Karolinska Comprehensive Cancer Center

Information Letter – Phase 1 Unit Solna,

Karolinska University Hospital

Dear Sponsor and Partner,

We would like to provide you with practical information about how the Phase 1 Unit at Karolinska University Hospital, Solna, operates. This overview is intended to facilitate a smooth and fast study start-up, efficient communication, and mutual understanding between our site and your organization.

> 📌 Please make sure you have familiarized yourself and relevant staff members with the Code of Conduct. This is a thorough guidance on how clinical trials are managed at our site and a mutual agreement between Lif (Swedish pharma organization), ASCRO (Swedish CRO organization) and NASTRO (network for all Oncology Clinical Trial Units at the University Hospitals in Sweden) Nastro | Code of Conduct
>
> 📌 We do not allocate formal resources to the study before it has passed through the Research Council Review, please see further details under section 1.
>
> 📌 Please also pay close attention to the different addresses to be used (section 12 of this document). This causes challenges at our site if not adhered to.
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> 📌 Confidentiality Disclosure Form is not required between our site and the sponsor as the public healthcare sector is covered by OSL (the Swedish Public Access to Information and Secrecy Act), providing an equivalent level of confidentiality, please see the Code of Conduct for further information.

Our site is inspected by Swedish Medical Product Agency every third year to keep a preapproval for First in Human trials and we conduct early clinical trials in various cancer diagnosis and types of therapy fields also including nuclear medicine, medtech as well as cell and gene-therapy at a JACIE certified department.

1. Research Council Review

All studies involving patients from Theme Cancer must be presented and reviewed at the Theme Cancer Research Council, which meets every Friday. Sponsor will be informed immediately after the meeting about the decision. Each meeting accommodates up to four study presentations. The Principal Investigator (PI) presents the study. Sponsors may provide 3–4 PowerPoint slides to support the presentation. External representatives cannot attend. For meeting details, please visit the Theme Cancer Research Council webpage: Forskningsråd Tema Cancer

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2. CTIS Application and Pre-meeting Documents

To secure an efficient start-up phase, the following documents **can be collected** to facilitate the CTIS application **before the Research Council meeting**:

- **PI's CV (in Swedish)**, already available at site at request
- **Site Suitability Statement (in Swedish)**, please prefill information about the specific trial. Site will fill in other information
- **Declaration of Interest (in Swedish)**

All forms for the national part of CTIS-application are available at Swedish Medical Products Agency webpage: Apply for a clinical trial | Swedish Medical Products Agency

We would also like to have a look at the Participant Information before submission and would like to get information regarding RFIs so that we can be of help during the process.

OMS-number for CTIS submission (Karolinska University Hospital Solna):

Karolinska University Hospital
Eugeniavägen 3, 171 64 Solna
ORG-number: ORG-100 000 573
LOCATION-number: LOC-100 031 783

3. Study Start-up

A Study Coordinator is assigned to your study when it has passed the Research Council Review and thereafter study specific activities can commence.

We need to have the most updated timelines available to provide the necessary resources and the best planning for study execution.

Please provide planned dates for Submission to CTIS, planned approval dates, planned dates for Site Initiation Visit and any other important milestones, like planned time for inclusion. Please note that it is very important to communicate any changes to planned dates. We do understand the complexity, and it can be difficult to set confirmed dates, but please communicate any changes as soon as they are available.

Please provide the following documents to the Study Coordinator (even if they are in draft) for us to speed up our internal processes to be ready to start at the agreed timelines. Please make sure to send updated documents as soon as they become available.

- Protocol
- Patient information sheets
- Biobank submission
- Lab/imaging manuals
- Pharmacy manual including information on what Pharmacy will be used in the study

- Study title (if there is a working title for the study, we need information about it, so we can use the same name for our internal processes)
- Site number
- Applications and approvals as soon as they become available, as we need these electronic for our internal processes
- Clearly mark all emails with the study name/protocol number so that it is clear which is being referred to
- At a later stage, login details for any e-training courses and other systems will also be required

We need to have a clear view on the contact persons from your side. Please provide name, title, contact details and role in the study.

4. Collection of Documents

The following documents can be collected before Site Initiation Visit, if deemed necessary: CV, GCP certificate and Financial Disclosure Form for PI (and one Sub-Investigator if deemed necessary from sponsor.)
CV and GCP certificate for Study Coordinator.
Remaining documents will be collected at the Site Initiation Visit when the complete study-team is selected.

5. Study Contract and Budget

The management of all Contract and Budgets are under the responsibility of the Head of Phase 1 Unit. Contact details: Caroline Brav: caroline.brav@regionstockholm.se

The allocated Study Coordinator needs to initiate the start-up process and understand the study execution before the budget negotiation can start.

If the sponsor has a Master Service Agreement in place with Karolinska University Hospital this should be used, and no separate Clinical Trial Agreement is required, only project agreement/study letter/study contract. The Lif-agreement templates (Ladda ned rapporter, avtal och mallar) will be added to the final document before signature process is initiated. (**Please note for CROs to check if the sponsor has a Master Service Agreement in place.**)

If Master Service Agreement is not in place the following process applies:

All Clinical Trial Agreements are reviewed by the legal department at Karolinska. Data Transfer Agreement must be attached, and Standard Clauses are added if needed.

We need the following documents to start the negotiation process:

- Clinical Trial Agreement
- Protocol
- Patient information
- Study manuals, e.g. lab, radiology, pharmacy etc
- Budget in an excel sheet with per visit specification

Karolinska University Hospital are working with official price lists for clinical trials. Please find them here: Forskningsprislistor

All study agreements are signed by the respective Head of the Department and the Head of Theme Cancer. Principal Investigator signs the contract as "read and acknowledged" only.

Medical Unit that is the "site" in the study and the **counterpart of the study agreement**:

Karolinska University Hospital, Theme Cancer, Centre for Clinical Cancer Studies (CKC), Eugeniavägen 3, 171 64 Solna, Sweden

6. Internal Agreements

We will establish Internal agreements and coordinate necessary planning, meetings with other units at Karolinska such as; Radiology, Pathology, Laboratory Medicine, Eye clinic, MR/Imaging units, and other hospital departments involved in study procedures. Please ensure all study-related requirements are clearly communicated early to avoid delays.

If central imaging reading is needed, sponsor needs to reach out to:
rtg.klinprov.karolinska@regionstockholm.se after site have made initial contact for the specific trial.

7. Local Laboratory and Biobank Applications

The address to the local laboratory is:
Karolinska Universitetslaboratoriet, Karolinska Universitetssjukhuset, SE 171 76 Stockholm

This is the accreditation information: SWEDAC SS-EN ISO 15189, GLP, CLIA, CAP, ISO
If the accreditation certificate is needed, please find it here: Kvalitetsarbete och ackreditering
Local Laboratory Reference Ranges can be found at the hospital web page: Provtagningsanvisningar A-Ö

The application to the Biobank is the sponsor's responsibility and should be applied in parallel with the CTIS application.
For information on the Biobank, please see A national infrastructure for biobanking – Biobank Sverige
We would like to review the application form before submission.

Stockholm Medical Biobank ID is: 914. If you need contact with the Pathology unit before the submission, please contact: mdk.studiestod.patologi.karolinska@regionstockholm.se

8. Investigational Medicinal Product (IMP) and Pharmacy Agreement

The Pharmacy agreement is the sponsor's responsibility. Please note that a separate Pharmacy agreement is mandatory in Sweden. Please start the agreement process with the Pharmacy early in the start-up phase as the agreement needs to be in place before the Site Initiation Visit. We need the information on what IMPs are provided by the sponsor.

Medovia handles, stores and prepares study drugs and can also handle investigational drugs that do not require preparation (e.g. tablets or similar). For IMP that does not require preparation, agreement can be made with other Pharmacies/Vendors as applicable per Swedish regulation.

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For all IMP that needs preparation, agreement with Medovia at Karolinska is mandatory. Please contact Medovia at kpavtal.stockholm@medovia.se

IMP tablets are ordered via requisition to the relevant pharmacy. We can store smaller quantities of IMP in our IMP medicine cabinet at our treatment unit, B8:09. If the sponsor enters into an agreement with Medovia for IMP tablets, we prefer that the IMP is stored at Medovia and that we collect per patient and visit.

IMP as Chemotherapy and similar (for intravenous, subcutaneous, intratumoural distribution) is prescribed and required through our internal system CytoDos. Our responsible Chief Medical Officer is responsible to enter applicable IMP information according to the study protocol in CytoDos.

Address to Medovia:
Medovia Clinical Trial Unit
Karolinska University Hospital
Eugeniavägen 23, C3:27
SE-171 64 Solna
SWEDEN

Internal address for delivery to Phase 1 Unit (only for Pharmacy distribution to site-please add in the Pharmacy Agreement):

Fas 1-enheten Solna, E8:59
Karolinska Solna

General information: Please make sure to confirm with the Study Coordinator the IMP management for the study and any study specific procedures. This should be done in parallel with the Pharmacy Agreement and before the Site Initiation Visit. Please provide us a copy of the finalized pharmacy agreement. You will receive information on who will have the right to order IMP from the Pharmacy during the Site Initiation Visit.

Infusions with chemo, antibodies and immunotherapy are administered by a research nurse at the Phase 1 Unit. IMP tablets are distributed by a research nurse.

If IMP handling requires a specially adapted room or other specially trained personnel, this is discussed during the start-up phase, for example for radioactive agents or cell/gene therapy and GMO/GMM.

9. Equipment and Calibration

If no sponsor equipment is provided, hospital equipment is used. All devices are calibrated regularly per our internal process by the MedTech department at Karolinska University Hospital. All individual equipment is labelled with the latest calibration date. Height meters are not calibrated. Additional documents related to the calibration can be provided upon request. All our freezers, refrigerators and cabinets are temperature controlled, alarmed and monitored via OpenLogger. This is our internal electronic system with measurement every minute. Documentation on the temperature for a given period can be provided upon request. In the event of deviations, persons on the alarm list are alerted around the clock. Backup equipment is available.

In addition, sponsor-provided electronic equipment to be used in patient care must be listed in the Site Equipment Log and undergo technical approval by the MedTech department before use. Calibration certificates and maintenance documentation must accompany any sponsor devices. Any equipment requiring special installation or temperature/environmental stability must be coordinated in advance with the Study Coordinator.

10. Site Initiation Visit (SIV)

We would like to get the Investigator Site File (ISF) and all other study specific material and documents including lab kits and waybills **approximately 2-3 weeks before the Site Initiation Visit**. The ISF will be stored at Fas 1-enheten Solna, Hotellet plan 3 during the study.

Please make sure to send to the correct addresses, see section 12.

We would ask to get all study documentation sent to us both electronically and per mail with clear filing instructions. Please address documents to Study Coordinator. Study Coordinator will arrange with PI signature as needed.

Please plan and schedule for SIV well in advance so that the SIV can be held as soon as the following are in place:

- Regulatory approval available
- Biobank approval available
- Signed CTA and budget approval
- Signed Pharmacy Agreement
- System training and accesses provided

Preferred time for Site Initiation Visit with ALL participants should be between 12:00–13:00 a clock to avoid too much interruption for the staff. PI may also suggest other times that suit the organisation. For the lunch meeting will staff from the Phase 1 team participate and possible other stakeholders for example from radiology, pathology department. This time should be devoted to the most important parts of the study. Please consider that the PI can devote additional 1-2 hours and the Study Coordinator 3 hours during the day.

It is the Study Coordinator responsibility to invite to the SIV so that room and connection is secured and to invite staff at Karolinska University Hospital. Sponsor can forward the invitation within the sponsors organization.

At SIV, we have the opportunity to collect outstanding signatures from the study team, and you as the sponsor have access to copy them. Please bring the confidentiality agreement so that it can be signed and ready for the first monitoring visit.

11. Monitoring, access to medical records and confidentiality

Please make sure that the confidentiality agreement for access to medical records is provided to Phase 1 Unit for signature by the Head of Department **at least one week in advance of the first monitoring visit.** No access to patient medical records can be given without the

confidentiality agreement in place. Please find a template for the confidentiality agreement: Mallar för kliniska prövningar - Apotekarsocieteten

Our electronic medical record system is called **Take Care**. Due to system design and Swedish data protection regulations, individual monitor access cannot be granted. Therefore, the Study Coordinator will print the relevant source documentation for each monitoring visit. Please ensure that required source data verification is performed during the on-site visit, as remote access is not possible.

We ask you to make sure that all necessary copying and access to data are made during the on-site visit to prevent unnecessary scanning of documents between visits.

12. Addresses

Address for study documentation:
Karolinska University Hospital
Att: Name of PI and Study Coordinator
Fas 1-enheten Solna
Hotellet plan 3
171 76 Stockholm
SWEDEN

Address for lab kits and lab supply:
Karolinska University Hospital
Att: Name of PI and Study Coordinator
Fas 1-enheten Solna B8:09
Eugeniavägen 11, plan 8
171 76 Stockholm
SWEDEN

Collection of lab samples and Dry Ice (address on the requisition forms):
Karolinska University Hospital
Att: Name of PI and Study Coordinator
Fas 1-enhten Solna B8:09
Eugeniavägen 11, plan 8
171 76 Stockholm
SWEDEN

Delivery of Investigational Medicinal Product to site from external Pharmacy (but if to Medovia, see section 8)**:**
Karolinska University Hospital
Att: Name of PI and Study Coordinator
Fas 1-enheten Solna B8:09

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Eugeniavägen 11, plan 8
171 76 Stockholm
SWEDEN

We look forward to collaborating with you and your team, ensuring high-quality, efficient clinical trial conduct at Karolinska University Hospital.

Warm regards,

Caroline Brav

Caroline.brav@regionstockholm.se
Head of Phase 1 Unit Solna
Karolinska University Hospital