LARA Quarterly Progress Report: 4/1/23 – 6/30/23

Wayne State Warriors Marijuana Clinical Research Program: Investigating the Impact of Cannabinoids on Veterans' Behavioral Health

Leslie H. Lundahl, PhD, Lead Principal Investigator
David Ledgerwood, PhD, Co-Principal Investigator

Project Aims:

In this randomized, controlled clinical trial we are recruiting veterans with PTSD who report using cannabis. **We are conducting two studies that are complementary and linked via their aims and methodology**. In **Study 1**, 200 veterans will be randomized into one of four different THC:CBD dose conditions (THC; CBD; THC+CBD, and placebo) for a 12-week treatment phase. In **Study 2**, 150 veterans will be randomized into *one of two groups:* a THC reduction group (n=75), tailored across THC products that are approximately 50% lower in THC than the products participants currently use; or a THC reduction + 1:1 THC:CBD group (n=75), also including tailored THC concentrations as in the first group but with CBD added in a 1:1 THC:CBD ratio. Within each Study 2 treatment group, participants will be randomly assigned on a 1:1 basis to either start the 12-week treatment after a 2-week baseline or a 6-week baseline so we can examine participant naturalistic cannabis use before introducing the new product. **Both studies** involve assessments weekly and bi-weekly throughout a 12-week treatment phase, and at 3- (post-treatment), 6-, 9, and 12-months post-baseline. **Primary outcomes** include clinical assessments of PTSD symptom severity, mood and anxiety symptoms, and suicidality. **Secondary measures** include (1) neurocognitive function; (2) overall health, sleep quality, pain, healthcare utilization, and quality of life; (3) individual differences in fear learning and extinction associated with PTSD symptom severity; (4) saliva for DNA analysis to examine genetic and epigenetic markers associated with the endocannabinoid system; and, (5) urine, blood, and saliva samples to quantify levels of endocannabinoids and their metabolites (e.g., anandamide [AEA] and 2-AG), as well as THC and CBD and their metabolites, to examine whether these levels vary as a function of THC:CBD dose mixtures and differentially affect outcomes. Data will be analyzed to determine which dose conditions might be associated with the outcome measures. These data will be used to (1) develop a predictive algorithm that will help determine personalized profiles of patients who may be at increased risk for suicide; and, (2) develop a profile of who might most benefit from cannabinoid therapeutics.

1). Project Milestones

Study 1 and Study 2 Protocols have been revised and finalized in accordance with discussion with CRA/LARA.

- **Project Progress**

During this period, we met with the University of Michigan team and officials from the Michigan Department of Military and Veterans Affairs (DMVA) to discuss recruitment strategies and opportunities for collaboration. We are developing advertising materials to be sent out to veterans in surrounding counties and updating the brochures that will be distributed at job fairs and events. We will send these materials to the DMVA for feedback prior to submitting them to our IRB for approval. We continue to update our project website (www.warriorCARE.net) regularly. Our studies are also listed on ClinicalTrials.gov, which also provides contact information to enhance referral efforts.

Our full-time recruiter continues to maintain contact with Veteran-related organizations we can approach for referrals and events like job fairs, where we can rent exhibition booths for our research staff to answer questions, provide information, conduct initial screening interviews and schedule in-person screening. We also continue to check in with the Veterans on our waitlist, ensuring we can ramp up recruitment quickly once all regulatory requirements are completed.

Dr. Lundahl met with NIDA Drug Supply Program (NDSP) leadership to finalize details about the cannabis products needed for the trials. We were told that cannabis bulk stocks are currently undergoing irradiation and testing, and once complete we will receive Certificates of Analysis (CoA) for the products we want. Once we receive the COAs we can then file the FDA IND application for NIDA Drug Supply. With regard to the second grower with whom we are working, the WSU legal department approved the NDA and DEA Letter of Intent the grower asked for and we are currently awaiting response from the grower.

The DEA Schedule I Protocols for both studies have been completed and will be submitted to the DEA for approval when we submit the INDs applications to the FDA.

• Noteworthy Accomplishments – Identify and describe any milestones reached or noteworthy accomplishments completed during the period.

The revised Study 2 (TRS) protocol has received Psychiatry Department Review Board approval and is currently undergoing minor revisions following review by the Wayne State University Institution Review Board.

We are currently awaiting installation of WarriorCARE logo decals, locking safe (to store cannabis being delivered), and shelving units for equipment for the study van. This van will allow us to deliver cannabis doses and conduct assessments at participant's homes which will be more convenient for veterans who may have transportation/mobility issues.

Research staff has been trained on all procedures.

2). Delays – Brief description of problems or delays, real or anticipated, which should be brought to the attention of the Grant Administrator.

While we await final IRB approval for Study 2 protocol changes and for DEA-approved research cannabis products to become available, we continue to operate under reduced salary support for research staff members.

3). Statement concerning any significant deviation from previously agreed-upon Statement of Work.

We have had several personnel changes:

Dr. Seth Norrholm will not be coming back onto the grant. Dr. Ledgerwood, who was appointed Co-Principal Investigator when Dr. Norrholm left Wayne State for his visiting professorship, will continue in this role.

Dr. Tanja Jovanovic came off the grant effective May 1, 2023, and her duties were taken over by Dr. Christine Rabinak, an Associate Professor in the Department of Pharmacy Practice in the College of Pharmacy and Health Sciences at Wayne State University. Dr. Rabinak is an expert on biomarkers of development, maintenance, and treatment of posttraumatic stress disorder (PTSD) and anxiety disorders, and on cannabinoid involvement during fear extinction learning and retention.

4). Financial expenditures of grant money and other contributions to the project, in-kind and/or direct funding.

Wayne State University: Veteran Marijuana Research 2021 Grant
Title: Investigating the Impact of Cannabinoids on Veterans' Behavioral Health

CATEGORY	TOTAL BUDGET	Expenses-thru 6/30/23	% of Budget Spent
Personnel/Fringe	3,925,223	970,684	
Equipment	129,404	79,650	
Supplies/Other	2,282,480	147,935	
Computers	45,575	9,321	
Travel	-	-	
DIRECT TOTALS	**6,382,682**	**1,207,590**	**18.92%**
Indirect Costs- 10%	638,268	120,759	
BUDGET TOTALS	**7,020,950**	**1,328,349**	**18.92%**

Attachments and Other Materials – Provide project materials developed and implemented during the reporting period (e.g. newspaper articles, newspaper advertisements, forms, brochures, announcements, studies, reports, analyses, audits, etc.)."

N/A

Respectfully submitted,

Leslie H. Lundahl, PhD
Lead/Contact Principal Investigator

David M. Ledgerwood, PhD
Co-Principal Investigator

July 14, 2023

WAYNE STATE UNIVERSITY

Sponsored Program Administration
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FINANCIAL STATEMENT

Agency	WSU Index No.	Report Period			Date
State of Michigan Dept of Licensing & Regulatory A	**370718M & 380156SUB**	04/01/23	Thru	06/30/23	**07/06/23**
Title:	Grant Code	Fund Code:	23T1C1	Project Period	
Veterans Marijuana Research 2021	**23T1C**	Org. Code:	06CMN1	08/16/21 Thru	07/31/24
Principal Investigator	Final	Reporting No.		Grant/Contract No.	
Dr. Leslie H. Lundahl	NO	**2**		VMR202101	

CATEGORY	EXPENDITURES		AGREEMENT	
	Current Period	Cumulative	Budget	Balance
Salaries & Wages	$55,200.51	$762,027.23	$3,080,771.00	$2,318,743.78
Fringe Benefits	$13,963.44	$208,657.94	$844,452.00	$635,794.07
Travel	$0.00	$0.00	$0.00	$0.00
Supplies & Materials	$1,151.13	$39,000.54	$2,328,055.00	$2,289,054.46
General Expenses	$0.00	$0.00	$0.00	$0.00
Equipment	$0.00	$79,649.88	$129,404.00	$49,754.12
Tuition	$0.00	$0.00	$0.00	$0.00
ROUNDING	$0.01			
TOTAL DIRECT	$70,315.08	$1,089,335.58	$6,382,682.00	$5,293,346.42
Indirect Costs Rate: 10.00%	$7,031.51	108,933.57	$638,268.00	$529,334.43
TOTAL EXPENDITURES	$77,346.59	$1,198,269.15	$7,020,950.00	$5,822,680.85

STATUS OF REVENUE

Previously Reported	$1,120,922.56
Current Billing	$77,346.59
Total Expenditures	$1,198,269.15
Total Payments to Date	$3,510,475.00
Outstanding Amount	($2,312,205.85)

outstanding

OUTSTANDING INVOICES

Date	Invoice No.	Amount
Total		$0.00

CERTIFICATION: BY SIGNING THIS REPORT, I CERTIFY TO THE BEST OF MY KNOWLEDGE AND BELIEF THAT THE REPORT IS TRUE, COMPLETE, AND ACCURATE, AND THE EXPENDITURES, DISBURSEMENTS, AND CASH RECEIPTS ARE FOR THE PURPOSES AND INTENT SET FORTH IN THE AWARD DOCUMENTS. I AM AWARE THAT ANY FALSE, FICTITIOUS, OR FRAUDULENT INFORMATION MAY SUBJECT ME TO CRIMINAL, CIVIL, OR ADMINISTRATIVE PENALTIES (U.S. CODE, TITLE 18, SECTION 1001)

NAME: Marlene Erno, Senior Director of Sponsored Program Administration

DATE: 7/6/23