

Press Release

CureVac Announces Study Publication in Molecular Therapy Demonstrating Wide-Ranging Benefits of Sequence-Optimized, Unmodified mRNAs

- **Peer-Reviewed Data Indicate that CureVac's RNArt® Technology Can Produce Therapeutically Relevant Protein Levels in Large Animals and Achieve Meaningful Biological Effects in Primates**
- **Sequence-engineered mRNA Described as Having "The Potential to Revolutionize Human Protein Therapies"**

TÜBINGEN, Germany, June 24, 2015 – CureVac, a clinical-stage biopharmaceutical company pioneering the field of mRNA-based technology, today announced that a study of its RNArt® technology platform was published in *Molecular Therapy* as an advanced article preview (Mol Ther doi:10.1038/mt.2015.103). The peer-reviewed study that was carried out in collaboration with Acuitas Therapeutics demonstrated for the first time that sequence-optimized, chemically unmodified mRNAs raised relevant protein levels in non-human primates without stimulating an unwanted immune reaction, indicating that mRNA achieves meaningful biological effects in large animals with body weight close to humans. Moreover, the study suggested that sequence-optimized, unmodified mRNAs offer advantages when compared to chemically-modified mRNAs, including more efficacious protein translation.

In the study, titled "Sequence-Engineered mRNA Without Chemical Nucleoside Modifications Enables an Effective Protein Therapy in Large Animals," investigators used erythropoietin (EPO) driven production of red blood cells as the biological model. Data demonstrated that sequence-engineered mRNA encoding EPO elicited meaningful physiological responses from mice to non-human primates, such as a considerable increase of serum EPO levels and reticulocyte counts, as well as a significant rise in hematocrit. Even in pigs of approximately 20 kg in weight, a single dose of engineered mRNA encapsulated in lipid nanoparticles induced high systemic EPO levels and strong physiological effects. There was neither cytokine release nor induction of EPO-specific antibodies upon repeated treatment.

The study also compared sequence-engineered, unmodified mRNA to various chemically-modified mRNAs, including mRNA from a commercial supplier. As suggested by protein levels and physiological responses, the sequence-engineered mRNA outperformed its modified counterpart.

Thus, the present study proves that protein (replacement) therapies are possible with mRNA, without any need for chemical modifications. CureVac's sequence engineering technology can be applied to any protein of interest, including complexes such as antibodies. Currently CureVac applies this technology, RNAntibody®, in collaboration with the Defense Advanced Research Projects Agency (DARPA, grant number HR0011-14-2-0006) for passive immunization with protecting antibodies encoded on mRNA.

Mariola Fotin-Mleczek, CSO of CureVac, stated, "The results we observed in this study demonstrate that sequence-engineered mRNA has the potential to revolutionize

human protein therapies. The data provide the first evidence that our mRNA enables therapeutic effects in large animals, even for systemically acting proteins. Although our mRNA is chemically unmodified, it does not elicit any immune response and, thus, allows for repetitive treatment.”

Ingmar Hoerr, CEO of CureVac, commented, “The results of this study confirm many of the benefits we understand are inherent to our RNArt[®] and RNAntibody[®] technologies, as well as our RNActive[®] and RNAdjuvant[®] technologies, and mirror what we have observed in our seven clinical trials involving more than 300 humans. We greatly look forward to leveraging this data to target molecular therapy-focused opportunities where our mRNA technology can be applied directly without chemical modifications.”

Read the accepted article preview published ahead of advance online publication under <http://www.nature.com/mt/journal/vaop/naam/pdf/mt2015103a.pdf>

About CureVac

CureVac, a German clinical stage biopharmaceutical company founded in 2000, is pioneering the field of mRNA-based technology for medical purposes, in which unmodified mRNA is specifically optimized and formulated. CureVac has been developing novel mRNA-based cancer immunotherapies and prophylactic vaccines against infectious diseases – both under the brand RNActive[®]. Moreover, CureVac's technology RNArt[®] is designed as molecular therapy to trigger the body's own production of therapeutic proteins without stimulating the immune system. The technology RNAntibody[®] is being developed to express therapeutic levels of RNA encoded antibodies.

CureVac has successfully established the first GMP (good manufacturing practice) facility worldwide for the manufacture of mRNA in 2006 and has pioneered mRNA-based drugs in various clinical studies.

www.curevac.com

About Acuitas

Acuitas Therapeutics Inc. is a privately held company developing LNP technology, including technology developed under limited license from Tekmira Pharmaceuticals Corporation, for delivery of mRNA therapeutics.

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