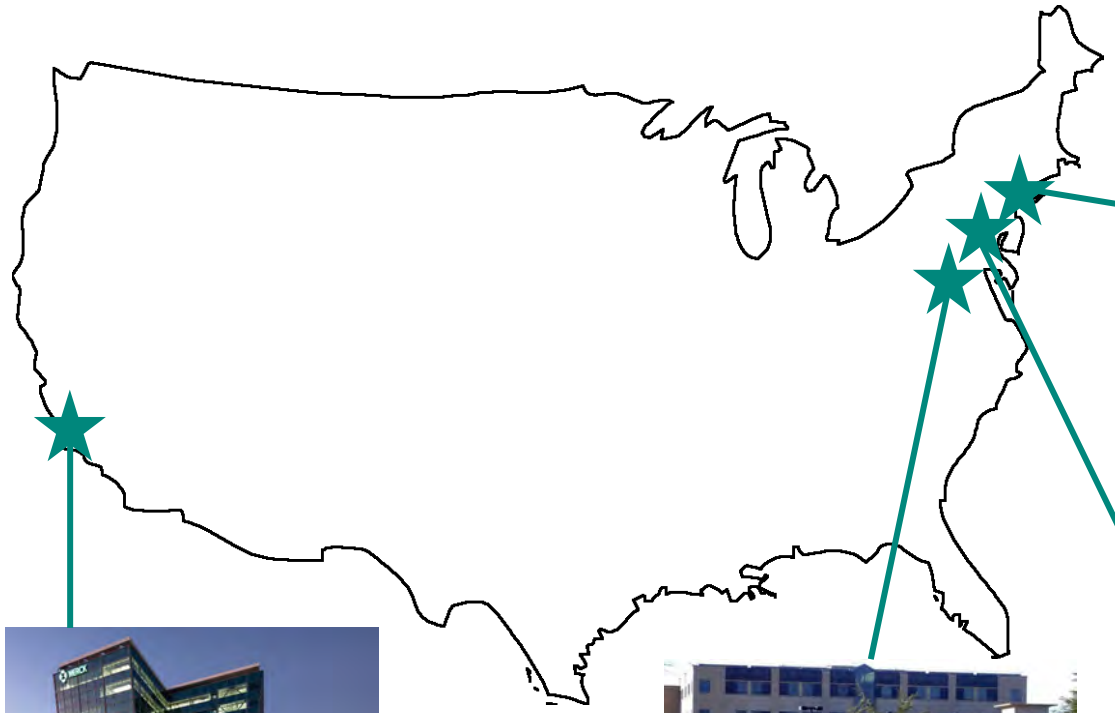
Merck

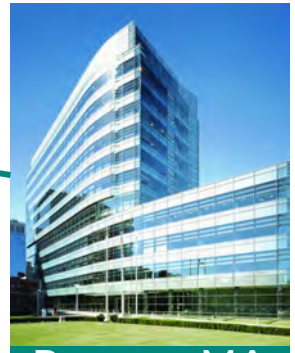
MERCK
INVENTING FOR LIFE

Agenda

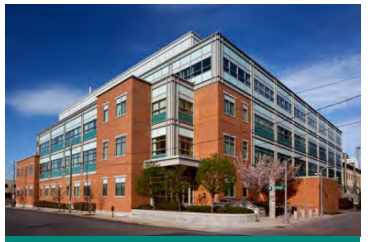
1. Functional Area Overviews (1:00 – 2:15)
2. Coffee Break (2:15-2:30)
3. Panel Discussion (2:30 – 3:00)
4. Resume Review (3:00 – 4:00)

OUR RESEARCH SITES





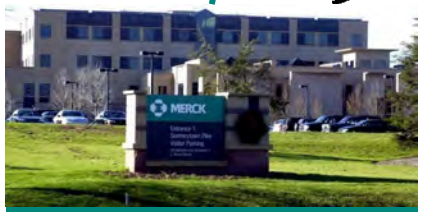
Boston, MA



Cambridge, MA

London, United Kingdom

San Francisco, CA



West Point, PA

Kenilworth, NJ

Rahway, NJ

Maximizing presence in key scientific innovation hub cities

WHO WE ARE… INVENTING FOR LIFE

We are a global healthcare company with a 130+ year history of working to make a difference

Patients First

- Deliver high-quality products & services to improve the health and wellness of people & animals
- Expand access to our medicines and vaccines

Respect for People

- Excel based on integrity, knowledge, imagination, skill, diversity, safety, and teamwork
- Work in an environment of mutual respect, inclusion, and accountability

Ethics and Integrity

- Committed to the highest standards of ethics and integrity
- Demonstrate responsibility and transparency in everything we do

Innovation and Scientific Excellence

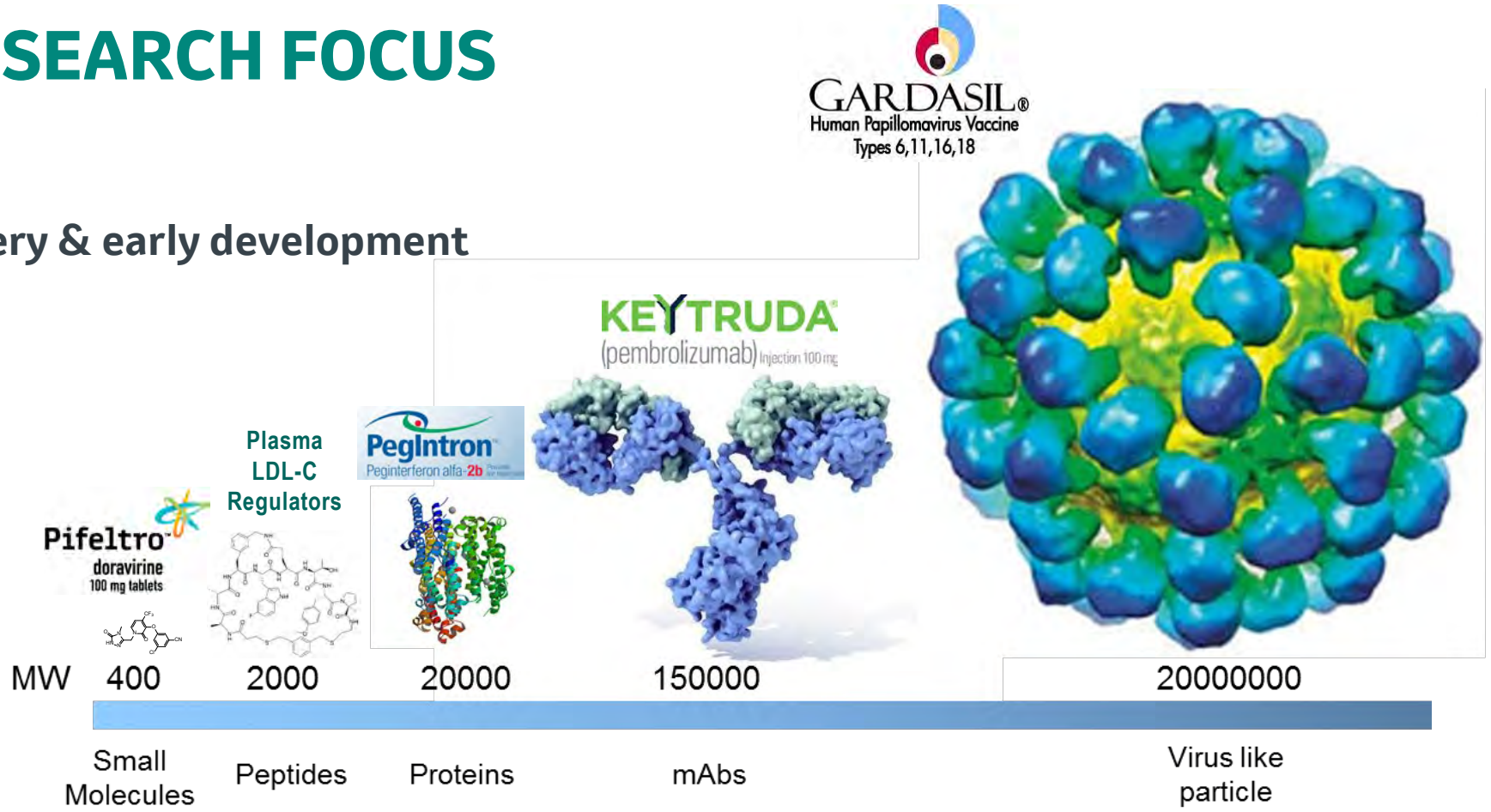
- Strive to identify the most critical needs of patients and customers
- Science-driven with strong support of R&D from the highest levels of leadership ($12.2B investment in 2021)
- Improve patients' health and quality of life through continuous innovation

OUR AREAS OF RESEARCH FOCUS

Diverse and Robust Pipeline

- **Over 150 programs in discovery & early development**
  - Oncology
  - Infectious Diseases
  - COVID-19
  - Vaccines
  - Cardio-metabolic Disorders

- **We take a modality-agnostic approach to solving human health challenges:**



- **Clinical Development**:

OUR COMMITMENT TO DIVERSITY

DE&I video link

What…
Who…
How…
Why…

Compel a more globally diverse and more inclusive workforce for our employees by creating an environment of belonging, engagement, equity, and empowerment so that we can ensure patients experience ultimate health outcomes.

seramount part of EAB — TOP COMPANY FOR EXECUTIVE WOMEN 2022

seramount part of EAB — INCLUSION INDEX COMPANY 2022

seramount part of EAB — 100 BEST COMPANY 2022

seramount part of EAB — BEST COMPANY FOR DADS 2022

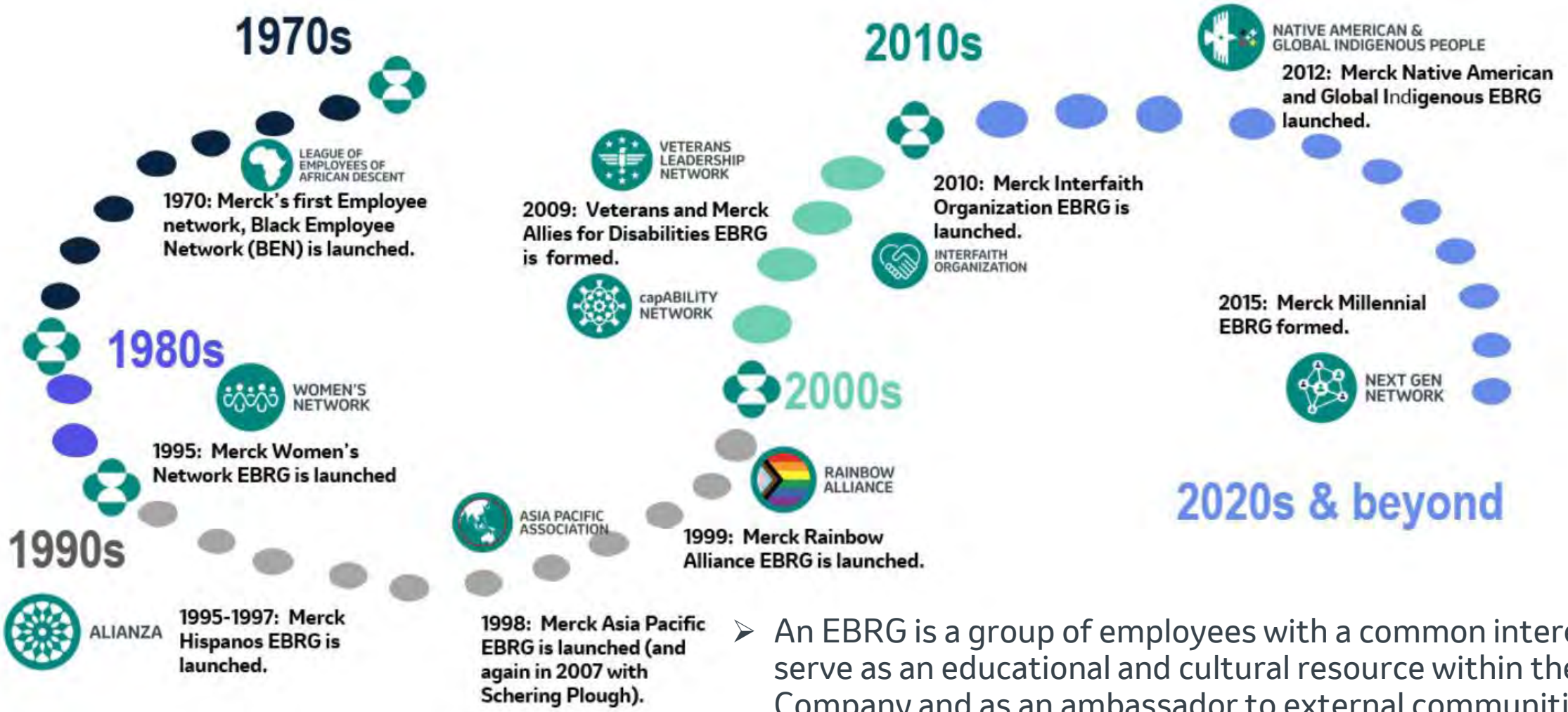
HUMAN RIGHTS CAMPAIGN FOUNDATION — BEST PLACES TO WORK for LGBTQ+ Equality 2022 — 100% CORPORATE EQUALITY INDEX

MILITARY FRIENDLY® SUPPLIER DIVERSITY PROGRAM 2022

DEI BEST PLACE TO WORK FOR DISABILITY INCLUSION 2021℠ — 100% DISABILITY EQUALITY INDEX

MERCK INVENTING FOR LIFE

MERCK EMPLOYEE BUSINESS RESOURCE GROUPS (EBRGS)



- An EBRG is a group of employees with a common interest to serve as an educational and cultural resource within the Company and as an ambassador to external communities.
- Current EBRG efforts include:
  - Reducing healthcare disparities among diverse populations
  - Enhance diverse talent acquisition
  - Increase health literacy

PRECLINICAL DEVELOPMENT OVERVIEW

Brian Vega

Background

University of Notre Dame
B.S. in Biology

Rutgers University
Ph.D. in Biomedical Sciences
Infection, Immunity, & Inflammation

- PI: Scott Kachlany
- Studied mechanisms of leukotoxin-mediated cell death

RUTGERS School of Dental Medicine

RSDM, Postdoctoral fellow
Leukotoxin as a therapeutic agent for treatment of Crohn's disease and Ulcerative Colitis

Actinobac Biomed, Inc.
Nonclinical Consultant
Pharmacology and toxicology support for IND filing

Actinobac Biomed. Inc.

Current role at Merck

Joined Merck in 2020 at West Point

Investigative Toxicology

- Immunotoxicology Group
- NDS lead for pseudoanaphylaxis de-risking strategy
- Investigative lead for unexpected toxicities
- Develop animal models for immunotoxicology assessments
- Provide SME input on drug hapten immune activation and T-cell activation
- Program development support
  - Discovery Program Leader
  - Compound Leader

Interests/Other

Live in Conshohocken, PA

- Grew up in North Jersey

Hobbies:
- Running
- Travel
- Cooking
- Beach
- Avid College Football fan

MERCK INVENTING FOR LIFE

Merck Preclinical Development (PCD) Ambassador Program

Our Mission

- Engage and nurture future talent to fortify scientific progress, develop the next-generation of scientists, innovate and apply novel drug modalities, and advance healthcare.
- Continue our commitment to building a diverse and inclusive workplace where scientific excellence thrives.

Our Scope

- Build direct relationships between Merck PCD scientists and key future talent
- Provide an overview of the PCD organization and desired scientific skills
- Introduce potential opportunities within PCD - internships/co-ops, post-doctoral training, and full-time positions per availability
- Provide educational support such as scientific lectures, consultation on curriculum if desired
- Offer mentorship opportunities and guidance on preparing for biopharma industry careers
- Tailor student engagement with feedback from academic leaders.

Our Team

- Merck PCD scientists with diverse expertise, educational, and cultural backgrounds.
- A volunteer-driven grassroots effort led by employees passionate about future talent engagement.
- Endorsed by Merck PCD Leadership.

Preclinical Development (PCD):

- ADME & Discovery Toxicology
- Bioanalysis
- Quantitative Pharmacology and Pharmacometrics
- Non-clinical Drug Safety
- Outsourcing
- Strategic Operations
- Laboratory Animal Resources (LAR)

Preclinical development designs, conducts and interprets studies that form the scientific basis of the decision to transition programs into and through clinical evaluation

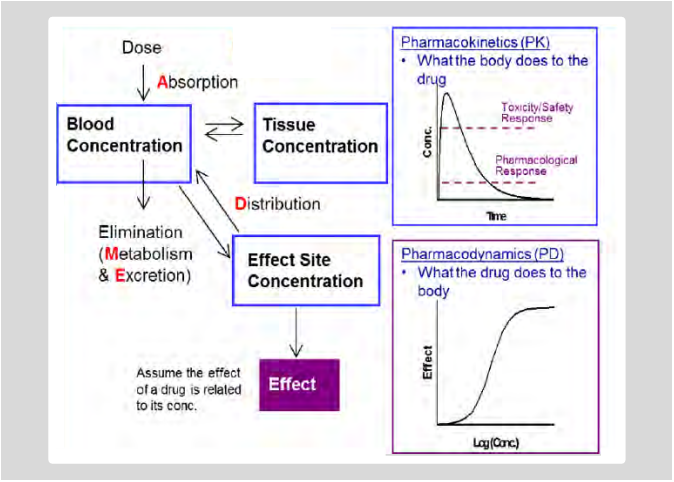
- Establish the safety profile for evaluation in the target patient population.
- Determine the safe and efficacious dose based on the understanding of the pharmacology and pharmacokinetics of the potential new drug
- Provide high quality bioanalytical data that enable decisions on progressing therapeutics and vaccines across the pipeline
- Elucidate the intersection of target biology and drug disposition and define the ADME characteristics needed for clinical success for any modality
- Identify clinical dose, justify dose for special populations or drug interactions and define therapeutic window through quantitative knowledge integrations

Preclinical Development (PCD) – bridging drug discovery and development

ADME & Discovery Toxicology (ADMEDT)

Mission: To influence molecular design to optimize drug disposition and biological properties that are integral to efficacy and safety through research and characterization that translate into differentiated labels.

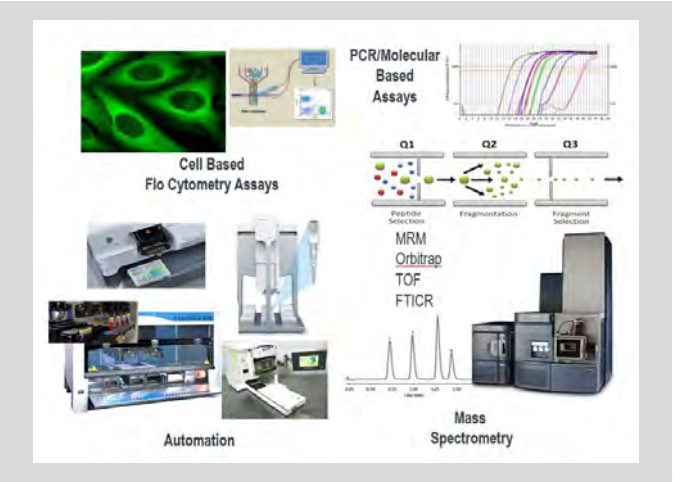
- ❑ Absorption, Distribution, Metabolism and Excretion (ADME) and Drug Metabolism Pharmacology
- ❑ Biotransformation and Distribution (BT&D)
- ❑ Transporter and In Vitro Technologies (T&IVT)
- ❑ Biochemical Toxicology (TK) and in vivo PK
- ❑ Discovery BA
- ❑ Genetic Toxicology (GT)
- ❑ In Vitro Toxicology
- ❑ In Vitro Safety Pharmacology



Regulated Bioanalytics (BA)

Mission: To impact pipeline decisions across all therapeutics and vaccines by understanding the questions our data seek to address and developing appropriately targeted bioanalytical methods and providing high quality bioanalytical data that enable decisions on progressing therapeutics and vaccines across the pipeline

- ❑ PK & ADA
- ❑ Immunogenicity and Molecular
- ❑ Lab Systems and Sample Management

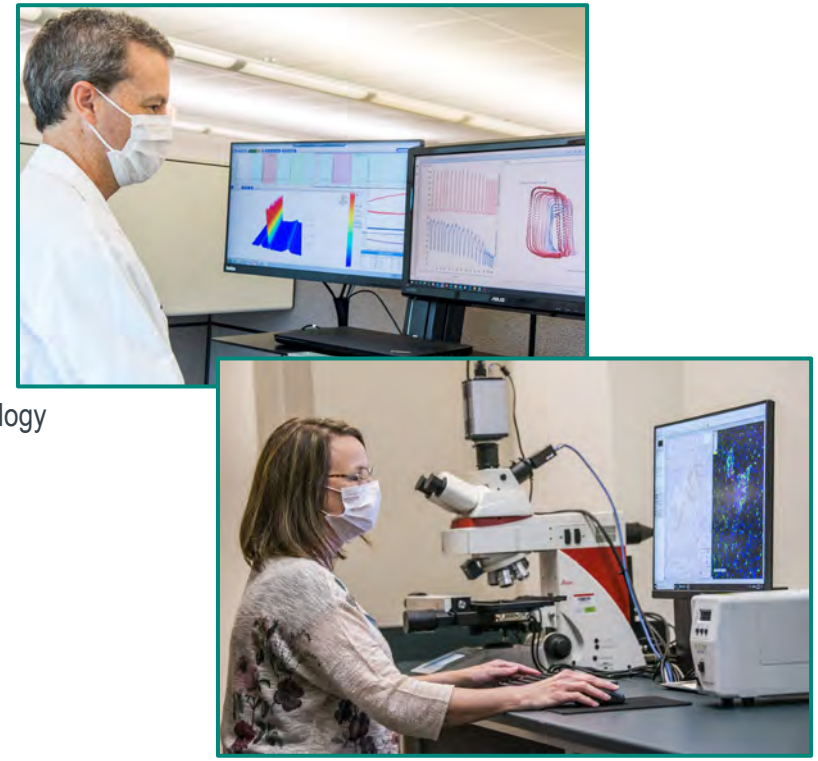


Preclinical Development (PCD) – bridging drug discovery and development

Nonclinical Drug Safety (NDS)

Mission: To empower ground-breaking discovery research that influences the development of safe therapeutics, develops insightful safety assessments for clinical trial safety & flexibility, and delivers the most appropriate commercial label

- ❑ Pathology
  - Anatomical Pathology
  - Clinical Pathology
  - Investigative Pathology
- ❑ Toxicological Sciences
  - Toxicology Operations
  - Central Pharmacy
  - Developmental & Reproductive Toxicology
- ❑ Program Discovery & Development
  - Program Planning and Submissions
  - Discovery Program Leaders (DPL)
  - Therapeutic Area Leaders (TAL)
  - Compound Leaders (CL)



- ❑ In Vivo Safety & Exploratory Pharmacology
  - GLP Safety Pharmacology
  - Investigative In Vivo Safety Pharmacology
- ❑ Investigative Toxicology
  - Immunotoxicology
  - Systems Toxicology
  - Analytical & Biochemical Toxicology
- ❑ Occupational Toxicology
- ❑ Operations
  - Project Planning & Sourcing
  - Digital Operations & Innovation
  - Information Management

Preclinical Development (PCD) – bridging drug discovery and development

Preclinical Development Outsourcing

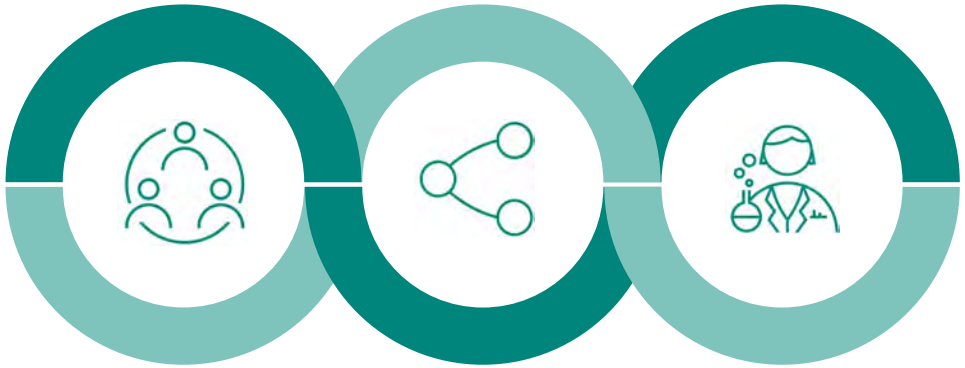
Mission: To advance MRL's therapeutic and vaccine portfolio by proactively developing and leading a network of external partners to generate high quality, timely and cost effective PCD data

- ❑ Preclinical, NDS, QP2 Sourcing
- ❑ Regulated Vaccines BA Sourcing
- ❑ Regulated PK/ADA Sourcing
- ❑ Sourcing Operations

Preclinical Development Strategic Operations

Mission: To generate, advance, and implement best practices that strengthen the broad PCD organization through innovative approaches, drive efficiencies in internal and external collaborative engagements, and create opportunities to ensure training compliance and professional development of PCD staff and leaders.

- ❑ Facilities and Project Management
- ❑ Regulatory Submissions and Document Management
- ❑ PCD Archives
- ❑ Training Strategy and Compliance



Preclinical Development (PCD) – bridging drug discovery and development

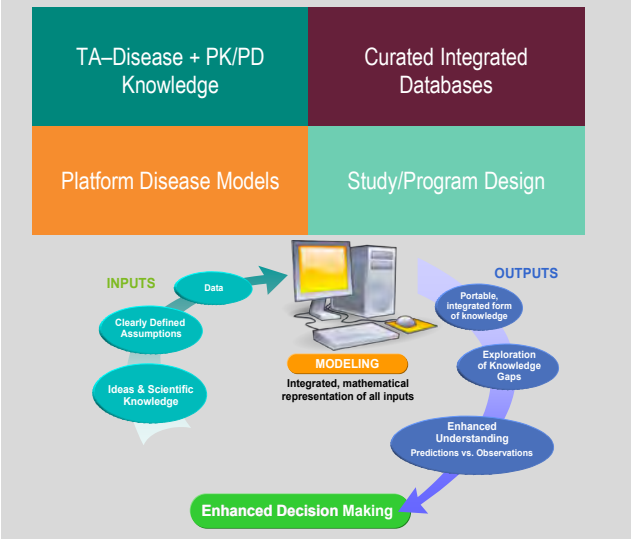
Laboratory Animal Resources (LAR)

Mission: To provide collaborative research support and technical expertise to MRL research programs while promoting the health, well-being and responsible use of animal models through optimal veterinary medical care. LAR is dedicated to advancing the development of safe and effective pharmaceutical products through partnerships, innovation and adaptability while ensuring a resolute commitment to maintaining full regulatory compliance.

- ❑ LAR Boston
- ❑ LAR South San Francisco
- ❑ LAR West Point

Quantitative Pharmacology and Pharmacometrics (QP2)

Mission: To deliver value through optimizing dosage, identifying opportunities to halt development of undifferentiated assets, and streamlining the development of promising compounds and biologics utilizing model-informed drug discovery/development and pharmacokinetics/pharmacodynamics.



External Collaborations

Mission: To deliver thorough and timely stage-appropriate PCD endorsed reviews for external business development opportunities across all TAs and assuring optimal transitions towards integration for agreement(s) with full cross-functional PCD engagement and in partnership with BD&L.

Summary

Identifying the *Right Target, Right Drug, Right Dose, Right Patient*

- PCD plays a pivotal role enabling the pipeline from early discovery through post-marketing
- Large lab footprint for experiment execution
  - In vitro assays
  - In vivo studies
  - Bioanalytical data generation
- We focus on understanding how the biological system impacts the molecule (ADME) and how the molecule impacts the biological system (Tox)
- We develop models based on our data to enable decisions across the portfolio (target selection, molecular design and compound selection, clinical study design)
- Collectively, our studies enable the translation of discovery data into clinically safe and effective doses for patients

- For more detailed information regarding our department and each sub-functional group please visit the PCD landing page in Merck Careers website
- If you have any questions, feel free to reach out!
  - James Schiller – BA – PCD Career Center Steward
  - Hillary Regan – PCD Strategic Operations

QUANTITATIVE PHARMACOLOGY & PHARMACOMETRICS (QP2)

Shuai Hu

Background

Peking University
B.S. in life sciences

University of Michigan College of Pharmacy
PhD in Medicinal Chemistry
MS in Bioinformatics
- Drug discovery in pancreatic cancer using multiomics analysis

FDA
- Intern and one-year fellowship after graduation
- Clinical data analysis, modeling & simulation

Current role at Merck

- Joined in 2021
- Senior Scientist, CMD group
- Based in Rahway NJ
- QP2 leads on multiple pipeline work to support trial design, dose decisions, and other strategic discussions using modeling and simulation (M&S)
- Collaborate closely with other functional area reps and provide

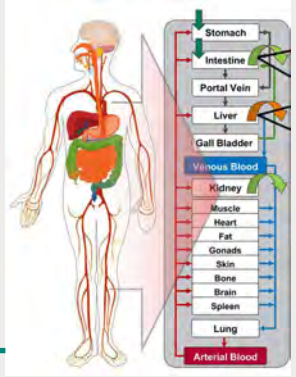
Interests/Other

- Travel
- Music
- Sports
- Family time

Would you like to use quantitative tools to bring benefit to patients around the world?

Pharmacy/
Pharmaceutical Sciences

Data Science



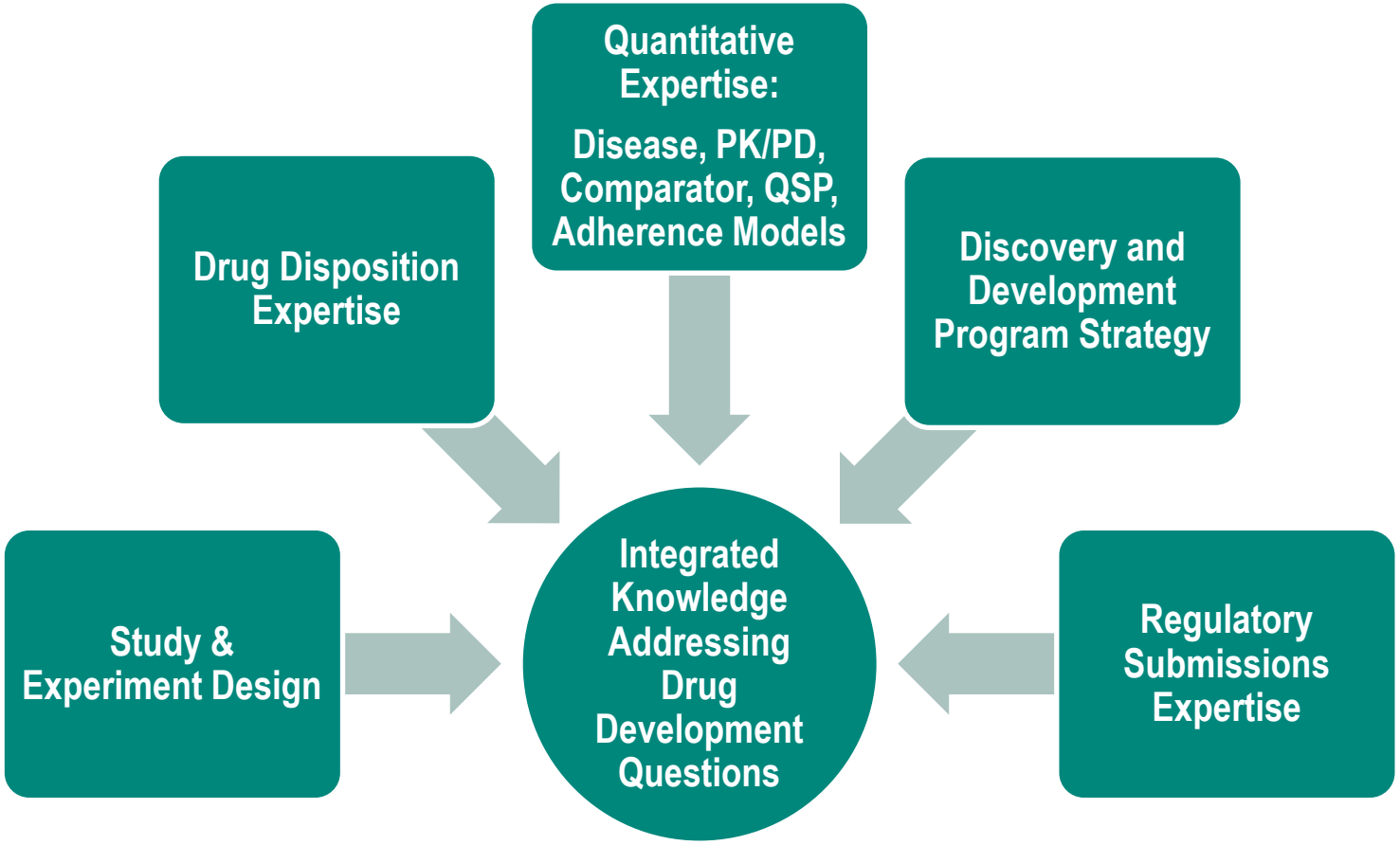
Physiology

Mathematics/Statistics

$$\frac{dx}{dt} = f(x_t, u_t, t, \theta)$$

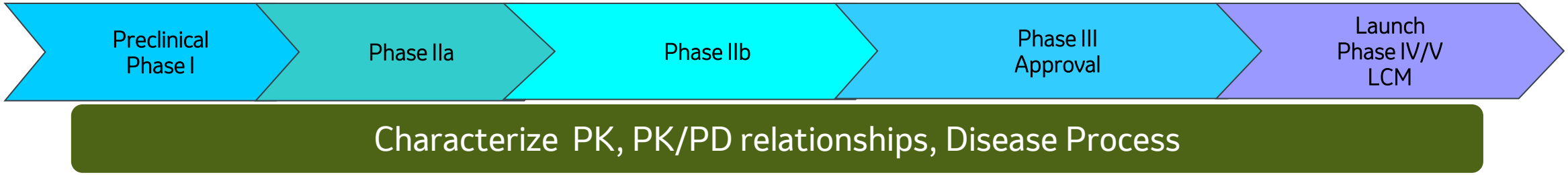
$$\frac{dC}{dt} = \frac{V_{max}\, Q}{(K_m + Q)V} - \frac{CL}{V} C$$

Engineering

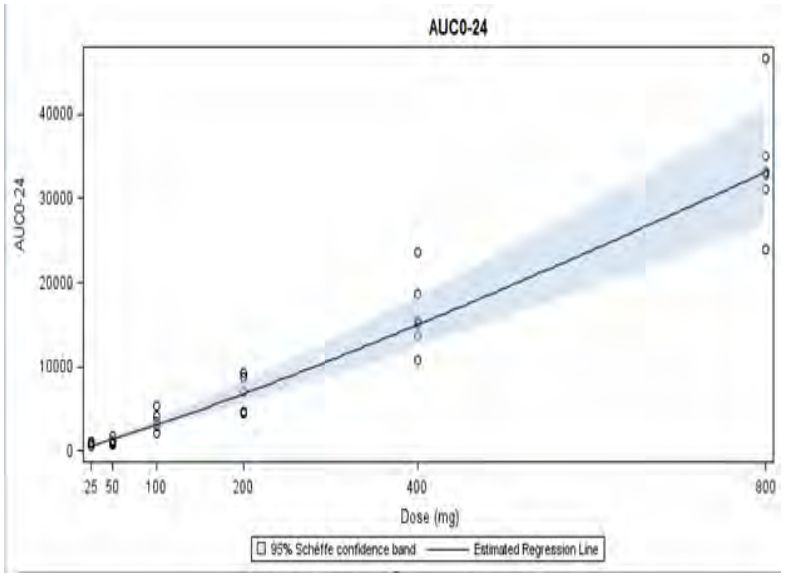


Right Target Right Drug | **Right Dose Right Patients**

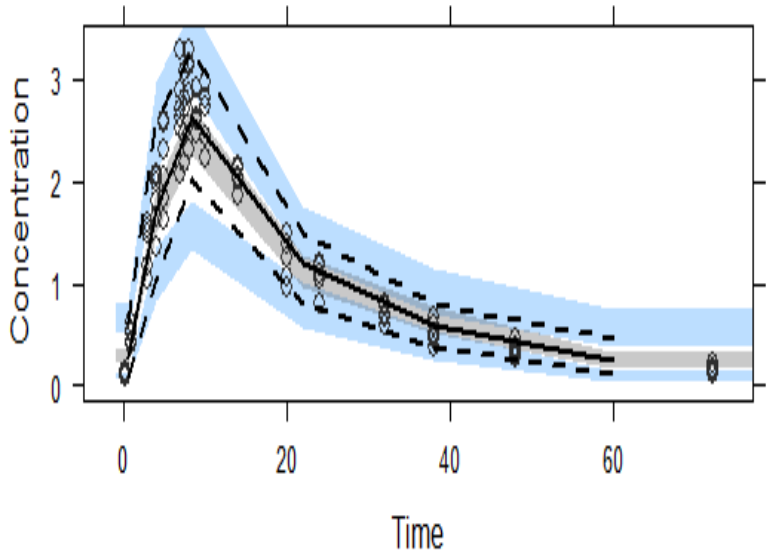
Leveraging Quantitative Approaches to Advance Novel Therapies Across All Stages of Drug Development



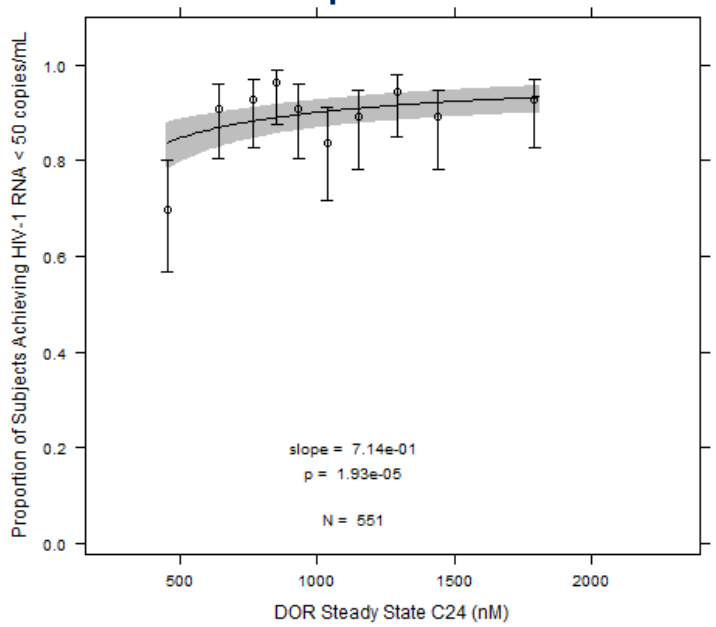
Dose and Exposure Relationship



Drug Concentration over Time Curve



Dose/Exposure- Response (PK/PD to define Therapeutic Window



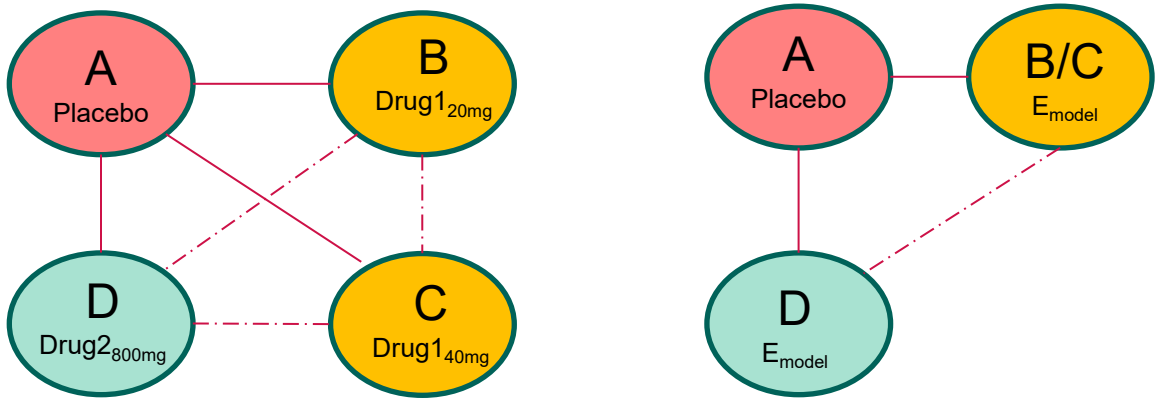
To inform label recommendations for Marketed Product

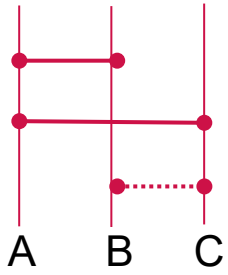
Model-Based Meta-Analysis (MBMA)

Network meta-analysis

$$\Delta Y_{ij} = A_i + f(E_j, x_i) + \epsilon_{ij}$$

$$\Delta Y_{ijt} = A_{it} + \frac{f(E_{max,class}, x_i).Dose_{ijt}}{Dose_{ijt} + f(ED_{50,drug}, x_i)} + \epsilon_{ijt}$$





ΔAB

ΔAC

ΔBC = ΔAC - ΔAB

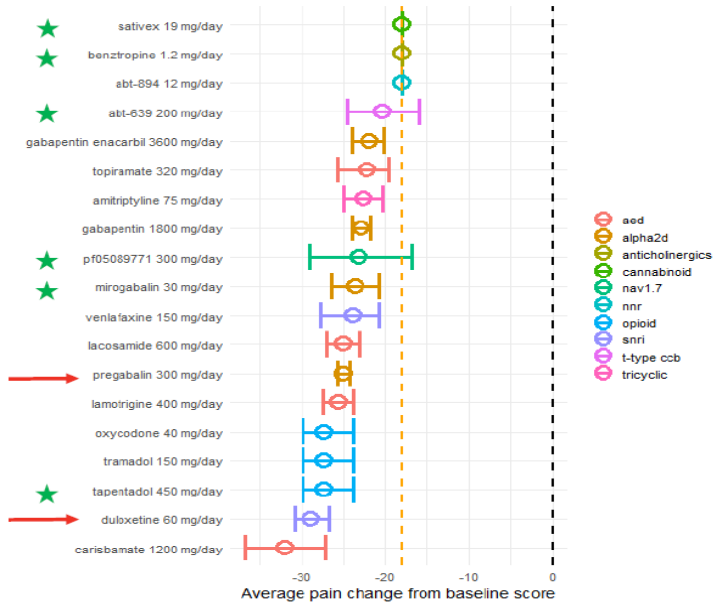
An extension of NMA, taking into consideration of dose responses, longitudinal effect and pharmacology.

MBMA to Support Development of Medicines for Treatment of DPN, PHN and Fibromyalgia

Database: publicly available, summary-level clinical trial data from 74 trials, 26,000 patients, 21 drugs across 9 classes

$$Effect_{ijt} = Eo_{it} + Emax_{class} \cdot \frac{Dose_{ijt}}{ED_{50,drug} + Dose_{ijt}} \cdot \frac{time_{ijt}^{\gamma}}{ED_{50,drug}^{\gamma} + time_{ijt}^{\gamma}} + \varepsilon_{ijt}$$

Average Pain Change from Baseline



MBMA predicted relative treatment effect at 12 weeks relative to placebo in diabetic peripheral neuropathy in Standard of care for benchmarking of internal compound

Interested? Want to learn more?

computational biology
mathematical modeling
strategic thinking
communications
experimental design
data science
informed drug development
machine learning
exposure
pk
clinical trial development
collaboration
pd
response modeling
pharmacology
programming
pharmacometrics

GLOBAL BIOANALYTICS:
ROLE AND IMPACT IN DRUG DISCOVERY AND DEVELOPMENT

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Nicole Revaitis

Background

B.S., Biology
Stockton University

M.S., Biology
Rutgers University
PI: Nir Yakoby

Ph.D., Computational and Integrated Biology
Rutgers University
PI:Nir Yakoby

Areas of Study:

- EGFR signaling and its ligand, Gurken
- Tissue patterning and morphogenesis during *Drosophila* oogenesis

WuXi Advanced Therapies: 2019-2021

- Based in Philadelphia
- Molecular Biology Group
- GMP testing (routine, assay qualification, and validation) for Residual Host Cell DNA, Mycoplasma, and Viral PCR platforms

Current Role

Joined Merck in 2021

Senior Scientist
PDMB Regulated BA

- Molecular Biologist supporting qPCR, dPCR, and NGS studies to support phases in the vaccine life cycle
- Recently moved to a new facility in Springhouse Innovation Park (SHIP)

Outside Work

Live in Franklinville, NJ
with my husband, 2 children (Ella:13, Michael:4), and pets

Interests:

- Outdoor activities (Gardening, Running, Beach)
- Crafting, Dining Out, Traveling
- Spectator for kids (Field hockey, Cheer, Soccer) and husband (Drag racing)

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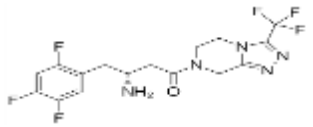
Bioanalytics: Definition and Role in Drug Discovery and Development

Bioanalytics (BA): Quantitative measurement of drug and/or drug effect/response markers in samples from preclinical and clinical studies

Goal/Impact: Create knowledge of drug and/or PD marker exposure at given time points in relevant sample types (e.g. serum, blood, saliva, urine, other) to enable establishment of pharmacokinetics and pharmacodynamics relationship for a given drug in a specific study environment (preclinical animal efficacy model, PK/PD study, clinical studies)

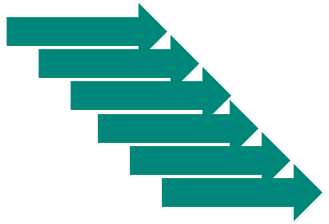
Global organization with site-based groups

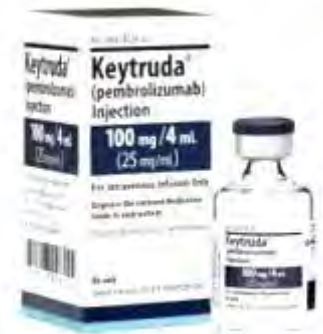


Discovery BA

Analyte	Dose	Regimen	mIFN-g [pg/mL]	mIL-1b [pg/mL]	mIL-6 [pg/mL]	mIL-8 [pg/mL]
mIgG	30 mg/Kg	Q7DX3	< MRC	1.7	2.3	38.0
mIgG	30 mg/Kg	Q7DX3	< MRC	2.8	3.3	107.6
mIgG	30 mg/Kg	Q7DX3	0.4	4.0	1.7	98.6
mIgG	30 mg/Kg	Q7DX3	0.8	5.5	2.8	33.5
mIgG	30 mg/Kg	Q7DX3	0.6	5.3	3.3	95.2
mIgG	30 mg/Kg	Q7DX3	0.7	2.4	2.1	100.4
mIgG	30 mg/Kg	Q7DX3	0.7	5.4	3.3	57.7
mIgG	30 mg/Kg	Q7DX3	0.5	2.4	2.5	65.6
mIgG	30 mg/Kg	Q7DX3	0.4	5.3	3.1	43.0
mIgG	30 mg/Kg	Q7DX3	0.6	11.0	2.6	81.1
mu0X400	5 mg/Kg	Q5DX5	1.7	5.2	4.5	36.1
mu0X400	5 mg/Kg	Q5DX5	2.9	6.2	10.6	22.1
mu0X400	5 mg/Kg	Q5DX5	0.6	2.5	2.6	103.0
mu0X400	5 mg/Kg	Q5DX5	0.8	8.4	2.7	23.8
mu0X400	5 mg/Kg	Q5DX5	1.2	10.9	5.5	34.8
mu0X400	5 mg/Kg	Q5DX5	1.6	6.0	9.3	18.6
mu0X400	5 mg/Kg	Q5DX5	0.7	4.2	3.9	69.7
mu0X400	5 mg/Kg	Q5DX5	1.2	6.2	8.9	17.3
mu0X400	5 mg/Kg	Q5DX5	1.0	4.4	19.9	39.5
mu0X400	5 mg/Kg	Q5DX5	1.5	4.2	96.0	14.9
E06	0.3 mg/kg	Q7DX3	0.4	6.7	2.6	25.7
E06	0.3 mg/kg	Q7DX3	0.4	4.7	3.4	92.1
E06	0.3 mg/kg	Q7DX3	0.7	3.9	2.3	33.1
E06	0.3 mg/kg	Q7DX3	0.4	2.2	2.5	82.3
E06	0.3 mg/kg	Q7DX3	0.5	3.9	3.0	42.3
E06	0.3 mg/kg	Q7DX3	1.5	2.6	2.2	64.0
E06	0.3 mg/kg	Q7DX3	0.4	6.9	2.2	45.0
E06	0.3 mg/kg	Q7DX3	0.4	11.2	2.1	39.8
E06	0.3 mg/kg	Q7DX3	0.8	10.5	4.2	50.8
E06	0.3 mg/kg	Q7DX3	1.1	4.4	3.2	46.6

Development BA
(preclinical, clinical)



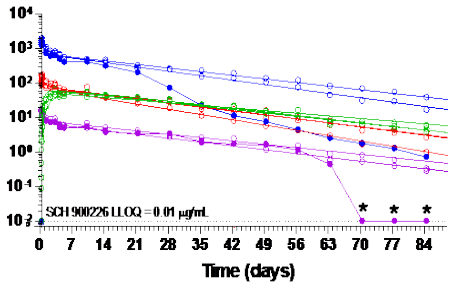


Quantitative Bioanalytical Assays In Support of Therapeutics

DISCOVERY → GLP → CLINICAL

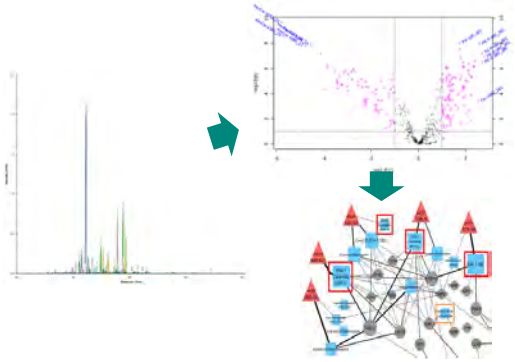
Pharmacokinetics

LC/MS LBA



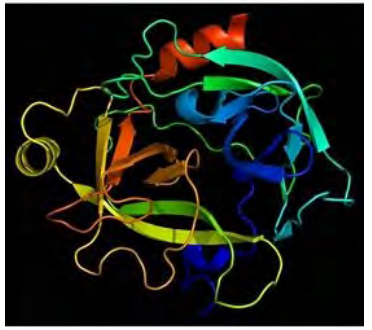
Pharmacodynamics/Target Engagement

LC/MS LBA



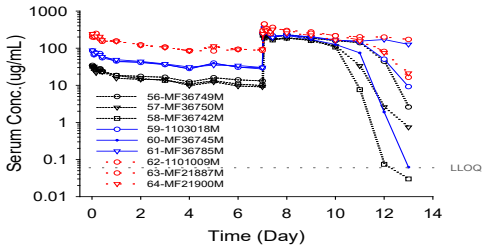
Target/Protein Quant.

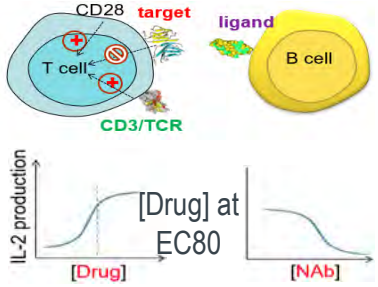
LC/MS LBA



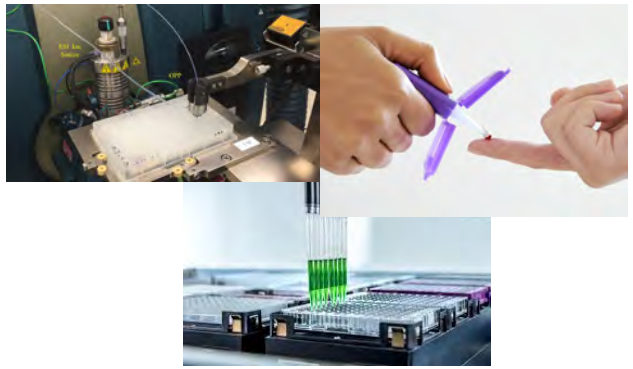
Immunogenicity

Capillary Electrophoresis LBA Cell-Based





New Technologies & Automation



High fidelity quantitative data are a foundation for model informed discovery and development (MIDD) work and decisions

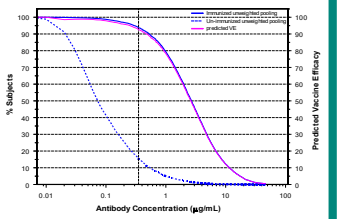
Quantitative Bioanalytical Assays In Support of Vaccines and Oncolytic Virus

DISCOVERY → GLP → CLINICAL

Immunogenicity – Total Antibodies

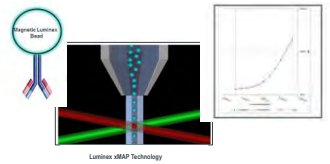
LBA

Correlate of Protection for pediatric PCV (WHO ELISA)

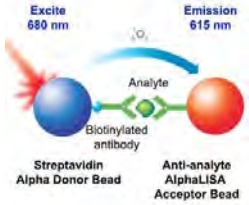


Data from Dr. Kohberger, WHO 2003

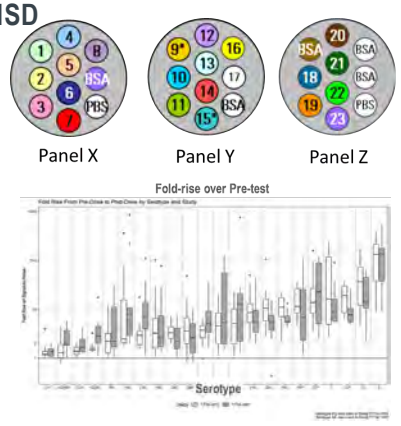
Luminex



AlphaLISA



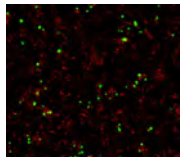
MSD

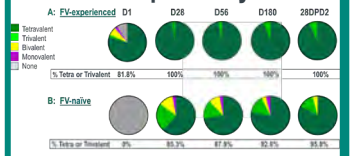


Immunogenicity – Functional Antibodies

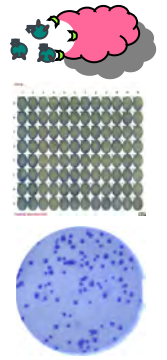
Cell-Based

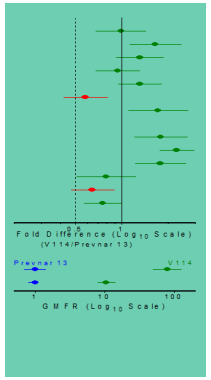
VRNT





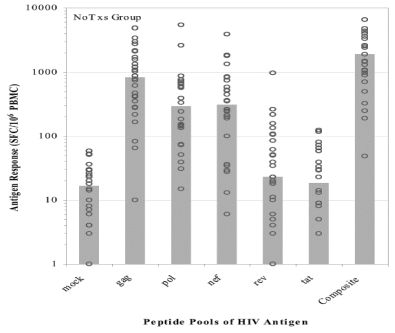
Bacteria + sera (containing **neutralizing antibodies**) + C'



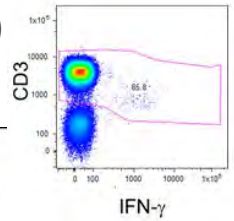


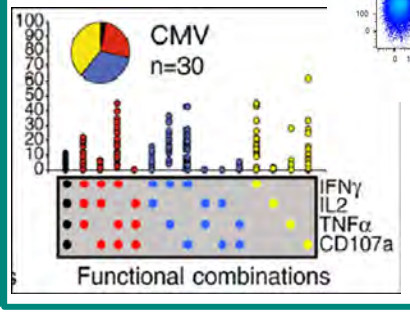
Immunogenicity – Functional T-cell

ELISPOT



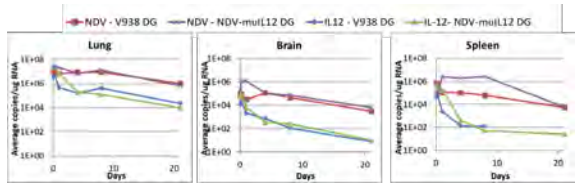
Flow Cytometry (ICS)





Molecular - qPCR

Blood
Brain
Lung
Heart
Kidney
Liver
Gonads
Lymph nodes
Injection Site



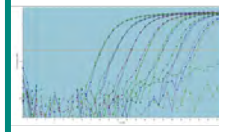


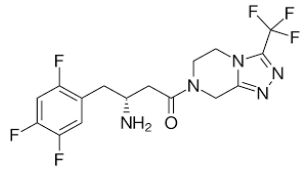
Table 6: Analysis of Efficacy of GARDASIL in the PPE* Population for Vaccine HPV Types

Disease Endpoints	GARDASIL N	GARDASIL Number of cases	AAHS Control N	AAHS Control Number of cases	% Efficacy (95% CI)
16- through 26-Year-Old Girls and Women†					
HPV 16- or 18-related CIN 2/3 or AIS	8493	2	8464	112	98.2 (93.5, 99.8)
HPV 16- or 18-related VIN 2/3	7772	0	7744	10	100.0 (55.5, 100.0)
HPV 16- or 18-related VaIN 2/3	7772	0	7744	9	100.0 (49.5, 100.0)
HPV 6-, 11-, 16-, or 18-related CIN (CIN 1, CIN 2/3) or AIS	7864	9	7865	225	96.0 (92.3, 98.2)
HPV 6-, 11-, 16-, or 18-related Genital Warts	7900	2	7902	193	99.0 (96.2, 99.9)
HPV 6- and 11-related Genital Warts	6932	2	6856	189	99.0 (96.2, 99.9)

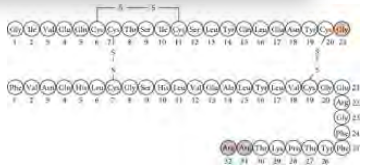
Immunogenicity and molecular data demonstrating a durable response/protection are often a basis for vaccines licensure

Bioanalysis: The Foundation of Drug Discovery and Development

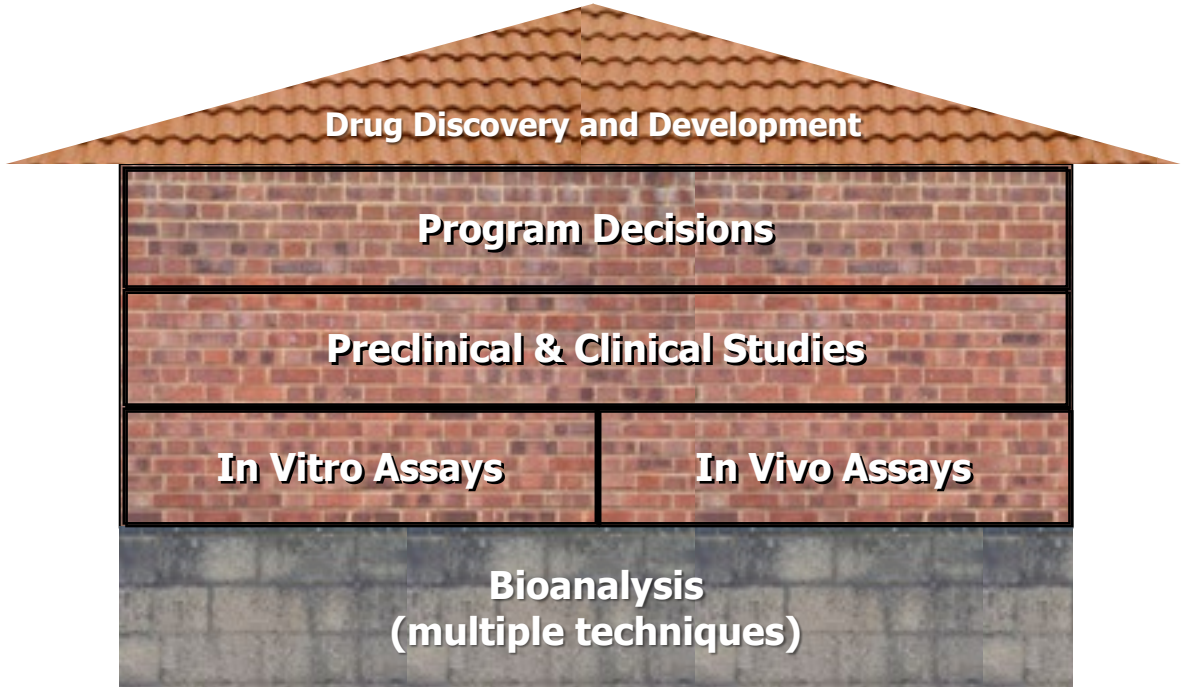
Small Molecules



Peptides

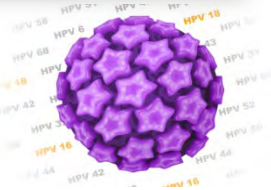


Oligonucleotides

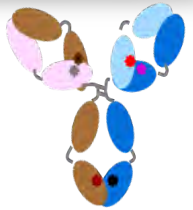


mAbs

Vaccines



Emerging Modalities
(example: Bispecific mAbs)

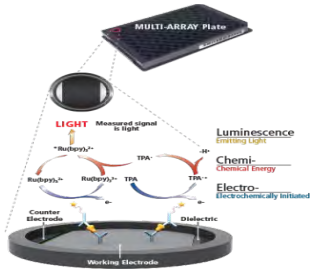


- Bioanalysis, or quantitative analysis, is used in all programs at Merck
- Liquid Chromatography Mass Spectrometry, Ligand Binding Assays, PCR, Cell-based assays, etc.

Bioanalytical Platforms (examples)

Ligand Binding Assays

Meso Scale Discovery



Luminex®

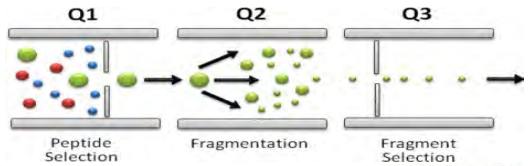
Gyrolab®

CE

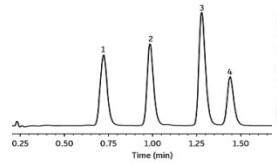
Automation

Deacon Automation System

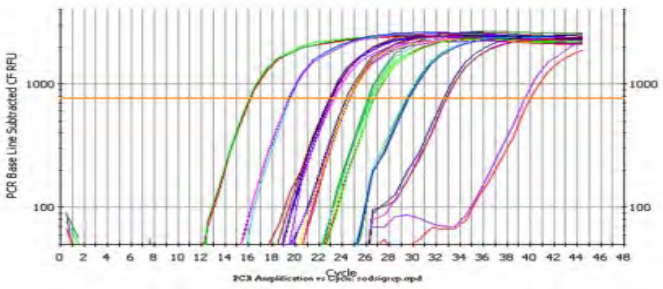
LC-Mass Spectrometry



MRM
Orbitrap
TOF
FTICR



PCR/Molecular Based Assays



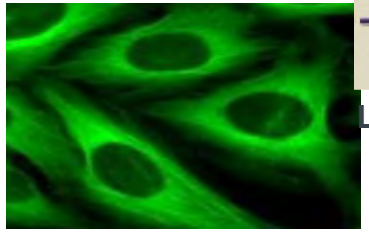
Hamilton®

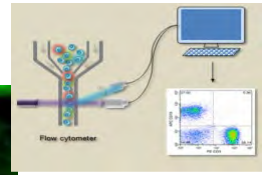
Assay Map

I.DOT

Cell Based Assays

Cytation/ EnSight Reader/Imager





LSRFortessa™ X-20

Academic, Regulatory, and Industry Engagement

Academic collaboration

Merck - Purdue Center for Measurement Sciences

Contributing to New Regulatory Guidance

ICH M10
Comments o
draft
guidances

Cross Industry Collaborations

IQ working groups

Organizing External Meetings

APA
ASMS
AAPS
Land O'Lakes

Leadership in the External BA Community

ASMS
AAPS
WRIB

Training the Regulators

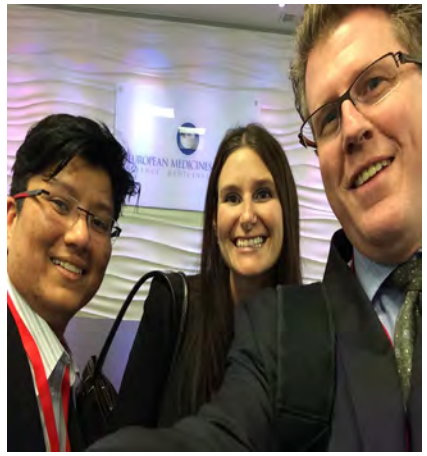
Presenting at FDA educational programs

Hosting tours for new FDA staff

White Paper Publications

Micro-sampling
Peptide Analysis

AAPS Meeting on **Global harmonization of regulated BA guidelines**



PPDM Staff at EMA Discussing Use of DBS

PPDM Team at NIFDC
Strengthening our relationship with regulatory authorities in China on vaccine clinical assays

aaps American Association of Pharmaceutical Scientists

FDA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

IQ INTERNATIONAL CONSORTIUM for INNOVATION & QUALITY in PHARMACEUTICAL DEVELOPMENT

MERCK INVENTING FOR LIFE

Training and Skillset for a BA Scientist

- A passion for new technology, data science, and problem solving
- Training in Analytical Chemistry, Biology, Biochemistry, Cell Biology, Immunology, Molecular Biology, Engineering, etc.
- A team player with strong oral and written communication skills as evidenced by scientific publications and presentations at scientific meetings.
- Be able to work collaboratively in a fast-paced environment and communicate effectively in presentations to stakeholders in partner organizations or at external scientific meetings
- A quantitative mindset!

Our ability to excel depends on the integrity, knowledge, imagination, skill, diversity and teamwork of our Scientists

NONCLINICAL DRUG SAFETY (NDS) & LABORATORY ANIMAL RESOURCES (LAR)

MERCK

INVENTING FOR LIFE

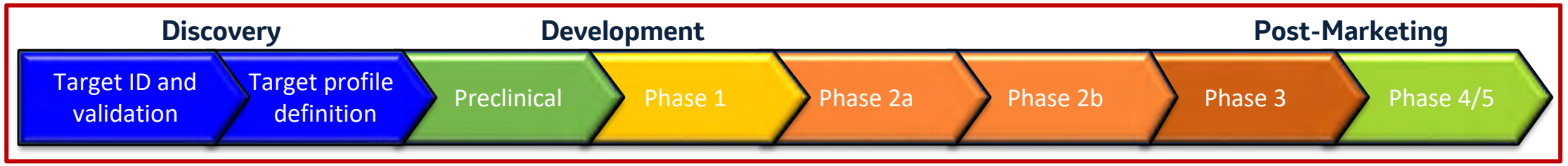
Mission: Discovery and Development of Safe Therapeutics

High Attrition Rate of Molecules Before Start of Clinical Trials*

*Source: *Current nonclinical testing paradigms in support of safe clinical trials: An IQ Consortium DruSafe perspective,* Lynne D. Butler et. al, Regulatory Toxicology and Pharmacology 87 (2017) S1 S15

Select molecules with the highest probability of success through early "predictive" screening

Our Integrated and Coordinated Organization Provides High Quality Risk Assessment



PCC Approval

WMA Approval

Discovery Team

Early Development Team

Product Development Team

Communication is the key to success

NDS Discovery Program Leaders (DPL)
dedicated, embedded at Discovery sites

NDS Compound Leaders (CL)
from all NDS functions and sites

Therapeutic Area Leaders

Labs, Operations and Project Management are the foundation

Information Management | Genetic Toxicology | Developmental and Reproductive Toxicology | Central Pharmacy

Project Planning | Anatomic Pathology | Clinical Pathology | Program Coordination and Planning | Toxicology

Digital Operations & Innovation | Safety and Exploratory Pharmacology | In Vitro Safety Pharmacology | Occupational Toxicology

Toxicokinetics | Immunotoxicology | Systems Toxicology | Analytical & Biochemical Toxicology | In Vitro Toxicology

Enabling Drug Development

Help to Select Best Drugs, Cheaper, Faster

- Maximize safety attributes of successful Preclinical Candidates (PCCs)

Help to Keep the Right Drugs Alive

- Implement effectual development strategies and effectively communicate risk assessments

Learn From Failures

- Application of learning from tox-related drug failure

Help Shape the External Environment

- Drive regulatory change through external scientific and regulatory engagement

Encouraging Growth through Scientific Contributions

CRITICAL PATH INSTITUTE

PhRMA RESEARCH • PROGRESS • HOPE

HESI®

imi innovative medicines initiative

USciences University of the Sciences

USC University of Southern California

GEORGE MASON UNIVERSITY

BOSTON COLLEGE

Tufts UNIVERSITY

Cornell University

Drexel UNIVERSITY

ILLINOIS

Northeastern University PhD Education

UNIVERSITY OF LIVERPOOL

UNIVERSITY OF MICHIGAN

Massachusetts Institute of Technology

PennState

The LEADERs Program
Partnerships in Research and PhD Education

External Consortia & Partnerships

Publications & Awards

Academic Collaborations & Internships

MERCK INVENTING FOR LIFE

We Want You To Join Our Team!

In vivo Experts

ACLAM
American College of Laboratory Animal Medicine

ALAT LAT LATG

AA®

ACADEMY of SURGICAL RESEARCH

Education, training and specialized certifications

Experience, BS, BA, MS, MBA, PhD, DVM, VMD

Biology
Pharmacology
Biochemistry
Zoology
Toxicology
Data Science
Chemistry
Molecular Biology
Immunology
Animal Science
Pathology
Management

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Career Opportunities at Merck

MRL Intern/Co-op Program

Intern/Co-Op positions in 4 states (CA, MA, NJ, PA)

Programs are open to undergraduate and graduate students

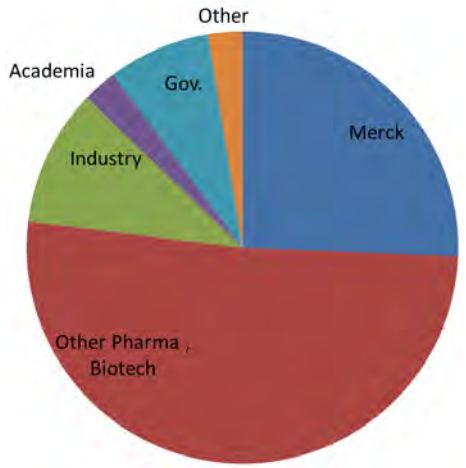
Merck covers travel expenses between school & Merck, while Intern/Co-Op responsible for housing

- **Co-Op:** 4- to 6-month assignments throughout year
- **Internship:** 9- to 11-week assignments between June and August
  - Intern job posting available late fall with offers extended before April
  - Final interview conducted by phone

For more info visit: https://www.merck.com/careers/student-opportunities.html

MRL Postdoctoral Program

- Program launched in 2012
  - Around 60 postdocs at any time, across all Merck sites
  - 30-36 new postdocs added each year - up to three years duration for each postdoc
- Original research projects in Merck Labs
  - Related to Merck's discovery and development work, but pre-competitive/non-proprietary projects
  - Objective is high profile publications and presentations by the postdoc
- Provides immersion for the postdoc in collaborative industrial research teams
  - an academic focus in a commercial environment
- Positions posted January-March
- More information: https://www.merck.com/research/fellow/home.html



Postdoc destinations - over 140 alumni have graduated from the MRL postdoc program

How to Apply – Finding open positions

- On the web -
  - Merck website: https://jobs.merck.com/us/en
    - Search Keywords such as:
    - Preclinical development, Bioanalytics, ADME, QP2, Toxicology
  - LinkedIn: https://www.linkedin.com/company/merck/careers
  - Twitter: @MerckIMInspired

- Resumes and applications are only processed and screened through our online Workday portal
- E-mail confirmation sent when your application is submitted

- Some example positions:

1. Senior Scientist, Data Science job in West Point, Pennsylvania, United States of America | Research & Development jobs at Merck
2. Boston ADME & Discovery Toxicology – Associate Principal Scientist job in Boston, Massachusetts, United States of America | Research & Development jobs at Merck
3. Senior Scientist, Quantitative Pharmacology and Pharmacometrics job in West Point, Pennsylvania, United States of America | Research & Development jobs at Merck
4. Associate Principal Scientist, Infectious Disease and Vaccines, Quantitative Pharmacology and Pharmacometrics job in West Point, Pennsylvania, United States of America | Research & Development jobs at Merck
5. Senior Scientist job in Rahway, New Jersey, United States of America | Research & Development jobs at Merck

Contact Information for Merck Participants

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Nicole Revaitis, Ph.D.	Bio-analytics (BA)	nicole.revaitis@merck.com
Brian Vega, Ph.D.	Nonclinical Drug Safety (NDS)	brian.vega@merck.com

THANK YOU FOR YOUR PARTICIPATION!

MERCK

Backup

Preclinical Development (PCD) – bridging drug discovery and development

- **ADME & Discovery Toxicology**: Characterizing absorption, distribution, metabolism, elimination, and toxicology profiles for drugs.
- **Quantitative Pharmacology and Pharmacometrics**: clinical PK/PD data analysis and trial design
- **Bioanalysis**: Quantification of critical drug and biomarker analytes to support PK/PD assessments
- **Non-clinical drug safety**: Assessing drug safety in preclinical species
- **Lab Animal Resources**: Preclinical species facilities and resource management
- **Strategic Operations**: Project Management & Facility Operations, Archiving, Submission Management, Training Strategy & Compliance
- **Outsourcing**: Managing Contract Research Organization partnerships and external studies

ADME & DISCOVERY TOXICOLOGY (DT)

MERCK

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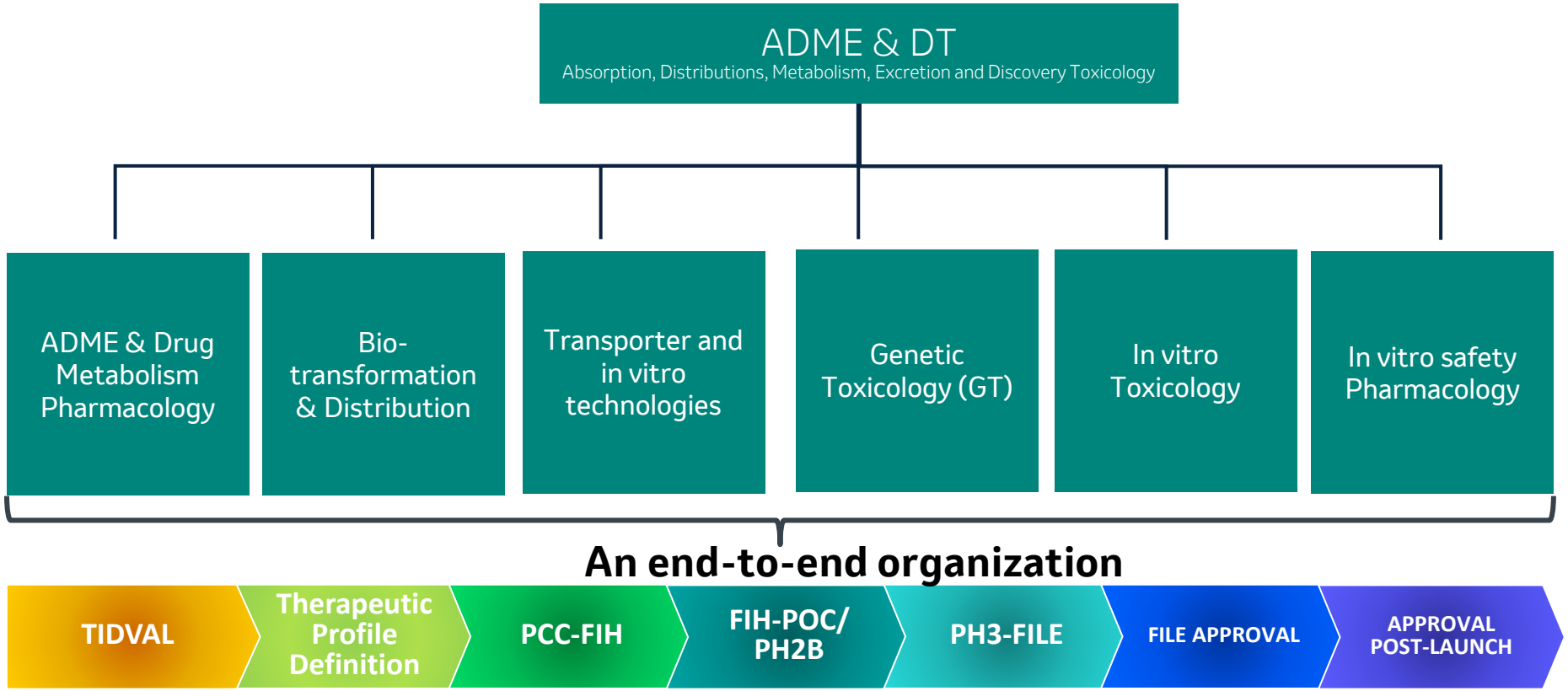
Global ADME-DT Organization



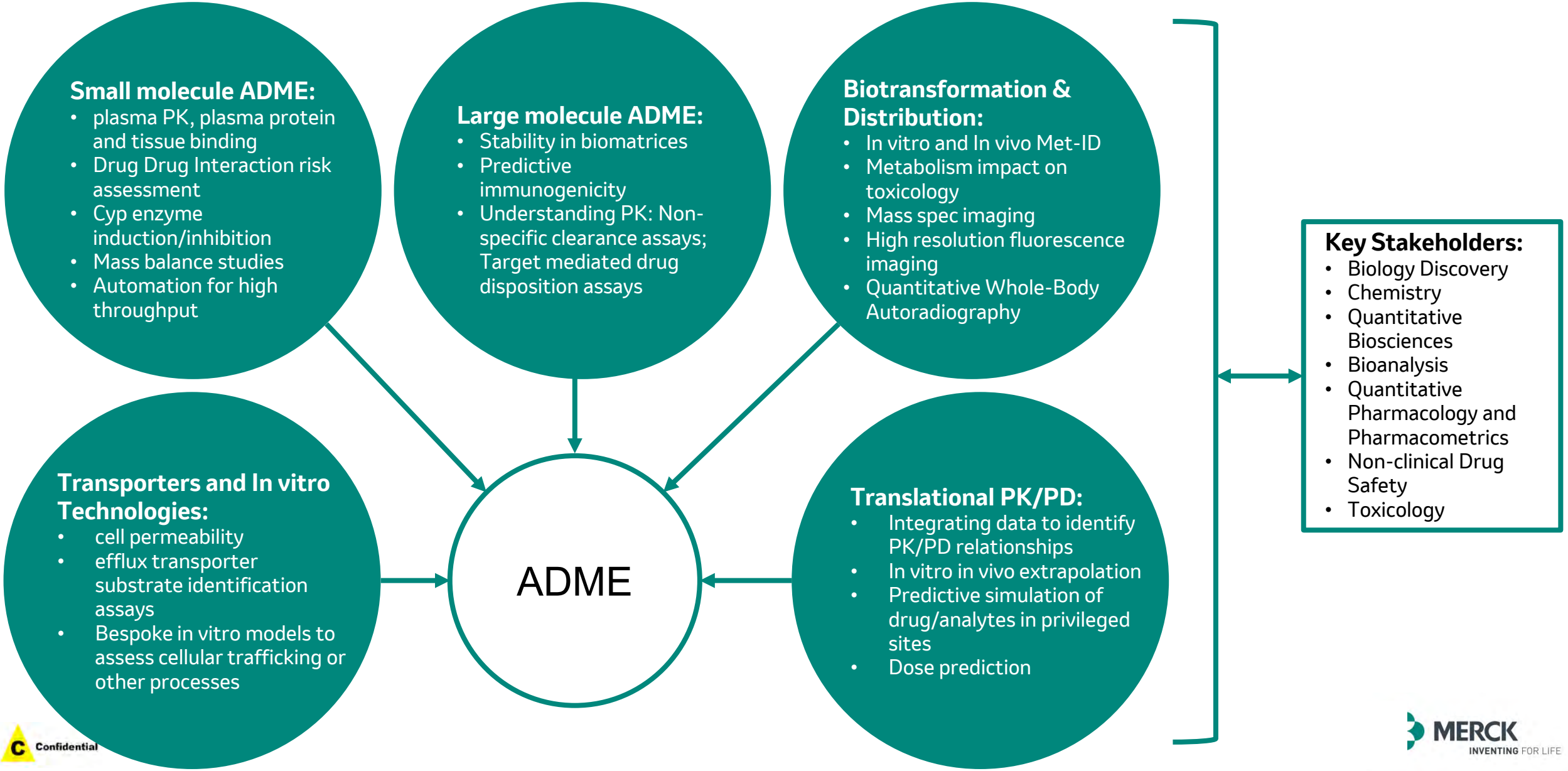
Our Vision:

To be the industry leader in advancing novel medicines to patients with unbridled efficacy and safety.

Our Core Mission:

Optimize the translation of preclinical ADME and Discovery Toxicology data to design molecules with maximal therapeutic safety and pharmacodynamics to achieve clinical success at unparalleled speeds.

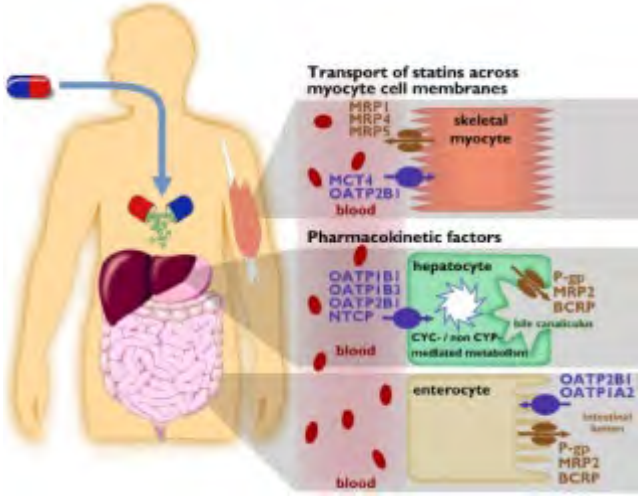
ADME functions support our diverse discovery and development pipeline



ADME's Goal: Elucidating the Intersection of Target Biology and Drug Disposition and Defining the ADME Characteristics Needed for Clinical Success for Any Modality

In silico, In Vitro, and In Vivo Relationships

- Inform on therapeutic strategy and molecular design.
- Build understanding of key factors affecting human dose.
- Incorporate tPKPD thinking on teams.



Regulatory Filings and Interactions

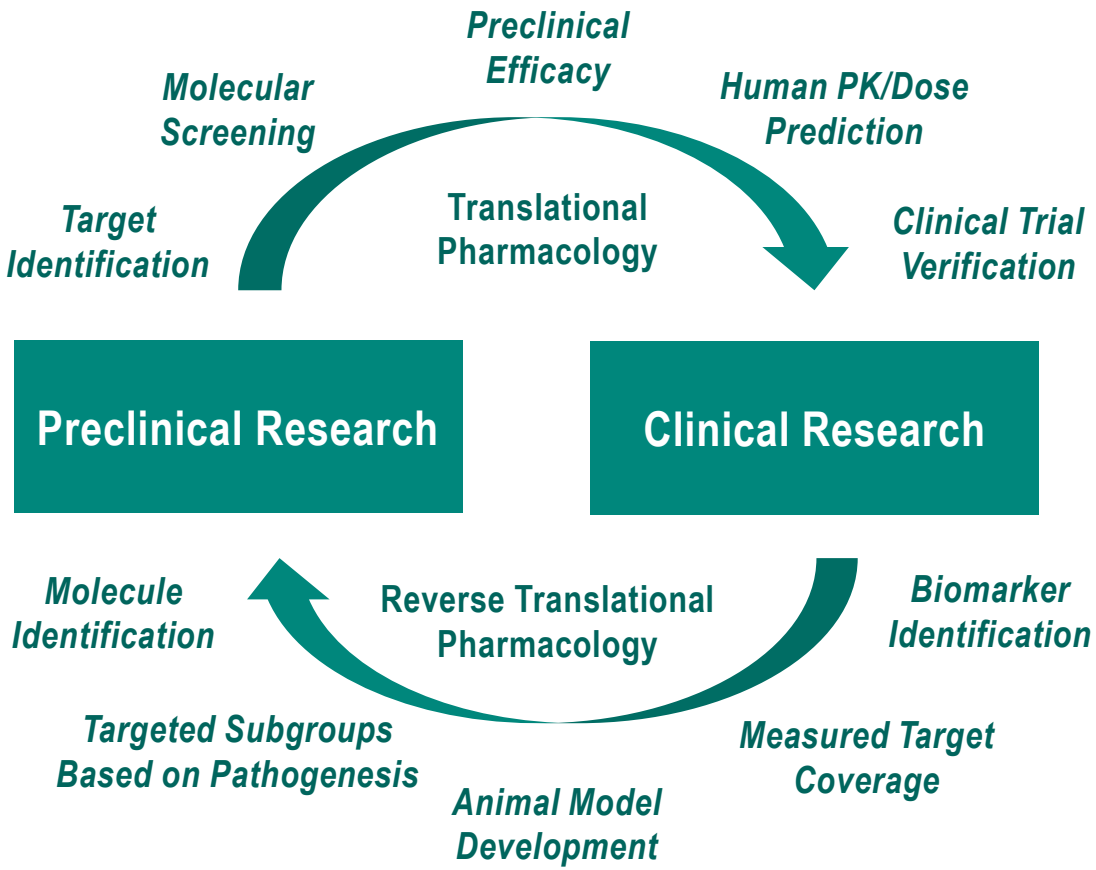
- Integrated mechanistic interpretation of clinical DDI data.
- Considerations of special populations (Pharmacogenomics- PGx)
- Drug product labeling

PRE-LEAD OPT → LEAD OPT → PCC-FIH → FIH-POC/ PH2B → PH3-FILE → FILE APPROVAL → APPROVAL POST-LAUNCH

Examples of ADME Characterization

- End-to-end and modality agnostic.
- Small molecules: Influencing ROP design, transporter assessments, CYP metabolism, DDI predictions, rolling dose predictions in conjunction with tPKPD.
- Biologics: PK/PD of bispecific mAbs, immunogenicity characterization.
- Peptides: Membrane permeability, stability, intracellular exposure, distribution to site of action.
- Vaccines: Biodistribution and tissue PK.
- Regulatory document authoring (IND/ IMPD/ IB/ NDA).

Translational and Reverse Translational ADME Capabilities



Translational ADME

- Analysis of parent drug, metabolites, target engagement and PD biomarkers
- Tumor imaging platforms
- 3D cell culture systems
- Flow cytometry capabilities

Reverse Translational ADME

- Modeling of target coverage and subsequent PK/PD relationships based on reported clinical biomarkers and patient outcomes
- Exploring relationships between TMDD, PK/PD and MOA in existing pembrolizumab samples and data sets

ADME-DT Encouraging Growth through Scientific Contributions

INTERNATIONAL CONSORTIUM for INNOVATION & QUALITY in PHARMACEUTICAL DEVELOPMENT

ISSX
International Society for the Study of Xenobiotics

American Society for Mass Spectrometry

aaps
American Association of Pharmaceutical Scientists

MANCHESTER 1824
The University of Manchester
Centre for Applied Pharmacokinetic Research (CAPKR)

PURDUE UNIVERSITY

External Consortia & Partnerships

Publications & Awards

Academic Collaborations & Internships

The ADME-DT team is looking for talent like YOU!

Analytical Chemistry

Biochemistry

Bioinformatics

Biology

Biophysics

Cell Biology

Chemistry

Data Science

Engineering

Immunology

Mathematics

Molecular Biology

Pharmaceutical Sciences

Pharmacology

Project Management

Toxicology

& MANY MORE ....

MERCK
INVENTING FOR LIFE

PRECLINICAL DEVELOPMENT (PCD) OUTSOURCING

MERCK

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PCD Outsourcing Mission

To advance MRL's therapeutic and vaccine portfolio by:

Proactively developing and leading a network of external partners to generate high quality, timely and cost-effective data that drive PCD portfolio decisions

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PCD Outsourcing… Who are we?

Preclinical, Nonclinical Drug Safety (NDS), Quantitative Pharmacology & Pharmacometrics (QP2) Sourcing

- Preclinical –supports most small molecule discovery screening assays (in vivo & in vitro) and biologics in vivo assays
- NDS –supports GLP and non-GLP studies (in vivo & in vitro)
- QP2 – supports modeling & simulation, NCA, MBMA, QSP, PKPD, PopPK

Regulated Vaccines Bioanalytical Sourcing

- Supports clinical and non-clinical vaccine sample analysis externally.
- Assays are externalized after internal method development, qualification and Ph1 support, to ensure robustness.
- Vaccines antigen/antibody binding, cell-based and molecular assays, many of which are multiplexed

Regulated Pharmacokinetics (PK)/Anti-Drug Antibody (ADA) Bioanalytical Sourcing

- Supports clinical and GLP small molecule and biologics PK/ADA/NAb sample analysis externally.
- Assays are externalized after internal method development, validation, and Ph1 support, to ensure robustness.
- LC/MS and ligand binding assays

Sourcing Operations

- Sourcing Operations align with Outsourcing subfunction
- Liaison with procurement and finance (forecasting/budget, PO generation, invoicing)
- Support Partner Relationship Management, Sourcing Management Process, Vendor Performance Process

Each PCD outsourcing subfunction:

- Aligns sourcing activities with the appropriate functional area scientific strategy
- Has robust quality processes and partnership with PCD Subject Matter Experts (SMEs) to ensure control over external work. Quality is #1.
- Provides access to flexible external resources.

PCD Outsourcing Provided Access to External Resources

ITERATIVE PROCESS

- **Build** a reliable external partner base
- **Source** well established & niche activities which are aligned with PCD scientific strategy. We have a global partner footprint.
- **Focus** spend on commoditized activities
- **Result** - internal resources focus on novel/complex work & partners focus on commoditized activities
- **Share/learn** –best practices

All working to ensure that data collected from external vendors matches Merck PCD expectations

Qualifications

Responsibilities

Quality

Ensure external data meet internal quality expectations

Flexibility

Provide flexible pool of quality providers to drive portfolio needs

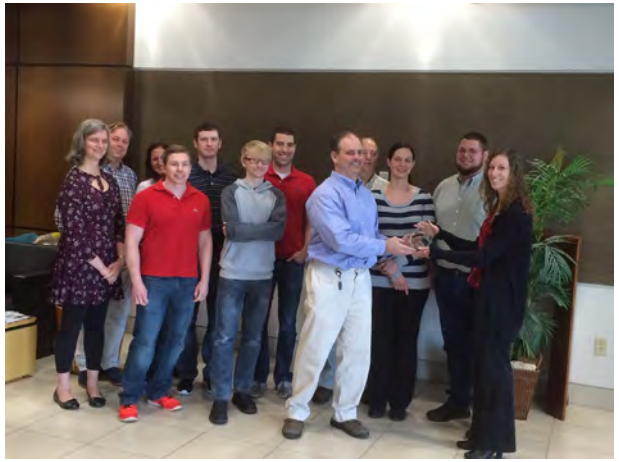
Speed

Ensure timely delivery of external data to our internal customers

Value

Provide high quality data at the best value for Merck

Activities



Our team works together to support charitable organizations and travels to vendor sites to complete performance reviews.