Public Hybrid Workshop

Generic Drug Repurposing: Exploring the Potential Role of the Regulator and Policy Solutions

May 29, 2025 | 10:00 a.m. – 4:00 p.m. ET

Duke | MARGOLIS INSTITUTE *for* Health Policy

Welcome & Opening Remarks

Gerrit Hamre, *Duke-Margolis Institute for Health Policy*

Statement of Independence

The Robert J. Margolis, MD, Institute for Health Policy is part of Duke University, and as such it honors the tradition of academic independence on the part of its faculty and scholars. Neither Duke nor the Margolis Institute take partisan positions, but the individual members are free to speak their minds and express their opinions regarding important issues.

For more details on relevant institutional policies, please refer to the Duke Faculty Handbook, including the Code of Conduct and other policies and procedures. In addition, regarding positions on legislation and advocacy, Duke University policies are available at http://publicaffairs.duke.edu/government.

Anti-Trust Compliance Policy

- Call participants are committed to free and open competition in the marketplace and compliance with all applicable laws, including compliance with antitrust and competition laws.
- Meetings, communications and other activities are not intended in any way to limit the individual competitive decisions of the Members or to restrict competition among them.
- By participating in this meeting, each participant agrees to comply with the Duke-Margolis Institute for Health Policy Antitrust Compliance Policy and Guidelines.
- Meetings, communications and other activities shall not be proposed for, or used for the purpose of, reaching or implementing any agreement concerning the competitive activities of others.
- If any discussions raise antitrust concerns, first, state the concern openly or directly to the meeting organizers. If your concerns are not resolved, (i) leave the meeting, (ii) document any conversation or activity that raises concerns and (iii) consult with counsel with any questions or to report concerning activity.

Anti-Trust Compliance Policy: Off-Limit Topics

When participating in activities, call participants and observers shall avoid discussing non-public, company-specific information relating to current or future competition in the marketplace.

- Company-specific prices, pricing methods, pricing policies, pricing plans.
- Sensitive cost information, including reimbursement rates or methods, pharmacy costs, and salaries/compensation information.
- Marketing and strategic plans, market or competitive evaluations, including any allocation of markets.
- Identity and other information about present or potential customers, healthcare clinicians or payers, including costs, prices, profitability, specific contract terms, marketing plans, and product development plans.
- Research & development plans.
- Other confidential or proprietary activities, strategies, processes or procedures.
- Refusals to deal with any company or supplier.
- Strategies or plans to award business or remove business from a specific company, to participate or not participate in any particular business opportunity or type of business opportunity.
- Status of negotiations with present or potential customers, suppliers, payers or healthcare clinicians.
- Any other confidential business information that could be used to reduce competition.

Meeting Logistics

- Attendees are encouraged to submit questions via Zoom or Slido and add comments in the chat if desired.
- In-person attendees may also raise their hand to ask questions directly
- All meeting materials for this workshop are available on the Duke-Margolis website

USE THIS QR CODE TO JOIN OUR SLIDO!

You can also go to Slido.com and use the code #4139881 to join

Agenda

10:00 am	Welcome and Opening Remarks
10:10 am	Background and Emerging Policy Solutions
10:25 am	Session 1: Identifying Opportunities for Generic Drug Repurposing
11:35 am	Break
11:50 am	Session 2: Regulatory Pathways for Non-Traditional Drug Developers
1:00 pm	Lunch Break
2:00 pm	Session 3: Updating Labels with Established Evidence & Encouraging Responsible Promotion
2:45 pm	Break
3:00 pm	Session 4: Additional Opportunities for Generic Drug Repurposing
3:50 pm	Closing Remarks and Adjournment

Background and Emerging Policy Solutions

Beth Boyer, *Duke-Margolis Institute for Health Policy*

Research Focus

Duke-Margolis aims to engage stakeholders on the role of drug repurposing to meet unmet patients' needs and to better understand the challenges and potential policy solutions for advancing drug repurposing efforts in the future.

Past Work on Drug Repurposing

Drug Repurposing for Pandemic Innovation *(2023)*

THE UNIVERSITY OF CHICAGO
MARKET SHAPING ACCELERATOR

Designing a pull mechanism for generic drug repurposing *(ongoing)*

Today's Focus

Generic Drug Repurposing: Exploring the Potential Role of the Regulator and Policy Solutions

Funded by Arnold Ventures

Aim: Take a deep dive on the **regulatory policy landscape** as it relates to generic drug repurposing and exploring the **potential role of FDA** in advancing research of new of uses of generic drugs **to meet patient needs**.

Defining 'generic drug repurposing'

There are many different terms used to describe finding new therapeutic uses for drugs and ways these terms are defined.

For purposes of this roundtable (and project), we define **drug repurposing** as:

The process of conducting research on new uses for established drugs on the market

We will also be focusing on repurposing **generic drugs,** which in this context we define as:

Drugs on the market for which the originator has lost exclusivity and other manufacturers may legally enter the market

Why generic drug repurposing?

1

Drug development is risky and expensive, costing as much as $2.8 billion.

Repurposed drugs have already demonstrated safety data and trials can start at later stages, increasing chances of success and reducing costs.

2

Drug development can take an average of 8-10 years.

Repurposed drugs can bypass early stages of development and therefore take less time to study and reach patients.

3

New, patented drugs can be expensive and may have delayed availability in some areas.

Repurposed generic drugs are often already widely available and less expensive.

https://www.sciencedirect.com/science/article/abs/pii/S0167629616000291?via%3Dihub; https://go.bio.org/rs/490-EHZ-999/images/ClinicalDevelopmentSuccessRates2011_2020.pdf; https://www.reuters.com/business/healthcare-pharmaceuticals/prices-new-us-drugs-rose-35-2023-more-than-previous-year-2024-02-23

Generic drug repurposing challenges

Lack of incentives for traditional drug developers to invest in research on new uses for generic drugs and/or sponsor label expansion:

- High costs of trials
- Low drug prices
- Limited profit margins

Limited resources and systematic efforts to identify repurposing candidates and conduct clinical trials to demonstrate efficacy for new use.

"**Non-traditional developers**" are more active in generic drug repurposing studies, however, may lack experience in navigating regulatory pathways and commercializing drug candidates.

Most generic drug repurposing studies are not intended to support label changes.

https://www.healthaffairs.org/doi/10.1377/hlthaff.2022.01083?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed
https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-022-08272-z#Sec1

Generic drug repurposing challenges

Lack of incentives for traditional drug developers to invest in research on new uses for generic drugs and/or sponsor label expansion:

- High costs of trials
- Low drug prices
- Limited profit margins

Limited resources and systematic efforts to identify repurposing candidates and conduct clinical trials to demonstrate efficacy for new use.

"**Non-traditional developers**" are more active in generic drug repurposing studies, however, may lack experience in navigating regulatory pathways and commercializing drug candidates.

Most generic drug repurposing studies are not intended to support label changes.

https://www.healthaffairs.org/doi/10.1377/hlthaff.2022.01083?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed
https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-022-08272-z#Sec1

Current Efforts in the U.S.

Identifying Repurposing Opportunities

CURE ID
Challenging cases... New approaches
at the FDA and NCATS/NIH

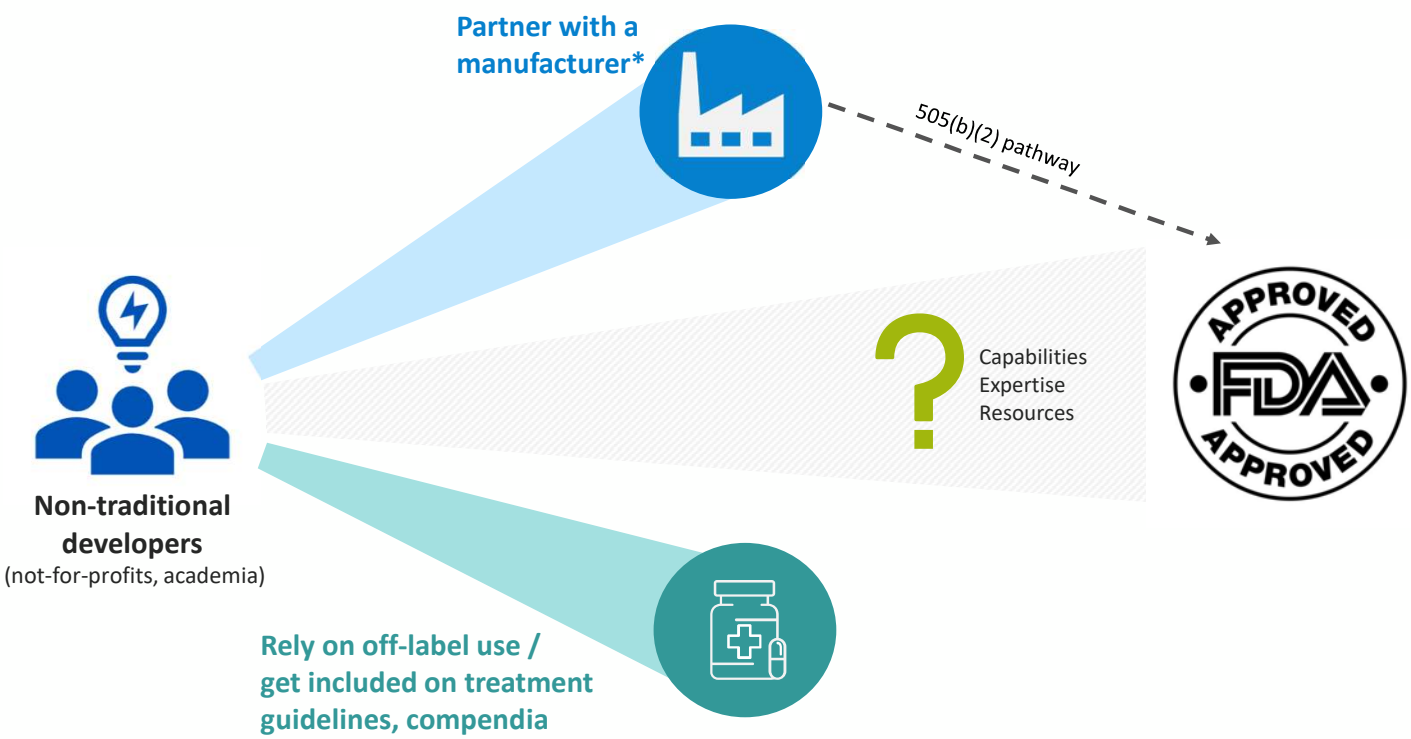
EVERY CURE

Updating Drug Labels

FDA

- Project Renewal
- Modern Labeling Act

The path for non-traditional developers to patient access



Non-traditional developers currently have two options when repurposing drugs for new indications.

Yet each option has its disadvantages or barriers.

What solutions might be considered to address the challenge for non-traditional developers to pursue label expansion for repurposed drugs?

*Companies may not be willing partner because of lack of financial incentives, resources required for regulatory approval, and liability concerns.

Duke | MARGOLIS INSTITUTE for Health Policy

Disadvantages of not pursuing label expansion

Despite the ubiquity of off-label use, it has several disadvantages:

- Lack of data generated on the drug's efficacy and safety for the off-label indication
- Uneven or slow uptake
- Reimbursement issues
- Limited awareness by providers and patients
- Patient concerns over using an unapproved therapy
- Supply issues (e.g., disruption or shortages from underestimated demand forecasting)
- Liability concerns from providers

https://www.medicinesforeurope.com/wp-content/uploads/2022/03/Advancing-medicines-repurposing-in-the-EU.pdf
https://www.scienceopen.com/document/read?vid=e0be8f6d-61e6-4f21-afb4-4beac8ad8611

International models to advance repurposing

STAMP Pilot

- Aims to **support not-for-profit organizations and academia** to gather and generate sufficient evidence on a new use of an established medicine to be formally authorized by a regulatory authority.
- EMA and national medicines agencies **provide regulatory support** to help generate a robust data package **to support application by a pharmaceutical company**

EU Pharmaceutical Reform Proposal

- Article 48: proposes a **pathway for a "not-for-profit entity" to submit data** to the agency for repurposing of products that **meet unmet medical need.**

Medicines Repurposing Programme

- **Identifies and progresses opportunities** to use existing medicines in new ways, outside of the current marketing authorization.
- **Prioritizes medicines** for the programme and **provides tailored support** including evidence generation, applying for a licence variation, and support for equitable patient access.
  - Open **competitive process** to select a marketing authorization holder to submit to MHRA
- Example: anastrozole for breast cancer prevention

EXPLORING POLICY SOLUTIONS

Areas of Exploration

- **Opportunities:** Exploring the potential role of the regulator in identifying possible repurposing opportunities

- **Approval:** Addressing challenges and disincentives that non-traditional drug developers may encounter in pursuing FDA approval for repurposed indications

- **Labeling:** Updating drug labels for new indications based on established evidence to encourage responsible promotion and ensure public health benefit of repurposed generic drugs

Generic Drug Repurposing: Regulatory Solutions Framework

Resources needed: Low → High

Building on Current Processes and Programs	New but Within Existing Authority	Legislative Action Needed
Programming – A program offering advice on research protocols and evidentiary needs to obtain regulatory approval/attract manufacturer partner (NCATS/FDA joint effort?), including workshops, individual meetings, and guidance documents	**Disease Prioritization -** Identification of priority uses cases or conditions for repurposing efforts for Federal efforts (i.e., within FDA, NCATS, NIH)	**Expand Modern Labeling Act-** Expand modern labeling act beyond withdrawn RDLs (criteria TBD; may be based on # of years since first ANDA); OR expand to allow nontraditional developers to compile and submit the data to FDA (reduce workload on FDA staff)
	User Fee Waivers - Waive user for repurposed drugs that meet or advance public health needs as defined by FDA (see above); if a pathway is created for nontraditional developers, user fee not to be required	**New Regulatory Pathways -** "Labeling only" 505(b)(2) pathways (Reboot Rx proposal) OR creation of other new pathway for nontraditional developers (similar to Article 48 in EU proposal)
Utilizing Modern Labeling Act – FDA can use authority provided to update labels of drugs with withdrawn RDLs based on existing data	**Sponsor Incentives –** Explore incentives for companies to partner with nontraditional developers on repurposing. This may include building on the "programming" solution to establish a program similar to the EU's STAMP Pilot.	**International Regulatory Reciprocity** – update labels based on evidence used for label expansion in other regulatory agencies (e.g., EMA, MHRA) for repurposed drugs that meet areas of unmet medical need
CURE ID Expansion - link CUREID with government funding partner to pull out promising candidates and prepare research protocols to meet regulatory standards (may include match making conferences)		**Addressing Liability Concerns -** Addressing liability concerns for pharmaceutical companies to share data or study new uses of generic drugs
Project Renewal Expansion – Expand Project Renewal to other disease areas where there is sufficient data and clear evidentiary targets (i.e., infectious diseases)	**Expand Federal Programming -** Expanding NCATS, NIA Alzheimer's Repurposing Program, or ARPA-H to establish a government-led repurposing initiative	**New Federal Initiative -** Create a new large-scale government initiative (e.g., BARDA) to advance drug repurposing for unmet medical need

- Opportunities
- Approval
- Labeling

Workshop Objective

The goal of this workshop is to **identify priority recommendations and opportunities** to address key regulatory challenges and help to unlock the full potential of generic drugs.

Session 1: Identifying Targets for Generic Drug Repurposing

Moderator: Beth Boyer, *Duke-Margolis Institute for Health Policy*

CURE ID

The Potential for the Regulator to Help Identify Generic Drug Repurposing Opportunities

Heather A. Stone, MPH
Email: heather.stone@fda.hhs.gov

Definition of Drug Repurposing

Drug repurposing is the identification of novel uses of existing* drugs.

Image Source: https://www.anticancerfund.org/en/drug-repurposing

*Drug repositioning is often used to refer to drugs that have made it through substantial development but have never been approved.

Why is Repurposing Important to FDA?

- There are many diseases that lack adequate approved treatment options
- De novo drug development has not satisfied these medical needs
- In these situations, drug repurposing is an important strategy to identify promising treatments

Examples include:

- Rare diseases which are hard to study and where the return on investment may be limited
- Infectious disease outbreaks where time for traditional drug development is lacking

Why we Developed the CURE ID Platform

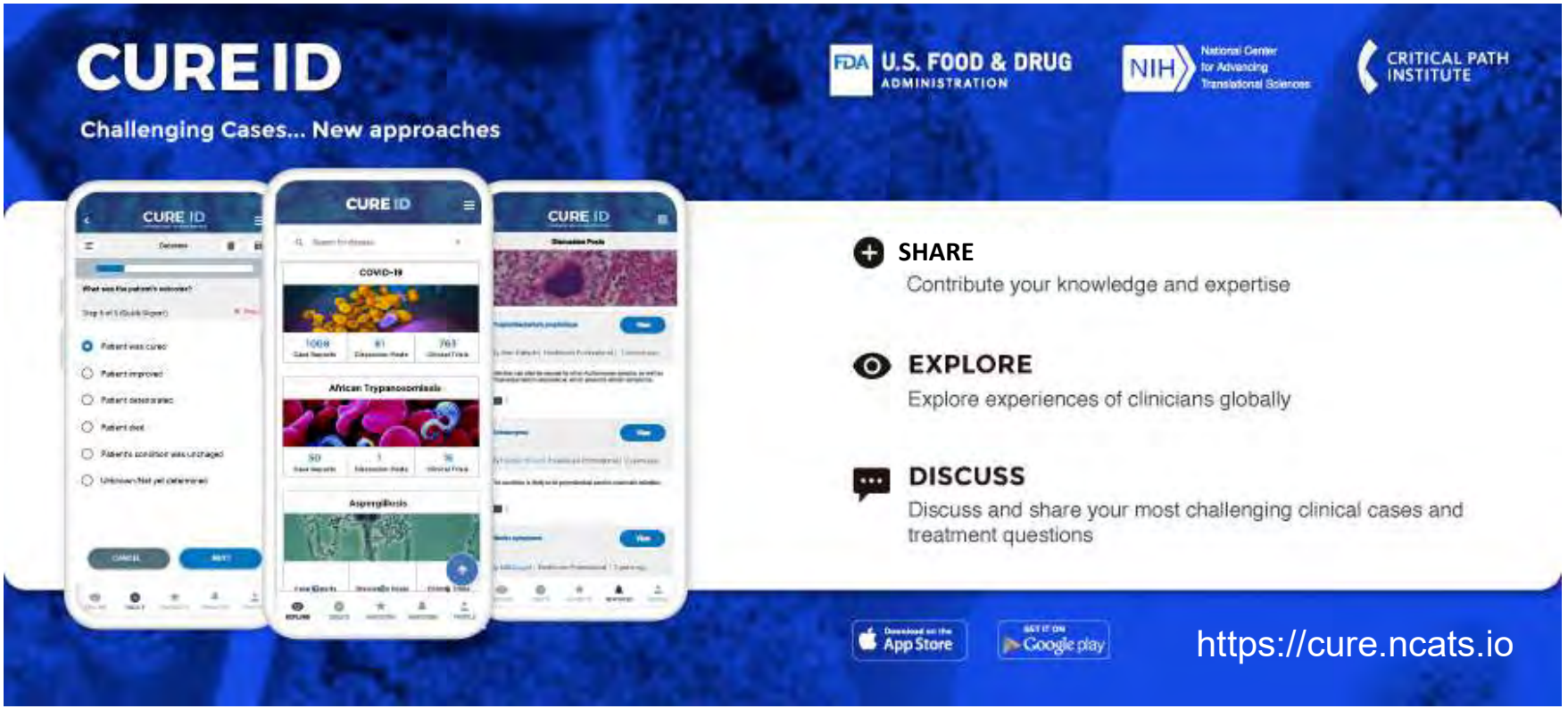
- Drug repurposing frequently begins in clinical practice through off-label use, when clinicians are faced with challenging diseases
- Their experiences are rarely captured
- We are unable to determine whether the drugs they use are effective, ineffective, or possibly harmful

What is CURE ID?

- A website and mobile app by FDA and NCATS/NIH designed to capture treatment experiences of healthcare providers and patients/care partners for diseases where we don't have good treatment options

- Serves as a treatment registry for FDA, NCATS, and the clinical community to review efficacy data when repurposed drugs are used for unmet medical needs

A Platform to Capture Novel Uses of Existing Drugs for Unmet Needs



Visit the website at: https://cure.ncats.io or download the “CURE ID” mobile app from the Apple App or Google Play Store

Strategy

- Crowd-sourcing **clinician** experience with repurposed drugs
- Crowd-sourcing **patient and caregiver** experience with repurposed drugs
- Automated extraction of drug repurposing data from **EHR**s

CURE ID Objectives

- To **identify signals** of potentially safe and effective treatments
- To **identify promising drugs** for further study
- To provide physicians and patients **information** where no FDA-approved drugs are available

What CURE ID Offers

- Provides healthcare providers and patients/care partners with a mechanism to rapidly share their treatment experiences with the global clinical community
- Collects the data in a manner that enables it to be immediately aggregated
- Makes the data openly accessible to all for free
- All cases are reviewed before public posting

Example of a Case Reported in CURE ID

Disease: Balamuthia

Organism: Balamuthia mandrillaris

Syndrome: Granulomatous Amoebic Encephalitis

Patient Characteristics:

Age: 51-60 years old

Sex: Male

Country: United States

Race: White

Ethnicity: Not Hispanic/Latino

Clinical Presentation:

Site of Disease: Brain

Method of Diagnosis:

- ☑ Clinical Assessment
- ☑ Imaging
- ☑ Molecular Diagnosis/PCR
- ☑ Pathology/Histopathology
- ☑ Culture
- ☑ Serology
- ❑ Unknown
- ❑ Other: _____

Challenge:

- ☑ There is no standard/approved therapy for this disease
- ❑ Standard therapy was contraindicated in this patient
- ☑ Patient experienced drug toxicity or AEs on prior therapy
- ☑ Patient failed previous therapy
- ❑ Organism was resistant
- ❑ Unusual disease presentation
- ☑ Patient did not complete prior therapy or was non-compliant
- ❑ Therapeutic options were inadequate

Treatment Setting: Inpatient (hospitalization)

Repurposed Drugs:

☑ **Nitroxoline (Primary drug added to failing regimen)**
250 mg, 3 times a day (TID), Oral (PO), 260 days

Concomitant Drugs:

Miltefosine - 50 mg, 3 times a day (TID), Oral (PO), 365 days
Azithromycin - 500 mg, Daily (QD), Oral (PO), 365 days
Albendazole - 400 mg, Daily (QD), Oral (PO), 365 days
Fluconazole - 12 mg/kg, Daily (QD), Oral, 365 days
Flucytosine - 37.5 mg/kg, 4 times a day (QID), Oral (PO), 340 days; AE: Decreased absolute neutrophil count

Method of Outcome Determination:

- ☑ Clinical Assessment
- ☑ Imaging
- ❑ Molecular Diagnosis/PCR
- ❑ Unknown
- ❑ Other: _____

Treatment Outcome:

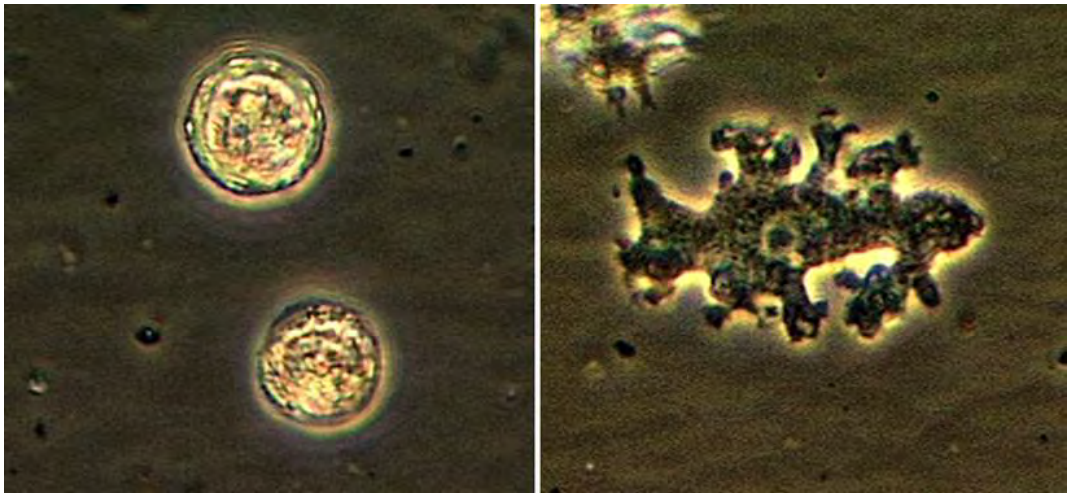
- ❑ Patient was cured/recovered
- ☑ Patient improved (Partial response)
- ❑ Patient's condition was unchanged
- ❑ Patient deteriorated
- ❑ Patient died
- ❑ Treatment was terminated due to adverse events
- ❑ Outcome is unknown/Not yet determined/Lost to follow-up

Recent Generic Drug Repurposing Experiences Reported in CURE ID

Nitroxoline in the treatment of *Balamuthia mandrillaris* causing Granulomatous Amoebic Encephalitis

What is *Balamuthia*?

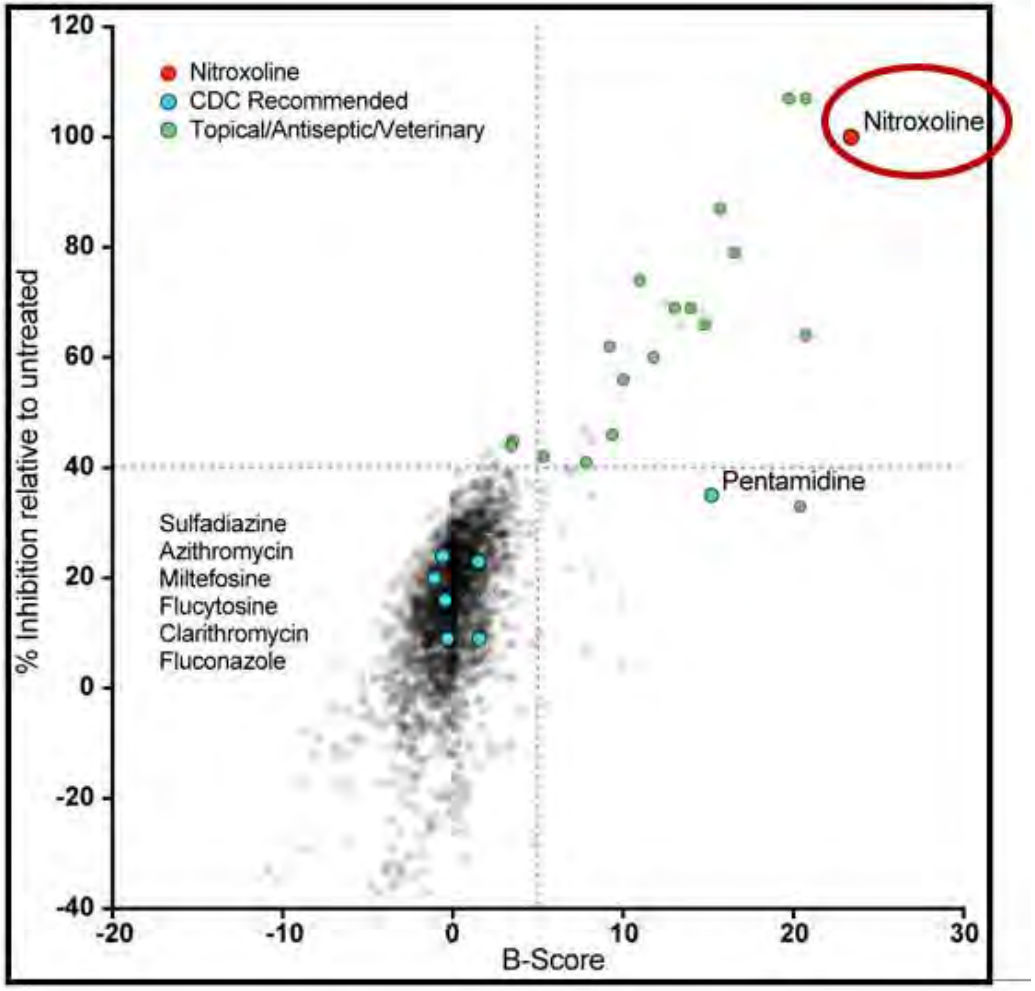
- *Environmental amoeba*
- Causes severe meningitis and encephalitis
- Fatality rate 75-90%
- No effective treatment



Source: https://www.cdc.gov/parasites/balamuthia/index.html

Adaptation of Slides on Background and First Balamuthia case courtesy of Dr. Natasha Spottiswoode, UCSF

High-Throughput Screen Identifies Nitroxoline



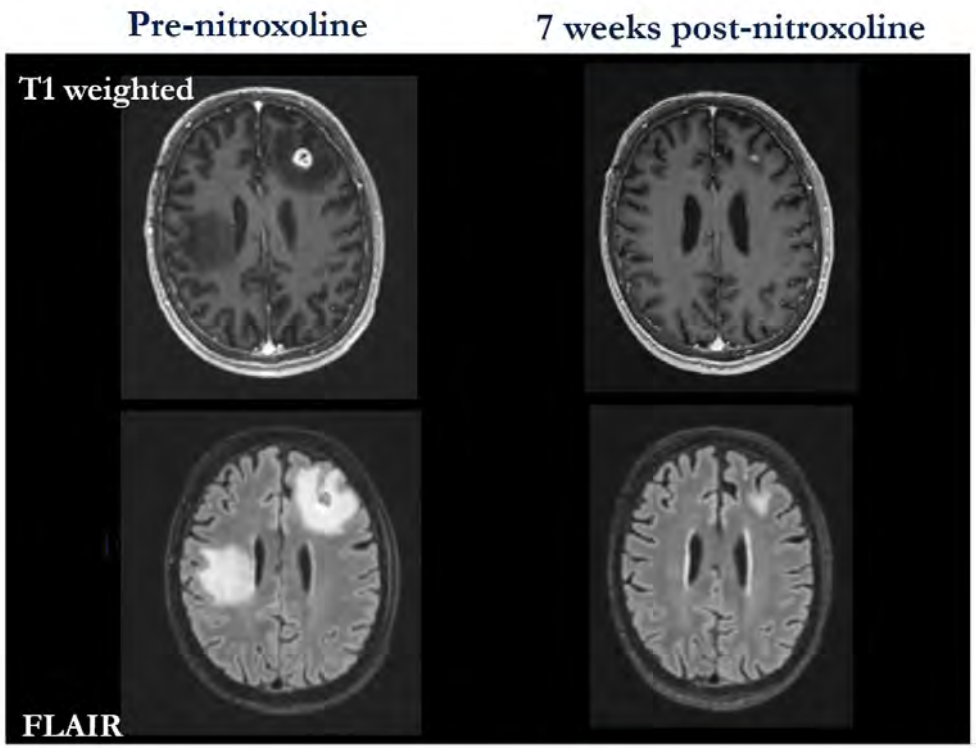
Laurie MT, White CV, Retallack H, Wu W, Moser MS, Sakanari JA, Ang K, Wilson C, Arkin MR, DeRisi JL. Functional Assessment of 2,177 U.S. and International Drugs Identifies the Quinoline Nitroxoline as a Potent Amoebicidal Agent against the Pathogen *Balamuthia mandrillaris*. mBio. 2018 Oct 30;9(5):e02051-18. doi: 10.1128/mBio.02051-18. PMID: 30377287; PMCID: PMC6212833.

Case 1: Repurposing for *Balamuthia* – First Treated Case with Nitroxoline

- Patient with Balamuthia was on a failing regimen
- His clinician found HTPS paper on nitroxoline
- Obtained emergency IND
- Patient was treated with nitroxoline and showed remarkable clinical and radiological improvement
- Patient was discharged alive

Spottiswoode N, Pet D, Kim A, Gruenberg K, Shah M, Ramachandran A, Laurie MT, Zia M, Fouassier C, Boutros CL, Lu R, Zhang Y, Servellita V, Bollen A, Chiu CY, Wilson MR, Valdivia L, DeRisi JL. Successful Treatment of Balamuthia mandrillaris Granulomatous Amebic Encephalitis with Nitroxoline. Emerg Infect Dis. 2023 Jan;29(1):197-201. doi: 10.3201/eid2901.221531. PMID: 36573629; PMCID: PMC9796214.

Pre- and post-nitroxoline MRIs



MRI progression

- Marked improvement on nitroxoline **in addition to** prior drugs, in the previously failing regimen
- Next MRI (17 weeks post nitroxoline) with continued improvement

See the case in CURE ID: https://cure.ncats.io/explore/cases/case-details/d98b5ec2-cb6a-49df-ba3d-09136ba48d02

Case 2: A little girl with *Balamuthia* is dying on the standard of care/CDC regimen…

Acknowledged in Dr. Spottiswoode's article; contacted by little girl's family

→

Helps clinician get eIND for the child

Photos used with permission of child's mother

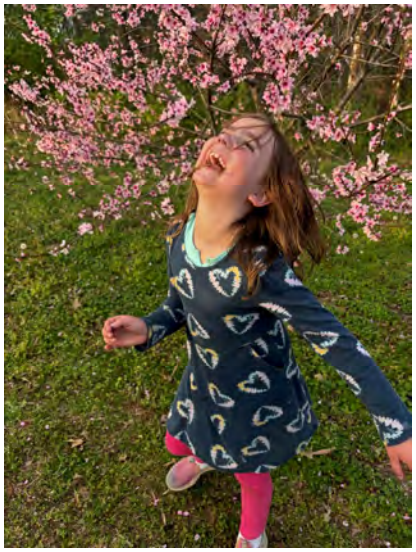
Connects clinician to Dr. Spottiswoode at UCSF, who supplies the drug, since Aseiris is unable to get it to the patient quickly enough from China

←

Child is improving, clinically and via MRI, is stable, and has been able to come off other toxic drugs that were severely impacting her QoL; Mother has inputted case into CURE ID

←

Heather Stone guided emergency authorization.



The little girl celebrated her 9th birthday in April 2025 and is doing great. Follow-up MRIs have looked good and all the medications, including nitroxoline have been stopped.

See the case in CURE ID - https://cure.ncats.io/explore/cases/case-details/9845598a-bca0-432c-87dd-c46bcdc4dcaa

CDC is now recommending nitroxoline for Balamuthia, based on these 2 patients who were successfully treated, and it is being examined for other amoebic infections. A third patient received the drug in the US, but sadly did not survive. Experience outside of the US has been more mixed and harder to assess, given delays in access.

Lessons from the experience with *Balamuthia*

- The process of translating pre-clinical findings to the clinic can be challenging and lengthy, especially for rare and rapidly fatal diseases, like *Balamuthia.*
- In such settings, case reports are important tools to identify potentially effective treatments
- Sharing data openly and freely is critical and may allow for more rapid dissemination of treatment experience, as well as interim results.
- Building and maintaining connections with all impacted parties is necessary to stimulate engagement with CURE ID.
- However, more is needed… not enough people are sharing their treatment experiences on CURE ID for it to reach its full potential.

Drug Repurposing and FDA

- FDA's website states:
  - "The Food and Drug Administration is responsible for protecting the public health by **ensuring the safety, efficacy**, and security **of human** and veterinary **drugs**, biological products, and medical devices…"
  - "**FDA is responsible** for advancing the public health by **helping to speed innovations that make medical products more effective**, safer, and more affordable **and by helping the public get the accurate, science-based information they need to use medical products** and foods to maintain and improve their health."

Emphasis added. Source: https://www.fda.gov/about-fda/what-we-do#:~:text=FDA%20is%20responsible%20for%20advancing,maintain%20and%20improve%20their%20health

- A drug repurposing program for unmet medical needs is a valuable strategy to achieve these goals.

What might the role of the regulator be in identifying potential repurposing opportunities?

- FDA's has extensive experience monitoring the **safety** of marketed drugs (Sentinel, FAERS, Medwatch)

- Modern IT developments have given us a new ability to look at the **efficacy** of post-marketed drugs
  - CURE ID is an example of an electronic tool that can be used to identify promising repurposed drugs

Challenges Moving Ahead

- How to encourage submission of cases to the CURE ID platform?
- How to support the study of candidate generic drugs in RCTs and robust observational studies?
- How to support non-traditional drug developers lacking the wherewithal to prepare an NDA for a repurposed generic drug?

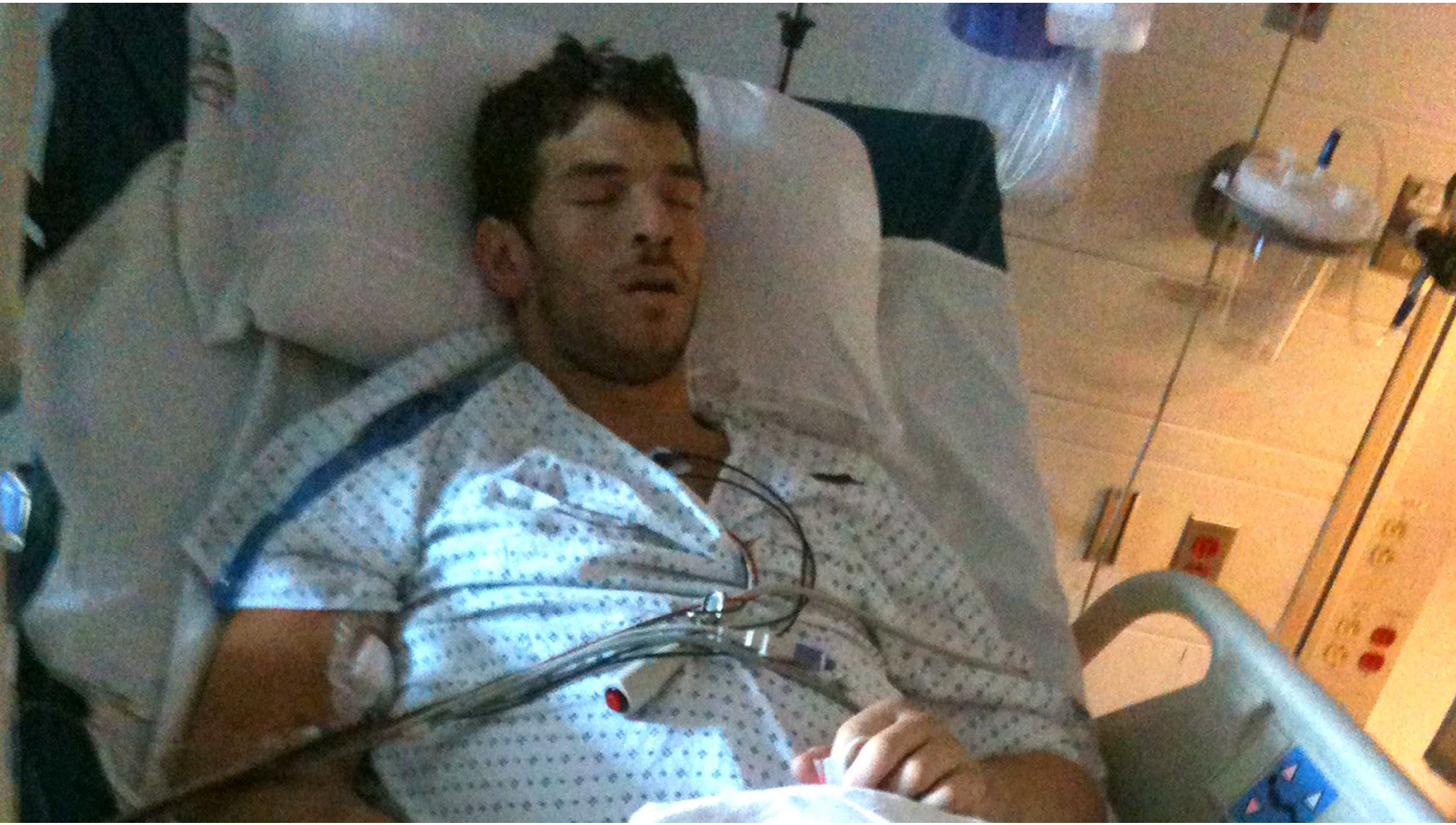

FDA
U.S. FOOD & DRUG
ADMINISTRATION

From ‘Chasing My Cure’ to ‘Every Cure’

David Fajgenbaum, MD, MBA, MSc
Founding Director, Center for Cytokine Storm Treatment & Laboratory, University of Pennsylvania
Co-Founder & President, Every Cure
Co-Founder & President, Castleman Disease Collaborative Network

May 29, 2025

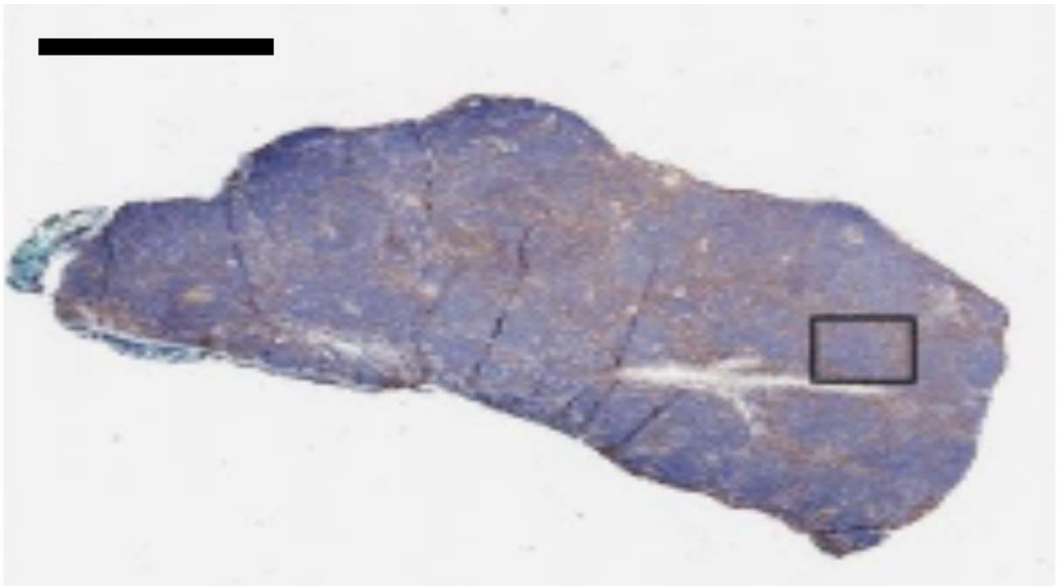
4,000 medicines are approved for 4,000 diseases, but 14,500+ diseases don't have a single approved therapy

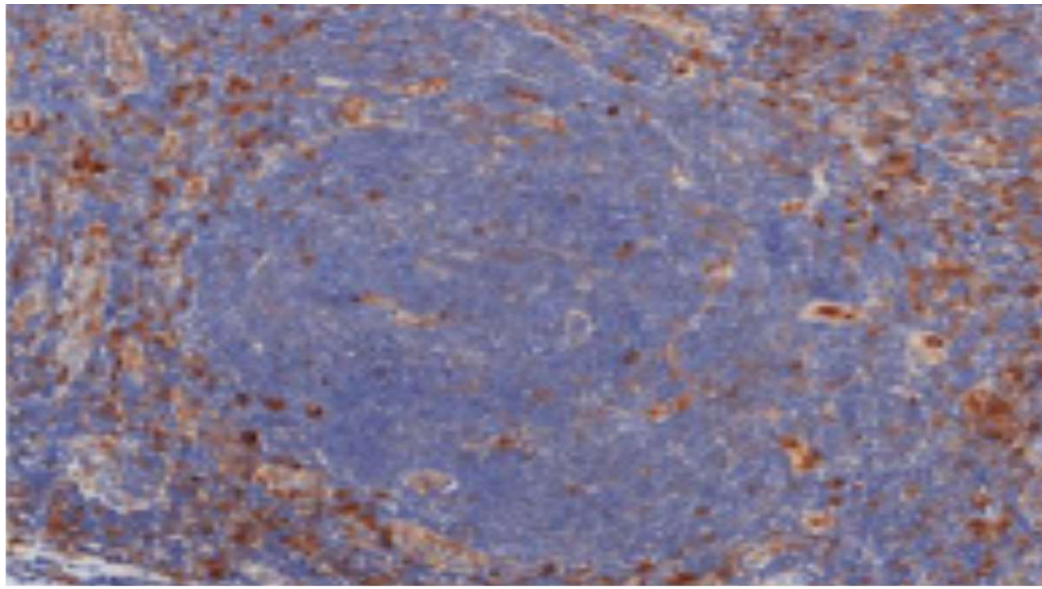


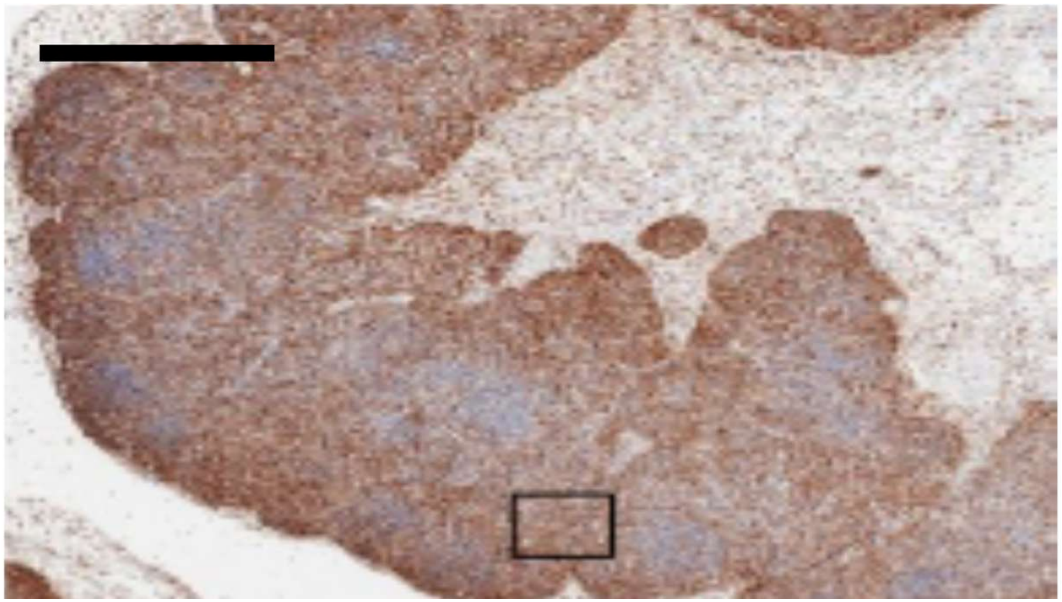

VIAGRA
100 mg film-coated tablets
Sildenafil
Pfizer
4 film-coated tablets
Thalidomide Celgene™ 50 mg
gélules
Thalidomide
28 gélules
Voie orale
Chaque gélule contient 50 mg de thalidomide.
Contient aussi du lactose. Pour plus d'informations, voir la notice.
MISE EN GARDE : Thalidomide entraîne des anomalies congénitales et la mort du fœtus.
Il est impératif de suivre le programme de prévention de la grossesse Thalidomide Celgene.
Celgene

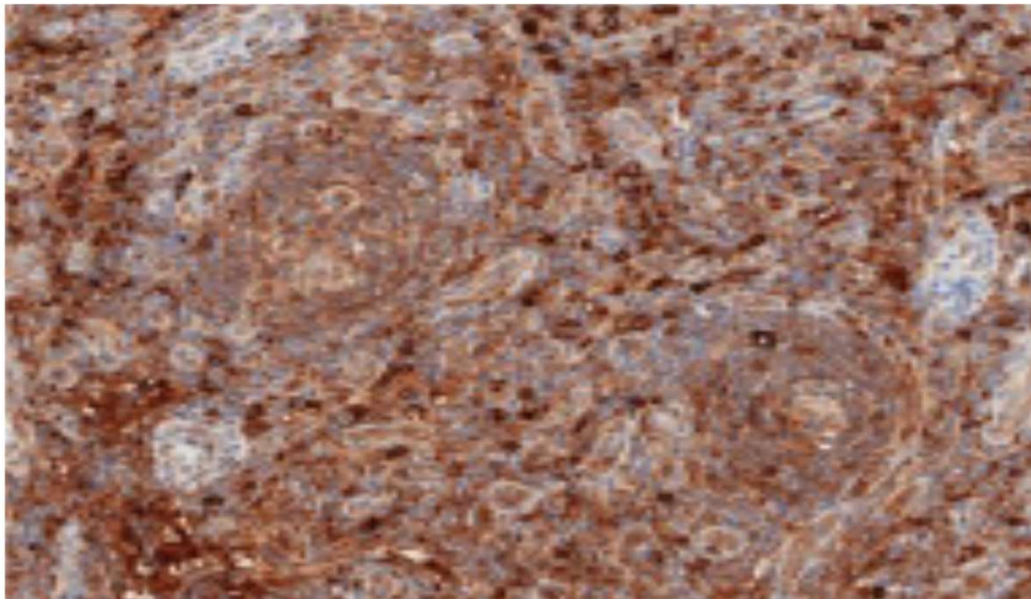
CDCN

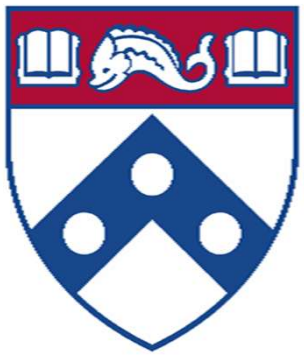
CASTLEMAN DISEASE COLLABORATIVE NETWORK











CSTL

Center *for* Cytokine Storm
Treatment & Laboratory

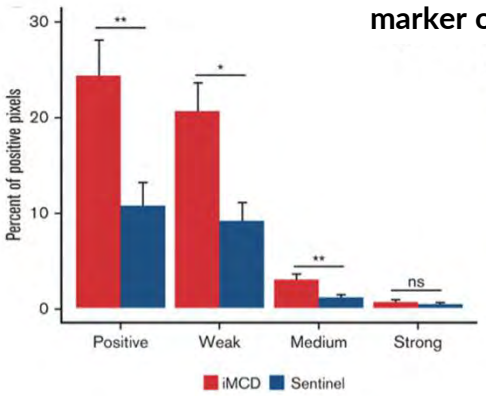

Hill-Rom

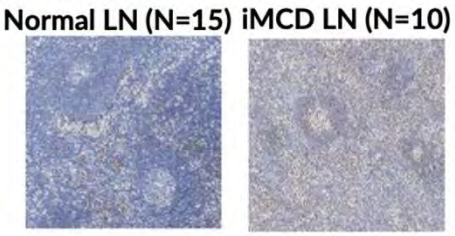
Ruxolitinib identified for iMCD by uncovering mechanistic insights

Table 1. Hallmark pathways significantly enriched in the discovery dataset among cluster 1 anti–IL-6 responders and in all siltuximab nonresponders

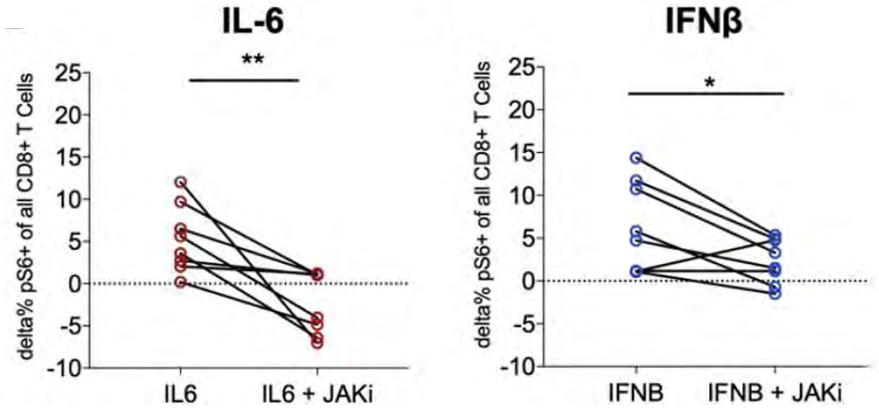
Pathway	Nominal *P* value	FDR q value
Enriched pathways in cluster 1 siltuximab responders vs HDs		
TNFα signaling via NF-κB	.004	0.090
Estrogen response early	.013	0.137
IFN-γ response	.033	0.149
Allograft rejection signature	.033	0.167
IL-6-JAK STAT3 signaling	.020	0.184
Enriched pathways in siltuximab nonresponders vs HDs		
KRAS signaling up	.029	0.118
IL-6-JAK STAT3 signaling	.031	0.144
TNFα signaling via NF-κB	.006	0.173
Allograft rejection signature	.043	0.177
IL2 STAT5 signaling	.018	0.179

Immunohistochemistry for pSTAT3, a marker of JAK1/2 activation





pFlow reveals JAK1/2 inhibition abrogates excess signaling

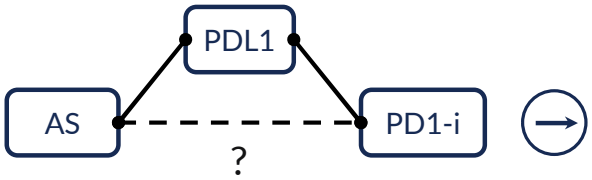


Pierson & Fajgenbaum. Blood Adv, 2020.
Pai & Fajgenbaum, JCI Insight, 2020.

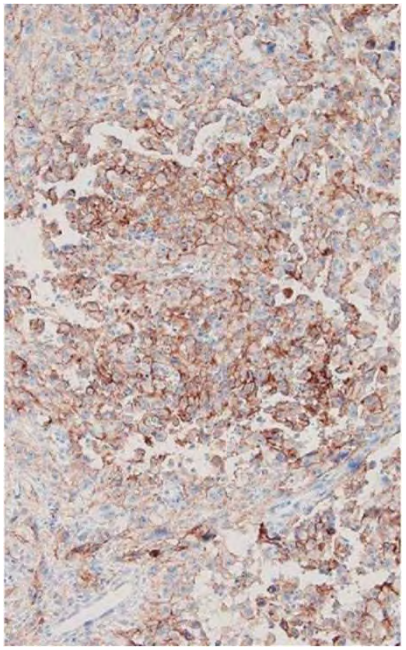

MARQUETTE
UNIVERSITY


LOVE

Treatment identified for AS by uncovering published link



2013 paper links PD1/PDL1 and angiosarcoma (AS)



Testing **confirmed increased PDL1** in 2016

First AS patient treated with PD1 inhibitor in **remission >9 years, many more benefitting**

Recommended by NCCN and widely used off-label worldwide

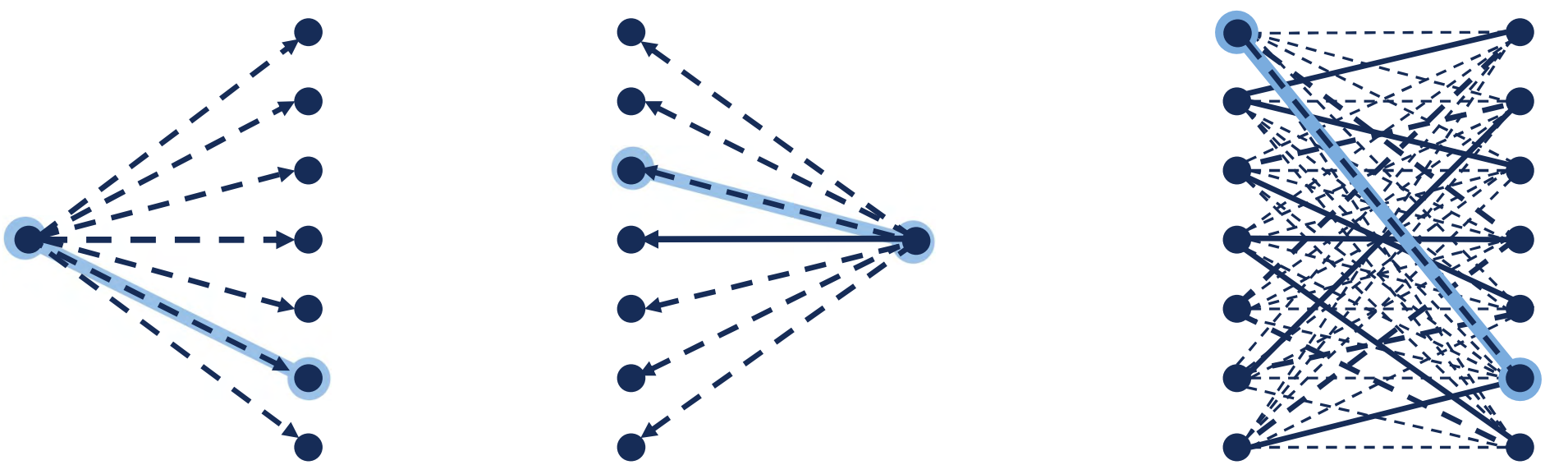
Kim et al. PLOS ONE. 2013.


ALL-DAY
EATERY
COFFEE
& DELI

Unleashing the potential of *every* approved medicine to **treat *every* disease** and ***every*** **patient possible**

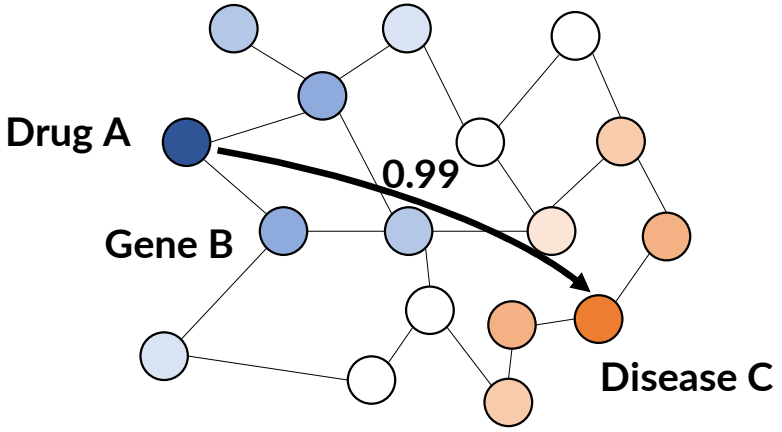
Advancing a new field of computational pharmaco-phenomics

Traditional Drug Repurposing + **Drug Repurposing: Indication Expansion** = **Computational Pharmacophenomics**

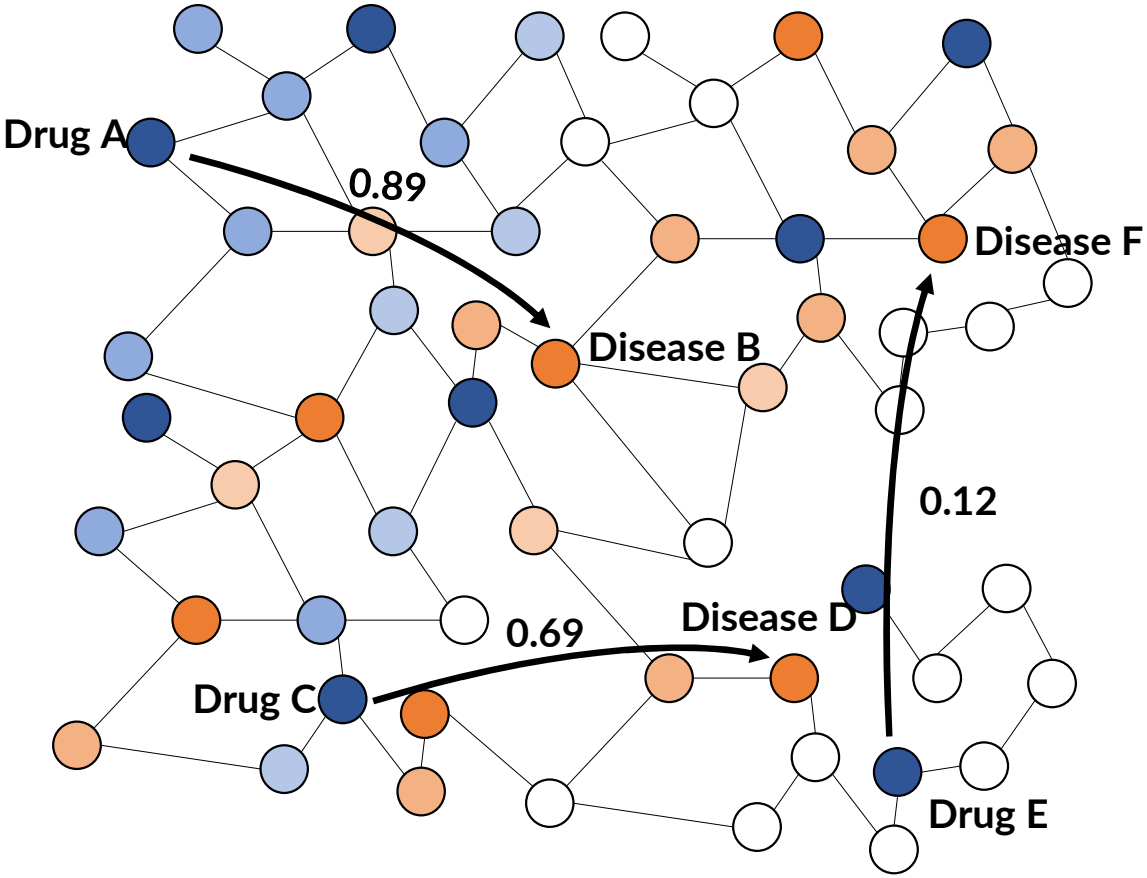


Fajgenbaum, et al. Lancet Haem, 2025.

We train on **known** treats relationships:

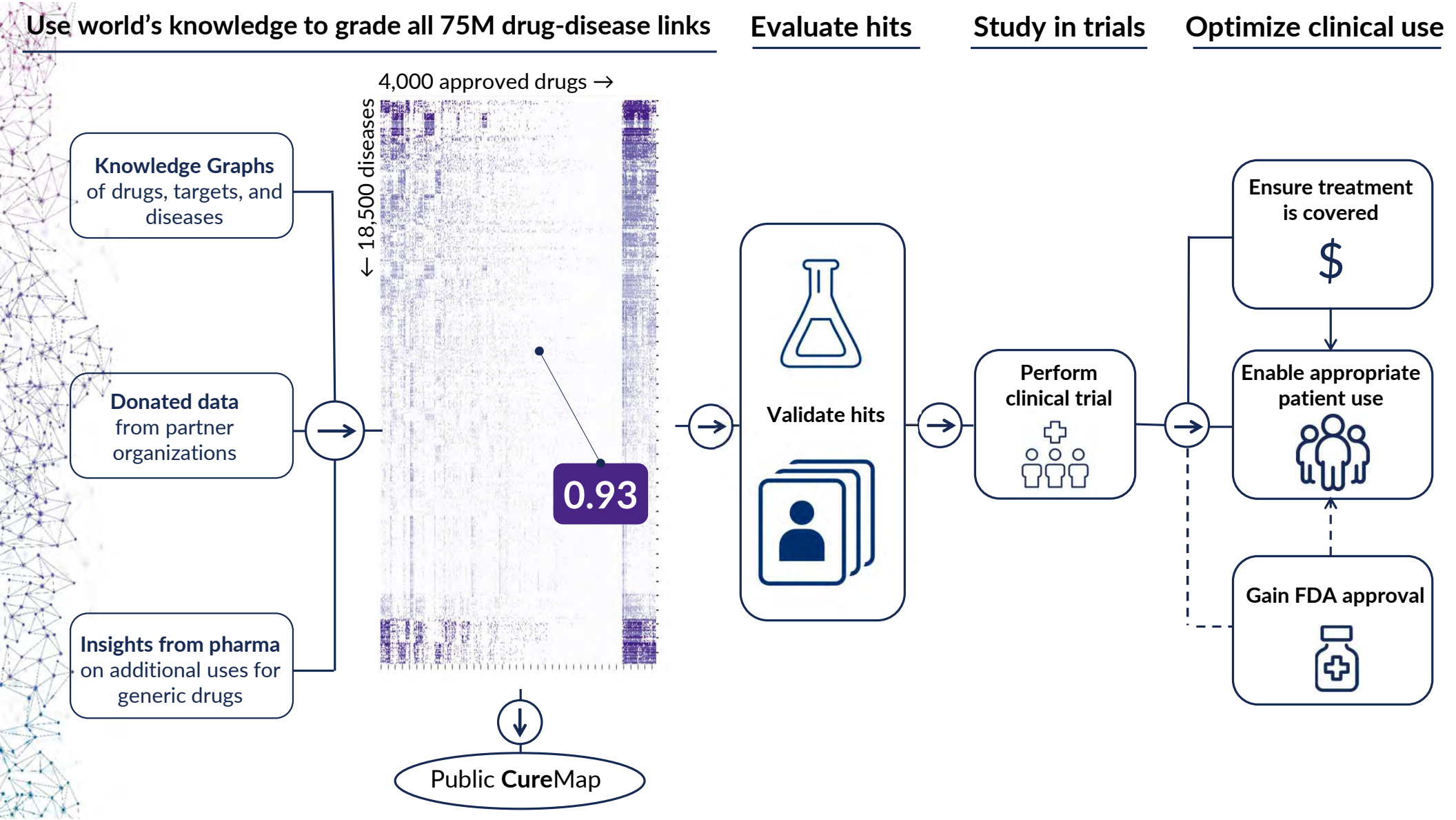


We unleash the algorithm on **unknown** relationships:



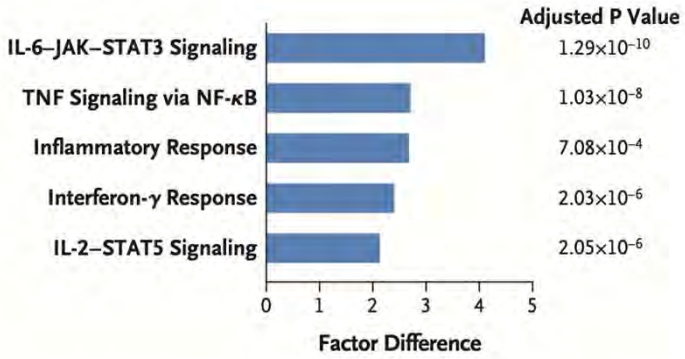
Scripps Research · monarch INITIATIVE · Penn State · UAB HUGH KAUL PRECISION MEDICINE INSTITUTE · UCSF University of California San Francisco · ISB Science Transforming Health · UNC · EVERY CURE

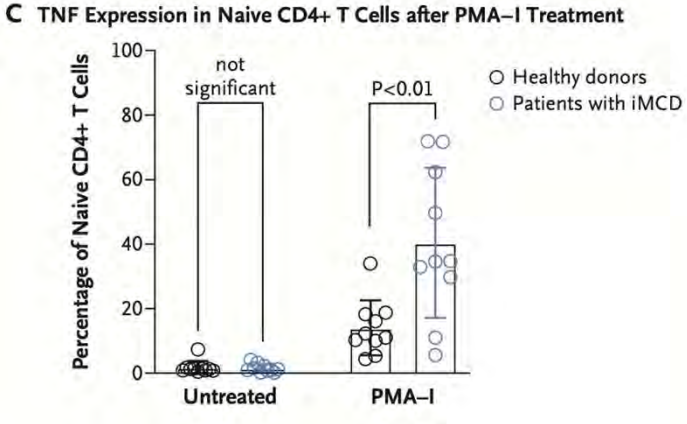
Ma, et al. GigaScience, 2023.

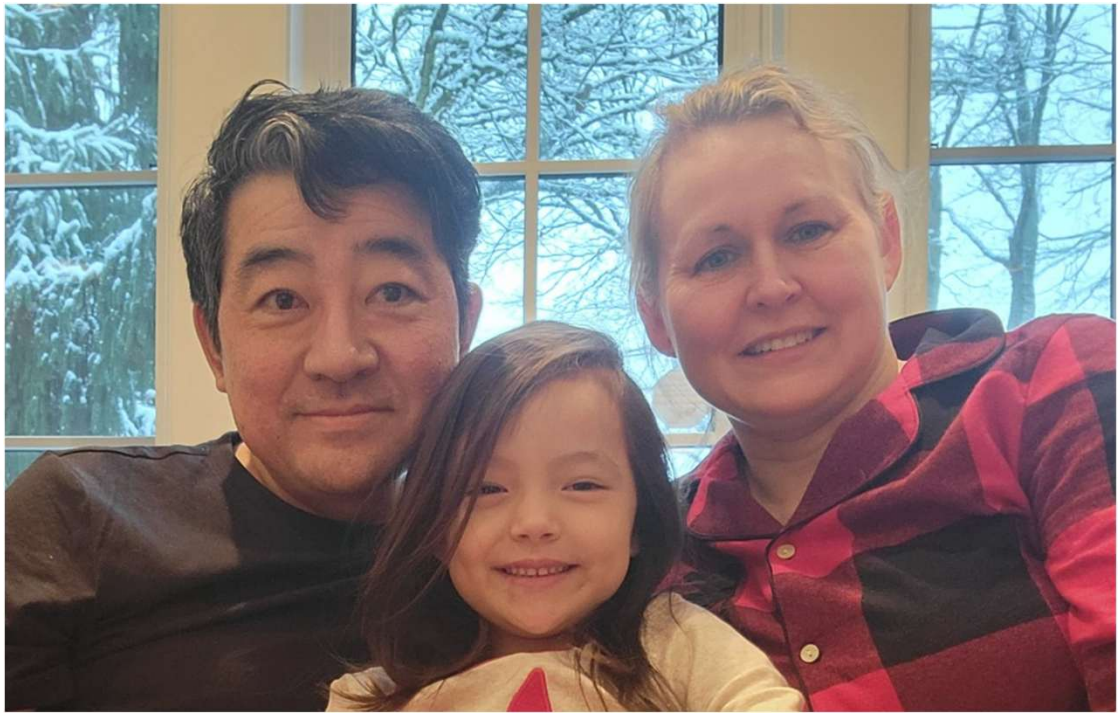

Use world's knowledge to grade all 75M drug-disease links
Evaluate hits
Study in trials
Optimize clinical use
4,000 approved drugs →
← 18,500 diseases
Knowledge Graphs of drugs, targets, and diseases
Donated data from partner organizations
Insights from pharma on additional uses for generic drugs
0.93
Public CureMap
Validate hits
Perform clinical trial
Ensure treatment is covered
$
Enable appropriate patient use
Gain FDA approval

The NEW ENGLAND JOURNAL of MEDICINE

Identifying and Targeting TNF Signaling in Idiopathic Multicentric Castleman's Disease

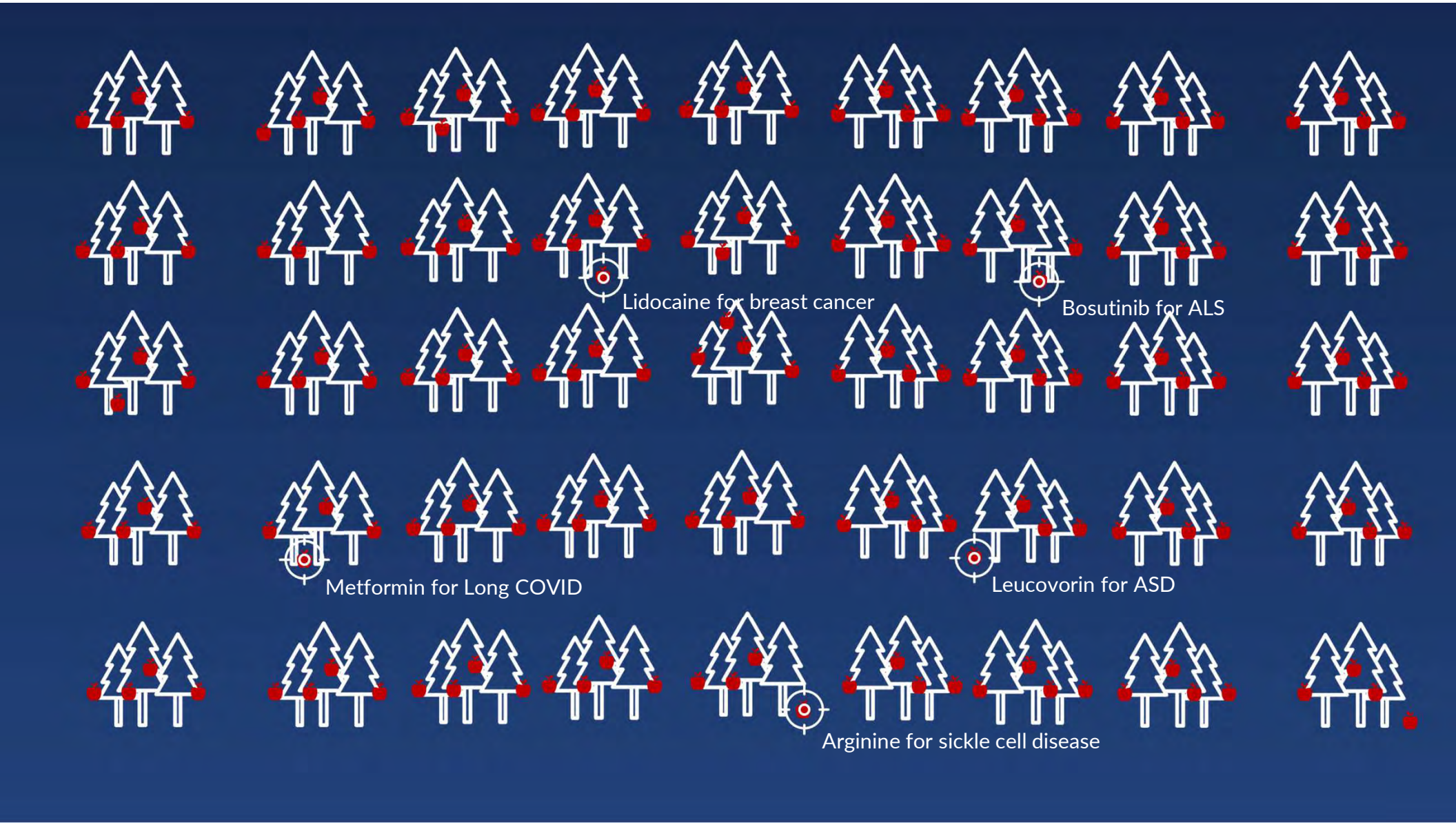






Mumau, …, & Fajgenbaum. NEJM, 2025.

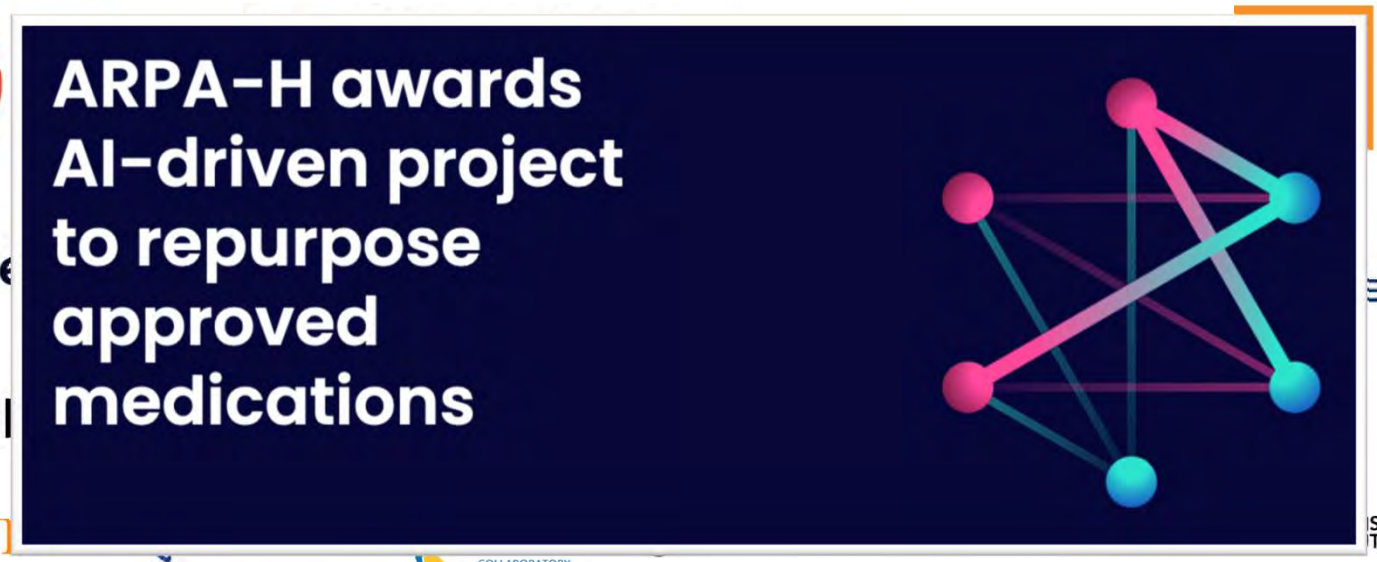

Santa
MAIL
PEACE
love &


Lidocaine for breast cancer
Bosutinib for ALS
Metformin for Long COVID
Leucovorin for ASD
Arginine for sickle cell disease

Our partners and key relationships in saving lives

EVERY CURE

Partners



LYDA HILL PHILANTHROPIES

aws

WORLDWIDE CLINICAL TRIALS

PennState

Key relationships

BROAD INSTITUTE

THE AUDACIOUS PROJECT

MILKEN INSTITUTE FasterCures

FDA

Kluwer

We need your help to unlock more uses for existing FDA-approved medicines

- Share drug repurposing ideas with us at everycure.org/ideas
- Volunteer to provide expertise at everycure.org/experts
- Help with obtaining key datasets from life sciences and data science companies
- Support the development of cutting-edge AI/ML algorithms
- Support Every Cure with evaluating top hits in studies and clinical trials (CROs, etc)
- Spread the word about treatments we're advancing
- Join our team or help with identifying amazing individuals for key roles (e.g., VP of Clin Dev)

davidfa@upenn.edu

Thank you!

CSTL/CDCN

Josh Brandstadter (Assoc Director, Clinical Research)
Michael Gonzalez (Assoc Director, Computational Res)
Melanie Mumau (Assoc Director, Translational Res)
Joe Zinsky (SRI)
Amber Cohen (Exec Admin)
Payton Morrissey (Exec Asst)
Bridget Austin (Biobank Coordinator)
Larissa Borys (Research Coordinator)
Criswell Lavery (Research Coordinator)
Mateo Sarmiento (Data Analyst)
Sai Shyamsundar (Data Analyst)
Abiola Irvine (Research Specialist)
Sally Nijim (MD student)
Mary Zuccato (CDCN Executive Director)
CDCN Board, Advisory Council, & SAB
Mentors: Dan Rader, Arthur Rubenstein

Partners/Funders:

NIH National Heart, Lung, and Blood Institute
CZI
CLINTON GLOBAL INITIATIVE
medidata
EUSA Pharma
PICI Parker Institute for Cancer Immunotherapy
FDA
Google Health
WORLDWIDE CLINICAL TRIALS

Every Cure

Grant Mitchell, MD, MBA; Co-Founder
Tracey Sikora, Co-Founder
Mary Zuccato, MBA; COO
Adam Green, MS; COS
Matej Macak, PhD
Daniel Korn, PhD
Charlie Hempstead, MBA
Chunyu Ma, PhD
Pascal Brokmeier, PhD
Sally Nijim
Vanessa Rostick
Jamie Babin
Brent Shaw

Tanisha Carino, PhD, Board of Directors
Bob Battista, Board of Directors
Tania Simoncelli, MS, Board of Directors
Eric Horvitz, MD, PhD, Board of Directors
Sec Bob McDonald, Board of Directors
Freda Lewis-Hall, Board of Directors
Janet Woodcock, MD, Board of Directors

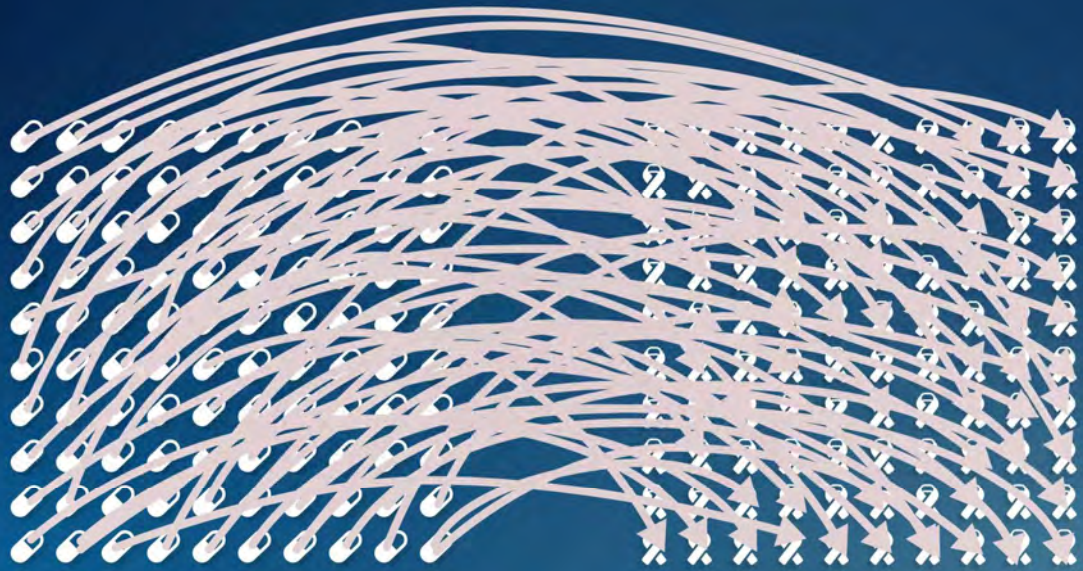
MATRIX Subcontractors:
Pennsylvania State University (Koslicki)
Scripps Research Institute (Su)
RENCI (Tropsha/Bizon)
UAB Precision Medicine Institute (Might)
Institute for Systems Biology
Monarch Initiative (Haendel)

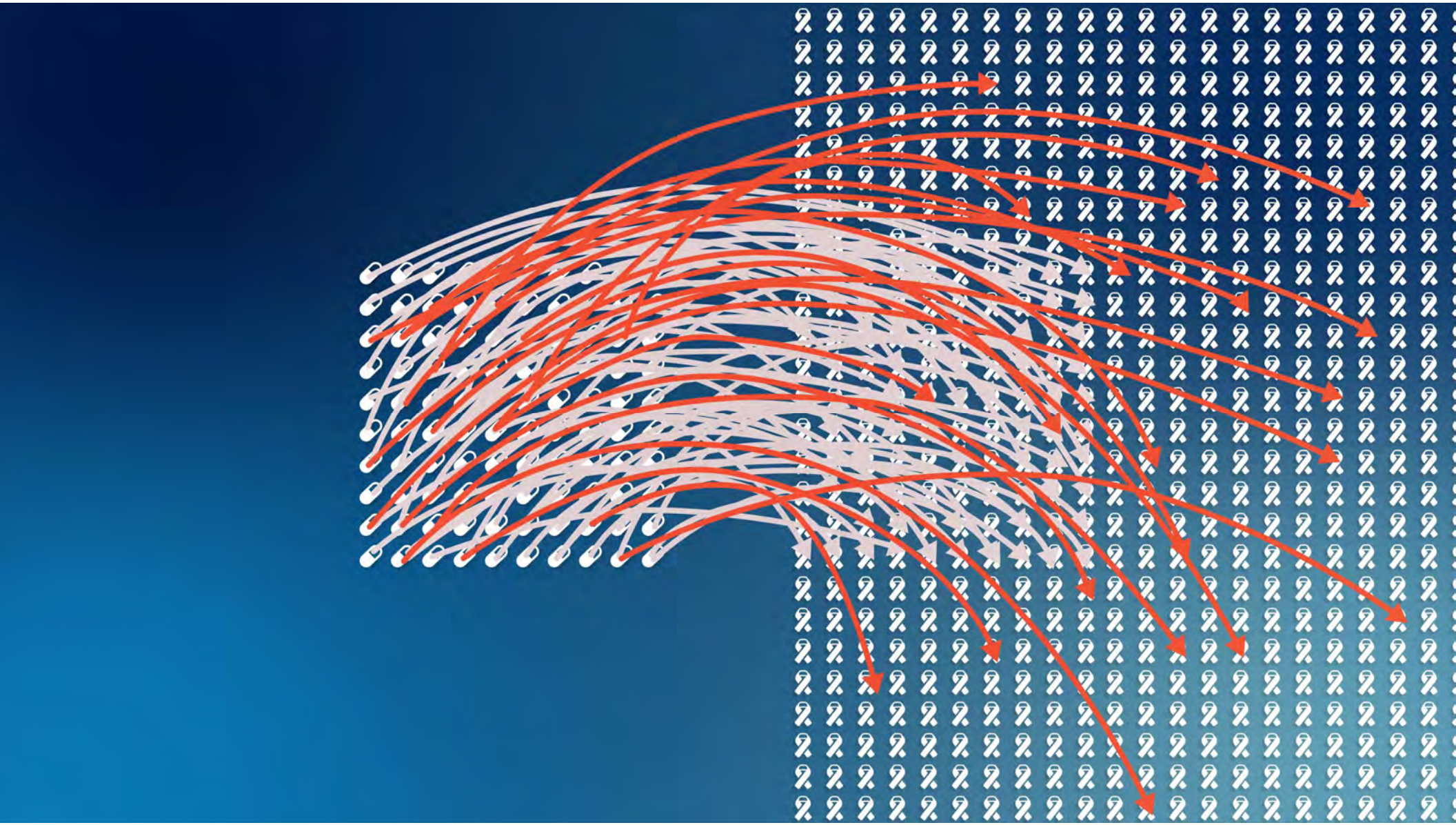
Funders

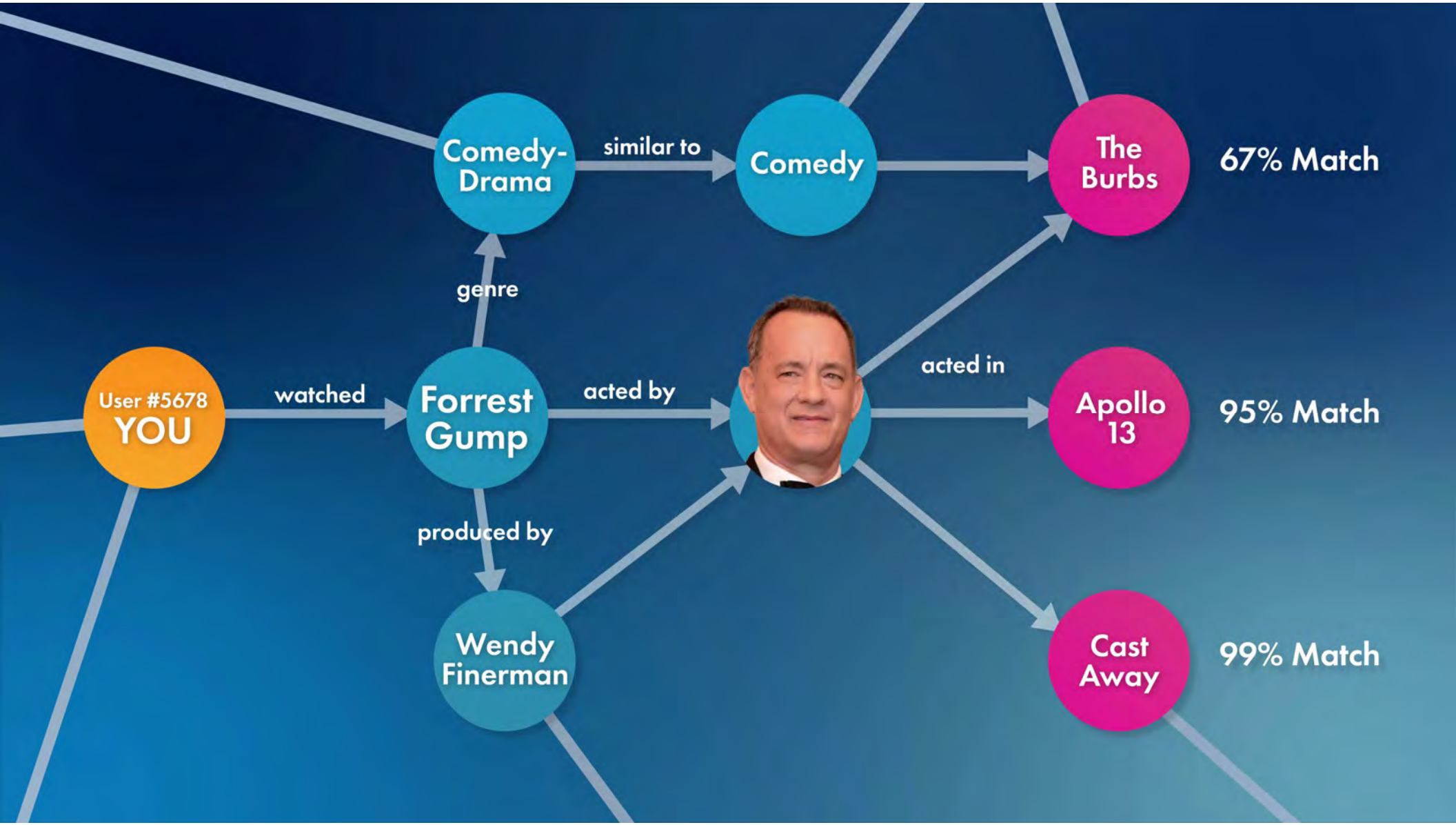
CHAN ZUCKERBERG INITIATIVE
LYDA HILL PHILANTHROPIES
ELEVATE PRIZE
Flagship Pioneering
THE CAROLYN SMITH FOUNDATION
SILC

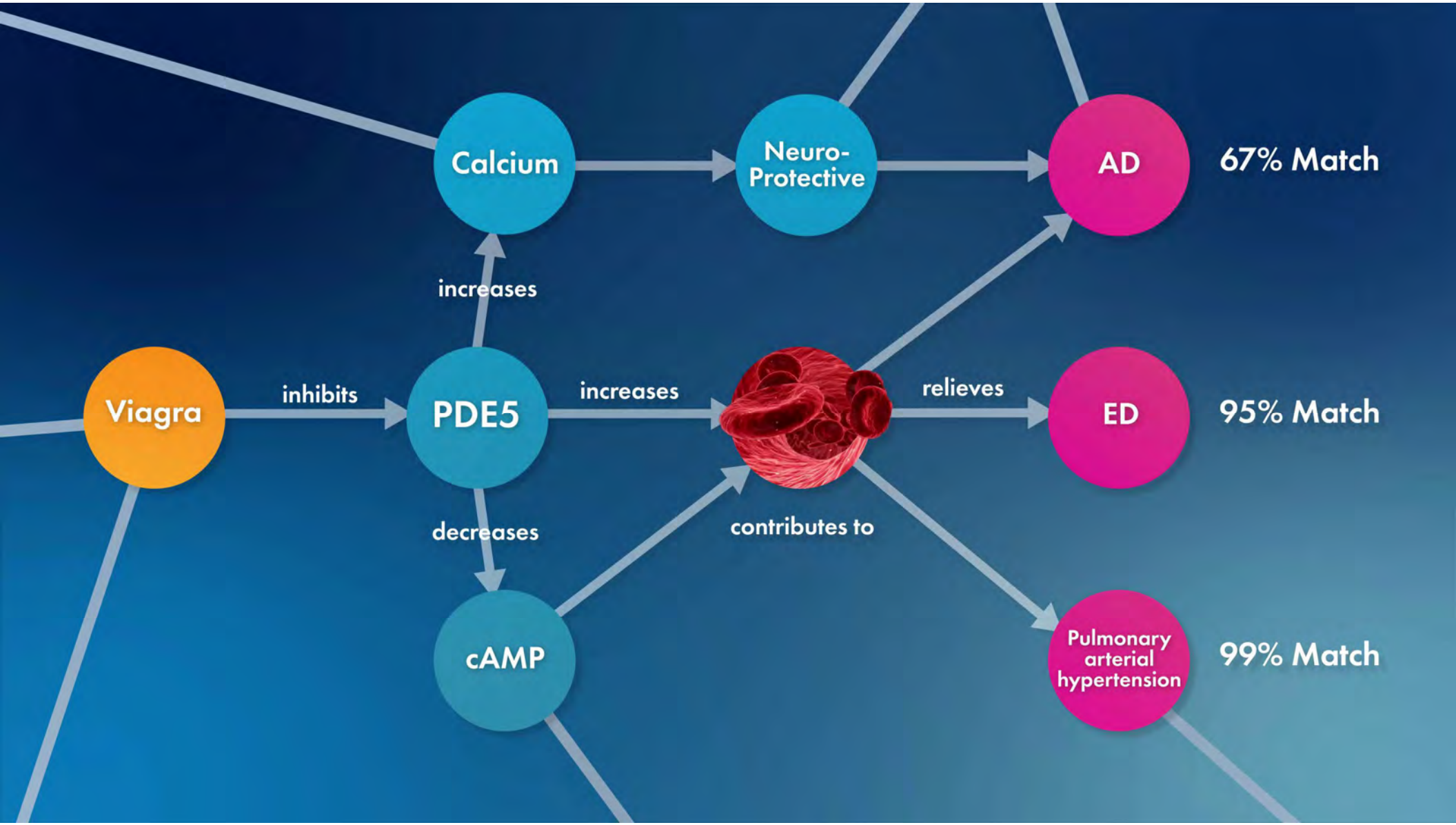
ChasingMyCure.com
@DavidFajgenbaum

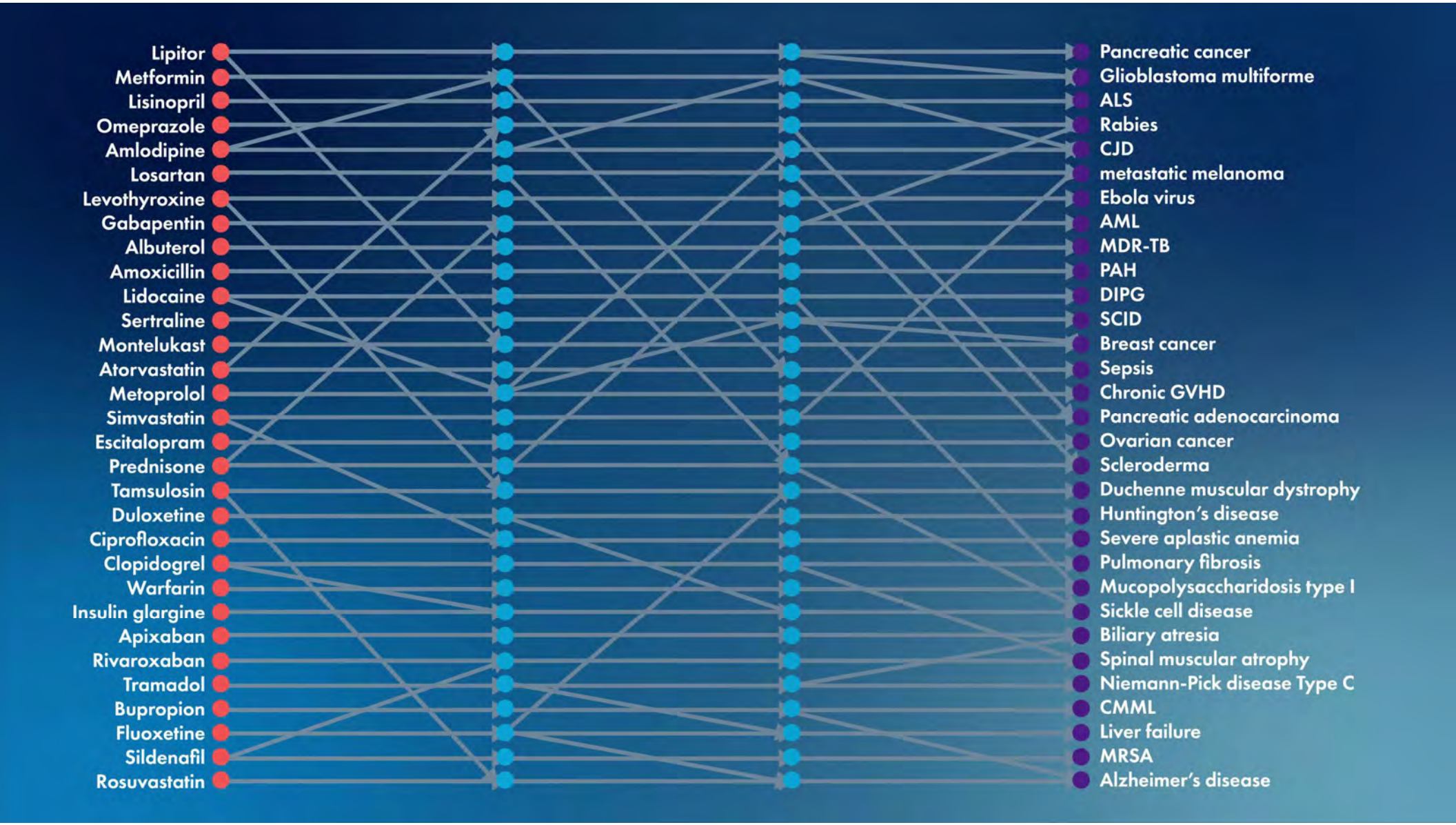
davidfa@pennmedicine.upenn.edu

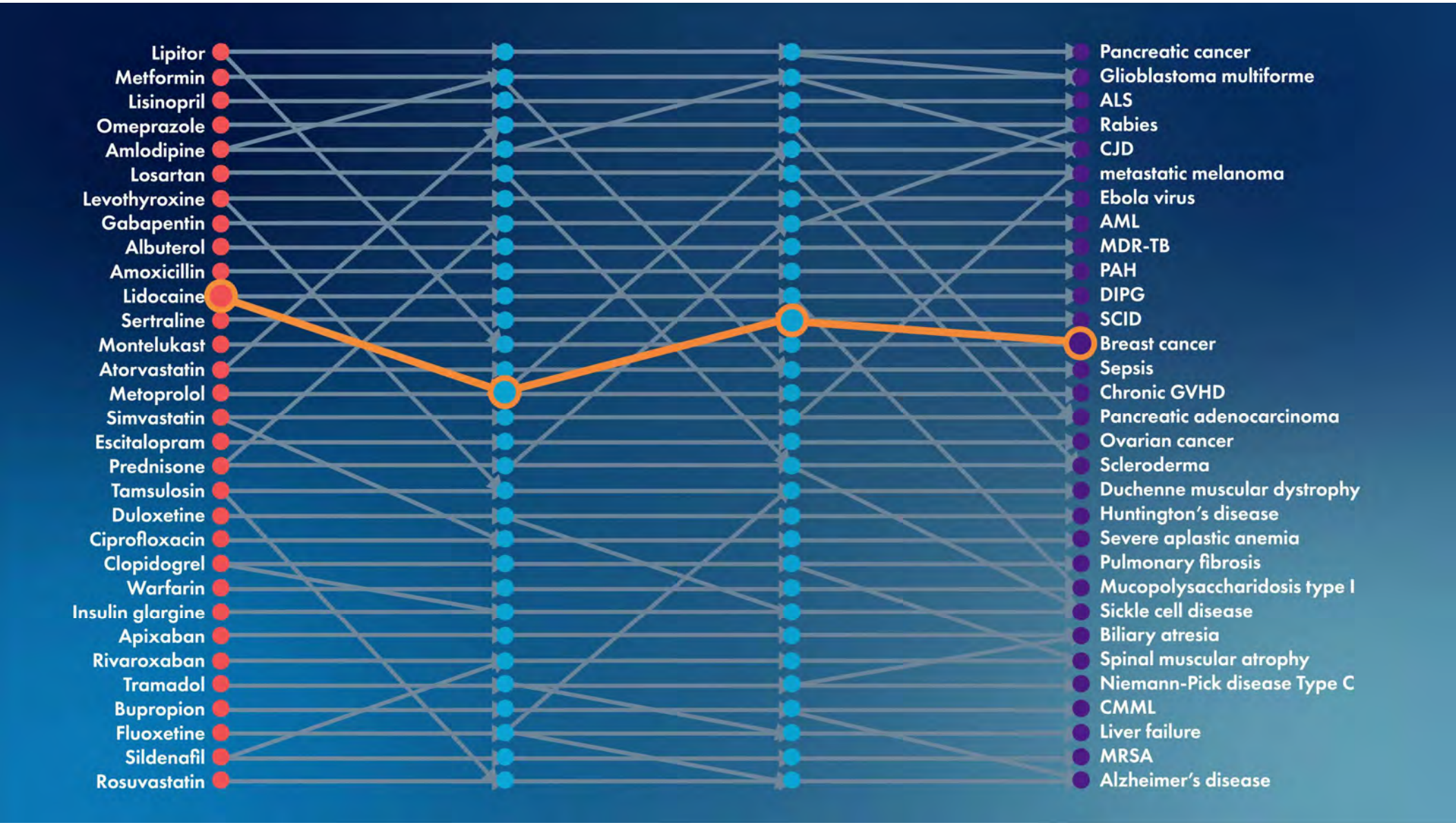





Comedy-Drama
similar to
Comedy
The Burbs
67% Match
genre
User #5678
YOU
watched
Forrest Gump
acted by
acted in
Apollo 13
95% Match
produced by
Wendy Finerman
Cast Away
99% Match


Calcium
Neuro-
Protective
AD
67% Match
increases
Viagra
inhibits
PDE5
increases
relieves
ED
95% Match
decreases
contributes to
cAMP
Pulmonary
arterial
hypertension
99% Match


Lipitor
Metformin
Lisinopril
Omeprazole
Amlodipine
Losartan
Levothyroxine
Gabapentin
Albuterol
Amoxicillin
Lidocaine
Sertraline
Montelukast
Atorvastatin
Metoprolol
Simvastatin
Escitalopram
Prednisone
Tamsulosin
Duloxetine
Ciprofloxacin
Clopidogrel
Warfarin
Insulin glargine
Apixaban
Rivaroxaban
Tramadol
Bupropion
Fluoxetine
Sildenafil
Rosuvastatin
Pancreatic cancer
Glioblastoma multiforme
ALS
Rabies
CJD
metastatic melanoma
Ebola virus
AML
MDR-TB
PAH
DIPG
SCID
Breast cancer
Sepsis
Chronic GVHD
Pancreatic adenocarcinoma
Ovarian cancer
Scleroderma
Duchenne muscular dystrophy
Huntington's disease
Severe aplastic anemia
Pulmonary fibrosis
Mucopolysaccharidosis type I
Sickle cell disease
Biliary atresia
Spinal muscular atrophy
Niemann-Pick disease Type C
CMML
Liver failure
MRSA
Alzheimer's disease


Lipitor
Metformin
Lisinopril
Omeprazole
Amlodipine
Losartan
Levothyroxine
Gabapentin
Albuterol
Amoxicillin
Lidocaine
Sertraline
Montelukast
Atorvastatin
Metoprolol
Simvastatin
Escitalopram
Prednisone
Tamsulosin
Duloxetine
Ciprofloxacin
Clopidogrel
Warfarin
Insulin glargine
Apixaban
Rivaroxaban
Tramadol
Bupropion
Fluoxetine
Sildenafil
Rosuvastatin
Pancreatic cancer
Glioblastoma multiforme
ALS
Rabies
CJD
metastatic melanoma
Ebola virus
AML
MDR-TB
PAH
DIPG
SCID
Breast cancer
Sepsis
Chronic GVHD
Pancreatic adenocarcinoma
Ovarian cancer
Scleroderma
Duchenne muscular dystrophy
Huntington's disease
Severe aplastic anemia
Pulmonary fibrosis
Mucopolysaccharidosis type I
Sickle cell disease
Biliary atresia
Spinal muscular atrophy
Niemann-Pick disease Type C
CMML
Liver failure
MRSA
Alzheimer's disease

Session 1

***Objective*:** This session will discuss the potential roles of the regulator in identifying generic drug repurposing opportunities. Participants will discuss opportunities to actively identify such targets including expansion of current programs, setting disease target priorities, and other policy solutions.

***Presentations*:**

- Heather Stone, U.S. Food and Drug Administration
- David Fajgenbaum, Every Cure

***Additional Panelists*:**

- Christine Colvis, NCATS

Moderated Panel Discussion & Audience Q&A

USE THIS QR CODE TO JOIN OUR SLIDO!

You can also go to Slido.com and use the code #4139881 to join

Generic Drug Repurposing: Regulatory Solutions Framework

Resources needed: Low → High

Building on Current Processes and Programs	New but Within Existing Authority	Legislative Action Needed
Programming – A program offering advice on research protocols and evidentiary needs to obtain regulatory approval/attract manufacturer partner (NCATS/FDA joint effort?), including workshops, individual meetings, and guidance documents	**Disease Prioritization -** Identification of priority uses cases or conditions for repurposing efforts for Federal efforts (i.e., within FDA, NCATS, NIH)	**Expand Modern Labeling Act-** Expand modern labeling act beyond withdrawn RDLs (criteria TBD; may be based on # of years since first ANDA); OR expand to allow nontraditional developers to compile and submit the data to FDA (reduce workload on FDA staff)
	User Fee Waivers - Waive user for repurposed drugs that meet or advance public health needs as defined by FDA (see above); if a pathway is created for nontraditional developers, user fee not to be required	**New Regulatory Pathways -** "Labeling only" 505(b)(2) pathways (Reboot Rx proposal) OR creation of other new pathway for nontraditional developers (similar to Article 48 in EU proposal)
Utilizing Modern Labeling Act – FDA can use authority provided to update labels of drugs with withdrawn RDLs based on existing data	**Sponsor Incentives –** Explore incentives for companies to partner with nontraditional developers on repurposing. This may include building on the "programming" solution to establish a program similar to the EU's STAMP Pilot.	**International Regulatory Reciprocity** – update labels based on evidence used for label expansion in other regulatory agencies (e.g., EMA, MHRA) for repurposed drugs that meet areas of unmet medical need
CURE ID Expansion - link CURE ID with government funding partner to pull out promising candidates and prepare research protocols to meet regulatory standards (may include match making conferences)		**Addressing Liability Concerns -** Addressing liability concerns for pharmaceutical companies to share data or study new uses of generic drugs
Project Renewal Expansion – Expand Project Renewal to other disease areas where there is sufficient data and clear evidentiary targets (i.e., infectious diseases)	**Expand Federal Programming -** Expanding NCATS, NIA Alzheimer's Repurposing Program, or ARPA-H to establish a government-led repurposing initiative	**New Federal Initiative -** Create a new large-scale government initiative (e.g., BARDA) to advance drug repurposing for unmet medical need

- Opportunities
- Approval
- Labeling

Duke | MARGOLIS INSTITUTE *for* Health Policy

Discussion Questions

1. What are some of the greatest challenges to identifying repurposing opportunities?

2. What role do you see within the FDA to support identification of repurposing opportunities?

3. What are your thoughts on expanding and linking CURE ID with a government agency to help identify potential repurposing candidates? How might that work and who do you see stepping into that role?

4. Which federal agency might be best positioned to house an effort to identify priority use cases for repurposing, beyond ARPA-H's efforts with Every Cure?

5. What potential do you see in expanding current federal programming, such as NCATS, NIA Alzheimer's Repurposing Program, or ARPA-H, to begin or expand upon efforts to identify repurposing opportunities? Which of these programs may be best suited for this?

USE THIS QR CODE TO JOIN OUR SLIDO!

You can also go to Slido.com and use the code #4139881 to join

BREAK

Our Program Will Resume at 11:50 AM ET

Upcoming Duke-Margolis Virtual Public Workshop

June 10, 2025|4:00 – 5:00 PM

Visit healthpolicy.duke.edu/events

Session 2: Regulatory Pathways for Non-Traditional Drug Developers

Moderator: Gerrit Hamre, *Duke-Margolis Institute for Health Policy*

Regulatory Background

May 29, 2025

Hyman, Phelps & McNamara PC

Overview of Drug Applications

"Full" New Drug Application (NDA) – 505(b)(1)

- Includes "full reports" of studies to prove safety and effectiveness

505(b)(2) Application – 505(b)(2)

- NDA where applicant does not have rights to some of the "full reports" necessary for approval

Abbreviated New Drug Application (ANDA) – 505(j)

- No requirement for "full reports"
- Approval based on showing of similarity to previously approved drug product, including bioequivalence

What is a 505(b)(2) Application?

A type of full NDA subject to the “full reports” requirement, BUT . . .

Some of the safety and effectiveness studies necessary to satisfy the “full reports” requirement were:

- NOT conducted by or for the 505(b)(2) applicant; and
- For which the applicant has no right of reference

Often viewed as a hybrid between full NDA and ANDA

Typically used for approval of changes to a previously approved drug, e.g., new dosage form, new indication

505(b)(2) Applications

New formulation requiring clinical studies

New dosage regimen

Different salt of previously approved active

New combination of previously approved actives

New indication

Rx-to-OTC switch

Complex drugs where clinical investigations necessary to show “same” active

505(b)(2) Applications – Data Requirements

Even though the statute indicates that “full reports” are required, FDA interprets it to permit reliance on:

- Published studies; or
- FDA’s prior finding of safety and effectiveness for a listed drug

Applicant only required to submit new data necessary to support S&E for change (e.g., new dosage form)

In some cases, no additional clinical studies may be necessary

What is an ANDA?

Primary means of approving generic drugs

Abbreviated Data Requirements

- Safety and effectiveness data is not required
- Safety and effectiveness is ***presumed*** if the generic drug is shown to be “the same as” a previously approved drug
- Clinical data generally limited to bioequivalence studies

Abbreviated time and cost

ANDA Eligibility – Two Routes

“Same” as a “Listed Drug”; or

Approved Suitability Petition

- Available only for certain differences from the listed drug

ANDA Eligibility

"Same as" means Identical in

- Active ingredient(s)
- Dosage form
- Strength
- Route of administration
- Conditions of use (except those uses protected by patents or non-patent exclusivity)

ANDA Eligibility

Suitability Petitions

- Permits submission of ANDA for drug with certain differences from the listed drug
- Allowable Differences
  - Active ingredient (combinations only)
  - Route of administration
  - Dosage form
  - Strength

ANDA Eligibility

Suitability Petitions (cont'd)

- Publicly available
- ANDA cannot be submitted until suitability petition is granted
- FDA will grant a suitability petition unless "investigations must be conducted" to show safety and effectiveness
- Drugs approved via suitability petitions are pharmaceutical alternatives, not pharmaceutical equivalents

ANDA Requirements

No “full reports” requirement

- FDA cannot require any clinical studies other than bioequivalence studies
- ***But*** has required “limited confirmatory testing”

Safety and efficacy presumed if generic is shown to be “the same as” the pioneer drug

Timing of ANDA approval depends upon patent and non-patent exclusivity of listed drug

User Fees for FY 2025

PDUFA

- Clinical data: $4,310,002
- No clinical data: $2,155,01

- Program Fees: $403,889 per strength

GDUFA

- $ 321,920

- Program Fees (small): $189,166

Hyman, Phelps & McNamara PC

THANK YOU!!

FDA Law Blog

(www.FDAlawblog.net)

Hyman, Phelps & McNamara PC

Reboot Rx

Because the solution may already exist

Regulatory Pathways for Nonprofits to Drive Generic Drug Repurposing

Devon Crittenden

Director of Strategy & Operations

www.rebootrx.org

Regulatory Approval Would Help Drive Adoption of Repurposed Generic Drugs

- Builds physician confidence and supports clinical adoption
- Enables guideline inclusion and payer reimbursement
- Allows broader communication to support patient access

Obtaining Regulatory Approval Is a Challenge

- Off-patent drugs offer no new exclusivity, so drug manufacturers lack financial incentive to act
- Nonprofits are stepping in to fill the gap
- Yet regulatory approval typically requires a sponsor, and nonprofits face barriers to applying on their own

A New Pathway for Repurposing: Labeling-Only 505(b)(2) NDA

Current 505(b)(2) approval pathway:

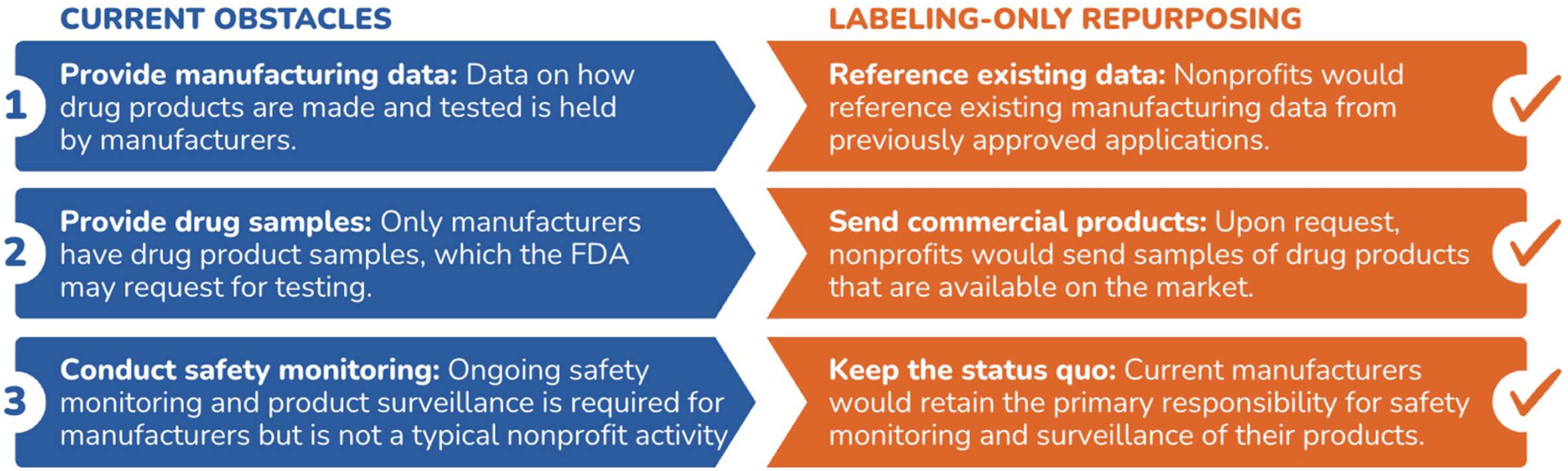
- Allows reliance on data not gathered by the sponsor (e.g., published literature, prior FDA findings), especially for safety
- Commonly used for new formulations, doses, or delivery methods
- Still requires a full NDA, including manufacturing data

Proposed Labeling-Only 505(b)(2) concept:

- Addresses the challenge that nonprofits do not manufacture drug products
- Extends reliance on third-party data to include manufacturing information; submit only the evidence needed to support a new indication
- Designed for generic drugs with no product changes, multiple interchangeable versions, and well-established manufacturing history

NDA - New Drug Application

Labeling-Only 505(b)(2) Pathway



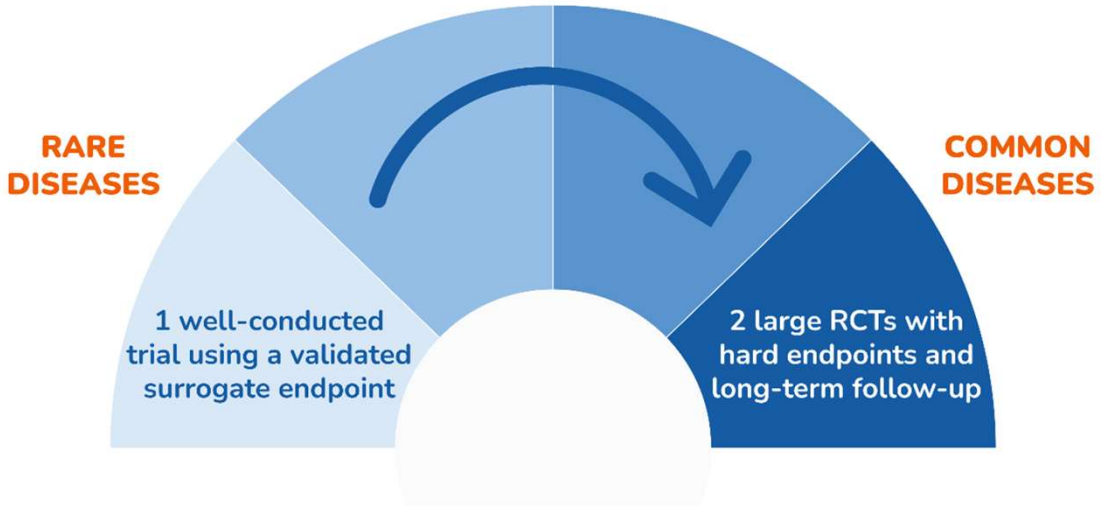
Crittenden D et al., *Front Pharmacol.* 2024.

Barriers to the Labeling-Only 505(b)(2) Pathway

- Generating or accessing regulatory-level efficacy data
- Managing post-marketing surveillance
- Taking on full legal liability
- High costs, including user fees

What is Regulatory-Level Data?

- Must meet regulatory expectations, which vary based on disease severity, rarity, and unmet need

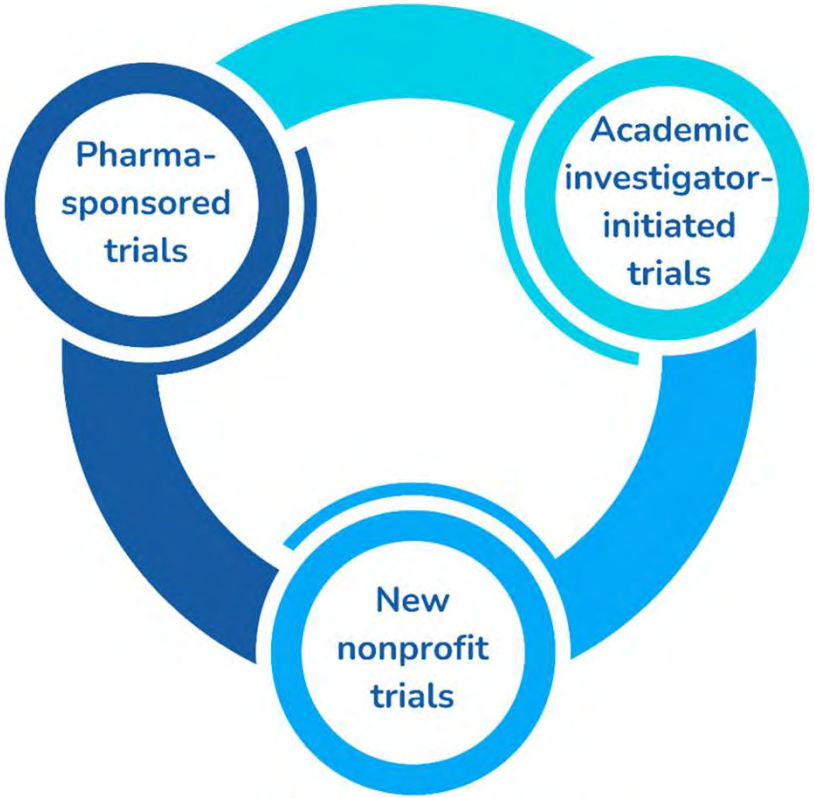


- Trials should be conducted under IND and follow GCP standards
- Access to patient-level data is often required

RCT - Randomized Controlled Trial; IND - Investigational New Drug; GCP - Good Clinical Practice

Sources of Regulatory-Level Data

Often from older, pre-patent-expiration studies; limited access and low incentive to share



May lack regulatory oversight or usable patient-level data

Costly to generate robust, regulatory-grade data under oversight

What It Might Take for the Labeling-Only Pathway to Work

- Access to data and funding to generate or compile regulatory-grade evidence
- FDA guidance on evidentiary standards and flexibility for repurposed generics
- User fee waivers for nonprofit sponsors
- Centralized third-party entity to manage post-marketing obligations
- Risk mitigation strategies for liability

Next Steps to Advance the Labeling-Only Pathway

- Pursue implementation through an FDA roadmap, pilot, or guidance — or through legislative action if needed
- Engage stakeholders to shape the pathway and ensure impact
- Identify strong use cases to demonstrate feasibility and value
- Assess when approval adds value, based on:
  - Product availability
  - Payer coverage
  - Clinician uptake
  - Patient population and unmet need

- We Have the Drugs.
- We Have the Data.
- Let's Deliver the Impact.

Reboot Rx

Because the solution may already exist

info@rebootrx.org

www.rebootrx.org

Boston, Massachusetts (USA)

Session 2

***Objective*:** This session will examine the pathways and programs that may be used to support non-traditional developers looking to pursue regulatory approval, including solutions to encourage sponsors to collaborate with non-traditional developers. Additionally, participants will explore opportunities for new federal authorities to support trial designs that meet evidentiary requirements and initiatives that enable increased direct engagement between non-traditional developers and FDA staff.

***Presentations*:**

- Sara Koblitz, Hyman, Phelps, & McNamara, P.C.

- Devon Crittenden, Reboot Rx

Moderated Panel Discussion & Audience Q&A

USE THIS QR CODE TO JOIN OUR SLIDO!

You can also go to Slido.com and use the code #4139881 to join

Generic Drug Repurposing: Regulatory Solutions Framework

Resources needed: Low → High

Building on Current Processes and Programs	New but Within Existing Authority	Legislative Action Needed
Programming – A program offering advice on research protocols and evidentiary needs to obtain regulatory approval/attract manufacturer partner (NCATS/FDA joint effort?), including workshops, individual meetings, and guidance documents	**Disease Prioritization -** Identification of priority uses cases or conditions for repurposing efforts for Federal efforts (i.e., within FDA, NCATS, NIH)	**Expand Modern Labeling Act-** Expand modern labeling act beyond withdrawn RDLs (criteria TBD; may be based on # of years since first ANDA); OR expand to allow nontraditional developers to compile and submit the data to FDA (reduce workload on FDA staff)
	User Fee Waivers - Waive user for repurposed drugs that meet or advance public health needs as defined by FDA (see above); if a pathway is created for nontraditional developers, user fee not to be required	**New Regulatory Pathways -** "Labeling only" 505(b)(2) pathways (Reboot Rx proposal) OR creation of other new pathway for nontraditional developers (similar to Article 48 in EU proposal)
Utilizing Modern Labeling Act – FDA can use authority provided to update labels of drugs with withdrawn RDLs based on existing data	**Sponsor Incentives –** Explore incentives for companies to partner with nontraditional developers on repurposing. This may include building on the "programming" solution to establish a program similar to the EU's STAMP Pilot.	**International Regulatory Reciprocity** – update labels based on evidence used for label expansion in other regulatory agencies (e.g., EMA, MHRA) for repurposed drugs that meet areas of unmet medical need
CURE ID Expansion - link CUREID with government funding partner to pull out promising candidates and prepare research protocols to meet regulatory standards (may include match making conferences)		**Addressing Liability Concerns -** Addressing liability concerns for pharmaceutical companies to share data or study new uses of generic drugs
Project Renewal Expansion – Expand Project Renewal to other disease areas where there is sufficient data and clear evidentiary targets (i.e., infectious diseases)	**Expand Federal Programming -** Expanding NCATS, NIA Alzheimer's Repurposing Program, or ARPA-H to establish a government-led repurposing initiative	**New Federal Initiative -** Create a new large-scale government initiative (e.g., BARDA) to advance drug repurposing for unmet medical need

Opportunities
Approval
Labeling

Duke | MARGOLIS INSTITUTE for Health Policy

Discussion Questions

1. What do you find to be the biggest challenges for nontraditional developers pursuing a label change for a repurposed drug?

2. How could a new regulatory pathway for nontraditional developers or “labeling only” pathway work?

3. What role might a federal advisory program play in supporting nontraditional developers pursuing regulatory approval?

    1. What are your thoughts on programs to prepare ready-to-submit evidentiary packages, similar to the STAMP Pilot in the EU? Is this sufficient to attract an industry partner?

4. What might be other methods of attracting industry partners to work with nontraditional developers on pursuing label expansion for new uses of generic drug?

USE THIS QR CODE TO JOIN OUR SLIDO!

You can also go to Slido.com and use the code #4139881 to join

BREAK

Our Program Will Resume at 2:00 PM ET

Upcoming Duke-Margolis Virtual Public Workshop

June 12, 2025|1:00 – 3:00 PM

Visit healthpolicy.duke.edu/events

Session 3: Updating Labels with Established Evidence & Ensuring Responsible Promotion

Moderator: Beth Boyer, *Duke-Margolis Institute for Health Policy*

Regulatory Options to Facilitate Drug Repurposing

Janet Woodcock M.D.

Diclosure: I’m on the Board of ”EveryCure” a nonprofit that does repurposing

The Problem: Societal

- **Repurposing generic drugs enables effective, low-cost treatments to be available**
- **Currently there are no real incentives to conduct repurposing**
- **Thus, for-profit pharmaceutical companies rarely work on repurposing for off-patent drugs**
- **Non-profits or similar entities lack the resources to both conduct studies and navigate the regulatory process to get new uses on label**
- **Off-label use often not reimbursed, may also raise patient concerns and practitioner liability worries; slow diffusion into practice**
- **Cancer drugs are often repurposed and often get reimbursed, due to special arrangements for cancer**

The Problems: For Regulators

- **Drug labels are supposed to the the ”gold standard” but they often get out of date, particularly once generics are available**
- **For this reason, labels rarely utilized by practitioners for old drugs**
- **Not a good look, undermines gold standard claim**
- **Reimbursement often tied to FDA approval**
- **Generic and new drug review processes (and user fee programs) were put in place with the for-profit industry in mind**
- **No FDA infrastructure for non-profit repurposers and current label update process does not fit**

EX-US Efforts

- **(NHS) Medicines Repurposing Program**
  - **Run by NHS**
  - **Submit proposals for funding with aim of submitting license variation to MHRA**

- **STAMP pilot**
  - **EU**
  - **EMA and national authorities help applicants with regulatory support**
  - **Proposed legislation for not-for-profits to submit**

Efforts to Improve Situation in US

- **Sporadic FDA efforts on particularly egregious old generic drug labels**
- **“Project Renewal” from FDA Oncology Center of Excellence**
  - **Update old labels (FDA led)**
  - **Work with RLD holder**
  - **Labor intensive for FDA**
  - **Data often assembled in some fashion by NCNN or other parties**
- **“Modern Labelling Act”**
  - **Enables FDA to direct label update of generics if innovator NDA withdrawn**
  - **Labor intensive for FDA; reviewers have to do a lot of work; appeal process**
  - **FDA has not used or set up process**

Non-legislative Proposals to Further Improve US situation

- **FDA should try harder (unlikely in prior or current situation) either by strengthening current programs or expanding them**
- **Expand user fee waiver program (I think would be legislative)**
- **New regulatory pathway (Reboot Rx): Label only 505(b)(2); they believe could be established by Guidance**
- **Incentives (generally would need to be financial, e.g., legislative**

Legislative Proposals

- **Haystack Project: Protect Rare Act**
  - **Mandate Federal reimbursement for off-label repurposed drugs for rare diseases if listed in compendium, etc**
  - **Modeled after cancer situation**
  - **Limited to rare diseases**
- **Expand overall Federal effort on repurposing (e.g., put some money behind it, or ARPA-H, or a new program at NIH etc)**
- **Expand Modern Labelling Act**
  - **Get rid of withdrawn NDA requirement**
  - **Allow submission, not have FDA do all the work**

Other Potential Legislative Approaches

- **Deal with liability concerns**
- **Enable International Regulatory Reciprocity**

What I Think Will Work

- **Label only 505(b)(2) pathway**
- **Why should non-profit developers have to have a "product" when there are FDA-blessed interchangeable products on the market?**
- **FDA could request commercially sourced samples if presentation a concern (not common)**
- **FDA could just post finding and label language; indication would be deemed "FDA approved"**
- **Pathway would need to have data submission process; submitters would simply refer to Orange Book drugs with USP monograph for CMC, tox etc, no right of reference needed. New data would be primarily clinical, sometimes with some non-clinical**
- **ANDA holders (and NDA holders if any) could would continue current postmarket activities**
- **I think this would help with liability concerns**

Session 3

***Objective*:** This session will discuss the utilization and potential expansion of existing federal authorities to update drug labels with new indications based on established evidence from real world use.

***Presentation*:**

- Janet Woodcock, Former Regulator

Moderated Panel Discussion & Audience Q&A

USE THIS QR CODE TO JOIN OUR SLIDO!

You can also go to Slido.com and use the code #4139881 to join

Generic Drug Repurposing: Regulatory Solutions Framework

Resources needed: Low → High

Building on Current Processes and Programs	New but Within Existing Authority	Legislative Action Needed
Programming – A program offering advice on research protocols and evidentiary needs to obtain regulatory approval/attract manufacturer partner (NCATS/FDA joint effort?), including workshops, individual meetings, and guidance documents	**Disease Prioritization -** Identification of priority uses cases or conditions for repurposing efforts for Federal efforts (i.e., within FDA, NCATS, NIH)	**Expand Modern Labeling Act-** Expand modern labeling act beyond withdrawn RDLs (criteria TBD; may be based on # of years since first ANDA); OR expand to allow nontraditional developers to compile and submit the data to FDA (reduce workload on FDA staff)
	User Fee Waivers - Waive user for repurposed drugs that meet or advance public health needs as defined by FDA (see above); if a pathway is created for nontraditional developers, user fee not to be required	**New Regulatory Pathways -** "Labeling only" 505(b)(2) pathways (Reboot Rx proposal) OR creation of other new pathway for nontraditional developers (similar to Article 48 in EU proposal)
Utilizing Modern Labeling Act – FDA can use authority provided to update labels of drugs with withdrawn RDLs based on existing data	**Sponsor Incentives –** Explore incentives for companies to partner with nontraditional developers on repurposing. This may include building on the "programming" solution to establish a program similar to the EU's STAMP Pilot.	**International Regulatory Reciprocity** – update labels based on evidence used for label expansion in other regulatory agencies (e.g., EMA, MHRA) for repurposed drugs that meet areas of unmet medical need
CURE ID Expansion - link CUREID with government funding partner to pull out promising candidates and prepare research protocols to meet regulatory standards (may include match making conferences)		**Addressing Liability Concerns -** Addressing liability concerns for pharmaceutical companies to share data or study new uses of generic drugs
Project Renewal Expansion – Expand Project Renewal to other disease areas where there is sufficient data and clear evidentiary targets (i.e., infectious diseases)	**Expand Federal Programming -** Expanding NCATS, NIA Alzheimer's Repurposing Program, or ARPA-H to establish a government-led repurposing initiative	**New Federal Initiative -** Create a new large-scale government initiative (e.g., BARDA) to advance drug repurposing for unmet medical need

Opportunities
Approval
Labeling

Discussion Questions

1. How could the Modern Labeling Act be utilized to support nontraditional developers pursing label expansion or updating labels with new uses of generic drugs?

    a. Could this be expanded beyond withdrawn RDLs or to allow nontraditional developers to submit data to the FDA themselves?

2. What disease areas may be best suited for the expansion of Project Renewal? What resources would be required? Is there a role for nontraditional developers to support data gathering for such a program?

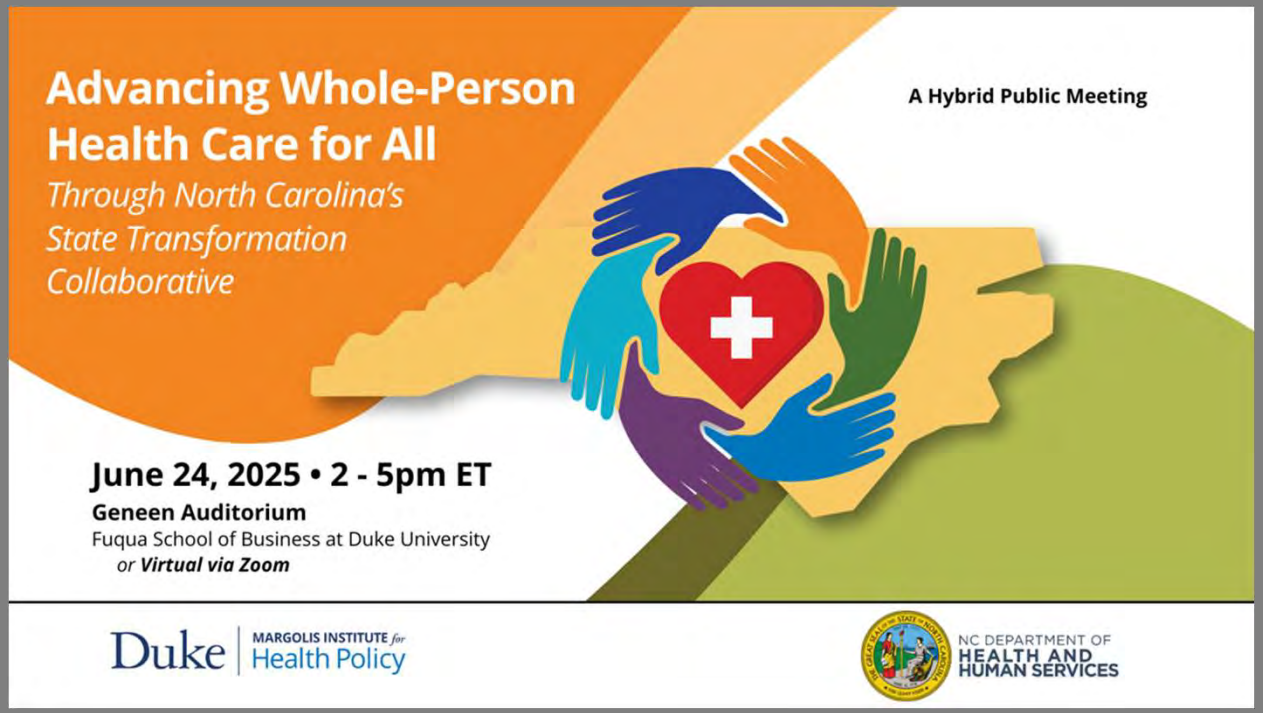
3. What's the feasibility for FDA to accept evidence used for label expansion by other regulatory authorities from other countries to expand labels here in the US?

USE THIS QR CODE TO JOIN OUR SLIDO!

You can also go to Slido.com and use the code #4139881 to join

BREAK

Our Program Will Resume at 3:00 PM ET



Upcoming Duke-Margolis Hybrid Public Workshop

June 24, 2025|2:00 – 5:00 PM

Visit healthpolicy.duke.edu/events

Session 4: Additional Opportunities for Generic Drug Repurposing & Next Steps

Moderator: Tanisha Carino, *Duke-Margolis Institute for Health Policy*

Session 4

***Objective*:** This session will open the floor up to participants to share new ideas and opportunities to support generic drug repurposing that have not already been discussed and potential next steps.

Open Discussion

Generic Drug Repurposing: Regulatory Solutions Framework

Resources needed: Low → High

Building on Current Processes and Programs	New but Within Existing Authority	Legislative Action Needed
Programming – A program offering advice on research protocols and evidentiary needs to obtain regulatory approval/attract manufacturer partner (NCATS/FDA joint effort?), including workshops, individual meetings, and guidance documents	**Disease Prioritization -** Identification of priority uses cases or conditions for repurposing efforts for Federal efforts (i.e., within FDA, NCATS, NIH)	**Expand Modern Labeling Act-** Expand modern labeling act beyond withdrawn RDLs (criteria TBD; may be based on # of years since first ANDA); OR expand to allow nontraditional developers to compile and submit the data to FDA (reduce workload on FDA staff)
	User Fee Waivers - Waive user for repurposed drugs that meet or advance public health needs as defined by FDA (see above); if a pathway is created for nontraditional developers, user fee not to be required	**New Regulatory Pathways -** "Labeling only" 505(b)(2) pathways (Reboot Rx proposal) OR creation of other new pathway for nontraditional developers (similar to Article 48 in EU proposal)
Utilizing Modern Labeling Act – FDA can use authority provided to update labels of drugs with withdrawn RDLs based on existing data	**Sponsor Incentives –** Explore incentives for companies to partner with nontraditional developers on repurposing. This may include building on the "programming" solution to establish a program similar to the EU's STAMP Pilot.	**International Regulatory Reciprocity** – update labels based on evidence used for label expansion in other regulatory agencies (e.g., EMA, MHRA) for repurposed drugs that meet areas of unmet medical need
CURE ID Expansion - link CUREID with government funding partner to pull out promising candidates and prepare research protocols to meet regulatory standards (may include match making conferences)		**Addressing Liability Concerns -** Addressing liability concerns for pharmaceutical companies to share data or study new uses of generic drugs
Project Renewal Expansion – Expand Project Renewal to other disease areas where there is sufficient data and clear evidentiary targets (i.e., infectious diseases)	**Expand Federal Programming -** Expanding NCATS, NIA Alzheimer's Repurposing Program, or ARPA-H to establish a government-led repurposing initiative	**New Federal Initiative -** Create a new large-scale government initiative (e.g., BARDA) to advance drug repurposing for unmet medical need

- Opportunities
- Approval
- Labeling

Duke | MARGOLIS INSTITUTE for Health Policy

USE THIS QR CODE TO JOIN OUR SLIDO!

You can also go to Slido.com and use the code #4139881 to join

Concluding Remarks

Beth Boyer, *Duke-Margolis Institute for Health Policy*

Thank You!

Contact Us

healthpolicy.duke.edu

Subscribe to our monthly newsletter at dukemargolis@duke.edu

1201 Pennsylvania Avenue, NW,
Suite 500 • Washington, DC 20004

DC office: 202-621-2800
Durham office: 919-419-2504

Follow Us

DukeMargolis

@dukemargolis

@DukeMargolis

Duke Margolis

Duke-Margolis Institute For Health Policy

Duke | MARGOLIS INSTITUTE *for* Health Policy