

# Passive Immunotherapy Against Influenza H5Nx

### **MARKET OPPORTUNITY**

H5N1, commonly known as "bird flu", outbreaks have wiped out large populations of birds and caused significant agricultural losses. Avian-human transmission is inefficient but handling of infected poultry had infected humans and resulted in mortality in more than half of those infected. Ongoing drift and prevalence pose worrying risks for the virus to mutate into a strain that can transmit easily amongst humans to result in pandemics. High antigenic diversity of the virus also hampers vaccination strategies and can render resistance to antivirals quickly. Some human and avian isolates of H5N1 have developed resistance to the two main classes of antivirals, namely neuraminidase inhibitors and adamantanes. Since 2008, the H5N1 virus has undergone reassortment with other circulating virus of different subtypes to give rise to several new viruses. They are collectively known as H5Nx viruses. Of these, the newly emerged H5N6 reassortant virus is of particular concern because of its prevalence over wide geographic areas. H5N6 human infection has resulted in approximately 75% fatality.

Passive immunity is a viable strategy to combat the viral attacks. Combination passive immunotherapy using a cocktail of noncompeting neutralizing monoclonal antibodies (mAbs) against hemagglutinin (HA) can reduce the degree of escape variants and the total dosage of antibodies required. The access to an increased repertoire of neutralizing mAbs against H5Nx viruses for preparation of a suitable efficacious combat cocktail may control infections and prevent their development into pandemics, thereby increasing our readiness to overcome the virus.

## Technology

Two mouse-human chimeric IgG and IgA monoclonal antibodies (mAbs) with high degrees of binding and neutralizing activity against H5N1 are available for development into passive immunotherapeutic agents. They bind to multiple influenza A H5Nx clades and neutralize at least six different H5N1 strains from different areas. The virus strains are representative of two different clades and seven years of ongoing drift.

### STAGE OF DEVELOPMENT

TRL 3 (Efficacy demonstrated in vitro and in vivo.)

### **APPLICATIONS**

Therapeutic treatment against Influenza A H5Nx infection.

### **ADVANTAGES**

- Monoclonal antibodies can be easily scaled up for production and inter-batch consistencies are highly achievable.
- The antibodies have potent neutralizing activity against multiple influenza A H5N1 clades and also H5Nx viruses, including the recently emerged H5N6 virus. Thus, they have the potential to combat against emerging H5Nx strains.
- The IgG and IgA mAbs share similar epitope but their different isotypes facilitate the selection of the ideal mAb for combining with other non-competing neutralizing antibodies to be the most effective passive immunotherapeutic cocktail against H5Nx.
- The mAbs have a different HA epitope from the majority of other anti-HA mAbs. They are candidates for development as therapeutics in combination with the other characterized anti-HA mAbs or antivirals available.

### **S**TATUS

Available for licensing and research collaboration. Patent pending in US and Europe.

Technology Manager: Dr Liting Lim E-mail: liting.lim@nus.edu.sg ILO Ref No: 13398N

Inventor: Associate Prof Yee-Joo Tan E-mail: MICTYJ@nus.edu.sg