Specific Guidelines for PIPELINE

CALL PIPELINE:
PharmaceutIcal Product dEveLopment from INnovativE academic research

Version 1, September 2023

Why academic pharmaceutical product development?

Treatment options remain unsatisfactory for many cancer types. Those patients that do not respond to current standard treatments face poor prognosis and suffer from severe side effects. The development of new, innovative pharmaceuticals that target unmet medical needs is needed to improve more patients' lives.

Rapid academic advancements in understanding molecular pathways and functioning of biological systems form the basis for the development of new pharmaceuticals (defined here as originator products manufactured for use as a medical product). Discoveries in the immuno-oncology field led to recent new breakthrough therapies such as checkpoint inhibitors and CAR-T cell therapy. New pharmaceuticals are typically brought to the market by industry after academic discovery. However, not all discoveries and innovations that target unmet medical needs are picked up by industry for clinical development because of market failure; products are considered non-commercially viable or too 'high-risk'. Innovations may be considered non-commercially viable by industry due to the rarity of the targeted disease or affected patient group, a highly personalized medicine approach, or weak Intellectual Property (IP) position. Complex production processes in a point-of-care setting may not fit well in the traditional pharmaceutical model of large-scale production and distribution. Venture capital and other private parties may hesitate to invest in innovations that are considered high-risk due to uncertainties.

When new pharmaceuticals are not, or not yet, commercially viable or interesting, academics are challenged to take on development themselves. However, the academic route for pharmaceutical product development has not fully matured. This ecosystem in which academic developers need to operate to develop new pharmaceuticals is full of bottlenecks. Ecosystem failures include social and operational reasons for early termination of product development, such as insufficient collaboration and a lack of resources. Furthermore, clinical trial conduct needs to be supported by strong business cases and regulatory strategies in order to reach marketing authorization and access in clinical practice. Academics face a wide range of bottlenecks along this development trajectory if they aim to reach clinical practice themselves. Efforts to transfer promising innovations to a commercial route through spin-offs, out-licensing or public-private collaboration may fail due to flaws in product design, regulatory strategy or business case, among others.

When market- or ecosystem failure arises for new academic innovations, academic efforts are needed to complete development trajectories and reach patients in need. Therefore, the Dutch Cancer Society (KWF) is organizing the call 'PIPELINE' to accelerate the development of academic innovations into new pharmaceuticals.

Aim

The PIPELINE call aims at the clinical development of new pharmaceuticals that originate from academic research and have the potential to substantially improve the treatment for cancer patients with unmet medical needs. Any type of pharmaceutical that is regulated as a medical product in the European Union is eligible.

Ambition

KWF sees an important role for academia in the development of new pharmaceuticals from academic research, when a commercial route is not, or not yet, viable. We aim to alleviate bottlenecks that academics face in pharmaceutical development by providing financial support, but also regulatory and business development support. KWF aims to anchor PIPELINE as a recurring call.

KWF collaborates with the Centre for Drug Development (CDD) in the United Kingdom, a charity-funded pharmaceutical development facility that is part of Cancer Research UK (CRUK). This collaboration is set up to alleviate bottlenecks and enable early clinical development for those academics that do not desire or cannot initiate trials themselves. However, if you apply to the call, engaging with the CDD is not mandatory. More information on the submission procedure and collaboration with the CDD is provided below.

We envision proposals on clinical trials that are supported by interdisciplinary teams (researchers, pharmacists, healthcare professionals), possibly in collaboration with centres in Europe, industry and/or service providers. Academics can aim to reach clinical practice with their innovations themselves. Other innovations could be de-risked for transfer to industry through the generation of clinical data. Public-private partnerships are another route for product development in this call.

Requirements and guidance

Project and applicants

Requirements		Guidance
Research type	Research project or consortia	- Projects that consist of 1 - 3 participating parties (research project) or 4 or more participating parties (consortia). - Project duration is between 4 and 8 years. - For consortia a project manager is mandatory.
Research phase	Clinical trials ranging from phase I to III.	- For the KWF route, phase I to III are eligible. For the CDD route, only phase I or I/II trials are eligible. - Confirmatory and/or 'pivotal' trials may be considered if they fit within the indicative budget. - The development and validation of GMP manufacturing can be part of a proposal for clinical trial conduct, if the duration from start of the project to start of patient inclusion does not exceed 2

		years and the total duration of the project does not exceed 6 years.
Trial design	Interventional, prospective, using the best-fitting trial design.	Best-fitting design for the trial phase, including single-arm and controlled designs. Consider regulatory requirements, and possibly HTA requirements and PASKWIL criteria for your design. Designs that make use of validated surrogate endpoints and real world data (for example as control arm) may be considered if these adhere to requirements and criteria mentioned above. Design should include the best suitable and most representative study population, with respect to the studied disease or patient subgroup.
Main applicant	Medical centre or research institute that must be located in the Netherlands.	Main applicants as well as public participating parties should fall within the following categories: Academic research groups (from universities or other higher education or research institutions); or Clinical/public health sector research groups (from hospitals/public health and/or other health care settings and health organizations).
Public participating parties	Medical centre or research institute that must be located in Europe.	A public participating party carries substantive and financial responsibility for a part of the project, the dissemination and/or exploitation of the results. A foreign participating party can perform parts of the work plan, when the project leader deems this necessary.
External inclusion centres	Medical centre or research institute that must be located in Europe.	- Centre outside the lead institute or participating organization(s) that only includes patients for clinical studies and has no active research role in the project. This centre has no right to the project results. An exception to this can be that an external inclusion centre retains the right on its own generated data, information, samples, knowledge and inventions. - External inclusion centres are not considered participating parties. A quotation for their services is obligatory.
Private participating parties	For-profit or industrial partners.	- Private participating parties are accepted if needed for the execution of the project, and as long as co-funding (in cash and/or in kind, see below 'Additional conditions') as well as appropriate agreements on intellectual property and fair pricing are in place (for full proposal). - Private participating parties cannot be the main applicant. - Both small- and medium enterprises and large industrial partners can

		participate in the project, yet the minimum required co-funding differs (see additional conditions).
Service providers	Department or organisation that provides a necessary service for the work plan.	- Internal service providers are departments of the lead institute or a participating organization that provides a necessary service for the work plan, such as data management or specific analyses. - External service providers are public or private organizations that provide a necessary service for the work plan, such as contract manufacturers, trial bureaus, and consultancy agencies. - Both internal and external service providers do not benefit from the project results and have no right to the project results. A quotation for their services is obligatory.
Patient participation	It is required to actively involve patients in the set up and execution of the trial.	Involvement of patients in the set up and execution of the trial is required. This may include, but not limited to, one or more of the following: letter of support from a patient organization, patient review of the Informed Consent Form, patient input on the protocol, dissemination of results to patients (including study participants), patient participation in steering committee.

Product

Requirements		**Guidance**
Intervention	New investigational pharmaceuticals (e.g. new chemical/biological entity, originator products)	Investigational pharmaceuticals intended to be used for treatment in humans (including but not limited to monotherapy, treatments in combination with standard treatment, (neo)adjuvant therapy, add-on therapy). These need to be new, originator products, meaning they have never been registered in any market before.
Product type	All types of experimental pharmaceuticals that fall under the EU definition of medicinal product (small molecules, biologicals, advanced therapy medicinal products).	Products are required to fall under the definition of medicinal product in the EU pharmaceutical legislation[1]. If it is unclear whether the product is a medicinal product, it may not be eligible.

[1] Article 1 of Directive 2001/83/EC.

Target Product Profile	A (preliminary) Target Product Profile (TPP) is mandatory.	- Key elements of a TPP are requested for the pre-application. - A (preliminary) TPP is mandatory for the pre- and full proposal.
Indication	All cancer types, including rare- and paediatric cancers	- All cancer types can be targeted, including paediatric, orphan, and non-orphan cancer types. - The target patient population (currently or in the future) needs to be specified. - Patient stratification or inclusion for therapeutic intervention(s) based on defined biomarkers or targets, as part of an interventional trial with relevant endpoints is allowed.
Scientific rationale	(Pre)clinical research supports expected safety and/or efficacy outcomes.	- For the pre-application, please provide high level findings from most relevant preclinical pharmacology/pharmacokinetics/ toxicology and clinical data. - For the pre- and full proposal, detailed outcomes that support expected safety and efficacy outcomes are mandatory.
Added value	Product development addressing unmet medical needs, with added value to the patient with respect to clinical safety and/or efficacy compared to current standard treatment.	- Unmet medical need is defined as addressing a life threatening or severely debilitating disease, which is associated with a remaining high morbidity or mortality under current standard treatment. - Added value to the patient is defined as: 1) a significant reduction in severe side effects, and/or 2) a meaningful expected reduction in disease morbidity or mortality for the relevant patient population as a result of treatment with the experimental product, in comparison to current standard treatment. The threshold for 'meaningful' has been defined in the PASKWIL criteria. - Unmet medical need and added value to the patient need to be substantiated with argumentation of prognosis and (expected) clinical outcomes.
Development plan	Clear development trajectory with supporting regulatory strategy and business development.	- The planned development trajectory needs to extend to the end goal; to reach the patient in clinical practice. - It is not mandatory to have a regulatory strategy or business development plan for the pre-application, yet previous or planned regulatory and/or business development activities are preferred

		(this is part of the selection criteria for pre-applications, see section 'pre-application' below). - The development plan needs to include a regulatory strategy and business development plan for the full proposal.

Out of scope

- Repurposing of registered pharmaceuticals for new indications.
- Combination therapy of registered pharmaceuticals only.
- Preclinical research cannot be part of the project.
- Private parties as a main applicant, or industry sponsored trials.
- (Early) diagnosis of (recurrent) disease and/or monitoring during therapeutic interventions and/or patient stratification for therapeutic interventions, without interventional and pharmaceutical development set-up (e.g., observational research).
- Investigational products with no or limited freedom to operate.

Additional conditions

If the for-profit private partner has an active role within the project, this party is considered a participating party and to this end must make a financial contribution: this is minimum 20% co-financing of the KWF requested budget (in cash and/or in kind). For partners with >250 FTE, co-financing must be at least 50% in cash. For small- and medium-sized enterprises (SME's) co-financing in cash is not mandatory, it may be contributed entirely in kind.

If the for-profit partner is involved on a fee-for-service basis, a contribution is not applicable. They are considered a service provider (see section on requirements).

Pre-application

The call starts with a pre-application. It must be written in English and submitted by the main applicant by sending a pre-application form to pharmaceuticals@kwf.nl in a PDF file. The form must be signed by the project leader. KWF will evaluate whether the pre-application is eligible for the call and fits the ambition of the call. Upon favourable decision, the main applicant will receive an invitation to submit a pre-proposal.

The selection procedure starts with an eligibility check. Pre-applications need to adhere to the requirements and scope of the call (see above). Eligible pre-applications are subsequently scored to which extent they fit the ambition of the call. There are four criteria used to rank eligible pre-applicants; 1) addressing unmet medical need, 2) expected added value to the patient compared to current standard treatment, 3) status of manufacturing, and 4) (proposed) development plan steps.

Collaboration with Centre for Drug Development

KWF collaborates with the CDD for phase I or I/II trials in the PIPELINE call. Applicants can indicate whether they prefer the CDD to be involved in their product development in the pre-application form. CDD involvement is not mandatory and selected preferences do not affect the pre-application selection procedure. The selected applicants can decide whether

to share their pre-proposal with the CDD in the next stage of the submission procedure, in dialogue with KWF.

KWF collaborates with the CDD to enable pharmaceutical product development that originates from academic research, which the academic party cannot or do not desire to undertake themselves. The CDD is a charity-funded drug development facility with preclinical and medical sciences, regulatory affairs, quality assurance, project management, legal, drug safety, clinical operations and data management capabilities. These capabilities are used to coordinate and monitor phase I or I/II conduct trials for promising new pharmaceuticals.

After early clinical research is completed, the CDD aims to license successful products out to the pharmaceutical industry for further development and market authorisation, under strict socially responsible terms. The CDD uses a case-by-case approach how to license out in order to reach patient access. Throughout this process, there is ample room for dialogue between the academic party and the CDD. KWF aims to enable product development via a semi-commercial route with the CDD-KWF collaboration, while stimulating socially responsible terms.

Projects that are granted in collaboration with the CDD will be funded under separate terms and conditions. More details regarding the collaboration with the CDD and relevant terms and conditions will be shared here in the next stage of the submission procedure.

Submission procedure

After the pre-application phase has ended, the submission procedure continues with a pre-proposal stage. Pre-proposals can be submitted by invitation only.

There are two routes for evaluation of submitted pre-proposals. Based on the approval of the main applicant, a selection of pre-proposals is sent to the CDD in het UK. The CDD will evaluate the pre-proposals on novelty of product and/or target, unmet medical need and feasibility of project. Those that are selected by the CDD are offered the possibility to collaborate with the CDD for development of their product and will not be part of the KWF evaluation procedure anymore. This is the CDD route (Figure 1). After the CDD evaluation is finalized, a KWF evaluation procedure starts to select projects for the full-proposal phase for the remaining pre-proposals (including projects not evaluated or rejected by the CDD). This is the KWF route (Figure 1). Applicants can choose to participate in the CDD or KWF route when the pre-proposal phase opens. KWF will only share pre-proposals with the CDD upon approval of the main applicant.

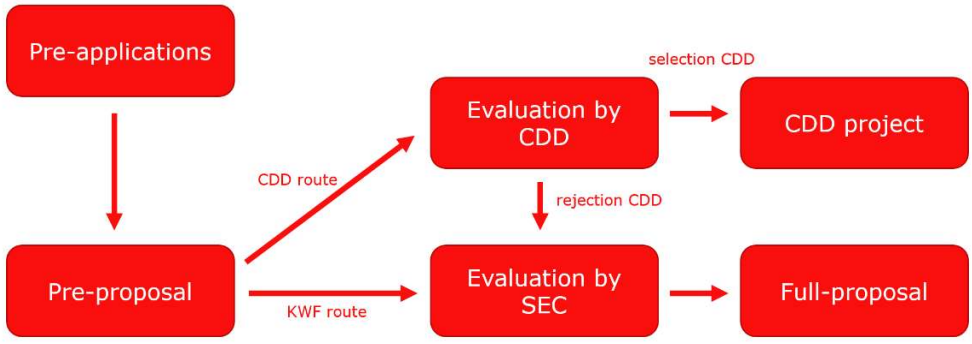

Figure 1: Evaluation routes (CDD and KWF). CDD = Centre for Drug Development, SEC = Scientific Evaluation Committee

The pre-proposals that are not selected by the CDD (due to too many applications for the capacity within the KWF/CDD collaboration, or products that fit better in an academic development route for example), are evaluated by the Scientific Evaluation Committee (SEC) with pharmaceutical development expertise. If a CDD evaluation is available it will be shared with the SEC. Pre-proposals are evaluated on excellence, developmental potential and patient impact potential. The best pre-proposals are selected for the full-proposal phase. The full-proposals are evaluated by the Scientific Evaluation Committee and Patient Advocacy Board on excellence, developmental potential and patient impact potential.

Both pre- and full proposals must be written in English and submitted exclusively by the main applicant through the electronic submission system (Grant Management System).

Timelines

Pre-applications opens:	September 19, 2023
Pre-applications closes:	November 30, 2023
Pre-proposal opens:	January 2024*
Pre-proposal closes:	March 2024*
Full-proposal opens:	June 2024*
Full-proposal closes:	September 2024*
Funding decision:	December 2024*

*Indicative timeline – subject to change.

Indicative budget:

The indicative total budget is 5 - 8 million euro. The budget indication per proposal is 1 – 4 million euro.