

Watson: Messenger RNA Encoded Abs for HIV Prophylaxis

OVERVIEW

This grant is focused on the development of mRNA-encoded antibodies to be used as prophylactic treatment against HIV. The research will be performed by Valera, LLC; Valera is an affiliate of Moderna Therapeutics, focused exclusively on the advancement of vaccines and therapeutics for the prevention and treatment of viral, bacterial and parasitic infectious diseases. It will utilize Moderna's modified messenger RNA (mRNA) platform, a technology that Valera has already utilized in preclinical settings to generate safe and effective prophylactic vaccines against multiple viruses. The enabling advantages of this technology are the ability to generate cocktails of antibodies as a single product, cost of production, and potentially increased duration of protein expression.

The program has a multi-stage framework.

- Stage One will involve production/formulation of mRNA constructs for both heavy and light chain of a selected set of broadly neutralizing anti-Env antibodies, for assessment of protein expression levels in vitro and in vivo (rodent models), allowing for sequence optimization of variants resulting in higher expression of antibodies.
- Stage Two proceeds by engineering the top candidates from Stage One into single chain versions that retain both variable and constant regions (scFv-Fc antibodies). Expressed versions of these scFv-Fc antibodies will be evaluated by affinity measurements, neutralization behavior, glycosylation, other biophysical properties, as well as other functional characteristics. The mRNA constructs for the ScFv-Fc antibodies, spanning a variety of sequence variants, will be evaluated for expression levels in murine models.
- Stage Three advances optimization in a research context, with selection of final mRNA constructs, and initial preclinical studies in rat and rhesus, testing ScFv-Fc's individually and as cocktails of antibodies. Evaluation in rhesus will have a challenge arm, as well as study arms for PK data capture.
- Stage Four is primarily focused on completing GLP toxicology studies in mouse and rhesus, with the prerequisites steps of Active Pharmaceutical Ingredient (API) and Drug Product (DP) manufacturing, with related analytics.
- Stage Five requires the GMP manufacturing of the API and DP for a Phase I study, using a CRO as subcontractor for the execution of the study.

This grant is led by Mike Watson, PhD, in the role of Chief Scientific Officer for Valera, LLC. Stages of the work will involve service contracts with a number of entities yet to be determined. The Central Services Facilities will be engaged during multiple stages to furnish functional assays such as neutralization testing and binding assays, and discrete analytical evaluations such as glycosylation features. The award began in January 2016 and has an anticipated duration of 48 months.

Grant at a Glance

Principal Investigator

Mike Watson, PhD

Grantee Institution

Valera, LLC, Cambridge, MA USA

Project Title

Messenger RNA encoded antibodies for HIV prophylaxis

OPPID

1147797

Grant Award

Up to \$20 million over 48 months