JSTO in the News

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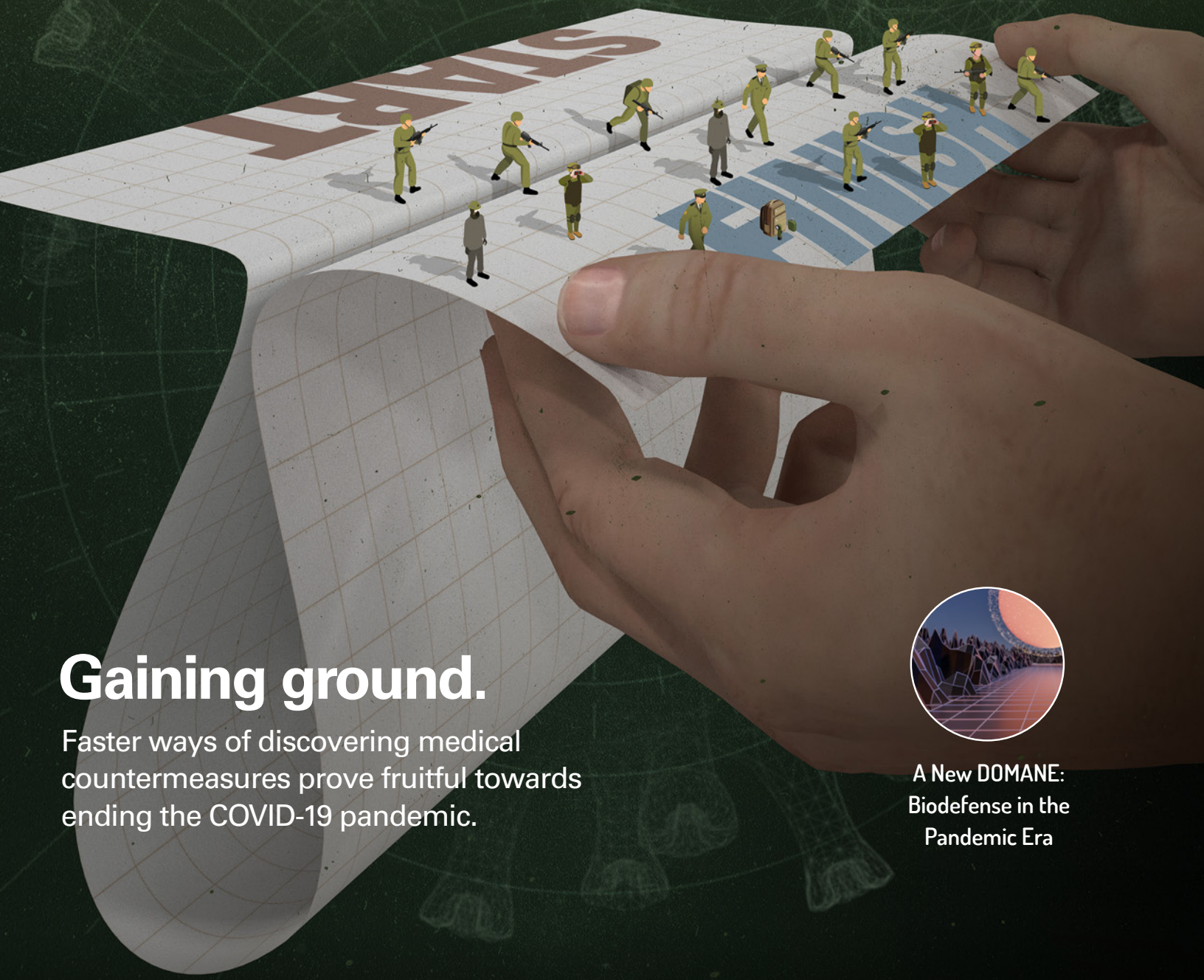

Gaining ground.

Faster ways of discovering medical countermeasures prove fruitful towards ending the COVID-19 pandemic.

A New DOMANE: Biodefense in the Pandemic Era

Lead DoD science and technology to anticipate, defend, and safeguard against chemical and biological threats for the warfighter and the nation.

DEFENSE THREAT REDUCTION AGENCY

Research and Development Directorate
Chemical and Biological Technologies Department
Joint Science and Technology Office for Chemical and Biological Defense

8725 John J Kingman Road, Stop 6201, Fort Belvoir, VA 22060

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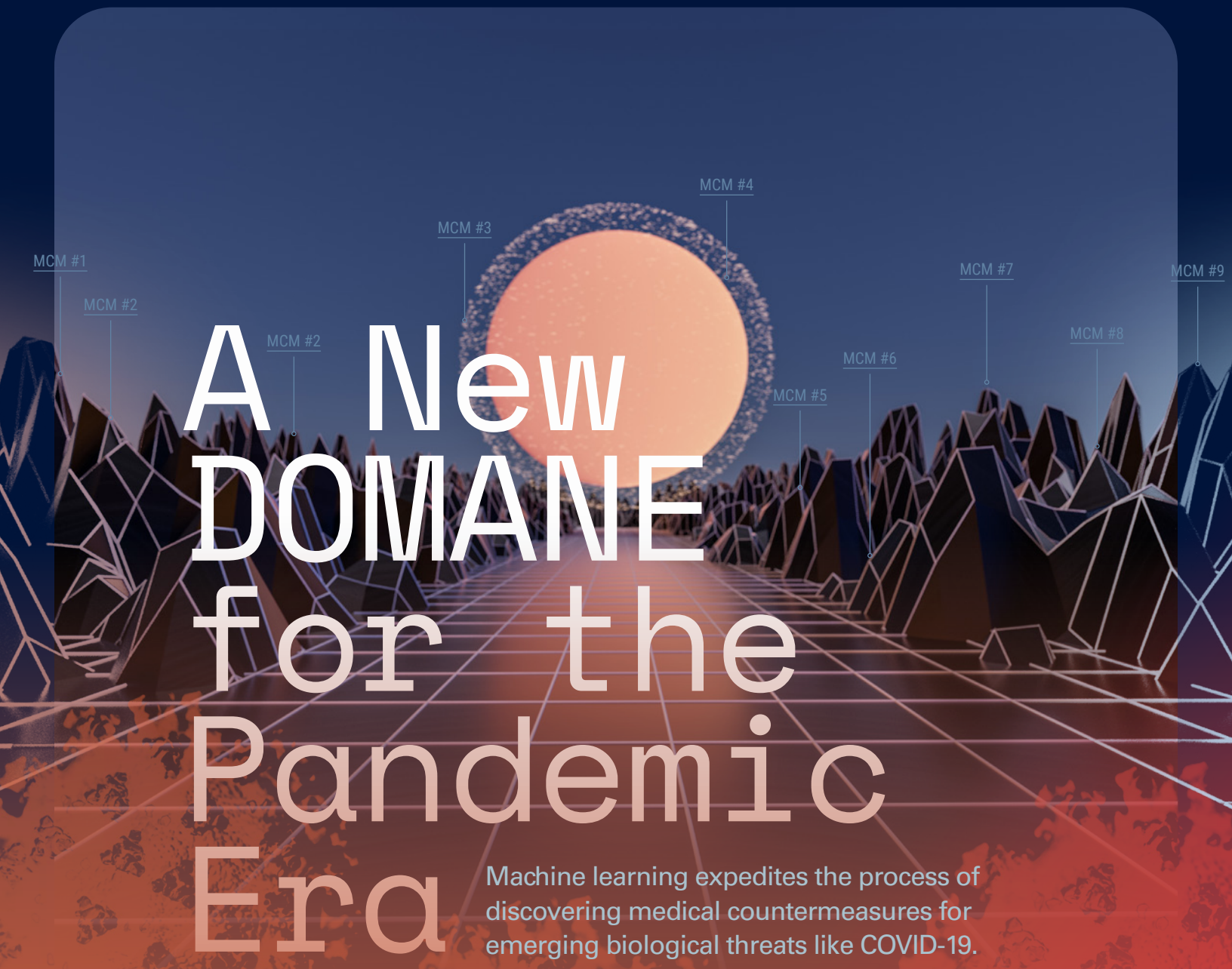
Front cover illustration courtesy of the Defense Threat Reduction Agency's Chemical and Biological Technologies Department.

Inside cover: A soldier prepares a sample to be tested for COVID-19 at Joint Base Elmendorf-Richardson, Alaska. Photo courtesy of the U.S. Air Force. Photo by Airman 1st Class Emily Farnsworth.

Back cover: A lab manager studies Coronavirus protein samples in an effort to produce a COVID-19 vaccine candidate. Photo courtesy of U.S. Army. Photo by Mike Walters.



A New DOMANE for the Pandemic Era

Machine learning expedites the process of discovering medical countermeasures for emerging biological threats like COVID-19.

The Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department, in its role as the Joint Science and Technology Office (JSTO), is developing a system-of-systems called DOMANE — Discovery of MCMs (medical countermeasures) Against Novel Entities — an interdisciplinary effort with team members whose expertise include computer science, physics, and medicine. DTRA CB posits that one drug may be insufficient towards countering a threat, so it is developing DOMANE to rapidly identify a combination of drugs to impact the novel biological threat from multiple targets, which may prove effective in promoting a disease-modifying effect to counter the biological threat.

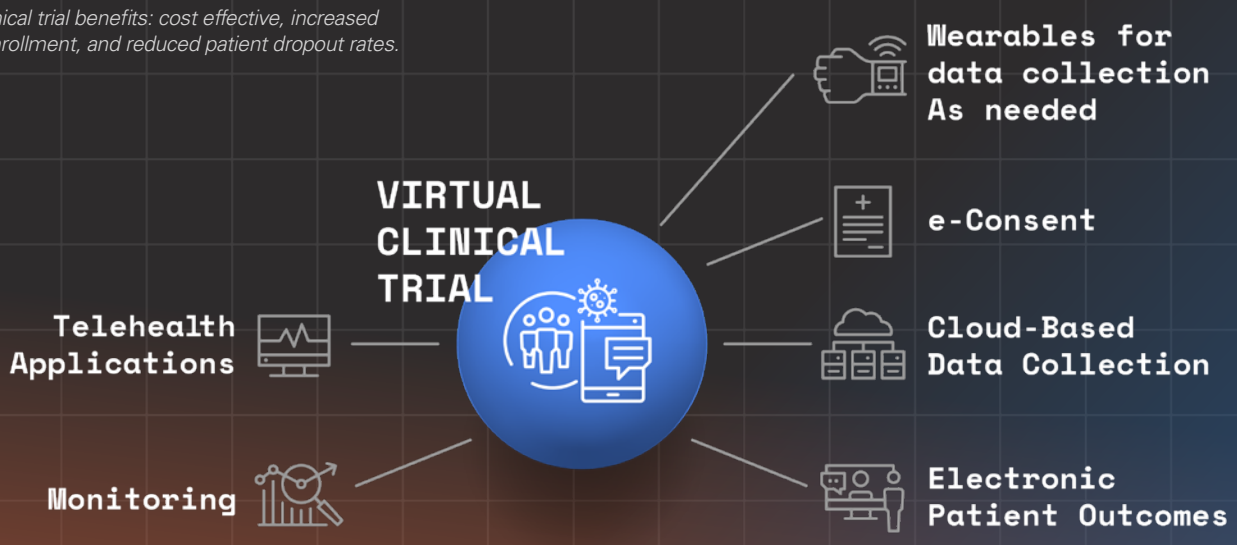
Systems within DOMANE include machine learning, high-throughput screening, *in silico* predictive tools, cryogenic electron microscopy (cryo-EM), organ-on-a-chip, and other emergent technologies. Machine-learning algorithms greatly reduce the time needed to search vast amounts of data on drugs and diseases. DOMANE is possible, in part, because of research studies that have occurred over the past several decades on biological threat agents and MCMs. The studies resulted in the global availability of a large repository of laboratory and clinical data ("big data") on how biological threats affect the human body.

The COVID-19 pandemic and the resulting national human and economic toll demonstrate a clear and present vulnerability of the U.S. to emerging and unknown contagious infectious diseases. For Joint Forces on the battlefield, the possibility of illness due to emerging biological threats can impact their mission. Ideally, they should be equipped with the MCMs they need to lessen the influence of emerging biological threats.

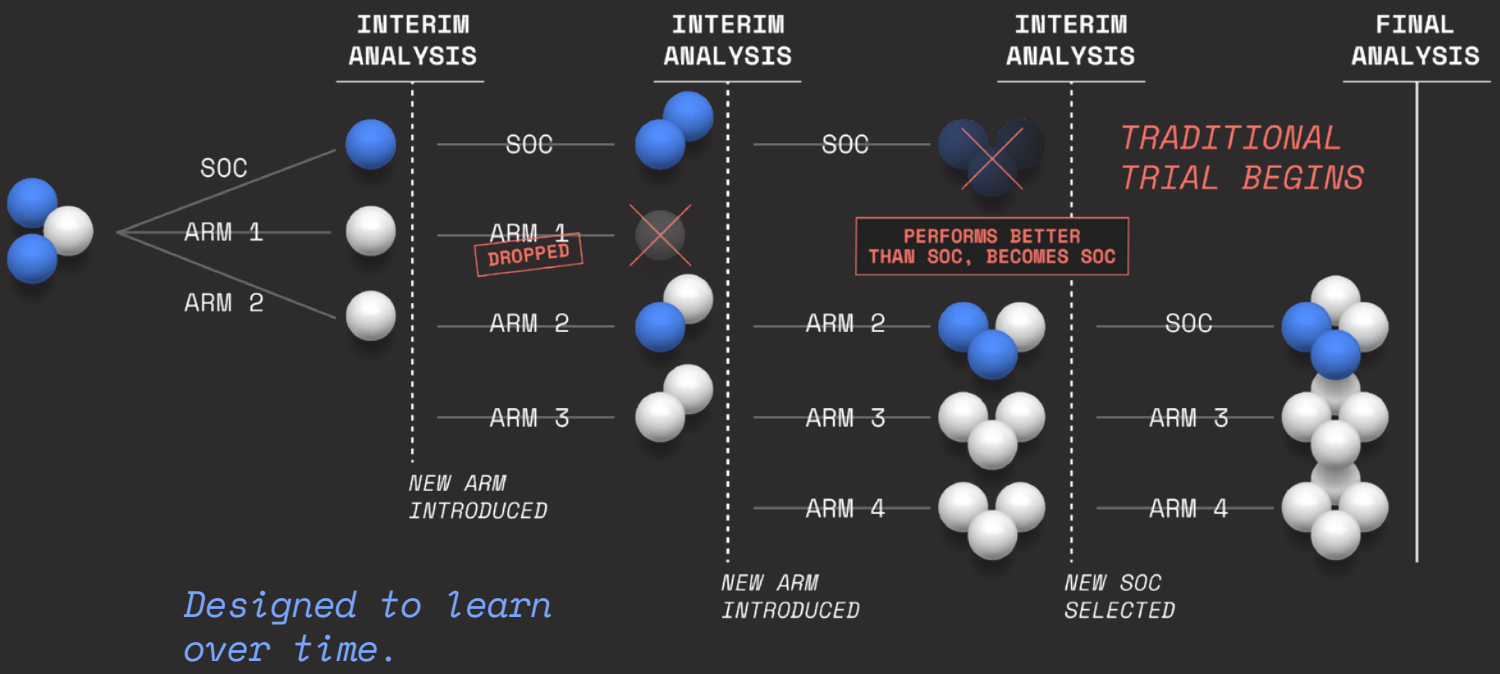
Utilizing drugs already approved by the Food and Drug Administration (FDA), DOMANE will evaluate the feasibility of repurposing them as MCMs to combat emerging threats.

DOMANE started in 2019, before the current pandemic, with the goal to shorten the traditional, multi-year timeline for developing MCMs to treat novel diseases. Utilizing drugs already approved by the Food and Drug Administration (FDA), DOMANE will evaluate the feasibility of repurposing them as MCMs to combat emerging threats. Some of the advantages to using FDA-approved drugs are that they are already manufacturable, have well-known toxicological profiles, and can proceed directly to human efficacy or Animal Rule studies. This can reduce or eliminate the time-intensive animal toxicology and human safety studies and enhance current good manufacturing practice to scale up process and ongoing stability assessment.

Virtual clinical trial benefits: cost effective, increased patient enrollment, and reduced patient dropout rates.



Adaptive Platform Trials



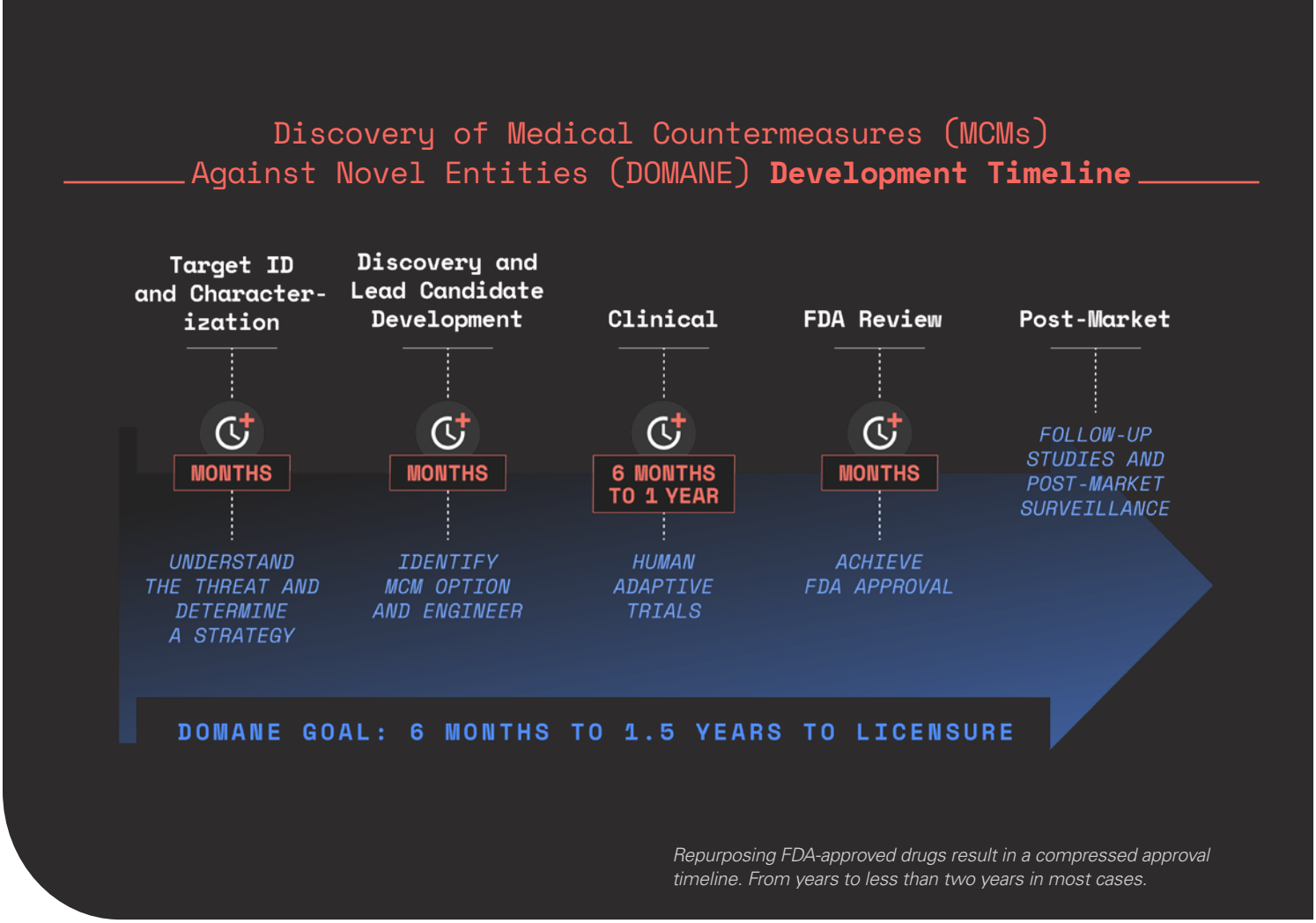
Adaptive Trials test multiple treatments against the Standard of Care (SOC) simultaneously. If one treatment performs well, it can become the new SOC, and future treatments are evaluated against it. If a treatment does poorly, it is removed from the trial. Additional treatment candidates can enter as new arms at any time.

The engine will produce in months, not decades, MCMs ready for pre-clinical and clinical development to protect the Joint Force and the nation against biological threats.

DTRA-JSTO is testing DOMANE using COVID-19 as a proof of concept to evaluate whether the DOMANE concept can identify drugs that are an effective treatment against the disease. DOMANE has already identified several FDA-approved drugs that can be repurposed to treat COVID-19, and these drugs have shown indications of potential efficacy in numerous case studies.

The next step is setting up randomized clinical trials to fully demonstrate the effectiveness of these repurposed drugs. To do this, adaptive, platform clinical trials will evaluate multiple drug combinations, dosages, and administration schedules performed in parallel. The adaptive nature of the trials enables clinical scientists to react to initial data from the trials. For example, if a drug and its approved dosage are ineffective or are having unanticipated effects, then clinicians can change the dosage or add another drug to the combination to pursue another therapeutic option.

The efficacy of COVID-19 drugs identified by DOMANE will be tested with two inpatient clinical trials and a planned virtual clinical trial. One inpatient trial is evaluating the efficacy of DOMANE-identified drugs for patients with severe, late-stage COVID-19 and the other inpatient trial is assessing the efficacy of drugs in COVID-19 patients newly admitted to hospitals. The virtual clinical trial will include outpatients who are newly diagnosed with COVID-19. Virtual outpatient trials dramatically reduce the cost of clinical trials and offer the Department of Defense (DoD) an opportunity to conduct these studies wherever patients with the disease are located, such as on a military ship or base.



Repurposing FDA-approved drugs result in a compressed approval timeline. From years to less than two years in most cases.

DTRA-JSTO recently held a two-day virtual workshop consisting of subject matter experts in synthetic biology, artificial intelligence and machine learning, organs-on-a-chip, high-throughput screening, microcrystal electron diffraction, cryo-EM, animal model development, and other fields. The goal of the workshop was to bring together a collaborative team with diverse technical capabilities to develop an operational workflow for rapidly discovering MCMs of interest. The workshop included presentations and panel discussions among experts from academia, industry, national laboratories, DoD, and other U.S. government organizations. The workshop identified capability gaps that will need to be addressed as well as collaborative opportunities to advance DOMANE that will begin the process of changing our defense against emerging biological and chemical threats.

The current COVID-19 pandemic has demonstrated the impact of biological diseases on national security and everyday life, which could set the stage for an era when there will be significant temptation for both state and non-state actors to intentionally execute a biological attack to cause pandemic-level devastation. Successful development of DOMANE will produce a discovery and verification engine for identifying MCMs for emerging biological threats. The engine will produce in months, not decades, MCMs ready for pre-clinical and clinical development to protect the Joint Force and the nation against biological threats. With DOMANE, DoD has the capability to fight not only COVID-19 but also diseases that have not yet surfaced, thereby ensuring the maintenance of a strong and lethal force. ●

POCs: Revell Phillips, Ph.D., l.r.phillips.civ@mail.mil; Dale Taylor, dale.e.taylor4.civ@mail.mil

Within the Defense Threat Reduction Agency's Research and Development Directorate resides the Chemical and Biological Technologies Department. The department serves as the Joint Science and Technology Office for Chemical and Biological Defense. This publication highlights the department's advancements in protecting warfighters and citizens from chemical and biological threats through the innovative application of science and technology. DTRA.mil