FOUR-YEAR RESULTS OF A PHASE 2 STUDY OF THE CATHEPSIN K INHIBITOR ODANACATIB IN POSTMENOPAUSAL WOMEN WITH LOW BONE MINERAL DENSITY

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Aim. Cathepsin K (CatK) is the primary collagenase in osteoclasts. In a 2-year phase 2 study and its 1-year extension, the selective cathepsin K inhibitor odanacatib (ODN) reduced bone resorption markers and progressively increased bone mineral density (BMD). The study was extended for 2 additional years to further assess ODN efficacy and long-term safety.

Methods. Postmenopausal women with BMD T-scores between -2.0 and -3.5 at the lumbar spine, femoral neck, trochanter or total hip received placebo or ODN at 3, 10, 25 or 50 mg weekly during the 2-year study. In Year 3, participants were re-randomized to ODN 50 mg weekly or placebo. In Years 4/5, women who received placebo or 3 mg ODN in Years 1/2 and placebo in Year 3 were switched to 50 mg ODN for Years 4/5; all others

continued with their Year 3 regimen. 141 women entered the extension, and 133 completed 4 years. Endpoints were BMD at the lumbar spine (primary), total hip and hip subregions, and 1/3 radius; levels of biochemical bone turnover markers; and assessments of safety.

Results. During year 4, 100 women received 50 mg ODN and 41 received placebo. Continuous treatment with 50 mg ODN for 4 years induced significant BMD increases from baseline at the spine (10.7%), total hip (8.3%), femoral neck (8.9%), and trochanter (10.3%) and maintained BMD (-0.1%) at the 1/3 radius; BMD changes from Year 3 were 2.8% (spine), 2.5% (total hip), 3.9% (femoral neck), and 2.9% (trochanter). Serum CTX remained low at Year 4 (-41%), whereas BSAP was relatively unchanged (-2%) from baseline. Women who received active treatment for 2 years and switched to placebo for 2 years experienced bone loss, with BMD near baseline for most sites and decreased by 4.5% at the 1/3 radius at the end of Year 4. Levels of bone turnover markers in women who discontinued active treatment after 2 years rose in the first month off-treatment, but all levels returned to baseline by the end of Year 4. ODN was generally well tolerated.

Conclusions. 4 years of ODN treatment increased lumbar spine and hip BMD and was generally well-tolerated in postmenopausal women with low bone mass. Bone formation markers remained relatively unaffected. Discontinuation of ODN after 2 years of treatment was promptly followed by resolution of effects on bone turnover and density such that BMD and bone biomarker levels at Year 4 were at or near baseline.

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WYNIKI CZTEROLETNIEGO BADANIA 2 FAZY ODANAKATIBU, INHIBITORA KATEPSYNY, U KOBIET POMENOPAUZALNYCH Z NISKIM BMD

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