Biotech drugs too little, too late for Ebola outbreak

The World Health Organization's (WHO) assistant director general, Marie-Paule Kieny, announced on August 12 that the agency would allow the use of unregistered therapies and vaccines to thwart the Ebola Zaire virus epidemic in West Africa. The WHO stressed, however, the importance of obtaining informed consent, maintaining confidentiality, preserving dignity, involving the community, and ensuring the release of safety and efficacy data to the wider scientific community. Several biotech companies stepped up to offer experimental treatments, although all had insufficient supplies to offer more than a trickle of therapeutic options.

Several days before the WHO announcement, San Diego–based Mapp Biopharmaceuticals had provided its Ebola treatment, ZMapp (MB-003) to two US health workers and a Spanish priest who had been infected with the virus in Liberia. As *Nature Biotechnology* went to press, the aid workers, who had returned to the US, were recovering, but the Spanish priest had succumbed to infection.

ZMapp is a cocktail of three monoclonal antibodies (mAbs) developed from work carried out at the US Army Medical Research Institute for Infectious Diseases in Frederick, Maryland, in the 1990s (*Science* **287**, 1664–1666, 2000). The current cocktail is a collaboration between Mapp, another San Diego–based startup LeafBio, biodefense company Defyrus of Toronto, and the Winnipeg, Manitoba–based level-4, National Microbiology Laboratory at the Public Health Agency of Canada, all largely funded by the US Department of Defense and the National Institutes of Health (NIH). The three mAbs target nonoverlapping Ebola virus epitopes (the mucin-like domain as well as the 6D31 and core epitopes of glycoprotein 1). They are murine mAbs engineered with human constant regions and manufactured in transgenic *Nicotiana benthamiana* tobacco lacking plant-specific N-glycan residues. By August 11, there was not much ZMapp to go around; the company announced it had given free of charge all the product it had in stock—enough to treat only six people. The company is currently gearing up to produce up to 50 treatment courses by the end of the year, enough for a small safety study.

The same month, Vancouver, British Columbia–based Tekmira Pharmaceuticals also announced it was making available its experimental drug TKM-Ebola after the US Food and Drug Administration (FDA) lifted a clinical hold on a phase 1 trial initiated in January in which volunteers had suffered several adverse events. Tekmira is the only company to have advanced an Ebola program as far as the clinic—all other companies with active programs are in the preclinic (**Table 1**).

TKM-Ebola has previously proved protective in non-human primates injected with an otherwise lethal dose of Ebola virus. Rather than a cocktail of mAbs, TKM-Ebola is a mixture of three intravenously injected 2′-*O*-methyl modified G/U short interfering RNA (siRNA) oligos targeting Ebola Zaire virus transcripts encoding polymerase L protein, viral protein 24 (VP24) and VP35. The siRNAs are packaged

CARL DE SOUZA/AFP/Getty Images/Newscom

Ebola treatments and vaccines have only been tested in animal models, with Tekmira's drug the only exception.

Organs-on-chips Harvard spinout

Emulate, a Cambridge, Massachusetts–based developer of 'organ-on-a-chip' systems, completed a $12-million series A round led by venture capital firm NanoDimension, Cedars-Sinai Medical Center and philanthropist Hansjorg Wyss, at whose eponymous Harvard incubator the startup was formed. The technology, a computer chip surrounded by living cells that mimic human physiology, could be ready for commercialization as soon as 2016, according to Emulate CEO James Coon.

Roche snaps up RNA-medicines firm Santaris

Roche announced in August that it is buying Copenhagen-based Santaris Pharma for $250 million upfront, with another $200 million tied to undisclosed milestones. Through the move, the Basel-based pharma picks up Santaris' locked nucleic acid platform for antisense drug discovery. Roche intends to keep Santaris' Denmark operations open. The acquisition follows two Roche purchases in June: it paid $125 million upfront (another $225 million tied to potential milestones) for the sequencing company Genia Technologies and $725 million in cash plus another $1 billion in potential milestone payments for Seragon Pharmaceuticals, which is focused on oral selective estrogen receptor degraders for breast cancer.

Rabbit milk Ruconest for hereditary angioedema

The US Food and Drug Administration approved in July Ruconest (C1 esterase inhibitor) in adults and adolescents with acute attacks of hereditary angioedema (HAE). The product, the first approved C1-esterase inhibitor manufactured in recombinant form, is purified from the milk of transgenic rabbits and restores levels of functional C1-esterase inhibitor in the plasma of patients, thereby reducing swelling often seen in the abdomens, extremities and faces of HAE sufferers. The drug is produced by Leiden, the Netherlands–based Pharming Group partnered with Salix Pharmaceuticals of Raleigh, North Carolina.

"'The Broad Gets $650 Million For Psychiatric Research'. That seems an awful lot of money for one woman." One person's reaction to the gift of $650 million from the Stanley Foundation to the Cambridge, Massachusetts Broad Institute. (*In the Pipeline*, 22 July 2014)

"More people are studying orphan diseases than have orphan diseases." Michael S. Kinch, of Yale Center for Molecular Discovery, commenting on pharma's disinterest in developing antibiotics. According to drug benefits manager Express Script, 70% of drugs approved by the FDA in 2013 were specialty drugs, used by less than 1% of the population. (*The New York Times*, 22 July 2014)