# Revisiting drugs that failed the efficacy phases of clinical trials

Emily Lorenzen
Metis Bootcamp
Project 3 - Business
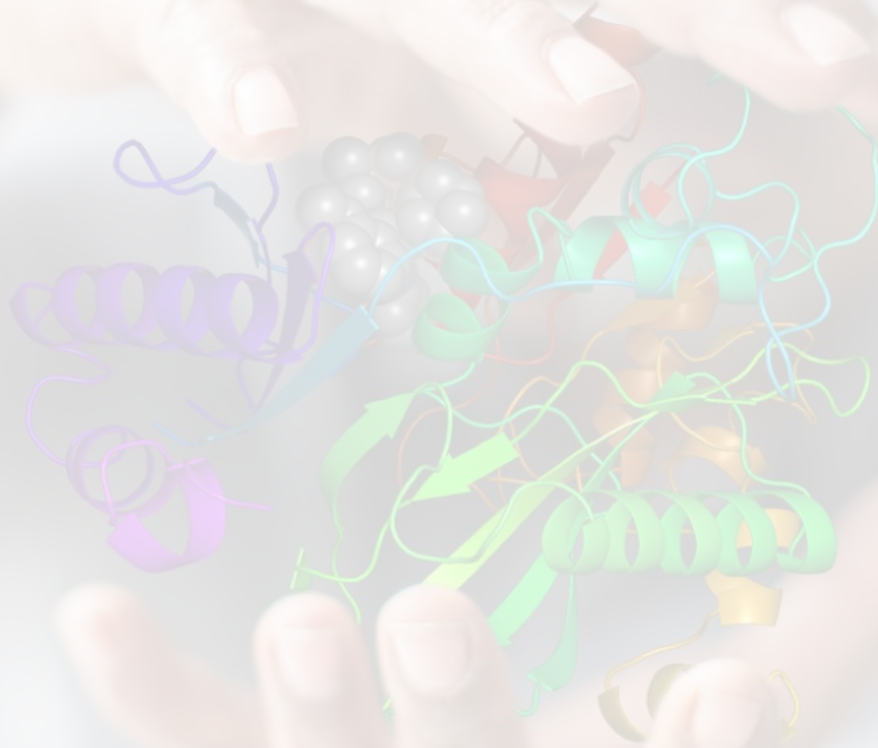
# Current process to form pharma parternerships
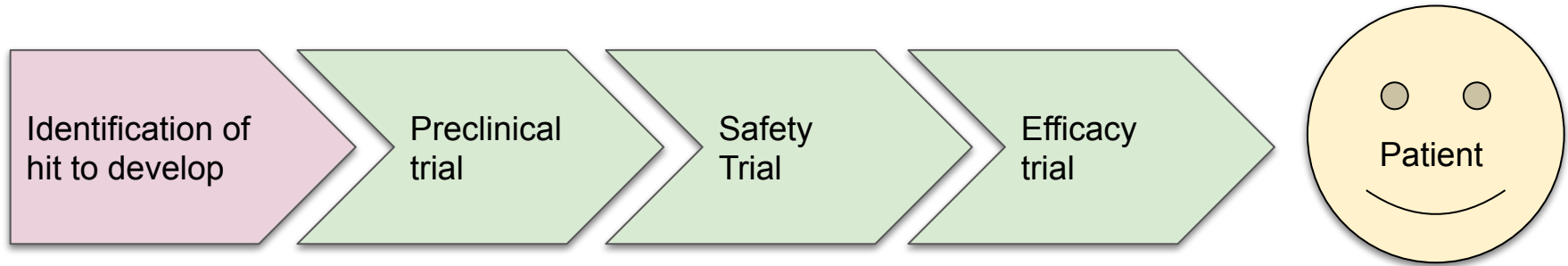
# Method to increase pharma partnerships



Identification development hit → Preclinical Trial → Safety Trial → Efficacy trial → Patient

$5 million

$2 million
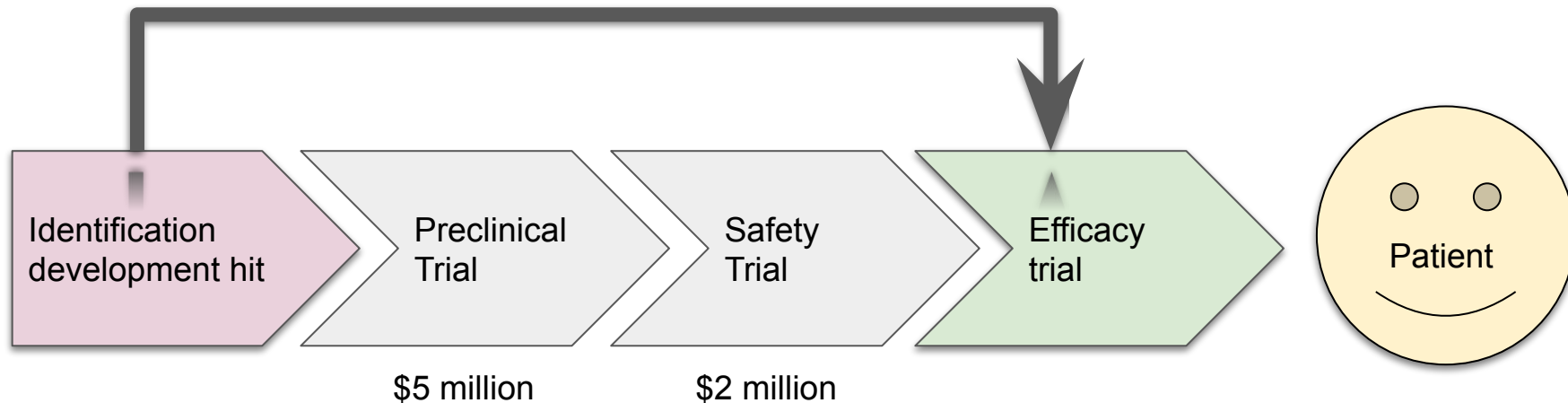
Repurpose drugs that failed in the efficacy phases of clinical trials.

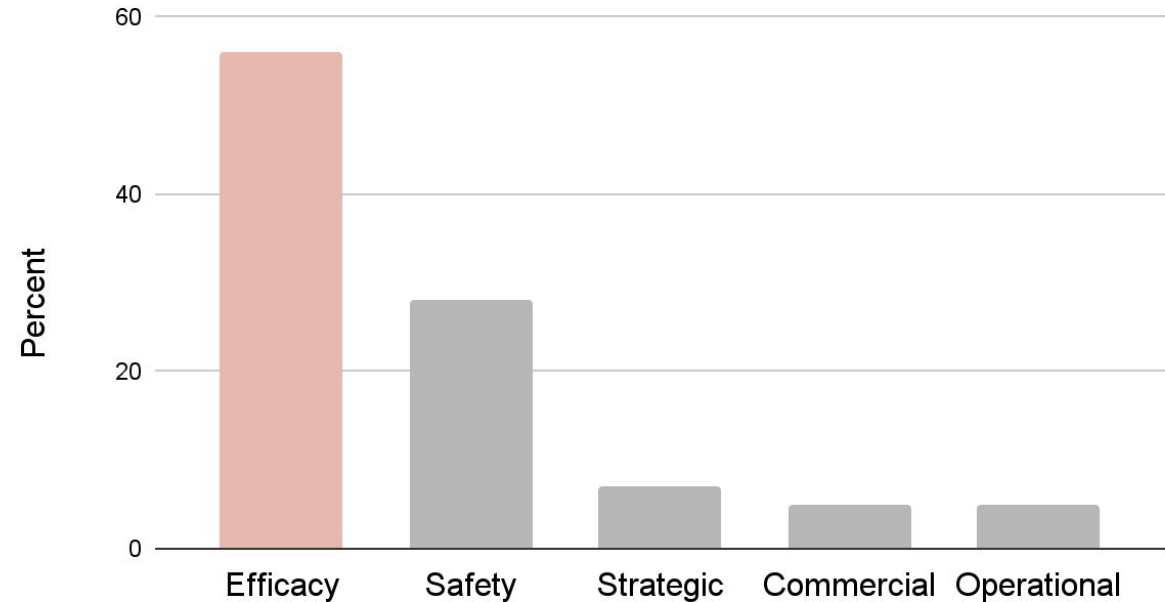# Identify drugs to investigate with molecular modeling

**83%**

drugs fail the efficacy trial

**21,200**

drugs that passed preclinical and safety trials, but failed efficacy trial

Reasons drugs fail efficacy trials

# Natural protein variation - now affordable to monitor
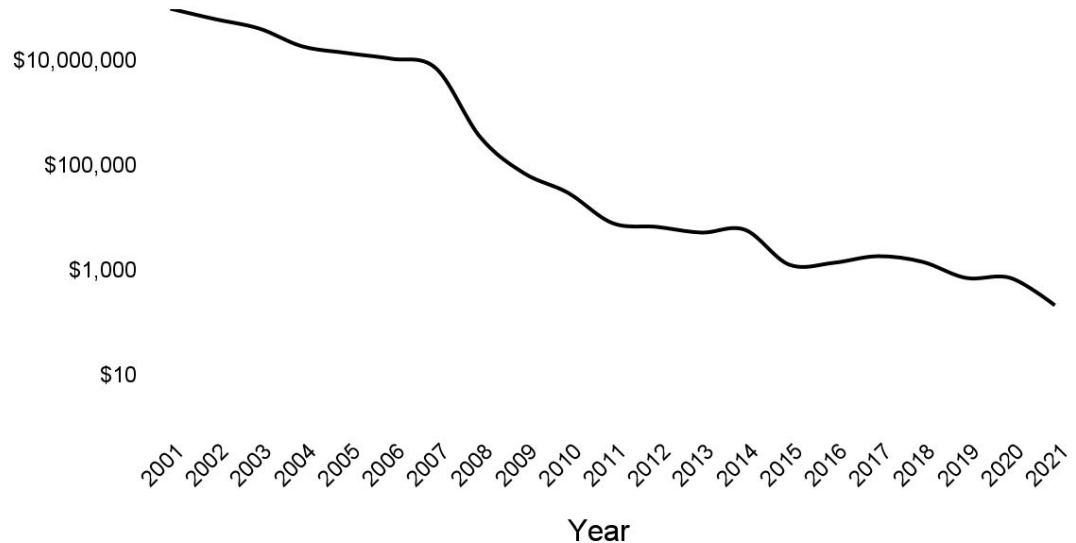
Proteins with variants:

# 12,896

Total proteins: ~20,000a
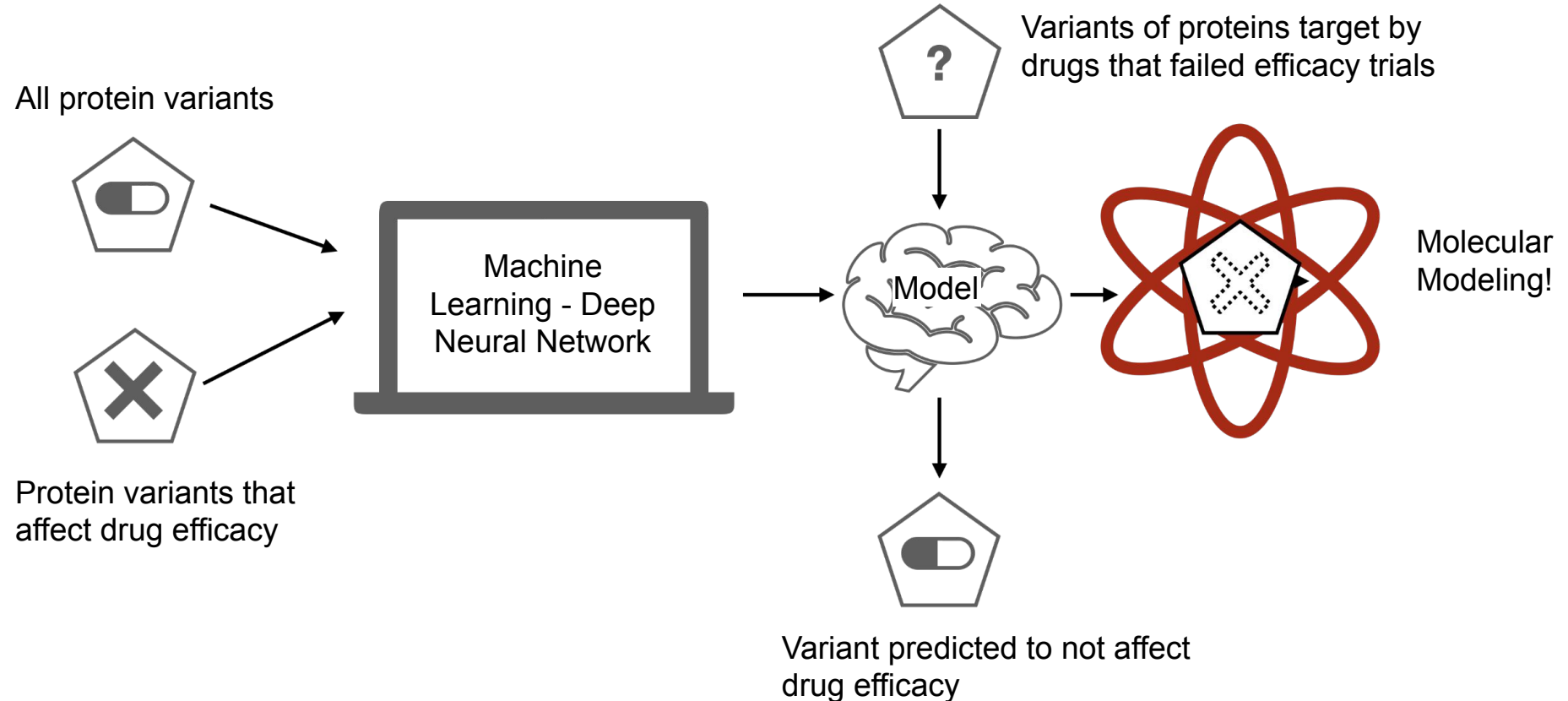
Drug targets with variants:

# 1,862

Total drug targets: 2,183

Genome sequencing costs are rapidly decreasing



$10,000,000

$100,000

$1,000

$10

2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021

Year

# Develop a model to classify variants

All protein variants

Protein variants that affect drug efficacy

Machine Learning - Deep Neural Network

?

Variants of proteins target by drugs that failed efficacy trials

Model

Molecular Modeling!

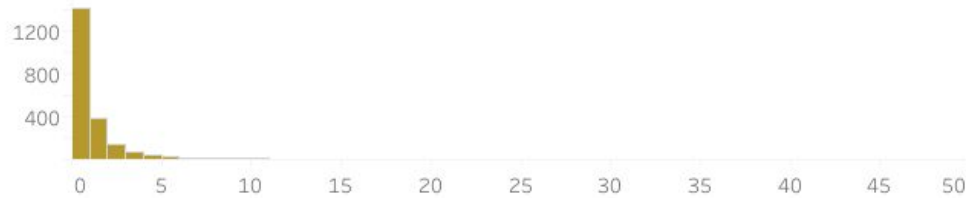Variant predicted to not affect drug efficacy

# Most proteins have few variants



All protein variants

# Most proteins have few variants



Drug target variants

# Most proteins have few variants

Drug efficacy variants



40
20

0   5   10   15   20   25   30   35   40   45   50

Number of protein variants (normalized by length)
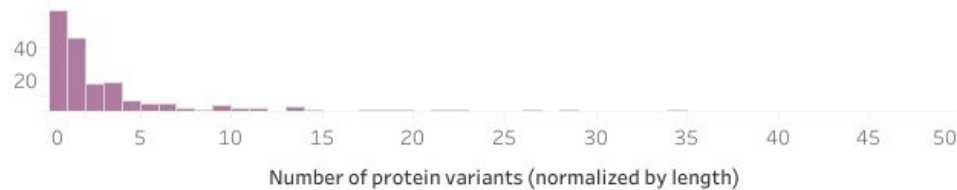
# Preliminary analysis - distribution of protein variation



All protein variants

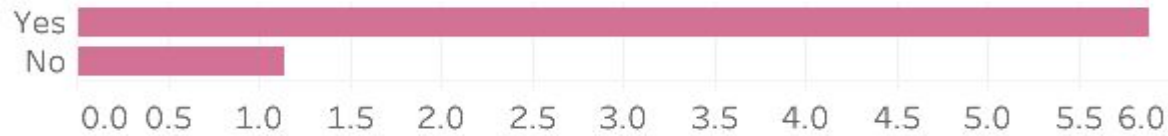Drug target variants

Drug efficacy variants

Number of protein variants (normalized by length)

Right skew becomes more shallow

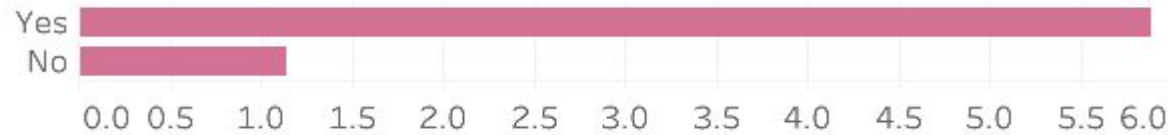# Preliminary analysis - average protein variation

Affects Drug Response

Statistical significance

Yes vs. No
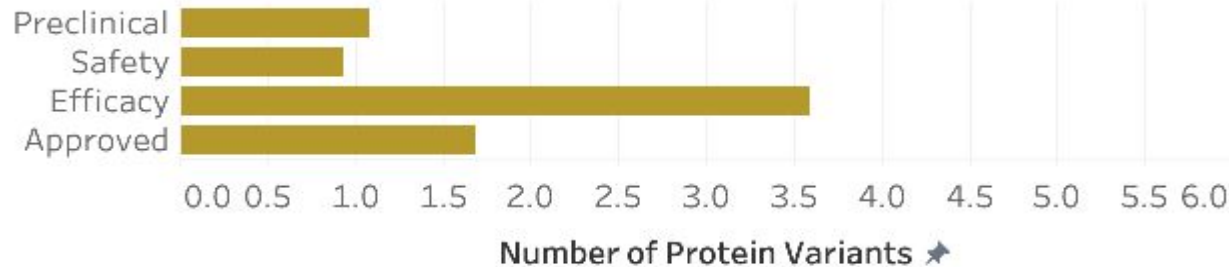P-value: 0.02

# Preliminary analysis - average protein variation

Statistical significance

### Affects Drug Response



Yes vs. No
P-value: 0.02

### Phase of Max Clinical Trial



Number of Protein Variants

Efficacy vs. approved
P-value: 0.19

# Preliminary analysis - average protein variation

## Affects Drug Response
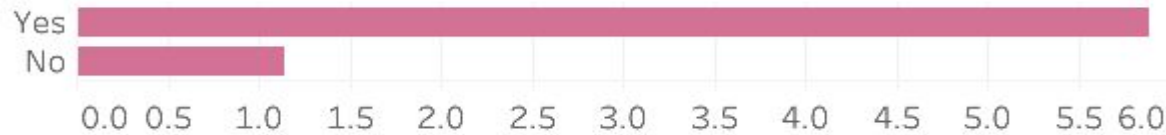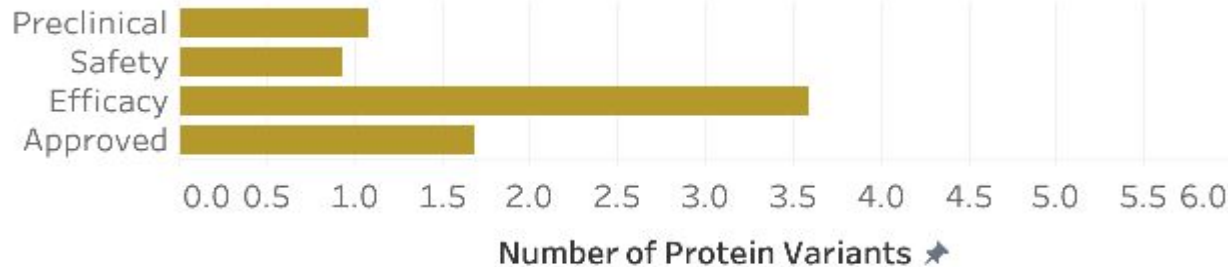
Statistical significance

Yes vs. No
P-value: 0.02

## Phase of Max Clinical Trial

Efficacy vs. approved
P-value: 0.19

Number of Protein Variants ✦

Efficacy vs. Yes,
Affects Drug
Response P-value:
0.41

# Conclusions

1) Biologically logical features can differentiate protein variants that affect drug response from other variants

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1) Biologically logical features can differentiate protein variants that affect drug response from other variants

2) Drugs that failed in efficacy trials target proteins that show feature characteristics similar to variants that affect drug response