Title: Development of in vivo-launched synthetic DNA-encoded antibodies employing CELLECTRA® electroporation technology.

Trevor Smith[1], Paul Fisher[1], Ami Patel[2], Elizabeth Parzych[2], Kevin Hollevoet[3], David B Weiner[2], Laurent Humeau[1]

[1] Inovio Pharmaceuticals, Plymouth Meeting, PA, USA.

[2] The Wistar Institute. Philadelphia, PA, USA.

[3] University of Leuven, Leuven, Belgium.

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Monoclonal antibodies have proved a simple passive immunization strategy to provide protection against infectious disease. However, access to potentially life-saving mAb biologics faces multiple challenges for broader population coverage including high doses (in milligrams/kilogram), shelf-stability, temperature stability and distribution barriers for low-/middle-income countries and resource-limited settings. Therefore, additional strategies that can further facilitate mAb uptake and global availability would be valuable for infection control. DNA-encoded monoclonal antibodies (dMAbs) offer a possible alternative technology to traditional recombinant mAbs. Synthetic DNA constructs are delivered to muscle tissues *with in vivo* electroporation to permit local tissue expression of the antibody transgene and transient production and secretion of mAbs into circulation. dMAbs have the potential to be a transformative mAb technology, allowing sustained trough levels, flexibility for administration of multiple constructs, rapid production at dramatically lower costs, and long-term drug product stability. Through a combination of optimizing EP parameters and drug formulations, circulating levels of mAbs providing disease protection can be achieved by this technology platform. Here we discuss the nonclinical path for development of DNA-encoded monoclonal antibodies. Through case studies we define the optimal delivery conditions, modeling and understanding the pharmacokinetics of *in vivo* mAb expression, and identify the requirements for scaling up the technology into clinically relevant models. This process has resulted in the successful translation of multiple dMAb candidates as medical countermeasures into clinical testing.