

The Role of Nonhuman Primate Studies in Preparation for Combination “Cure” Studies in Humans

Jeffrey D. Lifson
AIDS and Cancer Virus Program
Frederick National Laboratory*



**Supported with federal funds from the National Cancer Institute, National Institutes of Health, under Contract No. HHSN261200800001E*



Nonhuman Primate Combination “Cure” Studies: Considerations

- Which model? (macaque species, virus, match to question)
 - Well established natural history
- cART regimen (“fully suppressed”)
- Characterization of residual virus on cART (assays, levels, anatomic and cellular sources)
- Validate intended activity of individual agents in vitro and ex vivo, individually and together, *if possible* (*macaques are not humans, HIV/SHIV not HIV*)
- Confirm pharmacologically active drug exposure by drug level measurements and non-virologic pharmacodynamic readout, *if possible*



Nonhuman Primate Combination Studies: “Hypothetical” Examples

Validate rationale for combination

- Distinct, complementary mechanisms of action
- Additive or synergistic activity in vitro/ex vivo (HDACi + PKC agonist)
- “Kick” and “Kill” components (Therapeutic Vaccine/mAb + Viral inducer/LRA)



Nonhuman Primate Combination Studies: Take Home Message

Despite caveats, well conceived, well conducted studies in NHP models will be a critical component of the overall evaluation of combination treatment “Cure” intervention

Such studies can usefully inform the transition to clinical evaluation but need not be viewed as a strict “Gatekeeper” to progress to the clinic

