ZonMw-LSH 2Treat public-private partnership

LSH Roadmaps Regenerative Medicine, Molecular Diagnostics, Pharmacotherapy

Call for proposals

1. Programme ZonMw-LSH 2Treat public-private partnership

Deadline compulsory pre-proposal: 15 May 2014
Deadline final proposal: 2 September 2014
Keywords: top sector LSH, roadmaps, public-private partnership, health funds, SME, research organisations, translational research, www.lshplaza.nl, co-funding
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2. Aims and background

2.1 Background to programme

In the top sector Life Sciences & Health the route from idea to innovation is a long one. Due to the high costs and risks of the pre-clinical and early clinical phases new high-potential treatment methods do not sufficiently reach everyday practice. The funding within the programme 2Treat focuses on the phase in which the fundamental concepts of a new method, treatment or product are known, but where research is still needed before the first tests and use in humans can be performed. Examples are pre-clinical and clinical research in which the safety and efficacy of the method, product or treatment take centre stage and the research is aimed at validating and further developing products and new treatments/ combinations of treatments. In addition, the programme offers opportunities for early clinical research with new products or treatments/combinations of treatments.

Through the 2Treat programme public-private partnerships between businesses and research institutes will realise translational and/or early clinical research on a clearly described product. Proposals that are purely fundamental in nature do not fall within the research domain of the call. The 2Treat programme is therefore mainly focussed on a combination of fundamental and industrial research, with possibly a limited amount of experimental development.[1]

1 For the definition of these terms see the 'Note State Aid Rules' (*Toelichting Staatssteunregels*) under Section 5.1 Downloads.

In this call, health funds[2] are especially invited to invest together with knowledge institutions and SMEs and other companies (including health insurers) in bringing knowledge from scientific research to the clinic and the market.

ZonMw is realising this programme in collaboration with the top sector LSH. For background information you are explicitly referred to the websites of www.zonmw.nl and www.lshplaza.nl and the Innovation Contract Top Sector LSH (available under Section 5.1 Downloads).

2.2 Aims of the call

- Facilitating translational and/or early clinical research with a clearly described product or service
- Encouraging public-private partnerships between research organisations and private parties
- Addressing cost management in care
- Contributing to the three main goals from the ambition of the top sector LSH:
    - Maintain health, prevent health care
    - Maximize effect, minimize trauma
    - Manage disease extramurally

2.3 Research domain of the call

The call focuses on the subareas of the roadmaps Regenerative Medicine, Pharmacotherapy and Molecular Diagnostics in the Innovation Contract 2012 of the top sector LSH, namely:

A. Regenerative Medicine: Strategic Research
   Projects should aim for a phase I/IIa clinical trial within 1-5 years after the project is granted. The goal of the project should minimally be admission of a trial proposal at the CCMO or "METC".
   - *Area: Development of (biomaterials based) off-the-shelf technologies for in situ tissue regeneration and repair*
     - Establish patient stratification methodologies to predict the outcome of regenerative therapies.
     - Integration of genetic modification, imaging, stem cell and biomaterial manufacturing technologies to produce patient specific bioactive implants for tissues like bone, cartilage, heart valves, muscle, lung, intestine, and gastro-intestinal tract organs.
     - Development and evaluation of materials or material coatings for the controlled spatial and temporal delivery of cells, genes, pharmacological agents and/or bioactive molecules to affect biological functions, such as cell growth, inflammation and the immune response, and prevent biomaterial-associated infection.

B. Combination of the roadmaps Pharmacotherapy & Molecular Diagnostics
   - *Area: Companion diagnostics in rheumatoid arthritis (RA)*
     Development of diagnostic and stratifying tools to identify (subpopulations) of patients with very early, early, and established RA (VERA, ERA, and ESRA) with different characteristics of progression of the disease and different responses to treatment modalities. Currently, a rapidly-growing share of patients is continuously treated with highly effective and expensive biological disease-modifying drugs such as TNF inhibitors, interleukin inhibitors and B-cell modulators (rituximab). However, clinical experience shows that the targeted therapies with biologics are effective for approximately 50% of the RA patients treated, reflecting that there are responders and non-responders.

2 Health funds are so-called ANBI institutions and in this call - in line with the TKI regulation - are not considered to be companies but instead private parties insofar as the fund does not receive government funding.

The call invites consortia to develop and validate diagnostic tools to triage for responders and non-responders for one or more of these current (and potentially future) pharmacotherapies.

- *Area: Biomarkers for combination therapy in leukemia*
  It is increasingly obvious that heterogenicity of tumour characteristics exists between patients and even within patients. It seems feasible and cost effective to use this heterogenicity to target therapies to specific patient groups, thereby limiting treatment of non-responders and reducing side effects. By using combinations of therapies, a further increase in therapy effectiveness may be achieved. Combination therapy includes for instance treatment with drugs with different mechanisms of action, application of experimental and standard of care treatments or combination with previously failing clinical candidates.
  - Development and validation of biomarkers and companion diagnostics for treatment of leukemia using combination therapy.
  - Development of assays to test efficacy of combination of drugs for specific patients and specific leukemias. This may include methods to culture fresh primary tumour cells or tumour tissue slices to avoid effects of additional (arising in vitro) mutations.
  - Innovative clinical trial design for combination and/or innovative therapies and the monitoring of treatments with respect to effectiveness and the development of drug resistance. The use of new strategies and tools for the clinical development such as adaptive trial design are expected to increase its efficiency and to foster the approval of more targeted and safe therapies.

3. Limiting conditions

The admissibility of your proposal will be checked according to the limiting conditions described below.

3.1 Conditions for the project

The project proposal must satisfy the following conditions:

- ✓ The pre-proposal must be submitted no later than 15 May 2014 at 15.00 hours. Without a pre-proposal no final proposal may be submitted.
- ✓ The final project proposal must be submitted no later than 2 September 2014 at 15.00 hours.
- ✓ The pre-proposal and final proposal should be written in English.
- ✓ The research addresses one of the subjects stated under Section 2.3 of this call.
- ✓ The research is realised in a public-private partnership by a consortium with an optimum combination of expertise in which at least one or more companies (preferably including a health insurer), at least one or more research organisations, and preferably also a health fund participate.
- ✓ The partnership project is realised with all parties contributing to the costs and sharing the risks.
- ✓ The project proposal contains work packages aimed at bringing a clearly described service or product into the clinic, with tangible deliverables that are delivered after each phase and a realistic timetable.
- ✓ Each project has co-funding: besides the ZonMw contribution there is a compulsory matching of at least 50%. This contribution can come from research organisations and companies (including health insurers) but also from other private parties such as health funds.

- ✓ The duration of the proposed project must be at least two years and at most five years.
- ✓ If a project is awarded funding then a user committee will be appointed by ZonMw that will advise the consortium of public-private partnership partners and ZonMw, especially regarding application aspects. The primary objective of this user committee is to provide translational expertise for the project (for example, with respect to regulations, knowledge from pharmacies, expertise from patients and care providers). Throughout the course of the project the user committee will regularly meet with the project group.
- ✓ If a public or private party from outside of the Netherlands participates then ZonMw will not be able to make any grant funding available to this party for work performed outside of the Netherlands.

3.2 Intellectual Property Policy

Agreements must be made about the intellectual property arising from the knowledge acquired and products developed during the project. These agreements are recorded in the consortium agreement. One of the possibilities is a 'right of first refusal'.

Intellectual property agreements should be made in accordance with the Research, Development and Innovation State Aid Framework (specifically Article 3.3.2) and the TKI allowance regulation (Government Gazette 5 November 2013) to ensure that:

- Results from a partnership project to which no intellectual property rights can be granted may be widely disseminated and possible intellectual property rights that arise from the activities of the research organisation(s) may be fully awarded to the research organisation(s); or
- if they wish to appropriate the IP, the participating companies and/or health funds pay the research organisation(s) a remuneration in line with the market price for the intellectual property rights that emerge from the partnership project and these are then transferred to the participating private party/parties. Possible contributions from the participating private party/parties to the costs of the public party/parties will be deducted from the compensation paid.

3.3 Who can apply

The call is open to researchers from research institutes and private parties. A consortium is put together (see under 3.1 Conditions for the project) in which research institutions, companies (including health insurers) and preferably other parties as well such as health funds, retain their own identity and responsibility but jointly realise a project based on a clear and optimal distribution of the tasks and risks. The partnership project is realised with all parties contributing to the costs and sharing the risks. All parties make a financial (in cash/kind) and substantive contribution to the project. Within the public-private partnership the research institution provides the project leader (also the main applicant for the grant application) who will be the point of contact for ZonMw throughout the entire procedure. Every other public and private party within the consortium is a co-applicant. The main applicant should be located in the Netherlands. The call is open to co-applicants from Dutch and foreign institutes or companies but the project must benefit the Dutch knowledge infrastructure.

ZonMw applies the granting condition that projects submitted may not lead to state aid that necessitates registration with the European Commission. The document 'Explanation State Aid Rules' (see Section 5.1 Downloads: *Toelichting Staatssteunregels*) explains how this condition can be satisfied. The lower the percentage of funding provided by ZonMw, the greater the amount of experimental development possible. Please note: the main applicant is responsible for ensuring that the proposal contains an explanation of how this state aid condition has been satisfied.

The ZonMw Grant Terms and Conditions July 2013 and Procedures ZonMw 2002 apply (see Section 5.1 Downloads).

3.4 What amount can be applied for

ZonMw has a maximum of € 8 million available for this call and seeks to realise an even distribution of the funds across the research domains A and B (see Section 2.3 Research domains of the call). ZonMw's contribution to a consortium will be at least € 1 million and at most € 2.25 million.
The contribution of the company/companies to the project will be at least 25% of the total project costs, of which at least 10% of the total project costs in cash. ZonMw's contribution to the project is a maximum of 50%. Projects that need a contribution from ZonMw of 40% or less are preferred and will start with a higher relevance score. See Section 4.1 for an explanation of the relevance score.

Examples:

Contribution company/companies in kind	0.3 M	0.45 M	0.75 M
Contribution company/companies in cash	0.2 M	0.3 M	0.5 M
Contribution research institute(s)	0.5 M	0.45 M	0.5 M
Contribution other private parties	0	0.6 M	1.25 M
Contribution ZonMw	1.0	1.2 M	2.0 M
Total project costs	2.0 M	3.0 M	5.0 M
Percentage ZonMw	50%	40%	40%
Start score relevance	Relevant	Very relevant	Very relevant

The funding contributed can be used for scientific personnel and technical support. The budget can also be used for consumables and small-scale equipment specifically needed for the project. ZonMw also allows researchers to use the project budget to apply for services provided by the European infrastructure EATRIS[3]. The service must of course be in accordance with the budget. The general ZonMw Grant Terms and Conditions apply and where the granting conditions do not provide a clear outcome then the costs framework of the TKI regulation is taken as a guide.

A (preliminary) budget table is included in the pre-proposal form. For the drawing up of the final, full proposal and the final budget separate templates will be made available at a later stage (see Section 5.1 Downloads).
These forms (project proposal and budget) should be added as attachments when the full project proposal is submitted. If the proposal is awarded funding then the grant will be made available to the research institute where the main applicant is employed; the main applicant is responsible for any distribution of the funding to the consortium partners.

4. Assessment procedure

The application round takes place in two stages:

1. The first step is the compulsory pre-proposal in which a limited quantity of information must be supplied for each project. The pre-proposals are assessed by an

[3] EATRIS stands for European Infrastructure for Translational Medicine, it provides a new development pathway, open to researchers and companies in need of support for advancing biomedical innovations. More information: www.eatris.eu

independent international committee appointed by ZonMw that compares the pre-proposals on the basis of the assessment criteria and then prioritises the pre-proposals according to the chances of funding within the substantive and financial frameworks of this call. The evaluation committee will try to realise a spread across the research domains A and B. The main applicants of the circa 14 proposals with the highest chance of being awarded funding will be invited to elaborate their pre-proposals. Pre-proposals (and final project proposals) that do not satisfy the conditions will be rejected and not considered further.

2. The second step is the submission of the final project proposal and the assessment of this. The procedure for assessing the proposals includes a peer review and an advice issued by the international committee to support the ranking of the final proposals. Based on the assessment of relevance and quality the committee will prioritise (rank) the proposals according to the following matrix. Proposals should at least be assessed as Relevant and Very good to be eligible for granting. Proposals assessed as Very relevant receive a higher ranking than proposal assessed as Relevant. The international committee advises the ZonMw Board on the basis of the final proposal, referees reports' and an interview with the main applicant. The ZonMw Board informs the TKI LSH about the final prioritisation and the proposals awarded funding. The ZonMw Board takes the funding decision.

		RELEVANCE		
		Very relevant	Relevant	Not relevant
QUALITY	Excellent	1	3	-
	Very good	2	4	-
	Good	-	-	-
	Satisfactory	-	-	-
	Inadequate	-	-	-

Matrix ranking

4.1 Specific criteria

The project proposal will be assessed for general societal and economic relevance as well as quality of the science and translation according to the table above.

The project proposal starts with a score of very relevant or relevant dependent on the percentage contribution of ZonMw to the project costs (see Section 3.4). The idea behind this is that a larger financial contribution from companies and other partners is evidence of a wider support base, a greater commitment and a higher chance of a subsequent follow-up towards an actual application. If the project fails to achieve a satisfactory score on one or more of the following relevance criteria then the committee will deviate from the starting score in a negative sense.

Relevance criteria:
General relevance

- fits within the objectives of the call
- shows evidence of translational research
- gives insight into the expected business model to bring the product to clinical application or onto the market

Societal and economic relevance:
Described (as quantitatively as possible) in terms of improving quality of life, cost management, productivity and business, see matrix below for guidance.

- Addresses cost management in care and indicates the period in which this will be realised
- Compliance with criteria for responsible research innovation (RRI)[4]
- Involvement of professional support for the purpose of RRI/socially responsible innovation, data stewardship and implementation of results
- Step-by-step plan for implementing the project results and communicating about these both during and after the project

Measures of success: the objectives are accompanied by measures of success that guide the definition, selection, monitoring and evaluation of projects and sector achievements

	QUALITY OF LIFE	*AFFORDABILITY*	*PRODUCTIVITY*	*BUSINESS*
1. Maintain health, prevent health care	**Reduced DALYs** by preventing disease/ complications	**Reduced treatment costs** by preventing disease/ complications and thus reducing healthcare activities; corrected by cost of prevention	> **Limited loss of productive years** by preventing disease/ complications > **Reduced labor years in healthcare** by reducing healthcare demand; corrected by labor for prevention	> (Potential) worldwide **turnover** of commercial products associated with the solutions developed
2. Maximize effect, minimize trauma	**More years of good health** through more effective treatments and shorter recovery periods	**Reduced treatment costs** by reducing hospital time with more effective treatments, fewer unnecessary treatments, and reduced trauma revalidation/ care; corrected by cost to achieve that	> **More productive years** by reducing trauma > **Reduced labor years in healthcare** by reducing treatment; corrected by labor to achieve that	> **Share of turnover** from the commercial products for Dutch organizations
3. Manage disease extra-murally	**Less hospitalization/ institution time** by enabling patients to function at home	**Reduced treatment costs** by replacing expensive intramural care with less expensive extramural care	> **More productive years** by enabling patients to function in society > **Reduced labor years in healthcare** by reducing intramural care; corrected by extramural care labor	> (Foreign) **investments** in the Dutch Life Sciences & Health sector, including from partnering/ milestone deals

Matrix quality of life, cost management, productivity and business.

Scientific and translational quality:

- Innovativeness, clarity and scientific quality:
  The clarity of the intended product and the proposed research
  Innovativeness and quality of the scientific basis of the research
  Translational quality of the proposed research
- Suitability and quality of the planned approach:
  Feasibility of the project and completion of the proposed research within the duration of the project
  Concrete step-by-step plan with task allocation, milestones and deliverables
  Efficacy of the chosen approach
  Soundness of the budget
- Quality and expertise of the consortium:
  Academic excellence, demonstrated by scientific publications, grants and prizes obtained, education, mobility and supervision of personnel

[4] In the context of this call responsible research innovation (RRI) is understood to be: integration of ethical considerations and the involvement of stakeholders and users, including patient representatives and clinicians, in the articulation of criteria for quality of life and the translation of these into product development and implementation.

Translational expertise of the project group demonstrated for example by previously completed clinical studies, experience with the Central Committee on Research Involving Human Subjects (CCMO)
Experience with public-private partnerships
Optimal composition of consortium, preferably participation of health insurer and/or health fund as well

4.2 Procedural criteria

Pre-proposal submission

You should use the ZonMw pre-proposal form This form will be added as an attachment in ProjectNet after completion of the ProjectNet tab pages. No other attachments are permitted.

Final project proposal

You should use the ZonMw final project application form and budget form for a final project proposal. These forms (project proposal and budget) should only be added as attachments when the full project proposal is submitted.

The main applicant sends the following attachments with the project proposal:

- Specified budget (in ZonMw budget form) with, per co-funder, the financial contribution specified as in kind and in cash per year;
- Letters of commitment in which the pledges for the co-funding and the size of the payment by the companies and any other parties are confirmed. Companies and other parties state whether the contribution is in cash or in kind.

In the case of funding being awarded ZonMw expects that the official secretary will:

- ✓ ensure that within six months of a project being awarded funding, the consortium parties sign a partnership agreement (consortium agreement) which amongst other things describes how intellectual property (IP) arising from the project results will be dealt with. The in-kind and in-cash contributions from the individual consortium partners are also specified per year in this agreement. The main applicant is responsible for the realisation of the partnership agreement. A model agreement can be found under Section 5.1 Downloads. As soon as ZonMw has received a copy of the consortium agreement and the IP agreements and any other additional conditions have also been satisfied, ZonMw will start to make payments to the project.
- ✓ submit a substantive and financial progress report each year. The financial contribution of all consortium parties (in cash and in kind) and from other parties (in cash) must be demonstrated in this;
- ✓ regularly meet with the user committee during the course of the project;
- ✓ submit a financial and substantive final report as well as an auditor's statement within three months of the project being completed;
- ✓ cooperate with a mid-term review. Based on the mid-term review a go/no go decision will be taken by the board for the second half of the project;
- ✓ publish all project results. If applicable, publication takes place after the intellectual property has been safeguarded by the parties concerned;
- ✓ be responsible for Data Stewardship and reserve the funds for this;
- ✓ if possible ensure open access of publications that are the result of research funded by public funds;
- ✓ ensure a timely hours registration of the personnel on the project. For projects that are effectively those of existing partnerships it must be made clear that public funding has not already been awarded for the same research and that the private funding is indeed new funding;
- ✓ cooperate with activities related to exchanging knowledge about how the product under development is brought to the clinic and market (user committee meetings, project leaders meetings).

4.3 Intended timetable

Announcement of call	January 2014
Deadline for submitting pre-proposals	15 May 2014
Selection pre-proposals by committee	Second week of June 2014
Announcement outcome preselection	Third week of June 2014
Deadline submission final project proposal	2 September 2014
Receipt referees' comments	Before 10 October 2014
Presentation to committee and ranking	Last week of October 2014
LSH Foundation Board informed	
Funding decision and awarding by ZonMw Board	Second week of November 2014

Please note: this timetable is subject to change

5. Further information

5.1 Downloads

Template ZonMw 2Treat pre-proposal form
Innovation Contract Top Sector LSH 2012
General ZonMw Grant Terms and Conditions & ZonMw procedures 2002
Explanation State Aid Rules (Toelichting Staatssteunregels)
Model consortium agreement (available in June)
Template ZonMw 2Treat final project proposal (available in June)
Budget form 2Treat final project proposal (available in June)

5.2 Specific questions

For questions about the procedures please contact the secretariat: Petra van der Linden, e-mail 2treat@zonmw.nl, telephone number +31 70 349 5276

For call-specific questions please contact: Wilma van Donselaar, e-mail 2treat@zonmw.nl, telephone number +31 70 349 5418

5.3 Technical questions

ProjectNet can be accessed via a link on www.zonmw.nl
In the event of problems with ProjectNet please contact the helpdesk between 08.00 and 17.00 hours: +31 70 349 5178 or projectnet@zonmw.nl. Please state your telephone number in your e-mail so that we can phone you back if necessary.

6. Submission (via ProjectNet)

Closing date for submitting the compulsory pre-proposals is 15 May 2014 at 15.00 hours. The pre-proposal and the final project proposal can only be submitted electronically and in accordance with the guidelines via the ProjectNet system.
The complete submission of a pre-proposal consists of the filled in tab pages of ProjectNet and the pre-proposal form. You must submit this form as an attachment in ProjectNet. Other attachments are not permitted.

Deadline for the submission of the final project proposal is 2 September 2014 at 15.00 hours. Immediately after the digital submission of the final proposal you should print off the PDF. This should be signed by the "administratively responsible person" and "project leader and official secretary" and sent to ZonMw, f.a.o Wilma van Donselaar, PO Box

93245, 2509 AE The Hague, the Netherlands. ZonMw should receive this no later than one week after the digital submission.

Tips ProjectNet
If you have not previously worked with ProjectNet then you should register one day before as a 'New user'. Click here for a manual on opening an account. Before you submit your proposal electronically we advise you to print off a copy of the PDF of your application and to check this for irregularities. This is especially the case if you write your proposal in Word and then copy it to ProjectNet as then there is a risk that some symbols (such as quotes) might not be converted properly. You can correct such errors in ProjectNet.