Innovation Portfolio
14RMM003

Preventing MDR Gram-negative hospital-acquired infections

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HIGHLIGHTS

- ✓ **Synthetic polymer able to elicit protective immunity against MDR**
- ✓ **Faster developed immunity than vaccines**
- ✓ **Cost-effective treatment resulting in potential savings to the health system**

TECH STATUS

- ✓ **TRL: Late Pre-Clinical Studies**
- ✓ **IP: N. Phase On Process EP3183003**

(EU, US, CA, JP, CN, MX, AU, KR, RU, BR)

Problem to be solved

Nosocomial infections in Intensive Care Units (ICU), which affect to 30-50% of patients admitted to these units, are mainly caused by multidrug resistant (MDR) Gram-negative bacteria. These microorganisms evolve to develop mechanisms of resistance, which is a major challenge to prevent and control infectious diseases caused by these pathogens using current antibiotic therapies.

Background

Nosocomial bacterial infections remain a major problem for patients admitted to ICUs and are associated with considerable morbidity, mortality, and costs. These infections are the leading cause of death in non-cardiac ICUs, with mortality rates that reach 60%, and account for approximately 40% of total ICU expenditure. Gram-negative bacteria are responsible for more than 30% of nosocomial infections and account for 70% of infections acquired in ICUs. Consequently, protection against Gram-negative infections will have a major impact in improving the clinical outcome and reducing direct and indirect costs for patients admitted to ICU.

Circulating antibodies targeting Galactose α1-3 Galactose epitopes (αGal), the most abundant natural antibody in humans, may facilitate the survival in the blood of Gram-negative pathogens emerging from the gut microbiota. This suggests a possible role of circulating anti-αGal antibodies in the enhancement of Gram-negative bacterial infections by hampering the effective binding of protective (bactericidal and opsonic) antibodies.

Technology

RA-01 is a synthetic polymeric glycoconjugate that selectively removes inhibitory anti-αGal Abs, eliciting Protective Immunity against MDR Gram-negative bacteria. The transient removal of anti-αGal antibodies, achieved with the first intravenous (i.v.) or subcutaneous (s.c.) dose (1

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mg/Kg) of the polymeric glycoconjugate RA-01, immediately allows the activity of already existing bactericidal and opsonic antibodies, conferring protection against Gram-negative bacterial infections. According to our pre-clinical *in vivo* an *in vitro* proofs of concept we consider our approach relevant to elicit protective immunity against Gram-negative bacteria causing infections in humans.

Applications

RemAb Therapeutics aims to prevent Intensive Care Unit (ICU)-acquired Gram-negative bacterial infections by eliciting protective immunity against these pathogens, including those resistant to multiple antibiotics, using a novel approach based on the temporary intra-corporeal removal of inhibitory anti-αGal antibodies. If the removal of anti-αGal antibodies with RA-01 shows efficacy to prevent ICU acquired Gram-negative infections, the therapy will also be extended to patients admitted to other areas of the hospitals, at risk for prolonged admissions and the development of Gram-negative infections.

Technology status

Technology has been validated in lab. We are initiating the corresponding non-clinical regulatory studies and CMC work to support the submission of the first Clinical Trial Application (CTA). We have evidence that RA-01 efficiently binds *in vivo* to circulating anti-αGal antibodies, leading to the intra-corporeal removal of these antibodies in primates (*Cynomolgus* and *Rhesus* monkeys, and baboons) without apparent toxicity and lack of immune response to the compound. Furthermore, RA-01 also binds to the B-lymphocytes producing anti-αGal antibodies, inhibiting the production of new antibodies. The intra-corporeal removal of anti-αGal antibodies in GalT-KO mice with RA-01 reduced in 50% mice mortality by Gram-negative sepsis after cecal ligation and puncture. Additionally, inhibition of anti-αGal antibodies *in vitro* from human serum increases the bactericidal activity against *E. coli* O86:B7 and MDR *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*.

Market Opportunity

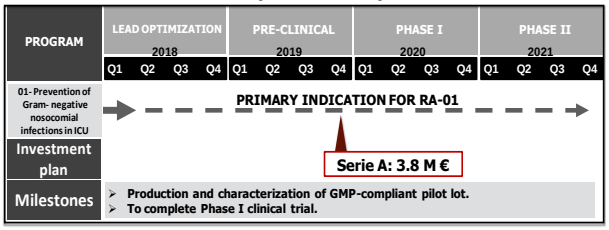
RemAb Therapeutics plans to cover an unmet clinical need. Vaccines, which could be our main competitors as a preventive strategy, take around two weeks to develop immunity, which is too late for patients already admitted into ICU, and prolonged prophylactic antibiotic therapies are associated with the generation of resistance mechanisms in Gram-negative bacteria.

Potential savings: direct cost of antibiotics, at least $ 300 per treatment using generic broad-spectrum drugs. Cost of ICU stays, around $ 2,000 per patient day in EU.

Peak-year commercial opportunity: we calculate a treatment cost for RA-01 between $ 600 and $ 1000, this result in $ 1.2 - $ 4 billion for treating from 2 to 4 million ICU patients.

Business Opportunity

RemAb Therapeutics is looking for investment to initiate clinical regulatory studies with RA-01 (Q4-2019).



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