The translation provided is for informational purposes only. The tender procedure is conducted in Polish. In the event of any discrepancies or disputes, the binding version of the agreement is the Polish version.

Annex No. 3 to the RFP/Agreement

ORDER DESCRIPTION

The subject of this order entails the meticulous supervision of a comprehensive clinical trial (CRO) within the territory of Great Britain, as an integral component of the ongoing project entitled: "Assessment of the Efficacy and Safety of Metoprolol as Adjunctive Therapy in Mitigating the Onset of Cardiomyopathy in Duchenne Muscular Dystrophy Patients Aged 8-17 Years." The trial is structured as a randomized, double-blind, parallel-group study, with placebo serving as the control variable. This initiative is registered under application number: 2019/ABM/01/00026.

I. SCOPE OF SERVICE PROVISION:

The purview of this order encompasses the oversight of a non-commercial clinical trial (CRO) in the Great Britain, in strict adherence to the funding agreement denoted as: 2019/ABM/01/00026.

The Ordering Party (Sponsor) shall mandate, while the Contractor (CRO) shall undertake, a series of pivotal activities as follows:

1. Registration of the study in Great Britain - applying to the competent authority and the bioethics committee. Follow-up activities such as sending additional information or documents, updating or amending the application, arranging meetings with the relevant authority and implementing recommendations from regulatory authorities. Review and submission of study documentation via the Integrated Research Application System (IRAS) for regulatory agency (MHRA) approval and ethics committee (REC) opinion. Responding to regulatory questions or comments. Informing the Sponsor of progress. Support for the administrative manager in Poland in activities related to the implementation of the study, particularly in the areas of communication, information management in the study, risk assessment, assessment of the achievement of basic milestones in the study, coordination of cooperation between centers.
2. Coordination and execution, in collaboration with the Ordering Party, of the clinical trial in accordance with the prescribed protocol at the designated research center. Compliance shall be upheld with extant regulations stipulated by the European Medicines Agency (EMA), Good Clinical Practice (GCP) guidelines of the International Conference on Harmonization (ICH), the Declaration of Helsinki, and pertinent national legislation.
3. Efficient project management, encompassing the strategic planning and facilitation of meetings and teleconferences, alongside the preparation of a comprehensive project management plan.

4. Regular and systematic dissemination of progress updates and prompt identification and resolution of any potential challenges to the Ordering Party.
5. Willingness to convene with representatives of the Ordering Party to deliberate on matters germane to the subject of this order.
6. Establishment of a pivotal liaison and information hub for researchers, administrative staff, laboratory personnel, pharmacists, and other pertinent stakeholders. Conducting active communication with all people involved in conducting the clinical trial at each site. Proactive communication shall be maintained with all involved parties at the research center.
7. Training of research teams in the conducted study, including in the scope of the protocol, procedures and GCP principles, together with issuing a certificate, as well as conducting training during the study for study coordinators at the site, research teams in GCP principles and training in the use of eCRF.
8. Preparation of a Quality Assurance Plan in English.
9. Adaptation of the procedure manual for the pharmacist in the study and information on the management of medications, including placebo (Pharmacy Manual) in English.
10. Adaptation of the Laboratory Manual into English.
11. Development of a comprehensive monitoring plan (Monitoring Plan) in English
12. Preparation of Investigator Study Files (ISF) in alignment with Good Clinical Practice (GCP) guidelines for the contracted research center.
13. Supervision of the electronic Case Report Form (eCRF), with dedicated coordination for data input.
14. Rigorous quality control of eCRF data, including proactive query resolution support.
15. Collation of laboratory standards, the curriculum vitae of the laboratory manager, and pertinent quality certifications for equipment deployed in the Clinical Trial.
16. Formulation of a Safety Monitoring Plan to ensure participant well-being throughout the trial.
17. On-site and remote monitoring of the clinical trial, encompassing opening, monitoring, and closing visits.
18. Oversight of patient safety profiles during diagnostic/therapeutic procedures, with timely submission of Serious Adverse Events Reports (SUSARs) via MHRA Gateway and ICSR Submissions.
19. Compilation and submission of annual safety reports to the Regulatory Agency.
20. Execution of pharmacovigilance activities on behalf of the Sponsor, in accordance with British regulatory frameworks.
21. Database cleansing and closure procedures.
22. Vigilant supervision of the quality of statistical data and derived results.
23. Preparation of sections of the final Clinical Study Report (CSR) in adherence to ICH E3 guidelines.
24. Timely submission of the final research report to the Regulatory Agency.

II. STAGES OF ORDER PROCESSING

STAGE I - Documentation Preparation:

Thorough verification of received documentation from the Sponsor for compliance with legal provisions. Compilation of any missing documents.

Submission of research documentation via the Integrated Research Application System (IRAS) to secure requisite approvals from the regulatory agency (MHRA) and the Research Ethics Committee (REC).

STAGE II - Clinical Trial Supervision and Result Compilation:

Rigorous monitoring of clinical trials at the designated research center, ensuring compliance with participant welfare standards, data accuracy, and protocol adherence.

Systematic documentation of all trial-related activities within a secure, IT-based data storage system, facilitating data access and verification.

Timely reporting of serious adverse events and other pertinent medical occurrences, in compliance with stipulated regulations, via the MHRA Gateway and ICSR Submissions, in addition to the Ordering Party.

Seamless collaboration with all stakeholders involved in service provision.

Facilitation of all requisite activities for the closure of the Clinical Trial at the contracted research center in Great Britain.

Comprehensive documentation retention and transfer to the Ordering Party upon trial completion or agreement termination.

Transfer of documents to the Sponsor for archival purposes post-trial completion.

To ensure the seamless execution of this order, the Ordering Party shall empower the Contractor to:

Act as the primary applicant to the Regulatory Agency, with the authority to sign and submit all requisite documents for trial conduct.

Undertake the signing of pertinent documents and respond to queries related to the application process.

Initiate and respond to change requests as necessitated.

Furthermore, the Ordering Party shall develop a Communication Plan, to be furnished to the Contractor post the execution of the service agreement.