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(54) Title: DISINTEGRIN VARIANTS AND PHARMACEUTICAL USES THEREOF

(57) Abstract: Disintegrin variants and pharmaceutical uses thereof are disclosed. The disintegrin variant includes an isolated polypeptide that has integrin avß3 receptor-antagonist activity and substantially reduced integrin aIIbß3 and/or a5ß1 receptor-blocking activity as compared to a wild-type disintegrin. The variant is encoded by a modified disintegrin nucleotide sequence that encodes a modified amino acid sequence, resulting in a polypeptide having substantially reduced affinity to integrin aIIbß3 and/or a5ß1 as compared to a wild-type disintegrin. The variant is useful for treatment and/or prevention of avß3 integrin-associated diseases in a mammal, which include osteoporosis, bone tumor or cancer growth, angiogenesis-related tumor growth and metastasis, tumor metastasis in bone, malignancy-induced hypercalcemia, angiogenesis-related eye diseases, Paget's disease, rheumatic arthritis, and osteoarthritis. The angiogenesis-related eye diseases include age-related macular degeneration, diabetic retinopathy, corneal neovascularizing diseases, ischaemia-induced neovascularizing retinopathy, high myopia, and retinopathy of prematurity.

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