***Long-Acting Monoclonal Antibody Platform Approaches for Pre-Exposure Prophylaxis (PrEP): Targeting Delivery to the Upper and Lower Respiratory Tracts***

**Overview**

Monoclonal antibodies (mAbs) and long-acting mAbs have been successfully developed to treat and provide protection against viral infections. Pre-exposure prophylaxis (PrEP) using long-acting mAbs was demonstrated recently during the COVID-19 pandemic. When considering approaches for PrEP, long-acting mAbs offer significant advantages in terms of speed of response, treatment duration, and safety profile. However, it is evident that further refinement is necessary to allow broader adoption of long-acting mAbs for use as PrEP for respiratory viral diseases. Development of effective, long-acting mAbs that address limitations currently associated with dosing and cost of manufacturing may ensure more general use.

We are interested in developing long-acting monoclonal antibody (mAb) platforms for prevention of infection with influenza and other respiratory viruses, particularly for vulnerable populations. Our goal is to identify and support transformative approaches that result in enhanced distribution of long-acting mAbs to the upper and lower respiratory tracts.

**To be considered responsive under this AOI, offerors should propose evaluation of platforms meeting the following requirements:**

1. Platform must support the development of long-acting mAb(s) that are dosed infrequently; ideally the drug should provide at least 6 months of protection from a single dose.
2. If the platform uses a parenteral route of administration, the proposed work must enhance delivery to the upper and lower respiratory tracts resulting in an appreciable reduction in overall dosing requirements.
3. If the platform uses an inhaled route of administration, the proposed work must enhance retention time in the upper and lower respiratory tract.
4. 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 clearly describe how improvements in targeting to the upper and lower respiratory tracts will be measured (e.g., animal model proposed and analytical methods for assessment).
2. Offerors should provide clear milestones and metrics that objectively measure the advancement of the platform. Example milestones may include but are not limited to:

a. Demonstrate improvements in targeting to the upper and lower respiratory tracts by >50% (over baseline) in small animal model(s) in the first 6 months with at least two different mAbs.
b. Demonstrate improvements in targeting to the upper and lower respiratory tracts by >80% (over baseline) in small animal model(s) in the first year with at least two different mAbs.
c. Demonstrate improvements in targeting to the upper and lower respiratory tracts by >80% (over baseline) in non-human primates (NHPs) with at least one mAb.
d. Demonstrate improvement in the biodistribution and enhanced retention time in the upper and lower respiratory tract by >50% in in vivo models.
e. Completion of IND enabling studies and filing of IND
f. Receipt of study may proceed letter from FDA

3. This solicitation is target agnostic, however, offerors utilizing mAb(s) targeting seasonal and pandemic influenza will increase the strength of the proposal.
4. 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.