Vision DMD: vamorolone drug development program for Duchenne muscular dystrophy

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Duchenne Muscular Dystrophy

- Caused by mutation in the dystrophin gene
- Incidence of 1: 5000 male births
- Onset: age 2-4 years
- Progressive muscle weakness and wasting
- Cardiac and respiratory involvement

- No cure available
- Corticosteroids can maintain muscle strength and function over a certain period of time, but associated with severe side effects
- Management of cardiac and respiratory complication

Characteristics of Vamorolone

- First-in-human dissociative steroid that has shown improved safety and efficacy in mouse models of Duchenne muscular dystrophy compared to corticosteroids.

- Preserves the anti-inflammatory actions of glucocorticoids
- Protects the muscle membrane
- Lacks transactivation sub-properties that may cause side effects of glucocorticoids, such as growth restriction and osteopenia

Phase I Study Results

- *Pharmacokinetic data* in single and multiple ascending doses up to 20 mg/kg/day for 14 days- study in healthy adult volunteers *shows* strong adherence to dose linearity and dose proportionality.
- No drug accumulation was observed, consistent with the short half-life.
- No adverse events precluding further escalations in dosing observed.

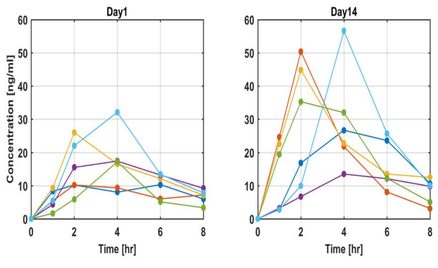
- Safety pharmacodynamics biomarker studies showed an improved safety window for adrenal suppression (100-fold increase in therapeutic window),
- No evidence of insulin resistance or immune suppression, compared to prednisone studies reported in the literature

Phase IIa Study

- 12 sites: USA (6), Canada(1), UK (1), Australia (2), Israel (1), Sweden (1)
- Multiple ascending dose-finding and safety study
- Inclusion Criteria: 4 - <7 years, genetically confirmed, steroid naive

- 14-day treatment trial followed by 6 month extension
- Opened recruitment in all country sides, 24 patients already enrolled
- DSMB report for the first cohort shows no alterations of pharmacodynamic biomarkers and no severe adverse events

Dose Level Group-	No. Subjects/ Group	Vamorolone Dose
1	12	0.25 mg/Kg
2	12	0.75 mg/Kg
3	12	2.0 mg/Kg
4	12	6.0 mg/Kg



- Pharmakokinetik run on initial 6 boys in 0.25 mg/kg/day
- PK in DMD children similar to fasted adults
- Increased bioavailability with milk likely offset by faster metabolism in children

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Primary Objective

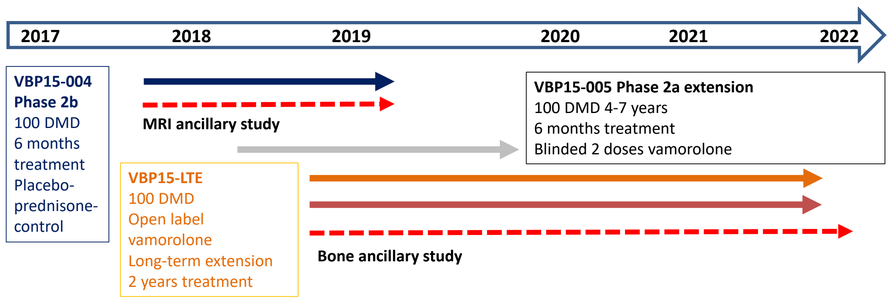
To evaluate the safety and tolerability of multiple ascending doses of vamorolone in ambulant boys ages 4-< 7 years with DMD.

Secondary Objectives

1. To investigate the single-dose and multiple-dose PK of vamorolone at multiple dose levels
2. To investigate the effects of single and multiple oral doses of vamorolone on serum PD

DMD Clinical Development Plan- Phase IIb Study

- 30 sites: EU (18), USA (6), Canada (3), Australia (2), Israel (1)
- Randomized, placebo-controlled study including steroid and placebo arms
- Inclusion Criteria: 4 - <7 years, genetically confirmed, steroid naive
- 24-weeks treatment followed by 6 month extension
- Exploratory Muscle MRI protocol to assess feasibility in a large study
- Expected recruitment start: August 2017



Planned Cohort	No. Subjects/cohort	Dose
1	25	2.0 mg/Kg
2	25	6.0 mg/Kg
3	25	Steroid
4	25	Placebo

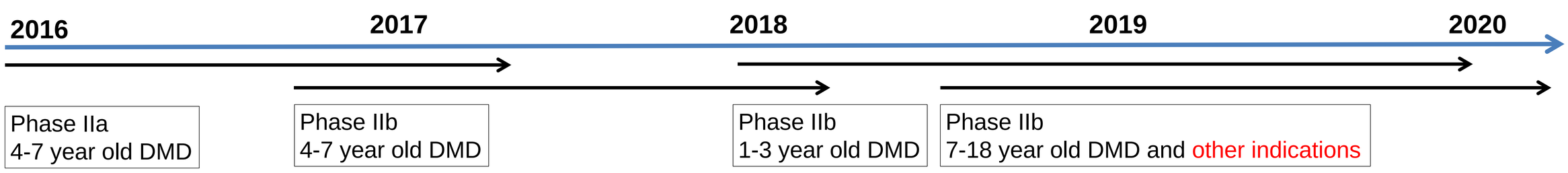
Primary Objectives

1. To evaluate the efficacy of multiple ascending doses of vamorolone vs. placebo in ambulant boys ages 4- <7 years with DMD, measured by the time to Stand (TTSTAND)
2. To evaluate the safety of multiple ascending doses of vamorolone vs. prednisone, as measured by body mass index (BMI) z-score

Secondary Objectives

1. To evaluate the safety and tolerability of vamorolone administered orally at daily doses over 24 week treatment
2. To compare the efficacy vs. placebo
3. To compare the effects of vamorolone vs. prednisone on serum pharmacodynamics (PD) biomarkers of safety

Projected Vamorolone Drug Development Timeline



References: Heier CR, et al. **VBP15**, a novel anti-inflammatory and membrane-stabilizer, improves muscular dystrophy without side effects. EMBO Mol Med. 2013 Oct;5(10):1569-85.; Reeves EK, et al. **VBP15**: preclinical characterization of a novel anti-inflammatory delta 9,11 steroid. Bioorg Med Chem. 2013 Apr 15;21(8):2241-9.

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