DRUG DEVELOPMENT COURSE: FROM MOLECULE TO PRESCRIPTION

Meeting Room: **WEILL CORNELL MEDICINE 1300 YORK AVE AUDITORIUM A-250 3:00PM - 5:00PM**

Dates: 1/11/2018, 1/18/2018, 1/25/2018, 2/1/2018, 2/8/2018, 2/15/2018, 2/22/2018, 3/1/2018, 3/15/2018, 3/22/2018, 3/29/2018, 4/5/2018, 4/12/2018, 4/19/2018, 4/26/2018 & 5/3/2018

Weill Cornell Graduate School - Tri-Institutional Therapeutics Discovery Institute

ABOUT THIS COURSE

This course has been designed in collaboration with drug development experts from Roche and provides a foundation of integrated knowledge of the multi-disciplined process of developing a new medication. It includes real world challenges encountered in the areas of discovery, development, manufacturing, global regulatory approval and commercialization of new medicines. In addition, the impact of emerging technologies to healthcare and the development process will be considered.

While each lecture could be a topic for one (or more) graduate course, the goal of this integrated program is to provide an introduction to the whole drug development process, to raise awareness of all the different aspects that need to be considered to bring new medicines to patients, and to elicit interest for young investigators.

WHO IT IS FOR

Graduate students in the life sciences who are future researchers, prescribers or potential participants in the development process will benefit from this comprehensive view of how drugs are developed.

FACULTY

The lectures will be given by professionals with expertise and long experience in drug development who work at Roche Innovation Center in New York City.
The current list of instructors is draft and will be defined based on recommendations and approval by Roche senior management for each specific subject matter

STRUCTURE

12 Lectures (1.5 - 2 hr. each) including real world case studies
Target size: approximately 40 students
Students will be divided in 6 groups, at the beginning of the course a “research problem’ will be assigned to each group. It is expected that at the end of the course each group will present their assignment and proposed solutions (i.e. 20 min presentation and 10 min for Q&A)
Assessment: Mid Term and Final Exams (multiple choice), plus evaluation of the research exercise

Session 1

Overview of the Discovery and Development Process
Instructor: Ignacio Rodriguez, MD, Senior Safety Science Leader, Pharma Development Site Head Roche Innovation Center New York

- Drug Development Pathway: how to go from molecule to medicine
- target product profile
- types of compounds (small molecules - biologics - antibody / drug conjugates, vaccines)
- different phases in development, approval, and life cycle management
- current and future drug development process

- success metrics, timelines, costs

Session 2

Drug Development is a Tightly Regulated Science

Instructor: Megan-Zoschg Canniere, Pharm D, Global Franchise Head Neurodegeneration & Rare Diseases, Regulatory Affairs, Roche Innovation Center New York

- History of Regulation
- Regulatory requirements in different countries (focus on FDA and EMA)
- Regulatory interactions at different phases of development
- CTA - IND - NDA
- Tools for expedited review and approval
- Safety database
- Regulatory compliance and post approval commitments
- Pediatrics

Session 3

Strategic & Tactical Considerations and Business Models

Instructor: Richard H. Christie MD, PhD. Global Head, Development Science and Innovation Head, External Development Group, Roche Innovation Center New York

- Indication Selection
- Risk Tolerance
- Target Product Profile
- Global Product Strategy
- Team Structure
- Roles and Functions
- Partners: Investigator Sites, CROs, Patient Advocacy Organizations, Disease Foundations
- Overview of business models in drug development
    - How to get funding
    - Commercial aspects of the TPP
    - Return on investment
    - Patent life

Session 4

Overview of the Discovery Process

Instructor: Paul Gillespie PhD. External Drug Discovery Director Roche Innovation Center New York

- Target identification and validation
- assay development and screening
- animal models of disease
- Lead identification, lead optimization and clinical candidate selection

Session 5

Chemistry, manufacturing, and control

Instructor: Hitesh Chokshi PhD. Senior Leader Therapeutic Modalities – Preclinical CMC. Roche Innovation Center New York

- Manufacturing Process and Formulation Activities and Requirements
    - Small vs Large Molecules
    - Different requirements and needs in different phases

Session 6

Non-Clinical safety and DMPK considerations

Instructors: Gaurav Tyagi, BVSc, PhD, DACVP, DABT Principal Scientist Pharmaceutical Sciences; Li Yu, Ph.D, Pharmaceutical Sciences Site Head, Expert Scientist Pharmacokinetics, Dynamics and Metabolism Leader, Roche Innovation Center New York

- What are desirable ADME properties?
- Points-to-consider in DMPK at different stages for drug discovery and development
- Translational PK/PD modeling
- Early in vitro tests to screen and predict toxicity
- Regulatory Toxicology (including ICH guidelines)
    - GLP vs non-GLP studies
    - Acute vs Chronic studies (selection of species, duration and evaluation)
    - Safety Pharmacology
    - Mutagenicity and Carcinogenicity studies
    - Reproductive and Developmental Toxicology studies
- Mechanistic Toxicology (including biomarkers)
- New trends in preclinical evaluation (integrated assessments, organ on a chip, stem cells, etc)
- Differences between evaluation of small molecules & biotherapeutics

Session 7

Overview of the Early Clinical Process (from First in Humans to Proof of Concept)

Instructor: Navita Mallalieu PhD, Director, Clinical Pharmacology Roche Innovation Center New York

- Key goals in early clinical development
- How to design and conduct EIH studies
    - Translating preclinical data to clinical
    - Study design questions: Study Design options- parallel group, crossover, adaptive, randomized, blinding, etc
    - Dose selection, dose progression (safety and PD/efficacy considerations)- small molecule vs biologic
    - Population (HVs vs. patients)
- Phase II Studies
    - Patient selection
    - Designs (e.g. adaptive, dose range finding, open-label vs blinded, dose selection)
    - Exposure response analysis: Biomarkers/surrogate efficacy measurements and the role of modeling and simulation
    - Proof of Mechanism / Proof of Concept
    - Dose selection
- Supporting Studies (DDI, Special Populations, Abuse Liability, TQT)

Session 8 MID-TERM EXAM

Session 9

Key Concepts in Clinical Pharmacology

Instructor: Patanjali Ravva PhD, Director, Clinical Pharmacology Roche Innovation Center New York

- Ultimate goal is a useful prescribing information
- Absorption, Bioavailability, Distribution, Metabolism, and Elimination
- Dose-Exposure relationships
- Quantitative Pharmacology/Pharmacometrics
- Clinical Pharmacodynamics

- Disease models
- Principles of PK/PD modeling and simulation

Session 10

Biostatistics in drug development

Instructor: Steven Blotner, Senior Statistical Scientist. Biometrics Roche Innovation Center New York

- role in the different phases
- novel designs (example: CRM vs. 3+3)
- Types of Endpoints in Clinical Trials
- Blinding, Randomization, and Stratification
- Hypothesis Testing and Error Probabilities
- Multiple Testing
- Interim Analyses
- Sample Size and Trial Duration
- Minimum Detectable Difference
- Confidence Intervals
- P-Values

Session 11

Confirmatory Phase and Post Approval Activities

Instructor: Judith Dunn, PhD Vice President, Head of Roche Innovation Center New York

- Pivotal Phase 3 studies
  - Key objectives
  - Logistical considerations
  - Choice of controls
  - Subgroup analysis
  - Interim Analyses (early stops for futility, safety or efficacy)
- Safety database
- What else is needed in this phase
- Regulatory submission for approval
- Post Approval Activities (surveillance, post approval safety studies, new indications)

Clinical Operations

- Challenges (clinical failure, participation rates, reimbursement)
- CROs
- Investigative sites

Session 12

Clinical Safety and Pharmacovigilance

Instructors: Ignacio Rodriguez, MD, Senior Safety Science Leader, Pharma Development Site Head Roche Innovation Center New York

- What is expected at each phase
- Principles of Pharmacovigilance
- Expected and Unexpected AE in clinical trials
- SUSAR and Reference Safety Information
- Safety Signals and Signal Detection Plan
- Risk Management Plans
- Post approval safety commitments

Session 13

Use of Emerging Technologies to Address Industry Challenges

Instructor: James Cai PhD. Head of Data Science, Roche Innovation Center New York

- Emerging Technologies and approaches in drug development
- Use of biomarkers and diagnostics
- PHC
- Real world data
- Use of electronic medical records

Session 14 & 15

Project Presentations (class)

- Each group will present their case study and the recommendations
- Sessions will be graded by a panel of experts from the lecturers and experts from Tri-I and the academic institutions

Session 16 FINAL EXAM