First study of a Self-amplifying mRNA (samRNA) Vaccine, GRT-R910, as a Booster to Protect against COVID-19 in Healthy Volunteers ≥60 Years of Age - Preliminary Evidence of Durable Immunity

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Background: First-generation of COVID-19 vaccines played a critical role in addressing the pandemic but have shown limited duration and breadth of protection because vaccine-elicted humoral immunity is transient (thus requiring boosters). Self-amplifying mRNA (samRNA), a next-generation platform technology, has demonstrated the potential to drive broad and durable cellular and humoral immunity against SARS-CoV-2. CORAL-BOOST (NCT05148962) is evaluating the safety and immunogenicity of a samRNA SARS-CoV-2 vaccine candidate (GRT-R910) in healthy adults.

Methods: This phase 1, open-label, multi-centre study was conducted in the UK. GRT-R910 encodes for Wild-type Spike (S) and highly conserved non-S T cell epitopes from ORF3a, Nucleopapsid, and Membrane (F1). Healthy adults ≥60 years were enrolled into cohorts 1 and 2 and received 1 dose of GRT-R910 after a primary series of Vaxzevria, with a subset receiving an optional second dose. Cohorts 3 and 4 assessed 2 doses of GRT-R910 after adenoviral or non-vaccine primary series, respectively (Fig. 2). The primary endpoint was to evaluate adverse events (AEs) and secondary objectives included magnitude and breadth of T cell response and SARS-CoV-2 specific IgG binding and neutralizing antibody (nAb) responses.

Results: Safety: Solicited AEs were predominantly mild/moderate, and transient. Nine grade 3 solicited AEs were observed in 3 subjects at 10µg and one subject at 30µg had grade 3 solicited AEs (mainly local pain and tenderness, and headache which were transient in nature – Data not shown). Immunogenicity: A single dose of GRT-R910 increased binding (IgG) and neutralizing (nAb) antibody levels to the vaccine-specific strain (WT) and VOCs (Cohorts 1 & 2; Fig. 3 & 4). Boosted antibody levels against WT and all VOC tested were maintained for at least 6 months after the GRT-R90 dose in subjects ≥60 years of age (Fig. 3 & 4). A single dose of GRT-R910 increased breadth and depth of T cell responses to S and non-S epitopes (Fig. 5). Administration of 2 doses of GRT-R910 increased Spike+ specific IgG responses irrespective of primary vaccination series (Cohorts 3 & 4; Fig. 6). Analyses assessing neutralization against WT and VOC and longitudinal responses in Cohorts 3 & 4 are ongoing.

Conclusions:
1. CORAL-BOOST (NCT05148962) is the first study assessing a samRNA-based SARS-CoV-2 vaccine in an older population (≥60 years of age)
2. GRT-R910 was well tolerated in this study population at all dose levels
3. Consistent longevity of neutralizing antibody response for at least 6 months was observed against different variants of concern not included in the vaccine construct
4. Administration of GRT-R910 increased breadth of T cell responses against Spike and non-Spike T cell epitopes included in the vaccine
5. This study is ongoing and final results will be communicated after the study has completed

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