# *2024 Area of Interest for HIV*

## HIV Areas of Interest

Effective August 2023, the HIV Investigator Studies Program Review Committee (MISP-RC) will accept proposals within our current Areas of Interest (AoIs). This is an ongoing competitive process that will be conducted throughout the year by the HIV MISP Review Committee. Decisions will be made on the basis of scientific merit and strategic fit within the AoIs. Please review the critical activities and abide by the timelines as outlined below. The program requests that investigators specify how they will support diversity in enrollment to include traditionally underrepresented minorities/ethnic groups.

**AOIs**

- **Optimization of ARV regimens:** Comprehensive management of HIV with a focus on current and evolving variants of antiretroviral therapy (e.g., long-acting regimens) in people living with HIV (PLWH). Special emphasis should be given to PLWH at risk for co-morbidities and toxicities such as CNS disease, cardiovascular disease, hyperlipidemia, weight gain, hepatic dysfunction, and metabolic, renal, and bone abnormalities. It will also be of great interest to identify new markers of metabolic dysfunction and/or novel ways of using already existing such markers in PLWH
- **Special populations of PLWH:**Different aspects of HIV disease prevention and treatment in PLWH from racial and ethnic backgrounds disproportionately affected by HIV infection and/or from populations that have historically been underrepresented in clinical trials such as women, children and adolescents, transgender individuals, members of ethnic minorities, and older adults. The focus should be on establishing the efficacy, tolerability, safety, and convenience of antiretroviral viral

therapy in these populations with particular emphasis on certain situations that include, but are not limited to, the following:
    - The impact of HIV and aging on the risk of co-morbidities and toxicities related to polypharmacy.
    - The impact of HIV and antiretroviral therapy on gender-/sex-based issues such as reproductive health, contraception, pregnancy, neonatal outcomes, and menopause.
- **HIV resistance:** Characterization of transmitted and acquired resistance to sponsor's antiretroviral products in treatment-naïve and treatment-experienced patients, respectively, with a focus on patterns of transmission, prevalence, characteristics, and response to therapy
- **Drug-drug interactions and drug toxicities:** Studies that focus on 1) interactions between regimens that contain the sponsor's antiretroviral agents and drugs used to treat underlying conditions (e.g., cardiovascular disease, hypertension, diabetes, bone and renal conditions, and neuro-affective disorders) and 2) toxicities associated with company antiretroviral products
- **HIV prevention (both pre-exposure and post-exposure):** Populations at high-risk of HIV infection; strategies to facilitate uptake and long-term adherence; alternative models that "de-medicalize" access to prevention modalities
- **Pathogenesis, viral reservoirs, and cure:** Different aspects of HIV-mediated inflammation and associated biomarkers; insights into the biology of viral reservoirs and methodologies for evaluating them; different strategies for achieving cure and its associated biomarkers

**Islatravir specific AOIs**

- **MOA** – studies to enable a deeper understanding of islatravir's mechanism of action and differentiate it as a novel NRTTI (biochemistry/structural biology/cell biology/virology)
- **Resistance studies** – studies that will elucidate pathways of resistance, fitness cost of mutations, genotypic and phenotypic characteristics of resistance, and barrier to resistance in HIV-1 clinical isolates across subtypes

- **Antiviral impact on reservoirs** – studies to evaluate impact on viral reservoirs (mathematical, animal, and ex-vivo models) in relationship to other ART agents
- **Biomarkers** – studies that measure the impact of islatravir on markers of inflammation, immune dysfunction, and cell biology