DRUG DEVELOPMENT COURSE - FROM MOLECULE TO PRESCRIPTION
WEILL CORNELL GRADUATE SCHOOL - TRI-INSTITUTIONAL THERAPEUTICS DISCOVERY INSTITUTE
THURSDAYS FROM 3:00PM - 5:00PM AT 1300 YORK AVE, NEW YORK, N.Y.

COURSE LEADERS: Dr. Paul Gillespie, External Drug Discovery Director Roche Innovation Center
Dr. Hitesh Chokshi PhD. Senior Leader Therapeutic Modalities – Preclinical CMC. Roche Innovation Center

COURSE FACILITATORS: Dr. Lorraine Gudas - Chair, Professor of Pharmacology, Weill Cornell Medicine
Dr. Daniel Heller, - Head, Cancer Nanomedicine Laboratory, Associate Member, Molecular Pharmacology Program, MSKCC, Associate Professor, Weill Cornell Medical College

TEACHING ASSISTANTS: George Liao - gel2017@med.cornell.edu
Corrin Pimentel - cop2002@med.cornell.edu

PLEASE NOTE DATES AND LOCATIONS:
Jan 10, 2019 3:00 PM-5:00 PM - AUDITORIUM A250
Jan 17, 2019 3:00 PM-5:00 PM - AUDITORIUM A250
Jan 24, 2019 3:00 PM-5:00 PM - AUDITORIUM A250
Jan 31, 2019 3:00 PM-5:00 PM - AUDITORIUM A250
Feb 7, 2019 3:00 PM -5:00 PM - AUDITORIUM C200
Feb 14, 2019 3:00 PM-5:00 PM - AUDITORIUM A250
Feb 21, 2019 3:00 PM -5:00 PM - AUDITORIUM C-200
Feb 28, 2019 3:00 PM-5:00 PM - AUDITORIUM A250

Mar 7, 2019 - SPRING BREAK NO CLASS
Mar 14, 2019 3:00 PM-5:00 PM - AUDITORIUM A250
Mar 21, 2019 3:00 PM-5:00 PM - AUDITORIUM A250
Mar 28, 2019 3:00 PM-5:00 PM - AUDITORIUM A250
Apr 4, 2019 3:00 PM-5:00 PM - AUDITORIUM A250
Apr 11, 2019 3:00 PM-5:00 PM - AUDITORIUM A250

Apr 18, 2019 – NO CLASS
Apr 25, 2019 3:00 PM -5:00 PM - AUDITORIUM C-200
May 2, 2019 3:00 PM-5:00 PM - AUDITORIUM A250
May 9, 2019 3:00 PM-5:00 PM - AUDITORIUM A950

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 courses, the goal of this integrated program is to provide an introduction to the whole drug development process, to raise awareness about all the different aspects that need to be considered to bring new medicines to patients, and to elicit interest of 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 much experience in drug development, most of whom work at Roche Innovation Center in New York City.
The current list of instructors is a draft and will be finalized 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 into 6 - 8 groups, and 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 group presentation and 10 min for Q&A)
Assessment: Mid Term and Final Exams (multiple choice), plus evaluation of the research exercise

January 2019
Session 1 – Jan 10th 2019
Overview of the Discovery and Development Process
Instructor: Ignacio Rodriguez, MD, Clinical Safety Therapeutic Area Head – CSL Behring
- 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 – Jan 17th 2019
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 3 – Jan 24th 2019
Transforming Novel Molecules to Medicines: Technical Perspective
Instructor: Hitesh Chokshi PhD. Senior Leader Therapeutic Modalities – Preclinical CMC. Roche Innovation Center New York
- CMC activities, partners, and deliverables
- How “drug like” is molecule?
  - Developability alerts
  - Target drug product profile
  - Scalability of API and drug product to meet clinic / market demand
  - Process and product quality attributes --> Robust product
- Drug Delivery – Past, Present and Future
- Future drug modalities – Challenges and Opportunities

Session 4 – Jan 31st 2019
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 5 – Feb 7th 2019
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 6 – Feb 14th 2019
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 7 – Feb 21st 2019
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 8 – MID-TERM EXAM – Feb 28th 2019

Spring Break – Mar 7th 2019

Session 9 – Mar 14th 2019
Clinical Safety and Pharmacovigilance
Instructor: Ignacio Rodriguez, MD, Clinical Safety Therapeutic Area Head – CSL Behring
- 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 10 – Mar 21st 2019
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
  o Translating preclinical data to clinical
  o Study design questions: Study Design options- parallel group, crossover, adaptive, randomized, blinding, etc
  o Dose selection, dose progression (safety and PD/efficacy considerations)- small molecule vs biologic
  o Population (HVs vs. patients)
• Phase II Studies
  o Patient selection
  o Designs (e.g. adaptive, dose range finding, open-label vs blinded, dose selection)
  o Exposure response analysis: Biomarkers/surrogate efficacy measurements and the role of modeling and simulation
  o Proof of Mechanism / Proof of Concept
  o Dose selection
• Supporting Studies (DDI, Special Populations, Abuse Liability, TQT)

Session 11 – Mar 28th 2019
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 12 – Apr 4th 2019
Confirmatory Phase and Post Approval Activities
Instructor: Mark Eisner, MD, Senior Vice President, Global Head of Immunology, Infectious Disease, and Ophthalmology Clinical Development, Genentech, South San Francisco, California
• Pivotal Phase 3 studies
  o Key objectives
  o Logistical considerations
  o Choice of controls
  o Subgroup analysis
  o 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)
Session 13 – Apr 11th 2019

Strategic & Tactical Considerations and Business Models
Instructor: Patrick Schleck, Pharm D, MBA, Global Head Business Development, Immunology, Infectious Diseases, and Specialty Care at Roche

- 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

NO CLASS - Apr 18th

Session 14 & 15 – Apr 25th 2019 – May 2nd, 2019

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 the academic institution

Session 16 FINAL EXAM – May 9th 2019 – A950