# Disrupting drug development with data-driven approaches:

## Insights for fast expanding data teams

Alice M Walsh, PhD
VP, Translational Research
Pathos

Katie Igartua, PhD
Sr Director, Computational Biology
Tempus

# Alice Walsh, Ph.D.

Penn
University of Pennsylvania

Bristol-Myers Squibb

PATHOS

Massachusetts Institute of Technology

janssen
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

R LADIES PHILLY

Oncology
Immunology
High-dimensional data
Data/stats/methods

Pharma ecosystems
Building teams and communities
How can teams be creative and innovative?

PATHOS



# Reimagining drug discovery and development through the lens of technology

OUR APPROACH

# Katie Igartua Ph.D.





TEMPUS

Oncology & Molecular Biology
Genomics
Population & statistical genetics

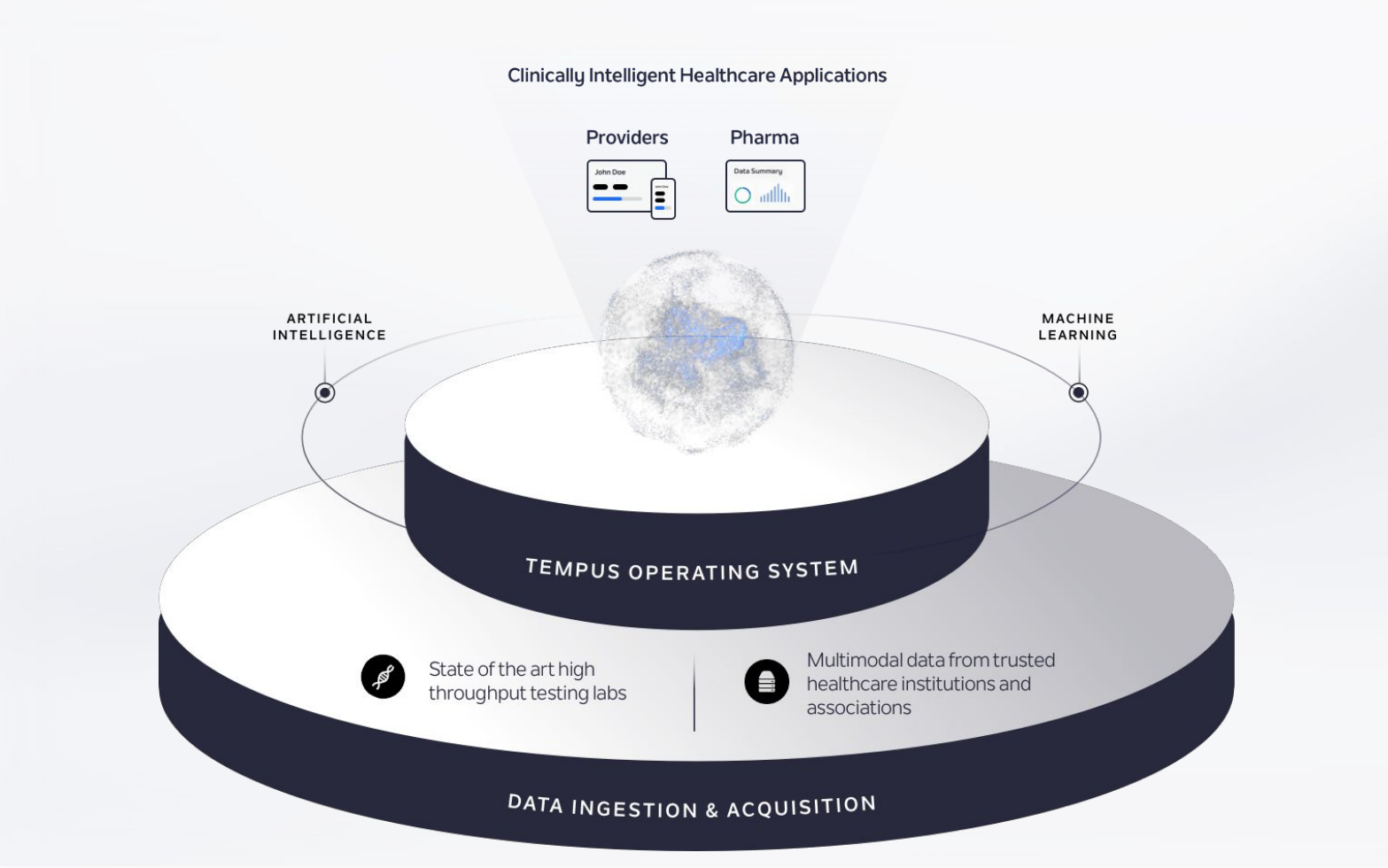
Pharma & Biotech
Building cross functional teams with a focus on
Systems Biology & Translational Research
Innovate to directly impact patients

# The Tempus Platform

We built both a technology platform to free healthcare data from existing silos and an operating system to make the resulting data useful.

Our end-to-end technology platform helps doctors make better decisions, drug companies make better drugs, and patients live longer and healthier lives.

TEMPUS

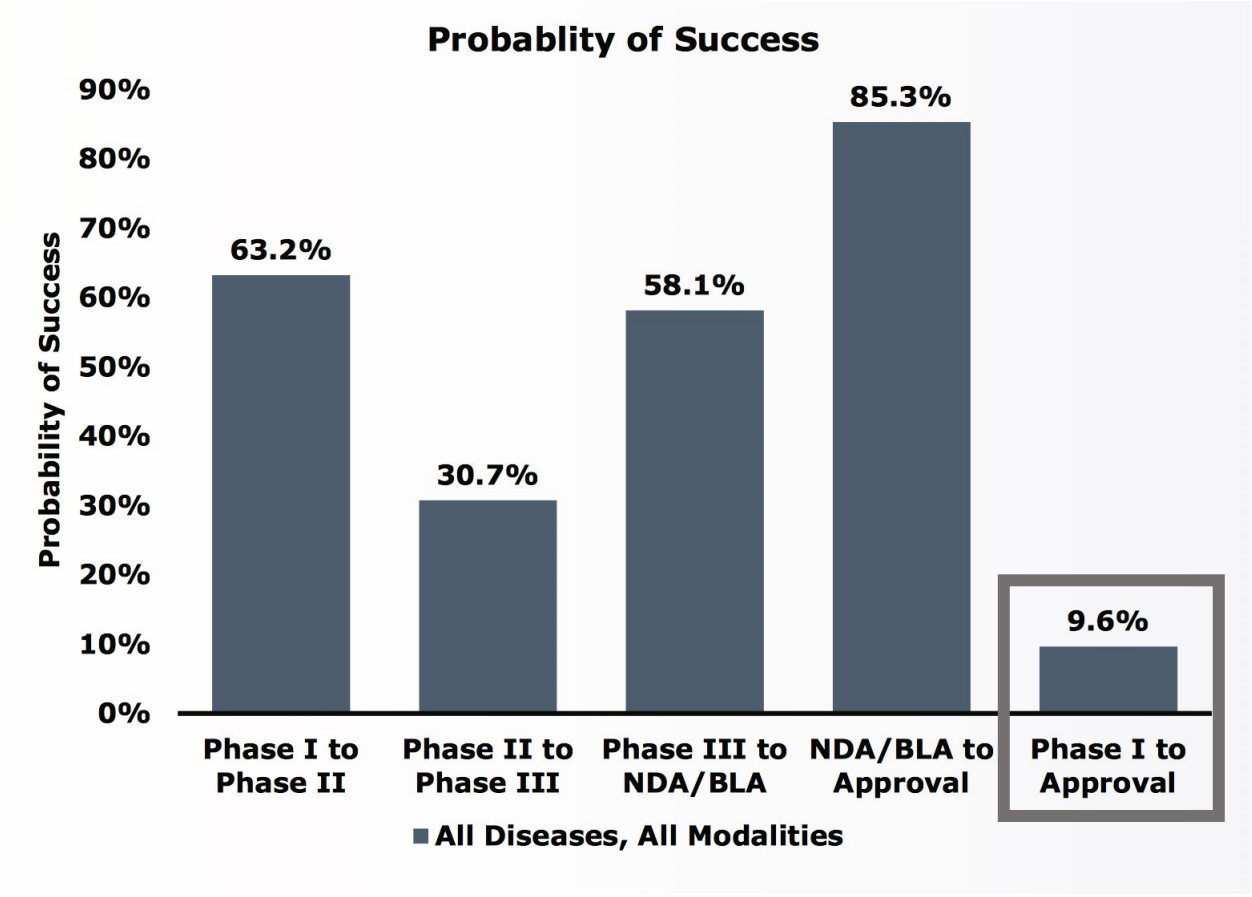


# What should we be excited about in drug development for the next 10 years?

Is the glass half-full or half-empty?

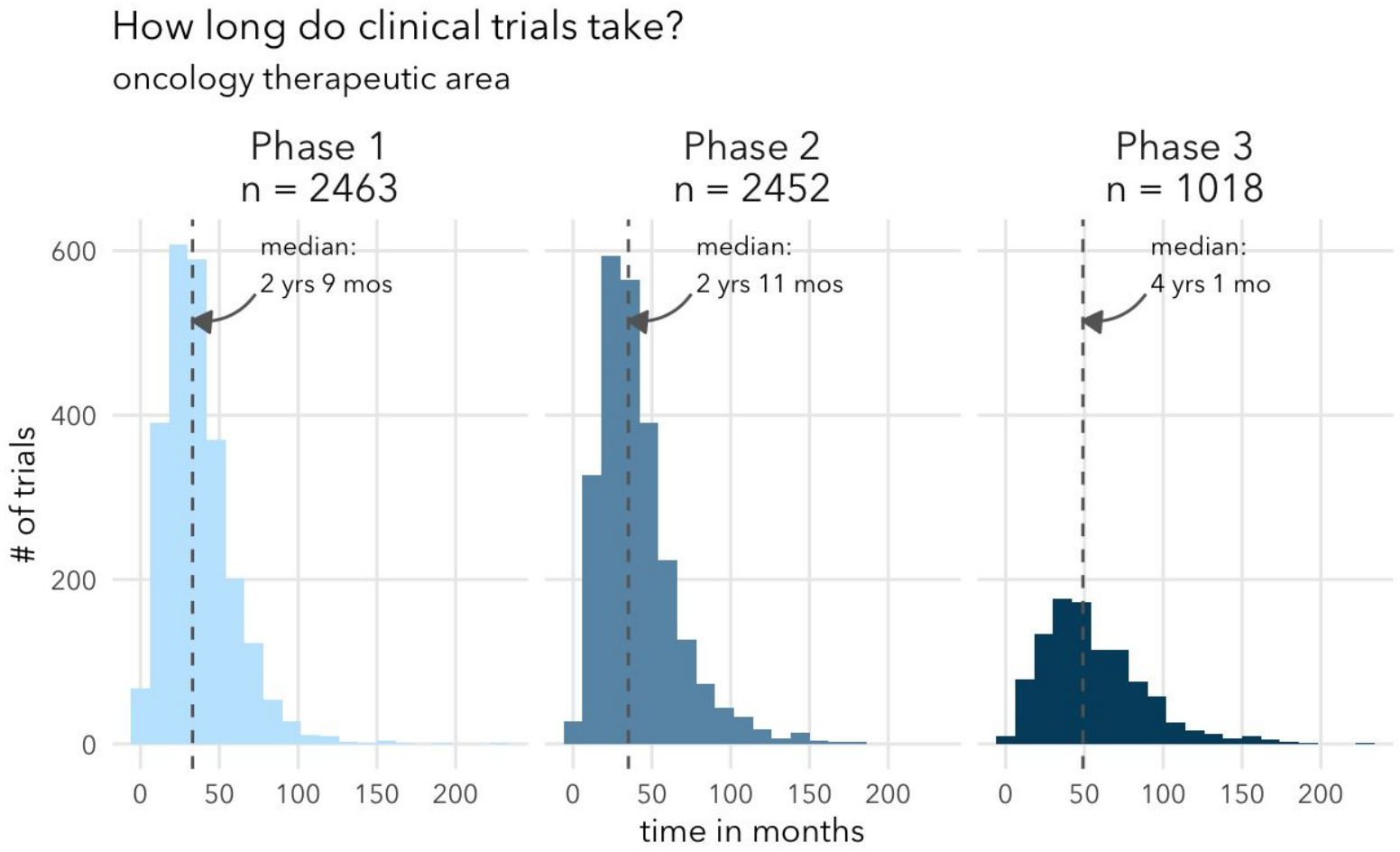
# The case for half-empty

# Probability of success is terrible




Source: Clinical Development Success Rates 2006-2015
https://www.bio.org/

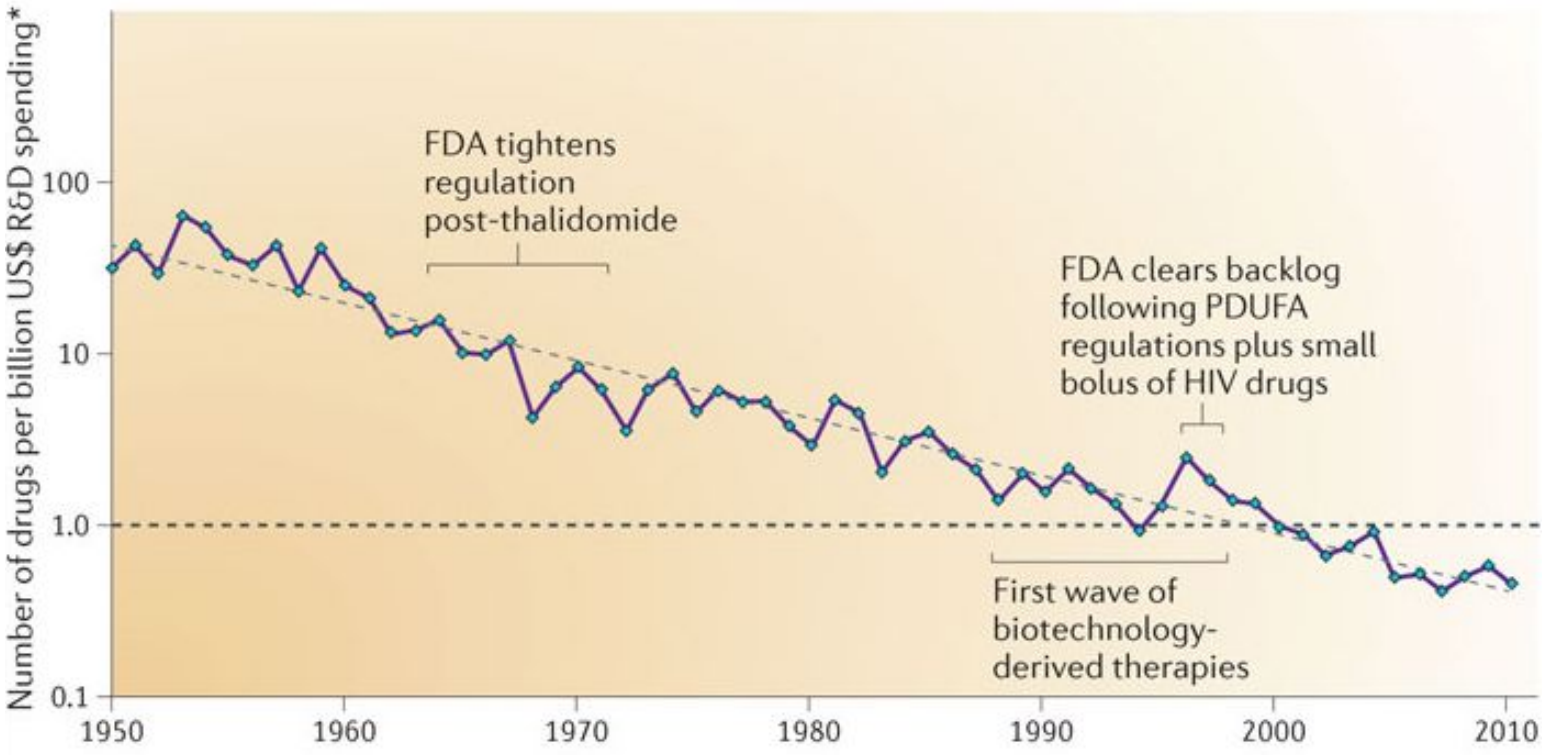
# Clinical trials take too long




data: clinicaltrials.gov

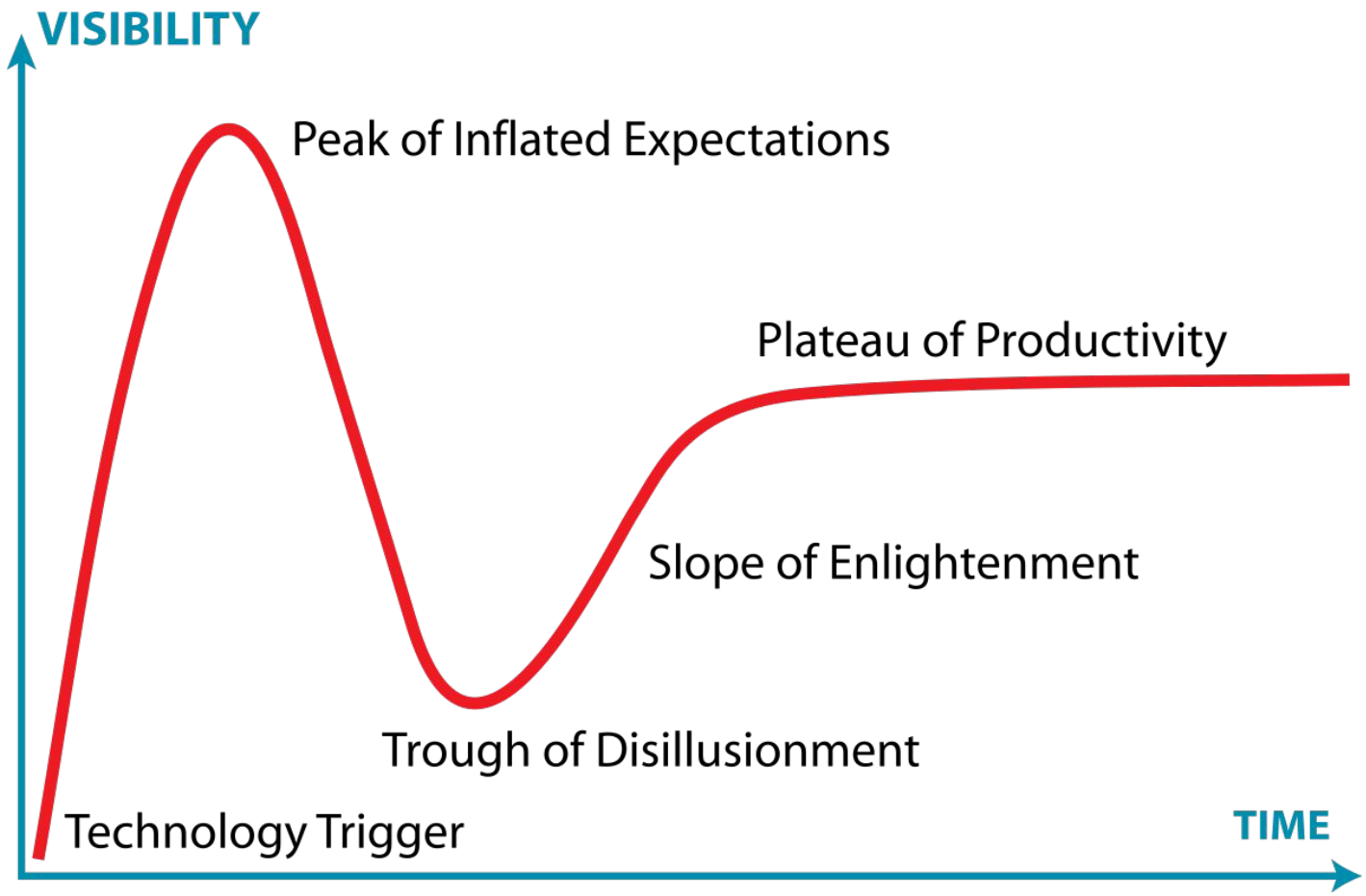
# Drug development is too expensive

Eroom's law

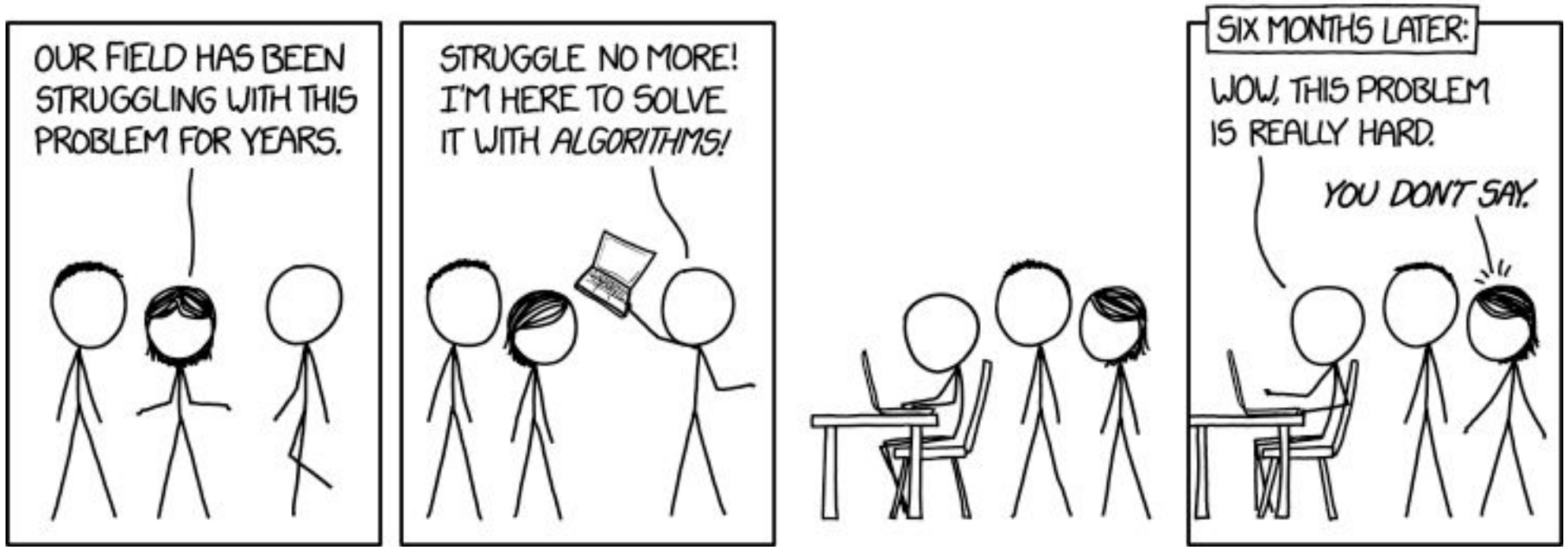



Scannell, J., Blanckley, A., Boldon, H. *et al.* Diagnosing the decline in pharmaceutical R&D efficiency. *Nat Rev Drug Discov* **11**, 191–200 (2012). https://doi.org/10.1038/nrd3681

We are in the peak of inflated expectations



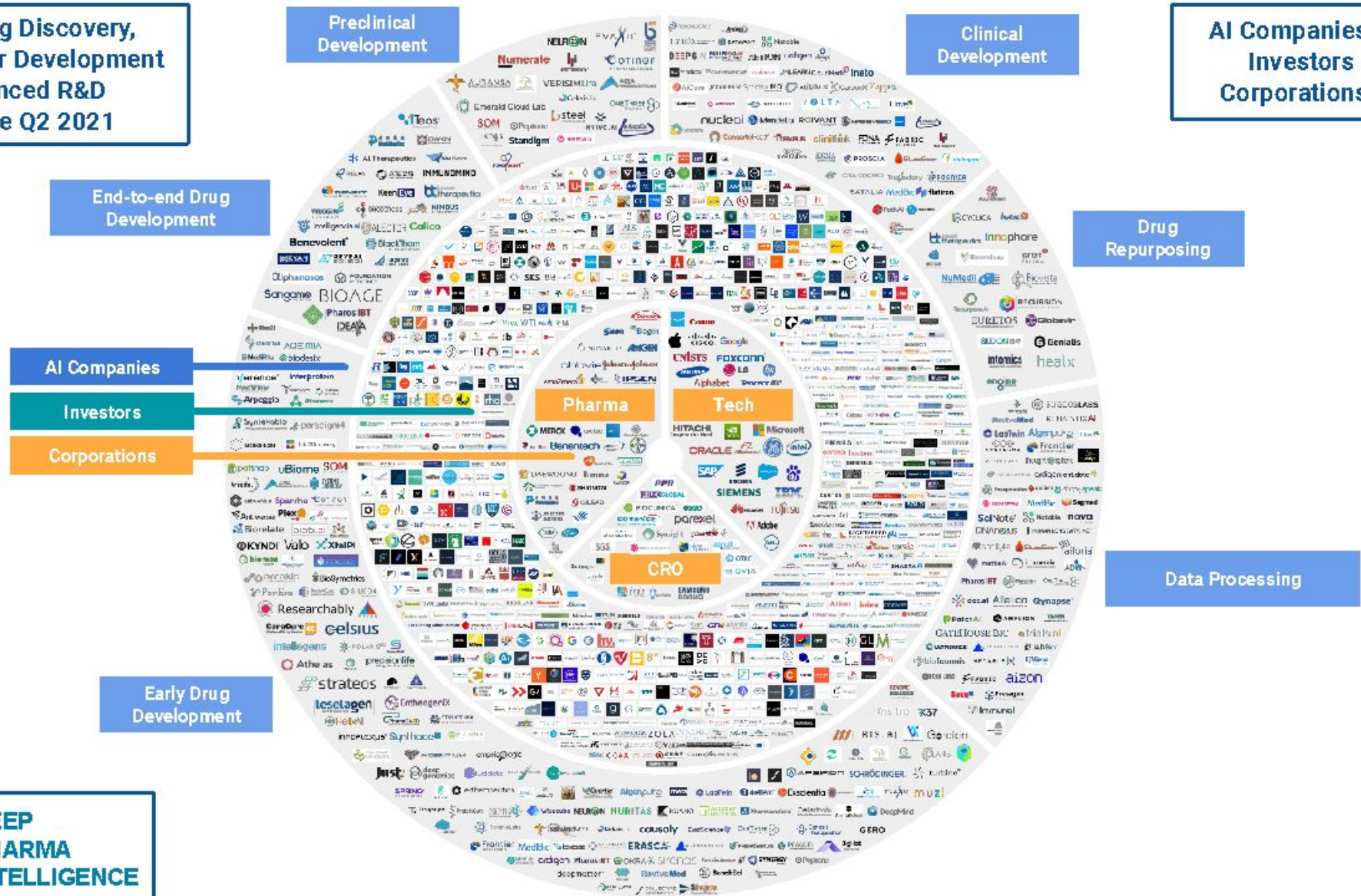

https://en.wikipedia.org/wiki/Gartner_hype_cycle




https://xkcd.com/1831/

# AI for Drug Discovery, Biomarker Development and Advanced R&D Landscape Q2 2021

**AI Companies - 300**
**Investors - 880+**
**Corporations - 100**




DEEP PHARMA INTELLIGENCE

https://www.deep-pharma.tech/landscape-overview-q2-2021

# We don’t have enough diagnostics

- 145 FDA approved/cleared companion diagnostics
- ~35 biomarkers
- 143/145 are for oncology

Source: FDA List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools) (11/1/2022)

# We don’t have enough diagnostics

**35** Biomarkers across

**~28** Indications

- ALK
- BRAF
- BRCA1 and BRCA2
- BRCA1, BRCA2 and ATM
- C-Kit
- deficient mismatch repair (dMMR) proteins
- EGFR (HER1)
- ERBB2
- ERBB2 (HER2)
- EZH2
- FGFR2
- FGFR3
- FLT3 (ITD/TDK)
- Homologous recombination repair (HRR) genes
- IDH1
- IDH2
- Ki-67
- KIT
- KRAS
- KRAS and NRAS
- Liver iron concentration imaging
- MET
- MSI-High
- Myriad HRD
- NTRK1, NTRK2 and NTRK3
- NTRK1, NTRK2 and NTRK3
- PD-L1
- PDGFRB
- PIK3CA
- POMC, PCSK1 and LEPR
- RET
- ROS1
- t(9;21) Philadelphia chromosome
- TMB
- TP53

**~20**

Manufacturers

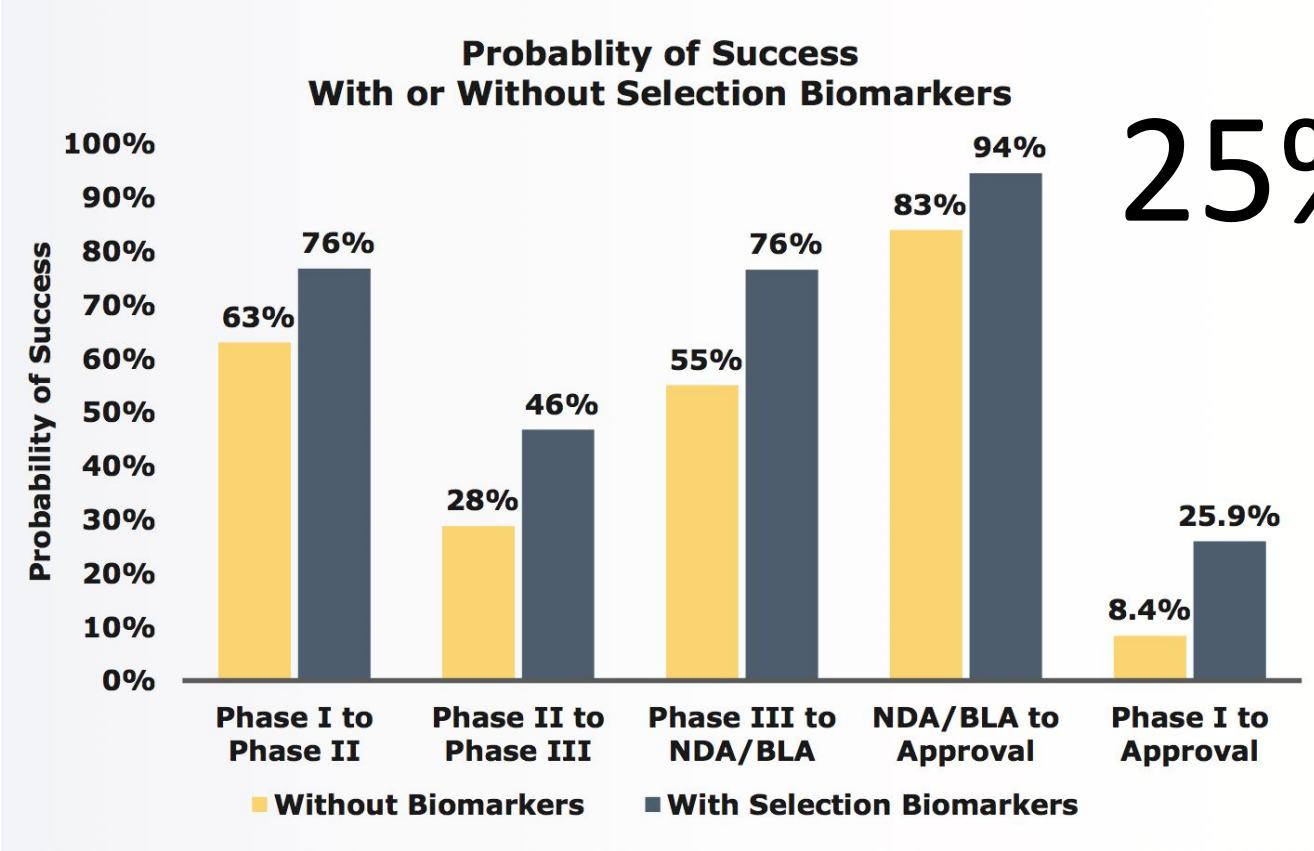
- Abbott Molecular Inc.
- Agilent Technologies
- ARUP Laboratories, Inc.
- Biogenex Laboratories, Inc.
- bioMérieux Inc.
- Dako Denmark A/S
- Dako North America, Inc.
- Foundation Medicine, Inc.
- Guardant Health, Inc.
- Illumina, Inc.
- Invivoscribe Technologies, Inc.
- Leica Biosystems
- Life Technologies Corporation
- MolecularMD Corporation
- Myriad Genetic Laboratories, Inc.
- Pillar Biosciences, Inc.
- PreventionGenetics, LLC
- Qiagen Manchester, Ltd.
- Resonance Health Analysis Services Pty Ltd
- Roche Molecular Systems, Inc.
- Ventana Medical Systems, Inc.

Source: FDA List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools) (11/1/2022)

# The case for half-full

# Finding the right patients can increase probability of success

Trials that utilized selection biomarkers had higher success rates at each phase of development




25%

Source: Clinical Development Success Rates 2006-2015
https://www.bio.org/

# Technologies are enabling

- NGS testing has become common practice, and in some cases routine for initial treatment (EGFR-mutated NSCLC)
  - Tissue agnostic drug approvals (rare fusions & I/O biomarkers)
  - Genomic DNA repair signatures to guide therapy (e.g. HRD)
  - Genomic drivers of resistance & logitudonal testing

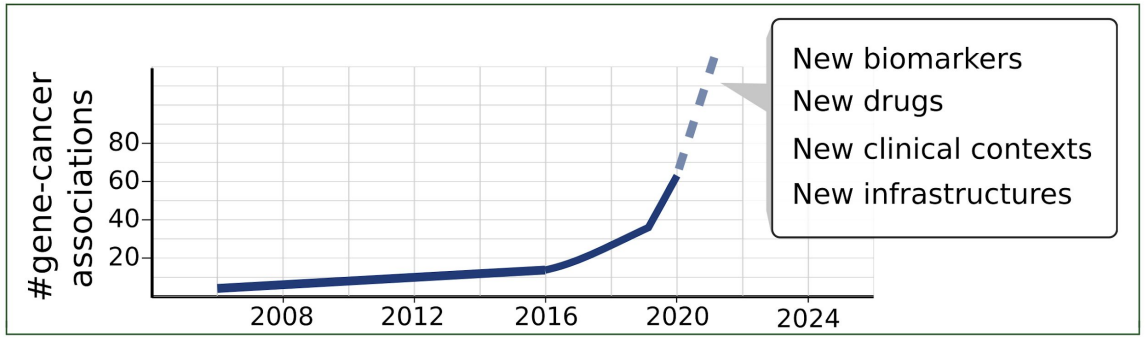



**Figure 1. Number of gene biomarker-cancer associations with approved targeted drugs from 2006 ($N = 6$) to 2020 ($N = 61$), based on estimates from Haslam et al.[1] and Chakravarty et al.[2]**
The dashed line represents the forecast for the coming years, which depends on precision cancer therapy enablers summarized in the box.

Dienstmann *et al.*, Annals Oncol 2021
Haslam *et al.*, Annals Oncol 2021

Response to genome informed therapy was 3.33% in 2006 and 11.10% in 2020

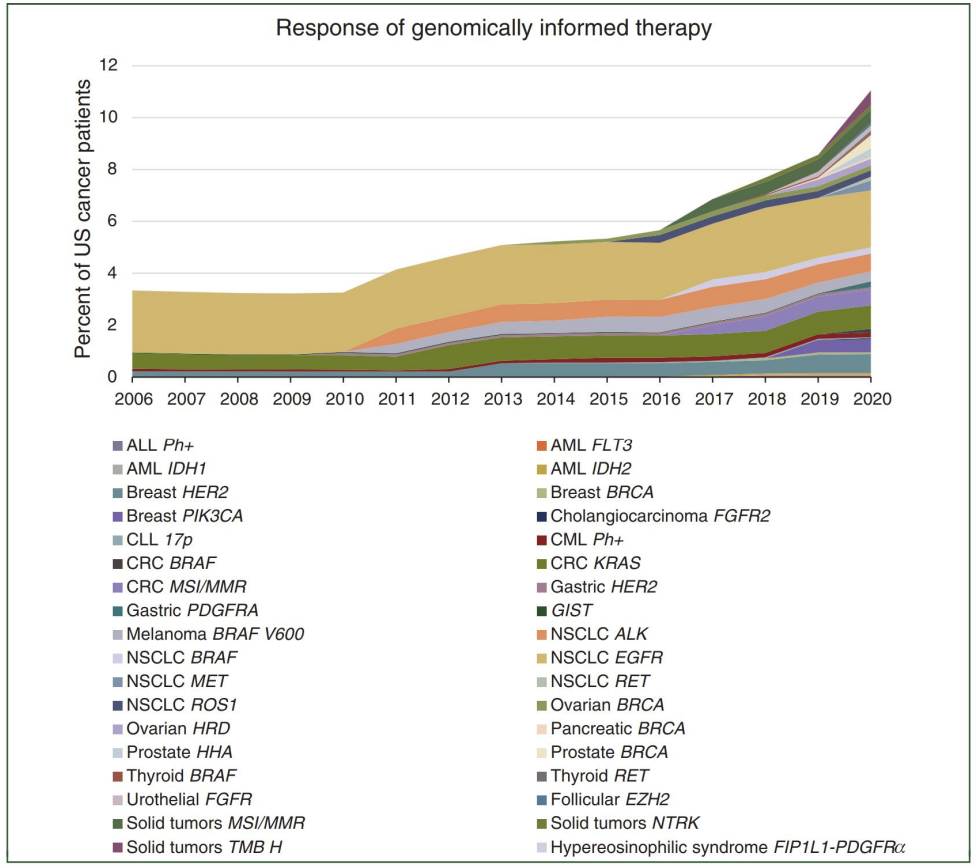
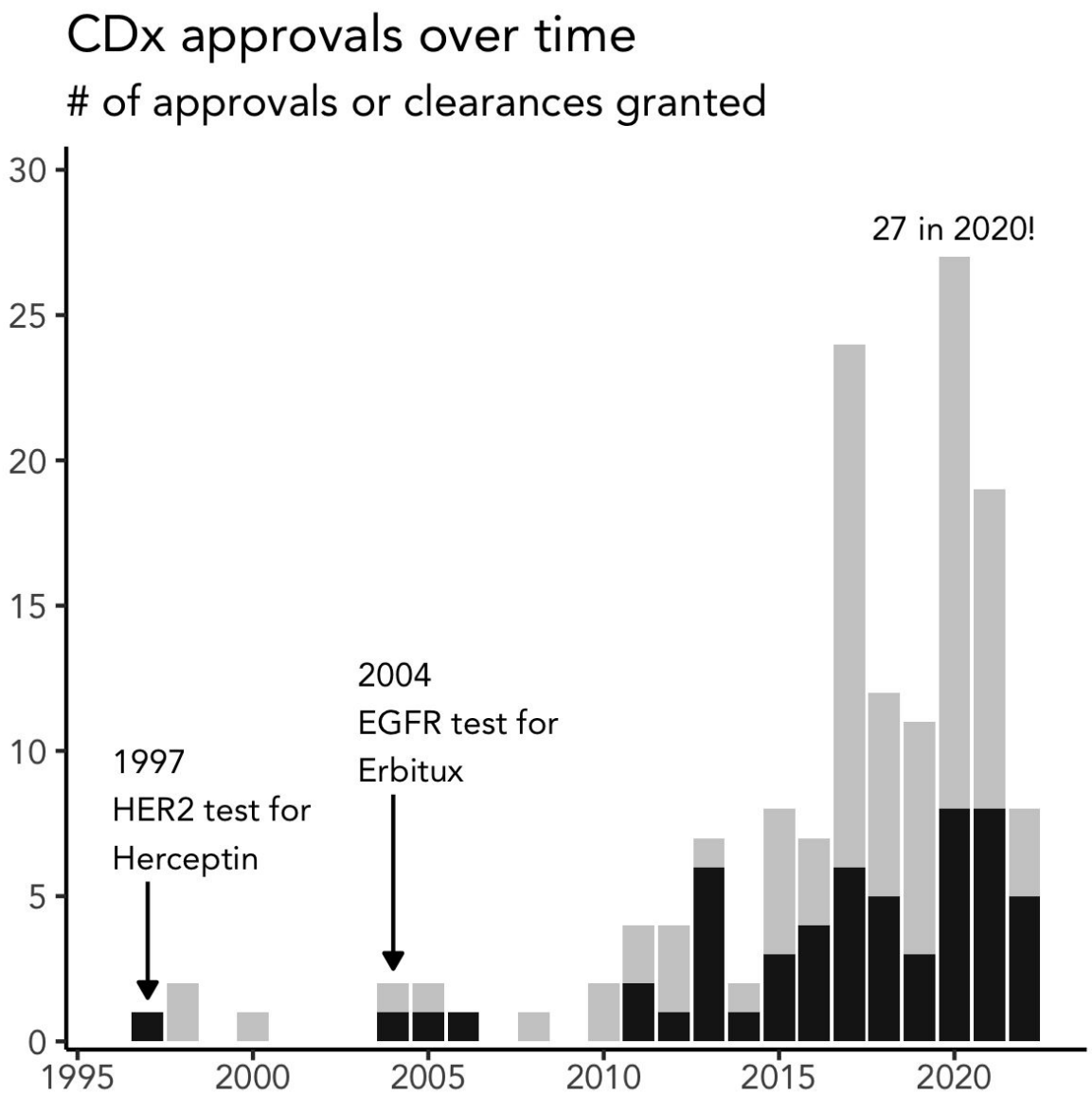



**Figure 4. Estimated response to genome-informed therapy in US cancer patients, 2006-2020.**
ALL, acute lymphocytic leukemia; AML, acute myelocytic leukemia; CLL, chronic lymphocytic leukemia; CML, chronic myelocytic leukemia; CRC, colorectal cancer; NSCLC, non-small-cell lung cancer.

# Companion diagnostics are becoming more common



Discovery & Translational Research

Clinical Development

Commercial & Medical Affairs

More data than ever before is available to impact all stages of development

# How is Real World Evidence data impacting Pharma?

RWE data can unlock data-driven insights and activities at every phase of target discovery & therapeutic development programs

## Indication Selection

Identify clinical biomarkers of response and indications enriched in those biomarkers. Develop **novel biomarkers strategies** based on DNA, RNA, or digital pathology images

## Preclinical Validation

Validate biomarkers/ signatures of response and identify combination therapies in three dimensions ex vivo with **tumor-derived biological models**

## Clinical Trial Design & Execution

Analyze RWD to inform I/E criteria to maximize probability of trial success.

## Companion Diagnostic Development

Design and launch validated algorithms as **NGS CDx's** with high biomarker stringency in select indications that have clinical benefit

Discovery & Translational Research

Clinical Development

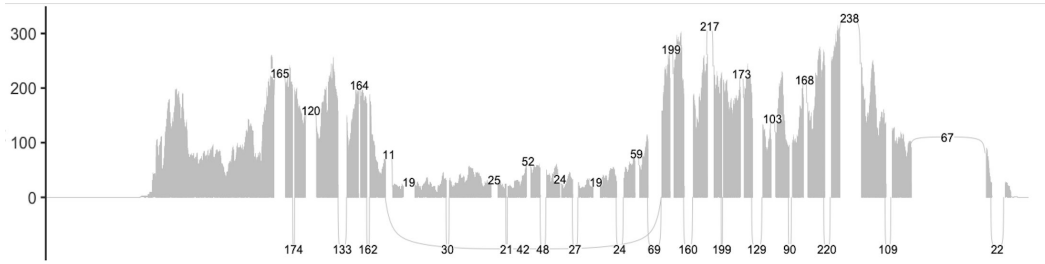
Commercial & Medical Affairs

CASE STUDY

# **Increased patient detection and clinical trial enrollment** through development of custom RNA exon skipping pipeline

**Background:** Partner was seeking help to determine eligibility for their phase II clinical trial. The eligibility criteria for the trial included variants in specific regions of interest across a family of four different genes determined through both DNA and RNA sequencing inputs.

- Developed a de novo RNA altered splicing pipeline, to increase the funnel of patients that are eligible for the trial
- Use of both DNA and RNA inputs to determine potential eligibility for the trial
- Custom reporting outputs provide principal investigators with information about a patient's potential eligibility for a trial
- CE marker the assays and supporting 30+ clinical trial sites across Europe, Israel and the US



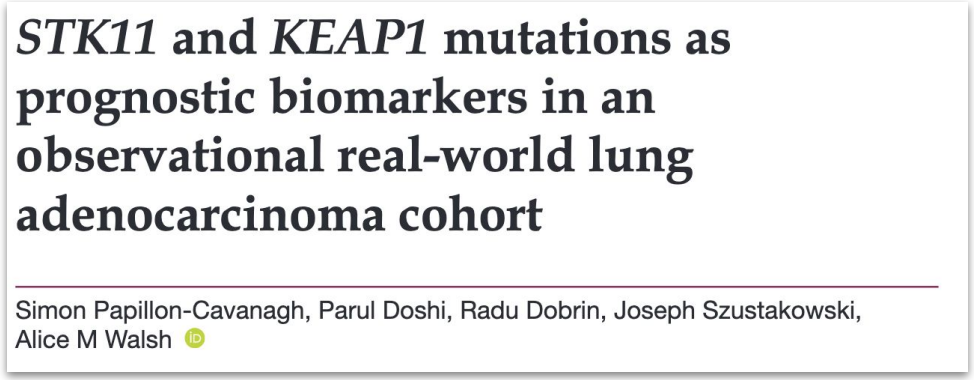

**Custom detection of *exon* splicing event.** Patient with detected splicing is likely eligible for the trial.

CASE STUDY

# **Real-world data** augments evaluation of clinical trials and enables faster decision making

**Background:** Internal research and external high-profile reports that ***STK11*** mutations are a negative biomarker for immune checkpoint blockade (ICB)

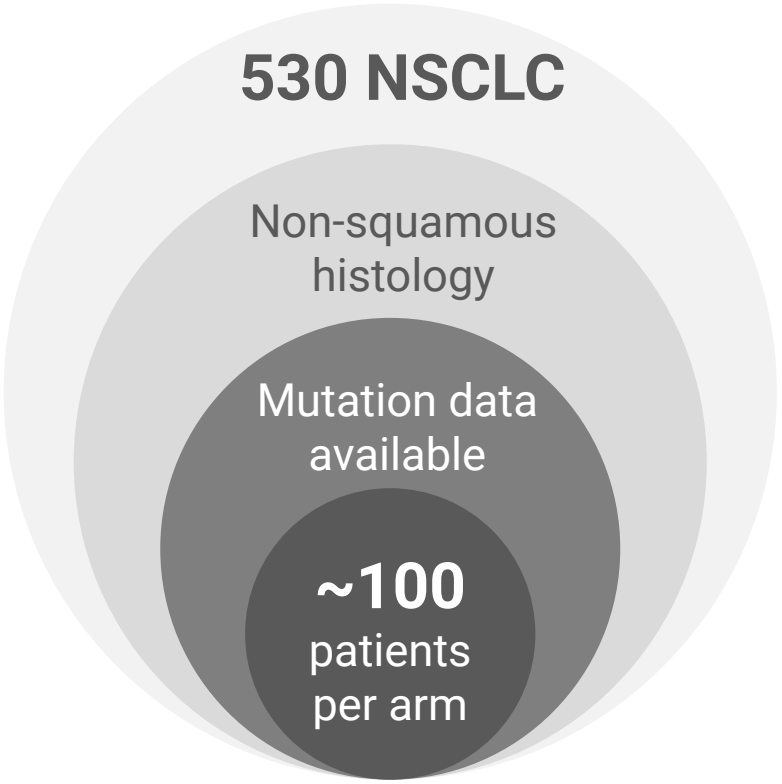
- Studies did not include non-ICB arms (**prognostic?**)
- Should we launch a new clinical study?
- **Do we need to exclude patients** from ongoing studies?



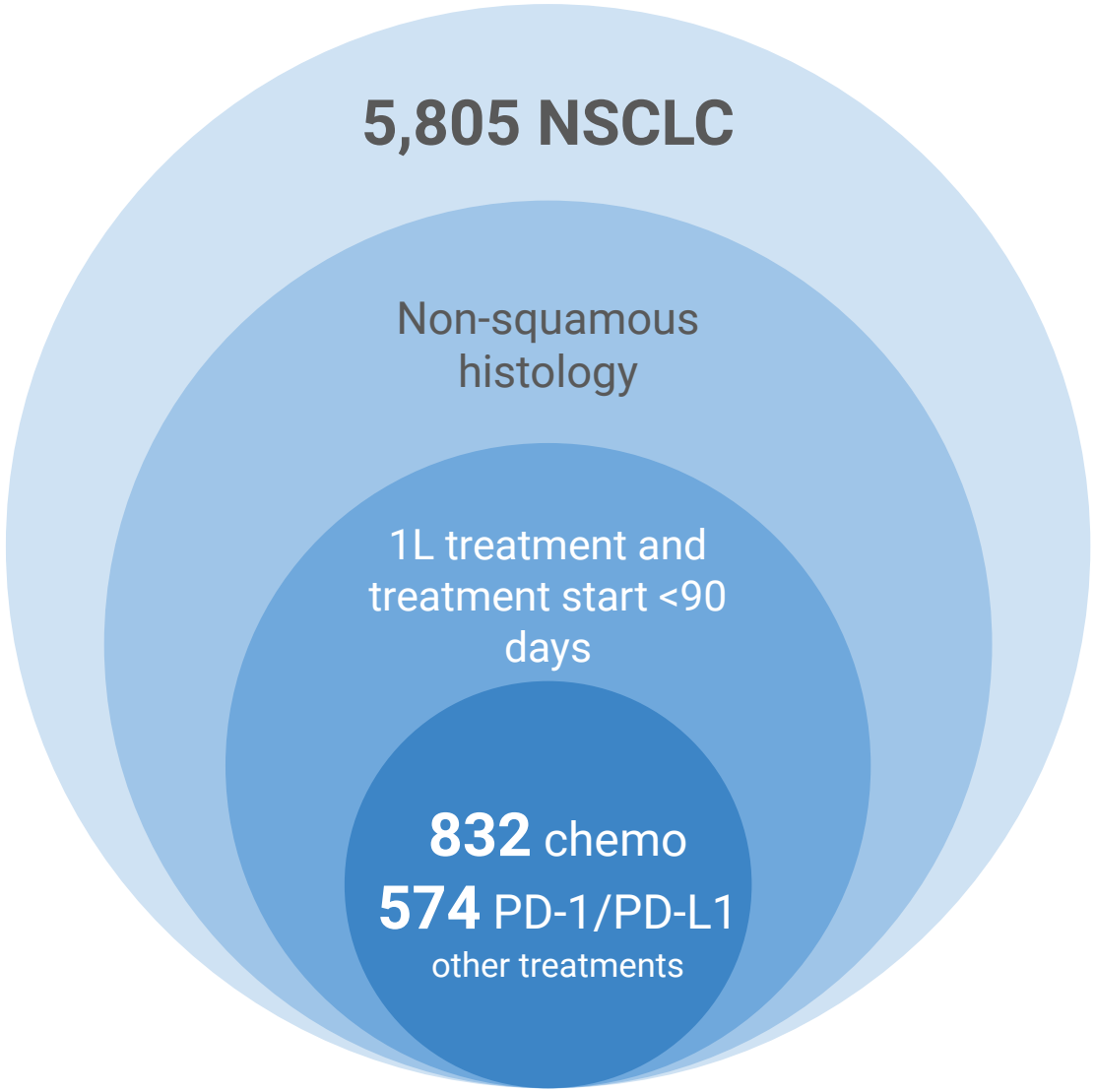

*Work done in 2017-2019 at Bristol Myers Squibb*

ref: 10.1136/esmoopen-2020-000706

## Randomized Controlled Trial




## Real-World Data

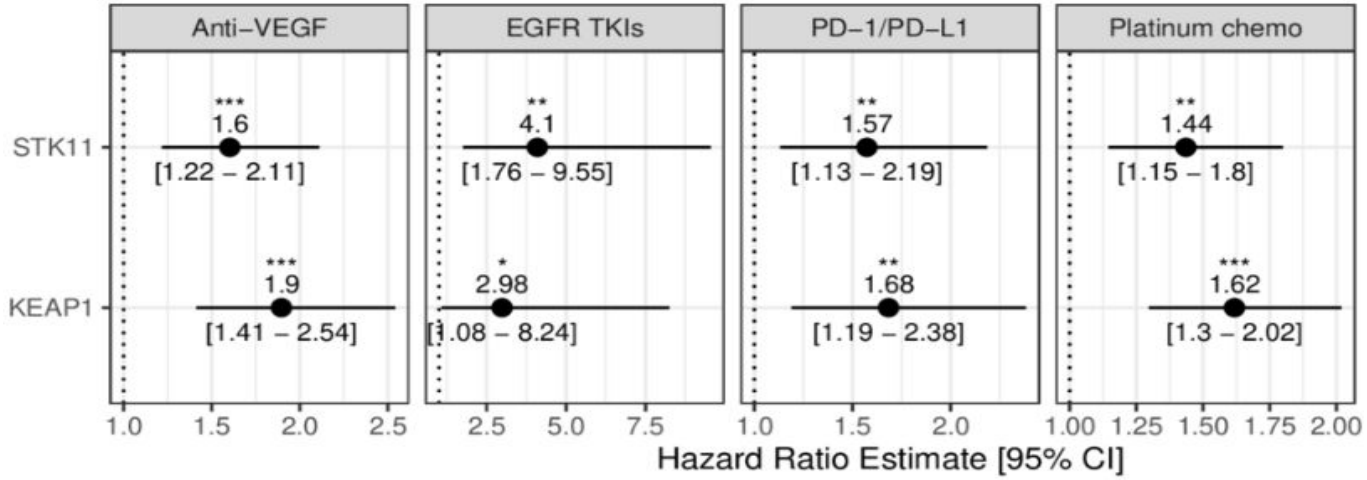



*Patients with Foundation Medicine tumor genetic testing and outcomes data (CGDB)

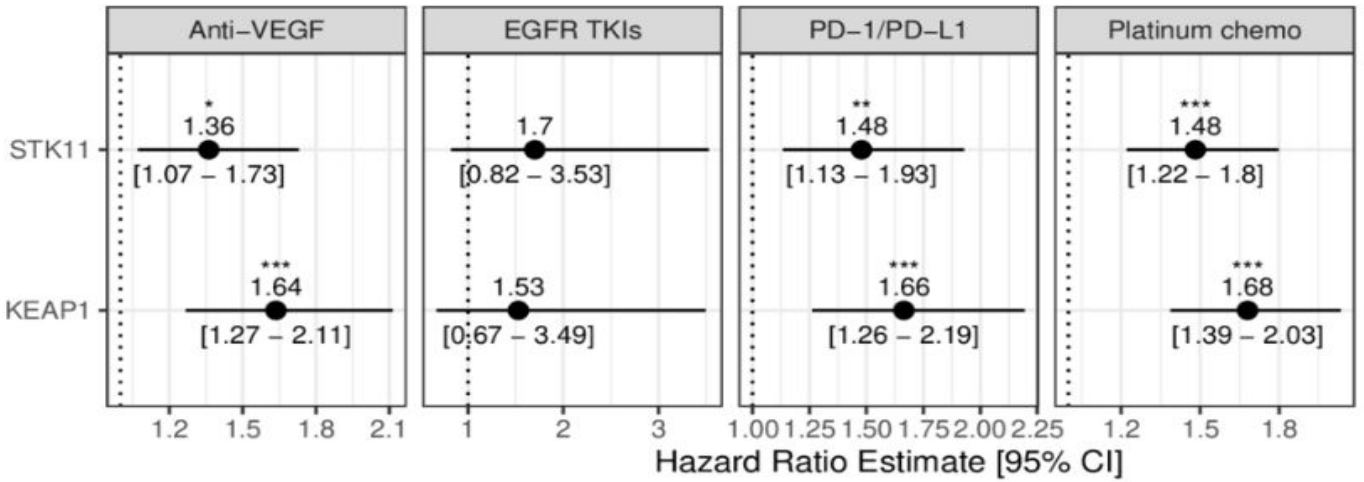
ref: 10.1136/esmoopen-2020-000706

# *STK11* and *KEAP1* mutations are deleterious across all treatments

OS




PFS

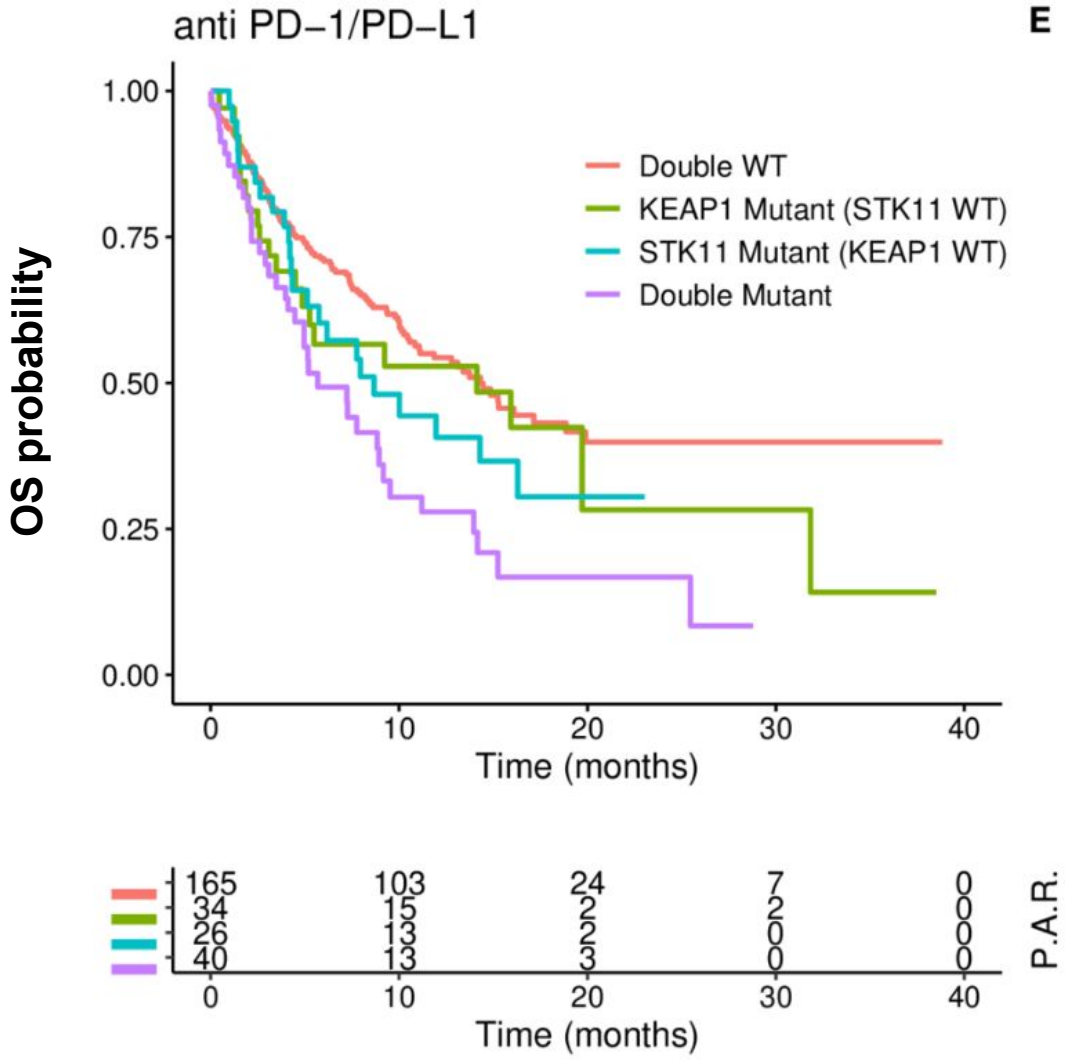


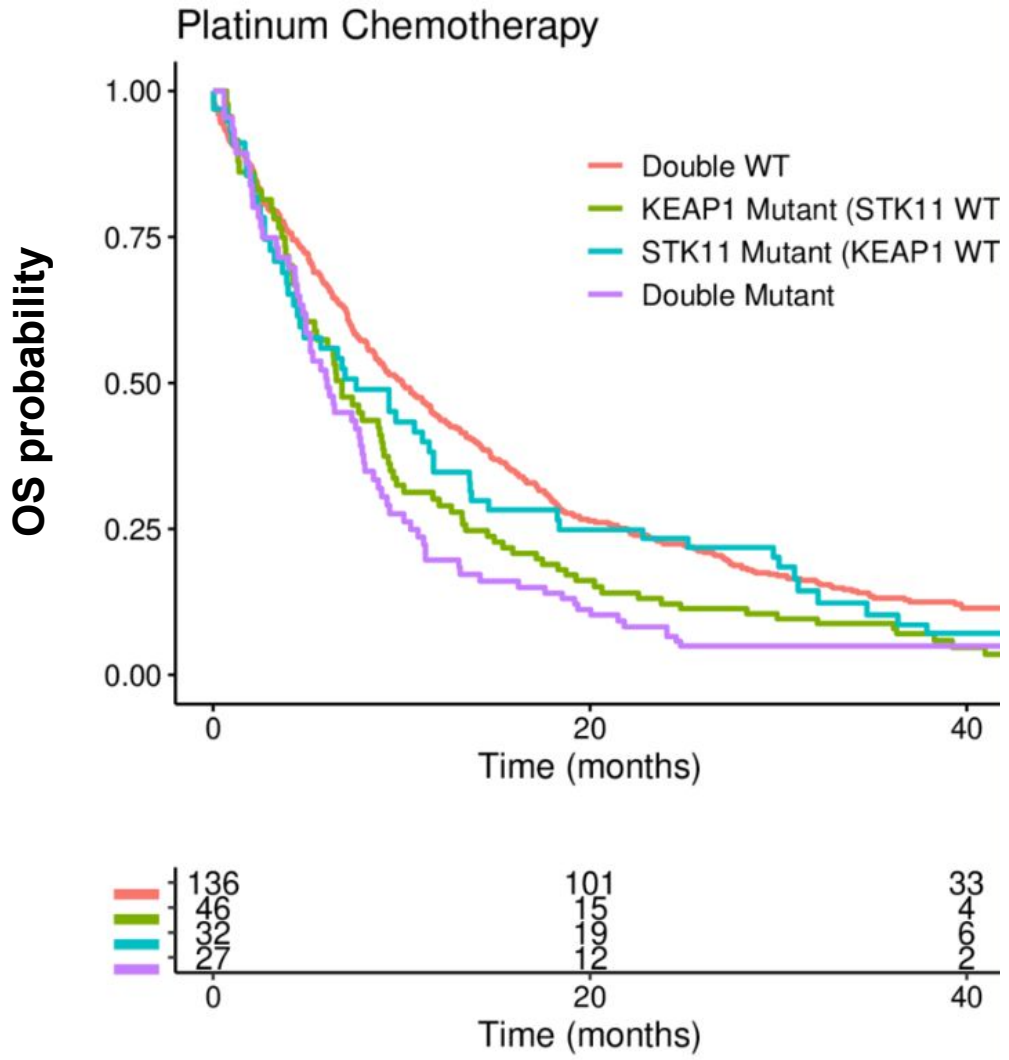

*STK11* mutations are found in **~20% of NSCLC** patients

*STK11* and *KEAP1* are **frequently co-mutated**

ref: 10.1136/esmoopen-2020-000706

# *STK11* and *KEAP1* mutations effects are additive (OS)

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We believe that data can help overcome challenges in drug development

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# Challenges growing teams

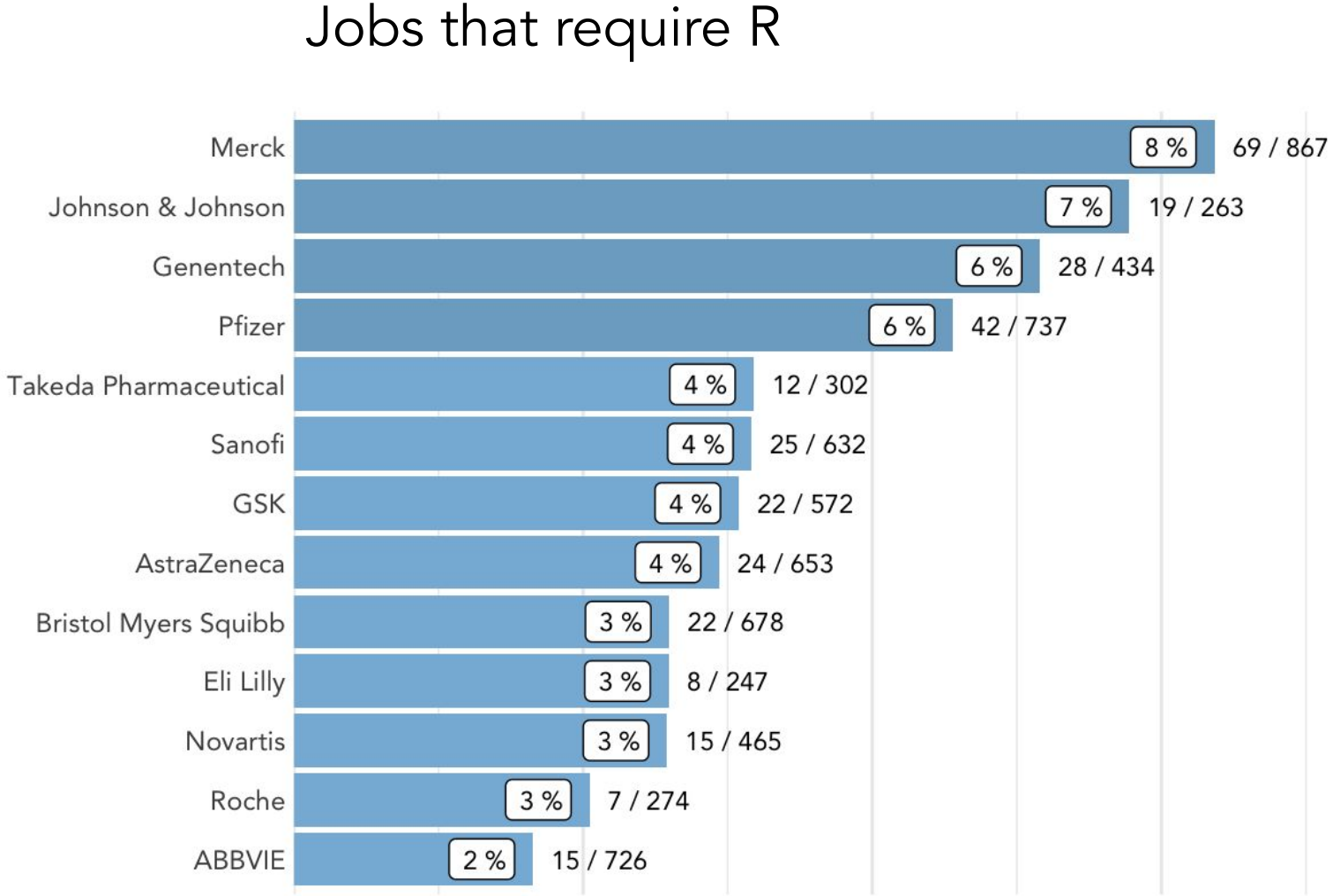
*Hiring*

*Lots of great companies to work for*

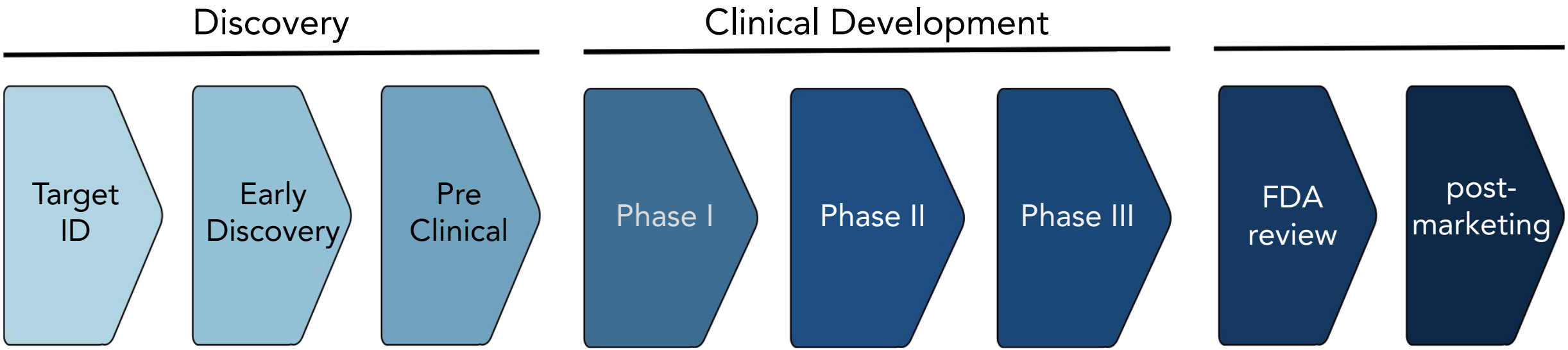
*Career development*

*Building & reinforcing culture*

# Companies need you!




Source: Job descriptions from Sept 2022




## *Who works with data?*

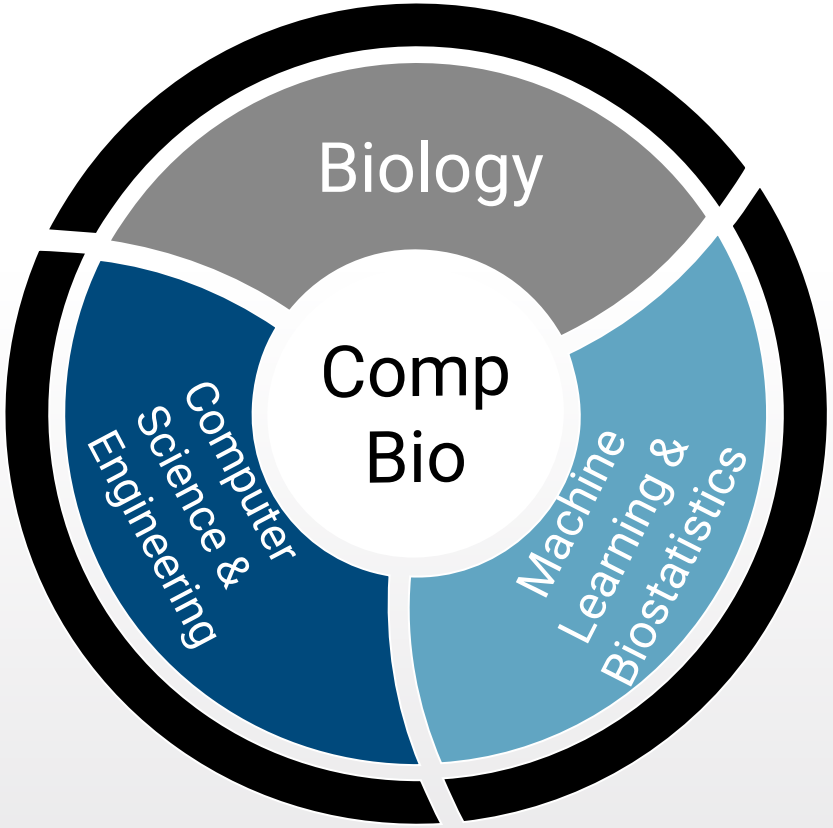
Preclinical stats teams
Discovery scientists
Bioinformatics
Computational biology

Clinical Biostats
Operations
Consultants
CROs

Partner companies
Academic collaborators

Regulatory agencies
Medical Affairs
RWD teams
HEOR teams

Can we communicate better job descriptions, company structures, and domain expertise?



# Data science roles in Pharma require a mix of skills

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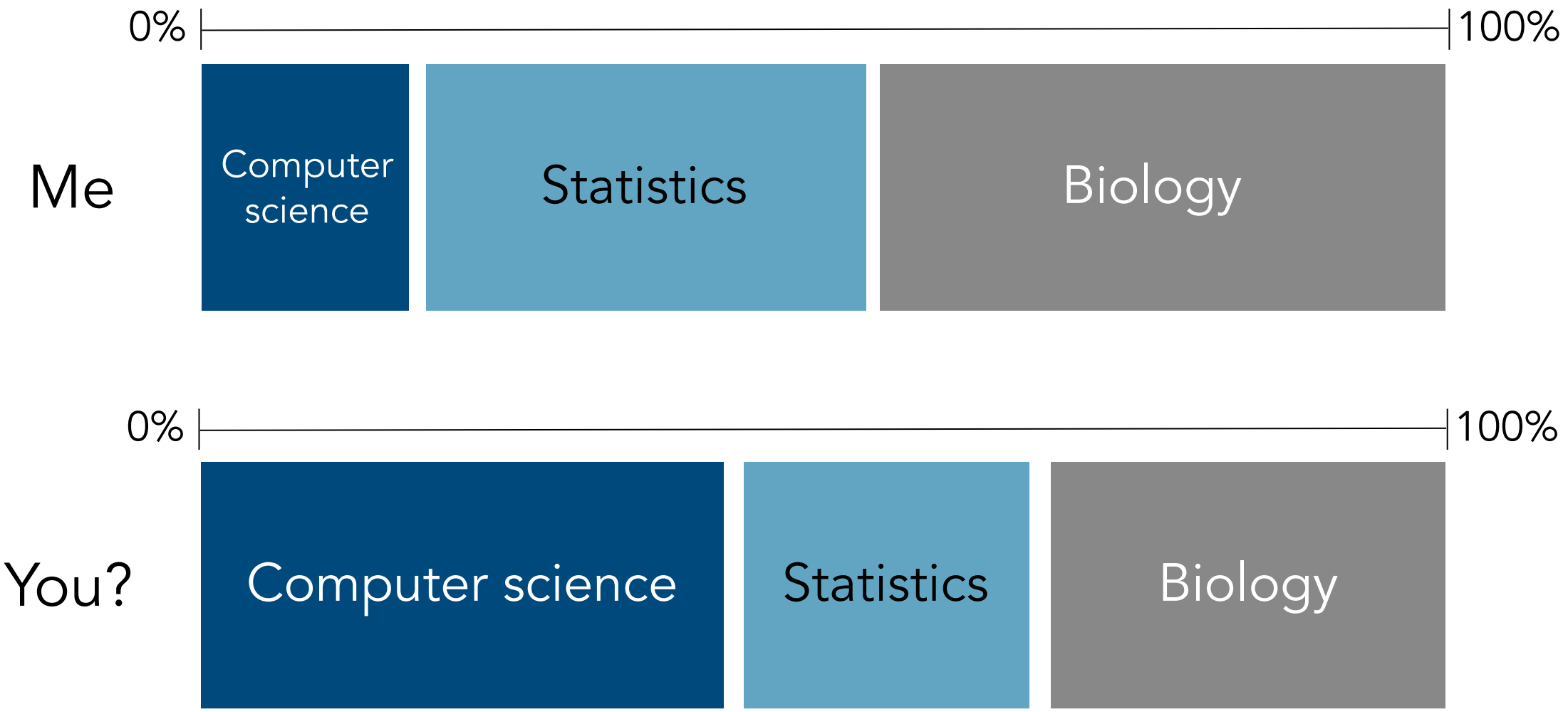

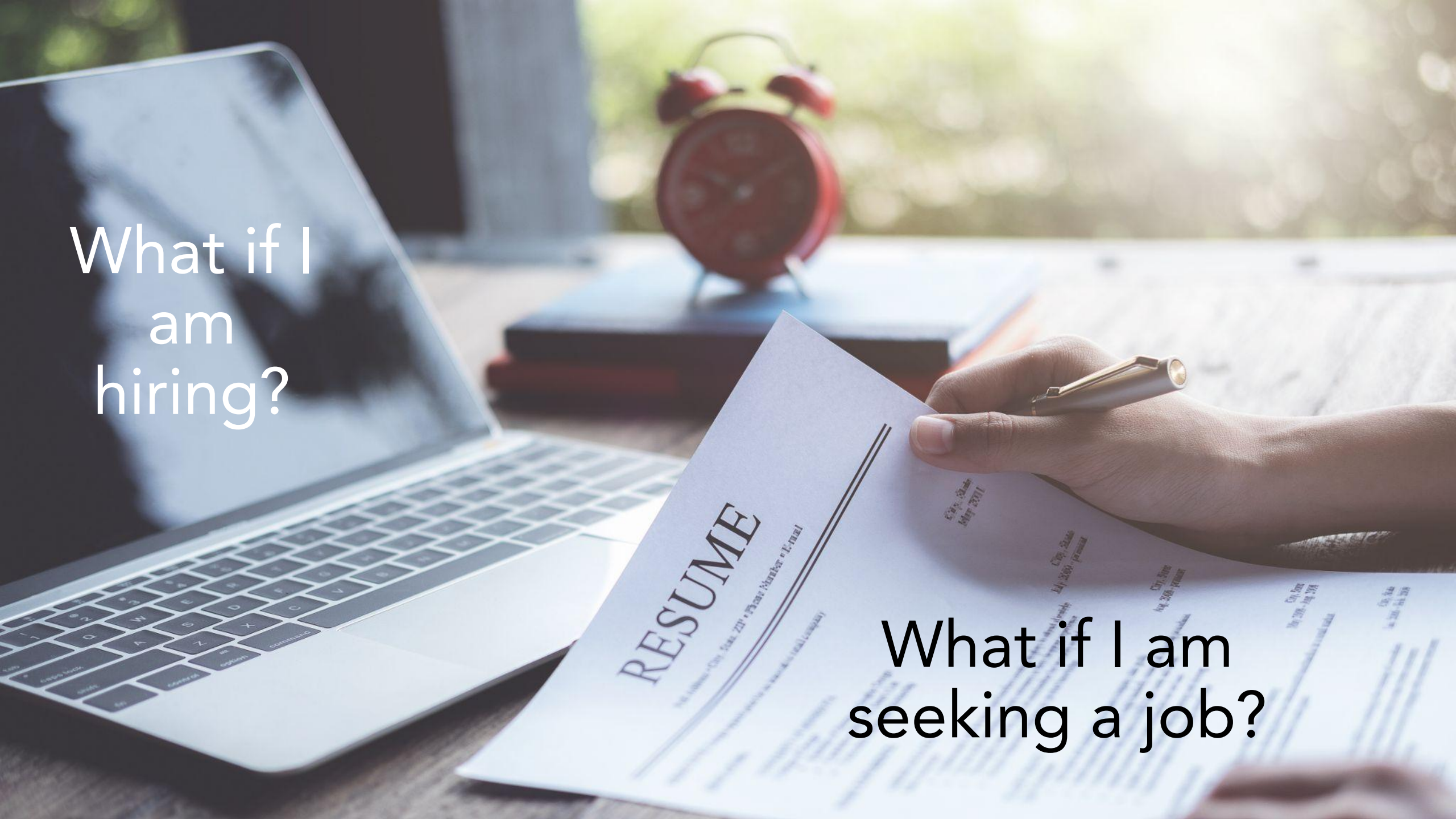
What if I am hiring?
RESUME
What if I am seeking a job?

# Hiring process and timeline

### Application Review

- Review publications
- Evaluate github
- Make guesses on CV
- Evaluate LinkedIN networks

### Technical assessment

- Take home assignment  challenge and/or technical interview
- Provide open ended questions to assess thought process and showcase expertise
- Evaluate written communication
- Request code and html report

### Offer Stage

- Act quickly!
- Ask for references and leverage shared connections
- Understand the competitive market

### Recruitment

- Lean on your network and community events!
- Build a ‘full-stack’ CompBio team
- Hire roles you need not who you have available

### Manager Informational Screen

- Describe team mission
- Ask about technical & scientific proficiency
- Assess culture fit
- Ask how their expertise will impact to team
- Evaluate if your role is the best company fit
- Ask about competitive offers and timeline considerations

### Virtual Interview

- Include scientific presentation to evaluate communication and expertise
- Discuss and ask open ended questions
- Ask about career development goals
- Engage the team in this process

**Aim to evaluate all candidates during this timeline and schedule all virtual interviews within 10 days of each other**

# Thank you!

Rx Pharma

@sciencealice

alice-walsh

pathos.com

@keir1016

catherineigartua

tempus.com

Careers at Tempus leveraging R!
Translational Research, Systems Biology, Immunology, Bioinformatics & Data Science