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Maps

MJP2 Quarterly Progress Report – Q4 2024 January 15, 2025

1. <u>% of completion and work done during project period:</u>

A) <u>% of Completion:</u>

MAPS has performed approximately 10-15% of the work initially proposed in the statement of work.

B) <u>Work Completed During Project Period - Clinical Hold Status Update:</u>

During this reporting period, MAPS made significant administrative and regulatory progress overcoming the long-held hurdles to receive clearance from the FDA for the proposed protocol.

As previously described, MAPS submitted the initial clinical study protocol for our Phase 2 Study of Cannabis for Veterans with PTSD (MJP2) on March 9, 2021; the FDA placed the study on Clinical Hold on May 10, 2021. In the more than three years that followed, the FDA Division of Psychiatry Products (DPP) issued and MAPS responded to five Partial Clinical Hold letters about potential risks associated with the proposed dosing and administration of cannabis which were designed to model real-world consumption of cannabis. Notably, in November 2023, MAPS submitted an extensive Clinical Hold Response, addressing previous discussions with FDA, including the June 2023 Type A meeting with the FDA Division of Psychiatry and the post-meeting communication by the Division of Pulmonology, Allergy, and Critical Care (DPACC). Despite this substantive submission, the FDA issued the 5th Partial Clinical Hold on December 28, 2023. This letter rejected the study of smoked marijuana and vaporized marijuana without addressing any of the substantive data in the MAPS' prior response.

Due to the lack of substantive engagement from the Division of Psychiatry and the rejection of the study of both smoked and vaporized marijuana, MAPS determined it was necessary to appeal this decision to the Office of Neuroscience through a Formal Dispute Resolution Request (FDRR). The FDRR was submitted in August 2024 to the FDA Office of Neuroscience, which oversees the FDA Division of Psychiatry. The FDRR asked the Office of Neuroscience to review the risk:benefit ratio in light of the scientific research data previously cited by MAPS. The FDRR appealed four key hold issues: 1) the proposed THC dose of the cannabis flower product, 2) smoking as a delivery method, 3) vaping as a delivery method, and 4) the enrollment of cannabis naïve participants. In September 2024, the Office of Neuroscience responded to the FDRR by denying the appeal but clarifying a pathway to remove the clinical hold. The Appeal Denied Letter indicated that the FDA now agreed with 3 of the 4 issues including MAPS' proposed dose and both smoking and vaporization administration methods.

In Q4 2024 during this reporting period, MAPS submitted (October 10, 2024) a fifth Complete Response to the Clinical Hold, including an updated protocol and ICF, which took into consideration

the updated thinking from the FDA "Appeal Denied" letter in Q3 2024. **On November 7, 2024, MAPS received notice from the FDA that MJP2 is cleared to "proceed with the protocol using smoking as a delivery method."** Due to ongoing persistence and data-driven evidence, the key elements of this real-world protocol – including the THC dose, self-titration, and a real-world administration method, smoking, are cleared to proceed by the FDA.

Notably, this communication also indicated that while the vaporization method is accepted by the Department of Psychiatry, the Center for Devices and Radiological Health now requires additional information to be provided on the technical features and safety of the vaporization device before MJP2 will be allowed to proceed with vaporization as a delivery method, and this portion of the protocol remains on clinical hold.

Following the partial removal of the clinical hold, MAPS worked with journalists to publish a New York Times article on November 20, 2024 to recognize the tremendous success of a three-year negotiation with the FDA, funded by the Michigan Veteran Marijuana Research Grant Program to permit the study of real-world cannabis use. This success will pave the way for other researchers to design similar studies that may lead to a new era of cannabis research. As an expression of our mission and values, MAPS publicly posted the FDA submissions and responses on our website following the NYT publication. All the prior regulatory submissions and correspondence related to this program are posted here: https://maps.org/marijuana/mjp2/. These resources provide an educational case study in regulatory negotiations for researchers and patient advocates in any discipline, and most importantly, ensure that current and future cannabis researchers can build upon our efforts to support more systematic and rigorous research into real-world cannabis use, which is currently grossly lacking.

In Q4 2024, following this initial regulatory clearance, MAPS moved to reinitiate the steps for study start-up after this long and unanticipated delay. In order to have a clear "active" protocol for study sites, MAPS prepared an updated protocol and ICF with the removal of vaporization as a delivery method so that the active protocol will reflect only the cleared method of administration, smoking. MAPS also prepared the 2024 Data Safety Update Report (DSUR) for the FDA. MAPS will submit the revised protocol and ICF with the 2024 DSUR at the start of Q1 2025.

In the meantime, MAPS has been in communication with the FDA and the vaporization device manufacturer to work toward removing the clinical hold on the use of the proposed vaporization device. We hope to remove this hold issue and reinstate vaporization as a delivery method prior to beginning study enrollment.

In Q4, MAPS also began study start-up activities with the CRO. MAPS reviewed the CRO budget and began preparing for a meeting to negotiate a new contract with the CRO. As previously described, many of the overall project and program management responsibilities were delegated to Lykos Therapeutics (formerly MAPS Public Benefit Corporation). Many of these responsibilities will need to be reassigned to the CRO in a new contract.

MAPS also continued to work with the vendor for the active cannabis product in order to determine a viable plan for packaging the active and placebo study product. In Q4 2024, MAPS obtained additional information from NIDA about the placebo cannabis product which can only be provided in bulk. The active cannabis vendor confirmed that they will likely be able to create matched placebo prerolled cigarettes with the NIDA cannabis product, however, they will need to test their packaging procedures with a sample of the NIDA product to definitively confirm. MAPS will work with NIDA in

Q1 2025 to export a sample to the active cannabis vendor for this purpose. Once we confirm a CMC packaging vendor, MAPS can work with that vendor to finalize the packaging design and randomization process.

Finally, the MAPS research team worked with leadership to inform the 2025 fiscal year organization strategy and personnel planning to ensure that MAPS is appropriately resourced across the internal and external teams to oversee and manage the proper execution of the study and the delegated vendors. MAPS will continue to assess the required personnel needed to ensure appropriate oversight as study development plans continue with external vendors.

2. Description of Problems and Delays:

During this reporting period, MAPS continued to work to resolve the FDA clinical hold, and the request for more information on vaporization. Start-up activities were previously on hold due to the FDA clinical hold but have resumed and are underway. MAPS will continue to assess the required personnel needed to ensure appropriate oversight as study development plans continue with external vendors.

3. Statement regarding any deviation from SOW:

On August 21, 2024, MAPS and the VMR executed a contract amendment which included formally extending the Grant Period to December 31, 2027, budgetary changes due to the removal or change of study procedures, and the reallocation of resources per the necessity to delegate additional responsibilities to contractors. No deviations from the SOW have occurred.

4. Quarterly Financial Expenditures:

In Q3 2024, MAPS billed $20,482.06 for direct administrative support of the VMR program for administrative information systems and administrative personnel and $54,079.38 for indirect administrative expenses as per the updated budget. MAPS billed $27,252.53 in project personnel expenses and $16,111.27 for VMR contracted services, for a total of $43,363.80 for VMR program expenses. Total expenditure to date equals 13.8% of the total contract value.