# *2025 Area of Interest for HIV*

## HIV Areas of Interest

Effective January 2025, 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.

### HIV AOIs

- **Optimization of ARV regimens**: Comprehensive management of HIV with a focus on current and evolving variants of antiretroviral therapy (e.g., long-acting oral and injectable regimens, rapid start modalities of therapy) in people living with HIV (PLWH). This comprehensive management would include but not be limited to therapeutic comparisons between regimens with a focus on:
    - Efficacy and safety
    - Treatment preferences and satisfaction with therapy of PLWH, health care providers, and health care systems
    - Implementation challenges and opportunities
    - 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, metabolic, renal, and bone abnormalities, and impact on other body systems. 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. As we move towards two-drug regimens that do not have activity against hepatitis B infection, it would be of interest to understand approaches that would increase rates of HBV vaccination among 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 including but not limited to 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 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, maternal lactation, neonatal outcomes, and menopause.
- **HIV resistance:** Characterization of transmitted and acquired resistance to the sponsor's various 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, neuro-affective disorders, and various infectious diseases), and 2) toxicities associated with the company's antiretroviral products.
- **HIV prevention (both pre-exposure and post-exposure):** Populations at high risk of HIV infection; strategies to facilitate uptake and long-term persistence; alternative models that "de-medicalize" access to prevention modalities; unmet needs in both the pre-exposure and post-exposure space; etc.
- **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; studies to evaluate impact of antiretroviral agents on viral reservoirs (mathematical, animal, and ex-vivo models); different strategies for achieving cure; studies to characterize biomarkers that could be used to

identify PLWH who would be good candidates for cure interventions and/or identify individuals in whom cure interventions have led to reservoir depletion.

**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
- Non-clinical studies that would address unmet medical needs that could be addressed by ISL and future translocation inhibitors either as individual drugs or combinations of antiretroviral agents in the treatment and prevention spaces administered orally or parenterally (e.g., PLWH and/or provider preference studies that address unmet needs of current therapies with regards to efficacy, frequence of dosing, route of administration, side effects, etc.).