AZIENDA OSPEDALIERA UNIVERSITARIA

Deliberazione n. 1157 del 31/08/2023

Emendamento n. 1 alla convenzione economica tra l'Azienda Ospedaliera Universitaria Policlinico e per essa l'UOC di Gastroenterologia e la Società ICON Holdings Clinical Research International Limited per la conduzione della sperimentazione clinica dal titolo: "Studio multicentrico di fase 3, randomizzato, in doppio cieco, controllato con placebo, volto a valutare l'efficacia e la sicurezza a lungo termine di lanifibranor in pazienti adulti con steatoepatite non alcolica e non cirrotic (NASH) e fibrosi epatica di stadio 2 (F2) di stadio 3 (F3) " Codice Prot. 337HNAS20011 Codice Eudract 2020-004986-38 - Sperimentatore: Prof. Salvatore Petta.

DIREZIONE GENERALE	**Area Gestione Economico - Finanziaria**
Il Responsabile dell'Ufficio atti deliberativi **Grazia Scalici**	Autorizzazione spesa n. Del Conto di costo _____ NULLA OSTA in quanto conforme alle norme di contabilità **Il Responsabile dell'Area Gestione** **Economico – Finanziaria**

Ai sensi del DPR n. 445/2000 e ss.mm.ii. e la Legge 241/90 e ss.mm.ii. e L.R. 7/2019, il sottoscritto attesta la regolarità della procedura seguita e la legalità del presente atto, nonché l'esistenza della documentazione citata e la sua rispondenza ai contenuti esposti.

Il Responsabile proponente

_____

Il Commissario Straordinario
Dott. Maurizio Montalbano
nominato con D. A. n. 19/2023 del
09 maggio 2023 prorogato con DA n. 28 del 29-06-2023
Con l'intervento, per il parere prescritto dall'art. 3 del D.L.vo n. 502/92
così come modificato dal D.L.vo n. 517/93 e dal D.L.vo n. 229/99
del Direttore Amministrativo Dott. Arturo Caranna
e del Direttore Sanitario Dott. Gaetano Cimò
Svolge le funzioni di segretario verbalizzante
Sig.ra Grazia Scalici

AZIENDA OSPEDALIERA UNIVERSITARIA

Delibera n. 1157 del 31/08/2023

IL COMMISSARIO STRAORDINARIO

PRESO ATTO che presso l'AIFA è stato istituito il Centro di Coordinamento nazionale dei Comitati Etici Territoriali e ricostituito con il Decreto del Ministro della Salute del 27/05/2021, garante dell'omogeneità delle procedure e del rispetto dei termini temporali;

PRESO ATTO dell'entrata in vigore in data 31/01/2022 del nuovo Regolamento (EU) n. 536/2014 del Parlamento Europeo sulla sperimentazione clinica di medicinali per uso umano;

VISTI il Decreto 26 gennaio 2023 recante: "individuazione di quaranta comitati etici territoriali (di seguito indicato con DM 40 CET);

il Decreto del 27 gennaio 2023, del Ministero della Salute recante misure relative all'individuazione e competenze dei Comitati Etici Territoriali;

il Decreto 30 gennaio recante "determinazione della tariffa unica per le sperimentazioni cliniche, del gettone di presenza e del rimborso spese per la partecipazione alle riunioni del Centro di coordinamento nazionale dei comitati etici territoriali per le sperimentazioni cliniche sui medicinali per uso umano e sui dispositivi medici, dei comitati etici territoriali e dei comitati etici a valenza nazionale";
il Decreto 30.01.2023 recante: "definizione dei criteri per la composizione e il funzionamento dei comitati etici territoriali";

PRESO ATTO che, con delibera n. 916 del 30/06/2023 e ss.mm.ii., è stato istituito il CET (Comitato Etico Territoriale) e la Segreteria Tecnico Scientifica, in applicazione al Decreto Regionale n. 541/2023;

che, con delibera n. 1017 del 19.07.2023 è stato istituito il CEL Palermo 1 (Comitato Etico Locale Palermo 1) e con delibera 1072 del 03.08.2023: Integrazione e recepimento del D.A. Assessorato Salute RS n. 746 del 25.07.2023;

VISTA La delibera n. 47 del 26/01/2023 di sottoscrizione della convenzione economica tra l'A.O.U.P. "P. Giaccone" e la Società Pharmaceutical Research Associates Italy S.r.l. per la conduzione della sperimentazione dal titolo: "Studio multicentrico di fase 3, randomizzato, in doppio cieco, controllato con

AZIENDA OSPEDALIERA UNIVERSITARIA

placebo, volto a valutare l'efficacia e la sicurezza a lungo termine di lanifibranor in pazienti adulti con steatoepatite non alcolica e non cirrotic (NASH) e fibrosi epatica di stadio 2 (F2) di stadio 3 (F3) " Codice Prot. 337HNAS20011 Codice Eudract 2020-004986-38 - Sperimentatore: Prof. Salvatore Petta.

PRESO ATTO Che in data 30/05/2023il Comitato Etico IRCCS Casa Sollievo della Sofferenza ha approvato l'emendamento n. 1 al protocollo ;

CONSIDERATO Che a seguito dell'emendamento si è reso necessario, modificare la convenzione economica originale sostituendo nella sua interezza l'Allegato A per tener conto delle modifiche apportate ai servizi e ai costi previsti dal contratto - Aggiornamento del titolo del Protocollo e Trasferimento da PRA a ICON .

SENTITO il parere favorevole del Direttore Amministrativo e del Direttore Sanitario cosi come prescritto dall'art. 3 del D.L.vo n. 502/92, cosi come modificato dal D.L. n. 517/93 e dal D.Lvo 229/99;

Per i motivi in premessa citati che qui si intendono ripetuti e trascritti

DELIBERA

Di procedere alla sottoscrizione dell' Emendamento n. 1 alla convenzione economica tra l'Azienda Ospedaliera Universitaria Policlinico e per essa l'UOC di Gastroenterologia e la Società ICON Holdings Clinical Research International Limited per la conduzione della sperimentazione clinica dal titolo: "Uno studio di fase 3, randomizzato, in doppio cieco, controllato con placebo, multicentrico, che valuta l'efficacia e la sicurezza di lanifibranor seguito da un'estensione del trattamento attivo in pazienti adulti con steatoepatite non alcolica non cirrotica (NASH) e stadio fibrosi 2 (F2)/fibrosi 3 di (F3) della fibrosi epatica " Codice Prot. 337HNAS20011 Codice Eudract 2020-004986-38 - Sperimentatore: Prof. Salvatore Petta.

L 'Emendamento n. 1 è allegato alla presente per farne parte integrante.

Il Direttore Sanitario
Dott. Gaetano Cimò

Il Direttore Amministrativo
Dott. Arturo Caranna

Il Commissario Straordinario

AZIENDA OSPEDALIERA UNIVERSITARIA

Dott. Maurizio Montalbano
Il Segretario Verbalizzante
Grazia Scalici

PUBBLICAZIONE

Si certifica che la presente deliberazione, per gli effetti dell'art. 53 comma 2 L.R. n. 30 del 03/11/1993, in copia conforme all'originale, è stata pubblicata in formato digitale all'albo informatico dell'Azienda Ospedaliera Universitaria Policlinico a decorrere dal giorno 03/04/2023 e che nei 15 giorni successivi:

- ☐ non sono pervenute opposizioni
- ☐ sono pervenute opposizioni da _____

Il Funzionario Responsabile

Notificata al Collegio Sindacale il _____

DELIBERA NON SOGGETTA AL CONTROLLO

☒ Delibera non soggetta al controllo , ai sensi dell'art. 4, comma 8 della L. n. 412/1991 e divenuta :

ESECUTIVA

☐ Decorso il termine (10 giorni dalla data di pubblicazione ai sensi dell'art. 53, comma 6, L.R. n. 30/93

☐ Delibera non soggetta al controllo, ai sensi dell'art. 4 comma 8, della L. n. 412/1991 e divenuta:

IMMEDIATAMENTE ESECUTIVA

Ai sensi dell'art. 53, comma 7, L.R. 30/93

Il Funzionario Responsabile

ESTREMI RISCONTRO TUTORIO

☐ Delibera trasmessa, ai sensi della L.R. n. 5/09, all'Assessorato Regionale Salute in data _____ prot. n. _____

SI ATTESTA

Che l'Assessorato Regionale Salute, esaminata la presente deliberazione:

☐ Ha pronunciato l'approvazione con atto prot. n. _____ del _____ come da allegato

☐ Ha pronunciato l'annullamento con atto prot. n. _____ del _____ come da allegato

☐ Delibera divenuta esecutiva con decorrenza del termine previsto dall'art. 16 della L. R. n. 5/09 dal _____

Il Funzionario Responsabile

Stamp duty is paid electronically by ICON HOLDINGS CLINICAL RESEARCH INTERNATIONAL LIMITED, with registered office in Via Benigno Crespi 19, 20159 Milan, Italy, Italian affiliate of the CRO, pursuant to art. 15 of the Presidential Decree (D.P.R.) 642 of 1972 (Authorization of the Revenue Agency of Milan registered on 14-June-2023 on the OFFICIAL REGISTER with number 203622).	*Imposta di bollo assolta in modo virtuale ICON HOLDINGS CLINICAL RESEARCH INTERNATIONAL LIMITED, con sede legale in Via Benigno Crespi 19, 20159 Milano, Italia, affiliata italiana della CRO, ex art. 15 del D.P.R. 642 del 1972 (Autorizzazione Agenzia delle Entrate di Milano protocollata in data 14-June-2023 sul REGISTRO UFFICIALE con il numero 203622).*
CONTRACT AMENDMENT #1	**EMENDAMENTO NO. 1 AL CONTRATTO**
This **CONTRACT AMENDMENT #1** ("Contract Amendment #1"), dated as of the date of the Last Signature below (the "**Contract Amendment #1 Effective Date**"), is by and between	Il presente **EMENDAMENTO #1 AL CONTRATTO** ("Emendamento No. 1") datato alla data dell'ultima firma sotto riportata (la ''**Data di Efficacia dell'Emendamento #1 al Contratto**''), da e tra
ICON Holdings Clinical Research International Limited" – Italian Branch (Sede Secondaria), with a place of business at Via Benigno Crespi, Maciachini Business Park, no. 19, 20159 Milano, Italy, tax code and VAT no. 12827880969, through its Proxy Gabriella Laurora as Director of Clinical Team Management, (hereinafter the "**CRO**"), acting in its own name and in the interests of **Inventiva S.A.**, located at 50 rue de Dijon, 21121 Daix, France (hereinafter the "Sponsor"), by virtue of the authority of attorney granted on July 19th, 2023	**ICON Holdings Clinical Research International Limited"** – Filiale Italiana (Sede Secondaria), con sede operativa in Via Benigno Crespi, Maciachini Business Park, n. 19, 20159 Milano, Italia, C.F. e P.IVA 12827880969, in persona della Procuratrice Gabriella Laurora in qualità di Director of Clinical Team Management, (d'ora innanzi denominato/a "**CRO**"), che agisce in nome proprio e nell'interesse di **Inventiva S.A.**, avente sede legale al 50 rue de Dijon, 21121 Daix, France (d'ora innanzi denominato/a "Promotore"), in forza di idonea delega conferita in data 19 luglio 2023
and	e

AZIENDA OSPEDALIERA UNIVERSITARIA POLICLINICO "PAOLO GIACCONE" DI PALERMO ["Paolo Giaccone" University Hospital Polyclinic of Palermo] (hereinafter referred to as "Institution"), with registered office in PALERMO, Via del Vespro 129 Tax Code and VAT No. 05841790826, represented by its Legal Representative, Dr. Maurizio Montalbano, who possesses the appropriate powers to sign this document hereinafter individually/collectively "the Party/the Parties"	**AZIENDA OSPEDALIERA UNIVERSITARIA POLICLINICO "PAOLO GIACCONE" DI PALERMO** (d'ora innanzi denominato/a"Ente"), con sede legale in PALERMO Via del Vespro 129 C.F. e P. IVA n. 05841790826, in persona del Legale Rappresentante, Dr. Maurizio Montalbano, munito di idonei poteri di firma del presente atto di seguito, individualmente/collettivamente, "la Parte/le Parti".
W I T N E S S E T H:	**SI ATTESTA:**
WHEREAS, under the terms of a certain Clinical Trial Agreement, dated January 26th, 2023 (the "Agreement") between and among the parties, ICON Italy retained the Institution, under the responsibility of Prof. Salvatore Petta (the "Principal Investigator") to perform the research study entitled "*A randomised, double-blind, placebo-controlled, multicentre, Phase 3 study evaluating long term efficacy and safety of lanifibranor in adult patients with non-cirrhotic non-alcoholic steatohepatitis (NASH) and fibrosis 2 (F2)/fibrosis 3 (F3) stage of liver fibrosis*" (the "Study"), bearing protocol number **337HNAS20011** version no. 1.0 of April 12th , 2021 as amended (the "Protocol") sponsored	**PREMESSO CHE,** in base ai termini di un certo Contratto di Sperimentazione Clinica, datato 26 gennaio 2023 (il "Contratto") tra le parti, ICON Italia ha incaricato l'Ente, sotto la responsabilità del Prof. Salvatore Petta (di seguito "Sperimentatore Principale") di eseguire lo studio di ricerca intitolato "*Studio multicentrico di fase 3, randomizzato, in doppio cieco, controllato con placebo, volto a valutare l'efficacia e la sicurezza a lungo termine di lanifibranor in pazienti adulti con steatoepatite non alcolica e non cirrotic* (NASH) *e fibrosi epatica di stadio 2 (F2)/di stadio 3 (F3)"* (di seguito la "Sperimentazione"), recante il numero di protocollo **337HNAS20011** versione 1.0 del

by the **Inventiva S.A.** (the "Sponsor"), as more particularly described in the Agreement;	12 aprile 2021 e suoi successivi emendamenti debitamente approvati, (il "Protocollo"), sponsorizzato da **Inventiva S.A.** (il "Promotore"), come descritto più dettagliatamente nel Contratto;
WHEREAS, ICON Italy has been engaged by Sponsor to arrange, monitor, oversee and perform, or have performed, the Study pursuant to the Protocol by the Institution, and	**CONSIDERANDO** che ICON Italia è stata incaricata dal Promotore di organizzare, monitorare, supervisionare ed eseguire, o far eseguire dall'Ente lo Studio ai sensi del Protocollo, e
WHEREAS, the parties hereto have entered into certain additional agreements with respect to modification of the Agreement, and which they desire to memorialize in this Contract Amendment #1;	**CONSIDERANDO** che le parti hanno stipulato alcuni accordi aggiuntivi relativi alla modifica dell'Accordo, che desiderano definire nel presente Emendamento n. 1 del Contratto;
NOW, THEREFORE, in consideration of the premises and of the following mutual promises, covenants and conditions hereinafter set forth, the parties hereto agree as follows:	**ORA, PERTANTO**, in considerazione delle premesse e delle seguenti promesse, patti e condizioni reciproche di seguito esposte, le parti convengono quanto segue:
1. Update to Budget. To account for changes to the services and costs under the Agreement due to Protocol Amendment 4.0 (dated 11-Jan-2023), the parties agree that the Budget attached to the Agreement as **Annex A** is hereby deleted and replaced in its entirety by the revised Budget attached hereto as **Amended Annex A – Amended Budget**	**1. Aggiornamento del budget.** Per tener conto delle modifiche apportate ai servizi e ai costi previsti dal Contratto in seguito all'Emendamento 4.0 del Protocollo (datato 11 gennaio 2023), le parti convengono che il Budget allegato al Contratto come **Allegato A** viene eliminato e sostituito nella sua interezza dal Budget rivisto allegato al presente documento come **Allegato A modificato – Budget modificato.**
2. Update to Protocol Title. Effective as of the Protocol Amendment 4.0 effective date, all references to the protocol title are hereby deleted and replaced in its entirety by "A randomized, double-blind, placebo-controlled, multicentre, Phase 3 study evaluating efficacy and safety of lanifibranor followed by an active treatment extension in adult patients with non-cirrhotic non-alcoholic	**2. Aggiornamento del titolo del Protocollo**. Con effetto dalla data di entrata in vigore dell'emendamento al protocollo 4.0, tutti i riferimenti al titolo del protocollo sono cancellati e sostituiti nella sua interezza da "Uno studio di fase 3 randomizzato, in doppio cieco, controllato con placebo, multicentrico, che valuta l'efficacia e la sicurezza di lanifibranor seguito da un'estensione del

steatohepatitis (NASH) and fibrosis 2 (F2)/fibrosis 3 (F3) stage of liver fibrosis"	trattamento attivo in pazienti adulti con steatoepatite non alcolica non cirrotica (NASH) e stadio fibrosi 2 (F2)/fibrosi 3 (F3) della fibrosi epatica"
3. Transfer from PRA to ICON. Effective 30 June 2023 as part of the business transfer all rights, title, interest and benefit in and relating to the Agreement between the Site and Pharmaceutical Research Associates Italy s.r.l. ("PRA"), which is currently in force will be assigned and transferred from PRA to ICON Italy with a business address at Via Benigno Crespi, Maciachini Business Park n. 19, 20159, Milan, Italy, with Tax Code/VAT: 12827880969. This is primarily an administrative change of legal entity and the Agreements shall continue on existing terms in all other respects. Effective as of 30 June 2023 all references to PRA should now read as ICON Italy.	**3. Trasferimento da PRA a ICON**. A partire dal 30 giugno 2023, nell'ambito del trasferimento aziendale, tutti i diritti, titoli, interessi e benefici relativi al Contratto tra il Centro e Pharmaceutical Research Associates Italy s.r.l. ("PRA"), attualmente in vigore saranno assegnati e trasferiti da PRA a ICON Italia con sede legale in Via Benigno Crespi, Parco Maciachini n. 19, 20159, Milano, Italia, con C.F./P.IVA: 12827880969. Si tratta principalmente di un cambiamento amministrativo di persona giuridica e per tutti gli altri aspetti i Contratti continueranno alle condizioni esistenti. A partire dal 30 giugno 2023 tutti i riferimenti a PRA dovranno ora intendersi riferiti ad ICON Italia.
4. Ratification of Balance of Agreement. In all other respects, the terms of the Agreement are hereby ratified and affirmed by each of the parties hereto.	**4. Ratifica del saldo dell'Accordo.** Per tutti gli altri aspetti, i termini del Contratto sono ratificati e affermati da ciascuna delle parti.
5. Headings. The headings in this Contract Amendment #1 are for convenience of reference only and shall not affect its interpretation.	**5. Titoli.** I titoli del presente Emendamento al Contratto #1 sono solo per comodità di riferimento e non influiscono sulla sua interpretazione.
6. Counterparts. This Contract Amendment #1 will be signed digitally pursuant to current regulations. The taxes and fees inherent in and consequent to the conclusion of this contract, including the stamp tax on the computer original referred to in Article 2 of the table in Annex A - Tariff Part I of Presidential Decree No. 642/1972 and the registration tax shall be paid, in accordance with applicable regulations.	**6. Controparti.** Il presente Emendamento al Contratto n. 1 sarà firmato digitalmente ai sensi della normativa vigente. Le imposte e tasse inerenti e conseguenti alla stipula del presente Contratto, ivi comprese l'imposta di bollo sull'originale informatico di cui all'art. 2 della tabella nell'Allegato A – Tariffa Parte I del DPR n. 642/1972 e l'imposta di registro devono essere versate nel rispetto della normativa applicabile.
IN WITNESS WHEREOF, the parties hereto, each by a duly authorized	**IN FEDE DI CIO',** le parti, ciascuna per mezzo di un rappresentante debitamente

representative, have executed this Contract Amendment #1 as of the Contract Amendment #1 Effective Date.	autorizzato, hanno sottoscritto il presente Emendamento al Contratto n#1 alla Data di entrata in vigore dell'Emendamento al Contratto #1.

For the CRO / Per la CRO

The Proxy/La Procuratrice

Dr/Dott.ssa Gabriella Laurora Gabriella Maria Laurora Firmato il 03-08-2023

Signature / Firma _____, ___/ ____/ ____

For the Entity / Per l'Ente

The Legal Rappresentative/ Il Legale Rappresentante

Dr/Dott. Dr. Maurizio Montalbano

Firmato digitalmente da:
Maurizio Montalbano
Data: 30/08/2023 13:34:04

Signature /Firma _____, ___/____/_____

Amended ANNEX A – Amended Budget	ALLEGATO A MODIFICATO – BUDGET MODIFICATO

Trial Information

Trial Name: Inventiva_IVPF2F3F-F2F3LF
Project: IVPF2F3F-F2F3LF
Protocol Number: 337HNAS20011 (NATiV3)
Protocol Version: V 4.0, dated 11-Jan-2023
Phase: III
Title: A randomised, double-blind, placebo-controlled, multicentre, Phase 3 study evaluating efficacy and safety of lanifibranor followed by an active treatment extension in adult patients with non-cirrhotic non-alcoholic steatohepatitis (NASH) and fibrosis 2 (F2)/fibrosis 3 (F3) stage of liver fibrosis
Arm: Main study

Location: Italy
Currency: EUR - Euro
Total Cost per Patient Main study: 9,994.00

PI Name: Salvatore Petta
Site Name: Azienda Ospedaliera Universitaria
Overhead Percent: 0.00%

Procedure Name	Selected Cost	Screening	Baseline	W4	W12	W24	W36	W48	Phone Visit, W50	W72	Phone visits (W84, W108)	W96	Site Visit (End of DBPC period - Maximum Week 120)	4 weeks after LV Part A	12 weeks after LV Part A	24 weeks after LV Part A	Phone visit 36 weeks after LV Part A	48 weeks after LV Part A	pEoT	Follow-up (4 weeks after last dose of study drug)
Informed consent, Main study	27,00	27,00						*		*										
Randomisation	20,00		20,00								Invoice									
Alcohol intake and Smoking habits	15,00								15,00		15,00									
Eligibility criteria	25,00	25,00	25,00																	
Concomitant medications	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00
Dietary and lifestyle monitoring	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	
Adverse events and Adverse events of special interest	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00	20,00
Drug accountability	12,00			12,00	12,00	12,00	12,00	12,00	12,00	12,00	12,00	12,00	12,00	12,00	12,00	12,00	12,00	12,00	12,00	
Initial Physical Exam, includes Demographics, Alcohol intake & smoking habits Medical and disease history, COVID-19 History/Symptoms, Vital signs	103,00	103,00																		
Follow-up Physical Exam, includes Alcohol intake & smoking habits, Vital signs, and monthly body weight measurements as applicable	75,00		75,00	75,00	75,00	75,00	75,00	75,00		75,00		75,00	75,00	75,00	75,00	75,00		75,00	75,00	75,00
ECG (singular or triplicate)	75,00	75,00				75,00		75,00		75,00			75,00					75,00	75,00	75,00
Blood draw for Central Lab**	30,00	30,00	30,00	30,00	30,00	30,00	30,00	30,00		30,00		30,00	30,00	30,00	30,00	30,00		30,00	30,00	30,00
Central: Venipuncture for Biomarkers and PK and/or Gene sampling, if applicable	30,00	30,00	30,00	30,00	30,00	30,00	30,00	30,00		30,00		30,00	30,00			30,00		30,00	30,00	
Central: Venipuncture for PK, Optional	30,00			Invoice x6	Invoice x5	Invoice x6	Invoice x7	Invoice x5												
Central: Urinalysis, includes Urinary ethyl glucuronide	6,00	6,00	6,00			6,00		6,00		6,00		6,00	6,00			6,00		6,00	6,00	6,00
Sample Handling and Shipping to Central lab	15,00	15,00	15,00	15,00	15,00	15,00	15,00	15,00		15,00		15,00	15,00						15,00	15,00
Liver biopsy (fresh)	1,041,00	Invoice								Invoice									Invoice	
Biopsy Sample Handling/Shipping	304,00	Invoice								Invoice									Invoice	
Historical Biopsy Sample Handling/Shipping	304,00	Invoice																		
Elastography and CAP***	65,00	65,00	65,00			65,00		65,00		65,00		65,00	65,00			65,00		65,00	65,00	
Patient training on mobile app	37,00		37,00																	
Site review/confirmation of PRO entry in mobile app	26,00		26,00			26,00		26,00		26,00			26,00						26,00	
Dexa Scan for optional sub-study	208,00		Invoice	Invoice						Invoice			Invoice							
cT1	87,00	Invoice								87,00										
MRI-PDFF	87,00	Invoice								87,00										
NASH-CLDQ	21,00		21,00			21,00		21,00		21,00			21,00			21,00		21,00	21,00	
SF-36	23,00		23,00			23,00		23,00		23,00			23,00			23,00		23,00	23,00	
WPAI	12,00		12,00			12,00		12,00		12,00			12,00			12,00		12,00	12,00	
Per Patient Activity Totals:		436,00	445,00	222,00	222,00	450,00	222,00	450,00	87,00	624,00	87,00	293,00	450,00	177,00	177,00	334,00	72,00	409,00	450,00	241,00

Non-Procedure Name	Selected Cost	Screening	Baseline	W4	W12	W24	W36	W48	Phone Visit, W50	W72	Phone visits (W84, W108)	W96	Site Visit (End of DBPC period - Maximum Week 120)	4 weeks after LV Part A	12 weeks after LV Part A	24 weeks after LV Part A	Phone visit 36 weeks after LV Part A	48 weeks after LV Part A	pEoT	Follow-up (4 weeks after last dose of study drug)
Day Bed fee	237,00	Invoice		Invoice	Invoice	Invoice	Invoice	Invoice		Invoice									Invoice	
Dispensing study drug	20,00		20,00	20,00	20,00	20,00	20,00	20,00		20,00		20,00	20,00	20,00	20,00	20,00				
Physician fee	69,00	69,00	69,00	69,00	69,00	69,00	69,00	69,00	17,25	69,00	17,25	69,00	69,00	69,00	69,00	69,00	17,25	69,00	69,00	69,00
Study Coordinator fee	118,00	118,00	118,00	118,00	118,00	118,00	118,00	118,00	59,00	118,00	59,00	118,00	118,00	118,00	118,00	118,00	59,00	118,00	118,00	118,00
Data Entry	29,00	29,00	29,00	29,00	29,00	29,00	29,00	29,00	14,50	29,00	14,50	29,00	29,00	29,00	29,00	29,00	14,50	29,00	29,00	29,00
Per Patient Other Direct Cost Totals:		216,00	236,00	236,00	236,00	236,00	236,00	236,00	90,75	236,00	90,75	236,00	236,00	236,00	236,00	236,00	90,75	216,00	216,00	216,00

	Screening	Baseline	W4	W12	W24	W36	W48	Phone Visit, W50	W72	Phone visits (W84, W108)	W96	Site Visit (End of DBPC period - Maximum Week 120)	4 weeks after LV Part A	12 weeks after LV Part A	24 weeks after LV Part A	Phone visit 36 weeks after LV Part A	48 weeks after LV Part A	pEoT	Follow-up (4 weeks after last dose of study drug)
Visit Cost Subtotal	652,00	681,00	458,00	458,00	686,00	458,00	686,00	177,75	860,00	177,75	529,00	686,00	413,00	413,00	570,00	162,75	625,00	666,00	457,00
Overhead at 0%	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Total Cost Per Visit	**652,00**	**681,00**	**458,00**	**458,00**	**686,00**	**458,00**	**686,00**	**177,75**	**860,00**	**177,75**	**529,00**	**686,00**	**413,00**	**413,00**	**570,00**	**162,75**	**625,00**	**666,00**	**457,00**
Visit Quantity	1,00	1,00	1,00	1,00	1,00	1,00	1,00	1,00	1,00	2,00	1,00	1,00	1,00	1,00	1,00	1,00	1,00	1,00	1,00
Cumulative Visit Cost	652,00	681,00	458,00	458,00	686,00	458,00	686,00	177,75	860,00	355,50	529,00	686,00	413,00	413,00	570,00	162,75	625,00	666,00	457,00
Total Cost per Patient Main study:	**9,994,00**																			

**Safety Labs for Central lab includes: Serology, Complete Blood count, Liver function, Biochemistry, Renal function, Coagulation, Glycemic metabolism, Other glycemic metabolism, Adiponectin, Lipid metabolism, Other lipid metabolism, Cardiac test NT-ProBNP, Fructosamine and Leptin. For additional detail, refer to Protocol section 1.3, footnotes 10-20.

***Controlled attenuation parameter (CAP) will be quantified by FibroScan® (only if available).

Invoiceable Name	Selected Cost	Overhead at 0%	Total Cost	Considerations
Local: COVID-19 test (infectious agent detection by DNA/RNA)	90.00	0.00	90.00	Upon receipt of detailed invoice; test may be performed at any time per Investigator's discretion
Informed Consent: Dexa scan sub-study	27.00	0.00	27.00	Upon receipt of detailed invoice for patients participating in the Dexa scan sub-study
Dexa Scan for optional sub-study	208.00	0.00	208.00	Upon receipt of detailed invoice, only for participates who consent to the Dexa scan sub-study, at Baseline and Weeks 4, 72 and 120
Informed Consent: Genetic testing	55.00	0.00	55.00	Upon receipt of detailed invoice as applicable
Informed Consent for female partners of male patients	27.00	0.00	27.00	Upon receipt of detailed invoice as applicable
ECG (singular or triplicate)	75.00	0.00	75.00	Upon receipt of detailed invoice if repeat assessment is required per protocol. Triplicate ECGs at arrival (fasting), breakfast in the investigational site with study treatment intake, triplicate ECGs 3 to 5 hours after breakfast.
Blood draw for Central Lab**	30.00	0.00	30.00	Upon receipt of detailed invoice if repeat assessment is required at the investigators discretion if medically necessary and in consultation with the Medical Monitor
Central: Venipuncture for PK, Biomarkers and/or Gene sampling	30.00	0.00	30.00	
Central: Urinalysis, includes Urinary ethyl glucuronide, Urine Pregnancy	6.00	0.00	6.00	
Sample Handling and Shipping to Central lab	15.00	0.00	15.00	Upon receipt of invoice if repeat serum and/or urine samples for central lab is required
Central: Venipuncture for PK, Optional	30.00	0.00	30.00	Upon receipt of detailed invoice, for patients who have consented to the optional PK sub-study, at Week 4, 12, 24, 36 OR 48, per the timepoint indicated in the visit grid for the applicable visit
Local: Chemistry Panel, includes ALT, AST, GGT, ALP, total and direct Bilirubin, Sodium Chloride, Potassium, Bicarbonate, Creatinine, Albumin	20.00	0.00	20.00	Upon receipt of detailed invoice at Investigator's discretion and/or in cases where initiation of IMP or safety follow-up is time-sensitive and the central laboratory results will not be available in time
Local: Liver Function Panel, includes ALT, AST GGT, ALP, total and direct Bilirubin	68.00	0.00	68.00	
Local: Renal Function Panel, includes Albumin, Chloride, Creatinine, Glucose, Potassium, Sodium chloride, Urea	41.00	0.00	41.00	
Local: Lipid Profile, includes Triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol	40.00	0.00	40.00	
Local: Other lipid metabolism tests, includes Apo A1, Apo B, total Apo C3, Apo C3 in LDL, Apo C3 in VLDL, Apo C3 in HDL	152.00	0.00	152.00	
Local: Fructosamine	65.00	0.00	65.00	
Local: Adiponectin	77.00	0.00	77.00	
Local: Leptin	77.00	0.00	77.00	
Local: Albumin	7.00	0.00	7.00	
Local: ALP	4.00	0.00	4.00	
Local: ALT	4.00	0.00	4.00	
Local: AST	4.00	0.00	4.00	
Local: Bicarbonate	17.00	0.00	17.00	
Local: Bilirubin, Direct	13.00	0.00	13.00	
Local: Bilirubin, Total	5.00	0.00	5.00	
Local: Chloride	4.00	0.00	4.00	
Local: Cholesterol, High Density	29.00	0.00	29.00	
Local: Density Cholesterol, High	37.00	0.00	37.00	
Local: Cholesterol, Total	17.00	0.00	17.00	
Local: Coagulation, APTT	7.00	0.00	7.00	
Local: Coagulation, INR	7.00	0.00	7.00	
Local: Complete blood count	20.00	0.00	20.00	
Local: CPK	26.00	0.00	26.00	
Local: Creatinine	2.00	0.00	2.00	
Local: eGFR	10.00	0.00	10.00	
Local: FPG (glycemic metabolism)	4.00	0.00	4.00	
Local: GGT	4.00	0.00	4.00	
Local: HbA1c (glycemic metabolism)	18.00	0.00	18.00	
Local: HBV (HBsAg)	24.00	0.00	24.00	
Local: HCV (HCV antibodies)	58.00	0.00	58.00	
Local: HCV RNA	490.00	0.00	490.00	
Local: HIV-1 and HIV-2, single assay	90.00	0.00	90.00	
Local: HOMA-IR (other glycemic metabolism)	311.00	0.00	311.00	
Local: Insulin (other glycemic metabolism)	23.00	0.00	23.00	
Local: Potassium	1.00	0.00	1.00	
Local: Sodium chloride	10.00	0.00	10.00	
Local: Triglycerides	16.00	0.00	16.00	
Local: Urea	4.00	0.00	4.00	
Local: Cardiac test, NT-ProBNP	35.00	0.00	35.00	
Local: Pregnancy, Serum, WOCBP	13.00	0.00	13.00	
Local: Pregnancy, Urine, WOCBP	8.00	0.00	8.00	
Liver biopsy (fresh)	1,043.00	0.00	1,043.00	Upon receipt of detailed invoice if fresh biopsy is required at Screening and/or if a repeat biopsy is required due to increased liver stiffness compared to Baseline. Also, at EOT and/or EOS unless there is previous confirmation of progression to F4, any liver outcome event or an available biopsy within the past 6 months prior. If there is no historical biopsy available at screening, it is recommended to not perform a liver biopsy in patients with low liver stiffness (i.e. FibroScan value<6kPa or other value if elastography performed with another tool) and AST/ULN<0.65.
Biopsy Sample Handling/Shipping	304.00	0.00	304.00	Upon receipt of detailed invoice if Fresh Biopsy is required at Screening, EOT and/or EOS
Historical Biopsy Sample Handling/Shipping	304.00	0.00	304.00	Upon receipt of detailed invoice at Screening if historical biopsy is available (historical biopsy must have been performed within 6 months of Screening). Upon receipt of detailed invoice at additional necessary visits according to the Protocol.
Anesthesia	651.00	0.00	651.00	Upon receipt of detailed invoice if required for Fresh Biopsy
CT Guidance for Needle Placement	531.00	0.00	531.00	Upon receipt of detailed invoice if required for Fresh Biopsy
Day Bed fee	237.00	0.00	237.00	Upon receipt of invoice if required for fresh biopsy at Screening and/or EOT/EOS. And at the applicable visit requiring extensive PK draws for the PK sub-study
FibroScan (or equivalent elastography exam approved by Inventiva)	65.00	0.00	65.00	Upon receipt of detailed invoice if repeat scan is required due to progression of cirrhosis
Unscheduled / Additional Phone Visit	20.00	0.00	20.00	Upon receipt of detailed invoice
Follow-up Patient training on mobile app	37.00	0.00	37.00	Upon receipt of detailed invoice if follow-up app training is required after Baseline
Mobile Device Dispense	29.00	0.00	29.00	Upon receipt of detailed invoice at Baseline for patients requiring a device for the app
Mobile Device Collection	18.00	0.00	18.00	Upon receipt of detailed invoice as patient returns device
Pharmacy Dispense	20.00	0.00	20.00	Upon receipt of detailed invoice for study drug replacement if patient's supply is lost, damaged or destroyed
Patient Meals: breakfast, per person	13.00	n/a	13.00	Upon receipt of detailed invoice with supporting documentation, up to the amount indicated. This applies if breakfast is not provided by site on the day of a study visit, applicable per visit requiring patient to fast, and for patients who are required to stay overnight due to long distance travel
Patient Meals: Lunch and/or Dinner, per person	26.00	n/a	26.00	Upon receipt of detailed invoice with supporting documentation, up to the amount indicated. This applies if patient is required to stay on-site during lunch hours and is not provided a meal by site, applicable per visit requiring patient to fast, and for patients who are required to stay overnight due to long distance travel
Patient Travel Reimbursement, includes: mileage, parking, uber/taxi, tolls, etc.	19.00	n/a	19.00	Upon receipt of detailed invoice with supporting documentation, up to the amount indicated.
Hotel	131.00	n/a	131.00	Upon receipt of detailed invoice and supporting documentation, up to the amount indicated, if applicable, only for patients participating in the ECG sub-study and/or PK sub-study
Hospitalization, includes meals	461.00	0.00	461.00	Upon receipt of detailed invoice for patient required overnight hospital stay for the ECG sub-study
Breakfast and/or Refreshments reimbursement to site	At cost			Upon receipt of detailed invoice with supporting documentation for fault breakfast/refreshments purchased to provide to patients who are required to fast for the ECG sub-study and/or the PK sub-study
Screen Failures (exclud. Biopsy)	489.00	0.00	489.00	Upon receipt of detailed invoice. Biopsy, if provided, will be invoiced based on archival or fresh, and in accordance to the cost provided in the invoiceable section.
Compensation for Time loss - biopsy	250.00	0.00	250.00	Upon receipt of detailed invoice. As needed.
Purchase of EtG Kits	At Cost			EtG kits purchase to be reimbursed at real cost upon presentation of a valid invoice
Randomisation	20.00	0.00	20.00	Upon receipt of detailed invoice. As applicable per protocol.
cT1	87.00	0.00	87.00	At screening, historical cT1 and MRI-PDFF assessed by LiverMultiScan®, i.e. performed before screening and for less than 7 months before randomisation will be retrieved. At Week 72,
MRI-PDFF	87.00	0.00	87.00	patients in a fasted state of at least 2 hours will undergo cT1 and MRI-PDFF measures.
Lunch & learn	At Cost			Upon receipt of detailed invoice. As necessary.
Pre-screening activities	1,500.00			Upon receipt of detailed invoice. As applicable.
	0.00	0.00	0.00	

Site Administrative Fee Name	Total Cost	Frequency	Considerations
Site Start-up	1,495.00	1	Upon receipt of detailed invoice
Archiving/Document storage	400.00	1	Upon receipt of detailed invoice
Pharmacy Start-up	500.00	1	Upon receipt of detailed invoice

Screening Failure(s)	Upon receipt of detailed invoice at the flat rate detailed in the invoiceable section. Biopsy, if provided, will be invoiced based on archival or fresh, and in accordance to the cost provided in the invoiceable section.
Unscheduled Visit(s)	Upon receipt of detailed invoice for procedures performed according to the protocol

Maximum Number of Screening Failures	Screen Failure payments must not exceed 8 per each randomized patient. Such maximum number may be increased with the written approval of Sponsor; the written approved increase will not require an amendment to this Agreement.

Trial Information

Trial Name: Inventiva_IVPF2F3F-F2F3LF
Project: IVPF2F3F-F2F3LF
Protocol Number: 337HNAS20011 (NATiV3)
Protocol Version: V 4.0, dated 11-Jan-2023
Phase: III
Title: A randomised, double-blind, placebo-controlled, multicentre, Phase 3 study evaluating efficacy and safety of lanifibranor followed by an active treatment extension in adult patients with non-cirrhotic non-alcoholic steatohepatitis (NASH) and fibrosis 2 (F2)/fibrosis 3 (F3) stage of liver fibrosis
Arm: ECG Sub-study

Location: Italy
Currency: EUR - Euro
Total Cost Per Patient ECG Sub-study: **10,324.00**

PI Name: Salvatore Petta
Site Name: Azienda Ospedaliera
Overhead Percent: 0.00%

Procedure Name	Selected Cost	Screening	Baseline	W4	W12	W24	W36	W48	Phone Visit, W60	W72	Phone visits (W84, W108)	W96	Site Visit (End of DBPC period - Maximum Week 120)	4 weeks after LV Part A	12 weeks after LV Part A	24 weeks after LV Part A	Phone visit 36 weeks after LV Part A	48 weeks after LV Part A	pEoT	Follow-up (4 weeks after last dose of study drug)
Informed consent, Main study & ECG sub-study	27.00	27.00						*		*										
Randomisation	20.00		20.00								Invoice									
Alcohol intake and Smoking habits	15.00								15.00		15.00									
Eligibility criteria	25.00	25.00	25.00																	
Concomitant medications	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00
Dietary and lifestyle monitoring	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	
Adverse events and Adverse events of special interest	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00
Drug accountability	12.00			12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	
Initial Physical Exam, includes Demographics, Alcohol intake & smoking habits Medical and disease history, COVID-19 History/Symptoms, Vital signs	103.00	103.00																		
Follow-up Physical Exam, includes Alcohol intake & smoking habits, Vital signs, and monthly body weight measurements as applicable	75.00		75.00	75.00	75.00	75.00	75.00	75.00		75.00		75.00	75.00	75.00	75.00	75.00		75.00	75.00	75.00
ECG (singular or triplicate)	75.00	75.00		75.00	75.00	75.00		75.00		75.00			75.00					75.00	75.00	75.00
Blood draw for Central Lab**	30.00	30.00	30.00	30.00	30.00	30.00	30.00	30.00		30.00		30.00	30.00	30.00	30.00	30.00		30.00	30.00	30.00
Central: Venipuncture for PK, Biomarkers, Gene sampling (if applicable)	30.00	30.00	30.00	120.00	120.00	30.00	30.00	30.00		30.00		30.00	30.00			30.00		30.00	30.00	
Central: Urinalysis, includes Urinary ethyl glucuronide, Urine Pregnancy	6.00	6.00	6.00			6.00		6.00		6.00		6.00	6.00			6.00		6.00	6.00	6.00
Sample Handling and Shipping to Central lab	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00		15.00		15.00	15.00						15.00	15.00
Liver biopsy (fresh)	1,043.00	Invoice								Invoice									Invoice	
Biopsy Sample Handling/Shipping	304.00	Invoice								Invoice									Invoice	
Historical Biopsy Sample Handling/Shipping	304.00	Invoice																		
Elastography and CAP***	65.00	65.00	65.00			65.00		65.00		65.00		65.00	65.00			65.00		65.00	65.00	
Patient training on mobile app	37.00		37.00																	
Site review/confirmation of PRO entry in mobile app	26.00		26.00			26.00		26.00		26.00			26.00						26.00	
Dexa Scan for optional sub-study	208.00		Invoice	Invoice						Invoice			Invoice							
cT1	87.00	Invoice								87.00										
MRI-PDFF	87.00	Invoice								87.00										
NASH-CLDQ	21.00		21.00			21.00		21.00		21.00			21.00			21.00		21.00	21.00	
SF-36	23.00		23.00			23.00		23.00		23.00			23.00			23.00		23.00	23.00	
WPAI	12.00		12.00			12.00		12.00		12.00			12.00			12.00		12.00	12.00	
Per Patient Activity Totals:		436.00	445.00	387.00	387.00	450.00	222.00	450.00	87.00	624.00	87.00	293.00	450.00	177.00	177.00	334.00	72.00	409.00	450.00	241.00

Non-Procedure Name	Selected Cost	Screening	Baseline	W4	W12	W24	W36	W48	Phone Visit, W60	W72	Phone visits (W84, W108)	W96	Site Visit (End of DBPC period - Maximum Week 120)	4 weeks after LV Part A	12 weeks after LV Part A	24 weeks after LV Part A	Phone visit 36 weeks after LV Part A	48 weeks after LV Part A	pEoT	Follow-up (4 weeks after last dose of study drug)
Hospitalization, includes meals	461.00			Invoice	Invoice															
Day Bed fee	237.00	Invoice		Invoice	Invoice	Invoice	Invoice	Invoice		Invoice									Invoice	
Dispensing study drug	20.00		20.00	20.00	20.00	20.00	20.00	20.00		20.00		20.00	20.00	20.00	20.00	20.00				
Physician fee	69.00	69.00	69.00	69.00	69.00	69.00	69.00	69.00	17.25	69.00	17.25	69.00	69.00	69.00	69.00	69.00	17.25	69.00	69.00	69.00
Study Coordinator fee	118.00	118.00	118.00	118.00	118.00	118.00	118.00	118.00	59.00	118.00	59.00	118.00	118.00	118.00	118.00	118.00	59.00	118.00	118.00	118.00
Data Entry	29.00	29.00	29.00	29.00	29.00	29.00	29.00	29.00	14.50	29.00	14.50	29.00	29.00	29.00	29.00	29.00	14.50	29.00	29.00	29.00
Per Patient Other Direct Cost Totals:		216.00	236.00	236.00	236.00	236.00	236.00	236.00	90.75	236.00	90.75	236.00	236.00	236.00	236.00	236.00	90.75	216.00	216.00	216.00

	Screening	Baseline	W4	W12	W24	W36	W48	Phone Visit, W60	W72	Phone visits (W84, W108)	W96	Site Visit (End of DBPC period - Maximum Week 120)	4 weeks after LV Part A	12 weeks after LV Part A	24 weeks after LV Part A	Phone visit 36 weeks after LV Part A	48 weeks after LV Part A	pEoT	Follow-up (4 weeks after last dose of study drug)
Visit Cost Subtotal	652.00	681.00	623.00	623.00	686.00	458.00	686.00	177.75	860.00	177.75	529.00	686.00	413.00	413.00	570.00	162.75	625.00	666.00	457.00
Overhead at 0%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Total Cost Per Visit	**652.00**	**681.00**	**623.00**	**623.00**	**686.00**	**458.00**	**686.00**	**177.75**	**860.00**	**177.75**	**529.00**	**686.00**	**413.00**	**413.00**	**570.00**	**162.75**	**625.00**	**666.00**	**457.00**
Visit Quantity	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	2.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Cumulative Visit Cost	652.00	681.00	623.00	623.00	686.00	458.00	686.00	177.75	860.00	355.50	529.00	686.00	413.00	413.00	570.00	162.75	625.00	666.00	457.00
Total Cost Per Patient ECG Sub-study:	**10,324.00**																		

**Safety Labs for Central lab includes: Serology, Complete Blood count, Liver function, Biochemistry, Renal function, Coagulation, Glycemic metabolism, Other glycemic metabolism, Adiponectin, Lipid metabolism, Other lipid metabolism, Cardiac test NT-ProBNP, Fructosamine and Leptin. For additional detail, refer to Protocol section 1.3, footnotes 10-20.
***Controlled attenuation parameter (CAP) will be quantified by FibroScan® (only if available).