Statement by the Dengue Vaccine Initiative on the Results of CYD-TVD Phase 3 Trial in Latin America

10 NOVEMBER 2014—Villar et al. recently published in The New England Journal of Medicine the results of the Phase 3 trial of the dengue vaccine candidate (CYD-TVD) of Sanofi Pasteur, the vaccines division of the French pharmaceutical company, Sanofi. The study was conducted in Brazil, Colombia, Honduras, Mexico and Puerto Rico with 20,869 children and teenagers aged 9 – 16 years, 13,920 in the vaccine group and 6,949 in the placebo group. It follows a CYD-TVD Phase 3 trial conducted in five countries in Asia, published by Capeding et al. in July.

The results show an overall vaccine efficacy against all dengue serotypes combined of 60.8 percent in the per-protocol analysis. The primary endpoint of the trial was met. Also reported is statistically significant protection against each of the four dengue serotypes, at varying levels: 50.3, 42.3, 74.0 and 77.7 percent against serotypes 1, 2, 3, and 4, respectively. No major concerns of safety were reported during the observation period of 25 months. The safety will be followed up for an additional four years. The preceding Phase 3 study in Asia showed overall vaccine efficacy against all serotypes combined of 57 percent in the per-protocol analysis and protection of 50, 35, 78 and 75 percent, against serotypes 1, 2, 3, and 4, respectively, wherein efficacy against serotype 2 was not statistically significant.

Exploratory analysis reported by the authors showed a vaccine efficacy against severe dengue of 95.0 percent, although the number of severe dengue cases was small (12 in total, 1 in the vaccine group and 11 in the placebo group) and 80.3 percent against hospitalizations (17 hospitalizations for virologically confirmed dengue were found after at least one injection in the vaccine group and 43 in the placebo group). Also reported is that the efficacy varied according to age and serostatus: vaccine efficacy was 83.7 percent in seropositive participants and 43.2 percent in seronegative participants. The efficacy in seronegative participants did not meet statistical significance. 79.4 percent of the children enrolled were seropositive against dengue at the time of the first vaccine administration. Additionally, the epidemiology between countries varied in terms of serotype distribution, incidence, and prior exposure to dengue disease. Vaccine efficacy was 77.5, 71.1, 67.5, 57.6, and 31.3 in Brazil, Honduras, Colombia, Puerto Rico and Mexico respectively (in the intent-to-treat analysis).

Although questions remain to be addressed, DVI finds these results encouraging. They confirm the efficacy and safety demonstrated in the findings of the trial in Asia and the feasibility of a vaccine to reduce cases of dengue fever. Additionally, while conducted as exploratory analysis on a limited number of cases, the study demonstrated a high protection against hospitalization and severe dengue disease. Topics that call for further attention include the duration of protection, given the serostatus and dengue epidemiology per country, the optimal vaccination age and vaccine schedule, among others.

About Dengue
No licensed dengue vaccine is currently available, however, dengue is one of the fastest spreading vector-borne viral diseases, with an epidemic potential in the world. Forty percent of the global population is currently at risk of contracting this disease, calling for urgent preventive intervention. A safe, effective and affordable vaccine would represent a major advance for the control of dengue.

- WHO Q&A.
- More about the burden of dengue here and dengue vaccines here.