Nucleic Acid Platform Approaches for Pre-Exposure Prophylaxis (PrEP): Targeting Delivery to the Upper and Lower Respiratory Tracts and Extending Half-Life

Overview

The recent success of mRNA-based vaccines has opened the door for further development of nucleic acid-based therapies. With their specificity and functional diversity, therapeutic nucleic acids hold enormous promise. However, challenges for applying nucleic acid therapeutic technologies to acute infectious diseases include organ-targeted delivery and short half-life. Tackling the development challenges of nucleic acid-based therapeutics can potentially benefit more expansive areas of medical needs, particularly in difficult-to-treat patient populations.

We are seeking to develop nucleic acid platform approaches for pre-exposure prophylaxis (PrEP) against influenza and other respiratory viruses, particularly for vulnerable populations. As such, our goal is to support the advancement of cost-effective nucleic acid platform technologies that target delivery of drug(s) to the upper and lower respiratory tracts and extend the half-life of drug(s). Technological improvements in these areas will be key to accelerating development of nucleic acid-based therapies for influenza PrEP.

To be considered responsive under this solicitation, offerors should propose evaluation of platforms meeting at least one of the following requirements (i.e., targeted delivery or half-life extension):

1. Platform must demonstrate improvements in targeted delivery of drug(s) to the upper and lower respiratory tracts over current or offeror's baseline formulations.
2. Platform must demonstrate improvements in half-life extension of the drug(s) over current or offeror's baseline retention times.
3. If delivering the drug directly to the upper and lower respiratory tracts, the proposed research plan must include half-life extension of the drug(s) in addition to targeted delivery.
4. If delivering the drug systemically, the proposed research plan must include at least one of these requirements (half-life extension or targeted delivery).
5. The platform should not be anticipated to cause respiratory complications or other significant toxicities in individuals with and without underlying comorbidities.

Additional considerations:

1. Offerors should provide clear milestones and metrics that objectively measure the advancement of the platform
    a. Offerors should clearly describe how improved delivery to the upper and lower respiratory tracts will be measured (e.g., animal model proposed and analytical methods for assessment).

b. Offerors should clearly describe proposed improvements to the formulation(s) over current formulations.

Example milestones may include but are not limited to:

- Demonstrate improvements in targeted delivery of drug(s) to the upper and lower respiratory tracts in small animal model(s) by 40% (over baseline) in the first 6 months
- Demonstrate improvements in targeted delivery of drug(s) to the upper and lower respiratory tracts in small animal model(s) by 80% (over baseline) in the first year
- Demonstrate improvements in half-life extension of drug(s) in small animal model(s) by 40% (over baseline) in the first 6 months
- Demonstrate improvements in half-life extension of drug(s) in small animal model(s) by 80% (over baseline) in the first year
- Completion of IND enabling studies and filing of IND
- Receipt of study may proceed letter from FDA

2. This solicitation is target agnostic; however, offerors proposing payloads that target seasonal and pandemic influenza will increase the strength of the proposal.

3. While this solicitation does not require it, future funding from the BARDA IEIDD Therapeutics Program for advanced development of a product would require activity against seasonal and pandemic influenza.