1. ABSTRACT

- **Title**

Prolia® Postmarketing Active Safety Surveillance Program (PASP) for Soliciting Adverse Events of Special Interest in the United States (US)

- **Keywords**

Prolia, denosumab, osteoporosis, adverse events of special interest, postmarketing active safety surveillance program

- **Rationale and Background**

The study was conducted to fulfill the postmarketing commitment for a long-term surveillance study in patients administered Prolia (denosumab) to prospectively evaluate the incidence of serious infection including skin infections, dermatologic adverse events, and over-suppresion of bone turnover.

- **Research Question and Objectives**

The objectives of this program were to monitor the long-term safety of Prolia and enhance the quality of data collection by proactively soliciting adverse event reporting of the 5 pre-specified adverse events of special interest (AESIs) from US healthcare providers (HCPs) who care for Prolia-treated patients using Practice Fusion (PF)-Electronic Medical Record (PF-EMR) in the following indications:

  - treatment of postmenopausal women with osteoporosis at high risk for fracture
  - treatment to increase bone mass in men with osteoporosis at high risk for fracture
  - treatment of glucocorticoid-induced osteoporosis in men and women at high risk for fracture

- **Study Design**

The program proactively solicited information on pre-specified AESIs from HCPs who care for Prolia-treated patients in the US.

- **Setting**

The original program (2010-2016) invited prescribers in the US to participate through active communication activites. The amended program (2016-2021) proactively solicited information from HCPs who participated in the PF-EMR system, a cloud-based electronic health record platform for HCPs and patients in the US.

- **Subjects and Study Size, Including Dropouts**

Over the amended PASP period, HCPs for 110 700 Prolia-treated patients were prompted for feedback through the PF-EMR system.

- **Data Source(s) and Methods**

Data were collected from 2 sources: the PF-EMR system and the secure Amgen website. Healthcare providers who care for Prolia patients were automatically prompted during a patient office visit or medication order to record any of the 5 pre-specified AESIs (hypocalcemia, osteonecrosis of the jaw [ONJ], atypical femoral fractures [AFF], serious infections, and dermatologic reactions) for the current Prolia-treated patient. The recording of the absence or presence of any AESI was captured in the AESI-soliciting questionnaire (PF form); for each such notification, 3 possible outcomes to the PF form could be collected ("YES," "NO," and "Unknown," representing at least 1 AESI, no AESI, and an incomplete PF form, respectively). A PF form was considered complete when the outcome was either "YES" or "NO." If the HCP recorded that the current patient has had 1 or more AESI (ie, "possible" AESI), the HCP was then alerted to report this safety information to Amgen via a direct link in the PF form. The link navigated the user to the secure Amgen website where the HCP could complete and submit the AESI-specific questionnaire (Amgen form). These potential PASP AESIs were entered into the Amgen Global Safety Database and medically reviewed to determine if the potential PASP AESIs met the AESI case definitions ("confirmed" PASP AESI).

- **Results**

Over the amended PASP period, 58.7% of the HCPs who were prompted completed the PF form. Of the 64 929 completed responses, 1.9% reported at least 1 AESI and 0.112% reported a potential PASP AESI through the Amgen form. Crude incidence rates over the amended program based on the medically confirmed AESIs reported to Amgen of hypocalcemia, ONJ, AFF, serious infections, and dermatologic reactions were 0.005%, 0.020%, 0.002%, 0.025%, and 0.014%, respectively. The review of AESI cases did not identify any new safety findings.

- **Discussion**

The results indicated that the incidence rates of AESIs remained low and consistent 12 years after Prolia's approval in the US, even with the addition of active safety surveillance.

- **Marketing Authorization Holder(s)**

Amgen Inc.

- **Names and Affiliations of Principal Investigators**

Not applicable.