

NIH Counter**ACT**Program

Status Epilepticus after
Benzodiazepines: Seizures and
Improving Long-term Outcomes

February 28 - March 1, 2023

Rapid Acquisition and Investigation of Drugs for Repurposing (RAIDR): Progress and Ambition

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Status Epilepticus after Benzodiazepines: Seizures and Improving Long-term Outcomes



Disclaimer

This certifies that the views expressed in this presentation are those of the author and do not reflect the official policy of NIH.

Disclosure

This certifies that I, Dr. Lauren Quattrochi, have no financial relationship that is relevant to the subject matter of the presentation.

BROAD SPECTRUM

Effective across multiple threats, offering a frontline defense and buying time to deploy targeted MCMs

Example: A broad-spectrum antiviral can be administered after exposure to multiple encephalitic viral diseases, to mitigate impact and spread



JPM CBRN MEDICAL STRATEGY

Protect the warfighter against known and unknown CBRN threats



Understand, mitigate, and protect warfighter against

priority threats with highly-specific tests and MCMs

TARGETED

Example: A Naloxone autoinjector provides immediate protection to warfighters following an exposure to ultra-potent opioids in the field

Repurposed MCMs

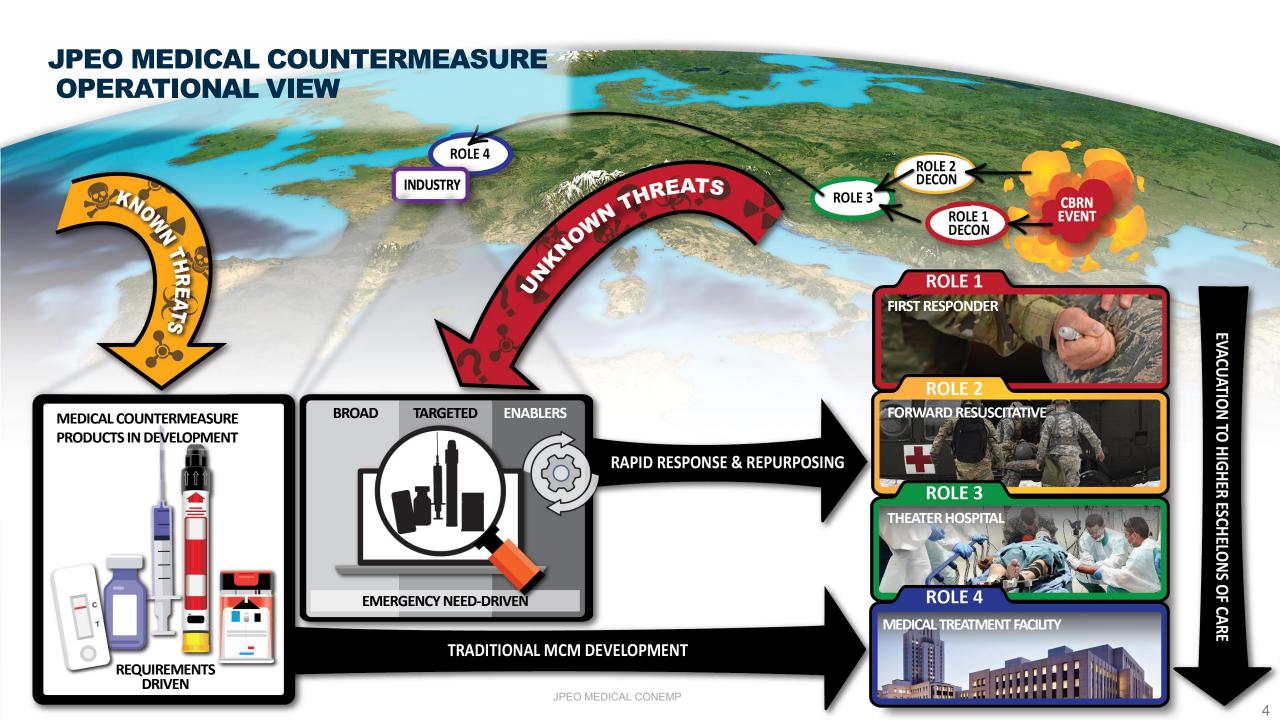
Symptomatic or hostimmune targeted treatment





EXPLOIT RAPID RESPONSE CAPABILITIES

Respond faster to the unknown

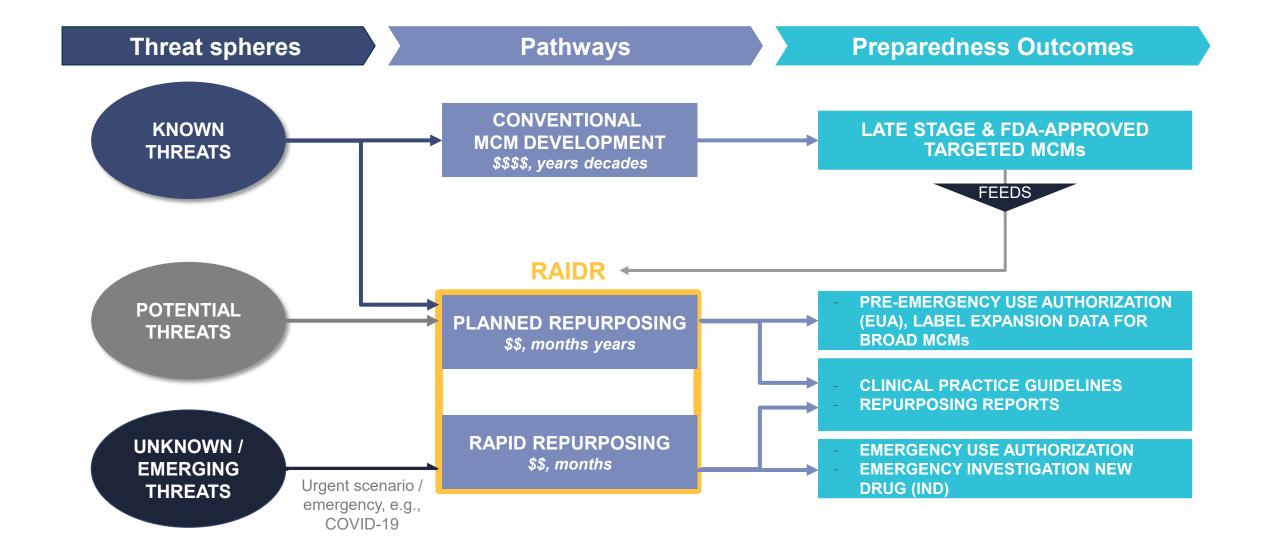


RAIDR PIPELINE HELPS DRIVE PREPAREDNESS









Conventional drug development is the primary means by which we build MCMs

RAIDR complements this approach with **drug repurposing**, testing approved MCM efficacy for additional indications



RAIDR repurposes proven medicines...



- Demonstrated safety in similar indications, lowering risk of failure
- Established manufacturing processes
- Faster and cheaper path to deploy, building from prior development efforts

...to provide a first line of defense to the warfighter



- Provides broad-spectrum
 MCMs to bridge between
 threat emergence and
 targeted therapy
 development
- Mitigates warfighter's
 symptoms, and expedites
 return to action

HOW INFRASTRUCTURE FEEDS INTO SUSTAINABLE CANDIDATE PIPELINE







Knowledge base

Data-Driven Models

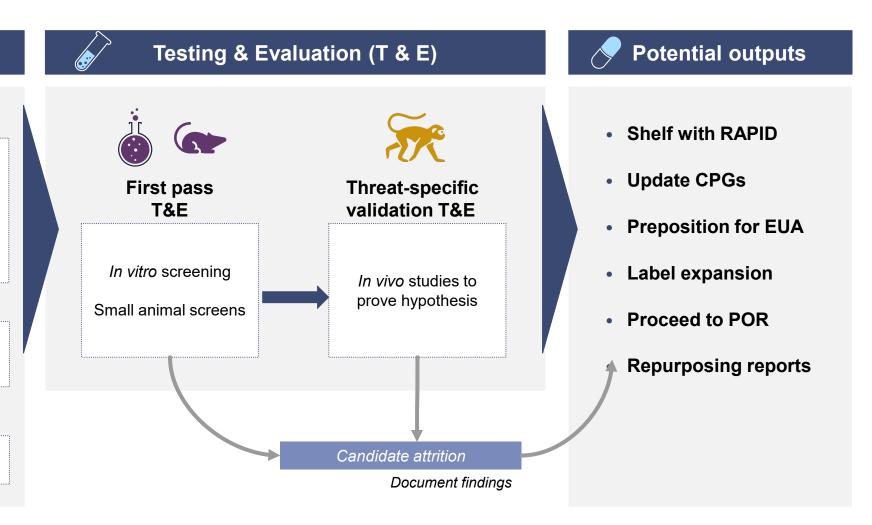
- Machine Learning / Artificial Intelligence Tools
- Discovery of MCMs Against Novel Entities (DOMANE)
- Agile MCM Decision Support Tool (AMDST)

Technical Experts

- Priority Sub-Working Group
- Tech watches
- Interagency Working Groups

Literature Reviews

- Market research
- Drug landscape analysis



Candidate approach will be dependent on knowledge base already available for a particular drug, against a threat of interest

RAIDR vision is to consistently contribute to a sustained MCM pipeline, via repurposing

Prioritized RAIDR efforts guided by:

- Level of threat risk and unmet needs
- Evidence for Mechanism of Action (MOA)/target knowledge
- Available partnerships
- Balance with existing portfolio
- Available Science & Technology Tools (e.g., animal models, existing assets)

Aiming for two repurposing target outcomes (repurposing reports, CPGs, EUA readiness¹) achieved per year

RAIDR LAUNCHED TO ADDRESS COVID-19 EMERGENCY









Low











High

Severity

COVID-19 Clinical Progress

Health, no infection

Not hospitalized, no limitations

Not hospitalize limitations Hospitalized, no active problems

Hospitalized, not on oxygen

Hospitalized, on oxygen

Hospitalized, noninvasive ventilation Hospitalized, mechanical ventilation

Death

Direct-Acting Therapies

Q-griffithsin / Univ. of Louisville

Blocks viral adhesion

Arakoda (tafenoquine) / 60Pharmaceuticals, LLC Blocks viral invasion

Mixed Therapies Tavalisse (fostamatinib) / Rigel Pharmaceuticals, Inc. Blocks viral evasion of immune system

Leukine (sargramostim) / Partner Therapeutics, Inc.
Restores immune cell control in the lungs

Humira (adalimumab) / Abbvie / Pharm - Olam Reduces cytokine response and amplification

Host-Directed Therapies

Pul-042 / Pulmotect, Inc.

Promotes innate immune response in lungs

Primary Department of Defense (DOD) focus is to maintain force readiness

Ultran MINI / The Ultran Group, Inc. Improves control of cytokine response

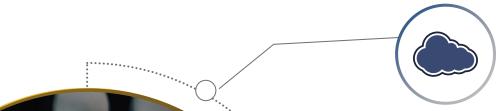
Clinical range of treatment efficacy

ONGOING EFFORTS AND CANDIDATES









Sulfur Mustard
Myelosuppressive effects

Leukine®

In FY22, the team launched, focusing on high-priority indication treatment efforts



Bunyaviruses
Post-exposure prophylaxis

Xofluza[®] Antiviral

Acute Respiratory Distress Syndrome (ARDS) Life-threatening lung condition

 MINI Wearable ultrasound



Nerve agents

Treatment for fatal seizures

- PRECEDEXTM
- Isoflurane
- Ketamine

Artificial Intelligence/Machine Learning (Al/ML) tool

Tests for potential FDA-approved drugs against virus targets with docking models, via crystallography

IN 2023 AND BEYOND, WE INVITE YOU TO WORK WITH RAIDR AS WE EXPAND CAPABILITIES AND THREAT SCOPE









Viruses

- All Coronaviruses
 - SARS-CoV
 - MERS-CoV
 - Excluding SARS-CoV-2
- Pandemic Influenza
- Western, Eastern, Venezuelan Equine Encephalitis
- Filovirus
 - Ebola
 - Sudan
 - Marburg
- Lassa virus
- Crimean-Congo Hemorrhagic Fever
- Nipah/Hendra virus



Bacteria

- Burkholderia mallei
- Burkholderia pseudomellei
- Coxiella burnetii
- Francisella tularensis
- Yersinia pestis
- Antimicrobial resistant bacteria
 - E. coli
 - P. aeruginosa
 - S. aureus



Toxins

- Staphylococcal Enterotoxin B (SEB)
- Mycotoxin
 - Aflatoxin
 - Diacetoxyscirpenol
 - T2
- Tetrodotoxin
- Conotoxin
- Ricin
- Botulinum Toxin A-G



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