Al-Farabi Kazakh National University
Higher School of Medicine
Department of Fundamental Medicine

The development of new drugs by using the Omics technologies.

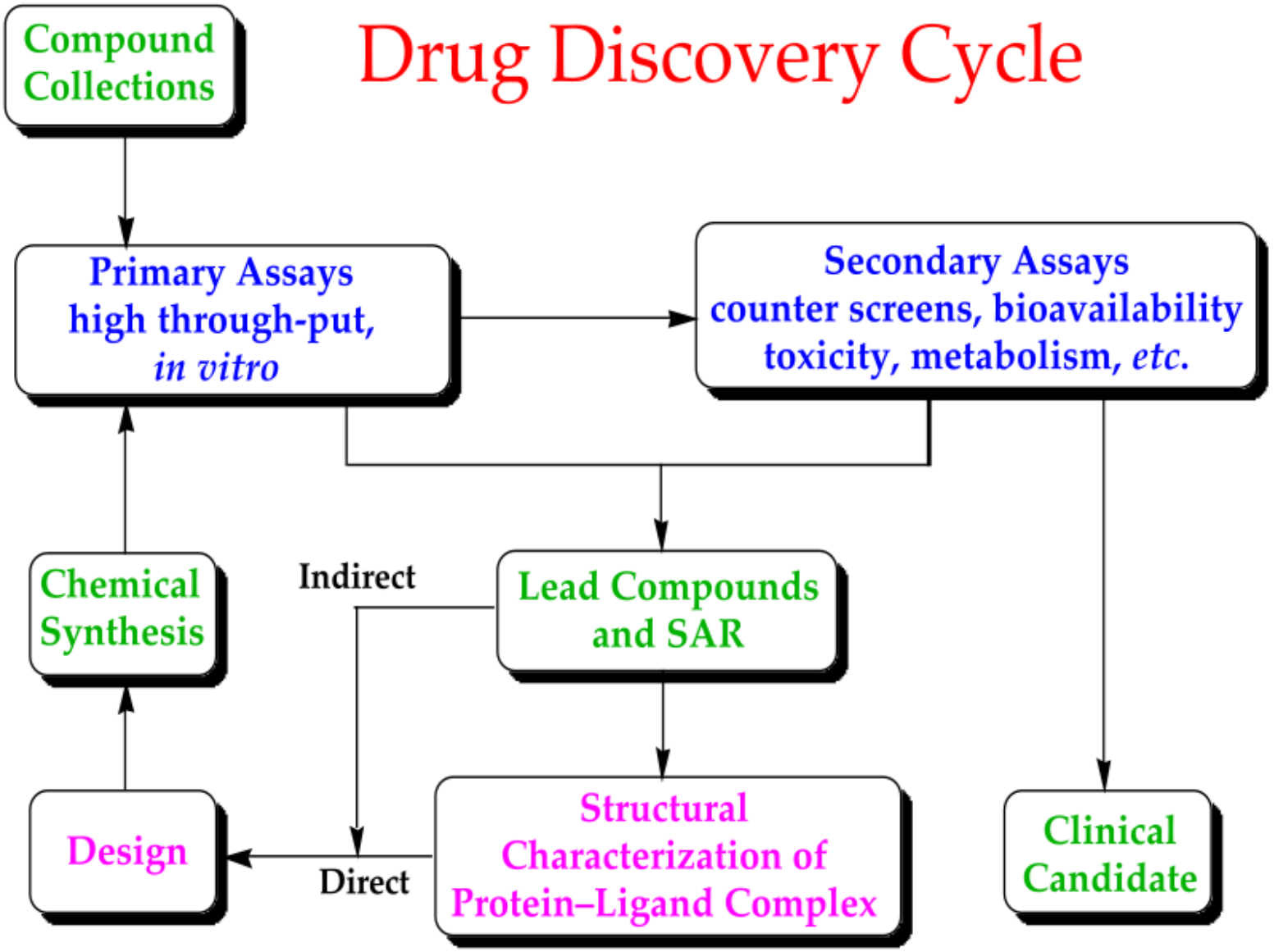
Lecturer and creator: PhD Pinsky Ilya Vladimirovich

LEARNING OUTCOMES
As a result of the lesson you will be able to:

Explain the each step of the drug development by using different “Omics” technologies, give the specific examples.

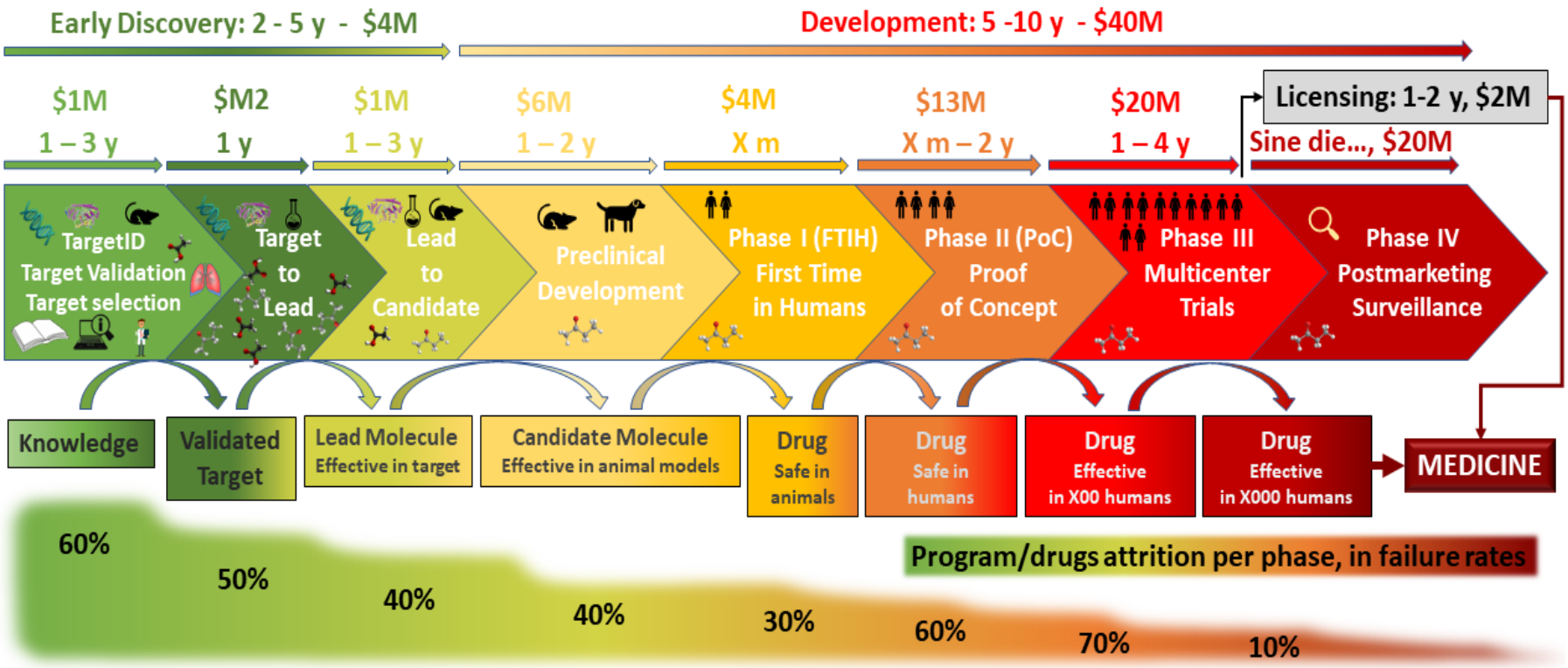
Definitions

Drug development is the process of bringing a new pharmaceutical drug to the market once a lead compound has been identified through the process of **drug discovery**. It includes preclinical research on microorganisms and animals, filling for regulatory status, such as via the United States **Food and Drug Administration** for an investigational new drug to initiate clinical trials on humans, and may include the step of obtaining regulatory approval with a new drug application to market the drug.[1][2] The entire process – from concept through **preclinical testing** in the laboratory to **clinical trial development**, including **Phase I–III trials** – to approved vaccine or drug typically takes more than a decade.[1][2][3]



https://commons.wikimedia.org/wiki/File:Drug_discovery_cycle.svg

The Drug Discovery Process



- Each stage output is the input of the next one.
- The system works like a pipeline, each phase feeding the following one with backups in prevention of program failures.
- Individual pipelines represent therapeutic concepts. Failed stages are not replaced by backups when there are no more appropriate molecules available, on target liabilities appear, compound does not prove therapeutic efficacy, or strategic decisions are applied.
- Costs and timelines represent the values for unique iterations of the respective phases.

Machine Learning applied to Drug Discovery
doctortarget.com

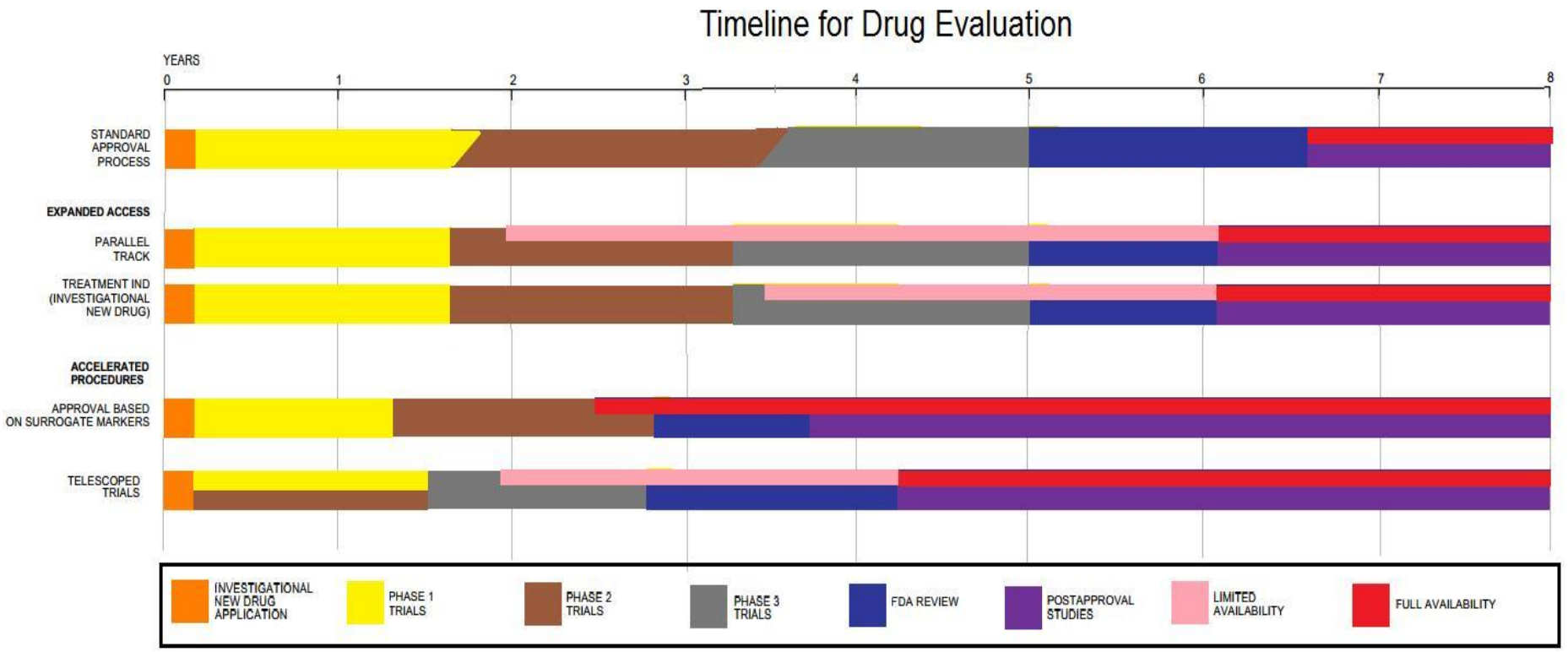
Pre-clinical development

- **New chemical entities** (**NCEs**, also known as **new molecular entities** or **NMEs**) are compounds that emerge from the process of drug discovery. These have promising activity against a particular biological target that is important in disease. However, little is known about the **safety, toxicity, pharmacokinetics, and metabolism** of this NCE in humans. It is the function of drug development to assess all of these parameters prior to human clinical trials. A further major objective of drug development is to recommend the dose and schedule for the first use in a human clinical trial **("first-in-human" [FIH] or First Human Dose [FHD**], previously also known as "**first-in-man" [FIM]**).
- In addition, drug development must establish the **physicochemical properties** of the NCE: its **chemical makeup, stability, and solubility**. Manufacturers must optimize the process they use to make the chemical so they can scale up from a medicinal chemist producing milligrams, to manufacturing on the kilogram and ton scale. They further examine the product for suitability to package as capsules, tablets, aerosol, intramuscular injectable, subcutaneous injectable, or intravenous formulations. Together, these processes are known in preclinical and clinical development as **chemistry, manufacturing, and control (CMC**). [4]

Clinical phase

Clinical trials involve three or four steps:[5]

- **Phase I trials**, usually in healthy volunteers, determine safety and dosing.
- **Phase II trials** are used to get an initial reading of efficacy and further explore safety in small numbers of patients having the disease targeted by the **NCE**.
- **Phase III trials** are large, pivotal trials to determine safety and efficacy in sufficiently large numbers of patients with the targeted disease. If safety and efficacy are adequately proved, clinical testing may stop at this step and the NCE advances to the **new drug application (NDA)** stage.
- **Phase IV** trials are post-approval trials that are sometimes a condition attached by the **FDA**, also called **post-market surveillance studies**.



Timeline showing the various drug approval tracks and research phases

Kessler DA, Feiden KL (March 1995). "Faster evaluation of vital drugs". Scientific American. 272 (3): 48–54. Bibcode:1995SciAm.272c..48K. doi:10.1038/scientificamerican0395-48. PMID 7871409.

References

1. Strovel J, Sittampalam S, Coussens NP, Hughes M, Inglese J, Kurtz A, et al. (July 1, 2016). "Early Drug Discovery and Development Guidelines: For Academic Researchers, Collaborators, and Start-up Companies". Assay Guidance Manual. Eli Lilly & Company and the National Center for Advancing Translational Sciences. PMID 22553881.
2. Taylor D (2015). "The Pharmaceutical Industry and the Future of Drug Development". Issues in Environmental Science and Technology. Royal Society of Chemistry: 1–33. doi:10.1039/9781782622345-00001. ISBN 978-1-78262-189-8.
3. "The Drug Development Process". U.S. Food and Drug Administration (FDA). 4 January 2018. Retrieved 21 March 2020.
4. Emanuel EJ. "The Solution to Drug Prices". New York Times.
5. Ciociola AA, Cohen LB, Kulkarni P (May 2014). "How drugs are developed and approved by the FDA: current process and future directions". The American Journal of Gastroenterology. 109 (5): 620–3. doi:10.1038/ajg.2013.407. PMID 24796999. S2CID 205100166.