| **EMENDAMENTO N. 1** | **AMENDMENT No. 1** |
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| **Protocollo numero: TAK-999-3001** | **Protocol Number: TAK-999-3001** |
| **Promotore: Takeda Development Center Americas, Inc.** | **Study Sponsor: Takeda Development Center Americas, Inc.** |
| QUESTO EMENDAMENTO N. 1 (l'**"Emendamento N. 1**") in vigore dalla data dell'ultima firma (la "**Data di entrata in vigore**"), da e tra Takeda Development Center Americas, Inc, con sede legale in 500 Kendall Street, Cambridge, MA 02142 USA, C.F. n. 383691673 in persona del suo legale rappresentante Paula Fischthal Director, Clinical Operations(d'ora innanzi denominato/a "**Promotore**"), e l' AZIENDA OSPEDALIERA UNIVERSITARIA POLICLINICO "PAOLO GIACCONE" DI PALERMO (d'ora innanzi denominato/a "**Ente**"), con sede legale in PALERMO Via del Vespro 129, C.F. e P. IVA n. 05841790826, in persona della Direttrice Generale, Dott.ssa Maria Grazia Furnari, modifica i termini del Contratto per la conduzione della Sperimentazione clinica sui medicinali stipulato in data 11 di febbraio 2025 apportati dalle parti a tale Contratto di | THIS AMENDMENT No. 1 (the **"Amendment No. 1**") effective as of the date of the last signature (the "**Effective Date**"), by and among Takeda Development Center Americas, Inc, headquartered in 500 Kendall Street, Cambridge, MA 02142 USA, Tax Code no. 383691673, in the person of legal representative Paula Fischthal, Director, Clinical Operations (hereinafter the "**Sponsor**"), and AZIENDA OSPEDALIERA UNIVERSITARIA POLICLINICO "PAOLO GIACCONE" of PALERMO (from now on the "**Institution**") headquartered in PALERMO Via del Vespro 129, Tax Code and VAT no. 05841790826, in person of General Director, Dr. Maria Grazia Furnari , amends the terms of the Agreement for the conduct of Clinical Trial on Medical Products dated as of the 11 day of February, 2025 made by the parties to that Sponsored Clinical Trial Agreement between |

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| sperimentazione clinica sponsorizzata tra le parti (il "**Contratto**"). Per le finalità del presente Emendamento N. 1, la CRO e l'Ente, potranno essere indicati ciascuno come una "Parte" e congiuntamente come le "Parti". I termini in maiuscolo non definiti nel presente documento devono avere lo stesso significato stabilito nel Contratto. | the parties (the "**Agreement**"). For purposes of this Amendment No. 1, each of the CRO and Institution, may be referred to as a "Party" and together as the "Parties". Capitalized terms not defined herein shall have the same meaning as set forth in the Agreement. |
| PREMESSO CHE le Parti intendono emendare il Contratto; | WHEREAS, the Parties desire to amend the Agreement; |
| TUTTO CIÒ PREMESSO, in considerazione dei patti e degli accordi reciproci ivi contenuti, le Parti, con l'intenzione di essere giuridicamente vincolate, hanno sottoscritto il presente Emendamento N. 1 e convengono specificamente quanto segue: | NOW THEREFORE, in consideration of the mutual covenants and agreements herein, the Parties, intending to be legally bound, have entered into this Amendment No. 1 and do specifically agree as follows: |
| 1. A seguito delle revisioni del budget richieste dall'Emendamento 4 al Protocollo, datato 30 settembre 2024- l'Allegato A - Budget (ossia "**Allegato A - Budget**") del Contratto verrà cancellato nella sua interezza e sostituito con l'Allegato A modificato allegato al presente documento e ivi incluso per riferimento. Le modifiche secondo il nuovo Allegato A - Budget entreranno in vigore alla data di autorizzazione di AIFA 17 febbraio 2025 (la "**Data di entrata in vigore del Budget**"). | 1. Further to budget revisions required by Protocol Amendment 4, dated 30th of September 2024- Annex A - Budget (the "**Annex A - Budget**") of the Agreement shall be deleted in its entirety and replaced with the revised Annex A - Budget attached hereto and incorporated by reference herein. -The changes per the new Annex A - Budget will go into effect per the AIFA authorization date 17 February 2025 (the "**Budget Effective Date**"). |
| 2. A partire dalla Data di entrata in vigore del | 2. Effective as of the Budget Effective Date, the |

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| Budget la clausola 6.1 del Contratto deve intendersi cancellata nella sua interezza e sostituita con la seguente clausola 6.1:<br>6.1 Il corrispettivo pattuito, preventivamente valutato dall'Ente, per paziente eleggibile, valutabile e che abbia completato il trattamento sperimentale secondo il Protocollo e per il quale sia stata compilata validamente la relativa CRF/eCRF, comprensivo di tutte le spese sostenute dall'Ente per l'esecuzione della Sperimentazione e dei costi di tutte le attività ad essa collegate, è pari ad € 34.549,95 (trentaquattromilacinquecentoquarantanove /95) per paziente, come meglio dettagliato nel Budget qui allegato sub A. | clause 6.1 of the Agreement is herewith deleted in its entirety and replaced with the following clause 6.1:<br>6.1 The remuneration agreed, assessed in advanced by the Institution, for each eligible, assessable patient whose trial treatment has been completed according to the Protocol and for whom the related CRF/eCRF has been duly compiled, including all the costs incurred by the Institution in execution of this Trial and the costs to cover all the related activities, is € 34.549,95 (thirty three thousand five hundred and forty nine/95) per patient as specified in more detail in the Budget attached hereto sub A. |
| 3. A partire dalla Data di entrata in vigore la clausola 4.3 del Contratto deve intendersi cancellata nella sua interezza e sostituita con la seguente clausola 4.3:<br>"I medicinali Sperimentali devono essere inviati dal Promotore alla Farmacia dell'Ente all' attenzione del Dott. Andrea Pasquale, che provvederà alla loro registrazione, conservazione, dispensazione ai pazienti, eventuale allestimento a mezzo del personale dell'UFA, contabilizzazione e stoccaggio dei resi fino al ritiro da parte del Promotore/ CRO | 3. Effective as of the Effective Date, the clause 4.3 of the Agreement is herewith deleted in its entirety and replaced with the following clause 4.3:<br>"The Trial Drugs shall be sent by the Sponsor to the Pharmacy of the Institution, to the attention of Dr. Andrea Pasquale, which will record them, store, provide to patients, possible setting up by UFA staff, accounting and storage of returns until withdrawal by the Sponsor/CRO and/or destruction in accordance with the provisions of the Protocol |

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| e/o distruzione secondo quanto previsto dal protocollo e normativa vigente. La farmacia si impegna a fornire assistenza ai CRA durante le visite di inizio studio, di monitoraggio e chiusura del centro fornendo tutte le certificazioni necessarie a garantire la corretta conservazione dei Medicinali loro affidati ed eventuale smaltimento". | and the current regulations.<br>The pharmacy undertakes to provide assistance to the CRAs during the SIV, monitoring and close-out visit by providing all the necessary certifications to ensure the correct storage of the medicinal products entrusted to them and possible disposal" |
| 4. Tutti gli altri termini e condizioni del Contratto rimarranno in pieno vigore ed efficacia. In caso di conflitto tra i termini del Contratto e il presente Emendamento N. 1, prevarranno i termini del presente Emendamento N. 1. | 4. All other terms and conditions of the Agreement shall remain in full force and effect. In the event of any conflict between the terms of the Agreement and this Amendment No. 1, the terms of this Amendment No. 1 shall govern and control. |
| Il presente Emendamento N. 1 viene sottoscritto con firma digitale ai sensi della normativa applicabile. Le imposte e tasse inerenti e conseguenti alla stipula del presente Emendamento 1, ivi comprese l'imposta di bollo sull'originale informatico di cui all'art. 2 della Tabella Allegato A – tariffa parte I del DPR n. 642/1972 e l'imposta di registro devono essere versate dal Promotore nel rispetto della normativa applicabile.<br>L'imposta di Bollo pari ad € 112,00 per complessive 7 marche da bollo viene assolta in modo virtuale dalla CRO. Autorizzazione N. | This Amendment No. 1 is being executed with digital signature in accordance with current regulations. The taxes and fees inherent to and consequent to the execution of this Amendment No. 1, including the stamp duty on the original electronic document under Art. 2 of the Table in Exhibit A – Tariff part I of Presidential Decree No. 642/1972, and registration tax must be paid by Sponsor, in accordance with applicable law.<br>Duty Stamps equal to € 112,00 for a total of 7 stamp duty is virtually paid by CRO pursuant to art.15 DPR 642/72 with authorization N. |

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| 28877/2015 del 05 febbraio 2015 Agenzia delle Entrate – Ufficio Territoriale Milano 2. | 28877/2015 dated 05 February 2015 by the Tax Agency – Ufficio Territoriale Milano 2. |
| A CONFERMA DI QUANTO PRECEDE, le Parti, con l'intenzione di essere giuridicamente vincolate, hanno sottoscritto il presente Emendamento N. 1 tramite i loro rappresentanti debitamente autorizzati a partire dalla Data di entrata in vigore. | IN WITNESS WHEREOF, the Parties hereto, intending to be legally bound, have executed this Amendment No. 1 by their duly authorized representatives as of the Effective Date. |

**Per il Promotore/ For the Sponsor**

Il Legale Rappresentante o suo delegato/ Legal Representative or her/his delegate

Dott./Dr. Paula Fischthal

Firma/Signature: DocuSigned by: Paula Fischthal 9A2C6425A16D406...

**Per l'Ente/ For the Institution**

Il Legale Rappresentante o suo delegato/ The legal Representative or her/his delegate

Dott.ssa/ Dr. Maria Grazia Furnari

Firma/ Signature

Maria Grazia Furnari
12.05.2026 15:41:48
GMT+02:00

| **ALLEGATO A – BUDGET** | **ANNEX A - BUDGET** |
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| **ONERI E COMPENSI** | **COSTS AND PAYMENTS** |
| **Parte 1 - Oneri fissi e Compenso per paziente coinvolto nello studio** | **Part 1 - Fixed costs and payment per patient included in the study** |
| Includere, a titolo di esempio le seguenti voci: | Include, by way of example, the following items: |
| - Fornitura del/i Medicinale/i Sperimentale/i e/o di ogni altro materiale in sperimentazione o necessario allo svolgimento della stessa affinché non vi sia aggravio di costi a carico del S.S.N. (kit diagnostici, dispositivi medici, ecc.). | - Supply of the Trial Drug(s) and/or of any other materials under trial or required for the trial provided that there are no extra costs for the Italian National Health Service (diagnostics kits, medical devices, etc.). |
| - Compenso lordo a paziente coinvolto nello studio: € 34.549,95 (fuori campo IVA) | - Gross payment per patient included in the study: € 34.549,95(VAT not applicable) |
| - Compenso per la Farmacia come da tariffe riportate nella tabella sottostante se la Sperimentazione non ricade in quanto normato con delibera dell'AOUP 406/2018 | - Pharmacy fee as per the rates shown in the table below if the Trial does not fall under what is regulated by AOUP resolution 406/2018. |
| Tabella 1/Table 1 – Compensi per la farmacia/ Pharmacy fees | |

| **Attività/Activity** | **Corrispettivo/Unit Cost** | **Frequenza/Quantity** | |
|---|---|---|---|
| Istruttoria Sperimentazione/Start-up fee | 500 € | 1 | |
| SIV | 150 (210) € | 1 | |
| Corrispettivo per ogni fornitura/IP supply fee | 50 € | Secondo attività/according to activity | Ogni arrivo/for each supply |
| Randomizzazione/Randomization | 10 € | Secondo attività/ according to activity | Ogni paziente/for each patient in |
| Assegnazione IWRS e Consegna farmaci al soggetto arruolato/ IWRS entailment and IP dispensation to patient enrolled | 40 € | Secondo attività/ according to activity | Ogni dispensazione/for each dispensation |
| Visita di monitoraggio/ monitoring visit | 100 € | Secondo attività/ according to activity | Ogni visita di monitoraggio/for each monitoring visit |
| Visita monitoraggio da remoto/ remote monitoring visit | 130 € | Secondo attività/ according to activity | Ogni visita di monitoraggio da remoto/ for each remote monitoring visit |
| Visita di chiusura/close-out visit | 150 (210) € | 1 | |
| Preparazione reso da rispedire (IMPs o contenitori termostati)/ Return IP shipment | 50 € | Secondo attività/ according to activity | Ogni collo preparato di IMPs o contenitori termostati/ for |

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| preparation (IMPs or thermostat containers) | | | Eeach shipment prepared or thermostat containers |
| Etichettatura/Labelling | 3 € | Secondo attività/ according to activity | Ogni confezione, unità Etichettata/ for each pack, unit Labeled |

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| Compenso per screening failure e unscheduled visit, nonché per la eventuale distruzione del farmaco sperimentale come previsto dall'art. 4.6 del Contratto. | Payment for screening failures and unscheduled visits, as well as for any destruction of the trial drug as provided for under art. 4.6 of the Agreement. |
| **Mancato superamento dello screening:** l'Ente riceverà un rimborso per un massimo di cinque (5) mancati superamenti dello screening (definiti sotto). Il Beneficiario riceverà un rimborso per procedura per ogni mancato superamento dello screening, sulla base del numero massimo sopra indicato al costo indicato nella tabella sottostante. Dopo aver raggiunto il numero massimo di mancati superamenti dello screening, qualsiasi mancato superamento dello screening aggiuntivo dovrà essere esaminato e sarà necessaria l'approvazione scritta del Promotore perché venga rimborsato. Non sono | - **Screen Failures**: The Institution will be compensated up to a maximum of five (5) Screen Failures (as defined below). Payee will be reimbursed on a per procedure basis per Screen Failure based on the above maximum number and at the rate set forth in the table below. After the maximum number of Screen Failures have been met, any additional Screen Failures must be reviewed and have written Sponsor approval prior to being reimbursed. No further amendments to the Agreement are required for these additional Screen Failure payments.<br><br>For purposes of this Amendment No. 1, a Screen Failure shall mean a subject who (i) |

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| necessari ulteriori emendamenti al Contratto per questi pagamenti dei mancati superamenti dello screening aggiuntivi.<br><br>Ai fini del presente Emendamento N. 1, viene considerato un mancato superamento dello screening un soggetto che (i) completa le procedure della Visita di screening indicate nel Protocollo (incluso, a titolo esemplificativo ma non esaustivo, il processo di consenso informato) e (ii) non è randomizzato. Per poter ricevere il rimborso per la Visita di screening, le pagine completate dell'eCRF dello screening devono essere confermate dalla CRO e qualsiasi altra informazione aggiuntiva, che possa essere richiesta dalla CRO, deve essere inoltrata per documentare in modo appropriato le procedure di screening del soggetto. | completes the Screening Visit procedures outlined in the Protocol (including, without limitation, the informed consent process) and (ii) is not randomized. To be eligible for reimbursement of Screening Visit, completed screening eCRF pages must be confirmed by CRO and any additional information, which may be requested by CRO must be submitted to appropriately document the subject screening procedures. |

| **Screening Visit /Visita di Screening** | **Costo Unitario (IVA esclusa e non applicabile) – incluse spese generali /Unit** |
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| | **Cost (VAT excluded and not applicable) – including Overheads** |
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| Informed Consent | € 31,32 |
| Inclusion/exclusion criteria | € 29,00 |
| Initial Physical Exam to include demographics, medication history, medical history, historical PFT data, vital signs, height, and weight | € 119,48 |
| ECG | € 87,00 |
| AE assessment | € 23,20 |
| Concomitant medications/procedures | € 23,20 |
| Central Lab blood samples: Hepatitis panel, HIV test, , FSH, Clinical laboratory tests, Alpha-fetoprotein, Serum sample for Z-AAT, Plasma sample for calprotectin, Blood sample for RNA, Serum sample for ELF score, Serum sample for circulation biomarkers , , Blood sample for DNA (optional), and Serum sample for immunogenicity | € 34,80 |
| Central Lab - Nasopharyngeal swab: COVID-19 PCR test | € 104,40 |
| Central lab urine samples: Urine drug screen, Urine cotinine, Clinical laboratory tests (urinalysis) | € 13,92 |
| Urine Cotinine (Local-point of care) at ET visit (N/A if tested within 6 months of termination) | €34,80 |
| Shipping, Handling, & processing to the Central Lab of blood/urine samples | € 13,92 |
| Abdominal Ultrasound | € 87,00 |
| MELD score | € 26,68 |

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| CTP classification | € 17,40 |
| West-Haven criteria | € 39,44 |
| CT lung densitometry | € 872,32 |
| Spirometry to include FEV1 and FVC | € 84,68 |
| Dispence and subject training on how to complete ePRO including CLDQ, EQ-5D-5L, SF-36, mMRC Dyspnea Scale, PGI-S, and HRU | € 33,64 |
| Review of ePRO for completion | € 30,16 |
| Physician's Fees without Exam Costs | € 290,00 |
| Study Coordinator Fee Per Visit | € 410,64 |
| Total | € 2.407,00 |

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| **Pagamenti per sospensione o interruzione anticipata:** il rimborso per i soggetti che sospendono o interrompono anticipatamente, sarà calcolato proporzionalmente in base al numero di visite/procedure completate confermate. | **Discontinued or Early Termination Payments:** Reimbursement for discontinued or early termination subjects will be prorated based on the number of confirmed completed procedures/visits. |
| **Avviamento della Sperimentazione:** un pagamento una tantum pari all'importo definito nel budget per le attività di avviamento della Sperimentazione sarà effettuato alla firma dell'Emendamento e quando la CRO avrà ricevuto dall'Ente una fattura originale completa dettagliata che includa i compiti rilevanti e i costi associati**.** | **Trial Start-up Costs:** A one-time payment, at the rate set forth in the budget for Trial Start-up activities will be made upon execution of the Amendment and upon receipt by CRO of an itemized original Complete Invoice including relevant tasks and associated costs from Institution. |

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| **Spese amministrative:** verrà effettuato un pagamento unico pari all'importo definito nel budget per le attività amministrative dello Sperimentazione alla firma del Contratto e quando la CRO avrà ricevuto dall'Ente una fattura originale completa dettagliata che includa i compiti rilevanti e i costi associati. | **Administrative Fee:** A one-time payment, at the rate set forth in the budget for Administrative activities will be made upon execution of the Agreement and upon receipt by CRO of an itemized original Complete Invoice including relevant tasks and associated costs from Institution. |
| **Spese di avviamento della farmacia:** verrà effettuato un pagamento unico per l'avviamento della farmacia, in base alle tariffe definite nella Tabella 1 sopra riportata, dietro ricevimento da parte della CRO di tutta la documentazione contrattuale e normativa e di una fattura originale valida. | **Pharmacy Set-Up Fee:** A one-time Pharmacy Set-Up payment, based upon the rates set forth in the Table 1 above, will be made upon receipt by CRO of all original contractual and regulatory documentation and receipt of an original Valid Invoice. |
| **Spese di conservazione dei registri/Spese di archiviazione:** verrà effettuato un pagamento unico per la conservazione dei registri, in base alle tariffe definite nel budget, per la conservazione dei registri dello Sperimentazione, secondo i requisiti definiti nel Contratto, dietro ricevimento di una fattura valida | **Record Storage Fee/Archiving Fee** A one-time record storage payment, based upon the rates set forth in the budget, for retaining Trial Records according to the requirements set out in the Agreement, will be made upon receipt of Valid Invoice. |
| **IND Safety Reports & SAE Reports**: Il pagamento alla tariffa stabilita nel budget | **IND Safety Reports & SAE Reports**: Payment at the rate set forth in the budget for |

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| per l'elaborazione di ciascun IND Safety Letter/External SAE report sarà effettuato al ricevimento della fattura non contestata e dettagliata e della documentazione di supporto. | processing each IND Safety Letter/External SAE report will be made upon receipt of undisputed and itemized invoice and supporting documentation. |
| **Visite di monitoraggio in loco (per visita di monitoraggio di persona):** L'Ente sarà rimborsato alla tariffa stabilita nel budget per il tempo e l'impegno spesi durante ogni visita di monitoraggio in loco. Il pagamento sarà effettuato al ricevimento di una fattura non contestata e dettagliata e della documentazione di supporto. | **On-site Monitoring Visits (Per visit for in-person monitoring):** The Institution will be reimbursed at the rate set forth in the budget for the time and effort spent during each on-site monitor visit. Payment shall be made upon receipt of undisputed and itemized invoice and supporting documentation. |
| **Audit:** Nel caso di un audit/ispezione per cause non direttamente connesse alla Sperimentazione, il Promotore rimborserà al beneficiario il tempo dedicato e le spese ragionevolmente sostenute dall'Ente e dallo Sperimentatore in relazione a tale audit/ispezione al tasso giornaliero stabilito nel budget fino ad un massimo di tre (3) giorni. Il pagamento sarà effettuato al ricevimento di una fattura non contestata e dettagliata e della relativa documentazione di supporto. | **Audits:** In the case of a not for cause audits/inspections directly relating to the Trial, Sponsor shall reimburse Payee for Institution's and Investigator's reasonable time and expenses in connection with such audit/inspection at the per day rate set forth in the budget with a cap of three (3) days. Payment shall be made upon receipt of undisputed and itemized invoice and supporting documentation. |

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| **Placebo:** l'Ente sarà rimborsato per le spese approvate per il placebo di provenienza locale al ricevimento da parte della CRO di una fattura completa originale che include numero di protocollo, sperimentatore, numero di fattura, data della fattura e documentazione di supporto appropriata ("Fattura valida") dal parte dell'Ente | **Placebo Materials:** Institution will be reimbursed for approved locally sourced placebo material expenses upon CRO's receipt of original complete invoice which includes Protocol number, Investigator, invoice number, invoice date, and appropriate supporting documentation ("Valid Invoice") from Institution |
| **Visite non programmate :** ai fini del presente Emendamento n. 1, per "Visite non programmate" si intende una visita del soggetto che non è espressamente prevista nel programma delle procedure del Protocollo della Sperimentazione, ma che (i) può essere richiesta per la Sperimentazione su indicazione dello Sperimentatore, oppure (ii) può essere correlata a un evento avverso manifestatosi durante la Sperimentazione o altrimenti richiesta per la Sperimentazione, su indicazione dello Sperimentatore, per la salute e il benessere di un soggetto che partecipa alla Sperimentazione. Le visite o le procedure standard del paziente che non sono richieste dal protocollo non costituiscono una Visita non programmata ai fini del presente Emendamento n. 1. | **Unscheduled Visits:** For purposes of this Amendment no. 1, an "Unscheduled Visit" means a Subject visit which is not expressly set forth in the schedule of Trial procedures of the Protocol, but that (i) may be required for the Trial as directed by the Investigator, or (ii) may be related to an adverse event experienced during the Trial or otherwise required for the Trial as directed by the Investigator, for the health and welfare of a Trial subject. Standard of care patient visits or procedures that are not required by the Protocol do not constitute Unscheduled Visits for purposes of this Amendment no. 1.<br><br>Unscheduled Visits will be reimbursed at the rate set forth in the budget following review and approval of any information and/or documentation required by Sponsor. |

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| Le Visite non programmate saranno rimborsate al valore forfettario stabilito nel budget dopo revisione e approvazione di qualsiasi informazione e/o documentazione richiesta dal Promotore. L'Ente dovrà cercare di avvisare il Promotore o il suo designato con un preavviso ragionevole e appena possibile, ottenere l'approvazione dello stesso prima di realizzare la procedura. Nel caso in cui i tassi di rimborso per procedure necessarie dal punto di vista medico non fossero inclusi nel budget, l'importo di rimborso per queste procedure sarà esaminato in buona fede dal Promotore prima che questi approvi o rifiuti le spese, senza irragionevoli sospensioni o ritardi. | Institution will endeavor to provide reasonable advance notice to Sponsor or its designee and whenever possible, seek Sponsor's prior approval before the procedure is performed. In the event that reimbursement rates for medically necessary procedures are not included in budget, the amount of reimbursement for those procedures will be reviewed in good faith by Sponsor prior to Sponsor's approval or disapproval of the expenditures, which shall not unreasonably be withheld or delayed. |
| Compenso per il Centro sperimentale a paziente completato (Compenso a paziente coinvolto – overhead aziendale - tutti i costi sostenuti dall'Ente per la sperimentazione): € 34.549,95 (IVA non applicabile). | Payment for the Trial Site for each completed patient (Payment per enrolled patient - company overheads - all the costs incurred by the Institution for theTrial): € 34.549,95 (VAT not applicable). |
| Fasi economiche intermedie (nel caso in cui i pazienti non completino l'iter sperimentale): | Interim financial phases (if the patients do not complete the trial procedure): |

| **Visit /Visita** | **Unit Cost (VAT excluded and not applicable) – including** |
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| | **Overheads/ Costo Unitario (IVA esclusa e non applicabile) – incluse spese generali** |
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| **Screen** | € 2,407.00 |
| **Day 1** | € 1,767.84 |
| **Week 4** | € 1,076.48 |
| **Week 8** | € 206,48 |
| **Week 12** | € 206,48 |
| **Week 16** | € 1,144.92 |
| **Week 20** | € 206,48 |
| **Week 24** | € 206,48 |
| **Week 28** | € 1,307.32 |
| **Week 32** | € 206,48 |
| **Week 36** | € 206,48 |
| **Week 40** | € 1,076.48 |
| **Week 44** | € 206,48 |
| **Week 48** | € 206,48 |
| **Week 52** | € 2,214.44 |
| **Week 64** | € 989.48 |
| **Week 76** | € 1,231.92 |
| **Week 88** | € 989.48 |
| **Week 100** | € 2,035.80 |
| **Week 106** | € 2,026.20 |
| **Week 112** | € 989.48 |
| **Week 124** | € 1,231.92 |
| **Week 136** | € 989.48 |
| **Week 148** | € 2,214.44 |

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| **Week 160** | € 989.48 |
| **Week 172** | € 1,231.92 |
| **Week 184** | € 989.48 |
| **Week 196** | € 2,035.80 |
| **Week 202** | € 1,978.64 |
| **Safety Follow-up (12 Weeks After Last Dose)** | € 946.56 |
| **Safety Follow-up (24 Weeks After Last Dose) EOS** | € 1,033.56 |
| **Total** | € 34.549,95 |
| **Early Termination Visit** | € 1.177,40 |

| **Site Costs/Costi del centro** | **Unit Cost (VAT excluded and not applicable) – including Overheads /Costo Unitario (IVA esclusa e non applicabile) – incluse spese generali** |
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| Trial Start-Up Fee / Site Set-Up Fee | € 1.495,00 |
| Archiving and Document Storage - Per Year | € 400,00 |
| Administrative Fee | € 2.000,00 |
| IND Safety Report (Per Report) | € 26,00 |
| SAE Reporting (Per Report) | € 67,00 |

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| On-Site Monitoring Fee (Per visit) | € 289,00 |
| Not-for-Cause Audit (€910 per day, 3 days max ) | € 910,00 |
| Unscheduled Visit | € 415,28 |

| **Invoiceable Items/Procedure Fatturabili** | **Unit Cost (VAT excluded and not applicable) – including Overheads/ Costo Unitario (IVA esclusa e non applicabile) – incluse spese generali** |
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| Vital Signs (post dose if clinically indicated at the discretion of PI) | € 11,60 |
| Serum pregnancy test in POCBP (hCG) | € 15,08 |
| Urine pregnancy test in POCBP (hCG) | € 9,28 |
| Urine Cotinine (Local-point of care) at ET visit (N/A if tested within 6 months of termination) | € 34,80 |
| ECG | € 87,00 |
| Liver Biopsy (fresh) | € 1.209,88 |
| Biopsy Sample Handling Complex (Fresh) | €32,16 |
| Biopsy Sample Handling (Archival) | €24,36 |
| Contrast-enhanced Abdominal CT (if contrast-enhanced MRI is not performed) | € 715,72 |
| Contrast-enhanced Abdominal MRI (if contrast-enhanced CT is not performed) | € 928,00 |
| EGD | € 1.125,20 |
| MRE | € 1.991,72 |

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| VCTE | € 75,40 |
| CT lung densitometry | € 872,32 |
| Spirometry to include FEV1 and FVC | € 84,68 |
| DLCOhgb | € 148,48 |
| Re-consent | € 39,44 |
| Clinical Laboratory- Hematology: Local Analysis may only be used in cases when the central laboratory results will not be available and the results are needed immediately to determine what actions to take for safety reasons. An amendment is not required for additional labs. **(Sponsor approval required prior to performing)** | € 24,36 |
| Clinical Laboratory- Clinical Chemistry: Local Analysis may only be used in cases when the central laboratory results will not be available and the results are needed immediately to determine what actions to take for safety reasons. An amendment is not required for additional labs. **(Sponsor approval required prior to performing)** | € 55,68 |
| Clinical Laboratory- Coagulation [Prothrombin Time (PT)]: Local Analysis may only be used in cases when the central laboratory results will not be available and the results are needed | € 9,28 |

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| immediately to determine what actions to take for safety reasons. **(Sponsor approval required prior to performing)** | |
| Clinical Laboratory- Coagulation [International Normalized Ratio INR]: Local Analysis may only be used in cases when the central laboratory results will not be available and the results are needed immediately to determine what actions to take for safety reasons. **(Sponsor approval required prior to performing)** | € 17,40 |
| Clinical Laboratory- Urinalysis: Local Analysis may only be used in cases when the central laboratory results will not be available and the results are needed immediately to determine what actions to take for safety reasons. An amendment is not required for additional labs. **(Sponsor approval required prior to performing)** | € 16,24 |

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| - Tutti i costi rimborsabili relativi alla Sperimentazione, inclusi quelli coperti dal contributo per paziente coinvolto nella Sperimentazione, non comporteranno aggravio di costi a carico del SSN | - All the reimbursable costs of the Trial, including those covered by the contribution per patient involved in the Trial, shall not lead to any extra costs payable by the Italian National Health Service. |

| **Parte 2 - Indennità per i pazienti/accompagnatori coinvolti nella Sperimentazione:** | **Part 2 - Allowance for patients/carers involved in the Trial:** |
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| Si fa rinvio al modello "Indennità per i partecipanti alla sperimentazione", incluso nel dossier della domanda ai sensi del Regolamento (UE) n. 536/2014, da intendersi richiamato nel presente Contratto come sua parte integrante e sostanziale. | Reference is made to the model "Allowance for trial participants", included in the application dossier pursuant to (EU) Regulation no. 536/2014, to be understood as cited in this Agreement as an integral and substantial part thereof. |
| LIQUIDAZIONE E FATTURE | LIQUIDATION AND INVOICES |
| - Il compenso deve essere liquidato entro 45 giorni (quarantacinque) dalla ricezione della fattura. | - The payment must be made within 45 days (forty-five) from receipt of the invoice. |
| - La fattura deve essere emessa con cadenza prevista trimestrale per soggetto e per visita, secondo quanto maturato nel periodo di riferimento, sulla base di apposita richiesta di emissione fattura da parte del Promotore. | - The invoice must be issued at the required intervals on quarterly basis on a per subject, per visit basis , based on the amounts accruing during the reference period and the specific request for invoice by the Sponsor. |
| - La visita di screening sarà rimborsata in base alle procedure completate; la CRO non rimborserà eventuali procedure eseguite dopo che il | - The screening visit will be reimbursed based on procedures completed; CRO will not reimburse for any procedures carried out after the subject has failed |

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| soggetto non ha superato lo screening. Tutte le visite saranno rimborsate sulla base di una visita completata per soggetto in conformità con il budget allegato. Il novanta percento (90%) di ogni pagamento dovuto, incluso qualsiasi mancato superamento dello screening che potrebbe essere versato ai sensi del presente Contratto, sarà effettuato sulla base dei dati di arruolamento del mese precedente confermati da schede di raccolta dati elettroniche ("eCRF") del soggetto completate dopo controllo dei dati a sostegno della visita del soggetto e/o dietro ricevimento di una fattura valida ove richiesto dalla regione. Il saldo degli importi dovuti, fino al dieci percento (10%), sarà calcolato su base proporzionale dopo controllo delle visite effettive del soggetto e sarà versato dalla CRO all'Ente all'accettazione finale del Promotore di tutte le pagine delle eCRF, dopo aver espresso tutti i chiarimenti, dopo ricevimento e approvazione di qualsiasi documento normativo in sospeso secondo le richieste della CRO e/o del Promotore, dopo restituzione | screening. All other visits will be reimbursed on a completed visit per subject basis in accordance with the attached budget. Ninety percent (90%) of each payment due, including any Screening Failure that may be payable under the terms of this Agreement will be made based upon prior month enrollment data confirmed by completed subject electronic Case Report Forms ("eCRFs") after data verification supporting subject visitation, and/or upon receipt of a Valid Invoice where required by region. The balance of monies earned, up to ten percent (10%), will be pro-rated upon verification of actual subject visits, and will be paid by CRO to the Institution upon final acceptance by Sponsor of all eCRFs pages, all data clarifications issued, the receipt and approval of any outstanding regulatory documents as required by CRO and/or Sponsor, the return of all unused supplies to CRO, and upon satisfaction of all other applicable conditions set forth in the Agreement. |

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| alla CRO di tutte le forniture non utilizzate e dopo soddisfacimento di tutte le altre condizioni applicabili definite nel Contratto. | |
| **Pagamento finale**: il pagamento finale, che include la trattenuta del dieci percento (10%) sarà pagabile dopo il completamento della visita di chiusura e dietro ricevimento di: (i) tutta la documentazione della sperimentazione, (ii) la contabilità di tutto il medicinale sperimentale non utilizzato, (iii) tutte le eCRF/domande completate e corrette e (iv) dopo la risoluzione di qualsiasi richiesta di chiarimento presentata dalla CRO o dal Promotore riguardante i dati o i registri della sperimentazione. | **Final Payment:** The final payment to include the ten percent (10%) withholding will be payable upon completion of the close-out visit and upon receipt of the following: (i) all Trial documentation, (ii) the accountability of any unused Trial Drug, (iii) all completed and correct eCRFs/queries and (iv) resolution of any clarification requests made by CRO or Sponsor regarding Trial data or records. |
| Si noti che le fatture non saranno elaborate se non riportano il nome del Promotore, il numero di protocollo, il nome dello sperimentatore e il numero del centro. | Please note that invoices will not be processed unless they reference the Sponsor name, Protocol number and Investigator name and site number. |
| Qualsiasi spesa o costo sostenuto dall'Ente nell'esecuzione del presente Emendamento N. 1 che non fosse specificatamente indicato come rimborsabile dalla CRO o dal Promotore ai sensi del presente Emendamento N. 1 | Any expense or cost incurred by the Institution in performing this Amendment no.1 that is not specifically designated as reimbursable by CRO or Sponsor under the Amendment no. 1 |

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| (incluso questo Allegato A) è di sola responsabilità dell'Ente.<br><br>Non sarà presa in considerazione alcun'altra richiesta di rimborso. | (including this Exhibit A) is Institution's sole responsibility.<br><br>No other additional funding requests will be considered. |
| **Metodo di pagamento:** i pagamenti saranno effettuati in EUR (Euro) tramite (bonifico bancario),<br><br>I pagamenti devono essere effettuati a:<br><br>Le Parti convengono che il beneficiario sotto indicato è il legittimo beneficiario del presente Emendamento N. 1 e che i pagamenti previsti ai sensi del presente Emendamento N. 1 saranno effettuati solo al seguente beneficiario (il "Beneficiario"): | **Payment Method:** Payments will be made in EUR (Euros) by (electronic bank transfer),<br><br>Payments should be made to:<br><br>The parties agree that the payee designated below is the proper payee for this Amendment No. 1, and that payments under this Amendment No. 1 will be made only to the following payee (the "Payee"): |

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| **NOME DEL BENEFICIARIO/ PAYEE NAME/ PAYEE NAME:** | AZIENDA OSPEDALIERA UNIVERSITARIA POLICLINICO "PAOLO GIACCONE" |
| **INDIRIZZO DEL BENEFICIARIO/ PAYEE ADDRESS**: | PALERMO Via del Vespro 129 |
| **NOME DELLA BANCA/BANK NAME** | BANCA NAZIONALE DEL LAVORO S.P.A. |
| **IBAN** | IT86P0100504600000000218030 SIC |
| **SWIFT/BIC** | BNLIITRR |

## Certificate Of Completion

Envelope Id: C2A9C497-6B3A-81A0-838B-9C13CA3BAEEA
Status: Completed
Subject: Please e-sign: Azienda Ospedaliera Universitaria Policlinico " Paolo Giaccone "
Source Envelope:
Document Pages: 25
Signatures: 1
Certificate Pages: 4
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Enabled
Time Zone: (UTC-08:00) Pacific Time (US & Canada)

Envelope Originator:
Takeda Contracts Management
5 Landsdowne St
Cambridge, MA 02139
global.next.generation.contracting@takeda.com
IP Address: 18.204.70.248

## Record Tracking

Status: Original
5/8/2026 2:58:24 AM

Holder: Takeda Contracts Management
global.next.generation.contracting@takeda.com

Location: DocuSign

| Signer Events | Signature | Timestamp |
|---|---|---|
| Paula Fischthal<br>paula.fischthal@takeda.com<br>Director, Clinical Operations<br>Director, Clinical Operations<br>Security Level: Email, Account Authentication (None), Login with SSO<br><br>**Electronic Record and Signature Disclosure:**<br>Accepted: 5/8/2026 5:46:18 AM<br>ID: 5ff960cc-071d-405f-91b3-ba0d642bb0e0 | DocuSigned by:<br>Paula Fischthal<br>9A2C6425A16D406...<br><br>Signature Adoption: Pre-selected Style<br>Using IP Address: 136.226.51.75 | Sent: 5/8/2026 2:58:28 AM<br>Viewed: 5/8/2026 5:46:18 AM<br>Signed: 5/8/2026 5:50:34 AM<br>Freeform Signing |

| In Person Signer Events | Signature | Timestamp |
|---|---|---|

| Editor Delivery Events | Status | Timestamp |
|---|---|---|

| Agent Delivery Events | Status | Timestamp |
|---|---|---|

| Intermediary Delivery Events | Status | Timestamp |
|---|---|---|

| Certified Delivery Events | Status | Timestamp |
|---|---|---|

| Carbon Copy Events | Status | Timestamp |
|---|---|---|
| Jovan Pjevac<br>Jovan.Pjevac@thermofisher.com<br>Security Level: Email, Account Authentication (None)<br><br>**Electronic Record and Signature Disclosure:**<br>Accepted: 12/29/2025 7:41:56 AM<br>ID: dc5fd240-2cc6-43a2-ae3d-47e9ad22291b | COPIED | Sent: 5/8/2026 2:58:27 AM<br>Viewed: 5/8/2026 2:59:05 AM |
| NA<br>jovan.pjevac@thermofisher.com<br>Security Level: Email, Account Authentication (None)<br><br>**Electronic Record and Signature Disclosure:**<br>Accepted: 12/29/2025 7:41:56 AM<br>ID: dc5fd240-2cc6-43a2-ae3d-47e9ad22291b | COPIED | Sent: 5/8/2026 2:58:27 AM<br>Viewed: 5/8/2026 3:04:10 AM |

| Witness Events | Signature | Timestamp |
|---|---|---|

| Notary Events | Signature | Timestamp |
|---|---|---|

| Envelope Summary Events | Status | Timestamps |
|---|---|---|
| Envelope Sent | Hashed/Encrypted | 5/8/2026 2:58:27 AM |
| Certified Delivered | Security Checked | 5/8/2026 5:46:18 AM |
| Signing Complete | Security Checked | 5/8/2026 5:50:34 AM |
| Completed | Security Checked | 5/8/2026 5:50:34 AM |

| Payment Events | Status | Timestamps |
|---|---|---|

| Electronic Record and Signature Disclosure |
|---|

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If you decide to receive notices and disclosures from us electronically, you may at any time change your mind and tell us that thereafter you want to receive required notices and disclosures only in paper format. How you must inform us of your decision to receive future notices and disclosure in paper format and withdraw your consent to receive notices and disclosures electronically is described below.

### Consequences of changing your mind

If you elect to receive required notices and disclosures only in paper format, it will slow the speed at which we can complete certain steps in transactions with you and delivering services to you because we will need first to send the required notices or disclosures to you in paper format, and then wait until we receive back from you your acknowledgment of your receipt of such paper notices or disclosures. Further, you will no longer be able to use the DocuSign system to receive required notices and consents electronically from us or to sign electronically documents from us.

### All notices and disclosures will be sent to you electronically

Unless you tell us otherwise in accordance with the procedures described herein, we will provide electronically to you through the DocuSign system all required notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you during the course of our relationship with you. To reduce the chance of you inadvertently not receiving any notice or disclosure, we prefer to provide all of the required notices and disclosures to you by the same method and to the same address that you have given us. Thus, you can receive all the disclosures and notices electronically or in paper format through the paper mail delivery system. If you do not agree with this process, please let us know as described below. Please also see the paragraph immediately above that describes the consequences of your electing not to receive delivery of the notices and disclosures electronically from us.

### How to contact Takeda Malbek:

You may contact us to let us know of your changes as to how we may contact you electronically, to request paper copies of certain information from us, and to withdraw your prior consent to receive notices and disclosures electronically as follows:
To contact us by email send messages to: freddy.sorto@docusign.com

### To advise Takeda Malbek of your new email address

To let us know of a change in your email address where we should send notices and disclosures electronically to you, you must send an email message to us at freddy.sorto@docusign.com and in the body of such request you must state: your

previous email address, your new email address. We do not require any other information from you to change your email address

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i. decline to sign a document from within your signing session, and on the subsequent page, select the check-box indicating you wish to withdraw your consent, or you may;

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- You can print on paper this Electronic Record and Signature Disclosure, or save or send this Electronic Record and Disclosure to a location where you can print it, for future reference and access; and
- Until or unless you notify Takeda Malbek as described above, you consent to receive exclusively through electronic means all notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you by Takeda Malbek during the course of your relationship with Takeda Malbek.