U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30329-4027

December 27, 2023

Agam Rao, MD
CDC National Center for Emerging and Zoonotic Infectious Diseases/Division of High-Consequence Pathogens and Pathology
ige4@cdc.gov

RE: CDC IRB Approval of Changes to CDC Protocol 6402, "Expanded Access IND #116039 Protocol: Use of Tecovirimat for Treatment of Human Orthopoxvirus Infections" Amendment #8

Dear Dr. Rao:

On December 20, 2023, the CDC Institutional Review Board (IRB) reviewed and approved changes to CDC Protocol 6402, "Expanded Access IND Protocol: Use of Tecovirimat for Treatment of Human Orthopoxvirus Infections" in accordance with 21 C.F.R. §56.109. This approval is effective as of December 20, 2023.

The CDC IRB has approved the following required changes:

- The risk of hallucination or similar psychotic event was added as a risk in the protocol's informed consent document.
- The treatment protocol was amended to clarify the boundary between treatment changes in dosing or duration permissible under treating providers' clinical discretion and those that require prior consultation or follow up consultation with CDC.
- Protocol Section 4.0 (Page 8) was edited to further clarify treatment duration, dose, or dosing interval modifications that can be made within the treating clinician's judgment versus those that require prior consultation with CDC.
- Informed Consent Form and Protocol Section 10.2 (Page 23) were edited to describe the risk of neurologic and neuropsychiatric adverse events such as hallucinations.

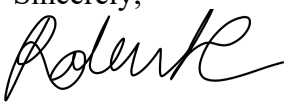
The CDC IRB finds that CDC Protocol 6402 involves more than minimal risk to subjects, consistent with its previous determination.

You are required to adhere to the protocol as approved on December 20, 2023, and implement the changes immediately in accordance with the approved amendment.

We appreciate your commitment to responsible conduct of the protocol and your cooperation with the IRB review process. If you have any questions or concerns regarding the conduct of

your protocol or the IRB review process, please do not hesitate to contact your Center Human Subjects Contact or Jerrell Little, IRB Administrator, at 404-639-3536, or via email at jiv4@cdc.gov.

Sincerely,



Robert Chirila, Lead
Human Research Protections Office