Summary Table of Study Protocol

Title	Real World Utilization and Effectiveness of Romosozumab among Osteoporosis Patients in Hong Kong
Protocol version identifier	20250006, Version 1.0
Date of last version of the protocol	Not applicable (NA)
EU Post Authorization Study (PAS) Register No	NA
Active Substance	NA
Medicinal Product	Romosozumab
Device	NA
Product Reference	NA
Procedure Number	NA
Marketing authorization holder(s)	Amgen Inc.
Joint PASS	No
Research Question and Objectives	Among patients treated with Romosozumab in Hong Kong: **Primary objectives:** • Describe characteristics of patients initiating Romosozumab and use of osteoporosis therapies • Describe change of bone mineral density among patients initiating Romosozumab CCI [redacted]
Country(ies) of Study	China
Author	PPD PPD

Marketing Authorization Holder (MAH)

MAH(s)	Amgen Inc.
MAH Contact	One Amgen Center Drive Thousand Oaks, CA 91320 USA 1-805-447-1000

This protocol was developed, reviewed, and approved in accordance with Amgen's standard operating procedures.

Protocol Version	Date of Protocol	Page Header Date
Original, Version 1.0	26 June 2025	26 June 2025

Confidentiality Notice

Investigator's Agreement

I have read the attached protocol entitled Real World Utilization and Effectiveness of Romosozumab among Osteoporosis Patients in Hong Kong, dated *26 June 2025*, and agree to abide by all provisions set forth therein.

I agree to ensure that Financial Disclosure Statements will be completed by:

- me (including, if applicable, my spouse [or legal partner] and dependent children)
- my Sub investigators (including, if applicable, their spouses [or legal partners] and dependent children)

at the start of the study and for up to 1 year after the study is completed, if there are changes that affect my financial disclosure status.

I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of Amgen Inc.

Signature	Date (DD Month YYYY)

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The University of Hong Kong

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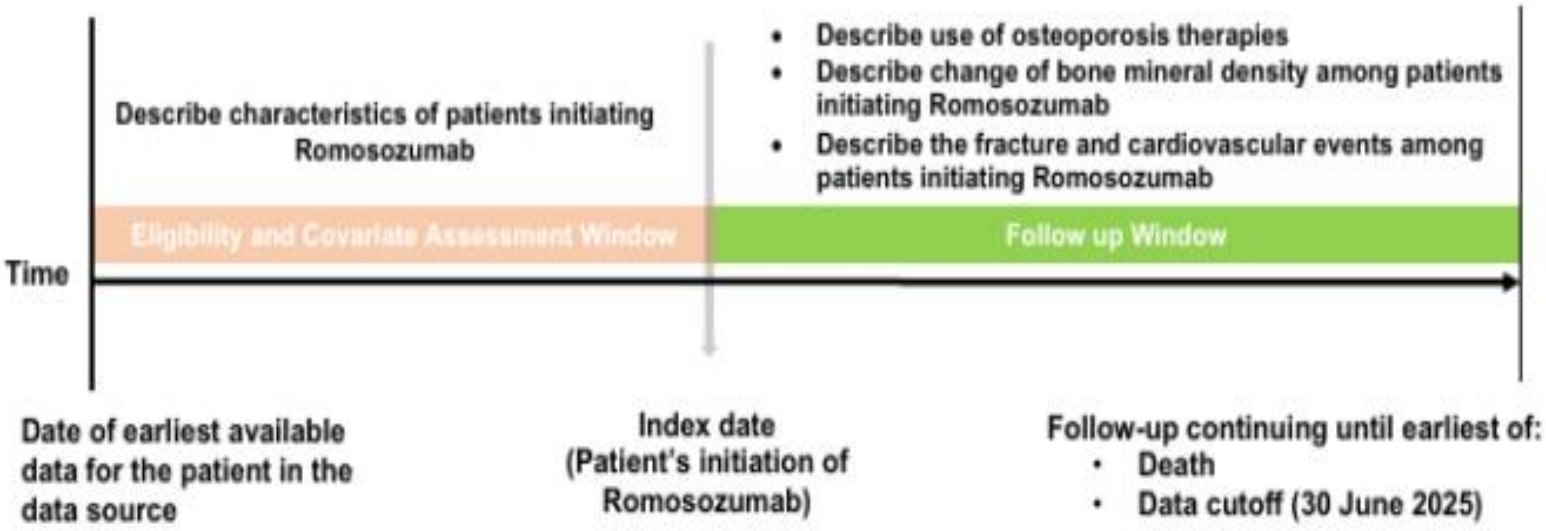
Study Design Schema



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2. List of Abbreviations

Abbreviation or Term	Definition/Explanation
AE	Adverse Events
BMD	Bone Mineral Density
CDARS	Clinical Data Analysis and Reporting System
CMS	Clinical Management System
EMR	Electronic Medical Records
EPR	Electronic Patient Records
HA	Hospital Authority
IEC	Independent Ethics Committee
IRB	Institutional Review Board
MI	Myocardial Infarction

3. Responsible Parties

Amgen

PPD

PPD

Academic Partner

PPD The University of Hong Kong

4. Abstract

- Study Title

Real World Utilization and Effectiveness of Romosozumab among Osteoporosis Patients in Hong Kong

- Study Background and Rationale

Despite the availability of osteoporosis treatments, osteoporosis continues to be a major public health concern in the Chinese population. This is especially true given the aging population, which causes a higher risk of fractures, decreased quality of life, and an increased healthcare burden. Romosozumab has been approved in Hong Kong in July 2020, based on the significant fracture risk reduction and bone mineral density (BMD) improvement observed in trials, when compared to placebo or alendronate. In Hong Kong, Romosozumab is indicated for the treatment of osteoporosis in postmenopausal women at high risk for fracture and contraindicated in patients with a history of myocardial infarction (MI) or stroke. However, the real-world utilization and effectiveness of Romosozumab in Hong Kong is unknown. The electronic medical records (EMR) from Hong Kong Clinical Data Analysis and Reporting System (CDARS) database can support the real-world study of Romosozumab users in Hong Kong and BMD records can be manually extracted from the chart review system named Clinical Management System (CMS)/Electronic Patient Records (EPR).This study aims to describe the real-world utilization and

effectiveness of Romosozumab among patients treated with Romosozumab in Hong Kong.

- Study Feasibility and Futility Considerations

The CDARS database is operational feasible and initial feasibility check demonstrated that around 1000 Romosozumab users have been identified in Hong Kong by the end of 2024. The CMS/EPR system can be used for chart review to manually extract BMD records for patients who ever used Romosozumab in the Hong Kong West cluster during feasibility check (over 200 Romosozumab users).

- Objective(s)

Objectives	**Endpoints**
Primary	

• Describe characteristics of patients initiating Romosozumab and use of osteoporosis therapies	• Demographics
	• Clinical characteristics[1]
	• Romosozumab utilization
	  - Dose and dosing schedule
	  - Total number of injections and duration of treatment
	• Use of osteoporosis therapies after Romosozumab

• Describe change of bone mineral density among patients initiating Romosozumab	• Percentage change of BMD from baseline of Romosozumab initiation to follow-up BMD
CCI [redacted]	
CCI [redacted]	

Note: [1] Clinical characteristic at initiation include demographics (eg, age, gender), prior osteoporosis treatment type and last dose date, history of recent fracture (hip, vertebral, or others, 1 year prior to initiation), history of fracture 3 years prior to initiation, history of cardiovascular events, other comorbidities and medication history.

– Hypothesis(es)/Estimation

Study objectives are descriptive in nature.

- Study Design/Type

This is a retrospective cohort study of patients initiated Romosozumab in Hong Kong.

- Study Population

The study population is patients initiated Romosozumab from 2 July 2020 (registration of Romosozumab in Hong Kong) to 31 December 2024 in Hong Kong.

- Summary of Patient Eligibility Criteria
  All patients received at least 1 injection of Romosozumab in Hong Kong will be included. Objective 2 will only include Romosozumab users identified in the Hong Kong West cluster.
- Follow-up
  The index date is defined as the date of initial Romosozumab prescription start date in Hong Kong, and patients will be followed until death or data cutoff (30 June 2025).
- Variables
  - *Outcome Variable(s)*
    Endpoints listed in objectives table.
  - *Exposure Variable(s)*
    Romosozumab use
  - *Other Covariate(s)*
    All available health records available before Romosozumab initiation will be used to describe history of comorbidities, procedures and records within 365 days before Romosozumab initiation will be used to describe history of medications. And up to 90 days before/at initiation will be used to describe lab covariate assessment including BMD.
- Data sources
  The data source is the CDARS, a territory-wide representative electronic medical database from the Hospital Authority (HA) of Hong Kong. CDARS serves $>$ 7.4 million Hong Kong residents through 43 hospitals and institutions, 49 specialist outpatient clinics, and 73 general outpatient clinics. CDARS covers approximately 80% of all hospital admissions in Hong Kong and has been extensively used for conducting high-quality population-based studies. It contains clinical records from outpatient, emergency, and inpatient, including diagnosis, dispensing, clinical procedures and operations, laboratory tests, and death registry records. The CMS/EPR system can be used to manually extract BMD records for patients who ever used Romosozumab in Hong Kong West cluster through chart review.
- Study Sample Size

  All Romosozumab users from 2020 to 2024, with an estimate of 1000 patients will be included for this study. Around 200 patients who ever used Romosozumab in Hong Kong West cluster will be included for chart review of BMD records.

- Data Analysis

  Objective 1: Describe characteristics of patients initiating Romosozumab and use of osteoporosis therapies

  Descriptive analysis will be conducted to describe the disease and medication history, lab values, treatment pattern of Romosozumab users, and use of other osteoporosis therapies after initiating Romosozumab.

  Objective 2: Describe change of bone mineral density among patients initiating Romosozumab

  For patients in Hong Kong West cluster, their BMD records can be manually extracted from CMS/EPR system. The change in baseline BMD (available BMD records up to 90 days before/at Romosozumab initiation) and BMD at 6 and 12 months after initiating Romosozumab will be described among patients with both BMD values at baseline and 6 months, or both BMD values at baseline and 12 months, respectively.

  CCI [redacted]

  CCI [redacted]

- Milestones

  The planned final report of study results will be available in June 2026.

5. Amendments and Updates

None

6. Milestones

Milestone	Planned date
Start of data extraction	July 2025
End of data extraction	December 2025
Final report of study results	June 2026

7. Rationale and Background

7.1 Diseases and Therapeutic Area

Despite the availability of osteoporosis treatments, including anti-resorptive agents (eg, bisphosphonates, denosumab) and anabolic agents (eg, teriparatide), osteoporosis continues to be a major public health concern in the Chinese population (Liu et al. 2025). This is especially true given the aging population, which contributes to a higher risk of fractures, decreased quality of life, and an increased healthcare

burden (Yu and Xia 2019; Si et al. 2015; Xiao et al. 2022). Romosozumab is a monoclonal antibody that targets sclerostin and works through a dual mechanism: it promotes bone formation while also reducing bone resorption, making it a promising treatment option. It has been approved in Hong Kong in July 2020 based on the rapid and substantial gains in bone mineral density (BMD), improved bone structure and strength, and significantly fracture risk reduction observed in trials, when compared to placebo or alendronate (Cosman et al. 2016; Saag et al. 2017). In Hong Kong, Romosozumab is indicated for the treatment of osteoporosis in postmenopausal women at high risk for fracture and contraindicated in patients with a history of myocardial infarction (MI) or stroke. However, the real-world utilization and effectiveness of Romosozumab in Hong Kong is unknown.

7.2 Rationale

The electronic medical records (EMR) from Hong Kong Clinical Data Analysis and Reporting System (CDARS) database can support the real-world study of Romosozumab users in Hong Kong and BMD records can be manually extracted from the chart review system named Clinical Management System (CMS)/Electronic Patient Records (EPR). Describing the real-world utilization and effectiveness of Romosozumab users can help us understand the profile of Romosozumab users in Hong Kong and support the generalization of clinical trial results to the broader Chinese population.

This study aims to describe the real-world utilization and effectiveness of Romosozumab among patients treated with Romosozumab in Hong Kong.

7.3 Feasibility and Futility Considerations

The CDARS database is operational feasible (Sing et al. 2017) and initial feasibility check demonstrated that around 1000 Romosozumab users can be identified in Hong Kong by the end of 2024. The CMS/EPR system can be used for chart review to manually extract BMD records for patients who have ever used Romosozumab in Hong Kong West cluster during feasibility check (the medical charts of over 200 Romosozumab users with records in Hong Kong West cluster can be reviewed to extract BMD records).

7.4 Statistical Inference (Estimation or Hypothesis[es])

Study objectives are descriptive in nature.

8. Research Question and Objectives

8.1 Primary

- Describe characteristics of patients initiating Romosozumab and use of osteoporosis therapies
- Describe change of bone mineral density among patients initiating Romosozumab

CCI [redacted]

9. Research Methods

9.1 Study Design

This is a retrospective cohort study of patients initiated Romosozumab in Hong Kong. The principal investigator's team will have data access and conduct the analysis

9.2 Setting and Study Population

9.2.1 Study Period

The study period will be from 2 July 2020 (registration of Romosozumab in Hong Kong) to 30 June 2025 (data cutoff).

9.2.2 Patient Eligibility

9.2.2.1 Inclusion Criteria

All patients received at least 1 injection of Romosozumab from 2 July 2020 to 31 December 2024 in Hong Kong will be included. Objective 2 will only include Romosozumab users identified in the Hong Kong West cluster.

9.2.2.2 Exclusion Criteria

Not applicable

9.2.3 Matching

Not applicable

9.2.4 Baseline Period

The index date is defined as the start date of initial Romosozumab prescription in Hong Kong. The baseline period is defined as the period starting from date of earliest available data for the patients to the index date. All available health records available before Romosozumab initiation will be used for comorbidities and procedures. Records within 365 days before Romosozumab initiation will be used for medications. And up to 90 days before/at initiation will be used for labs covariate assessment including BMD.

9.2.5 Study Follow-up

Follow up per patient will continue till the earliest date of death or data cutoff (30 June 2025).

9.3 Variables

9.3.1 Exposure Assessment

The exposure of interest is Romosozumab. Patients will be considered as exposed from the time of their initial Romosozumab administration through treatment discontinuation.

9.3.2 Outcome Assessment

Demographics and clinical characteristics

The baseline demographics and clinical characteristics will be described according to the covariate list in section 9.3.3.

Use of osteoporosis therapies

Treatment information of Romosozumab will be extracted through follow up including dose and dose schedule, as well as the total number of injections. Treatment of other osteoporosis therapies after Romosozumab will also be described.

BMD Endpoint

BMD data in grams / centimeter^2 and T-score, both the value and report, are available through manual extraction from the CMS/EPR system for Romosozumab users in the Hong Kong West cluster. BMD changes will be described by the difference between baseline BMD (available BMD records up to 90 days before/at Romosozumab initiation) and BMD at 6 and 12 months after initiating Romosozumab based on clinical practice.

CCI [redacted]

9.3.3 Covariate Assessment

The variables will be assessed during the baseline period. For variables that can change over time, the value nearest to the index date will be utilized.

- Demographic (eg age, gender, year at index date, health service use)
- Clinical characteristics
  - Smoking status or history of chronic obstructive pulmonary disease
  - Osteoporosis related (eg prior osteoporosis treatment type, last dose date and duration, prior glucocorticoid use, history of recent fracture (hip, vertebral, or others, 1 year prior to initiation), history of fracture 3 years prior to initiation)

- Comorbidities (eg myocardial infarction, ischemic stroke, hemorrhagic stroke, congestive heart failure, dyslipidemia, hypertension, diabetes mellitus, osteoarthritis)
- Concomitant treatments
- Baseline lab (eg BMD)

9.3.4 Validity and Reliability

Data validation has demonstrated high-coding accuracy of fractures in CDARS (Sing et al. 2017). BMD records are missing in CDARS but can be manually extracted from CMS/EPR system for patients who have ever used Romosozumab in the Hong Kong West cluster.

9.4 Data Sources

CDARS is a territory-wide representative electronic medical database from the Hospital Authority (HA) of Hong Kong. CDARS serves > 7.4 million Hong Kong residents through 43 hospitals and institutions, 49 specialist outpatient clinics, and 73 general outpatient clinics. CDARS covers approximately 80% of all hospital admissions in Hong Kong and has been extensively used for conducting high-quality population-based studies. It contains clinical records from outpatient, emergency, and inpatient, including diagnosis, dispensing, clinical procedures and operations, laboratory tests, and death registry records. The CMS/EPR system can be used to manually extract BMD records for patients in Hong Kong West cluster through chart review.

9.5 Study Size

By 31 December 2024, Around 1000 Romosozumab users have been identified in CDARS and over 200 Romosozumab users can be identified in Hong Kong West cluster for chart review of BMD records through initial feasibility check.

9.6 Data Management (Curation)

In order to use CDARS for research, analytical files must be built to define the study cohorts and algorithms are used to identify exposures, outcomes and covariates. Chart review needs to be conducted to obtain BMD records in CMS/EPR system.

9.7 Data Analysis

The analyses of all objectives will be performed using descriptive statistical methods. No hypotheses testing is planned.

9.7.1 Planned Analyses

9.7.1.1 Primary Analysis

<u>Objective 1: Describe characteristics of patients initiating Romosozumab and use of osteoporosis therapies</u>

Descriptive analysis will be conducted to describe the disease and medication history, lab values, treatment pattern of Romosozumab users, and use of other osteoporosis therapies after Romosozumab.

Objective 2: Describe change of bone mineral density among patients initiating Romosozumab

For patients in Hong Kong West cluster, their BMD records can be manually extracted from CMS/EPR system. The change in baseline BMD (available BMD records up to 90 days before/at Romosozumab initiation) and BMD at 6 and 12 months after initiating Romosozumab will be described.

CCI [redacted]

CCI [redacted]

9.7.2 Planned Method of Analysis

9.7.2.1 General Considerations

All data analyses will be performed using appropriate software such as R or SAS. All analyses will be descriptive. Continuous variables will be summarized by mean, median, standard deviation, 25th percentile, 75th percentile, minimum and maximum. Categorical variables will be summarized by number and percentage.

9.7.2.2 Missing or Incomplete Data and Lost to Follow-up

BMD records are not available in CDARS and can only be manually extracted for Romosozumab users in Hong Kong West cluster from the CMS/EPR system through chart review. Romosozumab users in other clusters of Hong Kong and those with missing BMD records in Hong Kong West cluster cannot be included for BMD analysis.

9.7.2.3 Descriptive Analysis

9.7.2.3.1 Description of Study Enrollment

All patients meet the eligible criteria will be included.

9.7.2.3.2 Description of Patient Characteristics

Patient demographics and clinical history during the baseline period will be summarized.

9.7.2.4 Analysis of the Primary, Secondary, and CCI [redacted] Endpoint(s)

Primary objective 1: Describe characteristics of patients initiating Romosozumab and use of osteoporosis therapies

The baseline characteristics will be described including fractures, cardiovascular events, comorbidities, and medication history. Fractures include history of recent fracture (overall and by subtypes: hip, vertebral, or others) within 1 year, history of fracture within 3 years, and ever fracture history before Romosozumab initiation. Fracture on the date of Romosozumab initiation will also be described. Cardiovascular events include history of recent events (overall and by subtypes: MI, ischemic stroke, hemorrhagic stroke) within 1 year, and ever cardiovascular events history before Romosozumab initiation. Cardiovascular events on the date of Romosozumab initiation will also be described.

The utilization of Romosozumab will be described including the total number of doses, dosing schedule, duration of treatment (defined as the time period from Romosozumab initiation to the prescription start date of last continued prescription + doses of last continued prescription * 30 days), etc. The use of other osteoporosis therapies after Romosozumab will also be described.

Primary objective 2: Describe change of bone mineral density among patients initiating Romosozumab

For patients in Hong Kong West cluster, their BMD records can be manually extracted from CMS/EPR system. The baseline BMD will be defined as the BMD record closest to index date within 90 days before/at index date. The BMD at 6 months after initiating Romosozumab is defined as the BMD record within the period of index date + 180 days ± 90 days; the BMD at 12 months after initiating Romosozumab is defined as the BMD record within the period of index date + 365 days ± 90 days. If multiple records can be identified during each period, the BMD record at the date closest to the date of index date + 180 days, or index date + 365 days will be chosen, respectively. The percentage change of BMD will be calculated for patients with both baseline BMD and follow-up BMD, and described as overall percentage change, and stratified by the follow-up BMD records during Romosozumab treatment (defined as before the prescription start date of last continued prescription + doses of last continued prescription * 30 + 90 days), and those who discontinued Romosozumab treatment.

CCI [redacted]

CCI [redacted]

CCI [redacted]

9.7.2.5 Sensitivity Analysis

9.7.2.5.1 Subgroup Analysis

For primary objective 1 and CCI [redacted], subgroup analysis will be conducted for patients who ever used Romosozumab in Hong Kong West cluster.

9.7.2.5.2 Stratified Analysis

For all objectives, stratified analyses will be conducted among patients with 6 or more doses of Romosozumab, and among patients with 5 or less doses of Romosozumab.

For description of Romosozumab utilization and CCI [redacted], stratified analyses will be conducted by patients with or without cardiovascular events (MI, ischemic stroke, hemorrhagic stroke) before index date, and by patients with or without cardiovascular events within 365 days before index date.

For primary objective 2, a stratified analysis of BMD change will be conducted by prior osteoporosis treatment types.

9.7.3 Analysis of Safety Endpoint(s)/Outcome(s)

Safety data will not be collected nor analyzed as part of this study.

9.8 Quality Control

Statistical analyses on the final analytical datasets will be conducted by two people and cross-checked for quality assurance.

9.9 Limitations of the Research Methods

9.9.1 Internal Validity of Study Design

9.9.1.1 Selection Bias

Only the BMD of Romosozumab users in Hong Kong West cluster can be manually extracted in CMS/EPR system through chart review for BMD analysis. Therefore, the results of BMD analysis can be biased from patients from other clusters in Hong Kong, and a subgroup analysis of patients from Hong Kong West cluster will be conducted to address potential difference from all patients from Hong Kong.

9.9.1.2 Confounding

In clinical practice, most Romosozumab initiators are with prior osteoporosis treatments. A stratified analysis will be conducted by the type and duration of prior osteoporosis treatments.

9.9.2 External Validity of Study Design

The clinical practice and treatment pattern might be different between Hong Kong and China mainland and whether the results of this study can be generalized to the broader Chinese population needs to be evaluated with caution.

9.9.3 Limitations Due to Missing Data and/or Incomplete Data

In clinical practice, BMD measurement before Romosozumab initiation may not be necessary for patients experienced recent osteoporotic fracture (ie at high risk of fracture) leading to potential missing baseline BMD. All BMD analyses will be conducted in patients with available baseline BMD among those who have ever used Romosozumab in the Hong Kong West cluster.

10. Protection of Human Participants

10.1 Informed Consent

Informed consent will not be applicable for a study containing only de-identified secondary data.

10.2 Institutional Review Board/Independent Ethics Committee (IRB/IEC)

This study protocol will be reviewed by the IEC in Hong Kong.

10.3 Patient Confidentiality

The investigator must ensure that the participant's confidentiality is maintained for documents submitted to Amgen.

Participant will be assigned a unique identifier by the sponsor. Any participant records or datasets that are transferred to the sponsor will contain the identifier only; participant names or any information which would make the participant identifiable will not be transferred.

For Serious Adverse Events (SAEs) reported to Amgen, participants are to be identified by their unique participant identification number, initials (for faxed/emailed reports, in accordance with local laws and regulations), and age (in accordance with local laws and regulations).

Documents that are not submitted to Amgen (eg, signed informed consent forms) are to be kept in confidence by the investigator, except as described below.

In compliance with [governmental regulations/ICH GCP Guidelines], it is required that the investigator and institution permit authorized representatives of the company, of the regulatory agency(s), and the [IRB/IEC] direct access to review the participant's original medical records for verification of data. Direct access includes examining, analysing, verifying, and reproducing any records and reports that are important to

the evaluation of the study. The investigator is obligated to inform and obtain the consent of the participant to permit such individuals to have access to their study-related records, including personal information.

11. Collection, Recording, and Reporting of Safety Information and Product Complaints (PCs)

This study is analyzing secondary data from *CDARS and CMS/EPR medical chart review*. The safety outcomes that are listed in section Outcome Assessment 9.3.2 will be documented and analyzed in this study. These will be reported in aggregate in the final study report as *number of events*. See section Outcome Assessment 9.3.2 for safety outcomes and definitions.

12. Administrative and Legal Obligations

12.1 Protocol Amendments and Study Termination

Amgen may amend the protocol at any time. When Amgen amends the protocol and distributes the protocol amendment to the sites, written agreement from the Investigator must be obtained where applicable per local governing law and/or regulations. The *IRB/IEC* must be informed of all amendments provided to the investigator by Amgen and give approval for all protocol amendments that Amgen provides to the site. The Investigator **must** send a copy of the approval letter from the *IRB/IEC* to Amgen.

Amgen reserves the right to terminate the study at any time. Both Amgen and the Investigator reserve the right to terminate the Investigator's participation in the study according to the contractual agreement. The Investigator is to notify the *IRB/IEC* in writing of the study's completion or early termination and send a copy of the notification to Amgen.

13. Plans for Disseminating and Communicating Study Results

13.1 Publication Policy

The study will be published.

Authorship of any publications resulting from this study will be determined on the basis of the International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals, which states authors need to fulfil all of the following criteria (defined in SOP-429662):

1. Make substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work
2. Draft the work or review it critically for important intellectual content
3. Approve of the version to be submitted for publication

4. Agree to be accountable for all aspects of the work by ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

All publications (eg, manuscripts, abstracts, oral/slide presentations, book chapters) based on this study must be submitted to Amgen for corporate review. The vendor agreement will detail the procedures for, and timing of, Amgen's review of publications.

14. References

Cosman, F., D. B. Crittenden, J. D. Adachi, N. Binkley, E. Czerwinski, S. Ferrari, L. C. Hofbauer, E. Lau, E. M. Lewiecki, A. Miyauchi, C. A. Zerbini, C. E. Milmont, L. Chen, J. Maddox, P. D. Meisner, C. Libanati, and A. Grauer. 2016. 'Romosozumab Treatment in Postmenopausal Women with Osteoporosis', *N Engl J Med*, 375: 1532-43.

Liu, Yi, Xuanyin Huang, Ke Tang, Jing Wu, Jiali Zhou, He Bai, Liying Zhou, Shiyi Shan, Zeyu Luo, Jin Cao, Peige Song, and Igor Rudan. 2025. 'Prevalence of osteoporosis and associated factors among Chinese adults: a systematic review and modelling study', *Journal of Global Health*, 15.

Saag, Kenneth G, Jeffrey Petersen, Maria Luisa Brandi, Andrew C Karaplis, Mattias Lorentzon, Thierry Thomas, Judy Maddox, Michelle Fan, Paul D Meisner, and Andreas Grauer. 2017. 'Romosozumab or alendronate for fracture prevention in women with osteoporosis', *New England Journal of Medicine*, 377: 1417-27.

Si, Lei, TM Winzenberg, Q Jiang, M Chen, and AJ Palmer. 2015. 'Projection of osteoporosis-related fractures and costs in China: 2010–2050', *Osteoporosis International*, 26: 1929-37.

Sing, C. W., Y. C. Woo, A. C. H. Lee, J. K. Y. Lam, J. K. P. Chu, I. C. K. Wong, and C. L. Cheung. 2017. 'Validity of major osteoporotic fracture diagnosis codes in the Clinical Data Analysis and Reporting System in Hong Kong', *Pharmacoepidemiol Drug Saf*, 26: 973-76.

Vestergaard Kvist, A., J. Faruque, E. Vallejo-Yagüe, S. Weiler, E. M. Winter, and A. M. Burden. 2021. 'Cardiovascular Safety Profile of Romosozumab: A Pharmacovigilance Analysis of the US Food and Drug Administration Adverse Event Reporting System (FAERS)', *J Clin Med*, 10.

Xiao, P-L, A-Y Cui, C-J Hsu, R Peng, N Jiang, X-H Xu, Y-G Ma, D Liu, and H-D Lu. 2022. 'Global, regional prevalence, and risk factors of osteoporosis according to the World Health Organization diagnostic criteria: a systematic review and meta-analysis', *Osteoporosis International*, 33: 2137-53.

Yu, F., and W. Xia. 2019. 'The epidemiology of osteoporosis, associated fragility fractures, and management gap in China', *Arch Osteoporos*, 14: 32.

15. Appendices

None

Approval Signatures

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Document Description:

Document Number: CLIN-000390725

Approval Date: 12 Aug 2025

Type of Study Protocol: Original

Protocol Amendment No.:

Document Approvals	
Reason for Signing: Functional Area	Name: PPD Date of Signature: 12-Aug-2025 23:51:50 GMT+0000