TO: IMPAACT P1108 Clinical Research Sites

FROM: Jacquelyn Mountcastle, Clinical Trials Specialist, on behalf of the IMPAACT P1108 protocol team

DATE: 20 October 2016

RE: IMPAACT P1108: change in IND Status

The purpose of this administrative notification is to provide an update on the change in IND status for IMPAACT P1108: "A Phase I/II, Open-Label, Single Arm Study to Evaluate the Pharmacokinetics, Safety and Tolerability of Bedaquiline (BDQ) in Combination with Optimized Individualized Multidrug-Resistant Tuberculosis (MDR-TB) Therapy in HIV-Infected and HIV-Uninfected Infants, Children and Adolescents with MDR-TB Disease."

IMPAACT P1108 protocol Version 1.0, dated March 3, 2016 was released to participating sites as a non-IND study on 9 March 2016. Bedaquiline is an orphan drug in the US, and there is no requirement from the FDA to conduct a pediatric program. However, because pediatric data from the P1108 trial will likely be submitted to obtain a pediatric indication in the US as well, the P1108 team requested that the protocol be submitted to the Food and Drug Administration (FDA). On 7 September 2016, the FDA notified the National Institutes of Health (NIH) Division of AIDS (DAIDS) Regulatory Affairs Branch that the protocol may proceed under an IND (#131, 832) and indicated that the protocol is safe to proceed.

This administrative notification may be submitted to appropriate Institutional Review Boards, Regulatory Ethics Committee and Drug Regulatory authorities to inform them of this change in IND status.

Language pertaining to regulatory oversight by the FDA will be formally added to the IMPAACT P1108 protocol via an amendment at a later date.