IRE ISTITUTO NAZIONALE TUMORI REGINA ELENA ISG ISTITUTO DERMATOLOGICO SAN GALLICANO
ISTITUTI DI RICOVERO E CURA A CARATTERE SCIENTIFICO

DELIBERAZIONE N. **229** DEL **11/03/2025**

OGGETTO: PRESA D'ATTO STIPULA STATEMENT OF WORK TRA IQVIA E ISTITUTI FISIOTERAPICI OSPITALIERI - ISTITUTO NAZIONALE TUMORI REGINA ELENA IRCCS (IFO-IRE) PER LA REALIZZAZIONE DELLE ATTIVITÀ DI FASE 2 E FASE 3 DELLO STUDIO "EXTERNAL CONTROL ARM STUDY TO SUPPORT HTA SUBMISSIONS FOR ENHERTU FOR PATIENTS WITH HER2-POSITIVE IHC3+ TUMORS" E ACCETTAZIONE DELLA QUOTA MASSIMA DI € 103.850,00 CHE IQVIA SI IMPEGNA A CORRISPONDERE A IFO-IRE SULLA BASE DEI PAZIENTI SCRUTINATI

Esercizi/o e conto 2025 Conto 401030401 Centri/o di costo 3020950 **- Importo presente Atto: € + 103.850,00** **- Importo esercizio corrente: € + 103.850,00** Budget **- Assegnato: € -** **- Utilizzato: € -** **- Residuo: € -** **Autorizzazione n°: -** Servizio Risorse Economiche: **Giovanna Evangelista**	STRUTTURA PROPONENTE **UOSD Servizio Amministrativo Ricerca** Il Dirigente Responsabile **Andrea Scotti** Responsabile del Procedimento **Andrea Scotti** L'Estensore **Simone Savina** Proposta n° DL-153-2025
PARERE DEL DIRETTORE SANITARIO Positivo Data 07/03/2025 IL DIRETTORE SANITARIO f.f. **Costanza Cavuto**	**PARERE DEL DIRETTORE AMMINISTRATIVO** Positivo Data 06/03/2025 IL DIRETTORE AMMINISTRATIVO **Laura Figorilli**

Parere del Direttore Scientifico IRE **Gennaro Ciliberto** data 24/02/2025 Positivo

Parere del Direttore Scientifico ISG **Maria Concetta Fargnoli** data 03/03/2025 Positivo

La presente deliberazione si compone di n° 9 pagine e dei seguenti allegati che ne formano parte integrante e sostanziale:
All. 1

Visto il decreto legislativo 30 dicembre 1992 n. 502 e successive modificazioni ed integrazioni;

Visto il decreto legislativo 16 ottobre 2003 n. 288 e il decreto legislativo 23 dicembre 2022 n. 200 di riordino della disciplina degli Istituti di ricovero e cura a carattere scientifico;

Vista la legge regionale 23 gennaio 2006, n. 2;

Visto l'Atto Aziendale adottato con deliberazione n. 153 del 19.02.2019 e approvato dalla Regione Lazio con DCA n. U00248 del 2.07.2019, modificato e integrato con deliberazioni n. 1254 del 02.12.2020, n. 46 del 21/01/2021 e n. 380 del 25.03.2021, approvate dalla Direzione Salute ed Integrazione Sociosanitaria della Regione Lazio, con Determinazione n. G03488 del 30.03.2021;

Visto il Decreto del Presidente della Regione Lazio n. T00015 del 12 febbraio 2025 avente ad oggetto "*Nomina del Direttore Generale dell'Azienda Sanitaria Locale dell'IRCCS Istituti Fisioterapici Ospitalieri (Art. 8, comma 7 bis, della legge regionale 16 giugno 1994, n. 18 e s.m.i.*";

Vista la deliberazione n. 160 del 18 febbraio 2025 di presa d'atto dell'insediamento del Direttore Generale dell'IRCCS Istituti Fisioterapici Ospitalieri Dott. Livio De Angelis;

Viste le deliberazioni n. 212 del 16 marzo 2022 e n. 367 del 23 aprile 2024 con le quali sono stati nominati rispettivamente la Dott.ssa Laura Figorilli quale Direttore Amministrativo e la Dott.ssa Costanza Cavuto quale Direttore Sanitario f.f. degli Istituti Fisioterapici Ospitalieri;

Visto il D.M. del Ministero della Salute del 20 giugno 2024 di conferma del riconoscimento del carattere scientifico dell'IRCCS di diritto pubblico a Istituti Fisioterapici Ospitalieri (IFO) relativamente alla disciplina di "oncologia" per l'Istituto Nazionale Tumori Regina

Elena (IRE) e alla disciplina di "dermatologia" per l'Istituto Santa Maria e San Gallicano (ISG);

Visti gli artt. 8 e 9 del decreto legislativo 16 ottobre 2003 n. 288, come da ultimo modificati dal D.lgs. 23 dicembre 2022, n. 200, che prevedono la possibilità per gli IRCCS di stipulare accordi e convenzioni, costituire e/o partecipare a consorzi e attuare misure di collegamento e sinergia con altre strutture di ricerca e assistenza sanitaria, pubbliche e private, nonché con le Università, per la realizzazione di comuni progetti di ricerca, in conformità all'art. 15 L. n. 241/1990;

gli artt. 7 e 10 del suddetto decreto, che contemplano le diverse tipologie di ricavi degli IRCCS;

Premesso che IQVIA Solutions Italy S.r.l. (di seguito "IQVIA") opera nel settore della fornitura di soluzioni informative strategiche e tecnologie abilitanti per le parti interessate del settore sanitario, compresi produttori farmaceutici, farmacie, ospedali e contribuenti;

che gli Istituti Fisioterapici Ospitalieri - Istituto Nazionale Tumori Regina Elena IRCCS (di seguito "IFO-IRE") e IQVIA sono impegnati nella conduzione di Studi Scientifici nel campo delle "*real-world evidence*" in oncologia;

che, con deliberazione n. 340 del 6 aprile 2023, IFO-IRE ha messo a disposizione di IQVIA dati e/o relative analisi, nel pieno rispetto del Regolamento (UE) 2016/679 del Parlamento Europeo e del Consiglio del 27 aprile 2016 relativo alla protezione delle persone fisiche con riguardo al trattamento dei dati personali;

che, con deliberazione n. 414 del 22 maggio 2024, si è preso atto della sottoscrizione, avventa in data 13 ottobre 2023, del Master Collaboration Agreement (di seguito "MCA") tra IFO-IRE e IQVIA, per meglio definire le attività di collaborazione tra i due enti;

Considerato che, sulla base del MCA, IFO-IRE e IQVIA hanno concordato la stipula di appositi Statements of Work relativi allo studio dal titolo: "*External Control Arm Study To Support*

HTA Submissions For Enhertu for Patients With HER2-Positive IHC3+ Tumors" (di seguito "studio"), formato da n. 3 Fasi di studio ("Patient Screening", "Sample Testing", "Data Extraction");

che, con deliberazione n. 117 del 4 febbraio 2025, si è preso atto dell'avvenuta sottoscrizione, in data 17 ottobre 2024, dello Statement of Work tra IFO-IRE e IQVIA, utile alla realizzazione delle attività di Fase 1 dello studio (Patient Screening), con contestuale accettazione della quota massima che IQVIA corrisponderà in favore di IFO-IRE pari a massimo € 51.550,00 fuori campo IVA, sulla base dei pazienti scrutinati;

Atteso che, in data 14 febbraio 2025, IQVIA e IFO-IRE hanno sottoscritto un successivo Statement of Work per disciplinare la Fase 2 di studio ("Sample Testing"), in cui IFO-IRE condurrà dei test HER2 su campioni di pazienti arruolati durante la Fase 1 di screening, e per disciplinare la Fase 3 dello studio ("Data Extraction"), in cui IFO-IRE estrarrà dei dati per i pazienti IHC3+, in accordo con il protocollo di studio;

che, per la realizzazione delle suddette Fasi di studio, IQVIA si impegna a corrispondere in favore di IFO-IRE una quota pari a massimo € 103.850,00 fuori campo IVA sulla base dei pazienti scrutinati, sulla base dei parametri di seguito riportati:

Breakdown of fees		
Phase	**Fee type**	**Value (€)**
Sample Testing	Fixed cost	€10,000.00
	Per sample cost (number of samples)	€125.00 (530)
	Total for Sample Testing	€76,250.00
Data Extraction	Fixed cost	€10,000.00
	Per patient cost (number of patient)	€400.00 (44)
	Total for Data Extraction	€27,600.00
	Grand total	€103,850.00

che IQVIA e IFO-IRE hanno disciplinato il trattamento dei dati personali attraverso un "*Vendor or Contractor Privacy & Security Standard*", allegato allo Statement of Work, il

quale prevede che il trattamento avrà luogo nel rispetto del Regolamento (UE) 2016/679 del Parlamento europeo e del Consiglio del 27 aprile 2016 ("GDPR"), nonché dalle correlate disposizioni legislative e amministrative nazionali, comprese le loro eventuali successive modifiche;

Acquisito con nota prot. n. 2622 del 18 febbraio 2025, il parere favorevole del Direttore Scientifico IRE;

Ritenuto opportuno prendere atto della sottoscrizione, avvenuta in data 14 febbraio 2025, dello Statement of Work tra IQVIA e IFO-IRE, per la realizzazione delle attività di Fase 2 ("Sample Testing") e Fase 3 ("Data Extraction") dello studio dal titolo: "*External Control Arm Study To Support HTA Submissions For Enhertu for Patients With HER2-Positive IHC3+ Tumors"* che, allegato al presente atto, ne costituisce parte integrante e sostanziale (All. 1);

opportuno accettare che IQVIA corrisponderà in favore di IFO-IRE una quota pari a massimo € 103.850,00 fuori campo IVA sulla base dei pazienti scrutinati, secondo la tabella di seguito riportata:

Breakdown of fees		
Phase	**Fee type**	**Value (€)**
Sample Testing	Fixed cost	€10,000.00
	Per sample cost (number of samples)	€125.00 (530)
	Total for Sample Testing	€76,250.00
Data Extraction	Fixed cost	€10,000.00
	Per patient cost (number of patient)	€400.00 (44)
	Total for Data Extraction	€27,600.00
	Grand total	€103,850.00

Attestato che il presente provvedimento, a seguito dell'istruttoria effettuata, nella forma e nella sostanza è totalmente legittimo e utile per il servizio pubblico, ai sensi dell'art. 1 della legge

20/94 e successive modifiche, nonché alla stregua dei criteri di economicità e di efficacia di cui all'art. 1, primo comma, della legge 241/90, come modificata dalla legge 15/2005.

Propone

Per i motivi di cui in narrativa che si intendono integralmente confermati di:

- prendere atto della sottoscrizione, avvenuta in data 14 febbraio 2025, dello Statement of Work tra IQVIA e IFO-IRE, per la realizzazione delle attività di Fase 2 ("Sample Testing") e Fase 3 ("Data Extraction") dello studio dal titolo: "External Control Arm Study To Support HTA Submissions For Enhertu for Patients With HER2-Positive IHC3+ Tumors" che, allegato al presente atto, ne costituisce parte integrante e sostanziale (All. 1);

- accettare che IQVIA corrisponderà in favore di IFO-IRE una quota pari a massimo € 103.850,00 fuori campo IVA sulla base dei pazienti scrutinati, secondo la tabella di seguito riportata:

Breakdown of fees		
Phase	**Fee type**	**Value (€)**
Sample Testing	Fixed cost	€10,000.00
	Per sample cost (number of samples)	€125.00 (530)
	Total for Sample Testing	€76,250.00
Data Extraction	Fixed cost	€10,000.00
	Per patient cost (number of patient)	€400.00 (44)
	Total for Data Extraction	€27,600.00
	Grand total	€103,850.00

- dare mandato alla UOC Risorse Economiche di iscrivere al piano dei conti n. 401030401 e al Centro di Costo n. 3020950 la somma di € 103.850,00 fuori campo IVA per l'anno 2025.

La UOSD Servizio Amministrativo per la Ricerca curerà tutti gli adempimenti per l'esecuzione della

presente deliberazione.

Il Dirigente della UOSD Servizio Amministrativo Ricerca

Andrea Scotti

Il Direttore Generale

Visto	il decreto legislativo 30 dicembre 1992, n. 502 e s.m.i.;
Vista	la legge regionale 23 gennaio 2006 n. 2;
Visto	il decreto legislativo 16 ottobre 2003 n. 288 e il decreto legislativo 23 dicembre 2022 n. 200 "Riordino della disciplina degli Istituti di ricovero e cura a carattere scientifico";
Visto	l'Atto Aziendale adottato con deliberazione n. 153 del 19 febbraio 2019 ed approvato dalla Regione Lazio con DCA n. U00248 del 2 luglio 2019, modificato e integrato con deliberazioni n. 1254 del 02 dicembre 2020, n. 46 del 21 gennaio 2021 e n. 380 del 25 marzo 2021, approvate dalla Direzione Salute e Integrazione Socio-sanitaria della Regione Lazio, con Determinazione n. G03488 del 30 marzo 2021;
Visto	l'art. 3 comma 6 del D.lgs. 502/92 e successive modificazioni ed integrazioni, nonché l'art. 8 comma 7 della L.R. del Lazio n. 18/94.
In virtù	dei poteri di cui alla delibera IFO n. 160 del 18 febbraio 2025 inerente l'insediamento del Direttore Generale Dott. Livio De Angelis;
Preso atto	che il Dirigente proponente il presente provvedimento, sottoscrivendolo, attesta che lo stesso a seguito dell'istruttoria effettuata, nella forma e nella sostanza è totalmente legittimo e utile per il servizio pubblico, ai sensi dell'art. 1 della legge 20/94 e s.m.i., nonché alla stregua dei criteri di economicità e di efficacia di cui all'art. 1, primo comma, della legge 241/90, come modificata dalla legge 15/2005.
Visto	il parere favorevole del Direttore Amministrativo e del Direttore Sanitario Aziendale;

ritenuto di dover procedere;

Delibera

di approvare la proposta così formulata concernente *"PRESA D'ATTO STIPULA STATEMENT OF WORK TRA IQVIA E ISTITUTI FISIOTERAPICI OSPITALIERI - ISTITUTO NAZIONALE TUMORI REGINA ELENA IRCCS (IFO-IRE) PER LA REALIZZAZIONE DELLE ATTIVITÀ DI FASE 2 E FASE 3 DELLO STUDIO "EXTERNAL CONTROL ARM STUDY TO SUPPORT HTA SUBMISSIONS FOR ENHERTU FOR PATIENTS WITH HER2-POSITIVE IHC3+ TUMORS" E ACCETTAZIONE DELLA QUOTA MASSIMA DI € 103.850,00 CHE IQVIA SI IMPEGNA A CORRISPONDERE A IFO-IRE SULLA BASE DEI PAZIENTI SCRUTINATI"* e di renderla disposta.

Il Direttore Generale

Dott. Livio De Angelis

Documento firmato digitalmente ai sensi del D.Lgs 82/2005 s.m.i. e norme collegate

Statement of Work: External Control Arm Study To Support HTA Submissions For Enhertu for Patients With HER2-Positive IHC3+ Tumors

This is a Statement of Work is entered into between **IQVIA Ltd.** ("IQVIA") and **IRCCS Istituto Nazionale Tumori Regina Elena** ("Institution") pursuant to the Master Collaboration Agreement with an Effective Date of **13th October, 2023** between **IQVIA Solutions Italy S.r.l.** and Institution (the "Agreement") and shall be effective as the last signature date ("SOW Effective Date"). Capitalized terms used but not otherwise defined in this Statement of Work ("SOW") shall have the meanings ascribed to them in the Agreement. Except to the extent otherwise set forth below for this SOW, the terms and conditions of the Agreement are incorporated by reference herein.

1. Study Specifications.

This study is formed of 3 Phases:

Phase 1: Patient screening
Phase 2: Sample testing
Phase 3: Data extraction

Phase 1 has been contracted separately in a Statement of Work executed on 17th October 2024. This Statement of Work refers only to Phase 2 and 3 (Sample testing and Data extraction).

Study title	External Control Arm Study To Support HTA Submissions For Enhertu for Patients With HER2-Positive IHC3+ Tumors (Phase 2: Sample Testing and Phase 3: Data Extraction)
Protocol number	D967VC00001
Study classification	Retrospective pharmacological non-interventional study
Indication	Colorectal adenocarcinoma, biliary tract cancer, bladder cancer, endometrial cancer, epithelial ovarian cancer, rare tumors
Institution Record Data type required	*Patient-Level Data*
Extent to which data will be de-identified	Patient level data will be pseudo-anonymised and shared with IQVIA
Analysis requirements	**Sample testing:** The Institution will identify IHC3+ samples and refer these patients for Phase 3: Data extraction **Data extraction:** The Institution will deliver patient level data to IQVIA. IQVIA will conduct analysis
Ethical and Regulatory requirements	
Ethics committee approval required	*Yes*

Ethics committee approval sought from	*Not confirmed at time of SOW execution (TBC at a later date)*
Ethics committee approval date	*Not confirmed at time of SOW execution (TBC at a later date)*
Regulatory/Supervisory authority approval/notification required	*Yes – Notification to AIFA (via RSO form)*
Regulatory/Supervisory authority approval/notification sought from/provided to	*Not confirmed at time of SOW execution (TBC at a later date)*
Regulatory/Supervisory authority approval date	*Not confirmed at time of SOW execution (TBC at a later date)*
Public registration of study	*Yes - RSO to be conducted once the protocol is final*
Study Description	
Context	While early results from the referent trials (DP-02, DC-02, DL-01) showed the response to Enhertu resulted in clinically meaningful survival outcomes across a broad range of HER2-expressing solid tumors, particularly in IHC3+ patients, the efficacy of Enhertu compared to the standard of care (SoC) for the indications of interest is not known. There is an unmet need for effective therapies for certain HER2-expressing solid tumors, particularly for those who have progressed on or are refractory to standard of care therapies. There are currently no approved HER2-directed therapies for these HER2-expressing cancers. In this study, a treatment comparison which utilizes real-world (RW) external control arms (ECAs) will be used to bridge the lack of data comparing Enhertu to SoC treatments for the 11 indications (including indication pooled cohorts) of interest in HER2+ IHC3+ patients. The results can be used to support market access and reimbursement of Enhertu in European markets for the tumor-agnostic indication. This study is formed of 3 Phases: Phase 1: Patient screening Phase 2: Sample testing Phase 3: Data extraction This Statement of Work covers Phase 2 and 3 only.
Research question and objectives	Primary objective:

<table>
<tr><td></td><td>
To evaluate the comparative efficacy with respect to overall survival (OS) for Enhertu vs SoC for patients with HER2+ IHC3+ expressing solid tumors in two pooled cohorts.
Secondary objectives:
To compare progression free survival (PFS) for Enhertu vs SoC for the pooled cohorts and indication subgroups included in the primary objective.
To describe the time to treatment discontinuation or death (TTD) for Enhertu and SoC for the pooled cohorts and indication subgroups included in the primary objective.
To compare time to next treatment or death (TNT-D) for Enhertu vs SoC for the pooled cohorts and indication subgroups included in the primary objective.
Exploratory objectives:
To describe the objective response rate (ORR) for Enhertu and SoC in the pooled cohorts and indication subgroups included in the primary objective.
To describe the duration of response (DoR) for Enhertu and SoC in the pooled cohorts and indication subgroups included in the primary objective.
</td></tr>
<tr><td>Data sources (Institution Source Data description)</td><td>Dedalus, RedCap, Medi Life</td></tr>
<tr><td>Number of patients (from feasibility if conducted)</td><td>
<u>Phase 2- HER 2 sample testing:</u>

The Institution will conduct HER2 testing on the samples of eligible patients identified in the patient screening phase (covered in previous Statement of Work executed on 17th October 2024). The Institution shall share the results of all tests conducted with IQVIA. Testing will be done in accordance with the protocol.
The Institution should conduct sample testing until the following number of confirmed IHC3+ patients have been identified (as feasible):

<table>
<tr><th>Indication</th><th>IHC3+ patients to be identified</th></tr>
</table>
</td></tr>
</table>

Colorectal adenocarcinoma	19
Biliary tract cancer	1
Urothelial cancer	2
Endometrial cancer	12
Epithelial ovarian cancer	4
Rare tumors	6

The number of tests to be conducted by the Institution is expected to be within the following ranges:

Indication	**Column A** **Minimum number of tests**	**Column B** **Maximum number of tests**
Colorectal adenocarcinoma	186	360
Biliary tract cancer	2	3
Urothelial cancer	5	7
Endometrial cancer	25	48
Epithelial ovarian cancer	46	88
Rare tumors	12	24

The Institution should conduct a minimum number of tests per indication (as feasible), as indicated in **Column A,** granted the patient screening phase has identified these samples. If the target number of IHC3+ patients is identified before this number of tests is conducted, the Institution should inform IQVIA. IQVIA will review the outputs of the testing activities and determine next steps.

If the Institution has conducted the number of tests in **Column A**, and the target number of IHC3+ patients has not been identified, the Institution should inform IQVIA. IQVIA will review the number of IHC3+ patients identified and inform the Institution of how many additional tests (up to the maximum in **Column B**) the Institution should conduct by indication.

	<u>Phase 3- IHC3+ data extraction</u> The Institution will conduct data extraction for IHC3+ patients, in accordance with the protocol. Following completion of sample testing and identification of IHC3+ patients, IQVIA will define the number of patients for which data extraction should be conducted.
Method(s)	Refer to protocol for full methodology. Statistical methods will be described in the statistical analysis plan (SAP).

Data variables required available in Institution Record Data, accounting for data missingness	Phase 2: Sample testing
	• Number of IHC3+ samples
	
	Phase 3: Data extraction
	Patient data
	• Patient ID
	• Date of birth
	• Age at index
	• Sex at birth
	• Age at advanced disease diagnosis
	• Height
	  ○ Height units
	• Weight
	  ○ Weight units
	• BMI
	  ○ BMI categories
	• Smoking
	
	Site
	• Site
	• Country
	
	Clinical data
	• Indication
	• Indication, other
	• Index date
	• Index year
	• Advanced disease diagnosis date
	• Year of advanced disease diagnosis
	• De novo disease

	• T-stage at advanced disease diagnosis date
	• N-stage at advanced disease diagnosis date
	• M-stage at advanced disease diagnosis date
	• Last visit date
	• Date of death
	• Vital status (at end of follow up)
	• Vital status date
	• Number of metastatic sites
	  ○ Bone
	  ▪ Date of first bone metastasis
	  ○ Lung
	  ▪ Date of first lung metastasis
	  ○ Liver
	  ▪ Date of first liver metastases
	  ○ Stable CNS metastasis
	  ▪ Date of first stable CNS metastasis
	  ○ Other
	  ▪ Other date
	• Number of Other metastasis
	  ○ Other - locations
	• Liver disease, leukaemia, aplastic anaemia or haemophilia
	• Record of primary malignancies
	• Record o spinal cord compression or active CNS metastases
	• MI or congestive heart failure
	• Lung-specific intercurrent clinically significant illness
	• Non-infectious ILD/pneumonitis
	• Autoimmune, connective tissue or inflammatory disorders
	• Complete pneumonectomy
	• Systemic infection
	• HIV, HEPB or HEP C
	• Pleural effusion, ascites, pericardial effusion, CART
	• Leptomeningeal carcinomatosis (CRC only)
	• Cerebrovascular disease
	• Dementia
	• Pulmonary disease
	• Diabetes mellitus with complications

	• Diabetes mellitus without complications • Hemiplegia and/or paraplegia • Peptic ulcer • Peripheral vascular disease • Renal disease • Charlson comorbidity index • Performance status type • Performance status value Pathology/biomarkers • Biomarker status/mutation date of collection • HER2 IHC value • HER2 ISH value • HER2 classification • HER3 classification • PI3K mutation • Ras mutation • RAF mutation • BRAF mutation • Tumour mutational burden • Microsatellite instability Treatment • LoT number • LOT start date • LOT end date • Number of prior lines • Prior treatment (CRC only) • Prior T-DXd or DXd-containing ADC • Clinical trial • Regimen Number • Regimen Name • Number of cycles • Drug start date • Drug end date • Drug name • Drug type • Reason for discontinuation • Dosage of individual drug • Dosage unit

	• Dosage unit, other Outcome data • Investigator Response • Date of response • Progression date • Progression data type Variables derived by IQVIA: • Progression free survival (PFS) • Overall survival • Time to treatment discontinuation (TTD) • Time to next treatment or death (TNT-D) • Overall response (OR) • Overall response rate (ORR) • Duration of Response (DoR)
Study team contact details	
IQVIA	PIC name/contact: Fernando Exposto, fernando.exposto@iqvia.com Day-to-day name/contact: Astrid Nardecchia, astrid.nardecchia@iqvia.com
Institution	PI name/contact: Eriseld Krasniqi, eriseld.krasniqi@ifo.it; Simonetta Buglioni, simonetta.buglioni@ifo.it Day-to-day name/contact: Remco Foppen, remco.foppen@ifo.it
Timeline	
Contracting completion (IQVIA and Institution)	3rd February 2025
Ethics approval (IQVIA and Institution)	Before end of March 2025
Start of sample testing (Institution)	1st April 2025
End of sample testing (Institution)	31st July 2025
Start of data extraction (Institution)	1st April 2025
End of data extraction (Institution)	30th September 2025

2. <u>Compensation.</u>

IQVIA shall compensate Institution for the provision of the Institution Record Data, as follows:

Breakdown of fees		
Phase	**Fee type**	**Value (€)**
Sample Testing	Fixed cost	€10,000.00
	Per sample cost (number of samples)	€125.00 (530)
	Total for Sample Testing	€76,250.00
Data Extraction	Fixed cost	€10,000.00
	Per patient cost (number of patient)	€400.00 (44)
	Total for Data Extraction	€27,600.00
	Grand total	€103,850.00

Phase 2 (Sample Testing):
Fixed cost: IQVIA shall submit payment of fixed costs to Institution within ninety (90) days of the later of (1) receipt of Institution's invoice; and (2) payment for the relevant fee by its client AstraZeneca, whichever is later. The invoice for fixed costs can be requested following last signature date of this SOW.

Per patient cost: IQVIA shall submit payment of per patient costs to Institution within ninety (90) days of the later of (1) receipt of Institution's invoice; and (2) payment for the relevant fee by its client AstraZeneca, whichever is later. The invoice for per patient cost can be requested following IQVIA accepting the Number of IHC3+ Samples as final. The Number of IHC3+ Samples will be considered final following completion of data query resolution by the Institution and data quality checks by IQVIA.

Phase 3 (Data Extraction):
Fixed cost: IQVIA shall submit payment of fixed costs to Institution within ninety (90) days of the later of (1) receipt of Institution's invoice; and (2) payment for the relevant fee by its client AstraZeneca, whichever is later. The invoice for fixed costs can be requested following completion of Phase 2 (Sample Testing).

Per patient cost: IQVIA shall submit payment of per patient cost to Institution within ninety (90) days of the later of (1) receipt of Institution's invoice; and (2) payment for the relevant Institution Record Data by its client AstraZeneca, whichever is later. The invoice for per patient cost can be requested following IQVIA accepting the Institution Record Data as final. The Institution Record Data will be considered final following completion of data query resolution by the Institution and data quality checks by IQVIA.

3. Term.

Unless earlier terminated in accordance with the Agreement, the term of this Statement of Work shall commence on the SOW Effective Date and shall expire on the completion of all obligations set forth in this SOW.

4. Data Processing.

For the purposes of Exhibit B of the Agreement, Schedule 1 of this Statement of Work (Data Processing Information Form) sets out the details of the data processing.

Following data extraction, the Institution will share pseudo-anonymized data with IQVIA. IQVIA will share such pseudo-anonymized data with the sponsor and stored on their EU-based server. An authorized third party may access the sponsor server to conduct analysis in accordance with activities of the Parties, however any party accessing the data will be appointed as Data Processor and will act in accordance with the Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 ("GDPR"), as well as the related national legislative and administrative provisions in force, with their possible subsequent amendments and/or additions. .

5. Signatures

IRCCS Istituto Nazionale Tumori Regina Elena	**IQVIA Ltd.**
Signature:	Signature:
Firmato da Gennaro Ciliberto Gennaro Ciliberto | Approvo il documento 04-feb-2025 | 7:59:05 AM PST 469FD06E53324C2E94F7912871F4E4F4	Signed by Edmund Drage Edmund Drage | I approve this do 14-Feb-2025 | 4: 5DEA468879B94C349744400256F9994C
Name: Professor Gennaro Ciliberto	Name: Edmund Drage
Title: Scientific Director	Title: Vice-president, Medical Evidence Practice
Date: 04-feb-2025	Date: 14-Feb-2025

Schedule 1
Data Processing Informations

Categories of data subject	Data Subjects include the following categories of Data Subjects: ☒ **Patients.** Former, current or future subjects participating in clinical research or other forms of medical research and/or patients who have received medical treatment, medications or other relevant healthcare services and/or their relatives, friends and carers. ☒ **Health Care Professionals**. General medical practitioners and health care professionals, including staff of hospitals, pharmacies and other facilities or bodies concerned with the treatment of patients, development or dispensing of medicines or other aspects of the healthcare system, such as pharmacists, physicians, nurses and other health care professionals. ☐ **Customer Personnel**. Personnel of IQVIA's customers (including former, current and future employees, contractors and agents). ☒ **IQVIA Personnel**. Personnel of IQVIA (including former, current and future employees, contractors and agents). ☐ **Other.**
Categories of pseudonymised **(key code) personal data**	Categories of personal data that will be pseudonymised include the following categories of Personal Data: ☒ **Patients:** o name, initials and contract details; o personal identification number; o demographic and medical data; o date of birth and/or age; o description of characteristics of physical features of the body; o connection data (e.g. logs, IP address, cookies). ☒ **Health Care Professionals:** o name and contact details; o personal identification number; o data regarding their experience and qualifications;

	○ data regarding expertise, interests and professional and academic affiliations, appointments, activities and publications; ○ connection data (e.g., logs, IP address, cookies). ☐ **Customer Personnel:** ○ name and contact details; ○ employment data (e.g. name and address of employer, job title / position, department); ○ data regarding their experience and qualifications; ○ connection data (e.g., logs, IP address, cookies). ☒ **IQVIA Personnel:** ○ name and contact details; ○ identification data (e.g. gender, date of birth, tax identification number, photographs); ○ employment data (e.g. job title, job category, location/department, employee number, date of joining, employment history, training and work experience, performance, reward, training, development and disciplinary data, system usage, duration and nature of leave of absence); ○ financial data (e.g. salary, bonus, tax details). ☐ **Other**.
Categories of sensitive pseudonymized data (if applicable)	Categories of sensitive data include the following categories of sensitive data: ☒ **Patients:** ○ (relevant elements of) medical history; ○ health data including clinical test results, samples and tissues, sample number and clinical visit number; ○ race and ethnicity so relevant for the data of the clinical research / other form of medical research; ○ sex life where so relevant for the data of the clinical research / other form of medical research. ☒ **IQVIA Personnel:** ○ only where required and lawfully permitted, race, ethnicity, religion, disability information; ○ leave of absence information; ○ maternity / paternity information.

	☐ **Other**.
Nature and purpose of the processing	☒ As necessary, in connection with the provision of the Services. ☐ **Other**
Subject matter of the processing, in pseudonymized form	☒ The Processing of Personal Information (as defined). ☐ **Other**
Duration of the processing	☒ The term of the Service Agreement. ☐ **Other**

Exhibit B

IQVIA Inc. and its Affiliates'
Vendor or Contractor Privacy & Security Standard
As revised March 2022

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1. Purpose and connection with Services Agreement.

This Vendor or Contractor Privacy & Security Standard ("Standard") including all schedules hereto stipulates confidentiality, security and privacy requirements with respect to Personal Information processed by any Vendor or Contractor ("Vendor") on behalf of IQVIA Inc. and/or its corporate affiliates ("IQVIA") or an IQVIA Customer in compliance with the provisions of Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 ("GDPR"), as well as the related national legislative and administrative provisions in force, with their possible subsequent amendments and/or additions (hereinafter, collectively, "Data Protection Laws") as well as any regulations of the Entities.
Vendor and IQVIA are collectively referred to as "the Parties". The purpose is to ensure that the processing by Vendor is compliant with (i) applicable privacy, security and data protection laws and regulations; (ii) the requirements of any applicable data protection or data privacy program adopted and approved by the governmental or regulatory authorities of the United States of America (U.S.), the European Union, the European Economic Area (EEA), Switzerland or the United Kingdom; (iii) the requirements of IQVIA Global Privacy Program with respect to adequate level of protection for the transfer of Personal Information from the European Economic Area, Switzerland and/or the United Kingdom to a country or territory which is not determined to offer adequate protection.
The Personal Information that will be processed pursuant to the Services is set out in a form attached to the Statement of Work for the Services.

2. Definitions

The following definitions are generally recognized and accepted by IQVIA. However, in the event that any of these terms are defined differently in applicable privacy laws and regulations in the jurisdiction(s) in which the Vendor will be providing Services to, or for and on behalf of IQVIA, the Vendor must comply with the legal definitions applicable to the Services in each jurisdiction.

(a) "Personal Information" means any information provided by IQVIA or collected by Vendor for IQVIA in connection with the Services to be performed by the Vendor (i) that identifies, or when used in combination with other information provided by IQVIA or processed by Vendor on behalf of IQVIA permits the identification, of a natural person ("Data Subject"), or (ii) from which identification or contact information of a natural

person can be derived. Personal Information can be in any media or format, including computerized or electronic records as well as paper-based files.

(b) "Personal Information" includes (without limitation) a person's name, address, phone number, fax number, email address, social security number or other government-issued identifier or identification number, and / or credit card information, location data, an online identifier or one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person. Additionally, to the extent any other information (such as, but not necessarily limited to, case report form information, clinical trial identification codes, personal profile information, IP addresses, other unique identifier, or biometric information) is associated or combined with Personal Information, then such information also will be considered Personal Information as long as, all together, information permits the identification of a Data Subject, directly or indirectly.

(c) "Sensitive Personal Information" consists of

(i) All government-issued identification numbers (including US Social Security numbers, EU Social Security numbers, Canadian Social Insurance numbers, driver's license numbers, and passport numbers);

(ii) All financial account numbers (bank account numbers, credit card numbers, and other information if that information would permit access to a financial account);

(iii) Reports of individual background checks;

(iv) Criminal records or allegations of crimes;

(d) "Special Categories of Data" which shall mean data revealing racial or ethnic origin, political opinions, religious or philosophical beliefs, or trade union membership, genetic data, biometric data for the purpose of uniquely identifying a natural person, data concerning health (including but not limited to medical records, biomedical specimens, health, disability, disease or product interests) or data concerning a natural person's sex life or sexual orientation.

(e) "Processing of Personal Information" ("Processing") shall mean any operation or set of operations which is performed upon Personal Information or on sets of Personal Information, whether or not by automatic means, such as collection, recording, organization, structuring, storage, adaptation or alteration, retrieval, consultation, use, disclosure by transmission, dissemination or otherwise making available, alignment or combination, restriction, blocking or dispersed erasure or destruction.

(f) "SCC Addendum" shall mean a separate Vendor SCC Addendum between IQVIA or an IQVIA Affiliate and Vendor or a Vendor Affiliate which will be entered into when applicable. In the event of any conflict or inconsistency between a provision in this

Standard and a provision in the SCC Addendum, the provision in the SCC Addendum shall prevail, but only to the extent of the conflict or inconsistency.

(g) "Services" shall mean any and all services that IQVIA's requests the Vendor to perform under any contract or agreement that involves Processing of Personal Information.

(h) "Services Agreement" shall mean the contract or agreement between IQVIA and Vendor for the provision of Services.

3. Vendor's General Obligations.

(a) Vendor shall process Personal Information only on behalf of IQVIA and exclusively for the purpose of the Services, and in accordance with IQVIA's instructions pursuant to the Services Agreement with IQVIA and this Standard;

(b) Vendor shall fulfill any obligations applicable in respect to the registration, transmission or any operation of Processing;

(c) Vendor hereby commits not to copy, reproduce, adapt, modify, change, erase or destroy the Personal Information exchanged or produced in the performance of Services to IQVIA, unless when specifically instructed to do so by IQVIA;

(d) Vendor shall immediately inform IQVIA, in writing:

(i) if Vendor cannot comply with the Services Agreement with IQVIA and/or this Standard regarding the Services. If this occurs, both parties shall use reasonable efforts to remedy the non-compliance. IQVIA shall be entitled to suspend the communication of Personal Information, and to terminate any of Vendor's further Personal Information Processing;

(ii) of any request for access to any Personal Information received by Vendor from a natural person who is (or claims to be) the subject of the data;

(iii) of any claims or questions raised by a natural person who is (or claims to be) the Data Subject;

(iv) of any request for access to any Personal Information received by Vendor from any government official (including any data protection agency or law enforcement agency);

(v) of any other requests with respect to Personal Information received from IQVIA's employees or other third parties, other than those set forth in the Services Agreement;

Vendor agrees that it is not authorized to respond to these requests, unless explicitly authorized by IQVIA and except for requests received from a governmental authority with a subpoena or similar legal document compelling disclosure by Vendor or as otherwise required by applicable law. In any case, the Parties agree to co-operate with each other to promptly and effectively handle and solve any enquiries, complaints, and claims relating to the processing of entrusted Personal Information from any court, government official (including but not limited to any data protection or law enforcement agency), third parties or natural persons (including but not limited to the Data Subjects). The Parties shall also co-operate with respect to the rectification, erasure and blocking of Personal Information resulting from interactions with Data Subjects indicated herein above.

(e) Vendor shall also, upon request from IQVIA, provide IQVIA's Data Protection department with the name and contact details of its Data Protection Officer.

(f) Any Personal Information collected or accessed by Vendor in the performance of the Services shall be limited to that which is necessary to perform such Services or to fulfill any legal requirements. Personal Information shall be kept reasonably accurate and current in accordance with document management provisions in the Services Agreement.

(g) If the Services involve the collection of Personal Information directly from natural persons, such as through a registration process or a webpage, Vendor will provide a clear and conspicuous notice regarding the uses of the Personal Information, in a form provided by (or approved in writing by) IQVIA. If applicable, Vendor shall retain documentation of consents or record of "opt-in" for a period of two years after completion of the Services as set forth in the Services Agreement or longer if required by applicable law. Notwithstanding the foregoing, Vendor shall ensure that it has appropriate process in place allowing Data Subject to object to the Processing.

(h) Vendor, and, if applicable, its representatives, shall, until termination of the Services Agreement keep an internal electronic record, in writing, of the Processing carried out on behalf of IQVIA. Said record shall include without limitation, (i) the operations of Processing and the categories of Personal Information processed (including indication on the processing of Sensitive Personal Information and specific indication on the Processing of Special Categories of Data), (ii) when applicable, transfers of Personal Information to a third country or international organization and the documentation of suitable safeguards that shall permit said transfer, and (iii) any other information as provided under the Services Agreement.

(i) Vendor shall not transfer the Personal Information across any national borders or permit remote access to the Personal Information unless such transfer or remote

access is specifically permitted in the Processing instructions provided to it by IQVIA and it has the prior written consent of IQVIA for such transfer or access. To receive or access Personal Information. from countries in the European Economic Area (EEA), Switzerland, or the United Kingdom in or from an Inadequate Jurisdiction (as defined in the SCC Addendum), Vendor agrees to provide an adequate level of protection for the Personal Information and comply with the terms of the SCC Addendum unless Vendor has provided IQVIA Data Protection department with evidence of having binding corporate rules (BCRs), or other data protection and privacy certification in place, approved by the applicable EEA, United Kingdom or Swiss regulatory or governmental authorities for the transfer and adequate protection of Personal Information in which case IQVIA shall be entitled to enforce the BCRs or other certification against Vendor.

(j) In the event of permitted transfer or remote access of Personal Information from the Vendor to a third party, Vendor undertakes to do so only by way of a written agreement with the said third party, which imposes the same obligations on the third party as are imposed on the Vendor under this Standard.

(k) Vendor shall provide any information, back-up documentation or other assistance required for IQVIA to carry out any privacy impact assessment regarding Processing in the context of the Services Agreement and this Standard, for the purposes of identifying and assessing reasonably foreseeable internal and external risks to the security, confidentiality and integrity of electronic, paper and other records containing Personal Information and evaluate and improve, where necessary, the effectiveness of Vendor's safeguards for limiting those internal and external risks.

4. Confidentiality of Personal Information.

(a) Consistent with the confidentiality provisions of the Services Agreement, Personal Information is considered Confidential Information of IQVIA or IQVIA's Customer (as the case may be) and Vendor must maintain all Personal Information in strict confidence. Unless compelled by government authority with a subpoena or similar legal document, Vendor shall not disclose, transmit, or by any way communicate or make available the Personal Information to third parties (including subcontractors), unless such disclosure, transmission, communication or making available has been explicitly authorized by IQVIA in writing and then only if the third party also certifies to the "Vendor or Contractor Privacy & Security Standard".

(b) Vendor shall make the Personal Information available only to its employees who need to access the Personal Information in order to perform the Services and the type of Personal Information made available shall also be provided on a need-to-

know basis approach. Vendor shall inform its employees having access to Personal Information of the confidentiality and security requirements set out in the Services Agreement and this Standard. Vendor's employees may handle Personal Information only if they are bound by legally enforceable and sound confidentiality obligations, and are qualified and trained to protect Personal Information. Upon request, Vendor shall provide to IQVIA a list of all employees (including former employees) who have accessed the Personal Information.

(c) When the Vendor ceases to perform Services for IQVIA, at IQVIA's option Vendor shall either return all Personal Information and any copies to IQVIA or a third party identified by IQVIA in writing or, upon IQVIA's written request, shall destroy all Personal Information and so certify to IQVIA. Destruction, when requested, shall include all existing copies. If, however, legally applicable document retention requirements do not permit the destruction, in whole or in part, of the Personal Information transferred, Vendor warrants that it shall ensure the continued confidentiality and security of the Personal Information and shall not actively process or in any way use the Personal Information transferred after termination of the relationship. In these cases, said Personal Information may only be retained for the period, purposes and in the terms required by the applicable law. If Vendor disposes of any paper or electronic record containing Personal Information, Vendor shall take all reasonable steps to destroy the information by

(i) shredding;

(ii) permanently erasing and deleting; or

(iii) otherwise modifying the Personal Information in such records to make it unreadable, un-reconstructable and indecipherable through any means.

Upon request, Vendor will certify to IQVIA that all forms of the requested Personal Information have been destroyed.

(d) The obligation of secrecy shall be kept by the Vendor (and, if any, its Affiliates and sub-processors) even after the termination of the Services Agreement, regardless of the reason of the termination.

5. Security.

(a) The Parties will have adequate operating methods,technical and organizational measures to protect Personal Information against accidental or unlawful destruction, alteration, unauthorized disclosure or access, and against all other unlawful forms of Processing, and shall have documented these measures. If the Processing involves the transmission of Personal Information over a network,

Vendor shall maintain appropriate supplementary measures aimed at protecting Personal Information against the specific risks presented by the Processing. The measures referred to above shall include, inter alia,: (i) pseudonymizing and encryption of IQVIA's Personal Information (at rest or during transmission, including, but not limited to data located on laptops, back-up tapes, USB flash drives and other portable devices); (ii) securing and safeguarding the ongoing confidentiality, integrity, availability and resilience of processing systems and Services; (iii) appropriate measures to restore the availability and access to Personal Information in a timely manner in the event of a physical or technical incident; and (iv) a process for regularly testing, assessing and evaluating the effectiveness of technical and organizational measures for ensuring the security of the Processing.

(b) The measures put into place shall ensure a level of security that is appropriate and commensurate with the nature of the Personal Information Processed.

(c) At IQVIA's request, Vendor shall submit, and shall ensure that its Affiliates and any subcontractors submit, its/their data processing facilities for audit which shall be carried out by IQVIA (or by an independent inspection company designated by IQVIA, which is subject to a confidentiality agreement covering Vendor's Services and data processing facilities). Vendor shall fully co-operate with any such audit, including providing IQVIA or such auditor with any necessary information and documents during the audit process. In the event that any such audit reveals material gaps or weaknesses in Vendor's security program, IQVIA shall be entitled to suspend transmission of Personal Information to Vendor and to suspend Vendor's Processing of such Personal Information until such issues are resolved.

6. Security Incident notification.

(a) Vendor shall immediately notify IQVIA in writing of any security incident that compromises the privacy, security, confidentiality and integrity of the Personal Information ("Security Incident"). A Security Incident shall include, but is not limited to, any accidental or unlawful destruction, loss, alteration, unauthorized transfer or access or disclosure to third parties, leakage of data or Processing, or any event directly or indirectly affecting the confidentiality, integrity, authenticity of Personal Information that is transmitted, stored or otherwise processed.

(b) Such notification shall include the details of Personal Information compromised, including, but not limited to: (i) information on the Data Subjects involved, including categories of the Data Subjects and number; (ii) a description on the nature of the unlawful or unauthorized disclosure and likely consequences; and (iii) the recommended measures to minimize possible harm.

(c) In the event of such Security Incident, and at its own cost, Vendor will implement appropriate measures, as approved by IQVIA, to secure the Personal Information and to mitigate any negative consequences for the affected Data Subjects and will furthermore assist IQVIA in pursuing any investigation or course of action, or an implementation of any measures deemed necessary to restore the security of the Personal Information.(d) Vendor shall notify IQVIA immediately in writing of any Security Incident of which Vendor has been notified by any third party.

7. Liability.

Vendor shall be liable before the competent authorities and/or affected Data Subjects for any damages incurred as a consequence of the Processing by the Vendor of Personal Information in violation of the applicable privacy, security and data protection laws and regulations or provisions set forth in this Standard. Without prejudice to the indemnification obligations of the Party that has violated the rules on privacy, security and data protection or the provisions established in this Standard.

8. Compliance with Laws.

Vendor agrees to stay informed of the legal and regulatory requirements applicable to Vendor for its Processing of Personal Information. Vendor's Processing of Personal Information shall be limited to the processing as set forth in the Services Agreement, and shall comply with applicable privacy or security laws and regulations, including legal definitions, as well as Vendor's own privacy notices.