Software and Service Offerings
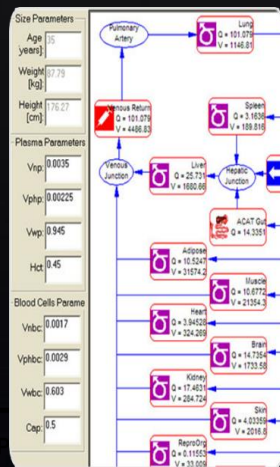
Saying "I do" to the
Machine Learning / PBPK / QST(P) marriage...
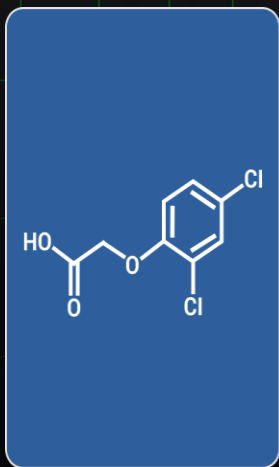
ADMET Predictor™

Permeability,
solubility vs. pH,
pKa(s),
logD vs. pH,
Fup,
blood:plasma
ratio, tissue Kps,
CLint, CLfilt

GastroPlus™

Local/systemic
exposure,
distribution,
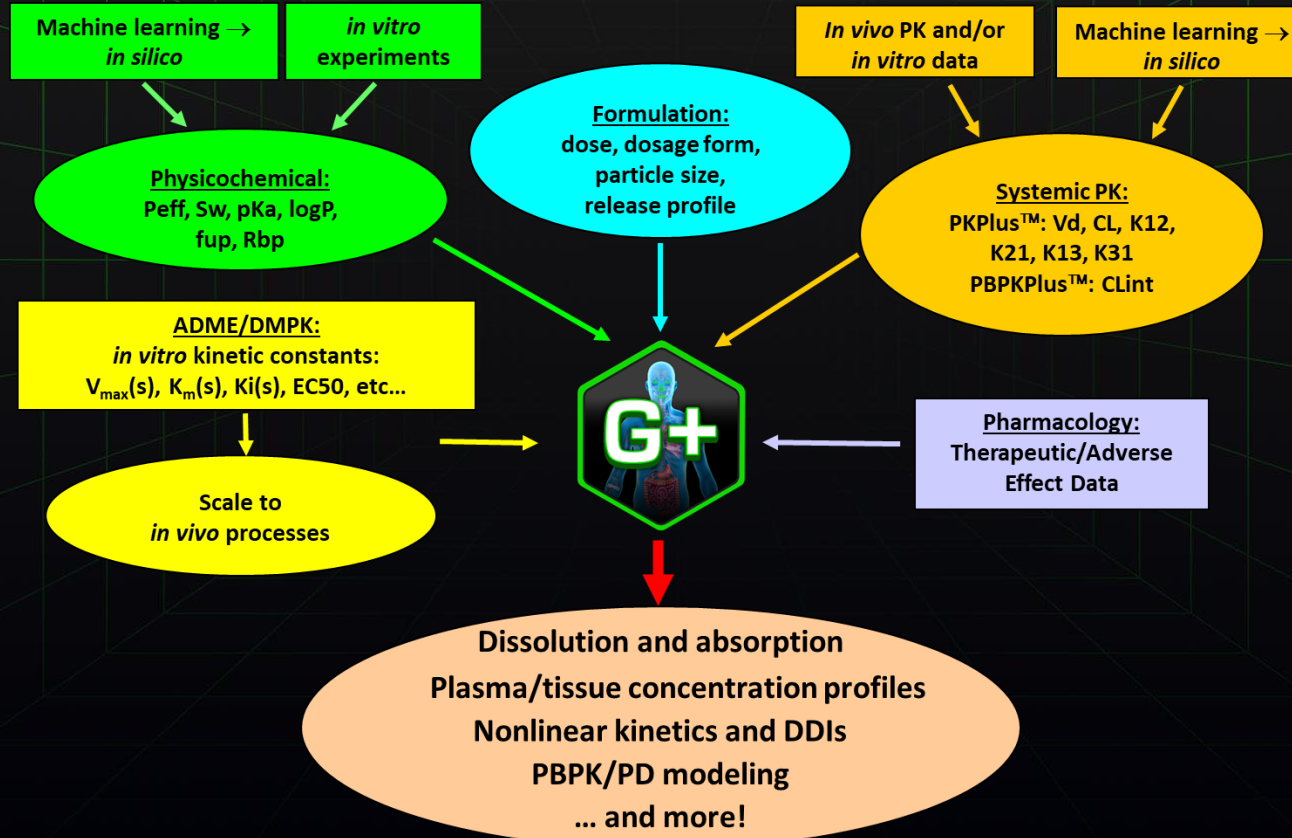parent/metabolite
levels,
patient variability

RENAsym™   DILIsym™

IPFsym™   NAFLDsym™
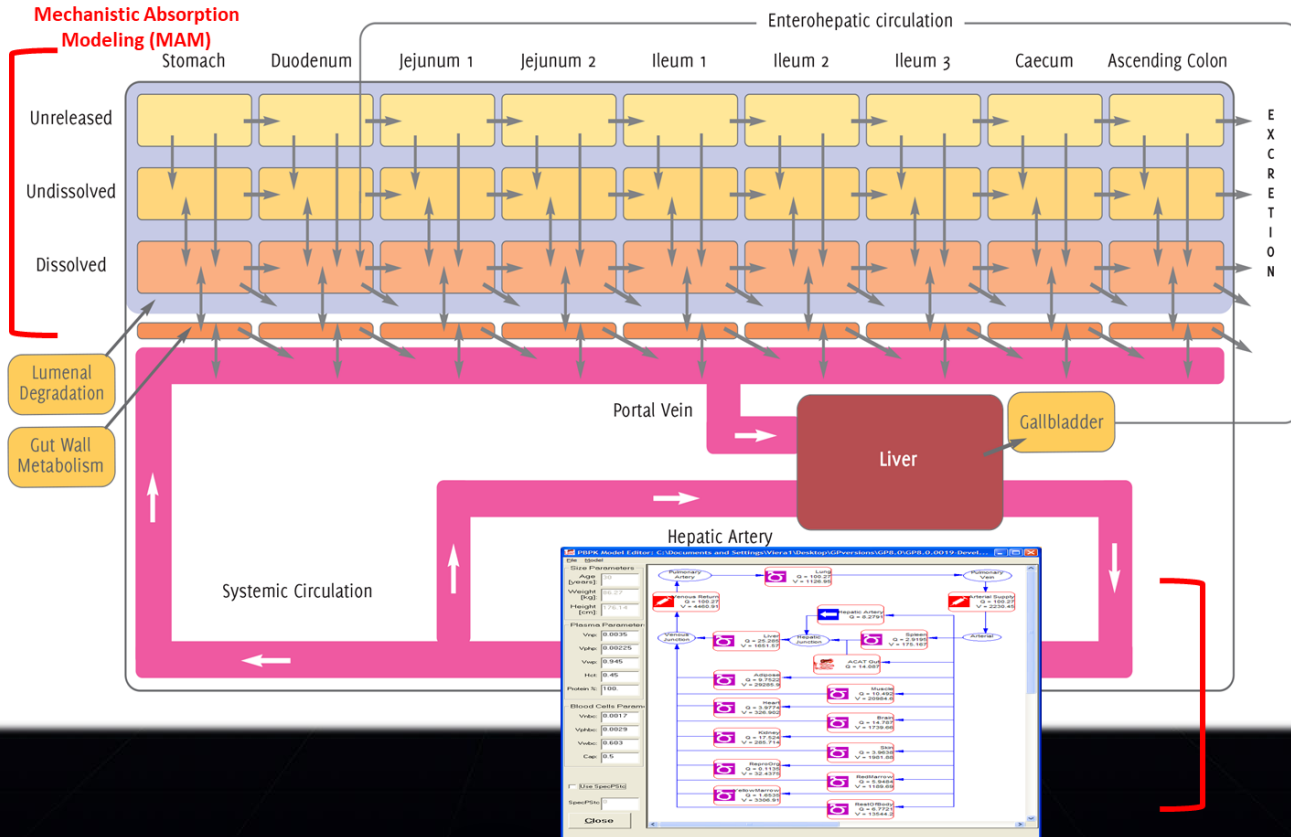
S+ SimulationsPlus
SCIENCE + SOFTWARE = SUCCESS

The Big Picture – Drug Inputs

Advanced Compartmental Absorption and Transit Model (ACAT™)

Mechanistic Absorption Modeling (MAM)

Enterohepatic circulation

| | Stomach | Duodenum | Jejunum 1 | Jejunum 2 | Ileum 1 | Ileum 2 | Ileum 3 | Caecum | Ascending Colon |

Unreleased

Undissolved

Dissolved

E X C R E T I O N

Lumenal Degradation

Gut Wall Metabolism

Portal Vein

Liver

Gallbladder

Hepatic Artery

Systemic Circulation

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Physiologically based Pharmacokinetics (PBPK)

Pulmonary

Ocular

Intra-muscular

Dermal

Intra-articular

Oral Cavity

Quantitative Systems Pharmacology/Toxicology (QSP/QST)

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Areas of Consulting Support

15 Clinical development plans based on pre-clinical PBPK models, de-risk analysis

14 Formulation selections based on pre-clinical PBPK models, de-risk analysis

10 DDI studies designed and biowaiver plans based on PBBK models, de-risk analysis

Preclinical	Clinical	Post Approval

FIH

Formulation Optimization

DDI

Drug Product Specifications

Special Populations/Dose Projections

PPI/Food Effects

CMC Changes/Oral BE

CMC Changes/Complex BE
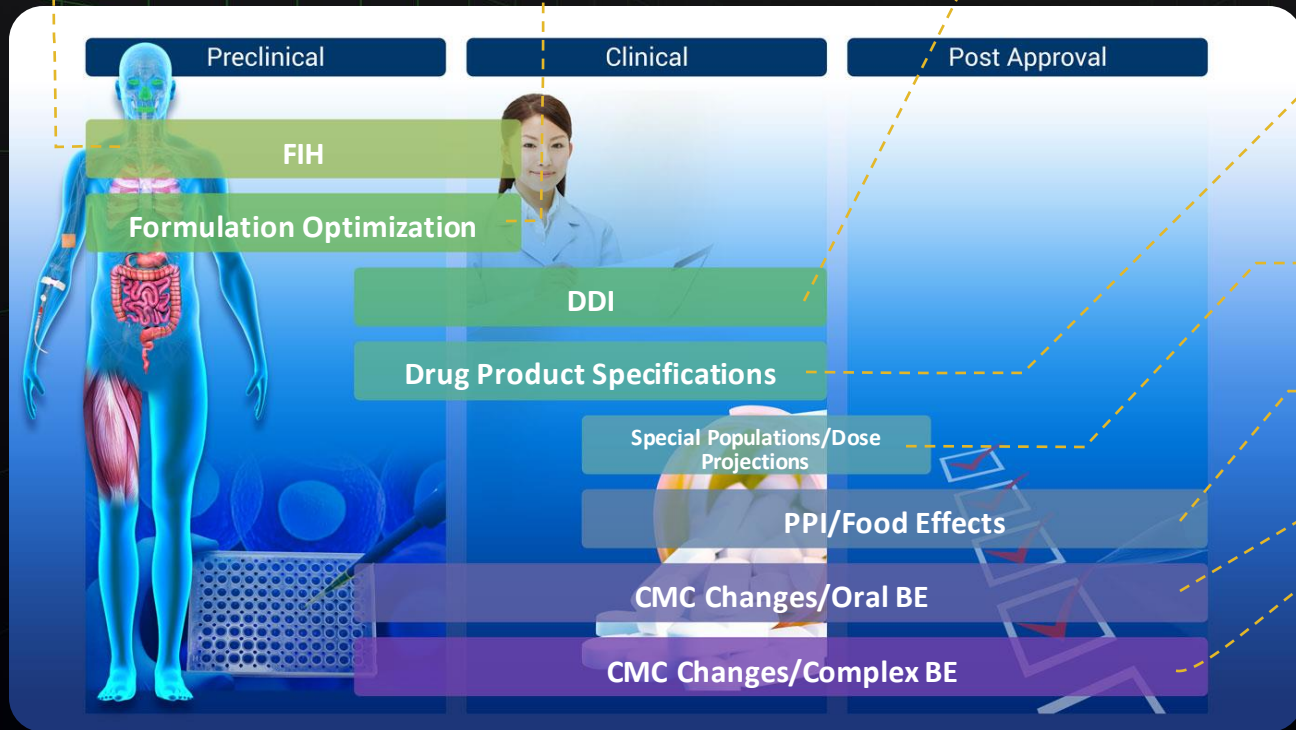
8
- Development of biopredictive dissolution methods
- Establish clinically relevant drug product specifications based on mechanistic IVIVR/IVIVC and de-risk analysis

8 Study design and biowaiver plans based on PBBM

9 Design studies and biowaiver plans based on PBBM

5 Design of BE studies and biowaiver plans for oral/non-oral route of administration based on PBBM

Numbers reflect the number of projects received in 2020

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Regulatory Scientists Trained on GastroPlus® PBBM/PBPK Modeling Software

Recent Approved Drug Product Applications

- ALECENSA® (**absorption/PPI DDI** informing drug labeling)
- BRAFTOVI® (**metabolism DDI** accepted by regulatory agencies)
- CALQUENCE® (**particle size specs** accepted by regulatory agencies)
- FARYDAK® (**food effect/PPI predictions** informing drug labeling)
- INLYTA® (**transporter DDI** accepted by regulatory agencies)
- KISQALI® (**gastric pH predictions** accepted by regulatory agencies)
- MEKINIST® (**transporter DDI** accepted by regulatory agencies)
- MEKTOVI® (**metabolism DDI** accepted by regulatory agencies)
- OPSUMIT® (**particle size specs** accepted by regulatory agencies)
- TAMIFLU® (**pediatric** PBPK predictions informing **dose selection**)
- ZURAMPIC® (**wider product specs** accepted by regulatory agencies)
- … and more!

No other PBBM/PBPK platform has the diversity in applications!

Thank you! Questions?

See you Stand 3 ☺