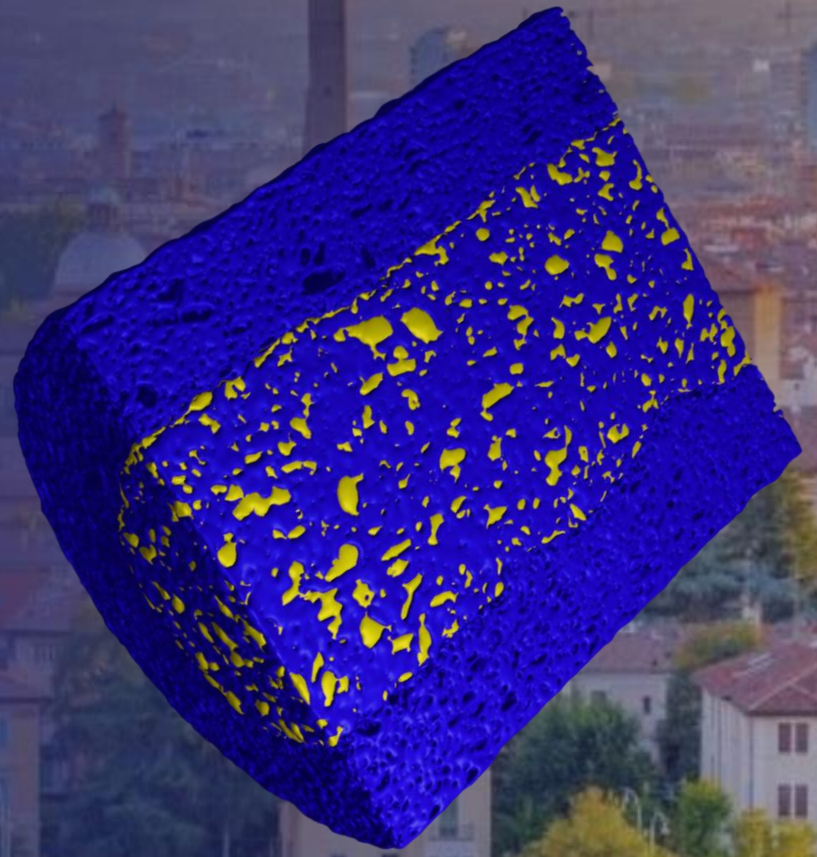
Digital Formulation of Ocular Implants: *In Silico* Release Predictions and Microstructure Synthesis of Drug Particle Networks



Innovation Showcase
July 9th, 2024

Joshua Lomeo
digiM solution

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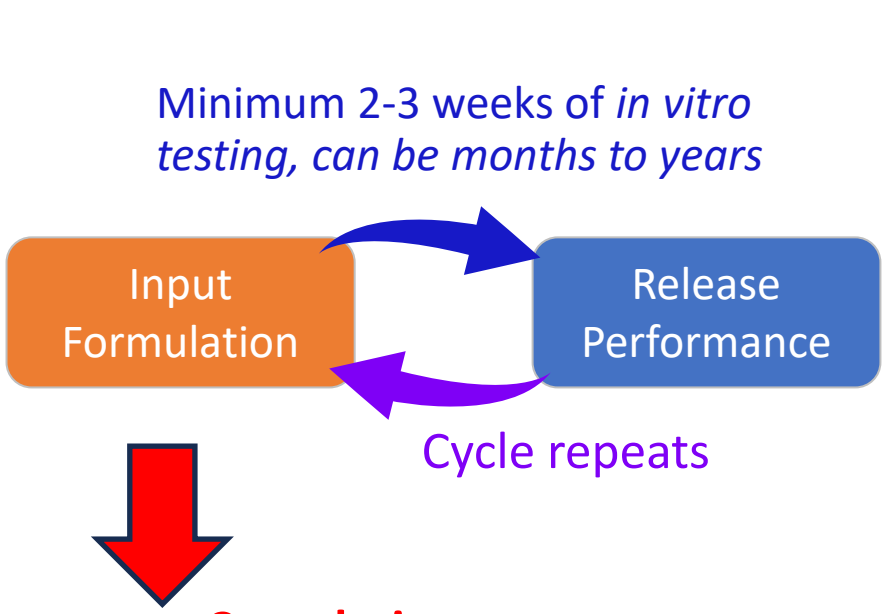
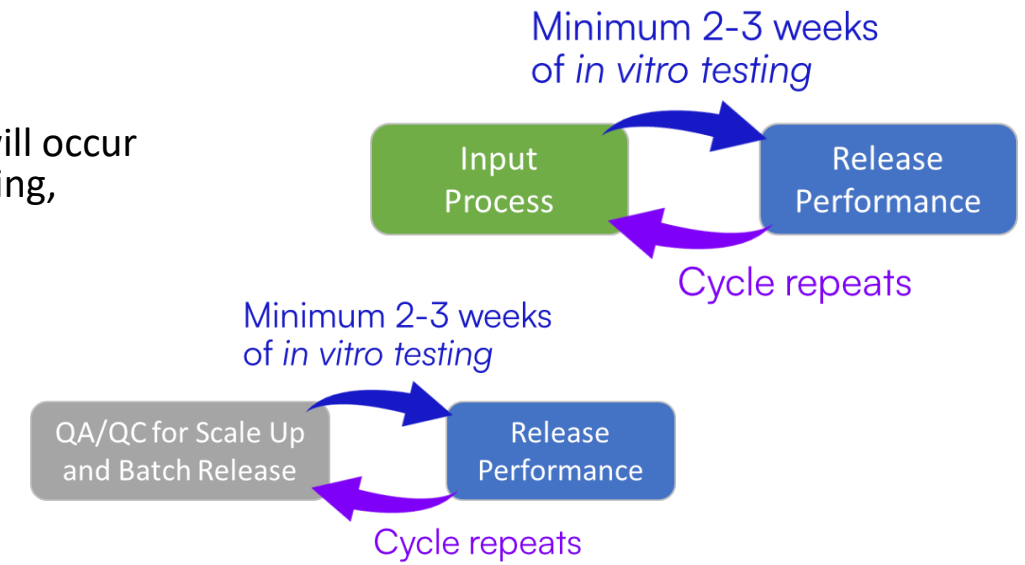
The Challenge with Traditional Approaches to Controlled and Long-acting Development

Conventional: Guessing the product's formulation and process to performance took 5+ years of trial and error.



Cumulative cost
months to years of iterative development

Similar cycles will occur for manufacturing, QA/QC, IVIVC



Total Program Costs – 5+ years with likely bottle necks in material availability, CDMO tech transfers, IVIVC, and performance variability

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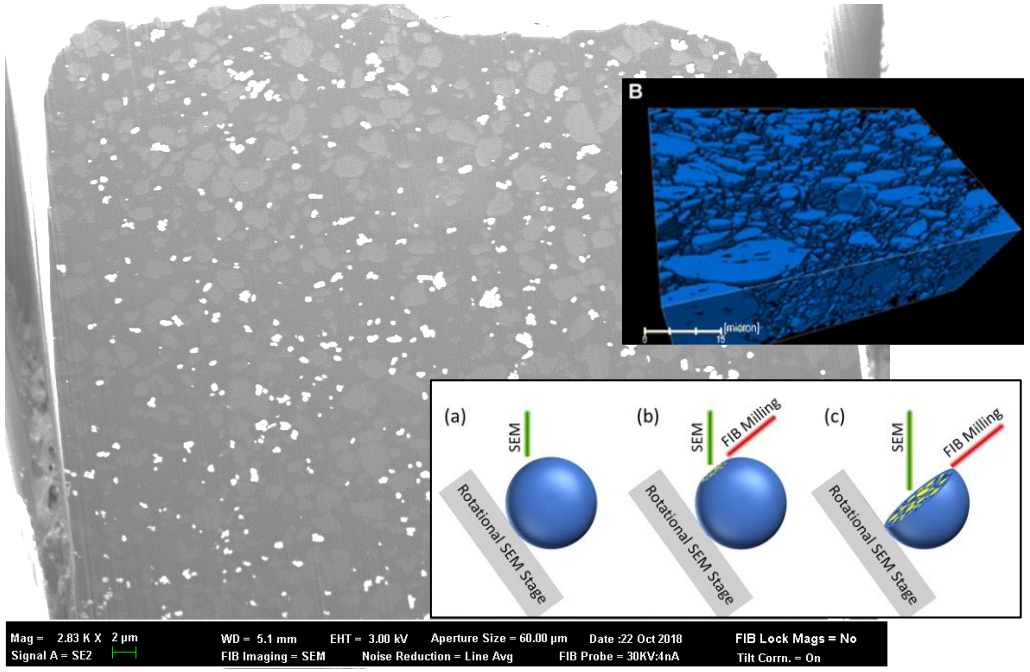
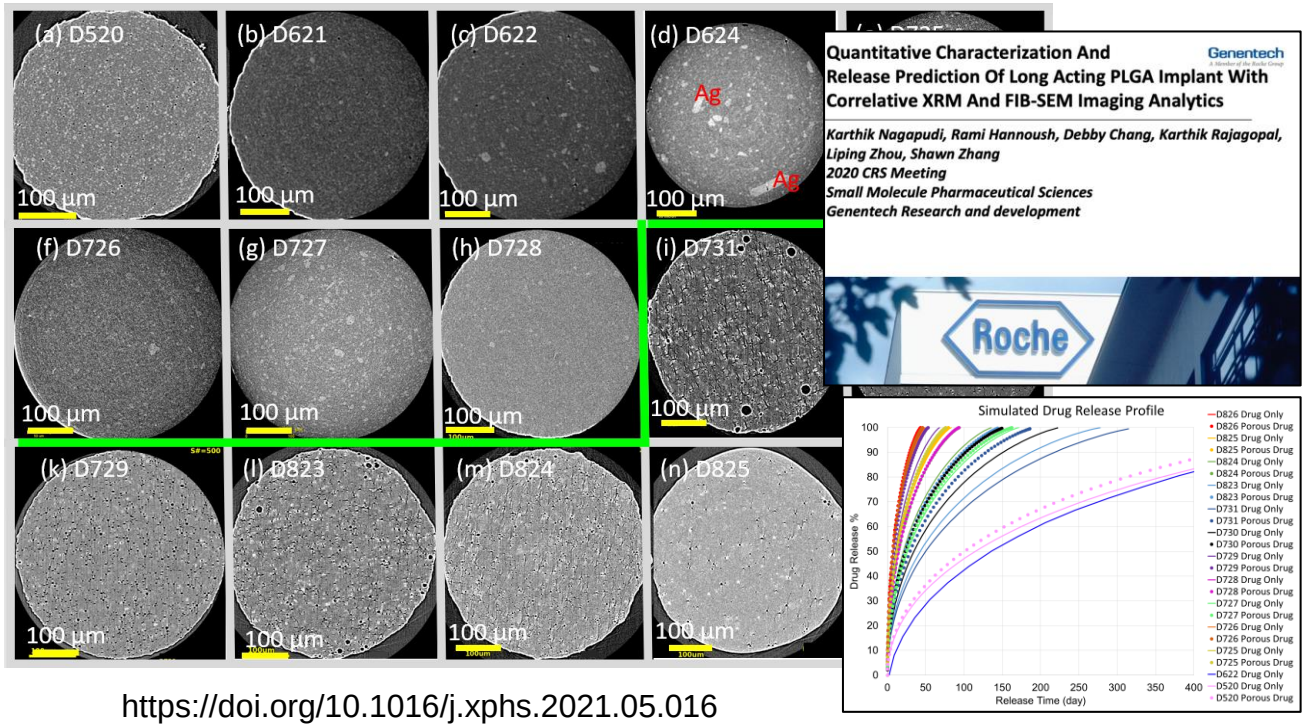
Innovation #1 – Quantitative Analysis of Drug Particle Networks with 3D FIB-SEM and micro-CT

Workflows that supported development of MK-8591 HIV-1 inhibitor EVA implant and Genentech ocular implant



https://doi.org/10.1007/s11095-021-03145-2



https://doi.org/10.1016/j.xphs.2021.05.016

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Innovation #2 – Image-based Simulation of Release Profiles from Drug Particle Networks

Simulation performed blindfold from *in vitro* release performance

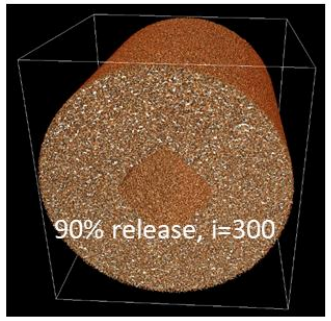
Voxel based approach integrates representativeness, computational cost, and accuracy.

External inputs for simulation:

- Bulk diffusion coefficient
- Drug load
- Drug solubility
- Implant diameter

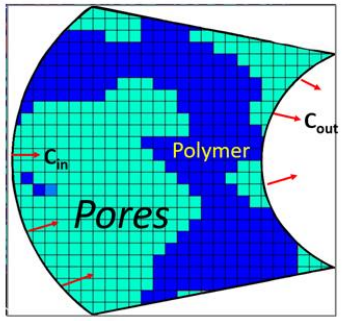
a. Percolation Simulation

Drug Release at Each Step



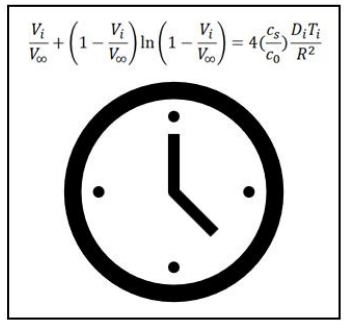
b. Effective Diffusivity

Dynamic Fick's Diffusion

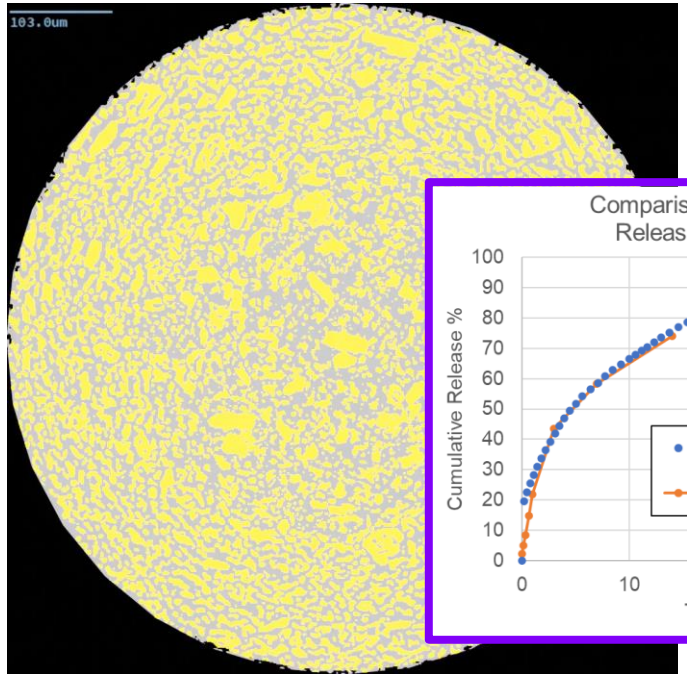


c. Time Conversion

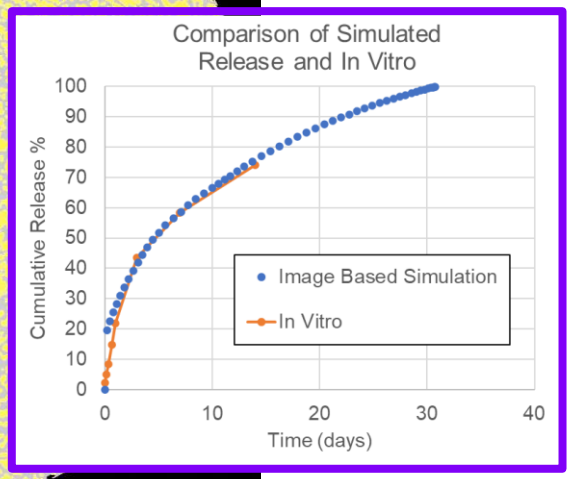
$$\frac{V_i}{V_\infty} + \left(1 - \frac{V_i}{V_\infty}\right)\ln\left(1 - \frac{V_i}{V_\infty}\right) = 4\left(\frac{c_s}{c_0}\right)\frac{D_i T_i}{R^2}$$



Patent US20190108322A1



With Purdue and Eli Lilly
https://doi.org/10.1016/j.jconrel.2023.05.049



Erosion and diffusion models

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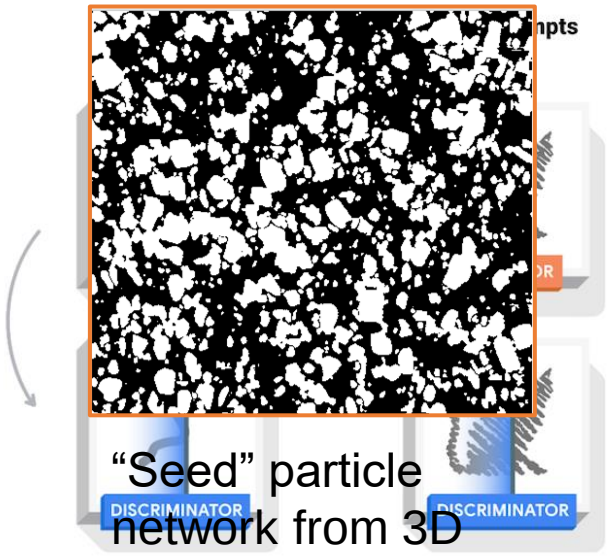
Innovation #3 – Generative Synthesis of New Microstructures for Digital Formulation

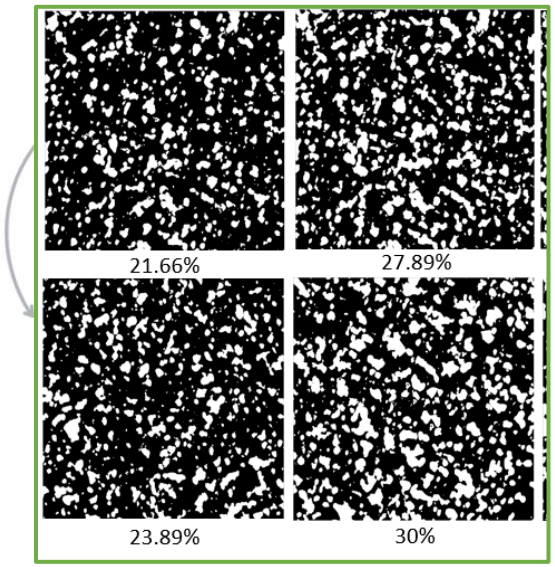
Technology Implements Controlled Changes on Microstructure While Fixing the Other Microstructure Variables

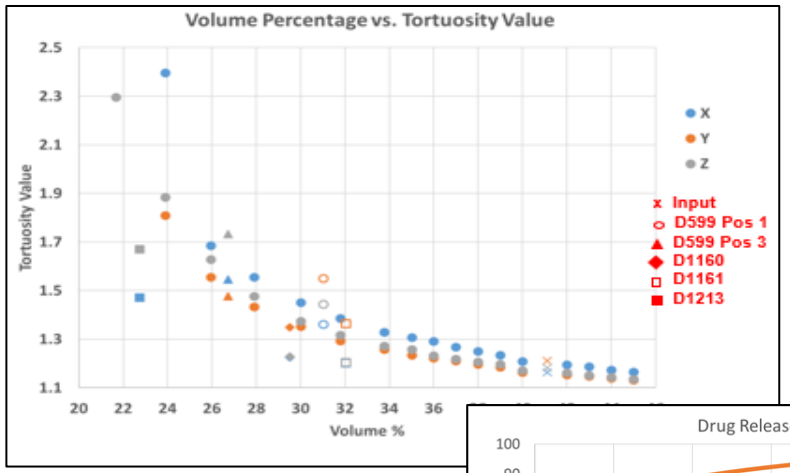


"Seed" particle network from 3D FIB-SEM at X_0% DL and $D_{50}=Y_0$

Patent Pending

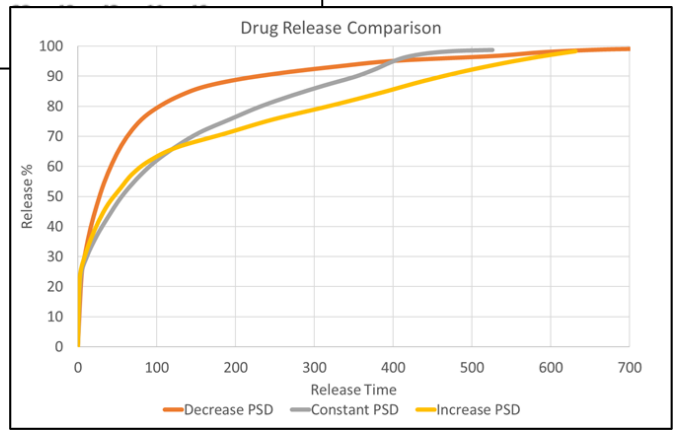
Synthesized networks with modified drug load





Fine tuning the digital formulation parameter space: Percolation threshold is found to occur at ~25%wt drug loading

Determining the optimal micronization size



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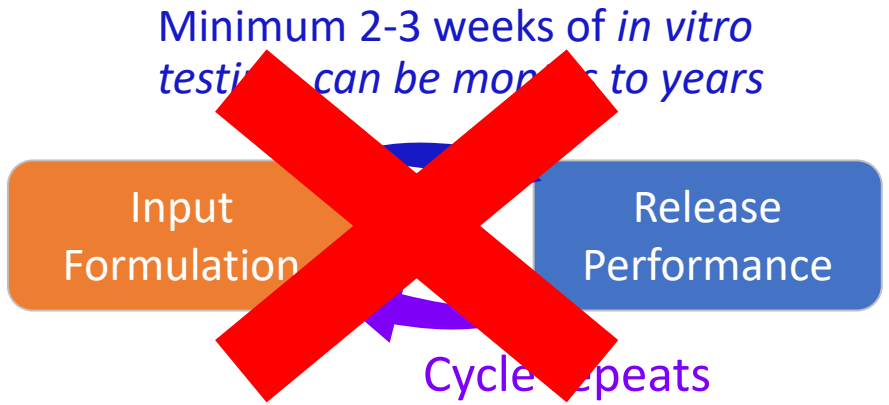
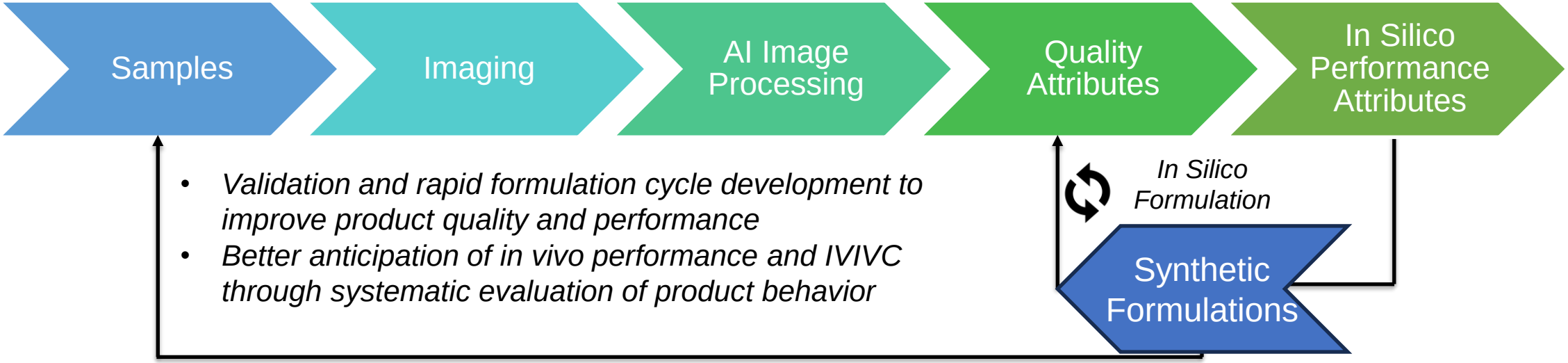


Stepping away from endless and long formulation development cycles



- *Validation and rapid formulation cycle development to improve product quality and performance*
- *Better anticipation of in vivo performance and IVIVC through systematic evaluation of product behavior*

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Questions?

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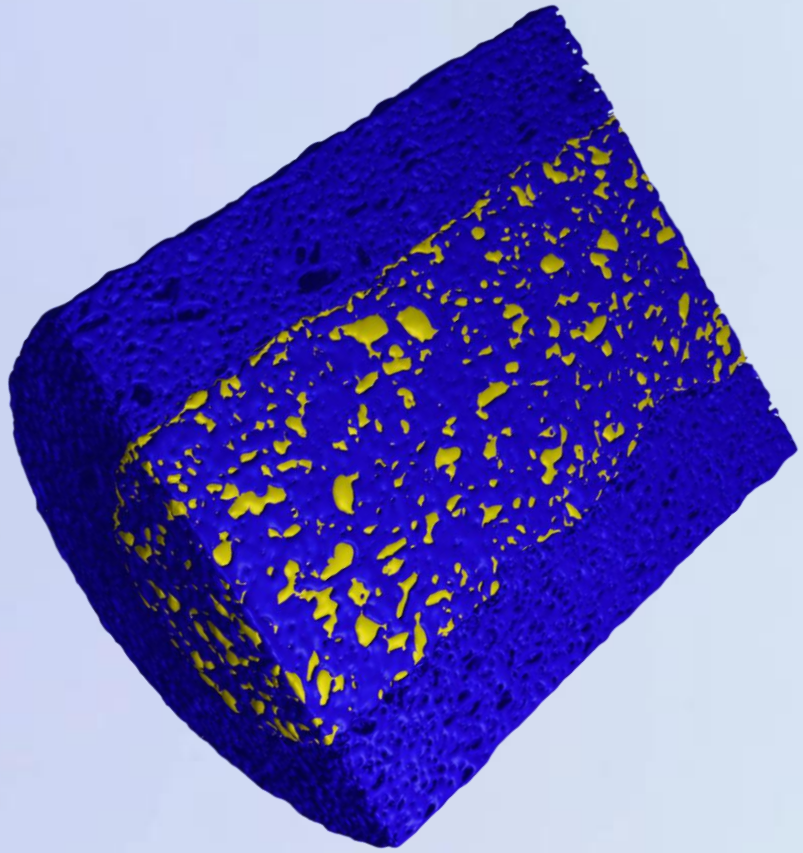
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