

CNS Drug Development (What is a “drug target”?)

a conversation to stimulate thinking

Sam Kongsamut, PhD

Executive Director, Entrepreneur Center, Institute for Life Sciences Entrepreneurship

RISE Associate Fellow, Drew University

President, Rudder Serendip LLC

October 21, 2016

Outline

- A little bit about me
- CNS drug development
- What is a drug target?
- If we only knew the pathological basis of disease we could fix it
- Why is pharmacology important?
- What do we want/need to know to put something into humans?
- It's the best time to be in science...

A little about Sam Kongsamut

- Ph.D. (Neuropharmacology) – Univ Chicago; Postdocs – Cornell, Yale
- Bridgewater NJ (1991-2012):



Hoechst Celanese



Hoechst Marion Roussel
Das Pharma-Unternehmen von Hoechst

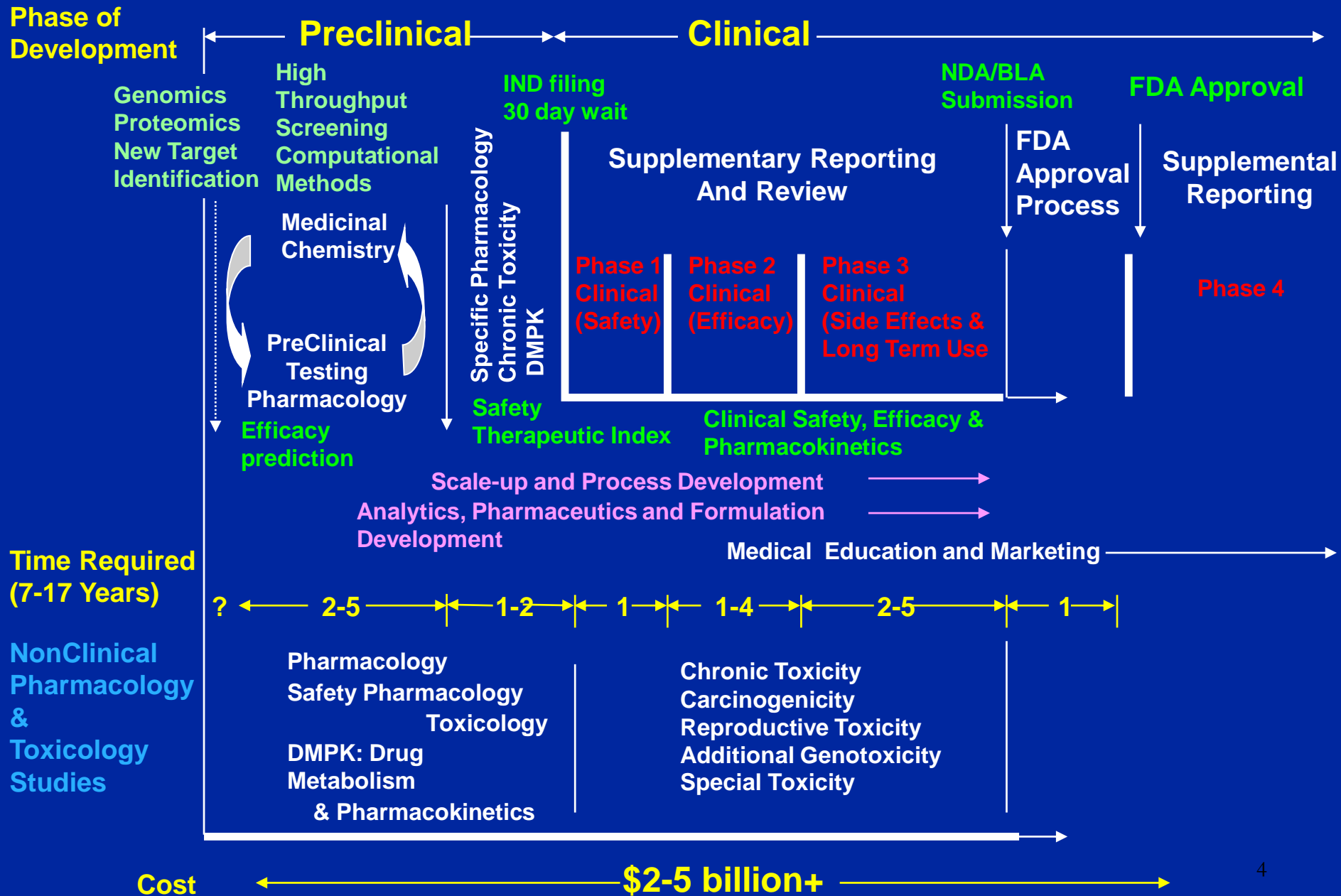


- R&D: Discovery → Development → Clinical Development → 2 Marketed Products
- Management (portfolio, people)
- External (open) Innovation / Business Development

-  **Rudder Serendip** (2012-present):

- Consulting in Neuroscience & Aging + other areas
- Universities and Foundations  Alzheimer's Drug Discovery Foundation  CHDI FOUNDATION  UNIVERSITEIT GENT
- Biochron Therapeutics
- Neurotrope BioScience Inc.  Neurotrope BioScience
- NSF iCorps, ELAB NYC  National Science Foundation WHERE DISCOVERIES BEGIN  ENTREPREURSHIP LAB BIO AND HEALTHTECH NYC
- Rutgers CTEC Entrepreneurship Mentor  RUTGERS
- Launch NJ Life Sciences Hub  Meetup
- Institute for Life Sciences Entrepreneurship  ILSE INSTITUTE FOR LIFE SCIENCE ENTREPRENEURSHIP
- RISE Associate, Drew University  DREW

US New Drug Development Process



CNS Drug development

Why is it so difficult?

Crossing the Blood Brain Barrier

Understanding of brain function

Redundant mechanisms and feedback loops

Neurodevelopmental abnormalities

Compensatory mechanisms

Acute vs chronic effects

Trial and error

What is a drug target?

Phenotypic screen – behavioral models

Molecular targets

Cloning of the human genome

Dictionary vs language – can you learn a language by studying the dictionary?

Disease pathology (up/downregulation)

humans vs. animal models

Mechanistic vs. pathological models

If we only knew the pathological basis of disease, we could fix it

Lysosomal storage disorders (ERT)

many CNS symptoms

Diabetes (insulin – successful?)

Alzheimer's as T3D?

Huntington's disease

Sickle Cell Anemia

Why is pharmacology important?

Pharmacodynamics

Pharmacokinetics

What the drug does to the body vs. what the body does to the drug

Benefit risk - everything is toxic

potency vs efficacy

Agonist or antagonist

Allosteric modulators

Pharmacokinetics – ADME

Structure Activity Relationships

What do we want/need to know to put something into humans?

Investigational New Drug application (IND)

Safety, safety, safety (first do no harm)

Benefit risk

Therapeutic index

Chronic treatment

CMC – we tend to take this for granted

It's the best time to be in science
We know more than ever

Change in R&D model from
big company to small company

Innovation occurs best in a resource-scarce environment

JOBShop Workshop: Drug Development in Biotechnology

9:30 – 9:45AM	Introduction and Purpose of the Symposium – Janet Alder
9:45 – 10:15	Overview of the Pharmaceutical Industry – Larry Wennogle
10:15 – 10:25	Questions/Discussion
10:25 – 10:55	Technologies for discovery of new drug candidates – Mary Konsolaki
10:55 – 11:05	Break
11:05 – 11:35	CNS Drug Development (What is a “drug target”) – Sam Kongsamut
11:35 – 12:05PM	Clinical Development of a Pharmaceutical Agent for Food and Drug Administration (FDA) approval – Ira Daly
12:05 – 12:35	The story of Entresto – Novel therapy for Heart Failure - Randy Webb
12:35PM	Working lunch will be served
1:00 – 1:30	Funding the Pharmaceutical and Biotechnology Industry – Ben Bowen
1:30 – 2:00	Break out groups – Attendee will break out into small ~6 person groups to develop a plan to organize a biotech company designed to develop pharmaceuticals. (More specific instructions will be supplied.)
2:00 - 2:30	The long and winding road to a marketed drug – Ron Steele
2:30 – 3:00PM	General Discussion including answers to questions submitted in advance of the symposium by participants.
3:00 – 4:00PM	Mixer