Proposal
R-11469846.P.1
GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS
OPBG-CUP code E83C22003170001 -009820NRT.BUK-Rossana

To:
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Submitted By:
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Issue Date:

21 November 2025

This proposal is valid until 31 December 2025.

Proposal for GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS

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OPBG-C009820NRT.BUK-Rossana

1. OBJECTIVE

The purpose of this study is to identify a dilution of the test material that is compatible with the replication competent retrovirus (RCR) testing platforms performed under the 009820GMP.BUK "Detection of Replication Competent Retrovirus (RCR) by Inoculation on 293 Detector Cells (5 passages)" and 011824GMP.BUK "Detection of Replication-Competent Retrovirus (RCR) by Co-cultivation with the 293 Detector Cell Line (5 passages)" assays.

2. SCOPE OF WORK

Based on the preliminary information provided by GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS, the following are considered to be the estimated milestones of this project. The scope of the project and price may change upon receipt of additional information. Upon signature of the proposal as intent to move forward, Project Management will schedule a project kick-off meeting with GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS to review deliverables, requirements and timelines.

- **Compliance Level Definition Summary**

NRT or non-GxP	No QA Oversight; No Specification Required. NRT = Non-Regulatory Testing
GLP	QA Oversight; No Specification Required
GMP	QA Oversight; Specification Required. If no specification is provided, then results will be reported as "Report Results. For Information Only" or similar terms.
Development	All activities prior to validation or transfer. This may include assay design, optimization, feasibility assessment and robustness evaluation
Validation	Study to determine the performance characteristics of the fully developed assay inducted in accordance with ICH Q2 (R2) or other relevant regulations

- **Milestone 1: Biocompatibility Assessment of Viral Vector (Non-GxP)**

  a. Assay code: C009820NRT.BUK

  b. This milestone covers assessment of the viral vector supernatant of two different Client products utilising the identifiers CLEC2A and B7H3.

  c. Each test material will be inoculated onto 293 detector cells, seeded at conditions replicating those of the 009820GMP.BUK assay. The test material will be inoculated at 3 dilutions:

  - Diluted 1 in 10
  - Diluted 1 in 50
  - Diluted 1 in 100

  d. The cultures will be maintained and routinely examined for cell health.

e. Regulatory Requirement:
   - Non-GxP

f. Deliverables to GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS:
   - A Final Report generated for each test material, capturing the test material conditions assessed (dilutions applied), along with a recommended condition to proceed with in the 009820GMP.BUK assay.

g. Requirement from GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS:
   - Confirmation of approval to proceed with an appropriately identified condition for use in the 009820GMP.BUK assay system.

h. If Milestone 1 is unsuccessful further development may be required. We will work with GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS to determine the scope of that work and generate a new proposal, an amendment to this proposal or a quote.

➢ **Milestone 2: Biocompatibility Assessment of Master Cell Banks (Non-GxP)**

a. Note: Milestone 2 may be performed in tandem with milestone 1.

b. Assay code: C009820NRT.BUK

c. This milestone covers assessment of the master cell bank (MCB) of two different Client products utilising the identifiers CLEC2A and B7H3.

d. A protocol amendment, for each test material, will be utilised to modify assay performance to replicate methodology of the 011824GMP.BUK assay. The protocol amendments will be approved by the Sponsor prior to commencement of this testing.
   - These protocol amendments will also be utilised to document the proposed number of test article cells to be inoculated per condition being assessed.

e. Each test material will be inoculated onto 293 detector cells, seeded at conditions replicating those of the 011824GMP.BUK assay. The test material will be inoculated at the conditions as specified, and approved by the Sponsor prior to testing, in the protocol amendments described above.

f. The cultures will be maintained and routinely examined for cell health.

g. Regulatory Requirement:
   - Non-GxP

h. Deliverables to GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS:
   - A protocol amendment, per study, capturing modification of the methodology to align with the 011824GMP.BUK assay.
   - A Final Report generated for each test material, capturing the test material conditions assessed (test article cells inoculated per

culture), along with a recommended condition to proceed with in the 011824GMP.BUK assay.

i. Requirement from GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS:

- Approval, and return, of the protocol amendments provided to allow commencement of the associated studies.
- Confirmation of approval to proceed with an appropriately identified condition for use in the 011824GMP.BUK assay system.

j. If further development is required, we will work with GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS to determine the scope of that work and generate a new proposal, an amendment to this proposal or a quote.

3. PROJECT WORKFLOW AND TIMELINE ESTIMATES

Upon signature of this proposal and receipt of a valid purchase order, BioReliance® Services Project Management will review capacity with operational leaders to determine actual timelines. BioReliance® Services Project Management will then generate a project plan/timeline to be reviewed and agreed to with the Client at a project kick-off meeting.

4. PROJECT PRICE

Description	Assay Number	QTY	Price (EUR)
Milestone 1: Generation of 009820NRT.BUK assay, and Biocompatibility Assessment of Viral Vector (CLEC2A and B7H3)	C009820NRT.BUK	2	€21,273
Milestone 2: Biocompatibility Assessment of Master Cell Banks (CLEC2A and B7H3)	C009820NRT.BUK	2	€13,852
Total:			€35,125

5. PAYMENT TERMS

Unless superseded by a separate, signed written agreement between BioReliance® Services and the Client, invoices shall be paid in accordance with the following terms, contingent on a satisfactory credit review:

Milestone 1: Generation of 009820NRT.BUK assay, and Biocompatibility Assessment of Viral Vector (CLEC2A and B7H3)	55% invoiced upon laboratory initiation, 40% invoiced upon laboratory completion and 5% invoiced upon order completion
Milestone 2: Biocompatibility Assessment of Master Cell Banks (CLEC2A and B7H3)	60% invoiced upon order booking and 40% invoiced upon laboratory completion

Unless otherwise agreed in writing by BioReliance® Services, payment shall be due **net 30** from the date of the invoice.

6. CLIENT CONTACTS

❖ **GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS point of contact for this project will be:**

Rossana Bugianesi
Quality Control Manager
+39 06 68597202
rossana.bugianesi@opbg.net

7. PROJECT CONTACTS

❖ **BioReliance® Services' project points of contact for this project will be:**

Dr. Christiane Hill
Account Manager
christiane.hill@merckgroup.com

8. CANCELLATIONS

Unless superseded by a separate, signed written agreement between BioReliance® Services and GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS, the following cancellation fee schedule will apply to each Project:

Cancellation <2 weeks before planned Lab Initiation date of any Milestone:	20% of the total price of applicable Milestone(s)
Cancellation after Lab Initiation of any Milestone:	50% of applicable Milestone(s)
Cancellation after Lab Completion of any Milestone:	90% of applicable Milestone(s)

9. REPEATS

Repeat testing may be subject to additional charges to GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS. Prior to initiating any work, including repeat testing, considered out of scope for this proposal, our Project Management or Account Manager will review with GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS and issue a quotation and/or proposal amendment.

10. RISK ASSESSMENTS AND SAFETY

Any known safety hazards associated with the test articles or reagents supplied for use in these studies must be reported to BioReliance® Services in order to allow a full risk assessment of the study to be conducted. Please be aware that there may be a requirement for licences to import and/or handle certain biological or infectious materials, and it is essential that these be in place before shipment of materials is arranged. Please note that no work shall commence until all relevant risk assessments and licences are in place.

Please also note that for studies under consideration at our UK facilities, BioReliance® Services is required by the UK Health and Safety Executive under European Commission Directive 94/51/EC to have a risk assessment of any GMO present in its facility. Therefore, if the material to be supplied is classified as a Genetically Modified Organism (GMO), we request that you inform us of the safety assessment for the test article. Alternatively, if requested by you, BioReliance® Services' own Genetic Safety Committee can do an assessment for you.

11. REGULATORY AND LEGAL NOTICES

Unless otherwise stated or expressly requested, this study will be conducted in laboratories compliant to GLP and GMP.

Any changes to the scope of this study including, but not limited to design, performance, materials and/or equipment are subject to the BioReliance® Services change control process, which may result in additional cost to the Client.

For method transfer projects, BioReliance® Services will endeavor to use the same critical reagent material as highlighted by the Client's SOP/Method/Protocol. However, if the supplier is not an approved vendor by the BioReliance® Services Quality Assurance Department, it will be the responsibility of the Client to provide the supplier quality details to confirm the reagent is acceptable for GxP use.

The pricing information provided in this proposal is the best estimate by BioReliance® Services based on the details available at this time. The price may vary upon further investigation by BioReliance® Services and additional information provided by the Client, prior to commencing the study.

Unless expressly stated herein, neither party grants nor implies the transfer of any Intellectual Property to the other party as a result of this contract. All data and results generated in this study are confidential and are owned solely by the Client. All data and results generated in this study will not be shared with any other entity without first receiving written permission from the Client.

BioReliance® Services is and shall continue to be the sole owner of, all concepts, inventions, improvements, designs, programs, formulas, know-how, methods, processes, and writings utilized or developed in conducting the Project to the extent relating solely and generally to the business, processes, practices, or services performed by BioReliance® Services for its customers.

If, in the course of providing the Services, Client requests and BioReliance® Services agrees to develop or make any improvement, design, process, documents or other material, the parties will reduce the agreement to writing in a contractual form, such as this Proposal or subsequent Individual Project Assignment (IPA), including the compensation to be paid for such developments. The copyrights, patent and all other intellectual property rights, and all legal and beneficial right, with and interest therein shall be identified therein; all other intellectual property developed by BioReliance® Services, in the course of providing the Services, shall belong to BioReliance® Services.

12. TERMS & CONDITIONS

Except to the extent superseded by a separate signed written agreement (i.e., a negotiated Master Service Agreement) between BioReliance® Services and GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS, the Services described in this quotation will be governed by the relevant BioReliance® Services' Statement of Terms and Conditions, which are included herewith, or incorporated herein by reference:

Testing and Storage Terms and Conditions.

13. SIGNATURES

We require a hard copy of a valid Purchase Order or equivalent prior to the initiation of the work quoted. If there will be delay in processing the PO, a signature is required below by an authorized company representative. At your earliest convenience, a hard copy should be scanned and forwarded to our Account Manager and/or Project Manager before testing is scheduled for completion.

If a Purchase Order will not be provided, please sign and complete a billing and shipping information form (provided separately) to ensure correct mailing of the invoices and reports/CofAs.

Signed on Behalf of:	**Signed on Behalf of:**
GMP Biopharmaceutical Facility	
Ospedale Pediatrico Bambino Gesù IRCCS:	**BioReliance Ltd.:**
_____	
Signature	Signature
_____	Dr. Christiane Hill
Name	Name
_____	Account Manager
Title	Title
_____	21 November 2025
Date	Date
_____	
Client PO Number	

Confidentiality

This document has been prepared by and remains the sole property of BioReliance Ltd. It is submitted to GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS solely for use in evaluating BioReliance Ltd. qualifications and/or quotations concerning the particular projects for which it was prepared. This document is confidential to BioReliance Ltd. and GMP Biopharmaceutical Facility Ospedale Pediatrico Bambino Gesù IRCCS agrees to treat the document in accordance with the terms of any Confidentiality Agreements previously signed and, in any event, shall not disclose to any third party without the consent of BioReliance Ltd. not to be unreasonably withheld.