Preclinical development of an anti-Dengue virus antibody that neutralizes all four serotypes

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GHIT R&D FORUM

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Background: Dengue disease

- Infectious disease by mosquito vector-transmitted dengue virus in the tropical and subtropical world
- The worldwide incidence of dengue has risen 30-fold compared with the situation 50 years ago
- Published estimates include total annual global cost of ~US$8-9 billion in 2013 (Shepard et al., 2016, Lancet Infect. Dis.)

**Epidemic area of dengue disease**

A novel anti-DENV cross-serotype neutralizing human antibody

- Anti-DENV cross-serotype neutralizing human antibody (3C) isolated in Singapore Immunology Network (SIgN)/A*STAR
- Potent and rapid neutralization of all four serotypes of dengue virus
  - Protective efficacy of Sanofi’s vaccine is not perfect (35-42% against DENV2)
- Applicable for all patient groups
  - Protective efficacy of current vaccine is weak in young children and naïve adults
- No ADE risk of our antibody therapy
  - Vaccination is suggested to increase severe dengue in infection naïve patients
- Applicable to prophylactic use because of long plasma half-life

- Accelerated recuperation from Dengue fever
- Prevention of severe Dengue
- Decrease disease, medical and economic burden
Partnership between Chugai and SIgN/A*STAR

SIgN/A*STAR in Singapore

- Government-affiliated institution which aim to bridge the gap between academia and industry in terms of research
- Singapore Immunology Network (SIgN) has expertise in immunology research including DENV research
  - Singapore is one of the endemic region of Dengue disease
  - SIgN has network of DENV research in Singapore and also other endemic countries

Chugai Pharmaceutical

- Chugai has expertise in antibody drug development
  - Various proprietary antibody engineering technologies
  - Know-how of antibody optimization, manufacturing and clinical development
- Chugai Pharmabody Research (CPR) in Singapore
  - 100% Chugai’s affiliate in Singapore for antibody drug discovery
Partnership between Chugai and SIgN/A*STAR

Co-development of anti-DENV antibody by Chugai and SIgN/A*STAR

- **Chugai**
  - Optimized SIgN’s anti-DENV antibody as a antibody drug
  - Conducts manufacturing and GLP-Tox for entry into human

- **SIgN**
  - Pharmacology studies by using living virus for IND submission
  - Support of the development of anti-DENV drug with the DENV research expertise and the research network

**Collaboration between Chugai and SIgN/A*STAR**

- Antibody engineering expertise
- DENV research expertise

**Optimization of the antibody**

**Preparation for IND**
(Manufacturing, GLP-Tox)

**Clinical study for PoC**

**GHIT Fund**
Critical aspects of the partnership between Chugai and SIgN/A*STAR

- Close relationship
  - Easy to establish close relationship by frequent F2F meeting
    - Geographical factor largely contributes

- Complementary role of each party
  - Complement the activities needed to develop anti-DENV antibody drug each other
    - Chugai is not familiar with tropical infectious diseases
    - SIgN is not familiar with drug development

- Governmental support
  - Support from Singapore government is expected in the future
    - Singapore government are putting great effort to reduce dengue disease
Future perspective of partnership

- Collaboration for clinical studies
  - Clinical studies in Singapore and/or other endemic countries
    - Possibility of investigator initiated clinical studies
  - Look for the opportunities of support from the government

- Identifying good collaboration partners as a key success factor of this project
  - Promote the clinical studies to achieve early launch of this drug
  - Understand the unmet needs in each endemic country
  - Establish the marketing strategy for each endemic country
Current status

- Preclinical development including cell line development for Ab manufacturing is progressing as planned.
- No significant findings were observed in preliminary toxicity study in cynomolgus monkeys.