# Krina Mehta, PhD

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- 15+ years in the biotech and pharmaceutical industry
- An experienced modeler with hands-on experience with a variety of modeling approaches, including population pharmacokinetic (PopPK) and pharmacodynamic (PopPKPD), exposure-response, physiologically based pharmacokinetic (PBPK), semi-mechanistic modeling, and quantitative systems pharmacology (QSP)
- Strong experience in oncology, infectious diseases, and rare diseases
- A technology enthusiast with hands-on experience using a variety of modeling and simulation tools, including, R, NONMEM, PK-Sim/Mobi, Simbiology, and Python.
- A pharmacist by background with strong skills for strategizing and implementing quantitative pharmacology approaches to support a variety of decision making in drug discovery and development
- A motivated and energetic leader, strong team player, and results-oriented scientist always looking to embrace innovative computational methods for data-driven decision making.

## Work Experience

**Kyowa Kirin Inc.**

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| Director, Pharmacometrics and Quantitative Pharmacology | Jan 2023 – Present |
| Associate Director, Pharmacometrics | June 2021 – Dec 2022 |
| Pharmacometrics Scientist (Contractor) | June 2020 – June 2021 |

- Collaborate with vendors and project teams to develop disease and modality mechanistic models, including acute myeloid leukemia (AML), immune-oncology (IO), and hematopoietic stem cell (HSC) gene therapy models to guide internal decision-making
- Participated in model-informed drug development strategy for two marketed drugs for regulatory submissions to support pediatric filing, indication expansion, and dosing change
- Developed and led execution of mechanistic modeling and simulation strategies for preclinical to clinical translation, IND filing, and early clinical development of several oncology therapeutics including using mechanistic approaches, i.e., bispecific antibodies, antibody-drug conjugates (ADCs), and small molecule protein degraders.
- As part of the clinical pharmacology leadership team, participated in cross-functional action plans, including process development and improvements, talent development, computer system validation, and review of numerous pharmacometric analysis plan and reports, clinical pharmacology development plans, and pre-IND briefing books.
- Provide guidance to the junior pharmacometrics team members, including two direct reports, and oversee vendors

**qPharmetra LLC.**

Associate Consultant, Pharmacometrics 2018 - 2020

- Provided pharmacometric consulting services to clients to inform various decisions in drug development, i.e., population M&S analyses, exposure-response analyses, non-compartmental analysis, and development of R shiny applications and submission ready reports.
- Key projects included a mechanistic combined PK/PD model building of an anti-FcRn receptor protein molecule, semi-mechanistic population PK (PopPK) and exposure-response (ER) analysis (tumor size, time to disease progression, adverse events) modeling of an ADC, and PopPK and ER (tumor size, overall response rate, progression free survival, and adverse events) modeling of a small molecule oncology drug leading to BLA filing and approval.

**Independent Contractor**

Pharmacometrician 2016 - 2018

- Halozyme Therapeutics Inc: Developed an R shiny application for simulations for subcutaneous absorption model of drugs of interest when administered with or without ENHANZE® platform; Performed miscellaneous modeling and simulation projects to inform decisions, i.e. conducted population PK modeling and simulations from preclinical data to inform FIH and clinical study design for subcutaneous route of administration of a large molecule, conducted prediction of QTc potential for a protein molecule based on a PK/PD model
- Center for Translational Medicine at University of Maryland: Delivered training modules on PBPK modeling; Conducted PBPK modeling and simulations-based drug-drug interaction (DDI) simulations to support regulatory filing of a small molecule.
- Alexion Pharmaceuticals Inc.: Conducted a population target-mediated drug disposition (TMDD) modeling for a bispecific monoclonal antibody for FIH dose selection. Conducted a PopPK analysis to simulate pediatrics profiles to inform pediatric filing.

**Genentech Inc.**

Regulatory Documentation Scientist (Contractor) 2010 - 2016

- Project managed and wrote a variety of clinical and nonclinical regulatory documents, including study protocols, investigator's brochures, periodic safety update reports, and clinical study reports.
- Collaborated in cross-functional teams to support regulatory submissions to the FDA and EMA.

**Lifescan Inc.,** 2007 - 2009

Medical Device Safety Associate

- Managed patient and providers complaints regarding blood sugar monitoring devices
- Prepared safety narratives and periodic safety regulatory submissions to the FDA and EMA.

## Education

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| Doctor of Philosophy (PhD), Quantitative Pharmacology | 2021 – May 2024 |
| Leiden University, The Netherlands | |
| Master of Science (MS), Pharmacometrics | 2015 – 2017 |
| University of Maryland, USA | |
| Bachelor of Pharmacy (BPharm) | 2001 – 2004 |
| Saurashtra University, India | |

## Professional Development Courses and Workshops

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| Python for Machine Learning, LinkedIn Learning Certificate | 2024 |
| Parameter Estimation with Simbiology, Mathworks | 2024 |
| PK/PD Modeling in Pumas Workshop, Pumas AI | 2022 |
| Protein Therapeutics PK/PD Modeling Workshop, University of Buffalo | 2019 |
| Systems Biology Certificate, Icahn School of Medicine through Coursera | 2018 |
| PK/PD Modeling Workshop, University of Buffalo | 2018 |
| PBPK Modeling, Kansas State University | 2017 |
| Advanced methods for NONMEM Workshop, Uppsala Pharmacometrics | 2017 |
| PBPK Modeling Using Gastroplus, Simulations Plus | 2016 |
| American Medical Writers Association Certificate | 2011 |
| Regulatory Affairs Professional Certificate | 2009 |

## Volunteer Positions

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| Communications Director on International Society of Pharmacometrics QSP special interest group leadership team | 2024 – Present |
| American conference of pharmacometrics planning – alumni committee | 2019 – 2021 |
| Peer reviewer on several occasions for various journals and conferences | 2020 – Present |

## Conference Presentations

Mehta K, et al. Leveraging QSP to Shape the Strategy for Early Phase Clinical Development in Immuno-Oncology. Invited oral presentation at QSP Summit May 2024, Boston, USA

## Journal Publications

Hruska, M.W., Sid-Otmane, L., Gosselin, N.H., Quattrocchi, E., Lee, S.K., Mascelli, M.A., Mehta, K, Jan de Beur, S.M. and Marsteller, D. (2024), Model-Informed Approach to Recommend Burosumab Dosing Regimens for Pediatric and Adult Patients With the Ultrarare Disease Tumor-Induced Osteomalacia. Clin Pharmacol Ther. https://doi.org/10.1002/cpt.3468

Mehta K, Storopoli J, Ramwani N, Quattrocchi E, Gobburu J, Weber T, Hruska M, Marsteller D, Pharmacodynamic Exposure–Response Analysis of Fracture Count Data Following Treatment with Burosumab in Patients with XLH. (2024) J Clin Pharm. https://doi.org/10.1002/jcph.6140

Mehta, K., Gosselin, N.H., Insogna, K., Barriere, O., Quattrocchi, E., Hruska, M.W. and Marsteller, D. (2024), Item Response Theory Quantifies the Relationship Between Improvements in Serum Phosphate and Patient-Reported Outcomes in Adults With X-Linked Hypophosphatemia. (2024) Clin Pharmacol Ther. https://doi.org/10.1002/cpt.3406

Mehta, K, Balazki P, van der Graaf, PH, Guo, T,van Hasselt, JGC. Predictions of bedaquiline central nervous system exposure in tuberculosis meningitis patients using physiologically-based pharmacokinetic modeling. Clin Pharmacokinet (2024). https://doi.org/10.1007/s40262-024-01363-6

Mehta, K, Guo, T, van der Graaf, PH, van Hasselt, JGC. Model-based dose optimization framework for bedaquiline, pretomanid and linezolid for the treatment of drug-resistant tuberculosis. Br J Clin Pharmacol. 2023; 1-12. doi:10.1111/bcp.15925

Mehta, K., Guo, T., van der Graaf, P.H. et al. Predictions of Bedaquiline and Pretomanid Target Attainment in Lung Lesions of Tuberculosis Patients using Translational Minimal Physiologically Based Pharmacokinetic Modeling. Clin Pharmacokinet 62, 519–532 (2023). https://doi.org/10.1007/s40262-023-01217-7.

Mehta K, Narayanan N, Heysell SK, Bisson GP, Subbian S, Kurepina N, Kreiswirth BN, Vinnard C. Pharmacogenetic variability and the probability of site of action target attainment during tuberculosis meningitis treatment: A physiologically based pharmacokinetic modeling and simulations study. Tuberculosis (Edinb). 2022 Dec;137:102271. doi: 0.1016/j.tube.2022.102271.

Mehta K, Guo T, Wallis RS, van der Graaf PH, van Hasselt JGC. Quantitative Systems Pharmacology Modeling Framework of Autophagy in Tuberculosis: Application to Adjunctive Metformin Host-Directed Therapy. Antimicrob Agents Chemother. 2022 Aug 16;66(8):e0036622. doi: 10.1128/aac.00366-22.

Mehta K, Spaink HP, Ottenhoff THM, van der Graaf PH, van Hasselt JGC. Host-directed therapies for tuberculosis: quantitative systems pharmacology approaches. Trends Pharmacol Sci. 2022 Apr;43(4):293-304. doi: 10.1016/j.tips.2021.11.016.

Oni-Orisan, A., Srinivas, N., Mehta, K., Das, J.L., Nguyen, T.T., Tison, G.H., Bauer, S.R., Burian, M., Funk, R.S., Graham, R.A. and (2021), Leveraging innovative technology to generate drug response phenotypes for the advancement of biomarker-driven precision dosing. Clin Transl Sci, 14: 784-790. https://doi.org/10.1111/cts.12973

Mehta K, Ravimohan S, Pasipanodya J, et al. (2019). Optimizing ethambutol dosing among HIV/tuberculosis co-infected patients: a population pharmacokinetic modelling and simulation study. The Journal of antimicrobial chemotherapy. https://doi.org/10.1093/jac/dkz265

## Posters

Takaichi D, Gewitz A, Okada H, Mehta K, Hosogi J, Nagata Y, Utsey K, Riggs M. Quantitative Systems Pharmacology Modeling of X-linked Hypophosphatemia Disease Pathway Normalization to Predict the Impact of Burosumab Treatment on Serum Biomarkers in Adult and Pediatric Patients. Poster presented at ACoP. 2024. https://acop2024.eventscribe.net/fsPopup.asp?PosterID=690782&mode=posterInfo.

Vupugalla R, Mehta K, Debir B, Kierzek A, Takada H, Adachi M, Ishida H, Ando M, Kierzek A, Debir B, Marsteller D, Hruska M. Development of a Pharmacokinetic-Tumor Target Engagement Model Using Nonclinical Data to Inform Phase 1 Dosing Scheme for a Novel Bispecific CD40-EpCAM Antibody, KK2269. Poster Number: 087, Presented at American College of Clinical Pharmacology Annual Meeting. September 2024. Poster Number 087. https://accp1.org/pdfs/documents/annualmeeting/2024/CPDDv13iS1AbstractBooklet.pdf

Mehta K, Storopoli J, Ramwani N, Quattrocchi E, Gobburu J, Weber T, Hruska M, Marsteller D, Pharmacodynamic Exposure–Response Analysis of Fracture Count Data Following Treatment with Burosumab in Patients with XLH. Poster presented at ACoP. 2023

Mehta K, Barriere O, Gosselin NH, et al., Burosumab treatment-induced increases in serum phosphate provide improvements in patient reported outcomes in adults with x-linked hypophosphatemia as assessed with graded item response analysis. Poster presented at ACoP. 2022

Mehta K, Patel D, Vupugalla R, et al., Rationale for the clinical use of less frequent dosing of mogamulizumab for T-cell lymphomas using population pharmacokinetic and exposure response analysis. Poster presentation at American Society of Hematology 2021 Conference. Abstract 2475 Dec 12, 2021. https://doi.org/10.1182/blood-2021-148099

Mehta K, Koshiba S, Hasegawa M, et al., Population pharmacokinetic-pharmacodynamic analysis of KHK2455 in patients with locally advanced or metastatic solid tumors. Abstract 1368. Poster presented at AACR 2021, July 01, 2021. https://doi.org/10.1158/1538-7445.AM2021-1368

Mehta K and Vinnard C. Impact of SLCO1B1 genotype and single nucleotide polymorphism on rifampin pharmacokinetics using linkage analysis and physiologically based pharmacokinetic (PBPK) modeling approach. Poster presented at ACoP10, October 2019.