

MPN Horizons
Understanding the
New Complexity of MPNs

13-15 October
Zagreb, Croatia

2023


The Life Cycle of Drug Development

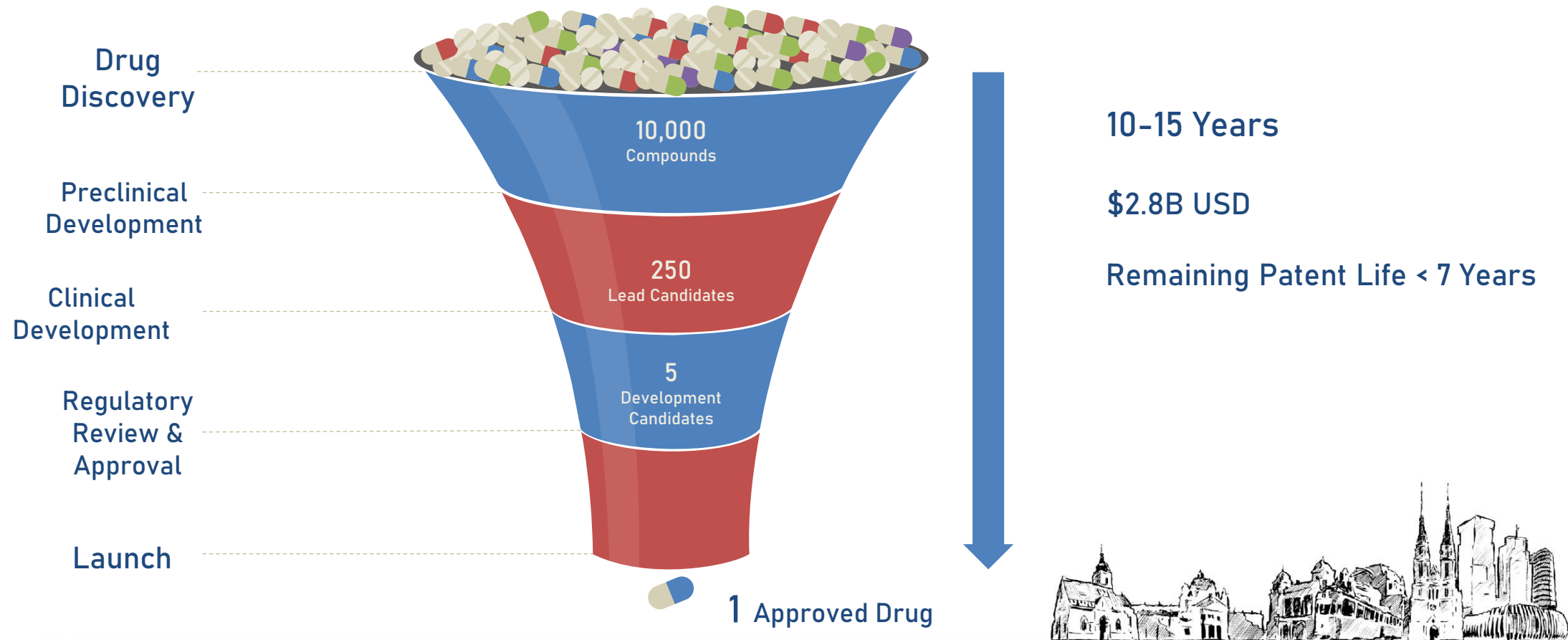
The Journey of Bringing New Therapies to Patients

14 October 2023

Scott J. Weir, PharmD, PhD



An Expensive, High-Risk Endeavor



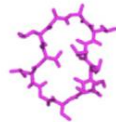
Types of Cancer Therapeutic Agents

Small Molecule Drugs

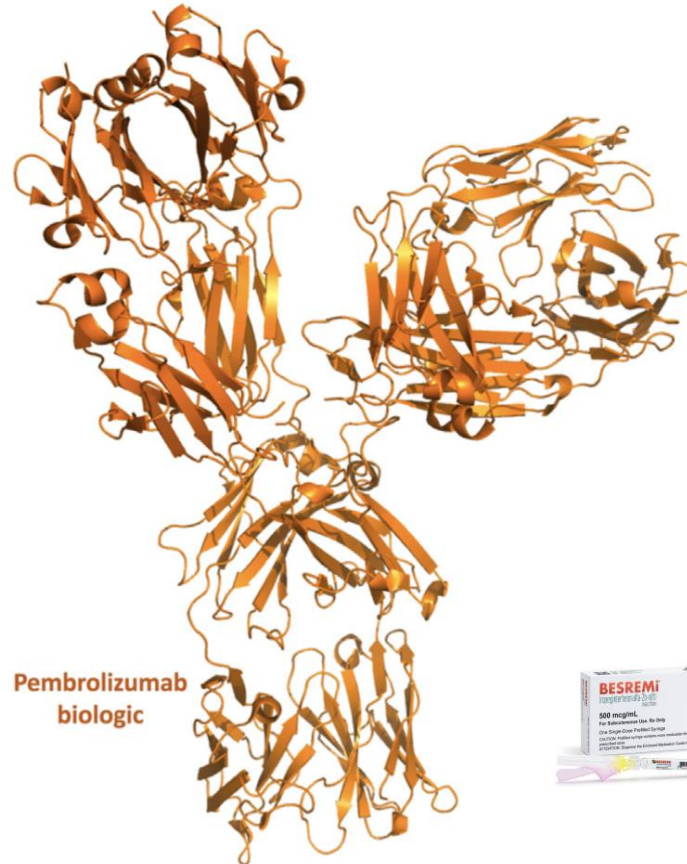
- Chemically synthesized and manufactured
- Stable at room temperature
- Often given orally
- Distribute throughout the body
- Development costs relatively low
- High failure rate



Rivaroxaban
small molecule



Cyclosporine
short peptide



Pembrolizumab
biologic



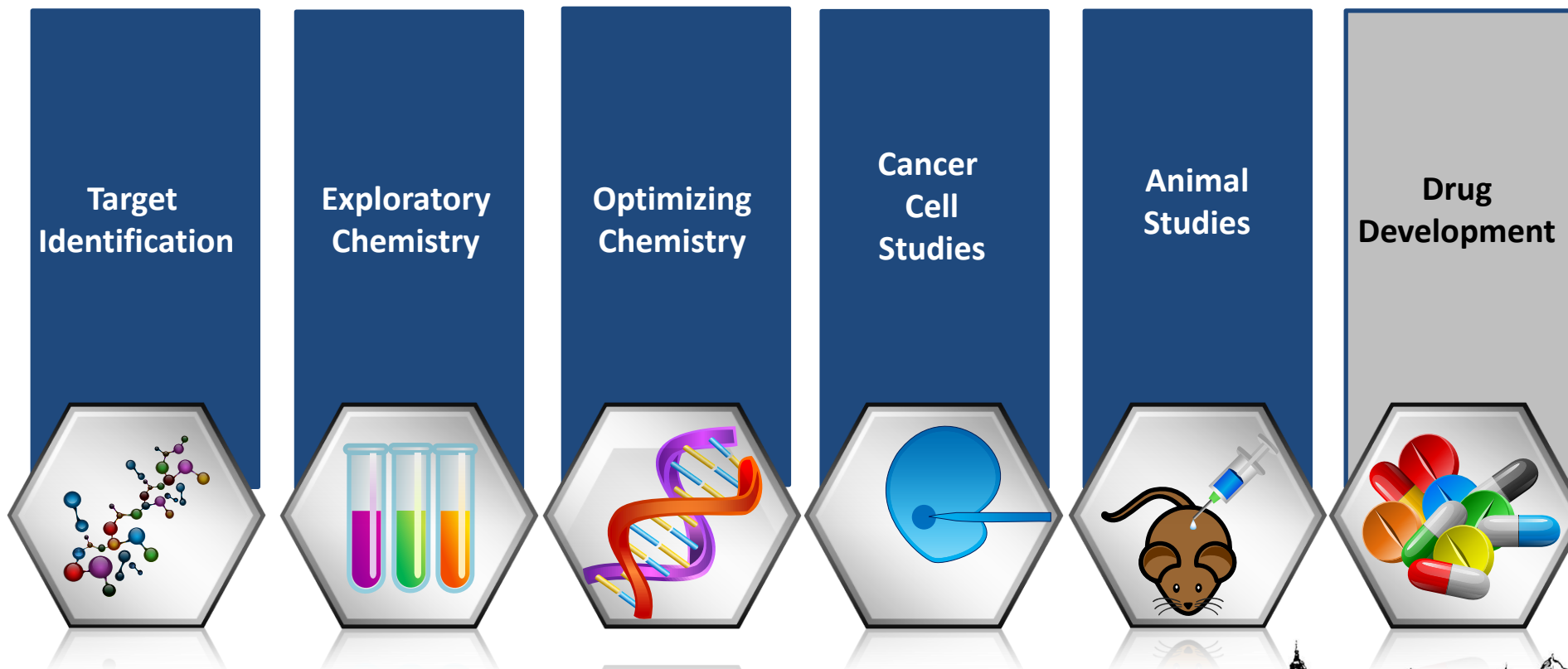
Biologics

- Derived from living organisms
- Vaccines, monoclonal antibodies, immunomodulators, growth factors
- Unstable at room temperature
- Given by injection
- Circulate in blood and lymphatics
- Development costs quite high
- Relatively low failure rate

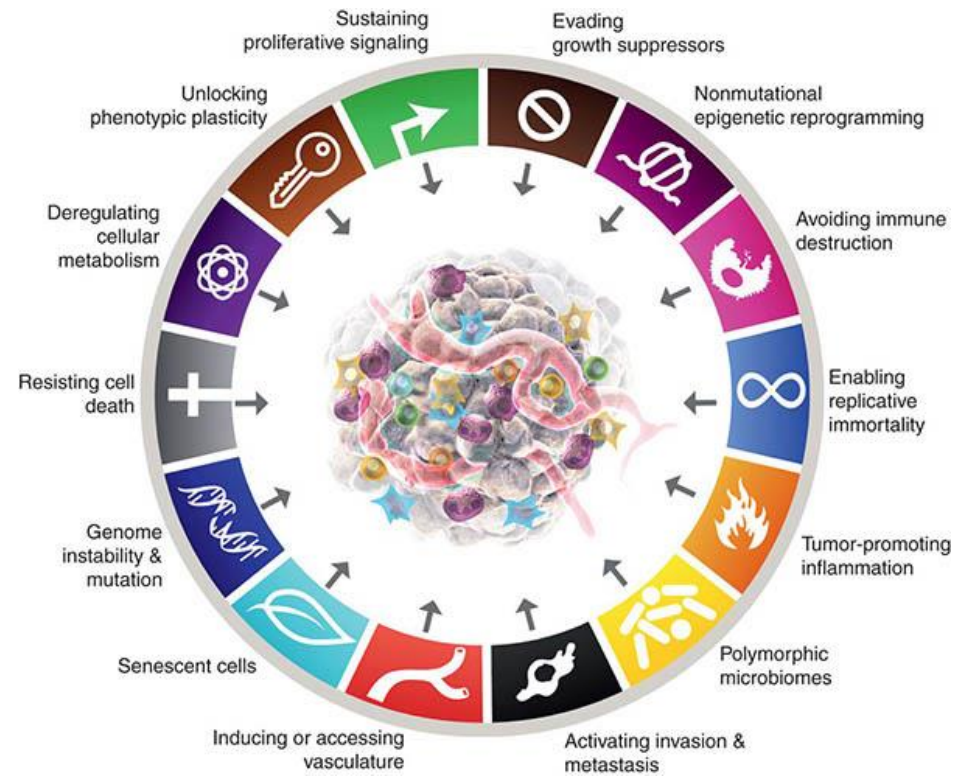
Jakafi[®]
ruxolitinib (tablets)



Drug Discovery Process



The Hallmarks of Cancer



The Concept of a Cancer Drug Target



What Makes a Good Drug Target?



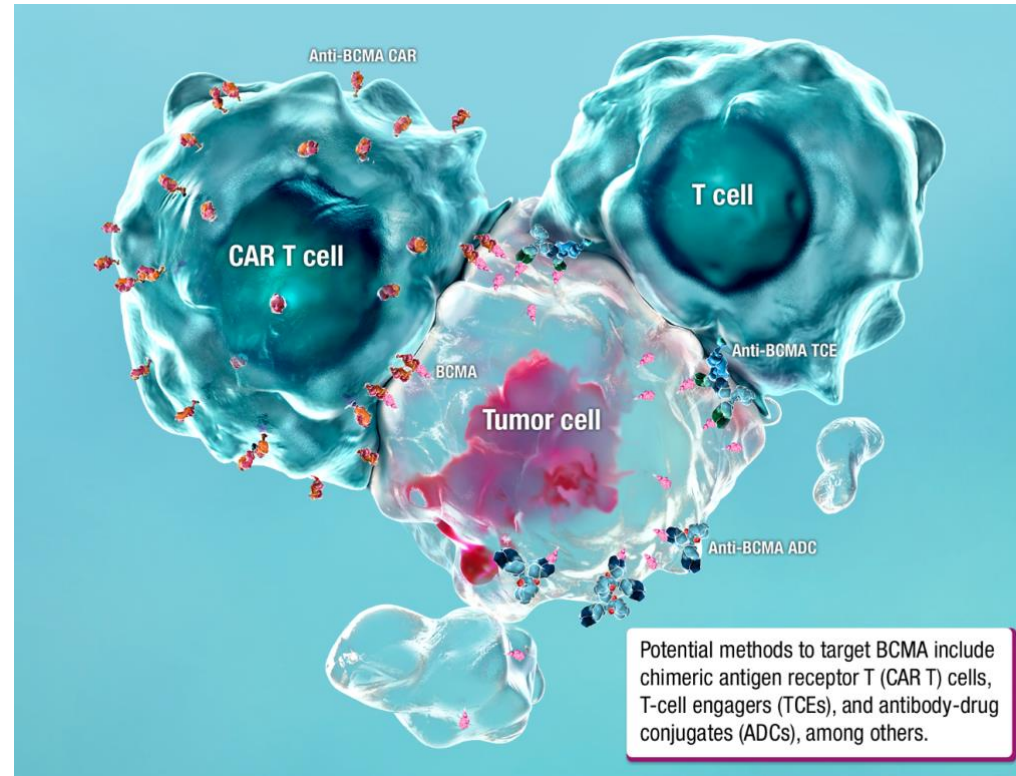
Target is involved in processes specific to cancer

Target is primarily found in cancer cells

Target can be reached by a drug



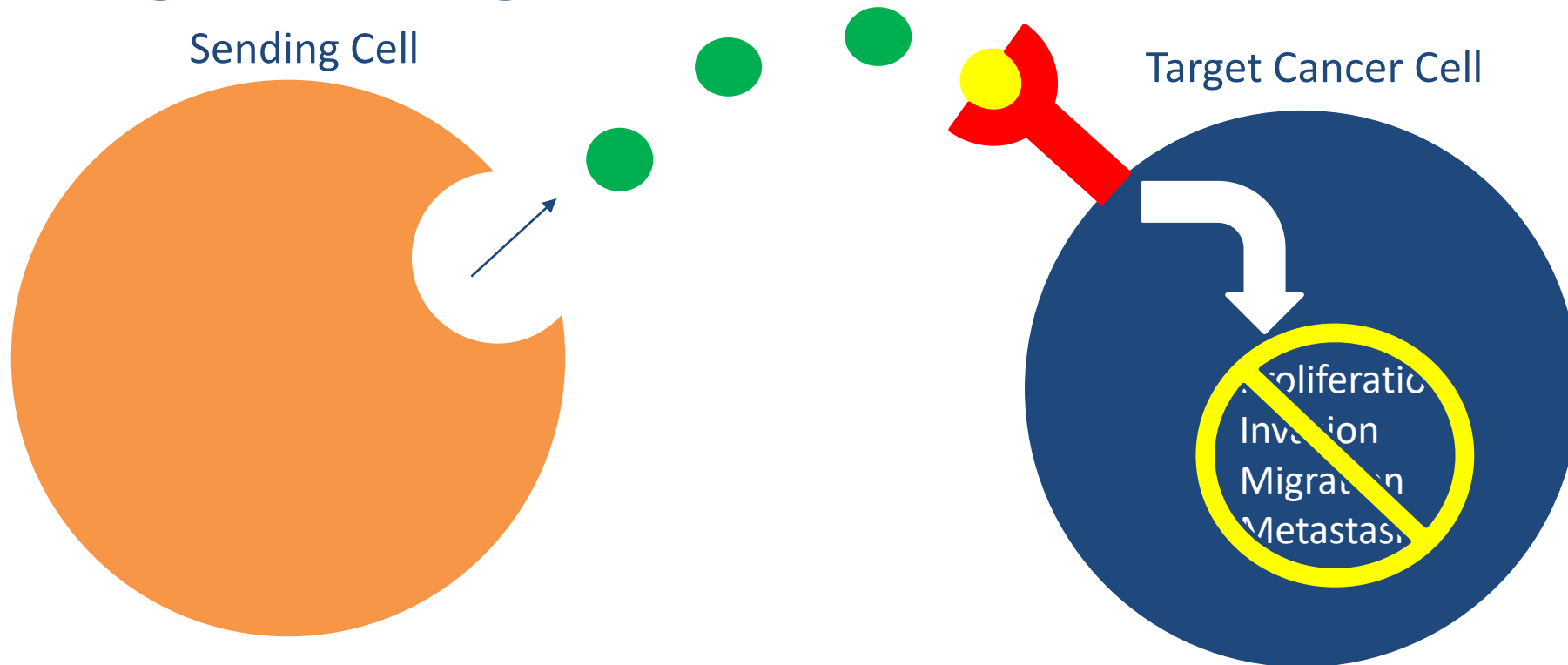
Drugs Directly Attacking the Cancer Cell






<https://www.bmsscience.com/pathways/b-cell-maturation-antigen-bcma/>



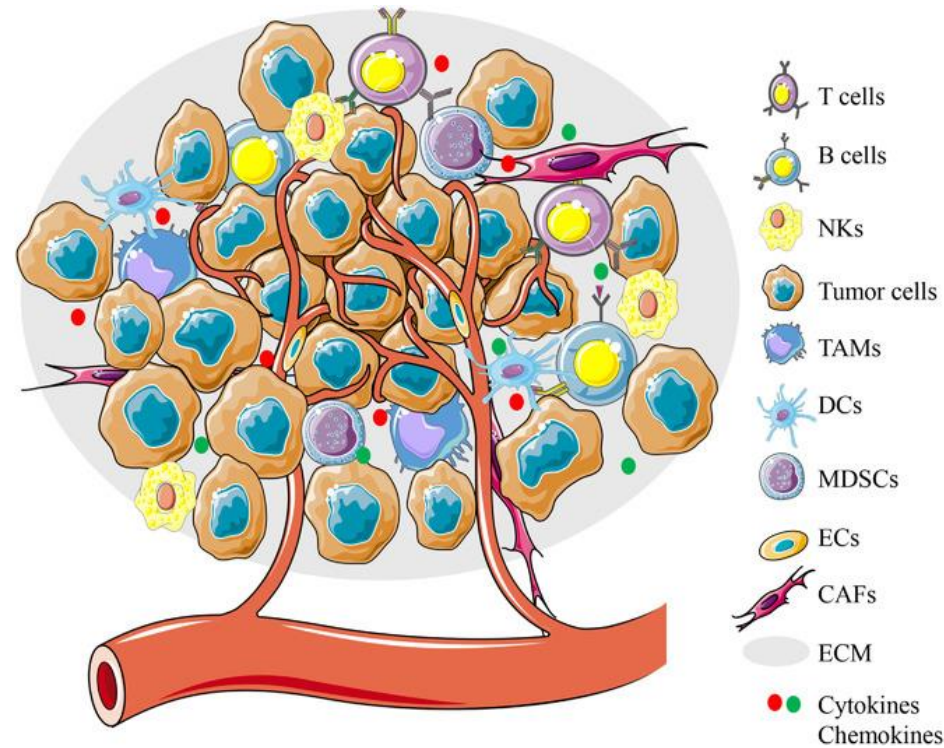
Drugs Blocking Communication between Cells



-  Signaling protein released by sending cell
-  Target receives signaling protein resulting in cancer cell growth
-  Drug blocks signaling protein from engaging with the target



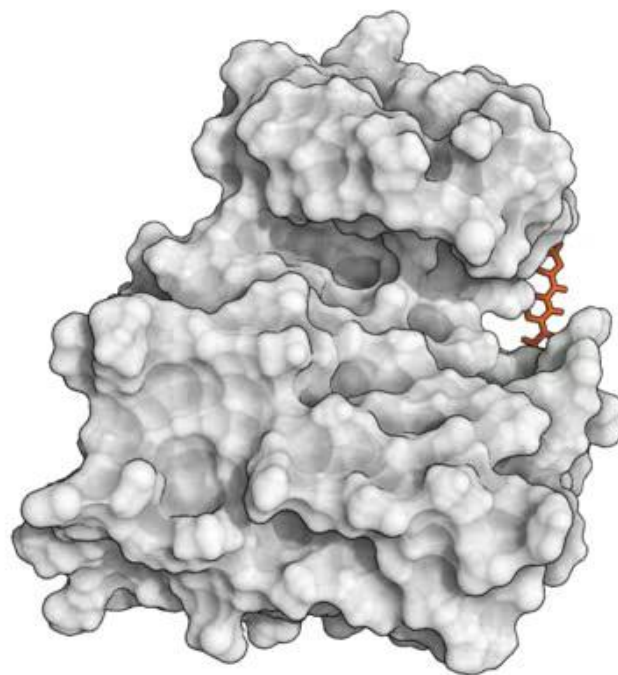
Drugs Attacking the Tumor Microenvironment



Shi, Tang, Miao, Med Comm 2020



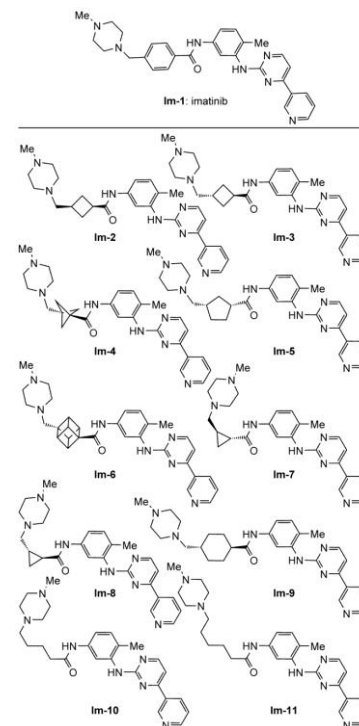
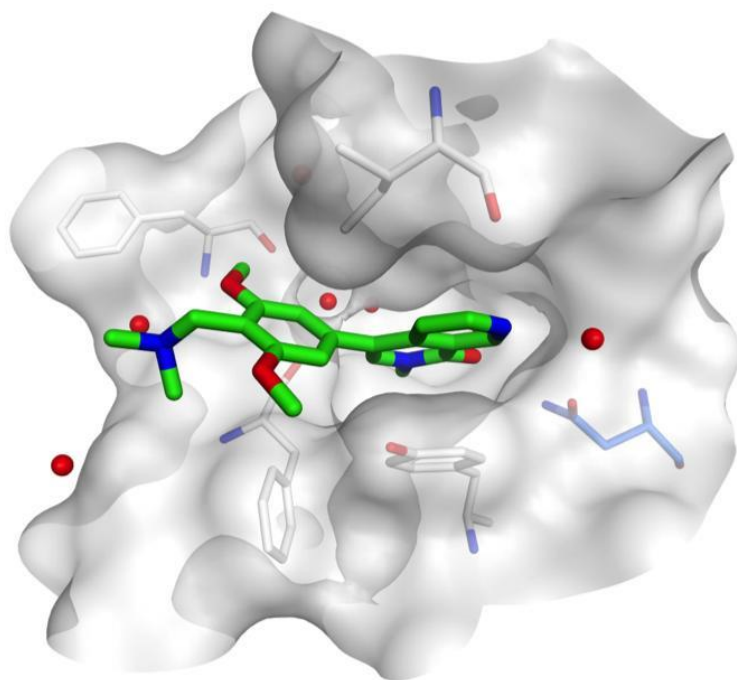
How a Drug Binds to the Target



Shan et al J Am Chem Soc 2011



Optimizing Chemistry

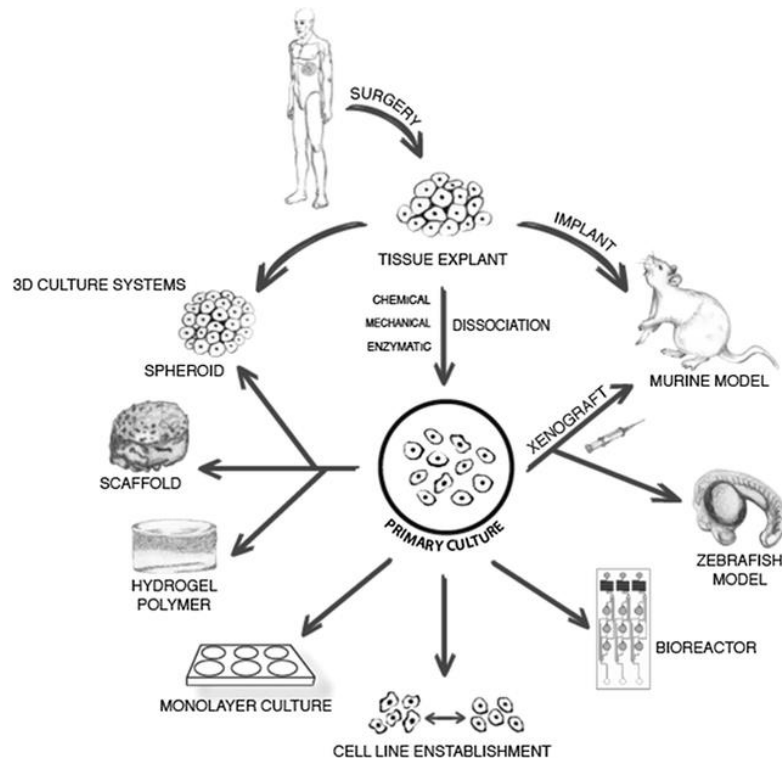


Nicolaou et al, Chem Med Chem 2015

<https://www.eurekalert.org/news-releases/874635>



Testing Drug Candidates for Anticancer Activity



Testing in Cancer Cells

Is it active?
Is it potent?
Is it stable?
How does it work?

Testing in Animal Models of Cancer

Does it get to the tumor?
Does it engage with the target?
Do tumors get smaller?



Seeking Permission to Proceed to Human Trials

IND and CTA submission

- Results from basic research and drug discovery studies
- Toxicities in animals
- Untoward (e.g., heart) effects in animals
- Manufacture clinical-grade drug substance
- Formulation research
- Manufacture drug product (e.g., tablet, vial) for human use
- First-in-Human Phase I trial protocol
- Early phase clinical research plan

IND = Investigational new drug application (US)

CTA = Clinical trial application (EU, Japan)



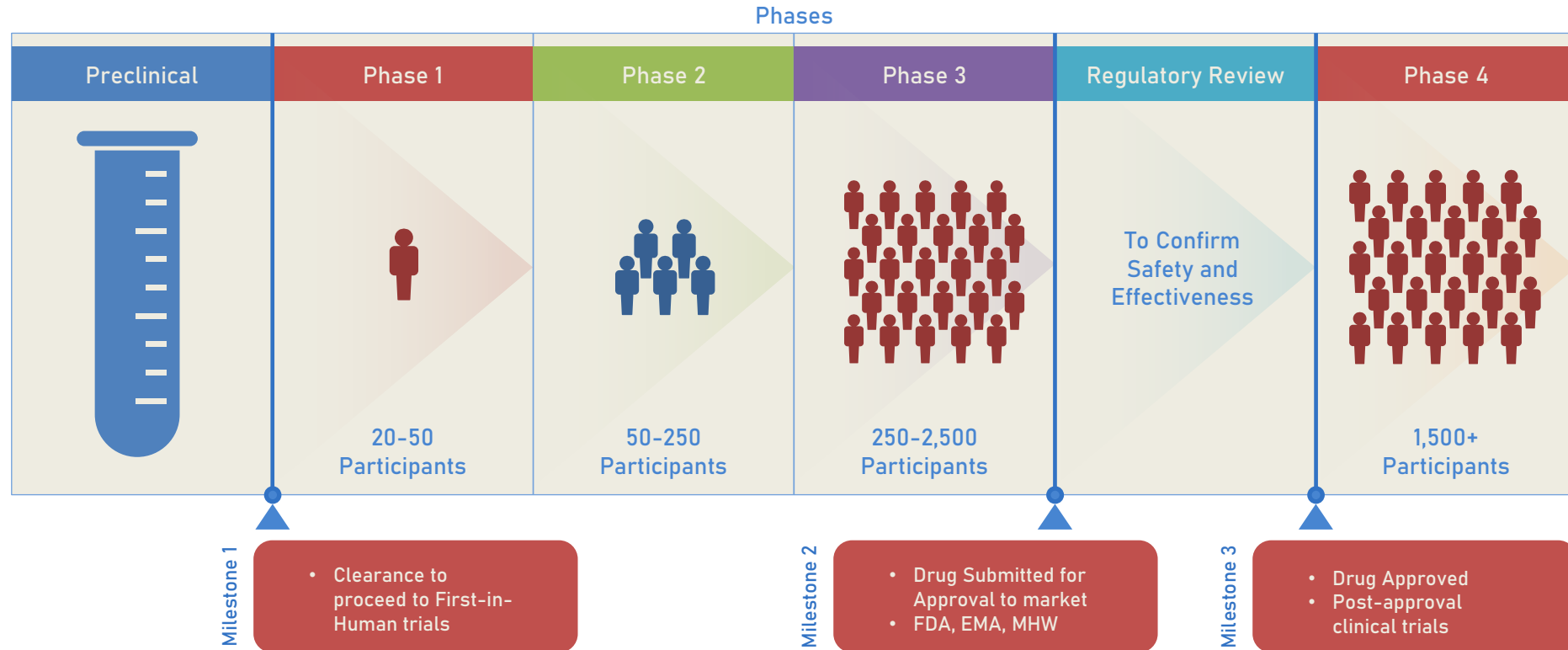
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH



厚生労働省
Ministry of Health, Labour and Welfare



Clinical Trials



Clinical Trial Considerations

Single Agent or In Combination
with Standard-of-Care Treatment

Improved treatment outcomes
versus standard-of-care

Improved treatment outcomes when
combined with standard-of-care

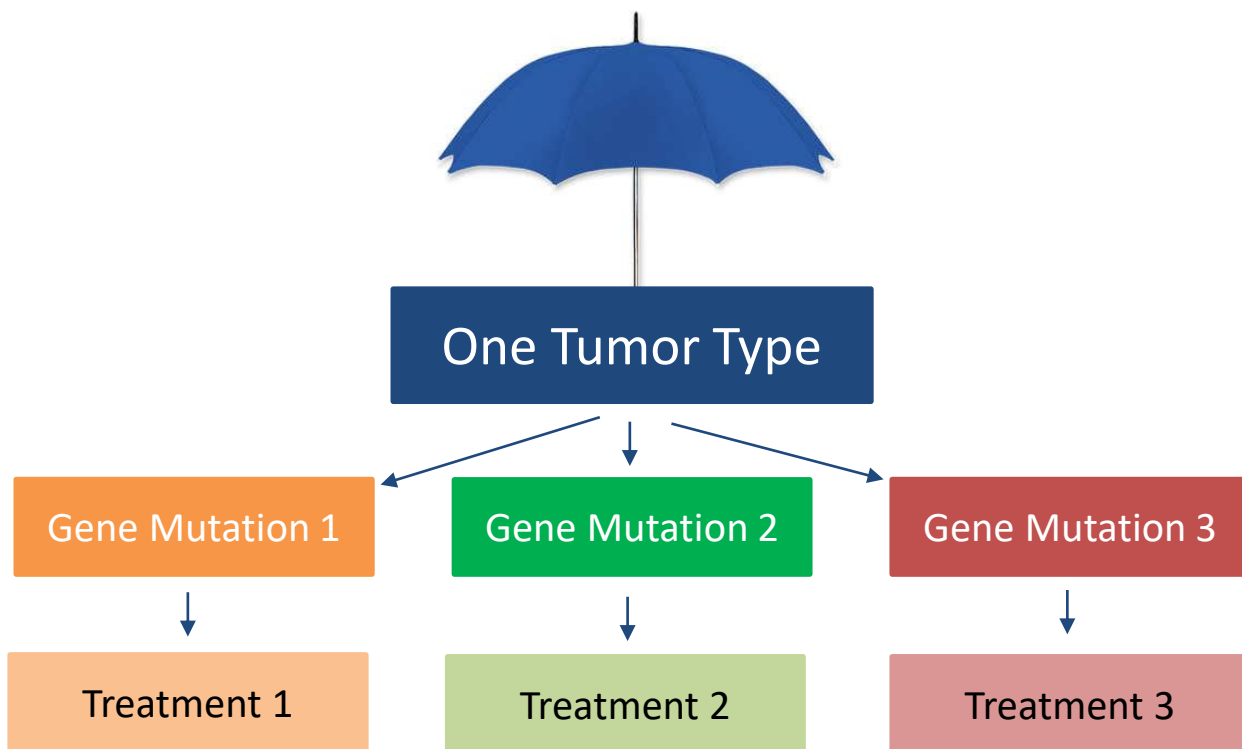
Neoadjuvant
or Adjuvant Treatment

Neoadjuvant - Before standard-of-care
treatment to reduce the size of tumor or
to kill cancer cells that have spread

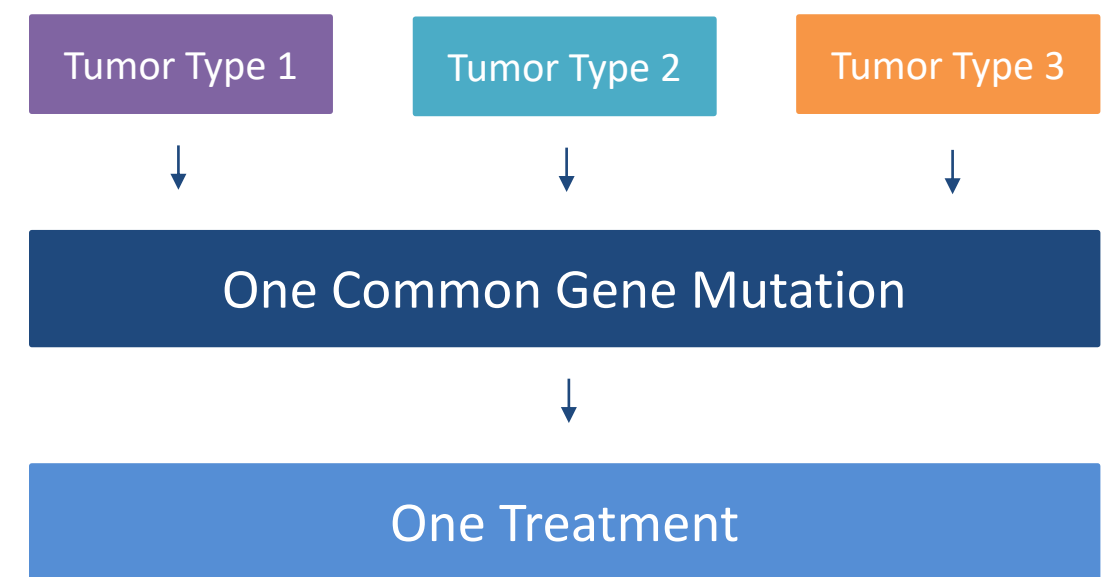
Adjuvant - after standard-of-care
treatment (e.g., surgery) to kill remaining
cancer cells



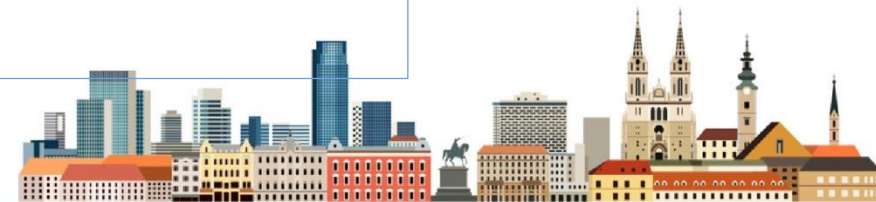
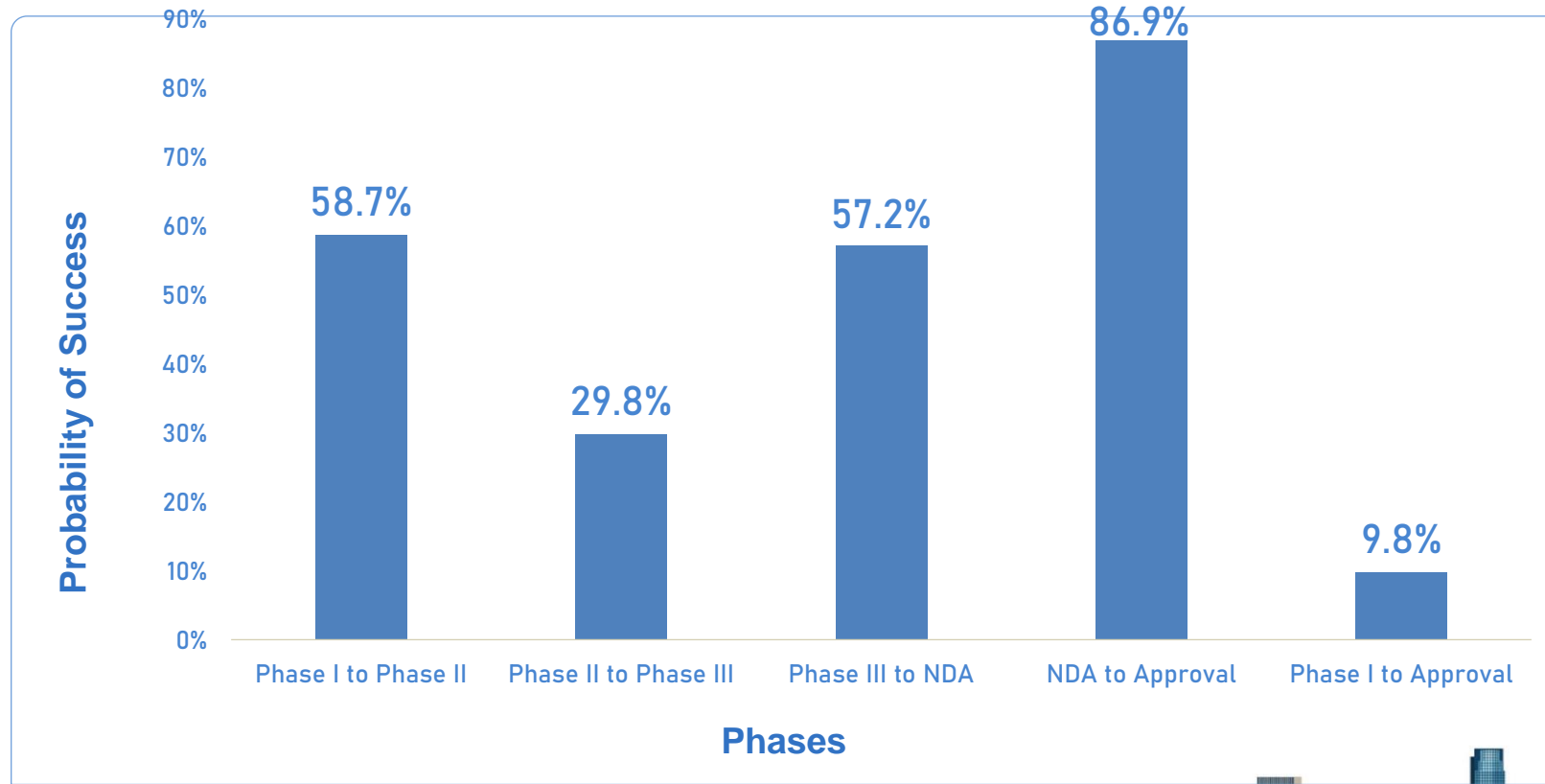
Umbrella Trial



Basket Trial



Trial Outcomes by Clinical Phase



Patient Partners in Drug Development



Immediate,
Relevant,
Patient-Honed
Feedback!



Researchers: Would you like patient feedback?



Rapid Reactor Team

- Immediate feedback to KUCC's researchers in a semi-structured, conversational setting
- A team approach to get patient research advocates' perspectives on all aspects of your research plan, including the research question
- Provides an opportunity to build relationships with patient partners and deepen your understanding of population of interest

Mondays or Thursdays from 5-6PM.

Sessions are scheduled upon researcher request

To schedule a session or for additional information, please contact us!

CALL

913-945-6873

EMAIL

PIVOT@kumc.edu

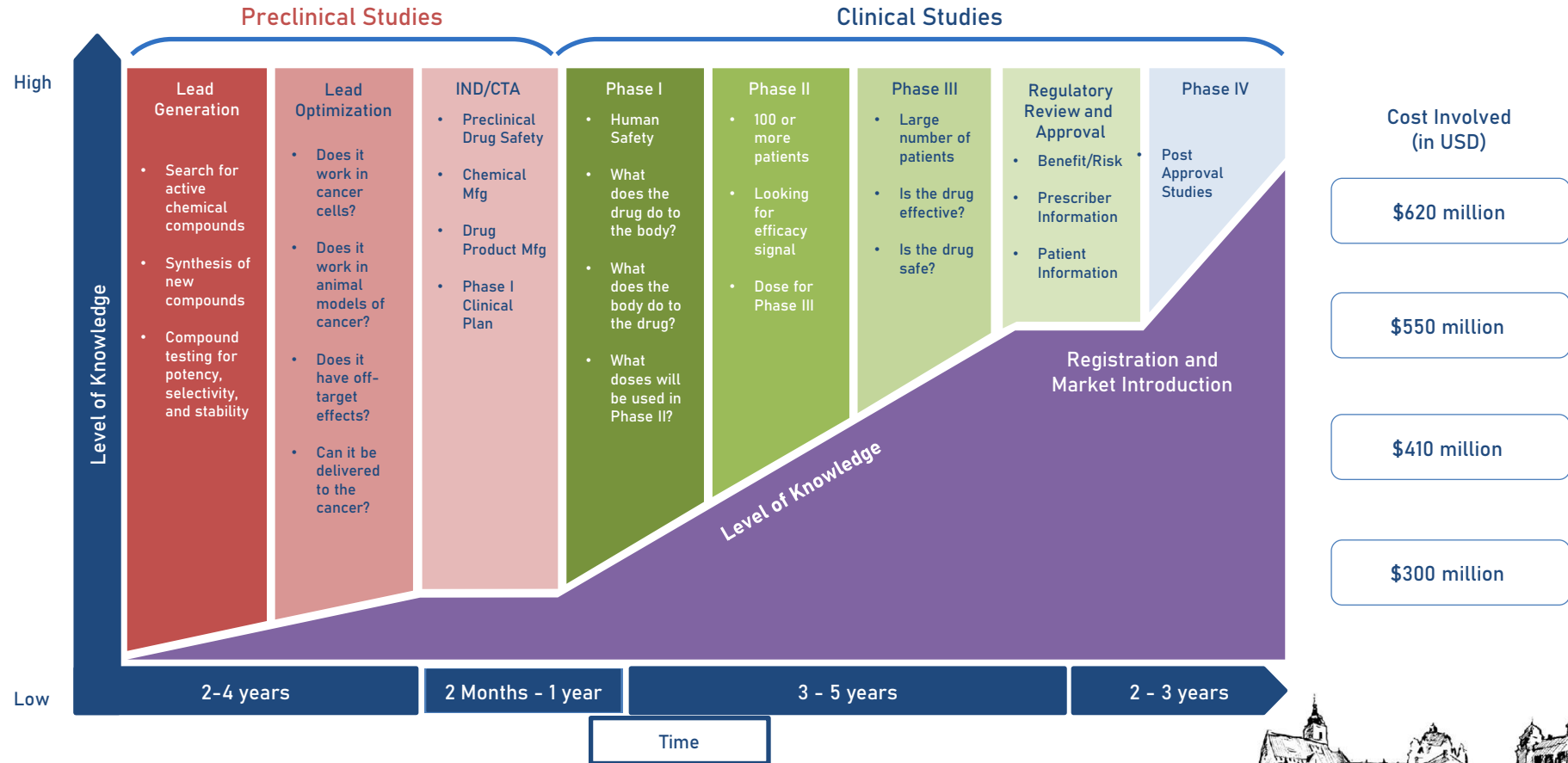
<http://www.midwestoncologyalliance.org/PIVOT>



THE UNIVERSITY OF KANSAS
CANCER CENTER



In Summary



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Thank You!

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