## RNActive®-AN mRNA-BASED VACCINE TECHNOLOGY FOR NEXT GENERATION PROPHYLACTIC VACCINES

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In recent years, messenger RNA (mRNA) based technologies have increasingly been applied in vaccine development, RNActive®, an mRNA based vaccination technology developed by CureVac, which uses sequence-optimized, unmodified mRNA, promises a powerful new platform for the development and production of prophylactic vaccines against infectious diseases. RNActive® vaccines have achieved promising results against a variety of viral pathogens such as influenza, rabies. Ebola and respiratory syncytial virus in several animal models. In previous studies we showed that intradermal application of RNActive® vaccines was able to confer protection against lethal influenza and rabies virus challenge infection in mice and induced protective levels of functional antibodies against both viruses in domestic pigs. In a first-in-human trial, the RNActive® vaccine against rabies, which was formulated with the cationic protein protamine, appeared safe with a reasonable tolerability and was able to induce boostable virus neutralizing antibodies (VNTs) after intradermal needle free injection whereas needle based injection was ineffective. This study provided important guidance for the development of improved vaccine candidates. Here, we describe a lipid nanoparticle (LNP) formulation of RNActive® vaccines that is able to induce potent immune responses when applied intramuscularly using low doses (ug) of mRNA. Vaccination of mice with this RNActive® vaccine encoding for influenza hemagglutinin or rabies glycoprotein led to the induction of both, humoral and cellular immune responses. Further experiments showed that the vaccine was able to induce potent and long lasting immune responses against influenza HA as well as high titers of rabies virus neutralizing antibodies in non-human primates following intramuscular administration by needle.