



◆ UNCOMPROMISING INTEGRITY ◆ RESPECT FOR ALL ◆ COMMITTED TO EXCELLENCE ◆ ALWAYS READY ◆

# JPEO-CBRND



## RAPID ACQUISITION AND INVESTIGATION OF DRUGS FOR REPURPOSING (RAIDR) AND VACCINE ACCELERATION THROUGH MODULAR PROGRESSION (VAMP)

April 2023

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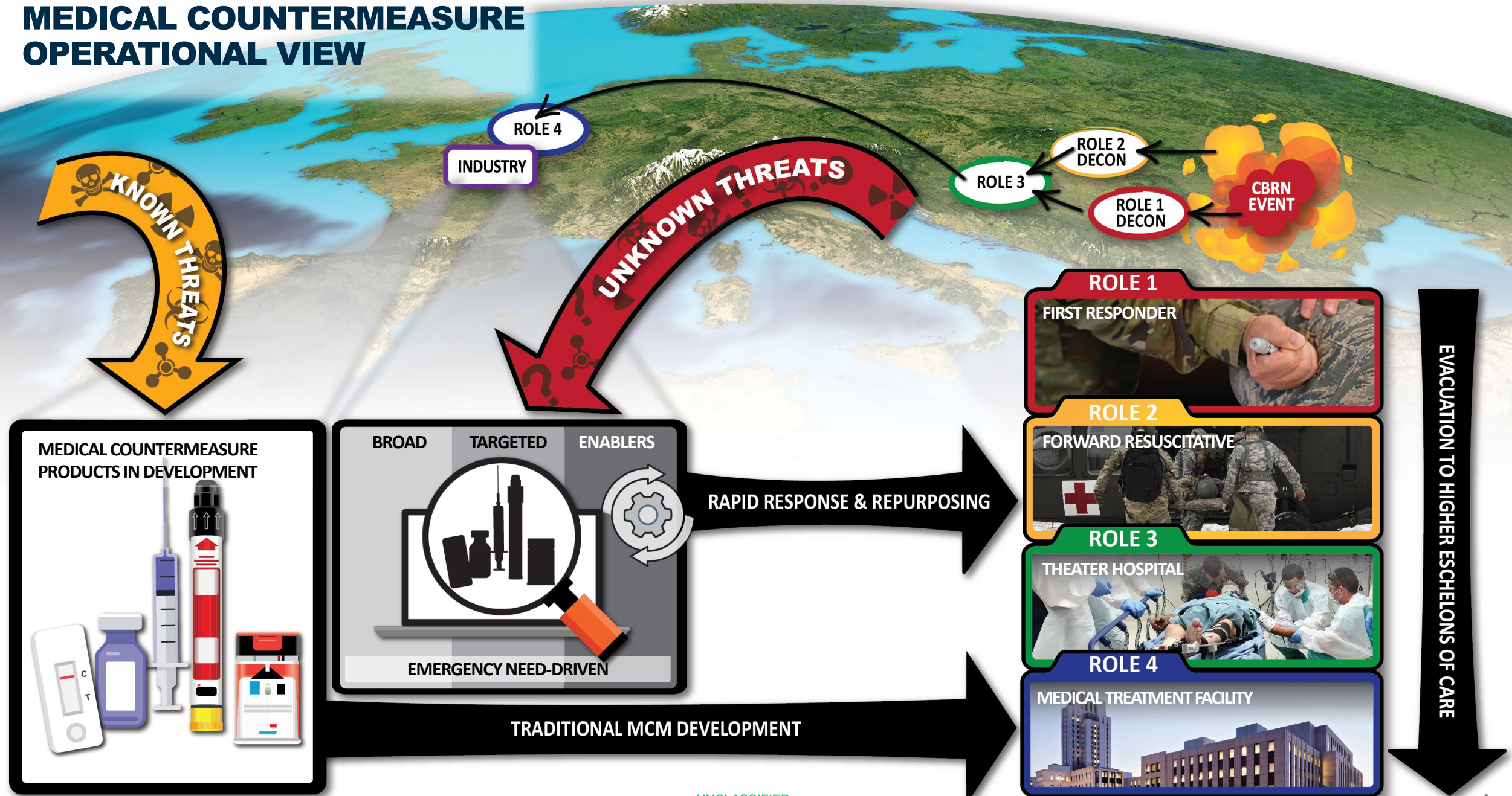
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PROGRAMS EXECUTED ON BEHALF OF THE CHEMICAL AND BIOLOGICAL DEFENSE PROGRAM



# MEDICAL COUNTERMEASURE OPERATIONAL VIEW



# CLINICAL PRACTICE GUIDELINE INFORMED DEVELOPMENT



To rapidly treat and contain threats, medical responders benefit from clinical guidelines, based on common symptoms presenting at different times. CPGs also inform concepts of use and operations and regulated product development.

**Predictive prodrome:** Flu-like symptoms, lethargy, fever, aches



## Respiratory

- Cough
- Chest pain
- Shortness of breath



## Cutaneous

- Rash
- Localized lesions



## Lymphadenopathy

- Swollen lymph nodes



## Gastrointestinal

- Vomiting
- Diarrhea
- Abdominal pain



## Hemorrhagic

- Bleeding
- Bruising
- Non-blanching rash



## Neurological (central)

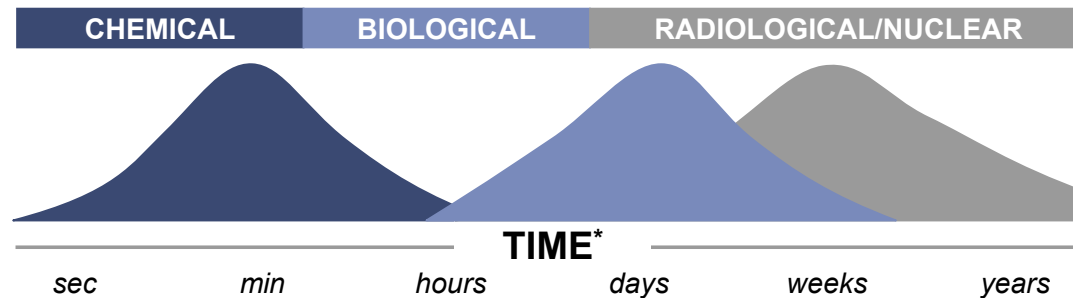
- Head and neck ache
- Confusion, hallucinations



## Neurological (peripheral)

- Paralysis
- Weakness of eyelids
- Speech & swallowing difficulty

**Origin of threat may vary onset, severity, and timing of symptoms.**



**Responders presented with a range of symptoms – many are non-specific**







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## VACCINE ACCELERATION THROUGH MODULAR PROGRESSION



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# VACCINE ACCELERATION BY MODULAR PROGRESSION (VAMP) PROGRAM IS BUILDING “BIOLOGICAL BODY ARMOR” TO PROTECT THE WARFIGHTER FROM WITHIN

## Delivering critical preparedness outcomes



### DEFENSE

Strategic reserve of “bio-armor” (e.g., vaccines) licensed or authorized for emergency use



### DETERRENCE

Capability to rapidly deploy vaccines deters adversaries considering exploiting vulnerabilities



## With increased operational agility



### SPEED

Industrial base for rapidly deploying partially developed, ‘on the shelf’ vaccine candidates



### RESPONSIVENESS

Ability to adapt to shifting priorities and ‘compete’ multiple prototypes in parallel for a single threat



# GEOGRAPHIC PRESENCE OF CURRENT DEVELOPMENT PRIORITIES DEMONSTRATES BREADTH OF THREAT LANDSCAPE



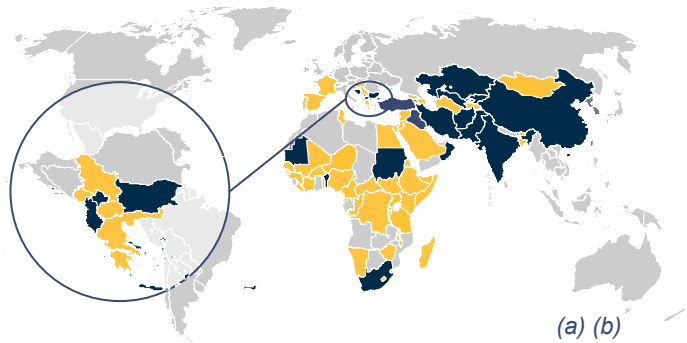
## Flu:

Globally endemic



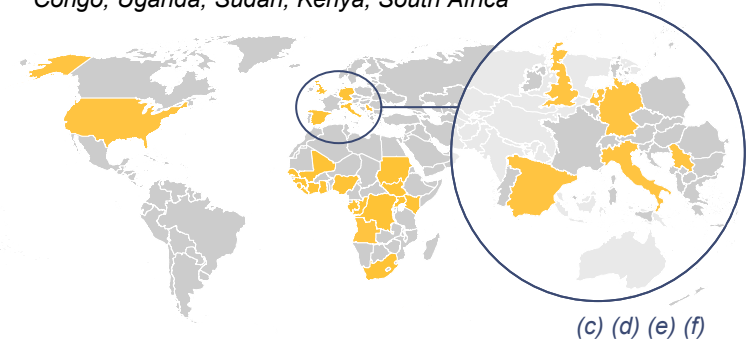
## CCHF:

Endemic: Albania, Kosovo, Bulgaria, Turkey, Iraq, Iran, Afghanistan, Pakistan, India, Kazakhstan, Kyrgyzstan, China, South Africa, Sudan, Mauritania



## Filovirus\*\*:

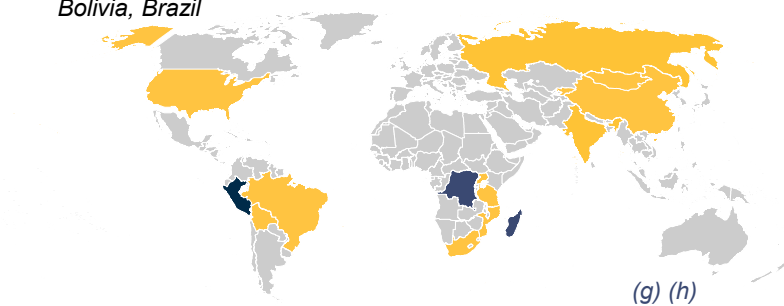
Historical outbreak: U.S., Italy, Spain, England, Germany, Netherlands, Serbia, Mali, Senegal, Sierra Leone, Guinea, Liberia, Cote d'Ivoire, Ghana, Nigeria, Gabon, Angola, DRC, Congo, Uganda, Sudan, Kenya, South Africa



## Plague\*:

Endemic: Peru, DRC, Madagascar

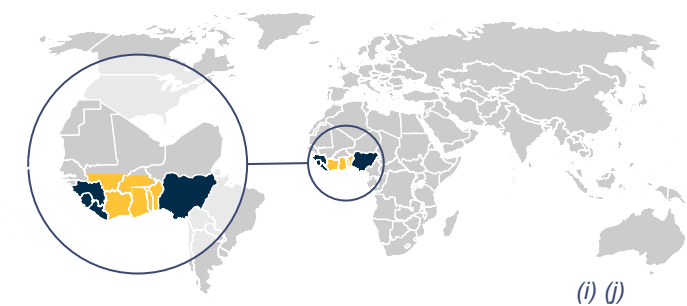
Historical outbreak: South Africa, Mozambique, Tanzania, Uganda, China, Mongolia, Russia, India, Kyrgyzstan, U.S., Bolivia, Brazil



## Lassa:

Endemic: Nigeria, Sierra Leone, Guinea, Liberia

Historical outbreak: Cote d'Ivoire, Ghana, Togo, Benin, parts of Mali and Burkina Faso



## Henipavirus:

Endemic: Malaysia, India, Singapore, Philippines, Australia, Bangladesh



### Upcoming development priorities (not mapped)

- Equine encephalitic viruses (Western, Eastern, Venezuelan)
- Q Fever
- Antimicrobial resistant bacteria
- Botulinum

\* Global distribution of natural plague foci (as of March 2016). Source: WHO/PED; \*\* Includes both Ebolavirus and Marburg  
• Sources: CDC, WHO

Source Links: CCHF [\(a\)](#) [\(b\)](#); Filovirus [\(c\)](#) [\(d\)](#) [\(e\)](#) [\(f\)](#); Plague [\(g\)](#) [\(h\)](#); Lassa [\(i\)](#) [\(j\)](#); Henipa [\(k\)](#) [\(l\)](#) [\(m\)](#)














# SYSTEM OF SYSTEMS: VACCINE DEVELOPMENT & DELIVERY







# VAMP EFFORTS

System		Sub-system	Carriers & Adjuvants	Delivery Method	Partners	Threat Families	Threats	Readiness
Traditional (Vaccines) Systems	RNA systems	mRNA	• Lipid Nanoparticles (LNP)	• Intramuscular • Alternative deliveries (options)	 	• Arenaviruses • Filoviruses	• Lassa • Aerosol Filoviruses (Ebola, Marburg, Sudan)	• Initial manufacturing • Pre-clinical animal work
			• Lipid Nanoparticles (LNP)	• Intramuscular • Skin patch		• Influenza	• Pandemic Avian Flu	• Initial manufacturing • Pre-clinical animal work
		saRNA	• Lipid Inorganic Nanoparticle (LION)	• Intramuscular • Skin patch (option)	 	• Henipaviruses • Nairoviruses	• Nipah • CCHF	• Initial manufacturing • Pre-clinical animal work
			• Nanostructured Lipid Carrier (NLC)	• Intranasal • Intramuscular		• Influenza	• Pandemic Avian Flu	• Initial manufacturing • Pre-clinical animal work
	Vector systems	Modified Vaccinia Ankara (MVA-BN®)	• N/A	• Intramuscular		• Togaviruses (Alphaviruses)	• WEVEE	• Pre-clinical animal work • Non-GMP, GMP manufacturing
	Subunit protein(s) system(s)	E.coli	• Alhydrogel	• Intramuscular		• Plague	• Plague	• GMP manufactured
Non-Traditional (Biological Response Modifier) Systems	Oligodeoxy-nucleotide	CpG 1018	• CpG 1018 • Recombinant IFN (Type I)	• Intramuscular		• Plague	• Plague	• GMP manufactured • Clinical trial on-going
	Lipid small molecules	TLR Agonists 4/7/8	• N/A	• Intranasal		• Pan viral	• Pan-Flu, Nipah	• Initial manufacturing
	Lipid small molecules	TLR Agonists 2/6	• N/A	• Intranasal		• Pan viral	• Flu, Rhinovirus, SARS-COV2, Nipah	• Initial manufacturing
	Lipid small molecules	Interferon Lambda	• N/A	• Intranasal	In negotiation	• Pan viral	• Flu, SARS-COV2, Marburg, Ebola, Nipah	• Initial manufacturing





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# **RAPID ACQUISITION AND INVESTIGATION OF DRUGS FOR REPURPOSING**



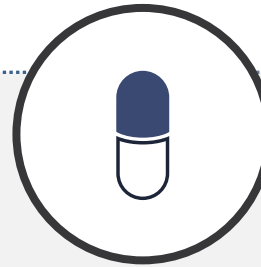
PROGRAMS EXECUTED ON BEHALF OF THE CHEMICAL AND BIOLOGICAL DEFENSE PROGRAM

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**





# RAIDR AIMS TO FEED INTO CLINICAL PRACTICE GUIDES (CPGS) THAT SERVICES USE FOR RAPID MEDICAL CARE

1

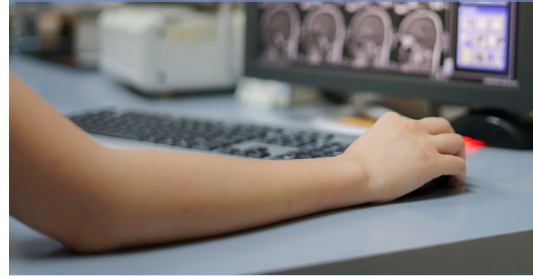
## Candidate Selection



- Identify FDA-approved drugs with high repurposing potential e.g.,
  - Favorable safety profile for new usage
  - Evidence for new target
  - Viable commercial partner/pathway to delivery

2

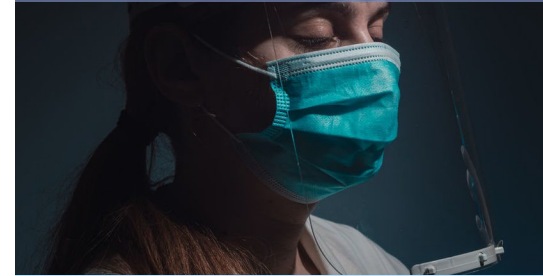
## Animal Model Studies



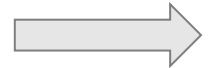
- Conduct animal studies to provide needed data package
- Demonstrate potent effect on desired target/mechanism through the efficacy studies

3

## Clinical Practice Guidelines



- Inform clinical practice guidelines used by responders for tactical approach to field treatment
- Incorporate data package into repurposing report and for EUA submission (if applicable)



... with potential to become Program of Record if clinical need is demonstrated / funding is available



# CET RAIDR EFFORTS

Threat	Etymology: MCM Candidate	Symptomology/MOA	RAIDR Purpose/Study Scope	Readiness	Approved Human Dosage
Acute Respiratory Disorder	Sulfur Mustard: Leukine	Stimulates macrophages in the lungs; blunts myelosuppression	NHP Challenge Study with Standard of Care against sulfur mustard	Approved for Radiation Exposure; May behave as BRM in some viral infections	For injection (lyophilized powder): 250 mcg of sargramostim in singledose vial for reconstitution. Injection (solution): 500 mcg per mL sargramostim in multiple-dose vial.
	Yersinia Pestis (Pneumonic Plague): Omadacycline	Synthetic Antibacterial, mitigates risk of antibacterial resistance	NHP aerosolized challenge study with standard of care at serial time points to test as PEP and treatment to aerosolized plague	Approved for Community Acquired Bacterial Pneumonia; Acute Bacterial Skin and Skin Structure Infections. Currently under investigation against Anthrax by BARDA.	For Injection: 100 mg of omadacycline as a lyophilized powder in a single dose vial for reconstitution and further dilution before intravenous infusion Tablets: 150 mg omadacycline
Refractory Status Epilepticus & Paralytic Toxin Intoxication	Nerve Agent: Dexmedetomidine	Counters overexcitement of central nervous system in status epilepticus	NHP challenge study to determine efficacy and neuroprotective qualities against chem exposure	Sedative. Approved as anesthetic; used in emergencies to treat refractory status epilepticus, existing rodent studies	Achieve required concentration (4 mcg/mL) prior to administration.
	Nerve Agent: Isoflurane	Counters overexcitement of central nervous system in status epilepticus	Mouse and rat challenge study to determine efficacy and neuroprotective qualities against chem exposure	Sedative. Approved as anesthetic; used in emergencies to treat refractory status epilepticus	Isoflurane induction requires 1.5% to 3% isoflurane for 7-10 minutes; then 1.0-2.5% isoflurane for the remainder of the time
	Nerve Agent: Ketamine	Counters overexcitement of central nervous system in status epilepticus	Minipig and NHP challenge study to determine efficacy against chem exposure	Sedative. Approved as anesthetic; used in emergencies to treat refractory status epilepticus, clinical trial for SE on-going, neuroprotective qualities demonstrated in rats	Intramuscular Route: range from 6.5 to 13 mg/kg. Intravenous Route: range from 1 mg/kg to 4.5 mg/kg.
Hemorrhagic Fever	Nipah/Hendra: TBD	Broad spectrum antiviral	Using AI/ML to find repurposing candidates to use in in vitro and subsequent in vivo studies	Approved drugs, various indications	TBD
	Lassa: TBD	Broad spectrum antiviral	Same as Nipah/Hendra	Approved drugs, various indications	TBD
	Crimean Congo Hemorrhagic fever (CCHF): TBD	Broad spectrum antiviral	Same as Nipah/Hendra	Approved drugs, various indications	TBD





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