BMS Clinical Pharmacology and Pharmacometric Networking Event at ASCPT

ASCPT Micro-Learning

Tunde Bello, Bindu Murthy, Li Zhu, Anna Kondic, Neelima Thanneer, and Brian Schmidt

Wednesday July 12th 2023

Bristol Myers Squibb™

Clinical Pharmacology, Pharmacometrics, Disposition & Bioanalysis

Akintunde (Tunde) Bello
Senior Vice President
Head of CPPDB

Sandra McVicar
Executive Associate II

Bindu Murthy
Executive Director
Head of Clinical Pharmacology
ICVNS

Neelima Thanneer
Executive Director
Head of Data Science &
Clinical Pharmacology
Analysis & Reporting

Vibha Jawa
Executive Director
Biotherapeutic
Bioanalysis

Li Zhu
Executive Director
Head of Clinical Pharmacology
HOCT

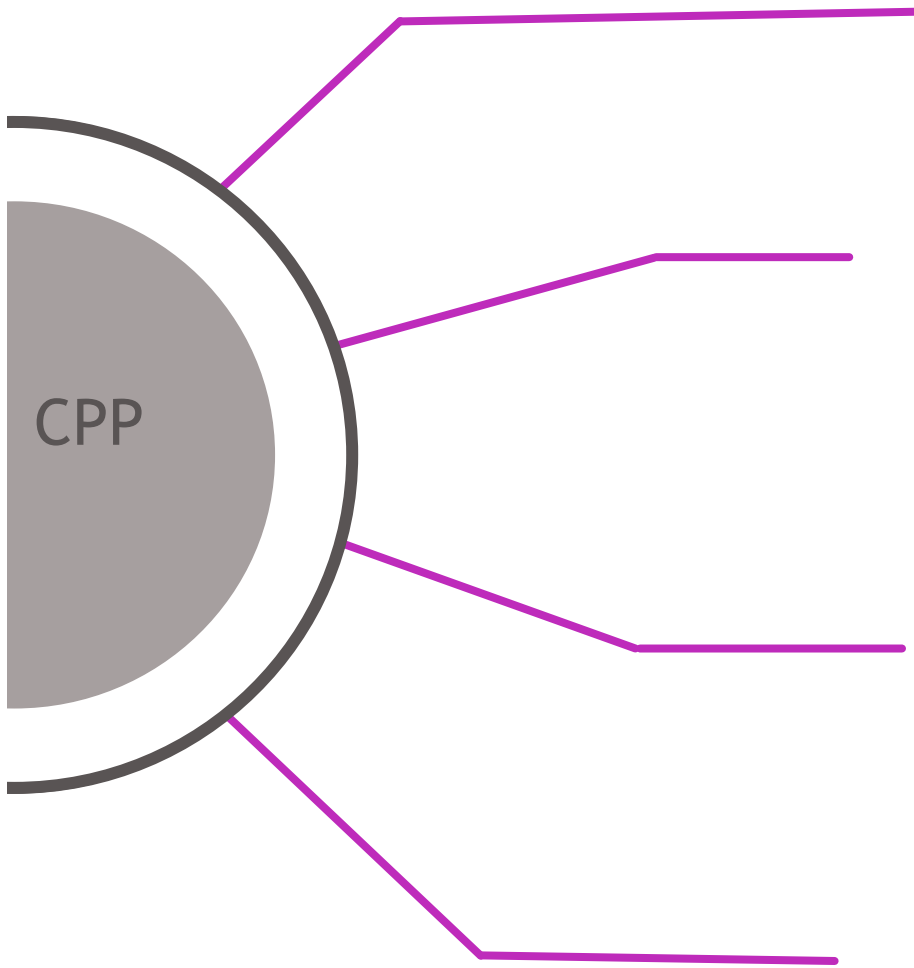
Brian Schmidt
Executive Director
Head of Mechanistic Modeling
(QSP &PBPK)

Jim Shen
Executive Director Head of
Regulated Bioanalysis (BA)
Operations

Ann Kondic
Executive Director
Head of Pharmacometrics

Matthew Hoffman
Senior Director Development
Biotransformation

CPP Groups & Functions



Clinical Pharmacology (ICVN & HOCT)

Bindu Murthy & Li Zhu

- Support early/late-stage dev programs
- Design & execute clin pharm strategy

Pharmacometrics (PMx)

Anna Kondic

- Perform/oversee Pmx analyses for submissions
- Oversee PMx modeling infrastructure and best practices

Clin Pharm Analysis & Reporting & Data Science

Neelima Thanneer

- NCA for clinical trials & regulatory submissions
  - Clin pharm sections to protocols and CSR's
- Programmers Integrate clinical trial & PK data for pop PK & PK/PD analyses

Mechanistic Modeling (QSP & PBPK)

Brian Schmidt

- Perform modeling activities to support early & late-stage programs

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Clinical Pharmacology & Pharmacometrics

Introduction & Overview of ICVN

July 2023

Bindu Murthy, PharmD, MS
ASCPT Microlearning Event

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ICVN Portfolio Consists of 3 Therapeutic Area Pillars Targeting a Broad Range of Novel Mechanisms & Modalities to Treat Disease with High Unmet Medical Need

Redefine standard of care

Build Industry-Leading Pipeline

ICVN Clinical Pharmacology & Pharmacometrics

Immunology

- Dermatology
- Rheumatology
- Irritable Bowel Disease
- Pulmonary

Cardiovascular

- Arterial Thrombosis & Embolism
- Heart Failure
- Cardiomyopathies

Neurosciences

- Multiple Sclerosis
- Alzheimers
- Neurodegenerative Diseases

ONCE-DAILY SOTYKTU™ (deucravacitinib) 6 mg tablets

ORENCIA® (abatacept) Injection for Intravenous Use Injection for Subcutaneous Use

once-daily ZEPOSIA™ (ozanimod) 0.92 mg capsules

LPA1

Eliquis® (apixaban) tablets

FXIa milvexian Collaboration

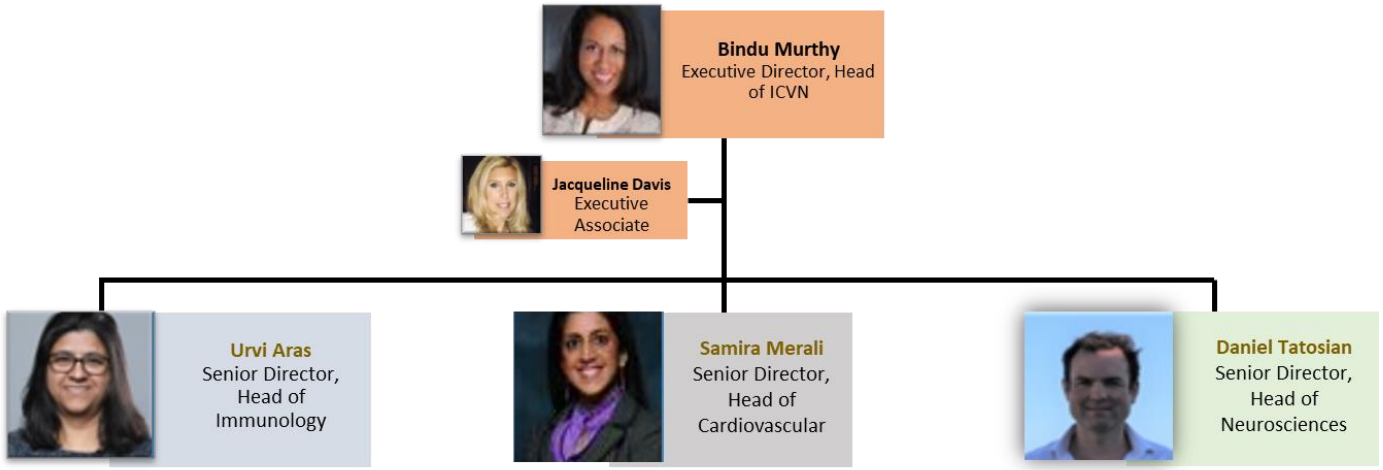
CAMZYOS™ (mavacamten) capsules

once-daily ZEPOSIA™ (ozanimod) 0.92 mg capsules

Novel Mechanisms

Join the ICVN Clinical Pharmacology & Pharmacometrics Community at Bristol Myers Squibb

Meet the Leadership Team



Mission: Design fit-for-purpose Clinical Pharmacology plan & Execute through a combination of innovative clinical studies & Quantitative Analysis Approaches to inform drug development decisions

Meet the Passionate Scientists

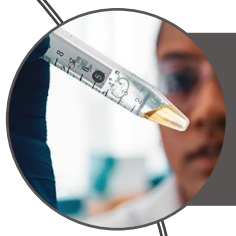
Clinical Pharmacology and Pharmacometrics

Hematology Oncology and Cell Therapy

Our Mission

To improve patient care by providing quantitative clinical pharmacology and drug development expertise to innovate breakthrough therapeutics that will help cancer patients

Our Deliverables

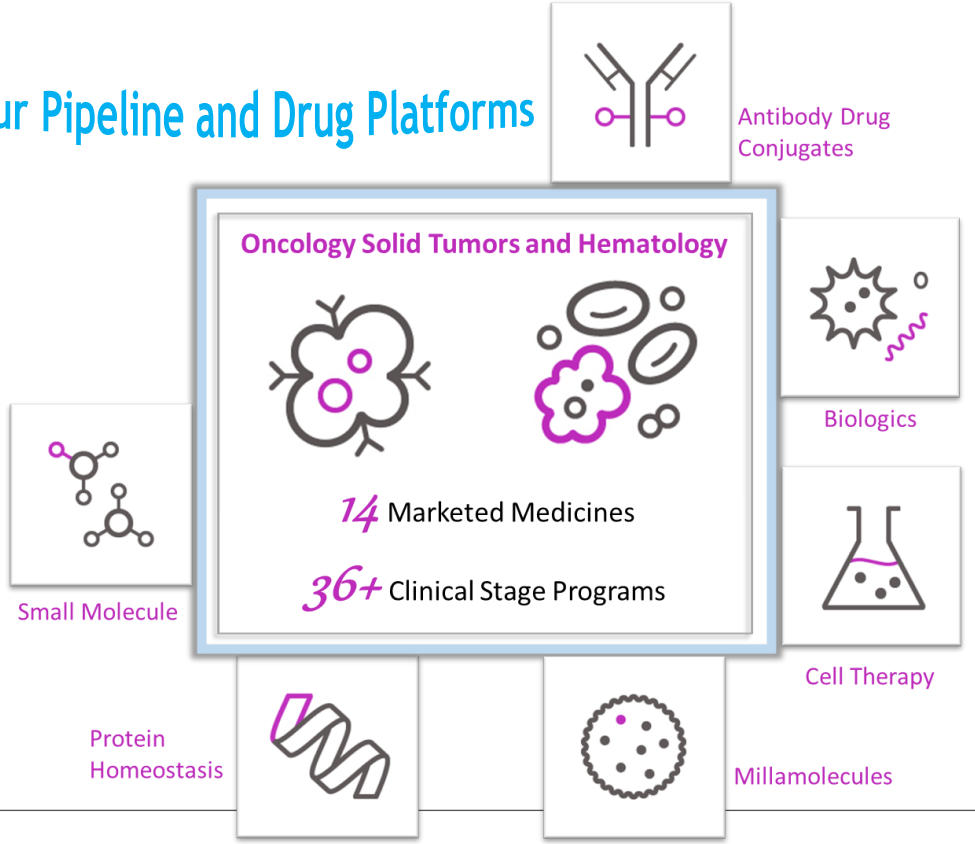


Phase I/II: Integrated PK, PK/PD and QSP modeling to support MoA and POC Go/No-Go decisions

Phase III: Comprehensive E-R analyses enable optimal dose selection and pivotal study design

Filing: Robust clin pharm package to support favorable benefit/risk assessment at the filing and during life cycle management

Our Pipeline and Drug Platforms



2023 ASCO ANNUAL MEETING

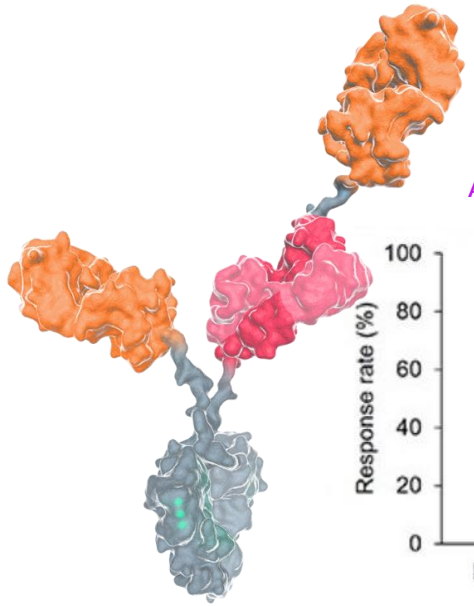
BMS presence by the numbers

106 Total Disclosures

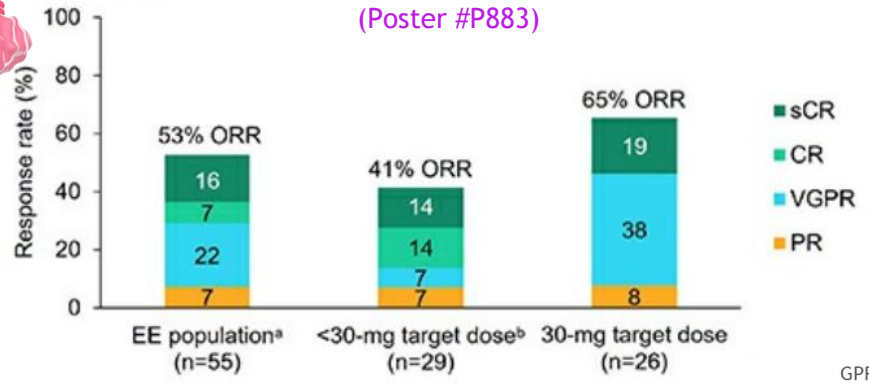
18 Orals
- 6 BMS
- 11 ISRs
- 1 Collaboration

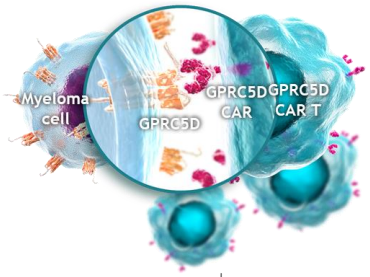
65 Posters
13 Poster Discussions
- 23 BMS
- 41 ISRs
- 14 Collaborations

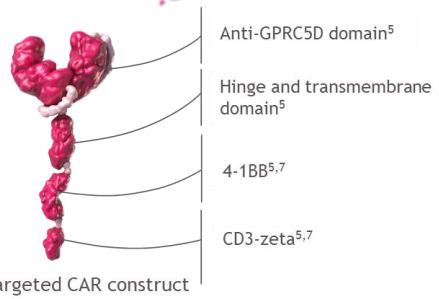
10 Abstract only Publications
- 4 BMS
- 4 ISRs
- 2 Collaborations



ALNUCTAMAB, A BCMA × CD3 T-CELL ENGAGER FOR RELAPSED/REFRACTORY MULTIPLE MYELOMA (Poster #P883)

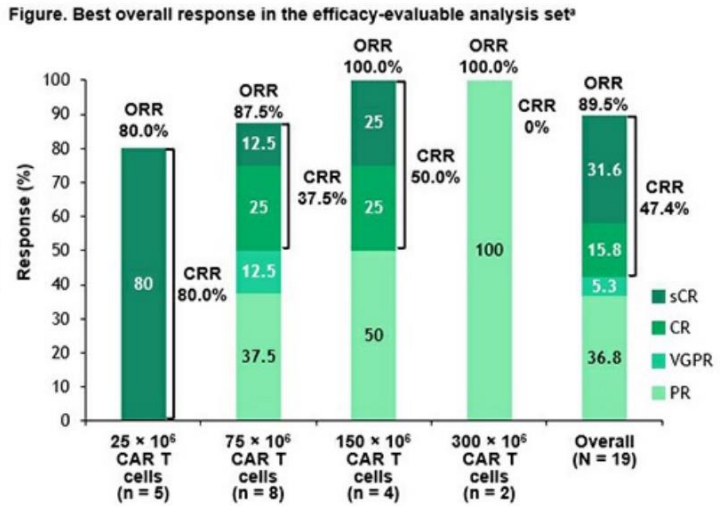






GPRC5D-targeted CAR construct

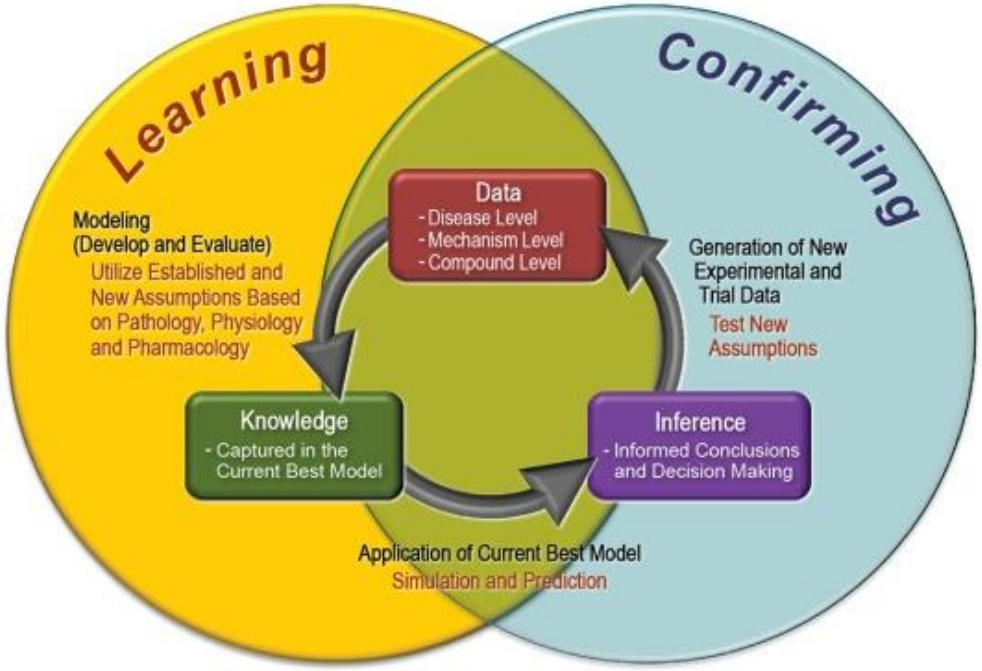
GPRC5D-TARGETED CAR T-CELL THERAPY FOR RELAPSED/REFRACTORY MULTIPLE MYELOMA (Poster #S193)



What is Pharmacometrics (PMx)
What is Model-Informed Drug Development (MIDD)?

- PMx is modeling & simulation applied to the characterization of pharmacokinetics, exposure-response (safety, efficacy, and biomarker), and disease progression
- MIDD is the use of model-based analyses to inform drug development and regulatory decisions by:
  - Bridging data gaps
  - Avoid or reduce scope of clinical studies

Learn & Confirm Paradigm of MIDD



PMx @BMS

Amit Roy
E-R, R

Chuanpu Hu,
CV/NS Discrete data
E-R, NM

Jun Shen,
ML/AI, NM,
Sci computing

Anna Kondic
Mech.-based
Models, Onc

Mayu Osawa
Hem CT, R

Yue Zhao,
ST Onc, NM

Julia Kessler
Exec. Assoc.
BMS system expert

Jian Zhou
MBMA, Monolix

Kiran Gautier
Bayesian inference,
R, Stan

Shengnan Du
PPK, R

Izumi Hamada
TGDOS, R

Sihang Liu
ST Onc, R

Sherry Zhao,
HOCT, R

VISION

Be a recognized leader and champion of Model Informed Drug Development methods and applications to address data gaps and enhance efficiency of drug development

MISSION

* *Partner strategically with CP on the characterization of PK and E-R relationship , quantifying impact of patient-specific factors*
* *Collaborate with IT and other BMS functions to aid in the development and adoption of new methodologies to streamline drug development with emphasis on key questions to CPP*

Data Science & Clinical Pharmacology Analysis and Reporting (DS/CPAR)

Mission: Build a high-quality foundation for quantitative analysis to better characterize drugs and bring them to patients.

Data Science:

- Integrate clinical and pharmacokinetic data to prepare analysis datasets for pharmacometric and non-compartmental analyses across all TAs for internal decisions and regulatory filings
- Follow rigorous, systematic processes to account for deficiencies in source data consistently across studies to enable modeling activities

CPAR:

- Responsible for study-level PK analysis and reporting and ensure it is standardized across protocols and programs
- Participate in continuous improvement initiatives related to optimizing PK data flow, PK analysis, reporting and outsourcing

External Focus:

- Developed programming standards and designed automation tools to create harmonization in pharmacometric datasets across the pharmaceutical industry

CPAR Tasks (PK sections)	DS Programming Tasks
Protocol and CRF review	Population PK datasets
Watson Setup	Exposure-Response Datasets
SAP/DPP Review	TLFs for Pharmacometric Report
PK data review prior to clinical DBL	Electronic Submission of Datasets and Model files
PK Non-compartmental Analysis (NCA)	NCA Datasets
PK TFLs and CSR	HA Responses

QSP & PBPK department: mechanistic modeling to advance drug discovery and development

Mechanistic modeling

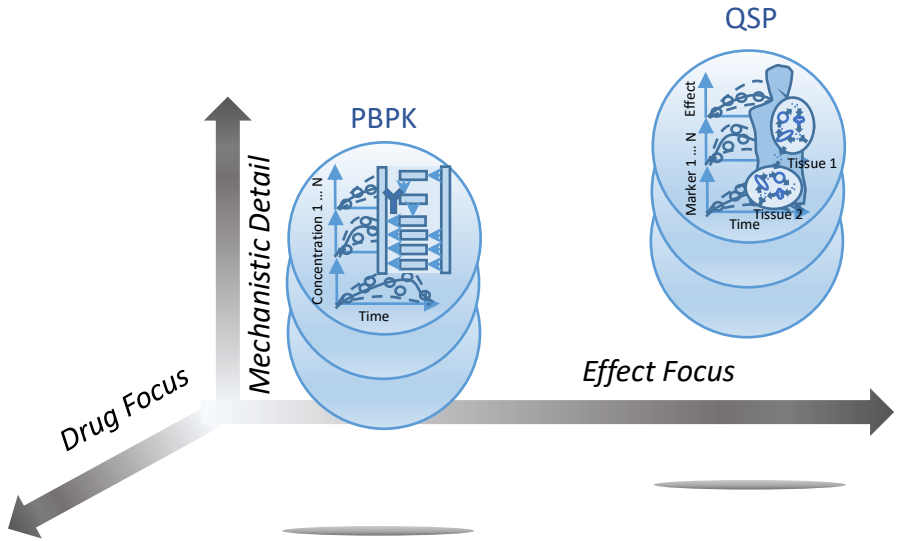
Application of mathematical models describing a biological system **to predict outcomes**

Physiologically Based Pharmacokinetics (PBPK)

Modeling of what body does to the drug

Quantitative Systems Pharmacology (QSP)

Modeling of what the drug does to the body



Adapted from CPT:PSP 2017 101 (1) 24-27

Mission

- Provide scientific, decision-enabling modeling and analysis derived from mechanistic data to support research & development
- Establish staged and long-term innovation in computational methods, modeling, and data utilization

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Mechanistic modeling can help with a variety of questions

Target: is a disease sensitive to targets of interest?

Properties: are drug properties appropriate (PK, binding, safety, tissue delivery)?

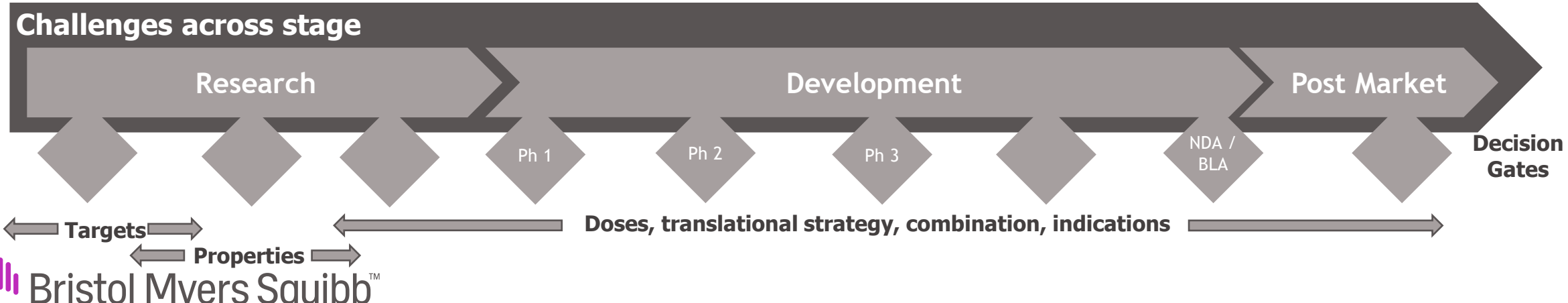
Translational strategy: what are mechanistic drivers and biomarkers, and what does a good target population look like?

Dose range for first-in-human and proof-of-mechanism: can I remove unnecessary low dose levels, assess efficacious dose range, and identify maximum dose

Dose for phase 2 and proof-of-concept: update with PK data, assess trial design, evaluate combinations, model patient groups, and assess biomarkers

Confirmatory and understanding for phase 3: improve prediction accuracy for new trial design, suggest new patient populations, and justify/confirm optimal results

Post Market: new indications, new combinations, and more convenient dosing regimens



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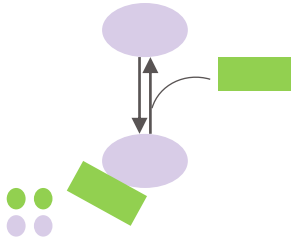
Mechanistic modeling strategies are applied fit-for-purpose to enhance discovery, translational, and development programs

Pathway Models

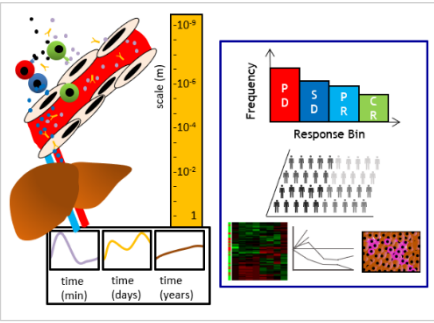


Mechanistic PK Models

Receptor Occupancy Models

Mechanistic PK-PD Models

Complex Disease Models for Clinical Trial Simulations



Mechanistic Model Scope (Breadth and Complexity)

Modeling approach considers:

- Timelines
- Scientific questions
- Available information and data

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