Fondazione Regionale per la Ricerca Biomedica

DECRETO NR. 133 del 28/11/2024

OGGETTO: BANDO ERAPERMED JOINT TRANSNATIONAL CALL FOR PROPOSALS 2020 – EROGAZIONE RATA IN FAVORE DELL'ISTITUTO DI RICERCHE FARMACOLOGICHE "M. NEGRI" IRCCS COORDINATORE DEL PROGETTO "DECODE" (ERAPERMED 2020-151) - CUP D12C20000360002.

L'atto si compone di 28 pagine
di cui 23 pagine di allegati

Fondazione Regionale per la Ricerca Biomedica

IL DIRETTORE GENERALE DELLA FONDAZIONE REGIONALE PER LA RICERCA BIOMEDICA

PREMESSO CHE:

- l'Istituto di Ricerche Farmacologiche "Mario Negri" IRCCS (di seguito "Beneficiario"), Coordinatore del progetto dal titolo *"Defining stratification of patients with C3 Glomerulopathies/immune complex-mediated glomerular diseases for better diagnosis and tailored treatment*", Acronimo DECODE, ERAPERMED2020-151, Responsabile Scientifico Dr.ssa Ariela Benigni, è risultato ammesso a finanziamento nell'ambito del programma europeo ERA PerMed JTC 2020 per un importo complessivo pari a € 450.000,00;
- il Beneficiario ha inviato, a FRRB, a mezzo PEC, in data 20.11.2020 (Prot. nr. 20200468E) la "*Dichiarazione di svolgimento di attività non economica ai sensi delle norme in materia di aiuti di Stato*" e la "*Dichiarazione di accettazione del contributo*";
- Con la DGR n. XI /1695 del 03.06.2019 è stato approvato il Piano d'Azione 2019 che prevede, al suo interno, l'allocazione fino ad un massimo di euro 1.000.000,00 per la partecipazione di FRRB al bando internazionale ERA PerMed JTC 2020;

CONSIDERATO CHE:

- il progetto Acronimo DECODE (ERAPERMED2020-151), ha avuto avvio in data 01.03.2021 per una durata di 36 mesi, come comunicato dal Responsabile Scientifico (PEC Prot. 20210003E) del 15.01.2021 e riportato nella Convenzione stipulata tra FRRB e l'Istituto di Ricerche Farmacologiche "Mario Negri" IRCCS;
- il Beneficiario, in fase di avvio progetto, ha comunicato la rinuncia all'anticipo con comunicazione via mail del 25.03.2021;
- secondo quanto stabilito dall'Articolo 8.1 della Convenzione sopracitata, l'erogazione al Beneficiario sarà effettuata da FRRB secondo le seguenti modalità:
  - "*due tranche successive entro 60 giorni dalla presentazione della prima e della seconda rendicontazione annuale, previa accettazione della documentazione ricevuta da parte di FRRB. L'importo del contributo sarà calcolato in base ai costi eleggibili effettivamente rendicontati da ciascun Beneficiario*";

DATO ATTO CHE:

- in data 16.05.2024 è pervenuta dal Beneficiario (PEC Prot. n. 20240184) la documentazione relativa al terzo anno di attività – periodo 01.03.2023 – 29.02.2024 - del progetto DECODE;
- in data 24.10.2024 FRRB ha comunicato al Beneficiario (PEC Prot. 20240378U) l'esito positivo dell'istruttoria di verifica della rendicontazione economica pervenuta richiedendo, al contempo, l'invio della richiesta di erogazione e della dichiarazione sulla ritenuta del 4%;

CONSIDERATO ALTRESI' CHE:

- all'art. 8.3 della Convenzione sopracitata si precisa che:
  - *"Nel caso di soggetti privati, l'erogazione del contributo sarà subordinata […] all'ottenimento, per il tramite della Banca Dati Nazionale Antimafia, della documentazione antimafia (solo nel caso di contributi superiori a € 150.000,00) nei modi e nei termini di cui all'Art. 92 D. Lgs. 159/2011 e* successive modifiche;
- in attuazione a tale articolo FRRB ha inviato, per il tramite della Banca Dati Nazionale Antimafia (BDNA), in relazione al Beneficiario, la seguente richiesta di informazione antimafia:
  - protocollo nr. PR_MIUTG_Ingresso_0337832_20241024 del 24.10.2024 per l'Istituto di Ricerche Farmacologiche "M. Negri" IRCCS con sede legale in Milano via Mario Negri nr. 2;
- alla data odierna, trascorso il termine minimo di 30 giorni dall'invio della nuova richiesta di informazione antimafia relativa al soggetto privato lombardo assegnatario di un contributo superiore a € 150.000,00 nell'ambito del progetto europeo DECODE, FRRB è in attesa del nulla osta da parte della competente Prefettura;
- ai sensi dell'art. 92 comma 3 del D. Lgs. 159/2011 i contributi, i finanziamenti, le agevolazioni e le altre erogazioni possono essere corrisposti sotto *condizione risolutiva* e l'amministrazione interessata può revocare le autorizzazioni e le concessioni o recedere dai contratti, fatto salvo il pagamento del valore delle opere già eseguite ed il rimborso delle spese sostenute per l'esecuzione del rimanente, nei limiti delle utilità conseguite. Le facoltà di revoca e di recesso si applicano anche

quando gli elementi relativi a tentativi di infiltrazione mafiosa siano accertati successivamente alla stipula del contratto, alla concessione dei lavori o all'autorizzazione del subcontratto;

PRESO ATTO che il Responsabile dell'Area Amministrativa, Dr. Marco Trincavelli, ha verificato che lo stanziamento di € 117.557,32 è finanziariamente sostenibile al capitolo di spesa 20.15.5023, rientrante nei bandi previsti nel Piano di Azione FRRB relativo all'esercizio 2019, approvato da Regione Lombardia con DGR n. XI/1695 del 03/06/2019 e incassato da FRRB in data 10/07/2019;

VERIFICATA la regolarità contributiva del beneficiario – Istituto di Ricerche Farmacologiche "Mario Negri" – tramite acquisizione d'ufficio del DURC da parte di FRRB;

RICHIAMATI:

- la DGR nr. IX/2401 del 26.10.2011 con la quale la Regione Lombardia ha costituito la "Fondazione Regionale per la Ricerca Biomedica" (di seguito "FRRB"), il cui scopo statutario è quello di promuovere la ricerca scientifica e sanitaria nel settore delle Scienze della Vita;
- la DGR n. XI/5786 del 21.12.2021 con la quale è stato approvato il nuovo Statuto di FRRB;
- la DGR n. XII/1670 del 28 dicembre 2023 con la quale è stato approvato lo schema di Accordo di collaborazione tra FRRB e Regione Lombardia;
- la DDG n° XII/64 del 27/03/2023 avente ad oggetto: "Determinazioni in ordine alla Designazione del Direttore Generale della Fondazione Regionale per la Ricerca Biomedica (Frrb)" e la Deliberazione del Consiglio di Amministrazione di FRRB del 31/03/2023 che ha nominato la Dott.ssa Veronica Comi quale Direttore Generale;

VISTI:

- il Regolamento (UE) nr. 1291/2013 del Parlamento Europeo e del Consiglio dell'11 dicembre 2013 che istituisce il Programma Quadro di Ricerca e Innovazione (2014-2020) "*Horizon 2020*" quale strumento di finanziamento della ricerca scientifica e dell'innovazione per progetti di ricerca o azioni volte all'innovazione scientifica e tecnologica che portino un significativo impatto sulla vita dei cittadini europei;

- il Grant Agreement nr. 779282 firmato il 21.11.2017 tra la Commissione Europea ed un partenariato internazionale coordinato dall'Instituto de Salud Carlos III e composto da 32 enti provenienti da 23 paesi con il quale è stato approvato il progetto *"ERA-Net Cofund in Personalised Medicine — ERA PerMed";*

DECRETA

per i motivi espressi in premessa, parte integrante del presente provvedimento:

1. di autorizzare l'erogazione in favore dell'Istituto di Ricerche Farmacologiche "M. Negri" IRCCS con sede legale in Milano, via Mario Negri nr. 2, di un importo pari a € **117.557,32** corrispondente alle spese sostenute e considerate eleggibili da FRRB a conclusione delle attività relative alla seconda annualità del progetto Acronimo DECODE (ERAPERMED2020-151) di cui € **4.702,29** che FRRB verserà all'erario a titolo di ritenuta 4%;
2. di provvedere alla pubblicazione del presente Decreto sul sito web di FRRB, a cura del Responsabile del procedimento ai sensi della Legge 241/1990, Dott.ssa Giulia Maria Rossignolo.

IL DIRETTORE GENERALE
Veronica Comi

Veronica
Comi
28.11.2024
17:57:13
GMT+02:00

COST STATEMENT

NAME OF LOMBARDY BENEFICIARY: ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI
NAME OF PRINCIPAL INVESTIGATOR: Dott.ssa Ariela Benigni
PROJECT ID: ERAPERMED2020-151
CUP NUMBER: D12C20000360002
REPORTING PERIOD (FROM-TO): from 1/03/2023 to 29/02/2024
IS VAT RECOVERABLE? (YES/NO): YES

COST CATEGORIES	TOTAL BUDGET	REPORTING PERIOD 1	REPORTING PERIOD 2	REPORTING PERIOD 3	TOTAL COST STATEMENT	DEVIATION FROM ORIGINAL BUDGET
TOTAL PERSONNEL COSTS	€ 180.000,00	€ 87.933,53	€ 50.538,77	€ 30.617,30	€ 169.089,60	€ 10.910,40
-Scientist	€ 0,00	€ 0,00	€ 0,00		€ 0,00	€ 0,00
-PhD Student	€ 0,00	€ 0,00	€ 0,00		€ 0,00	€ 0,00
-Technician	€ 0,00	€ 0,00	€ 0,00		€ 0,00	€ 0,00
-Other (*please specify*)	€ 0,00	€ 0,00	€ 0,00		€ 0,00	€ 0,00
CONSUMABLES	€ 167.000,00	€ 17.956,29	€ 60.398,87	€ 63.239,10	€ 141.594,26	€ 25.405,74
EQUIPMENT (LEASING OR ON HIRE)	€ 0,00	€ 0,00	€ 0,00		€ 0,00	€ 0,00
STUDY/CLINICAL TRIAL	€ 0,00	€ 0,00	€ 0,00		€ 0,00	€ 0,00
TRAVEL & ACCOMODATION	€ 10.000,00	€ 0,00	€ 2.856,67	€ 2.856,67	€ 5.713,34	€ 4.286,66
OTHER DIRECT COSTS	€ 15.500,00	€ 1.120,91	€ 4.630,01	€ 1.251,36	€ 7.002,28	€ 8.497,72
SUBTOTALE	**€ 372.500,00**	**€ 107.010,73**	**€ 118.424,32**	**€ 97.964,43**	**€ 323.399,48**	**€ 49.100,52**
OVERHEADS	€ 74.500,00	€ 21.402,15	€ 23.684,86	€ 19.592,89	€ 64.679,90	€ 9.820,10
SUBCONTRACTING COSTS	€ 3.000,00	€ 0,00	€ 0,00	€ 0,00	€ 0,00	€ 3.000,00
TOTAL REQUESTED BUDGET	**€ 450.000,00**	**€ 128.412,88**	**€ 142.109,18**	**€ 117.557,32**	**€ 388.079,38**	**€ 61.920,62**

PERSONNEL COSTS
(in case of public IRCCS and ASST ONLY temporary contracts will be considered eligible)
Max 50% of direct costs

NAME	POSITION	CONTRACT TYPE	PERIOD (FROM - TO)	EURO AMOUNT
Benigni Ariela	P.I. - Project Coordination	coordinated and continuous collaboration agreement	from 1/03/2023 to 29/02/2024	8.391,15
Buelli Simona	Researcher	Indefinite period	from 1/03/2023 to 29/02/2024	8.791,22
Noris Marina	Laboratory chief	Indefinite period	from 1/03/2023 to 29/02/2024	10.335,45
Piras Rossella	Clinician	Indefinite period	from 02/01/2024 to 29/02/2024	3.099,48
			TOTAL € AMOUNT	30.617,30

CONSUMABLES
(Under this cost categories animal costs can be listed)

NAME	ITEM DESCRIPTION	INVOICE NR.	INVOICE DATE	PAYMENT DATE	EURO AMOUNT
Agilent Technologies Italia S.p.A.	Rb a Hu C3c Complement/FITC	199301347/301485/P1	29/01/2024	seguirà pagamento	1.235,00
ALIFAX S.R.L.	ADAMTS-13 ATTIVITA CROMOGENICO ELISA	663/1	14/03/2023	12/05/2023	1.815,00
CARLO ERBA REAGENTS SRL	FL9352200 3522 ULTRAMICRO 10 NON-STER.96OTIPS	2123027685	30/06/2023	30/10/2023	154,44
DISA RAFFAELE E F.LLI SNC	Cilindro graduato in TPX basso cc. 100	145	12/05/2023	30/08/2023	232,87
Eppendorf s.r.l.	epTIPS Reload PCRcl 0.1-10MyL, 960 pcs	0220046527	12/07/2023	28/12/2023	64,88
Eppendorf s.r.l.	Research plus 8 canali 30-300 MyL aranc	0220048434	17/10/2023	28/02/2024	627,00
Eppendorf s.r.l.	epDualfilter 2-200 MyL PCRSter 960	0220049369	23/11/2023	11/03/2024	2.326,64
Eppendorf s.r.l.	epDualfilter 2-20 MyL PCRSter 960	0220050012	21/12/2023	29/04/2024	2.258,16
Eppendorf s.r.l.	epDualfilter 2-20 MyL PCRSter 960	0220051071	14/02/2024	seguirà pagamento	2.031,92
EUROCLONE SPA	ECL Select WB detection reagent	2802	10/03/2023	27/07/2023	947,85
FISHER SCIENTIFIC SAS	X12 Cap GL45, PP, Red, winner seal	4180145657	12/07/2023	30/10/2023	97,46
FISHER SCIENTIFIC SAS	X800 ADESIVO PE 134X80MM STERILE	4180160150	09/02/2024	seguirà pagamento	312,55
FISHER SCIENTIFIC SAS	1LT Sulfuric acid, 5% v/v aq. soln. 1l	4180139598	24/04/2023	28/06/2023	88,92
Life Technologies Italia	BDT V3.1 RR-100 & SEQ BUFFER	23039597	17/07/2023	28/11/2023	2.952,44
Life Technologies Italia	PCR, 0.2ML TUBE W/ ATTACHED FL	23046806	18/08/2023	28/12/2023	76,20
Life Technologies Italia	MIN HANDLING CHARGE FR CATALOG	23059842	17/10/2023	28/02/2024	1.129,48
Life Technologies Italia	MINI GEL TANK	23065561	09/11/2023	28/03/2024	1.433,82
Life Technologies Italia	HU C3A COATED ELISA	23073119	06/12/2023	29/04/2024	3.352,44
Life Technologies Italia	MICROAMP 96-WELL RXN PLATE -	23002784	26/01/2023	31/05/2023	137,40
Life Technologies Italia	GENESCAN-500(LIZ) SIZE STD KIT	23004242	06/02/2023	28/06/2023	1.848,30
Life Technologies Italia	CAPILLARY ARRAY 48 X 50CM	23005128	10/02/2023	28/06/2023	4.284,00
Life Technologies Italia	EXOSAP-IT 2000 REACTIONS	23005611	14/02/2023	28/06/2023	2.727,12
Life Technologies Italia	BOLT BIS-TRIS PLUS 10% 10 WELL	23008686	03/03/2023	27/07/2023	803,20
Life Technologies Italia	TUBE,5X SEQ BUFFER SMALL	23009237	07/03/2023	27/07/2023	4.170,31
Life Technologies Italia	ION AMPLISEQ FOR ION CHEF, DL8	23017903	25/04/2023	30/08/2023	5.245,20
Life Technologies Italia	510 & 520 & 530 KIT - CHEF	23019666	03/05/2023	29/09/2023	4.009,60
Life Technologies Italia	MICROAMP 96-WELL RXN PLATE -	23019665	03/05/2023	29/09/2023	137,40
Life Technologies Italia	ION AMPLISEQ ON-DEMAND PANEL	23027634	02/06/2023	03/11/2023	1.199,68
Life Technologies Italia	0.2ML FLAT CAP THERMO-TUBE, PU	23029136	08/06/2023	03/11/2023	209,22
Life Technologies Italia	AMPLITAQ GOLD 1000U BUFFER II	23033020	22/06/2023	03/11/2023	1.623,80
Merck Life Science S.r.l.	BOVINE SERUM ALBUMIN, LYOPHILIZED POWDE	8230576714	14/03/2023	15/06/2023	478,80
PRODOTTI GIANNI SRL	Iptacopan	A10168	13/11/2023	28/03/2024	177,00
PRODOTTI GIANNI SRL	Human Complement C2 -Kit ELISA-	A10651	22/11/2023	28/03/2024	769,00
PRODOTTI GIANNI SRL	Human Lysozyme -Kit Elisa- (LZM)	A888	30/01/2024	seguirà pagamento	749,50
PRODOTTI GIANNI SRL	Human Thrombin -Kit Elisa- (Factor II)	A1514	15/02/2024	seguirà pagamento	749,50
RESNOVA S.R.L.	SALSA MLPA P236 ARMD MIX-1 PRO	001509/23	03/08/2023	28/11/2023	2.896,00
RESNOVA S.R.L.	SALSA MLPA P352 PKD1 PKD2 PROB	001913/23	20/10/2023	28/12/2023	1.597,00
Technogenetics S.p.A.	MICROVUE BA EIA KIT	0010001298	16/11/2023	28/02/2024	1.900,00
Technogenetics S.p.A.	MICROVUE SC5B 9 EIA KIT	0010001535	11/12/2023	28/03/2024	2.460,00
Technogenetics S.p.A.	MICROVUE BA EIA KIT	0010001659	19/12/2023	28/03/2024	3.520,00
Technogenetics spa	QA311 A311 ANTI-HUMAN FACTOR B GOAT2 ML CND:-	23001094	27/03/2023	31/05/2023	410,00
				TOTAL € AMOUNT	63.239,10

EQUIPMENT (LEASING OR ON HIRE)

NAME	ITEM DESCRIPTION	INVOICE NR.	INVOICE DATE	EURO AMOUNT	% OF USE OF THE EQUIPMENT FOR PROJECT'S PURPOSES	AMORTISATION MONTHS	EURO AMOUNT
						TOTAL € AMOUNT	0,00

TRAVEL AND ACCOMODATION
Max 10% of direct costs

NAME	MOTIVATION	DESTINATION	PERIOD (FROM - TO)	EURO AMOUNT
Cuneaz Beatrice	Partecipazione studio clinico DECODE	Ranica	13/06/2023	162,04
Rota Federico	Partecipazione studio clinico DECODE	Ranica	16/06/2023	205,18
Franchini Miriam	Partecipazione studio clinico DECODE	Ranica	21/07/2023	243,00
Fabbri Rebecca	Partecipazione studio clinico DECODE	Ranica	24/07/2023	81,16
Branca Marco Andrea Luca	Partecipazione studio clinico DECODE	Ranica	24/07/2023	154,30
Sammarone Longo Trisha Federica	Partecipazione studio clinico DECODE	Ranica	31/07/2023	101,50
Pozzato Federico	Partecipazione studio clinico DECODE	Ranica	31/07/2023	158,32
Dondelli Roberta	Partecipazione Congresso ICW 2023	NewCastle	31/08/23 - 5/09/23	1149,77
Mamone Marco Luis	Partecipazione studio clinico DECODE	Ranica	11/09/2023	146,08
Redaelli Valeria	Partecipazione studio clinico DECODE	Ranica	31/10/2023	32,96
Poropat matteo	Partecipazione studio clinico DECODE	Ranica	20/09/2023	257,24
Teggi Ada	Partecipazione studio clinico DECODE	Ranica	28/09/2023	165,10
			TOTAL € AMOUNT	2.856,67

SUBCONTRACTING
Max 20% of direct costs

NAME	PROCEDURE APPLIED	DESCRIPTION (provide details on service duration)	INVOICE NR.	INVOICE DATE	EURO AMOUNT
				TOTAL € AMOUNT	0,00

OTHER DIRECT COSTS
Publication costs can be listed here up to a maximum of 5% of direct costs

NAME	DESCRIPTION	INVOICE NR.	INVOICE DATE	PAYMENT DATE	EURO AMOUNT
DESCO SRL	Servizio catering per meeting "DECODE" per Vostri Ospiti	01/95	30/03/2023	28/06/2023	350,00
Maver Viaggi SNC	20 PAX 17.45 Ranica Centro Ricerche Cliniche Aldo e Cele D. / Bergamo Htl	FT23/47	31/03/2023	30/08/2023	300,00
COOPERATIVA CITTA' ALTA SOC.COOP.SOC. A R.L.	Pranzo	A/1087	28/03/2023	19/07/2023	318,36
International Society of Nephrology	FEE	2023020000126	21/11/2023	seguirà pagamento	37,30
DHL EXPRESS (ITALY) S.R.L.	Spedizione merce - prodotti chimici	MIL0006387590	29/02/2024	28/03/2024	247,70
				TOTAL € AMOUNT	1.251,36

The accounting documentation relating to the prospectus indicated above is kept in the records at the headquarters of the Beneficiary and will be made available in the event of checks.

Name of the Legal Representative: Dott. Stefano Giovanni Paroni

Position held at Host Institution:

Signature of the Legal Representative: [redacted]

Date and stamp:

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

ISTITUTO DI RICERCHE
FARMACOLOGICHE
MARIO NEGRI · IRCCS

RICHIESTA EROGAZIONE CONTRIBUTO
DICHIARAZIONE SOSTITUTIVA DI ATTO NOTORIO
(D.P.R. 445/2000)

Spett.le
Fondazione Regionale
per la Ricerca Biomedica
Piazza Città di Lombardia 1
20124 Milano

PEC:
fondazioneregionalericercabiomedica@pec.it

OGGETTO: Bando ERA PerMed Cofund Joint Transnational Call 2020

TITOLO PROGETTO: Defining stratification of patients with C3 Glomerulopathies/immune complex-mediated glomerular diseases for better diagnosis and tailored treatment (acronimo DECODE ID 151)

RESPONSABILE SCIENTIFICO: Dott.ssa Ariela Benigni

CODICE CUP: D12C20000360002

Il sottoscritto Giuseppe Remuzzi
Nato a [redacted] il [redacted]
Residente a [redacted]
CAP [redacted]
In qualità di Legale Rappresentante dell'Istituto di Ricerche Farmacologiche Mario Negri IRCCS partecipante al progetto in oggetto
con sede legale in comune di Milano
CAP 20156 Via Mario Negri, 2
CODICE FISCALE/PARTITA IVA 03254210150
INDIRIZZO E-MAIL direzione@pec.marionegri.it

CHIEDE

l'erogazione della 3° rata pari a € 117.557,32

Le coordinate per il versamento sono le seguenti:

- Banca Intesa Sanpaolo Spa
- Agenzia Filiale n.1876- Milano
- IBAN IT12D0306909400000008816112

Cordiali saluti,

Milano, 24 ottobre 2024

F.to DIGITALMENTE
DAL LEGALE RAPPRESENTANTE
(o suo delegato, ai sensi dell'Art. 24
del DLgs n. 82/2005)

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI · IRCCS

MODELLO DICHIARAZIONE RITENUTA 4%*

Il/La Sottoscritto/a DOTTOR STEFANO PARAZZI
nato/a a [redacted] il [redacted]
in qualità di Chief Financial Officer con delega della società/ente non commerciale:
ISTITUTO DI RICERCHE FAMACOLOGICHE MARIO NEGRI
P. IVA / Cod. Fiscale 03254210150
residente a [redacted] in (via/piazza) [redacted]

consapevole che le dichiarazioni mendaci sono punite penalmente ai sensi dell'art. 76 del D.P.R. 28 dicembre 2000, n. 445, e che codesta Amministrazione effettuerà controlli, anche a campione, sulle dichiarazioni rese

DICHIARA

che, ai fini dell'applicazione della ritenuta del 4% prevista dal secondo comma dell'art. 28 del D.P.R. 29 settembre 1973, n. 600, il contributo oggetto della richiesta a cui viene allegata la presente dichiarazione è da considerarsi come segue: (1)

SOLO PER ENTI COMMERCIALI

☐ L'ente beneficiario svolge attività commerciale in via esclusiva o principale; **(soggetto a ritenuta)**

SOLO PER ENTI NON COMMERCIALI

x L'ente beneficiario, pur non svolgendo attività commerciale in via esclusiva o principale, destina il contributo alla riduzione di oneri gestionali o alla copertura di disavanzi di gestione cui concorrono entrate derivanti da attività di natura commerciale; **(soggetto a ritenuta; nel caso di quota di finanziamento/cofinanziamento U.E., tale quota non è soggetta a ritenuta)**

☐ Il contributo è destinato unicamente alla copertura di spese o di disavanzi alla cui formazione concorrono solo entrate di carattere istituzionale; (2) **(non soggetto a ritenuta)**

☐ L'ente beneficiario è un'organizzazione non lucrativa di utilità sociale ONLUS (organizzazione iscritta nel registro provinciale di volontariato, cooperativa sociale, ecc., di cui all'art. 10, D. Lgs. n. 460/97); (3) **(non soggetto a ritenuta)**

IN GENERALE

☐ Il contributo viene dichiarato esente dalla ritenuta medesima in virtù di un'espressa deroga ai *sensi della legge* _____; (4) **(non soggetto a ritenuta)**

Il sottoscritto **dichiara**, altresì, che provvederà a comunicare tempestivamente eventuali variazioni che dovessero intervenire a modificare la presente dichiarazione, ivi comprese, in particolare, quelle previste dall'art. 149 del D.P.R. 22 dicembre 1986, n. 917 (in rif. alla perdita della qualifica di ente non commerciale).

Data 24/10/24

[redacted]zzi

***Allegare fotocopia della Carta di Identità o di un documento equipollente.**

INFORMATIVA per il consenso al trattamento dei dati personali ai sensi del D.LGS 30.06.2003 n. 196 ("PRIVACY"): i dati sopra riportati sono previsti dalle disposizioni vigenti ai fini del procedimento amministrativo per il quale sono richiesti e verranno utilizzati solo per tale scopo.

(1) apporre una crocetta sul punto interessato
(2) rif. art. 143, comma 1 D.P.R. 22 dicembre 1986, n. 917; le entrate derivano esclusivamente da contributi dei soci o degli Enti Pubblici e comunque, anche nel caso in cui ci fossero entrate di altro genere di natura commerciale, queste ultime vengono gestite con contabilità separata rispetto a quella istituzionale per la quale si richiede il contributo (art. 144, co. 2 D.P.R. 917/86)
(3) rif. art. 16 D.Lgs 460/97.
(4) indicare gli estremi della disposizione normativa

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Fondazione per ricerche eretta in ente morale, D.P.R. 361 Del 5/4/1961 - Registro Persone Giuridiche Prefettura Milano N.227
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Joint Transnational Call for Proposals (2020) for

"Multidisciplinary Research Projects on Personalised Medicine – Pre-/Clinical research, Big Data and ICT, Implementation and User's Perspective"

Annual Report

1. General information

Project title	**Defining stratification of patients with C3 Glomerulopathies/immune complex-mediated glomerular diseases for better diagnosis and tailored treatment**
Project acronym	**DECODE**
Project duration (months)	**36**
Starting date	**01/03/2021**
Period covered by the report:	**01/03/2023 – 29/02/2024**
Periodic report:	**[3rd]**
Project website and social media accounts	**era-decode.eu/**

2. Project Consortium

Coordinator (Partner 1):

Affiliation, Address:	Istituto di Ricerche Farmacologiche Mario Negri IRCCS
Country:	Italy
Name of Principal Investigator:	Ariela Benigni
E-Mail:	ariela.benigni@marionegri.it
Phone:	+39-035-4213410
Type of institution (academic, clinical, industrial)	No profit research organization
Funding Organisation:	Fondazione Regionale per la Ricerca Biomedica (FRRB)

Project Partners:

Partner no.	Affiliation	Country	Name of Principal Investigator	Type of partner (academic, clinical, industrial)
2	ASST-Papa Giovanni XXIII	Italy	Piero Ruggenenti	Clinical
3	Biomedical Research Foundation Academy	Greece	Antonia Vlahou	Academic
4	Helmholtz Zentrum München	Germany	Philippe Schmitt-Kopplin	Academic

5	Norwegian Institute of Public Health	Norway	Isabelle Budin Ljøsne	Clinical
6	University of Leipzig, Germany (ULEI)	Germany	Henry Loeffler-Wirth	Academic

Please indicate any changes in the project team.

3. Publishable summary of the context and overall objectives of the project

*Please summarize the project **objectives and major achievements** using language accessible to the public (max. 2000 characters including spaces). **This abstract may be published (e.g. ERA PerMed website).***

Primary membranoproliferative glomerulonephritis represents a group of rare kidney disorders associated with complement activation. There is no specific therapy and the prognosis is unfavorable: about half of all patients, mostly children, develop end-stage renal disease and need dialysis within 10 years of onset. MPGN is heterogeneous and patients have abnormal activation at different levels of the complement system. Several drugs targeting complement have been already approved or are investigated in trials for other conditions. However, trials to test new therapeutics will be heavily influenced by the heterogeneity MPGN. The current classification into C3 glomerulopathy (C3G) and immunecomplex- mediated MPGN (IC-MPGN) based on only histological data, does not reflect the etiology and is inefficient. Thus, there is an obligation in future trials to ensure that each patient is maximally characterized in order to receive the right drug.

Previous studies identified four patient clusters, instrumental to define early and late complement activation. DECODE will implement this strategy by combining omics approaches (i.e. WES, proteomics and metabolomics) and hierarchical clustering analysis to define a precise stratification of patients with C3G/IC-MPGN, and to identify specific biomarkers, which will be instrumental for diagnosis, predicting prognosis and tailoring the right therapeutic strategy for the right patients.

4. General overview of the objectives and deliverables for the period covered

Objectives/Deliverables			
No.	***Title***	***Partner in charge***	***Short Description***
D1.4	**A user-friendly platform to assign patients to a cluster and SOM portrayal of the cohort**	**Partner 6**	Creation of computational tool that allows assignment of patients to a cluster using a limited set of genetic, laboratory and clinical data with the final goal of making a correct diagnosis and of orienting among treatment options.
D2.3	**Data integration and selection of the most informative proteomic and/or metabolomic parameters**	**Partner 3, Partner 4, Partner 6**	The most informative proteomic and/or metabolomic parameters (3 to 5) will be selected for each cluster based on differential levels, correlation to other -omics and functional annotation. Multi-omics analysis is complemented by SOM portrayal for improved resolution of feature-clusters.
D2.4	**Validation of the selected parameters**	**Partner 1 (Coordinator), Partner 2, Partner 3**	Validation of proteomic and metabolomic parameters as cluster-specific biomarkers is performed using advanced techniques such as multiple reaction monitoring (MRM) MS, and, where applicable, western blot/ELISA for proteins and HPLC for metabolites. The validation is performed using plasma and/or urine samples collected from all patients before treatment.
D2.5	**Verification of the selected parameters with the original clusters**	**Partner 1 (Coordinator), Partner 2,**	Selected proteomic and metabolomic parameters are used to verify the concordance of biomarker levels with the original clusters

		Partner 3	
D3.1	**Data of in-vitro study on fluid phase activation**	**Partner 1 (Coordinator)**	Evaluation of fluid phase complement activation in selected patients from each cluster and the effects of complement inhibitors.
D3.2	**Data of in-vitro study on solid phase activation**	**Partner 1 (Coordinator)**	Evaluation solid phase complement activation on C3b-coated microplates treated with serum from selected patients from each cluster and the effects of complement inhibitors.
D3.3	**Data of complement activation by ex-vivo study**	**Partner 1 (Coordinator)**	Cultured endothelial cells activated with ADP, or cultured podocytes are exposed to serum from selected patients from each cluster, with subsequent assessment of C3 and C5b-9 deposits by confocal microscopy.
D3.4	**Data of cell phenotype and functions by ex-vivo studies**	**Partner 1 (Coordinator)**	Studies to evaluate serum-induced modifications in inflammatory markers of endothelial cells and podocytes by ELISA or confocal microscopy. Studies to assess leukocyte adhesion to endothelial cells using a laminar flow chamber.
D4.1	**OFF-ON-OFF-ON Protocols**	**Partner 2**	Design of protocols for cluster-specific exploratory phase 2 studies with complement inhibitors or other drugs targeting biomarkers identified by omics-studies of WP2, and selected by in-vitro and cell-based studies of WP3. The OFF-ON-OFF-ON approach allows performing within-patient comparisons between different treatment periods which reduced random data fluctuations and increased the power of statistical analyses despite the small sample size.
D4.2	**Randomized placebo design protocols**	**Partner 2**	Design of a Randomized Placebo-Phase: patients are first randomly allocated to either an experimental or a control group. After a short, fixed placebo-phase all controls will be blindly switched to the experimental treatment.
D4.3	**Protocols with sequential design or a response adaptive randomization design**	**Partner 2**	Protocols with a sequential or a response-adaptive randomization design based on identified clusters, patient availability, and anticipated treatment effects are designed to produce robust evidence on the risks and benefits of various complement inhibitors.
D5.2	**Report on stakeholders'views on PM and stratification**	**Partner 5**	To investigate the perspectives, hopes, concerns, and views of both patients and healthcare professionals regarding personalized medicine and patient stratification approaches in healthcare.

D5.3	**Informed consent tools to support PM in multi-site clinical research**	**Partner 5**	Development of informed consent tool supporting the use of personalized and stratification approaches in multi-site clinical trials with study centres in several countries.
D5.4	**Multi-stakeholder workshop to increase patient literacy in PM**	**Partner 5**	Development of recommendations for increase patient literacy in PM and stratification approach using results from qualitative and quantitative research performed in task 2 and an international stakeholder workshop.
D6.2	**Consortium Annual meeting**	**All**	
D6.3	**Scientific publications**	**All**	
D6.4	**Dissemination events**	**All**	

Add lines as relevant.

5. Work performed during the reporting period and main results achieved so far

Please describe the work performed per WP.

WP 1	**Patient stratification by cluster analysis**
Leading Partner: Partner 1 (Coordinator)	
Additional involved Partners: partner 2, partner 6	
Planned timeline (according to GANTT chart): (from M1 to M20)	**Actual timeline:** (from M1 to M28)
Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*) Deliverable D1.4: A user-friendly platform to assign patients to a cluster and SOM portrayal of the cohort: The browser tool was developed by partner 6 for classification of MPGN patients based on clinical parameters. Implementation of the prototype was finalized during the reporting period and presented to the project and clinical partners during a working stay in October 2023. Based on the provided feedback and the discussions, utilization of the tool was improved with focus on handling of missing parameters and incomplete data. Partner 1 recruited 14 new patients with primary C3G /IC-MPGN for testing the user-friendly platform. Clinical biochemical histology data at onset were collected, and complement profile, and screening for C3NeF and rare gene variant was performed.	
Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces.* The deliverable, originally scheduled for Month 20, was delayed due to the absence of complete data from the full set of patients belonging to the 5 clusters. Consequently, it was completed in Month 28.	

WP 2	**Omics profiles of clusters**
Leading Partner: Partner 3	

Additional involved Partners: Partner 1 (Coordinator), partner 4, partner 6	
Planned timeline (according to GANTT chart): (from M16 to M32)	**Actual timeline:** (from M16 to M40)

Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*)

BRFAA successfully completed the proteomic analysis of 80 plasma samples (10 from each of the 5 clusters defined in WP1 and 30 controls). Cluster-specific biomarkers were identified following all possible pairwise comparisons among groups. Prioritization for further validation was based on frequency, significant difference against controls and availability of reliable ELISA kits. Elisa assays were then performed for Lysozyme C (LYZ), a biomarker specific for Cluster 1, fibronectin (FN1) and prothrombin (F2), biomarkers specific for Cluster 5 using the 80 plasma samples. The trend observed in the proteomic analysis was also observed following ELISA for LYZ and F2 and to a lesser extend for FN1 (results for LYZ and FN1are described in more detail in Deliverable 2.3).

Helmholtz finished the metabolomic analysis of eighty urine samples (10 of each of the 5 clusters, 20 healthy controls and 10 proteinuric patients). Multivariate statistical analysis of metabolomic data did not identify meaningful cluster specific metabolite, despite the difference observed between healthy controls and all patient groups. Amino acid derivatives were decreased, and phosphatidylcholines were increased in all Cluster groups. Univariate pairwise comparison resulted in highest count of significant features comparing Cluster_1 and healthy controls or Cluster_4 and healthy controls. We did not find any unique Cluster specific metabolites, because levels of metabolites did not differ significantly to proteinuric samples. Until now, we could not find metabolites for validation tests.

Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces.*

Deliverable 2.3. Data integration and selection of the most informative proteomic and/or metabolomic parameters using self-organizing map (SOM) machine learning. This deliverable is delayed from month 23 to month 40. The reason for deviation is some delay in the availability of full set of proteomic and metabolomic data.

WP 3	Pre-clinical identification of cluster-specific therapies
Leading Partner: Partner 1 (Coordinator)	
Additional involved Partners:	
Planned timeline (according to GANTT chart): (from M24 to M32)	**Actual timeline:** (from M24 to M40)

Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*)

We selected 25 patients (5 for each cluster) **D3.1 In-vitro study on fluid phase complement activation.** Preliminary experiments documented that the evaluation of C3a release in 20% serum is the best assay to identify patients with complement iperactivation in fluid phase. Experimental evaluations are ongoing. **D3.2 In-vitro study on solid phase complement activation.** We evaluated serum induced formation of C5b-9 on C3b-coated wells and the effect of different complement inhibitors. The assay was done in all

patients and showed a broad response to C3 inhibition and a variable response to alternative pathway inhibitors (highest inhibition in clusters 3 and 5). **D3.3 Complement activation ex –vivo.** We evaluated serum induced C3b deposition on human podocytes and microvascular endothelial cells (HMEC-1). Results showed higher than normal C3b deposits on podocytes with serum from most C3G/IC-MPGN patients with highest values recorded in cluster 4, whereas excessive serum-induced C3b deposition on HMEC-1 was mainly restricted to cluster 5. Serum-induced C5b-9 formation on podocytes was generally lower than C3b in most patients. **D3.4 Cell phenotype and function.** We have set-up the experimental conditions.

Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces.*

The deliverables of this WP, originally scheduled for Month 26 (D3.1 and D3.2), month 29 (D3.3) and month 32 (D3.4) were delayed because the set-up of the many methods of complement activation analysis took longer than expected. The GmEC cell line proved unstable and with variable results depending on passage so we decided to use another human endothelial cell line, HMEC-1 of proven efficiency in ex-vivo tests with human serum.

WP 4	**Clinical Protocols**
Leading Partner: Partner 2	
Additional involved Partners: partner 1 (Coordinator), partner 4, partner 6	
Planned timeline (according to GANTT chart): (from M30 to M35)	**Actual timeline:** (from M34 to M40)

Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*)

According to results of cluster analyses, specific complement inhibitors to be tested to target specific complement pathways involved in disease pathogenesis in each single cluster have been identified along with their modality and timing of administration (Table). Considering the number of patients identified for each cluster (Table) and the proportion of those who currently have normal kidney function without urine abnormalities or are on dialysis therapy and that approximately one third with pre-terminal kidney dysfunction will be involved in ongoing clinical trials, less than 50% of identified patients are expected to be potentially eligible for innovative trials. According to the number of available and consenting patients three study designs have been identified:

Deliverable D4.1

- Less than 10 patients: 48-week, OFF(Baseline)-ON-OFF-ON-OFF design (Figure 1)

Deliverable D4.2

- 10 to 20 patients: 12-month, Randomized, Placebo-Controlled, Cross-Over-design (Figure2)
- > 20 Patients: 6-month, Randomized, Placebo-Controlled design followed by 6-month active treatment for all participants (Figure 3)

Deliverable D4.3

- To be finalized by final DECODE meeting on June 2024

Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces.*

WP 5	Ethical, legal and social aspects
Leading Partner: Partner 5	
Additional involved: PAOs	
Planned timeline (according to GANTT chart): (from M 1 to M36)	**Actual timeline:** (from M1 to M36)
Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*) The work on D5.2 (Report on stakeholders' views on PM and stratification) is completed and consists of two outcomes: 1) A public report providing an overview of the IMPACT survey results and a summary of key findings, published on the DECODE website in September 2023 and 2) a scientific paper summarizing results from interviews with patients and parents of patients regarding their views on participation in potential future clinical trials. The paper was submitted to the ELSEVIER journal "Rare" in February 2024 and is under peer review. The work on D5.3 (Informed consent tools to support PM in multi-site clinical research) was pursued during the period and a complete draft of a guideline on "Informed consent in clinical trials for MPGN" was shared in March with the DECODE partners for review. The guideline will be finalized in May and published on the DECODE website. WP5 is currently preparing the final workshop (D5.4 multi-stakeholder workshop to increase patient literacy in PM) to be held in Bergamo on June 22 in connection with the final DECODE consortium meeting. Invitations to relevant stakeholders will be sent in May 2024	
Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces.*	

WP 6	Communication, Dissemination ad Exploitation
Leading Partner: Partner 1	
Additional involved Partners: All (partners and PAOs)	
Planned timeline (according to GANTT chart): (from M1 to M36)	**Actual timeline:** (from M1 to M41)
Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*) D6.2 Consortium Annual meeting: We organized the Second Consortium annual meeting in person in order to discuss the state of the art of the project and in particular the issues and the subsequent delays faced during the second year. The second year meeting has taken place on March 28th-29th, 2023 in Ranica (Bergamo). Specific dissemination activities are detailed in section 10. The final meeting is planned for 21st and 22nd of June 2024.	
Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces.* *D6.2, D6.3 and D6.4 are delayed as consequence of the project delay due to the incomplete data from the full set of patients and the delay in setting up of methods of complement activation analysis.* *For this reason the consortium has requested a 5-months extension.*	

6. Transnational Collaboration, Meetings and Mobility

Describe consortium meetings (physical and virtual) including more than 2 partners (date, location, purpose, results).

Participants	*Date*	*Location*	*Purpose*	*Results*
All	*April 12, 2021*	*Virtual*	*Kick off Meeting: Presentation and planning of the project*	*- Choice of the project logo and DECODE website;* *- Updating related to patient selection and data collection*
All	*April 5, 2022*	*Virtual*	*First year Meeting: activity updating*	*WP1: Patient identification and stratification* *WP1: Adaptation of algorithm to preliminary DECODE data* *WP2: Preliminary data on mass spectrometry metabolomics* *WP5: Presentation of the questionnaire for patient data collection*
All	*March 28-29, 2023*	*Clinical Research Center for Rare Diseases "Aldo e Cele Daccò"* *Via GB Camozzi, 3* *24020-Ranica (Bergamo), Italy*	*Second year meeting: activity updating*	*Reminder of project plan and timelines* *WP1: presentation of results* *WP2: preliminary data of proteomics and metabolomics and planning of future analises* *WP5: preliminary results from the IMPACT survey and interviews and future programmed activities* *WP6: updating of the communication and dissemination activities*
Partners 1,2 & 6	*18th October 2023*	*Clinical Research Center for Rare Diseases "Aldo e Cele Daccò"*	*Working stay of partner 6, demonstration of*	*Identification of desirable features for the tool: mapping of protein and metabolite markers, information on*

			the interactive classification tool	*parameter weighting, and possibility to classify patients with incomplete data*

Please describe the benefits and the synergies of the collaboration including: any joint project or initiative, any staff exchange or cross-country recruitment, training opportunities for new staff, any obstacles to the transnational collaboration and the proposed solution (max 2,000 characters including spaces).

7. Data Management Plan

Please describe all changes (if any) from the strategy described in the Data Management Plan (DMP) sent to the ERA PerMed Joint Call Secretariat. (Max. 2,000 characters including spaces).

The plan is not changed

8. Patients Involvement

Does your project involve a patient representative/organization? yes/no

Yes

What is the role(s) of the patient representative(s)/organization(s) in your project (please select all that apply)?

INVOLVEMENT (where patient representative/organization are actively involved in the research project):

X Involvement in identifying research priorities within the project
☐ Serving as members of the project advisory or steering committee(s)
X Commenting and developing patient information leaflets or other research materials
☐ Undertaking interviews with research participants
☐ Carrying out specific aspects of the research projects
X Other (please specify): contribute to set up ethical documents

PARTICIPATION (where patients take part in the research study):

☐ People being recruited to a clinical trial
X Completing a questionnaire or participating in a focus group as part of a research study
☐ Other (please specify)

ENGAGEMENT (where information and knowledge about research is provided and disseminated):

☐ Scientific conferences/open day with debates and discussions on research where patient representative(s)/organization(s) are invited to find out about the research projects
X Raising awareness of the project through media such as television programmes, newspapers and social media
X Dissemination to patient organizations and the patient community on the findings of a study
X Other (please specify): lobby for development of any diagnostic tests and orphan drug therapies emerging from this project

9. Peer Reviewed Articles

Only include publications after the start date of the project, ***with clear acknowledgement of ERAPerMed funding:*** *"This project was supported by [name of funding organization, or an acknowledgment as requested by your national funding organization], under the frame of ERA PerMed."*

Type of Publication *	Partners involved	Publication (authors, title, journal, year, issue, pp.)	DOI	Open access (yes/no)	Confir-mation **
Article in journal	1	Noris M, Daina E, Remuzzi G. Membranoproliferative glomerulonephritis: no longer the same disease and may need very different treatment. Nephrol Dial Transplant. 2021 Oct 1:gfab281. Online ahead of print.	10.1093/ndt/gfab281.	yes	X
Article in journal	1	Piras R, Breno M, Valoti E, Alberti M, Iatropoulos P, Mele C, Bresin E, Donadelli R, Cuccarolo P, Smith RJH, Benigni A, Remuzzi G, Noris M. *CFH* and *CFHR* Copy Number Variations in C3 Glomerulopathy and Immune Complex-Mediated Membranoproliferative Glomerulonephritis. Front Genet. 2021 Jun 11;12:670727. eCollection 2021.	10.3389/fgene.2021.670727	yes	X
Article in journal	1	Noris M, Galbusera M. The complement alternative pathway and hemostasis. Immunol Rev. 2023 Jan;313(1):139-161	10.1111/imr.13150	yes	X
Article in journal	1	Noris M and Remuzzi G. Eculizumab-Every Fifteen Days Forever? Kidney International Reports Volume 8, Issue 1, January 2023, Pages 4-7	https://doi.org/10.1016/j.ekir.2022.11.006	yes	X
Article in journal	1	Noris M, Remuzzi G. C3G and Ig-MPGN-treatment standard. Nephrol Dial Transplant. 2024 Jan 31;39(2):202-214.	10.1093/ndt/gfad182.	yes	X
Article in journal	1	Zanchi C, Locatelli M, Corna D, Cerullo D, Fishilevich E, Desai D, Rottoli D, Donadelli R, Noris M, Zoja C, Remuzzi G, Benigni A. Liver factor B silencing to cure C3 glomerulopathy: Evidence from a mouse model of complement dysregulation. Mol Immunol. 2023 Sep;161:25-32.	10.1016/j.molimm.2023.07.010.	yes	X

Add lines as relevant.

** Type of publication: Article in journal, Publication in conference proceedings, Books-Monographs.*

*** I, the coordinator, confirm that this publication includes content generated within our ERA PerMed project and that ERA PerMed was acknowledged as indicated above.*

10. Further Dissemination Activities

Only include publications and activities after the start date of the project.

Type of dissemination activity*	Partner No	Description	Link	Target audience**
Organization of the International Frontiers Meeting	1	Complement-mediated kidney diseases, with a focus on C3G and IC-MPGN. The DECODE consortium gave the patronage to the meeting	https://www.theisn.org/frontiers/	Clinicians, Scientists, Patients, Patient's Associations
Dissemination to the general public	1	The project is mentioned in the Coordinator Institutional website in a section focused on the MPGN diseases	https://www.marionegri.it/magazine/glomerulonefrite-membranoproliferativa	General public
Dissemination to the general public	1	The project and its aim is mentioned in the Coordinator Institutional website within a section dedicated to renal diseases and MPGN	https://www.marionegri.it/magazine/reni-malattie-e-cure	General public
Recruitment campaign	5	The IMPACT survey link was posted on the DECODE website with invitation to MPGN patients to participate	http://www.era-decode.eu/survey.html	MPGN Patients
IMPACT survey flyer	5	The survey flyer was shared with approx. 25 researchers/research groups and patient organizations internationally (Europe and USA) for dissemination among patients. The groups/organizations helped post the flyer on their websites and Facebook groups and inform patients.	Shared by email	Relevant research groups and patient organizations
Dissemination	5	The IMPACT survey report was posted on the DECODE website.	The IMPACT study (era-decode.eu)	MPGN Patients, researchers, clinicians, other
Dissemination to the general public	PAO	On the DDD Onlus website, a brief description of the DECODE project and a link to DECODE have been added.	http://www.dddets.org/link.html	General public
Dissemination to the stakeholders	1	The project is mentioned in the ASN meeting kidney week, Philadelphia 2-5 November 2023 within a	https://www.asn-online.org/education/kidneyweek/2023/KW23_Onsite_Guide_web.pdf	Clinicians, Scientists, Patient's Associations

		lecture on Complement inhibition in nondiabetic kidney diseases towards translation.		

Add lines as relevant.

** Type of publication or dissemination activity: Master/PhD/MD thesis; Communication in scientific conferences or workshops; dissemination to the general public; e.g. Organisation of a Conference/Workshop, Press Release, Exhibition, Flyers, Social media, Web-site, Communication campaign; Other (please specify).*

*** Target audience: scientific community, general public, policymakers, industry, etc.*

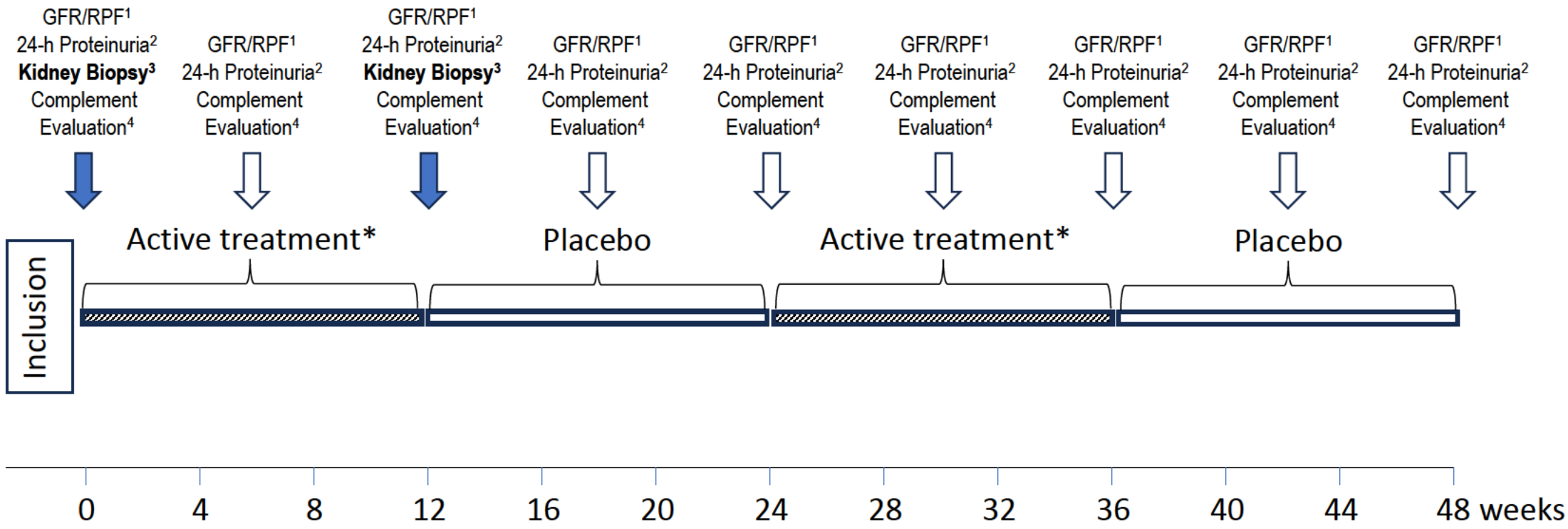
DECODE STUDY DESIGN

*Less than **10** patients available*

Primary Outcome:

12-week 24-hour proteinuria reduction (Post- vs. Pre- Active Treatment as compared to Post- vs. Pre- Placebo changes)

For each individual patient two active treatment periods are compared with two placebo treatment periods



*To be decided according to Cluster (See Table)

[1]By iohexol and para-amino-hippuric acid plasma clearance
[2]Mean of three consecutive urine collections
[3]Structural, Immunohistochemical and ultrastructural evaluation
[4]In blood and biopsy samples when available

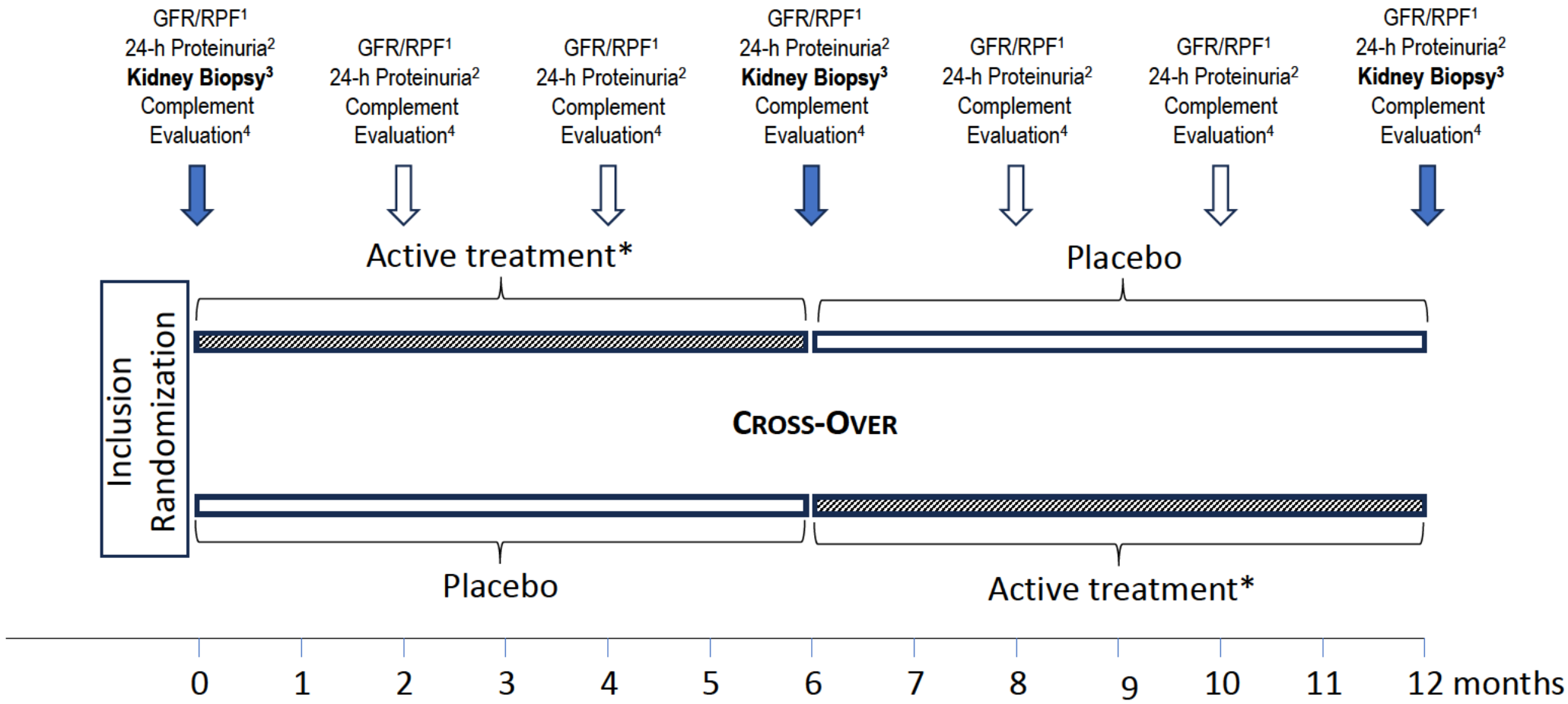
Figure 1

DECODE STUDY DESIGN

10 to 20 *patients available*

Primary Outcome:

Six-month 24-hour proteinuria (Post- vs. Pre- ActiveTreatment as compared to Post- vs. Pre- Placebo changes)



* To be decided on the basis of Cluster analyses *(see Table)*

[1]By iohexol and para-amino-hippuric acid plasma clearance
[2]Mean of three consecutive urine collections
[3]Structural, Immunohistochemical and ultrastructural evaluation
[4]In blood and biopsy samples when available

Figure 2

DECODE STUDY DESIGN

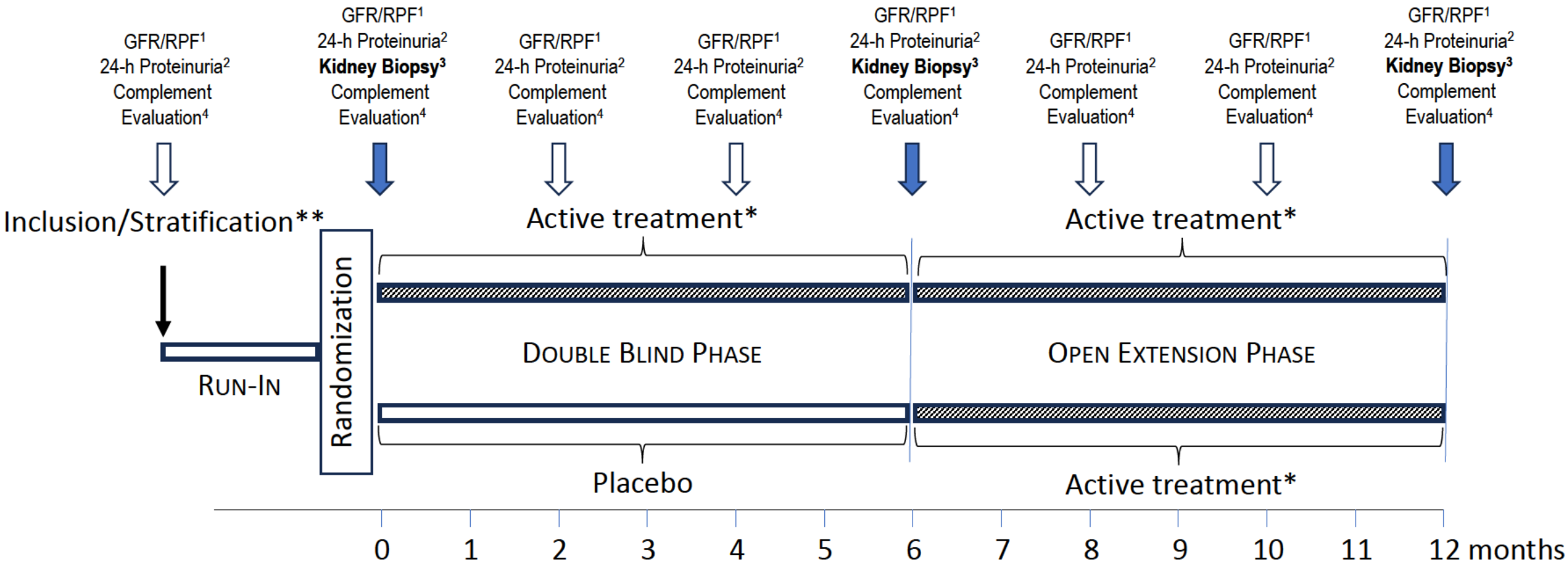
*>**20** patients available*

Co-primary Outcomes:

Six-month 24-hour proteinuria (Post- vs. Pre- Active Treatment as compared to Post- vs. Pre- Placebo changes)

Six- vs. 12-month 24-hour proteinuria (Post- vs. Pre- Active Treatment changes)

Changes during two 6-month Active Treatment periods can be compared with changes during one 6-month Placebo treatment period



* To be decided on the basis of Cluster analyses

** By gender, eGFR and proteinuria

[1]By iohexol and para-amino-hippuric acid plasma clearance

[2]Mean of three consecutive urine collections

[3]Structural, Immunohistochemical and ultrastructural evaluation

[4]In blood and biopsy samples when available

Figure 3

CLUSTER Number of patients	#1 N=44	#2 N=67	#3 N=73	#4 N=41	#5 N=70
DRUG	CFH-RGD coupled (ALXN1920)	1) C3 inhibitor 2) C5 inhibitor	CFH-RGD coupled (ALXN1920)	1) Factor B inhibitor 2) C3 inhibitor	1) Factor B inhibitor 2) C5 inhibitor 3) C3 inhibitor
TARGET	Alternative pathway on cell/tissues	1) Classical and alternative pathway systemic 2) Terminal pathway systemic	Alternative pathway on cell/tissues	1) Alternative pathway systemic 2) Classical and alternative pathway systemic	1) Alternative pathway systemic 2) Terminal pathway systemic 3) CP and AP systemic
ADMINISTRATION MODALITY	Subcutaneous	1) Subcutaneous 2) I.v.	Subcutaneous	1) Oral 2) Subcutaneous	1) Oral 2) I.v. 3) Subcutaneous
DOSE INTERVAL	Weekly	1) Twice weekly 2) Every other week/monthly	Weekly	1) Twice daily 2) Twice weekly	1) Twice daily 2) Every other week/monthly 3) Twice weekly

INAIL
ISTITUTO NAZIONALE PER L'ASSICURAZIONE CONTRO GLI INFORTUNI SUL LAVORO

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Istituto Nazionale Previdenza Sociale

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Numero Protocollo	INPS_42665153	Data richiesta	26/09/2024	Scadenza validità	24/01/2025

Denominazione/ragione sociale	ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI
Codice fiscale	03254210150
Sede legale	VIA MARIO NEGRI 2 MILANO MI 20156

Con il presente Documento si dichiara che il soggetto sopra identificato RISULTA REGOLARE nei confronti di

I.N.P.S.
I.N.A.I.L.

Il Documento ha validità di 120 giorni dalla data della richiesta e si riferisce alla risultanza, alla stessa data, dell'interrogazione degli archivi dell'INPS, dell'INAIL e della CNCE per le imprese che svolgono attività dell'edilizia.