UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND READINESS

FEB - 9 2024

The Honorable Patty Murray
Chair
Committee on Appropriations
United States Senate
Washington, DC 20510

Dear Madam Chair:

The Department's response to House Report 117–388, pages 267-268, accompanying H.R. 8236, the Department of Defense Appropriations Bill, 2023, "Metastatic Cancer Research," is enclosed. Unfortunately, due to the nature and complexity of this report, and required coordination with Departmental stakeholders, our response took longer than expected.

The report provides an update on the implemented recommendations contained in the 2018 Metastatic Cancer Task Force report to Congress; includes efforts to advance diverse research opportunities for metastatic cancer research; summarizes metastatic cancer research efforts undertaken by the Congressionally Directed Medical Research Programs (CDMRP) from Fiscal Years 2017 to 2021; and highlights success stories from CDMRP metastatic cancer research investments. All clinical trial award budgets include research-related subject costs and may support costs to address potential barriers to participation, if requested (such as transportation, lodging, participation incentives, etc.). CDMRP investments have also ultimately led to various therapeutics shown to improve patient outcomes, including progression-free survival and overall survival.

Thank you for your continued strong support for the health and well-being of our Service members, veterans, and their families. I am sending a similar letter to the House Appropriations Committee.

Sincerely,

[redacted]

Ashish S. Vazirani
Acting

Enclosure:
As stated

cc:
The Honorable Susan Collins
Vice Chair

UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND READINESS

The Honorable Kay Granger
Chairwoman
Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

FEB - 9 2024

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Sincerely,

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Ashish S. Vazirani
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Enclosure:
As stated

cc:
The Honorable Rosa L. DeLauro
Ranking Member

Report to the Committees on Appropriations of the Senate and the House of Representatives

Metastatic Cancer Research

February 2024

The estimated cost of this report for the Department of Defense (DoD) is approximately $1,800.00 for Fiscal Year 2023. This includes $800.00 in expenses and $1,000.00 in DoD labor.

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BACKGROUND AND PURPOSE

This report is in response to House Report 117–388, pages 267–268, accompanying H.R. 8236, the Department of Defense (DoD) Appropriations Bill, 2023, which requests the Assistant Secretary of Defense for Health Affairs to provide a report to the House and Senate Appropriations Committees on the progress of implementing the recommendations contained in the 2018 Task Force report to Congress on metastatic cancer, including an identification of any barriers to implementation and further recommendations to improve diverse research opportunities for metastatic cancer research for congressional consideration. House Report 117–388 reiterates the Committee's interest in areas where assistance from other Federal agencies is required for full implementation of the recommendations within the Task Force's report.

As defined for the purposes of this report, metastatic cancer is cancer that has spread beyond the primary organ of origin and regional lymph nodes into other major organ sites. Metastatic cancer is responsible for the majority of cancer-related deaths in the general population. Distant recurrence refers to cancer that has metastasized. A recurrence signifies cancer that returns after a period of remission.

CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS (CDMRP): METASTATIC CANCER RESEARCH EFFORTS

The DoD CDMRP funds nine congressionally directed research programs focused on cancer. Table 1 summarizes total CDMRP investments in metastatic cancer research from Fiscal Year (FY) 2017–FY 2021.

Table 1. FY 2017–FY 2021 CDMRP Investments in Metastatic Cancer Research

Program	Cancer Type/Topic	Number of Awards	Funding
Peer Reviewed Cancer Research Program (PRCRP)*	Adrenal Cancer	3	$1.6M
	Bladder Cancer	24	$18.7M
	Blood Cancers	3	$1.2M
	Brain Cancer	12	$7.8M
	Cancer In Children, Adolescents, and Young Adults	3	$1.4M
	Colorectal Cancer	27	$19.9M
	Endometrial Cancer	1	$2.2M
	Esophageal Cancer	4	$5.4M
	Germ Cell Cancers	1	$0.6M
	Head and Neck Cancer	7	$3.7M

Program	Cancer Type/Topic	Number of Awards	Funding
	Immunotherapy	9	$6.6M
	Liver Cancer	10	$6.9M
	Lymphoma	6	$5.6M
	Melanoma and Other Skin Cancers	10	$6.2M
	Metastatic Cancers	2	$2.3M
	Myeloma	1	$0.7M
	Neuroblastoma	7	$6.0M
	Pancreatic Cancer (FY11-19)	12	$8.8M
	Pediatric Brain Tumors	5	$2.0M
	Pediatric, Adolescent, and Young Adult Cancers	9	$13.3M
	Rare Cancers	2	$2.3M
	Sarcoma	6	$5.1M
	Stomach Cancer	5	$5.3M
	Thyroid Cancer	1	$1.9M
	PRCRP Total:	***170***	***$135.5M***
Breast Cancer Research Program (BCRP)	Breast	280	$397.0M
Kidney Cancer Research Program (KCRP)	Kidney	53	$31.5M
Lung Cancer Research Program (LCRP)	Lung	61	$20.4M
Melanoma Research Program (MRP)	Melanoma	53	$24.7M
Ovarian Cancer Research Program (OCRP)	Ovarian	78	$48.8M
Pancreatic Cancer Research Program (PCARP) (FY 2020–FY 2021)	Pancreatic	19	$10.3M

Program	Cancer Type/Topic	Number of Awards	Funding
Prostate Cancer Research Program (PCRP)	Prostate	247	$203.7M
Rare Cancers Research Program (RCRP)	Rare Cancers	12	$3.4M
	Total:	***973***	***$875.3M***

** Each fiscal year, Congress directs the topic areas for inclusion under PRCRP funding. Therefore, topic areas are subject to change each year based on Defense Appropriations legislation.*

CDMRP invested in preclinical, translational, and/or clinical research that ultimately led to Food and Drug Administration (FDA) approval and/or commercialization for the products and clinical approaches for metastatic cancers identified in Table 2. All the therapeutics listed have demonstrated improvement in patient outcomes, such as progression-free survival or overall survival.

Table 2. Metastatic Cancer Success Stories from CDMRP-Funded Research

Clinical Approaches	Overview	Cancer Type
XPOVIO® (selinexor)	An FDA-approved drug used to treat relapsed/refractory multiple myeloma and diffuse large B-cell lymphoma.	Blood Cancers
Herceptin® (trastuzumab)	An FDA-approved monoclonal antibody that targets the human epidermal growth factor receptor 2 (HER2) and is part of standard-of-care treatment regimens for HER2-positive early-stage and metastatic breast cancers.	Breast
Ibrance® (palbociclib)	An FDA-approved treatment in combination with an aromatase inhibitor or hormone therapy used to treat hormone-positive metastatic breast cancer.	Breast
Kisqali® (ribociclib)	An FDA-approved treatment in combination with an aromatase inhibitor or hormone therapy used to treat hormone-positive metastatic breast cancer in premenopausal and menopausal women.	Breast
Verzenio™ (abemaciclib)	An FDA-approved treatment in combination with an aromatase inhibitor or hormone therapy, as well as a monotherapy, used to treat hormone-positive metastatic breast cancer.	Breast
Adjuvant Tamoxifen Longer Against Shorter (ATLAS)	The ATLAS clinical trial determined that tamoxifen reduced risk of recurrence or death from breast cancer among women who took tamoxifen for 10 years versus those who took it for 5 years. These findings changed clinical practice.	Breast

Clinical Approaches	Overview	Cancer Type
MetaSite Breast™	A clinically validated test that measures Tumor Microenvironment of Metastasis sites to predict metastatic potential of the primary tumor. MetaSite Breast™, licensed to MetaStat, Inc., is analytically validated under the Clinical Laboratory Improvement Amendments and publicly available.	Breast
MenaCalc™	MenaCalc™, licensed to Metastat, Inc. and clinically validated for use in treatment decision making, serves as a prognostic marker for distant recurrence of breast cancer. MenaCalc™ has also served as an independent prognostic factor and predictor of metastasis for other cancer types, including non-small cell lung carcinoma.	Breast; Others
Breast Cancer Index	A commercially available (bioTheranostics) biomarker-based quantitative assessment test used to evaluate risk of early and late recurrence of breast cancer.	Breast
Sentinel Lymph Node Biopsy	A standard-of-care method that enables clinicians to determine both tumor staging and the need for more extensive surgery to address breast cancers that have invaded the lymph nodes.	Breast
Velcade® (bortezomib)	An FDA-approved chemotherapy used for multiple myeloma that inhibits proteasomes, leading to cancer cell death.	Multiple Myeloma
Rubraca® (rucaparib)	A poly adenosine diphosphate-ribose polymerase inhibitor approved by the FDA as a maintenance therapy for women with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer to prevent progression to advanced (metastatic) disease.	Ovarian; Prostate
DANYELZA® (naxitamab)	An FDA-approved monoclonal antibody targeting a ganglioside molecule called GD2, in combination with granulocyte-macrophage colony-stimulating factor, to treat metastatic relapsed neuroblastoma in the bone or bone marrow.	Neuro-blastoma
XGEVA® (denosumab)	An FDA-approved antibody that blocks the bone resorption protein receptor activator of nuclear factor kappa-B ligand (RANKL), slows the progression of prostate cancer bone metastasis, and prevents skeletal-related events (such as fractures), which often occur after androgen deprivation therapy.	Prostate
Xtandi® (enzalutamide)	An FDA-approved androgen receptor (AR) inhibitor used to treat both non-metastatic and metastatic castration-resistant prostate cancer (CRPC) patients.	Prostate

Clinical Approaches	Overview	Cancer Type
Zytiga® (abiraterone)	An FDA-approved cytochrome P450 17A1 (CYP17) inhibitor used to treat metastatic CRPC.	Prostate
NuSAP1	A biomarker associated with metastatic prostate cancer that is part of two commercially available assays (Decipher; Prolaris) used to help guide prostate cancer treatment.	Prostate
ERLEADA™ (apalutamide)	An AR inhibitor and the first FDA-approved drug used for patients with non-metastatic CRPC. It was the first drug to be FDA-approved based on a new intermediate clinical endpoint measuring improvements in metastasis-free survival (time before disease metastasizes).	Prostate
Oncotype IQ AR-V7 Nucleus Detection Test	A commercially available liquid biopsy assay that measures the AR variant, AR-V7, in circulating tumor cells to guide treatment (precision medicine) of metastatic CRPC.	Prostate
JEVTANA® (cabazitaxel)	Anti-microtubule taxane chemotherapy approved for the treatment of metastatic CRPC in patients previously treated with a docetaxel-containing regimen.	Prostate
Pylarify® (PSMA-Targeted PET Imaging Agent)	Radioactive diagnostic agent that identifies prostate-specific membrane antigen (PSMA) positive lesions in men with suspected prostate cancer metastasis using positron emission tomography (PET).	Prostate
Quantitative Total Bone Imaging Software (QTxI 1.0)	An FDA 510(k)-cleared software tool that automatically identifies and contours tracer uptake in bone for full or partial body imaging scans. QTxI 1.0 fuses a series of scans from a patient over time, allowing for evaluation of changes to each tumor hotspot and determination of treatment response by individual tumor metastases.	Prostate; Breast
ZEJULA (niraparib)	An orally administered ADP-ribose polymerase (PARP) inhibitor that was granted Breakthrough Therapy Designation as a treatment for metastatic castration-resistant prostate cancer.	Prostate

DOD IMPLEMENTATION OF RECOMMENDATIONS FROM THE TASK FORCE ON METASTATIC CANCER

Table 3 summarizes each of the implemented recommendations in the 2018 Task Force Report on Metastatic Cancer.

Table 3. Update on Implemented Task Force Recommendations

CLINICAL TRIALS	
Recommendation:	**Expand the interdisciplinary approach to research to include clinicians, translational and basic researchers, data scientists, and experts in fields other than medicine (e.g., engineers, chemists, mathematicians).**
DoD Status:	Fully Implemented in DoD.
Update:	CDMRP has made significant efforts to expand the interdisciplinary approach to research. Multiple programs offer funding opportunities to promote translational and clinical research through interdisciplinary teams, including partnerships among basic, translational, and clinical scientists, and experts in other fields. Applications for these funding opportunities undergo evaluations that consider how well the proposed research integrates different scientific disciplines to enhance current understanding of cancer research complexities. Examples include: 1) Transformative Breast Cancer Consortium Award, which focuses on "[r]esearch that includes different disciplines that come together to address ending breast cancer with an ecologic approach;" 2) Translational Team Science Award, which intends to "support multi-investigator, multidisciplinary teams to perform clinical research studies;" 3) Virtual Cancer Center Director Award, which aims to "[e]ncourage multi-disciplinary, convergent collaborative research;" and 4) the Convergent Science Cancer Consortium Development Award, which requires the consortium to "be a diverse discipline coalition." At the Murtha Cancer Center[1](MCC), the APOLLO[2] (Applied Proteogenomics Organizational Learning and Outcomes) research Program implements this interdisciplinary aspect to research, which became operational in 2022 at the eight largest Defense Health Agency (DHA) medical centers and hospitals[3]. In addition, at MCC, Cancer Moonshot 2.0 began in 2022 and is spearheaded by the

[1] The MCC is the DoD Center of Excellence for cancer care and research, performing clinical, basic, and advanced translational research for military relevant cancers. The ultimate goal is to prevent, screen for, detect early, treat with precision and personalized approaches, and cure with minimal side effects as possible, as well as mitigate the impact of cancer and cancer treatment on Service members and their caregivers and family members to enable them to return to duty, become re-classified to a new duty position, or reintegrate into civilian life with highest possible quality of life.

[2] APOLLO is a DoD-led, tri-agency (DoD, National Cancer Institute (NCI), and Department of Veterans Affairs (VA)) translational clinical research program developed from the 2016 Federal Cancer Moonshot program. APOLLO enrolls cancer patients across DHA and VA hospitals and performs gene sequencing of the tumors and blood of all patients; identifies genetic changes and targets in tumors for precision-targeted therapies, as well as genetic risks for other diseases and cancers; and performs full-scale tumor protein assessments. These efforts enable MCC to offer the latest precision oncology treatments and research for its DoD and VA patients. MCC-funded DoD laboratories conduct all molecular analyses and sequencing.

[3] The 10 DHA medical centers and hospitals are Walter Reed National Military Medical Center (WRNMMC); Navy Medical Center Portsmouth; Womack Army Medical Center; Keesler Medical Center; San Antonio Military Medical Center; Tripler Army Medical Center; Naval Medical Center San Diego; Madigan Army Medical Center, William Beaumont Medical Center (El Paso, TX); and Fort Belvoir Community Hospital.

	PROMETHEUS (PROject for Military Exposures and Toxin History Evaluation in U.S. Service members) research portfolio consisting of over 175 personnel from across the Federal government, multiple agencies, and public-private partnerships and representing multiple non-medical disciplines such as chemists, experts in exposure science, and multiple other areas.
Recommendation for Assistance Required:	None.
Recommendation:	**Consider trial designs that add strata for patients with metastatic cancer who are frequently ineligible for clinical trials (such as worse performance status, abnormal laboratory values, location of metastases, rare tumor types, comorbidities, and other conditions).**
DoD Status:	Being Implemented in DoD.
Update:	Eight of CDMRP's nine cancer-focused programs offer funding opportunities for clinical trials. CDMRP references the Metastatic Cancer Task Force's recommendations in its cancer research program funding opportunity announcements, stating, "[a] congressionally mandated Metastatic Cancer Task Force was formed with the purpose of identifying ways to help accelerate clinical and translational research aimed at extending the lives of advanced state and recurrent patients. As a member of the Metastatic Cancer Task Force, the CDMRP encourages applicants to review the recommendations (https://health.mil/Reference-Center/Congressional-Testimonies/2018/05/03/Metastatic-CancerResearch) and submit research ideas to address these recommendations provided they are within the limitations of this funding opportunity and fit with the FY 2022 [program] priorities." This includes the recommendation to consider trial designs that add strata. CDMRP considers this specific recommendation at the time of negotiations for awards that include a clinical trial for metastatic cancer. For MCC, its APOLLO research program allows for enrollment of patients with any cancer type, disease stage, and performance status. Likewise, for MCC's new PROMETHEUS 8A research study, all patients with metastatic cancer and any performance status, comorbidities, or lab values will be eligible.
Recommendation for Assistance Required:	None. DoD Agencies will continue collaboration in this area.
Recommendation:	**Develop strategies to ease the regulatory burden of the clinical trials process (e.g., increase utilization of centralized institutional review boards (IRBs); refine adverse event reporting; provide additional guidance for the consistent application of regulations across IRBs).**
DoD Status:	Being Implemented in DoD.
Update:	Consolidation of oversight for the Human Research Protections Program (HRPP) at military medical treatment facilities (MTFs) under the DHA Office of Research Protections (ORP), in accordance with the National Defense Authorization Act for FY 2017, was completed in October 2020 for MTFs within the continental United States and in October 2021 for MTFs located outside the continental United States. DHA ORP has implemented standardized policies and procedures for institutional HRPPs and IRBs and has centralized IRB review to 5 DHA IRBs (from 11 DoD IRBs) at the MTFs. Additionally, the use of the electronic IRB system has standardized the

	forms and processes used for protocol submission and review across all DHA-managed MTFs/institutions and all other DoD institutions using the system. The U.S. Army Medical Research and Development Command (USAMRDC) manages CDMRP funding. The CDMRP uses standard processes to facilitate USAMRDC review and approval of DoD-funded clinical trials, which is required before any research may begin and, in accordance with the Defense Federal Acquisition Regulation Supplement, is in addition to the local IRB or Ethics Committee (EC) review, wherein a non-DoD IRB or EC conducts the review. CDMRP uses the Office of Management and Budget-mandated Federal-wide Research Performance Progress Report to monitor the technical aspects of clinical trial progress (e.g., monitoring subject accrual) and to standardize investigators' annual and final progress reporting on DoD-funded projects. Additionally, CDMRP provides investigators with a suggested quarterly report template to facilitate standardized reporting. The DoD adheres to the Common Rule (45 CFR Part 46 and 32 CFR Part 219), including 32 CFR § 114(b), which requires all institutions located within the United States engaged in cooperative research (i.e., any project involving non-exempt human research at more than one institution) conducted or supported by a Federal agency to rely upon approval by a single IRB for the portion of the research that is conducted in the United States. Specifically with respect to NCI-funded metastatic cancer clinical trials and other cancer research, DoD institutions may use NCI Central IRB review and approval for DoD-conducted research funded through NCI.
Recommendation for Assistance Required:	None. DoD continues to achieve progress in this area.

DIAGNOSTICS

Recommendation:	**Invest in novel diagnostic imaging tracers and techniques that are more sensitive and specific for the detection of early metastatic disease states.**
DoD Status:	Fully Implemented in DoD.
Update:	DoD has fully implemented this recommendation through the CDMRP research program. CDMRP cancer-focused programs will continue to invest in this type of research. MCC at WRNMMC, through its Nuclear Medicine department, has clinically available novel diagnostic imaging tracers and continues to be on the leading edge of offering these to its cancer patients especially in the search for metastatic disease. MCC also has a sustained collaboration with the NCI intramural research program in radiology, which develops the next generation of imaging agents in coordination with industry. MCC cancer patients have access to these novel agents through this partnership.
Recommendation for Assistance Required:	None. DoD continues to invest in this area.

Recommendation : Streamline and facilitate biomarker development for the diagnosis and monitoring of metastatic disease.	
DoD Status:	Fully Implemented in DoD.
Update:	CDMRP cancer-focused programs have and will continue to offer funding opportunities that support biomarker development for diagnosis and monitoring of metastatic disease. Streamlining biomarker efforts may undergo consideration for future funding opportunities as the scientific community achieves advances and establishes recommendations. MCC has been very active in this area through its DoD Federal Cancer Moonshot 1.0 (of 2016) and 2.0 (of 2022). For example, MCC Moonshot programs of APOLLO and DoD Framingham (both from Cancer Moonshot 1.0) have already discovered new biomarkers for oropharyngeal squamous cell cancer (in DoD Framingham 1) and lung adenocarcinoma (in DoD APOLLO 1), both of which have been peer-reviewed and published in high-impact journals. Moreover, all of MCC's raw molecular sequencing and proteomic data from APOLLO 1 have been shared publicly through the NCI's data commons (Genomic Data Commons, Proteomic Data Commons, and The Cancer Imaging Archive), resulting in over one terabyte of publicly-shared data from MCC Moonshot projects to date.
Recommendation for Assistance Required:	None.
Recommendation: Encourage tissue acquisition, when appropriate, and liquid biopsies throughout the duration of metastatic disease for clinical decision-making, laboratory research, and molecularly-driven clinical trials.	
DoD Status:	Fully Implemented in DoD.
Update:	Metastatic cancer studies funded by CDMRP cancer-focused programs already support tissue acquisition and/or liquid biopsy. Biorepositories that include metastatic samples were established by the following programs/funding opportunities: PCRP Prostate Cancer Biorepository Network; OCRP Program Project Award; OCRP Outcomes Consortium Award; OCRP Resource Development Award; LCRP Lung Cancer Biospecimen Resource Network; and RCRP Resource and Community Development Award. MCC has implemented and operationalized DoD's largest-ever tissue banking network and one of the highest quality in existence, across the 10 largest DoD DHA MTFs. MCC has implemented the MCC Research Program (MCCRP) tissue research protocols, which acquire cancer tissues from all stages of all types of cancers, including stage 4 (metastatic) cancer, and robust amounts of liquid biopsy materials from all patients. Currently, the MCC biobank holds over half a million biospecimens from tens of thousands of enrolled, consented patients, which have been used in hundreds of research studies with partners across the United States and the NCI. Additionally, MCC at WRNMMC, in collaboration with industry partners, has a clinical trial underway funded by the non-DoD civilian Breast Cancer Research Foundation that enrolls breast cancer patients with metastatic disease and studies their blood samples using four separate liquid biopsy platforms to find the best blood biomarkers for determining treatment response and enabling early detection of disease recurrence.
Recommendation for Assistance Required:	None.

BIOLOGY OF DISEASE	
Recommendation : Increase research investigating the etiology, progression, and treatment of metastatic disease.	
DoD Status:	Fully Implemented in DoD.
Update:	Research that investigates metastatic disease etiology, progression, and treatment is a priority or focus area of CDMRP's cancer-focused programs. In the 5-year period from FY 2017 to FY 2021, CDMRP funded 973 awards totaling $875.3M on metastatic cancer research. MCC has this aspect incorporated in its APOLLO research program, which is operational at eight DHA facilities.
Recommendation for Assistance Required:	None.
Recommendation: Encourage and support studies to develop more accurate and representative models of metastatic disease.	
DoD Status:	Fully Implemented in DoD.
Update:	The RCRP, initiated in FY 2020 and one of CDMRP's newest programs, has a specific focus area for development and validation of rare tumor-specific models. This focus area is especially important because of the paucity of metastatic disease models for rare cancers. Although the focus areas of other CDMRP-funded cancer-focused programs do not specifically include development of metastatic cancer models, CDMRP's funding opportunities support this type of research. CDMRP has funded several projects that are developing or have already developed representative models of metastatic disease. For example, the BCRP-funded research at the University of Utah resulted in publicly available, patient-centric tumor graft mouse models that replicate the diversity of human breast cancer and enhance the study of metastasis and drug efficacy.
Recommendation for Assistance Required:	None.
Recommendation: Explore novel funding mechanisms to support longer-term basic and translational studies of metastatic disease.	
DoD Status:	Fully Implemented in DoD.
Update:	CDMRP cancer-focused programs will continue to offer funding opportunities along the full spectrum of basic, translational, and clinical research, including clinical trials, for up to a four-year period of performance. Openly competed funding opportunities allow investigators who led successful studies to submit a new proposal for CDMRP funding to support the next phase of research. Some CDMRP cancer-focused programs offer an Expansion Award mechanism, which allows previously funded investigators to continue to

	expand upon their successful CDMRP-funded research in a limited competition. In 2023, MCC is looking to begin an organoid research lab program (representing metastatic cancer model development) within our Cancer Moonshot portfolio of APOLLO, in collaboration with scientists at the Veterans Health Administration.
Recommendation for Assistance Required:	None.
THERAPIES	
Recommendation: Study the metastatic process to identify therapeutics that will treat existing metastases, prevent the development of metastases, and/or target dormant cancer cells.	
DoD Status:	Fully Implemented in DoD.
Update:	CDMRP cancer-focused programs will continue to invest in this type of research. CDMRP cancer-focused programmatic priorities and strategic goals already include identifying or developing therapeutics to treat or prevent metastases or target dormant cancer cells. Through the MCC Cancer Moonshot research programs, MCC laboratories are studying the metastatic process across various aspects for cancers such as prostate, breast, pancreatic, lymphoma, glioblastoma brain cancer, testicular germ cell tumors, and other cancers of interest and importance to Service members.
Recommendation for Assistance Required:	None.
Recommendation: Optimize use of existing therapies (e.g., chemotherapy, hormonal, targeted, and immunotherapy).	
DoD Status:	Fully Implemented in DoD.
Update:	CDMRP cancer programs already offer funding opportunities supporting this type of research and have invested in studies to optimize the use of existing therapies. For example, the BCRP encourages research to revolutionize treatment regimens by replacing them with ones that are more effective, less toxic, and impact survival. MCC, at its main Center of Excellence (CoE) clinical site at WRNMMC, has implemented robust Tumor Boards that conduct ongoing reviews of all cancer patient treatments. These reviews ensure that existing patient therapies are optimized and align with the highest standard of national clinical cancer care at CoEs by adhering to National Comprehensive Cancer Network® (NCCN®) guidelines. Additionally, MCC has implemented a new Molecular Tumor Board (MTB) that incorporates tumor-specific molecular data, such as tumor gene sequencing, to further refine and align existing therapy treatments to best predicted effectiveness at a molecular level. MCC intends to expand this MTB into other DoD DHA hospitals through implementation of a virtual molecular tumor board so more patients can benefit across its direct care organization.

Recommendation for Assistance Required:	None.
Recommendation: Evaluate medications that are currently FDA-approved for other indications, as well as underdeveloped investigational agents for the treatment or prevention of metastasis.	
DoD Status:	Fully Implemented in DoD.
Update:	CDMRP cancer programs already offer funding opportunities supporting this type of research and have invested in studies on medications currently FDA-approved for other indications. For example, the BCRP is supporting a Phase II clinical trial for metastatic breast cancer that is testing the efficacy of a combination treatment consisting of fulvestrant (an estrogen receptor antagonist) and enzalutamide, which is an FDA-approved treatment for metastatic prostate cancer. The clinical trial has completed patient treatments, and data analyses are ongoing. MCC commonly approaches FDA for Compassionate Use allowance for medications for stage 4 metastatic cancer patients that are FDA-approved for other indications, but not for a patient's specific need.
Recommendation for Assistance Required:	None.
Recommendation: Identify the determinants of efficacy for immunotherapy.	
DoD Status:	Fully Implemented in DoD.
Update:	Funding opportunities offered by CDMRP cancer-focused programs support cancer immunotherapy studies. CDMRP cancer programs currently have a portfolio with 262 immunotherapy-focused awards totaling $267.9M, including $47.3M invested in clinical trials. The determinants of efficacy are under investigation, such as: "Targeting the Microbiome to Enable Immunotherapeutic Efficacy in Pancreatic Carcinoma," funded by the PCARP; "Targeting the Genetic Determinants of Immune Escape and Immunotherapy Failure in Castration-Resistant Prostate Cancer," funded by the PCRP; and "DNA [Deoxyribonucelic Acid] Damage as a Predictive Biomarker for Immunotherapy Response in Ovarian Cancer," funded by the OCRP.
Recommendation for Assistance Required:	None.

SYSTEM INFRASTRUCTURE	
Recommendation: Increase research on less widely studied cancers.	
DoD Status:	Fully Implemented in DoD.
Update:	As directed by Congress in FY 2020, CDMRP launched the RCRP to increase research on less widely studied cancers. The PRCRP congressionally directed topic areas include rare cancers and rare cancers subtypes. Research on rare subtypes of breast, ovarian, kidney, melanoma, and other cancers may also receive funding under the other cancer-specific congressionally directed programs. The KCRP has a specific focus area, to "[d]efine the biology of rare kidney cancers and develop treatments to improve outcomes and reduce death." The MRP released an FY 2022 funding opportunity, the Focused Program Award, for funding research on rare melanomas. In MCC, the Cancer Moonshot 1.0 program of APOLLO 5 is operational at the 10 largest DoD DHA direct care hospitals. APOLLO 5 enrolls all patients with cancer seen at these facilities, including rare cancers and those less widely studied, and performs full molecular analysis of DNA whole-genome sequencing, ribonucleic acid sequencing, and four different protein analysis platforms on these rare and poorly-studied cancers. In future years, APOLLO 5 will be able to make the molecular data currently being collected, available to the world-wide research community through uploading into the NCI Data Commons, as done for the APOLLO 1 lung adenocarcinoma molecular data in 2022 and 2023.
Recommendation for Assistance Required:	None.
Recommendation: Promote interdisciplinary collaborations by developing specific funding mechanisms, incentives, and resources for data sharing.	
DoD Status:	Fully Implemented in DoD.
Update:	CDMRP has made significant efforts to expand the interdisciplinary approach to research. Multiple programs offer funding opportunities designed to promote translational and clinical research by interdisciplinary teams, including partnerships among basic, translational, and clinical scientists, as well as experts in other fields.
Recommendation for Assistance Required:	None.

Recommendation:	**Incentivize investigator career development in metastatic cancer research through recognition of group and collaborative science by academic promotion and tenure committees.**
DoD Status:	Fully Implemented in DoD.
Update:	The OCRP, PRCRP, KCRP, and MRP incentivized Early Career Investigators (ECIs) to study metastatic cancer through the establishment of virtual academies or cancer centers, which are innovative researcher development platforms that provide intensive mentoring, national networking, collaborations, and a peer group for ECIs. In the longest standing of these efforts, several ECIs funded under the OCRP's Ovarian Cancer Academy successfully advanced in their careers through academic promotion, a result of the collaborative science fostered by this award mechanism.
Recommendation for Assistance Required:	As noted in the recommendation, this recommendation applies to academic promotion and tenure committees.
Recommendation:	**Streamline the proposal requirements and timelines for Federal funding agencies.**
DoD Status:	Fully Implemented in DoD.
Update:	USAMRDC, U.S. Army Medical Research Acquisition Activity, and CDMRP coordinate to streamline proposal requirements and funding timelines to the maximum extent practicable. CDMRP uses Federal-wide Grants.gov, including common forms, for grant submissions. New ideas for streamlining the proposal submission process undergo consideration every year. In contrast to other Federal agencies consisting of broad institutes or programs encompassing multiple diseases, CDMRP funding opportunities are disease-specific and based on annual guidance provided by Congress. CDMRP funding opportunities are refined each year based on this guidance, identified research gaps, and needs of the cancer communities. Timelines are dependent upon when the President signs the annual Defense Appropriations bill into law. Delays caused by continuing resolutions affect CDMRP proposal submission timelines.
Recommendation for Assistance Required:	None.
Recommendation:	**Recruit and incentivize senior scientists to serve on review panels to ensure that the most qualified reviewers are providing scientific evaluations of research proposals.**
DoD Status:	Fully Implemented in DoD.
Update:	CDMRP uses a two-tier review process that was originally recommended by the National Academy of Medicine (NAM) in 1993 and reviewed favorably by NAM, most recently in 2016. This process includes a robust peer-review recruitment strategy to ensure the most qualified reviewers scientifically evaluate research proposals. CDMRP does not use standing peer review panels. Rather, CDMRP recruits reviewers based on the expertise needed for the proposals received. Robust recruitment efforts ensure peer review panels include senior scientists, but not exclusively.

Recommendation for Assistance Required:	None.
Recommendation:	**Implement warm/rapid autopsy programs and establish metastatic tissue repositories of annotated clinical samples (with primary and metastatic tumor specimens) to be widely accessible to the research community.**
DoD Status:	Fully Implemented in DoD.
Update:	CDMRP has funded efforts to develop and/or expand tissue repositories that are widely accessible to research communities. For example, the PCRP funded the development of a multi-institutional biorepository for annotated primary and metastatic tumor specimens, which also includes a warm/rapid autopsy program, while the OCRP funded the development of the Australian Ovarian Cancer Study, which established an extensive biorepository of primary tumor tissue and ascites fluid. Samples from both biorepositories were collected with the intent for distribution to the research community. The RCRP is offering the Resource and Community Development Award to develop platforms (e.g., tumor tissue repository with clinical annotation; centralized databanks; patient registry with common data structure; research model and molecular database; and longitudinal studies of natural history and treatment response) to facilitate sharing of data, bio-specimens, and resources, and foster collaboration among stakeholders within the rare cancers community.
Recommendation for Assistance Required:	None.
PATIENT-RELATED FACTORS	
Recommendation:	**Improve access to care and clinical trial participation for patients with metastatic cancer particularly for underrepresented groups.**
DoD Status:	Fully Implemented in DoD.
Update:	CDMRP Program Announcements supporting clinical trials and clinical research include language highlighting special attention given to inclusion of women and/or minorities, consistent with the Belmont Report. In FY 2021, CDMRP established an Inclusion of Women and Minorities in Clinical Research policy. Since then, CDMRP Program Announcements supporting clinical trials and clinical research also require applicants to submit a strategy for inclusion of women and minorities in their research studies, and a planned inclusion enrollment table with proposed enrollment distributed based on sex/gender, race, and ethnicity to ensure inclusion of underrepresented groups, as appropriate to each study. Funded investigators are subsequently required to submit updated inclusion enrollment report forms with their annual reports for CDMRP review. Additionally, research-related subject costs are included in all clinical trial award budgets and may be requested to support costs (such as transportation, lodging, participation incentives, etc.) to address potential barriers to participation. Moreover, multiple programs are addressing this recommendation at the strategic level. For example, the PRCRP includes an overarching challenge to "[i]mprove prevention strategies, diagnosis, treatment, and outcomes for patients in underserved or under recognized populations." The MCC/MCCRP has a diverse cancer care and research program with diverse patient and participant

	representation that reflects the military and general population, as well as strong percentages of underrepresented minority (URM) enrollees and participants in all research studies and clinical trials, including the Cancer Moonshot programs.
Recommendation for Assistance Required:	None.
Recommendation: Ensure enrollment in clinical trials reflects the demographics of the U.S. population.	
DoD Status:	Fully Implemented in DoD.
Update:	CDMRP adopted the Public Health Service Inclusion Enrollment Report for funded researchers to submit with their annual and final technical progress reports. This reporting requirement, implemented in FY 2021 following CDMRP's Inclusion of Women and Minorities in Clinical Research policy, enables CDMRP to monitor enrollment based on sex/gender, race, and ethnicity, as well as compare actual enrollment with planned enrollment. Previous reporting on clinical trial enrollment did not provide such demographics for CDMRP-funded awards. It is anticipated that this recently implemented approach, adopted from the National Institutes of Health's approach, will enhance oversight of clinical trial inclusion across different demographics. MCC/MCCRP has a diverse cancer care and research program with diverse patient and participant representation that reflects the military and general population, as well as strong percentages of URM enrollees and participants in all research studies and clinical trials, including Cancer Moonshot programs.
Recommendation for Assistance Required:	None.
Recommendation: Increase cancer patient awareness of healthcare resources, encourage adherence to treatment, and inform patients about risk factors for metastasis (e.g., compliance, obesity, smoking, alcohol use).	
DoD Status:	Fully Implemented in DoD.
Update:	DoD cancer centers accredited by the American College of Surgeons Commission on Cancer (ACS CoC) meet these criteria as part of their Professional and Community Outreach standard and through help from Oncology Social Workers and Nurse Navigators. Patients receive information about risk of cancer recurrence, including metastasis, at surveillance appointments in accordance with NCCN follow-up guidelines and as part of their survivorship programs. Additionally, as a CoE of the DoD and having the highest accreditation status of the ACS CoC, MCC holds many successful annual seminars and outreach programs for cancer patients, with potential for replication across the Military Health System (MHS). In Calendar Year 2022, MCC/MCCRP held eight DoD-wide seminars and educational programs attended by over 800 participants (through in-person and virtual learning) and offered 28 continuing medical education credits. Additionally, MCC/MCCRP continued its monthly Patient Cancer Survivorship series, which brings caregivers, advocates, and patients together one evening a month to learn and discuss a topic of interest to the cancer community.

Recommendation for Assistance Required:	None.
Recommendation: Evaluate the role of social networks as they relate to outcomes for patients with metastatic cancer.	
DoD Status:	Fully Implemented in DoD.
Update:	Applicants can submit proposals on this topic to CDMRP cancer-focused program funding opportunities. This specific recommendation is relevant to CDMRP funding opportunities and research priorities of the PRCRP, PCRP, OCRP, KCRP, LCRP, and PCARP. These programs have focus areas on survivorship, quality of life, supportive care, and patient-reported outcomes. MCC, in partnership with a civilian national organization, implemented the Adolescent and Young Adult (AYA) program to support young adults with cancer. In the MCC AYA, young adults between 18 and 39 years of age who are diagnosed and treated for cancer at MCC WRNMMC receive special support groups, resources for the patient's social and family network, and access to a MCC social worker assigned specifically to AYA who offers special expertise and resources. Additionally, MCC conducts surveys and studies focused on this critical issue through its AYA program, and publishes an annual report. In 2022, the MCC AYA program served over 100 unique patients, over 60 percent of whom are active duty Service members with cancer.
Recommendation for Assistance Required:	None.
SURVIVORSHIP AND PALLIATIVE CARE	
Recommendation: Study whether inclusion of palliative care for patients with metastatic cancer extends life and determine which patients and families would most benefit from these resources.	
DoD Status:	Fully Implemented in DoD.
Update:	Applicants can submit proposals on this topic to CDMRP cancer-focused program funding opportunities. This specific recommendation is relevant to CDMRP funding opportunities and research focus areas of the PRCRP, PCRP, OCRP, KCRP, LCRP, and PCARP. These programs have focus areas on survivorship, quality of life, supportive care, and patient-reported outcomes. The PRCRP also offers a Patient Well-Being and Survivorship Award (formerly Behavioral Health Science Award) supporting studies to advance preservation of function, quality of life, supportive care, symptom management, resilience, relief from neurocognitive deficits, and support for psychosocial issues related to cancer diagnosis, treatment, and survivorship.
Recommendation for Assistance Required:	None.

Recommendation:	**Create standardized survivorship care plans for patients with metastatic cancer and validate whether their use improves outcomes for these patients.**
DoD Status:	Being Implemented in DoD.
Update:	Applicants can submit research proposals on standardizing survivorship care plans for patients with metastatic cancer. This specific recommendation is relevant to CDMRP funding opportunities and research focus areas of the PRCRP, PCRP, OCRP, KCRP, LCRP, and PCARP. These programs have focus areas on survivorship, quality of life, supportive care, and patient-reported outcomes. The Office of the Assistant Secretary of Defense for Health Affairs and DHA established the "Oncology Clinical Community" (OCC), which has the ability to be a "coordinating center" for implementation of cancer-related initiatives across the MHS. The OCC has made progress in standardizing cancer care and research across the MHS by developing a Standardization and Centralization of Cancer Care Initiative based on getting a large medical center in each Market accredited by the ACS CoC, considered the "gold standard" for cancer accreditation of hospitals. The OCC is working on all DoD cancer centers having the ability to become ACS CoC accredited. DoD cancer centers that are ACS CoC accredited meet these criteria as part of their survivorship program standard. The survivorship program focuses on patients with non-metastatic cancer, as recommended by national guidelines. Additionally, MCC provides all patients treated at MCC with a survivorship care plan; this was noted as one of many significant achievements during the most recent ACS CoC accreditation site visit at MCC.
Recommendation for Assistance Required:	None.

SUMMARY

The recommendations included in the 2018 Task Force report to Congress on Metastatic Cancer were primarily intended for the national cancer efforts undertaken by Federal funding organizations that support cancer research, including the DoD CDMRP. The Task Force recommendations are applicable to the cancer research community as a whole (e.g., scientists, clinicians, survivors) for concerted research efforts. DoD has achieved substantial progress on implementing the Task Force's recommendations within its authority.

ACRONYMS

ACS CoC	American College of Surgeons Commission on Cancer
APOLLO	Applied Proteogenomics Organizational Learning and Outcomes (research program)
AR	androgen receptor
ATLAS	Adjuvant Tamoxifen Longer Against Shorter (Clinical Trial)
AYA	Adolescent and Young Adult
BCRP	Breast Cancer Research Program
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
CoE	Center of Excellence
CRPC	castration-resistant prostate cancer
DHA	Defense Health Agency
DoD	Department of Defense
EC	Ethics Committee
ECI	Early Career Investigator
FDA	Food and Drug Administration
FY	Fiscal Year
HER2	human epidermal growth factor receptor 2
HRPP	Human Research Protections Program
IRB	institutional review board
KCRP	Kidney Cancer Research Program
LCRP	Lung Cancer Research Program
MCC	Murtha Cancer Center
MCCRP	Murtha Cancer Center Research Program
MHS	Military Health System
MRP	Melanoma Research Program
MTB	Molecular Tumor Board
MTF	military medical treatment facility
NAM	National Academy of Medicine

NCI	National Cancer Institute
NCCN	National Comprehensive Cancer Network
OCC	Oncology Clinical Community
OCRP	Ovarian Cancer Research Program
ORP	Office of Research Protections
PCARP	Pancreatic Cancer Research Program
PCRP	Prostate Cancer Research Program
PET	positron emission tomography
PRCRP	Peer Reviewed Cancer Research Program
PROMETHEUS	PROject for Military Exposures and Toxin History Evaluation in U.S. Service members
PSMA	prostate-specific membrane antigen
RCRP	Rare Cancers Research Program
URM	underrepresented minority
USAMRDC	U.S. Army Medical Research and Development Command
VA	Department of Veterans Affairs
WRNMMC	Walter Reed National Military Medical Center