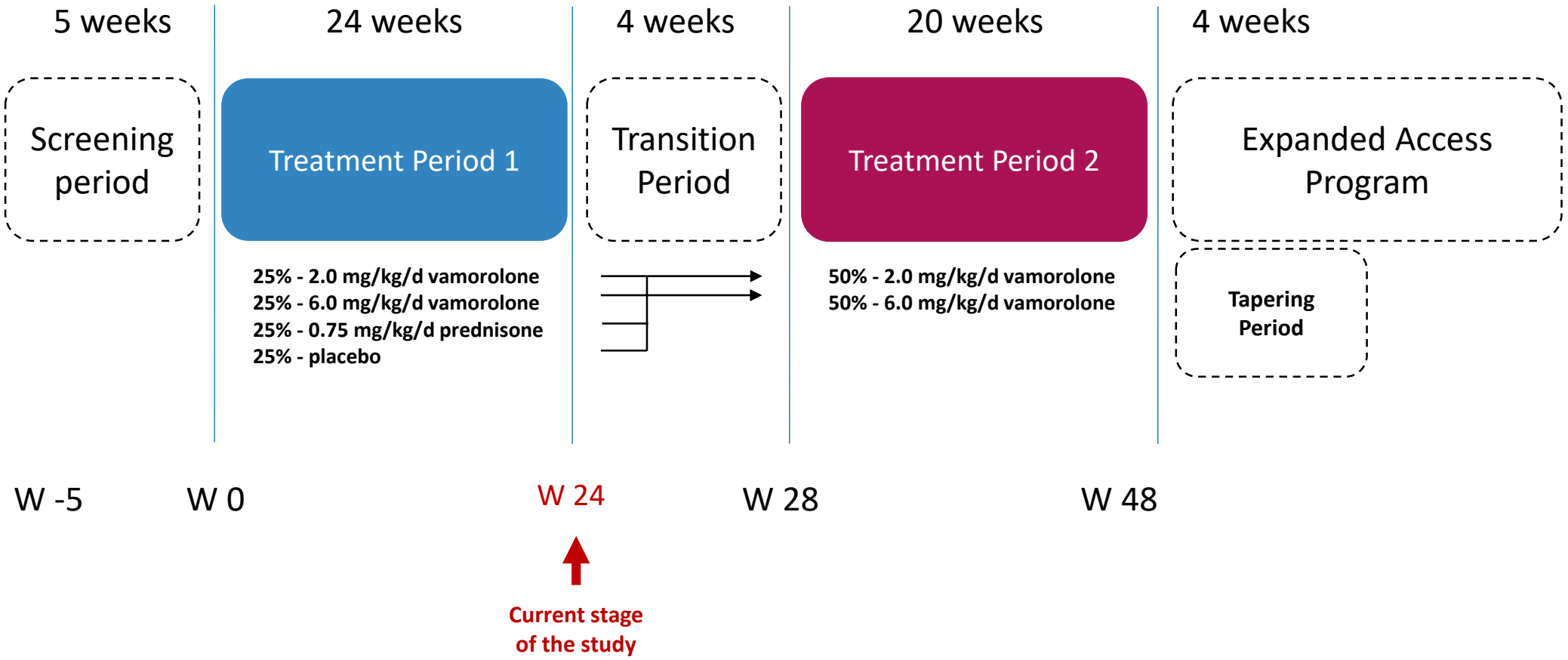
Brackets indicate mixed-model repeated-measures p values
- black for comparisons to CINRG Duchenne Natural History Study [DNHS]
- blue for within-trial dose group comparisons

Adapted from Hoffman et al 2019

Conklin et al. Ph. Res. (2018); Hoffman et al. Neurology. (2019) ; Smith et al. PLOS Medicine. (2020); Dang et al. MDA Abstr. #47 (2021)

VISION-DMD: investigated efficacy and safety of 2 doses of vamorolone

Randomized, double-blind, placebo controlled trial in 121 steroid-naive patients, aged 4 - 7 yrs



https://www.clinicaltrials.gov/ct2/show/NCT03439670?term=vamorolone&cond=Duchenne+Muscular+Dystrophy&draw=2&rank=4

VISION-DMD: Efficacy endpoints and pre-defined comparisons

Primary endpoint:

- Change baseline to wk 24 in Time to Stand (TTSTAND) velocity, vamorolone 6 mg/kg/d versus placebo

Secondary endpoints were tested in pre-defined hierarchical order (at Week 24 and tested):

- TTSTAND velocity, vamorolone 2 mg/kg/d versus placebo
- 6-minute walk test (6-MWT) distance, vamorolone 6 mg/kg/d versus placebo
- 6-minute walk test (6-MWT) distance, vamorolone 2 mg/kg/d versus placebo
- Time to Run/Walk 10 meters (TTRW) velocity, vamorolone 6 mg/kg/d versus placebo
- Time to Run/Walk 10 meters (TTRW) velocity, vamorolone 2 mg/kg/d versus placebo

Other exploratory efficacy endpoints

- Time to Climb 4 stairs (TTCLIMB), vamorolone 6 mg/kg/d versus placebo
- Time to Climb 4 stairs (TTCLIMB), vamorolone 2 mg/kg/d versus placebo
- North Star Ambulatory Assessment (NSAA), vamorolone 6 mg/kg/d versus placebo
- North Star Ambulatory Assessment (NSAA), vamorolone 2 mg/kg/d versus placebo

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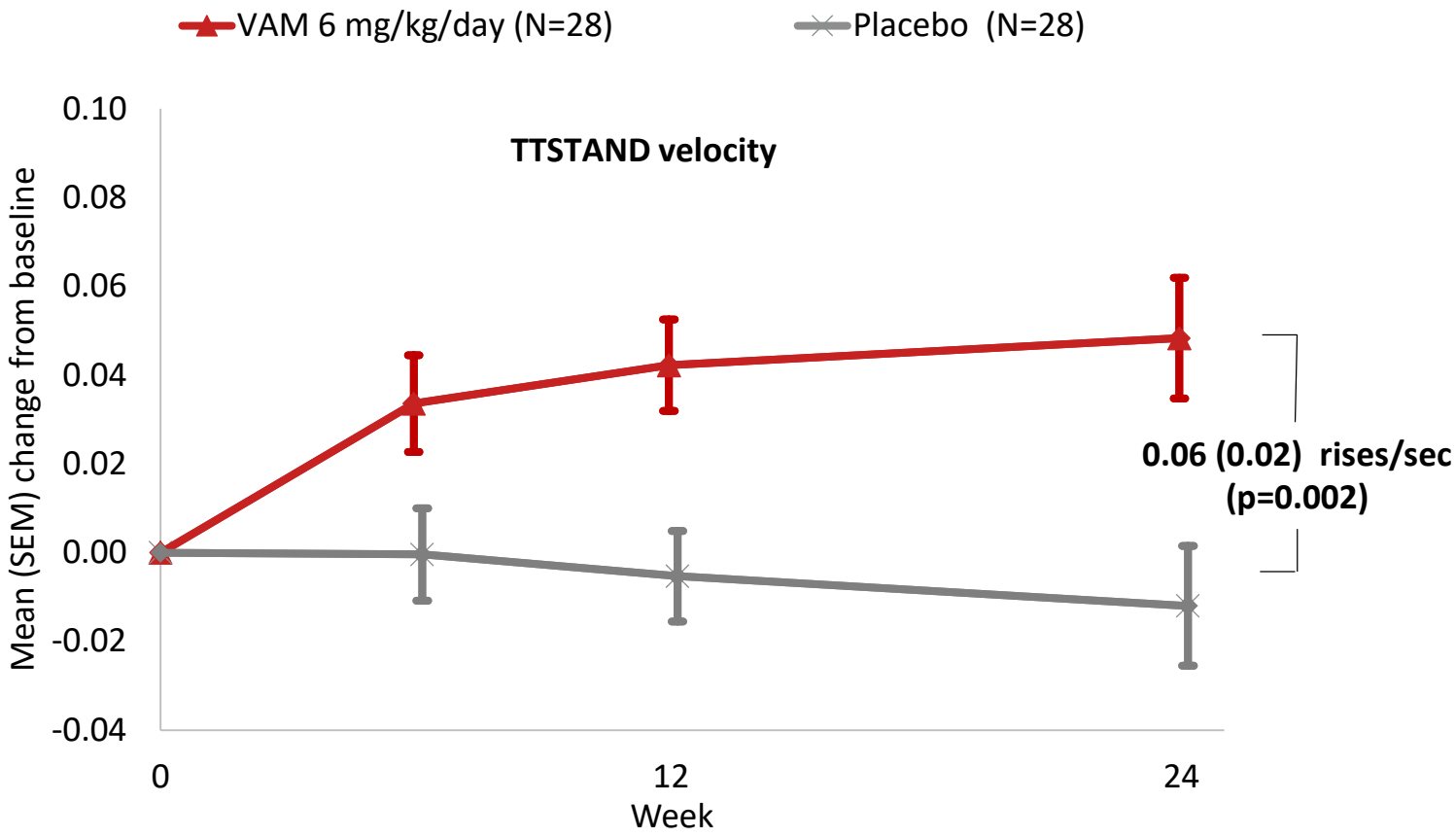
VISION-DMD: Demographics characteristics
(n=121 randomized)

	Placebo (N=29)	PDN 0.75 mg/kg/d (N=31)	VAM 2 mg /kg/d (N=30)	VAM 6 mg/kg/d (N=28)	Total[1] (N=118)
Age (years)	5.4 (0.8)	5.5 (0.9)	5.3 (0.9)	5.4 (0.9)	5.4 (0.9)
Height (cm)	109 (9)	111 (6)	108 (9)	107 (7)	109 (8)
Weight (kg)	20 (3)	21 (3)	19 (4)	19 (3)	20 (3)
BMI (kg/m^2)	16.3 (1.2)	16.8 (1.3)	16.2 (1.2)	16.6 (1.4)	16.5 (1.3)

Data shown as mean (SD) or % of patients
[1] Safety population

Primary Endpoint: Change in TTSTAND velocity (rises/sec)

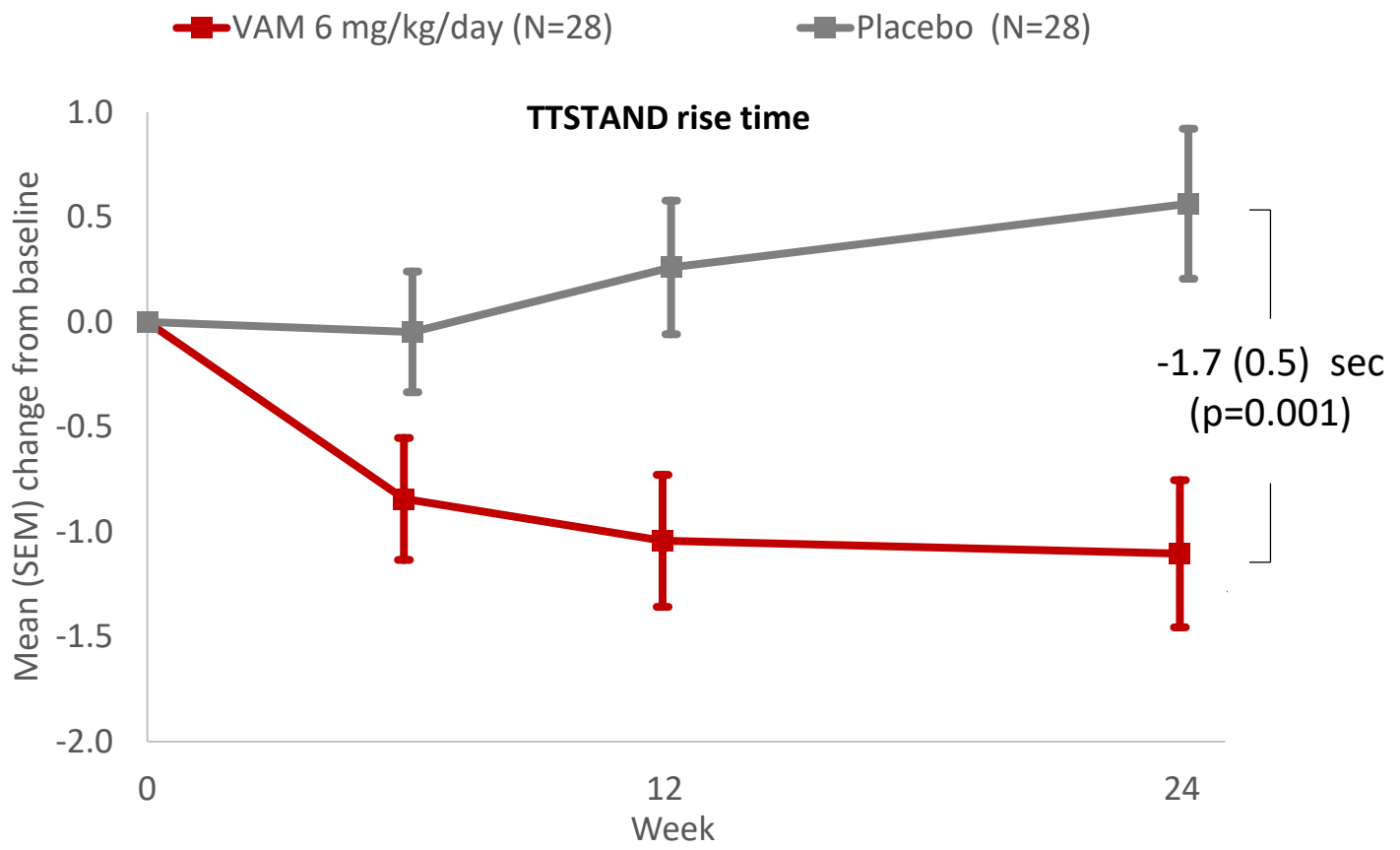
Mean change vamorolone 6 mg/kg/d vs placebo baseline to wk 24 (mITT Set, MMRM)



mITT set, patients who received study medication and had at least 1 post-baseline efficacy assessment.

TTSTAND improved on average from 5.1 sec to 3.4 sec

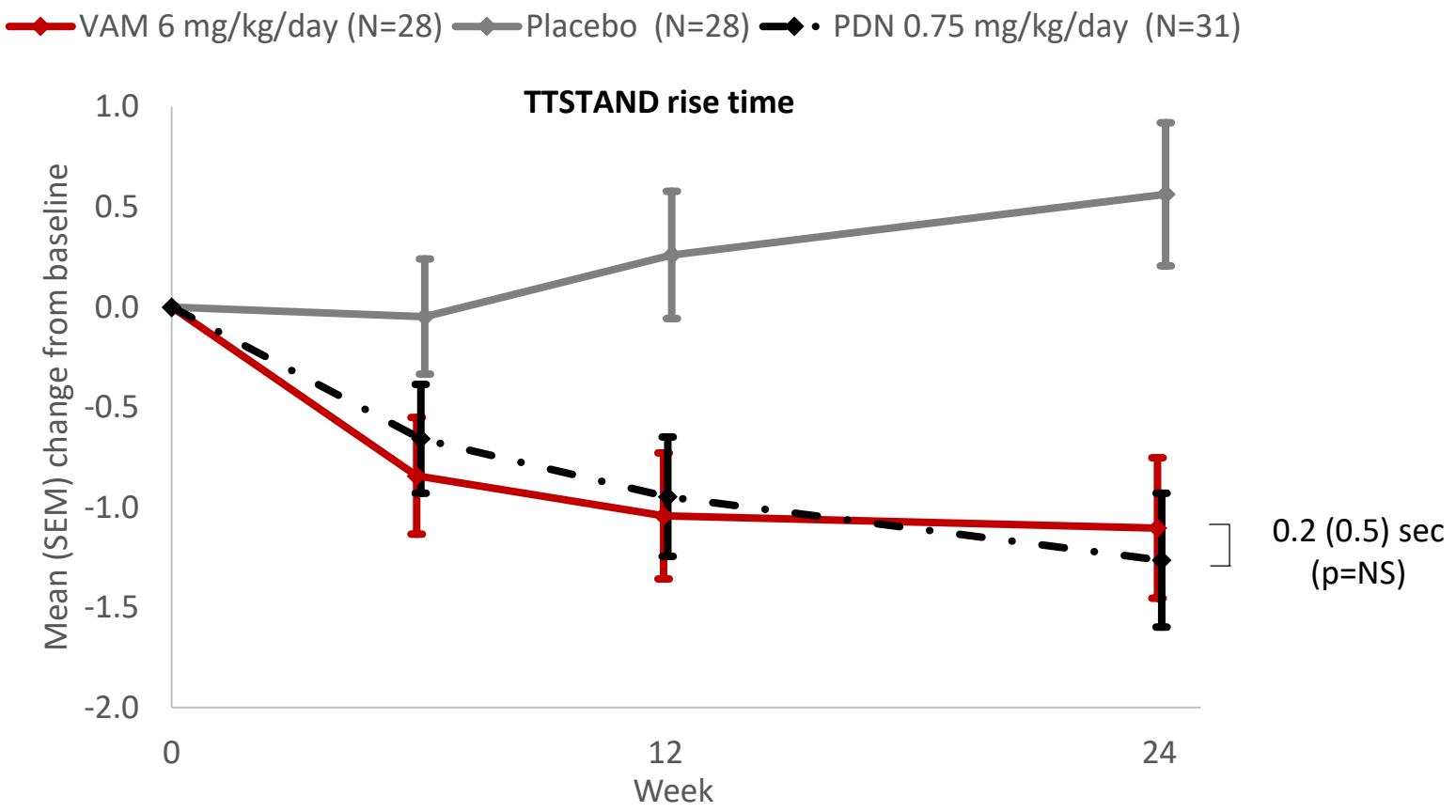
Mean change vamorolone 6 mg/kg/d vs placebo baseline to wk 24 (mITT Set, MMRM)



mITT set, patients who received study medication and had at least 1 post-baseline efficacy assessment.

No significant difference between vamorolone and prednisone was seen

Mean difference vamorolone 6 mg/kg/d vs prednisone 0.75 mg/kg/d at wk 24 (mITT Set, MMRM)



mITT set, patients who received study medication and had at least 1 post-baseline efficacy assessment.
mITT, modified intention-to-treat; MMRM, mixed model repeated measures; NS, non-significant; PDN, prednisone; TTSTAND, time to stand; VAM, vamorolone.

VISION-DMD: Summary of efficacy outcomes

Rank	Endpoint	Comparison	Difference	P-value
Primary	TTSTAND velocity	vam 6 mg/kg/d vs placebo	0.06 rises/s	0.002
Secondary	TTSTAND velocity	vam 2 mg/kg/d vs placebo	0.04 rises/s	0.017
	6MWT	vam 6 mg/kg/d vs placebo	42 m	0.003
	6MWT	vam 2 mg/kg/d vs placebo	37 m	0.009
	TTRW velocity	vam 6 mg/kg/d vs placebo	0.24 m/s	0.002
	TTRW velocity	vam 2 mg/kg/d vs placebo	0.13 m/s	0.103
Exploratory	TTCLIMB velocity	vam 6 mg/kg/d vs placebo	0.07 tasks/s	<0.001
	TTCLIMB velocity	vam 2 mg/kg/d vs placebo	0.06 tasks/s	0.006
	NSAA	vam 6 mg/kg/d vs placebo	3.4 points	<0.001
	NSAA	vam 2 mg/kg/d vs placebo	3.2 points	<0.001

Summary of efficacy:

- Vamorolone effective in improving outcomes **across a broad dose range from 2 mg/kg/d to 6 mg/kg/d**
- Thanks to patient families, expert clinical trial sites (11 countries), expert trial management (TRiNDS, Camden)

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Time to Stand (TTSTAND), 6 Minute Walk Test (6-MWT), Time to Run/Walk 10m (TTRW), Time to Climb 4 Stairs (TTCLIMB), North Star Ambulatory Assessment (NSAA)

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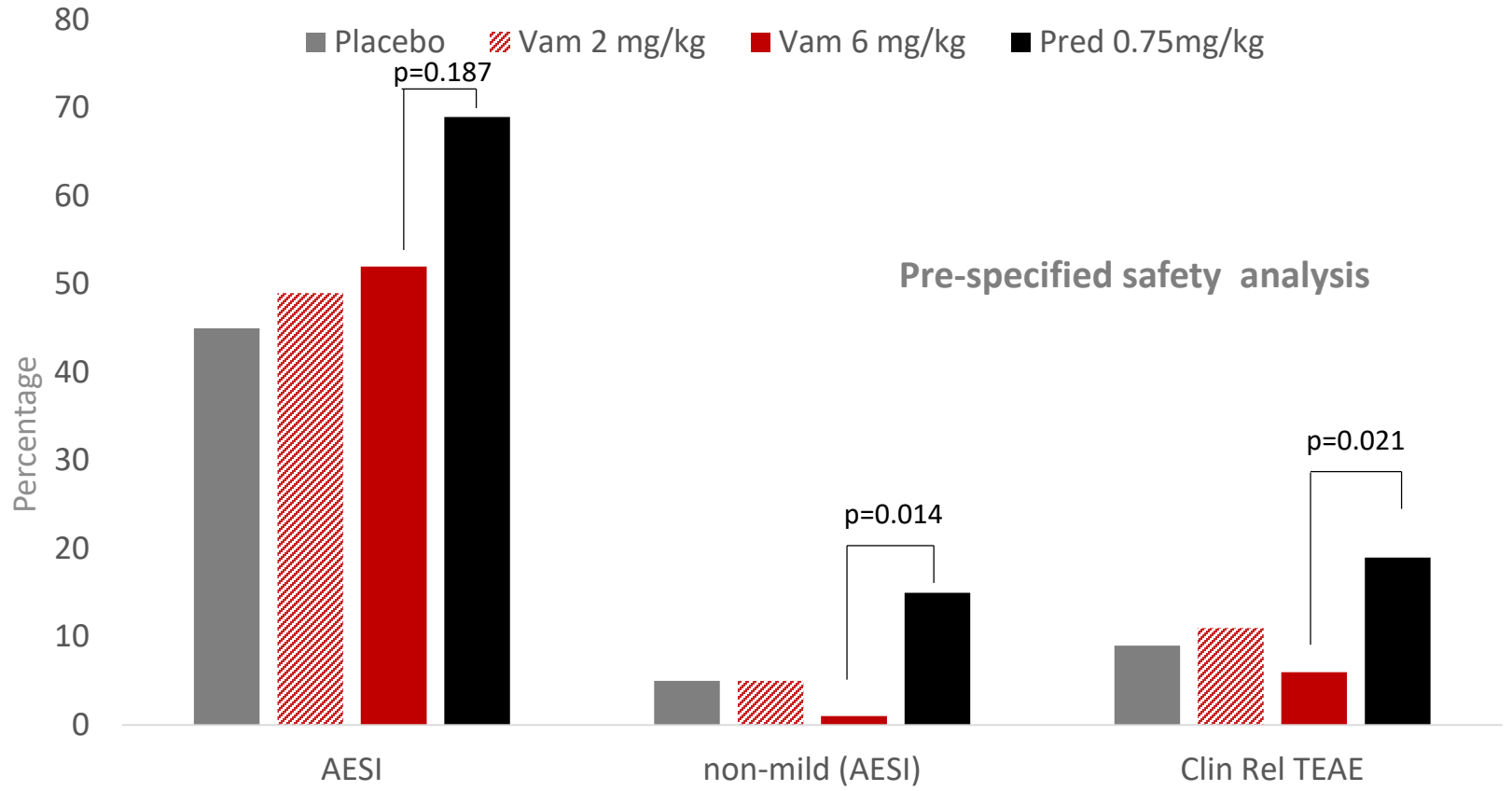
VISION-DMD: Safety Summary

Safety population

Event type	Placebo (N=29) N (%); Events	PDN 0.75 mg/kg/d (N=31) N (%); Events	VAM 2 mg/kg/d (N=30) N (%); Events	VAM 6 mg/kg/d (N=28) N (%); Events
Total TEAEs	23 (79.3) ; 77	26 (83.9) ; 121	25 (83.3) ; 97	25 (89.3) ; 91
Severe (or worse) TEAEs	-	1 (3.2) ; 1[1]	-	-
Serious TEAEs (other than deaths)	-	-	1 (3.3) ; 1[2]	-
Deaths	-	-	-	-
TEAEs leading to discontinuation [a]	-	1 (3.2) ; 1[3]	-	-

[a]Leading to permanent discontinuation of study treatment
[1]Severe TEAE: Gastroenteritis viral
[2]Serious TEAE: Aggression
[3]TEAE leading to discontinuation: Personality change

Fewer clinically relevant adverse events typically associated with corticosteroids seen with vamorolone 6 mg/kg/d compared to prednisone at 24 weeks



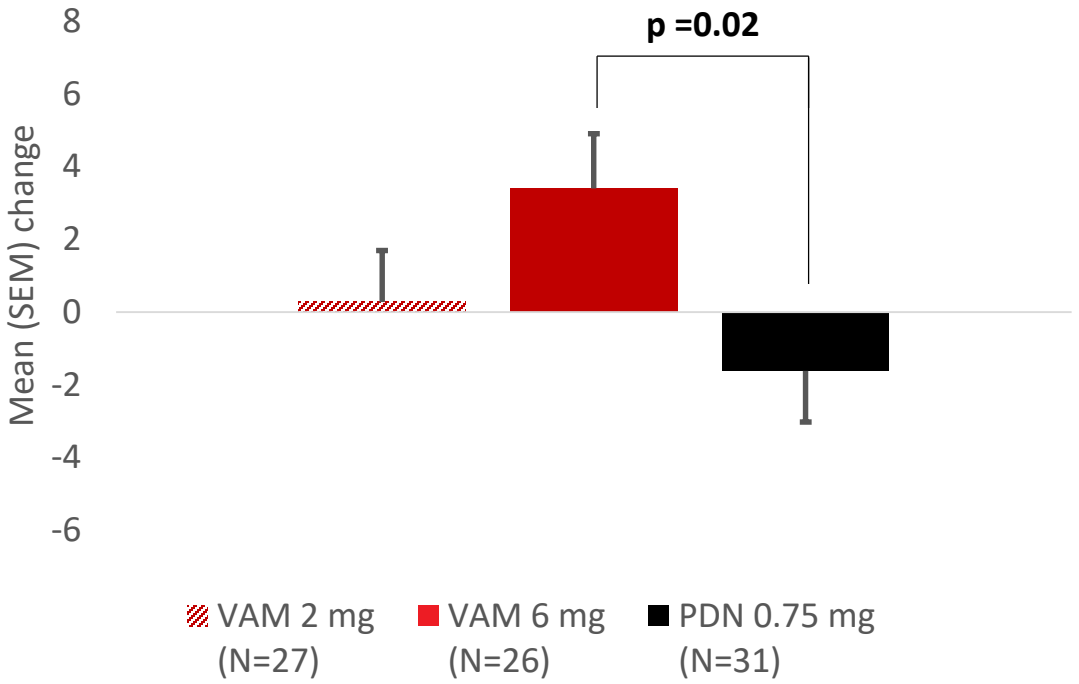
AESI, Adverse Events of Special Interest (typically associated with corticosteroids); clinically relevant TEAE, TEAEs defined as moderate, severe, serious and leading to treatment discontinuation; non-mild AESI, AESI graded as moderate or severe; Pred, prednisone; TEAE, treatment-emergent adverse events; Vam, vamorolone.

Vamorolone preserves growth trajectory compared to prednisone

Comparison from VISION-DMD and Long Term Extension studies (VBP15-LTE)

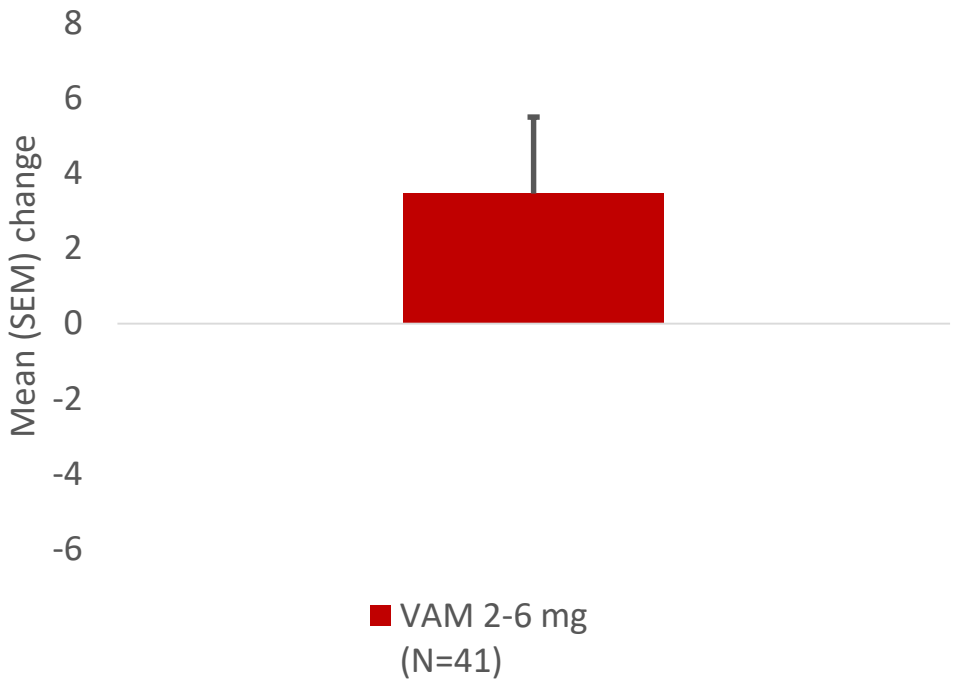
Growth trajectory in pivotal study

VBP015-004: change in height percentiles baseline to week 24



Growth trajectory in long term open label study

VBP015-LTE: change in height percentiles baseline to 2.5 years



VBP015-LTE is a LTE, open-label, multiple dose study to evaluate the long-term safety, tolerability, efficacy and PD of vamorolone over 24 months in participants from the VBP15-002 Phase IIa and VBP15-003 Phase IIa studies.
LTE, long-term extension; PD, pharmacodynamics; Pred, prednisone; SEM, standard error of mean; Vam, vamorolone.

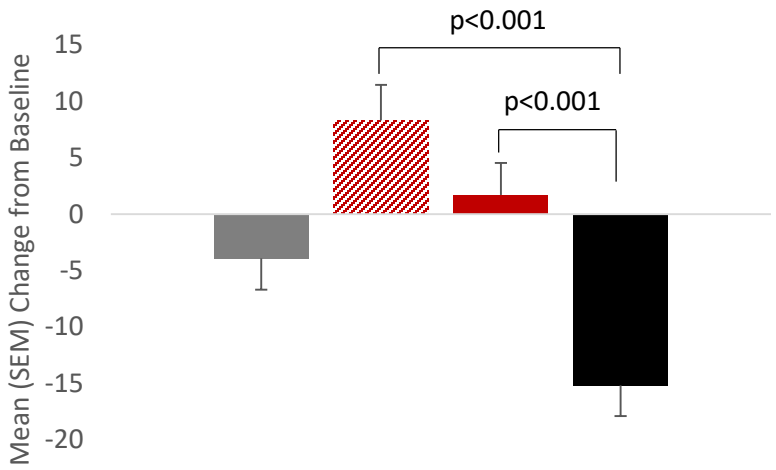
Vamorolone did not adversely impact biomarkers of bone health unlike prednisone

Comparison of changes from baseline to week 24 in bone biomarkers for vamorolone vs prednisone

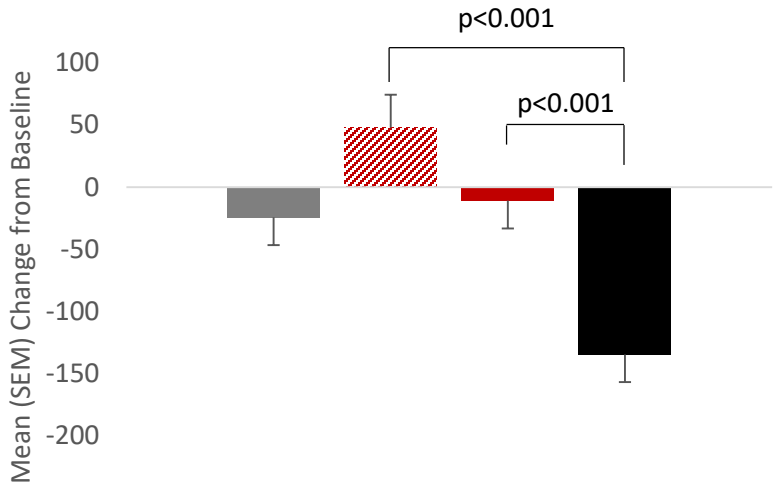
Biomarkers of bone formation

Biomarkers of bone remodelling

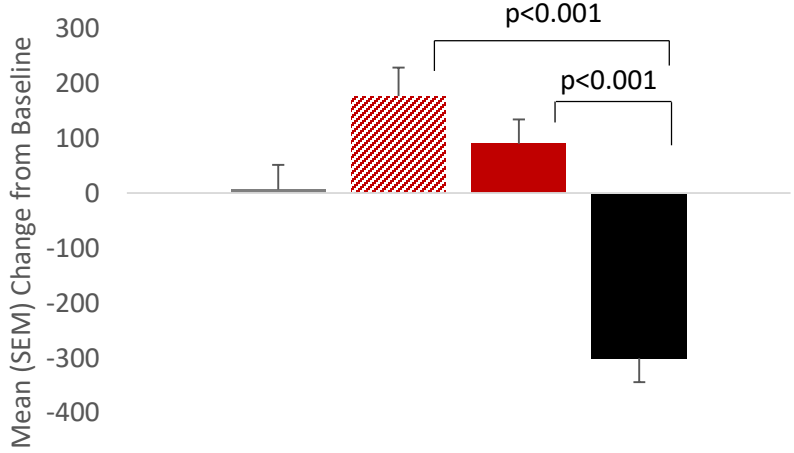
Osteocalcin (ng/ml)



P1NP (ng/ml)



CTX1 (pg/ml)



Placebo Vam 2 mg/kg Vam 6 mg/kg Pred 0.75mg/kg

Pred, prednisone; SEM, standard error of mean; Vam, vamorolone.
CTX, C-terminal telopeptide of type 1 collagen; P1NP, procollagen type 1 N-terminal propeptide

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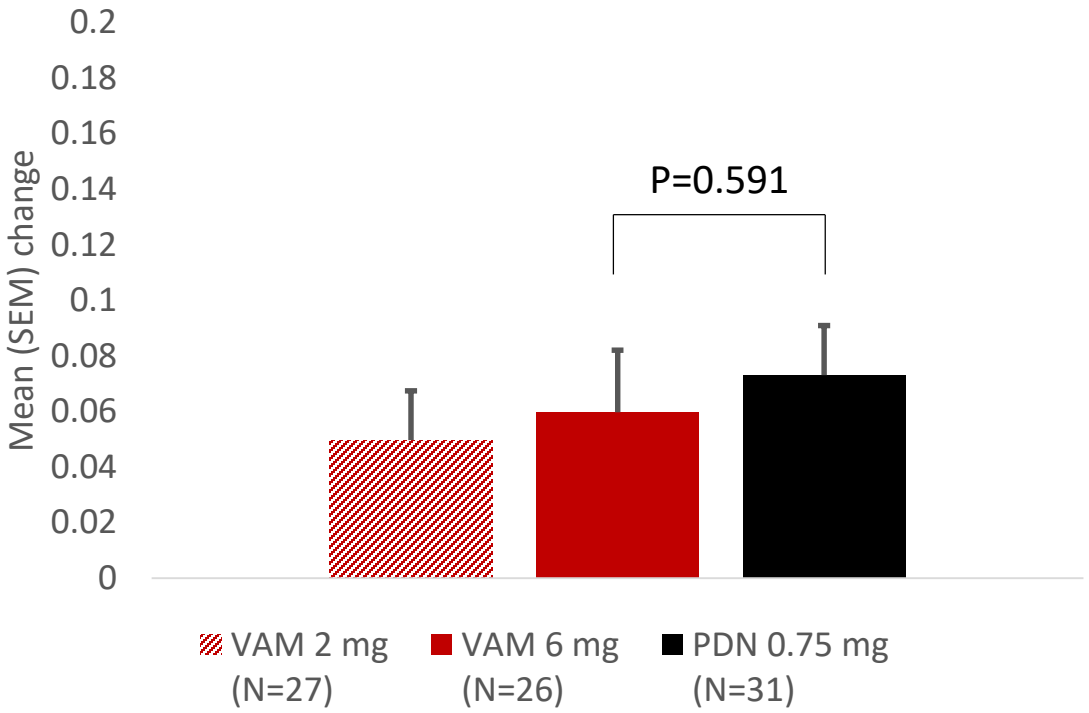
No difference in weight gain seen at 24 weeks between vamorolone and prednisone

Comparison of changes from baseline to week 24 in BMI z-score vamorolone vs prednisone



In the open label Long Term Extension study **(24 months)** weight gain was reported as an adverse event in

- 12 (26%) participants on vamorolone 6 mg/kg/d and were down titrated to 2mg/kg/d and continued in the study
- 2 (5%) participants on 2 mg/kg/d events who continued in the study

Pred, prednisone; SEM, standard error of mean; Vam, vamorolone

Summary

- Vamorolone is being investigated as a first-in-class dissociative steroid with lower incidence of corticosteroid-associated adverse effects
- VISION-DMD 24-week study showed statistically significant and clinically relevant improvements across 5 functional outcome measures across a broad dose range from 2 – 6 mg/kg/d
- Vamorolone did not adversely impact growth trajectory or biomarkers of bone health
- Treatment was well tolerated with fewer physician reported adverse events typically seen with corticosteroids at 24-weeks in a dose dependent manner
- Vamorolone is the first dissociative steroid with proven efficacy for 2 doses across a wide dose range allowing physicians to tailor treatment to the individual without loosing efficacy

Thank you to all the families who participated in vamorolone trials and contributed to the investigation of this potential therapy

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