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TIP1. TRIALS IN PROGRESS: CLASSICAL HEMATOLOGY

Velora pioneer, Phase 1/2 study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of HMB-002 for prophylaxis in von Willebrand disease: A trial in progress

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Abstract Background: Von Willebrand Disease (VWD), the most common inherited bleeding disorder, results from quantitative or qualitative defects in von Willebrand factor (VWF). This deficiency impairs both platelet adhesion and factor VIII (FVIII) stabilization, resulting in recurrent and often unpredictable mucocutaneous bleeding events that significantly diminish quality of life. These bleeding manifestations can be life-threatening and profoundly impact patients' physical, emotional, and social well-being, with the burden frequently compounded by chronic complications including iron deficiency anemia and heavy menstrual bleeding. Current management strategies remain suboptimal. Desmopressin provides only transient benefit and is limited by tachyphylaxis, while plasma-derived or recombinant VWF/FVIII concentrates require frequent, burdensome intravenous infusions. These challenges underscore a significant unmet need for convenient prophylactic therapy. HMB-002, an investigational monovalent antibody, binds to and stabilizes endogenous VWF, elevating circulating VWF and FVIII levels. The goal of HMB-002 is to offer long-acting subcutaneous prophylaxis, shifting the treatment paradigm from reactive to preventative in VWD.
Methods and Trial Design: VELORA Pioneer (NCT06754852) is an ongoing Phase 1/2, multi-center, open-label study evaluating safety, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary efficacy of HMB-002 in adults with VWD. The study has two parts:

- Part A (ongoing): Single ascending dose (SAD) cohorts evaluating multiple dose levels to assess safety, tolerability, PK, and PD.

- Part B (upcoming): Multiple dose (MD) cohorts evaluating safety and tolerability of repeat dosing. Participants may transition directly from the observational VELORA Discover study (NCT06610201).

Study is ongoing and actively enrolling participants in the US, UK, and Australia.
Current Eligibility Criteria: Adults ≥18 and ≤65 years for VELORA Pioneer, with a confirmed Type 1 VWD diagnosis. Inclusion requires VWF activity ≤40 IU/dL and FVIII:C ≤70 IU/dL at screening. Part B additionally requires an annualized treated bleed rate of ≥3 and completion of the VELORA Discover observational study. Additional VWD subtypes may be included in later cohorts. Documented residual VWF levels are required, and exclusion criteria include concurrent participation in interventional trials or medical conditions confounding study results. Part B requires participants to have completed the VELORA Discover observational study.

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