Osteoporosis has been transformed from something that was previously considered an inevitable consequence of aging - grandma getting increasingly kyphotic with age, then falling and breaking a hip - to its recognition as a disease that can be diagnosed, prevented, and now on the verge of being reversed. Significant scientific advances since 1970 include changing the paradigms for understanding how bone functions, particularly the identification of Cbfa1/runx2 as the "master regulator" of skeletogenesis. Among the landmarks that are used for targeting therapies are the mapping out of hormone effects on bone cells, the RANKL-RANK-OPG regulation of osteoblast and osteoclast communication, and the anabolic effects of Wnt signaling on the adult skeleton: each of these discoveries has been translated into novel therapeutic approaches for osteoporosis, with additional compounds in the pipeline.