



NEWS RELEASE

Merck Announces Data from Pivotal Phase 3 Fracture Outcomes Study for Odanacatib, an Investigational Oral, Once-Weekly Treatment for Osteoporosis

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Merck now expects to submit the New Drug Application for odanacatib with the U.S. Food and Drug Administration (FDA) in 2015

Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced data from the pivotal Phase 3 fracture outcomes study for odanacatib in postmenopausal women with osteoporosis. Odanacatib is Merck's investigational once-weekly cathepsin K inhibitor. In the Long-Term Odanacatib Fracture Trial (LOFT), odanacatib met its primary endpoints and significantly reduced the risk of osteoporotic hip, spine and non-vertebral fractures compared with placebo. The results from this trial were presented today at the American Society for Bone and Mineral Research (ASBMR) Annual Meeting in Houston, Texas.

The rates of adverse events overall in LOFT were generally balanced between patients taking odanacatib and placebo. Adjudicated events of morphea-like skin lesions and atypical femoral fractures occurred more often in the odanacatib group than in the placebo group. Adjudicated major adverse cardiovascular events were generally balanced overall between the treatment groups. There were numerically more adjudicated stroke events with odanacatib than with placebo.

"Despite the important and serious consequences of fractures related to osteoporosis and our ability to identify patients who would benefit from therapy, many patients with osteoporosis are not being treated. There is a need for additional treatment options. The effects of odanacatib on fracture risk from the LOFT study are very encouraging," said Michael McClung, M.D., LOFT leader and founding director of the Oregon Osteoporosis Center,

Portland, Oregon.

In the study, odanacatib significantly reduced osteoporotic fracture risk

In LOFT, odanacatib significantly reduced the risk of three types of osteoporotic fractures compared to placebo in the primary efficacy analysis, and also reduced the risk of the secondary endpoint of clinical vertebral fractures. Specifically, compared to patients receiving placebo, patients who received odanacatib had a:

- 54% relative risk reduction of new and worsening morphometric (radiographically-assessed) vertebral fractures ($p < 0.001$),
- 47% relative risk reduction of clinical hip fractures ($p < 0.001$),
- 23% relative risk reduction of clinical non-vertebral fractures ($p < 0.001$), and
- 72% relative risk reduction of clinical vertebral fractures ($p < 0.001$).

In addition, treatment with odanacatib led to progressive increases over five years in bone mineral density (BMD) at the lumbar spine and total hip. Compared to placebo, the change in BMD from baseline at five years with odanacatib for lumbar spine was 11.2% ($p < 0.001$) and for total hip was 9.5% ($p < 0.001$).

Safety and tolerability data from LOFT

Prior to the start of the study, certain adverse events of interest were identified for adjudication: morphea-like skin lesions, systemic sclerosis, serious respiratory infections, osteonecrosis of the jaw, atypical femoral shaft fractures, delayed fracture unions, atrial fibrillation and major adverse cardiovascular events (MACE). Adjudicated morphea-like skin lesions occurred more frequently on odanacatib: in 12 patients in the odanacatib group (0.1% incidence) and 3 patients in the placebo group ($< 0.1\%$ incidence). These skin lesions resolved or improved after discontinuation of the study drug. Adjudicated atypical femoral shaft fractures were reported for 5 patients in the odanacatib group (incidence of 0.1%) and not reported in patients in the placebo group. No meaningful differences were observed in adjudicated events of systemic sclerosis, serious respiratory infections or delayed fractured unions between groups. There were no adjudicated cases of osteonecrosis of the jaw.

Adjudicated atrial fibrillation was reported in 92 patients in the odanacatib group (incidence of 1.1%) and 80 patients in the placebo group (incidence of 1.0%). In the MACE analysis, events were reported for 215 patients in the odanacatib group and 194 patients in the placebo group (hazard ratio 1.12 (95% confidence interval (CI) 0.93, 1.36)). There were 271 deaths reported in the odanacatib group and 242 deaths in the placebo group (hazard ratio 1.13 (95% CI 0.95, 1.35)); this numeric difference does not appear to be related to a particular reported cause or causes of death. There was a numeric imbalance in adjudicated strokes with more events occurring in the odanacatib group. Based on the adjudication committee assessment, 109 patients in the odanacatib group experienced stroke

(incidence 1.4%) and 86 patients (incidence 1.1%) in the placebo group (hazard ratio 1.28 (95% CI 0.97, 1.70)). Investigator-reported cerebrovascular events occurred in 305 patients in the odanacatib group (incidence 3.8%) and 290 patients taking placebo (incidence 3.6%) (hazard ratio 1.06 (95% CI 0.91, 1.25)).

Merck continues to collect data from the blinded extension study and is planning additional analyses of data from the trial, including an independent re-adjudication of major adverse cardiovascular events, in support of regulatory submissions.

“Merck believes the currently available data support a favorable benefit/risk profile for odanacatib,” said Dr. Keith Kaufman, vice president, Clinical Research, Diabetes and Endocrinology, Merck. “We want to thank our investigators who conducted the study and the thousands of patients who participated in this study, which is yielding critical insights into the potential of odanacatib in the treatment of postmenopausal osteoporosis.”

Largest outcomes study in postmenopausal women with osteoporosis

LOFT is a randomized, double-blind, placebo-controlled, event-driven trial, including a pre-planned, blinded placebo-controlled extension study. The trial enrolled 16,713 women, 65 years of age or older, diagnosed with osteoporosis, who have been postmenopausal for five years or more. Patients were randomized to receive odanacatib 50 mg/week (n=8,357) or placebo (n=8,356). All patients received vitamin D (5600 IU/week) and calcium up to 1200 mg/day, if required. Safety and efficacy analyses were conducted for 16,071 patients randomized at 387 centers in 40 countries, with patients enrolled across the Americas, Europe and the Asia-Pacific region.

About odanacatib

In osteoporosis, bone loss occurs because of an imbalance in bone remodeling (the rate of bone resorption exceeds that of bone formation). Osteoclasts, cells that resorb bone, secrete signaling factors to stimulate osteoblasts, cells that form bone. Odanacatib selectively inhibits cathepsin K, the primary enzyme in the osteoclasts that digests proteins during bone resorption. Progressive increases in BMD have been demonstrated with odanacatib.

Merck now plans to submit a New Drug Application to the Food and Drug Administration for odanacatib in 2015. Merck also plans to submit applications to the European Medicines Agency and the Ministry of Health, Labour, and Welfare in Japan.

About Merck

Today's Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside the

United States and Canada. Through our prescription medicines, vaccines, biologic therapies, and consumer care and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies, programs and partnerships. For more information, visit www.merck.com and connect with us on **Twitter**, **Facebook** and **YouTube**.

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Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; Merck’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of Merck’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

Merck undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in Merck’s 2013 Annual Report on Form 10-K and the company’s other filings with the Securities and Exchange Commission (SEC) available at the SEC’s Internet site (www.sec.gov).

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