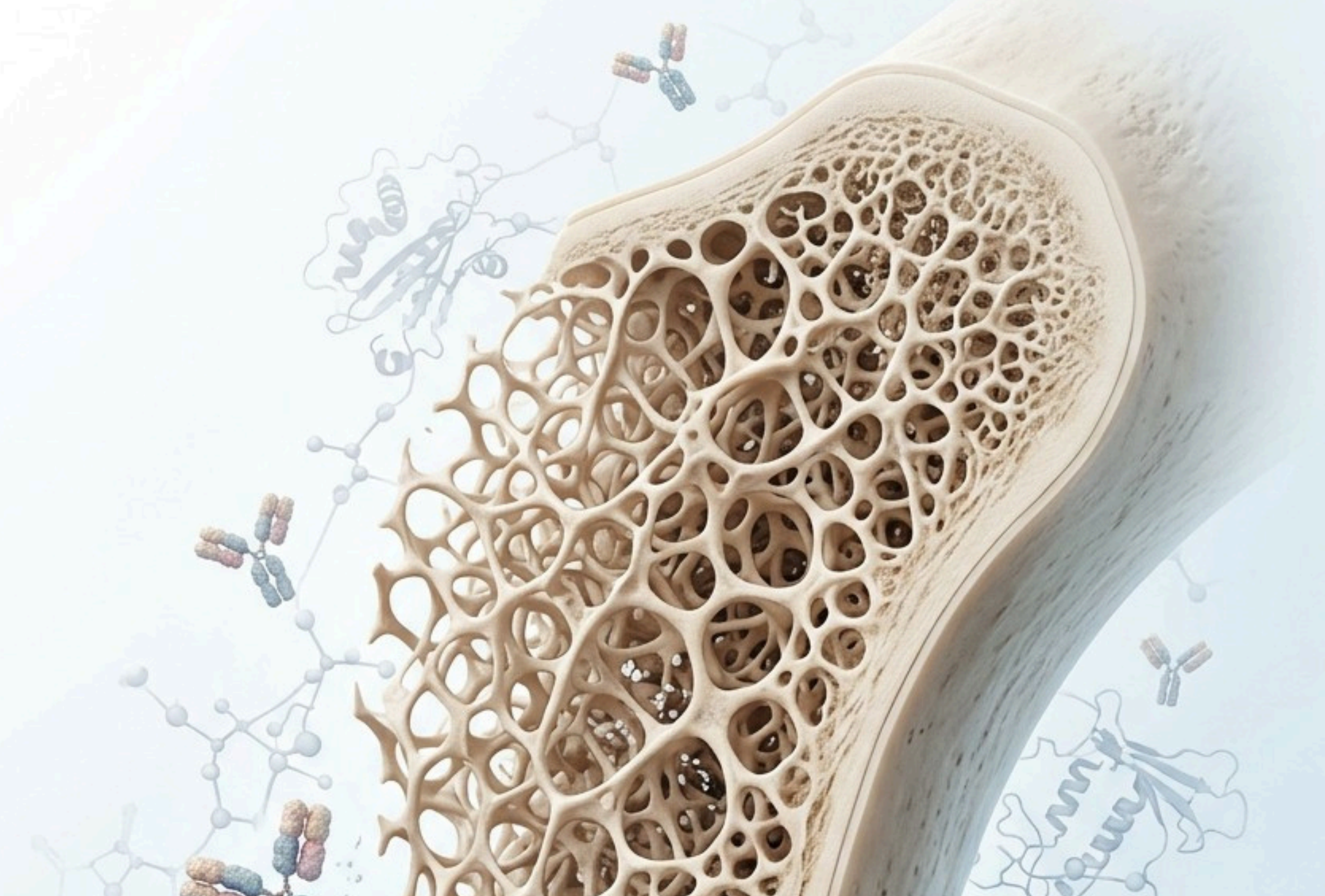
LAMBDA Research Accelerated | Novum PHARMACEUTICAL RESEARCH SERVICES

Global Full-service CRO

STUDY INSIGHTS

Delivering a Multicenter **Denosumab Clinical Trial** with Integrated Clinical & Bioanalytical Expertise



Study Objective

A global pharmaceutical company partnered with Lambda Therapeutic Research to conduct a global multicenter clinical trial evaluating a Denosumab biosimilar in postmenopausal women with osteoporosis. The study compared the biosimilar with the reference medicinal product to establish pharmacokinetic (PK), pharmacodynamic (PD), and immunogenicity equivalence, while evaluating safety and efficacy.

Designed to support regulatory submissions to the US FDA and EMA, the study required coordinated clinical execution across multiple countries, centralized bioanalytical testing, advanced immunogenicity assessment, imaging coordination, and long-term patient follow-up, including a treatment-switch extension phase.

Molecule Overview

Denosumab is a fully human monoclonal antibody that binds to receptor activator of nuclear factor kappa-B ligand (RANKL), inhibiting osteoclast formation, function, and survival. By reducing bone resorption, Denosumab increases bone mineral density and lowers fracture risk in patients with osteoporosis.

Because Denosumab targets circulating RANKL, bioanalytical assessment requires highly sensitive methods capable of overcoming target interference while accurately measuring pharmacokinetics, immunogenicity, and pharmacodynamic biomarkers. These analytical complexities make biosimilar development particularly challenging.

Study Overview

This randomized, double-blind, active-controlled, parallel-arm, multicenter study enrolled approximately 552 postmenopausal women with osteoporosis across India and Georgia. Participants received 12 months of treatment followed by a 6-month treatment-switch extension phase to further evaluate safety and immunogenicity after switching from the reference medicinal product to either the reference product or the investigational biosimilar.

Study Design	Randomized, double-blind, active-controlled, parallel-arm, multicenter study
Therapeutic Area	Osteoporosis
Study Population	Approximately 552 postmenopausal women (55 to 90 years)
Countries	India and Georgia
Treatment Duration	12 months
Extension Phase	6-month re-randomized switching study
Primary Objective	Demonstrate PK, PD, and immunogenicity equivalence
Secondary Objectives	Evaluate efficacy, safety, and immunogenicity following treatment switching
Regulatory Objective	Support US FDA and EMA regulatory submissions

Challenges & Solutions

Challenge	Lambda's Solution
Patient enrollment and long-term retention Identifying eligible postmenopausal women with osteoporosis while maintaining patient retention throughout the 12-month treatment period and extension phase.	Selected experienced investigator sites with strong osteoporosis patient pools and appropriate infrastructure. Continuous patient engagement, proactive site coordination, and dedicated site support ensured efficient enrollment and sustained patient retention throughout the study.
Complex study design and protocol execution Managing a global, randomized, double-blind study involving PK, PD, immunogenicity, efficacy, safety, and imaging assessments across India & Georgia.	Established standardized site-level operational workflows, conducted comprehensive investigator training, and maintained close coordination across investigative sites, laboratories, imaging facilities, and project teams to ensure consistent protocol execution.
Extension study & patient re-randomization Transitioning eligible patients into the treatment-switch extension phase within stringent timelines.	Planned monitoring visits, aligned cross-functional stakeholders, and coordinated closely with study sites to enable seamless patient re-randomization and timely initiation of the extension phase.
Imaging coordination Ensuring patient compliance for imaging endpoint assessments performed at the central imaging facility.	Established structured imaging workflows, patient visit tracking, and coordination between investigative sites and the central imaging facility to ensure timely image review and endpoint evaluation.
Global database lock Achieving a global database lock within aggressive timelines for a first-to-file biosimilar development program across multiple countries.	Implemented centralized project tracking, proactive data reconciliation, and continuous coordination across global teams, enabling completion of the global database lock within three weeks of Last Patient Last Visit (LPLV).

Challenges & Solutions

Challenge	Lambda's Solution
Global sample management and project timelines Managing intensive PK, PD, and immunogenicity sample collection, shipment, and centralized bioanalysis across global study sites.	Deployed dedicated phlebotomy teams for intensive PK sampling, centralized bioanalysis at Lambda's laboratory in India, and implemented robust sample tracking and validated logistics to ensure sample integrity & timely analysis across global study sites.
Immunogenicity assay development Overcoming interference from circulating RANKL during anti-drug antibody (ADA) assessment while maintaining high assay sensitivity, drug tolerance, and target tolerance.	Developed an immunogenicity assay with high sensitivity, high drug tolerance, and RANKL tolerance, minimizing false-positive ADA results and enabling accurate assessment of immunogenicity.
Neutralizing antibody assay development Developing a sensitive neutralizing antibody (NAb) assay while overcoming the limitations of conventional cell-based assays, including low sensitivity, assay variability, & high operational cost.	Established a highly sensitive competitive ligand-binding NAb assay based on Denosumab's mechanism of action. The assay provided high sensitivity, drug tolerance, reproducibility, and operational efficiency compared with conventional cell-based methods.
PK and PD bioanalytical methods Developing robust analytical methods for Denosumab quantification and pharmacodynamic biomarker evaluation in a disease population.	Developed and validated an in-house ligand-binding PK assay for Denosumab and optimized PD biomarker assays for CTX and PINP using in-vitro diagnostic platforms adapted for drug development. Method validation and Incurred Sample Reanalysis (ISR) ensured robust bio analytical performance.
Regulatory-ready bioanalytical performance Generating reliable bioanalytical data that met the stringent expectations of global regulatory agencies for biosimilar development.	Developed innovative bioanalytical methods that improved assay sensitivity, specificity, target tolerance, reproducibility, and overall analytical reliability, generating high-quality data aligned with the regulatory expectations of the US FDA and EMA for biosimilar development.

Key Outcomes

- Successfully enrolled approximately 552 postmenopausal women across investigator sites in India and Georgia.
- Executed a global, randomized, double-blind clinical trial with integrated PK, PD, immunogenicity, efficacy, imaging, and safety assessments.
- Successfully transitioned eligible participants into the treatment-switch extension study within protocol-defined timelines.
- Successfully coordinated centralized bioanalysis of PK, PD, and immunogenicity samples collected across India and Georgia.
- Completed the global database lock within three weeks of Last Patient Last Visit (LPLV), supporting the sponsor's first-to-file biosimilar development program.
- Developed and validated highly sensitive immunogenicity, neutralizing antibody, PK, and PD bioanalytical methods capable of overcoming target interference and supporting comprehensive biosimilar evaluation.
- Generated clinical and bioanalytical data to support the sponsor's planned regulatory submissions to the US FDA and EMA.

Conclusion

This study demonstrates Lambda Therapeutic Research's ability to execute large, global biosimilar clinical trials that integrate clinical operations, centralized bioanalytical testing, immunogenicity assessment, imaging coordination, and regulatory-focused project management. Through coordinated global execution and advanced laboratory capabilities, Lambda generated high-quality clinical and bioanalytical data while maintaining protocol compliance, patient safety, and accelerated development timelines for a complex biosimilar program.

Connect with us to explore how we can accelerate your clinical development programs.

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