

**THIS RESEARCH AGREEMENT is effective from the date of the last signature**

**AMONG**

- (1) **THE EHE RARE CANCER CHARITY** a charitable incorporated organisation registered with the Charity Commission with charity number 1162472 whose registered office is at 23 Geneva Road, Kingston-Upon-Thames, Surrey, KT1 2TW ("**FUNDER**"); and
- (2) **FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI** whose address is Via Giacomo Venezian N. 1 -20133 Milano Italy ("**RESEARCH PARTY**").

(FUNDER and RESEARCH PARTY shall be each a "**party**" and together the "**parties**" to this Agreement as the context requires).

## **BACKGROUND**

Following RESEARCH PARTY approaching FUNDER for funding of the proposed introduction of a European EHE prospective study entitled "Prospective EHE Registry (PROSPHERES)" (the "Study"), FUNDER agrees to engage RESEARCH PARTY, and RESEARCH PARTY agrees to accept the engagement, to undertake the new Programme of Research (as defined hereunder) on the terms and conditions of this Agreement.

**IT IS HEREBY AGREED** as follows:

### **1. DEFINITIONS AND INTERPRETATION**

- 1.1 In this Agreement (unless the context otherwise requires), the following words and phrases shall have the following meanings:

**"Affiliate"** means in relation to a party, any entity or person which controls, is controlled by or is under common control with that party. For the purposes of this definition, "control" shall mean direct or indirect beneficial ownership of 50% or more of the share capital, stock or other participating interest carrying the right to vote or to distribution of profits of that entity or person, as the case may be.

**"Agreement"** means this agreement, the schedules and any document referred to, completed or to be completed in accordance with its provisions.

**"Background Intellectual Property"** means the Intellectual Property Rights (excluding Foreground Intellectual Property) owned or controlled by a party prior to the Commencement Date, or developed independently from the Programme of Research, and used in or disclosed in connection with the performance of the Programme of Research.

**"Commencement Date"** means the commencement date as set out in Schedule 1 hereto.

**"Deliverables"** means any results, materials, information or Intellectual Property to be provided under this Agreement as described in Schedule 2.

**"Force Majeure Event"** means any circumstance beyond the reasonable control of the parties including, but not limited to acts of God, pandemics, fire, explosion, adverse weather conditions, flood, earthquake, terrorism, riot, civil commotion, war, hostilities, strikes, work stoppages, slow-downs or other industrial disputes, accidents, riots or civil disturbances, acts of government, lack of power and delays by suppliers or materials shortages.

**"Foreground Intellectual Property"** means individually and collectively all Intellectual Property which is conceived and/or made by one or more members or other agents of RESEARCH PARTY acting either on their own or jointly with one or more employees of FUNDER in the direct performance of the Programme of Research.

**"Intellectual Property" or "Intellectual Property Rights"** includes patents, inventions, know-how, trade secrets and other confidential information, registered designs, copyrights, database rights, design rights, rights affording equivalent protection to copyright, database rights and design rights, semiconductor topography rights, trademarks, service marks, logos, domain names, business names, trade names and all registrations or applications to register any of the aforesaid items, rights in the nature of any of the aforesaid items in any country or jurisdiction, rights in the nature of unfair competition rights and rights to sue for passing-off. For the avoidance of doubt, Intellectual Property shall include the Deliverables of the Programme of Research.

**"Irrecoverable Costs"** means all costs whatsoever incurred by RESEARCH PARTY in performing their duties in the Programme of Research up to the date of termination of the Agreement in accordance with the terms herein. For the avoidance of doubt, such costs shall not include costs of facilities or personnel after the date of termination unless agreed by FUNDER, such agreement not to be unreasonably withheld or delayed.

**"Payment Terms"** means the payment terms as set out in Schedule 1 hereto.

**"Price"** means the price as set out in Schedule 1 hereto.

**"Principal Investigator"** means the individuals appointed to direct the Programme of Research for RESEARCH PARTY, as specified in Schedule 1 hereto.

**"Programme of Research"** means the programme of research set out in Schedule 2.

**"Registry"** means the database in which data of the patients enrolled in the Study are collected.

**"Term"** means the period starting on the Commencement Date and finishing on the Termination Date.

**"Termination Date"** means the termination date as set out in schedule 1 hereto or if no termination date is set out in Schedule 1 then the date when the Deliverables are delivered or any other date of termination agreed in accordance with the terms of this Agreement.

**"VAT"** means value added tax and includes any substituted or similar tax. As the Programme of Research involves medical research, the VAT rate shall be zero; and

**"Working Day"** means any day from Monday to Friday (inclusive) which is not Christmas Day, Good Friday or a statutory holiday in the appropriate jurisdiction for each party.

1.2 In this Agreement (unless the context otherwise requires):

1.2.1 construction of this Agreement shall ignore the headings, contents list and frontsheet (all of which are for reference only); and

1.2.2 any reference to any legislative provision shall be deemed to include any subsequent re-enactment or amending provision.

## **2. ENGAGEMENT**

FUNDER hereby engages, and RESEARCH PARTY agrees to accept the engagement, to carry out the Programme of Research in accordance with the terms of this Agreement.

## **3. TERM**

This Agreement shall come into force on the Commencement Date and shall continue in force until the Termination Date.

## **4. PRINCIPAL INVESTIGATOR(S)**

The Programme of Research shall be supervised by the Principal Investigators. In the event that a Principal Investigator becomes unable to supervise the Programme of Research, and no other Principal Investigator has been pre-agreed as shown in Schedule 1, then RESEARCH PARTY shall propose one or more alternatives, and if reasonably practicable, prior to the existing Principal Investigator becoming

unavailable. The parties shall enter into good faith negotiations to agree a substitute. In the event that the parties cannot agree a mutually acceptable substitute, then the Agreement may be terminated in accordance with Article 13 of this Agreement.

## **5. PERFORMANCE OF THE PROGRAMME OF RESEARCH**

### **5.1 Each party shall:**

- 5.1.1 notify the other party in writing as soon as reasonably practicable if it becomes aware of an unexpected technical or scientific problem which (i) makes it impossible to achieve or (ii) is likely to cause a material delay to achievement of the Programme of Research or any material increase in the costs of the Programme of Research or if any party becomes aware of the action of any third party which threatens to affect adversely completion of the Programme of Research or the reasonable expectations of either party hereunder;
- 5.1.2 ensure that the work conducted under the Programme of Research is conducted in accordance with generally accepted standards of good practice at the time applicable to such work (including all relevant statutory safety standards from time to time in force) and each party will be responsible for the implementation of and compliance with all safety and the other legislative requirements which apply to the work assigned to it under the Programme of Research;
- 5.1.3 procure that such Background Intellectual Property, facilities, resources, materials and equipment as are reasonably required for the proper execution of the Programme of Research are made available by it for the Programme of Research. For the avoidance of doubt, nothing in this clause 5 purports to permit any party to reverse engineer or otherwise analyse any of the materials provided to it under the Agreement except in accordance with the provisions of this Agreement and to the extent not prohibited by law.
- 5.1.4 As detailed in the Schedule 2, the Programme of Research foresees the participation of several centers across the European Union in order to develop the Registry. The terms and conditions of the Registry will be set out in a separate agreement between the involved centers.

## **6. PAYMENT**

- 6.1 In consideration of RESEARCH PARTY performing its duties in the Programme of Research, FUNDER shall pay RESEARCH PARTY the Price in accordance with the Payment Terms as set out in Schedule 1.

- 6.2 FUNDER is not entitled to withhold payment of any amount due to RESEARCH PARTY by way of any set-off or counterclaim.

## **7. DELIVERABLES**

RESEARCH PARTY will use reasonable endeavours to deliver all Deliverables of the Programme of Research.

## **8. LIABILITY**

- 8.1 RESEARCH PARTY will use reasonable endeavours to ensure that its work pursuant to this Agreement is carried out in accordance with accepted scientific standards but makes no representation or warranty that any Deliverables will be fit for any particular purpose and accepts no responsibility for any use which may be made of any Deliverables and/or Foreground Intellectual Property arising from its work or otherwise supplied to or to which a party gains access. It is therefore agreed that any party utilising such Deliverables and/or Foreground Intellectual Property is fully responsible and liable for any losses, costs, claims or demands arising from that party's own direct use.

- 8.2 Except as set out in this clause 8, all conditions, warranties and representations, expressed or implied by statute, common law or civil law, in relation to the carrying out of the Programme of Research or the supply, non-supply or delay in supplying the Deliverables are excluded to the fullest extent permitted by law.

- 8.3 Subject to the provisions in clause 8.7 below, neither party shall be liable to the other party in contract, tort (including negligence or breach of statutory duty) or otherwise for any of the following losses or damages, whether direct or indirect, arising out of, or in connection with, the Programme of Research or the supply, non-supply or delay in supplying the Deliverables or otherwise in connection with this Agreement:

8.3.1 loss or damage incurred by a party as a result of third-party claims;

8.3.2 loss of actual or anticipated profits;

8.3.3 loss of business opportunity;

8.3.4 loss of anticipated savings;

- 8.3.5 loss of goodwill;
- 8.3.6 injury to reputation; or
- 8.3.7 any indirect, special or consequential loss or damage howsoever caused even if a party was advised of the possibility of them in advance.
- 8.4 RESEARCH PARTY gives no guarantee and makes no representation or warranty to FUNDER:
  - 8.4.1 that particular results, materials, information or Intellectual Property will arise from the Programme of Research;
  - 8.4.2 that any Deliverables will not infringe third party rights and RESEARCH PARTY does not accept any responsibility whatsoever for infringement of such rights; and
  - 8.4.3 as to the merchantable or satisfactory quality of any product or process developed through the Programme of Research, its fitness for purpose, or its viability, safety or non-toxicity.
- 8.5 Subject to clause 8.6, each party shall indemnify and keep indemnified the other party, their servants or agents against all claims, actions, losses, damages, costs and expenses which may be brought against or incurred or suffered by the other party, their servants or agents in connection with the carrying out of work pursuant to the Programme of Research which arise as a result of or due to the negligence of the indemnifying party, its servants or agents.
- 8.6 Subject to clauses 8.3 and 8.7, the entire liability of any party arising out of or in connection with the Programme of Research or otherwise in connection with this Agreement, whether in contract, tort (including negligence or breach of statutory duty) or otherwise, is limited to the Price.
- 8.7 Nothing in this Agreement shall operate to exclude or restrict any party's liability for:
  - 8.7.1 death or personal injury resulting from negligence;
  - 8.7.2 fraud or deceit; or
  - 8.7.3 any other matter which may not be excluded or restricted by law.
- 8.8 Subject to clauses 8.3, 8.5, 8.6 and 8.7 each party will be responsible for its own (and its Affiliates') officers, employees, students, consultants, agents and representatives ("Staff") and will indemnify the other party against all claims that may arise out of any injury, loss or damage suffered by such Staff in connection with the breach, performance or non-performance of this Agreement by that party or the use of any Deliverables.

- 8.9 Each party undertakes to make no claim in connection with this Agreement or its subject matter against any Staff of the other party (apart from claims based on fraud or wilful misconduct).

## **9. PUBLICATION**

- 9.1 FUNDER recognises that RESEARCH PARTY may make reference to or publish information concerning the Programme of Research and the Deliverables, in the interests of the exchange of scientific information, in journals, theses, dissertations or other such published material. Before such publication, the RESEARCH PARTY shall notify FUNDER, with a copy of any proposed publication. FUNDER shall have the right to review and comment upon any proposed publication and to remove any information it can reasonably demonstrate would be damaging to its charitable interests. FUNDER shall notify RESEARCH PARTY within fifteen (15) days of the date of receiving the proposed publication of any requested amendments. Should FUNDER reasonably believe that publication should be delayed in order to enable any Intellectual Property Rights arising from the information or the Deliverables to be registered then it shall notify the RESEARCH PARTY in writing within fifteen (15) days of the date of notification. RESEARCH PARTY shall use reasonable efforts to comply with FUNDER's request to delay publication.
- 9.2 Neither party may include Confidential Information or confidential Background Intellectual Property belonging to the other party in any publication.
- 9.3 Published information will include reference to FUNDER and the RESEARCH PARTY.

## **10. INTELLECTUAL PROPERTY RIGHTS**

- 10.1 For the avoidance of doubt all Background Intellectual Property used in connection with the Programme of Research shall remain the property of the party introducing the same. Neither party will make any representation or do any act which may be taken to indicate that it has any right, title or interest in or to the ownership or use of any Background Intellectual Property belonging to the other party except under the terms of this Agreement. Each party acknowledges and confirms that nothing contained in this Agreement shall give it any right, title or interest in or to the Background Intellectual Property of the other party save as granted by this Agreement.
- 10.2 The parties agree that any improvements or modifications arising from the activities described in this Agreement to a party's Background Intellectual Property which are not severable from that party's Background Intellectual Property will be deemed to form part of that party's Background Intellectual Property.
- 10.3 Each party grants to the other party a non-exclusive, royalty free, fully paid up, licence to use such of its Background Intellectual Property, and any Foreground Intellectual Property belonging to it, as may be necessary to effect the performance of this Agreement.

- 10.4 Each party shall promptly disclose to the other party all Foreground Intellectual Property generated by it. All rights to Foreground Intellectual Property created by the employees, students and/or agents of a party in the performance of this Agreement shall belong to the party employing such persons.
- 10.5 Each party grants the other party a royalty free, fully paid up, non-exclusive licence to use the Foreground Intellectual Property for academic, teaching and non-commercial research purposes. Use of Foreground Intellectual Property for commercial purposes shall only be permitted in strict accordance with the remainder of this clause 10.
- 10.6 Should the grant of a licence of any of a party's Background Intellectual Property be necessary in order for the other party to exploit any Foreground Intellectual Property, then the owner of the Background Intellectual Property may, on written request, consent to grant a non-exclusive licence (such consent not to be unreasonably withheld or delayed). Such licence shall only be given to the extent necessary to enable the party to comply with this Agreement, and shall be subject to commercially reasonable terms (which if not agreed by the parties shall be determined by the arbitrator referred to under this Agreement's Dispute Resolution procedure).
- 10.7 Each party owning Foreground Intellectual Property independently may commercially exploit that Foreground Intellectual Property (the "Exploiting Party") upon consultation with the other party. In such circumstance, the Exploiting Party agrees to pay the other party a fair and reasonable royalty rate/revenue on the value of any products or processes commercially exploited by it which incorporate any Foreground Intellectual Property taking into consideration: (a) the respective financial, intellectual and technical contributions of the parties to the development of the Foreground Intellectual Property, (b) the expenses incurred in securing intellectual property protection thereof, (c) the costs of its commercial exploitation and (d) the proportionate value of the Foreground Intellectual Property in any such product or process (which if not agreed by the parties shall be determined by an appropriate independent expert in such matters agreed to by the parties, and if such expert cannot be agreed, then by the Dispute Resolution procedure under Article 15 of this agreement).
- 10.8 Where any Foreground Intellectual Property is created or generated by the parties jointly and it is impossible to segregate each party's intellectual contribution to the creation of the Foreground Intellectual Property, the Foreground Intellectual Property will be owned by the parties in equal shares. Where Foreground Intellectual Property is identified in accordance with this clause, representatives of the parties shall promptly meet (either in person or via teleconference) to decide upon one party (the "Lead Exploitation Party") to take the lead on the exploitation of all Foreground Intellectual Property. The Lead Exploitation Party should be the party that, in the opinion of the parties, is best placed to manage such Foreground Intellectual Property. The Lead Exploitation Party may take such steps as it may decide from time to time, at the Lead Exploitation Party's expense, to



register and maintain any protection for the Foreground Intellectual Property, including filing and prosecuting patent applications for any of the Foreground Intellectual Property, and taking any reasonable action in respect of any alleged or actual infringement of the Foreground Intellectual Property.

- 10.9 The Lead Exploitation Party of joint Foreground Intellectual Property shall be subject to the same exploitation terms set out in clause 10.7.
- 10.10 Each party will promptly notify the other party in writing of any Foreground Intellectual Property conceived and/or made pursuant to this Agreement and the parties shall co-operate, where required, in relation to the preparation and prosecution of patent applications and any other applications relating to Foreground Intellectual Property.
- 10.11 The party/parties owning Foreground Intellectual Property shall be responsible for making decisions regarding the registration (including patent applications) of Foreground Intellectual Property and the scope and contents of such application(s).
- 10.12 If a party elects not to exercise its right to apply for registration of any Foreground Intellectual Property or decides to discontinue the financial support of any prosecution or maintenance of such registration, the other party shall be entitled (but not obliged) to file or continue prosecution or maintain any such registration(s) and to maintain any registration issuing thereon in the United Kingdom and/or other country, at their own expense. The party filing or continuing prosecution or maintenance shall be free to exploit and license to third parties the Foreground Intellectual Property without any obligation to share any of the revenues of such exploitation or licensing. For the avoidance of doubt, this clause 10.12 is without prejudice to the provisions concerning ownership and licensing of Foreground Intellectual Property elsewhere in this Agreement, and nothing in this clause 10.12 shall operate to grant or transfer any right, title or interest in or under any Foreground Intellectual Property.
- 10.13 Following completion of the Programme of Research should one party choose not to exploit the Foreground Intellectual Property and not to receive Royalties under clause 10.7, then the other parties may request that the Foreground Intellectual Property is assigned to it at its own expense upon payment of a fair and commercially reasonable one-off fee to be agreed between the parties. Following such an assignment the owner of the Foreground Intellectual Property shall be responsible for all costs incurred in connection with the preparation, filing, prosecution and maintenance of UK and/or other applications associated with the assigned Foreground Intellectual Property.
- 10.14 Each party will ensure that work undertaken by it pursuant to this Agreement will be undertaken by personnel under arrangements whereby any Intellectual Property generated by the personnel in undertaking the work vests in the party.

## 11. PUBLICITY

Neither party shall use the name, logo, or trade mark of the other party, its employees or Affiliates in any publicity, advertising or news release without the prior written approval of that party.

## 12. MEETINGS AND REPORTS

12.1 RESEARCH PARTY and FUNDER will hold meetings in the periods set out in schedule 1, or if no periods are set out by agreement on the reasonable request of a party.

12.2 Written progress reports and presentations shall be provided by RESEARCH PARTY to FUNDER as set out in schedule 1.

## 13. TERMINATION

13.1 FUNDER may terminate this Agreement by giving the RESEARCH PARTY not less than sixty (60) days' prior written notice.

13.2 RESEARCH PARTY may terminate this Agreement by giving the FUNDER not less than sixty (60) days' prior written notice.

13.3 A party ("**Initiating Party**") may terminate this Agreement with immediate effect by written notice to the other party on or at any time after the occurrence of any of the following events in relation to the other party ("**Breaching Party**"):

13.3.1 the Breaching Party being in material breach of an obligation under this Agreement and, if the breach is capable of remedy failing to remedy the breach within thirty (30) days of receipt of written notice from the Initiating Party giving details of the breach and requiring the Breaching Party to remedy the breach and stating that a failure to remedy the breach may give rise to termination under this Agreement;

13.3.2 the Breaching Party passing a resolution for its winding up or a court of competent jurisdiction making an order for the Breaching Party to be wound up or dissolved or the Breaching Party being otherwise dissolved;

13.3.3 the appointment of an administrator of, or the making of an administration order in relation to, the Breaching Party or the appointment of a receiver or an administrative receiver of, or an encumbrancer taking possession of or selling, the whole or part of the Breaching Party's undertaking, assets, rights or revenue;

13.3.4 the Breaching Party being unable to pay its debts or being deemed unable to pay its debts under applicable legislation that is in force and applies in the place where the defaulting Party is located;

- 13.3.5 the Breaching Party entering into an arrangement, compromise or composition in satisfaction of its debts with its creditors or any class of them or taking steps to obtain a moratorium or making an application to a court of competent jurisdiction for protection from its creditors;
- 13.3.6 the Breaching Party entering into an arrangement, compromise or composition in satisfaction of its debts with its creditors;
- 13.3.7 a change of control of the Breaching Party, where "**control**" means the ability to direct the affairs of another whether by way of contract, ownership of shares or otherwise.

#### 14. CONSEQUENCES OF TERMINATION

- 14.1 Upon termination of this Agreement all rights and obligations of the parties shall cease to have effect immediately except that termination shall not affect accrued rights and obligations of the parties under this Agreement at the date of termination or any express obligations in this Agreement of a continuing nature.
- 14.2 Upon termination by FUNDER, FUNDER shall reimburse RESEARCH PARTY for all Irrecoverable Costs (such reimbursement not to exceed the Price specified in Schedule 1).
- 14.3 Upon termination:
  - 14.3.1 by RESEARCH PARTY, RESEARCH PARTY shall provide the reasons for termination to FUNDER together with a full reconciliation of all Irrecoverable Costs ("**Total Costs**") and all payments made by FUNDER to RESEARCH PARTY ("**Total Payments**"). For the avoidance of doubt, Total Costs cannot exceed the Price specified in Schedule 1. Where the reason for termination is accepted by FUNDER, such acceptance not to be unreasonably withheld or delayed, and the Total Costs are in excess of Total Payments, FUNDER shall pay the amount of such excess to RESEARCH PARTY. If, however, the Total Costs are less than the Total Payments RESEARCH PARTY shall return the amount of such over-payment to FUNDER. If FUNDER does not accept the reason for termination, then FUNDER shall have no obligation to make any further payments under this Agreement. For the avoidance of doubt, termination by RESEARCH PARTY shall be accepted by FUNDER as acceptable reasons for termination if: (i) RESEARCH PARTY believes that ongoing research progress and results demonstrate that the Programme of Research cannot provide the Deliverables; or (ii) circumstances beyond RESEARCH PARTY's control make performance of the Programme of Research materially different to, or uneconomic compared with, that reasonably contemplated by RESEARCH PARTY

at the date of entering into this Agreement; or (iii) termination is in accordance with clause 13.3; or

14.3.2 by FUNDER, and the Total Costs are in excess of Total Payments, FUNDER shall pay the amount of such excess to RESEARCH PARTY, and thereafter shall have no obligation to make any further payments under this Agreement. If, however, the Total Costs are less than the Total Payments RESEARCH PARTY shall return the amount of such over-payment to FUNDER.

## 15. DISPUTE RESOLUTION

15.1 If any dispute arises between the parties under or in connection with this Agreement either party may serve notice upon the other setting out brief details of the dispute that has arisen ("**Notice of Dispute**") and the parties shall use their reasonable endeavours to resolve the dispute by good faith negotiations.

15.2 If the dispute is not resolved by the earlier of: (i) three (3) months from the date of the Notice of Dispute; or (ii) the date either party decides not to continue such good faith negotiations at any time; then the matter shall be referred to arbitration.

15.3 Without prejudice to clause 15.1 above, any dispute arising out of or in connection with this Agreement which cannot be resolved within three (3) months from the date of the Notice of Dispute, shall be finally resolved by arbitration in accordance with the provisions of the Arbitration Act 1996 and conducted pursuant to the rules of the Chartered Institute of Arbitrators at present in force and subject to English law.

15.4 The parties acknowledge and agree that:

15.4.1 the tribunal shall consist of a single arbitrator;

15.4.2 the arbitrator shall be appointed by the parties jointly or (failing agreement within five (5) further Working Days) to be selected and appointed by the President for the time being of the Chartered Institute of Arbitrators of London;

15.4.3 any right of application or appeal to court concerning any question of law arising in the course of the arbitration shall be excluded insofar as the law allows; and

15.4.4 the place of the arbitration shall be London and all submissions and awards shall be made in English.

## 16. CONFIDENTIALITY

- 16.1 In this clause 16, "**Confidential Information**" means all information disclosed (whether in writing, orally or by another means and whether directly or indirectly) by a party ("**Disclosing Party**") to the other party ("**Receiving Party**") including, but not limited to, reports and financial statements, information relating to the Disclosing Party's products, operations, processes, plans or intentions, product information, know-how, design rights, trade secrets, market opportunities and business affairs. The obligations of confidentiality under this clause 16 shall continue for a period of five (5) years after the Date of Termination except where the Confidential Information relates to matters that are the subject of a patent, licence or other form of protection of rights, in which case the obligation of confidentiality shall last for the duration of such patent, licence or other form of protection of rights.
- 16.2 During the Term and after termination or expiry of this Agreement the Receiving Party:
- 16.2.1 shall not use Confidential Information for a purpose other than the performance of its obligations under this Agreement;
  - 16.2.2 shall not disclose Confidential Information to any person except with the prior written consent of the Disclosing Party or in accordance with clauses 16.3 and 16.4;
  - 16.2.3 shall make every effort to prevent the unauthorised use or disclosure of Confidential Information.
- 16.3 During the Term of this Agreement the Receiving Party may disclose Confidential Information to any of its directors, other officers, employees, students and sub-contractors ("**Recipient**") to the extent that disclosure is necessary for the purposes of this Agreement.
- 16.4 Before disclosure of Confidential Information to a Recipient, the Receiving Party shall ensure that such Recipient is made aware of and is under their own obligation to comply with no less stringent obligations of confidentiality than under this Agreement.
- 16.5 Clauses 16.2 to 16.4 do not apply to Confidential Information which:
- 16.5.1 is at the Commencement Date or becomes at any time after that date publicly known other than by the Receiving Party's or Recipient's breach of this Agreement;
  - 16.5.2 can be shown by the Receiving Party to the Disclosing Party's reasonable satisfaction to have been known by the Receiving Party before disclosure by the Disclosing Party to the Receiving Party;

16.5.3 is or becomes available to the Receiving Party otherwise than pursuant to this Agreement and free of any restrictions as to its use or disclosure; or

16.5.4 is required to be disclosed by law, in which case the party that is subject to the legally-required disclosure shall, where it is legally permitted to do so, inform the other party prior to such disclosure being made, and if this is not reasonably possible, as soon as possible thereafter.

## 17. FREEDOM OF INFORMATION

Nothing in this Agreement shall be interpreted as contravening any of the provisions of the Freedom of Information Act 2000, and the Italian Legislative Decree on privacy on personal data [196/2003 as implemented by the Italian Legislative Decree 101/2018] and Regulation (EU) 2016/679 GDPR and FUNDER acknowledges and accepts that RESEARCH PARTY is subject to the same legislation if and when applicable.

## 18. BRIBERY

Both parties shall comply with all applicable laws, regulations and sanctions relating to anti-bribery and anti-corruption including (to the extent applicable) but not limited to the Bribery Act 2010 and Italian Legislative Decree 231/2011 and Law 190/2012 and shall not give, provide or offer to any other party or any third parties any loan, fee, reward, gift (except items of negligible or intrinsic value), or any emolument or advantage whatsoever to such other parties. Non-compliance or suspected non-compliance shall constitute a material breach of this Agreement and this Agreement may be terminated by the non-breaching party with immediate effect without prejudice to any other rights the non-breaching party may possess.

## 19. FORCE MAJEURE

19.1 If a party ("**Affected Party**") is prevented, hindered or delayed from or in performing any of its obligations under this Agreement by a Force Majeure Event:

19.1.1 the Affected Party's obligations impacted by the Force Majeure under this Agreement are suspended while the Force Majeure Event continues and to the extent that it is prevented, hindered or delayed. For the avoidance of doubt, obligations under Clauses: 9 (Publication); 10 (Intellectual Property); 11 (Publicity); 16 (Confidentiality); 18 (Bribery); and 20 (Assignment and Sub-Contracting) shall not be suspended during Force Majeure;

19.1.2 as soon as reasonably possible after the start of the Force Majeure Event, the Affected Party shall notify the other party ("**Non-Affected Party**") in writing of the Force Majeure Event, the date on which the Force Majeure Event started and the effects of the Force Majeure Event on its ability to perform its obligations under this Agreement;

19.1.3 the Affected Party shall make reasonable efforts to mitigate the effects of the Force Majeure Event on the performance of its obligations under this Agreement; and

19.1.4 as soon as reasonably possible after the end of the Force Majeure Event, the Affected Party shall notify the other parties in writing that the Force Majeure Event has ended and resume performance of its obligations under this Agreement.

19.2 If the Force Majeure Event continues for more than three (3) months starting on the day the Force Majeure Event starts, either party may terminate this Agreement by giving not less than thirty (30) days' notice in writing to the other party.

19.3 For the avoidance of doubt, Force Majeure shall not excuse FUNDER from any payment obligations under this Agreement.

## **20. ASSIGNMENT AND SUB-CONTRACTING**

Neither party may sub-contract the performance of any of its obligations or assign or deal in any way with all or any part of the benefit of, or its rights or obligations under, this Agreement without the prior written consent of the other party (which consent shall not be unreasonably withheld or delayed). The sub-contracting party shall be responsible for all acts and omissions of its sub-contractors as if they were its own.

## **21. NOTICES**

Any notice given by one party to the other under this Agreement must be in writing and may be delivered personally or by pre-paid first class post and in the case of post will be deemed to have been given two (2) Working Days after the date of posting, or by email. Notices shall be delivered or sent to the addresses of the parties as referenced in Schedule 1 or to any other address notified in writing by one party to the others for the purpose of receiving notices after the date of this Agreement.

## **22. SEVERANCE**

If any provision of this Agreement is found by any court or administrative body of competent jurisdiction to be invalid or unenforceable, such invalidity or unenforceability shall not affect the other provisions of this Agreement which shall remain in full force and effect.

## **23. THIRD PARTIES**

A person who is not party to this Agreement shall have no rights under the Contracts (Rights of Third Parties) Act 1999 and the European Civil Law of Agreements to enforce any term of this Agreement. This clause 23 does not affect any right or remedy of any person which exists or is available otherwise than pursuant to that Act.

**24. NO PARTNERSHIP OR AGENCY**

Nothing in this Agreement is intended to create a partnership or joint venture or legal relationship of any kind that would impose liability upon one party for the act or failure to act of the other party between the parties, or to authorise any party to act as agent for the other party between the parties. Save where expressly stated in this Agreement, neither party shall have authority to make representations, act in the name or on behalf of or otherwise to bind the other party.

**25. WAIVER**

No forbearance or delay by a party in enforcing its rights will prejudice or restrict the rights of that party, and no waiver of any such rights or of any breach of any contractual terms will be deemed to be a waiver of any other right or any later breach.

**26. VARIATION**

No variation of this Agreement or any of the documents in the agreed form referred to in it shall be valid unless it is in writing signed by or on behalf of each of the parties to this Agreement.

**27. ENTIRE AGREEMENT**

27.1 This Agreement, together with the documents referred to in it, constitutes the entire agreement and understanding between the parties in respect of the matters dealt with in them and shall take precedence over any conflicting terms in any subsequent purchase order terms and conditions issued for the Project.

27.2 Each of the parties acknowledges and agrees that in entering into this Agreement, and the documents referred to in it, it does not rely on, and shall have no remedy in respect of, any statement, representation, warranty or understanding (whether negligently or innocently made) other than as expressly set out in this Agreement. The only remedy available to either party in respect of any such statement, representation, warranty or understanding shall be for breach of contract under the terms of this Agreement.

27.3 Nothing in this clause 27 shall operate to exclude any liability for fraud.

**28. GOVERNING LAW AND JURISDICTION**

28.1 This Agreement and any matter arising from or in connection with it shall be governed by and construed in accordance with English law.

**29. GENERAL**



The Parties agree to execute this Agreement by way of an electronic certified signature, and agree this shall constitute a valid and enforceable agreement between the Parties.

**IN WITNESS** whereof the parties have executed this Agreement the day and year shown below their respective following signatures.

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**SIGNED by**

for and on behalf of Fondazione  
IRCCS Istituto Nazionale dei Tumori  
(INT):

Name: Dr. Carlo Nicora  
Title: General Manager  
digital signature

**Read and Acknowledged:**

Principal Investigators

DocuSigned by:  
*Silvia Stacchiotti* 03-dic-2022  
3D6853D2922B42C...  
Name: dr. Silvia Stacchiotti

DocuSigned by:  
*Nadia Zaffaroni* 04-dic-2022  
7463E5653BB5464...  
Name: dr. Nadia Zaffaroni

DocuSigned by:  
*Annalisa Trama* 05-dic-2022  
BD77E28EA2E44C3...  
Name: dr. Annalisa Trama

**SIGNED** by:

DocuSigned by:



ED7087580076445

for and on behalf of The EHE Rare  
Cancer Charity (UK) :

Name: Howard Hugh I Leonard

Title: Chair of Trustees

Date: 03-Dec-2022

## SCHEDULE 1

### Programme of Research

TITLE	<b><u>Prospective EHE registry (PROSPHERES)</u></b>
PROGRAMME OF RESEARCH	The Programme of Research is described in Schedule 2.
COMMENCEMENT DATE	The date on which RESEARCH PARTY has received the First Tranche of payment as defined below after confirming that it is ready to proceed.
TERMINATION DATE	The earlier of; (i) the date that occurs 36 (thirty-six) calendar months after the Commencement Date ; or (ii) the date when the Deliverables are delivered; or (iii) any other date of termination of this Agreement in accordance with its terms.
WORK PROGRAMME	The work programme is described in Schedule 2.
PRICE	<p>Total price for the three year Programme of Research comprises € 91,500 (ninety-one thousand, five hundred) Euros; all as more fully detailed in Schedule 3.</p> <p>The Price is RESEARCH PARTY's estimate of the cost of the Programme of Research and includes allocation of personnel, materials and all other items required to deliver the Programme of Research described in Schedule 2.</p> <p>Due to the uncertain nature of research, RESEARCH PARTY and the FUNDER recognise that the scope of work may vary once started. RESEARCH PARTY may propose variations to the scope of work and associated increases or decreases in costs, and if agreed by FUNDER at its sole and absolute discretion, an amendment to the Price stipulated in this section of schedule 1</p>

	<p>shall be agreed in writing. RESEARCH PARTY shall be under no obligation to deliver any increase in the scope of work if FUNDER does not agree to an associated increase in costs.</p> <p>At the end of each year of the Programme of Research, RESEARCH PARTY shall provide an account for all costs of the Programme of Research incurred by RESEARCH PARTY in that year, including a reconciliation of all costs paid to the other establishments as listed in Schedule 2 against patients recruited.</p> <p>If costs incurred are less than the payments made by FUNDER to RESEARCH PARTY, RESEARCH PARTY and FUNDER will discuss if such overpayment should be: (i) credited to and subtracted from the next year's budget; or (ii) repaid to FUNDER with no adjustment to the following year's budget.</p>
PAYMENT TERMS	<p>The Price shown above is payable to RESEARCH PARTY in a single payment each year, with annual amounts shown in Schedule 3. The first payment shall be made within 30 days of the signing of this Agreement, and subsequent two annual payments shall be made on each anniversary of the date of the first payment, based on RESEARCH PARTY reporting progress at the end of the prior year period that FUNDER agrees is reasonable, such agreement not to be unreasonably withheld or delayed.</p> <p>RESEARCH PARTY shall deliver an invoice to FUNDER prior to the payment of any sums. The parties shall agree the structuring of the invoices prior to the first invoice being submitted. The</p>

	<p>invoice shall include details as listed in Schedule 4. There shall be no VAT payable.</p> <p>Invoices shall be payable within 15 (fifteen) days of the date of the invoice.</p> <p>For the avoidance of doubt, sums specified as payable to The Royal Marsden Hospital, London (RMH) in Schedule 3 shall be paid by FUNDER to RESEARCH PARTY who shall then transfer the funds on to RMH, unless an alternative direct payment structure between FUNDER and RMH is agreed with RESEARCH PARTY.</p>
PRINCIPAL INVESTIGATOR(S)	<p>Dr Silvia Stacchiotti MD at s.c. Oncologia Medica 2 – Tumori mesenchimali e rari, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Venezian 1 - 20133 Milano</p> <p>Dr Annalisa Trama, Head of s.s.d. Epidemiologia Valutativa, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan</p> <p>And</p> <p>Dr. Nadia Zaffaroni, PhD, Head of s.c. Farmacologia Molecolare, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Amadeo 42 - 20133 Milano.</p>
DELIVERABLES, REPORTING AND PRESENTATIONS	<p>The deliverable of the Programme of Research is the establishment of a prospective, EHE dedicated, clinical registry across the UK and EU, as more fully described in the Programme of Research in Schedule 2</p> <p><b>Reporting:</b></p>

	<p>RESEARCH PARTY shall provide progress reports every six months after the Commencement Date. Such reports shall be delivered to the FUNDER at the address given below, and by email.</p> <p>For the avoidance of doubt, all reporting shall be to the FUNDER at the address given below, and by email.</p> <p><b>Presentations:</b></p> <p>In order to maximise the benefit of EHE research and the sharing of knowledge, information and ideas, FUNDER will be coordinating a programme of presentations under which each research team funded by FUNDER is required to provide an annual presentation of their research to a small audience comprising: (i) members of the FUNDER'S management and Advisory Board; (ii) other EHE researchers funded by the EHE foundations; and (iii) external EHE research and EHE clinical specialists. In accepting funding for this project, the RESEARCH PARTY agree to: (i) provide such annual presentation; and (ii) provide senior personnel to attend presentations by other researchers. The date and timing of such presentations given by the RESEARCH PARTY shall be mutually agreed between the parties.</p>
SPECIFIC PROVISIONS	<p>IP specific to the project: results will be made available to other academic users based on cost recovery, any commercial exploitation would be subject to negotiation between the FUNDER and RESEARCH PARTY.</p>
ADDRESSES FOR NOTICES	<p><b>For INT PARTY:</b></p> <p>Dr Silvia Stacchiotti</p> <p>Dr Annalisa Trama</p>

	<p>Dr. Nadia Zaffaroni, PhD</p> <p>Fondazione IRCCS Istituto Nazionale dei Tumori, Via Venezian 1 - 20133 Milano</p> <p><b>For FUNDER:</b></p> <p>Mr Hugh Leonard:</p> <p>EHE Rare Cancer Charity (UK)</p> <p>23 Geneva Road</p> <p>Kingston-Upon-Thames</p> <p>Surrey</p> <p>KT1 2TW</p>
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## SCHEDULE 2

### Programme of Research Description

#### Prospective EHE Registry (PROSPHERES)

##### 1. Background and Rational of the study

Epithelioid hemangioendothelioma (EHE) is an ultra-rare, vascular sarcoma, with an incidence of 0.038/100000/year<sup>1-3</sup>. It peaks in the IV-V decade of life<sup>1,3-6</sup>, with a predominance in females<sup>7</sup>. Up to 90% of EHEs are marked by the fusion of Transcriptional Co-activator with a PDZ-motif (TAZ) with Calmodulin Binding Transcription Activator 1 (CAMTA1), that is a diagnostic hallmark and help differential diagnosis with other mimics. The 10% of EHEs that lack the TAZ–CAMTA1 fusion instead have a fusion of Yes-associated Protein (YAP) and Transcription Factor E3 (TFE3) genes (YAP-TFE3)<sup>8,9</sup>.

At the time of presentation >50% of patients show metastatic disease, with liver (21%), lung (12%), and bone (14%) being the most commonly involved sites<sup>4-6,11,12</sup>. The extent of the disease can be variable, with essentially 3 possible different clinical scenarios: unifocal lesion (i.e. localized disease characterized by a single tumour lesion), locoregional metastases (i.e. a disease with multifocal single-organ involvement or multiple lesions to a single anatomic compartment) or systemic metastases (i.e. a disease with multi-organ involvement)<sup>1,6,11</sup>. The clinical course of EHE is unpredictable upfront and ranges from indolent tumours that lay dormant for years to highly aggressive disease, rapidly progressive and often fatal. As of today, the natural history of this entity is not fully understood and reliable, validated clinical and/or molecular prognostic factors are lacking.

Patients presenting with a unifocal lesion are usually managed with surgery, as there is no evidence today that complimentary treatment can impact survival. For those presenting with asymptomatic metastatic disease, given the unpredictable clinical behaviour of EHE, upfront surveillance can be reasonably offered, while a systemic therapy is offered to symptomatic or progressive patients. Conventional chemotherapy has a very limited activity in this disease, while better results have been reported with m-Tor inhibitors and anti-angiogenic compounds. Overall, the best treatment strategy is still to be defined, and there is still a high variability in the approach across institutions.

With the aim of addressing these outstanding questions, we propose a collective effort across the EU and UK, with the establishment of a prospective EHE dedicated, clinical registry which will be called the PROSPHERES study.

## 2. Study objectives

This study aims to provide a description of the population affected by EHE, giving an insight into the natural history of the disease and its variants, leading to the possible identification of clinical and biochemical prognostic and predictive factors and answering some of the outstanding questions on its management. The primary objectives of the study will include:

- Demographic description of the population affected by EHE
- Description of the natural history and outcome of the disease as a whole and of EHE 3 main variants based on disease extension:
  - 1) Primary, localized, single lesion (unifocal disease);
  - 2) Loco-regional (multifocal single-organ involvement)
  - 3) Systemic metastases (multi-organ involvement including loco-regional lymph-node involvement)
- Description of tumour-related symptoms and their changes over time
- Description of tumour-related pain and changes overtime
- Description of current treatment approach for localised disease
- Description of current treatment approach for metastatic disease
- Assessment of disease response to local therapies (radiation therapy, local ablative techniques, ILP, others)
- Assessment of disease response to systemic therapies (cytotoxic chemotherapy, mTOR inhibitors, anti-angiogenic compounds, others)
- Identification of biological and clinical predictors of response to medical therapies
- Identification of biological and clinical prognostic factors
- Description of outcome

## 3. Study design

The PROSPHERES study will be incorporated in and administered within the STARTER project. STARTER is a Health Programme funded project, coordinated by dr Annalisa Trama (Department of Research, Evaluative Epidemiology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan) aiming to set-up a clinical registry for EURACAN, the European Reference Network (ERN) dedicated to rare adult solid cancers. The project was launched in April 2020 and will be running for 36 months. It will exploit at a European level, data coming from individual expert health care providers, from national and European registries and it will be interoperable with already existing rare disease registries.

The EURACAN registry will progressively cover all the 10 families of rare adult solid cancers included in EURACAN (sarcomas; rare neoplasms of the female genital organs and placenta; rare genitourinary cancers; rare neuroendocrine tumours; rare digestive cancers; rare endocrine cancers; rare head and neck cancers; rare

thoracic cancers; rare skin/eye melanoma and rare brain tumours). However, sarcomas together with rare head and neck cancers have been selected as the two case-use to get the project started.

Among the sarcoma domain (coordinated by Prof. Paolo G. Casali, Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan) ultra-rare sarcomas, such as EHE, have been selected as the topic to start with, as the community believe that, given the exceeding rarity of these sarcoma types, international prospective registries could provide an invaluable contribution, both by allowing a better understanding of the natural history of the different diseases and in order to provide external control data, potentially useful in the process of drug development and approval.

Incorporating and operating the PROSPHERES study within and as part of the STARTER project represents an extraordinary opportunity to develop an EHE prospective study that would be broader, larger and more cost effective than if PROSPHERES was run as a standalone study, and will deliver the following benefits:

- The establishment of a full registry in EHE, which with appropriate funding can be maintained on an ongoing basis with no pre-defined duration over time.
- The use of the existing free-of-charge web application (RedCap) offered by the Fondazione IRCCS Istituto Nazionale dei Tumori in Milan, which is fully set up and used for data collection in the head and neck domain including data quality checks.
- A simplification in terms of administrative, legal and ethical issues implicit in the project as the STARTER project team has already addressed and is compliant with very complex ethical and administrative issues such as current GDPR requirements.
- The supervision of a dedicated coordination team of data manager, CRF developers and statisticians.
- The potential enrolment of a large number of patients through the contribution of multiple sarcoma reference centers, within and outside EURACAN.

By joining STARTER, the project may be able to include, as a start, approximately 11 sarcoma reference centers across the European Union and the UK, including:

1. Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
2. Royal Marsden Hospital, London, United Kingdom
3. Fundación Jimenez Diaz University Hospital, Madrid, Spain
4. Sahlgrenska Universitetssjukhuset, Gothenburg, Sweden
5. Oslo University Hospital, Oslo, Norway
6. University Hospital Graz, Graz, Austria
7. Centre Leon Berard, Lyon, France

8. Mannheim University Medical Centre, Mannheim, Germany
9. Maria Skłodowska Curie Institute - Oncology Centre, Warsaw, Poland
10. Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, Netherlands
11. Istituto Oncologico Veneto / Università di Padova, Padua, Italy
12. Policlinico Universitario P. Giaccone , Palermo, Italy

Two centers (Fondazione IRCSS Istituto Nazionale dei Tumori, Milan; and the Royal Marsden Hospital, London) will be covered by EHERCC funding under this contract. The possible inclusion of additional centers, some of whom have previously expressed interest in joining the EURACAN sarcoma registry, will be discussed, but will be dependent on their expertise on sarcomas and EHE in particular, and additional funding availability.

The European contributing institutions all belong to the sarcoma domain of EURACAN, the European Reference Network dedicated to the Rare Adult Solid Cancers, to ensure data quality and a concrete expertise in the sarcoma field.

This prospective registry will include all consecutive patients with a histological diagnosis of EHE and treated at participating sarcoma reference centers as listed above.

For every patient included, a confirmation of the histological diagnosis performed by the expert sarcoma pathologist of each contributing institution will be performed, and molecular testing for WWTR1-CAMTA1 and/or YAP-TFE3 will be required.

Clinical data (demographic, symptoms, disease clinical and pathological features, treatment, outcome) will be prospectively collected through an electronic CRF which will be put in place and shared with all contributing institutions. Data quality check will be performed by a dedicated study coordinator.

#### **4. Study population**

The initial plan is to include a minimum of approximately 100 patients (range: 80-120), in 36 months, followed by a follow up time of at least 3 years.

##### *Inclusion criteria:*

- Histological diagnosis of EHE according to 2020 WHO classification, confirmed by an expert sarcoma pathologist and molecularly confirmed, as previously described.
- Adequate patient compliance

## References

1. Lau, K. *et al.* Clinical patterns and outcome in epithelioid hemangioendothelioma with or without pulmonary involvement: insights from an internet registry in the study of a rare cancer. *Chest* **140**, 1312–1318 (2011).
2. Stacchiotti, S. *et al.* Epithelioid hemangioendothelioma, an ultra-rare cancer: a consensus paper from the community of experts. *ESMO open* **6**, 100170 (2021).
3. de Pinieux, G. *et al.* Nationwide incidence of sarcomas and connective tissue tumors of intermediate malignancy over four years using an expert pathology review network. *PLoS One* **16**, e0246958 (2021).
4. Rosenbaum, E. *et al.* Prognostic stratification of clinical and molecular epithelioid hemangioendothelioma subsets. *Mod. Pathol. an Off. J. United States Can. Acad. Pathol. Inc* **33**, 591–602 (2020).
5. Guo, Q., Xue, J., Xu, L., Shi, Z. & Zhou, B. The clinical features of epithelioid hemangioendothelioma in a Han Chinese population: A retrospective analysis. *Medicine (Baltimore)*. **96**, e7345 (2017).
6. Flucke, U. *et al.* Epithelioid Hemangioendothelioma: clinicopathologic, immunohistochemical, and molecular genetic analysis of 39 cases. *Diagn. Pathol.* **9**, 131 (2014).
7. Sardaro, A., Bardoscia, L., Petruzzelli, M. F. & Portaluri, M. Epithelioid hemangioendothelioma: an overview and update on a rare vascular tumor. *Oncol. Rev.* **8**, 259 (2014).
8. Antonescu, C. R. *et al.* Novel YAP1-TFE3 fusion defines a distinct subset of epithelioid hemangioendothelioma. *Genes. Chromosomes Cancer* **52**, 775–784 (2013).
9. Errani, C. *et al.* A novel WWTR1-CAMTA1 gene fusion is a consistent abnormality in epithelioid hemangioendothelioma of different anatomic sites. *Genes. Chromosomes Cancer* **50**, 644–653 (2011).
10. Lamar, J. M., Motilal Nehru, V. & Weinberg, G. Epithelioid Hemangioendothelioma as a Model of YAP/TAZ-Driven Cancer: Insights from a Rare Fusion Sarcoma. *Cancers (Basel)*. **10**, 229 (2018).
11. Shiba, S. *et al.* Clinical characteristics of Japanese patients with epithelioid hemangioendothelioma: a multicenter retrospective study. *BMC Cancer* **18**, 993 (2018).
12. Wu, X., Li, B., Zheng, C., Hong, T. & He, X. Clinical characteristics of epithelioid hemangioendothelioma: a single-center retrospective study. *Eur. J. Med. Res.* **24**, 16 (2019).

## SCHEDULE 3

### Project Costs

BUDGET PROPOSAL : PROSPHERES PROSPECTIVE STUDY WITHIN STARTER			
Funder:	The EHE Rare Cancer Charity (UK)		
International Coordinating Centre:	Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy		
Other involved Institutions:	As listed in Schedule 2 : Programme of Research Description		
PROPOSAL			
Study Information			
Study Title	PROSPHERES		
Estimated number of participants	Initially 100 patients with additional patients added as available		
Estimated project duration	3 years		
Principal Investigators Contact Information			
Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy	First name Last name Investigator Institution Country	Silvia Stacchiotti Italy	
Other institutions	To be confirmed as each institute agrees to join the project.		
Budget			
Funding details Total Planned Study Budget			
Fondazione IRCCS Istituto Nazionale Tumori, Milan	Italy	Costs included in project figures below	
EU participating sarcoma reference centres	Others as applicable	Funded from existing alternative sources	
UK	London	Costs included in project figures below	
Local EU Study Currency	EUR €		
Local UK Study Currency	Pound £		
Average Exchange Rate per EUR	0.86		
Direct cost covered by this contract		Costs in Euros	
		Per year	For 3 years
Administrative costs for Study Set-up at Fondazione IRCCS INT (Year 1 sum only)		1,500 €	1,500 €
Study Coordinator: Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy (dedicated to work with the STARTER team to set-up an EHE specific CRF, established a contact with all the contribution institutions and coordinate work over the first 3 years, ensure patients enrolment and data entry at INT over the first 3 years)		20,000 €	60,000 €
Royal Marsden Hospital, London : Costs for all analysis and data entry for Royal Marsden patients included in the study		10,000 €	30,000 €
	Total	31,500 €	91,500 €

## **SCHEDULE 4**

### **Invoice Requirements**

The following information should be included within all invoices relating to the Programme of Research:

- You must clearly display the word ‘invoice’ on the document;
- A unique invoice identification number;
- Invoicer’s full name, address and contact information for queries;
- FUNDER’s name and address, which is:

**The EHE Rare Cancer Charity**

23 Geneva Road  
Kingston-Upon Thames  
Surrey  
KT1 2TW

- Description and dates of works being invoiced. For example “PROSPHERES Research contract Year 1 payment”;
- The amount(s) being charged;
- The total amount owed;
- The payment due date; and
- Full bank details for international payments

FUNDER will ask for re-issuance of invoices that do not include this information.

Invoices should be submitted by email to Hugh Leonard at [hleonard@ehercc.co.uk](mailto:hleonard@ehercc.co.uk) with copy to Mr Jeffery Collins at [jcollins@ehercc.co.uk](mailto:jcollins@ehercc.co.uk)