Clinical Trial Site Agreement

Dated: _____

Full Title of Clinical Trial:	**A phase II study of nivolumab monotherapy in patients with relapsed/refractory Hodgkin lymphoma, fit for autologous stem cell transplant, who fail to reach complete metabolic remission after first or second line salvage therapy**
Short Title and/or Acronym:	**ANIMATE**
EudraCT Number:	**2017-002544-32**
REC ref:	**18/LO/0204**
Sponsor:	**University College London**
Sponsor's Project ID Number:	**UCL/15/0515**
Funder:	**Bristol-Myers Squibb Pharmaceuticals Ltd (BMS protocol reference CA-209-445)**

Between:

(1) University College London (**"UCL"**) hereby represented by the CANCER RESEARCH UK & UNIVERSITY COLLEGE LONDON CANCER TRIALS CENTRE, (**"CTC"**) of 90 Tottenham Court Road, London W1T 4TJ (together the **"Sponsor"**); and

(2) [add NHS TRUST / NHS HEALTH BOARD NAME and address] (Please see list at Appendix 1 of associated hospital sites with the same Principal Investigator for which the Site is responsible, and where Trial activities are to be undertaken) (the **"Site"**).

together: "**the Parties**"

Whereas:

(A) The CTC and UCL are coordinating and sponsoring the ANIMATE trial (the "**Trial**"), which will be conducted according to the Protocol (as amended from time to time), a copy of which is attached to this Agreement as Appendix 2;

(B) The CTC is part of UCL but does not have separate legal status from UCL; UCL is sponsoring the Trial and the roles and responsibilities of the CTC and UCL are as set out in the Memorandum of Understanding ("MoU") (as defined below);

(C) The Site is interested in undertaking the conduct of the Trial pursuant to the terms and provisions of this Agreement;

(D) The Funder has agreed to provide funds for the central co-ordination of the Trial at the CTC and “per site” payments (as per Appendix 5);

(E) The Sponsor has entered into an agreement with the Supplier to cover the supply of Trial Drug (nivolumab).

Operative Provisions

1. **DEFINITIONS IN THIS AGREEMENT:**

The following words and phrases have the meanings set out here:

“Adverse Event (AE)” means any untoward medical occurrence in a patient treated on a trial protocol, which does not necessarily have a causal relationship with a trial treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a trial treatment, whether or not related to that trial treatment;

“Adverse Event of Special Interest (AESI)” means an AE that requires reporting even if does not meet the standard criteria for seriousness, or it occurs outside the standard AE reporting timeframes for the trial;

“Adverse Reaction (AR)” means all untoward and unintended responses to a trial treatment related to any dose administered. A causal relationship between a trial treatment and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out;

“Confidential Information” means all information, data, results and Intellectual Property and Know How relating to the Trial including Trial Treatment, its/their use(s), any new indication or novel use of Trial Treatment and all information concerning arrangements contemplated by this Agreement or the business affairs of one Party that it discloses to the other Party pursuant to or in connection with this Agreement;

“Data Protection Legislation” means the Data Protection Act 2018 and the General Data Protection Regulation (EU 2016/679), and any other applicable UK and EU data protection legislation and regulations, and any amendments or replacements thereto;

“Force Majeure" means in relation to either Party any circumstances beyond the reasonable control of that Party (including without limitation any strike lock-out or other industrial action);

“Framework” means the ‘UK Policy Framework for Health and Social Care Research’, issued by the Health Research Authority in October 2017, as may be amended from time to time;

“Funder” means the organisation providing monetary funds for the purpose of carrying out the Trial;

“Good Clinical Practice (GCP)” refers to the principles of ICH Harmonised Tripartite Guideline for Good Clinical Practice (CPMP/ICH/135/95) as set out in Schedule 1 (Conditions and Principles of Good Clinical Practice and for the Protection of Clinical Trial Subjects) of the Medicines for Human Use (Clinical Trials) Regulations 2004 and the GCP Directive 2005/28/EC, as set out in SI 2006/1928, and any amendments thereto;

"Good Manufacturing Practice (GMP)" refers to European Commission Directive 2003/94/EC laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use, and any amendments thereto;

"Independent Data Monitoring Committee (IDMC)" means the committee responsible for the independent monitoring of Trial data in order to assess the safety and efficacy of Trial Treatment(s);

"Intellectual Property" means all patents, trade marks, copyrights, database rights, design rights and all rights (whether registered or unregistered) or forms of protection of a similar nature or having equivalent or similar effect to any of them anywhere in the world, whether registered or not and including applications for registration of any of them;

"Know How" means all technical and other information which is not in the public domain, including information relating to concepts, discoveries, data, designs, formulae, ideas, inventions, methods, models, procedures, designs for experiments and tests, the results of experiments and testing, processes, specifications and techniques, laboratory records, clinical data, manufacturing data and information whether or not contained in submissions to regulatory authorities;

"Materials" means all tissue samples or other biological materials and any derivatives, portions, progeny or improvements and shall include all patient information and documentation supplied in relation to them as detailed in the Protocol;

"Memorandum of Understanding (MoU)" means the document describing the roles and responsibilities between UCL and the CTC for the management and conduct of clinical trials sponsored by UCL;

"MHRA" means the Medicines and Healthcare products Regulatory Agency;

"Personal Data" means data which falls within the definition of "Personal Data" in the relevant Data Protection Legislation as is then in force;

"Principal Investigator" or **"Investigator"** means the authorised health care professional who will lead and co-ordinate the work of the Trial on behalf of the Site or any other person as may be agreed from time to time between the Parties as a replacement;

"Protocol" means the document set out in Appendix 2 (and as amended from time to time) which describes the objectives, design, methodology, statistical considerations and the organisation of the Trial and is, or will be, approved by Research Ethics Committee and the MHRA;

"Regulations" mean the Medicines for Human Use (Clinical Trials) Regulations 2004, as are amended from time to time, including the Medicines for Human Use (Clinical Trials) Amendment Regulations 2006 and the Medicines for Human Use (Clinical Trials) Amendment (No.2) Regulations 2006;

"Research Ethics Committee (REC)" means the research ethics committee which provides a single favourable opinion for the Trial;

"Serious Adverse Event (SAE)", "Serious Adverse Reaction (SAR)" means an Adverse Event or Adverse Reaction that at any dose:

- Results in death
- Is life threatening (The term “life-threatening” refers to an event in which the patient was at risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it were more severe.)
- Requires in-patient hospitalisation or prolongs existing hospitalisation
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly or birth defect
- Is otherwise medically significant (e.g. important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed above);

“Serious Breach” means a breach of GCP or of the Protocol which is likely to affect to a significant degree, the safety or physical or mental integrity of the Trial Subjects; or the scientific value of the Trial;

“Site” means the hospital or any premises in which the Trial will be conducted and which is approved by the NHS Trust or Health Board which is a Party signatory to this Agreement;

“Sponsor” means the organisation that takes responsibility for the initiation, management and financing (or arranging the financing) of the Trial;

“Supplier” means the company providing Trial Drug for the Trial namely Bristol-Myers Squibb Pharmaceuticals Ltd. providing nivolumab (Opdivo®);

“Suspected Unexpected Serious Adverse Reaction (SUSAR)” means a Serious Adverse Reaction, the nature or severity of which **is not consistent** with the applicable reference safety information;

“Trial Drug” means the investigational medicinal product and the medicinal product under investigation, nivolumab (Opdivo®); for use in the Trial;

“Trial Management Group (TMG)” means the committee which provides advice and oversight of day to day management decisions for the Trial and whose input is aimed at ensuring the safe conduct and progress of the Trial in accordance with the Protocol;

“Trial Steering Committee (TSC)” means the oversight committee which provides supervision of the overall conduct of the Trial on behalf of the Funder(s) and Sponsor. The TSC reviews recommendations of the Independent Data Monitoring Committee and, on consideration of this information, recommends appropriate amendments/actions for the Trial as necessary;

“Trial Subject” means a patient recruited onto the Trial for the purpose of participation in the Trial;

“Trial Treatment” means all therapeutic activity under investigation in the Trial, including Trial Drug(s), as dictated by the Protocol.

“Urgent Event” means a safety event that requires urgent reporting to the Sponsor via a specific case report form. Events that require reporting as Urgent Events for the Trial are identified in the Protocol.

2. CONDUCT OF THE TRIAL

2.1 UCL and CTC shall undertake the Trial as Sponsor according to the approved Protocol, the Regulations, GCP and any other applicable local laws and regulations.

2.2 The Trial shall be conducted by the Parties:

2.2.1 At the Site and in accordance with the terms of this Agreement;

2.2.2 In accordance with the Protocol and any amendments to the Protocol;

2.2.3 With Trial Subjects selected in accordance with the criteria specified in the Protocol;

2.2.4 Only after all necessary legal, regulatory and/or other approvals have been granted including, without limitation, REC approval, Clinical Trial Authorisation granted by the MHRA and NHS permission (Health Research Authority approval in England) and strictly in accordance with the terms of any of such approvals.

2.3 The Parties shall comply with all guidance, laws and statutes applicable to the performance of clinical trials including, but not limited to, the Human Rights Act 1998, Data Protection Legislation, The Freedom of Information Act 2000, The Human Tissue Act 2004, the Medicines Act 1968, the Regulations, GMP, and with all relevant guidance relating to medicines and clinical trials from time to time in force including, but not limited to, GCP, the World Medical Association Declaration of Helsinki entitled *'Ethical Principles for Medical Research Involving Human Subjects'* (1996 version), the Framework and any amendments thereto.

2.3.1 In addition to clause 2.3 above, Scottish, Welsh and Northern Irish Sites shall comply with all their local laws and statutes applicable to the performance of clinical trials.

3. RESPONSIBILITIES OF THE PARTIES

In exchange for their mutual obligations to each other, the Parties agree that they will do the following:

3.1 The **Site** shall:

3.1.1 Ensure that the Protocol has been reviewed by the Site R&D Department and it has been agreed that there are no resource or cost implications that would prevent the Trial from being conducted at the Site;

3.1.2 Procure the services of a Principal Investigator for the duration of the Trial and ensure that the Principal Investigator undertakes the duties contained in Appendix 4 and elsewhere in this Agreement and complies with other responsibilities reasonably expected from the Principal Investigator in the performance of the Trial. The Site represents that the Principal Investigator holds the necessary qualifications and has the necessary expertise, time, supporting staff and resources to conduct the Trial;

3.1.3 Ensure that if the Principal Investigator is no longer able to perform his/her duties at the Site under this Agreement for whatever reason, the Site will use its reasonable endeavours to replace the Principal Investigator, and shall procure that any such replacement, shall have the same level of experience and skill for the purposes of the conduct of the Trial as the current or outgoing Principal Investigator ensuring that the CTC is notified promptly of any changes;

3.1.4 Ensure that all members of Site staff (including any sub-contractors) involved in the Trial are suitably qualified and experienced to undertake the duties delegated to them and that this is adequately documented;

3.1.4.1 The Site shall ensure that up to date CVs are held for all members of Site staff involved in the Trial;

3.1.4.2 The Site shall ensure that delegation of Trial duties to Site staff by the Principal Investigator is documented and signed for by the Principal Investigator on the Site staff delegation log and a copy sent to the CTC;

3.1.5 Provide to the Sponsor appropriate financial disclosures and any conflicts of interest relating to the Trial, as the Sponsor may reasonably request, and shall communicate to the Sponsor any changes to the foregoing during the Trial and for a period of one (1) year thereafter;

3.1.6 Ensure that the required training in the Protocol and any Trial specific duties is provided and maintained for all new Site staff during the Trial;

3.1.7 Ensure that all medical care given to, and medical decisions made on behalf of, Trial subjects will be the responsibility of an appropriately qualified doctor;

3.1.8 Assess a potential Trial Subject's capability to give informed consent;

3.1.9 Ensure that Trial Subjects receive the current version of the patient information sheet, are fully informed about the Trial and, having been given at least the minimum timeframe required by the Protocol to consider their participation in the Trial, have confirmed their willingness to take part by signing the consent form for the Trial;

3.1.10 Ensure that Trial Subjects are given appropriate contact details for twenty four (24) hour access to medical advice;

3.1.11 Ensure that the Trial is commenced at Site only after Site confirmation of capacity and capability (English and Welsh sites), and all necessary local approvals have been granted including without limitation, where applicable, local R&D approval, and strictly in accordance with the terms of any such approvals;

3.1.12 Ensure that the Trial is commenced only after the Site has received written confirmation from the Sponsor;

3.1.13 Ensure that all Trial data and information are collected at the Site and that data are recorded, handled and stored in a way that allows accurate

reporting, interpretation and verification, and are provided to the CTC in the format and within the timescales required by the CTC and/or the Protocol;

3.1.14 Maintain a Site file and ensure the content of the Site file complies with the requirements of the Regulations;

3.1.15 Ensure that the Trial Drug provided for the Trial by the Supplier is used solely for the purpose of the Trial;

3.1.16 Ensure that the Sponsor is informed promptly of any intended or actual inspection, written enquiry and/or visit to the Site (relating to the Trial) by any regulatory authority and forward to the CTC copies of any correspondence from any regulatory authority relating to the Trial. The Site will use all reasonable endeavours to ensure that the Sponsor may have a representative present during such a visit;

3.1.17 Ensure that staff involved in the conduct of the Trial at the Site co-operate fully in any Site monitoring or auditing activities (including submission of requested documents for central monitoring and participation in site quality control checks) requested by representatives of the Sponsor, or inspection by the MHRA or any other relevant regulatory or other authority where this relates to the Trial;

3.1.18 Ensure that clinical negligence insurance is available by the Site for the Trial as part of the Clinical Negligence Scheme for Trusts (CNST) in England or Clinical Negligence and Other Risk Indemnity Scheme (CNORIS) (Scottish Sites only) or Welsh Risk Pool (Welsh Sites only) or equivalent clinical negligence schemes as provided by the Department of Health, Social Services and Public Safety (DHSSPS) in Northern Ireland (Northern Irish Sites only);

3.1.19 Ensure that all staff taking part in the Trial that are not employed by the Site, hold NHS honorary contracts (or equivalent) that include provisions covering their participation in the Trial and that such contracts are issued prior to the participation of staff in the Trial at the Site;

3.1.20 Ensure that Trial Drug management duties outlined in Appendix 3 and 4 are managed effectively at the Site. Delegation of any duties to pharmacy staff by the Principal Investigator must be documented on the Site staff delegation log and a copy sent to the CTC;

3.1.21 Ensure that Trial Drug accountability records are kept which may include but are not limited to:

3.1.21.1 records of Trial Drug delivery;

3.1.21.2 the use of Trial Drug by each Trial Subject;

3.1.21.3 Trial Drug reconciliation records;

3.1.21.4 Trial Drug destruction records;

3.1.21.5 Trial Drug storage records.

3.1.22 Observe and comply with any notice of recall or any other instructions or information received directly from a manufacturer, and/or the Supplier and/or the Sponsor and shall use reasonable endeavours to ensure that the Trial Drug is not administered or provided to any Trial Subject in contradiction of any such notice or instruction or other information from the manufacturer, Supplier or Sponsor;

3.1.23 Ensure that the CTC is informed immediately if any Trial Drug affected by a recall has been administered to a Trial Subject;

3.1.24 Destroy or return any unused Trial Drug pursuant to the Sponsor's instructions contained in Appendix 3. In case of destruction, written confirmation shall be supplied to the Sponsor;

3.1.25 Ensure that all safety events requiring immediate reporting, i.e. SAEs (including AESIs, SARs and SUSARs), Urgent Events and Protocol-defined pregnancies at the Site are reported to the CTC within twenty four (24) hours of awareness of the event (or as required by the Protocol for Urgent Events), and that all additional information requested by the CTC is provided within timeframes specified by the CTC to enable the CTC, where required, to undertake expedited reporting in compliance with the Regulations;

3.1.26 Ensure that all SAEs, Urgent Events and Protocol-defined pregnancies reported to the CTC in accordance with clause 3.1.25 above, are followed to their conclusion and all additional reports and information in connection with the SAE, Urgent Event and Protocol-defined pregnancy are provided to the CTC at regular intervals and, in any event, upon the conclusion of such event;

3.1.27 Promptly notify the CTC of any deviation from the Protocol and/or GCP or any other event or condition adversely affecting the satisfactory running or completion of the Trial at the Site;

3.1.28 Ensure that the CTC is informed of any Serious Breach occurring at the Site within one (1) business day of identification of the Serious Breach and provide any necessary follow up information to ensure the CTC are able to comply with requirements for reporting under the Regulations;

3.1.29 Undertake the PET-CT scanning responsibilities or procure that such responsibilities are undertaken by an external PET-CT scanning facility, as outlined in Appendix 6;

3.1.30 Ensure handling and transfer (where applicable) of data and documentation relating to a Trial Subject's participation in the Trial is in accordance with all applicable regulations and the Protocol;

3.1.31 Procure a named individual to be responsible for archiving documents relating to Trial conduct in accordance with the Regulations;

3.1.32 Ensure that all Trial-related documentation held at the Site is appropriately stored and indexed at the end of the Trial for the required duration (as stated in the Protocol) after the Trial has ended.

3.2 the **Sponsor** shall:

3.2.1 Ensure that all regulatory and ethical submissions that are the responsibility of the Sponsor are undertaken and that approvals are granted for the conduct of the Trial;

3.2.2 Ensure that the documentation required for the Trial (including patient information sheets and consent forms) are provided to the Site prior to the commencement of the Trial;

3.2.3 Conduct training on the Protocol for Site staff on initiation of the Site;

3.2.4 Notify the Site in writing when recruitment may commence at Site;

3.2.5 Ensure that the Site is promptly notified of any changes to the Protocol and related documents and procedures;

3.2.6 Ensure that systems are in place (including appropriate agreements) to ensure that sufficient supplies of the Trial Drug provided for the Trial by the Supplier are provided to the Site to conduct the Trial, pursuant and subject to the terms of this Agreement;

3.2.6.1 Ensure that through its agreement with the Supplier, the Trial Drug provided by the Supplier complies with current quality requirements and is packaged and labelled in accordance with relevant guidelines and the Regulations;

3.2.7 Ensure that the Site is notified of all necessary safety information related to the Trial;

3.2.8 Undertake data management and analyses of data received from the Site in accordance with the requirements of the Protocol;

3.2.9 Provide the Site and Principal Investigator with relevant contact numbers for the CTC to be used throughout the Trial as listed in the Protocol;

3.2.10 Inform the Site, in writing, when a decision has been made to cease follow-up.

3.3 *Audit*

3.3.1 The Sponsor may, at its sole discretion, by itself, or by its agents, conduct audits of the Trial documentation, source data and procedures relating to the Trial, at the Site's premises in order to ascertain that the Trial is being properly conducted to the requisite standards, during normal office hours and upon reasonable notice to the Site.

4. TRANSFER OF MATERIALS

4.1 It is envisaged that from time to time over the term of this Agreement that Materials may be transferred from the Site to the Sponsor and/or a third party or third parties named in the Protocol (the **"Authorised Third Party"**) for the purpose of undertaking the Trial in accordance with the Protocol or future research as approved by an

appropriate ethics committee. If such Material transfer is applicable to the Trial the Parties agree that they shall both abide by the terms of this clause 4.

4.2 The Sponsor shall and, where applicable, shall procure that the Authorised Third Party shall keep the Materials and associated documents secure at the Sponsor's laboratory or that of the Authorised Third Party and ensure that access to the Materials and associated documents is restricted to the Sponsor and Authorised Third Party, their respective authorised co-workers and agents who have entered into legally binding obligations with the Sponsor or Authorised Third Party on terms equivalent to those set out in this Agreement concerning the Materials, associated documents, data, Intellectual Property and Confidential Information.

4.3 The Site shall ensure that Materials are (or have been) collected and handled in accordance with the Human Tissue Act 2004, any amendments thereto and any other applicable relevant legislative and regulatory requirements and codes of practice.

4.4 The Sponsor shall and shall procure that the Authorised Third Party shall ensure that the Materials will be stored, accessed and processed in accordance with the Human Tissue Act 2004, any amendments thereto and any other applicable relevant legislative and regulatory requirements and GCP and use any Material or other information provided by or derived from a Trial Subject and/or provided by or on behalf of the Site to the Sponsor or Authorised Third Party only as outlined in the Protocol (or associated future ethically approved research) and in accordance with the consent provided by the Trial Subject.

4.5 All documents and information provided with the Materials including patient data shall be considered Confidential Information.

4.6 The Parties acknowledge that the Materials may be fully used up during the Sponsor's or Authorised Third Party's processing of the Materials.

4.7 The Sponsor shall and shall procure that the Authorised Third Party shall ensure that the Materials are traceable at all times while in the possession of the Sponsor or Authorised Third Party.

4.8 The Materials are supplied without cost but the CTC shall pay the costs of shipping that may be incurred as part of the 'per patient' payments outlined in Appendix 5.

4.9 Subject to clause 4.10 the Materials are supplied without warranty as to their properties, merchantable quality or fitness for any particular purposes and without any other warranty whatsoever, expressed or implied.

4.10 In supplying the Materials the Site warrants that the original supply from the Trial Subject complied with all legal and ethical requirements and guidelines and that it has obtained the Trial Subject's express informed consent to the use of such Materials in accordance with the patient information sheet and consent form for the Trial.

4.11 The Site shall provide proof of consent upon request of the Sponsor as evidence of compliance with the provisions of clause 4.10;

4.12 The Sponsor shall and shall procure that the Authorised Third Party shall comply with all applicable laws and any relevant guidance issued by the Department of Health or equivalent authority and all ethical guidelines relating to the use, storage,

transportation and disposal of Materials (including where relevant, human tissue) for research purposes laid down by the competent body or authority.

5. LIABILITY AND INDEMNITY

5.1 Nothing in this clause 5 shall operate so as to restrict or exclude the liability of any Party in relation to death or personal injury caused by the negligence of that Party or its employees, students, consultants and subcontractors, including researchers, or to restrict or exclude any other liability of any Party which cannot be so restricted in law.

5.2 Subject to clauses 5.3, 5.4, 5.5, 5.6, 5.7 and 5.8 the Sponsor shall indemnify and keep the Site and its employees, students, consultants and subcontractors, including researchers, indemnified against any claims, proceedings and related costs, expenses, losses, damages and demands to the extent they arise or result from the Site:

5.2.1 Undertaking the Trial in accordance with the Protocol; and/or

5.2.2 Preparing, manufacturing or assembling any medicinal product, medical device or other equipment in accordance with the Protocol or other written instructions of the Sponsor, where such instructions differ from the instructions of the manufacturer.

5.3 The indemnity shall only apply if the Site:

5.3.1 Informs the Sponsor in writing as soon as reasonably practicable following receipt of notice of such claim or proceeding;

5.3.2 Upon the Sponsor's request and at the Sponsor's cost gives the Sponsor full control of the claim or proceedings and provides all reasonable assistance; and

5.3.3 Makes no admission in respect or such claim or proceedings other than with the prior written consent of the Sponsor.

5.4 The indemnity shall not apply to the extent any claims, proceedings and related costs, expenses, losses, damages and demands arise or result from:

5.4.1 The wrongful acts or omissions or negligence or breach of statutory duty of the Site or its students, consultants and subcontractors, including researchers; or

5.4.2 A treatment or procedure routinely undertaken as part of NHS treatment.

5.5 If a Party incurs any loss or damage (including costs and expenses) ("Loss") arising or resulting from this Agreement and:

5.5.1 All Parties are NHS bodies as defined in Section 9(4) of the National Health Service Act 2006 or Section 17 of the National Health Service (Scotland) Act 1978 or Articles 16 and 26 of the Health and Personal Social Services (Northern Ireland) Order 1972, which established the Boards and Central Services Agency respectively and Article 10 of the Health and Personal

Social Services (Northern Ireland) Order 1991: which established Trusts in Northern Ireland as appropriate; or

5.5.2 One or more Party is a NHS body and the other Party(ies) is a NHS Foundation Trust; or

5.5.3 All Parties are NHS Foundation Trusts;

Then clauses 5.6, 5.7 and 5.8 shall apply.

5.6 If all Parties are NHS bodies / NHS Foundation Trusts in England, Wales or Northern Ireland and are indemnified by the same Indemnity Scheme (being one of the NHS Litigation Authority clinical negligence or the Welsh Risk Pool or the Clinical Negligence Fund in Northern Ireland) and the Party incurring any loss can recover such loss under one of the Indemnity Schemes, then such Party shall rely on the cover provided by the Indemnity Scheme and not seek to recover the Loss from the other Party(ies). Where the other Party(ies) caused or contributed to the Loss, it undertakes to notify the relevant Indemnity Scheme(s) to take this into account in determining the future levies of all Parties in respect of the indemnity schemes.

5.7 If:

5.7.1 The Parties are members of the same Indemnity Scheme in England, Wales or Northern Ireland and the Party incurring the Loss is not indemnified for that Loss by its Indemnity Schemes; or

5.7.2 All Parties are NHS bodies in Scotland; or

5.7.3 The Parties are NHS bodies/Foundation Trusts established in different jurisdictions within the United Kingdom;

Then the Parties shall apportion such Loss between themselves according to their respective responsibility for such Loss. Should the Parties be unable to agree the apportionment the matter shall be resolved in accordance with clause 14.

5.8 If one or more Parties are NHS Foundation Trusts and the Party incurring the Loss is not responsible for all or part of the Loss and is not indemnified in respect of the Loss by one of the Indemnity Schemes then the Party incurring the Loss shall be entitled to recover the Loss from the other Party(ies) pursuant to the provisions of this Agreement.

5.9 The liability of the Site to the Sponsor in respect of any contractual liability the Sponsor may or does incur to a third party arising or resulting from this Agreement shall be limited to all fees payable by the Sponsor to the Site in accordance with clause 6.

5.10 No Party shall be liable to another in contract, tort, breach of statutory duty or otherwise for any loss of profits, revenue, reputation, business opportunity, contracts, or any indirect, consequential or economic loss arising directly or indirectly out of or in connection with this Agreement.

6. FINANCIAL SUPPORT

6.1 It is hereby agreed that the Site will receive payments from the Sponsor in consideration of the conduct of the Trial. Payments will be made as outlined in Appendix 5.

7. INTELLECTUAL PROPERTY AND DATA

7.1 It is recognised and understood that the existing inventions, Intellectual Property, Know How and technology of the Sponsor and the Site are their separate property respectively and are not affected by the terms of this Agreement (including but not limited to, Trial Treatment, and information and technology related to the Protocol) and no Party shall have any claims to or any rights in such existing inventions, Intellectual Property, Know How and technologies of the other Party.

7.2 Subject to clause 7.1, in the event that any discovery, Intellectual Property and/or Know How made and/or developed by the Site during the course of the Trial, arising out of the Trial, connected to the performance of the Protocol and/or related to a new use, improvement and/or modification of Trial Treatment, such discovery or invention shall be communicated to and be the property of the Sponsor.

7.3 The Site hereby assigns (on behalf of itself and its employees), its rights in and to all Intellectual Property and, to the extent possible in and to all Know How, arising out of the Trial, clinical intervention, clinical practice relating to the performance of the Protocol or to any new use, improvement and/or modification of Trial Treatment to the Sponsor. At the request and expense of the Sponsor, the Site and the Investigator shall execute all such documents and do all such other acts as the Sponsor may reasonably require in order to vest fully and effectively all such Intellectual Property and Know How in the Sponsor or its nominee.

7.4 Nothing in this clause 7 shall be construed so as to prevent or hinder the Site from using Know How gained during the performance of the Trial in the furtherance of its normal activities of providing or commissioning clinical services, teaching and research to the extent that such use does not result in the disclosure or misuse of Confidential Information or the infringement of any Intellectual Property right of the Sponsor.

8. CONFIDENTIALITY, DATA ACCESS, PUBLICATION AND FREEDOM OF INFORMATION

8.1 *Confidentiality*

8.1.1 All Confidential Information, this Agreement and the terms and conditions hereof shall be treated as strictly confidential and none of the Parties shall, without the prior written permission of the disclosing Party, disclose the same to any third party except to the extent this may be required by a regulatory authority or by applicable law or as necessary for the conduct of the Trial.

8.1.2 The Site shall ensure that only those of its employees or officers directly concerned with the conduct of the Trial at the Site shall have access to the Confidential Information relating to the Trial.

8.1.3 The obligations set out in the above clauses 8.1.1 and 8.1.2 will not apply to Confidential Information that is:

8.1.3.1 published or generally available to the public through no fault of the Party receiving the data;

8.1.3.2 in the possession of the receiving Party prior to commencement of this Agreement and not already subject to obligations of confidentiality;

8.1.3.3 independently developed by the receiving Party and not subject to obligations of confidentiality;

8.1.3.4 obtained by the receiving Party from a third party not the subject of the obligations of confidentiality;

8.1.3.5 necessarily disclosed by a Party by virtue of its status as a public authority in terms of the Freedom of Information Act 2000 or the Freedom of Information (Scotland) Act 2002 (Scottish sites only); or

8.1.3.6 necessarily disclosed by a Party by laws applicable to clinical trials or pursuant to a court order, provided that prior to such disclosure, the disclosing Party shall notify the other Party of its obligation to disclose the other Party's Confidential Information and the other Party shall be permitted to advise the disclosing Party of the proposed form of disclosure.

8.1.4 The aforementioned confidentiality restrictions shall continue to apply after the termination of the Agreement for ten (10) years.

8.2 *Data access*

8.2.1 The Parties will adhere to all applicable principles relating to medical confidentiality and data protection of all potential and actual Trial Subjects (including the NHS Code on Confidentiality, Data Protection Legislation and the Caldicott Principles). Neither Party will disclose patient data to the other Party except as is required by the Protocol or for the purposes of monitoring or reporting adverse events.

8.3 *Publication*

8.3.1 The Parties recognise that the Framework places an obligation on the Site as an NHS organisation carrying out health and social care research to publish their work. The Parties agree that this clause 8.3 should be interpreted in light of such obligation.

8.3.2 Following completion of the Trial, the Sponsor shall use all reasonable endeavours to ensure the appropriate publication or other dissemination of the conclusions of the Trial. Should the Trial form part of a Trial being undertaken at a number of separate Sites this obligation shall arise following completion of the entire multi-site Trial.

8.3.3 The Site shall not publish or otherwise disseminate the conclusions of the Trial, including all or any part of the results of the Trial without the prior written consent of the TMG or TSC, such consent not to be unreasonably withheld or delayed. Any publication or other dissemination of the conclusions of the Trial by the Site shall not occur until the Sponsor has published the conclusions of the Trial in accordance with clause 8.3.2 and shall refer to publication by the Sponsor in such form as the Sponsor may reasonably direct.

8.4 *Freedom of Information:*

8.4.1 Parties to this Agreement which are subject to the Freedom of Information Act 2000 (FOIA) or the Freedom of Information (Scotland) Act 2002 (FOI(S)A) and which receive a request under FOIA or FOI(S)A to disclose any information that belongs to another Party shall notify and consult that Party in accordance with clause 17, as soon as reasonably practicable, and in any event, not later than five (5) working days after receiving the request.

8.4.2 The Parties acknowledge and agree that the decision on whether any exemption applies to a request for disclosure of recorded information under FOIA or FOI(S)A is a decision solely for the Party responding to the request.

8.4.3 Where the Party responding to an FOIA or FOI(S)A request determines that it will disclose information it will notify the other Party in writing, giving at least two (2) working days notice of its intended disclosure.

9. DATA PROTECTION

9.1 The Parties agree that the processing of all Personal Data is subject to the provisions of Data Protection Legislation, even if such Personal Data is processed outside the United Kingdom.

9.2 The Site will only process Personal Data in relation to the Trial in accordance with the express instructions of the Sponsor and the Protocol, and shall co-operate fully in the fulfilment of any request for information that may be received by the Sponsor from a Trial Subject.

9.3 The Site shall give all Trial Subjects the approved patient information sheet and consent form and shall ensure that it receives the explicit consent of all Trial Subjects in relation to the processing of their Personal Data for the purposes of the Trial.

9.4 The Site shall procure that any other body or person that it recruits to process Personal Data shall enter into terms that are substantially the same as those imposed by this clause 9.

9.5 Neither Party shall disclose the identity of any Trial Subject or any confidential medical information relating to Trial Subjects to any third party except in accordance with the Data Protection Legislation or, as appropriate, the NHS Confidentiality Code of Practice or the Scottish Executive Health Department NHS Code of Practice on Protecting Patient Confidentiality or the Confidentiality; Code of Practice for Health and Social Care in Wales or the Code of Practice on Protecting the Confidentiality of Service Users in Northern Ireland.

10. TERM AND TERMINATION

10.1 This Agreement comes into effect in accordance with the date on the first page of the Agreement and will expire after the date the CTC informs the Site that the Trial has ended (in accordance with the Protocol).

10.2 The Agreement may be prematurely terminated by the Sponsor where:

10.2.1 the TSC, IDMC, TMG, or any applicable regulatory authority or ethics committee recommend stopping the Trial on grounds of safety, or the emergence of new information that invalidated or rendered irrelevant the original hypotheses to be tested;

10.2.2 in the event that insufficient number of Trial Subjects (according to the Protocol) are recruited for the Trial;

10.2.3 the Trial fails to open;

10.2.4 the Principal Investigator ceases to be employed by or associated with the Site and a suitable replacement cannot be found within three (3) months in accordance with clauses 3.1.2 and 3.1.3 above;

10.2.5 one of the Parties is declared insolvent or an administrator or receiver is appointed over all or any part of its assets, or such Party ceases or threatens to cease to carry on its business;

10.2.6 the Funder withdraws or terminates its funding for any reason or if it has been agreed between the Sponsor and the Funder that there is insufficient funds available to continue the Trial;

10.2.7 the arrangements between the Sponsor and the Supplier are terminated.

10.3 The Site will act on any notification received from the Sponsor or MHRA of the Trial being suspended or terminated at the Site, and will adhere to any instructions therein.

10.4 This Agreement may be terminated by either Party, for any breach of the obligations set out in this Agreement, by giving three (3) months written notice to the other of its intention to terminate. The notice shall include a detailed statement describing the nature of the breach. If the breach is capable of being remedied and is remedied within the above mentioned notice period, then the termination shall not take effect.

10.5 The Site may terminate this Agreement on one (1) month's notice in writing to the Sponsor. Prior to so terminating this Agreement the Site shall discuss with the Sponsor the reasons for wishing to terminate and explore alternative arrangements to termination and the Site shall ensure appropriate care is provided to Trial Subjects already recruited to the Trial according to the Protocol.

10.6 Termination of this Agreement will not relieve either Party of any obligation that may have accrued prior to termination.

10.7 Provisions of Transfer of Materials (clause 4), Liability and Indemnity (clause 5), Intellectual Property and Data (clause 7), Confidentiality, Data Access, Publication

and Freedom of Information (clause 8) and Applicable Law and Jurisdiction (clause 20) shall continue beyond the expiry or termination of this Agreement.

11. FORCE MAJEURE

11.1 If the performance by a Party of its obligations under this Agreement is delayed by a Force Majeure, the affected Party shall promptly notify the other Party, specifying the details of the delay and how long it expects the delay to continue. In the event the delay lasts for more than four (4) weeks, the unaffected Party shall be entitled to terminate this Agreement forthwith on written notice to the other Party.

12. ENTIRE AGREEMENT

12.1 This Agreement, including its Appendices, constitutes the full understanding of the Parties and a complete and exclusive statement of the terms of their Agreement. No terms, conditions, understanding or Agreement purporting to modify or vary the terms of this Agreement will be binding unless hereafter made in writing and signed by both Parties.

13. AMENDMENT

13.1 This Agreement cannot be amended or modified except by the express written consent of both Parties.

14. DISPUTE RESOLUTION

14.1 If any dispute arises from this Agreement, the Parties shall refer the dispute to the Director of the CTC for the Sponsor and R&D Director or Chief Executive for the Site, for resolution. If no resolution is achieved within five (5) days of the date of referral, the dispute shall be referred to Vice-Provost (Biomedicine) and Dean of the Medical School for the Sponsor and Chief Executive for the Site.

14.2 If no resolution has been reached, in accordance with clause 14.1 above, within ten (10) days of the date of referral, then either Party may call for the dispute to be referred to mediation in accordance with the Centre for Dispute Resolution ("CEDR") Model Mediation Procedure.

14.3 If no resolution has been reached, in accordance with clauses 14.1 and 14.2 above, within twenty eight (28) days of the call for mediation, then either Party may call for the dispute to be referred to arbitration under the UNCITRAL Rules, which rules are deemed to be incorporated by reference to this clause.

14.4 Notwithstanding the other provisions of this clause 14, the Parties may seek any interim or interlocutory relief from the courts at any time.

15. ASSIGNMENT AND SUB-CONTRACTING

15.1 The Site may not assign its rights under this Agreement, or any part of it, or subcontract the performance of any of its obligations, without informing the Sponsor.

15.2 If either Party does sub-contract its obligations, it shall remain responsible for the acts and omissions of its sub-contractors as if they were its own employees.

16. **GENERAL PROVISIONS**

16.1 The Sponsor or the Site has no obligation to renew this Agreement. The Sponsor is not under any obligation to enter into another type of Agreement with the Site at this time or in the future.

16.2 The Sponsor and the Site warrant and represent to each other that both have the full right and authority to enter into this Agreement and that both are not aware of any impediment which would inhibit their ability to perform their obligations hereunder.

16.3 If any provision herein is found to be unenforceable, it is the intent of the Parties that such provision be replaced, reformed or narrowed so that its original business purpose may be accomplished to the extent permitted by law. The invalidity or unenforceability of any provision of this Agreement shall not affect the validity or enforceability of any other provision(s) of this Agreement, which shall remain in full force and effect.

16.4 Should there be any inconsistency between this Agreement and the Protocol, the Protocol shall prevail except insofar as such inconsistency relates to issues of intellectual property, and liabilities and indemnities related to the Trial.

17. **NOTICES**

17.1 All notices to be given under this Agreement shall be in writing and delivered to the following addresses:

for CTC:

Professor Jonathan Ledermann
Director
Cancer Research UK and University College London Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

for the Site:

Principal Investigator
[insert details - name, title and address]

and

[insert details – name *(name is optional)*, title and address of relevant individual or post *(e.g. R&D manager, Chief Executive of NHS Trust/Health Board or NHS Trust/Health Board R&D Director)*]

18. **RIGHTS OF THIRD PARTIES**

18.1 Nothing in this Agreement is intended to confer on any person any right to enforce any term of this Agreement which that person would not have had, but for the Contracts (Rights of Third Parties) Act 1999.

19. **WAIVER**

19.1 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 future exercise of it, or the exercise of any other right under this Agreement.

20. **APPLICABLE LAW AND JURISDICTION**

20.1 The validity, construction and performance of the Agreement will be governed by and construed for all purposes in accordance with the laws of England and Wales.

20.2 The Parties submit to the exclusive jurisdiction of the English courts.

Compulsory Sign Off Page

Signed on behalf of University College London by:

_____ Date:

Professor Jonathan Ledermann, Director
Cancer Research UK and University College London Cancer Trials Centre

Signed on behalf of [insert Site name i.e. name of NHS Trust/Health Board] by:

_____ Date:

(authorised NHS Trust/Health Board signatory – e.g. Chief Executive or NHS Trust/Health Board R&D Director)

[Name:] [or insert title & name]
[Position:] [or insert position]

Appendix 1

Hospital(s) within the Site where Trial activities will be undertaken

(*please list name and address of all hospital locations in the NHS Trust/Health Board where trial activities are to be undertaken* ***and the same PI*** *is involved:)*

Appendix 2

The Protocol

Provided as a separate document

Appendix 3

Pharmacy Agreement - [Name of Site(s) covered in this pharmacy agreement]* *See CTSA guidance notes*

This appendix summarises the pharmacy requirements for the ANIMATE Trial.

Nivolumab (Opdivo®) will be supplied free of charge by Bristol-Myers Squibb Pharmaceuticals Ltd. to sites for Trial Subjects in accordance with the Trial Protocol. Further details are given in the 'summary of drug arrangements' document for the Trial

Please confirm each of the following statements and respond to <u>all</u> questions by ticking each box:	**Yes**
All relevant pharmacists/technicians have read (or will have read prior to working on the Trial) the Protocol and 'summary of drug arrangements' document for the Trial, and agree to adhere to both documents	☐
Trial Drug will be segregated & stored according to the 'summary of drug arrangements' document	☐
Trial Drug will be dispensed according to the Trial Protocol	☐
Trial Drug will be dispensed only for individual Trial Subjects	☐
Trial Drug will be provided to Trial Subjects free of charge unless NHS prescription charges apply	☐
Pharmacy will keep and maintain a Trial Pharmacy Site File with essential documents for the Trial	☐
Pharmacy has a procedure for shelf life extension ☐ Y or ☐ N	
Pharmacy would undertake relabelling if instructed by the Sponsor	☐
Pharmacy policies/procedures will be available when requested	☐
Nivolumab (Opdivo®) - specific requirements:	
Pharmacy are able to comply with arrangements for nivolumab (Opdivo®) re-ordering	☐
Pharmacy will maintain records of nivolumab (Opdivo®) delivery	☐
Pharmacy will add required information to the nivolumab (Opdivo®) label upon receipt at Site as per the instructions detailed in the 'summary of drug arrangements' document.	☐
On dispensing, nivolumab (Opdivo®) will be labelled according to the 'summary of drug arrangements' document for the Trial	☐
Nivolumab (Opdivo®) accountability logs will be maintained *(template accountability logs will be provided, however in-house forms may be acceptable provided they capture the same information requested on the template accountability log as a minimum, and a copy is provided to the CTC for review prior to use)*	☐
Completed Nivolumab (Opdivo®) accountability logs will be provided to CTC on request	☐

Please confirm each of the following statements and respond to **all** questions by ticking each box:	Yes
Pharmacy has a policy/procedure to deal with the destruction of unused nivolumab (Opdivo®) *(once reconciled, unused nivolumab (Opdivo®) will be destroyed according to local destruction procedure/policy upon written authorisation by the Sponsor. All destruction will be documented and records supplied to CTC on request).*	☐

Name of Site(s) covered in this agreement*:		
Pharmacy Address:		Post code:
Signed (by responsible individual in pharmacy):		**Date:**
Name *(please print clearly)*:		Position:
Tel:	Fax:	E-mail:

***** Where pharmacy supplies a satellite pharmacy or other sites for the trial, all sites involved must be named in this agreement and please ensure appropriate details of arrangements are documented in the Pharmacy Site File (PSF) at each site/satellite pharmacy. **Please forward a copy of these arrangements to the CTC.**

Data protection: Please note your name and contact details will be held on our contacts database so that you receive appropriate trial information.

Appendix 4

Principal Investigator's Responsibilities

Principal Investigator main responsibilities include, but are not limited to:

Trial Set-up & Conduct
Ensuring staff at the Site are suitably qualified and experienced to undertake their duties in the Trial, and that this is documented and signed/dated CVs are held at Site.
Providing a current signed and dated copy of the Principal Investigator's CV to the CTC, and updates, as requested, during the Trial
Ensuring staff involved in the conduct of the Trial at Site are trained in the Protocol and GCP, and that records are maintained
Ensuring that delegation of any Trial duties to Site staff by the Principal Investigator are documented and signed for by the Principal Investigator on the Site staff delegation log and a copy sent to the CTC
Notifying the CTC of any conflicts of interest relating to the Principal Investigator or any staff involved in the conduct of the Trial
Ensuring that there are no resource or cost implications that would prevent the conduct of the Trial in accordance with the Protocol
Forwarding to the CTC any documentation required to be reviewed by the Sponsor
Ensuring that the necessary local approvals to participate in the Trial have been obtained
Forwarding to the CTC copies of all applicable local approvals
Ensuring that an Investigator Site File and a Pharmacy Site File are maintained
Ensuring the Trial is commenced at Site only after written confirmation is received from the CTC
Ensuring that potential Trial Subjects are assessed for their ability to give informed consent
Providing potential Trial Subjects with current patient information for the Trial and ensuring required reflection time is given
Ensuring written informed consent is obtained from each Trial Subject entered into the Trial and that the process is recorded in the medical records at Site
Ensuring Trial Subjects are given appropriate contact details for 24 hour access to medical advice
Ensuring any new information provided by CTC that may require forwarding to the Trial Subject is forwarded appropriately
Trial Drug Management
Ensuring that the Trial Drug provided for the Trial is used solely for the Trial
Ensuring that the Trial Drug is appropriately labelled and stored
Ensuring that records of accountability for Trial Drug are kept
Submitting to the CTC records of Trial Drug accountability
Ensuring that any unused Trial Drug(s) at the end of the Trial are destroyed or returned and records maintained, as required in Appendix 3
Complying with notices of recall and related instructions from a manufacturer, the Sponsor, the Supplier and/or the CTC
Submitting records of Trial Drug destruction or return to the CTC
Ensuring that systems are implemented that will allow adequate reconstruction of the movement and administration of non-investigational medicinal products

Trial Documentation and Data
Ensuring that a Trial Site staff delegation log is maintained
Submitting to the CTC copies of Trial Site staff delegation logs
Ensuring accurate completion and timely submission of Case Report Forms to the CTC as required by the Protocol
Responding to data queries from the CTC
Ensuring all amendments to Trial documentation, and their approvals, supplied by the CTC are disseminated and actioned at Site according to CTC instructions and local requirements
Submitting to the CTC any other Trial documentation, as required by the CTC or the Protocol
Archiving all Site Trial documentation for required duration after the termination of the Trial
Pharmacovigilance
Ensuring that all AEs are recorded in Site records and according to the Protocol
Ensuring that all SAEs (including AESIs) requiring immediate reporting, Urgent Events and Protocol-defined pregnancies are reported to the CTC within the timeframes specified in the Protocol
Ensuring that all SAEs (including AESIs), Urgent Events and Protocol-defined pregnancies are followed appropriately and all additional reports provided to the CTC at regular intervals and until their resolution
Forwarding all SUSAR reports, received from the CTC, to individuals and departments at Site in line with local requirements
Forwarding any other safety reports, received from the CTC, as required by the CTC or the Protocol
Monitoring and audit
Cooperating in any site monitoring or audit activities, including submission of requested documents for central monitoring and participation in site quality control checks, requested by representatives of the Sponsor
Data Protection
Ensuring that Data Protection Legislation is complied with and appropriate measures against unauthorised or unlawful processing of Personal Data and against accidental loss or destruction of, or damage to Personal Data are taken
Other
Promptly notifying the CTC of any deviations from the Protocol and/or GCP occurring at Site
Notifying the CTC of any Serious Breaches occurring at Site within the timeframe required in the Protocol
Informing the CTC of any intended or actual inspection by a regulatory authority or audits that may involve the Trial
Forwarding to the CTC copies of correspondence from any regulatory authority
Include only for Sites where PET-CT will be performed – otherwise delete row Ensuring relevant license(s) is/are in place where required in relation to medical radiation exposure, and renewed as required
Include only for Sites where PET-CT will be performed – otherwise delete row: Ensuring the PET-CT Quality Assurance programme has been completed
Ensuring Materials are obtained, processed and shipped to the appropriate central laboratory by the Site according to the Protocol and Trial laboratory manual

Signed in acknowledgement of the Agreement and the roles and responsibilities to be undertaken as Site Principal Investigator:

_____ Date:

[Name:] [or insert title & name]
[Position:] [or insert position]
[insert Site name i.e. Trust name]

Appendix 5

Financial Arrangements

This Appendix specifies those payments to be made by the Sponsor to the Site under clause 6 of the Agreement. In consideration of the successful completion of all work to be performed by the Site on the Trial, payments will be made according to the schedule below and the conditions set forth herein.

1. **Schedule of payments:**

A. Per-Trial Subject Payments:

i) For Trial Subjects who are **ineligible for nivolumab treatment**, the Sponsor agrees to pay the site up to a maximum of £126 as follows:

- £126 for each Trial Subject registered upon completion of the "eligibility for treatment" visit and receipt of appropriate scans and tissue samples for research, as set out in the Protocol

ii) For Trial Subjects patients who are **eligible for nivolumab treatment**, the Sponsor agrees to pay the Site up to a maximum of £2,287 as follows:

- £126 for each Trial Subject registered upon completion of the "eligibility for treatment" visit and receipt of appropriate scans and tissue samples for research, as set out in the Protocol
- £858 upon a Trial Subject's completion of 4 cycles of Trial Treatment and receipt of appropriate scans, tissue and blood samples for research, as set out in the Protocol;
- For Trial Subjects who are PET-positive after cycle 4, an additional £1,103 upon a Trial Subject's completion of Trial Treatment and 1 month post treatment assessment, and receipt of appropriate scans, tissue and blood samples for research, as set out in the Protocol;
- £200 upon resolution of all Trial data queries

UCL reserves the right to amend/withhold final payments in cases where the Site has not performed their duties according to the terms of the protocol and/or this Agreement.

B. One off Trial Payments:

In addition, the Sponsor agrees to pay the Site a **one off archiving payment of £21.06 at the end of the Trial** in consideration of administration time for the preparation for archiving of Trial documentation held at Site.

2. **Arrangements for Invoicing and payment**

- Payments by the Sponsor during the course of the Trial are dependent on continued availability of funds from the Funder.

- The amounts agreed in this Appendix shall not be exceeded without the Sponsor's agreement, and formal amendment of the Agreement.

- The Site shall submit invoices to the Sponsor for the attention of the person designated contact for the Trial given below.

- The Site is expected to keep accurate accounts of all costs incurred in the performance of the Agreement.

- Financial records supporting documents and other records pertinent to the sums paid by the Sponsor to the Site shall be retained by the Site for a period of five (5) years from the date of submission of the final expenditure report, except that records pertaining to audits, appeals, litigation or settlement of claims arising out of performance of the Agreement shall be retained until such audits, appeals, litigation or claims have been disposed of.

- All costs incurred under the Agreement will be subject to audit by Sponsor. The Site shall allow the appropriate Sponsor representatives (including the Funder) access to records where necessary to support costs relating to this Agreement.

- Payment shall be made in Pounds Sterling by Bank transfer to the account advised by the Site in the invoice.

- Payment will be made according to the schedule below on presentation of VAT (if applicable) invoices from the Site.

  Per Trial Subject payments: The Site will raise invoices at six monthly intervals to include payments for all Trial Subjects reaching a relevant 'milestone' as listed in the schedule of payments above, during the preceding 6 months. Full details of the payments included in the invoice must be given, including Trial Subject number.

  Payments will be made within sixty (60) days of receipt of the valid invoice provided satisfactory completion of relevant case report form(s) received at the CTC.

  The one off payment to Site for archiving may be included in the final invoice from the Site, which will precede Trial and Site closure notification from the Sponsor.

  At the end of the Trial an invoice for any outstanding amount should be submitted within three (3) months of the end of Trial notification, after which time no further invoices can be paid.

Invoices, quoting UCL purchase order number, should be sent to:

Name:	ANIMATE Trial Coordinator
Address:	Haematology Trials Group CR UK & UCL Cancer Trials Centre 90 Tottenham Court Road London W1T 4TJ
Tel. No. (in event of queries)	0207 679 9860
Email	ctc.animate@ucl.ac.uk
Organisation to be invoiced	University College London
N.B. a purchase order number (obtained from contact above) must be quoted on each invoice	

Appendix 6

PET-CT agreement

This appendix summarises the PET-CT responsibilities for the ANIMATE Trial. PET-CT scan images must be sent for central review as part of the Protocol. It is important that PET-CT facilities are aware of, and can comply with, the scanning and data transfer requirements as outlined in the Protocol and the Imaging Manual for the Trial.

[ASCERTAIN WHICH OF THE 2 STATEMENTS APPLY TO THE SITE'S CIRCUMSTANCES AND SELECT THE APPROPRIATE TABLE]

Either:

If Trial Subjects are to have PET-CT investigations performed at the Site – in a PET-CT scanning facility within the Site [or external to the Site but with which they are considered to be a single site. For this to apply the Site must take full responsibility for the PET-CT scanning facility under the Framework and NHS indemnity must apply etc]:

Please confirm the following:	**Initial to confirm**
All relevant nuclear medicine physicians/technicians have read and agreed to adhere to the Trial Protocol and Imaging Manual	☐
The PET-CT facility will undergo, and obtain written confirmation of undertaking, formal Trial-specific PET-CT scan accreditation process as outlined in the Imaging Manual prior to commencing the ANIMATE Trial	☐
Relevant license(s) in relation to medical radiation exposure will be obtained prior to commencing the ANIMATE Trial and the license(s) will be updated prior to expiry as necessary. A copy of the license(s) and each renewal will be provided to the Cancer Research UK & UCL Cancer Trials Centre (UCL CTC).	☐
The PET-CT facility will provide UCL CTC with an updated Site contact list if there are any staff changes	☐
Trial Subjects will be scanned in accordance with the Protocol guidelines and Imaging Manual, and the same scanner will be used each time a Trial Subject has a scheduled Trial scan	☐
Data will be uploaded to a secure ftp-server or saved to CD and sent for central review (as outlined in the Imaging Manual)	☐
The PET-CT scan at the end of initial salvage is standard of care at the Site, however all other PET-CT scans performed in the ANIMATE trial are in excess of standard treatment and will be reimbursed via the trial as detailed in Appendix 5.	☐
I understand that failure to comply with the requirements above may result in the Site being suspended from recruitment to the Trial	☐

NB) Complete following if PET-CT scanning facility is not a department of the Trust but is considered by the Trust to be a single site. (ie the Site takes full responsibility for the PET-CT scanning facility under the Framework and NHS indemnity applies) ***– if not relevant delete next 4 lines only***	
Name of PET-CT scanning facility:	

Please confirm the following:	**Initial to confirm**
Contractual arrangements are in place between the Trust/Health Board and the PET-CT scanning facility to cover all arrangements for PET-CT scanning in the Trial, including any financial arrangements	☐
The Trust/Health Board assumes full responsibility under the Framework for all procedures undertaken at the PET-CT scanning facility, and indemnity provision is in place under the relevant clinical negligence scheme	☐

Signed (by Trust Signatory):		**Date:**
Name *(please print clearly)*:		Position:
Tel:	Fax:	E-mail:
Name of Site:		
Address of nuclear medicine department:		
		Post code:

Data protection: Please note your name and contact details will be held on our contacts database so that you receive appropriate trial information.

OR:

If patients are to be referred to a PET-CT scanning facility at another Trust/Health Board which is also a site in the Trial:

Specify Trial site where PET-CT scanning facility is to which Trial Subjects are being referred for scanning	

Please confirm the following:	**Initial to confirm**
The above named PET-CT scanning facility has agreed to accept Trial Subject referrals from the Site for the ANIMATE Trial.	☐
Contractual arrangements are in place between the Site and the PET-CT scanning facility to cover all arrangements including insurance provision and financial issues	☐
The Site must make all reasonable endeavours to ensure that the PET scanning facility complies with the data scanning and data transfer requirements for the ANIMATE Trial	☐

Signed (by Trust signatory):		**Date:**
Name *(please print clearly)*:		Position:
Tel:	Fax:	E-mail:
Name of Site:		

Data protection: Please note your name and contact details will be held on our contacts database so that you receive appropriate trial information.

FOR CTC USE *Before recruitment to the ANIMATE Trial can commence at the Site, the CTC must confirm the following:*	Initial to confirm
The nominated PET-CT scanning facility is part of a site that is approved to participate in the ANIMATE trial	☐
The nominated PET-CT scanning facility has signed an ANIMATE PET-CT agreement as part of their CTSA (at appendix 6), undertaking to comply with the Trial requirements (CTC to append copy of PET-CT scanning site's PET-CT agreement to the CTC copy of this Agreement)	☐

Signed (by member of CTC team)	Date:
Name (print clearly)	Position: