REAGAN-UDALL FOUNDATION FOR THE FDA

Drug Repurposing:

Considerations for Selection Criteria and Prioritization

Hybrid Public Meeting

This project is supported by the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) as part of an award of $118,960 in federal funds (100% of the project). The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by FDA, HHS, or the U.S. Government. For more information, please visit FDA.gov.

REAGAN-UDALL FOUNDATION FOR THE FDA

WELCOME

Susan C. Winckler, RPh, Esq.

CEO, Reagan-Udall Foundation for the FDA

Housekeeping

REAGAN-UDALL FOUNDATION FOR THE FDA

Joining Online

Microphone and video will remain off during the meeting

Share questions using the Zoom Q&A function

Public Commenters: Make sure your Zoom name matches the name you used to register

Recording

This public meeting is being recorded

Slides, transcript, and video will be available at www.ReaganUdall.org

Joining in Person

Please write questions on the index cards provided

Agenda

All times listed in Eastern Time

REAGAN-UDALL FOUNDATION FOR THE FDA

10:30am	Welcome
10:35am	Opening Remarks
10:40am	FDA's Drug Repurposing Framework
10:50am	**Session 1:** Snapshots of Repurposing Efforts
11:15am	**Session 2:** Selection Criteria and Prioritization
12:15pm	Break for Lunch
1:15pm	**Session 3:** Evidence & Submission Expectations
2:15pm	**Session 4:** Federal Partner Discussion
3:15pm	Public Comment
5pm	Adjourn

Public Comment Topics

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1. What are examples of successful prioritization approaches from other programs or jurisdictions that could be adapted?

2. What factors should guide selecting repurposing candidates, and how should they be prioritized?

3. What evidence gaps or policy/regulatory barriers most hinder advancing promising repurposing opportunities?

No direct questions will be posed to speakers or panelists

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Opening Remarks

Brian Fahey

Senior Advisor, Immediate Office of the Commissioner

FDA

REAGAN-UDALL FOUNDATION FOR THE FDA

FDA's Drug Repurposing Framework

Marta Sokolowska, PhD

Deputy Center Director for Substance Use and Behavioral Health
Center for Drug Evaluation and Research
FDA

Drug Repurposing for Unmet Medical Needs: FDA's Drug Repurposing Framework

Marta Sokolowska, PhD

Deputy Center Director for Substance Use and Behavioral Health

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

Disclaimer

- This presentation reflects the views of the author and should not be construed to represent FDA's views or policies.
- The author has no conflicts to disclose.

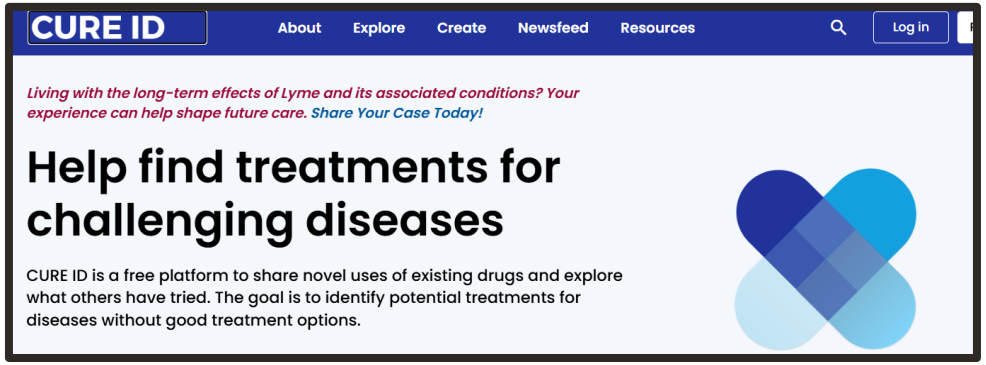
Alignment of Priorities

"The NIH and FDA will jointly investigate opportunities to strengthen the use of repurposed drugs for the treatment of chronic disease, while harmonizing authorization processes through collaborative clinical trial designs to achieve FDA approval."

Building on Prior Work

Duke | MARGOLIS INSTITUTE for Health Policy

- Drug Repurposing for Pandemic Innovation
- Design of a Pull Incentive for Generic Drug Repurposing
- Generic Drug Repurposing Regulatory Policies and Pathways
- Barriers and Solutions Across Drug Repurposing Archetypes



Success Stories

2001 — Anthrax Countermeasure

FDA published a notice clarifying approved indications for doxycycline and penicillin G procaine for treatment of inhalational exposure to *Bacillus anthracis*

2004 — Radiological Countermeasure

FDA published a notice supporting the use of calcium trisodium (Ca-DTPA) and penetrate zinc trisodium (Zn-DPTA) for treatment of certain kinds of radiation exposure

2022 — Capecitabine

FDA approved updated drug labeling including new indications and dosing regimens for capecitabine tablets under Project Renewal

2023 — Temozolomide

FDA approved new and updated indications for temozolomide under Project Renewal

2024 — Fludarabine Phosphate

FDA approved updated drug labeling for fludarabine phosphate under Project Renewal

2026 — Leucovorin Calcium

FDA approved expanded use of leucovorin calcium tablets for the treatment of cerebral folate deficiency with confirmed variant in the folate receptor 1 gene (CFD-FOLR1)

MODERN Labeling Act of 2020: What's in the Law

1. DEFINITION OF COVERED DRUGS
2. IDENTIFICATION OF COVERED DRUGS
3. SELECTION OF DRUGS FOR UPDATING
4. RESPONSE TO NOTIFICATION
5. REVIEW OF APPLICATION HOLDER'S RESPONSE
6. CHANGES TO LABELING

FDA Requests Labeling Updates for Generic Isotretinoin Products

Yesterday, the U.S. Food and Drug Administration requested labeling updates for all generic drugs referencing Accutane (isotretinoin) capsules as their reference listed drug (RLD). These updates are necessary because new scientific evidence exists that is not reflected in current labeling, and the approved labeling does not follow the current format that better serves healthcare providers.

Listserv Message from 6/17/26

Source: MODERN Labeling Act of 2020 / FD&C Act §503D

FDA's Drug Repurposing Framework

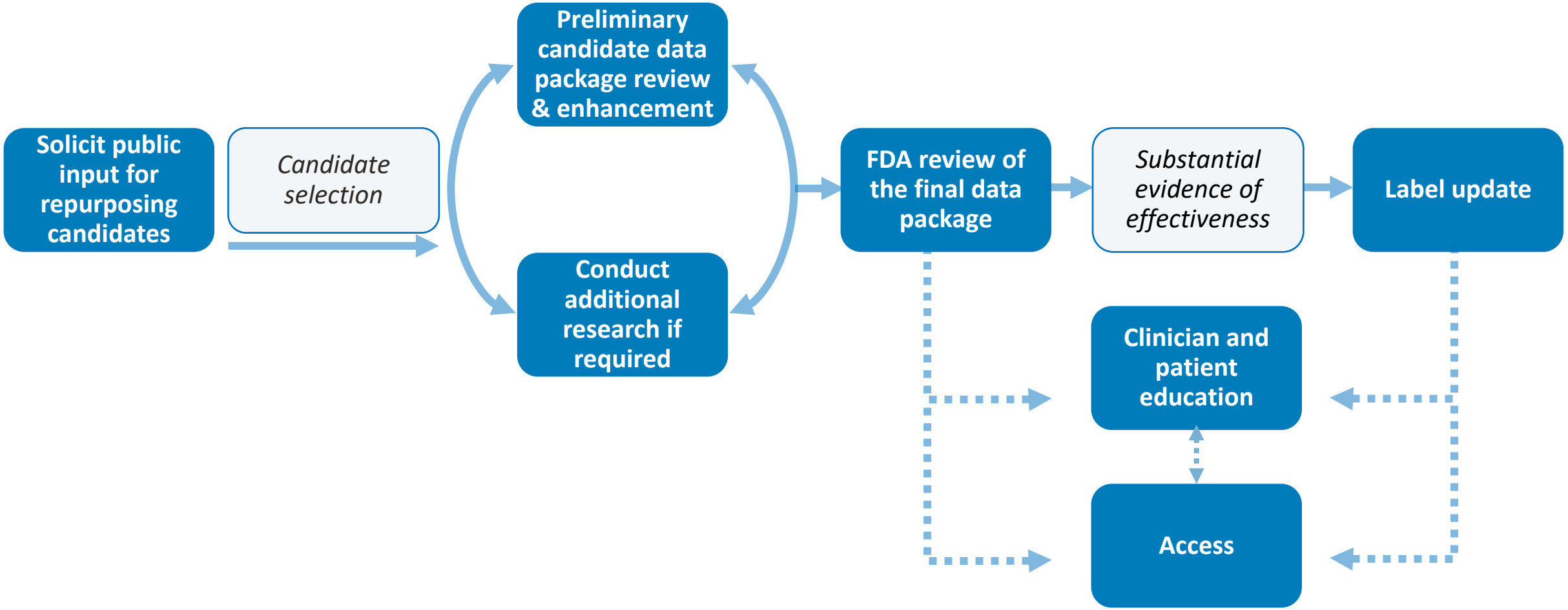
SCOPE OF ELIGIBLE DRUG CANDIDATES

- FDA-approved drugs for which there currently appears to be no commercial interest in adding a new use through a supplemental application.
- Criteria for a new use:
    1) There is compelling scientific evidence to support the effectiveness of the drug for the new use,
    2) the dosage form(s) and route(s) of administration for the new use are the same as for an approved indication, and
    3) there is a comparable safety profile for the patient populations for the new use and approved indications.

FRAMEWORK

FDA's Drug Repurposing Framework

FOR OFF-PATENT DRUGS WITHOUT COMMERCIAL INTEREST



What We Asked

On May 12, 2026, FDA published a Request for Information in the Federal Register on "Drug Repurposing for Unmet Medical Needs." FDA requested public input on four topics:

PRIORITY AREAS

Do the proposed priority areas align with your understanding of areas with significant unmet medical needs and high repurposing potential?

APPROACHES TO IDENTIFICATION

What innovative approaches could be used to identify new drug repurposing opportunities?

REPURPOSING CANDIDATES

What candidates for drug repurposing have the greatest potential for effective treatment of particular identified medical conditions?

BARRIERS & OPPORTUNITIES

What are the key barriers to drug repurposing for stakeholders, and what specific actions could be taken to address them?

Today's Meeting

SESSION 1 | SNAPSHOTS OF REPURPOSING EFFORTS
Highlights ongoing activities that feed into FDA's broader framework

SESSION 2 | SELECTION CRITERIA AND PRIORITIZATION
Provides high-level summary of responses to the Request for Information and next steps for FDA, including development, evaluation, and prioritization of candidates

SESSION 3 | EVIDENCE AND SUBMISSION EXPECTATIONS
Clarifies what is needed after a candidate is selected, including evidence generation regulatory considerations, submission pathways, and barriers to adoption and success

SESSION 4 | FEDERAL PARTNER DISCUSSION
Identifies opportunities for federal coordination and considers how existing programs, partnerships, real-world data, and AL/ML could support repurposing efforts

PUBLIC COMMENT SESSION
Provides an opportunity for more stakeholders to share perspectives and recommendations

Acknowledgments

- CDER Office of the Center Director
  - Brian Gac, PharmD
  - Anika Haque, PharmD
  - Caroline Huang, PhD
  - Bic Nguyen, PharmD

Session 1

Snapshots of Repurposing Efforts

REAGAN-UDALL FOUNDATION FOR THE FDA

Mitra Ahadpour, MD

FDA

Matt Hall, PhD

National Center for Advancing Translational Sciences

Heather Stone, MPH

FDA

A New Approach to Repurposing Generic Drugs

Mitra Ahadpour, MD
Principal Deputy Director
Office of Translational Sciences
August 5, 2026

U.S. FOOD & DRUG ADMINISTRATION

Noah

- Noah is 4 years old with Kabuki Syndrome (no approved treatment).
- 52 diagnoses across 18 pediatric subspecialties.
- Open heart surgery at 8 days of life: 5 months in PICU.
- Communicates through ASL, word approximations, and assistive technology.

"He redefines what it means to live a meaningful life."

Photo of Noah courtesy of Kimberly Maxfield.

Shared with permission of Kimberly Maxfield · For illustrative purposes only · FDA is not working on this individual case.

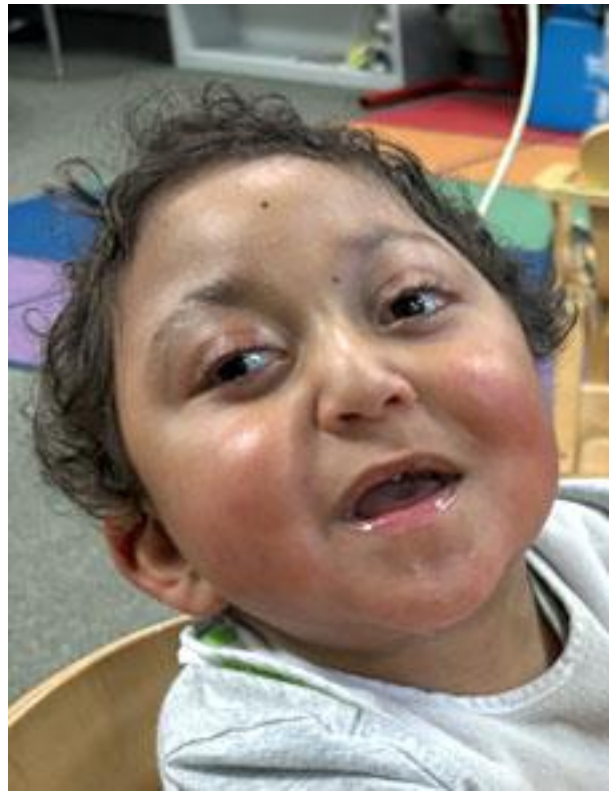
The Scale of Unmet Need

RARE DISEASES BY THE NUMBERS

>10,000 Rare diseases identified—most with no approved treatment

80% Of rare diseases estimated to have a genetic origin

1/2 Of those affected by rare diseases are children



Noah.

Photo courtesy of Kimberly Maxfield.

Rare Diseases at FDA | FDA

Artificial Intelligence

AI-driven computational methods now enable systematic evaluation of FDA-approved drugs for new indications.

Formal Research Collaborative Agreement

FDA & Every Cure

Identifying existing generic drugs with potential therapeutic value for rare diseases where no approved treatment exists.

How the Matching Works

Every Cure • MATRIX platform: Computational

The Biomedical Knowledge Graph

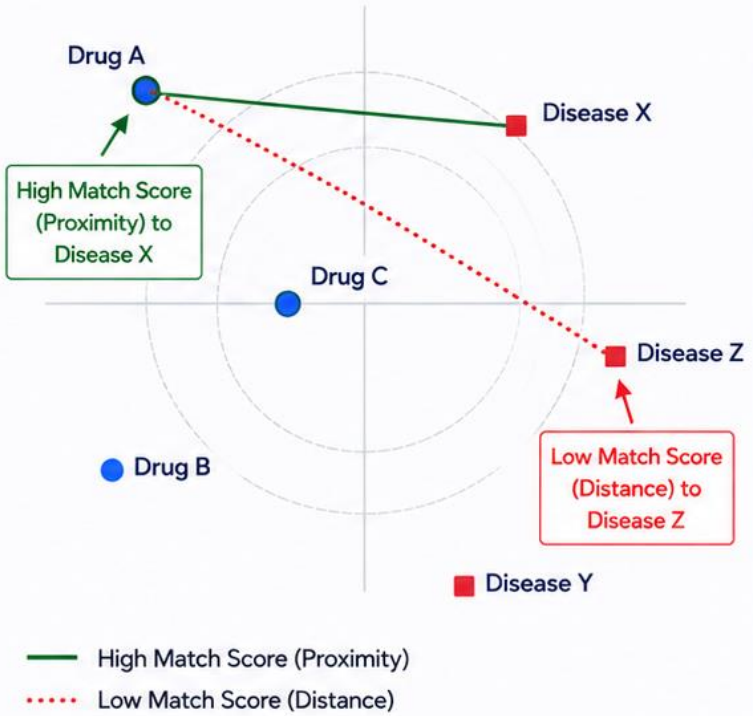
An AI-readable map of human biology built from 100+ datasets

- Drug Mechanisms
- Gene–Gene Interactions
- Protein–Protein Interactions
- Disease Pathways
- Phenotypes
- Clinical Trial Outcomes
- Real-World Evidence

ML models convert graph to mathematical map
(high-dimensional embeddings)

The Match Score

Biological plausibility score from drug–disease proximity in a high-dimensional space



Source: MATRIX, an ARPA-H-funded program, enables Every Cure to systematically identify promising drug repurposing opportunities.

MODERN Authority: One Tool for Drug Repurposing

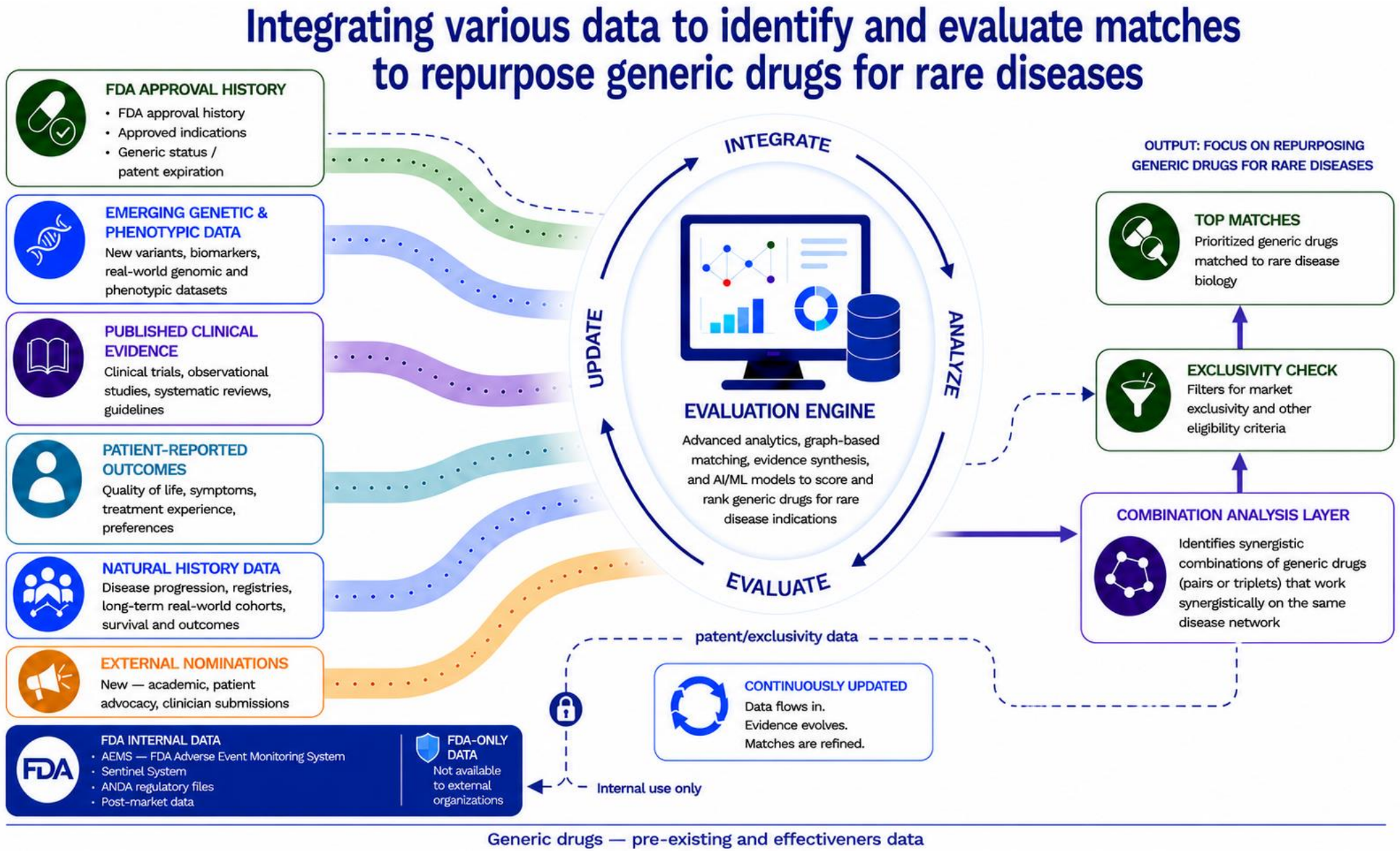
Using our authority under section 503D of the FD&C Act (commonly referred to as **"MODERN"**), FDA can require certain updates to the labeling of generic drugs when the brand version of the drug is **no longer protected by patents/exclusivity** and approval of the brand drug has been **withdrawn for reasons other than safety/efficacy**

This includes the authority to require updates to **add new uses** to the labeling of these generic drugs when the uses are **supported by data that meets FDA's approval standards**

MODERN thus gives FDA a **useful tool for repurposing older drugs** with wholly generic markets, and has the potential to **expand affordable access to treatment** for patients

21 USC 353d: Process to update labeling for certain generic drugs

A Vision: Continuously Updated Evaluation System



Why Try AI Matching to Repurpose Generic Drugs?

- For Noah and every patient still waiting for an approved treatment for their rare disease.
- Approved drugs may have untapped potential for rare diseases with no approved treatment.

Photo of Noah courtesy of Kimberly Maxfield.


FDA
U.S. FOOD & DRUG
ADMINISTRATION

Matthew Hall, PhD
Scientific Director
National Center for Advancing Translational Sciences (NCATS)
National Institutes of Health

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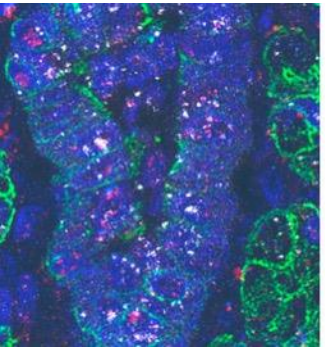
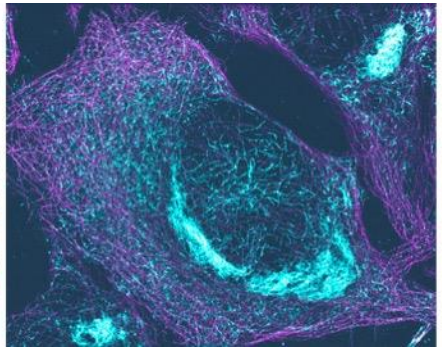
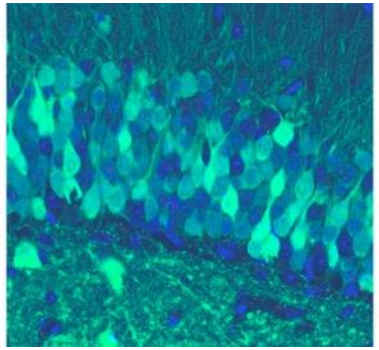
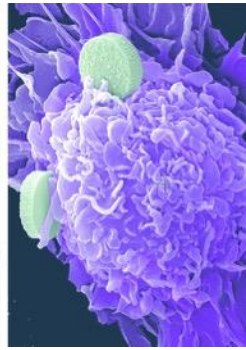








The pathway from a disease to a drug

Understanding the disease

Develop a therapeutic strategy

Find therapies that affect the target

Test candidates to improve activity and safety

IND application

Clinical trials to prove safety, activity

FDA review & approval

Basic science

Clinical research

NCATS is the Preclinical Center

Understanding the disease

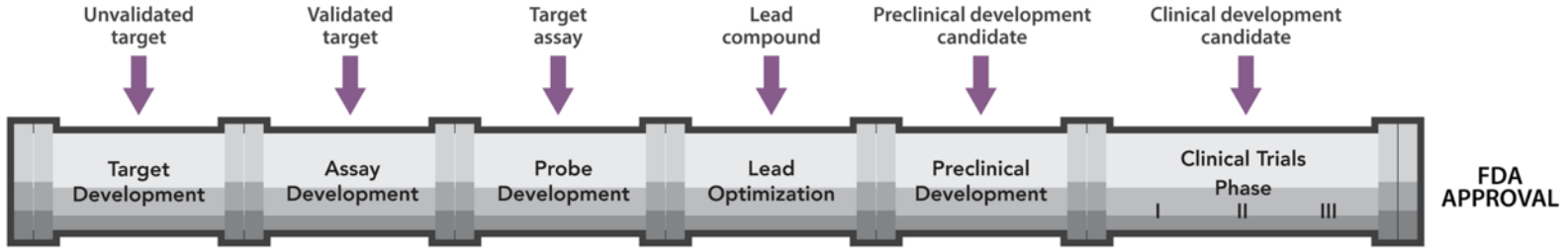
Basic science

NIH Clinical Center

Clinical research

NIH National Center for Advancing Translational Sciences

NCATS | An integrated pipeline for drug discovery & development



Understanding the disease

Clinical trials to prove safety, activity

Assay biology

Medicinal Chemistry

Data Science

Project Management

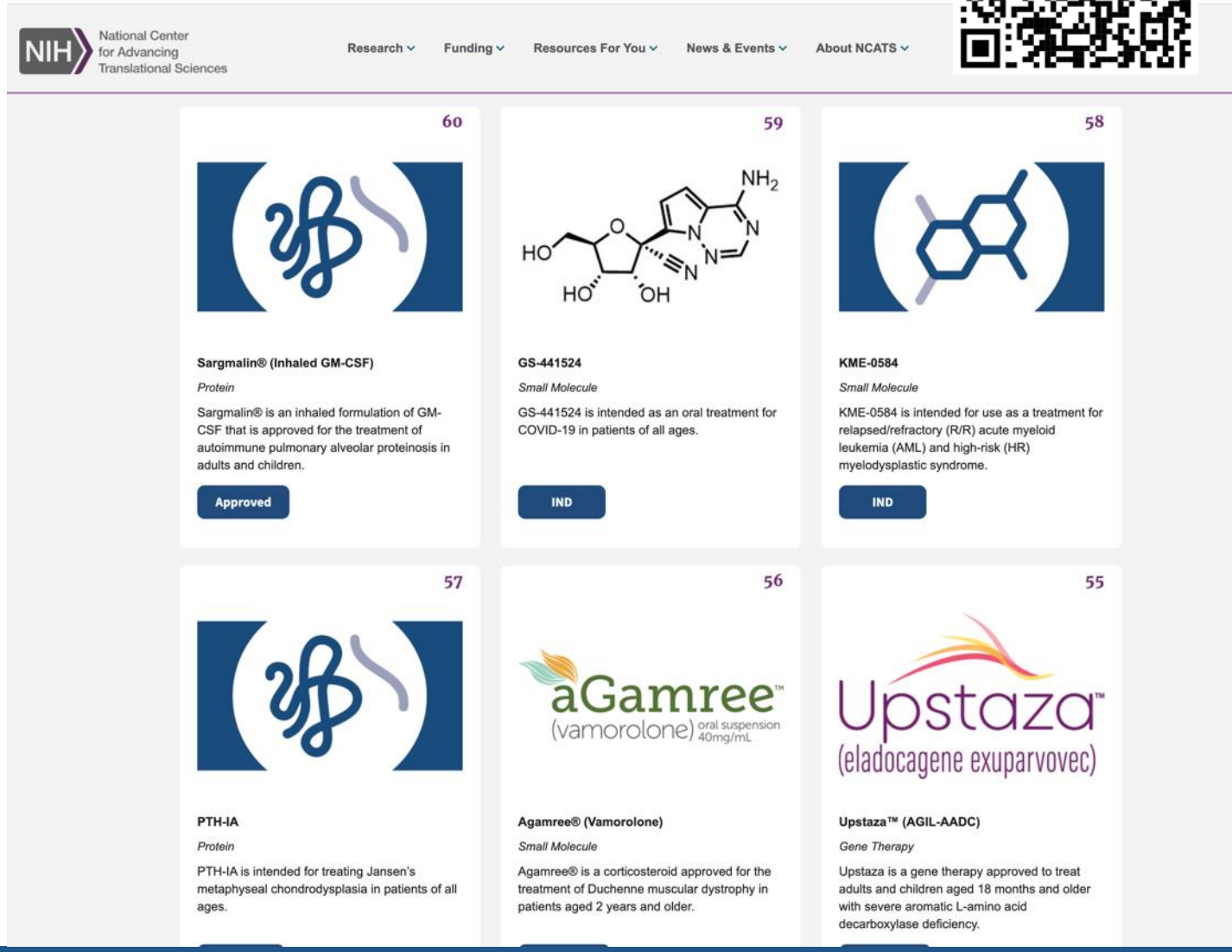
Regulatory Expertise

NCATS Intramural has a record of clinical success

65
INDs

5
drug approvals

Read more about these **success stories** here!



If you've seen one drug repurposing story....
you've seen **one drug repurposing story**

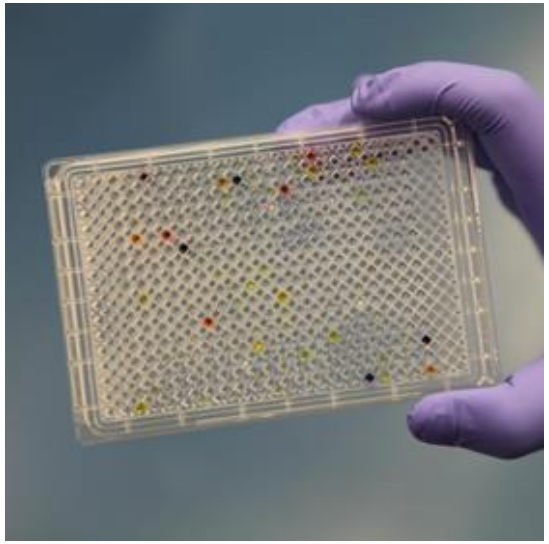
There are many definitions, and many challenges

What it does....
Leverages prior studies
Saves time
Saves money
Can get more treatments to patients more quickly

What it does not do...
Does NOT replace development of new drugs

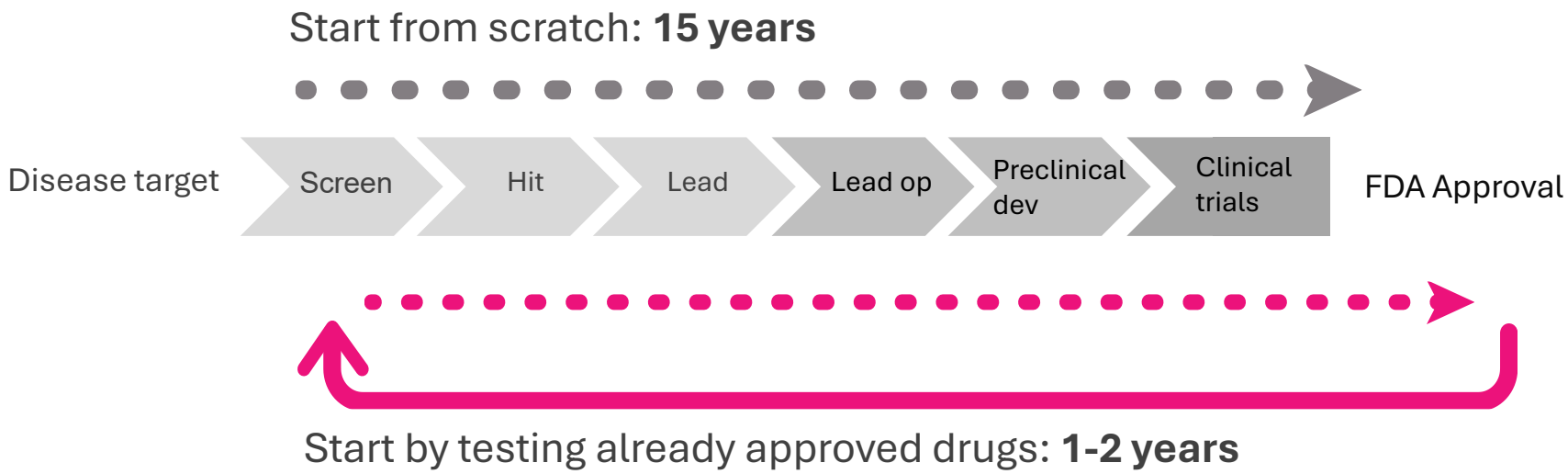
	Patented	Off-patent
Approved	**Market exclusivity** (mechanistic repositioning)	**Generic**
Not approved	**Asset held by someone**	**Abandoned candidate**
Commercial opportunity?	YES	NO
Freedom to operate for repurposing?	NO	YES

Repurposing is an efficient strategy for drug development



NCATS Pharmaceutical Collection (NPC)

Since 2009

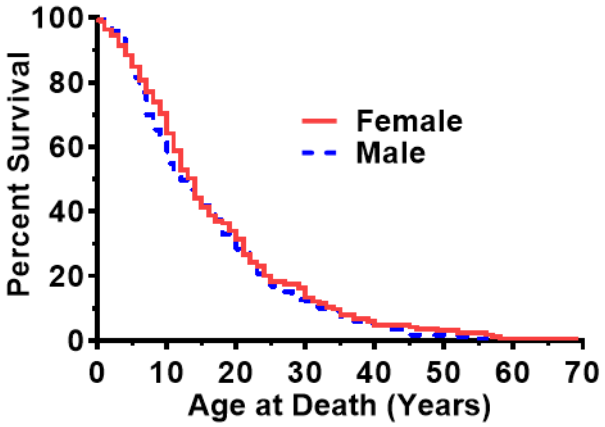


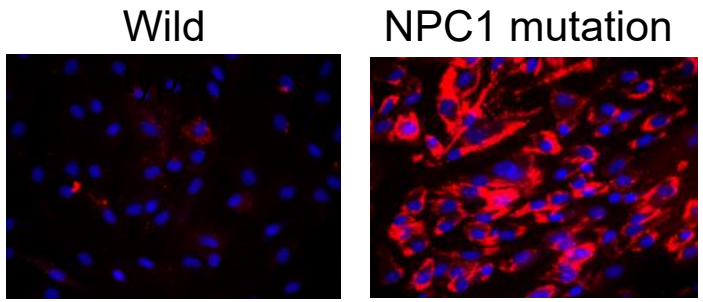
- Contains 3,000 drugs approved for use in US, Europe, Japan, Australia and Canada
- Much is known about these compounds, how they work and how they behave in patients
- Clinical trial candidates emerge from testing these approved agents

Cyclodextrin for Niemann-Pick C Disease

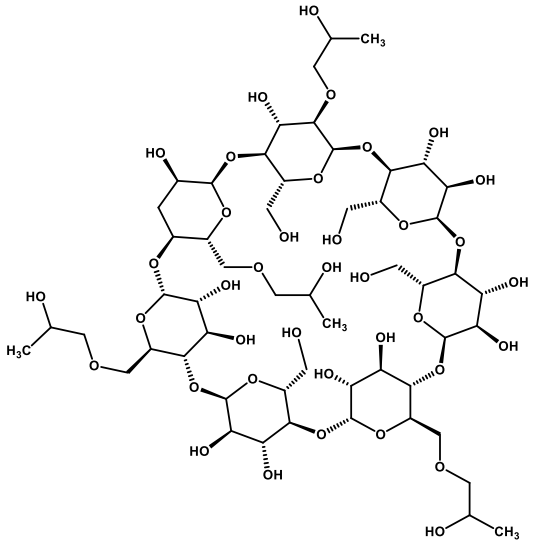
Rare Disease

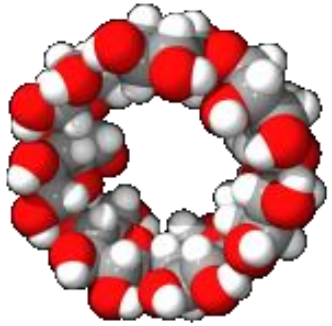
- Autosomal recessive, progressive, lethal, neurodegenerative disorder (*NPC1/NPC2 mutation)*
- Incidence: ~1/100,000
  - Late Onset 1/20,000-1/40,000
- Progressive neurological impairment
  - Cerebellar ataxia
  - Cognitive impairment and dementia





Lysosome size enlarged in NPC1 cells.
Red: lysosome, Blue: nuclei





2-hydroxypropyl-b-cyclodextrin (HPBCD)

Repurposing candidate

Original use: Pharmaceutical excipient to increase solubility of poorly water-soluble drugs

Repurposed use: Niemann-Pick C disease

Beta-cyclodextrin is found in the FDA "generally recognized as safe" (GRAS) list and its derivative is in the FDA's list of inactive pharmaceutical ingredients

Cyclodextrin for Niemann-Pick C Disease

Project Milestones

NIH National Center for Advancing Translational Sciences

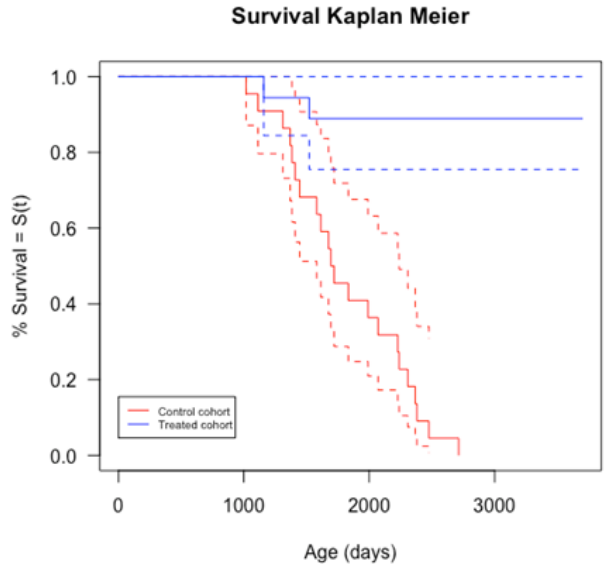
NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

NIH Clinical Center

- 2006 | **Natural History Study** (Dr. Forbes (Denny) Porter)
- 2011-2013 | **HP-β-CD Pre-Clinical Studies**
  - **Biomarker/Bioanalytical Assays**
  - **Chemistry and Manufacturing**
  - **Toxicology Studies**
  - **Regulatory Support**
- 2013-2015 | **Phase 1/2 Clinical Trial (NIH CC)** NIH Clinical Center
- 2022-2023 | **Phase 2/3 Efficacy Trials (Pharma)** Vtesse, SUCAMPO The Science of Innovation, Mallinckrodt Pharmaceuticals
  - | **Early Infantile Trial (<2 yr old, Pharma)** Mandos® By Beren Therapeutics, a Public Benefit Corporation
- 2025 | **New Drug Application Submitted**

FDA Breakthrough Therapy Designation

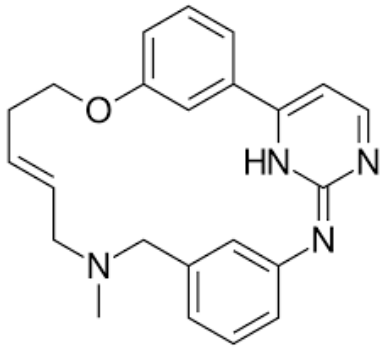
Early Infantile NPC1 Survival



Mandos® By Beren Therapeutics, a Public Benefit Corporation

Beren, Through its Subsidiary Mandos, Submits New Drug Application to U.S. FDA for Adrabetadex in Infantile-Onset NPC

Identifying new uses for cancer drugs



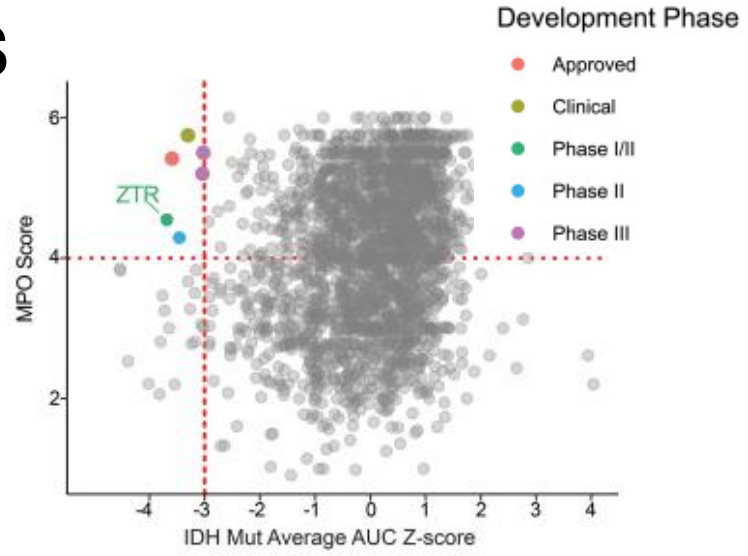
Zotiraciclib

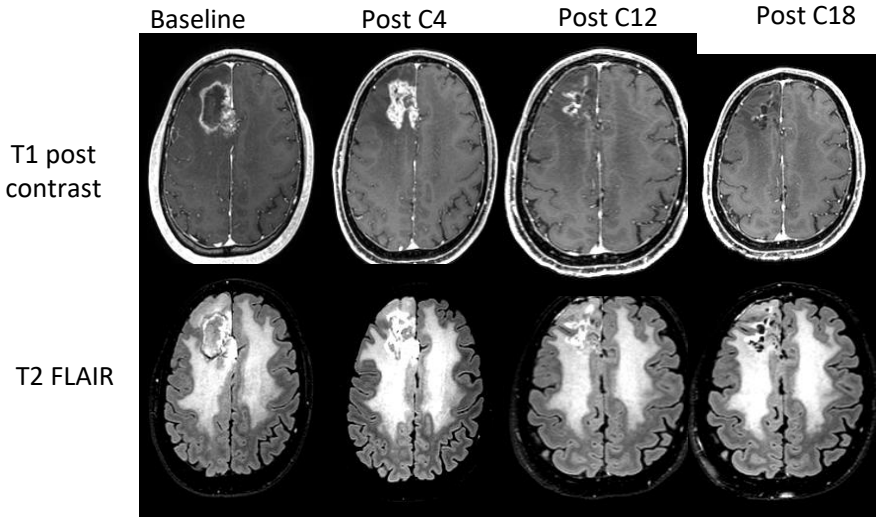
Repurposing candidate

Original use: Potent oral kinase inhibitor for the treatment of cancer

Repurposed use: Recurrent high-grade glioblastoma multiforme (GBM)

- Recurrent high-grade glioma has MST < 1yr
- Mutation in IDH1 or IDH2 is a key ‘biomarker’
- Tested 2,700 cancer ‘drugs’ against six patient lines





FDA grants fast track designation to zotiraciclib for the treatment of recurrent high-grade glioma

NCATS Translator for Precision Medicine Research

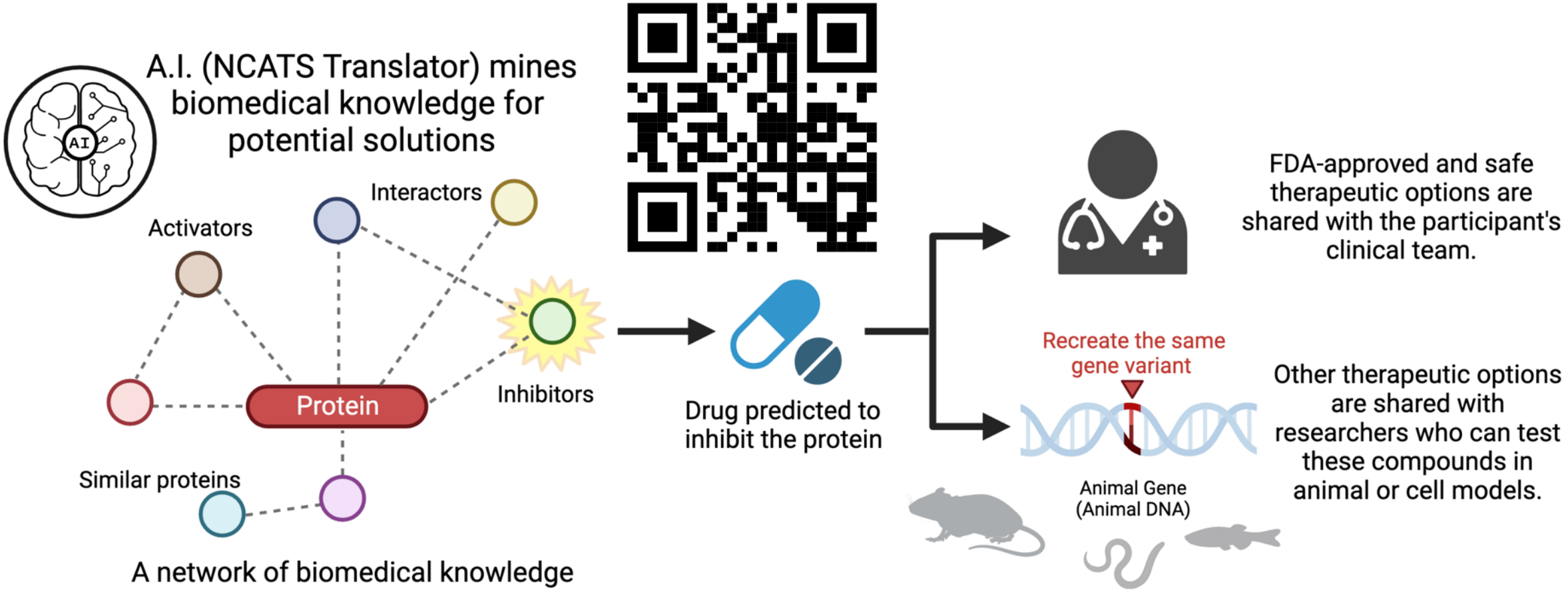


Image courtesy of Andy Crouse, BMA

ui.transltr.io

SHINE Syndrome

An NCATS Repurposing Case Study

National Center for Advancing Translational Sciences

The University of Alabama at Birmingham

SHINE syndrome, also known as DLG4-related synaptopathy, is an extremely rare neuro-developmental disorder characterized by:

Sleep Disturbances

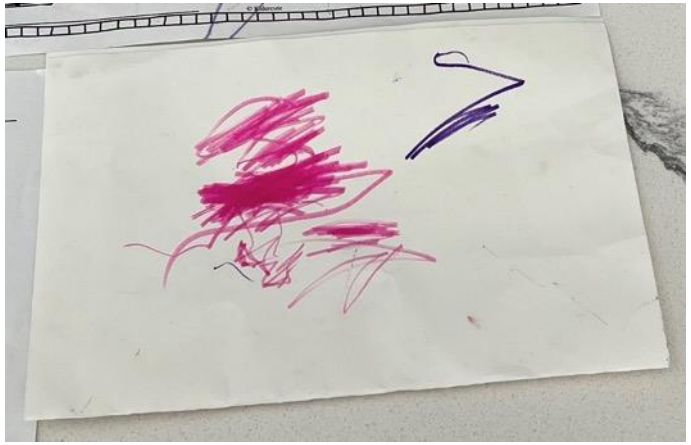
Hypotonia

Intellectual Disabilities

Neurological Disorders (e.g. motor disruption)

Epilepsy

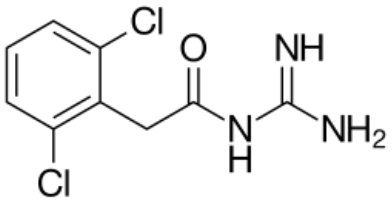
Drawings from a young SHINE patient, treated with guanfacine



Before

After (5 months later)

Translator tools returned many potential treatments, including →



Guanfacine

Repurposing candidate

Original use: Common blood pressure treatment

Repurposed use: SHINE syndrome, *a* rare neurodevelopmental disorder

NCATS Translator for Precision Medicine Research

DeSanto-Shinawi syndrome (DESSH)

- Recent report by KARE 11 in Minneapolis focusing on Jorie, patient with a rare chromosomal deletion including the gene WAC (WW domain-containing adaptor with coiled coil)
- Investigators at the Mayo Clinic used Translator tools to find a potential treatment.
- Jorie's WAC protein has been restored to typical levels

KARE 11 news story

Genetics in Medicine Open article

Normal WAC gene expression pattern based on Human Protein Atlas and displayed in PHAROS

MAYO CLINIC

Laura Lambert, PhD
Whitney Thompson, MD

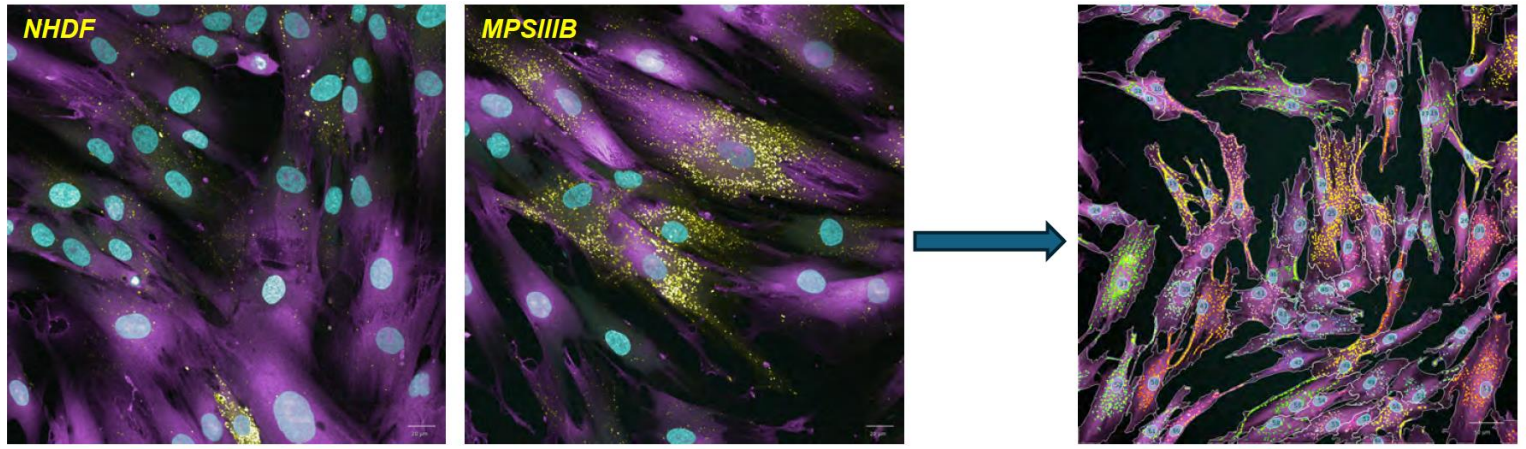
Challenges with generalized prediction

Assay: Sanfilippo syndrome is classified as a lysosomal storage disorder (LSD). Lysotracker for detection and quantification of lysosomes

- LysoTracker Red DND-99 – a commercially available cell-permeable red fluorescent dye that stains acidic compartments.
  Can use this to assess lysosome number, localization, size.

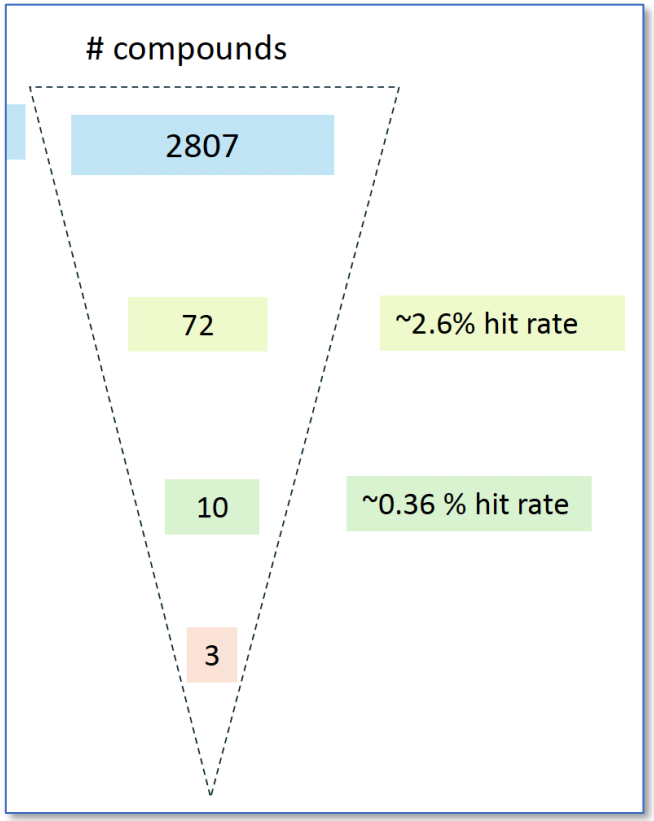
- High-content imaging in 384-well plates

Developed an analysis pipeline



Teal=Nuclei ; Yellow=Lysotracker Red
Purple=Cell Mask

Kathleen McDaniel and Zeenat Shyr

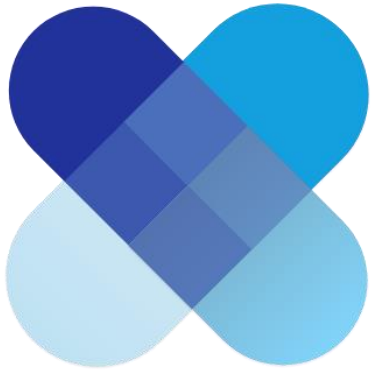


"The child that the cell line came from has been on drug for 2 months now, increasing dose every 2 weeks. The child has gone 2 years without formal communication. 2 weeks ago, out of the blue, he started simple sign language. This has built up over the past 2 weeks to include strings of 6 signs to tell his mom which episode of the Disney channel he wants to watch".

THANK YOU

matt@nih.gov

CURE ID: A Drug Repurposing Tool for Areas of Unmet Medical Need



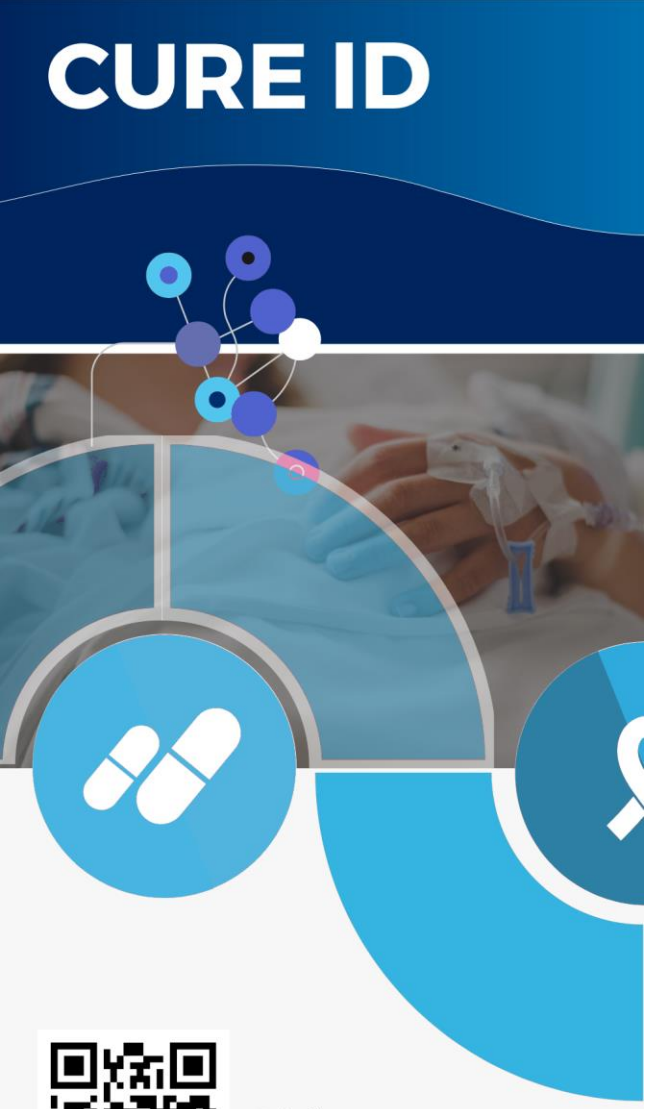
Heather A. Stone, MPH
Email: heather.stone@fda.hhs.gov
August 5, 2026

What is CURE ID?

- A **website** and **mobile app** developed by FDA and NCATS/NIH
- Designed to capture **de-identified** treatment experiences of **healthcare providers and patients/care partners** for diseases where we don't have good treatments
- **Crowdsources** experiences with off-label treatments
- Serves as a **treatment registry of repurposed drugs** for the community to review efficacy data for treatments that are tried in clinical practice

FDA U.S. FOOD & DRUG ADMINISTRATION

NIH National Center for Advancing Translational Sciences



Objectives

- To **identify signals** of potentially safe and effective treatments that can then be **studied further** in appropriate trials and studies

- To provide physicians and patients **real-time information** where no FDA-approved drugs are available

Ideal Use Cases

- Diseases **where RCTs are difficult or impossible** (e.g., ultra-rare diseases)
- Diseases/drug development where there are **insufficient financial incentives**
- **Infectious disease outbreaks** where there is limited time for novel drug discovery and clinical trials and need for rapid, real-time dissemination of treatment information

CURE ID Program History

2012 — CURE ID Conceptualized

Collaboration with NCATS/NIH begins, and website starts to be designed

2015 — Mobile App Developed

Supported by the HHS IDEA Lab and user-tested around the world

2019 — Global Launch to ID Clinicians

CURE ID launched formally at FDA–NCATS–RUF Off-Patent Repurposing Conference

2020 — Public–Private Partnership

CDRC launched as PPP convened by C-Path and recruits dozens of partner orgs

2021 — EHR Automated Extraction

$8.3M grant Automated EHR extraction COVID-19 and future outbreaks

2022 — Patient & Caregiver Reporting

New reporting platform launched to expand users and get patient perspectives

2023 — Platform Expansion

Rare Cancer and Rare Genetics Case Report Forms added to platform

2024 — Preliminary Case Targets Reached

500+ patient & clinician reports 115,000 EHR cases CDRC concludes

2025 — Need for CURE ID Receives Press

Featured in The Washington Post Michael Lewis series “Who is Government?”

2026 — National Conversation Continues

Featured on NPR’s Freakonomics Radio to discuss Off-Patent Repurposing

CURE ID is an FDA and NIH-led, Patient-Centered Innovation Delivering Real-World Impact for Unmet Medical Needs

386
diseases with at least 1 case report

115,000
cases extracted from electronic health records

5,500
cases extracted from published literature

1,500
clinician and patient/ caregiver-submitted cases

Including treatments of ultra-rare diseases

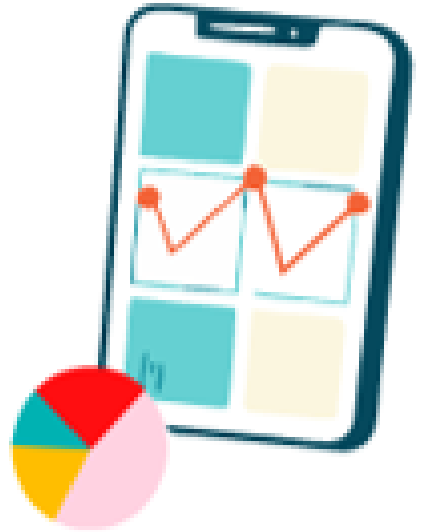
Primary Functionalities of CURE ID

SHARE

Share your treatment experience

EXPLORE

Explore what others have tried



What CURE ID Offers

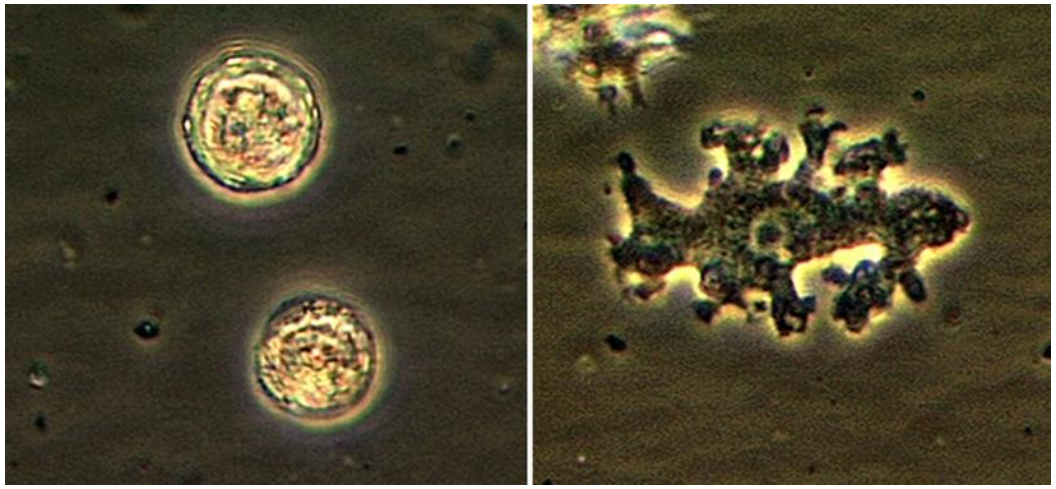
- Provides users a **mechanism to rapidly share their treatment experiences** with a global community and to capture and maintain clinical knowledge in a structured way that is **supported by the government as a public good**
- Collects **fully de-identified data** and immediately aggregates it
- Makes the **data openly accessible to all for free**
- **All cases are reviewed** before public posting to improve quality

Highlighting the Power of CURE ID

When can a case report really make a difference?

The “Brain-Eating” Amoeba

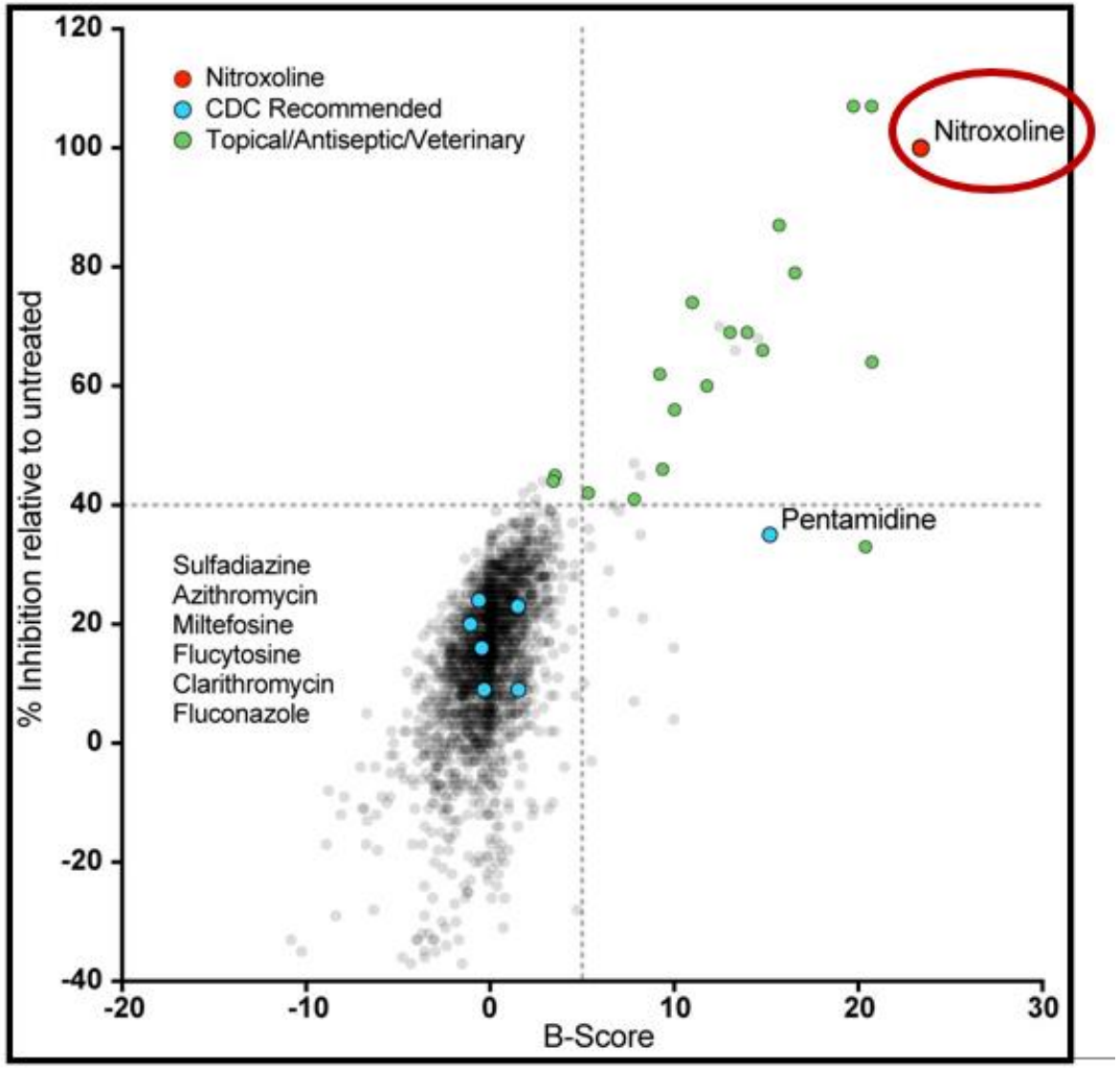
- *Balamuthia mandrillaris* is an environmental amoeba, one of three “Free-Living Amoeba”
- Causes severe meningoencephalitis
- **Fatality rate >95%** when encephalitis
- No effective treatment
- **Less than 200 cases ever reported**



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

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

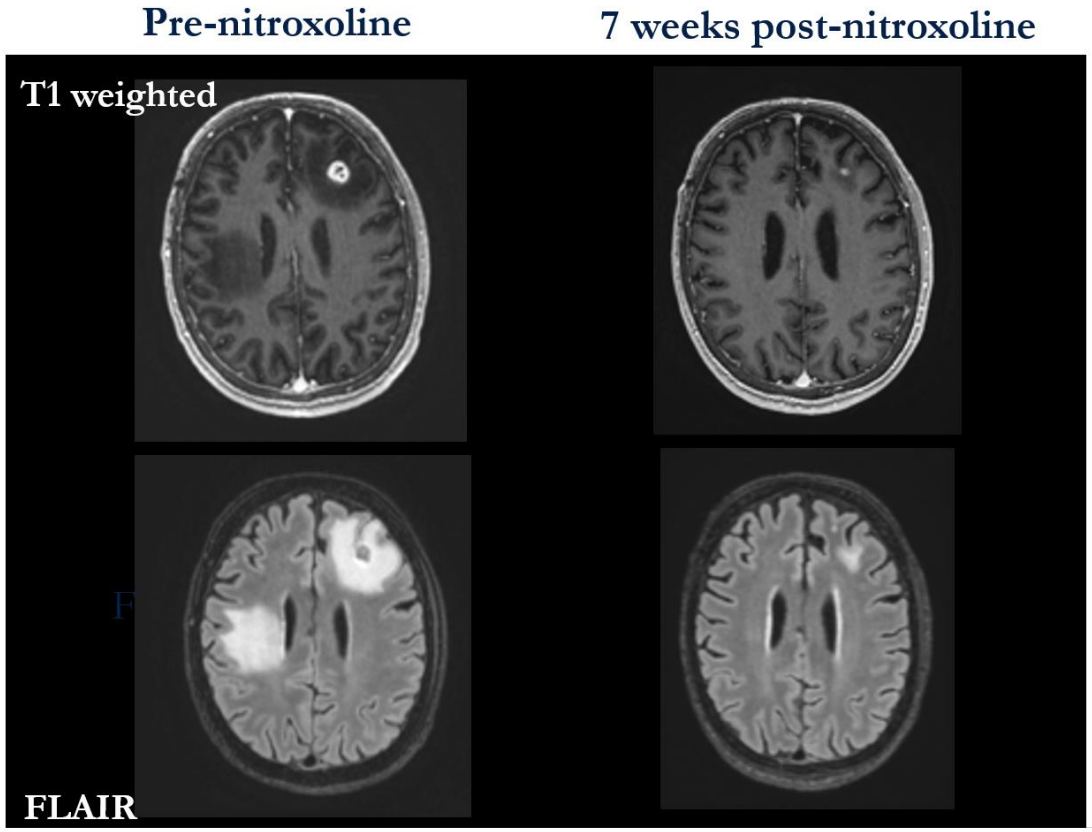
High-Throughput Screen Identifies Nitroxoline



- Nitroxoline is a quinolone antibiotic with decades of safety data
- Has been approved in Europe for 50 years for urinary tract infections; is not approved in US
- Preclinical Findings Published in 2018 showed remarkable, unanticipated activity

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.

First Patient Treated with Nitroxoline



- Patient is dying of Balamuthia and in multi-organ failure from other toxic meds
- Finds pre-clinical article and obtains Nitroxoline under eIND as last-ditch effort
- Patient has remarkable recovery and is discharged alive to the community

Spottiswoode N, et al. 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.

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

A little girl with *Balamuthia* is dying

Photos used with permission of the child's parents

- Child is dying of Balamuthia while on CDC-recommended regimen
- Acknowledgement in Dr. Spottiswoode's article leads to contact by patient's mother
- Helped her doctor obtain eIND for nitroxoline, as medication approved in Europe but not US
- Negotiated approval by FDA of bridge supply of drug from UCSF

Her Remarkable Recovery

- Child showed robust improvement clinically and radiologically and has now recovered and has been able to stop all meds
- Mother submitted case to CURE ID
- **For several years, CURE ID was the only place this case experience was publicly available**

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

It Works for Some, but Not All

- **There have been patients** with Balamuthia who received the drug **who did not survive**
  - Many of these cases have been ex-US and have involved long delays in getting access to the medication

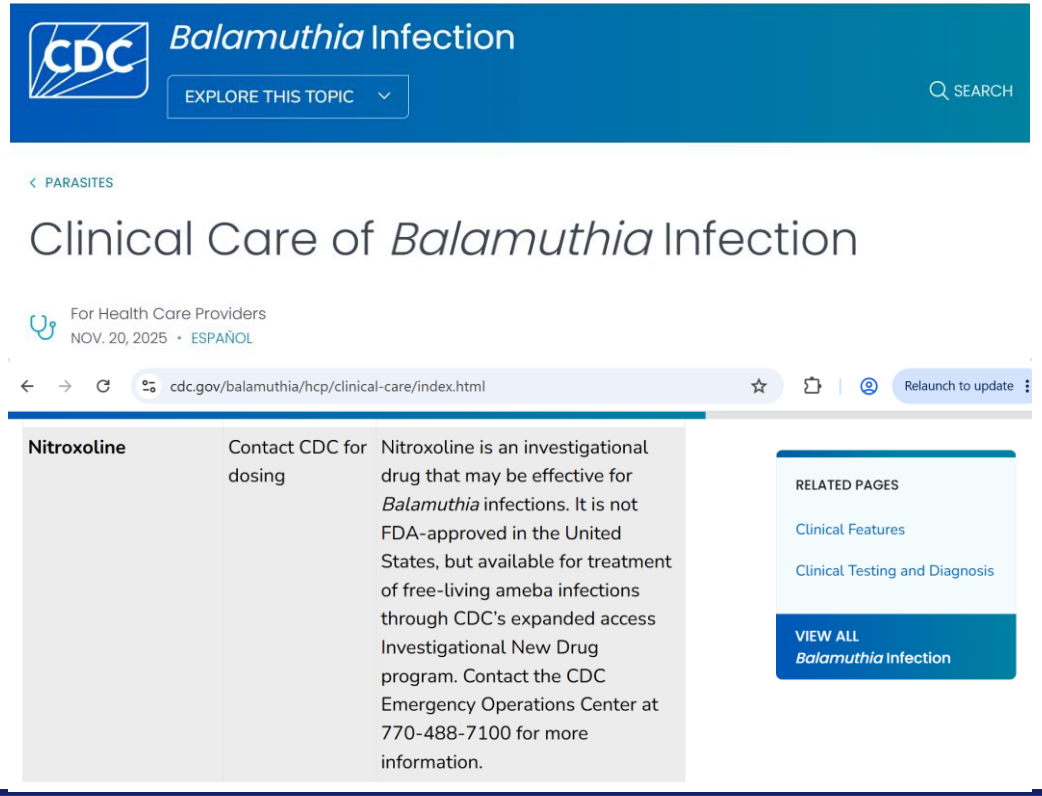
- **The best estimate is that 50% of patients with this infection are now surviving, compared to 5%**

Why the 2nd Case was as Important as the 1st

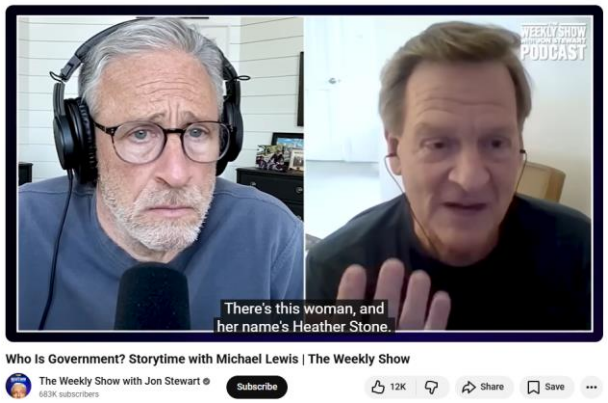
- **CDC is now recommending nitroxoline to all patients with free-living amoeba infections based on these two case reports** and pre-clinical/ mechanistic findings

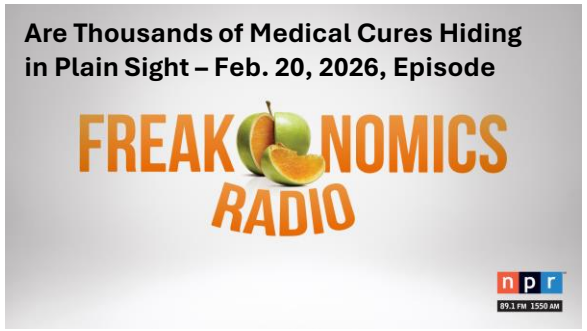
- **Would not make recommendation based on only one case**

- With our encouragement, they **have opened an intermediate IND to provide a supply of the drug that is housed in the US** so it can be administered to patients rapidly upon diagnosis

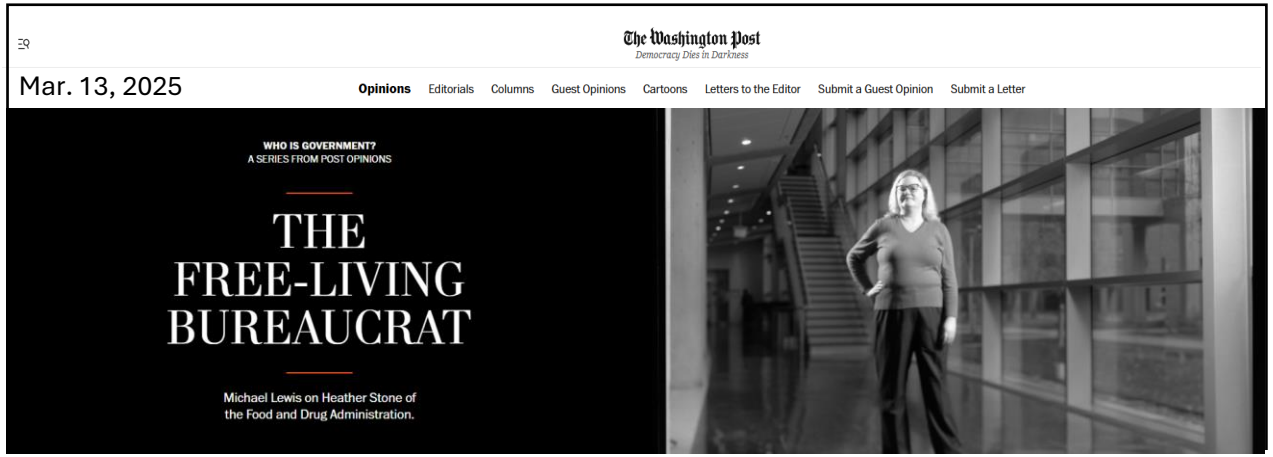


Response has shown the public wants to see FDA facilitating repurposing for unmet needs





Author Michael Lewis went behind the scenes to meet…



To read more about this incredible case, visit: https://www.washingtonpost.com/opinions/interactive/2025/michael-lewis-fda-who-is-government/

Lessons from the *Balamuthia* experience

- **Translating basic science discoveries to treatment impacting patients takes time**, especially for rare diseases and requires a clinician to take a leap of faith
- **Case reports can bridge the gap**, helping surface promising treatments when trials aren't feasible or haven't yet been conducted
- **Open data sharing accelerates learning**, spreading treatment insights
- **Greater participation is needed** to unlock CURE ID's full potential

Where do we go from here?

- Need to **envision the full pipeline** from preclinical and initial case signal generation to regulatory approval and determine what role FDA can play
- **Expand patient, caregiver, and clinician-reporting**, along with EHR and published case extraction, including through exploration of the use of AI tools to facilitate
- Proof-of-concept needs to be demonstrated with **clinical trials of signals generated in CURE ID**

How I Envisage the Drug Repurposing Pathway for Unmet Needs

Off-Label Use or Preclinical Research

Initial Discovery

One method:
CURE ID
(a RWD treatment registry)

Hypotheses generated and selected for formal testing

Clinical Trials

Testing & Evaluation

FDA Partners with NIH to design and fund needed trials

Trials with positive outcomes may be used to support regulatory approval

FDA Approval for New Indication

Regulatory Approval

Leverage Existing Legislation to Help Seek Approval of New Indications for Conditions with Substantial Evidence

CURE ID

Help us turn treatment insights into action

Visit CURE ID at https://cure.ncats.io or download the mobile app

FDA U.S. FOOD & DRUG ADMINISTRATION

NIH National Institutes of Health

Session 2

Selection Criteria & Prioritization

REAGAN-UDALL FOUNDATION FOR THE FDA

Susan Cantrell, RPh, MHL
Academy of Managed Care Pharmacy

Caroline Huang, PhD
FDA

Emily Einstein, PhD
American Society of Addiction Medicine

Huong Huynh, PhD
Critical Path Institute

Pam Gavin, MBA
National Organization for Rare Diseases

Janet Woodcock, MD
Former FDA Acting Commissioner

Request for Information on Drug Repurposing: Preliminary Analysis and Next Steps

Caroline J. Huang, PhD

Supervisory General Health Scientist

Office of the Center Director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration

Disclaimer

- This presentation reflects the views of the author and should not be construed to represent FDA's views or policies.
- The author has no conflicts to disclose.

Agenda

- RFI at a Glance
- RFI Deep(er) Dive
- Next Steps

Timeline

May 12, 2026	RFI publishes in Federal Register
June 11, 2026	Deadline for initial public comment period
June 11, 2026	Comment period extended another 30 days; Reagan-Udall Foundation/FDA public meeting announced
July 13, 2026	Deadline for extended public comment period
July 21, 2026	Deadline for public comment requests for Reagan-Udall Foundation/FDA public meeting
August 5, 2026	Reagan-Udall Foundation/FDA public meeting

What We Asked

On May 12, 2026, FDA published a Request for Information in the Federal Register on "Drug Repurposing for Unmet Medical Needs." FDA requested public input on four topics:

PRIORITY AREAS

Do the proposed priority areas align with your understanding of areas with significant unmet medical needs and high repurposing potential?

APPROACHES TO IDENTIFICATION

What innovative approaches could be used to identify new drug repurposing opportunities?

REPURPOSING CANDIDATES

What candidates for drug repurposing have the greatest potential for effective treatment of particular identified medical conditions?

BARRIERS & OPPORTUNITIES

What are the key barriers to drug repurposing for stakeholders, and what specific actions could be taken to address them?

RFI AT A GLANCE

Preliminary Analysis Process

608
Total number of public comments received

547
Deduplicated public comments (removing ≥95% textual duplicates)

420
Comments with ≥ 1 drug candidate recommendation (deduplicated)

132
Distinct recommendations for drug candidate-disease pairings

167
Public comments with ≥1 attachment (deduplicated)

2
Total number of additional comments received from federal partners

INITIAL EXPLORATORY REVIEW PROCESS

1. Organize input
2. Screen and deduplicate
3. Extract and standardize
4. Validate
5. Synthesize preliminary signals

MANUAL REVIEW WITH HHSGPT SUPPORT

Examples where AI-assisted review helped

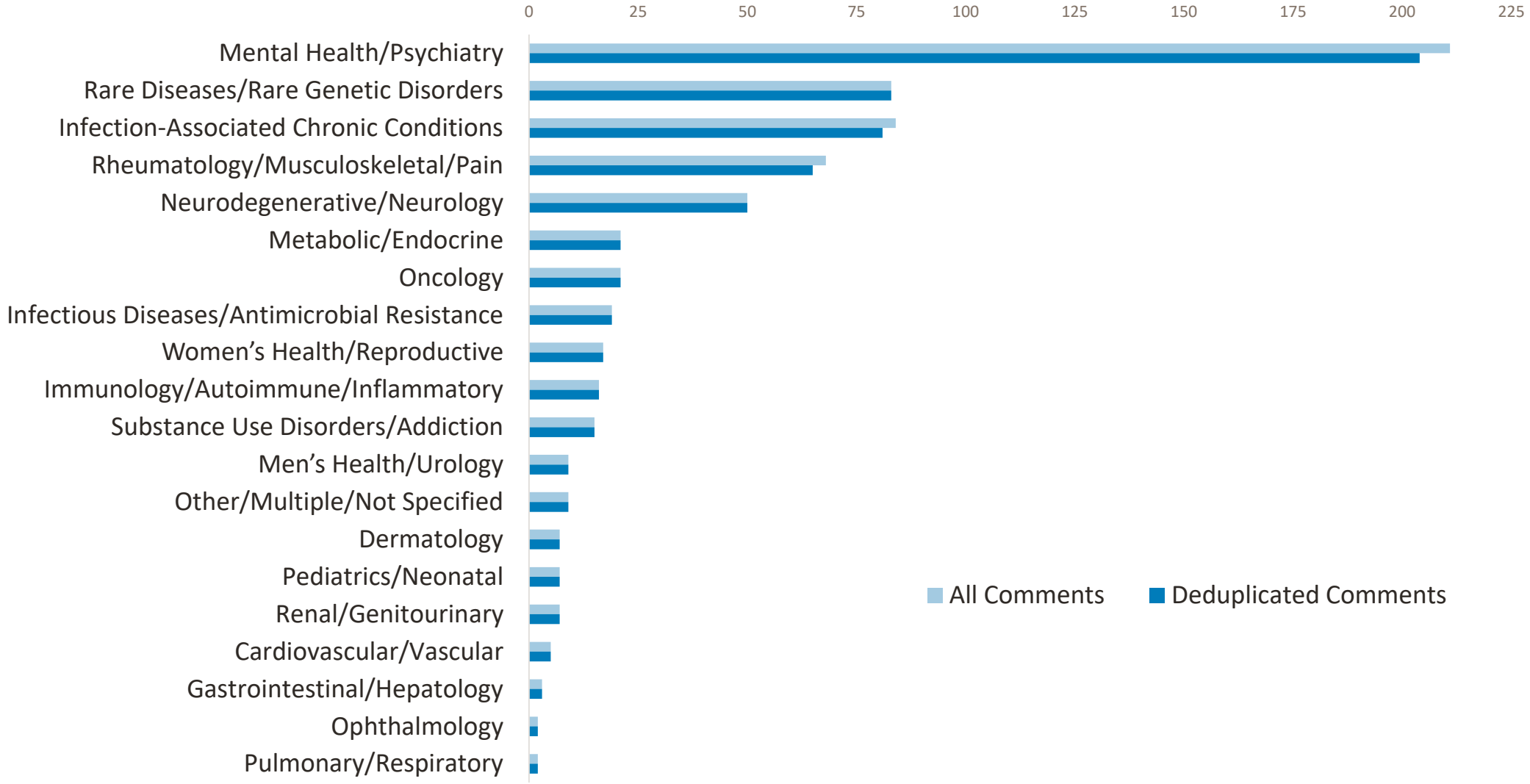
- Text-similarity and duplicate-adjacent screening
- High-level summary of high-frequency drug candidates, disease areas, barriers, and opportunities

Examples where manual QC is (especially) needed

- Drug candidate/disease relationships, especially in long attachments and dense technical submissions

This information reflects preliminary analysis and should not be interpreted as final findings; subject to further review and validation.

Priority Disease Areas



This information reflects preliminary analysis and should not be interpreted as final findings; subject to further review and validation.

RFI DEEP(ER) DIVE

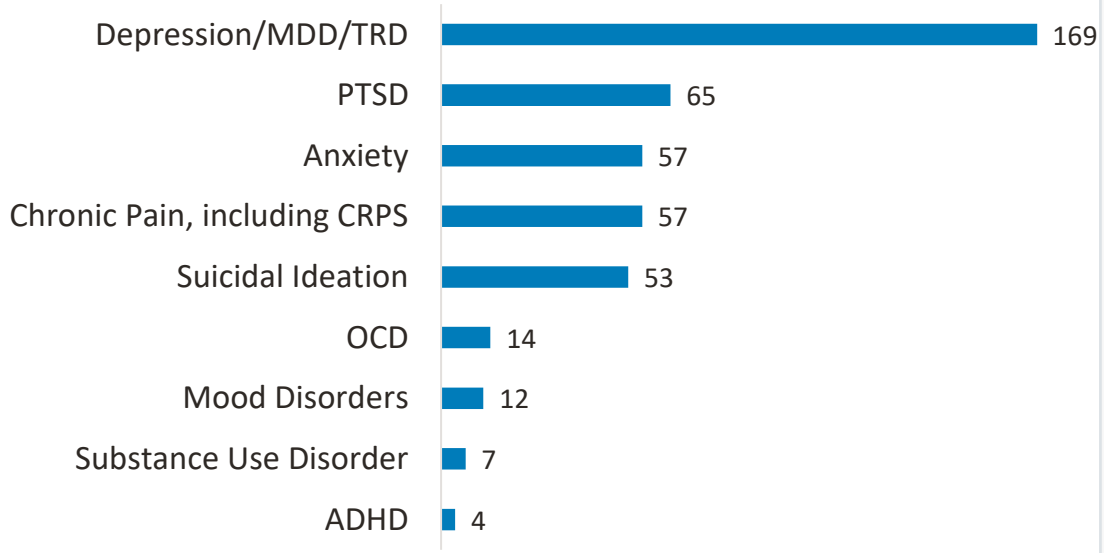
High-Volume Signal: Ketamine

223
Deduplicated Comments

~40%
Of All Deduplicated Comments

16
Proposed Uses

Top Proposed Uses for Ketamine



POINTS OF INTEREST

- Most frequently recommended drug candidate in the docket, suggested for a variety of mental health and pain conditions and substance use disorders.
- A subset of comments recommending ketamine used verbatim or substantially similar advocacy language, e.g., a public campaign by Ember Health.

This information reflects preliminary analysis and should not be interpreted as final findings; subject to further review and validation.

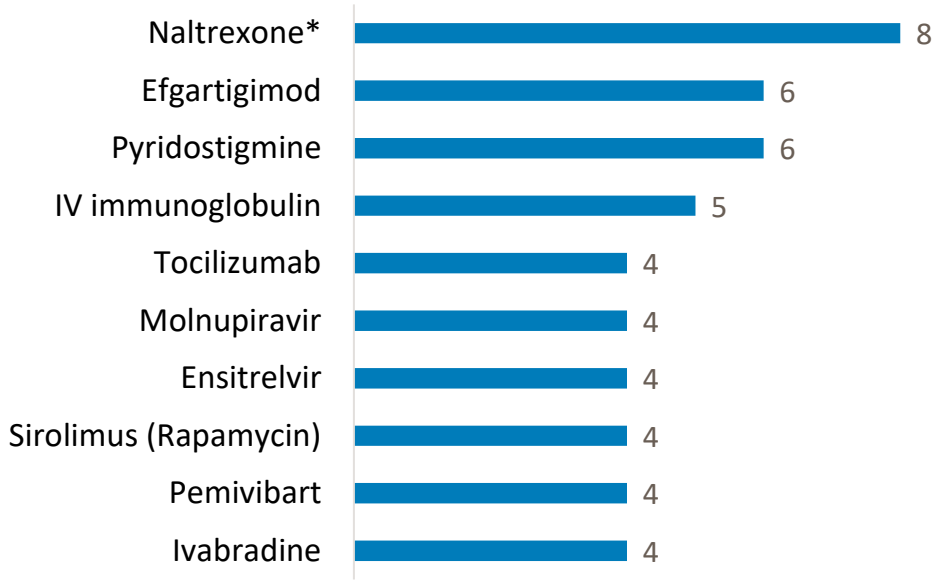
High-Volume Signal: Long COVID

139
Deduplicated Comments

~25%
Of All Deduplicated Comments

23
Distinct Candidate Recommendations

Top 10 Drug Recommendations for Long COVID



*Mostly low-dose

POINTS OF INTEREST

- Comments related to Long COVID were wide-ranging, with recommendations distributed across many drug candidates, mechanisms of action, and evidence types.
- A subset of comments on Long COVID used verbatim or substantially similar advocacy language. Some of these referenced CURE ID using substantially similar framing and recommendations for support.

This information reflects preliminary analysis and should not be interpreted as final findings; subject to further review and validation.

RFI DEEP(ER) DIVE

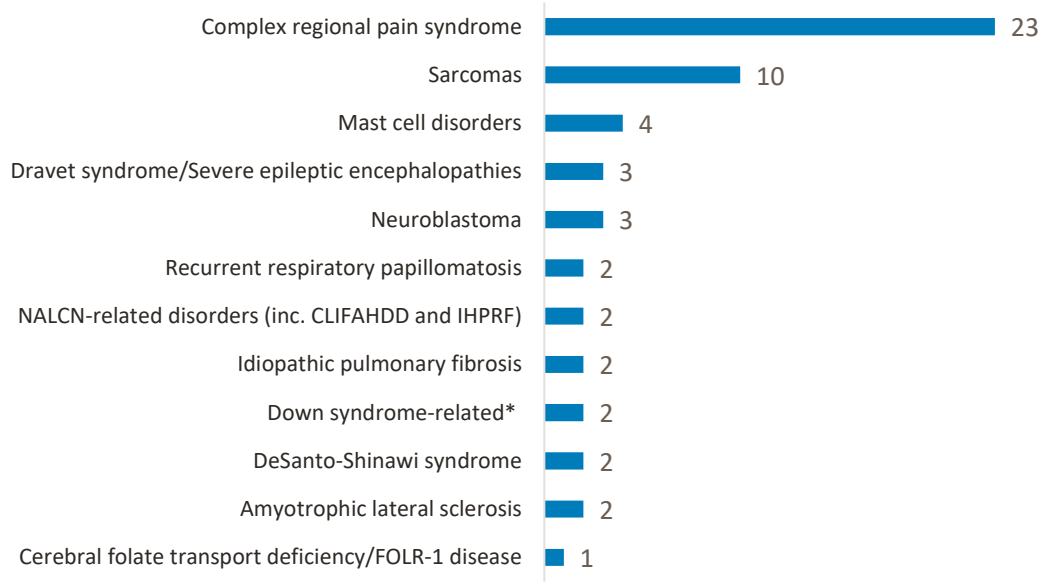
High-Volume Signal: Rare Diseases

93
Deduplicated Comments

~20%
Of All Deduplicated Comments

82
Distinct Diseases Mentioned

Top 12 Rare Diseases Mentioned in the RFI



* Includes Down syndrome-related Alzheimer's disease

POINTS OF INTEREST

- Wide variety of distinct diseases highlighted in comments with few similar/duplicative comments, which was not particularly surprising given the nature of rare diseases.
- Largest collection of comments were for complex regional pain syndrome (CRPS), largely tied to comments advocating for ketamine.

This information reflects preliminary analysis and should not be interpreted as final findings; subject to further review and validation.

Summary of Barriers and Opportunities

Barriers

- Access and affordability
- Commercial viability
- Evidence and safety
- Regulatory process concerns

Opportunities

- Clinical trial design
- Data and evidence generation
- Partnership and support
- Regulatory and policy clarifications

This information reflects preliminary analysis and should not be interpreted as final findings; subject to further review and validation.

Next Steps

What We're Planning to Do Next

- Complete the RFI analysis, including attachment review and manual validation, and publish on FDA's website
- Develop Candidate Selection and Prioritization Framework, incorporating public meeting and post-meeting written feedback, and publish on FDA's website
- Share additional findings and opportunities for engagement as this initiative progresses

How Stakeholders Can Engage Now

- Submit written feedback on prioritization, selection, and evidence gaps/regulatory barriers to repurposing@reaganudall.org through Friday, August 21
- Share novel uses of existing drugs and explore what others have tried through CURE ID
- Look for Reagan-Udall Foundation meeting report on Foundation's website

This information reflects preliminary analysis and should not be interpreted as final findings; subject to further review and validation.

Acknowledgments

- CDER Office of the Center Director
  - Brian Gac, PharmD
  - Anika Haque, PharmD
  - Bic Nguyen, PharmD
- CDER Office of Medical Policy
  - Mili Duggal, PhD, MPH
  - Heather Stone, MPH
  - Larissa Stabinski, MD, MPH

Session 2

Selection Criteria & Prioritization

REAGAN-UDALL FOUNDATION FOR THE FDA

Susan Cantrell, RPh, MHL
Academy of Managed Care Pharmacy

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Emily Einstein, PhD
American Society of Addiction Medicine

Huong Huynh, PhD
Critical Path Institute

Pam Gavin, MBA
National Organization for Rare Diseases

Janet Woodcock, MD
Former FDA Acting Commissioner

REAGAN-UDALL FOUNDATION FOR THE FDA

Break for lunch

The meeting will resume at
1:15pm Eastern

Session 3

Evidence & Submission Expectations

REAGAN-UDALL FOUNDATION FOR THE FDA

Sundeep Agrawal, MD

FDA

Amy Abernethy, MD, PhD

Highlander Health

Marie Bradley, PhD

FDA

David Fajgenbaum, MD, MSc

Every Cure

Donald Lo, PhD

REMEDi4ALL

Emily Freilich, MD

FDA

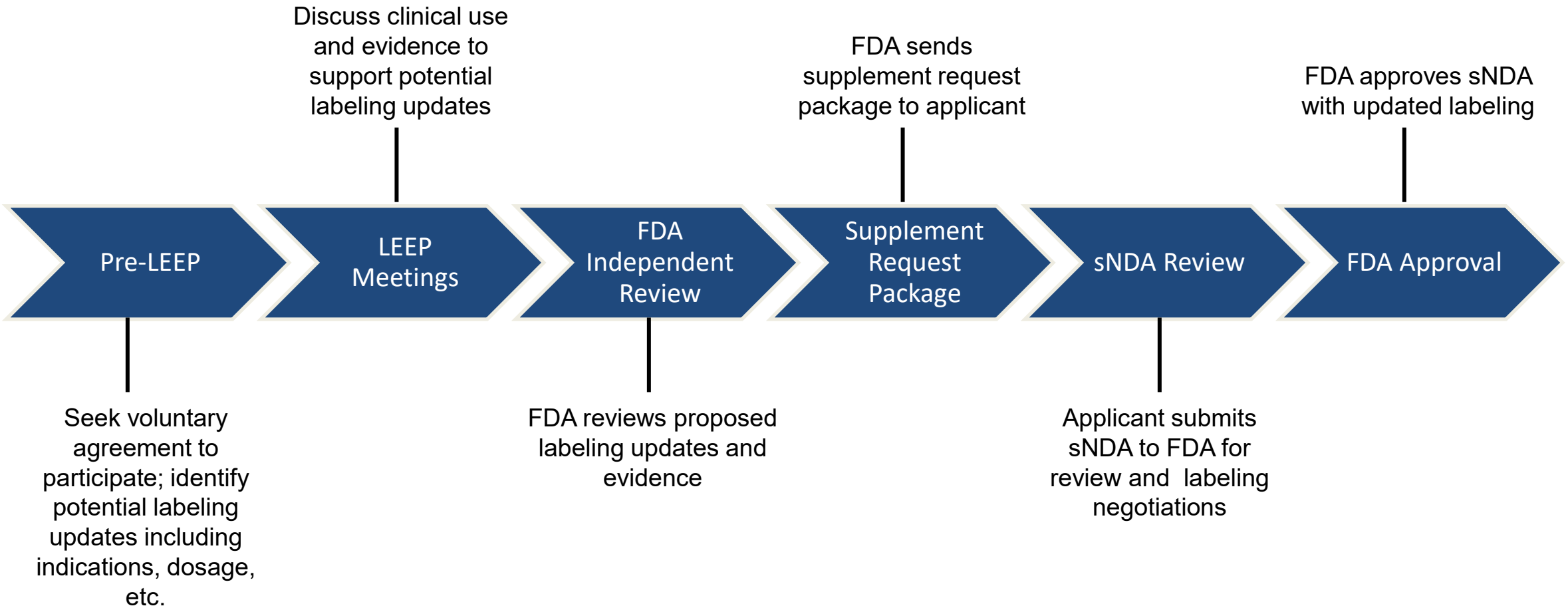
PROJECT RENEWAL
Lessons Learned

Sundeep Agrawal, M.D.
FDA Oncology Center of Excellence
August 5, 2026

What is Project Renewal?

- **A public health initiative to update certain older oncology drug labels**
  - Off-patent drugs that have been used to treat cancer for decades
- **Goal: Provide most accurate labeling information to inform safe and effective use**
  - Establishes repeatable, objective, and scientific processes for efficient labeling updates
  - Creates opportunity to engage the oncology community
  - Provides an educational opportunity for oncology/hematology fellows
- **Labeling updates can:**
  - Expand and/or add indications if there is substantial evidence
  - Remove outdated information
  - Modernize into Physician Labeling Rule (PLR) and Pregnancy and Lactation Labeling Rule (PLLR) format

Project Renewal – The Process



Unique Ability to Expand Indications in Oncology

- Decades of clinical experience in multiple disease settings
- Multiple trials with acceptable endpoints to support labeling updates
  - Large cooperative groups and NCI funding unique to the oncology field (many high-quality trials)
  - Reliable, consistent endpoints (e.g., tumor response rate, overall survival)
- Mechanism of most cytotoxic chemotherapies well-understood and correlated with response measurements
- Well-characterized safety across multiple cancer types and treatment settings

Project Renewal IS:

- An FDA project to update longstanding labels for off-patent products
- Initially only reviewing a subset of high priority indications
- An opportunity to collaborate on a transparent review of evidence

Project Renewal IS NOT:

- A way to expand indications for drugs on patent or with exclusivity
- A review of all possible indications that may be in use
- Related to cost, payment, or coverage decisions

The Role of Guidelines and Compendia in Project Renewal

- Guidelines and compendia ≠ evidence
- Compendia for off-label oncology indications are not definitive:
  - Can lack transparency in evidence evaluation process
  - May cite little current evidence
  - Often lack systemic methods to review or update evidence
- Help prioritize which uses to evaluate further but have limitations that should be considered
- FDA must do its own review of the evidence

Abernethy at al. Ann Intern Med. 2009

Substantial Evidence of Effectiveness

- Quantity of Evidence
  - # of trials and supportive evidence
- Quality of Evidence
  - Adequate and well-controlled trials
- Magnitude and Statistical Persuasiveness of Result
  - E.g., large median OS improvement $p<0.001$
- Source of Evidence
  - Controlled Clinical Trial, Real World Evidence, Published Literature
- Context
  - Rarity of disease, unmet need, additional safety and efficacy data across diseases

Data Source: Published Literature

- Who conducted the study?
- How detailed is the published report?
- How objective are the outcomes?
- Was the analysis prespecified?
- Clinically meaningful and statistically persuasive result?
- Additional internal consistency within trial secondary outcomes?
- Are there multiple studies? External validation?

Does the published report provide enough detail to be considered substantial evidence from an adequate and well-controlled trial?

Project Renewal – Lessons Learned

- Dependent on voluntary participation from sponsors
  - Reducing burden to companies is important to enable voluntary participation
- Evidence often generated with different historical standards
  - Context and quantity of studies can mitigate some of these concerns
- Allocating FDA resources
  - Resource intensive but we are generating process efficiencies
- Successful engagement efforts
  - Bi-directional learning between the community and the FDA

Value of Project Renewal

- More accurate labeling information to allow for safe and effective use of older drugs that are still used frequently
- Modernization of labeling into the PLR/PLLR format
- Increased engagement with oncology community
  - Educational outreach with oncology fellows
  - Potential recruiting opportunities
- Expansion of Project Renewal to other therapeutic areas

Summary

- Candidate drugs have established safety and efficacy
  - Often used for decades
  - Clinical practice patterns supported by strong data (overall survival or other relevant oncology endpoints)
- Compendia and expert guideline recommendations are not enough
  - We review the source references from these guidelines to ensure meeting of statutory requirements
- Potential challenges with extrapolation to other diseases:
  - Is there adequate data to support a claim of effectiveness?
  - Can safety be extrapolated from other diseases when populations are small in size?
  - Will “repurposing approvals” set a precedent that might affect contemporary drug regulation?

Acknowledgements

- Clara Lee
- Esther Park
- Doris Auth
- Evan Bryson
- Angelo DeClaro
- Tamy Kim
- Laleh Amiri-Kordestani
- And many others!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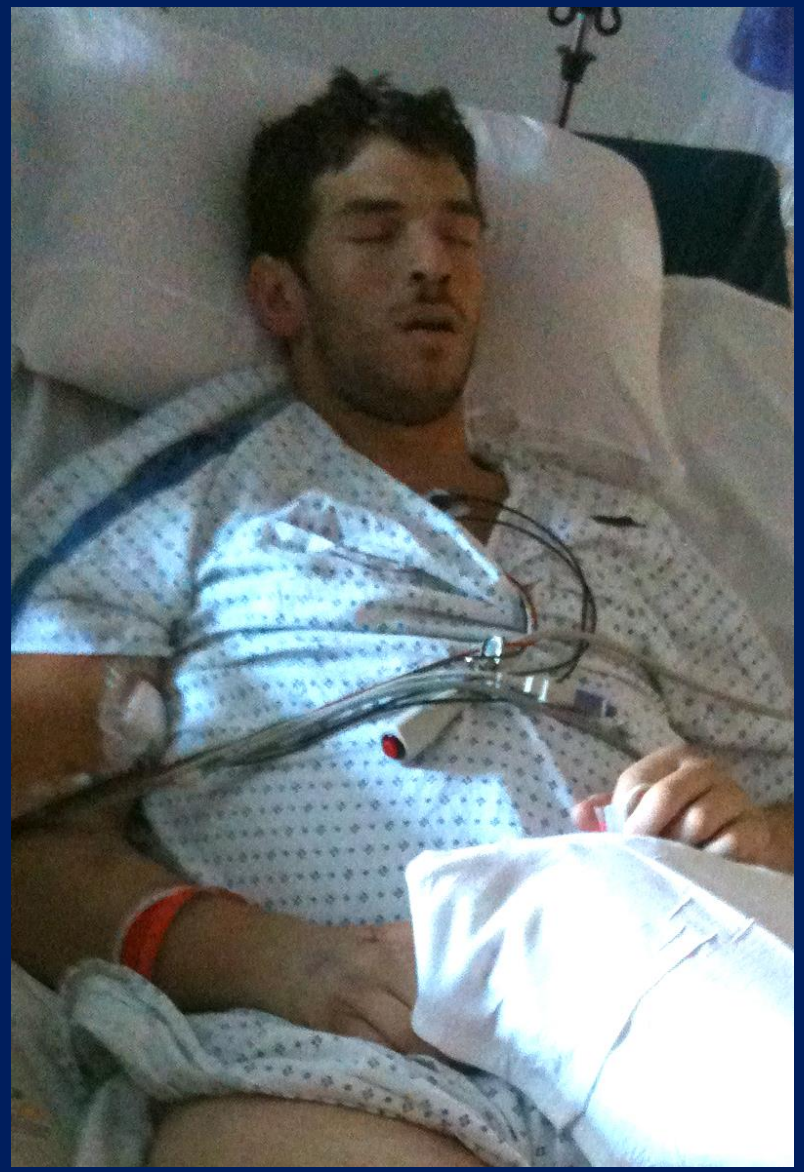
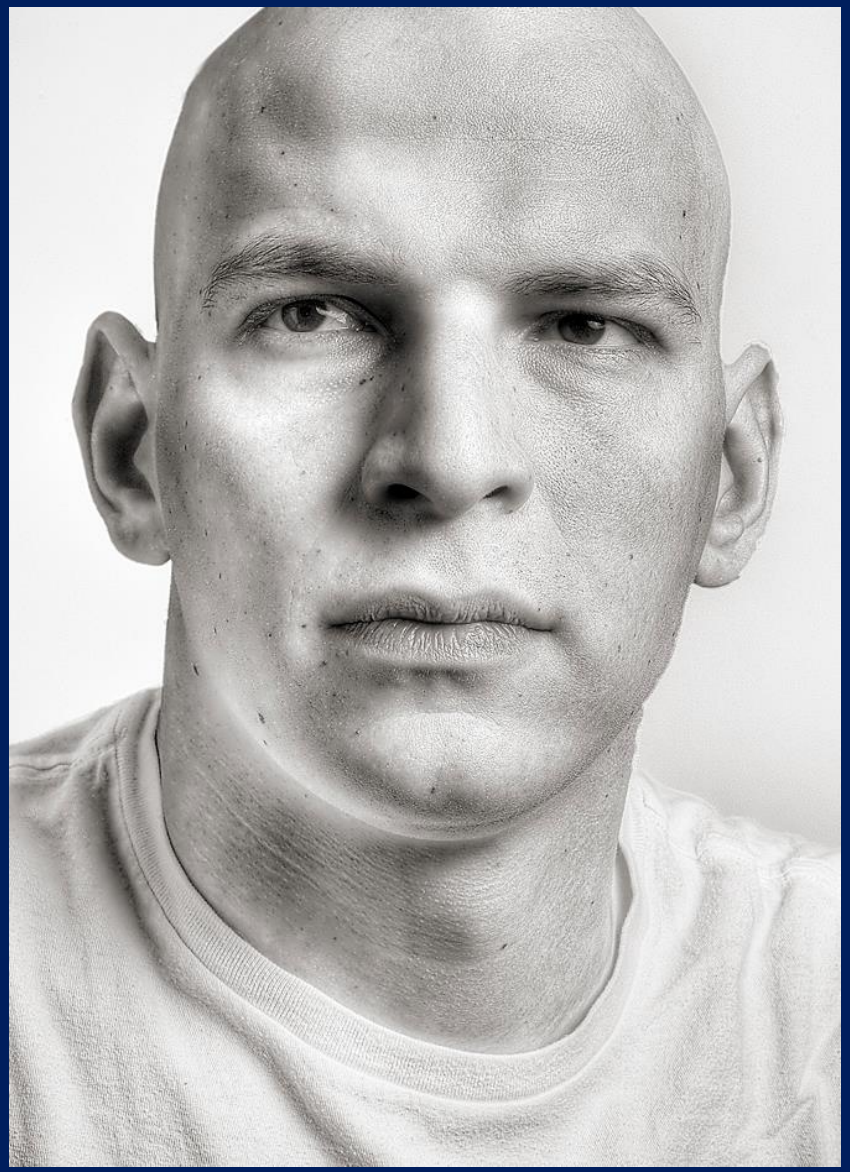
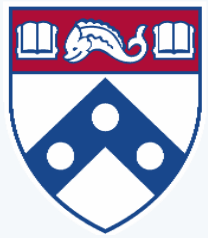
ADMINISTRATION

EVERY CURE

Lessons Learned on Drug Repurposing







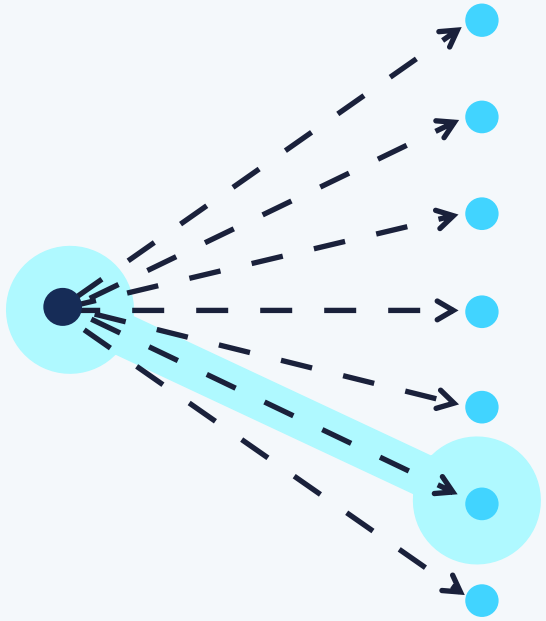

CSTL
Center for Cytokine Storm
Treatment & Laboratory


EVERY
CURE

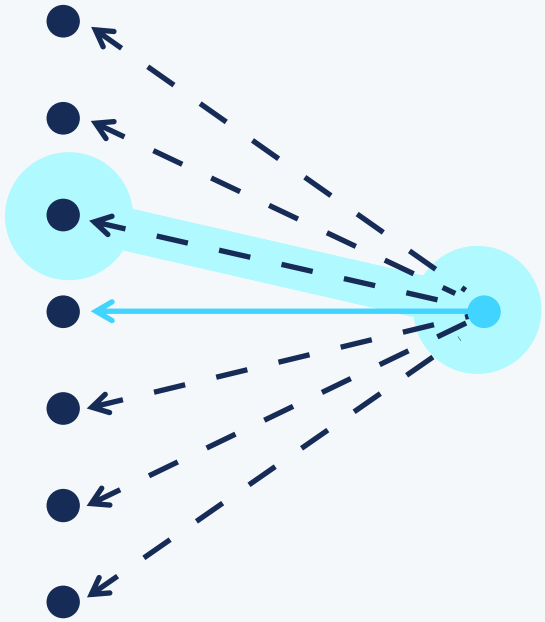
Lesson 1: AI helps us scale the challenging effort of discovering repurposing opportunities across all drugs vs all diseases

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

Disease Drugs



Diseases Drug



Diseases Drugs

*In addition to AI discovery, we also love receiving repurposing ideas from physicians, researchers, and patients at **everycure.org/ideas**.*

EVERY CURE

Lesson 2: Not all repurposing opportunities are the same, so evidence generation must be tailored to the situation

Lab studies to establish mechanistic rationale

Real world data to study associations in existing utilization

Clinical trials to prove efficacy

Guideline change & education when existing evidence is strong and compelling

We must ask: *What is the most efficient path to generating sufficient evidence for doctors and guideline committees to be able to assess this specific opportunity for patients?*

EVERY CURE

Lesson 3: Making impact for patients with repurposed treatments takes an ecosystem of accountability from end-to-end

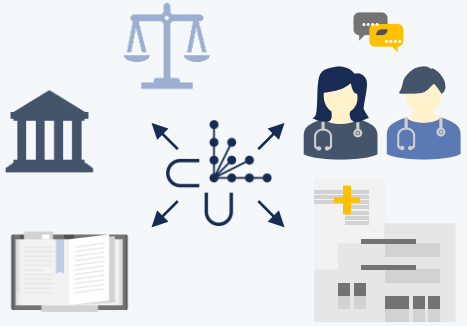
Discover

Computational discovery to select the best repurposing opportunities

Evaluate

Data generation to fill the gaps required to prove efficacy and safety

Impact



Dissemination of findings and treatments to patients

At Every Cure, we are end-to-end; we don't stop advancing repurposing opportunities until we've reached patients in need

EVERY CURE

Our pipeline includes 14 active repurposing programs, and we're reviewing 500-1,000 new opportunities per month!

- 75M potential drug repurposing opportunities
- Beta blocker–neurodegenerative disease*
- Epigenetic modifier–muscle degenerative disorder*
- Fibrosis modifier–rare genetic syndrome*
- mTOR inhibitor–rare vascular disorder*
- Metabolism modifier-fibrotic lung disease*
- Immune modulator-vascular malignancy*
- ARB-rare blistering disorder*
- mTOR inhibitor-inflammatory granulomatous disease*
- Amino acid-rare mitochondrial disease*
- Small molecule-rare genetic syndrome*
- Glabellar Botulinum toxin-major depressive disorder
- Lidocaine-breast cancer
- DFMO-Bachmann-Bupp syndrome
- Lenalidomide-Rosai-Dorfman

EVERY CURE

Session 3

Evidence & Submission Expectations

REAGAN-UDALL FOUNDATION FOR THE FDA

Sundeep Agrawal, MD

FDA

Amy Abernethy, MD, PhD

Highlander Health

Marie Bradley, PhD

FDA

David Fajgenbaum, MD, MSc

Every Cure

Donald Lo, PhD

REMEDi4ALL

Emily Freilich, MD

FDA

Session 4

Federal Partner Discussion

REAGAN-UDALL FOUNDATION FOR THE FDA

Andrew Brack, PhD

ARPA-H

Christine Colvis, PhD

National Center for Advancing Translational Sciences

Shari Ling, MD

Centers for Medicare and Medicaid Services

Marta Sokolowska, PhD

FDA

Danielle Turley, PhD

BARDA

Public Comment

REAGAN-UDALL
FOUNDATION
FOR THE FDA

Virtual Public Comment Process

REAGAN-UDALL FOUNDATION FOR THE FDA

Make sure your Zoom name matches the name you used to register.

Foundation staff will send you a Zoom chat in advance with a panelist invitation. Please watch for and accept that prompt.

We will announce the commenters in sets of three, so you know when your slot is coming up.

---

1. First time your name is called: **PREPARE TO SPEAK**
2. Second time your name is called: **TURN ON YOUR CAMERA**
3. When introduced: **UNMUTE AND BEGIN SPEAKING**
4. You will have **10 seconds** to begin speaking

Commenters will have 2.5 minutes (150 seconds) to speak. A countdown timer will be provided.

Open public comment forum: neither the Foundation nor the FDA will respond.

In-Person Public Comment Process

REAGAN-UDALL FOUNDATION FOR THE FDA

Virtual commenters will speak first. In-person commenters will then be called by last name, in alphabetical order.

The moderator will provide a verbal cue when your turn is coming up.

A staff member will direct you to the podium.

---

1. First time your name is called: **MOVE TO THE STAGE STAIRS**
2. Second time your name is called: **MOVE TO THE PODIUM**
3. When introduced: **SPEAK FROM THE PODIUM**

Commenters will have 2.5 minutes (150 seconds) to speak. A countdown timer will be provided.

Open public comment forum: neither the Foundation nor the FDA will respond.

TOPIC 1

What are examples of successful prioritization approaches from other programs or jurisdictions that could be adapted?

REAGAN-UDALL FOUNDATION FOR THE FDA

Public Comment

Andrea DiCarlo-Cohen

HHS Repurposes Products for Radiation Disaster Preparedness

Andrea DiCarlo, PhD, Director; Radiation and Nuclear Countermeasures Program, NIAID, NIH, HHS

Bone Marrow Death

2015

2015

2018

2021

+ 10 Generics

Repurposing Workshop

RADIATION RESEARCH 190, 659–676 (2018)
0033-7587/18 $15.00

DOI: 10.1667/RR15137.1

WORKSHOP REPORT

Challenges and Benefits of Repurposing Products for Use during a Radiation Public Health Emergency: Lessons Learned from Biological Threats and other Disease Treatments

Andrea L. DiCarlo,[a,1] David R. Cassatt,[a] William E. Dowling,[b] John L. Esker,[c] Judith A. Hewitt,[b] Oxana Selivanova,[c] Mark S. Williams[b] and Paul W. Price[d]

2018

DiCarlo AL, et al. Radiat Res. 2018;190(6):659-676.

Skin Injuries

2022

Product Classes Under Study

- Blood pressure
- GLP1s
- Cancer meds
- Statins
- Antibiotics

Partner with industry early & collaboratively; Know end use/user; Involve regulatory throughout

Public Comment

Linda Feinstein

Example: Successful repurposing of UCAs in Canada, Europe, China, Brazil

Ultrasound contrast agents (UCAs): Enhance ultrasound scans to better assess tumors, perfusion and CV risk.

FDA approval: Adult heart and liver; additional pediatric indications.

Common uses outside USA: Heart, liver AND kidneys, breast, thyroid, bowel, ovaries, pancreas, spleen, etc.

UCAs are ideal candidates for drug repurposing. Clinical trial safety data are robust and easily leveraged to support broader use because UCAs are systemic agents, a single IV injection shows perfusion in all organs of the body, target does not alter risk, studies confirm accuracy in other organs, and broader use changes therapy and patient outcomes.

Advantages: Safe, accurate, affordable, real-time results → reduction in downstream tests and procedures, lower costs, improved outcomes, and avoidance of delays and risks associated with contrast-CT and MR.

Accessibility: Ultrasound is cheaper and more widely available than CT or MR. And, for some patients, contrast-enhanced ultrasound is the only option for advanced imaging. (E.g., pregnancy, kidney impairment, logistics, cost.)

Stakeholders: It is not profitable to pursue new approvals, organ by organ. Motivation for expanding use is led by clinician-scientists and professional societies focused on best interests of patients and improving health care outcomes.

Priority for repurposing: Low-hanging fruit = whole-body UCA, leveraging existing safety data, guidelines and experience in Canada, Europe, China and Brazil → expanded access to safe, reliable, affordable health care.

Public Comment

Barbara Goodman

Additional Prioritization Approaches

CuresWithinReach

since 2005

>160 repurposing trials funded

>100 institutions funded

>90 diseases funded

Pediatrics

Often excluded from initial trials and approvals

CWR Success: sirolimus for ALPS

Neurology: Mental Health, Chronic Pain and TBI

Unmet needs beyond neuro-degeneration and SUD

CWR Success: N-acetylcysteine for TBI

Refractory / Recurrent Oncology

Few options exist once known therapies fail

CWR Success: interferon gamma for AML/MDS

Cures Within Reach is testing already approved treatments for unsolved diseases:
driving more treatments to more patients more quickly

www.cureswithinreach.org a 501(c)3 tax-exempt organization info@cureswithinreach.org

Public Comment

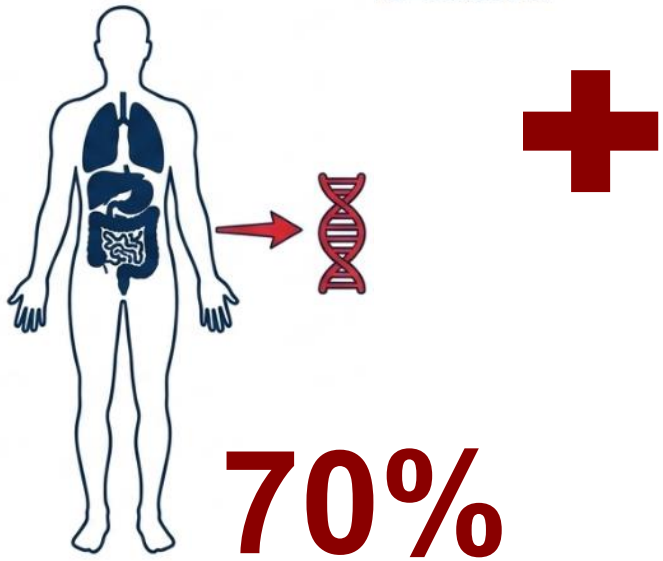
Jacqueline Perez

The TAPUR Study Blueprint for Drug Repurposing

Joint Public Comment by: Richard L. Schilsky, MD, FACP, FSCT, FASCO, Founding PI; Neal J. Meropol, MD, FASCO, PI; Elizabeth Garrett-Mayer, PhD, FASCO, FSCT, Vice President, Center for Research and Analytics (CENTRA); Laurie Smith, MA, Division Director, CENTRA; Jacqueline K. Perez, MPH, Director, Clinical Research, CENTRA

Genomic Targets

Utilizes pre-specified genomic criteria to match a drug to a gene alteration, regardless of tumor type or location.



70%

Of screened patients find a drug match and enroll

The Statistical Engine

Enroll 10 patients

- Disease control in < 2 patients → **STOP** → X Conclude disease control rate ≤ 15%
- Disease control in ≥ 2 patients → **Enroll 18 more patients**
  - Disease control in < 7 patients → X Conclude disease control rate ≤ 15%
  - Disease control in ≥ 7 patients → ✓ Conclude disease control rate > 15%

- Identifies Early Futility/Efficacy Signals
- Minimizes Patient Risk
- Optimizes Resource Utilization

Learn more about the TAPUR Study or view our publications:

NCT#: NCT02693535

(Disease Control = Complete Response, Partial Response or Stable Disease ≥ 16 weeks)

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

Public Comment

Barbara Binzak Blumenfeld

TOPIC 2

What factors should organizations consider when selecting repurposing candidates, and how should these factors be prioritized in the decision-making process?

REAGAN-UDALL FOUNDATION FOR THE FDA

Public Comment

Olugbenga Ajulo

WHAT FACTORS SHOULD ORGANIZATIONS CONSIDER WHEN SELECTING REPURPOSING CANDIDATES, AND HOW SHOULD THESE FACTORS BE PRIORITIZED IN THE DECISION-MAKING PROCESS?

OLUGBENGA MATTHEW AJULO, PHD
PROFESSOR OF CLINICAL PHARMACY
DEPT. OF CLINICAL PHARMACY & BIOPHARMACY,
FACULTY OF PHARMACY, UNIVERSITY OF UYO
AKWAIBOM STATE, NIGERIA
EMAIL: matthewajulo@uniuyo.edu.ng
MOBILE: +2347030262468

Public Comment

William Fitzsimmons

A Framework for Prioritizing Drug Repurposing Candidates

William E. Fitzsimmons, Pharm.D., M.S.
University of Illinois at Chicago

PRIORITIZATION FRAMEWORK

1. **Unmet Medical Need**
2. **Clinical & Real-World Evidence**
3. **Potential Public Health Impact**
4. **Development Feasibility**
5. **Impact on Patient Access**

WHY SOLID ORGAN TRANSPLANTATION?

47,995
Solid Organ Transplants
United States (2025)

Kidney	27,574	Liver	12,344
Heart	4,587	Lung	3,490

15 YEARS
No New Mechanism Approved for Solid Organ Transplantation

OPTN/SRTR
National Registry
Captures All U.S. Solid Organ Transplants

Solid organ transplantation satisfies all five prioritization criteria.

- Lifelong immunosuppression with substantial unmet need
- Robust real-world evidence through OPTN/SRTR
- Multiple standard-of-care drugs remain unlabeled for certain organs
- Label expansion improves reimbursement, access and preserves donated organs

Proposed FDA Prioritization Principle: FDA should prioritize diseases where **unmet medical need**, **compelling clinical and real-world evidence**, and the **potential to improve patient access** converge.

OPTN = Organ Procurement and Transplantation Network | SRTR = Scientific Registry of Transplant Recipients

Public Comment

Anna Hedden

PRIORITIZING DRUG REPURPOSING CANDIDATES

Anna V. Hedden
Patient, Legislative & Research Advocate
2-time Survivor of Rare, Metastatic Ovarian & Endometrial Cancers

Selection Criteria

1. **Target High Unmet Need**
   (Lethality | Recurrence | Rarity | Underinvestment) → Ovarian & Endometrial Cancers
   4 Surgeries → Chemotherapy → Immunotherapy → Targeted Therapy → 3 Hormonal Therapies → Phase I Trial → Radiation → Antibody-Drug Conjugate (ADC) → **What's Next? → Drug Repurposing**
2. **Prioritize Overcoming Resistance**
   (Distinct biological mechanisms)
3. **Leverage FDA-Approved Safety**
   (Rapid clinical translation)
4. **Ensure Mechanism Over Organ Origin**
   (Securing commercial access)

↓

Population Inequity: Restrictive organ labels create structural therapeutic exclusion for smaller populations.
Commercial Disparity: Narrow organ labels trigger initial insurance denials—causing critical delays in care—followed by automated unenrollment from Patient Assistance Program (PAP).

↓

THE FIX? → PROTECT REAL-WORLD PATIENT ACCESS & COMMERCIAL SAFETY NETS

Application: Prioritizing ANKTIVA via Mechanism-Driven, Tissue-Agnostic Repurposing Pathways.

Public Comment

Rachel Heilmann

FACTORS TO PRIORITIZE WHEN SELECTING DRUG REPURPOSING CANDIDATES

Rachel Heilmann, PharmD, BCPS - rePURPOSEd Pharmacy Practice/The Rory Belle Foundation

- **Disease burden & unmet need** – Prioritize serious, rare neurogenetic diseases with high care burden that have limited or no approved therapies and allow greater flexibility for rare diseases.
- **Established safety profile/human evidence** – Existing human safety data from published literature reduce development risk and accelerate translation.
- **Mechanistic rationale** – Strong biological plausibility and targeting direct or indirect disease pathways.
- **Accessibility and availability** - The ability to access and administer the drug without extensive investment in further drug development.

Public Comment

Kimberly Juroviesky

KETAMINE

(RACEMIC)

DRUG REPURPOSING GREATEST UNMET NEED:

Approximately 21 million Americans suffer with disabling chronic pain

Approximately 17 million adult Americans suffer with a mental illness.

PRIORITIZATION

Medications like (racemic) Ketamine that already have FDA approval and a proven safety record should be prioritized for new uses based on new potential life-saving properties.

RESEARCH FOCUS

Preliminary studies have shown great efficacy in mitigating physical pain and mental illness. Over a 50% reduction in pain conditiona such as CRPS 95% Reduction in SI, 70% reduction in symptoms in patients with TRD, and PTSD.

FUNDING

Funding for research for drug repurposing needs to be prioritized at the federal level to make it more accessible for small companies pursuing repurposing.

ACCESS DELAYED IS ACCESS DENIED!

We not only need FDA approval for these new uses for these medicines but we also need the AMA to create new pathways for insurance coverage. Without insurance coverage only the very wealthy will be able to access these medications. There are over 700 Ketamine clinics in the USA which are all cash pay making it accessible only for the wealthy. Insurance coverage for Ketamine infusions would ensure safe medical treatement for all who would benefit from it.

Public Comment

Sarah Philbin

CEREBRAL PALSY FOUNDATION

0

FDA-approved therapies that that modify cerebral palsy

1 in 345 children in the U.S. have cerebral palsy

The most common lifelong physical disability: about 1 million Americans, 50 million+ worldwide.

FOUR FACTORS TO WEIGH

1. **Economic, not scientific**
   prioritize where the market won't act
2. **Mechanistic convergence**
   approved drugs already hit pathways
3. **Durable benefit**
   lifelong condition · developmental windows
4. **Trial readiness**
   registries · outcome measures · networks

Cerebral palsy meets all four
Name it a priority.
Leverage foundations like ours.

Sarah Philbin, PhD MPH · Cerebral Palsy Foundation · Public Comment · August 5, 2026

Public Comment

Muhammad Ahmed Qamar

DRUG REPURPOSING: How Organizations Should Select & Prioritize Candidates

Muhammad Ahmed Qamar, PharmD, MS Drug Regulatory Affairs ·

Start with what is already happening: active off-label use + real-world safety data (FAERS & FDA Sentinel). Then ask, can we responsibly formalize this use?

HOW COMPANIES SHOULD FILTER CANDIDATES

1. **Unmet Medical Need**
   Filter for conditions where patients have limited or no adequate options. Off-label prescribing volume is a direct signal of unmet need.

2. **Strength of Evidence**
   Gather evidence from existing off-label experience, published data, company pharmacovigilance, and request FDA Sentinel / FAERS analyses for the new population.

3. **Disease Burden**
   Assess prevalence, disability, and economic impact of the condition being treated off-label. Higher burden strengthens the case for formalization.

4. **Public Health Impact**
   Evaluate potential to reduce morbidity/mortality at scale, improve equity of access, and deliver feasible real-world benefit once labeled.

COMPANY–FDA COOPERATION

Companies share utilization & safety data from their sources → request FDA input from Sentinel and FAERS → jointly review the combined picture → advance 505(b)(2) or labeling supplement when the profile supports formalization. Incentives: expedited designations, enhanced meetings, early RWE advice, existing exclusivity.

EXAMPLES STILL OFF-LABEL: Metformin for PCOS & prediabetes · GLP-1 agonists for PCOS · Historical success: Propranolol for infantile hemangiomas

Closing: Select by real-world off-label signal + safety data, then cooperate with FDA to convert high-value experience into labeled indications that improve access, equity, and characterization.

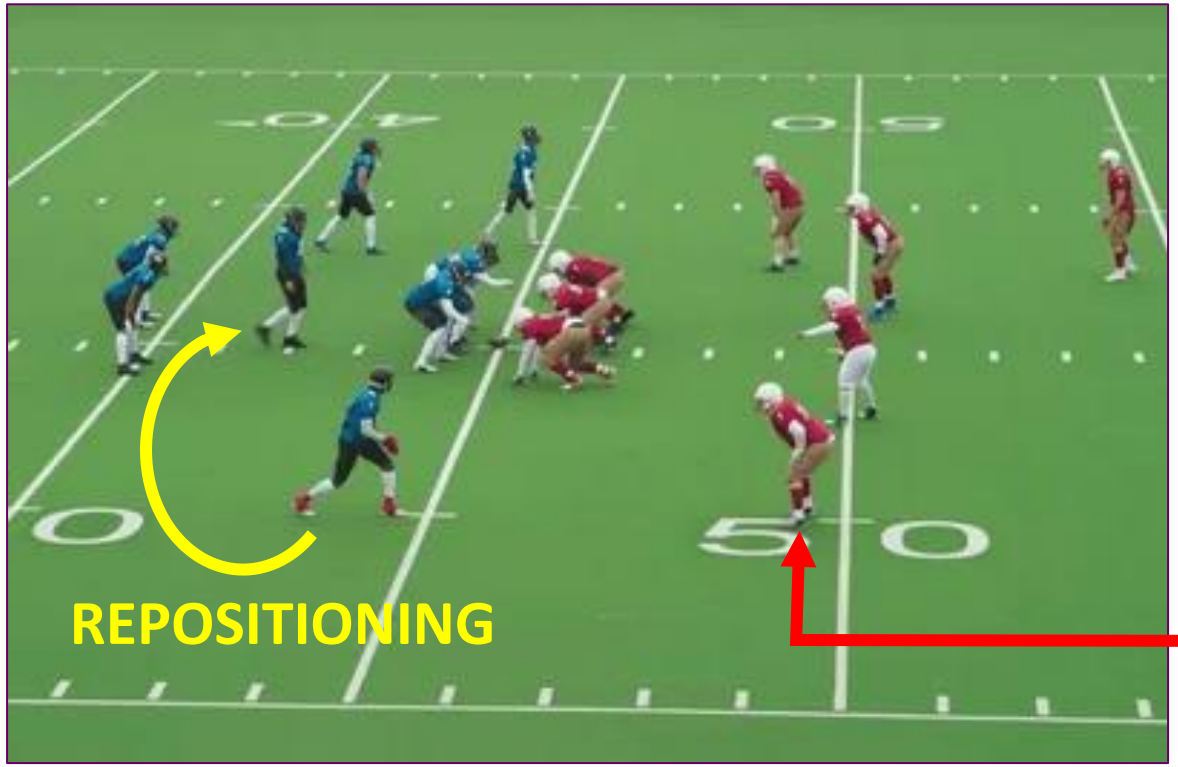
mahmedk10797@gmail.com

Public Comment

Appu Rathinavelu

‘DRUG REPOSITIONING Vs REPURPOSING’

A CONSIDERATION FOR PARADIGM REFINEMENT



CANCER

(Can be Target and Biomarker-driven strategy)

CARDIOVASCULAR

(Can be PK/PD-driven strategy)

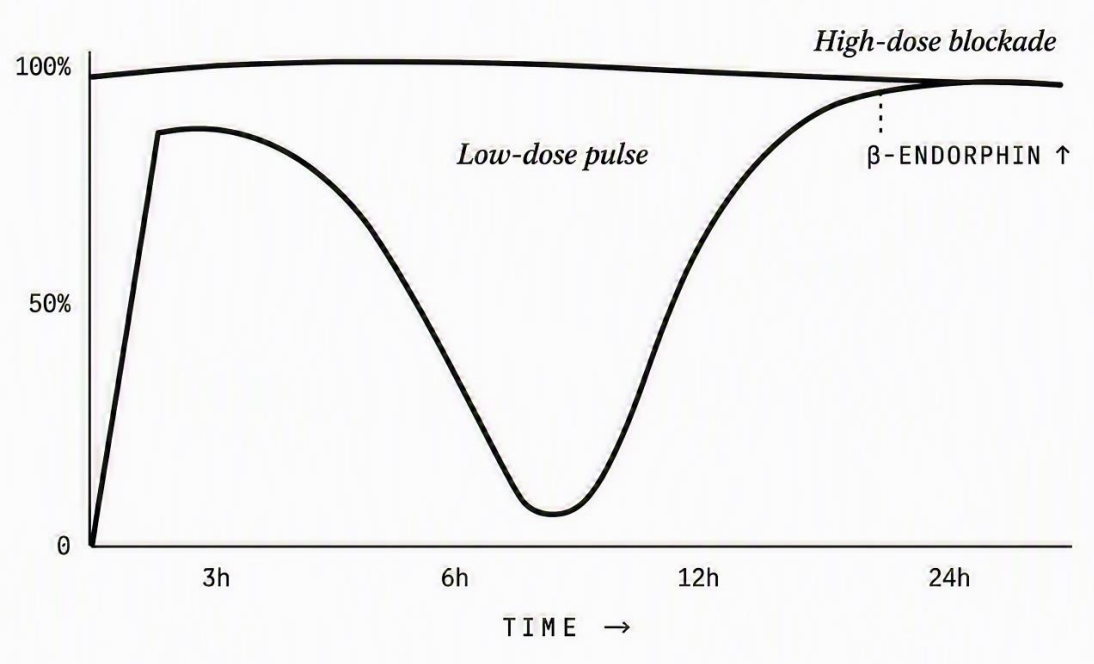
Public Comment

John Rosa

ATTUNE BIOTECH

Built on an FDA-Approved Molecule. Differentiated by Science.

Focused on repurposing chemistry, not a previously approved mg strength.



Naltrexone is a well-established molecule with FDA approval for alcohol and opioid dependence.

In 1985, researchers observed that naltrexone exhibited markedly different biological effects when administered at lower doses. Today, low-dose naltrexone (LDN) is widely prescribed off-label in the United States, yet no FDA-approved low-dose product exists.

Lodonal™, IR capsule and oral dissolvable film formulations, are built upon the well-established safety and clinical foundation of naltrexone, leverging the distinct biological effects associated with daily doses of **0.01-10mgs.**

Public Comment

Shane Wald Altman

REAL-WORLD, CLINICALLY VALIDATED THERAPEUTIC DISCOVERY PLATFORM

Drug Repurposing for an Ultra-Rare, Lethal Vasculopathy

QR GENETICS

Match a disease-causing variant to an FDA-approved drug, prove it in a patient, then extend the mechanism to large unmet-need populations · Docket FDA-2026-N-4492

QRGenAI PLATFORM

Maps disease-causing genetic variants to FDA-approved drugs

16T data points · Harvard / Mass General Brigham · Yale

180+	34	20+
Different rare disease cases analyzed	Treated with different FDA approved drugs	Meaningful outcomes

4-STAGE DISCOVERY — SAPROPTERIN, A GENERIC PKU DRUG, REPURPOSED FOR ULTRA-RARE ACTA2 R179H MSMDS

1 Model the variant

Build a digital protein structure, run functional-dynamics simulations, detect the defect, and define the target to rescue.

2 Match an FDA drug

Screen thousands of FDA-approved drugs; sapropterin (originally a PKU drug) fits the pocket and restores function.

3 Validate in cells + mouse

Patient fibroblasts restore actin (↓ G/F ratio); an ACTA2 R179H mouse model shows improved survival, blood pressure & sensorimotor recovery.

4 Treat the patient

Treated a 6-year-old girl for 18 months, off-label; cerebrovascular disease stabilized.

Bottom line The model turns a variant of uncertain consequence into a physically-grounded, druggable target to the foundation every downstream repurposing step is built on.

We validate the mechanism in a rare-genetic case, then extend it to a much larger unmet population that also lacks approved therapy.

p=0.0007	+225%	0
ICA ratio improved	PedsQL physical health	adverse events

~35M patients

cardiovascular disease · no approved disease-modifying therapy · pre-IND, Phase 2 repurposing trial planned

Our ask to FDA a dedicated repurposing pathway for candidates with human clinical validation (incl. compassionate use), peer-reviewed publication, and mechanistic pre-clinical data and recognition of rare genetic disease as a priority source of mechanistic signals.

Published case: Hausman-Kedem M, Bielopolski N, Wald-Altman S, et al. Ann Clin Transl Neurol 2026 (doi:10.1002/acn3.70493, open access). Preclinical in-vivo (ACTA2 R179H mouse): Krishnan, Weil, Altman … Musolino et al. (MGH / QR Genetics) presented 2023, Platform validation: npj Genomic Medicine 2026 · Frontiers Mol Neurosci 2023 · Epilepsy Research 2022.

~35M = projected addressable population; expansion is pre-IND / Phase-2-planned.

Dr. Shane Wald-Altman, PhD · Co-Founder & CTO, QR Genetics · Aug 5, 2026 · Docket FDA-2026-N-4492

shanewa@qrgenetics.com

Public Comment

Daniel Jacobson

MENTOR-EV: Mechanistic Digital Twin-Guided Drug Repurposing

From Drugs to Mechanisms to Patients

Dan Jacobson, Oak Ridge National Laboratory

1. Inputs:
Drugs + Disease Signals

Drugs
- FDA-approved drugs
  Drug databases
- Targets & mechanisms

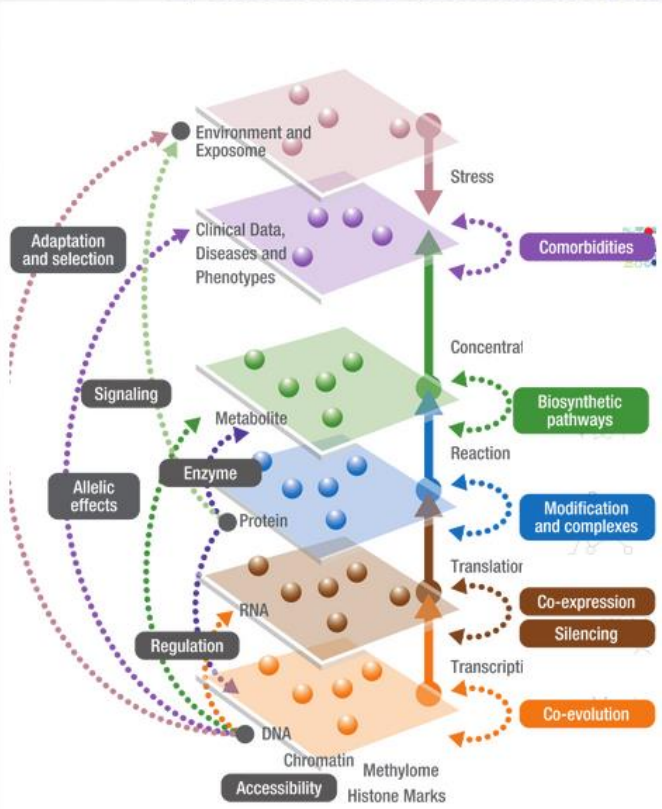
Disease Signals
- GWAS
- Methylation
- Transcriptomics
- Proteomics
- Imaging / Phenotypes

FRONTIER
ORNL HPC + AI

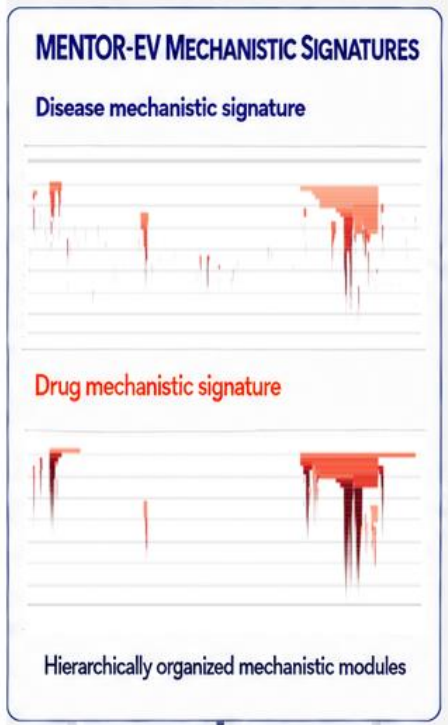
AI

Scalable • Repro

2. Project Into Mechanistic Digital Twin



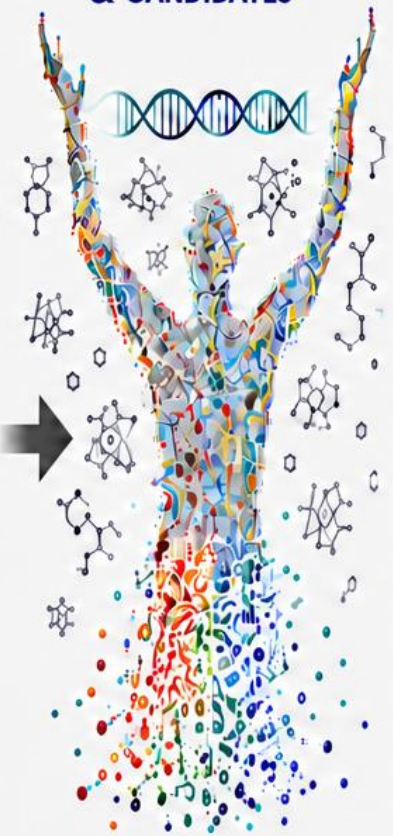
MENTOR-EV Mechanistic Signatures



Compare signatures

Mechanistic overlap

3. Prioritize Mechanisms & Candidates



4. Outputs: Candidates & Insights

- **Ranked drug candidates**
  Repurpose with mechanistic justification
- **Actionable mechanisms**
  Pathways & modules linked to disease
- **Model system recommendations**
  Ortholog & topology conservation
- **EHR Retrospective Clinical Trial Simulations**
- **Data & reports**
  Machine-readable tables, visualizations & audit trail

Accelerating Safe, Effective Therapies

- Leverages existing approved drugs
- Mechanism-first precision
- Cross-omics convergence
- Better models, better translation
- Faster path to patients with unmet need

Systems Biology • Network Medicine • AI-Driven Discovery

Public Comment

Susan Lin

Road Back Foundation's Comments

Factors to Consider When Selecting Drugs for Repurposing

1. Rare diseases without an affordable and accessible cure

   Example: Scleroderma (diffuse)

2. Effects of the disease and Impact on Life

3. Strength of Evidence

Public Comment

Mariia Markitanova

PUBLIC COMMENT

Selecting Repurposing Candidates

Prioritize the factors *in sequence* — not in parallel

Mariia Markitanova
Founder & Director
Curada PBC
www.curada.bio

1 GATE

Public health impact

Prioritize the greatest public-health gain.

2 RANK

Strength of evidence

Human evidence already in hand.

3 SCREEN

Regulatory cost of entry

MODERN §503D offers a viable path — no commercial sponsor needed.

4 DECIDE

Deployability — the critical factor

A label fixes the legal barriers — not deployment. Deployment needs **an owner with underwritable economics** to acquire a non-interchangeable position (OTC switch; distinct PDURS, 505(j)(2)(A)(v)).

Why off-label use alone struggles to scale

- No data for the new use
- **Uneven, slow uptake**
- Reimbursement gaps
- **Low provider & patient awareness**
- **Patient hesitancy**
- **Supply & shortage risk**
- Provider liability concerns

— Duke-Margolis, 2025

Bottom line: impact gates → evidence ranks → pathway cost screens → deployability decides whether a new use is adopted in clinical practice.

Docket FDA-2026-N-4492 · Drug Repurposing for Unmet Medical Needs; Request for Information · Public Meeting · Aug 5, 2026

mariia@curada.bio

Public Comment

Simon Vukelj

CHILDREN'S TUMOR FOUNDATION

Selecting Drug Repurposing Candidates

When an already-approved drug could serve an unmet rare-disease need.

FACTORS TO WEIGH

1 **Severity of unmet need**

No approved therapy; morbidity, disability, shortened life expectancy.

2 **Established safety profile**

Already FDA-approved, with a mature clinical safety record.

3 **Disease-specific evidence**

Real preclinical or clinical signal, not just plausibility.

HOW TO PRIORITIZE: ACTION TIERS

TIER 1

Proven, then abandoned

Clinical benefit already shown, but the sponsor has no incentive to file.

FDA lever: facilitate label expansion • e.g., brigatinib for *NF2*-SWN

TIER 2

Proven, but at risk

Strong clinical data exists, but sponsor engagement could still lapse.

FDA lever: keep sponsors committed • e.g., cabozantinib ± selumetinib

TIER 3

Promising, but blocked

A compelling preclinical case exists, but the owner will not release the drug.

FDA lever: unlock access for trials • e.g., deucravacitinib + mirdametinib

Rank highest where the evidence is strongest. Regulatory facilitation can close the gap between an approved drug and the patients who need it.

TOPIC 3

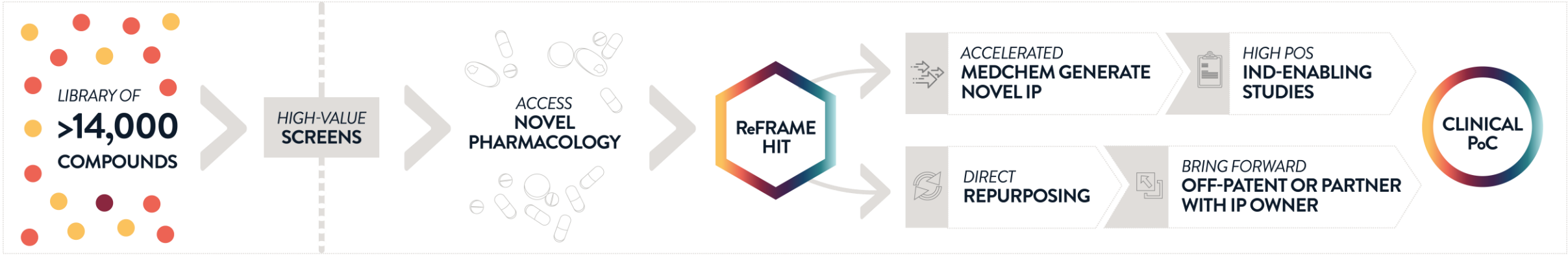
What evidence gaps or policy/regulatory barriers most commonly hinder the advancement of promising repurposing opportunities?

REAGAN-UDALL FOUNDATION FOR THE FDA

Public Comment

Arnab Chatterjee

Repurposing **F**ocused **R**escue and **A**ccelerated **ME**dchem (**ReFRAME**) Drug Repurposing Platform



- FDA-approved drugs (39%)
- Investigational new drugs (58%)
- Preclinical compounds (< 3%)

Reframedb.org has all drug information and screening data

Calibr-Skaggs Institute for Innovative Medicines | Scripps Research

Gates Foundation

In 10 years has put 6 new drugs in clinical trials and 5 at IND-enabling studies with 25M USD investment with average program from screen to clinic in 1 year

Public Comment

Megan Golden

Megan Golden, CEO, Mission: Cure

Mission:Cure

PUBLIC COMMENT · EVIDENCE GAPS & REGULATORY BARRIERS

When the patent holder won't act, patients have no path.

1

No owner

Generic (no one to file)

2

Unwilling owner

e.g. perceived risk to primary market

3

Expiring patent

No runway to invest

THE ASK A route to the label that doesn't depend on the patent holder: a clear evidence pathway and an incentive for whoever does the work.

Public Comment

Nicolas Grundmann

Ember Health

IV Ketamine for Depression

AN OPPORTUNITY TO IMPROVE SAFETY, ACCESS, AND OUTCOMES

1 IN 9

U.S. adults experience Major Depressive Disorder

Only ~1 in 3 achieve remission with first-line antidepressants

7,000+

Peer-reviewed publications over 30+ years

~75% response rate when administered within established parameters

Rapid effects—often within days

SAFETY DEPENDS ON THE MODEL OF CARE

- ✓ Intravenous administration
- ✓ Standardized dosing
- ✓ Clinician oversight
- ✓ Continuous monitoring
- ✓ Trained medical staff

Guidance from APA, VA, and ASKP3

REAL-WORLD EVIDENCE: EMBER HEALTH

42,000+	IV ketamine infusions
2,600+	Patients treated
84%	Treatment response
~1 IN 1,600	Medically serious adverse events

Largest known single-practice dataset on IV ketamine for depression (with Harvard Medical School collaborators)

WHY FDA ACTION MATTERS

Millions are already seeking ketamine for mental health, often in lower-cost, minimally supervised settings because IV ketamine remains off-label for depression.

An FDA-approved indication with clear safety standards would:

- ✓ Improve patient safety
- ✓ Establish national clinical guardrails
- ✓ Increase access to evidence-based care

FDA reclassification of IV ketamine for Major Depressive Disorder will help address an unmet medical need affecting millions of Americans.

Public Comment

Lisa Kane

Drug Repurposing for Chronic Refractory Systemic Demodicosis (CRSD) : Precision Rx

Disease Burden

Demodicosis is recognized by NIH GARD (GARD:1802) and ICD-10 B88.0. (Genetic And Rare disease)
Often diagnosed as rosacea, blepharitis, acne, seborrheic dermatitis, rash, psychogenic illness, or dismissed.
Current status: Substantial impact on quality of life, productivity, and healthcare utilization. Devastating social stigma.

Age-related Prevalence

3–15 yr: 13%
31–50 yr: 69%
≥60 yr: 84%
≥70 yr: Up to 100%

Research Opportunity

Repurpose medications with established safety data (e.g., ivermectin, moxidectin, permethrin
Evaluate dosing, formulations, combination therapy, and life-cycle management.
Compare veterinary rotation (e.g., flurilaner. lufenuron, pyrethrins, piperonyl butoxide)
Rigorous human research to ensure safety/monitor for toxicity / ADME / Precision Rx

AI-Facilitated Research

Reduce development time and cost by prioritizing promising adaptive and interventional therapies.
Integrate clinical, imaging, microscopy, genetics, proteomics, immunology, PK/PD, wearables, and patient-reported outcomes.
Support adaptive Bayesian trials, precision medicine, resistance detection, and optimized dosing.
AI serves as a scientific decision-support platform—helping investigators generate, prioritize, and continuously refine evidence while keeping clinical judgment and regulatory oversight central to the research process.

Regulatory Requests

Support investigator-initiated adaptive interventional drug-repurposing research.
Modernize regulatory pathways and standardized outcomes.
Prior authorization hurdles and “red tape” lead to delay in treatment , vermin colonization
Enable evidence-based FDA updates that inform insurance quantity limits and coverage.
I.e. full body / affected area

Sources: NIH GARD • AAO EyeWiki • American Academy of Dermatology • PubMed (Demodex blepharitis, Demodex rosacea, Drug Repurposing) • CDC

Public Comment

Nichelle Santos

Public Comment

Marian Saxon

Public Comment

Sarah Tompkins

Public Comment

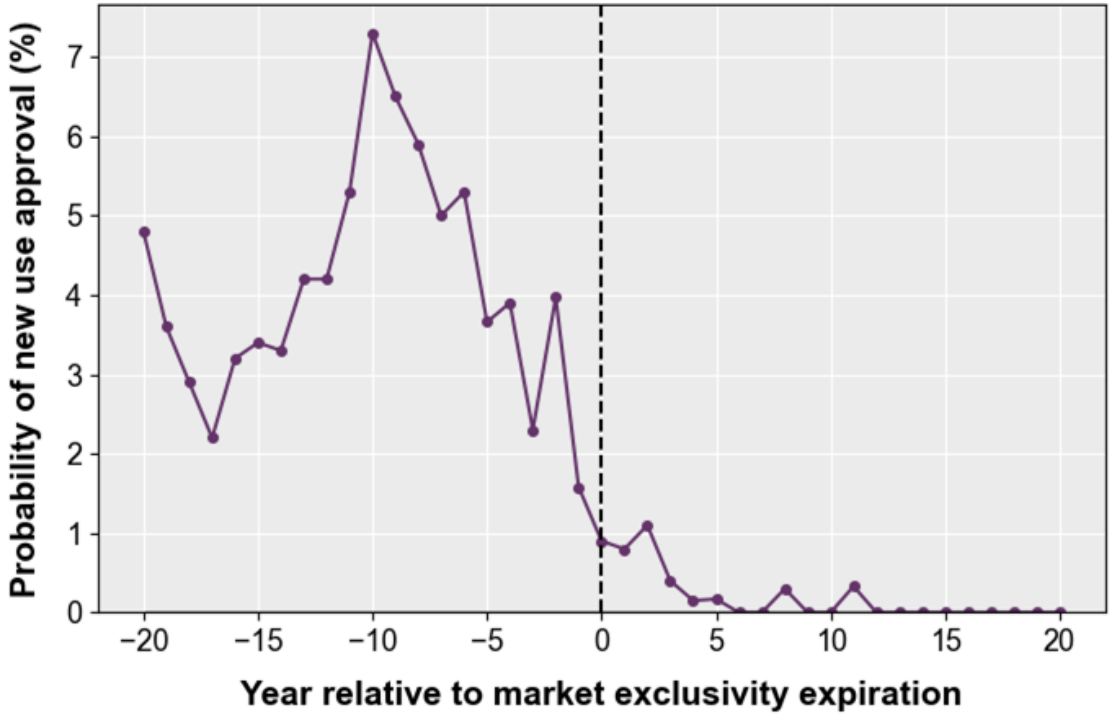
Sarrin Chethik

Missing incentives

(1) Patents expire
(2) Generic entry reduces profits
(3) Nearly no financial incentive to repurpose drugs

Budish, et al. (2025) estimate appropriate incentives would've led to **200-800 additional drug-use combinations**

Probability of approval for new use (%)



Source: Budish, et al., 2025
Note: A standard patent expires after *20 years*.

Email: schethik@marketshapingacceleartor.org

Public Comment

Laura Ford

Public Comment

Laura Kleiman

Reboot Rx
Because the solution may already exist

Laura Kleiman, PhD | Founder & CEO
Nonprofit advancing affordable cancer treatments by repurposing generic drugs

Overcoming key barriers to repurposing generic drugs

Need for definitive randomized controlled trials

Recommendations: Dedicate NIH funding for repurposing clinical trials; modernize Investigational New Drug (IND) requirements

No practical FDA approval pathway without manufacturer involvement

Recommendations: Create "labeling-only" 505(b)(2) pathway; expand MODERN Labeling Act; leverage Citizen Petitions and Federal Register

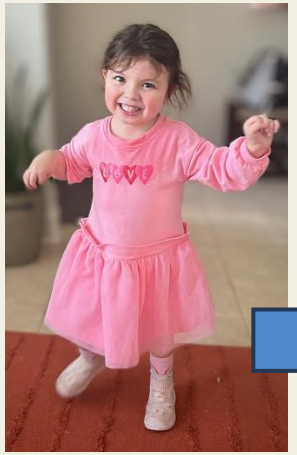
View full FDA RFI response

Includes additional policy recommendations and Scenario 1 drug candidates

info@rebootrx.org

Public Comment

Shayanne Martin



2022 2023 2024 2025 2026 2027

CHANNELING HOPE FOUNDATION

NEEDS

- FDA engagement pathway for patient advocacy organizations to be trial leaders
- Incentives for drug repurposing trials for ultra-rare diseases – including for generic drug manufacturers

Public Comment

Jeffrey Martini

Public Comment

Thomas Seoh

Incentives and Regulatory Clarity to Unlock Repurposed Generics

- **Biggest hurdle:** lack of private sector incentives to overcome 'free rider' problem (toolkit includes e.g. extended market exclusivity, Priority Review Vouchers, prizes and grants)

- **Dedicated pathway:** create a dedicated accelerated pathway (structural, like a dedicated Office, or guidance-based), for repurposed generics ***with substantial human safety experience***
- **Scale safety exposures:** to residual risk - e.g., 100's (not 1,000's) may suffice where safety is already well characterized
- **FDCs:** clarify and sensibly prune factorial-design expectations under the combination drug rule facturing mechanistic support and safety/tolerability experience
- **Dose/formulation optimization:** permit dose and formulation optimization for new indications without automatically restarting phase 2 development
- **Compress adoption of endpoints and biomarkers:** fit-for-purpose, transparent standards and predictable evidentiary tiers (~15 years for BMD, >20 years for C-peptide **too long**)

Principle: evidence requirements proportionate to known risk and prior human experience

Thank you

Slides, transcript, and recording will be available at
www.ReaganUdall.org

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