AGREEMENT FOR THE PERFORMANCE OF THE TRIAL

Prophylactic oropharyngeal surfactant for preterm-infants: a randomized trial (POPART)

Project ID: 2016---004198---41

Coordinating Investigator:
[redacted]

INVOLVING

European Clinical Research Infrastructure Network (ECRIN-ERIC)
www.ecrin.org

Hereinafter referred to as "ECRIN"

and

Masaryk University, Brno, Czech Republic
Hereinafter referred to as "ECRIN PARTNER"

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THIS AGREEMENT IS MADE BY AND BETWEEN (hereinafter referred to as the **"Agreement"**):

European Clinical Research Infrastructure Network (ECRIN-ERIC), registered under SIRET n°801 933 235 00021, established in 5-7 rue Watt, 75013 Paris, France, represented by Prof. Dr. Jacques Demotes, Director General of ECRIN ERIC

Hereinafter referred to as **"ECRIN"**

AND

Masaryk University, whose registered office at Zerotinovo nam. 617/9, Brno 601 77, Czech Republic, ID number 00216224, VAT num.: CZ00216224

Represented by: prof. MUDr. Martin Bareš, Ph.D., the dean of **Faculty of Medicine,** contact address: Kamenice 5, Brno-Bohunice, 625 00, Czech Republic

Hereinafter referred to as **"ECRIN PARTNER"**

Hereinafter individually or collectively referred to as the "Party" or the "Parties".

WHEREAS

A clinical trial entitled **"Prophylactic oropharyngeal surfactant for preterm-infants: a randomized trial" (POPART)** (hereinafter referred to as the "Clinical trial") is to be conducted in different European countries pursuant to the protocol current version (hereinafter referred to as the "Protocol").

The Clinical trial is part of the work package 4 of the PedCRIN project which receives funding (as "transnational access") from the European Union Horizon H2020 Programme under Grant Agreement no. 731046.

The **University College Dublin, National University of Ireland, Dublin**, whose business address is at **Belfield, Dublin 4, Ireland,** is the Sponsor of the Clinical trial in the European Union (EU).

The Sponsor has delegated specified tasks to ECRIN, as stated in a separate Agreement signed by the Sponsor and ECRIN on July 16th, 2018.

ECRIN will perform the tasks delegated by the Sponsor in the different EU countries through subcontracting to its Partners as stated in the above-mentioned agreement.

Masaryk University (hereinafter referred to as ECRIN PARTNER), hereby agrees to undertake the tasks specified for ECRIN PARNER in the Tasks list (see appendix 1) according to the Protocol current version (see Appendix 3) subject to the terms and conditions of this Agreement.

The purpose of this Agreement (hereinafter referred to as the "Agreement") is:

- to state the tasks (hereinafter referred to as the Tasks) subcontracted by ECRIN to ECRIN PARTNER;
- in particular, to set forth the terms and conditions governing the performance of the Tasks in the **Czech Republic**

THEREFORE, IT IS HEREBY AGREED AS FOLLOWS:

1. PERFORMANCE OF CLINICAL TRIAL RELATED TASKS

The clinical trial-related tasks shall be conducted by the participating Parties:

1.1.1. in all respects in accordance with their respective roles and responsibilities as described in the present agreement and Tasks list (*see Appendix 1*)

1.1.2. in accordance with the protocol (*see Appendix 3*)

1.1.3. in accordance with the requirements laid down by laws and regulations applicable in the participating countries

1.1.4. Each Party has a duty to inform the other Party as soon as possible of any difficulties encountered in carrying out the Tasks assigned to it and which may compromise the objectives of the Clinical trial.

2. DUTIES

2.1. Obligations of ECRIN

2.1.1. ECRIN shall be responsible for the coordination of the Clinical Trial in the following countries: **Sweden, Italy, Czech Republic, Belgium, Norway, Portugal**

2.1.2. ECRIN shall centralize and transmit clinical trial-related documents and information from following countries **Sweden, Italy, Czech Republic, Belgium, Norway, Portugal** to the Sponsor or to any person authorized by the Sponsor for the completion of the Clinical trial as described in the aforementioned Tasks list.

2.1.3. ECRIN shall transfer to ECRIN PARTNER the monitoring manual and all documents necessary to perform the tasks

2.1.4. For the avoidance of doubt, ECRIN has no obligation to transfer to ECRIN PARTNER any data or information other than data and information strictly needed by ECRIN PARTNER for the performance of the Tasks assigned to ECRIN PARTNER

2.2. Obligations of ECRIN PARTNER

ECRIN PARTNER shall be responsible for carrying out its Tasks as described in the Tasks list (*see Appendix 1*). In particular, ECRIN PARTNER shall:

2.2.1. be responsible for applications to National Competent authorities, Ethics Committees and any relevant Authorities, in the Czech Republic

2.2.2. be responsible for monitoring of the Clinical trial in the trial sites in the concerning country according to the Monitoring Manual written and validated by the Sponsor

2.2.3. be responsible for the sending of SUSARs and Safety reports to National Competent authorities, Ethics Committees and any relevant Authorities, in the **Czech Republic**

2.2.4. is responsible for ensuring that the tasks related to the Monitoring as described in the Protocol current version and Monitoring Manual are fulfilled strictly in accordance with the terms of this Agreement, and all applicable international and national laws, regulations and guidelines, including without limitation, the Declaration of the Helsinki (latest updated version), "ICH Harmonised Tripartite Guideline, Guideline for Good Clinical Practice", the Directive on Clinical Trials (2001/20/EC) of the European Parliament and of the Council of 4 April 2001 and the EU GCP Directive 2005/28/EC.

2.2.5. for all work involving databases of personal data, electronic or otherwise, including but not limited to medical information and genetic information the ECRIN PARTNER shall fully comply with prevailing data protection provisions, in particular the EU Data Protection regulation (the GDPR) and any related law and regulations applicable in the participating countries.

In addition, ECRIN PARTNER represents and warrants to ECRIN that:

2.2.6. shall fulfill its obligations under this Agreement and during the term of this Agreement and will not enter into any agreement which would in any way prevent it from performing its Tasks under this Agreement.

2.2.7. has disclosed any existing relationship, which may adversely impact the execution of the Tasks.

2.2.8. has, and shall continue to have at its own expense for the duration of this Agreement, all of the authorizations required under any applicable laws and regulations to perform the work involved in performing the Tasks at its facilities

3. COST AND PAYMENTS

For the performance of the Tasks, both Parties agree on the costs, which are based on the assumptions described in **Appendix 2.**

The tasks for this Study are provided under the non-economic activity model according to the Framework agreement signed on 16.11.2016. ECRIN PARTNER shall charge price at the level of costs (including overheads) without profit.

The total price for the all Tasks described in Appendix 2 is 77 960 EUR excluding VAT. The Tasks are exempt from Value added tax, based on the Commission implementing decision of 29 November 2013 on setting up the European Clinical Research Infrastructure Network (ECRIN) as a European Research Infrastructure Consortium (ECRIN-ERIC) 2013/713/EU and article 151 (1)(b) of Council Directive 2006/112/EC.

The remuneration and payment is agreed on under presumption that 4 sites will be initiated in the Czech Republic. In case that more sites are initiated, the parties will enter into negotiation immediately regarding new payment schedule.

Payments will be made pro-rata for work completed. On a quarterly basis, ECRIN PARTNER shall submit original invoice and report summarizing the work completed to ECRIN at the address below. The clinical trials reference **POPART** should be mentioned on the invoice. Invoices for the work completed will be paid within thirty (30) days of receipt.

INVOICING DETAILS:
ECRIN
Attn: Alicja Szofer-Araya
5-7 RUE WATT
75013 PARIS - FRANCE
VAT N°: FR91 801933235

In the event of early termination of the Agreement, if payment (whether for salaries or otherwise) has been made by ECRIN to ECRIN PARTNER in advance for work not completed, funds received in advance at the exception of duly justified expenses already incurred by ECRIN PARTNER, shall be returned to ECRIN within thirty (30) days of the effective date of termination.

Misuse of funds, if discovered or suspected, will result in immediate suspension of the Tasks and reimbursement of the already received funds shall/may be expected.

4. CLINICAL TRIAL DATA& RESULTS

ECRIN PARTNER agrees not to make claims to possible intellectual property rights (the "IPR") from data and results obtained during the conduct of the Clinical Trial (hereinafter referred as to "Data" and "Results") and not to pursue IPR protection that would prevent or block access to or use of any data, conclusions drawn directly from those Data and Results.

5. CONFIDENTIALITY

For the purpose of this AGREEMENT, confidential information should include but not limited to any and all information related to the Clinical Trial which is disclosed by ECRIN to ECRIN PARTNER as a result of this AGREEMENT. (Hereinafter referred to as the "CONFIDENTIAL INFORMATION")

5.1. Confidentiality of Provided Information

5.1.1.1. ECRIN PARTNER hereby agrees that at all times during the term of this Agreement, ECRIN PARTNER with its professional staff, affiliates, independent consultants and any other cooperating partners, will hold and maintain in confidence all proprietary and CONFIDENTIAL INFORMATION related to the Clinical Trial, written or oral, provided by ECRIN.

5.1.2. ECRIN PARTNER undertakes to use such CONFIDENTIAL INFORMATION only in relation to the execution of the Tasks unless otherwise agreed with the disclosing Party.

5.1.3. ECRIN PARTNER agrees that it will not permit CONFIDENTIAL INFORMATION in its possession to be reproduced, disseminated or otherwise disclosed to any third party or used for any purpose not previously authorized in writing by ECRIN other than those contemplated by this Agreement.

5.1.4. In the event ECRIN PARTNER becomes legally compelled to disclose any confidential information, it shall immediately provide ECRIN with notice thereof prior to any disclosure, shall use its best efforts to minimize the disclosure of any CONFIDENTIAL INFORMATION, and shall cooperate with ECRIN.

5.1.5. The obligations set forth in this Article shall not apply to information for which the Party it is able to prove that:

-the Confidential Information becomes publicly available by means other than a breach of confidentiality obligations;

- the disclosing Party subsequently informs the recipient that the Confidential Information is no longer confidential;

-the Confidential Information is subsequently communicated to the recipient without any obligation of confidence by a third party who is in lawful possession thereof and under no obligation of confidentiality;

- that the disclosure or communication of the Confidential Information is foreseen by law or by other provisions of this grant agreement or the supplementary agreement;

- that the disclosure or communication of Confidential Information is required by the Laws and Regulations.

5.2. Confidentiality of Results

5.2.1. ECRIN PARTNER including its professional staff, agrees not to disclose or transfer or publish or commit to any third party the data, in whole or in part, and the results of the Clinical trial which are confidential information.

5.2.2. In the event ECRIN PARTNER's independent consultants or any other cooperating partners (hereinafter "PARTNERS") shall be involved, ECRIN PARTNER will undertake that such PARTNERS are obliged to respect the commitment specified in this Agreement to the same extent.

5.2.3. In any case, all CONFIDENTIAL INFORMATION containing personal data shall be handled in accordance with all applicable laws, including, but not limited to the European Data Protection Directive EC/95/46 and the locally applicable laws and regulations on Data Protection.

5.2.4. The terms and conditions of these obligations of confidentiality and restricted use contained herein are applicable during the term of the Agreement and shall survive its date of termination, whether by expiration or by earlier termination.

5.3. Specific obligations of ECRIN PARTNER under national law of the Czech Republic

5.3.1. ECRIN acknowledges that the ECRIN PARTNER is an obligated subject under the Czech act no. 340/2015 Coll. of the Czech Republic, on special conditions for the effectiveness of some contracts, the disclosure of these contracts and the Registry of contracts (Act on the Registry of contracts). Provisions of the Act on the Registry of contracts obligates public institutions (such as Masaryk university) to transparently publish a copy of this agreement (including metadata) in a central repository of contracts (Registry of contracts) before the agreement enters into force.

5.3.2. ECRIN and ECRIN PARTNER declare that they agree that this Agreement and all its amendments will be published by the ECRIN PARTNER in the Register of contracts under the conditions of the Act on the Registry of contracts.

5.3.3. ECRIN and ECRIN PARTNER declare that the confidential parts of this Agreement and its amendments, third party trade secrets and parts protected by intellectual property, such as the Protocol, will not be published in the Register of contracts.

5.3.4. The parties have agreed, that the annexes (appendices) of this Agreement will not be published, because they contain intellectual property, know-how and trade secrets of the Sponsor and/or ECRIN or ECRIN PARTNER.

6. SUBCONTRACTING

6.1. ECRIN PARTNER represents and warrants to ECRIN that shall not sub-contract part of its Tasks to a third party in the framework of this Agreement without notifying ECRIN through a written notice and having received ECRIN's written consent and, if necessary, the authorization of the Sponsor. The prior information shall be notified to ECRIN at least thirty (30) days before the date of signature of any subcontracting agreement.

6.2. Notwithstanding such ECRIN consent, ECRIN PARTNER shall ensure that :

- its agreement with the subcontractor(s) is made on terms that reflect the requirements of this Agreement
- the subcontractor shall not claim any intellectual property right or right of use of Data and Results pertaining to Clinical trial.

6.3. In any event, ECRIN PARTNER shall remain fully liable for the completion of the share of the Tasks that it entrusts to said third party subcontractor as well as for the acts and omissions of any such permitted third party.

7. LIABILITY AND INDEMNITY

7.1. ECRIN PARTNER is exclusively and fully liable for its assigned Tasks related to the Clinical trial and for the implementation of all technical, organizational, human, material, legal operations, and safety rules required by the performance of its tasks.

7.2. ECRIN PARTNER shall take out appropriate insurance cover in respect of its potential liability and shall produce to ECRIN, on request, a copy of the insurance certificate as evidence to confirm that it has such coverage. Failure to maintain adequate insurance coverage does not relieve or reduce ECRIN PARTNER liability under this Agreement.

7.3. ECRIN PARTNER undertakes to carry out its assigned Tasks with outmost care, observing approved and recognized scientific standards.

7.4. ECRIN PARTNER shall indemnify and hold ECRIN harmless from any and all claims, demands, damages, liabilities and costs incurred by ECRIN which directly or indirectly result from, or arise in connection with, any negligent act or omission of ECRIN PARTNER, its agents, or employees, pertaining to its activities and obligations under this Agreement.

8. INSPECTION AND AUDIT

8.1. Should ECRIN PARTNER become aware of an upcoming inspection or audit related to the Clinical Trial, ECRIN PARTNER should inform ECRIN and Sponsor in writing within 72 hours.

8.2. ECRIN PARTNER hereby allows any Regulatory Authorities may inspect the facilities and all related documents being used by ECRIN PARTNER for the performance of the Tasks.

8.3. ECRIN PARTNER agrees that, during an audit or an inspection by a Regulatory Authority it will not disclose information and materials that are not required to be disclosed to such Regulatory Authority without the prior written consent of ECRIN

8.4. ECRIN PARTNER shall provide ECRIN with a copy of all correspondence related to such audit or inspection and a summary of the audit findings or the inspection report

8.5. If any inspection, audit or examination by a Regulatory Authority results in a finding that ECRIN PARTNER has failed to comply with the terms of this Agreement, ECRIN PARTNER promptly take such measures at its own cost and expense as are necessary to correct such default identified in any such inspection, audit or examination.

9. MODIFICATION

9.1. This Agreement, including the attached Annexes, constitutes the entire and only Agreement between the parties relating to the Clinical trial.

9.2. Any agreement to change the terms of this Agreement and its Appendices in any way shall only be valid if the change is made in writing and approved by mutual agreement of authorized representatives of all the Parties. Such amendments shall be assigned by all the Parties and annexed to this Agreement.

10. INTUITU PERSONAE

The Agreement is executed *intuitu personae*. Consequently, ECRIN PARTNER is not authorized to transfer all or part of the rights and obligations hereunder to a third party without the prior and written agreement of ECRIN and of the Sponsor.

11. TERM AND TERMINATION OF THE AGREEMENT

11.1. This Agreement is considered concluded as from the date of signature of the last Party to sign the agreement. The effective date is the date when a copy of this agreement has been published in a Registry of contracts pursuant to Art. 5.3. of this Agreement. The Agreement shall remain in effect up to December 31th, 2019. The agreement may be extended by amendment. Any and all extension shall be subject to the drafting of an amendment to be signed by an authorized representative of each Party.

11.2. This Agreement can, only after discussing between the Parties, be terminated by written notice in case of

- early termination of the Study
- any technical, administrative cause (e.g. Study not authorized, suspended or prohibited by the Authorities) or methodological impossibility to pursue the Study
- termination for Breach

11.3. In the event of a breach by any Party of any of its obligations under this Agreement, the other Party may provide written notice to the breaching Party, such notice specifying the breach and requiring that the default be remedied within thirty (30) days. If the breach has not been remedied by the breaching Party to the satisfaction of the other Parties within thirty (30) days of receipt by the breaching Party of the notice identifying the breach and requiring its remedy, the Parties may terminate automatically, totally or partially, this Agreement with respect to the Defaulting Party with immediate effect. Such termination shall become effective with respect to such Defaulting Party as of the date of the notice of termination. Fees in relation with Tasks carried out up to this termination remain payable.

11.4. The defaulting Party concerned by the termination undertakes to communicate to the other Party or subrogated third parties, free of charge and immediately, all the files and information required to allow them to continue the implementation of the Study.

11.5. Exercising this cancellation right does not exonerate the defaulting Party from fulfilling its contracted obligations until the effective date of the termination and shall not, in any case be interpreted as a waiving, by the Party or Parties requesting the termination, of damages and interest in any way whatsoever.

12. FORCE MAJEURE

For the avoidance of doubt, force majeure means any unforeseeable and exceptional event affecting performance of the Agreement, which is outside the control of the Parties, and which cannot be avoided in spite of the efforts which the Parties may reasonably make.

No Party shall be considered to be in breach of this Agreement if such breach is cause by Force Majeure. Each Party shall notify the other Party of any Force Majeure as soon as possible. If impossibility or delay in fulfillment due to a case of force majeure continues for longer than three (3) months, the latter Party may automatically terminate the Agreement at any time by written notification sent to the other Party.

13. SURVIVAL

Upon termination of expiration of the Agreement for any reason, the provisions relating to the Clinical Trial Data and results, Confidentiality, Liability, Indemnity and Litigation shall survive termination of this Agreement.

14. WAIVER

No failure, delay, relaxation or indulgence by any Party in exercising any right conferred on such Party by this Agreement shall operate as a waiver of such right, nor shall any single or partial exercise of any such right nor any single failure to do so, preclude any other or future exercise of it, or the exercise of any other right under this Agreement.

15. NOTICES

All notices or other communications required or permitted to be made or given hereunder shall be deemed so made or given when hand-delivered or sent in writing by registered or certified mail, postage prepaid and return-receipt requested, or by a recognised courier service, charges prepaid and properly addressed to the representatives of the Parties at their addresses mentioned herein:

ECRIN-ERIC	ECRIN PARTNER
European Clinical Research Infrastructure Network (ECRIN-ERIC) **BioPark, 5-7 rue Watt** **75013 Paris, France**	**Masaryk University, Faculty of Medicine (CZECRIN)** **Kamenice 5** **625 00 Brno – Bohunice** **Czech Republic**

16. LITIGATION

In the event of any dispute arising between the Parties in relation to the terms of this Agreement, the parties shall use their best endeavors to resolve the matter on an amicable basis.

To initiate conciliation, a Party must give notice in writing to the other Party, requesting conciliation in accordance with this clause. Within thirty (30) days after this notification, the Parties shall try to appoint a single conciliator, but in the absence of agreement, each Party shall appoint one conciliator. The mission assigned to the Conciliator(s) by the Parties is to suggest a solution in order to resolve amicably such dispute within sixty (60) days after the notification.

In the event the Parties are unable to resolve the dispute informally within a reasonable time, any action brought by either party to this Agreement shall be heard by the appropriate court of competent jurisdiction.

17. GOVERNING LAW

This Agreement and all disputes arising hereunder will be governed by and interpreted in accordance with the laws of France without giving effect to the principles of conflict of laws. The parties hereby consent to and agree that the competent courts, where the ERIC has its statutory seat, shall have the sole and exclusive jurisdiction to resolve all such disputes.

18. GENERAL PROVISION

The invalidity of one or more provisions of this agreement does not affect the validity of the others. The invalid provision is to be replaced by a provision, which, in compliance with the legal prescriptions, suits the purpose best. The modification shall be made in writing and approved by mutual agreement of authorized representatives of all the Parties as specified in article 8.

19. APPENDICES

The following documents are appended to the Agreement and form an integral part hereof:

- Appendix 1: Tasks list (Version n° Version 1.0, 08 02 2018)
- Appendix 2: Financial Table (Version n° 01, 03/08/2018)
- Appendix 3: Protocol (Version n° UCDCRC/16/003 FINAL, V1.1, 09-JAN-2017)

20. SIGNATURE

This Agreement is executed in two counterparts, depending on the number of the parties, each of which shall be considered an original hereof but which together shall constitute one agreement.

IN WITNESS WHEREOF, the parties, acting through their duly authorized representatives, have executed three (2) copies of this Agreement

1. For and on behalf of ECRIN

European Clinical Research Infrastructure Network (ECRIN-ERIC)
BioPark, 5-7 rue Watt
75013 Paris, France

LEGAL REPRESENTATIVE :
Prof. Dr. Jacques Demotes
Director General of ECRIN ERIC

DATE: 3-8-2018 SIGNATURE: [redacted]

2. For and on behalf of the ECRIN PARTNER

Masaryk University, Faculty of Medicine
Žerotínovo nám. 617/9, 601 77 Brno, Czech Republic

LEGAL REPRESENTATIVE:
Prof. MUDr. Martin Bareš, Ph.D.
The dean of Faculty of Medicine

[redacted]

DATE: - 4 -10- 2018 SIGNATURE:

TABLE OF RESPONSIBILITIES – Europe-wide (ex-Ireland)

Protocol Number: UCDCRC/16/003

Study Title : PROPHYLACTIC OROPHARYNGEAL SURFACTANT FOR PRETERM INFANTS: A RANDOMISED TRIAL (THE POPART TRIAL)

EudraCT Number: 2016-004198-41

As per the European Commission Directive 2001/20/EC, the sponsor takes overall responsibility for the initiation and management of a clinical trial, however as the sponsor, UCD formally delegates responsibility for certain trial deliverables as assigned and agreed within this Table of Responsibilities.

Abbreviations

AE : Adverse Event
CRA : Clinical Research Associate
CRF : Case Report Form
CTA : Clinical Trial Application
CV : Curriculum vitae
DSMB : Data Safety Monitoring Board
DSUR : Development Safety Update Report
ECRIN : European Clinical Research Infrastructure Network
GCP : Good Clinical Practice
GMP : Good Manufacturing Practice
IMP : Investigational Medicinal Product
QC : Quality Control
SAE : Serious Adverse Event
SAR : Serious Adverse Reaction
SOP : Standard Operating Procedure
SUSAR : Suspected Unexpected Serious Adverse Reaction

Task Delegation Key:

A	**Accountable**
R	**Responsible**
C	**Consulted**
I	**Informed**
S	**Subcontracted by ECRIN to ECRIN PARTNER**

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
I Administrative and Regulatory issues						
1. Drawing up of the investigator brochure – NOTE: Summary of Product Characteristics will be used in place of the Investigator's Brochure.	C/I	A/R		C/I		
2. Provision of validated Core Regulatory Submission pack for each country adaptation.	A/R			C/I	C/I	Sponsor will provide this to ECRIN and ECRIN partners
3. Preparation, translation and QC of local regulatory submissions in accordance with country requirements	C/I			A/R	S	
4. Preparation, translation and validation of Ethics Committee application and follow up in accordance with country requirements including collection of CVs, preparation of CTA and payment of fees.	C/I/A			A/R	S	
5. Submission and follow-up of all clinical trial submissions to Regulatory Authorities and National Ethics Committee, payment of fees	C/I/A			R	S	
6. Review and validation of any changes required by the Regulatory	C/I/A	C/I		R	S	

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
Authority						
7. Providing the answers to all applicable questions raised by regulatory authorities and ethics committees	A/R	A/R		C/I	**C/I**	
8. Providing Sponsor with the final response given by individual country Regulatory Authorities and Ethics Committees (translated as required)	C/I/A	I		R	**S**	
9. Local Country-specific Amendments and Notifications implemented and submitted to Regulatory Authorities and Ethics Committees as required locally. This is to be done only after confirming with the Sponsor.	C/I/A	C/I	A/R	R	**S**	
10. Providing Sponsor with all communications and clinical trial documentation between applicant and Regulatory Authority per country – including notifications, amendments, reports and end of trial submissions in a timely manner.	C/I			A/R	**S**	
11. Contract between ECRIN & Sponsor	A/R			A/R		
12. Obtain advice on requirements and options/quotations for insurance per country for Sponsor	C/I	C/I		A/R	**S**	

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
13. Insurance in accordance with individual country requirements	C/I/A			R	S	
14. Assignment of local contact person per country for management of all local country clinical trial activities (including regulatory and ethics submissions) and for direct communication between Sponsor/ECRIN/Countries	C/I	C/I		A/R	S	
15. Contracting of translation activities per country for the Sponsor files	C/I/A			A/R	S	
16. Maintenance, update and completion of Study Activities status report, Clinical Trial Submissions & Document tracker on a country basis and provided to the Sponsor in accordance with agreed timelines	C/I			A/R	S	
II Investigators						
A. Selection						
1. Proposal of potential investigators and national coordinator – ensure all sites have adequate experience, staffing, resource and expertise in conduct and management of the clinical trial per site	C/I/A	A/R		C/I		
2. Organisation of pre-trial visit or teleconference with investigational	C/I/A	A/R		C/I		

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
site personnel to evaluate the capability of the centers to recruit patients within the time frame						
3. Provide Sponsor with complete staff contact list with contact information and CVs for all staff delegated to work on any trial activities on site at all sites in countries	C/I		A/R	A/R	S	
B. Agreement with investigators/institutions						
1. Identification of all the agreements for each potential site to be obtained before study start	C/I	C/I		A/R	S	
2. Drawing and negotiating all contractual agreements	A/R			C/I		
3. Coordination of the submission and translations (where applicable) of the contractual agreements to the investigators/institutions for signature	C/I			R	S	
4. Initiation of the signature of the contractual agreements by investigators/institutions for sponsor	C/I/A			R	S	
III Trial drug supplies						
A. Randomization/allocation of treatments						
1. Programming and development of a randomization list	C/I	A/R				

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
2. Issue of decoding envelopes to be sent to investigators for decoding in case of medical emergency	C/I	A/R				
3. Allocation of treatments through a Central Randomisation system	C/I	A/R				
B. Management of trial drug supplies						
1. Manufacturing/provision of drug supplies (or subcontracting)		A/R				
2. Management of packaging and labeling of IMP locally for each site	C/I		A/R			
3. Validation and distribution of Master English IMP labeling according to Annex 13 GMP requirements for country adaptation.	A/R			C/I		
4. Adaptation, validation, finalisation, translation, back-translation and QC of IMP labeling in accordance with local requirements per country.	C/I			A/R	S	
5. Ensure correct and compliant storage, management and traceability of IMP on site in accordance with storage requirements for the drug and temperature monitoring records maintained.	C/I		A/R			
6. Monitoring of storage, management and traceability of IMP on site in accordance with storage				A/R		

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
requirements for the drug and temperature monitoring records maintained.					S	
7. Recall, quarantine and destruction of drug where required and recorded and handled appropriately on site	C/I		A/R	C/I		
8. Forwarding of required regulatory documentation to Sponsor	C/I			R	S	
C. Retrieval and disposal of study drug						
1. Manage retrieval of all study drugs from site	NA	NA	NA	NA		
2. Perform a reconciliation of all drugs supplied and returned	NA	NA	NA	NA		
3. Destruction of IMP			A/R	C/I		
IV Study documentation						
A. Drawing up study documents						
1. Final protocol: writing, review and validation	A/R/C	A/R/C		C/I		
2. Master English Informed consent form for trial	C	A/R/C		C/I		
3. Validation of Master informed consent form according to GCP and regulations	A/R	A/R				
4. Local Country Informed Consent Form in English: Adaptation of Master English version in	C/I			A/R		

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
accordance with local requirements and provided to Sponsor before translation.					S	
5. Translation, back-translation and validation of Local informed consent form in compliance with GCP and local requirements	C/I			A/R		
6. Investigator Site File contents page and relevant documentation provided for local sites in electronic format for sites to compile site file before study start.	A/R		C/I	C/I		
7. CRF	A/R					
8. Printing of CRFs			A/R			
B. Filing and archiving of study document						
1. Management of the Site-specific information for Trial Master File	C/I		A/R	C/I		
2. Filing of all original administrative study documents in Trial Master File		A/R	A/R			
3. Ensure that patients' names and addresses are masked prior to returning documents to Sponsor but assure that the documents are still identifiable with protocol number, patient's initials and number			A/R			

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
4. Ensure the maintenance of the Trial Master File throughout the study period			A/R			
5. Management of all original documents of the Trial Master File from sites upon request of Sponsor, after database closure			A/R	R	S	
V – Monitor activities on clinical sites						
A. Initiation site visit						
1. Performing the site initiation after obtaining all Regulatory and Ethics Approvals	C/I/R	C/I	C/I	A/R	S	
2. Check that all critical points of the study including scientific, administrative and logistic matters are well understood by all members of the study team prior to enrollment of the first subject	C/I	C/I	A/R	R	S	
3. Check that all study documents and/or material such as CRF, investigator study file have been forwarded to the investigator prior to the visit or handed over during the visit	A/R			R	S	
4. Written confirmation obtained by each site from the Sponsor before recruitment of first patient can begin (once all SIV and site-start-up actions have been completed).	C/I		A/R	C/I		

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
B. Patient selection and recruitment						
1. Check patient recruitment in the site in order to randomize the total number of patients as defined in the protocol in the planned timelines	C/I	A/R	C/I	C/I	**C/I**	
2. Decision to increase the number of sites, if needed	C/I	A/R		C/I	**C/I**	
C. Monitoring						
1. Allocation of a CRA to conduct site monitoring visits during the course of the trial.	C/I			A/R	**S**	
2. Monitoring Plan finalisation	A/R	C/I		C/I		
3. Monitoring of Pharmacy/IMP Storage facility	C/I			R	**S**	
4. Detection and report to Sponsor of potential problems during study conduct including any/all of the following – Protocol deviations, protocol violations, serious breeches, GCP or SOP non-compliance as well as possible proposed actions for discussion with the Sponsor	C/I		A/R	A/R	**S**	
5. Monitoring visits and schedule completing in accordance with Monitoring Plan	C/I			A/R	**S**	
6. Verification of source documents for the following, in accordance				A/R		

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
with Monitoring Plan: all criteria listed below (demographics, inclusion/exclusion criteria, primary efficacy and safety assessments, AEs (serious and non-serious), drug dispensing record and informed consent form, reason for premature termination.					S	
7. Check maintenance of the investigator's trial file at the site monitoring visit	C/I			A/R	S	
8. Completion of a visit report form and forwarding to Sponsor within 15 working days after the visit (or in accordance with the Monitoring Plan – including initiation, monitoring, close-out)	C/I			A/R	S	
9. Provide sponsor with all communications, reports and follow-ups in relation to monitoring visits conducted				A/R	S	
10. Monitoring of documented GCP Training to all site staff	C/I			A/R	S	
11. Provision of documented Protocol Training to all Investigators		A/R	C/I	C/I		
12. Provision of documented Protocol Training to all site staff		C/I	A/R			
13. Monitoring of documented Protocol Training to all site staff	C/I/A			A/R	S	

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
14. Provision of any specific training or training materials related to study/Sponsor processes	A/R	C/I		C/I		
D. Drug accountability						
1. Check of study drug accountability for all subjects			A/R			
2. Ensure proper completion of the Drug Dispensing and Accountability Forms for the selected monitored subjects			A/R			
3. Perform a reconciliation of all drugs supplied and returned at the site			A/R			
4. Monitoring of drug accountability as detailed above D. Drug Accountability: points 1, 2 &3				A/R	S	
E. Study closure						
1. Perform close-out visit to the site on Sponsor's/Principal investigator's instruction and ensure that all the documents are ready for archiving	C/I			A/R	S	
2. Ensure that essential documents are archived properly	C/I		A/R			
3. Collection of all study documents as per sponsor's instruction	C/I		A/R	R	S	
VI Serious Adverse Events follow up and reporting						
1. Provide investigator site with Serious Adverse Event (SAE) forms	A/R	C/I	C/I	C/I	C/I	

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
and training materials on Pharmacovigilance procedures for reporting of serious adverse events						
2. Timely alert to Sponsor and CI of all or any of the following important safety events in accordance with standard pharmacovigilance practice: SAE/SAR/urgent safety measure/life-threatening safety event/fatality	C/I	C/I	A/R	C/I		
3. Review of all Serious Adverse Events Forms on an ongoing basis	A/R	C/I/R/A				
4. Shipment of SUSARs reports to the Regulatory Authorities as applicable according to expedited timelines on a country basis	C/I/A	C/I		R	S	
5. Preparation of DSUR	A/R	A/R		C/I		
6. Submission of SUSARs and DSURs to National Ethics Committees (reports provided by Sponsor) per country according to local requirements	C/I		C/I	R	S	
7. DSMB Charter: Preparation, review and implementation	A/R	C/I		C/I		

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
VII Sample Management						
1. Local Sample Management: collection, processing, storage, destruction and destruction			A/R	C/I		
VIII Data-Entry, Data management and Coding						
A. Data management						
1. Compile Data Management Plan	A/R					
2. Creation of the database structure	A/R	A/R				
3. Data entry for all data of the CRFs and DCFs completed according to ICH GCP E6 R2 principles (attributable, legible, contemporaneous, original, accurate, and complete). Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry.	C/I		A/R	C/I		
4. Data-cleaning – Coherent review in order to ensure validity and consistency of the information contained within the electronic CRFs. Run checks, raise queries, QC, coding, generating listings and status reports, SAE and external data reconciliation)	C/I	A/R				
5. Supervision of coherence review,	C/I	A/R				

	Sponsor	Chief Investigator	Principle Investigator (per site)	ECRIN	ECRIN Partner	Comments
issue of data clarification forms (DCFs) if needed						
6. Supervision of resolution of data clarification forms (DCFs) if needed	C/I	A/R				
7. Monitoring of CRF completion, site data entry and DCF resolution	C/I			A/R	S	
8. Database Lock	C/I	A/R				
IX Statistical analysis						
1. Entire responsibility for statistical analysis	C/I	A/R				
X Clinical study report						
1. Issued by Sponsor.	C/I	A/R				
XI Quality Assurance						
1. Compile Quality Management Plan	A/R					
2. Conduct on site QA audits	A/R	I/C		C/I		
3. Implement corrective actions and follow up	A/R	A/R	A/R	C/I		
4. Monitoring of corrective actions at site during the duration of the study	C/I		C/I	R	S	

POPART (31.05.2018)

4 sites. 80 patients

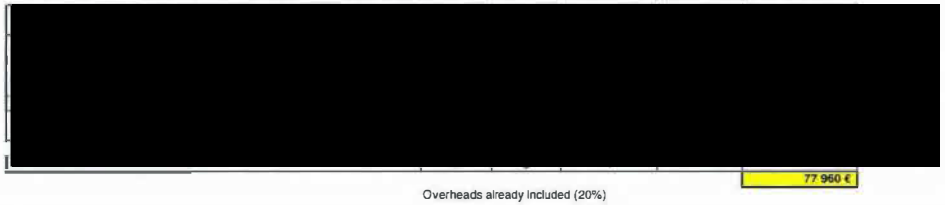
CTU = Masaryk University Brno

[redacted]

Duration - 2y 9m

Cost/Hour = 40 €

	Requested (Yes/No)	Nº HOURS	UNITS	Cost/Hour	TOTAL COST
[redacted]					



Overheads already included (20%)