Drug Development – Clinical

Brian Appleby, MD

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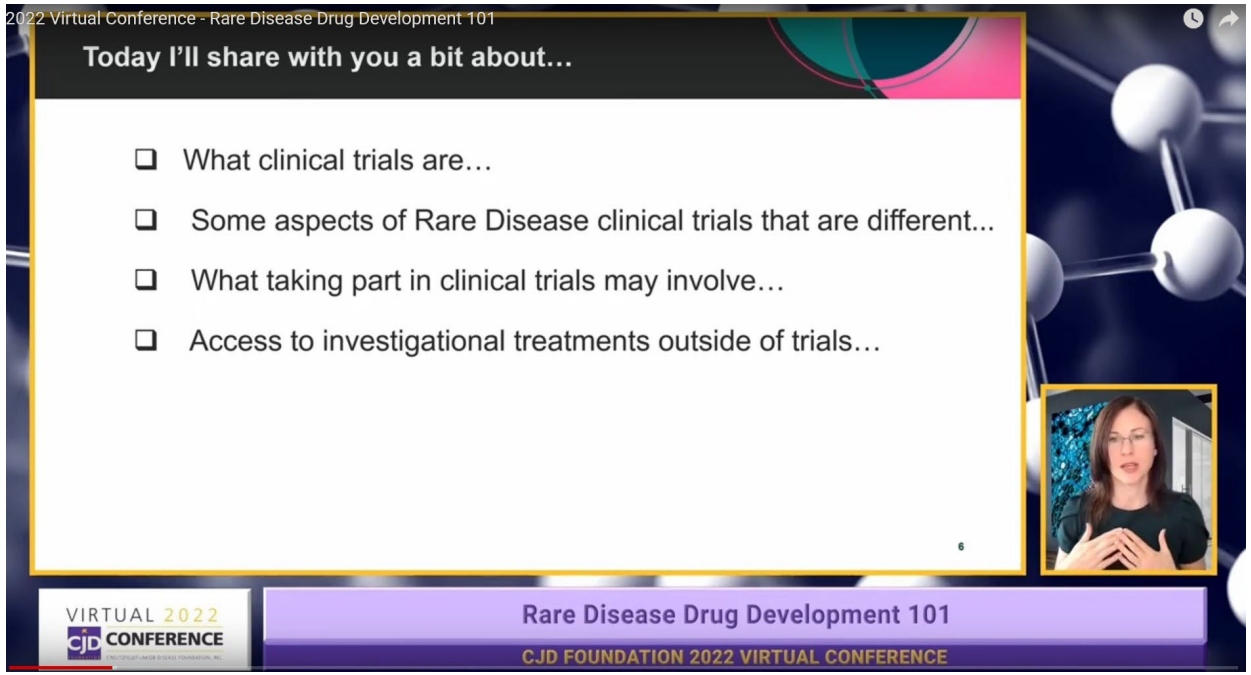
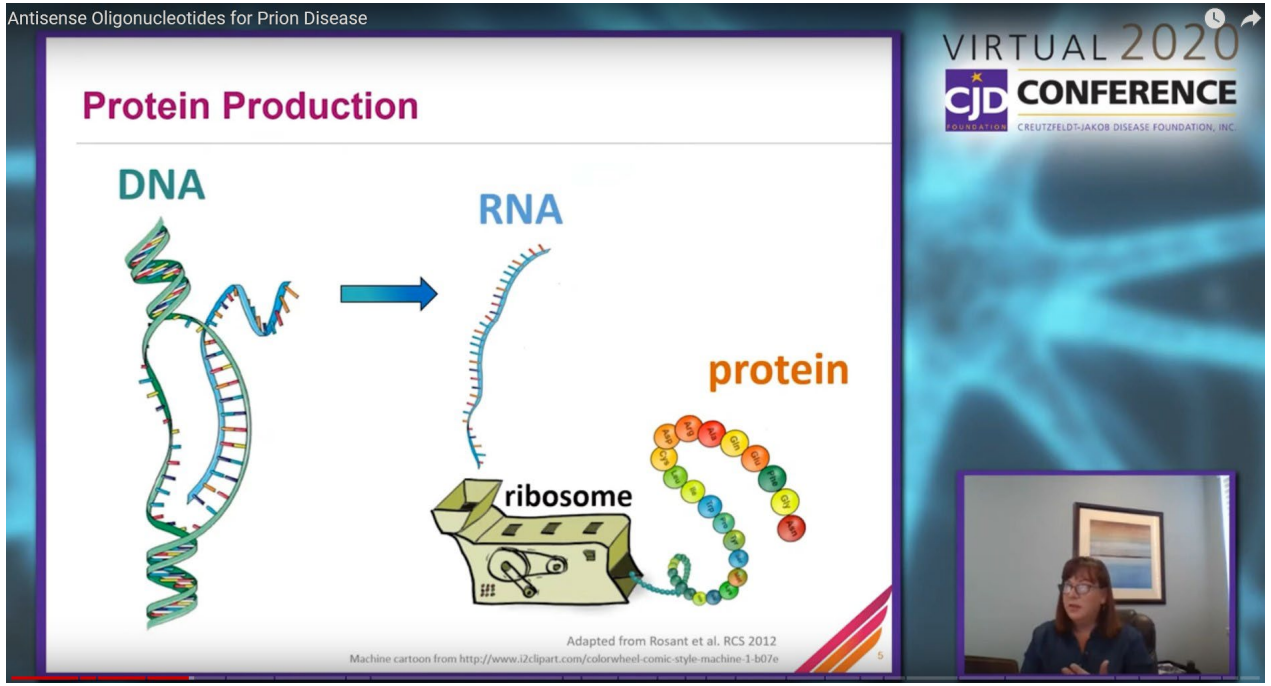
Prior Talks on this Topic



Laura Iliescu, MSc, Director, Patient Advocacy Strategy, Center for Rare Diseases



Anne Smith, PhD, Executive Director of Clinical Development at Ionis Pharmaceuticals

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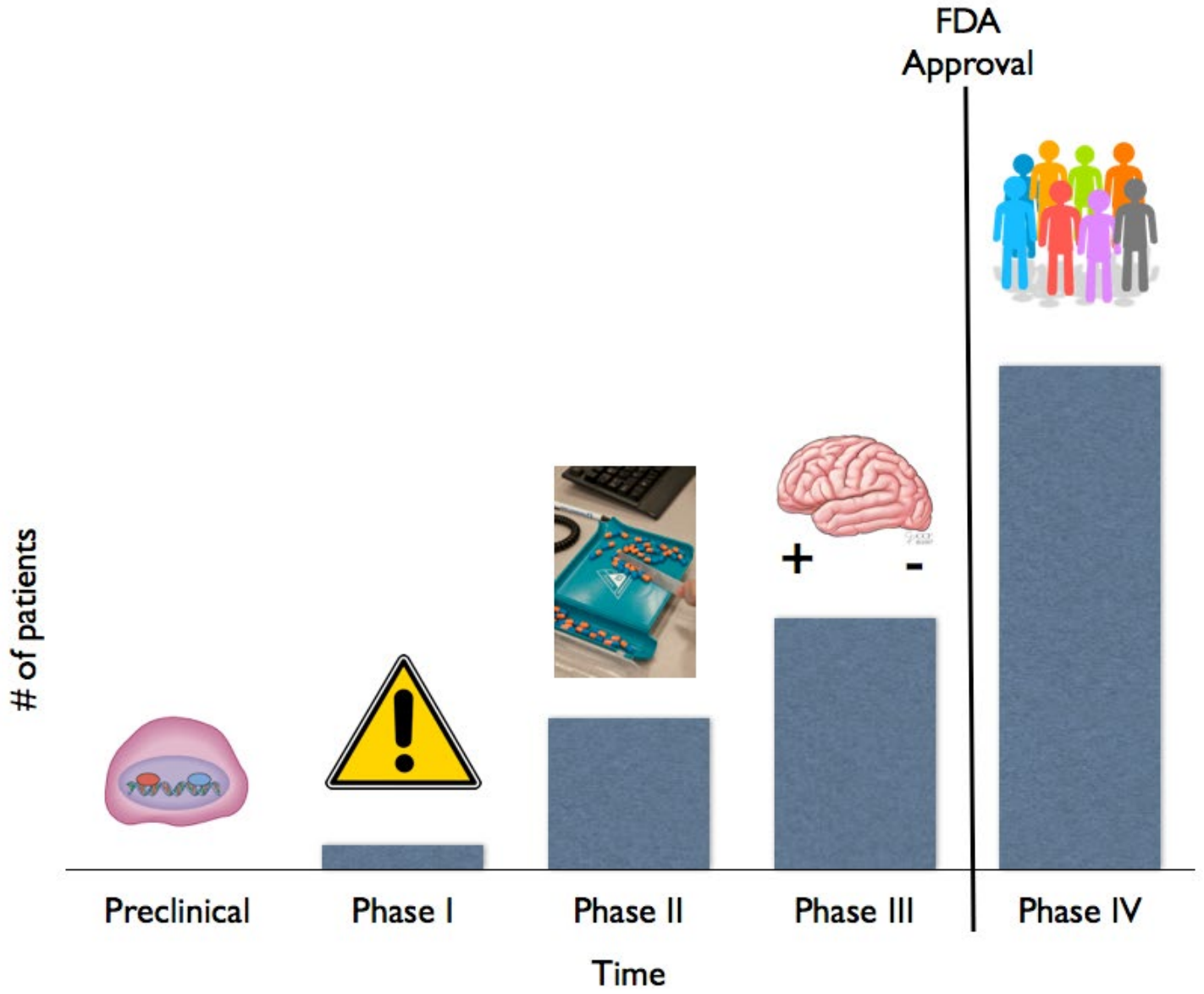
Types of Research

- Basic science
- Natural history studies
- Biomarker focused studies
  - Prognosis
  - Diagnostic test development
  - Influence treatment decisions
- Treatment studies (e.g., clinical trials)
  - Pharmacological
  - Non-pharmacological
  - Device

Clinical Trial Phases



Clinical Trial Caveat

Which picture most appropriately depicts a clinical trial?

A.

B.

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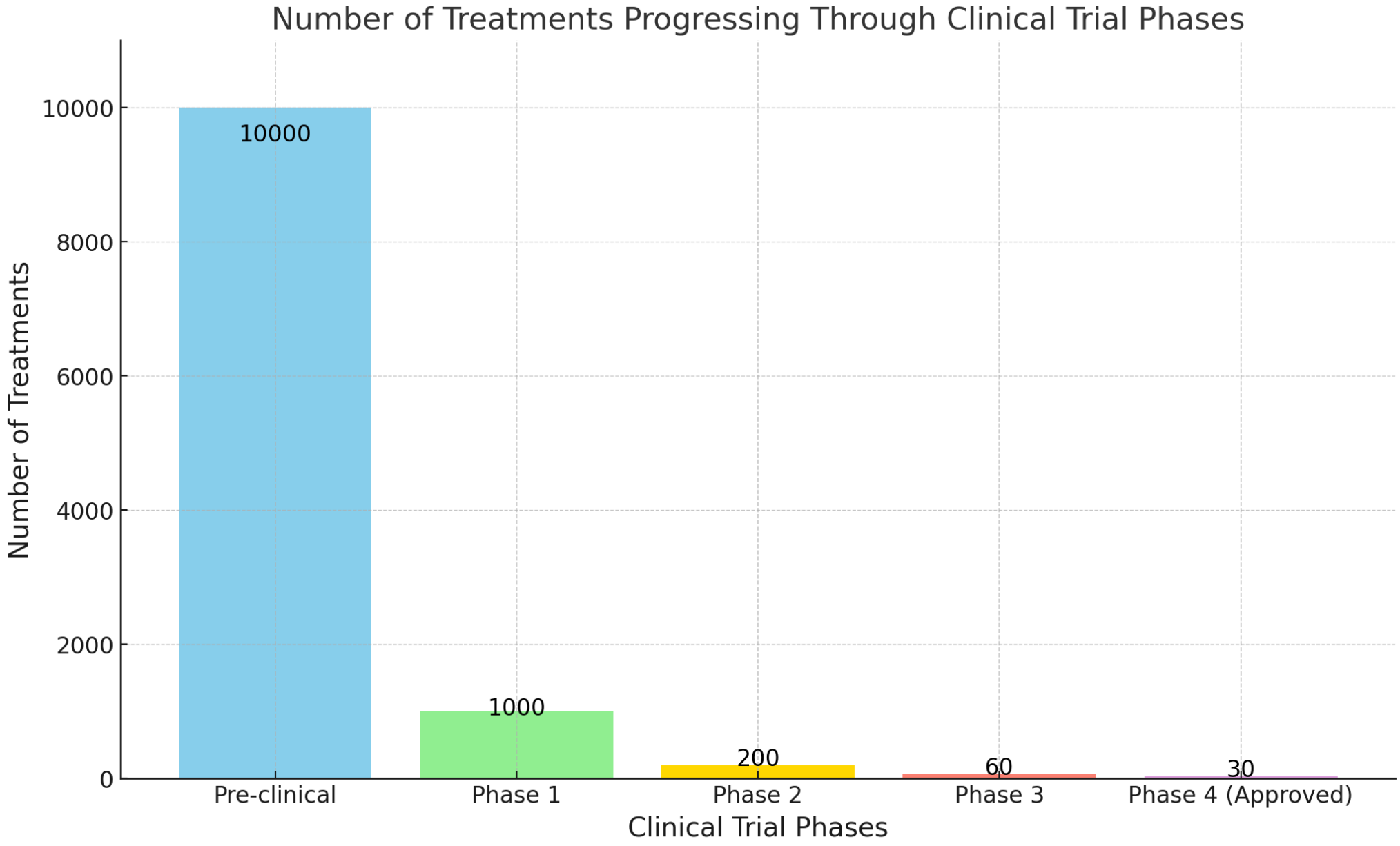

Why don’t we see more prion disease clinical trials?

Discovery and Development Phase	Out-of Pocket Costs ($-millions)	Total Cost (Capitalized at 11%, $-millions)
Target-to-hit	$24	$94
Hit-to-lead	$49	$166
Lead optimization	$146	$414
Preclinical	$62	$150
Phase I	$128	$273
Phase II	$185	$319
Phase III	$235	$314
Submission to launch	$44	$48
TOTAL:	$873	$1,778

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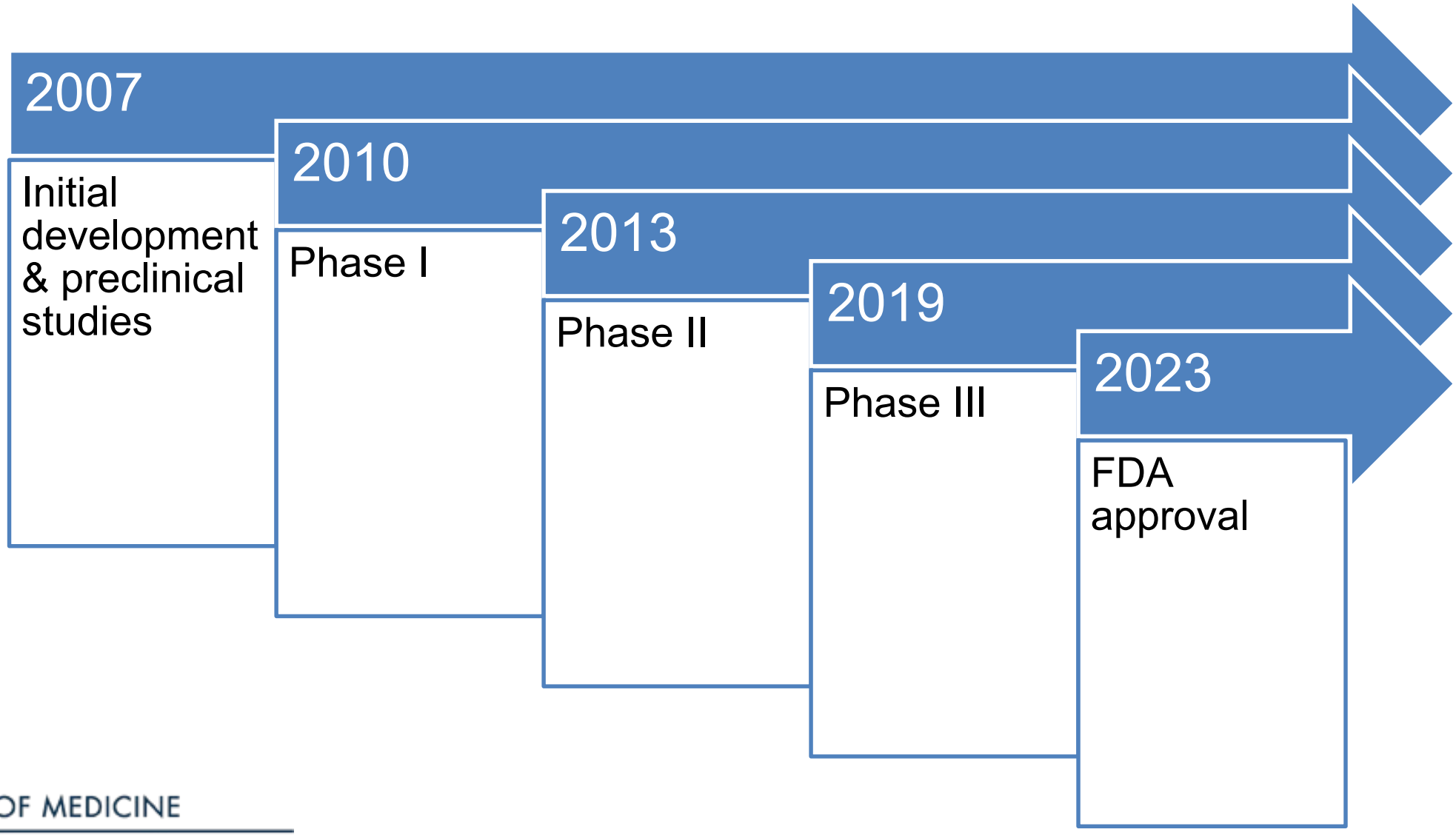
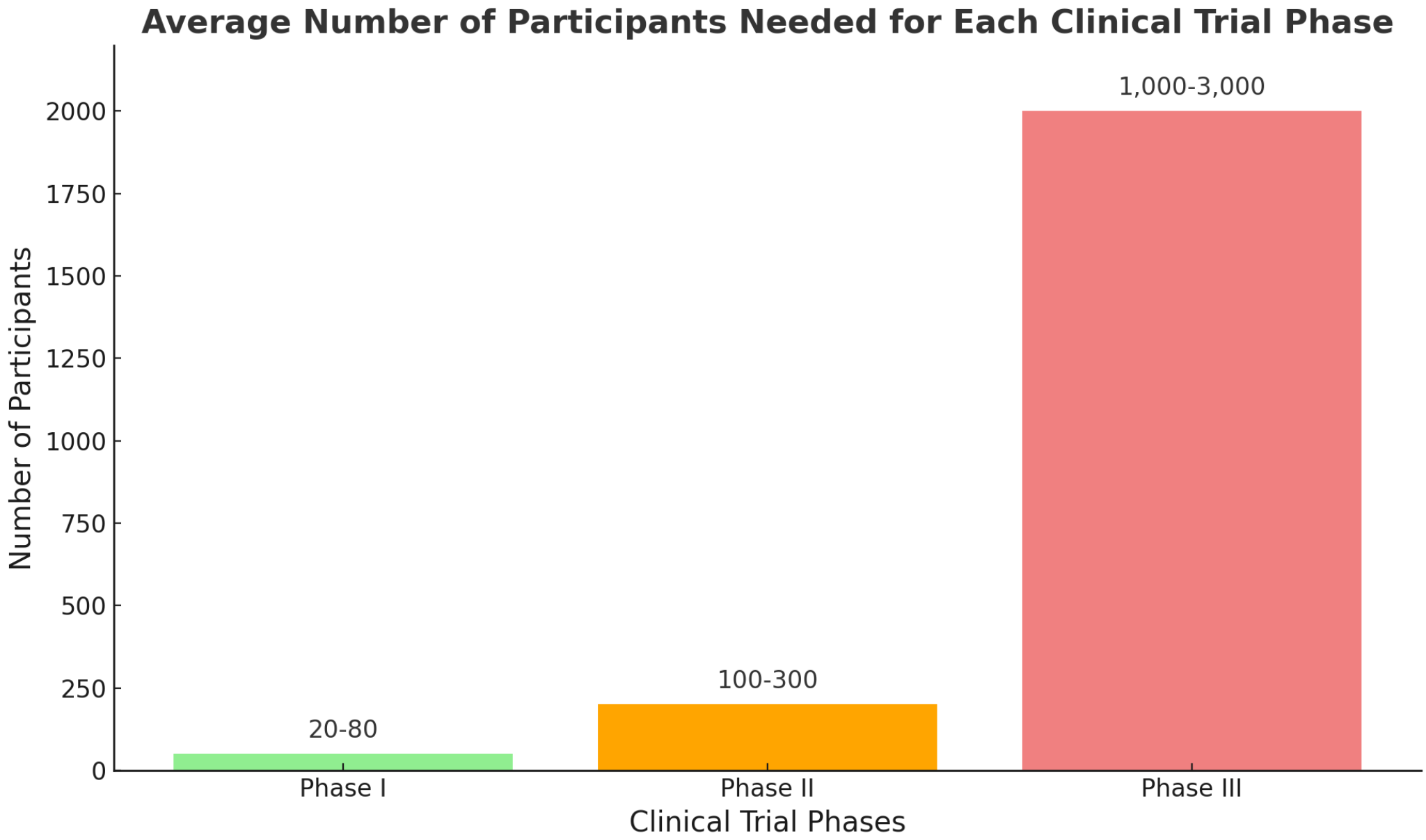
https://www.genengnews.com/insights/what-is-the-real-drug-development-cost-for-very-small-biotech-companies/

Drug Development Timeline for New Alzheimer's Drug (Lecanemab)





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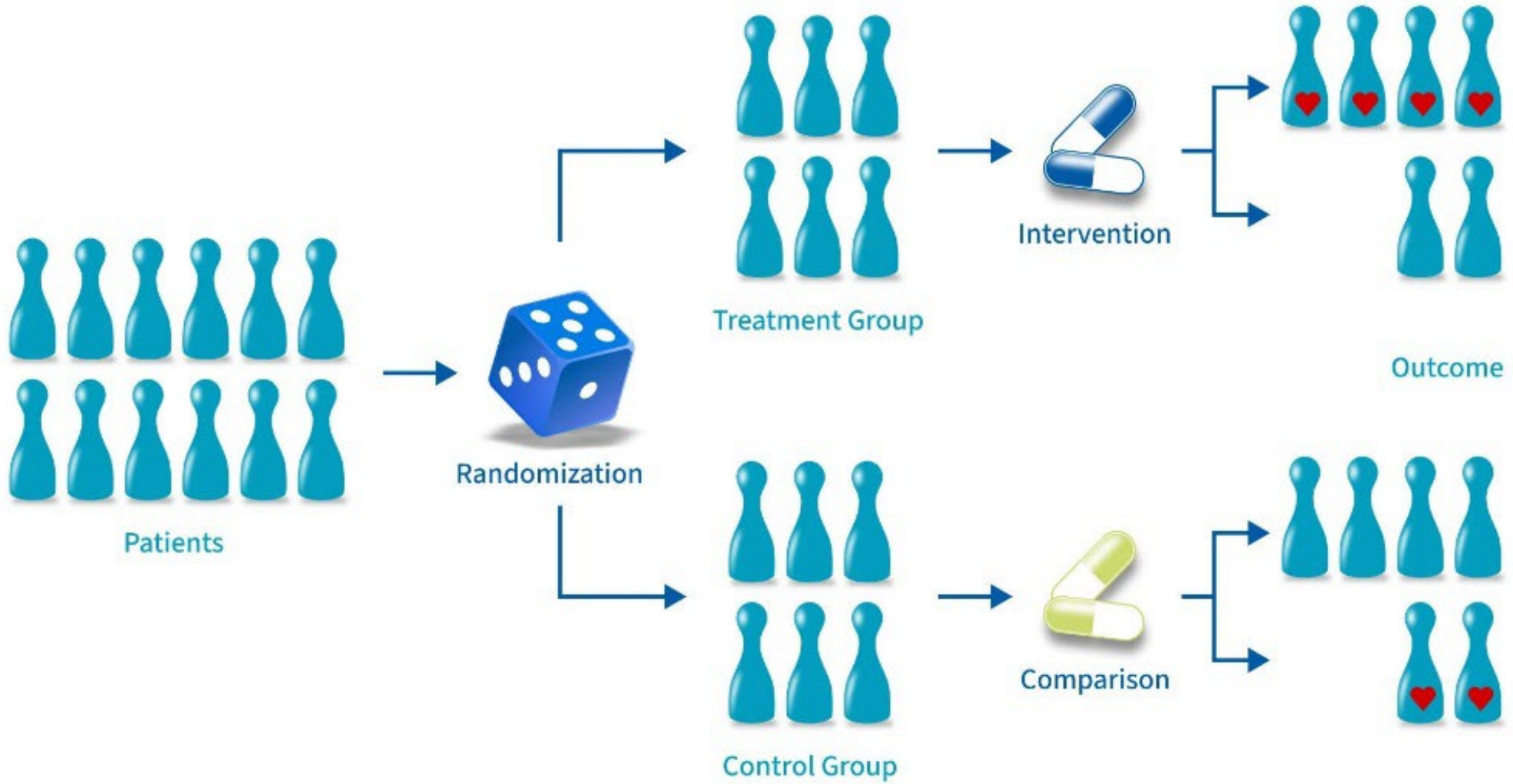
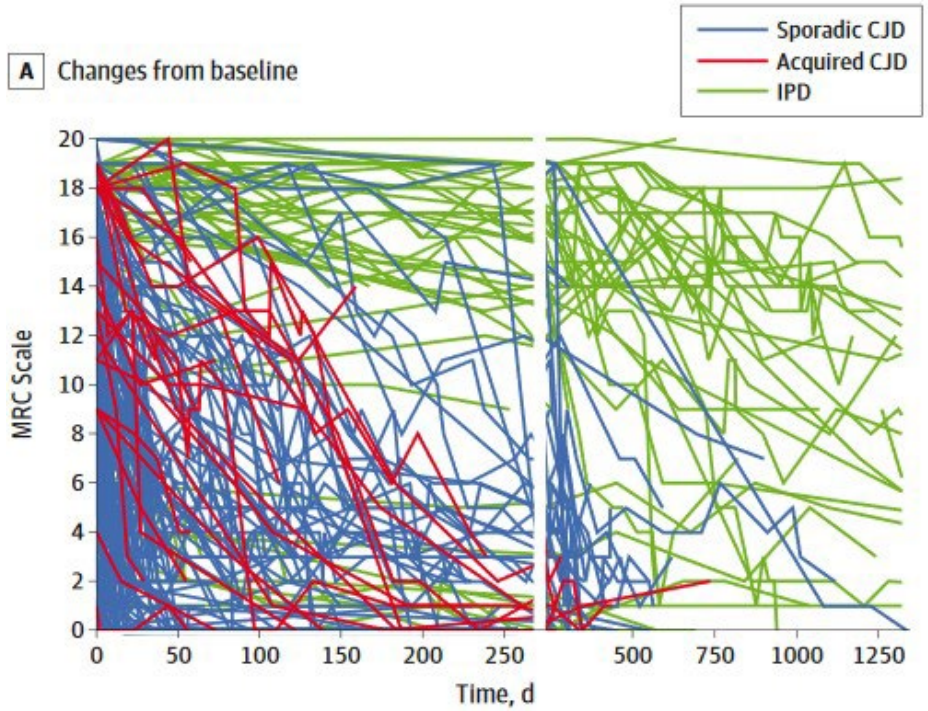
https://www.fda.gov/patients/drug-development-process/step-3-clinical-research

Randomized Controlled Trial





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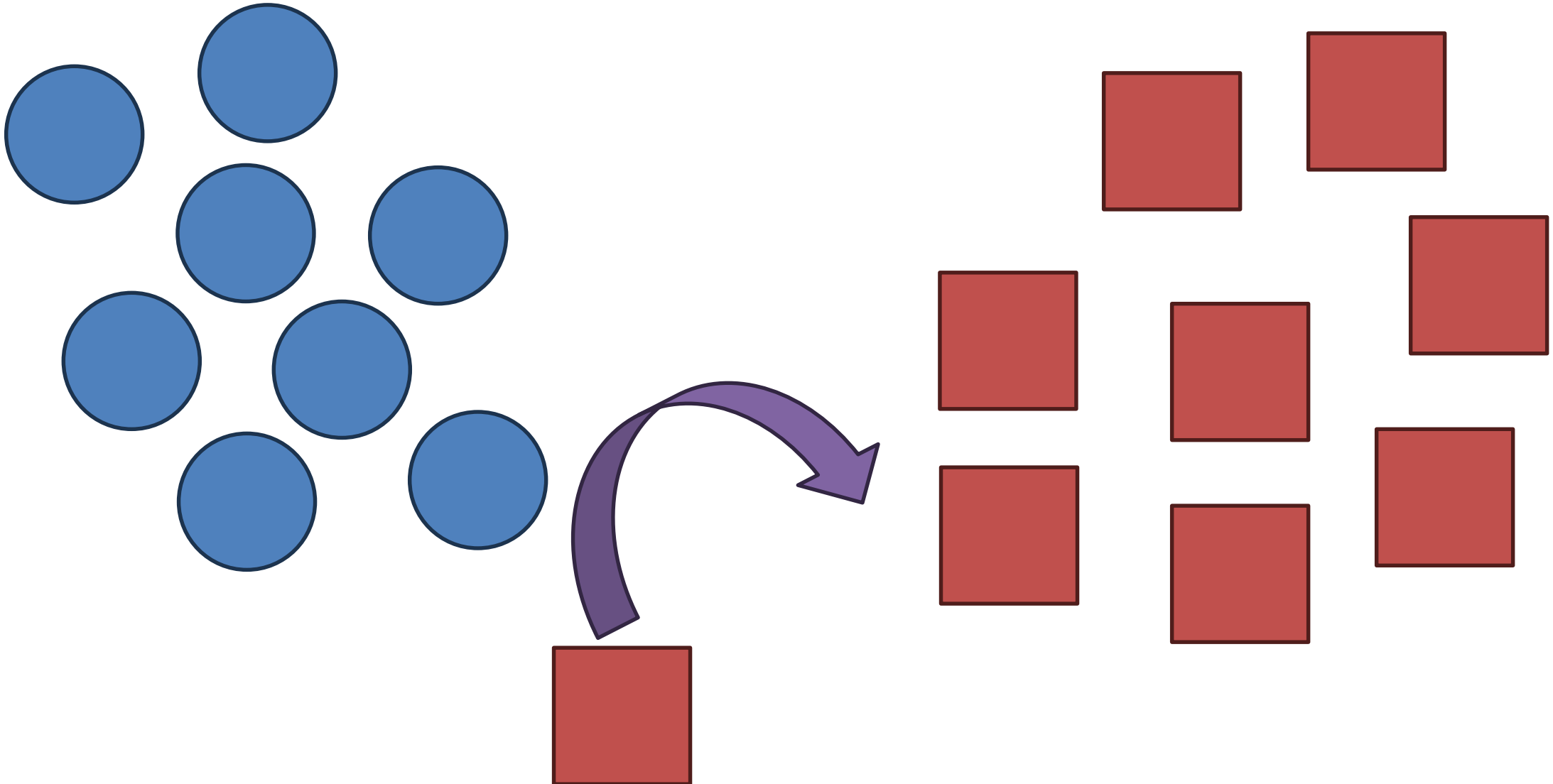
Mead S, JAMA Neurol 2016

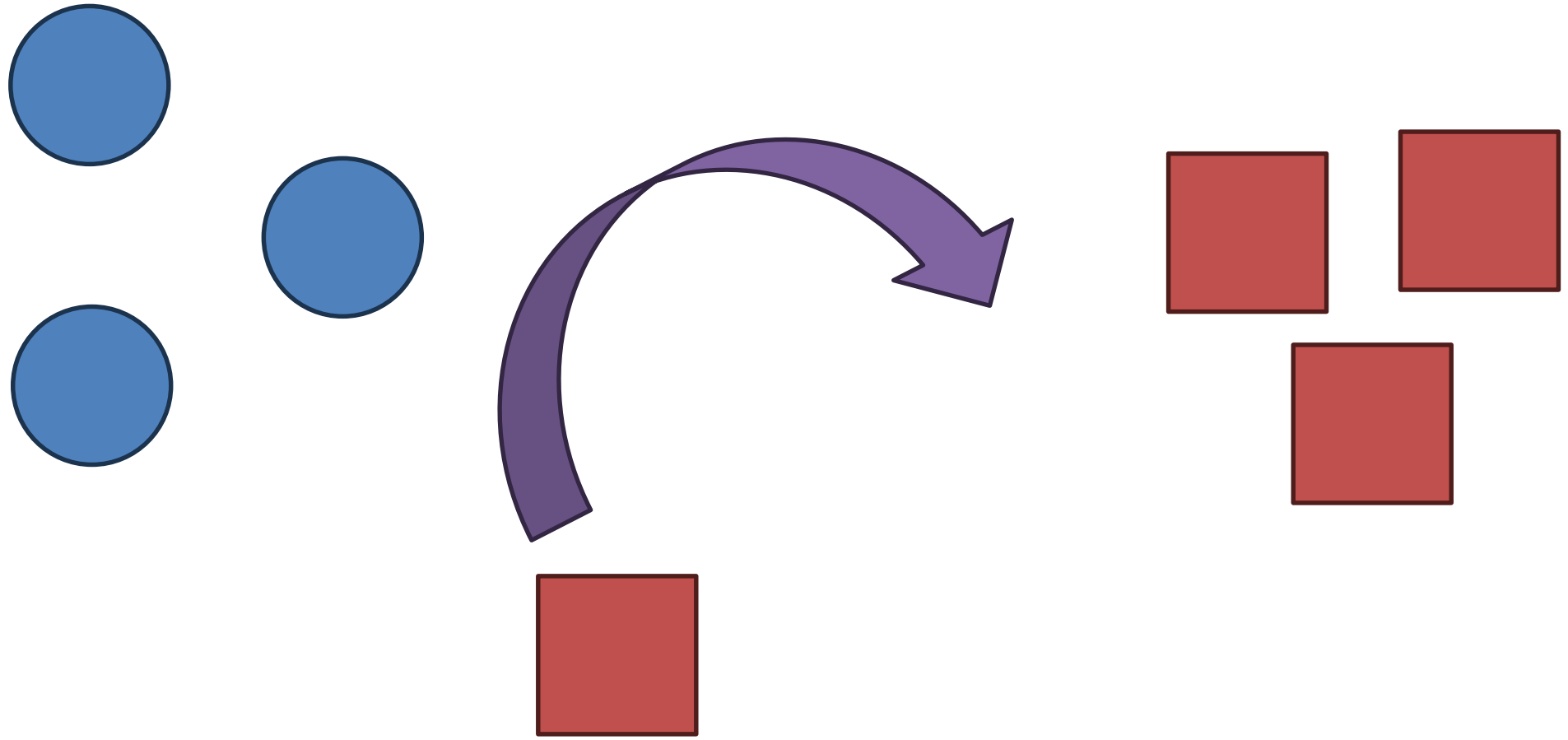
Accelerated Approval Program

The FDA instituted its Accelerated Approval Program to allow for earlier approval of drugs that treat serious conditions, and fill an unmet medical need based on a surrogate endpoint. A surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. The use of a surrogate endpoint can considerably shorten the time required prior to receiving FDA approval.

Drug companies are still required to conduct studies to confirm the anticipated clinical benefit. If the confirmatory trial shows that the drug actually provides a clinical benefit, then the FDA grants traditional approval for the drug. If the confirmatory trial does not show that the drug provides clinical benefit, FDA has regulatory procedures in place that could lead to removing the drug from the market.

Lowering the Normal Prion Protein as a Surrogate Endpoint





Things they may ask you to do as a participant

- Send prior medical records
- Physical/Neurologic examination
- Cognitive testing (paper/pencil or computerized testing)
- Informant interviews
- Blood and/or spinal fluid tests
- Brain and other type of body scans
- Follow-up in certain time intervals
- Visits may be in person, virtual, or a mix of both
- Engage in some type of intervention

Useful Information as a Potential Participant

- Specifics of your disease (e.g., type of prion disease, mutation)
- What medications you take and why
- What other medical conditions you have
- The purpose of the study
- The time requirements for the study
- What will be required from you and your family?
- If a clinical treatment trial:
  - Will you have access to any test results done through the study?
  - Is it randomized? Placebo controlled?
  - Do you have an option of continuing the intervention when the study is completed?

Where to find information about clinical trials?

- Clinicaltrials.gov: search for prion disease
- NPDPSC: tinyurl.com/priontrials
- CJD Foundation: cjdfoundation.org/drug-development
- Prion Registry: prionregistry.org/study-listing