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Maps

MJP2 Quarterly Progress Report – Q1 2024 April 15, 2024

1. % of completion and work done during project period:

A) % of Completion:

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

B) Work Completed During Project Period - Clinical Hold Status Update:

As previously described, MAPS developed an extensive formal response to the Clinical Hold in Q4 2024. This in-depth 28-page response addressed and incorporated the various communications and discussions with the FDA, including the Type A meeting with the FDA Division of Psychiatry, which took place on June 15, 2023, and the post-meeting communication provided by the Division of Pulmonology, Allergy, and Critical Care (DPACC) on August 11, 2023. The response directly addressed the Clinical Hold Comments received from the FDA on December 16, 2022, as required by the regulations, and took into account the FDA Type A meeting in June, the guidance and advice from the DPACC, and a thorough review of the relevant literature. MAPS addressed each point of scientific evidence and literature provided by the FDA, speaking to the strength and merit of the presented evidence and provided additional scientific and data-driven literature to support the proposed dosing and administration paradigms in the protocol. MAPS additionally consulted with several leading experts in the field who wrote letters of support to the FDA on behalf of this study program.

As part of the proposal to lift the clinical hold, MAPS once again made targeted revisions to the protocol to reduce the risk of the study to support clearance by the FDA, while ensuring that the study design remains consistent, in purpose and spirit, with the study description provided in the VMR agreement. These changes included: emphasizing the research focus of the protocol, reduction of the maximum daily allotment of cannabis from 2.0 g to 1.5 g, as well as changes to the eligibility to only include participants who have previously or were considering using cannabis and to exclude participants who have a current or history of chronic obstructive pulmonary disease or asthma. These protocol changes reflected a significant effort to address the reasonable concerns of the FDA, while maintaining the critical real-world elements of the proposal that make this data collection meaningful to the Veteran population this research is intended to serve.

MAPS formally submitted this Complete Response to the Clinical Hold to the FDA on November 30, 2023, which included the updated protocol and supportive letters from scientific leaders in the field. On December 28, 2023, the FDA Informed MAPS that the Partial Clinical Hold on our Phase 2 Study of Cannabis for Veterans with PTSD (MJP2) would be continued. This clinical hold letter rejected the study of smoked marijuana and vaporized marijuana without addressing any of the substantive responses in the Complete Response to the clinical hold submitted by MAPS in November.

Importantly, the letter did not indicate if the FDA will consider scientific evidence to support the use of either smoking or vaporization in future cannabis clinical research.

In this quarter, MAPS consulted with regulatory advisors to determine the most effective pathway forward to address the clinical hold. Due to the lack of substantive engagement from the Division of Psychiatry on the merits of the November response and the outright rejection of the study of smoked or vaporized marijuana, MAPS has determined it is necessary to appeal this decision to the Office of Neuroscience though a Formal Dispute Resolution Request (FDRR). This request will be based on both regulatory review standards and the scientific research cited by MAPS in the prior Complete Response which was not addressed by the Division of Psychiatry. The FDRR will ask the overseeing Office of Neuroscience to review this evidence and the risk:benefit ratio of the proposed research to allow Study MJP2 to proceed. We completed a competitive bid process and identified an experienced and economical partner to support the FDRR process.

The complete response, supporting letters, FDA Type A meeting minutes, DPACC post-meeting communication, and FDA clinical hold letter were all shared on the MAPS website in keeping with the mission of public benefit and transparency in our research. Practicing transparency with regard to the clinical hold process ensures that the public has access to pertinent information about FDA policies and practices, as well as summaries of cutting-edge literature on cannabis safety, provides an educational case study in regulatory negotiations for researchers and patient advocates in any discipline, and most importantly, ensures that current and future cannabis researchers are able to build upon our efforts in order to support more systematic and rigorous research into real world cannabis use, which is currently grossly lacking. See here for all the submissions related to this program: https://maps.org/marijuana/mjp2/.

In tandem with the vendor selection process, we initiated a review of all MJP1 and MJP2 documents transferred to MAPS by Lykos Therapeutics (formerly MAPS PBC) in preparation for the FDRR. An inventory of all provided and outstanding documentation was completed in January, and Lykos was promptly notified of the status of documentation transfer to ensure that outstanding documentation is provided to MAPS. We expect this documentation to substantially improve the rigor of the FDRR.

As described in detail below, MAPS has been in communication with the VMR to amend the budget according to substantial and necessary changes in program management and the necessity of additional regulatory and CMC support to address the ongoing FDA clinical hold issues. MAPS initially requested a budget amendment and update to the grant terms in the Q3 2023 report submitted October 15, 2023. Per VMR request, MAPS submitted a formal amendment request by email on December 18, 2023. The VMR requested additional information pertaining to the formal request on January 24, 2024. Following the completion of the vendor selection processes, MAPS submitted a 3-column budget amendment request, amendment justification, and description of the competitive bid process for contracted services to the VMR on April 8, 2024, in accordance with the VMR request.

While MAPS' priority is the removal of the clinical hold, MAPS has continued to work on 1) resolving issues related to cannabis packaging and 2) managing cannabis vendors to ensure adequate study supply and product testing. MAPS is judiciously managing the vendors that were previously identified through a bidding process to both ensure that undue expenses are not committed prior to the clinical hold being lifted and that there are no unnecessary delays during the study start-up

period once the clinical hold is removed.

2. Description of Problems and Delays:

MAPS continues to work to resolve the FDA clinical hold and continue trial activities.

3. Statement regarding any deviation from SOW:

A) Project Change Request: Personnel and Contracted Services

As documented in the initial approved grant budget, overall project and program management was delegated to Lykos Therapeutics (formerly MAPS Public Benefit Corporation) and a CRO was selected to primarily oversee trial site conduct while Lykos conducted the internal Sponsor roles. However, at the end of 2022, Lykos reallocated a significant amount personnel resources to the organization's other clinical research efforts including an NDA submission for MDMA-assisted therapy for the treatment of PTSD and informed MAPS that they would no longer be able to act as delegate of Sponsor roles on this program. As of Q1 2023, MAPS is directly overseeing and conducting this work and no longer delegating the trial oversight and conduct to Lykos. As we discussed with VRM last year, the MAPS staff does not have the scope of internal positions needed to take over the functions delegated to the Lykos "internal program staff" or the infrastructure to host the information systems, data, and trial recruitment.

Therefore, MAPS proposed in the Q3 2023 report submitted 15 Oct 2023 to amend the proposed budget in order to shift funds from the specified internal personnel to both expand the role of the external functions, specifically the Contract Research Organization (currently Alira Health) and incorporate additional contracted service providers to fulfill the previous internal Lykos roles related to CMC, Regulatory Affairs, and Independent Rating. A budget amendment request and brief amendment justification was initially provided in writing in the Q3 2023 VMR grant report. Per VMR request, a formal amendment request was then submitted by email to the VMR on December 18, 2023. Additional information was requested by the VMR on January 24, 2024.

As described above, the FDA informed MAPS on December 28, 2023 that the Partial Clinical Hold placed on our Phase 2 Study of Cannabis for Veterans with PTSD (MJP2) would be continued. During this quarter, MAPS completed an exhaustive bid process to identify a cost-effective and suitable contractor for regulatory affairs support to remove the clinical hold. Following the completion of this process, MAPS submitted a 3-column budget amendment request, amendment justification, and description of the competitive bid process for contracted services to the VMR on April 8, 2024 per VMR request.

B) Project Change Request – Grant Term:

MAPS' original Work Plan describes a sponsored clinical trial planned as a 35-month project, commenting with Last Patient, Last Visit (LSLV) in December of 2023 and the final Clinical Study Report filed to the FDA in 2024. The FDA clinical hold persisting from 2021 into 2024 has greatly affected this proposed timeline for initiating the study sites. If the FDA clinical hold is removed by the end of 2024, and if the original study duration assumption stays the same, study completion would take place near the end of 2027. MAPS understands from prior communications that the

Grant Period can be extended to carry over allocated funds in order to accommodate the completion of the clinical trial and requests that this updated timeline be reflected in the formal amendment that has been requested.

4. **Quarterly Financial Expenditures:**

During this reporting period, MAPS has billed $20,618.68 in administrative support of the VMR program for administrative information systems and administrative personnel. VMR Program expenses in Q4 totaled $19,911.24. The VMR contracted services expenses in this quarter totaled $8,815.75. Total expenditure to date equals 11.2% of the total contract value.

VMR contracted services billed in this quarter included expenses incurred in the last quarter to support the submission of the clinical hold response in Q4 2024. These expenses are tracked in this reporting period because they were either erroneously omitted from previous reports or were paid this quarter.

- Two invoices for contracted CMC contracted services
- One invoice for regulatory affairs contracted services
- One invoice for CRO contracted services (to support formal submission to FDA)