CLINICAL STUDY COORDINATION AND SITE AGREEMENT

This Clinical Study Coordination Agreement ("**Agreement**") is valid as of last Party's signature to this Agreement and becomes effective as of the date of its publication in the Register of Contracts is made between:

1. **Princess Máxima Center for Pediatric Oncology B.V.**, Heidelberglaan 25, 3584 CS Utrecht, the Netherlands, lawfully represented by [redacted] (hereinafter referred to as "Máxima" or "SPONSOR")

and

2. Motol University hospital, government contributory organization, V Úvalu 84, 150 06 Prague 5, The Czech Republic, represented by [redacted] (hereinafter referred to as "National Coordinating Center" or "NCC");

in the presence of:

NCC's employee, [redacted]
(hereinafter referred to as "**NCC Investigator**")

SPONSOR and NCC hereinafter individually or collectively referred to as "**Party**" or "**Parties";**

NCC may hereinafter also be individually and collectively referred to as "**Institution**".

Preambles

WHEREAS SPONSOR has assumed legal SPONSOR responsibilities defined in article 2(14) of Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC for the conduct and co-ordination of a clinical study **("CTR")** entitled ***"Interfant-21: International collaborative treatment protocol for infants under one year with KMT2A-rearranged acute lymphoblastic leukemia or mixed phenotype acute leukemia" (including its substudies)*** (the "**Study**") as described in the protocol and its amended versions with EUDRACT number 2021-000213-16 ("**Protocol**"), attached to this Agreement as **Exhibit B**, under the supervision and co-ordination of Dr. Janine Stutterheim (hereafter "***Coordinating Investigator***"), employee of SPONSOR;

WHEREAS SPONSOR wishes to delegate certain of its legal sponsor responsibilities and tasks to NCC as set out in the task list attached hereto as **Exhibit A** ("**Task List and Table**") for the conduct and co-ordination of the Study in the Czech Republic ***("Country")*** and for NCC to contract the sites participating in the Study in the Country ("**Participating Site**");

WHEREAS NCC shall also conduct the Study in its own institution in its role as research site participating in the Study under the supervision of Site Investigator [redacted];

WHEREAS NCC wishes to conduct the Study and is willing to assume national delegated sponsor tasks;

WHEREAS SPONSOR has entered into an agreement with a pharmaceutical company named [redacted] (hereafter "**Pharma**"). Pharma has agreed with the SPONSOR to supply the investigational medicinal product [redacted] (the "**Study Drug**") free of charge to SPONSOR (or to SPONSOR's authorized distributing third party) for the conduct of the Study;

Any supply of investigational medical product has to be in compliance with the Protocol, the GMP-Guideline, Annex 13 and Laws and Regulations. An investigational medical product can only be supplied to Participating Sites by SPONSOR's authorized distributing third party on account of an explicit written order of SPONSOR and on behalf of SPONSOR.

WHEREAS Parties wish to clarify the respective responsibilities of SPONSOR and the NCC;

Therefore, Parties agree the following:

1 SPONSOR RESPONSIBILITIES

1.1 SPONSOR shall respect and follow all applicable laws, rules, regulations and guidelines of any type, including but not limited to the ICH Harmonised Tripartite Guideline for Good Clinical Practice (CPMP/ICH/135/95) and other good clinical practice requirements as are specified in the CTR and the Directive 2005/28/EC of the European Parliament and the Council relating to medicinal products for human use and published by the European Commission, and all legislation and guidelines regarding the privacy of persons and the protection of personal data, and all rules and regulations of the governmental agencies governing the testing and approval of pharmaceuticals for use in humans ("**Regulatory Authority**") (collectively: "**Laws and Regulations**").

1.2 SPONSOR shall coordinate internationally and be the international legal SPONSOR of the study.

1.3 SPONSOR will provide NCC with all documents, to the extent necessary to perform the Study, including the Protocol, except those which are specific for the Country, all as set out in the Task List and Table for Allocation of NCC's and Sponsor's Responsibilities attached hereto in **Exhibit A**.

1.4 SPONSOR is responsible for ensuring all required approvals mandatory under local Laws and Regulations, such as the approval of an institutional review

board/institutional ethics committee (hereafter " **IRB/IEC**"), and the approval of the competent authority or other competent local regulatory authority, are in place before Study initiation. SPONSOR may delegate such responsibility to NCC, or request NCC to apply for such approval on behalf of SPONSOR in which case NCC shall keep SPONSOR fully informed on the progress of the procedures, all as set out in the Tasklist for Allocation of NCC's and Sponsor's Responsibilities attached hereto in **Exhibit A**. Any Protocol amendment requested by the IRB/IEC must be approved in writing by SPONSOR in advance.

1.5 Parties agree that NCC will not proceed with the Study until such time as the Study has received the IRB/IEC positive opinion and a written approval of Sponsor. Upon receipt of the IRB/IEC positive opinion and competent authority approval NCC will provide a copy of it to Sponsor. Should such positive opinion be withdrawn or modified, in whole or in part, the NCC or NCC Investigator will notify Sponsor in writing immediately and in no event later than 48 hours following the receipt of notice from the IRB/IEC.

2. NCC RESPONSIBILITIES

2.1 NCC shall and ensures that each Participating Site shall respect and follow all applicable laws, rules, regulations and guidelines of any type, including but not limited to the ICH Harmonised Tripartite Guideline for Good Clinical Practice (CPMP/ICH/135/95) and other good clinical practice requirements as are specified in the CTR and in the Directive 2005/28/EC of the European Parliament and the Council relating to medicinal products for human use and published by the European Commission, and all legislation and guidelines regarding the privacy of persons and the protection of personal data, and all rules and regulations of the governmental agencies governing the testing and approval of pharmaceuticals for use in humans.

2.2 NCC shall and ensures each Participating Site shall perform the obligations as listed in the Task List and Table attached in (**Exhibit A**). Any third party to whom responsibilities are delegated to by SPONSOR are referred to.

2.3 NCC shall conduct and coordinate the Study under the direct supervision and responsibility of NCC Investigator and in full compliance with this Agreement. NCC shall ensure all required approvals and permissions of the competent IRB/IEC and institutional approvals are in place prior to the Study commencement, including all approvals and permissions at Participating Site's site (as applicable under the Task List and Table).

2.4 Prior to Study conduct and Study subject enrollment, NCC shall ensure all required approvals and permissions and institutional approvals are in place, all as set out in the Tasklist for Allocation of NCC's and Sponsor's Responsibilities, attached hereto in **Exhibit A**.

2.5 NCC is responsible that all Participating Sites, including the NCC in its role as Participating Site in the Study, shall enter the Study data within (ten) 10 working days after an event into the electronic Case Report Form as outlined in the Protocol.

2.6 NCC represents and warrants that it will properly contract Participating Sites for the conduct of the Study, and it shall be fully liable and responsible for Participating Site's actions, errors and omissions with respect to Participating Site's involvement in the Study and its compliance to the terms of this Agreement. NCC shall ensure that all Participating Sites shall comply with the obligations of NCC as a site pursuant to this Agreement.

2.7 NCC shall use reasonable efforts to enroll [redacted] patients in the Study.

2.8 The estimated duration of the Study is from [redacted] and the estimated duration of the Study in the Czech Republic is from [redacted].

3. SUPPLY OF STUDY DRUG

3.1 Study Drug support by Pharma. SPONSOR warrants that it has a written agreement in place with Pharma according to which Pharma (or the third party provider selected by SPONSOR, as applicable) will provide the Study Drug [redacted] for the Study. NCC shall adhere to sections 3.2 -3.3 below. All other drugs will be obtained as commercial supply.

3.2 NCC ensures and will ensure Participating Site's ensure that Study Drug provided by SPONSOR's authorized distributing third party to the site under the terms of this Agreement shall be used only for this Study and its enrolled subjects, in compliance with this Agreement, and that complete drug accountability in accordance with ICH-GCP and Laws and Regulations is kept.

3.3 NCC agrees it will, and shall oblige Participating Sites to agree they will store the Study Drugs adequately, and that no expired Study Drugs will be given to any subject in this Study. NCC must and shall oblige Participating Sites to maintain accurate records of all Study Drug received and dispensed and all Study Drug will be stored in a secure and locked location to prevent theft or misuse. Upon the conclusion or termination of this Study or at Sponsor request, NCC will account in writing for all Study Drug provided by Sponsor on behalf of Pharma, and at Sponsor's option, either (a) return unused Study Drug to Sponsor or its designee or (b) destroy any unused Study Drug, with documentation or written confirmation to Sponsor, in each case in accordance with the Protocol, as well as Laws and Legislation

3.4 SPONSOR has an agreement in place with Pharma and SPONSOR's authorized distributing third party, in which Pharma and SPONSOR's authorized distributing third party ensure that the Study Drug that is to be supplied for the Study, is in accordance with the 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 ("**GMP-guidelines**") and the Study Drugs is appropriately labelled.

3.5 NCC ensures that each Participating site:
a) has an adequate supply, at its own costs, of the other commercially available drugs (when applicable) for the sole purpose of performing the Study as required in the Protocol.
b) shall not represent to any third party, including Study subjects, that Pharma is a regulatory sponsor;
c) shall notify SPONSOR immediately in case of any suspected quality defect in the Study Drug or the provided packaging or labeling;
d) shall verify and report any temperature excursions to SPONSOR immediately;
e) shall provide SPONSOR with reasonable notice if resupply is needed because of pending expiration of existing supplies.

3.6 NCC agrees that the Study Drug will not be provided to any third party without the prior written approval of Sponsor.

3.7 SPONSOR shall supply the Study Drug to the pharmacy of NCC where a pharmacist will take the consignment over and check it (to the same extent as other consignments - i.e. for damage, whether all transport requirements were met, if everything is received in good order, the pharmacist shall confirm receipt of the consignment), subsequently the NCC shall ensure the Site Investigator shall collect the Study Drug for the NCC and becomes fully responsible for the Study Drug. SPONSOR will make reasonable efforts to notify the authorized pharmacist by e-mail of the time when the consignment is supposed to be delivered to the pharmacy no later than three (3) business days prior to such delivery.
SPONSOR shall ensure delivery of the Study Drug to the following address:

Nemocniční lékárna FN Motol (MOTOL UH Pharmacy)
V Úvalu 84, 150 06 Praha 5

and shall specify the name of the authorized pharmacist on the package.

4. PHARMACOVIGILANCE

4.1 NCC shall comply with all applicable Laws and Regulations regarding safety reporting, and with this article 4 and shall comply with the provisions of **Exhibit D**: pharmacovigilance.

4.2 NCC shall ensure that all Investigators notify the SPONSOR immediately upon becoming aware during the conduct of the Study of any of the following information or circumstances relating to the Study Drugs, even if complete information is not yet

available all as set out in the Tasklist for Allocation of NCC's and Sponsor's Responsibilities, attached hereto in **Exhibit A**: imposition by an applicable competent regulatory authority in any area of the world in which the Study Drugs are marketed of any prohibition or restriction of the Study Drugs use; or any new information that might influence the evaluation of the risks and benefits of the Study Drugs. Such information may include both positive and negative results from clinical trials or other studies in relation to all indications and populations, whether or not use of the Study Drugs in that indication or population is approved under the relevant marketing authorization.

4.3 SPONSOR shall distribute to NCC all new information provided by Pharma, that might influence the evaluation of the risks and benefits of the Study Drugs. NCC shall distribute such information to Participating Site all as set out in the Tasklist for Allocation of NCC's and Sponsor's Responsibilities attached hereto in **Exhibit A**.

5. OWNERSHIP AND USE OF STUDY DATA

5.1 All case report forms and other data (including without limitation, written, printed, graphic, video and audio material, and information contained in any computer database or computer readable form) arising from and directly relating to the Study and the Protocol (the "**Data**") shall be the property of SPONSOR, which may utilize the Data in any way it deems appropriate, subject to and in accordance with applicable Laws and Regulations and the terms of this Agreement. To the extent permitted by Laws and Legislation, including data protection laws, SPONSOR shall have reasonable access to (I) the facilities where the Study is being performed and (II) all Data relevant to the Study under the terms and conditions of this Agreement and (III) all other data, documents or information related to the performance of this Agreement and required for regulatory, legal, financial, insurance or record keeping purposes. Study Data will be maintained and provided to SPONSOR in accordance with this Agreement, the Protocol and case report forms. For the avoidance of any doubt, Participating Site shall remain the owner of all the original study subject medical records ..

5.2 NCC warrants that each Participating Site and/or sub-investigators (if any) and all Study staff members have executed or shall execute a written agreement with NCC in which each such entity and/or person assigns to NCC all right, title and interest in and to Study data and Data, in order that NCC may fully assign the rights to SPONSOR as provided above.

5.3 Records-Keeping and Access to Records. NCC shall and shall have all Participating Sites maintain complete, accurately written records, accounts, notes, reports, data and radiographic examinations ("**Records**") relating to the Study and the Protocol which will be used to prepare and submit patient case report forms to SPONSOR, as detailed in the Protocol and/ or SOP's.

5.4 Record Retention. NCC shall retain, maintain and archive the essential documents related to the Study for the period defined (at least twenty-five (25) years) in a

way that ensures that they are readily available, upon request, to the competent authorities. NCC shall at SPONSORS costs retain the records beyond the twenty-five (25) years period if so requested by SPONSOR.

5.5 Intellectual Property

a) All Intellectual Property Rights and know how owned by or licensed to any of the Parties prior to and after the date of this Agreement, other than any Intellectual Property Rights and know how arising from the Study are their separate property and are not affected by this Agreement. Any developments to existing inventions and technologies that are not detailed as part of the Protocol but which may be developed during the Study will be owned by the owner of the pre-developed background.

b) The entire right, title and interest in and to any inventions, discoveries or other intellectual property rights that are conceived or developed from the Study, including all improvements or modifications which are anticipated by the Protocol, or rely on, use, or incorporate any Confidential Information provided by SPONSOR, or that relates to the Study Drug, or the delivery, manufacture, form, formulation, or use of the Study Drugs (including uses of the Study Drugs in combination with other products or agents), or that relates to a biomarker that is or may be useful in selecting patients for treatment with the Study Drugs ("**Inventions**"), shall be the exclusive property of SPONSOR. SPONSOR shall use and/or exploit all Data and Inventions in line with for the purposes of the Interfant Consortium.

c) The NCC shall and makes sure each Participating Site shall promptly report in writing to the SPONSOR each invention or discovery and hereby assigns, and shall ensure that all Study staff assign to the SPONSOR all of the rights, title and interest, if any, in and to each such Invention. In case Laws and Regulations do not establish the ownership of an Invention as intended above, NCC will ensure that the respective owner(s) of such Inventions grant SPONSOR the applicable license to enable SPONSOR to exercise the rights above. Subject to section (f) below, any such assignment will be free of any further obligation or consideration to NCC, the Participating Investigator(s) or the Participating Site(s), or the owner beyond that provided for in this Agreement, if so permitted by law.

d) The Parties shall execute such documents as are necessary to give effect to these provisions.

e) The SPONSOR hereby grants to the Participating Sites a fully paid up, non-exclusive, non-sub-licensable right to use the Inventions relating to research methods, documentation techniques, know-how, information and other aspects of the performance of the Study that do not arise out of the use of the Study Drug or Confidential information provided by the Sponsor for internal non-commercial research and teaching purposes, subject to the terms of this Agreement.

6. PAYMENT

6.1 SPONSOR will not provide any funding to NCC/Participating site for the conduct of the Study.

6.2 SPONSOR's support for the conduct of the Study is limited to having arranged the supply of Study Drug by Pharma and SPONSOR's authorized distributing third party.

6.3 To the extent NCC is contracting any Participating Site that will participate in the sub-study entitled "Pharmacokinetic study on Anticancer Treatment in Infant ALL to support Optimal dosing (PATIO)" the Parties agree that payment for the services provided by such Participating Site(s) in accordance with this Agreement for the sub-study PATIO shall be made directly by SPONSOR. Therefore, Parties hereby explicitly allow SPONSOR to discharge NCC from NCC's payment obligations resulting from Participating Site's provision of services in accordance with this Agreement and to make payments to satisfy NCC's payment obligations for such services towards Participating Site, as further described in Exhibit G to this Agreement. NCC agrees to incorporate the payment agreement as included in Exhibit G in their contract/s with the relevant Participating Site(s).

7. CONFIDENTIAL INFORMATION

7.1 "**Confidential Information**" means, information, data and material of any nature belonging to a Party and disclosed by one Party (the "**Disclosing Party**") to the other Party (the "**Receiving Party**") in connection with this Agreement, which is personal data which relates to any patient of NCC/Participating Site (as applicable) or his or her treatment or medical history, or other information, which reasonably should be known as Confidential Information of the Disclosing Party, or which is a trade secret, including know how, or, in case of Study Drug information: which is Pharma's Confidential Information, whether disclosed before or after execution of this Agreement, except the information specified in Section 7.3 below. Confidential Information may be written or spoken. It includes pictures, diagrams and electronically stored information. The obligations of confidentiality concerning Confidential Information which is not personal data, shall survive for a period of ten (10) years following termination or expiry of this Agreement. The obligations of confidentiality of this clause 7 regarding Confidential Information which is personal data shall remain in full force and effect after termination or expiry of this Agreement.

7.2 Disclosure of Confidential Information

a) Each Party shall use the other Party's (and if applicable: Pharma's) Confidential Information only in the conduct of the Study and shall return to the Disclosing Party all written Confidential Information at the request of the Disclosing Party.

b) No Party shall disclose Confidential Information to any third party not involved with the Study, without prior written consent of the other Party, and shall take all reasonable precautions to prevent the disclosure of Confidential Information to third parties. In the event that Confidential Information is required to be disclosed to a third party to allow the performance of the Study then the Party disclosing the information to

the third party will ensure that said third party are bound by terms of confidentiality no less stringent than those contained herein and will at all times remain liable for the use made by the third party of the Confidential Information.
c) NCC will oblige Investigator(s) and Study Staff to comply with the provisions of the section "confidential information".

7.3 The provisions of Section 7.2 do not apply to any Confidential Information which:
a) the Receiving Party can demonstrate by written records was known to the Receiving Party prior to receiving that Confidential Information either directly or indirectly from the Disclosing Party;
b) is generally known to the public or which becomes generally known to the public through no act or omission on the part of the Receiving Party; or
c) is lawfully obtained by the Receiving Party from sources independent of the Disclosing Party and who, to the best of their knowledge after due inquiry, have a lawful right to disclose such Confidential Information.
d) is developed independently by receiving party without use of or reference to any Confidential Information of the disclosing's Party which the receiving party can demonstrate.

7.4 Specifically authorized is the disclosure of Confidential Information:
a) under obligation of law, regulation or court order, provided the information disclosed is necessary to comply with legal requirements, and confidentiality is maintained to other third parties;
b) to the EC/IRB, Competent Authority and representatives of the health-care inspectorate or a medicines evaluation board;
c) as part of publication of the results of the Study based on Study Data, subject to the provisions of section "confidential agreement" of this Agreement, and section 8 regarding publications and disseminations of results.

8. PUBLICATION

8.1 NCC will, and will oblige their Investigator and other Study Staff to comply with the provisions of this paragraph. NCC agrees that the first publication of the results of this Study shall be made in conjunction with the presentation of a joint, multi-center publication of the Study results with the investigators and the institutions from all participating sites contributing to Data, analyses and comments, and coordinated by SPONSOR, as described in the Protocol, unless otherwise agreed by Parties. The results of the final analysis as well as all analyses that deal with the primary and secondary endpoints listed in the Protocol will be initiated and/or authorized by SPONSOR.

8.2 If there is no multi-site publication within twelve (12) months after the Study has been completed or terminated at all Participating Sites and all data has been received by the SPONSOR, the NCC and any sub-contractors shall have the right to publish results from the Study, subject to the following notice requirements.

a) The NCC shall send the SPONSOR a draft of all intended publications in advance of publication for the SPONSOR to review for the possible inclusion of any of its Confidential Information. The SPONSOR shall have 45 days, after the receipt of the draft to request in writing the delay or amendment of such proposed publication on the grounds that there is subject matter which needs patent protection or similar protection or to prevent publication of any Confidential Information of the SPONSOR failing which, without comment after the expiry of this period, the NCC will be free to publish.

b) The SPONSOR may request the NCC to refrain from publishing for a maximum of another period of 45 days in order to allow for application for patent protection in the name and at the cost of the relevant owner of any Inventions.

c) A copy of all publications and publicity communications related to the Study shall be sent to NCC for information by the SPONSOR. NCC shall distribute such communications to Participating Site (if/as applicable).

8.3 The contributions of either Party and Pharma's support of the Study shall be referenced and credited in all publications and communications related to the Study and authorship determined in accordance with the Protocol.
The results of the clinical trial will be published after complete data collection and evaluation. Partial or preliminary results may not be published beforehand.
Publications and/or presentations are to be initiated and/or authorized by the principal investigators, and will be prepared by the principal investigators as first and last author of the paper.
The following persons will be considered as co-authors:
• Investigators who have recruited at least 1 patient into the trial. In case the journal we want to publish the paper in does not allow a large number of co-authors this may have to be restricted to investigators enrolling at least 2 patients.
• Members of the trial steering committee
The final publication manuscript should be prepared within six months after last patient's last visit (LPLV). The co-authors must notify the main author in writing concerning their approval or proposed changes to the manuscript within four weeks after receiving the publication draft. Failing to do this, their approval will be assumed.
Any publication in the form of a lecture, poster or publication of data must be approved by the Coordinating Investigator. Such publication should generally not occur before the joint publication of the study group. Enquiries from the press and general public concerning study results may only be answered by the Coordinating Investigator of the clinical trial after consultation with the sponsor.

8.4 In accordance with the Act No. 340/2015 Coll. on Registry of Contracts, this Agreement and/or any amendment shall be published on the Ministerial Contract Registry within thirty (30) days from last signature. The Parties agree that NCC shall publish this Agreement, its Exhibits and any future amendments, and shall limit its disclosure to the information required by law.

Prior to publication, NCC shall remove all information related to Confidential Information, personal information, and business and trade secrets, as defined by the Civil Code from the Agreement to be published (hereinafter, collectively "Excluded

Information"), including, without limitation, the Protocol, the investigator brochure and the budget exhibit detailing the costs per procedures. Only the expected total study budget (contract value) shall be published.

NCC shall draft the final form of the Agreement (hereinafter "Draft Publication Document") for publication (which shall not contain any Excluded Information) and shall submit the Draft Publication Document to SPONSOR for review at least thirty (30) calendar days before the Agreement is expected to be executed. SPONSOR shall provide any comments to NCC on the Draft Publication Document within fifteen (15) days and NCC shall make any amendments reasonably suggested by SPONSOR. The Agreement shall only be executed after the parties have agreed the final form and format of the Agreement for publication on the Ministerial Contract Registry (hereinafter "Final Document").

NCC agrees to publish the Final Document and complete the metadata on the Ministerial Contract Registry within five (5) working days after final signature of the Agreement. The Institution shall add trialmanagement@prinsesmaximacentrum.nl as a secondary recipient. The parties understand that the site shall not be initiated until the Final Document has been published.

9. SAMPLES

9.1 For the purpose of this clause Samples shall mean any human biological materials, including but not limited to blood, body tissue, plasma and any other material containing human cells.

9.2 As part of the Protocol, Samples derived from Clinical Study Subjects may be transferred to SPONSOR or a third party indicated by SPONSOR (hereinafter: "SPONSOR's Designee") subject to the informed consent form ("ICF") signed by the Study subject.

9.3 The SPONSOR and SPONSOR's Designee shall have the right to store, transfer and use the Samples only in accordance with applicable laws, the Protocol and ICF. If this is done in non-anonymous form, SPONSOR and SPONSOR's Designee shall adhere to the provisions of the GDPR by concluding the necessary agreements with each other. The NCC shall promptly notify the SPONSOR of any withdrawal of or changes in the informed consent of a Study subject, which may affect the use of such subject's Samples under this Agreement and as such each Party will comply with the request of the patient as per the ICF requirements accordingly.

9.4 Upon termination or expiration of the Study, and at least at any time the Samples are no longer needed to be retained by the SPONSOR for any procedures described in the Protocol or as defined in the ICF, or as required per any applicable law or regulation, the remainder of the Samples in SPONSOR's or any of its designee's possession will be

stored by the SPONSOR and used for future research, to the extent further use of the Samples after termination or expiration of the Clinical Trial is provided for in the ICF pending ethical approval.

For the avoidance of any doubt, the control of the Samples remains at all times with the Clinical Study Subjects they are derived from, while the Site Parties and/or SPONSOR are acting as custodian of the Samples, as described in the Protocol.

9.5 The NCC as Participating Site warrants that where required by applicable laws the Samples have been obtained from humans with the appropriate consent, and with ethical approval and the NCC shall be liable for any claims arising due to the breach of this warranty. Each Party will notify the other Party of any specific requirements required under applicable laws. The NCC hereby grants to the SPONSOR a non-exclusive, sub-licensable, irrevocable research licence to use the Samples for the Study and to retain custody of the Samples for future use including but not limited to research and teaching. The NCC further warrants that it has not provided any information (and does not intend to provide any information) which has led or may lead to the SPONSOR being able to identify the person from whom the relevant material came.

10. PUBLICITY

SPONSOR will not use the logo or name of the NCC, nor of any member of the NCC's Study Staff, for promotional purposes or in any publicity without the prior written approval of an authorized representative of NCC, such approval not to be unreasonably withheld. SPONSOR will not use the logo or name of Participating Site, nor of any member of the Participating Site's Study Staff, for promotional purposes or in any publicity without the prior written approval of an authorized representative of Participating Site, such approval not to be unreasonably withheld. NCC will not, and will ensure that the their (Principal) Investigator and Study Staff will not, use the name or logo of SPONSOR or Pharma or of any of their employees, nor the name of the Study, nor the name of the Study Drug, for promotional purposes or in any publicity without the prior written approval of SPONSOR, such approval not to be unreasonably withheld. Notwithstanding the abovementioned, Parties may use the other Party's name however, if required for transparency purposes and to comply with Laws or regulations. NCC agrees that Pharma may identify the NCC as Participating Site and their Investigators, provided that in any such disclosure, Pharma will clearly differentiate between payments or other transfers of value to institutions and those made to individuals. Disclosures may include identifying information for institutions and investigators such as name, business address, specialty, licensure numbers.

11. INDEMNIFICATION AND LIMITATION OF LIABILITY

11.1 Both Parties are responsible for obtaining adequate liability insurance to cover their respective responsibilities as set out in **Exhibit A** and shall provide evidence of the same to the other Party upon request.

11.2 NCC ensures and, if applicable, shall assure that each Participating Site in the Country has taken out insurance including professional liability coverage, to cover their liabilities under the Agreement and under the Study, and in full compliance with Laws and Regulations. SPONSOR shall be provided evidence thereof upon request, either through presentation of an insurance certificate or confirmation that NCC is covered under the relevant government scheme.

11.3 NCC has taken out clinical trials insurance as required by applicable regulatory requirements, including article 76.1 of the CTR, to provide compensation or indemnity to all Study patients in the Country, and shall indemnify SPONSOR against all claims from or on behalf of Study subjects, in connection with personal injury or death as a result from such Study subject's participation in the Study, on the condition that the personal injury or death is not caused by SPONSOR's or Coordinating Investigators negligence, failure to comply with this Agreement, the Protocol or with applicable Laws and Regulations.

11.4 Without prejudice to Article 11.3, NCC acting as Participating Site shall indemnify, defend and hold harmless SPONSOR and Coordinating Investigator from any and all liability, loss, including attorney's fees, or damage they may suffer as the result of claims, demands, costs or judgments against them which arise from or are connected with:

a) injury or death to a Study patient as a result of negligence or willful misconduct on the part of the NCC, its agents, officers, employees, or NCC Investigator; or

b) a failure to comply with this Agreement, the Annexes, the Protocol, the SOPs, any reasonable written instructions from SPONSOR or any applicable law, by NCC or NCC Study Staff.

11.5 SPONSOR shall indemnify, defend and hold harmless NCC, their respective agents, officers, and employees including NCC Investigator from any and all liability, loss, including attorney's fees, or damage it may suffer as the result of third party claims, demands, costs or judgments against it which arise from or are connected with: a breach of this Agreement, or failure to comply with applicable law, by SPONSOR or SPONSOR's Study Staff or Coordinating Investigator.

11.6 Nothing in this section 11 shall operate so as to restrict or exclude the liability of a Party in relation to death or personal injury caused by the negligence of that Party or its servants or employees or to restrict or exclude any other liability of either Party which cannot be so restricted or excluded in law.

11.7 Neither Party has any liability to the other under this Agreement for incidental, indirect or consequential damages (including lost profits, business, revenue or opportunity or damage to reputation or goodwill) arising from any breach of this

Agreement. This limitation will not apply to the extent such liability cannot be so restricted or excluded under Laws and Regulations and in case of gross negligence or wilful misconduct.

11.8 The aggregate liability of each Party for a claim or proceeding of the other Party under this Agreement shall be limited to EUR 250.000, except and to the extent such claim or proceeding is made for damages caused by: A) gross negligence, wilful recklessness or wilful conduct or wilful misconduct of any of the Participating Site and cannot be so restricted or excluded by Law, or B) claims or proceedings between the Parties arising from the joint and several liability in connection with the joint controllership of the Parties under the GDPR as further laid down in clause 14 below.

11.9 Conditions for Indemnification

Each Party's agreement to indemnify, defend and hold the other harmless is conditioned on the indemnified Party:

a) providing written notice to the indemnifying party of any claim, demand or action arising out of the indemnified activities within seven (7) days after the indemnified party has knowledge of such claim, demand or action;

b) permitting the indemnifying party to assume full responsibility to investigate, prepare for and defend against any such claim, demand or action;

c) assisting the indemnifying party, at the indemnifying party's reasonable expense, in the investigation of, preparation for and defense of any such claim, demand or action; and;

d) not compromising or settling such claim, demand or action without the indemnifying party's written consent.

11.10 Limited Warranty and Disclaimer:

It is understood that the Study Drug distributed and provided under this Agreement is experimental in nature. SPONSOR makes no representation of any kind, express or implied, regarding the safety or efficacy with respect to the Study Drug and and/or the Protocol. However SPONSOR assures to conclude an appropriate contract with Pharma supplying the Study Drug and to take all necessary efforts to reasonably oblige Pharma under that contract to be liable for the manufacture of Study Drug according to Laws and Regulations.

12. TERM AND TERMINATION

12.1 The term of this Agreement shall commence on the date upon which this Agreement is executed by all Parties and shall remain in effect, for the duration of the study, unless terminated in accordance with 12.2. The term may be extended by a written amendment to the Agreement signed by both Parties.

12.2 Termination

a) By SPONSOR: SPONSOR may terminate this Agreement upon thirty (30) days written notice in the event no Study subjects are enrolled in the Study, unless termination

is due to serious adverse reactions to Study Drugs and such reactions represent a unreasonable and significant risk to patients, which shall result in an immediate termination .

b) Each Party may terminate this Agreement upon written notice to the other party with immediate effect in the following events:

i. if one of the Parties is dissolved;
ii. if one of the Parties becomes or is declared insolvent or a petition in bankruptcy has been filed against it;
iii. if the purpose of the Study, as confirmed by the IRB/EC, becomes obsolete;
iv. if, through no fault of a Party, the Study does not receive official approval from the EC/IRB or Study Authorities, or this approval is permanently revoked;
v. if the Study ceases to be in the interests of the health of the Study patients as determined by the EC/IRB or Study Authority;
vi. any material breach of or failure to comply with any of the terms or conditions of this Agreement or Protocol by the other Party, which breach or failure, if capable of remedy, is not remedied within thirty (30) days after notice from the aggrieved Party demanding such remedy, and provided the termination is in reasonable proportion to a termination for such cause;
vii. if, for reasons beyond a Party's reasonable control, the performance of the obligations under this Agreement, reasonably can no longer be demanded from that Party
viii. if Study recruitment is significantly slower than planned and impacting Study overall timelines as set forth in the Protocol, which makes it unlikely to generate statistically or clinically meaningful results; or
ix. as long as no research subjects have undergone treatments or have had conduct requirements imposed on them, for any reason upon providing a minimum of sixty (60) days prior written notice to the other party.

12.3 Survival

Clauses 3, 5, 8, 9, 10, 11, this clause 12.3, 13, 14 and 15.2, or other clauses contemplating performance after termination, shall remain in full force and effect upon termination or completion of this Agreement without regard to whether the Parties have fully performed their obligations under this Agreement, and, as the case may be, during a time period mentioned in each respective section.

13. MONITORING and AUDITING

13.1 Monitoring

SPONSOR hereby delegates its monitoring responsibility to NCC. NCC is therefore responsible for monitoring the Clinical Trial in the Country as set out in the Tasklist for Allocation of NCC's and Sponsor's Responsibilities attached hereto in **Exhibit A**.

13.2 Auditing

To satisfy its duties as sponsor of the Study, SPONSOR will conduct during regular business hours quality oversight reviews and audits of the facilities, services, systems and process of NCC in Study execution, when it sees reason to do so. However such audit

will be at reasonable times and without causing unreasonable disruption to NCC's daily practice.

13.3 Regulatory inspections
NCC will notify SPONSOR as soon as reasonably possible if it or any of the Participating Sites is, or will be inspected by a regulatory agency in relation to the Study, and will promptly share with SPONSOR the results of any such inspection, who is hereby granted approval to share the results with Pharma.

14. DATA PROTECTION

14.1 Each Party shall ensure that it complies with the requirements of all legislation and regulatory requirements in force from time to time relating to the use of Personal Data, including, without limitation, Regulation (EU) 2016/679 (General Data Protection Regulation) and the equivalent legislation in the country of the SPONSOR ('Data Protection Laws').

14.2 The Parties each acknowledge and agree that they may need to process Personal Data relating to each Party's representatives (in their respective capacities as Controllers) in order to (as appropriate): (a) administer and perform their respective activities and obligations under this Agreement; (b) compile, dispatch and manage any payments agreed under this Agreement; (c) manage this Agreement and resolve any disputes relating to it; (d) respond and/or raise general queries relating to this Agreement; and (e) comply with their respective regulatory obligations.

14.3 Each Party shall process such Personal Data relating to each Party's representatives for the purposes set out in clause 14.2 above in accordance with their respective privacy policies. The Parties acknowledge that they may be required to share Personal Data with their affiliates, group companies and other relevant parties, within or outside of the country of origin, in order to carry out the activities listed in clause 14.2, and in doing so each Party will ensure that the sharing and use of this Personal Data complies with applicable Data Protection Laws.

14.4 In addition to the Personal Data described in clause 14.2 the Parties hereby agree that they will need to transfer Personal Data in order to fulfill the requirements of the Study ('the Study Personal Data'). The Study Personal Data to be processed by the NCC is detailed in **Exhibit E**.

14.5 Each Party agrees to comply with its obligations as set out in **Exhibit E** (Data Protection) of this Agreement.

14.6 Sponsor shall refrain from tracing and/or identifying any Study Patient, except where Sponsor is under a legal obligation to do so. In the event any Study Patient, for any other than aforementioned reason, becomes identifiable to Sponsor, Sponsor agrees to preserve, at all times, the confidentiality of information pertaining to such Study Patient.

15. MISCELLANEOUS

15.1 General Terms

a) This Agreement, including those documents attached hereto as Exhibits or referenced herein, constitutes the entire understanding of SPONSOR, NCC, Participating Site and NCC Investigator and Principal Investigator.
b) In the event of any inconsistency between the terms of this Agreement and the terms of any Exhibit attached hereto such as the Protocol, the terms of the Protocol shall prevail with respect to the conduct of the Study and the treatment of patients in connection therewith; in all other respects, the terms of this Agreement shall prevail.
c) No changes, amendments, or alterations shall be effective, unless in writing and signed by both Parties.
d) If for any reason a court of competent jurisdiction finds any provision of this Agreement, or portion thereof, to be unenforceable, that provision of this Agreement shall be enforced to the maximum extent permissible so as to affect the intent of the parties, and the remainder of this Agreement shall continue in full force and effect. Failure by either Party to enforce any provision of this Agreement shall not be deemed a waiver of future enforcement of that or any other provision.
e) In case NCC uses a translated native language version of documents for the Study and/or of this Agreement, this English language version Agreement shall remain the working document and the terms of this English language Agreement shall prevail over the translated documents.
f) The Parties agree that Pharma is the intended third party beneficiary of this Agreement and may, enforce its rights and interests under this Agreement.

15.2 Governing Law

This Agreement shall be exclusively governed by the laws of The Netherlands, excluding its conflicts of laws rules. The Parties consent to the exclusive jurisdiction of the competent court of Midden-Nederland, location Utrecht, for the resolution of all disputes or controversies between the Parties hereto that Parties are unable to settle amicably. However, both parties agree to comply with the laws regarding the conduct of clinical studies being applicable in the country of NCC.

15.3 Notice

Any notice required to be given under this Agreement shall be sent to the other Party by certified mail, return receipt requested or by other method reasonably capable of proof of receipt thereof and addressed to the Parties as set forth below, and shall be deemed given as of its date of receipt, which shall be no later than five (5) days after the date of postmark. Notice shall be given to each Party at the address set forth below, or such address a Party may indicate:

To SPONSOR:

Formal Notices:

Princess Máxima Center for pediatric oncology
Trial and Data Center
Heidelberglaan 25
3584 CS Utrecht
The Netherlands

TDCSecretary@prinsesmaximacentrum.nl

Science / medical matters: [redacted]

To NCC:

Formal Notices:

NCC: [redacted] *V Úvalu 84, 150 06 Prague 5, The Czech Republic.*

Eva.Aljamal@fnmotol.cz
Medical / Science matters: [redacted] *V Úvalu 84, 150 06 Prague 5, The Czech Republic.*

[redacted]

15.4 Relationship of the Parties

a) Neither NCC nor the NCC Investigator shall be deemed an agent or employee of SPONSOR, and neither has authority to bind SPONSOR. As an independent contractor, neither NCC nor NCC Investigator nor any associated staff performing the protocol shall participate in any SPONSOR employee benefit plans nor receive any other compensation.

b) Payments for services rendered under this Agreement shall be made in full at the agreed rate without any deductions for employment taxes of any kind whatsoever, this being in conformity with non-employee status. It is understood that any employment taxes that may be due and payable as a result of the payments herein specified by SPONSOR shall be entirely the NCC's responsibility. It is understood that, as part of this Agreement, the recipient undertakes to pay all employment taxes on such payments for which it may be liable when due.

15.5 Assignment

This Agreement shall not be assignable in whole or in part by either party, without the express prior written approval of the other Parties. However, both Parties shall be entitled to subcontract their responsibilities arising from this Agreement to a CRO or similar third

party contractor. Any Party who so sub-contracts shall be responsible for the acts and omissions of its sub-contractors as though they were its own.

IN WITNESS WHEREOF, Parties have executed this Agreement by their respective officers hereto duly authorized on the day and year hereinafter written.

SPONSOR Princess Máxima Center for Pediatric Oncology B.V.

Legal representatives
By:_____
Print Name: [redacted]
Title: Head Trial & Data Center
Date: _____

Read and acknowledged:

Coordinating Principal Investigator
By:_____
Print Name: Dr. J. Stutterheim
Title: pediatric oncologist, Coordinating Investigator
Date: _____

NCC, Motol University Hospital:

By:_____
Print Name: [redacted]
Title: Deputy Director, acting on power of attorney
Date: _____

Read and acknowledged

NCC:

NCC Investigator
By:_____
Print Name: __ [redacted] _____
Title:___pediatric oncologist, NCC investigator_____
Date: _____

APPENDICES:

EXHIBIT A: TASK LIST AND TABLE SPONSOR/NCC
EXHIBIT B: PROTOCOL
EXHIBIT C: REGULATORY DOCUMENTATION
EXHIBIT D: PHARMACOVIGILANCE
EXHIBIT E: DATA PROTECTION
EXHIBIT F: PRIVACY NOTICE

EXHIBIT A: TASKLIST SPONSOR/NCC

Tasklist for Allocation of NCC's and Sponsor's Responsibilities

Responsibility	Sponsor	NCC	Participating site
Trial Development			
Trial Design	✓		
Risk Assessment	✓		
Obtain EudraCT number	✓		
Register trial in clinical trial registration database	✓		
Protocol development	✓		
Select and subcontract external vendors plus vendor oversight plan	✓		
Develop Patient Information Sheet, Consent Form and other patient focused documents in English	✓		
Arrange for translation of Patient Information Sheet, Consent Form and other patient focused documents from English into local language		✓	
Ensure the translated Patient Information Sheet, Consent Form and other patient focused documents comply with national requirements and standards		✓	
Case Report Form development	✓		
Develop, test and maintain trial database, including randomisation system (if applicable)	✓		
Develop Procedure manual	✓		
Provision of finalised trial essential documents and guidance in English where needed. Including but not limited to: • Protocol summary/protocol • Investigational Medicinal Product (IMP) Labels • XML of CTA • Sponsor proof of clinical trial insurance	✓	✓ translation of documents when required	
Train NCC Investigator, staff at NCC on protocol and study responsibilities	✓		
Train monitor and site staff of participating sites on protocol and study responsibilities		✓	
Develop country specific protocol appendix when required for regulatory submission in order to comply with national laws and regulatory requirements and provide copy (in English) to sponsor for approval		✓	
Approval of country specific protocol appendix, required for regulatory submission	✓	Advisory role	

Responsibility	**Sponsor**	**NCC**	**Participating site**
Develop Country specific guidance documents e.g. Pharmacy Manual, Laboratory Guidelines. Provide copies to SPONSOR on request		✓	
Develop Country specific Patient Information Sheet, Consent Form and other patient focused documents, including translation and adaption where required, to comply with national requirements Provide copy of Country specific patient documents to SPONSOR		✓	
Obtain Country specific clinical trial insurance/indemnity and provide copy to Sponsor		✓	
Provision and sign off of contracts and agreements with Country specific third party suppliers (if applicable) Details of third party suppliers to be provided to SPONSOR on request		✓	

Contracts, legal and financing			
Obtain funding for conduct of trial within Country/Participating Sites		✓	
Manage financial budget within Country		✓	
Provide draft contract to NCC and if applicable NCC investigator.	✓		
Creation and provision of written agreement between NCC and Participating Site(s). Provide copy of signed agreement(s) to sponsor.		✓	
Send invoices based on agreed budget template and time-lines as specified in the contract		NA	
Pay invoices according to agreed time-lines	NA		
Trial Authorization			
Register the Clinical Trial in CTIS and obtain EU CT number	✓		
Decide on publication deferral rules in CTIS	✓		
Decide on user rights in CTIS	✓		
User administration management in CTIS	✓		
Check if all participating sites are registered in OMS (Organization Management Service) system		✓	
Ensure that all Participating Sites in Country are registered in OMS		✓	
Registration of Participating Sites in OMS system			✓
Develop required Part I documents for regulatory approval (initial and modifications)	✓		
Responsibility	**Sponsor**	**NCC**	**Participating**

			site
Translate required Part I documents for regulatory approval (initial and modifications), where applicable		✓	
Develop required Part II documents for regulatory approval in Country, share with Sponsor (initial and modifications)		✓	
Translate required Part II documents for regulatory approval in Country, share with Sponsor (initial and modifications)		✓	
Distribute initial regulatory documents and (substantial) modifications, reports and other documentation to the NCC after approval	✓		
Distribute initial regulatory documents and (substantial) modifications, reports and other documentation to the Country's Participating Sites after approval		✓	
Complete Form section in CTIS: create, redact and upload documents and fill in text fields	✓		
Complete Member States Concerned (MSCs) section in CTIS		✓	
Redact Part I documents (initial and substantial modifications)	✓		
Complete Part I in CTIS: upload documents and fill in text fields (initial and substantial modifications)	✓		
Redact Part II documents (initial and substantial modifications)		✓	
Complete Part II in CTIS: upload documents and fill in text fields (initial and substantial modifications)		✓	
Submit the clinical trial application in CTIS (initial and substantial modifications)	✓		
Respond to Requests for Information (RFI's) about Part I	✓		
Respond to RFI's about Part II		✓	
Respond to RFI's about Form and/or MSCs section	✓		
Submit RFI's	✓		
Determine whether part I modifications are needed, which modifications are substantial, and supply documentation to NCC	✓		
Determine whether part II modifications are needed, which modifications are substantial, and supply documentation to NCC	✓		
Prepare and submit required documents in Country for additional national approval as needed (e.g. local Review Board or Scientific Committee), and provide proof to Sponsor		✓	
Ensure Participating Sites obtain additional local approval as needed, and provide proof to Sponsor		✓	
Obtain additional local approval as needed			✓
Responsibility	**Sponsor**	**NCC**	**Participating**

			site
Report start of study in Country to regulatory authority via the CTIS portal	✓		
Notify Sponsor of First patient First Visit FPFV in Country		✓	
Report FPFV of Country to regulatory authority via the CTIS portal	✓		
Trial participation			
Patient allocation and recruitment			✓

Trial Management			
Medical and scientific supervision global	✓		
Medical supervision participating country		✓	✓
Ensure trial conducted according to protocol and GCP	✓	✓	✓
Conduct NCC, Participating Site feasibility	✓		
Act as point of contact for Country specific Participating Site feasibility		✓	
Maintain a list of Country Participating Sites contacts e.g. medically qualified investigators (physicians), research nurses, etc.	✓	✓	
Grant permissions to access trial database	✓		
Act as country-based point of contact for routine trial management		✓	
Act as a point of contact for clinical queries (including eligibility)	✓	✓	
Provide electronic Investigator Site File index to the Country's Participating Sites	✓		
Maintain trial master file (where applicable)	✓		
Maintain country specific trial master file		✓	
Maintain Investigator Site file			✓
Participate in study progress teleconferences (as needed)	✓	✓	
Decide on the need for implementation of urgent safety measures	✓		
Report urgent safety measure to regulatory authority via the CTIS portal	✓		
Implement urgent safety measure. Provide confirmation to Sponsor		✓	✓
Report potential serious breaches of GCP/Protocol to the Sponsor		✓	✓
Perform assessment of potential serious breaches	✓		
Propose and implement Corrective and Preventive Actions (CAPA) plan and ask Sponsor approval	✓ (approve)	✓	✓ (draft CAPA plan)
Responsibility	**Sponsor**	**NCC**	**Participating**

			site
Report serious breaches and CAPA to the regulatory authority via the CTIS portal as required	✓		
Decide on need for temporary halt to trial (when applicable)	✓		
Report temporary halt of recruitment, follow-up actions and restart of recruitment (if applicable) in Country to regulatory authority via the CTIS portal	✓		
Site Management			
Site selection	✓	Advisory role	
Site initiation visit (SIV) including training	✓	✓	
Site essential documents collection	✓	✓	
Site initiation confirmation	✓		
Site close out (visit) (SC(V)) as per monitoring manual	✓	✓	
Site close out confirmation	✓		
Data Management			
Central Data management	✓		
Data entry by electronic remote data capture (eRDC)			✓
Reminders for timely data entry to Participating Sites	✓	✓	
Adverse Event Reporting			
Report SAEs and AESIs to sponsor in a timely fashion			✓
Clinical evaluation and categorisation of Serious Adverse Events (SAEs)	✓		
Generate SUSAR report in EVWEB	✓		
Provide SUSAR report to reporting Site and concerned NCC	✓		
Provide SUSAR report to non-EU NCCs if required	✓		
Generate Suspected Unexpected Serious Adverse Reactions (SUSARs) reports and provide to Country	✓		
Evaluation of the impact of the SUSAR on the trial (i.e. if the SUSAR necessitates a change in the trial)	✓		
Report SUSARs to local investigators with a cover letter/e-mail with instructions to file the report in the investigator trial		✓	
Report SUSAR to Participating Sites according to local requirements		✓	
Report SUSAR to local authorities if required		✓	
Notify the Participating Sites and Investigators in the country of safety issues as specified by the Sponsor. Provide proof of notification to Sponsor		✓	
SAE reconciliation	✓		
Preparation of Development Safety report (DSUR) and	✓		

provide to country as applicable			
Submission of DSUR to regulatory authority via the CTIS portal	✓		

Responsibility	**Sponsor**	**NCC**	**Participating site**
Submission of DSUR to EC & CA in accordance with national laws and regulatory requirements. Provide sponsor with proof of submission.		✓	
Medicinal Supply Management			
Supply of labelled IMP	✓ (Outsourced to CSM)		
Maintaining an IMP inventory and monitor study drug supply to sites	✓		
Preparation of pharmacy related documents	✓		
Investigative Site drug accountability including drug inventory, storage, dispensing, compliance and drug reconciliation and IMP destruction (when applicable)			✓
Monitor drug accountability	✓ (at study level)		✓ (at site level)

Responsibility	Sponsor	NCC	Participating site
Monitoring and Audit			
Preparation of monitoring plan (detailing minimal monitoring requirements)	✓		
Preparation of monitoring manual	✓		
Arrange on site monitoring of Participating Sites in accordance with GCP, protocol and monitoring plan according to monitoring manual.		✓	
Review monitoring reports and decide on actions to be taken	✓	✓	
Communicate actions to be taken to sites (if applicable)		✓	
Follow up of required actions resulting of monitor visits			✓
Report follow up of required actions resulting of monitor visits to sponsor		✓	
Oversight of implementation of actions which resulted from monitoring sites	✓		
Prepare Audit Plan	✓		
Prepare potential audits of participating sites	✓		
Report inspection report of Country to regulatory authority via the CTIS portal	✓		
Report inspection reports of third countries to regulatory authority via the CTIS portal	✓		
Data Provision, Statistical Analysis and Publication			
Development of Statistical Analysis Plan (SAP)	✓		
Provide summaries (e.g. number patients recruited, CRF return, etc.) for TCs, newsletters, monitor visits, etc.	✓		
Perform analyses in accordance with the Statistical Analysis Plan	✓		
Preparation and submission of main trial abstract(s)/publication(s)	✓		
Report formal (interim) reports to regulatory authority via the CTIS portal (if applicable)	✓		
Central Laboratories and/or Central Review			
Coordinate central review/analysis for MRD		✓	
Perform and document central data review/analysis	✓		
Data collection of central review/analysis outcomes	✓		

Preparation and transfer of data sets from central review/analysis results for statistical analysis	✓		
Responsibility	**Sponsor**	**NCC**	**Participating site**
End of Trial			
Report early termination of study to regulatory authority via the CTIS portal (if applicable)	✓		
Report end of recruitment in Country to regulatory authority via the CTIS portal	✓		
Report end of study (LPLV) of Country to regulatory authority via the CTIS portal	✓		
Report end of study (LPLV) of all Member States to regulatory authority via the CTIS portal	✓		
Report end of study (LPLV) in all countries (Member States and third countries) to regulatory authority via the CTIS portal	✓		
Preparation of End of Trial Report (ETR) and provide to country as applicable	✓		
Submit ETR to regulatory authority via the CTIS portal	✓		
Prepare Lay Summary of trial results in English	✓		
Translate Lay Summary into local language(s)		✓	
Submit Lay Summary to regulatory authority via the CTIS portal	✓		
Ensure archiving of country trial master file		✓	
Ensure archiving of investigator site file			✓
Archiving of sponsor's trial master file	✓		

EXHIBIT B: PROTOCOL

EXHIBIT C: REGULATORY DOCUMENTATION

NCC (or, if applicable: Participating Site, in which case each referral to NCC shall read as Participating Site) will collect the Regulatory Documentation identified in this schedule, whenever applicable for each Participating **SITE**, whenever applicable in close collaboration with SPONSOR**.**

1. NCC will submit the following Regulatory Documentation to SPONSOR immediately upon its receipt by NCC:

   1.1. Initial IRB/IEC approval for the first Participating Site, along with annual renewal(s) of IRB/IEC approval for those Sites if applicable (if/to the extent more than one site is participating in the Study in such country);

   1.2. documentation of competent regulatory authority approval to conduct the Study;

   1.3. Documentation of approval by competent regulatory authorities of all substantial amendments to the clinical trial authorization for Participating Sites.

2. NCC will collect the following Regulatory Documentation as it is generated, share it with the SPONSOR via the webportal (dcog-ectc website) and shall retain it until the Study is completed/terminated or as required under Laws and Regulations, whichever occurs first last:

   2.1. Curriculum Vitae (CV) for the Principal Investigator and each sub-Investigator of all Participating Sites;

   2.2. Initial IRB/IEC approval for all Participating Sites other than the first one;

   2.3. Annual renewal of IRB/IEC approval for all Participating Sites other than the first one;

   2.4. A completed form detailing about the Participating Sites' and their investigator's qualifications to conduct clinical trials as required under Laws and Regulations, or, if feasible at their sole discretion (of note: this was captured under the feasibility checklist by SPONSOR);

EXHIBIT D: PHARMACOVIGILANCE

1. Reporting of SAEs

This section identifies the nature and extent of safety reporting obligations.

Study Drugs = [redacted]

1.1. Timing and Scope.

Within 24 hours of first awareness of an SAE by the Participating Site Investigator, or within 24 hours upon awareness by the Participating Site Investigator if the SAE is fatal or life-threatening, the Participating Site Investigator will notify SPONSOR by e-mail of any SAE for which reporting to SPONSOR is required under this provision. With respect to the obligations of reporting SAE's, the hours between Fridays 17.00 hrs till 09.00 hrs on the Mondays thereafter, and Bank Holidays are not taken into consideration. The Participating Site Investigator will notify SPONSOR of any SAE reported or modified in the last 24 hours by email to the SPONSOR safety desk. SAEs that are subject to the reporting requirement are those that occur in:

- participants who are assigned to receive the Study Drugs; or
- individuals otherwise exposed to the Study Drugs.

The Participating Site Investigator will notify SPONSOR of any such SAE within timeframes established by this section 1.1 even if complete information concerning the SAE is not yet available and irrespective whether causality is related to the Study Drugs.

1.2. Reporting Format. Participating Site Investigator will report SAEs using a study specific serious advents reporting form provided by the sponsor.

1.3. Report Information. The SAE report shall include the following information:

- Participant study ID
- Date of SAE form completion
- Description of event
- Reason for seriousness
- Date of event
- Name of hospital/doctor
- Outcome
- Causality of the event to the IMP
- Name of person completing the form.

1.4. Patient Level Data. patient level data, including the following, will also be collected and made available to SPONSOR through the SPONSOR database:

- Height and weight at screening
- Trial relevant medical history
- Latest drug history (drug names only)

1.5. New Information. If new information is added to a prior SAE report, the Participating Site Investigator will forward the updated version of the SAE report to SPONSOR.

1.6. Exclusions from SAE Reporting Requirements. It is not necessary to report SAEs that only require hospitalization or prolonged hospitalization during the chemotherapy courses, because the intensity of the therapy will lead to too many well-known SAEs by this definition (mainly fever and febrile neutropenia), and the chemotherapy is considered standard of care and was similarly applied in the Interfant99 and Interfant06 protocols.

Hospitalization under the following circumstances do not require reporting as SAEs. However, note that some of these satisfy criteria for an AESI and these will need AESI reporting.

a) Planned medical/surgical procedure as per protocol.
b) Routine health assessment requiring admission for health status documentation.
c) Medical/surgical admission for planned purpose prior to entry into study trial.
d) Admission due to other life circumstance that carries no bearing on health status and requires no medical/surgical intervention (i.e. lack of housing, economic inadequacy, care-giver respite, family or administrative circumstances).
e) Routine treatment not associated with any deterioration in condition. (e.g. a blood transfusion)
f) Neutropenic fever.
g) Slow methotrexate elimination without impaired kidney-function.
h) Parenteral nutrition or IV rehydration due to mucositis, in appetence/anorexia or vomiting/diarrhea.
i) AESIs during chemotherapy courses (see section 13.2.2 in the protocol).

Of Note, during blinatumomab courses all SAEs do need to be reported. During blinatumomab courses AESIs are not exempted from expedited reporting according to the rules of SAEs.

1.7. Reporting Period for SAEs. SAEs that are subject to this reporting provision are those that (i) occur from after signing informed consent until 30 days after end of treatment; or (ii) occur any time after the 30 days period if Participating Site Investigator suspects a causal relationship between the Study Drugs and the event. Serious adverse events occurring to a patient after the active reporting period has ended should be reported to the Sponsor if the Investigator becomes aware of them; at a minimum, all serious adverse events that the Investigator believes have at least a reasonable possibility of being related to study drugs are to be reported to the Sponsor.

1.8. Follow-Up Information. NCC / Participating Site / Investigator will assist SPONSOR in investigating any SAE and will provide any follow-up information reasonably requested by SPONSOR.

1.9. Regulatory Reporting. Reporting an SAE to SPONSOR does not relieve Participating Site Investigator of responsibility for reporting it to appropriate regulatory authorities, if such reporting is required.

1.10. SPONSOR-Provided Safety Information. SPONSOR will be responsible for distributing the SUSAR reports to the NCC's, who will distribute these reports to the Participating Sites as appropriate.

1.11. Notifications to SPONSOR. If Participating Site Investigator becomes aware during the conduct of the Study of any of the following information or circumstances relating to the Study Drugs, the Participating Site Investigator will promptly notify SPONSOR:

- Any new information that might influence the evaluation of the risks and benefits of the Study Drugs. Such information may include both positive and negative results from clinical trials or other studies in relation to all indications and populations, whether or not use of the Study Drugs in that indication or population is approved under the relevant marketing authorization.
- The Participating Site Investigator is to provide such notification upon awareness, even if complete information is not yet available

2. Reporting of non-serious Adverse Events

All non-serious AEs will be collected and the following information will be captured in the SPONSOR database:

- Participant ID
- Description of event
- Date of event
- Outcome
- Causality of the event to the IMP

EXHIBIT E: DATA PROTECTION

This Exhibit ("Exhibit") sets forth the General Data Protection Regulation EU 2016/679 ("**GDPR**") roles and requirements that are applicable to Personal Data processed by SPONSOR and Site with respect to the Agreement and the Study. For the purposes of this Exhibit E NCC is herein referred to as "Site".

DATA PROTECTION

1. In this Exhibit the following words and phrases have the following meanings:
   "**CCMO**" means the Dutch clinical trial authority, namely the Central Committee on Research involving Human Subjects (in Dutch: '*Centrale Commissie Mensgebonden Onderzoek*' or '*CCMO*');

   "**GDPR**" means Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation);

   "**ICF**" means the Informed Consent Form as approved by the IRB/IEC, in which the Study subject consents to his participation in the Study, including a consent, as defined in article 4 paragraph 11 of the GDPR, regarding the processing of the Study subject's Personal Data which shall meet the requirements relating thereto of the GDPR;

   "**Personal Data**" means personal data as defined in article 4(1) of the GDPR, i.e. any information relating to an identified or identifiable natural person, e.g. such information of a Study subject;

   "**Personal Data Breach**" means a personal data breach as defined in article 4 paragraph 12 GDPR and further determined by articles 33 and 34 of the GDPR.

2. In line with the current position of the CCMO, the Site and SPONSOR are considered joint controllers for the processing of the Personal Data provided by the Site to SPONSOR for the Study, if such Personal Data is processed and maintained by the Site for purposes of the Study and the Agreement. SPONSOR is the joint data controller together with Amgen (referred to as "Pharma" in the Agreement) for safety data (such as SUSAR reports and other information about SAE's and non-serious AE's) collected from Site and transferred thereof to Pharma, as long as such Personal Data are maintained by SPONSOR for the purposes of the Study and SPONSOR's agreement with Pharma. Parties will both handle all Personal Data in accordance with the GDPR and any other to the performance of the Study applicable laws or regulations covering the protection of Personal Data (collectively "**Data Protection Law**"). Parties will fully cooperate with each other as joint controllers and shall take the necessary measures in order to comply with the Data Protection Law, such cooperation shall duly reflect the respective roles and relationships of the joint controllers vis-à-vis the Study subjects as data subjects, in particular as regards the exercising of the rights of these data subjects and the Parties' respective duties to provide the information referred to in Articles 13 and 14 of the GDPR. Each joint controller shall maintain a record of processing activities

under its responsibility. The Parties respective obligations are described below and in the Joint Controller Matrix added as **Annex P1 (JOINT CONTROLLER MATRIX)** to this Exhibit.

3. In the event law and interpretation by the CCMO and/or a relevant data protection authority or a court decision should prescribe or indicate another qualification of the roles of the parties in clinical trial agreements, the Parties hereto shall consult with each other and shall adapt the qualification of their roles and change arrangements as may be deemed appropriate.

4. The Site shall continue to be an independent controller for the processing of Personal Data of Study subjects as well as of the Site Investigator and the Study Staff processed by the Site for purposes unrelated to the Study or the Agreement.

5. The Parties agree to adhere to the principles of medical confidentiality in relation to Study subjects.

6. SPONSOR shall provide a template ICF to Sites. The Site is responsible for the adequacy of the ICF collection and storage of the ICFs, and for compliance with applicable requirements. The Site will only process Personal Data of a Study subject if such Study subject has signed the ICF. SPONSOR is allowed to share the Personal Data with the parties for which the Study subject has provided its written informed consent.

7. SPONSOR acknowledges that Study subjects – and/or their legal representatives on their behalf – may withdraw, in whole or in part, their initial informed written consent. Site Investigator shall promptly notify SPONSOR of any such withdrawal of the informed written consent of a Study subject, which may affect the use of such Study subject's Personal Data under the Agreement. The Site Investigator will communicate with SPONSOR on behalf of the Study subject. However, the procedure followed upon such withdrawal of a Study subject's consent will be according to the instructions, to the extent laid down in the Protocol and the ICF, and in accordance with the applicable (Data Protection) Law.

8. SPONSOR shall refrain from tracing and/or identifying any Study subject, except where SPONSOR is under a legal obligation to do so. In the event any Study subject, for any other than aforementioned reason, becomes identifiable to SPONSOR, SPONSOR agrees to preserve, at all times, the confidentiality of information pertaining to such Study subjects.

<u>Site Investigator and Study Staff Personal Data</u>

9. Where applicable, SPONSOR shall inform the Site Investigator, and to the extent applicable other Study Staff involved in the Study as well, of the collection, the use and the transfer of his/her/their Personal Data and his/her/their rights in respect of such processing as set forth in articles 13 and 14 GDPR, as well as the essence of the arrangement between the Parties as joint controllers referred to in article 26 paragraph 1 GDPR.

10. The Site agrees to help SPONSOR obtain any express consents, to the extent allowed and/or as may be necessary in accordance with applicable Data Protection Law from the Site Investigator, and to the extent applicable and necessary from other Study Staff involved in the Study as well, for any intended processing of his/her/their Personal Data by SPONSOR.

11. The SPONSOR Privacy Notice is added as **Annex P2 (Princess Máxima Center Privacy Notice)** to this Exhibit. The Site will ensure that the Site Investigator and the involved Study Staff receive a copy of the Princess Máxima Center Privacy Notice.

Annexes:
Annex P1 (JOINT CONTROLLER MATRIX)
Annex P2 (Princess Máxima Center Privacy Notice)

ANNEX P1 JOINT CONTROLLER MATRIX

Princess Máxima Center and Site are joint controllers with regard to the Personal Data that will be processed by virtue of the Agreement. In this context Parties determine and agree on - in accordance with article 26 of the GDPR - their respective obligations with regard to compliance with the GDPR.	
Privacy obligation	**Responsible party and/or arrangements**
1. Provide information on the processing of the Personal Data to data subjects in accordance with article 13, 14 GDPR, The Medical Treatment Contracts Act (WGBO) and article 12 of the Medical Research Involving Human Subjects Act (WMO).	*The ICF will contain all information that should be provided to the Study subjects. If reasonably possible, the Site will publish the ICF, together with the Site's privacy notice on its website.* *In respect of the Personal Data of the Site Investigators and Study Staff, the Site will inform them about the processing of their Personal Data in line with article 9, 11 and 12 and will ensure that the Princess Máxima Center Privacy Notice (Annex P2) is provided to the Site Investigators and the Study Staff.*
2. Safeguarding that informed consent for the processing of the Personal Data is obtained (article 6 GDPR).	*The Site will use a template ICF provided by Princess Máxima Center in order to collect the necessary consents, see article 6*
3. Safeguarding that the data subjects can exercise their right of access, to rectification, erasure, restriction of processing and to object to the processing (articles 15 to 18 and article 21 GDPR). Safeguarding that the data subjects can exercise their right to data portability (article 20 GDPR) in case the relevant Personal Data was obtained under informed consent or for the purposes of the performance of an agreement to which that subject was a party. The rights set out in clauses 15 (access), 16 (rectification), 17 (erasure) and 18 (Restriction) of the GDPR are not applicable in case of research.	*All requests from Study Subjects can be submitted at the Site in accordance with the procedure as laid down in the ICF. The Site will inform Princess Máxima Center about the requests and parties will assist each other where necessary in order to timely address such requests and will discuss which Party will respond to the specific request. If a request is directly submitted to Princess Máxima Center, Princess Máxima Center will contact the Site in order to discuss which Party shall deal with the request.* *With regard to the procedure relating the withdrawal of the informed written consent, Parties refer to article 9.* *Requests from the Site Investigator and the Study Staff are dealt with in accordance with the procedure as described in the Princess Máxima Center Privacy Notice. If such a request is sent to the wrong Party, Parties will forward the request to the correct Party.*
4. Safeguarding the security of the Personal Data in accordance with article 32 GDPR and in accordance with other arrangements in the Agreement.	*Both Parties as long as they process Personal Data related to the Study and/or the Agreement.*
5. Comply with data breach obligations (articles 33 and 34 GDPR).	*If any Party becomes aware of a Personal Data breach in connection with the Study or the performance of the Agreement, that Party shall promptly notify the other Party. Parties will fully*

	cooperate with each other in order to fulfil the (statutory) notification obligations timely.
6. Safeguarding that employees who have access to Personal Data are instructed by a binding agreement or binding instruction(s) in accordance with Article 32 lid 4 GDPR, to process the Personal Data in conformity with the instructions of the Controllers to the Personal Data, including observing the duty of confidentiality with regard to the Personal Data.	*Each Party.*
7. Safeguarding that engaged (sub) processors who have access to Personal Data are instructed by a binding agreement (data processor agreement) to process the Personal Data in accordance with the requirements stated in article 28 of the GDPR, including among others the documented instruction of the Controllers to the Personal Data and all other GDPR requirements applicable to the processor.	*Each Party for the Processors engaged by the respective Party.*
8. Safeguarding that: (1) regular monitoring takes place in order to assess if the processing of the Personal Data by the (sub) processor is in compliance with the data processor agreement entered into with the (sub) processor; and (2) that breach of the data processor agreement is addressed by appropriate measures.	*Each Party for the Processors engaged by the respective Party.*
9. Safeguarding that the transfer of Personal Data takes place in accordance with the transfer requirements of the GDPR.	*Each Party for the data transfers initiated by the respective Party.*
10. Safeguarding the compliance with the requirements regarding retention periods, destruction, return and/or migration of the Personal Data.	*Each Party.*
11. Safeguarding that a Privacy Impact Assessment (PIA) is executed prior to the collection, including obtaining and further processing of the Personal Data (Article 35 AVG).	*Each Party in accordance with the applicable law. If and when necessary, Parties will assist each other.*
12. Cooperation with and audits by the supervisory authorities.	*Each Party agrees to co-operate with any competent supervisory authority and to allow such supervisory authority to audit each Party's compliance with the GDPR.*

ANNEX P2 PRINCESS MÁXIMA CENTER PRIVACY NOTICE

PRIVACY NOTICE
SITE INVESTIGATORS AND STUDY STAFF

As part of your involvement in the study/studies identified above (the "Study"), Princess Máxima Center, an institution organized in accordance with public law of The Netherlands, having an address at Heidelberglaan 25, 3584 CS, Utrecht, the Netherlands will collect information about you and your working relationship with the Site. We refer to such information as "Personal Data." We collect Personal Data from you as well as from other sources and process it for a variety of reasons. This Privacy Notice for Site Investigators and Study Staff ("Notice") describes how your Personal Data will be used, maintained, and shared by Princess Máxima Center (collectively "Processed" or "Processing").

If you fail to or are unwilling to provide your Personal Data for the purposes described in this Notice, you will not be able to be involved in the Study.

The data controller for purposes of this Notice is Princess Máxima Center.

Types of Personal Data Collected and Processed

As part of your involvement in the Study, the following types of Personal Data may be Processed by Princess Máxima Center for Princess Máxima Center's purposes as described in this Notice:

- Information that directly identifies you, such as your name, contact information, and age;
- Information about your training and qualifications, such as your organizational or institutional affiliations, place of employment, educational history, publications and professional experience;
- Information relating to your Study involvement, such as Study participation, quality events, adverse event reports, and Study reports;
- Information about your relationship with Princess Máxima Center, e.g. including financial payments made to you.

Uses and Disclosures of Your Personal Data

Princess Máxima Center will use and disclose your Personal Data when this is necessary for compliance with a legal or regulatory obligation to which we are subject and/or when this is necessary for based on our legitimate interests, as explained in more detail below:

(i) To fulfill regulatory and legal obligations in connection with the Study. This means that Princess Máxima Center may disclose your Personal Data to other parties in order to comply with any applicable regulatory or legal requirements including to ethics committees and institutional review boards, as well as health regulatory authorities throughout the world.

(i) To administer the Study, Study implementation, management, monitoring, related to your participation in the Study. This means that Princess Máxima Center may disclose your Personal Data to partners, authorized representatives, contractors, and service providers.

(ii) To publicly disclose your involvement in the Study, including (if applicable) your association as an investigator, for posting online by Princess Máxima Center or its agents on Princess Máxima Center's website, the European Clinical Trials Database, ClinicalTrials.gov, and similar sites, and in printed materials.

(iii) To conduct background checks, including to verify your credentials, training and licensing and to ensure that we are not precluded from working with you.

(iv) To disclose your relationship with Princess Máxima Center, including any amounts Princess Máxima Center may have paid to you, including reports to government authorities, as required by applicable law.

(v) To other companies with which we collaborate regarding joint development, distribution and/or marketing of particular products or services.

(vi) To identify and, if applicable, engage with you for other research collaboration and professional consulting opportunities based on your professional expertise and opinions.

(vii) To prepare, complete and implement any reorganization, merger, sale, joint venture, transfer or other disposition of all or any portion of our business, assets or stock (including any bankruptcy proceedings).

(viii) To comply with regulatory requirements, judicial proceedings, court orders, government requests or legal process served on us.

(ix) To take legal action or otherwise protect safety, rights or property of our customers, the public and Princess Máxima Center and our affiliates.

If you are an investigator, Princess Máxima Center may contact you to discuss possible future research studies.

Transfer

Your Personal Data may be transferred and stored of in countries other than where you are based, including the United States and other countries located outside of the EU, EEA, and Switzerland. Some non- EU, EEA, and Swiss countries are recognized by the European Commission as providing an adequate level of data protection according to EU standards (the full list of these countries is available on the EU Commission website: https://ec.europa.eu/info/law/law-topic/data-protection/data-transfers-outside-eu/adequacy-protection-personal-data-non-eu-countries_en.

For transfers from the EU to countries that are not recognized by the European Commission to provide an adequate level of data protection, Princess Máxima Center will ensure that such a transfer of Personal Data is in accordance with the applicable laws and regulations, for example

by concluding a model contract drawn up and approved by the European Commission for that purpose.

Your Personal Data Rights

If you have any questions, complaints, or concerns about how Princess Máxima Center processes your Personal Data; if you would like to request access, correction (if you believe the data is incomplete or inaccurate), suppression or deletion of your Personal Data or if you would like to request a copy or the portability of your Personal Data or that we cease using it; please contact Princess Máxima Center at fg@prinsesmaximacentrum.nl. Please note, however, that certain Personal Data may be exempt from such requests pursuant to applicable laws and regulations.

Retention

Your Personal Data may be retained by Princess Máxima Center for so long as is reasonably necessary to ensure Princess Máxima Center's compliance with any legal or regulatory requirements. The criteria used to determine our retention periods include: (i) as long as we have an ongoing relationship with you; (ii) as required by a legal obligation to which we are subject; and (iii) as otherwise necessary for legal purposes (such as in regard of applicable statutes of limitations, litigation, or regulatory investigations).

Data Protection

Princess Máxima Center will take reasonable organizational, technical and administrative measures to protect the confidentiality and security of your Personal Data that are consistent with applicable privacy and data security laws and regulations, including requiring service providers to use appropriate measures to protect the confidentiality and security of Personal Data; however, no data transmission or storage system can be guaranteed to be 100% secure.

Complaints & Data Protection Officer Contact Information

If at any time you have any concerns, complaints or requests regarding Princess Máxima Center's use of your Personal Data, please contact our Data Protection Officer at: FG@prinsesmaximacentrum.nl.

You may also file a complaint with a Data Protection Authority for your country or region or in the place of the alleged mishandling of your Personal Data.