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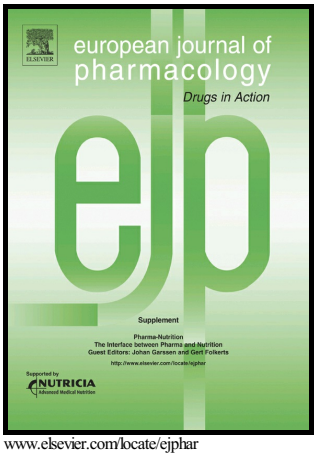

www.elsevier.com/locate/ejphar

PII: S0014-2999(18)30106-7
DOI: https://doi.org/10.1016/j.ejphar.2018.02.028
Reference: EJP71681

To appear in: *European Journal of Pharmacology*

Received date: 9 November 2017
Revised date: 15 February 2018
Accepted date: 19 February 2018

Cite this article as: Sharmistha Bhattacharyya, Subhashis Pal and Naibedya Chattopadhyay, Targeted inhibition of sclerostin for post-menopausal osteoporosis therapy: a critical assessment of the mechanism of action, *European Journal of Pharmacology,* https://doi.org/10.1016/j.ejphar.2018.02.028

Targeted inhibition of sclerostin for post-menopausal osteoporosis therapy: a critical assessment of the mechanism of action

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Abstract

Promising news in the treatment of osteoporosis is that sequestering sclerostin from circulation with antibodies stimulates robust bone formation. Pre-clinical studies on rodents and monkeys have confirmed that treatment with anti-sclerostin monoclonal antibody (Scl-Ab) increases bone mass improves bone strength and enhances fracture repair. Clinical trials show that bone gain (anabolic effect) is transient and are primarily at central (spine and hips) than peripheral (wrist) sites. Interestingly Scl-Ab also inhibited bone resorption. Thus Scl-Ab is being regarded as the pharmacologic agent with dual properties - stimulating bone formation and decreasing bone resorption. Sclerostin neutralization transiently increases bone formation markers in post-menopausal women and like parathyroid hormone (PTH) activates osteoblasts and lining cells resulting in bone anabolic effect. However, unlike PTH, sclerostin antibody also decreases bone resorption (anti-catabolic). Although, the U.S. Food and Drug Administration have accepted the