Bambino Gesù
OSPEDALE PEDIATRICO

Project - Hub Life Science – Advanced Therapy (LSH-TA) PNC-E3-2022-23683269 - funded by the Ministry of Health as part of the National Complementary Plan for the Innovative Health Ecosystem

CUP Code E83C22006230001

Technical Specifications for the provision of the service Quote Type: Cell Line Characterization, Modality: Viral Gene Therapies

For research activities at the Tumor Gene Therapy Research Unit, part of the Oncohematology Research Area, the Bambino Gesù Children's Hospital (OPBG) requests Solvias NL (hereinafter the Company) to provide a characterization service for cell banks and viral vectors, according to standard protocols and standard reports in accordance with GMP regulations and aimed at the production of pharmaceutical products for gene therapy to be used in Phase I/II clinical trials.

Cell banks and viral vectors can be used in the production process of gene therapy drugs only after verifying the stability of the transgene during the proliferation of the producing cell bank and the efficiency of the viral vector derived from it in correctly transferring and integrating (intact and identical to the initial plasmid sequence) the transgene into the genome of the cell undergoing transduction (in this case, T lymphocytes). The reference legislation is reported below:

- **ICH Q5B** – *Quality of Biotechnological Products: Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products*
- **ICH Q5D** – *Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products*

Therefore, the following analytical and support services are specifically required for the activities of 3 production lines:

<u>Project B7H3</u>

- Genetic analysis consisting of:
    - MCB (monoclonal sample) analysis for transgene identity, integrity and integration
    - EPCB (monoclonal sample) analysis for transgene identity, integrity and integration
    - estimate of the number of vector copies per cell (VCN)
- analysis of transduced lymphocytes (heterogeneous sample) with VV B7H3 for transgene identity, integrity and integration (transduction efficiency)

<u>Project CLEC2A</u>

- Genetic analysis consisting of:

  - MCB (monoclonal sample) analysis for transgene identity, integrity and integration
  - EPCB (monoclonal sample) analysis for transgene identity, integrity and integration
  - estimate of the number of vector copies per cell (VCN)
- analysis of transduced lymphocytes (heterogeneous sample) with the VV CLEC2A for transgene identity, integrity and integration (transduction efficiency)

Project GD2
- Genetic analysis consisting of:
  - MCB (monoclonal sample) analysis for transgene identity, integrity and integration
  - EPCB (monoclonal sample) analysis for transgene identity, integrity and integration
  - estimate of the number of vector copies per cell (VCN)
- analysis of transduced lymphocytes (heterogeneous sample) with VV GD2 for transgene identity, integrity and integration (transduction efficiency)

Other support services for the 3 projects listed above:
- Documentary and IT activation of analytical services
- Sample preparation kit
- sample collection

Delivery methods of the supply

Analytical services are deemed to be provided upon issuance and submission to OPBG of the final analytical reports relating to the above-mentioned activities, accompanied by verification by the Company's Quality Assurance Department for aspects relating to the compliance of the activities performed with current legislation and internal standard procedures.

Acceptance of the reports by the staff of the Hospital's Tumor Gene Therapy Research Unit does not exempt the Company from being responsible for any comments and clarifications from OPBG.