

R as the Core Technology to Support Modeling and Simulation in Pharma Research, Development, and Post Approval Activities

Marc R. Gastonguay, Ph.D.

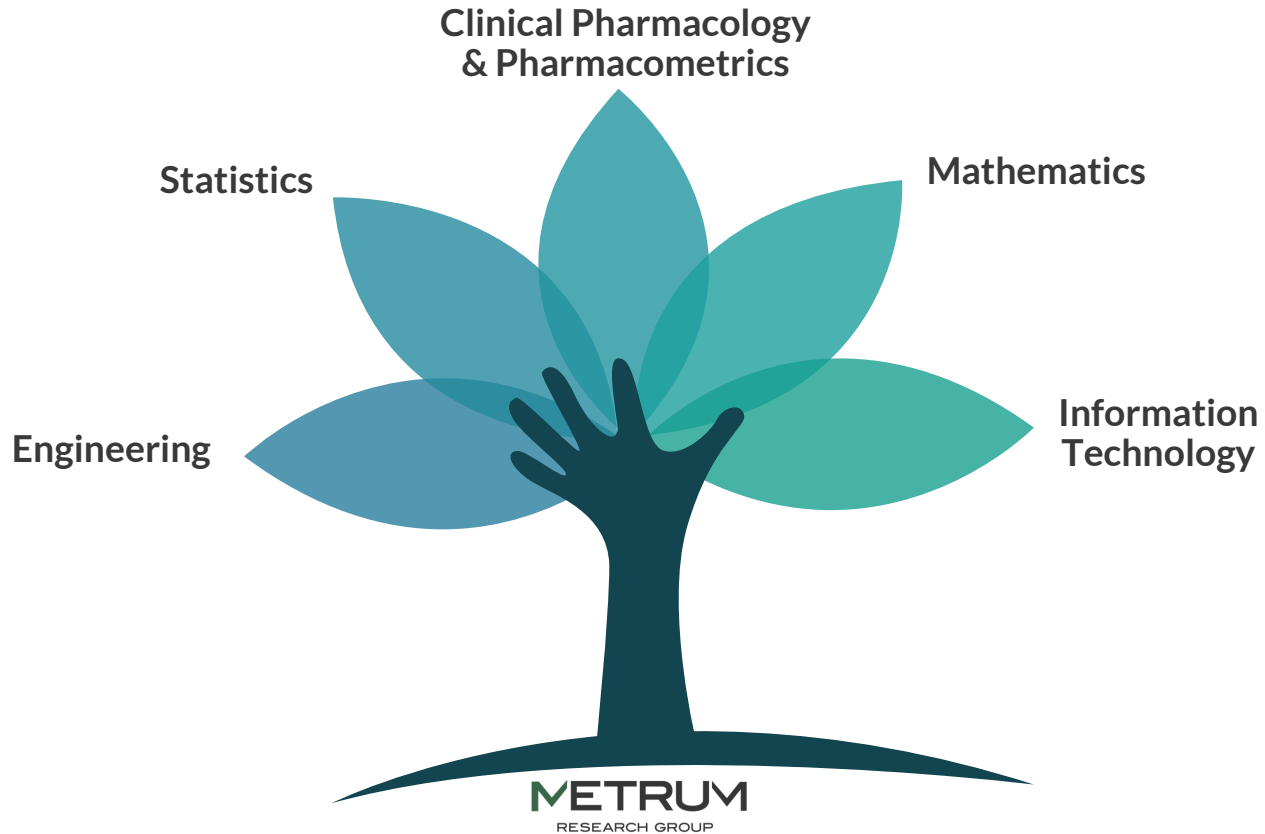
Founder & CEO

Metrum Research Group LLC

metrumrg.com

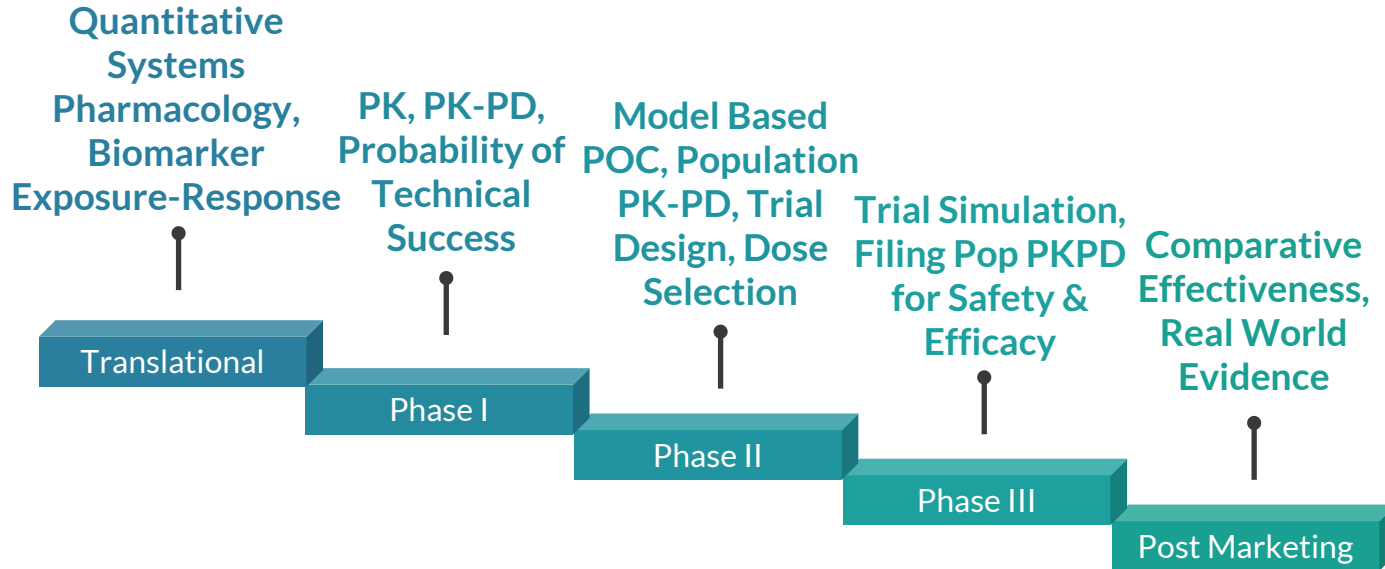
Who We Are

Founded in 2004, Metrum Research Group is a multidisciplinary team.



Model-Informed Drug Development

Just some of the methods and services we provide throughout development programs.



Off-The-Shelf Disease Area Platform Content: Disease Progression, Quantitative Systems Pharmacology, Competitor Model-Based Meta-Analysis, Trial Simulation Tools

Strategic Modeling and Simulation

General Hourly Consulting Services - Fixed Scope Contract Research Projects - Collaborative Scientific Partnership

Understanding
Translational &
Systems Pharmacology

Probability of
Technical Success

Quantitative Due
Diligence Assessment

Dose Selection

Trial Design Evaluation
& Optimization

Comparative
Effectiveness

Internal Decision
Support

Preparation of
Regulatory Documents

Therapeutic Areas and Regulatory Settings

small molecules, biologics, diagnostics, devices

>150 Sponsors	>500 Projects	>100 Regulatory Filings
Bone Health	Cardiovascular	Neurodegeneration
Ophthalmology	Pediatrics	Pain
Infectious Disease	Hematology	Inflammation
Oncology	Rare & Ultra Rare Disease	Immunology
Growth and Development	CNS	Endocrine & Metabolic Disorders

Open Source Tools



Growing the science with open-source tools

At Metrum Research Group, we are strong advocates of open-source software development efforts. We make several of the useful tools we've developed (or co-developed) for our own work available as free, open-source software.

mrgsolve
metrumrg
nmqual
qapply
fork
review

SASexport
audited
BUGSModelLibrary
BUGSParallel
Torsten (Stan PKPD)

Training Workshops and Open Courseware

We offer open, free training courses and materials as well as custom, fee-based workshops.

R Programming

Intro & Advanced Pop PKPD

Intro through Advanced Bayesian Data Analysis

Categorical, Count, Time-To-Event Models

Model-Based Meta-Analysis

Exposure-Response Models

Intro and Advanced Stan for PKPD Modeling

Simulation Concepts and Strategies

PKPD Simulation with mrgsolve

Metworx Elastic Cloud Computing

PBPK Modeling (with mrgsolve)

Systems Pharmacology (with mrgsolve)

R-Shiny Web Apps for Decision Making

Communication of M&S to Non-Technical Audiences



On site



YouTube
courses



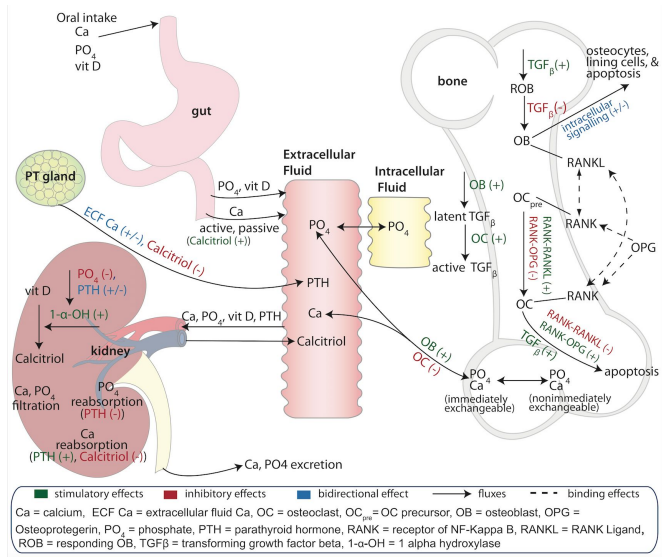
Online/
Webinars



Partnerships with
scientific meetings



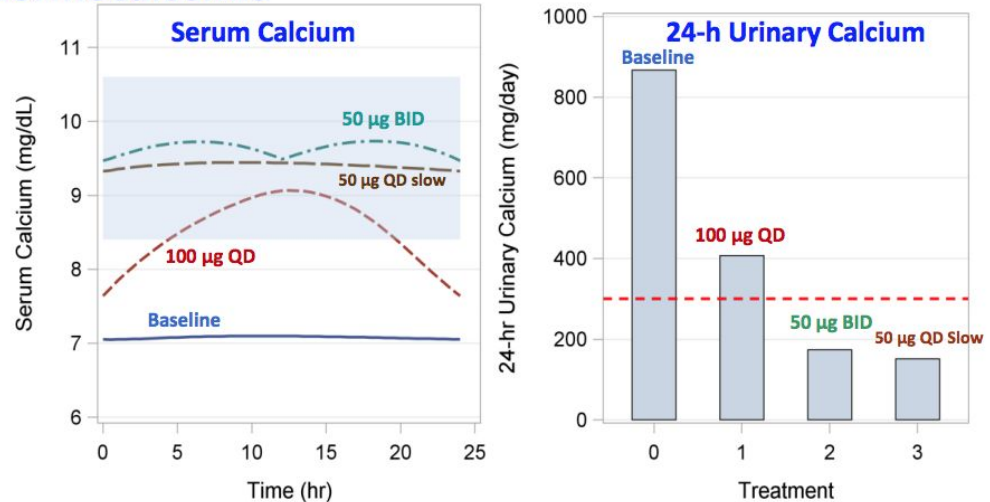
Open Models Utility & Impact



<https://github.com/metrumresearchgroup/OpenBoneMin>

"Using systems pharmacology model we showed that control on hypercalciuria is feasible with more frequent regimen or a slow release PTH profile at lower systemic exposure than 100 µg QD"

Altering Regimen (QD to BID) or Release Profile Controls Hypercalciuria While Maintaining Normocalcemia



<https://wayback.archive-it.org/7993/20170405215559/https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/UCM416168.pdf>

Computational Infrastructure and Workflow



Since its foundation in 2004, Metrum Research Group has relied on R as the core technology and central framework for all of the company's biomedical modeling and simulation (M&S) service activities, spanning more than 475 projects with 150+ different sponsors. Projects include pharmacokinetic-pharmacodynamic modeling, quantitative systems pharmacology models, simulation-based trial design evaluations, disease progression and patient population modeling, model-based meta analysis of competitor data, model-based comparative effectiveness assessments, and data management activities, etc., all within a regulated environment. Analyses were conducted in R or via other software tools which are managed via R scripts, functions, or packages. Key deliverables of M&S projects are routinely provided as R packages or interactive simulation applications, driven by R (and R Shiny). R has also been an essential component of Metrum's vision for Open Science in biomedical M&S, allowing for accessibility and reproducibility of platform models developed for multiple disease areas.