Inmazeb™ (atoltivimab/maftivimab/odesivimab-ebgn) – New orphan drug approval

- On October 14, 2020, the FDA announced the approval of Regeneron's Inmazeb (atoltivimab/maftivimab/odesivimab-ebgn), for the treatment of infection caused by *Zaire ebolavirus* in adult and pediatric patients, including neonates born to a mother who is RT-PCR positive for *Zaire ebolavirus* infection.

    - The efficacy of Inmazeb has not been established for other species of the *Ebolavirus* and *Marburgvirus genera*.
    - *Zaire ebolavirus* can change over time, and factors such as emergence of resistance, or changes in viral virulence could diminish the clinical benefit of antiviral drugs. Consider available information on drug susceptibility patterns for circulating *Zaire ebolavirus* strains when deciding whether to use Inmazeb.

- *Zaire ebolavirus*, commonly known as Ebola virus, is one of four Ebolavirus species that can cause a potentially fatal human disease. Ebola virus is transmitted through direct contact with blood, body fluids and tissues of infected people or wild animals, as well as with surfaces and materials, such as bedding and clothing, contaminated with these fluids. Individuals who provide care for people with Ebola virus, including health care workers who do not use correct infection control precautions, are at the highest risk for infection.

- Inmazeb is the first FDA-approved treatment for *Zaire ebolavirus* infection in adult and pediatric patients.

    - Inmazeb targets the glycoprotein that is on the surface of Ebola virus. Glycoprotein attaches to the cell receptor and fuses the viral and host cell membranes allowing the virus to enter the cell. The three antibodies that make up Inmazeb can bind to this glycoprotein simultaneously and block attachment and entry of the virus.

- The efficacy of Inmazeb was established in PALM, an open-label, randomized controlled study. The study was conducted in the Democratic Republic of Congo, where an Ebola outbreak began in August 2018, and enrolled 681 patients of all ages. Patients were randomized to receive Inmazeb as a single infusion intravenously (IV), an investigational control IV every third day, for a total of 3 doses, or other investigational drugs. The primary efficacy endpoint was 28-day mortality.

    - The PALM trial was stopped early on the basis of a pre-specified interim analysis showing a statistically significant reduction in mortality for Inmazeb compared to control. The 28-day mortality was 34% and 51% in the Inmazeb and control groups, respectively (difference of -17.2, 95% CI: -28.4, -2.6; p = 0.0024).

- A warnings and precaution for Inmazeb is hypersensitivity reactions including infusion-associated event.

- The most common adverse reactions (≥ 20%) with Inmazeb use were pyrexia, chills, tachycardia, tachypnea, and vomiting.

- The recommended dosage of Inmazeb is 50 mg of atoltivimab, 50 mg of maftivimab, and 50 mg of odesivimab per kg diluted and administered as a single intravenous infusion.

- As part of an agreement announced in July 2020, Regeneron will deliver an established number of Inmazeb treatment doses over the course of six years to the Biomedical Advanced Research and

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Development Authority (BARDA), as part of the U.S. Department of Health and Human Services' (HHS) goal of building national preparedness for public health emergencies.

- Inmazeb will be available as a 241.7 mg of atoltivimab, 241.7 mg of maftivimab, and 241.7 mg of odesivimab per 14.5 mL (16.67 mg/16.67 mg/16.67 mg per mL) single-dose vial.