CHUGAI
Roche Roche Group

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

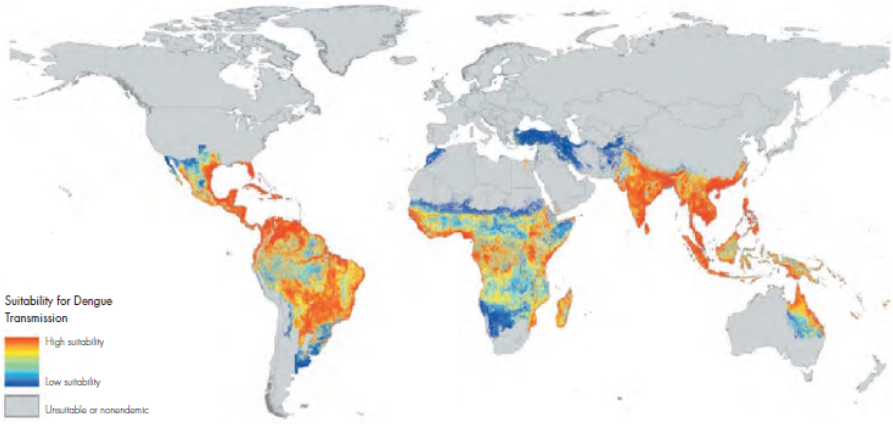
Dec 8, 2017
GHIT R&D FORUM

Hisafumi Okabe, PhD
Senior Vice President
Chugai Pharmaceutical Co., Ltd.

Background: Dengue disease

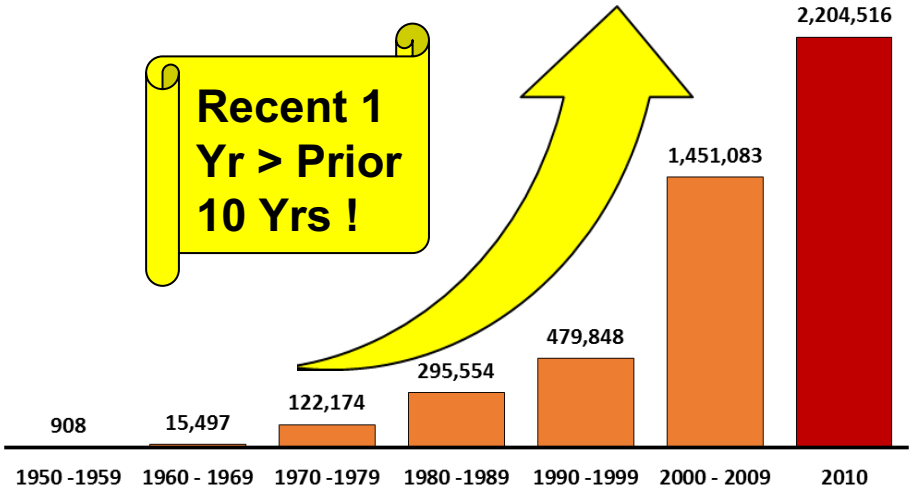
- Infectious disease by mosquito vector-transmitted dengue virus in the tropical and subtropical world
- The worldwide incidence of dengue has risen 30-fold compared with the situation 50 years ago
- Published estimates include total annual global cost of ~US$8-9 billion in 2013 *(Shepard et al., 2016,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

Epidemic area of dengue disease



WHO Global strategy for dengue prevention and control (2012)

Dengue Virus Active Cases (Ten Years Ending except 2010)



Guidelines for Diagnosis, Treatment, Prevention, and Control. 2009; 1-160. WHO
Simmons CP, et al. Dengue Fever. NEJM. 366(15): 1423-1432.

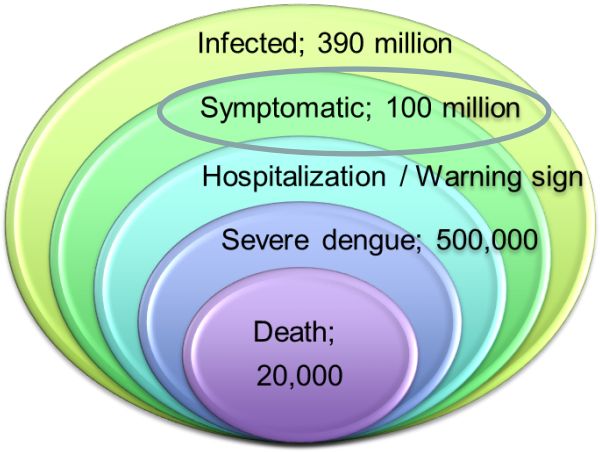
A novel anti-DENV cross-serotype neutralizing human antibody

Innovation all for the patients

CHUGAI

Roche A member of the Roche group

- 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

Innovation all for the patients

CHUGAI

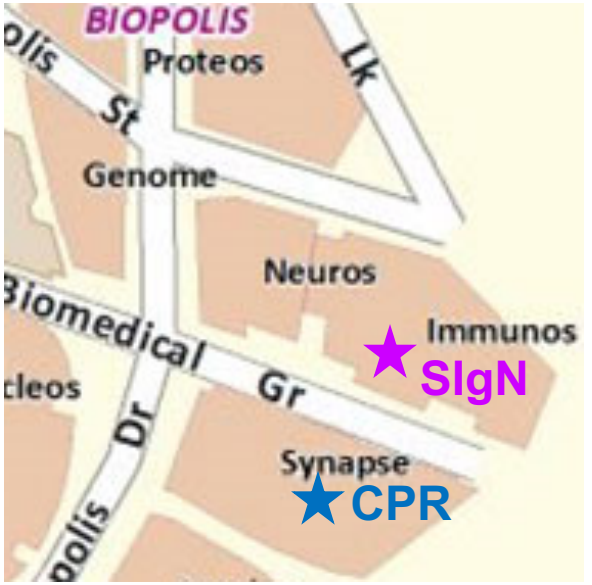
Roche A member of the Roche group

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

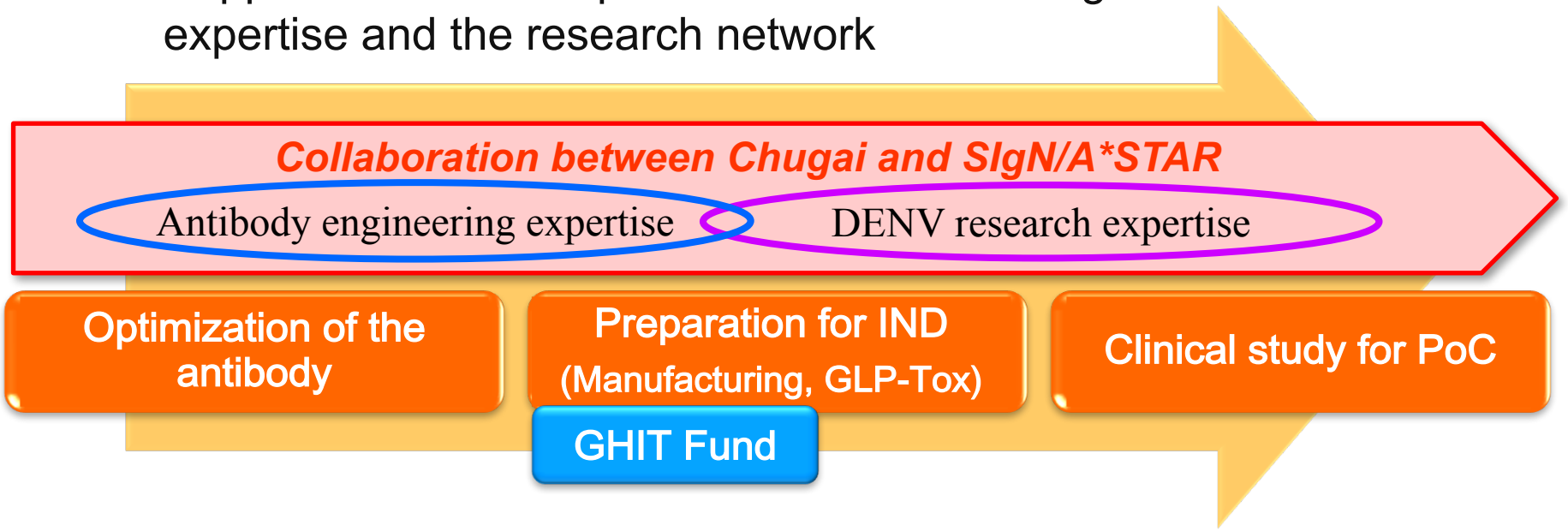
Innovation all for the patients

CHUGAI

Roche A member of the Roche group

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



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.