METHODS AND COMPOSITIONS FOR TREATING HEMOPHILIA AND LOW BONE MINERAL DENSITY

RELATED APPLICATIONS

[0001] This application claims the benefit of priority to U.S. Provisional Application No. 62/863,831, filed June 19, 2019, and U.S. Provisional Application No. 62/968,785, filed January 31, 2020, both of which are incorporated herein by reference in their entireties.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on June 16, 2020, is named 706564_SA9-503PC_ST25.txt and is 46,080 bytes in size.

BACKGROUND OF THE DISCLOSURE

[0003] Hemophilia is a group of bleeding disorders caused by defects in the genes encoding coagulation factors and affects 1-2 in 10,000 male births. Graw *et al.,* Nat. Rev. Genet. 6(6): 488-501 (2005). Hemophilia A is characterized by the absence of functional endogenous coagulation factor VIII (FVIII). Patients with severe hemophilia A suffer not only from poorly-controlled traumatic bleeds but also from spontaneous bleeding into the joints. The current standard of care for treatment of hemophilia is intravenous factor replacement therapy with the aim of preventing serious life- and limb-threatening bleeding including recurrent joint hemorrhage (hemarthrosis) which could lead to hypertrophic synovitis and cartilage degradation (hemophilic arthropathy). Manco-Johnson et al, NEJM 357(6):535-4 (2007). Over decades, optimal prophylaxis reduces but does not eliminate joint bleeding. Manco-Johnson at al, Blood 129(17):2368-2374 (2017).

[0004] People with hemophilia are at higher risk for reduced bone mineral density (BMD) and osteoporosis compared to the general population. Gerstner et al, Haemophilia, 15(2):559-65 (2009). According to one study, 27% of hemophiliacs have osteoporosis and 43% have low bone density. *Id.* Growing global observations of BMD indicate it is often lower in hemophilia patients than control cases or lower than expected in general populations based on age. Despite this association, the mechanism of reduced BMD in hemophilia patients is currently unknown.