Horizon 2020

Call: H2020-MSCA-ITN-2017

(Marie Skłodowska-Curie Innovative Training Networks)

Topic: MSCA-ITN-2017

Type of action: MSCA-ITN-ETN

(European Training Networks)

Proposal number: 765497

Proposal acronym: THERACAT

Deadline Id: H2020-MSCA-ITN-2017

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How to fill in the forms?

The administrative forms must be filled in for each proposal using the templates available in the submission system. Some data fields in the administrative forms are pre-filled based on the previous steps in the submission wizard.

Proposal ID **765497** *Acronym* **THERACAT**

1 - General information

Topic	MSCA-ITN-2017
Call Identifier	H2020-MSCA-ITN-2017
Type of Action	MSCA-ITN-ETN
Deadline Id	H2020-MSCA-ITN-2017

Acronym	THERACAT
Proposal title	Bio-orthogonal catalysis for cancer therapy

Note that for technical reasons, the following characters are not accepted in the Proposal Title and will be removed: < > " &

Duration in months	*48*
Panel	CHE

Please select up to 5 descriptors (and at least 3) that best characterise the subject of your proposal, in descending order of relevance. Note that descriptors will be used to support REA services in identifying the best qualified evaluators for your proposal.

Descriptor 1	*Chemical reactions: mechanisms, dynamics, kinetics and ca*	Add	
Descriptor 2	*Macromolecular chemistry*	Add	Remove
Descriptor 3	*Medicinal chemistry*	Add	Remove
Descriptor 4	*Intelligent materials, self-assembled materials*	Add	Remove

Free keywords	*Bio-orthogonal catalysis, nanomedicine, catalysis in living cells, Chemical Biology*

Abstract

THERACAT is an international and multidisciplinary consortium aiming at the training of 13 ESRs on the innovative topic of novel bio-orthogonal catalysis-based tools for cancer therapy. This ETN comprises 6 academic partners, 3 industrial partners active in the pharmaceutical market (1 large pharmaceutical company, Teva, and 2 SMEs, BiogelX and Tagworks) and 3 partners with focus on science communication (Cancer research UK), gender and minorities (UAB-Observatory for Equality) and management and entrepreneurship (ESADE business school). The combination of academic, private and society-involved organisations will provide a broad training for the 13 ESRs recruited, equipping them with the necessary skills to succeed as scientists, industrial researchers and entrepreneurs.
The development of novel cancer therapies is a major challenge for academic research and pharmaceutical industries. THERACAT aims to establish a training programme focused on the development of THERApeutic CATalysts. In this strategy, materials bearing a catalytic unit are delivered to the tumour and subsequently non-active prodrugs are administered. The prodrugs are non-toxic and therefore generate limited side effects. Only at the tumour site the catalytic particles convert the prodrugs into active compounds that generate a therapeutic effect. This approach presents several advantages on the classical drug delivery paradigm including limited side effects and prolonged efficacy.
This multidisciplinary research programme will be the setting for the training of 13 ESRs. The combination of the research

expertise, the cutting-edge facilities and the complementary skills present in the consortium holds a great promise for the advancement of their careers, as well as of the knowledge of catalysis-based anticancer therapies and the development of marketable technologies and products.

Remaining characters 122

Has this proposal (or a very similar one) been submitted to a H2020-MSCA-ITN call? ○ Yes ◉ No

Proposal ID **765497** *Acronym* **THERACAT**

Declarations

1) The coordinator declares to have the explicit consent of all applicants on their participation and on the content of this proposal.	☒
2) The information contained in this proposal is correct and complete.	☒
3) This proposal complies with ethical principles (including the highest standards of research integrity — as set out, for instance, in the European Code of Conduct for Research Integrity — and including, in particular, avoiding fabrication, falsification, plagiarism or other research misconduct).	☒

4) The coordinator confirms:

- to have carried out the self-check of the financial capacity of the organisation on http://ec.europa.eu/research/participants/portal/desktop/en/organisations/lfv.html or to be covered by a financial viability check in an EU project for the last closed financial year. Where the result was "weak" or "insufficient", the coordinator confirms being aware of the measures that may be imposed in accordance with the H2020 Grants Manual (Chapter on Financial capacity check); or	○
- is exempt from the financial capacity check being a public body including international organisations, higher or secondary education establishment or a legal entity, whose viability is guaranteed by a Member State or associated country, as defined in the H2020 Grants Manual (Chapter on Financial capacity check); or	◉
- as sole participant in the proposal is exempt from the financial capacity check.	○

5) The coordinator hereby declares that each applicant has confirmed:

- they are fully eligible in accordance with the criteria set out in the specific call for proposals; and	☒
- they have the financial and operational capacity to carry out the proposed action.	☒

The coordinator is only responsible for the correctness of the information relating to his/her own organisation. Each applicant remains responsible for the correctness of the information related to him/her and declared above. Where the proposal to be retained for EU funding, the coordinator and each beneficiary applicant will be required to present a formal declaration in this respect.

According to Article 131 of the Financial Regulation of 25 October 2012 on the financial rules applicable to the general budget of the Union (Official Journal L 298 of 26.10.2012, p. 1) and Article 145 of its Rules of Application (Official Journal L 362, 31.12.2012, p.1) applicants found guilty of misrepresentation may be subject to administrative and financial penalties under certain conditions.

Personal data protection

The assessment of your grant application will involve the collection and processing of personal data (such as your name, address and CV), which will be performed pursuant to Regulation (EC) No 45/2001 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data. Unless indicated otherwise, your replies to the questions in this form and any personal data requested are required to assess your grant application in accordance with the specifications of the call for proposals and will be processed solely for that purpose. Details concerning the purposes and means of the processing of your personal data as well as information on how to exercise your rights are available in the privacy statement. Applicants may lodge a complaint about the processing of their personal data with the European Data Protection Supervisor at any time.

Your personal data may be registered in the Early Detection and Exclusion system of the European Commission (EDES), the new system established by the Commission to reinforce the protection of the Union's financial interests and to ensure sound financial management, in accordance with the provisions of articles 105a and 108 of the revised EU Financial Regulation (FR) (Regulation (EU, EURATOM) 2015/1929 of the European Parliament and of the Council of 28 October 2015 amending Regulation (EU, EURATOM) No 966/2012) and articles 143 - 144 of the corresponding Rules of Application (RAP) (COMMISSION DELEGATED REGULATION (EU) 2015/2462 of 30 October 2015 amending Delegated Regulation (EU) No 1268/2012) for more information see the Privacy statement for the EDES Database).

Proposal ID **765497** *Acronym* **THERACAT**

List of participants

#	Participant Legal Name	Country
1	FUNDACIO INSTITUT DE BIOENGINYERIA DE CATALUNYA	Spain
2	TECHNISCHE UNIVERSITEIT EINDHOVEN	Netherlands
3	RIJKSUNIVERSITEIT GRONINGEN	Netherlands
4	UNIVERSITAT BASEL	Switzerland
5	THE UNIVERSITY OF EDINBURGH	United Kingdom
6	TEL AVIV UNIVERSITY	Israel
7	Teva Pharmaceutical Industries Ltd.	Israel
8	TAGWORKS PHARMACEUTICALS BV	Netherlands
9	Biogelx Limited	United Kingdom

Information on partner organisations

Partner Organisation number	PIC Search PIC	Organisation legal name	Country	Academic Sector	Role of associated		
					Provide training	Host secondmends	
1	999494888	Cancer Research UK	United Kingdom	No	Yes	Yes	
2	999863876	Fundación ESADE	Spain	Yes	Yes	No	
3	999986484	Universitat Autonòma de Barcelona	Spain	Yes	Yes	No	

2 - Administrative data of participating organisations

Coordinator

PIC	***Legal name***
999528450	*FUNDACIO INSTITUT DE BIOENGINYERIA DE CATALUNYA*

Short name: IBEC

Address of the organisation

Street CARRER BALDIRI REIXAC PLANTA 2A 10-12

Town BARCELONA

Postcode 08028

Country Spain

Webpage www.ibecbarcelona.eu

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... no
Non-profit ..... yes
International organisation ..... no
International organisation of European interest ..... no
Secondary or Higher education establishment ..... no
Research organisation ..... yes
Legal person ..... yes
Academic Sector ..... yes

Enterprise Data

SME self-declared status ..... 2013 - no
SME self-assessment ..... unknown
SME validation sme ..... unknown

Based on the above details of the Beneficiary Registry the organisation is not an SME (small- and medium-sized enterprise) for the call.

Nace code 721 -

Department(s) carrying out the proposed work

Department 1

Department name: Nanoscopy for Nanomedicine ☐ not applicable

☐ Same as organisation address

Street: Baldiri Reixac 15-21, 1a planta

Town: Barcelona

Postcode: 08028

Country: Spain

Dependencies with other proposal participants

Character of dependence	***Participant***	

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **IBEC**

Person in charge of the proposal

Title: Dr. Sex: (•) Male ( ) Female

First name: **Lorenzo** Last name: **ALBERTAZZI**

E-Mail: **lalbertazzi@ibecbarcelona.eu**

Position in org.: Group Leader

Department: Nanoscopy for Nanomedicine [ ] Same as organisation

[ ] Same as organisation address

Street: Baldiri Reixac 15-21, 1a planta

Town: Barcelona Post code: 08028

Country: Spain

Website: http://www.ibecbarcelona.eu/nanoscopy

Phone: +34 934020517 Phone 2: +xxx xxxxxxxxx Fax: +xxx xxxxxxxxx

Other contact persons

First Name	***Last Name***	***E-mail***	***Phone***
Rosa	Miralles	rmiralles@ibecbarcelona.eu	+34934031145
Esther	Gallardo	projects@ibecbarcelona.eu	+34934039705

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **TU/e**

Participant

PIC	***Legal name***
999977269	*TECHNISCHE UNIVERSITEIT EINDHOVEN*

Short name: TU/e

Address of the organisation

Street GROENE LOPER 5

Town EINDHOVEN

Postcode 5612 AE

Country Netherlands

Webpage www.tue.nl/en/

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... yes
Non-profit ..... yes
International organisation ..... no
International organisation of European interest ..... no
Secondary or Higher education establishment ..... yes
Research organisation ..... no
Legal person ..... yes
Academic Sector ..... yes

Enterprise Data

SME self-declared status ..... 2007 - no
SME self-assessment ..... unknown
SME validation sme ..... 2007 - no

Based on the above details of the Beneficiary Registry the organisation is not an SME (small- and medium-sized enterprise) for the call.

Nace code 853 -

Department(s) carrying out the proposed work

Department 1

Department name: Institute for Complex Molecular Systems ☐ not applicable

☐ Same as organisation address

Street: Groene Loper 5

Town: Eindhoven

Postcode: 5612 AE

Country: Netherlands

Dependencies with other proposal participants

Character of dependence	***Participant***	

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **TU/e**

Person in charge of the proposal

Title: Dr.

Sex: ○ Male ◉ Female

First name: **A.R.A** Last name: **Palmans**

E-Mail: **a.palmans@tue.nl**

Position in org.: Associate Professor

Department: Institute for Complex Molecular Systems ☐ Same as organisation

☐ Same as organisation address

Street: Groene Loper 5

Town: Eindhoven Post code: 5612 AE

Country: Netherlands

Website: www.tue.nl/icms

Phone: +31-40-2473105 Phone 2: +31-402473101 Fax: +xxx xxxxxxxxx

Other contact persons

First Name	***Last Name***	***E-mail***	***Phone***
E.W.	Meijer	e.w.meijer@tue.nl	+31-402473101
K.A.	Duijvesz	k.a.duijvesz@tue.nl	+31-402472491

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **RIJKSUNIVERSITEIT GRONINGEN**

Participant

PIC	***Legal name***
999989782	*RIJKSUNIVERSITEIT GRONINGEN*

Short name: RIJKSUNIVERSITEIT GRONINGEN

Address of the organisation

Street Broerstraat 5

Town GRONINGEN

Postcode 9712CP

Country Netherlands

Webpage www.rug.nl

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... yes

Non-profit ..... yes

International organisation ..... no

International organisation of European interest ..... no

Secondary or Higher education establishment ..... yes

Research organisation ..... yes

Legal person ..... yes

Academic Sector ..... yes

Enterprise Data

SME self-declared status ..... 2015 - no

SME self-assessment ..... 2015 - no

SME validation sme ..... 2007 - no

Based on the above details of the Beneficiary Registry the organisation is not an SME (small- and medium-sized enterprise) for the call.

Nace code 853 -

Department(s) carrying out the proposed work

Department 1

Department name: Stratingh Institute for Chemistry, University of Groningen ☐ not applicable

☐ Same as organisation address

Street: Nijenborgh 4

Town: Groningen

Postcode: 9747 AG

Country: Netherlands

Dependencies with other proposal participants

Character of dependence	***Participant***	

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **RIJKSUNIVERSITEIT GRONINGEN**

Person in charge of the proposal

Title: Prof.

Sex: (•) Male ( ) Female

First name: **Gerard**

Last name: **Roelfes**

E-Mail: **j.g.roelfes@rug.nl**

Position in org.: Full professor Biomolecular Chemistry & Catalysis

Department: Stratingh Institute for Chemistry, University of Groningen ☐ Same as organisation

☐ Same as organisation address

Street: Nijenborgh 4

Town: Groningen

Post code: 9747 AG

Country: Netherlands

Website: https://roelfesgroup.nl/

Phone: +31503637745

Phone 2: +31503636933

Fax: +xxx xxxxxxxxx

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **UNIVERSITAT BASEL**

Participant

PIC	***Legal name***
999907914	*UNIVERSITAT BASEL*

Short name: UNIVERSITAT BASEL

Address of the organisation

Street PETERSPLATZ 1

Town BASEL

Postcode 4051

Country Switzerland

Webpage www.unibas.ch

Legal Status of your organisation

Research and Innovation legal statuses

Public body .....yes

Non-profit .....yes

International organisation .....no

International organisation of European interest .....no

Secondary or Higher education establishment .....yes

Research organisation .....yes

Legal person .....yes

Academic Sector .....yes

Enterprise Data

SME self-declared status.....2012 - no

SME self-assessment ..... unknown

SME validation sme..... unknown

Based on the above details of the Beneficiary Registry the organisation is not an SME (small- and medium-sized enterprise) for the call.

Nace code 853 -

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **UNIVERSITAT BASEL**

Department(s) carrying out the proposed work

Department 1

Department name: Department of Chemistry ☐ not applicable

☐ Same as organisation address

Street: Spitalstrasse 51

Town: Basel

Postcode: 4056

Country: Switzerland

Dependencies with other proposal participants

Character of dependence	***Participant***	

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **UNIVERSITAT BASEL**

Person in charge of the proposal

Title: Prof. Sex: (•) Male ( ) Female

First name: **Thomas** Last name: **Ward**

E-Mail: **thomas.ward@unibas.ch**

Position in org.: Full professor, director NCCR "Molecular Systems Engineering"

Department: Department of Chemistry [ ] Same as organisation

[ ] Same as organisation address

Street: Spitalstrasse 51

Town: Basel Post code: 4056

Country: Switzerland

Website: http://www.chemie.unibas.ch/~ward/

Phone: +41 61 207 1004 Phone 2: +xxx xxxxxxxxx Fax: +41 61 207 1022

Other contact persons

First Name	***Last Name***	***E-mail***	***Phone***
Eve	Silfverberg	eve.silfverberg@unibas.ch	+41 61 207 2883

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **UEDIN**

Participant

PIC	***Legal name***
999974941	*THE UNIVERSITY OF EDINBURGH*

Short name: UEDIN

Address of the organisation

Street OLD COLLEGE, SOUTH BRIDGE

Town EDINBURGH

Postcode EH8 9YL

Country United Kingdom

Webpage www.ed.ac.uk

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... yes

Non-profit ..... yes

International organisation ..... no

International organisation of European interest ..... no

Secondary or Higher education establishment ..... yes

Research organisation ..... yes

Legal person ..... yes

Academic Sector ..... yes

Enterprise Data

SME self-declared status ..... 2007 - no

SME self-assessment ..... unknown

SME validation sme ..... 2007 - no

Based on the above details of the Beneficiary Registry the organisation is not an SME (small- and medium-sized enterprise) for the call.

Nace code 853 -

Department(s) carrying out the proposed work

Department 1

Department name: Cancer Research UK Edinburgh Centre ☐ not applicable

☐ Same as organisation address

Street: Crewe Road South

Town: Edinburgh

Postcode: EH4 2XR

Country: United Kingdom

Dependencies with other proposal participants

Character of dependence	***Participant***	

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **UEDIN**

Person in charge of the proposal

Title: Dr.

Sex: (•) Male ( ) Female

First name: **Asier** Last name: **Unciti-Broceta**

E-Mail: **asier.ub@ed.ac.uk**

Position in org.: Reader in Medicinal Chemistry

Department: Cancer Research UK Edinburgh Centre ☐ Same as organisation

☐ Same as organisation address

Street: Crewe Road South

Town: Edinburgh Post code: EH4 2XR

Country: United Kingdom

Website: http://www.ed.ac.uk/cancer-centre/research/unciti-broceta-group

Phone: +44 1316518500 Phone 2: +44 1316518702 Fax: +xxx xxxxxxxxx

Other contact persons

First Name	***Last Name***	***E-mail***	***Phone***
Alan	Kennedy	europe@eri.ed.ac.uk	+44 1312429420

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **TAU**

Participant

PIC	***Legal name***
999901609	*TEL AVIV UNIVERSITY*

Short name: TAU

Address of the organisation

Street RAMAT AVIV

Town TEL AVIV

Postcode 69978

Country Israel

Webpage http://www.tau.ac.il/

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... yes

Non-profit ..... yes

International organisation ..... no

International organisation of European interest ..... no

Secondary or Higher education establishment ..... yes

Research organisation ..... yes

Legal person ..... yes

Academic Sector ..... yes

Enterprise Data

SME self-declared status ..... unknown

SME self-assessment ..... unknown

SME validation sme ..... unknown

Based on the above details of the Beneficiary Registry the organisation is not an SME (small- and medium-sized enterprise) for the call.

Nace code 853 -

Department(s) carrying out the proposed work

Department 1

Department name: Dpt. of Physiology and Pharmacology, Sackler Faculty of Medicine ☐ not applicable

☐ Same as organisation address

Street: Haim Levanon St., Ramat Aviv

Town: Tel-Aviv

Postcode: 69978

Country: Israel

Department 2

Department name: School of Chemistry ☐ not applicable

☐ Same as organisation address

Street: Ramat Aviv

Town: Tel-Aviv

Postcode: 6997801

Country: Israel

Dependencies with other proposal participants

Character of dependence	***Participant***	

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **TAU**

Person in charge of the proposal

Title: Prof. Sex: ○ Male ◉ Female

First name: **Ronit** Last name: **Satchi-Fainaro**

E-Mail: **ronitsf@post.tau.ac.il**

Position in org.: Chair, Department of Physiology and Pharmacology

Department: Department of Physiology and Pharmacology ☐ Same as organisation

☐ Same as organisation address

Street: Haim Levanon St.

Town: Tel-Aviv Post code: 69978

Country: Israel

Website: http://medicine.mytau.org/satchi-fainaro

Phone: +97236407427 Phone 2: +97236408733 Fax: +97236409113

Other contact persons

First Name	***Last Name***	***E-mail***	***Phone***
Anna	Scomparin	anna.scomparin@gmail.com	+97236408733
Ayelet	Hashdi	ayelethashdi@tauex.tau.ac.il	+97236408733
Lea	Pais	leap@tauex.tau.ac.il	+97236408774
Roey	Amir	amirroey@tau.ac.il	+97236408435

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **Teva Pharmaceutical Industries Ltd.**

Participant

PIC	***Legal name***
923869808	*Teva Pharmaceutical Industries Ltd.*

Short name: Teva Pharmaceutical Industries Ltd.

Address of the organisation

Street Basel 5

Town Petch Tikva

Postcode 4951033

Country Israel

Webpage http://www.tevapharm.com/

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... no

Non-profit ..... no

International organisation ..... no

International organisation of European interest ..... no

Secondary or Higher education establishment ..... no

Research organisation ..... no

Legal person ..... yes

Academic Sector ..... no

Enterprise Data

SME self-declared status ..... unknown

SME self-assessment ..... unknown

SME validation sme ..... unknown

Based on the above details of the Beneficiary Registry the organisation is not an SME (small- and medium-sized enterprise) for the call.

Nace code

Department(s) carrying out the proposed work

Department 1

Department name: NTE (new therapeutic area) R&D ☐ not applicable

☐ Same as organisation address

Street: Eli Horovitz 18

Town: Kfar Saba

Postcode: 4410202

Country: Israel

Dependencies with other proposal participants

Character of dependence	***Participant***	

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **Teva Pharmaceutical Industries Ltd.**

Person in charge of the proposal

Title: Dr.

Sex: ○ Male ◉ Female

First name: **Hila** Last name: **Epstein-Barash**

E-Mail: **hila.barash@teva.co.il**

Position in org.: Dir, Head of NTE Development GxR&D NTE - KFS

Department: NTE Development GxR&D ☐ Same as organisation

☐ Same as organisation address

Street: Eli Horovitz 18

Town: Kfar Saba Post code: 4410202

Country: Israel

Website: http://www.tevapharm.com/

Phone: +972-54-888-6282 Phone 2: +972-9-7638880 Fax: + 972-9-7654952

Other contact persons

First Name	***Last Name***	***E-mail***	***Phone***
Hemda	Cohen	hemda.cohen19@teva.co.il	+972-9-7638799

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **TAGWORKS PHARMACEUTICALS BV**

Participant

PIC	***Legal name***
947414133	*TAGWORKS PHARMACEUTICALS BV*

Short name: TAGWORKS PHARMACEUTICALS BV

Address of the organisation

Street Vondellaan 11

Town Eindhoven

Postcode 5611 NX

Country Netherlands

Webpage www.tagworkspharma.com

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... no

Non-profit ..... no

International organisation ..... no

International organisation of European interest ..... no

Secondary or Higher education establishment ..... no

Research organisation ..... no

Legal person ..... yes

Academic Sector ..... no

Enterprise Data

SME self-declared status ..... 2013 - yes

SME self-assessment ..... 2013 - yes

SME validation sme ..... unknown

Based on the above details of the Beneficiary Registry the organisation is an SME (small- and medium-sized enterprise) for the call.

Nace code 72 - Computer & related activities

Department(s) carrying out the proposed work

No department involved

Department name		☒ not applicable
	☐ Same as organisation address	
Street	*Please enter street name and number.*	
Town		
Postcode		
Country		

Dependencies with other proposal participants

Character of dependence	***Participant***	

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **TAGWORKS PHARMACEUTICALS BV**

Person in charge of the proposal

Title: Dr.

Sex: (•) Male ( ) Female

First name: **Marc** Last name: **Robillard**

E-Mail: **marc.robillard@tagworkspharma.com**

Position in org.: CEO

Department: TAGWORKS PHARMACEUTICALS BV ☒ Same as organisation

☒ Same as organisation address

Street: Vondellaan 11

Town: Eindhoven Post code: 5611 NX

Country: Netherlands

Website: http://www.tagworkspharma.com/

Phone: +31625021525 Phone 2: *+xxx xxxxxxxxx* Fax: *+xxx xxxxxxxxx*

Participant

PIC	***Legal name***
941323309	*Biogelx Limited*

Short name: Biogelx Limited

Address of the organisation

Street BioCity Scotland, Bo'Ness Road

Town Newhouse

Postcode ML1 5UH

Country United Kingdom

Webpage www.biogelx.com

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... no

Non-profit ..... no

International organisation ..... no

International organisation of European interest ..... no

Secondary or Higher education establishment ..... no

Research organisation ..... no

Legal person ..... no

Academic Sector ..... no

Enterprise Data

SME self-declared status ..... 2015 - yes

SME self-assessment ..... 2015 - yes

SME validation sme ..... unknown

Based on the above details of the Beneficiary Registry the organisation is an SME (small- and medium-sized enterprise) for the call.

Nace code

Department(s) carrying out the proposed work

No department involved

Department name ☒ not applicable

☐ Same as organisation address

Street *Please enter street name and number.*

Town

Postcode

Country

Dependencies with other proposal participants

Character of dependence	***Participant***	

Proposal ID **765497** *Acronym* **THERACAT** *Short name* **Biogelx Limited**

Person in charge of the proposal

Title: Dr.

Sex: ○ Male ◉ Female

First name: **Laura** Last name: **Goldie**

E-Mail: **laura.goldie@biogelx.com**

Position in org.: Research Chemist

Department: Biogelx Limited ☒ Same as organisation

☒ Same as organisation address

Street: BioCity Scotland, Bo'Ness Road

Town: Newhouse Post code: ML1 5UH

Country: United Kingdom

Website: http://biogelx.com/

Phone: +44 1698534656 Phone 2: +xxx xxxxxxxxx Fax: +xxx xxxxxxxxx

Other contact persons

First Name	***Last Name***	***E-mail***	***Phone***
Eleanore	Irvine	eleanore.irvine@biogelx.com	01698534655

Proposal ID **765497** *Acronym* **THERACAT**

3 - Budget

Researcher Number	Recruiting Participant (short name)	Planned start month	Duration (months)
1	RIJKSUNIVERSITEIT GRONINGEN	6	36
2	TAU	6	36
3	Teva Pharmaceutical Industries Ltd.	6	36
4	TU/e	6	36
5	UEDIN	6	36
6	IBEC	6	36
7	IBEC	9	36
8	TU/e	9	36
9	Biogelx Limited	9	36
10	UNIVERSITAT BASEL	9	36
11	UEDIN	9	36
12	TAGWORKS PHARMACEUTICALS BV	9	36

Proposal ID **765497** *Acronym* **THERACAT**

Researcher Number	Recruiting Participant (short name)	Planned start month	Duration (months)
13	TAU	9	36
Total			468

Participant Number	Organisation Short Name	Country	IOEI	No of researchers	Number of person.months	Researcher Unit Cost			Institutional Unit Cost		TOTAL
						Living allowance	Mobility Allowance	Family Allowance	Research, training and networking costs	Management and overheads	
1	IBEC	ES	no	2	72	218545,92	43200,00	18000,00	129600,00	86400,00	495745,92
2	TU/e	NL	no	2	72	233548,56	43200,00	18000,00	129600,00	86400,00	510748,56
3	RIJKSUNIVERSITEIT GRO	NL	no	1	36	116774,28	21600,00	9000,00	64800,00	43200,00	255374,28
4	UNIVERSITAT BASEL	CH	no	1	36	126626,76	21600,00	9000,00	64800,00	43200,00	265226,76
5	UEDIN	UK	no	2	72	269375,76	43200,00	18000,00	129600,00	86400,00	546575,76
6	TAU	IL	no	2	72	243401,04	43200,00	18000,00	129600,00	86400,00	520601,04
7	Teva Pharmaceutical Indust	IL	no	1	36	121700,52	21600,00	9000,00	64800,00	43200,00	260300,52
8	TAGWORKS PHARMACEU	NL	no	1	36	116774,28	21600,00	9000,00	64800,00	43200,00	255374,28
9	Biogelx Limited	UK	no	1	36	134687,88	21600,00	9000,00	64800,00	43200,00	273287,88

Proposal ID **765497** *Acronym* **THERACAT**

Participant Number	Organisation Short Name	Country	IOEI	No of researchers	Number of person.months	Researcher Unit Cost			Institutional Unit Cost		TOTAL
						Living allowance	Mobility Allowance	Family Allowance	Research, training and networking costs	Management and overheads	
Total				13	468	1581435,00	280800,00	117000,00	842400,00	561600,00	3383235,00

4 - Ethics issues table

1. HUMAN EMBRYOS/FOETUSES		Page
Does your research involve Human Embryonic Stem Cells (hESCs)?	○ Yes ◉ No	
Does your research involve the use of human embryos?	○ Yes ◉ No	
Does your research involve the use of human foetal tissues / cells?	○ Yes ◉ No	
2. HUMANS		**Page**
Does your research involve human participants?	○ Yes ◉ No	
Does your research involve physical interventions on the study participants?	○ Yes ◉ No	
3. HUMAN CELLS / TISSUES		**Page**
Does your research involve human cells or tissues (other than from Human Embryos/ Foetuses, i.e. section 1)?	◉ Yes ○ No	27,47
Are they available commercially?	◉ Yes ○ No	47
Are they obtained within this project?	○ Yes ◉ No	
Are they obtained from another project, laboratory or institution?	○ Yes ◉ No	
Are they obtained from biobank?	○ Yes ◉ No	
4. PERSONAL DATA		**Page**
Does your research involve personal data collection and/or processing?	○ Yes ◉ No	
Does your research involve further processing of previously collected personal data (secondary use)?	○ Yes ◉ No	
5. ANIMALS		**Page**
Does your research involve animals?	◉ Yes ○ No	28,29
Are they vertebrates?	◉ Yes ○ No	28,29
Are they non-human primates?	○ Yes ◉ No	
Are they genetically modified?	○ Yes ◉ No	
Are they cloned farm animals?	○ Yes ◉ No	
Are they endangered species?	○ Yes ◉ No	

The specific strains of mice that will be used correlate with the tumor type and source of the cells. For human tumors inoculated in mice, we will use either SCID or nu/nu mice, whereas for murine tumors, we will use C57BL/6 or BALB/c mice depending on the specific tumor type.		
6. THIRD COUNTRIES		Page
In case non-EU countries are involved, do the research related activities undertaken in these countries raise potential ethics issues?	○ Yes ◉ No	
Do you plan to use local resources (e.g. animal and/or human tissue samples, genetic material, live animals, human remains, materials of historical value, endangered fauna or flora samples, etc.)?	○ Yes ◉ No	
Do you plan to import any material - including personal data - from non-EU countries into the EU?	○ Yes ◉ No	
Do you plan to export any material - including personal data - from the EU to non-EU countries?	○ Yes ◉ No	
In case your research involves low and/or lower middle income countries, are any benefits-sharing actions planned?	○ Yes ◉ No	
Could the situation in the country put the individuals taking part in the research at risk?	○ Yes ◉ No	
7. ENVIRONMENT & HEALTH and SAFETY		Page
Does your research involve the use of elements that may cause harm to the environment, to animals or plants?	○ Yes ◉ No	
Does your research deal with endangered fauna and/or flora and/or protected areas?	○ Yes ◉ No	
Does your research involve the use of elements that may cause harm to humans, including research staff?	○ Yes ◉ No	
8. DUAL USE		Page
Does your research involve dual-use items in the sense of Regulation 428/2009, or other items for which an authorisation is required?	○ Yes ◉ No	
9. EXCLUSIVE FOCUS ON CIVIL APPLICATIONS		Page
Could your research raise concerns regarding the exclusive focus on civil applications?	○ Yes ◉ No	
10. MISUSE		Page
Does your research have the potential for misuse of research results?	○ Yes ◉ No	
11. OTHER ETHICS ISSUES		Page
Are there any other ethics issues that should be taken into consideration? Please specify	○ Yes ◉ No	

I confirm that I have taken into account all ethics issues described above and that, if any ethics issues apply, I will complete the ethics self-assessment and attach the required documents. ☒

How to Complete your Ethics Self-Assessment

5 - Call Specific Questions

Extended Open Research Data Pilot in Horizon 2020

If selected, applicants will by default participate in the Pilot on Open Research Data in Horizon 2020[1] , which aims to improve and maximise access to and re-use of research data generated by actions.

However, participation in the Pilot is flexible in the sense that it does not mean that all research data needs to be open. After the action has started, participants will formulate a Data Management Plan (DMP), which should address the relevant aspects of making data FAIR – findable, accessible, interoperable and re-usable, including what data the project will generate, whether and how it will be made accessible for verification and re-use, and how it will be curated and preserved. Through this DMP projects can define certain datasets to remain closed according to the principle "as open as possible, as closed as necessary". A Data Management Plan does not have to be submitted at the proposal stage.

Furthermore, applicants also have the possibility to opt out of this Pilot completely at any stage (before or after the grant signature). In this case, applicants must indicate a reason for this choice (see options below).

Please note that participation in this Pilot does not constitute part of the evaluation process. Proposals will not be penalised for opting out.

We wish to opt out of the Pilot on Open Research Data in Horizon 2020.	◉ Yes	○ No

If opting out please indicate the reason(s) for not being able to participate in the Pilot:

- the project does not generate any data	☐
- to allow the protection of results (e.g. patenting)	☒
- incompatibility with the need for confidentiality linked to security	☐
- incompatibility with privacy/data protection	☐
- achievement of the project's main aim would be jeopardised	☐
- other legitimate reasons	☐

Further guidance on open access and research data management is available on the participant portal: http://ec.europa.eu/research/participants/docs/h2020-funding-guide/cross-cutting-issues/open-access-dissemination_en.htm and in general annex L of the Work Programme.

[1] *According to article 43.2 of Regulation (EU) No 1290/2013 of the European Parliament and of the Council, of 11 December 2013, laying down the rules for participation and dissemination in "Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020)" and repealing Regulation (EC) No 1906/2006.*

START PAGE

MARIE SKŁODOWSKA-CURIE ACTIONS

Innovative Training Networks (ITN)
Call: H2020-MSCA-ITN-2017

PART B

THERACAT

Bio-orthogonal catalysis for cancer therapy

This proposal is to be evaluated as:

ETN

TABLE OF CONTENTS

LIST OF PARTICIPATING ORGANISATIONS

Consortium Member	Legal Entity Short Name	Academic	Non-academic	Awards Doctoral Degrees	Country	Dept./ Division/ Laboratory	Scientist-in-Charge	Role of Partner Organisation
ACADEMIC BENEFICIARIES								
1 – Fundació Institut de Bioenginyeria de Catalunya	IBEC	X			Spain	Nanoscopy for Nanomedicine	Lorenzo Albertazzi	
2 - Technische Universiteit Eindhoven	TUE	X		X	Netherlands	Institute for Complex Molecular Systems	Anja Palmans	
3 - Rijksuniversiteit Groningen	GRO	X		X	Netherlands	Stratingh Institute for Chemistry	Gerard Roefles	
4 - Universitat Basel	BAS	X		X	Switzerland	Dpt. of Chemistry	Thomas Ward	
5 - University of Edinburgh	EDI	X		X	United Kingdom	Cancer Research UK Edinburgh Centre	Asier Unciti-Broceta	
6 - Tel Aviv University	TAU	X		X	Israel	(a) Dpt. of Physiology & Pharmacology	Ronit Satchi-Fainaro	
						(b) School of Chemistry	Roey Amir	
NON-ACADEMIC BENEFICIARIES								
7 - TEVA Pharmaceutical Industries Ltd.	TEVA		X		Israel	NTE (new therapeutic area) R&D	Hila Barash	
8 - Tagworks Pharmaceuticals BV	TAG		X		Netherlands	N/A	Marc Robillard	
9 – Biolgelx Limited	BGX		X		United Kingdom	N/A	Laura Goldie	
PARTNER ORGANISATIONS								
10 - Cancer Research UK	CRUK		X		United Kingdom	Research Information and Engagement	Fionnuala Ratcliffe	Training, Host Secondment
11 – Fundación ESADE	ESADE	X			Spain	Dpt of Strategy and General Management	Jordi Vinaixa	Training
12 – Universitat Autònoma de Barcelona	UAB	X		X	Spain	Observatory for Equality	Joana Gallego	Training

Data for non-academic beneficiaries:

Name	Location of research premises (city / country)	Type of R&D activities	No. of full-time employees	No. of employees in R&D	Web site	Annual turnover (in Euro)	Enterprise status (Yes/No)	SME status (Yes/No)
TEVA	Kfar Saba/ Israel	Generic/ New therapeutic area/ Specialty	58.000	5.162	http://www.tevapharm.com/	18.8 billion	Yes	No
TAG	Nijmegen/ Netherlands	In vivo chemistry	3	3	www.tagworkspharma.com	140.000	Yes	Yes
BGX	Newhouse/ United Kingdom	Design and synthesis of peptide hydrogels	10	4	www.biogelx.com	168.000	Yes	Yes

Declarations

Name (institution / individual)	Nature of inter-relationship
N/A	N/A

1. Excellence

1.1 Quality, innovative aspects and credibility of the research programme

THERACAT is an international and multidisciplinary consortium aiming at the training of 13 ESRs on the innovative topic of bio-orthogonal catalysis for cancer therapy. This ETN comprises 6 academic partners from top European institutions, 3 industrial partners active in the pharmaceutical market (1 large pharmaceutical company, Teva, and 2 SMEs, BiogelX and Tagworks) and 3 partners with focus on science communication (Cancer research UK), gender and minorities (UAB-Observatory for Equality), management and entrepreneurship (ESADE business school). The combination of academic, private and society-involved organisations will provide a broad and effective training for the 13 ESRs recruited, equipping them with the necessary skills to succeed as scientists, industrial researchers and entrepreneurs.

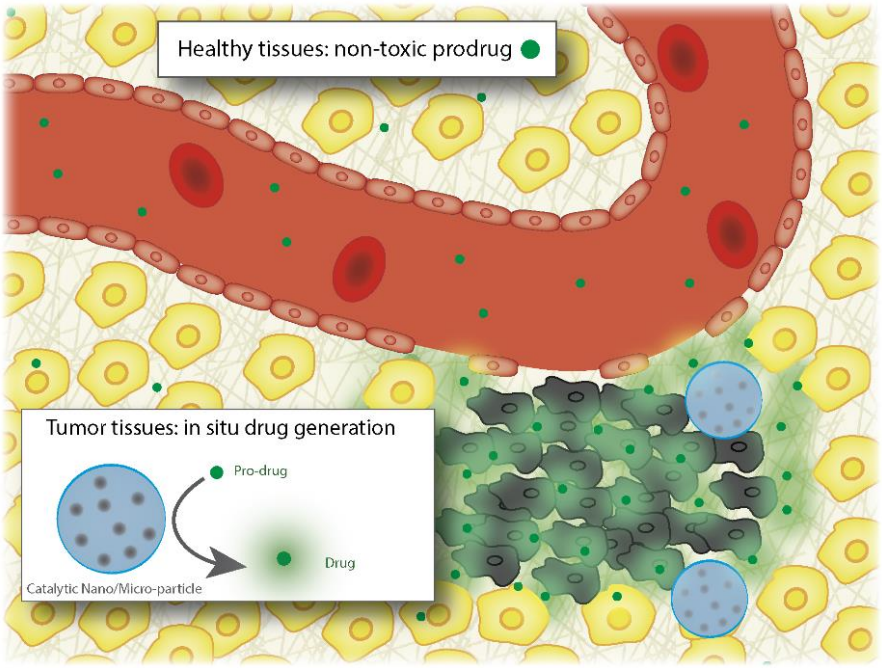


Fig.1 – Overview of THERACAT

The development of novel cancer therapies is a major challenge for academic research and pharmaceutical industries. Although the recent progress in traditional treatments such as surgery and chemotherapy improved the clinical outcome of cancer patients, there is a strong need for new and effective approaches as well as for a new generation of young scientists trained to tackle these challenges from a multidisciplinary perspective. THERACAT aims to establish an international training programme focused on the development of catalysis-based approaches towards the cure of cancer. In this strategy (see Fig.1), nano- and micro-particles bearing a catalytic unit are delivered to the tumour site and subsequently non-active prodrugs are administered to the patient. The prodrugs are non-toxic and therefore generate limited side effects. Only at the tumour site the catalytic particles convert the prodrugs into active anticancer compounds that generate a local and strong effect, as single catalytic species can uncage a large number of drugs. This approach presents several advantages on the classical drug delivery paradigm including limited side effects and prolonged efficacy.

The scientific aims of the consortium include:

- Synthesis and characterization of bio-orthogonal catalytic materials
- Design of novel anti-cancer prodrugs and catalytic strategies for their activation
- Development of delivery strategies for the catalytic materials in vitro and in vivo
- Evaluate the in vitro and in vivo performances for cancer therapy

This multidisciplinary research programme, at the interfaces of chemical synthesis, catalysis and cancer biology, will offer the setting for the training of 13 ESRs, providing them the scientific and transferable skills to be successful as academics, industrial researchers and entrepreneurs. The combination of the research expertise, the cutting-edge facilities and the complementary skills present in the consortium holds a great promise for the advancement of our knowledge of catalysis-based anticancer therapies as well as for the development of marketable technologies and products.

1.1.1 Introduction, objectives and overview of the research programme

Introduction - Societal impact of cancer. The social and economic relevance of cancer in Europe is continuously growing, with 2.6 million people diagnosed with cancer in the EU in 2012[1] and 14.1 million

[1] J Ferlay et al, Eur J Cancer. 2013 Apr;49(6):1374

people worldwide[2] (see Fig. 2). The devastating effects of difficult-to-treat cancers (pancreatic, ovarian, breast, prostate, liver, lung, etc.) do not only impose an overwhelming affliction to hundreds of thousands of patients and families, but also burden the European Health Systems resources. It is estimated that cancer costs European countries 124 billion euros per year.[3] To address this rapidly growing problem, it is thus essential that Pharma and public investments are driven towards more efficient/selective drugs and focal treatment strategies. Health constitutes one of the priority research actions within Horizon 2020, with particular focus on finding new ways to prevent diseases, developing better diagnostics and more effective therapies, as well as taking up new technologies promoting health and wellbeing. **In this context, the research activities proposed herein aims at the development of novel approaches for cancer treatment and are fully integrated into the EU strategy.**

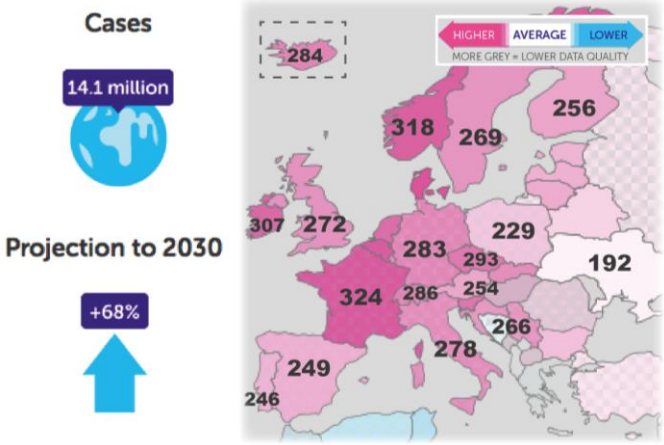


Fig. 2 – Cancer incidence in Europe (cases per 100.000 people). Source: Cancer Research UK.

Up to date, the three most established treatments for cancer are surgery, radiotherapy and chemotherapy. Surgery, when possible, is generally the first treatment option after which cancers may be further treated with radiotherapy or chemotherapy. Chemotherapy uses cell-killing drugs that target cells that are dividing and multiplying, which cancer cells do far more frequently than normal cells. However, both radiotherapy and chemotherapy lead to numerous adverse effects that affect the quality of life of the patient and limit the treatment of the disease. **Therefore, new therapeutic strategies beyond the current paradigm are required to treat the most aggressive forms of cancer.** Here we propose new solutions for more effective and side effect-free chemotherapy. The key feature of THERACAT strategy is the use of bio-orthogonal catalysis to activate chemotherapeutic prodrugs selectively and efficiently in the tumour site. The development of a chemical arsenal of catalysts able to function in the complex biological media is therefore a main scientific target of THERACAT.

Catalysis in biological media - State of the art. Combining the progress made in the field of bio-orthogonal chemical reactions — i.e. that can occur inside of living systems without interfering with their processes — and the development of air and water stable transition-metal complexes resulted in the **emerging of the young field of bio-orthogonal catalysis.[4]** Transition metals are particularly powerful catalysts for this purpose because they catalyse a great diversity of chemical transformations and several of them (Pd, Pt, Rh, Ru) do not occur in living cells[5], permitting to access a variety of non-natural reactions. In a landmark example, Meggers and co-workers showed that Ru-based complexes enabled the deallylation of allylcarbamate protected rhodamine dyes in living mammalian cells.[6] In 2011, Unciti-Broceta and co-workers showed that polystyrene particles comprising Pd(0) nanoparticles were also capable of this deprotection reaction, but in addition catalysed Suzuki-Miyaura cross-coupling reactions inside cells.[7] Later, Chen and co-workers showed that also ligand free Pd(II) complexes were efficient in catalysing Sonogashira and Suzuki-Miyaura cross-coupling reactions between fluorescent dyes and proteins inside bacterial cells.[8] Moreover, Ward and co-workers recently showed that the well-known Ru metathesis chemistry could be conducted in the periplasm of Escherichia coli as a reaction compartment.[9] **These pioneering reports, many of them published by members of the THERACAT consortium, opened the way for the use of bio-orthogonal catalysis as a therapeutic tool.** Recently, Unciti-Broceta and co-workers put forward an innovative approach for chemotherapy using the concept of bio-orthogonal catalysis.[10] In this approach, prodrugs such as fluorouracil and gemcitabine are locally deprotected by catalytic polystyrene particles in vivo, being toxic only in the implant site.[11] These results represent the first example of catalysis-based chemotherapy and highlight the potential of the THERACAT approach to develop bio-orthogonal tools for cancer therapy.

[2] http://www.cancerresearchuk.org/health-professional/cancer-statistics/worldwide-cancer; [3] R Luengo-Fernandez et al, The Lancet Onchology (2013), 14 (12), 1165 [4] Sasmal et al, Chem. Comm. (2013), 49 (16), 1581. [5] Yang et al, Chem. Soc. Rev. (2014), 43 (18), 6511; [6] C. Streu et al, Angew. Chem. Int. Ed. (2006), 45, 5645; [7] R. M. Yusop et al, Nat. Chem. (2011), 3, 239; [8] Li, et al, Nat. Chem. (2014), 6, 352.; [9] M. Jeschek et al, Nature, (2016), 537, 661. [10] J. T. Weiss et al, Nature Commun.(2014), 5, 3277; [11] J. T. Weiss et al, J. Med. Chem. (2014), 57, 5395

Future challenges and THERACAT scientific objectives.

In order to exploit the therapeutic potential of bio-orthogonal catalysis, several scientific and technical issues have to be addressed such as: i) the availability of metal-labile protective groups fully stable under physiological conditions; ii) highly stable and active catalysts system that can be implanted or targeted at the site of interest; and iii) a full understanding of in vivo catalysts localization, catalytic activity, toxicity and anticancer activity. Clearly these challenges exceed the field of chemistry and catalysis and require a broad expertise in a variety of fields ranging from chemistry and catalysis to biology and imaging. The THERACAT consortium comprises several renowned European players, both academic and industrial, in fields necessary for the development of bio-orthogonal therapies and combines the knowledge required starting from material synthesis, catalysis activation, in vitro and in vivo cancer cell studies up to in vivo animal studies to test the efficacy of the developed systems. The collaborations fostered by the ESR secondments as well as by the network-wide meetings will support the achievement of objectives that will be unreachable for an individual group or at a national level.

The main scientific objectives of THERACAT are:

S1 - Synthesis and characterization of bio-orthogonal (nano)catalysts (WP1)

S2 - Design of novel catalytically-activable prodrugs and prodyes (WP2)

S3 - Effective strategies for the selective delivery of catalysts in the cancer site (WP3)

S4 - An in vivo validation of the antitumor strategy using imaging and animal models (WP4)

Consortium Overview. THERACAT comprises 6 academic partners from 5 different countries and 3 private sector beneficiaries: TEVA and 2 SMEs, Tagworks and Biogelx. Moreover, the consortium comprises 3 partners active on scientific communication (Cancer Research UK), on management and entrepreneurship (ESADE Business School) and on gender and minorities (UAB-Observatory for Equality). The combination of academic, private and society-involved organisation will provide a broad and effective training for the 13 ESRs recruited, equipping them with the necessary skills to succeed as scientists, industrial researchers and entrepreneurs.

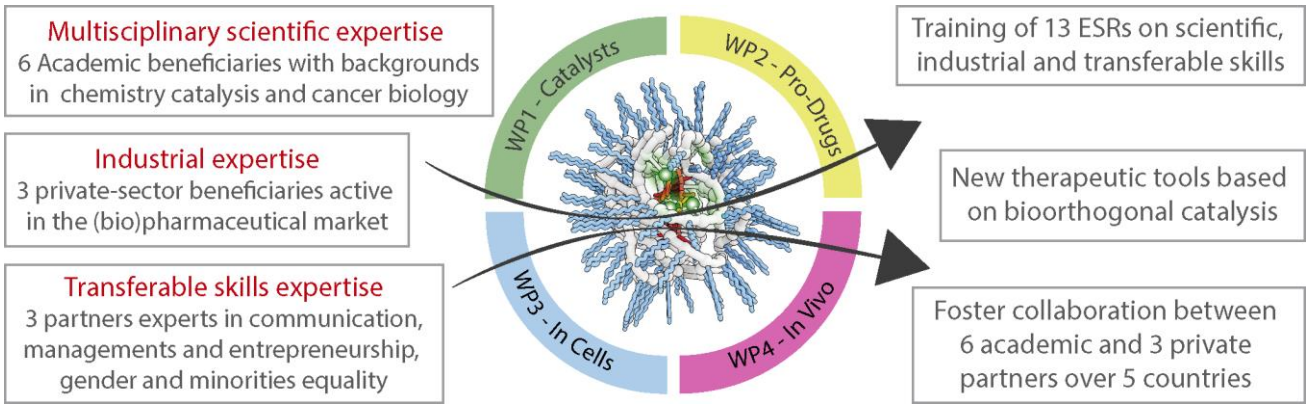


Fig. 3 – Overview of the consortium

The 6 academic beneficiaries are outstanding European institutions covering all the expertise necessary to achieve the scientific goals of THERACAT, ranging from synthetic chemistry to cancer biology and biological imaging. The three industrial beneficiaries (1 large pharma company, TEVA, and two SMEs, Tagworks and Biogelx) will be strongly involved in all the issues related to large-scale production, product development and industrial manufacturing under GMP conditions. Moreover, they will prepare the ESRs with the skills needed for a career in the industrial field. Notably the 3 partner organisations will uniquely strengthen THERACAT for transferable skills. Cancer Research UK (CRUK) is among the largest charities in Europe with the purpose to promote cancer research and awareness, and will take the crucial role to ensure the communication to the general public of the network purposes and results. ESADE Business & Law School is one of the most prestigious business schools worldwide according to numerous

THERACAT:

- 5 countries (ES, NL, UK, CH, IL)
- 3 of 9 beneficiaries from industry
- 1 large pharma, 2 SMEs, 1 business school, 1 charity
- 6 of 13 PI are women

rankings, with more than half century of experience. ESADE will provide support and training in the fields of project management and entrepreneurship. Finally, the UAB Observatory for Equality will raise awareness on gender issues in research and monitor the development of THERACAT in light of gender and minorities' equality. Therefore, the THERACAT consortium holds a great promise towards the training of the ESRs to develop the skills necessary for the next generation of highly-qualified scientists and entrepreneurs as well as to strengthen the European competitiveness in academic research and the market of novel anticancer therapies.

1.1.2 Research methodology and approach

THERACAT aims at the development of bio-orthogonal catalysts as innovative anticancer therapies. In our approach, anticancer drugs will be caged and rendered inactive by the conjugation of a protective group (prodrugs). These compounds are designed to be deprotected by a metal catalyst that locally releases the cytotoxic compound. Therefore, we envision a novel therapy based on the following steps: i) selective delivery and accumulation of the catalysts to the cancer site; ii) systemic administration of the prodrug; iii) localized drug catalytical activation to devise a selective and side effects-free cancer therapy. **The advantages of this approach over classical therapies are multiple.** The catalytic activation in situ of the prodrug will allow limiting the side-effects typical of anti-cancer remedies as the active drug will be created only in the tumour site. Moreover we expect an enhancement of efficacy compared to classical drug delivery approaches; while drug carriers currently used in the clinic (e.g. Doxil[12]) have a limited drug loading, a single catalyst can potentially generate an extremely high number of active drug, according to its turnover frequency and turnover number.[13] Of course the proposed approach is not exempted of challenges. Catalysts with tumour targeting capabilities have not yet been developed, while the stability of the catalyst in the complex biological environment needs to be optimized for maximal prodrug activation capacity. Moreover, a two-step administration (catalyst and the prodrug) is necessary and the dosage and timing of both needs to be optimized. **For these reasons the THERACAT programme has the fundamental goal of gaining a detailed understanding of the behaviour of bio-orthogonal catalysts in the biological environment using state-of-the-art techniques and maximizing the targeted potential of the strategy.** To achieve this ambitious goal we propose a multidisciplinary research programme structured in four work packages as illustrated in Fig. 4.

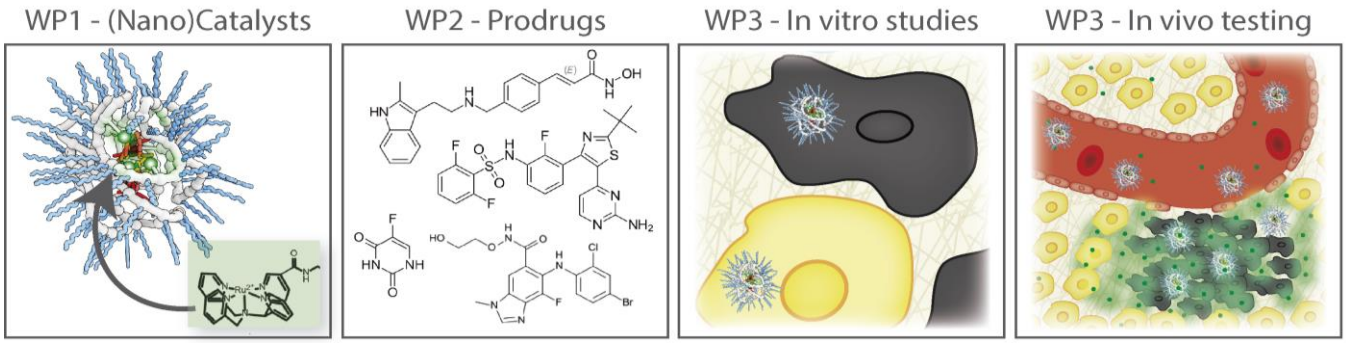


Fig. 4 – Overview of the work packages

In WP1 novel metal catalysts (ESR1) and catalytic nanoparticles (ESR2-4) will be synthesized and characterized). WP2 will focus on the design and synthesis of novel prodrugs (ESR5) and prodyes (ESR6) and their in vitro testing. The performances of catalyst-prodrug combinations will be tested in vitro using 2D cultures (ESR7-8) and 3D cell models (ESR9) in WP3 and in vivo studies using animal cancer models in WP4 (ESR11-13). In order to gain a fundamental understand of bio-orthogonal therapies - a crucial step towards the design of effective therapies - two relevant technologies will be provided by the THERACAT members: sophisticated in vitro[14,15] and in vivo cancer models[16] (BGX, TAU) and advanced imaging techniques such as super resolution microscopy (IBEC)[17,18], click-based PET imaging (TAG)[19] and intravital imaging (TAU)[20,21]. These methods will be instrumental towards the understanding of bio-orthogonal catalysis in complex biological media, for advancing our knowledge in the field of in vivo catalysis and enabling the rational design of effective and applicable catalytic materials. Advanced imaging

[12] Y Barenholz, J. Controlled Release (2012), 160(2):117; [13] Beller et al, Catalysis: From Principles to Applications (2012) Wiley; [14] H Greco Song et al, Adv. Drug Deliv. Rev. (2014), (0)19; [15] Alakpa et al, Chem. (2016), 1(2), 298; [16] A Kruczynski et al, Curr. Prot. Pharm. (2002), 5.24; [17] L Shermelleh et al, J. Cell. Biol. (2010), 190(2), 165; [18] Van der Zwaag et al, ACS Apll. Mater. Interafaces, (2016), 8(10), 6391; [19] Rossin et al, Bioconjg. Chem. (2013), *24* (7), pp 1210; [20] Pittet et al, Cell, (2011), 147(5); [21] Segal et al, Plos One, (2009), 4(4), e5233

techniques such as super resolution imaging (ESR7), in vivo positron emission tomography (PET, ESR 12) and intravital microscopy (ESR13) will be employed to track in real time the catalytic events in vivo and provide crucial information to devise future therapies. Notably this will be extremely beneficial for the scientific training of the ESRs that will be exposed to the most advanced methodologies, developing strong expertise for their future career steps. To complement the research-based sections, two additional work packages focusing on training (WP5) and dissemination and outreach (WP6) have been designed to support the training and the impact of THERACAT. The details of the ESRs research projects are described in details in table 3.1d.

Table 1.1: Work Package (WP) List

WP No.	WP Title	Lead No.	Start Month	End month	Activity Type	Lead Short Name	ESR involvement
WP0	Management and coordination	1	1	48	Management	IBEC	All
WP1	Catalysts synthesis	2	6	42	Research	TUE	ESR1-4
WP2	Prodrugs design and synthesis	5	6	42	Research	EDI	ESR5-6
WP3	In vitro delivery and imaging	1	9	45	Research	IBEC	ESR7-10
WP4	In vivo evaluation	6	9	45	Research	TAU	ESR11-13
WP5	Training	6	1	48	Training	TAU	All
WP6	Dissemination and outreach	5	1	48	Dissemination	EDI	All

WP1 – Catalysts synthesis. In WP1, THERACAT will evaluate a number of transition-metal-based catalysts with the ultimate aim to activate selected, clinically relevant chemotherapeutic agents that are currently applied in cancer treatment therapies. First, synergistically with WP2, we will select several protective groups (e.g. (dimethyl)propargyloxycarbonyl) to be introduced into prodyes and prodrugs. Then, biocompatible transition-metal-based catalytic systems able of drug uncaging will be developed. We will focus on Ru- and Pd-based metal-complexes as these metals are absent in living cells and have high affinities for the aforementioned protective groups. A number of approaches will be evaluated to form the catalytically active complexes. Polypyridine-based ligands will be used because they have a broad catalytic scope and are efficiently taken up by cancer cells (ESR1). Such catalysts can be used as such or loaded on nanoscaffolds to enhance their catalytic properties as well as their biological behaviour. Micellar catalysts based on amphiphilic block copolymers will be developed that comprise mono- and bivalent ligands between the hydrophobic and hydrophilic blocks so that the metal catalysts will be present in very high local concentrations (ESR2). Apart from developing carrier materials for catalysts, we will also work on industrial-scale formulation of carrier materials that are applicable for oral delivery (ESR3). Herein, the different technologies will be combined, e.g. catalysts developed in ESR1 with vesicles of ESR3. Amphiphilic polymers with pendant ligands will be developed that fold around catalytic centres and shield the active site to induce enzyme-like activities (ESR4). All catalytically active nanomaterials will be fully characterized in vitro (size, shape, catalyst loading). In a next step, the catalytic efficiencies will be quantified for the differently protected dyes in vitro. Alongside with WP2, which focuses on the synthesis of prodrugs, selected prodrugs and catalytic systems will be tested in vitro and the nature of the prodrug/drug (polarity, size, reactive groups) on catalysts activity and the toxicity of the waste products will be evaluated. The best performing systems will enter the in vivo evaluation studies in WP3 and WP4.

WP2 – Prodrugs design and synthesis. The aims of WP2 is to expand the arsenal of therapeutics that can be activated by bio-orthogonal organometallic catalysts (ESR5) and to develop novel spectroscopy and microscopy methods that will enable to test the probe/prodrug activating capacity of the nanomaterials proposed in THERACAT by measuring single fluorescent events (ESR6). Metal-labile protecting groups (e.g. propargylation) will be inserted into FDA-approved drugs such as doxorubicin, selumetinib and panobinostat. Moreover fluorescent model compounds (i.e. prodyes) will be synthesized to allow the study of catalyst performances in vitro and in vivo. Microscopy methods to study catalyst performances in prodye deprotection will be developed based on single molecule imaging. These methods will allow to address

turnover rates, stability and heterogeneity at the single catalyst level. The highly qualified multidisciplinary training required to complete the research programme described in WP2 will be provided by the EDI and IBEC nodes. EDI will offer training and supervision in prodrug design, synthesis and screening. IBEC will lead the super resolution imaging studies. Materials and methods will be mutually shared between ESR5 and ESR6. For example, fluorescent doxorubicin prodrugs will be developed and used in both projects (as a prodrug in ESR5 and as a probe in ESR6). Importantly, WP2 will also feed from other work packages: outputs from WP1 will provide novel nanocatalysts to be tested by ESR5 and ESR6, while they will also capitalize on the targeted strategies, assays and tools developed across WP3 and WP4.

WP3 – In vitro delivery and imaging. The pairs of catalytic materials and prodrugs developed in WP1 and WP2 will be evaluated in in vitro biological models. Few crucial issues will be addressed such as: i) the biocompatibility and bio-orthogonality of the materials (ESR7,9); ii) the development of delivery strategies to localize the catalyst in the desired cellular location and to enhance the selective targeting of cancer cells (ESR8,10) and iii) the effectiveness of the catalysis in the complex cellular environment (ESR7-10). The materials will be studied in 2D cellular cultures of cancer cell lines and in more realistic 3D-gel based cancer models developed at BGX (ESR9). In order to understand the behaviour of these new materials in the complex cellular environment imaging techniques will play a pivotal role. For this purpose the catalysts will be labelled with suitable fluorescent dyes (ESR 1,2,4) and catalytically activable fluorophores (i.e. prodyes, ESR6) will be used to study the kinetic and the spatial localization of drug activation in cells. Confocal microscopy for 2D cell culture and 2-photon microscopy for 3D gels will be used as main imaging techniques. Moreover ESR7 will implement super resolution microscopy as a tool to image catalysts localization and number with unprecedented spatial accuracy in cells.

WP4 – In vivo evaluation. Two-dimensional (2D) cell cultures have a tremendous value in biomedical research in general and in drug screening in particular, however, they do not support tissue-specific and differentiated functions of multiple cell types in disease progression nor do they predict the in vivo effect of drug activities. Therefore, a main purpose of WP4 is to establish mCherry-labeled orthotopic models of cancer in mice. Then, we will evaluate the biodistribution of the newly synthesized prodyes and catalysts and the anticancer activity of the activated prodrugs in vivo. ESR13 will establish the mouse models of cancer. These models will enable the biocompatibility evaluation of polymers of various compositions synthesized by other groups in the consortium (ESR2,3,4,9,11). As the mouse models are mCherry labelled, we will follow-up tumour progression by intravital non-invasive optical imaging and nanoparticles' biodistribution by labelling the NPs with near infra-red fluorescent dyes. Once the various prodrugs and prodyes are synthesized and characterized (WP1-2), we will evaluate their in vitro and in vivo biological activity, including tumour accumulation, biodistribution in healthy organs, safety profile (WBC count, neurotoxicity, cardiotoxicity, blood chemistry), and antitumor activity. These optical measures will be corroborated by PET imaging (ESR12), a complementary technique endowed with enhanced sensitivity. During the project period, compounds will be screened for their safety, activity and optimized according to the acquired results and then re-tested following improvement of synthesis.

Preliminary and collaborative results. The feasibility of the scientific objectives of THERACAT is strongly supported by the preliminary results recently obtained in several nodes of the consortium as shown in Fig. 5. Notably several THERACAT groups pioneered the field of bio-orthogonal catalysis reporting the first examples of metal complexes able to perform efficient substrate conversion in the biological environment. Striking examples among others are the prodrug (pro5FU) activation and consequent cancer cell killing by a palladium-loaded microparticles[10] from EDI and the ruthenium-catalysed metathesis in living bacteria from BAS.[9] Moreover, **several members of the THERACAT consortium are currently collaborating and joint preliminary results are available.** As examples, we report in Fig.5 the fluorescent study in cancer cells of palladium-loaded single chain polymeric nanoparticles by IBEC and TUE and the high resolution microscopy study of micelles

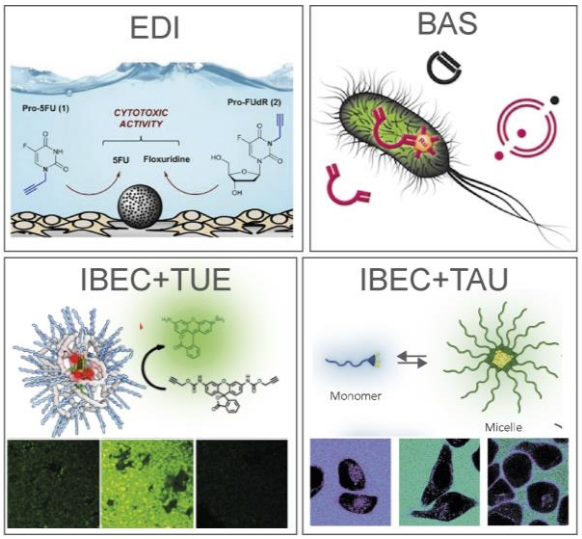


Fig. 5 – Preliminary and collaborative results

localization in cancer cells jointly performed by IBEC and TAU.

1.1.3. Originality and innovative aspects of the research programme

The THERACAT consortium propose an innovative training programme with several aspects of originality:

Advancing the state of the art in the new field of therapeutic bio-orthogonal catalysis. The idea of using synthetic metal-based catalysts in a biological environment is extremely new as the first reports date less than ten years ago.[4] The field grew extremely rapidly in the last 5 years due to the many points of academic interest associate to the challenge of performing catalysis inside a living cell. The next big step for the field is therefore moving from academic proof of principle to the use of bio-orthogonal catalysis for biomedical applications. For this purpose, THERACAT gathers several pioneers of the field of bio-orthogonal catalysis and joins them with experts in microscopy, cancer biology and medicinal chemistry into a unique multidisciplinary consortium. **THERACAT associate scientists with different expertise into a unique collaborative network encompassing the chemical design of biocompatible catalysts to the in vivo testing of novel therapies**. This is another unique aspect of innovation as it is not very common to have networks covering all the disciplines (chemistry, biophysics, biology) and expertise (synthesis, catalysis, microscopy, in vitro and in vivo evaluation) for the creation of new therapies.

Unique multidisciplinary and varied programme. Many other ITN networks such as SUBICAT, CATSENSE, NONOMECAT are focusing on catalysis for industrial purposes. THERACAT aims to be the first ITN network joining catalysis and biology, taking on the challenge to bring metal catalysis to the biological world pursuing a therapeutic anticancer effect. Therefore, this ITN will provide a unique multidisciplinary training to the recruited ESRs. THERACAT aims to join not only different scientific disciplines but to expose the ESRs to a consortium offering a high variety in terms of nationality, gender, expertise and mixture of scientific skills, industrial skills and transferable skills. THERACAT extends over 5 European countries and is composed of 8 academic and 4 private-sector members, including large industries and SMEs, a large cancer-related charity, a world-renowned business school and an observatory for equality. **Such a comprehensive consortium is uniquely positioned to provide an excellent and diverse training to the ESRs as well as to advance the multidisciplinary field of bio-orthogonal therapies.**

Attention to gender importance. THERACAT is committed to analyse and take in account the importance of gender in research in all its facets. The implication of gender in the scientific aspects of the project will be taken in account. Gender is known to play a crucial role in cancer occurrence, progression and response to therapy. In this framework, clinical trials and preclinical research in animal models have been often gender unbalanced resulting in the formulation of biased therapies. **Taking in account this gender dimension will allow to provide more targeted and effective therapies**. THERACAT is committed to consider, investigate and provide adequate solution for the gender relevance in cancer therapies development and testing (e.g. in the choice animal models). Moreover, gender is taken in account for the recruitment and management of the project. **Notably 46% of THERACAT PIs are women and the management committees are composed to ensure gender balance.** The executive committees and especially Prof. Gallego from the Observatory for Equality, have a long-standing experience in promoting gender equality at all levels, aiming for a stronger and more innovative European science programme by creating a diverse workforce.

1.2 Quality and innovative aspects of the training programme

1.2.1 Overview and content structure of the training programme

THERACAT aims to establish an outstanding multidisciplinary and intersectoral training programme that will give ESRs broad scientific background and skills in order to provide them the tools to become the next generation of scientific leaders and entrepreneurships in the EU.
To achieve this goal, THERACAT sets several training activities, which are detailed below and include research excellence, intersectional and international research environments, as well as broad multi-disciplinary scientific education and communication skills, which are essential for the ability to conduct top-end multi-and inter-disciplinary research. THERACAT training programme includes 10 leading research groups at 5 universities and 1 research institute, one big and two small private sector organisations, which are speared over five different countries. The programme aims to recruit 13 ESRs, which will be trained through the following activities:

The main training objectives of THERACAT are:

T1: Research Excellence is the foundation of the scientific training of the ESRs. This will be ensured by supervisors with established international reputation in their respective fields.

T2: Industrial and entrepreneurship training of ESRs by the private sector partners aims at closing the gap between Industry and Academia, facilitating the future transition of ESRs from their academic studies into the EU scientific industries.

T3: The acquisition of **transferable skills** including scientific communication and dissemination, project management, entrepreneurship, ethics and gender awareness is envisioned to prepare the ESRs towards their future careers in academia, industry and governmental agencies.

Training through research. The ESRs will develop their PhD project under the direct supervision of the THERACAT PIs, consisting of a balanced mix of established and young professors and industrial leaders. The ESRs will therefore benefit from the mentorship of the experienced THERACAT PIs, all of them having experience in mentoring students, as well as of the stimulating environment of the beneficiaries' institutions. ESR projects are carefully designed to maximize the learning experience of the ESRs as well as to have an impact in the field of bio-orthogonal catalysis. The projects are challenging and make use of state-of-the-art techniques and instrumentation, preparing the ESRs for their future careers and supporting employability.

ESR secondments. To achieve the scientific and training objectives of the proposed research programme, ESRs will be trained in highly multi-disciplinary and intersectoral environments. Towards this goal ESRs will undertake secondments in other labs and groups within the network. This will enhance the collaboration between the different members of the network as well as broaden the scientific education of the ESRs, training them to become truly multi- and interdisciplinary researchers. Notably, all ESRs will have at least one intersectoral secondment, ensuring the exposure of the ESRs to the different aspects of conducting research in academia and industry. In addition to the substantial benefit of training the ESRs in different laboratories, the planned secondments are also envisioned to allow the visiting ESRs to contribute from their diverse background and skills to the hosting lab and allow them to expand their personal professional networks.

THERACAT secondments:

100% of secondment plans are intersectoral

100% ESRs visit another country

100% secondments are at least 3 months

Researcher No.	Recruiting Participant	Planned Start Month	Duration (months)
ESR 1	GRO	M6	36
ESR 2	TAU - b	M6	36
ESR 3	TEVA	M6	36
ESR 4	TUE	M6	36
ESR 5	EDI	M6	36
ESR 6	IBEC	M6	36
ESR 7	IBEC	M9	36
ESR 8	TUE	M9	36
ESR 9	BGX	M9	36
ESR 10	BAS	M9	36
ESR 11	EDI	M9	36
ESR 12	TAG	M9	36
ESR 13	TAU - a	M9	36
Total: 13			**468**

Table 1.2 a Recruitment Deliverables per Beneficiary.
TAU-a: Prof. Satchi-Fainaro; TAU-b: Dr. Amir.

Local PhD programmes and training. All ESRs in the THERACAT network will enrol in a PhD program either at their host university or in an affiliated university in the case that their recruiting node cannot directly award a PhD degree (ESR3,6,7,9,12; Section 1.3.2). The ESRs will participate in the PhD programs and their curriculum will be built with the guidance of their PIs. In addition to courses that are required for their research objectives, the ESRs will be encouraged to participate in courses from other disciplines in order to expand their intellectual horizons. PIs will promote the participation of ESRs in the local training activities of the beneficiaries (e.g. at IBEC, the ESRs training program includes periodic seminars given by external renowned scientists and experts in public funding, and complementary skills sessions on career development, Tech Transfer and grant writing, among others). The academic progress of the ESRs will be closely monitored by the corresponding PIs to ensure the graduation of the ESRs within the set time. As the PhD programme in TAU, TUE and GRO take four years to complete, sufficient funds will be allocated by the relevant PIs to support the ESRs at their fourth year.

Personal Career Development Plans (PCDP). A valuable tool in the implementation of the training of the ESRs will be the individual PCDPs. The PCDP will contain the ensemble of research objectives and training actions to be undertaken by each researcher of the Network, in particular: (i) the scientific objectives and methodology of the Individual Research Project, ensuring originality and feasibility; (ii) the local and network-wide scientific training necessary to ensure the successful completion of the research project; (iii) the individual secondment plan to expose the ESRs to multidisciplinary, intersectoral and multicultural environments; (iv) the transferable skills training actions to be undertaken; (v) the communication and dissemination activities; (vi) the details on the supervision and assessment procedures to monitor the development of the acquired training and (vii) a prospective on the professional career. The PCDP will be agreed between the ESR and the Supervisor(s). The present ETN considers the PCDP a key instrument in the ESR professional development and for this reason all PCDPs will be approved by the Training Committee. Special care will be taken to ensure that the PCDP fulfil the needs of the current employment market. The PCDPs should be prepared within one month after the ESRs recruitment and will be updated at least every six months.

ETN conference. In addition to the network training events, we will organize an ETN conference in Barcelona to cover the wide aspects of the THERACAT project. This will serve as the ideal opportunity to share both the academic and industrial challenges in drug developments, prodrugs design, catalysis and polymeric carriers in cancer therapy. Lectures will be delivered by the different PIs, ESRs and invited external experts. The conference will be open also to non-member students, with the aim to bring together around 50 students including the THERACAT ESRs. This will enable us to contribute also to the education and training of students beyond the network as well as encourage the member **ESRs to take an active role in the organisation of the conference, helping them develop their management and organisation skills.** Furthermore, allowing the ESRs to select and invite some of the external speakers, will offer them the opportunity to directly interact with the invited experts. The conference will take place as a satellite of the NanoBio&Med conference in Barcelona (co-organized by IBEC), which annually brings together experts in Nanobiotechnology and Nanomedicine. The participation of the ESRs in the NanoBio&Med conference will also allow all ESRs to expand their scientific knowledge and networking.

Specific training events – network-wide training events. In addition to the training of the ESRs at their home institutes and through secondments, we will also have network-wide training events, which are aimed at providing a holistic view of the multi- and interdisciplinary nature of the proposed research and at preparing them with key transferable competences. All training events will include a combination of both technical hard-skills and transferable soft-skills and special emphasis will be given to hands-on training of the ESRs. The training events are detailed in table 1.2b.

Table 1.2 b Main Network-Wide Training Events, Conferences and Contribution of Beneficiaries

	Main Training Events & Conferences	ECTS[1]	Lead Institution	Action Month
1	Training event 1	2	BAS	12
2	ESR meeting 1	-	BAS	12
3	Training event 2	2	TUE	18
4	Training event 3	2	EDI	24
5	ESR meeting 2	-	EDI	24
6	Training event 4	2	TAU	30
7	ESR meeting 3	-	TAU	30
8	Training event 5	3	IBEC	36
9	ESR meeting 4	-	IBEC	36
10	ETN Conference	2	IBEC	42

[1] ECTS have been estimated according to the European Higher Education Area regulations; each ESR will obtain an attendance letter after the event; doctoral schools will be responsible of allocating to the ESR the corresponding ECTS according to their internal regulation.

The key idea is to provide to the ESR the right training at the right time of their PhD. Therefore, the first training event will focus on skills such as research planning, project management and scientific ethics, skills essential to start a PhD. The last event will concentrate on the complementary skills necessary for the ESRs transition to their new scientific careers in industry and academia. In this event the ESRs will be guided in their choice and prepared both to find and obtained their most suitable job as well as to correctly face this transition. This training event will include a special course on innovation and entrepreneurship by

the ESADE Business School, a partner organisation in the network with great experience and highly ranked MSc programme in innovation and entrepreneurship. Taking advantage of the multidisciplinary and multisectoral nature of the network, each of the training events will consist on a mixture of: i) theoretical lessons on the scientific disciplines of THERACAT **(SCI)**; ii) hands-on sessions on the innovative technologies present in the consortium **(LAB)**; iii) training on transferable complementary skills **(COMP)**. The programme for the training events is detailed in the table below.

1 - Introducing the THERACAT Network & How to plan and start a PhD	**M12, 4 days**	**2 ECTS**	**BAS**
Content: The first training event will start with a general introduction of the network and its scientific and training goals. It will also include a comprehensive training of transferable skills aimed to accelerate the implementation of the ESRs into the training programme			
General introduction of the network and its scientific goals	**All PIs** (all nodes)	**SCI**	1 day
Introduction of the training programme	**All PIs** (all nodes)	**SCI**	½ day
Skills to start a successful PhD: Time management, team work, ethics, intercultural, gender and diversity awareness	**All PIs** (all nodes)	**COMP**	1 ½ day
Scientific communication: writing papers, the peer-review process, open science, oral and poster presentations	**IBEC** (Outreach office)	**COMP**	1 day
ESR Meeting 1	**ESR representatives**	**-**	½ day
2 – Chemical synthesis & catalysis	**M18, 5 days**	**2 ECTS**	**TUE**
Content: This event will introduce the ESRs to the fundamental principles of designing the structure and synthesis of the prodrugs and the catalysts that will be studied throughput the project. It will also include an important chemical safety session.			
Catalysts and catalysis: from the synthetic utilization to artificial enzymes	**BAS** (T.Ward)	**SCI**	1 day
Prodrugs: design principles, synthesis and preliminary evaluation	**EDI** (A.Unciti-Broceta)	**SCI**	1½ day
Safety in chemical laboratories and research in industry and academia	**TUE** (A.Palmans)	**LAB**	1 day
How can we do better in bringing new molecules to the market: scaling up, formulations, regulations, procedures and economical aspects	**TEVA** (H.Barash)	**SCI COMP**	1 day
Entrepreneurship and translation: IP and commercial exploitation	**IBEC Tech Transfer**	**COMP**	1 day
3 – Drug delivery & microscopy	**M24, 5 days**	**2 ECTS**	**EDI**
Content: This training event will focus on the design of polymeric platforms for delivering the catalysts and on in-vitro imaging, which is utilized for preliminary evaluation of the performance of the proposed therapeutic approach.			
Designing delivery systems: concepts, examples and concerns	**TAU** (R. Amir)	**SCI**	1 day
Introduction to in-vitro imaging and cell assays	**EDI** (A.Unciti-Broceta)	**SCI**	1 day
The power of microscopy techniques in biomedical research: principles and challenges	**IBEC** (L.Albertazzi)	**SCI**	1½ day
Lab tours in a microscopy facility including hands-on experience	**EDI** (EDI lab members)	**LAB**	½ day
Gender balance in academia, current situation and future perspectives	**UAB** (J.Gallego)	**COMP**	½ day
ESR Meeting 2	**ESR representatives**	**-**	½ day
4 – Going in vivo, chemistry and cancer biology	**M30, 5 days**	**2 ECTS**	**TAU**
Content: This training event will give broader introduction to cancer and will focus on the different aspects of developing in vivo models and pharmacological studies for the proposed therapeutics.			
Fighting Cancer – biomedical, social and economic aspects	**CRUK** (F.Ratcliffe)	**SCI COMP**	1 day
Animal experiments – ethical and practical aspects	**TAU** (R.Satchi-Fainaro)	**SCI LAB**	1 day
Designing in vivo models and choosing the right controls	**TAU** (R.Satchi-Fainaro)	**SCI**	1 day
In Vivo imaging	**TAG** (M.Robillard)	**SCI**	1 day

How to communicate to and engage the public	**CRUK** (F.Ratcliffe)	COMP	½ day
ESR Meeting 3	**ESR representatives**	-	½ day
5 – Getting ready for the next career step	**M36, 7 days**	**3 ECTS**	**IBEC**
Content: The last training event will be dedicated to preparing the ESRs towards completion of their studies and the development of their independent careers in industry, academia and EU agencies, including job hunting.			
Career opportunities in industry and interview simulations	**Industrial PIs**	COMP	1½ day
Searching for post-doc and setting the path for academic careers	**Academic PIs**	COMP	1 day
Innovation and Entrepreneurship including managing strategies, IPs, financing and marketing.	**ESADE** (J.Vinaixa)	COMP	4 day
ESR Meeting 4	**ESR representatives**	-	½ day

1.2.2 Role of non-academic sector in the training programme

The Training programme of the THERACAT Network includes a **strong involvement of the non-academic beneficiaries and partner organisations of the consortium**. A total of 3 ESRs out of 13 (23%) will be recruited by non-academic beneficiaries. In addition, the non-academic beneficiaries and non-academic partner organisations will be in charge of organizing 7 of the 27 Training Workshops. Moreover, non-academic beneficiaries will actively participate in the secondment plan of the network, offering secondment opportunities to all ESRs for a total of 28 months (33% of the total), and will promote the participation of their hosted-ESRs into the secondments to other partners' places. Finally, all non-academic beneficiaries will be part of at least one of the THERACAT Committees (Section 3.2.1; notably, BGX partner will participate in the Training Committee and TEVA will lead IP & Innovation Committee). The non-academic members have been carefully chosen to complement the training provided by the 6 academic beneficiaries. TEVA is a large pharmaceutical company with a world-leading position in the production of drugs for several therapeutic areas. TEVA brings technical knowledge, technology and support for moving a drug from the academia to the market. As a large pharmaceutical company, TEVA has the ability to mentor and support the ESRs through all challenging process of drug development: regulatory requirements, working under GMP conditions, valid analytical methods and preclinical and clinical demands. TAG and BGX are SMEs with a focus on specialty markets such as in vivo chemistry and hydrogels for 3D cellular cancer models. They will offer technical training on such fields providing ESRs with knowledge on the start-up and spin-off system, entrepreneurship (in collaboration with the Business School ESADE) and career development in industries and SMEs. Finally, Cancer Research UK is among the biggest European charities involved in public engagement and scientific dissemination. They will give a fundamental contribution to the WP6 (Dissemination and Outreach) as well as to the outreach sessions of the network-wide training events.

THERACAT non-academic training:

TEVA: industrial production of materials, oral delivery, career in the pharmaceutical market

TAG: in vivo chemistry, PET imaging, start-up development

BGX: hydrogel synthesis and characterization, career development

CRUK: communication and science-society link

1.3 Quality of the supervision

1.3.1 Qualifications and supervision experience of supervisors

The consortium is a balanced mix of senior experienced professors and young group leaders in academia and industry. The academic partners are from some of the premier research universities in Europe, which have been involved in many European consortia and training networks. The scientific quality of the academic PIs is of the highest level, as is evidenced by their track records and the prestigious grants and awards they have received, which includes several ERC grantees and awardees of prestigious national grants. Moreover, they have a proven track record of training young researchers, ensuring a high-quality training and mentorship. Furthermore, THERACAT supervisors have excellent technical background in key technologies such as catalysis, microscopy and imaging, realistic models of diseases. These strong technological backgrounds will play an important role in the training of the ESRs.

Overview of scientific excellence of academic PIs

Academic PIs	ESR	Field	No papers	H index	Grants and Awards
Roelfes	1	Catalysis	69	30	ERC starting (consolidator level), NWO vici
Meijer	4,8	Supramolecular Chemistry	>600	>100	ERC advanced / National Research Center
Ward	10	Catalysis	155	42	ERC advanced / National research Center
Unciti -Broceta	5,11	Medicinal Chemistry	39	14	EPSRC Healthcare Technology Challenge Award
Amir	2	Polymer Chemistry	33	18	Alon fellowship
Satchi-Fainaro	13	Cancer Drug Delivery	80	32	ERC consolidator, EuroNanoMed II (coordinator)
Albertazzi	6,7	Microscopy	43	18	Ramon Y Cajal fellowship, NWO veni
Palmans	4,8	Polymer Chemistry	>100	37	NWO Vidi

The industrial partners have diverse expertise, covering the various aspects of this programme. The involved industrial supervisors have demonstrated scientific excellence through their career, as is evidenced from both their CV's and track records, and have ample experience with the training and supervision of students at various levels in their education. The combination of the research expertise and the cutting-edge facilities provided by the various partners of the consortium hold a great promise for the establishment of an excellent training programme.

1.3.2 Quality of the joint supervision arrangements

All ESRs of the Network will be enrolled in a Doctoral Programme at a University. Each ESR will be supervised by the PI from the corresponding host institution and co-supervised by the secondment partner during the planned secondments, thus ensuring that all ESRs have both an academic and industrial supervisor. We will promote the continuous interaction of the ESRs with the secondment co-supervisors by including them in the individual Assessment Commission (AC) that will be created for each ESR, composed of the secondment co-supervisor and two additional members belonging to partners other than the host partner and with different expertise and profiles (academic/non-academic). The ACs will meet with the ESRs three times coinciding with Network Meetings 1, 2 and 3 and will assess the ESR regarding the training and research being conducted in a broader perspective, acting also as intermediary between the ESR and supervisor in case of conflicts. The list of Universities, Doctoral programmes, and co-supervisors at universities corresponding to each fellow are detailed in the Table below:

ESR	University	Doctoral programme (co-supervisor)
ESR1	Groningen University	Doctoral studies at University of Groningen
ESR2, ESR3, ESR13	Tel Aviv University	TAU School of Chemistry, TAU School od medicine
ESR4, ESR8	Eindhoven University of Technology	PhD programme molecular science and technology
ESR6, ESR7	University of Barcelona	Nanoscience doctoral program (Prof. Samitier)
ESR5, ESR9, ESR11	University of Edinburgh	Molecular and Clinical Medicine
ESR10	University of Basel	Doctoral Studies at UniBas
ESR12	Radboud University Medical Center	Molecular life science (Prof. Boerman)

1.4 Quality of the proposed interaction between the participating organisations

1.4.1 Contribution of all participating organisations to the research and training programme

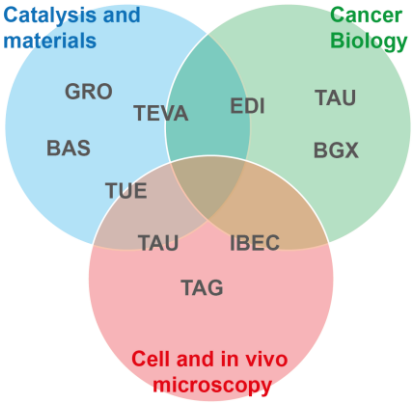
The introduction of the bio-orthogonal chemistry paradigm in medicine is one of the latest advances in experimental cancer therapy. The first examples of prodrugs activated by bio-orthogonal chemistry —either by click chemistry or transition metal-mediated catalysis— were reported by two of the consortium partners (TAG and EDI, respectively). To expand the scope and fulfil the clinical potential of this emerging therapeutic approach, a multidisciplinary training network composed of 6 world-class academic institutions and 6 commercial partners has been created. The wide expertise of the consortium ranges from organometallic catalysis (TUE, BAS), drug design (EDI), super resolution microscopy (IBEC), tumour-targeting strategies (BAS, TAU) and in vivo models (TAU) to technology transfer (BGX, TAG). Moreover,

THERACAT expertise:

Organic and Polymer Chemistry (TAU, TUE)
Metal catalysis (GRO, BAS)
Medicinal chemistry (EDI)
Drug delivery (TAU, IBEC, EDI)
Imaging (IBEC, TAU, TAG)
In vitro and in vivo cancer models (TAU, BGX)
Industrial formulation of materials (TEVA)
Entrepreneurship and management (ESADE)
Communication and engagement (CRUK)
Gender and minorities (UAB)

the industrial partners will provide valuable contributions to product commercialization (TEVA), public engagement activities (CRUK), entrepreneurship (ESADE) and gender issues (UAB). The research activities across all WPs have been carefully created to maximize training opportunities, with students realizing multidisciplinary and intersectoral secondments in two different institutions in addition to attending annual meetings to share their results and get trained in translational research and outreach activities. The active role of industrial partners will enhance the career perspective of the ESRs, provide them with industrial experience and create a route for technology commercialization of the project outcomes.

1.4.2 Synergies between participating organisations



One of main goals of THERACAT is promoting synergies between partners in different research fields to achieve results not possible with a single discipline. In particular, in light of the therapeutic application of bio-orthogonal catalysis this programme joins experts in catalysts synthesis with partners in complementary disciplines such as cancer biology and microscopy. Given the multidisciplinary nature of the research actions, the career development plan of each ESR will been designed to take full advantage of the expertise and facilities of the primary hosting institution and two secondments hosts. Notably several collaborations are already ongoing between partners (see section 1.1.2 –preliminary data and collaborations) and more will be fostered during the project. Data sharing will be made available by confidential disclosure agreements, while exchange of information and materials will be promoted across ESRs to maximize individual training and research results. The consortium will strongly support academic-industry collaborations to generate added value. In this framework, the consortium is designed to gather academic experts with pharmaceutical industries that will support the translation of proof-of-concepts into marketable products.

1.4.3 Exposure of recruited researchers to different (research) environments, and the complementarity thereof

At the hosting institution, each student will benefit from world-class local expertise, equipment and facilities, including local support and guidance for the exploitation of viable commercial opportunities from the corresponding transfer technology office. The 6 academic members cover different areas of chemistry physics and biology ensuring an exposure to different research environments. **Secondments will take place in the lab of a partner with complementary expertise,** allowing effective training activities and facilitating the establishment of new collaborations between partners. This will aid in providing enhanced career perspectives in both the academic and non-academic sectors through international, interdisciplinary and intersectoral mobility combined with an innovation-oriented mind-set. The aim is to train a new generation of creative, entrepreneurial and innovative early-stage researchers able to face current and future challenges and to convert knowledge and ideas into products and services for economic and social benefit. Additionally, in the case of commercial partners, these actions might provide a direct route for the translation of new discoveries. Notably the 6 non-academic partners will allow to expose the ESRs to a whole set of different experiences ranging from a large company (TEVA), 2 SMEs (BGX and TAG), a societally-engaged charity (CRUK) and a business school (ESADE).

2. Impact

The THERACAT programme aims to impact the European scientific and industrial community in several ways as schematically reported in the impact objectives below. The key point of impact and the focus of the proposal are the young researchers participating in the programme as ESRs. The consortium will provide them the scientific, technical and soft skills necessary to excel. This will enhance their career perspectives and at the same time provide a human capital that will contribute to the future development of European academic and private institutions in the field and the market of anticancer pharmaceuticals. Moreover, the knowledge exchange during the training events and the secondments of the ESR will promote the collaboration between the participating institutions, tightening the connections between excellent European academics. This section describes the impact of THERACAT on European academia, private sector and society and is the results of a detailed **stakeholder analysis** (see tables) aiming at individuate the entities affected by the project and the most effective way to maximize the positive effects as well as their engagement.

The main impact objectives of THERACAT are:

I1 – Develop new strategies for anticancer therapy strengthening the European position in the pharmaceutical market for oncology.

I2 – Create career perspectives for the ESRs in the public or private sector as well as provide a human capital of highly trained researchers for European academia and industry

I3 - Strengthen international and intersectoral collaborations in Europe

2.1 Enhancing the career perspectives and employability of researchers and contribution to their skills development

The ITN will bring together a team of leading academic researchers and innovative industrial leaders to create high quality collaborative training programme to a cohort of early stage researchers aimed to provide alterative innovative strategies to combat cancer using hybrid catalyst to deliver active anti-cancer drugs in a highly localized and directed manner. A complementary network of supervisors and mentors spanning both academia and industry will offer students novel research projects and a **fully integrative academic-industrial experience that encompasses both basic- and applied research while providing high quality technical, transferable and employability skills**. ESRs will gain formal PhD training with primary oversight by 1 of 8 experienced research Faculty with a proven track record of excellence in mentoring young scientists (see section 1.3.1). The ESRs will work as a multidisciplinary and integrated team, mimicking the collaborative research environment found in an industrial setting rather than working along the classical “one-student one-project” scheme. **Participants will benefit from hands-on exposure with state-of-the-art techniques/instrumentation** and expert training at the select research hubs within the academic and industrial research network to gain research skills in areas including but not limited to: i) Advanced organic, medicinal and polymer chemistry; ii) In vitro characterization methodology (i.e. small angle X-ray Scattering (SAXS), transmission electron microscopy (TEM), etc.); iii). State of the art imaging techniques (i.e. super resolution microscopy, single particle tracking, etc.); iv) The utilization of in vitro and in vivo models to assess drug therapy efficacy (hydrogel 3D cell matrix, whole mouse, etc.). **The ESRs will also have opportunities to participate in research beyond their host institution with 3-4 months carefully planned secondments** at our academic and industrial partner’s laboratories over their course of their PhD studies (See section 1.3.2). The high flexibility and ease of mobility within the research network are designed to foster the transfer of knowledge and innovative thinking between academia and industry, student exposure to different research areas, and offer a high level of peer-support and community in effort to provide an outstanding learning experience. Additionally, we will offer students several opportunities to

Stakeholder	Impact	Method
13 ESRs	Provide ESRs the scientific, technical and soft skills to guarantee employability	Training and mentorship
Scientific community	Provide 13 young researchers highly trained for an academic career	Training through research, transferable skills
Industrial community	Provide 13 young researchers highly trained for an industrial career	Training and secondments in THERACAT companies
	Provide 13 young researchers highly trained for entrepreneurship	ESADE entrepreneurship course and training

promote scientific efficacy and professional development. This includes **project management skills** by organizing collaborative aspects of projects, **team working skills**, developing effective **scientific communication skills** by dissemination of their research findings at departmental seminars or formal scientific meetings, community outreach events at host institutions aimed to **bring general scientific public awareness**, and networking opportunities with academic and industrial partners to create opportunities to accelerate their own independent scientific future careers. **This will result in increased employability with future job prospects beyond what would be available by training via a traditional PhD programme.** We are confident that, after the rigorous scientific training and exposure to industrial practices, our alumni will form the next generation of exceptionally trained, highly innovative and collaborative European scientists, prepared for competitive careers throughout Europe in academia, industry, private research institutions and government. On a final note: we acknowledge that in current days there is a still gender disparity both within the academic and industrial science research workforce (See section 1.3). Therefore, we will actively recruit young female participants to our research programme and educate all our fellows in gender-related issues in accordance with the Marie Curie Carter and Code with the support of the UAB observatory for equality (UAB). **This is in effort to minimise gender-related barriers and lead to a stronger and more innovative European science programme by creating a diverse workforce.**

2.2 Contribution to structuring doctoral/early-stage research training at the European level and to strengthening European innovation capacity

The social and economic burden of cancer in western society is main point of intervention of the European strategy for health (H2020 Societal Challenge: Health, demographic change and wellbeing). In this framework, new therapeutic strategies beyond the current paradigm are required to limit the effects of this disease on society and represent a key point for European innovation strategy. THERACAT aims to strengthen European position on novel cancer therapies on several sides: i) developing new approaches and clinical solutions based on bio-orthogonal catalysis; ii) training the new generation of multidisciplinary scientists for future medicine; iii) training of young entrepreneurs to promote European competitiveness on the strategic market of cancer therapies. Moreover, THERACAT will have a long lasting effect on the European training structure providing new ideas for the multidisciplinary training of young scientists. The approach of THERACAT will be in the future implemented in the local doctoral programmes in order to extend the too sectorial training offer. The consortium will promote interactions between the doctoral programmes of the members' countries, resulting in a more connected European academia. Finally, the consortium will pursue the goals of THERACAT applying for further funding for the consortium.

Stakeholder	Impact	Method
European innovation capacity	Novel anticancer therapies and marketable products	Research on novel catalysis-based therapies
	New generation of multidisciplinary scientists	Excellent multidisciplinary training of 13 ESRs
	Entrepreneurship	Training of 13 ESRs for entrepreneurship (ESADE)
European doctoral research training	Provide innovative training	THERACAT training programme (section 1.3.2)
	Improve intersectoral connections	Secondments, intersectoral training events

2.2.1 Contribution of the non-academic sector to the doctoral / research training

The aforementioned student-training programme described in Section 1.2 stems from a consultation between our industrial partner and academic beneficiaries in effort to identify and fulfil a workforce need for researchers with a strong multidisciplinary skillset and collaborative mind set for solving problems. Our industrial partners will significantly contribute to our training programme by providing access to state-of-the-art instrumentation, to research materials and **mentors that can help navigate the challenges from initial concept to a deliverable product.** Such interactions will lead to opportunities to learn scientific creativity and entrepreneurship skills in addition to receiving technical training. The on-site secondments at our industrial partner's campuses will give the participants of this programme first-hand exposure to life as an industrial scientist. Such interactions with industry are rare and provide a unique perspective for our ESRs. We will establish a personal Career Development Plan (see section 1.2.1) with each of our students. This will be discussed openly on an annual basis with a paired academic and industrial mentor for constructive input into the student's project progress and career goals (see Gantt Chart). **This dual**

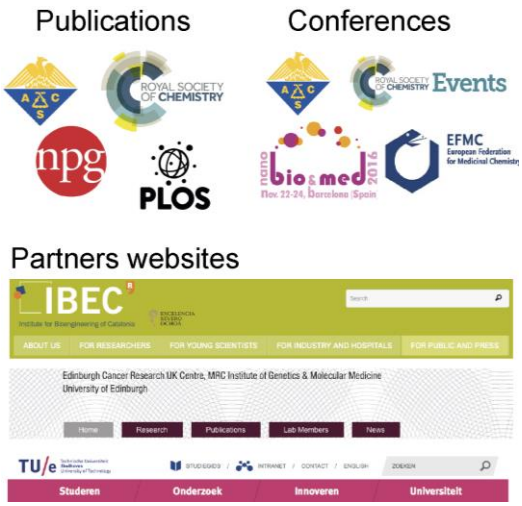
academic and industrial mentoring of the scientific development of the ESRs will afford a European workforce with enhanced research- and innovation capacity. Thanks to the close interactions with industry, our alumni, will have the “know-how” to traverse the complex interface of academia and industry with the potential to identify and forge new opportunities to enhance European biomedical science and European scientific innovation.

2.3 Quality of the proposed measures to exploit and disseminate the results

2.3.1 Dissemination of the research results

Effective dissemination of research results is one of the key aspects of the European Charter for Researchers, aimed at increasing the European science awareness and maximizing scientific impact. The THERACAT programme will fulfil these requirements by establishing a comprehensive dissemination programme.

Publications on scientific journals. We will set priority to publishing in high-impact journals and comply with the guidelines outlined in the Horizon 2020 calls, i.e., provide "open access" to our publications whenever possible/allowed to increase public accessibility and to attract talent and resources to Europe from abroad. Journals in the fields of chemical synthesis and catalysis, drug delivery and cancer research will be targeted as well as multidisciplinary journals. **Conferences.** Students will be encouraged to present their research findings and results at International conferences throughout their PhDs such as: the biennial International Symposium on Medicinal Chemistry (EFMC-ISMC), the National Meetings organized by the American Chemical Society (ACS), international cancer meetings (e.g. AACR Annual Meetings) and drug discovery meetings (e.g. BPS, ELRIG and MIpTec meetings which promote industry engagement). Together, these research conferences span both basic research and translational medicine increasing the scientific exposure and potential impact of the project. Notably THERACAT partners are involved in the organisation of conferences such as NanoBioMed Conference (IBEC) and the international symposium on bio-orthogonal strategies (CRUK in collaboration with the Royal Society of Chemistry). **Institutions websites.** Research findings will also be highlighted in the consortium labs’ websites (e.g. www.boomchemistry.com, http://www.ibecbarcelona.eu, http://www.meijerlab.nl) and in the CRUK’s website to attract traffic from broader audiences (http://www.cancerresearchuk.org/homepage). CRUK is a global leader in scientific innovation and promotion of the research outcomes will attract interests from academics and pharma industry alike, will be instrumental in promoting European Excellence and Competitiveness.



2.3.2 Exploitation of results and intellectual property

There is an increasing economic and societal drive for the development of novel cancer therapies with limited side effects and increased drug efficacy. Cancer care remained a mixed picture in 2015. Declining mortality rates, growing numbers of survivors, and exciting progress in treatment were set against the backdrop of increasingly unsustainable costs and a volatile practice environment. In 2015 the US Food and Drug Admiration (FDA) added 15 new drugs and biologic therapies to its list of more than 180 approved anticancer agents and expanded use for 12 previously approved treatments. With the change of patient population and aging of our population treatment requires constant improvement, offering new technologies with increase complexity of treatment of cancer, innovation is a requirement. This project aims to make this idea a reality by utilizing hybrid catalysts that can produce active anticancer drugs on site from biologically inactive prodrugs. The development of this technology could serve as an effective method for future cancer therapies and therefore holds a promise for the development of marketable products. **We foresee some possible exploitable technologies: i) novel implantable catalysts (peptide hydrogels, polystyrene resins) for solid tumour treatment; ii) targetable catalytic nanoparticles for metastatic cancer treatment and iii) new prodrugs.** We will work in close collaboration with the R&D teams at our industrial partners to discuss opportunities for technological product development or innovation opportunities (e.g. patents, biotech start-ups, technology transfer agreements, etc.). We will negotiate co-owner agreements for any joint technologies and commercial

agreement when and if they become necessary over the course of this collaborative research programme. Prior to all public releases research materials including poster, slides and flyers will be approved by both academic- and industrial partners for potential conflicts with respect to intellectual property matters.

2.4 Quality of the proposed measures to communicate the activities to different target audiences

2.4.1 Communication and public engagement strategy

The academic beneficiaries participating in this project have a strong track record in dissemination of scientific results and public community engagement. The consortium partners recognize the importance of public engagement in science and, to address this, the **Research Information & Engagement team of Cancer Research UK has joined the consortium activities.** The communication with the public will take place on several platforms and modalities. **Cancer-related charities.** Given the importance of gaining patients' trust for them to accept being treated by such novel technology, informing the public about the technology, the treatment and its unique benefits will be one of the primary objectives of the present ITN. With the support of CRUK, the students will become directly involved in speaking to patients. This will be done through charitable events organized by CRUK and arranging meetings with members and support groups of cancer organisations, e.g. Breast Cancer Now, Prostate Cancer Support Federation. Similar initiatives will be activated with the national cancer association (e.g. IBEC organizes events with AECC in Spain). **Social Media.** The results of THERACAT will be communicated to the public with social media such as Facebook, Twitter and LinkedIn. Dedicated accounts for the consortium will be created and used in synergy with the accounts of the single institutions **(e.g. CRUK has 284.000 followers on Twitter and over a million on Facebook). Blogs**. Several THERACAT institutions such as IBEC and CRUK publish divulgation blogs. These platforms will be used to disseminate the results in a simple and comprehensible way to the general public. **Videos.** TUE hosts an animation studio which activity focuses on the creation of 3D animation videos to explain scientific achievements to the general public. ESRs in collaboration with TUE will prepare videos explaining for a general audience the main goals of the project, its societal implications as well as promoting the value of mobility on a personal example. The videos will be added to the ETN and partners' websites, social media and blogs. **Conferences**. CRUK will provide engagement and communication training sessions at an annual scientific meeting organized for the consortium students. Through various programmes, including interactive shows, experiment demonstrations and workshops, this annual event will enable the students to improve their communication skills and share their research work across the consortium members. **General press articles** about the research being conducted and its implications will be submitted to media such as CORDIS website and related webs (News, research*eu results magazine, Horizon Magazine). **Science festivals**. Members of the consortium will participate to public events such as: the Edinburgh International Science Festival, one of largest science festivals in Europe (http://www.sciencefestival.co.uk/), the European Researchers' Night, and Night of art and Science in Groningen. **Local media.** The students will

Stakeholder	Action	Method
Scientific community	Disseminate the results of THERACAT	Conferences, Publications, Partners websites
Industrial community	Disseminate the results of THERACAT	Conferences
	Promote intersectoral collaborations	Secondments, intersectoral training events
General public	Disseminate the results of THERACAT	Social media, Websites, Blogs, Radio/TV, videos
	Engage the public	Science Festivals, "open doors" events
Cancer patients	Engage and inform patients	Charitable events (CRUK)

also promote their works in university newsletters, local press or radio/TV programmes to inform the general public of the discoveries and benefits related to the project proposed herein.

3. Quality and Efficiency of the Implementation

3.1 Coherence and effectiveness of the work plan

3.1.1 Work Packages description

Table 3.1 a Description of Work Packages

WP0	**Management and coordination**
Lead Beneficiary: IBEC	**Start Month: 1 – End Month: 48**
Objectives: To ensure a smooth management of the Network, including administrative coordination, contractual and financial management, and meetings organisation.	
Description of Work and Role of Specific Beneficiaries / Partner Organisations **Task 0.1.** Gender-balanced ESRs recruitment (**TUE**, UAB). **Task 0.2.** Coordination of the ETN, including scientific and financial management and reporting to EC (IBEC). **Task 0.3.** Network meetings organisation (IBEC).	
Deliverables: D0.1-D0.5. Network Meetings minutes (M1, M12, M24, M36, M48). **D0.6.** Recruitment completion (M12). **D0.7-D0.10.** Periodic management, economic and scientific reports (M12, M24, M36, M48).	
WP1	**Catalysts synthesis**
Lead Beneficiary: TUE	**Start Month: 6 – End Month: 42**
Objectives: **1.** Synthesis of metal complexes for bio-orthogonal catalysis; **2.** Synthesis and formulation of nano/micro particles loaded with catalysts; **3.** Characterization of (nano)catalysts structure and activity.	
Description of Work and Role of Specific Beneficiaries / Partner Organisations **Task 1.1.** Synthesis of palladium (TUE) and ruthenium (GRO) complexes for dye/drug uncaging. **Task 1.2.** Formulations of catalytic polymeric nanoparticles (TUE), micelles (TAU) and vesicles (TEVA). **Task 1.3.** Studying of (nano)catalysts structure using spectroscopy (GRO, TUE), SAXS (TUE, TAU), fluorescence spectroscopy (TUE), light scattering (TEVA, TAU, TUE).	
Deliverables: D1.1. Novel metal complexes for bio-orthogonal catalysis (M16). **D1.2.** Novel nanostructures loaded with Ru or Pd catalysts (M28). **D1.3.** Structure-activity relations description for the selected catalysts (M42).	
WP2	**Prodrugs design and synthesis**
Lead Beneficiary: EDI	**Start Month: 6 – End Month: 42**
Objectives: 1. Synthesis of prodrugs; **2.** Synthesis of prodyes; **3.** Understanding prodrug/dyes activation kinetics, stability and turnover rates.	
Description of Work and Role of Specific Beneficiaries / Partner Organisations **Task 2.1.** Synthesis of a library of anti-cancer drugs (e.g. selumetinib and panobinostat) protected with propargyl/allyl groups (EDI). **Task 2.2.** Synthesis of fluorescent dyes such (rhodamines, cyanines) protected with propargyl/allyl groups (IBEC). **Task 2.3.** Spectroscopic (bulk) and microscopic evaluation (single molecule) study of catalysis (EDI, IBEC).	
Deliverables: D2.1. Library of anticancer prodrugs (M16). **D2.2.** Set of 2-3 fluorescent prodyes (M28). **D2.3.** Structure-activity relations description for the selected catalysts (M42).	
WP3	**In vitro delivery and imaging**
Lead Beneficiary: IBEC	**Start Month: 9 – End Month: 45**
Objectives: 1. Synthesis of a library of cell-targeted catalysts carrier; **2.** Understanding cell-material interactions with optical microscopy; **3.** Screen the best-performing catalysts in in vitro models.	
Description of Work and Role of Specific Beneficiaries / Partner Organisations **Task 3.1.** Synthesis catalysts carriers bearing targeting ligands (TUE, BAS, BGX). **Task 3.2.** Fluorescence and super resolution optical imaging of carriers' interactions with cancer cells (IBEC, TUE). **Task 3.3.** Test the efficiency of prodrug conversion in 2D and 3D cancer models (BGX, TUE, BAS, IBEC).	
Deliverables: D3.1. Library of targeted catalysts carriers (M18). **D3.2.** Description of the structure-activity relations of the material-cell interactions (M30). **D3.3.** Selection of the best catalyst in vitro (M36).	

WP4	In vivo evaluation
Lead Beneficiary: TAU	**Start Month: 9 – End Month: 45**
Objectives: 1. Establish reliable in vivo cancer models; **2.** Study toxicity and biocompatibility of the selected catalysts; **3.** In vivo imaging of catalyst localization and efficacy; **4.** Test in vivo anticancer efficacy.	
Description of Work and Role of Specific Beneficiaries / Partner Organisations **Task 4.1.** Create mCherry fluorescent tumour in vivo models (TAU). **Task 4.2.** In vivo administration of the catalysts and study of biocompatibility (TAU, EDI, TAG). **Task 4.3.** Use intravital optical and PET imaging to study catalyst localization and efficacy (BGX, TUE, BAS, IBEC). **Task 4.4.** Test in vivo efficacy against melanoma, breast and prostate cancer (TAU).	
Deliverables: D4.1. Set of mCherry-labeled orthotopic models of cancer in mice (M18). **D4.2.** Results of the biocompatibility tests for the catalysts (M22). **D4.3.** Results of in vivo imaging of catalysts localization and efficacy (M36). **D4.4.** Results of in vivo evaluation of anticancer activity (M45).	
WP5	**Training**
Lead Beneficiary: TAU	**Start Month: 1 – End Month: 48**
Objectives: To coordinate all actions related to the training, supervision and progress monitoring of ESRs.	
Description of Work and Role of Specific Beneficiaries / Partner Organisations **Task 5.1.** Training events organisation containing scientific and complementary training courses (TAU). **Task 5.2.** Personal Career Development and Employment Plans for all ESRs (TAU). **Task 5.3.** Periodic individual assessment of ESRs (IBEC). **Task 5.4.** Doctoral studies (GRO).	
Deliverables: D5.1-D5.5. Training events (M9, M18, M24, M30, M36). **D5.6-D5.8.** Personal Career Development Plans (M10, M24, M36. Responsible: supervisor). **D5.9-D5.13.** ESRs periodic short reports and AC recommendations (M12, M18, M24, M30, M36). **D5.14.** Personal Employment Plans (M40. Responsible: supervisor).	
WP6	**Dissemination and outreach**
Lead Beneficiary: EDI	**Start Month: 1 – End Month: 48**
Objectives: To promote the efficient and effective awareness of academic and industrial scientists as well as general public about THERACAT, its training potential and results.	
Description of Work and Role of Specific Beneficiaries / Partner Organisations **Task 6.1.** THERACAT webpage including a private intranet for internal communication (**EDI**). **Task 6.2.** Open-access publications in high-impact journals and patents (EDI). **Task 6.3.** Work presented in international conferences and workshops (EDI). **Task 6.4.** THERACAT social media account creation and management (**EDI**, CRUK). **Task 6.5.** Communication activities incl. cancer-related charity events, science festivals, European Researchers' Night, general press articles, THERACAT video (**EDI**, CRUK). **Task 6.6.** ETN international conference (IBEC).	
Deliverables: D6.1. Website completion (M6). **D6.2-D6.5.** Periodic report on dissemination (papers, patents, presentations in conferences) and participation in outreach activities (M12, M24, M36, M48). **D6.6.** THERACAT video (M24). **D6.7-D6.8.** General press articles submitted to EU magazines (M30, M48). **D6.9.** THERACAT conference (M42).	

3.1.2 List of major deliverables

Table 3.1 b Deliverables List

Scientific Deliverables						
Number	**Deliverable Title**	**WP**	**Beneficiary**	**Type**	**Diss.**	**Date**
D1.1	Novel metal complexes for bio-orthogonal catalysis	1	GRO	R	CO	M16
D2.1	Library of anticancer prodrugs	2	EDI	R	CO	M16
D3.1	Library of targeted catalysts carriers	3	TUE	R	CO	M18
D4.1	Set of mCherry-labeled orthotopic models of cancer in mice	4	TAU	R	CO	M18
D4.2	Results of the biocompatibility tests for the catalysts	4	TAU	R	CO	M22
D1.2	Novel nanostructures loaded with Ru or Pd catalysts	1	TEVA	R	CO	M28
D2.2	Set of 2-3 fluorescent prodyes	2	IBEC	R	CO	M28
D3.2	Description of the mechanisms material-cell interactions	3	IBEC	R	CO	M30
D4.3	Results of in vivo imaging of catalysts localization and efficacy	4	TAG	R	CO	M36
D1.3	Structure-activity relations description for the selected catalysts	1	TUE	R	CO	M42

D2.3	Structure-activity relations description for the selected prodrugs	2	EDI	R	CO	M42
D3.3	Selection of the best catalyst in vitro	3	BGX	R	CO	M36
D4.4	Results of in vivo evaluation of anticancer activity	4	EDI	R	CO	M45

Management, Training, Recruitment and Dissemination Deliverables						
Number	**Deliverable Title**	**WP**	**Beneficiary**	**Type**	**Diss.**	**Date**
D0.1-D0.5	Network Meetings minutes (5)	0	IBEC	ADM	CO	M1,12,24,36,48
D6.1	Website completion	6	EDI	ADM	PU	M6
D5.1-D5.5	Training events (5)	5	TAU	ADM	PU	M9,18,24,30,36
D5.6-D5.8	Personal Career Development Plans (3)	5	Recruiting beneficiary	ADM	CO	M10,24,36
D0.6	Recruitment completion	0	TUE	ADM	CO	M12
D5.9-D5.13	ESRs periodic short reports and AC recommendations (5)	5	IBEC	R	CO	M12,18,24,30,36
D0.7-D0.10	Periodic management, economic and scientific reports (4)	0	IBEC	R	CO	M12,24,36,48
D6.2-D6.5	Periodic report on dissemination (papers, patents, presentations in conferences) and participation in outreach activities (4)	6	EDI	R	CO	M12,24,36,48
D6.6	THERACAT video	6	IBEC	PDE	PU	M24
D6.7-D6.8	General press articles submitted to EU magazines	6	IBEC	PDE	PU	M30,48
D5.14	Personal Employment Plans	5	Recr. Benef.	ADM	CO	M40
D6.9	THERACAT conference	6	IBEC	PDE	PU	M42

3.1.3 List of major milestones

Table 3.1 c Milestones List

Milestones					
Number	**Title**	**WP**	**Beneficiary**	**Date**	**Means of Verification**
M01	Guidelines for recruitment and assessment of ESRs, PCDPs, strategy for dealing with scientific misconduct	WP0	IBEC	4	Guidelines available to all partners and approved by SB
M02	Assessment Commissions	WP5	IBEC	6	AC designated and operative
M03	Intranet and extranet website	WP6	EDI	6	Tool completed and functional
M04	ESRs Recruitment and PCDPs	WP0, WP5	Recruiting beneficiary	12	Employment contracts and agreement on the strategy for dealing with scientific misconduct properly signed and PCDPs ready for all ESRs
M05	ESR local doctoral studies	WP5	Recruiting beneficiary	12	All ESRs accepted and enrolled in the corresponding doctoral programme
M06	Synthesis of the first prodye	WP2	IBEC	18	Spectroscopic characterization
M07	Synthesis of the first catalyst	WP1	GRO	18	Spectroscopic characterization and activity test
M08	Synthesis of the first prodrug	WP2	EDI	18	Spectroscopic characterization
M09	Establishments of the protocol for super resolution imaging in cells	WP3	IBEC	18	Image resolution analysis
M10	Establishments of the protocol for in vivo cancer imaging	WP4	TAG	18	Image analysis
M11	First catalyst supported on a nanoparticle	WP1	TUE	21	Spectroscopic characterization
M12	Establishment of an mCherry orthotopic cancer model	WP4	TAU	21	Histology
M13	Midterm project assessment	WP0	IBEC	24	Project follows as planned
M14	Midterm dissemination and outreach activities assessment	WP6	TAU	24	Number and quality of publications, conferences attended, outreach activities conducted
M15	Synthesis and evaluation of the first cell-targeted nanocarrier	WP3	TUE	24	Cell targeting experiments
M16	Achievement of a library of prodrugs for several cancer types	WP2	EDI	28	Spectroscopic characterization

M17	A library of supported catalysts fully characterized and ranked in efficiency	WP1	EDI	30	Spectroscopic characterization
M18	Toxicity and delivery screening in a 3D cancer model	WP3	BGX	32	Biological assays
M19	Anticancer activity of the nanocatalysts against melanoma, breast and prostate cancer	WP4	TAU	36	In vivo assays

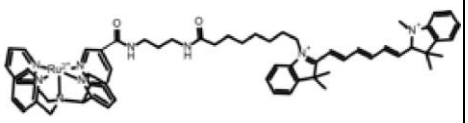
3.1.4 Fellow's individual projects

Table 3.1 d Individual Research Projects

ESR 1 - GRO	Novel Ru and Pd Complexes of Polypyridine for Catalysis in Living Cells	PhD: Yes	Deliv.: 1.1, 3.1	Start date: M6	Duration 36	WP1

Objectives: **1.** Development of Ru and Pd complexes for catalytic uncaging of prodrugs in cancer cells; **2.** Synthesis of targeted metal complexes by conjugation to targeting moieties; **3.** Development of light activable Ru complexes for spatial and temporal control over catalytic uncaging of prodrugs.

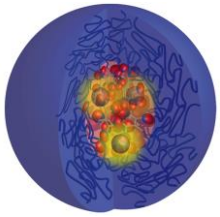
Description: In this project, we aim to develop Ru(II) and Pd(II) complexes of polypyridine ligands for catalytic uncaging of anti-tumour drugs in cancer cells. Metal complexes of polyridyl ligands such as phenanthroline, terpyridine, TPA and N4Py are of interest because of their broad catalytic scope and, as recently shown in our group, are efficiently taken up by cancer cells. Moreover, targeting to specific cellular location can be achieved by conjugation to hydrophobic dyes targeting, for example, the mitochondria. We will prepare a variety of Ru(II) and Pd(II) complexes and investigate them in uncaging of prodrugs, first in model reactions and then in vitro. When required, the complexes will be incorporated in delivery vehicles such as single chain polymer nanoparticles, micelles and lipidic nanoparticles developed in WP1. Finally, light activable variants of active Ru(II) complexes will be prepared and tested by ligation of nitrile ligands to the open coordination sites, which can be dissociated by light irradiation.



Planned secondments: EDI – Prodrug uncaging in vitro (M12, 3 months); TEVA – Formulation (M24, 3 months).	Expected results (deliverables): Pd and Ru complexes for catalytic uncaging of prodrugs (D1.1); specific targeting of complexes to cellular location (D3.1); light activable Ru complexes for uncaging of prodrugs (D1.1)

ESR 2 – TAU (Amir)	Micellar catalysts	PhD: Yes	Deliv.: 1.1, 1.2	Start date: M6	Duration 36	WP1

Objectives: **1.** Develop synthetic methodology for amphiphilic polymers with a ligand; **2.** Metal complexation and self-assembly of micelles; **3.** Demonstrating catalytic capability and its optimisation.

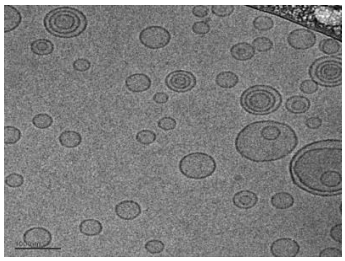


Description: ESR2 will develop block-copolymer amphiphiles bearing mono or bivalent ligands at the focal point of the amphiphilic polymer exactly between the hydrophilic and hydrophobic blocks. The ligand will be utilized for complexation of transition metals, which will serve as catalytic centres for the activation of the proposed prodrugs (WP2). Upon their self-assembly in water, these amphiphiles will form polymeric micelles, which will contain high local concentration of catalytic entities at the interface of the hydrophilic shell and the hydrophobic core. The hydrophobic part will be based on dendritic structures due to their high structural precision and modularity, which will allow fine-tuning of the amphiphilicity of the polymers and their micellar stability. Polymers of various compositions will be synthesized and studied (WP1, 3-4)

Planned secondments: GRO – Metal catalyst synthesis (M12, 3 months); TAG – in vivo micelle imaging (M32, 4 months).	Expected results (deliverables): Polymeric amphiphiles with metal binding ligands (D1.1); metal containing polymeric micelles (D1.2); Micelles with catalytic activity (D1.2)

ESR 3 - TEVA	Oral nano delivery – Formulation design and characterization	PhD: Yes	Deliv.: 1.2, 1.3	Start date: M6	Duration 36	WP1

Objectives: **1.** Develop an oral nano-delivery formulation; **2.** In-vitro characterization of the obtained system via different spectroscopies, such as SAXS, SLS and TEM; **3.** Large-scale GMP manufacturing of an oral formulation

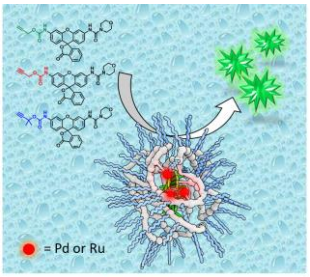


Description: The emerging field of nanotechnology seeks to exploit distinct technological advantages of nanoscience. It is not only about the realization of devices, constructs, methods, and techniques at this size scale, but also about the functional enhancement gains over conventional technology. Although development of an oral-nano formulation is very challenging, it serves as an unmet need, which we would like to address. Nanoparticles (NPs) formation represents a significant industrial challenge because of the physical limitation for sub-micron sizing, physicochemical stability, purity, and concerns about the large-scale cGMP-compliant manufacturing of such products. TEVA has the capabilities and the experience in moving a product from the academy to the market, finding the best formulation, which will exhibit improved pharmacokinetic profile and reduced toxicity. *In-vitro* and *in-vivo* characterization of the NPs will help us better understand our systems and find the best candidate for scale-up manufacturing.

Planned secondments: IBEC – NP imaging (M18, 4 months); **TUE** – SAXS characterization of NP (M30, 3 months).	**Expected results (deliverables)**: Development of lipid/polymer-based nano formulation in lab scale (D1.2); Extensive physicochemical characterization of the NPs (D1.3); NPs GMP Manufacturing in larger scale (scale-up) (D1.2)

ESR 4 - TUE	Single chain polymeric nanoparticles for fast prodrug activation	PhD: Yes	Deliv.: 1.1 - 1.3	Start date: M6	Duration 36	WP1

Objectives: **1.** Fast and scalable synthesis of SCPNs with Pd(0), Pd(II) or Ru(II) catalytic centres; **2.** Quantification of the turnover frequencies of catalysts and substrates; **3.** Identification of a few best performing ligand/metal and protective group combinations.

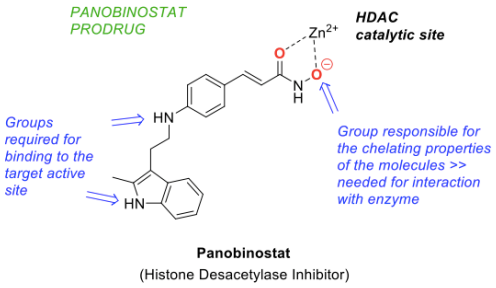


Description: ESR4 will focus on 1) the evaluation of protecting groups that cleave fast in the presence of selected transition metals and 2) the synthesis of a family of catalytically active amphiphilic polymers that, driven by supramolecular interactions, fold around a transition-metal based centre into compact conformations: single chain polymeric nanoparticles (SCPNs). We select Pd(0), Pd(II) and Ru(II) as the transition-metal-based catalysts of choice because of their relatively high compatibility with complex media. The SCPN's catalysts activity will be assessed *in vitro* by a catalyst-activable caged fluorescent rhodamine (Rho, WP2). By screening appropriate ligands attached to the SCPNs that are (1) stable in biological conditions, (2) show sufficiently strong binding to the metal to prevent leaching, and (3) show high activity in the deprotection reactions, we will identify a fast SCPN for Rho deprotection. With the best performing system, we will also investigate the *in vitro* deprotection rates of selected prodrugs based on 5-FU and Panobinostat (developed in WP2), with the aim to investigate in how far the structure of the drug affects the catalyst efficiency.

Planned secondments: BAS – synthesis of Ru catalysts (M22, 3 months); **TEVA** – industrial formulation of SCPN (M30, 3 months).	**Expected results (deliverables)**: Prodyes activated by Pd or Ru catalysts (D1.1); Optimised SCPN catalysts for prodyes and prodrugs (D1.2); Catalysts stable and active in a complex medium (D1.3)

ESR 5 - EDI	Prodrug design and synthesis	PhD: Yes	Deliv.: 2.1, 2.3	Start date: M6	Duration 36	WP2

Objectives: **1.** Synthesis of prodrugs; **2.** Validation of Pd-mediated drug release in vitro; **3.** Reduction of prodrugs' activity by 100-fold relative to parent drug; **4.** Demonstration of Pd-triggered release of the functional drug in cell culture.

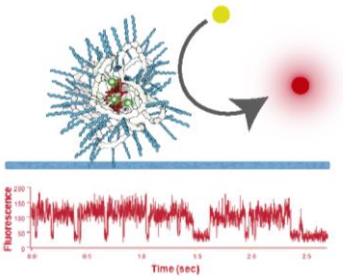


Description: ESR5 will investigate the development of a series of biochemically-stable (= bio-orthogonal) prodrugs specifically designed to become active upon reaction with Palladium (Pd) catalysts. We will generate and test Pd-activated prodrugs using a range of Pd-labile protecting groups. Such studies will enable to expand the arsenal of chemotherapy drugs that can be exploited through this novel spatially-targeted strategy, including therapeutics that are either currently used in the clinic for melanoma and breast cancer treatment. To maximize the clinical impact of the strategy, Pd-labile prodrugs will be developed from a selection of therapeutics with different mode of actions, e.g. HDAC inhibitors (panobinostat), kinase inhibitors (dabrafenib and selumetinib) and alkylating agents (duocarmycin). Prodrugs' sensitivity to Pd will be tested using the methodology developed by ESR6. The efficacy of the deactivation strategy (= bio-orthogonality) will be determined by performing dose response studies with the prodrug and the parent drug in cancer cell lines, which will be followed by the study of the Pd-mediated release of each drug using standard phenotypic assays.

Planned secondments: TAG – Pro-imaging PET agents (M24, 4 months); **TAU** – Test micelles catalysts (M34, 3 months).	**Expected results (deliverables)**: Synthesis of 6-10 prodrugs (D2.1); Pd-mediated drug release ranked by reaction kinetics (D2.3); 2-4 prodrugs showing >100-fold reduction in activity (D2.3); Prodrug activation in cell culture (D2.3).

ESR 6 - IBEC	Single molecule imaging of prodyes activation	PhD: Yes	Deliv.: 2.2, 2.3	Start date: M6	Duration 36	WP2

Objectives: **1.** Synthesis of prodyes; **2.** Develop a method for single catalytic events imaging and measure of the turnover rate and stability of nanocatalyst; **3.** Measure and compare different families of natural and synthetic catalysts.



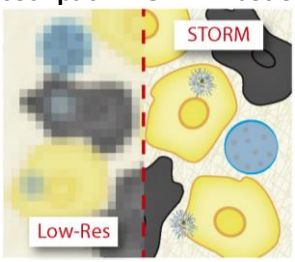
Description: ESR6 will develop a super resolution method to test at the single molecule level the catalytic efficiency of the nanomaterials proposed in THERACAT. Catalytically-activable prodyes (e.g. rhodamines and cyanines) will be synthesize to probe the efficiency of the catalyst developed in WP1. We anticipate that measuring catalytic activity and the single molecule level is crucial for synthetic structures due to the heterogeneity induced by the polydispersity in the synthesis. Individual catalyst will be anchored on a glass surface and a prodye substrate added to the solution. Single fluorescence events will be observed at any catalytic conversion using a TIRF microscope. The time profile of such events will provide information of the catalytic efficiency, turnover and stability of the catalyst and the distribution of such properties among a large population of nanostructures. A variety of structures created in WP1 (ESR1-4) will be tested and compared with natural enzymes.

Planned secondments: TUE – synthesis of SCPN for imaging (M24, 3 months); **CRUK** – training in outreach (M38, 3 months).	**Expected results (deliverables)**: Prodyes synthesis (D2.2); Data on catalyst turnover and stability (D2.3); Overview of the structure-catalysis relations (D2.3)

ESR 7 - IBEC	Super resolution imaging of catalytic nanoparticles delivery	PhD: Yes	Deliv.: 3.2, 3.3	Start date: M9	Duration 36	WP3

Objectives: **1.** Develop a method for STORM nanocatalyst imaging; **2.** Imaging the localization and amount of nanocatalyst in different models; **3.** STORM imaging of prodye activation in different models.

Description: ESR7 will use super resolution imaging to track the delivery and the activity of nanocatalysts in different biological models. Super resolution microscopy allows for multicolour imaging in cells and tissues with 20 nm resolution and is therefore an ideal tool to study the interactions of nanostructured materials with living matter. Different nanostructures (e.g. ESR1-4) will be labelled with Cyanine dyes suitable for Stochastic Optical Reconstruction Microscopy (STORM) and administered to i) culture of cancer cells; ii) 3D models of tissue environment (ESR9). At the desired time point the sample will be fixed and imaged with STORM revealing with high accuracy the localization and amount of catalyst that reach the target. With an analogous procedure, we will be able to localize and quantify the amount of activated prodye in different biological model simply using a STORM-compatible prodyes.

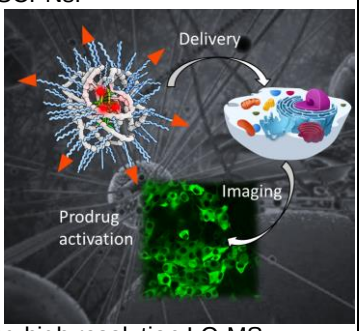


Planned secondments: BGX – imaging of gel models (M21, 3 months); **TAU** – in vivo and ex vivo imaging of catalysis (M30, 4 months).	**Expected results (deliverables)**: Protocol for nanocatalyst STORM imaging (D3.2); Data on nanocatalyst localization in cell and 3D cultures (D3.2); Map of catalytic activity in cells and tissues (D3.3)

ESR 8 - TUE	Catalytic single chain polymeric nanoparticles targeted delivery	PhD: Yes	Deliv.: 3.1, 3.3	Start date: M9	Duration 36	WP3

Objectives: **1.** Preparation of SCPN with peripheral GE11 peptide; **2.** Assessment of targeted delivery of GE11-SCPNs into cancer cells; **3.** Development of a protocol for inter- and/or intracellular prodrug activation by SCPNs.

Description: ESR8 will focus on (1) assessing targeted delivery strategies to cancer cells for the SCPNs developed in WP1 and (2) evaluating the efficacy of prodrug activation of protected Panobinostat and fluorouracil in cells. The best performing SCPN will be functionalised with the GE11 peptide which shows high specific binding to the EGFR receptors overexpressed in cancer cells (e.g. breast cancer). The obtained SCPNs will also be provided with a suitable fluorescent label and untargeted and targeted delivery strategies will be investigated using imaging techniques (confocal fluorescence microscopy, STORM, ESR7) and compared for their efficiency. Then, the SCPNs will be provided with the best performing catalytic system and extracellular and intracellular catalytic activity of the catalytically active SCPNs will be assessed. The SCPNs will be used to activate selected prodrugs (protected 5-FU and Panobinostat) inside and outside cells. Toxicity assays will be applied to see the efficacy of the deprotection reactions, and the results will be quantified using high resolution LC-MS.



Planned secondments: IBEC – STORM imaging of SCPN delivery (M21, 4 months)**; BGX** – test activity in gel cancer models (M36, 3 months).	**Expected results (deliverables)**: Synthesis of GE11-targeted SCPN (D3.1); Synthesis of catalytical targeted SCPN (D3.1); prodrug activation in cancer cells (D3.3)

ESR 9 - BGX	Development of Peptide Hydrogels for Use in Anti-Cancer Strategies	PhD: Yes	Deliv.: 3.1, 3.3	Start date: M9	Duration 36	WP3

Objectives: **1.**Design and synthesise hydrogels mimicking both healthy and cancerous tissue; **2.** Development of a realistic *in vitro* 3D cancer model using peptide hydrogels; **3.** Gain insight into the ability of peptide hydrogels to act as nanoparticle carriers

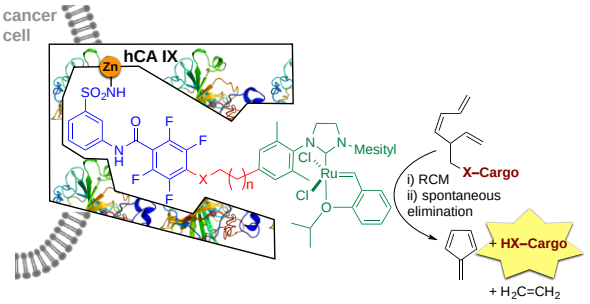
Description: ESR9 will design and optimise peptide-based hydrogels to aid in the development of the proposed bio-orthogonal catalysis approach to cancer treatment. The project will focus on two main areas of investigation. (1) It is known that cancer tissues have different, much stiffer microenvironments compared to those of normal tissues. The stiffness of the extra cellular matrix (ECM) has considerable impact on cell behaviour, as it affects the differentiation, proliferation, and migration of cells. As such, using Biogelx technology, the ESR will develop hydrogels with defined chemical compositions and tuned mechanical properties, which will possess the ability to mimic the properties of both healthy and cancerous tissue. ESR9 will use these newly developed hydrogels to build a realistic *in vitro* 3D model with which to test the nanoparticle and prodrug delivery strategies developed in other WPs. (2) A second aspect to the project will involve investigating peptide hydrogels as the nanoparticle carrier material itself. Both aspects of the project will involve assembly and characterisation of these peptide based nanostructures using a range of spectroscopy and microscopy techniques, as well as analysis of mechanical properties using rheology.

Planned secondments: TUE – synthesis of gel-based catalysts (M27, 3 months); **IBEC** – imaging gels with STORM (M36, 4 months).	**Expected results (deliverables)**: Peptide hydrogel formulations tuned to mimic cancer (D3.3); In vitro model for testing nanoparticle delivery (D3.3); Peptide hydrogel formulations for therapeutic delivery of catalytic NP (D3.1)

ESR 10 - BAS	Targeting Human Carbonic Anhydrase IX for Drug Release via Metathesis	PhD: Yes	Deliv.: 3.1, 3.3	Start date: M9	Duration 36	WP3

Objectives: **1.** Identify metathesis catalyst activated upon binding to hCA IX; **2.** Uncage cargo (fluorophore or drug) by ring-closing metathesis; **3.** Fluorophore- or Drug-release by ring-closing metathesis on the surface of cancer cell overexpressing hCA IX.

Description: In the past decade, the Ward group has developed a series of artificial metalloenzymes for a variety of bio-orthogonal reactions. For this purpose, a catalyst precursor (green) is activated upon incorporation within a host protein (ribbon display) via a high affinity anchor (blue). We have shown in the past that i) hCA II is an outstanding host for the creation of artificial metathases and ii) artificial metathases are fully biocompatible, air stable and can be performed *in vivo*.[4] To target the tumour site, it is proposed to exploit hCA IX to specifically accumulate and activate a metathesis catalyst on the surface of cancer cells. With this goal in mind, the fluorinated sulfonamide anchor will be linked via a spacer (red) to a metathesis catalyst. Initial experiments will be carried out with diallyl-*N*-tosylamide as model substrate. Having identified an active metathesis catalyst for incorporation within hCA IX, the artificial metathase will be screened for its RCM activity towards an heptatriene substrate bearing either a caged fluorophore or a caged drug. Upon RCM, a spontaneous elimination occurs via an aromatic transition state, thus uncaging the fluorophore or the drug. For the synthesis of the triene substrates, ESR10 will spend three months at EDI. Having identified a suitable precatalyst, activated upon incorporation in hCA IX, experiments will be performed in the presence of cells overexpressing hCA IX on their cell surface. To facilitate its delivery to cancer cells, the catalyst precursor will be non-covalently incorporated in a variety of delivery vectors including:, hydrogels, micelles, SCNPs, lipidic NPs. For this purpose, ESR10 will spend 3 months at TEVA to adapt their NPs to the delivery of the metathesis catalyst.

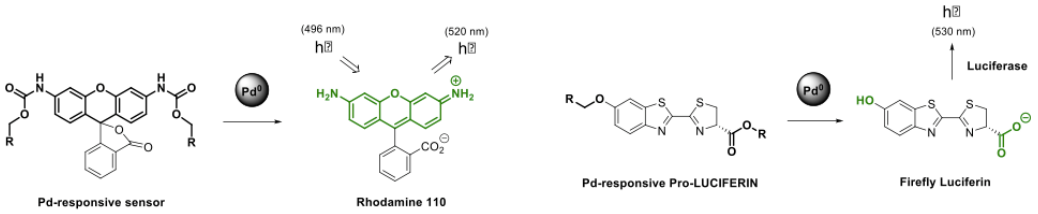


Planned secondments: EDI – synthesis of caged prodrugs (M27, 3 months); **TEVA** – encapsulate catalyst in lipid NP (M36, 3 months).	**Expected results (deliverables)**: synthesis of five metathesis catalysts (D3.1); reactivity profile of two caged fluorophores and one drug uncaged upon RCM (D3.3); reactivity profile upon incorporation within hCA IX (D3.3)

ESR 11 - EDI	Pd in vivo implants and Pd-activatable tools	PhD: Yes	Deliv.: 4.2 - 4.4	Start date: M9	Duration 36	WP4

Objectives: **1.** Synthesis of Pd-implants; **2.** Synthesis of probes; **3.** Validation of Pd-mediated activation in vitro; **4.** In vivo compatibility studies of Pd-implants; **5.** Demonstration of Pd-triggered probe activation in vivo.

Description: The student will develop novel implantable Pd-devices and a range of chemical tools that will allow us to evaluate the catalytic activity of metallic Pd *in vivo* (e.g. surgically-implanted in tumour xenografts or tissues) and expend its scope. To facilitate surgical implantations, Pd-devices of appropriate size (> 4mm) will be developed. ESR11 will investigate the manufacture of larger devices by physically merging them in an appropriate mould. To enable the localised use of naked Pd nanoparticles (NP), a novel technique will be tested in which NP are "bagged" in sealed sachets made out of dialysis tubing. The catalytic capabilities of Pd-implants will be investigated using Pd-responsive sensors prepared from well-established fluorescent, bioluminescent and chemoluminiscent reagents (see Figure) and tetrazines (for click-to-release strategies, ESR12). Masking of reagents' strategic groups will block their reporting properties, which will only be restored upon Pd catalysis (see Figure). In vitro comparative analysis of the probes will allow ranking the best probes for in vivo sensing. In collaboration with consortium partners, animal studies will be performed to determine the compatibility of the devices. After tumour mass formation, devices will be surgically implanted in the tumour and the chosen sensor/protetrazine intravenously-administered. Mice health will be monitored over time and sensor activation analysed by non-invasive in vivo optical imaging.

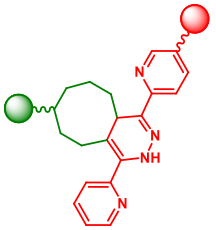


Planned secondments: BGX – gel-based implants (M21, 3 months); **TAU** – in vivo imaging (M36, 3 months).	**Expected results (deliverables)**: Synthesis of Pd-implants (D4.2); Synthesis of 6-8 probes (D4.2); Pd-mediated sensor activation ranked by reaction kinetics (D4.3); 2-4 implants show total biocompatibility (D4.2); In vivo activation of probes / tools (D4.4)

ESR 12 - TAG	in vivo click and click-to-release strategies for catalysts	PhD: Yes	Deliv.: 4.3, 4.4	Start date: M9	Duration 36	WP4

Objectives: **1.** Develop in vivo radioimaging approaches for bio-orthogonal catalysts; **2.** Develop in vivo radioimaging approaches for the bio-orthogonal substrate; **3.** Develop catalyst activation approaches based on click-release chemistry in vivo.

Description: ESR12 will develop in vivo click-conjugation and click-release chemistry to aid the development and improve the function of bio-orthogonal catalysts. Click-conjugation chemistry will be used to radiolabel and image catalysts and their activity in vivo. Depending on the nature of the catalyst the radiolabeling will occur pre- or post-catalyst administration. In addition, radioimaging agents will be designed that localize at the target following catalyst-mediated uncaging. Regarding

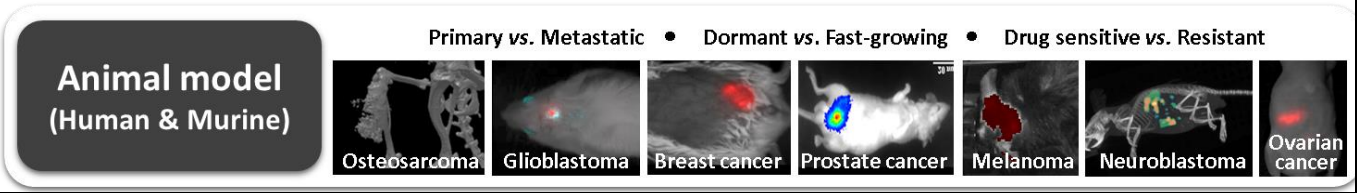


click-release chemistry, the ESR will develop strategies to activate target-localized catalysts, enabling temporal control over catalyst activity, for example to reduce premature catalyst deactivation. Likewise, click-release concepts will be applied to selectively destabilize catalyst-containing nanoparticles at the target site, unveiling the delivered catalysts and thus enabling efficient catalyst-substrate interaction.	
Planned secondments: EDI – pro-PET agents synthesis (M18, 3 months); **BAS** – activable PET probe (M28, 3 months).	**Expected results (deliverables)**: In vivo imaging of NP- and protein-based catalysts (D4.3); In vivo imaging of radiolabeled substrate activated by catalyst (D4.3); In vivo release and/or activation of a target-bound catalyst by click-release chemistry (D4.4)

ESR 13 – TAU (Satchi-Fainaro)	**In vivo imaging and biological activity of prodrug activation**	**PhD**: Yes	**Deliv.**: 4.1 - 4.4	**Start date:** M9	**Duration** 36	**WP4**

Objectives: **1.** Establish mCherry-labeled orthotopic models of cancer in mice; **2.** Evaluation of biodistribution of the newly-synthesized prodyes; **3.** Evaluation of anticancer activity of the activated prodrugs.

Description: ESR13 will establish mCherry-labeled orthotopic models of cancer in mice. These models will enable the biological evaluation of polymers of various compositions. Intravital non-invasive optical imaging will be used to follow-up tumor progression (mCherry/GFP) and nanoparticles' biodistribution (near infra-red fluorescence). Once the various prodrugs and prodyes will be synthesized and characterized (WP 1-2), they will be evaluated for their in vitro and in vivo biological activity, including tumour accumulation, biodistribution in healthy organs, safety profile (WBC count, neurotoxicity, cardiotoxicity, blood chemistry), and antitumor activity (WP 3-4). During the project period of 3 years, compounds will be screened for their safety, and activity and optimized according the acquired results and then re-tested following improvement of synthesis.



Planned secondments: IBEC – imaging of ex-vivo samples (M21, 4 months); **TEVA** – oral formulations (M36, 3 months).	**Expected results (deliverables)**: Establish mCherry orthotopic models (D4.1); Intravital non-invasive imaging of catalyst and prodye activation (D4.3); Biocompatibility and toxicity profile (D4.2); *In vivo* anticancer efficacy (D4.4).

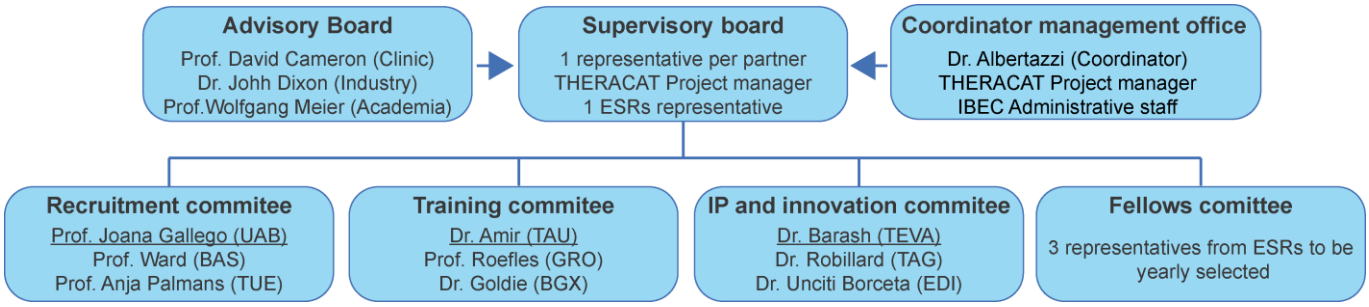
3.1.5 Gantt Chart

Please find the THERACAT Gantt Chart containing secondment plan in Section 4 (document 2).

3.2 Appropriateness of the management structures and procedures

3.2.1 Network organisation and management structure

The management structure of THERACAT is detailed in the scheme below.



Overall, this will (i) make management functions clear and verifiable, (ii) facilitate and manage the interaction between the different groups in the consortium and the integration of different backgrounds from academic and industrial environments, (iii) ensure the maintenance of research integrity, and (iv) guarantee the highest quality in the recruitment, research and training programmes, as well as in the assessment of the scientific outcomes of the project in terms of IP and innovation. The composition of the Committees has been agreed upon considering gender and academic/industrial balance. A Consortium Agreement will specify the management structure and the relationship among the partners, the decision-making procedures and the rights and obligations of the partners concerning liability, access rights, dispute resolution and intellectual property.

Project Management Team. The Coordinator, Dr. Albertazzi, will be responsible for the day-to-day management and liaison with the European Commission (EC). The coordinator will be assisted by the ***Coordinator Management Office***, composed by administrative staff at IBEC and a Project Manager to be hired for the Network. IBEC, with only 9 years of history and being awarded in 2015 with the prestigious Severo Ochoa Excellence Award by the Spanish Economy and Competitiveness Ministry, has coordinated 4 European research projects (incl. a recently awarded FET Proactive, MECHANO-CONTROL) and 2 Research and Training projects (FIBROGELNET-IAPP, SPM2.0-ETN); has been beneficiary in 7 additional EU projects; and is one of the core members of the KIC INNOLIFE. This broad experience in managing multi-institutional, multi-national projects will be applied to ensure the proper management of this Network. Tasks: (i) day-to-day management and support to the coordinator in the preparation of documents to be reported to the EC; (ii) financial and administrative management between the participants and the EC; (iii) ensuring transfer of information between the different boards and partners; (iv) support in the organisation of meetings and training events.

Recruitment Committee. It is responsible for advertising vacancies within the ETN, as well as implementing the Recruitment Strategy detailed in Section 3.2.3. Tasks: (i) developing a recruitment plan defining the step by step process of employment; (ii) ensuring gender balance within the recruitment; (iii) advertising positions internationally; (iv) dealing with any problem that may arise in the recruitment process.

Training Committee. It will supervise training activities and regularly monitor the progress of trainees. The TC will be chaired by Dr. Amir, leader of WP5 (Training), and will be also composed by a mixture of academia and industry experts. Tasks: (i) defining the Network training activities, (ii) evaluating the integration of the Network into local training programmes, (iii) supervising and managing all the training activities, (iv) supporting the definition of the **Personal Career Development Plan (PCDP)** for each ESR under the guidance of their supervisors outlining the individual learning objectives and skills to acquire throughout their doctoral/research training for their career development.

IP & Innovation Committee. It is the body responsible for advising on Intellectual Property and Innovation activities related to the research developed within the project, with the support of the Tech Transfer departments of the members' institutions. Tasks: (i) periodic monitoring of the project scientific results, assessing the scientific achievements and progress; (ii) determining whether some results are patentable; (iii) investigating competitive landscapes and potential exploitation issues.

Fellows Committee. Representing all fellows, the 3 lead ESRs will be initially selected by the RC, while successors will be selected yearly by all ESRs by majority vote. Tasks: (i) discussions on the network strategies and transfer to other relevant Committees when needed; (ii) launching fellow-related initiatives, (iii) supply input for the improvement of the programme (e.g. new training activities).

Advisory Board. It is composed of three experts external to the network in the different scientific areas related to THERACAT. **To reflect the intersectoral nature of THERACAT the three advisory board members are from academia, hospitals and private sector:** (i) Prof. David Cameron, Director of Cancer Services in NHS Lothian and Clinical Cancer Research Champion for Scotland; (ii) Dr. John Dixon, Director of JD Consulting and former VP of Drug Discovery in AstraZeneca Charnwood (iii) Prof. Wolfgang Meier, full professor of Chemistry at Basel University. Tasks: (i) provide an independent perspective of the progress of the Network and training progress of the ESRs; (ii) give impartial advices on potential areas for improvement and new possible avenues to explore; (iii) act as mediator in conflicts between beneficiaries. AB members will attend the project annual meetings, read the annual reports and write a critical review with recommendations for the next period.

Management of the network

Internal communication strategy. The intranet section of the THERACAT webpage, restricted to SB members and fellows, will be the main tool used to ensure and effective and continuous exchange of information among partners. It will contain an up to date schedule of activities and a repository of official documents (deliverables, dissemination, meeting minutes and presentations, progress reports, guidelines, and templates), and will be also used for the submission of reports on the deliverables to the Coordinator. This will be complemented by discussions at Network Meetings and bi-/multilateral meetings via video/web/phone based conferencing

Decision making. All committees including the SB will try at every moment to make unanimous decisions after discussion of a given issue. In case that unanimous consensus is not achieved, decisions will be taken by a simple majority, with each member having one vote. In case of even votes, the Coordinator's vote as chair of the SB will decide (details on the decision-making structures and procedures will be described in the Consortium Agreement).

Financial management. The Network Coordinator together with the Network Management Office will be responsible for the proper financial management of the project. As agreed among Network partners, the funding received by each beneficiary will be redistributed proportionally to the number of person months to create common budgets that will be managed by the Coordinator: (i) *training budget* (€300 per person month from the "Research, training and networking costs" of each beneficiary); (ii) *management budget* (€600 per person month from the "Management and overheads costs"). Therefore, each beneficiary will keep €1,500 per person month for the local research and training related expenses, and €600 per person month for local management and overheads. Individual budgets of the partners could be subject to updating and reallocation if milestones are not met and/or reallocation of budgets between Network partners is required for improved functioning of the Network. In such cases, prior approval of the European Commission Services will be requested. Each partner will send all documents necessary to justify rightful use of the funds (in accordance with the contract signed with the EC) to the Coordinator. Such documents will help the Coordinator and the Management Office to prepare financial reports. The Network will supply financial reports in accordance with the financial guidelines of the EC at the end of each reporting period.
Strategy for dealing with scientific misconduct. All Network members are strongly committed to prevent any potential misuse of research and research misconduct, complying with principles of research integrity as set out in the European Code of Conduct for Research Integrity that will be also presented to all ESRs once incorporated to the Network. The SB will actively contribute to preserve and promote research integrity by carefully monitoring all projects in terms of scientific progress and financial management, following the guidelines reported in the Code for Research Integrity as well as in the document "A comprehensive strategy on how to minimize research misconduct and the potential misuse of research in EU funded research" based on discussions among Ethics Experts with previous experience in EU Ethics Screening, Review and Audit. If despite these measures there is an alleged or suspected case of scientific misconduct incurred, it will be duly assessed by the SB and informed to the EC (if necessary).

3.2.2 Supervisory board

This board will be the ultimate decision-making body of the project, being responsible for implementing the project strategy, both from the scientific and training perspectives, within the budget and time frame of the project, always maintaining research integrity according to the "European Code of Conduct for Research Integrity". The SB will be chaired by the Coordinator and include one representative from each beneficiary and from partner organisations, the THERACAT Project Manager as well as one representative from the recruited ESRs (selected by majority vote among all ESRs). The responsibilities of the SB will be: (i) ensuring that recruitment procedures are open, transparent and internationally comparable, (ii) overseeing the integration of the fellows in the hosting institution and their mentoring, (iii) ensuring that scientific and technological training through personalised research projects is balanced with complementary skills training to guarantee future ESR employability in all sectors, (iv) monitoring the implementation of the research and training plan and solving any problem that may arise, (v) guaranteeing the exchange of best practices among the partners, and (vi) providing uniform procedures to the Network through the elaboration and approval of the guidelines for the elaboration of PCDPs, the recruitment and assessment of ESRs, and the Strategy for dealing with scientific misconduct.

3.2.3 Recruitment strategy

The recruitment of researchers will be open, transparent, international, competitive, and based on an equal opportunity policy following the "European Charter for Researchers" and the "Code of Conduct for the Recruitment of Researchers". Notably, all academic partners are part of EURAXESS and 50% of them (including the coordinator) have been awarded the "HR Excellence in Research", reflecting their commitment to continuously improve their HR policies in line with the EC principles. The **Recruitment Committee (RC)** will be in charge of implementing the recruitment strategy, together with the host scientific supervisor. The available positions will be widely advertised by the RC one month after the project granting and through relevant international websites (including EURAXESS, Find a PhD, European Technology Platform for Nanomedicine –IBEC is member-, etc.), the beneficiaries' websites, the ETN website and in selected high profile scientific journals. Application will be by submission of a CV, list of publications, two letters of support and a letter describing why they wish to study in this particular research area to the corresponding PI. Three candidates will be pre-selected for each position according to their education, student skills and motivation. Subsequent interviews will be held by videoconferencing in order to minimise the travel expenses. The PIs will send to the RC a ranked list of candidates properly justified, always

promoting equality of opportunities between women and men (Section 3.2.7). The RC will revise the selection process and invite the best candidate to enter the network, after proper validation of all data and documents provided by the applicants.

3.2.4 Progress monitoring and evaluation of individual projects

The day-to-day **progress monitoring of the ESRs** will be performed by the corresponding Supervisor, while at a Network level each ESR will be periodically assessed by his/her own Assessment Commission (AC). ESRs will send a short report describing the training received and research performed to both the AC members and to the Coordinator, main obstacles and future plans every 6 months. The AC will oversee the progress of the ESR, especially in comparison with the PCDPs, and provide recommendations which will be forwarded to the ESR and his/her Supervisor (e.g. specific training events interesting for the ESR like conferences or courses, best practices that could be implemented in the following period). Moreover, ESRs will meet with their AC during the Network Meetings 1-3: (i) in the 1st meeting, the ESR will present and discuss his/her PCDP as agreed with the Supervisor and the initial results of the research; (ii) in the 2nd meeting, the ESR will report on the evolution of his/her research project and of the obtained results; (iii) in the 3rd meeting, he/she will present the main conclusions on the work obtained so far and a draft version of the PhD thesis (even if preliminary for those ESRs starting at M9). The **progress monitoring of the Network** as a whole will be achieved by a continuous monitoring and assessment of the actions made on the Research and Training Programmes, mainly through the individual reports on the ESRs progresses as well as through the yearly Meetings of the Network, in which each partner will report in front of the other partners on the recruitment, research and training actions performed for a one year period. The typical duration of a **Network Meeting** will be one day and a half. During the first day (except for the Kick-off meeting), ESRs will shortly present the progress of their individual research projects, and discuss the results with the network members. The SB will use these presentations to evaluate the scientific progress of the Network. During the remaining half day (restricted only to Board members), the different boards will meet and evaluate the scientific, training and management evolution of the network. The organisation of the Meetings will be responsibility of the host institution supported by the SB. The meetings will be organized, in order, by IBEC (kick-off), BAS (M12), EDI (M24), IBEC (M36) and IBEC (M48). The dates and organizers of the 1st, 2nd and 3rd Network Meetings will be made to coincide with the Training events described in Section 1.2.1 to minimise travel expenses and organisation tasks.

3.2.5 Risk management at consortium level

The main risks involved in the management of the ETN and their contingency plans are detailed in Table 3.2.a. Scientific and technological risks identified for the research programme are also listed.

Table 3.2a Implementation Risks

No.	Description of Risk	WP	Proposed mitigation measures
R1	One participant is not able to fulfil the plan of recruitment	WP0	Extension of the recruitment period and intensive advertising of the available position among members' colleagues
R2	ESR not integrated in the host institution	WP0	Mediation of the conflict between the ESR and the supervisor by the RC and the AB. The SB may offer the ESR the transfer to another beneficiary
R3	Partner leaving the project	WP0	The SB will re-allocate its pending research and training tasks and associated funding between other beneficiaries, and will offer the possibility to the hosted ESR to transfer to another beneficiary
R4	Cancellation of a planned secondment due to force majeure reasons	WP0	Preferably, postpone the planned secondment; if not possible, definition of a new secondment agreed between supervisor, ESR, AC, the new secondment co-supervisor and coordinator
R5	Conflicts among partners, including IPR conflicts	WP0	The Coordinator will mediate between the parties. Should agreement not be reached, the conflict will be resolved by the SB, in line with the recommendations of the EC and the Consortium Agreement
R6	Delay in the synthesis of the materials in WP1	WP1	Synthetic work packages start 3 months earlier than WP3 and WP4. The optimisation of imaging and evaluation (WP3 and WP4) will start in time using materials already available in the consortium as preliminary results
R7	Delay in the prodrugs synthesis	WP2	Several prodrugs and prodyes are already available in the consortium to start the optimisation of the biological assays, providing time for the synthesis of the novel compounds
R8	Technical issue with one imaging modality	WP3,4	To avoid excessive dependence on one imaging method the use of several techniques (STORM, Confocal, PET, Intravital imaging) as well as experts in such methods are included

R9	Poor efficiency in biological tests in vitro and in vivo	WP3,4	The consortium is endowed with the analytical tools (e.g. in vitro and in vivo imaging) to understand the possible cause of lack of efficiency and feedback towards the synthesis of novel more efficient catalysts

3.2.6 Intellectual Property Rights (IPR)

The IP and innovation committee (led by TEVA) will be responsible to supervise the activity of the consortium to find potential marketable occasions. The IP and innovation committee will be in touch with the local tech transfer offices to manage the strategy for successful translation of the know-how generated in the consortium into marketable products. The beneficiary or beneficiaries responsible for the new technology will own the IP and will have to responsibility to patent it and exploit it. In case of joint IP or IP generated during secondments the involved beneficiaries will sign an agreement on IP exploitation. All beneficiaries will be allowed to access the research results for research or training purposes. IPR regulations will be detailed in the consortium agreement between beneficiaries and partners and serve as a reference. If required secondments, meeting or results sharing will be performed under a non-disclosure agreement. However, attention will be dedicated in order to do not prevent the possibility of publication of the ESRs.

3.2.7 Gender aspects

Following the EC recommendation on the implementation of Responsible Research and Innovation as a cross-cutting issue in H2020 projects, as well as in direct relation with national policies of gender impact, gender equality has been and will be carefully considered in THERACAT. **Indeed, 46% of the consortium members are led by women (75% regarding the non-academic sector), and women are included in all the different boards and committees forming the decision-making bodies of the project**. In addition, the Network will take all reasonable measures to actively pursue the objective of receiving more than 40% women candidates and achieving at least 40% recruitment of women, always in the framework of the excellence of the candidates. The RC and especially Prof. Gallego from the Observatory for Equality, with a long-standing experience in promoting gender equality at all levels, will oversee the recruitment of candidates. Some other actions planned to promote gender parity are focused on addressing equal employment policies, including family-friendly plans (incl. flexible working hours for ESRs having a family in charge), and ensuring that all partners fully respect the EU regulations on awarding parental leaves during the course of the Network.

THERACAT gender aspects:
- 46% of the PIs are women
- 75% of private sector PIs are women
- 66% of the committees are led by women
- UAB Observatory for Equality involved

3.3 Appropriateness of the infrastructure of the participating organisations

All ESRs will be assisted by well-established support services and research infrastructure available at the participants' institutions:

Research infrastructure: all partners have powerful state-of-the-art equipment and access to scientific services needed to perform their tasks, including synthesis and characterization facilities (WP1-2), cell culture and in vitro/vivo imaging facilities (WP3-4), radiochemistry (WP4) and animal facilities (WP4).

- *Each ESR will follow a specific planning to get acquaintance with the main technologies and facilities available at the host and secondment institutions provided by the technical staff.*
- *Each ESR will be provided with a desk, phone, computer and access to libraries and bibliographic and IT databases (e.g. SciFinder).*

Experience in supervision of ESRs: all PIs → *PIs will supervise their ESRs offering the highest standards in ESR mentoring. Non-academic beneficiaries regularly host and supervise PhD students in their facilities, and will provide supervision standards equivalent to those of academic institutions.*

Participation in European projects: 75% of PIs participate in EU-funded projects; 66% of them in MSCA actions → *the PIs supported by their Projects Offices will work for the proper implementation of the project thanks to their experience in EU projects.*

EURAXESS Network of Service Centres: all academic beneficiaries & partner organisations → *HR Departments of each institution will help ESRs in their settlement (i.e. housing, language courses, etc.) as they have well-informed staff used to assist researchers in their movement to a foreign country.*

"HR Excellence in Research" Award from EC: 50% of the academic partners (including beneficiaries & partner organisations) → *The European Charter for Researchers and The Code of Conduct for the Recruitment of Researchers principles will be strictly followed by all partners.*

3.4 Competences, experience and complementarity of the participating organisations and their commitment to the programme

3.4.1 Consortium composition and exploitation of organisations' complementarities

The consortium shaped for the THERACAT Network is composed of 5 high education centres, 1 research institute, 1 large industrial company and 2 SMEs as beneficiaries, plus 1 non-academic and 2 academic institutions as partner organisations, carrying out top quality fundamental and applied research activities. The consortium provides a well-balanced intersectoral approach between research and transfer into industrial practice and covers the entire chain from materials (catalysts and prodrugs) synthesis to their oral formulation.

Partner	Expertise	WP1	WP2	WP3	WP4	WP5	WP6
IBEC	supramolecular materials, drug delivery, super resolution microscopy		X	X		X	X
TUE	polymer chemistry, catalysis, supramolecular chemistry	X		X		X	X
GRO	bio-inorganic chemistry, bio-inspired catalysis, chemical biology	X				X	X
BAS	organometallic catalysis, biotechnology, in vivo catalysis			X		X	X
EDI	medicinal chemistry, prodrug activation, biorthogonal catalysis		X		X	X	X
TAU	polymers and micelles, cancer therapies, intravital imaging	X			X	X	X
TEVA	industrial formulation, oral delivery, nanomaterials	X				X	X
TAG	in vivo chemistry, PET imaging				X	X	X
BGX	gel-based 3D cancer models, hydrogels for delivery			X		X	X
CRUK	*dissemination on cancer social impact, support to patients*					*X*	*X*
ESADE	*entrepreneurship, business, from science to market*					*X*	
UAB	*gender equality promotion, gender perspective in science*					*X*	

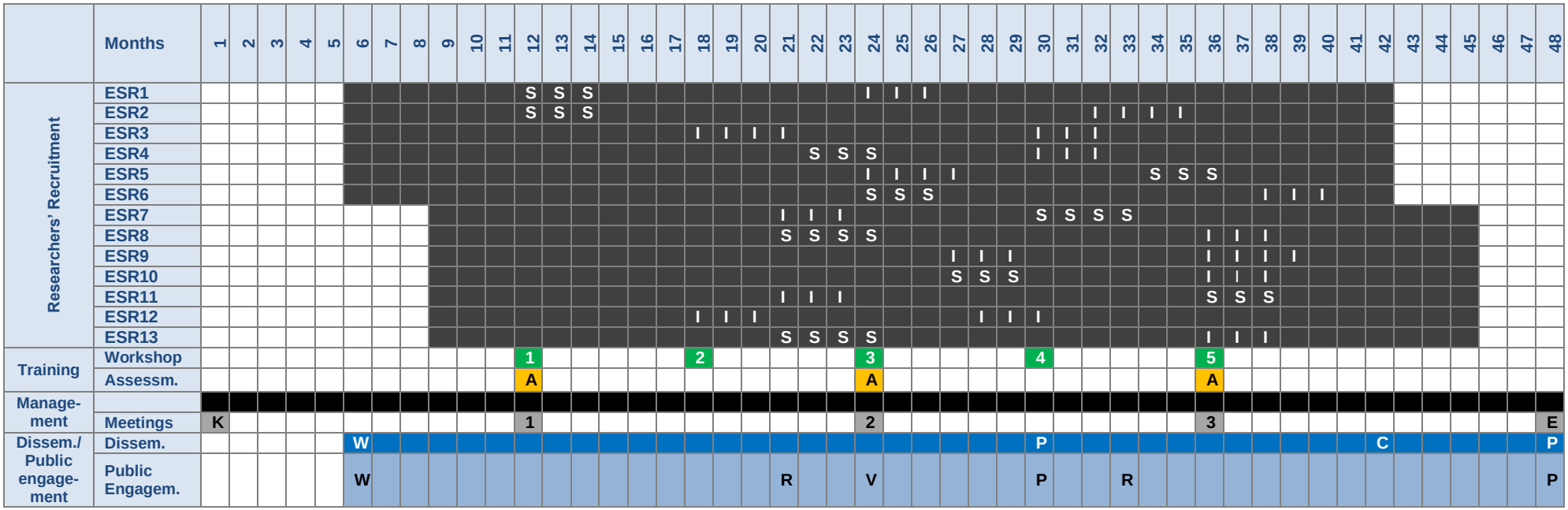
With this composition, the consortium covers all the research fields required to train the next generation of multidisciplinary researchers in the field of bio-orthogonal catalysis for cancer therapy. The interaction of the researchers with different supervisors having complementary expertise will contribute to the formation of professional profiles showing a distributed background, with the ability to manage research activities having a common denominator from quite different disciplines. This multidisciplinary and multisectorial approach could not be performed by national initiatives, having 12 partners from 5 different countries, sharing a wide range of knowledge competences and technological facilities. The geographical distribution constitutes a living example of collaboration in the European Research Area.

3.4.2 Commitment of beneficiaries and partner organisations to the programme

All partners are deeply committed to both the research and training programme of the Network and have actively collaborated in the preparation of the current proposal. Regarding beneficiaries, this is demonstrated by the fact that all of them assume leadership roles either in tasks or WPs (or both), are responsible for deliverables, recruit and host ESRs, organise training courses and host secondments. This serious commitment of the network beneficiaries, which is shown at the same level for both academic and non-academic partners, is a guarantee for the success of implementation of the Network. Concerning partner organisations, all of them are responsible for one or more courses on their topics of expertise and are moreover committed to collaborate in some key tasks: CRUK – raising awareness about the Network implications and results through communication and outreach activities, courses on social aspects of cancer and public engagement, training of ESR6; ESADE – 4-days training on entrepreneurship, marketing and IPR; UAB – promotion of gender equality in recruitment and gender perspective in scientific tasks, training in gender aspects.

DOCUMENT 2

4. Gantt Chart



S = Secondment
I = Intersectoral secondment
A = ESRs individual meetings with Assessment Commissions
K = Kick-off meeting
E = End of action
W = Website
P = General press articles in EU Magazines
C = THERACAT Conference
R = European Researchers' Night
V = THERACAT Video

5. Participating Organisations

Beneficiary Legal Name: Fundació Institut de Bioenginyeria de Catalunya (IBEC)	
General Description	IBEC (www.ibecbarcelona.eu) is a research institute covering most bioengineering fields, from basic research to medical applications, aiming to act as an international reference in this field. IBEC was established in 2005 by the Government of Catalonia, the University of Barcelona (UB) and the Technical University of Catalonia (UPC) and was awarded in 2015 with the prestigious Severo Ochoa Excellence Award by the Spanish Ministry of Economy and Competitiveness. IBEC is located at the Barcelona Science Park (PCB) and hosts around 200 researchers and technicians, which are part of its own staff or are associated to the UB and UPC. Within IBEC, the "Nanoscopy for nanomedicine" group (www.ibecbarcelona.eu/nanoscopy) led by Dr. Lorenzo Albertazzi is an international group currently focused on the application of Super Resolution Microscopy to visualize and track self-assembled nanomaterials with therapeutic potential in living cells and tissues.
Role and Commitment of key persons (including supervisors)	Dr. Lorenzo Albertazzi (Group Leader). ETN Coordinator; Research, training and supervision. Super Resolution Microscopy, nanomaterials, drug delivery (30%). Dr. Rosa Miralles (Project Manager). Project management and coordination (50%).
Key Research Facilities, Infrastructure and Equipment	The Nanoscopy for Nanomedicine lab offers the necessary infrastructure and facilities required for the completion of this project proposal, including a state-of-the-art super resolution N-STORM setup. Other existing equipment consists of: fluorescence spectroscopy instrumentation, cell culture facilities, fluorescence microscopes, electron microscopes, and atomic force microscopes, among others. Also accessible are the powerful state-of-the-art Scientific Services and Platforms at the Barcelona Science Park, including Genomics, Proteomics, Confocal Microscopy and the Laboratory Animal Applied Research Platform with specific pathogen-free areas, and the IBEC Nanotechnology Platform in nanofabrication and bionanocharacterisation, a research facility featuring 150 m2 of class 10,000 clean room space and laboratories offering state-of-the-art equipment for the fabrication and characterisation of micro- and nanodevices and structures.
Status of Research Premises	The Nanoscopy for Nanomedicine Lab is independently supervised and guided by Dr. Lorenzo Albertazzi. The group has its own space and equipment. Moreover, the group also has access to the facilities of University of Barcelona and of the Parc Cientific de Barcelona. IBEC's research premises are wholly independent from other beneficiaries and partner organisations in the consortium.
Previous Involvement in Research and Training Programmes	IBEC possess a strong track record in the training of students and postdocs within the Institute. Moreover, IBEC has coordinated or been involved in several European networks including a research training network such as IMMUNONANOMAP (ITN), as well as other EU projects such as Angiofrac (EURONANOMED) and STRUCTGEL (EURONANOMED). IBEC is also involved in the organization of training events like the biyearly summer school "Advanced Summer School Interrogations at the Biointerface" besides the regular training sessions and seminars that are organized all throughout the year. Dr. Albertazzi has a strong track record in training students from the undergraduate up to the postdoctoral level and was PI of a Veni Grant from the Netherlands Organisation for Scientific Research.
Current involvement in Research and Training Programmes	IBEC is currently coordinating the MC-IAPP project FIBROGELNET, the MSCA-ITN-ETN project SPM2.0 and acting as beneficiary for NANOMICROWAVE (MSCA-ITN-ETN project). Moreover, Dr. Albertazzi is currently supervising three PhD students and two postdoctoral researchers in addition to several master students. The group is active in a variety of outreach activities such as hosting and training high school students in the Barcelona area. In addition, Dr. Albertazzi is IP of the National project TARGETSTORM (SAF2016-75241-R, 2016-2019), and partner in the EuroNanoMed-II project NanoVax (2017-2019). He has been recently awarded with the prestigious Ramon y Cajal grant from the Spanish Ministry of Economy and Competitiveness (2017-2022).
Relevant Publications and/or research/innovation products	[1] Baker, Albertazzi, Voets, Leenders, Palmans, Pavan, Meijer. Consequences of chirality on the dynamics of a water-soluble supramolecular polymer. **Nat. Commun**. 6, 6234 (2015). [2] Albertazzi, Martinez-Veracoechea, Leenders, Voets, Frenkel, Meijer. Spatiotemporal control and superselectivity in supramolecular polymers using multivalency. **Proc. Natl. Acad. Sci.** 110(30), 12203-12208 (2013). [3] Albertazzi, van der Zwaag, Leenders, Fitzner, van der Hofstad, Meijer. Probing exchange pathways in one-dimensional aggregates with super resolution microscopy. **Science** 344(6183), 491-495 (2014). [4] van der Zwaag, Vanparijs, Wijnands, De Rycke, De Geest, Albertazzi. Super Resolution Imaging of Nanoparticles Cellular Uptake and Trafficking. **ACS Appl Mater Interfaces** 8(10), 6391-6399 (2016). [5] Bakker, Lee, Meijer, Dankers, Albertazzi. Multicomponent Supramolecular Polymers as a Modular Platform for Intracellular Delivery. **ACS Nano** 10(2), 1845-1852 (2016).

Beneficiary Legal Name: Technische Universiteit Eindhoven (TUE)	
General Description	The Laboratory of Macromolecular and Organic chemistry is part of the Institute for Complex Molecular Systems (ICMS) located at the TU/e, and focuses on supramolecular systems and how individual molecules can influence the properties of the assembly of multi-component systems. Special attention is given to the use of supramolecular interactions to fold synthetic polymers into conformations that show enzyme-like catalysis. The research performed in our group takes place at the interface between supramolecular chemistry, polymer chemistry and catalysis. Our strength is our ability to combine small molecule synthesis with complex polymer synthesis, and perform detailed catalysis studies on the formed macromolecular complexes. Our interdisciplinary approach also permits detailed characterisations of the formed macromolecular systems using spectroscopic, microscopic and scattering techniques. With these, information of the systems on multiple length scales are be obtained.
Role and Commitment of key persons (including supervisors)	Dr. A.R.A. Palmans (Associate Professor at the Department of Chemical Engineering and Chemistry). Research, training and supervision (10%). Prof. E.W. Meijer (full professor at the Departments of Chemical Engineering and Chemistry and Biomedical Engineering, and Scientific Director of the ICMS at the TU/e). Research and training (10%).
Key Research Facilities, Infrastructure and Equipment	The Laboratory of Macromolecular and Organic Chemistry is part of the Institute for Complex Molecular Systems (ICMS) and is equipped with state-of-the-art analytical techniques (LCMS, GCMS, Maldi-ToF MS, ESI-MS, SEC), spectroscopy techniques (CD, UV, IR, fluorescence, NMR), scattering techniques (SAXS, DLS, SLS) and microscopy techniques (STORM, POM, AFM). All equipment and characterisation tools necessary for complex macromolecular synthesis and characterisation are available.
Status of Research Premises	The beneficiary's research facilities are owned by the beneficiary and its research premises are wholly independent from other beneficiaries and/or partner organisations in the consortium. The group is run by Prof. Meijer, who is also the scientific director of the ICMS and co-run by Dr. ARA Palmans.
Previous Involvement in Research and Training Programmes	EU-funded projects: LAMINATE (HPRNCT-2000-00135); CODE (HPRN-CT-2000-00003); MC: POSE (MCFH-1999-01243).
Current Involvement in Research and Training Programmes	[1] EURO-SEQUENCES (MSCA-ITN-ETN: SEP-210157074). [2] For PhDs and postdocs, the ICMS organizes courses in professional skills, on experimental techniques and PhD courses on specific research themes. These can be easily incorporated and/or adopted in new research training networks. See http://www.tue.nl/en/research/research-institutes/top-research-groups
Relevant Publications and/or Research / Innovation Product	[1] Stals PJM, Cheng C-Y, van Beek L, Wauters AC, Palmans ARA, Han S, Meijer EW. Surface water retardation around single-chain polymeric nanoparticles: critical for catalytic function? **Chem. Sci**. 7(3), 2011-2015 (2016). [2] Artar M, Souren ERJ, Terashima T, Meijer EW, Palmans ARA. Single Chain Polymeric Nanoparticles as Selective Hydrophobic Reaction Spaces in Water. **ACS MacroLett.** 4(10), 1099-1103 (2015). [3] Liu Y, Pauloehrl T, Presolski SI, Albertazzi L, Palmans ARA, Meijer EW. Modular Synthetic Platform for the Construction of Functional Single-Chain Polymeric Nanoparticles: From Aqueous Catalysis to Photosensitization. **J. Am. Chem. Soc.** 137(40), 13096-13105 (2015). [4] Gillissen MAJ, Terashima T, Kohlbrecher J, Meijer EW, Palmans ARA, Voets IK. Sticky Supramolecular Grafts Stretch Single Polymer Chains. **Macromolecules** 46(10), 4120-4125 (2013). [5] Terashima T, Mes T, De Greef TFA, Gillissen MAJ, Besenius P, Palmans ARA, Meijer EW. Single-Chain Folding of Polymers for Catalytic Systems in Water. **J. Am. Chem. Soc**. 133(13), 4742-4745 (2011).

Beneficiary Legal Name: Rijksuniversiteit Groningen (GRO)	
General Description	The University of Groningen has a long tradition of academic excellence, being one of the oldest research universities in Europe. It ranks the top 4% of research institutions in the world on the basis of the number of citations per publication. Currently approximately 30,000 students are enrolled and every year about >400 PhD students defend their theses. Of these 60% are from abroad. The chemistry department is the strongest in the Netherlands and houses around 35 different research groups that are organised in separate institutes that provide critical mass on selected priority areas. Institutes relevant to the present proposal are the Stratingh Institute for Chemistry and the Groningen Biomolecular Sciences and Biotechnology Institute (GBB) with several world-leading scientists, including Prof. Dr. Ben L. Feringa, Nobel laureate in chemistry 2016.
Role and Commitment of key persons (including supervisors)	Prof. Dr. G. Roelfes (head of the Biomolecular Chemistry & Catalysis group). Research, training and supervision (20%).
Key Research Facilities, Infrastructure and Equipment	**Roelfes lab:** Excellent facilities for routine organic synthesis, biochemical and biotechnological research. **Stratingh Institute for Chemistry and GBB:** central NMR, MS (LC-MS, MALDI-TOF, Orbitrap) and chromatography (GC, HPLC) facilities. State-of-the-art spectroscopic (UV/BIS, fluorescence, IR, Raman) and biological (plate readers, robotized pipetting and screening systems) equipment.
Status of Research Premises	The Biomolecular Chemistry & Catalysis group headed by Prof. Roelfes is a fully independent unit within the Stratingh Institute and has its own lab space and facilities. In addition, it has unrestricted access to all state of the art facilities of the Stratingh Institute and the GBB institute, whose research premises are independent from other beneficiaries and partners in the consortium.
Previous Involvement in Research and Training Programmes	The University of Groningen and in particular the Stratingh Institute has coordinated or been involved in several European networks ITN's such as READ, DYNAMOL and RESMOLSYS. **Roelfes lab**: Intra-European Marie Curie Fellowship (FP7-PEOPLE-2010-IEF, Contract No. 274987). ERC starting grant (PE5, ERC-2011-StG, Project number 280010). Member of the national research school combination "Catalysis", a recognized top institute in the area of catalysis. Prof. Roelfes has guided 10 PhD students (defended) and 4 postdocs.
Current Involvement in Research and Training Programmes	**Roelfes lab**: Member of the Dutch research school on catalysis (NIOK), which provides training to Ph.D. and postdoctoral researchers. Member of the national research centre "Functional Molecular Systems", a recognized top programme that provides training in the area of supramolecular chemistry (Ph.D. courses). Prof. Roelfes currently guides 11 PhD students and 3 postdocs.
Relevant Publications and/or Research / Innovation Product	[1] A. Rioz-Martínez, J. Oelerich, N. Ségaud, G. Roelfes. DNA-Accelerated Catalysis of Carbene Transfer Reactions by a DNA/Cationic Iron Porphyrin Hybrid. **Angew. Chem. Int. Ed.,** 55, 14136-14140 (2016). [2] J. Bos, W.R. Browne, A.J.M. Driessen, G. Roelfes. Supramolecular Assembly of Artificial Metalloenzymes Based on the Dimeric Protein LmrR as Promiscuous Scaffold. **J. Am. Chem. Soc.**, 137, 9796-9799 (2015). [3] I. Drienovská, A. Rioz-Martínez, A. Draksharapu, G. Roelfes. Novel artificial metalloenzymes by in vivo incorporation of metal-binding unnatural amino acids. **Chem. Sci.**, 6, 770-776 (2015). [4] Q. Li, M.G.P. van der Wijst, H.G. Kazemier, M.G. Rots, G. Roelfes. Efficient Nuclear DNA Cleavage in Human Cancer Cells by Synthetic Bleomycin Mimics. **ACS Chem. Biol.,** 9, 1044–1051 (2014).

Beneficiary Legal Name: Universitat Basel (BAS)	
General Description	The University of Basel has a long tradition of excellence in teaching and research (est. 1460, 7 faculties with > 12'000 students and > 3'000 researchers). Life Sciences and Nanotechnology, which lie at the centre of the present proposal, are among the focus areas of the University of Basel (https://www.unibas.ch/en.html). The University is integrated in the Basel Life Science hub and enjoys privileged contacts with world-leading companies including: Novartis, Roche, Actelion, etc.
Role and Commitment of key persons (including supervisors)	Prof. Ward (full professor and head of the Artificial Metalloenzymes Laboratory). Research, training and supervision (10%). Prof. Ward has significantly contributed to establish the field of artificial metalloenzymes in the last decade. He is highly respected in the field as reflected by: i) his excellent publication record (150 refereed publications) ii) former co-worker's academic track record including professor positions at: Princeton; Nottingham; ENSCP, Osaka University etc.; iii) plenary lectures at international conferences including: BIOTRANS, ICBIC, ICCC, GRC, etc.
Key Research Facilities, Infrastructure and Equipment	**Lab equipment**: hoods, laminar flow hoods, centrifuges, 20 l fermenter, ICP-OES, incubators, FPLC, HPLC, UPLC-MS, GC-MS, multiwell plate readers, pipetting robots, etc. **Facilities at the UniBas**: NMR and X-ray facility; high-throughput facility; FACS facility; proteomics facility; quantitative genomics facility; biophysics facility. **Infrastructure for career development and results dissemination**: Career Service Center; Unitectra; Department of Communications & Marketing.
Status of Research Premises	Following the recent award of the National Center of Competence in Research ("Molecular Systems Engineering", Prof. Ward director), the University of Basel is investing 40 mio. € to renovate its chemistry research facility. The Ward group is scheduled to move into fully renovated laboratories in June 2017, whose research premises are and will be independent from other beneficiaries and partners in the consortium. The chemistry department, as part of the faculty of natural sciences, offers state of the art infrastructures to carry out research at the interface between Life Sciences and Nanotechnology.
Previous Involvement in Research and Training Programmes	Prof. Ward has participated in several research and training programmes, including: -Marie Curie ITNs: IBAAC, BIOTRAINS, BioChemLig. -KBBE Metacode olefin metathesis *in vivo*. Proof-of-principle of the use of artificial metalloenzymes *in vivo.* -COST CM1003: biotin streptavidin technology as tool for supramolecular catalysis in water. -NIH GM050781: joint project with Prof. A. Borovik, UC Irvine-
Current Involvement in Research and Training Programmes	-**ERC** Advanced Grant (DrEAM): Directed evolution of artificial metalloenzymes based on the biotin-streptavidin technology for white biotechnology applications (yearly budget 0.5 mio. €). -**Director** of the National Center of Competence in Research "**Molecular Systems Engineering**" (Coordinating the research efforts of 29 research groups at the interface of chemistry and biology - yearly budget 5 mio. €). The MSCA fellow will have access to the comprehensive training programme set-up by the NCCR including: soft-skills, ethics, workshops, communications, networking etc.
Relevant Publications and/or Research / Innovation Product	[1] Jeschek, Reuter, Heinisch, Trindler, Klehr, Panke, Ward. Directed evolution of artificial metalloenzymes for in vivo metathesis. **Nature**, 537, 661-665 (2016). [2] Mallin, Hestericová, Reuter, Ward. Library design and screening protocol for artificial metalloenzymes based on the biotin-streptavidin technology. **Nature Protoc.** 11, 835-852 (2016). [3] Heinisch, Ward. Artificial metalloenzymes based on the biotin-streptavidin technology: challenges and opportunities. **Acc. Chem. Res.** 49, 1611-1622 (2016). [4] Köhler, Wilson, Dürrenberger, Ghislieri, Churakova, Quinto, Knörr, Häussinger, Hollmann, Turner, Ward. Synthetic cascades are enabled by combining biocatalysts with artificial metalloenzymes. **Nat. Chem.** 5, 93-99 (2013). [5] Hyster, Knörr, Ward, Rovis. Biotinylated Rh(III) complexes in engineered streptavidin for accelerated asymmetric C-H activation. **Science** 338, 500-503 (2012).

Beneficiary Legal Name: University of Edinburgh (EDI)	
General Description	The **University of Edinburgh** (EDI) is the leading research university in Scotland and also is amongst the top ten in the United Kingdom with an international reputation as a centre of academic excellence. The proposed project will be performed at the **Cancer Research UK Edinburgh Centre** (CRUK-EC), which sits within the **Institute of Genetics and Molecular Medicine** (IGMM), one of the largest centres internationally for human genetics, molecular medicine & cancer research with >500 research staff.
Role and Commitment of key persons (including supervisors)	Dr. Unciti-Broceta (Reader = Associate Professor in Medicinal Chemistry, Head of the *Innovative Therapeutics Lab* at the CRUK-EC and chemistry director of the Edinburgh Cancer Discovery Unit-ECDU). Research, training and supervision (20%).
Key Research Facilities, Infrastructure and Equipment	The PhD students will benefit from the wide range of specialised facilities, services and research expertise across the IGMM and the EDI, including full access to an impressive library, on-line access to most scientific journals and training in the use of IT databases (e.g. SciFinder). Dr. Unciti-Broceta's lab is equipped with state-of-the-art synthesis and characterisation facilities, e.g. brand new fumehoods, buchi's, vacuum ovens, fluorescence spectrometer, a microwave synthesizer (Biotage), a miniaturized MS device (Microsaic), HPLC with UV detector and last generation LCMS (Dionex RSLCnano UPLC). Cell culture facilities, access to cancer cell lines and primary tumoral cells from the IGMM cell bank and hospital cancerous human tissues, imaging facilities (FV1000 confocal microscope, OV100 fluorescence reflectance imaging system, IncuCyte ZOOM™ for real-time studies), zebrafish facilities, rodent animal house, reagents/fungibles store and bioinformatics will be available in the CRUK-EC/IGMM. The students will also have access to characterisation facilities (NMR, SEM, TEM, etc.) at the School of Chemistry of the EDI.
Status of Research Premises	The Innovative Therapeutics Lab is independently supervised and led by Dr. Unciti-Broceta. The group has its own space and equipment. All research premises at the CRUK-EC used are wholly owned by EDI and are independent from other beneficiaries and partner organisations in the consortium.
Previous Involvement in Research and Training Programmes	Dr. Unciti-Broceta is an active participant on research / training programmes. In the last 6 years, Dr. Unciti-Broceta has supervised BSc / MSc students (4), Erasmus students (2) and PhD students (8). He has participated in knowledge exchange training programmes such as the SULSA's Bio-industry Skills Knowledge and People Exchange Programme. Through an international collaboration with the GENyO research centre in Spain, he co-supervised a Talentia Postdoc (FP7-Andalusian government) and 2 additional postdocs funded by UK and Spanish research charities. During this time, he has led 7 research projects as a PI, which has resulted in 24 publications and 5 patent applications.
Current involvement in Research and Training Programmes	Dr. Unciti-Broceta is currently first supervisor of 4 PhD students and second supervisor of 2. He is PI of 4 research grants, highlighting a CRUK Pioneer Award (2016-18) and an EPSRC Healthcare Technology Challenge Award (2016-21), with over £1.7M available for research funding for the next 5 years. 3 postdocs are full time members of his lab, including a H2020 MSCA Fellow. He participates as a mentor in the Mentoring Programme of the UoE, providing guidance in career progress to a number of postdocs.
Relevant Publications and/or research/innovation products	[1] Rubio-Ruiz, Weiss, Unciti-Broceta*. Efficient Palladium-Triggered Release of Vorinostat from a Bioorthogonal Precursor. **J. Med. Chem.** 59, 9974 (2016). [2] Unciti-Broceta*. Bioorthogonal Catalysis. Rise of the Nanobots. **Nat. Chem.** *7*, 538–539 (2015). [3] Weiss, Dawson, Fraser, Rybski, Torres-Sánchez, Bradley, Patton, Carragher, Unciti-Broceta*. Development and Bioorthogonal Activation of Pd-Labile Prodrugs of Gemcitabine. **J. Med. Chem.** 57, 5395-404 (2014). [4] Weiss, Dawson, Macleod, Rybski, Fraser, Torres-Sánchez, Patton, Bradley, Carragher, Unciti-Broceta*. Extracellular Pd-Catalyzed Dealkylation of 5-Fluoro-1-Propargyl-Uracil as a Bioorthogonally-Activated Prodrug Approach. **Nat. Commun.** 5, 3277 (2014). [5] Yusop, Unciti-Broceta, Johansson, Sánchez-Martín, Bradley. Palladium-Mediated Intracellular Chemistry. **Nat. Chem.** 3, 241–245 (2011).

Beneficiary Legal Name: Tel Aviv University (TAU)	
General Description	TAU is the largest comprehensive research university in Israel. In 2013 Tel Aviv University was ranked 18th in the world in the criteria citations per faculty member. Recently TAU has been ranked 9th in the world, by Venture Capital monthly, in the top universities for vc-backed entrepreneurs. The commercial arm of TAU, Ramot at TAU Ltd., has many years of experience in translating basic research achievements to products that benefit society. On top of the wide range of programs that TAU offers its 29,000 students, TAU has introduced an ever-increasing number of interdisciplinary programs in vital fields, such as nanotechnology and biotechnology. With its 17 affiliated hospitals and 600 cancer researchers, TAU is an internationally-renowned centre of excellence in the cancer field. More than any other institution in Israel, TAU has placed an emphasis on and committed extensive resources promoting multidisciplinary projects among its faculties of medicine, life sciences, exact sciences, engineering and social sciences. Dozens of collaborative projects have led to significant breakthroughs, over 100 patents and revolutionary biomedical technologies in the cancer field.
Role and Commitment of key persons (including supervisors)	Prof. Ronit Satchi-Fainaro (Group Leader). Research, training and supervision. Intravital non-invasive imaging of drug delivery systems (10%). Dr. Anna Scomparin (Researcher). Research & training (20%). Dr. Roey Amir (Group Leader). Training coordinator; Research, training and supervision. Design and synthesis of amphiphilic polymeric materials, self-assembly, polymeric nanocarriers for controlled drug and gene delivery applications (20%).
Key Research Facilities, Infrastructure and Equipment	Prof. Satchi-Fainaro's laboratory consists of 10 PhD students, 4 MSc students, 2 postdoctoral fellows, 1 MD neurosurgeon, 5 experienced Research Associates, 5 Undergraduate students and an Administrative Assistant. Equipment consists of microscopes (Nikon TS-100 inverted, TE-2000E inverted fluorescence live cell imaging system with high resolution CCD camera and incubator, Leica M165 FC dissecting microscope), SpectraMax M5e microplate reader, 2 tissue culture facilities, 3 Chemical hoods, Rotavap, lyophilizer, 2 AKTA FPLCs, Ultimate3000 Dionex analytical HPLC, Coulter Counter, thermocycler PCR and real-time PCR, FACS Aria. Imaging center enables advanced in vitro/vivo imaging, e.g. intravital imaging systems (Ivis SpectrumCT, Maestro® fluorescence imaging system, fibered confocal fluorescence microscopy Cell-VizioTM, Bruker Biospec 7 Tesla MRI unit, VisualSonics Vevo 2100 Ultrasound), Leica TCS SP5 and SP8, Multiphoton + FLIM for Zeiss LSM 710, STED Leica High resolution confocal imaging systems. Image analysis software: Huygens and Imaris. SPF Animal facilities and operating suites are available under 3 veterinarians. The Amir group has state of the art laboratory equipment for the preparation and characterisation of polymeric materials including microwave and photo-reactors, chromatography systems (HPLC and GPC), UV-Vis spectrophotometer, fluorimeter and DLS. In addition to group equipment, NMR, IR, and MS are available as departmental instruments and TEM, SEM, and AFM are available through the Center for Nanoscience and Nanotechnology (TAU-NST).
Status of Research Premises	Owned by beneficiary; fully independent from others in the consortium.
Previous Involvement in Research and Training Programmes	TAU participates in the European Framework Programmes since FP5 with 50 projects in FP5, 75 projects in FP6 and 225 in FP7 (33 of which are ERC's and 108 Marie Curie Grants). Since the beginning of H2020, TAU researchers already obtained 40 ERC grants and participate in numerous projects including a coordination of a project under SC1. TAU is also a core member of the Human Brain Project Flagship since its beginning. Over the years TAU has also participated in hundreds of research and training actions under the Israeli Science Foundation (ISF) and under other national and international funding schemes including ongoing National I-CORE (centers of excellence), Bi –national (BSF, GIF) and others, including international student exchange programs. Notably, Prof. Satchi-Fainaro received the Consolidator ERC grant POLYDORM for 2014-2019.
Current Involvement in Research and Training Programmes	Since the beginning of H2020 TAU is participating in 69 projects including 3 IF, 4 ETNs and 2 RISE projects. Prof. Satchi-Fainaro has 3 more years of funding from the ERC and was recently awarded the EuroNanoMed Consortium as coordinator (MultiNano@MBM, 2017-2020). The Amir group is active in several national research and training programs. These include a research project in the field of enzyme-responsive polymers funded by the Israel Science Foundation (ISF966/14). In addition, the Amir group hosts several outreach programs such as guiding high-school students through a research project as part of their chemistry studies and the TAU Alpha program for talented high school students.
Relevant Publications and/or Research / Innovation Product	[1] Ferber, Baabur-Cohen, Blau, Epshtein, Kisin-Finfer, Redy, Shabat, Satchi-Fainaro. Polymeric nanotheranostics for real-time non-invasive optical imaging of breast cancer progression and drug release. **Cancer Lett.**, 352 (1), 81-89 (2014). [2] Redy-Keisar, Kisin-Finfer, Ferber, Satchi-Fainaro, Shabat. Synthesis and Use of QCy7-derived Modular Probes for Detection and Imaging of Biologically Relevant Analytes. **Nat. Protoc.**, 9(1), 27-36 (2014). [3] Markovsky, Baabur-Cohen, Satchi-Fainaro. Anticancer polymeric nanomedicine bearing synergistic drug combination is superior to a mixture of individually-conjugated drugs. **J Control Release**, 187, 145–157 (2014). [4] Amir, Albertazzi, Willis, Khan, Kang, Hawker. Multifunctional Trackable Dendritic Scaffolds and Delivery Agents. **Angew. Chem. Int. Ed.**, 50(15), 3425-3429 (2011). [5] Albertazzi, Mickler, Pavan, Salomone, bardi, Panniello, Amir, Kang, Killops, Bräuchle, Amir, Hawker. Enhanced Bioactivity of Internally Functionalized Cationic Dendrimers with PEG Cores. **Biomacromolecules**, 13(12), 4089-4097 (2012).

Beneficiary Legal Name: TEVA Pharmaceutical Industries Ltd. (TEVA)	
General Description	Teva Pharmaceuticals was established at 1901 and since then gained 115 years of experience in GMP-manufacturing and marketing drugs all over the world. Today TEVA has a portfolio of more than 1,000 molecules, producing approximately 64 billion tablets and capsules a year at 66 manufacturing facilities. TEVA has the most extensive product portfolio in the industry, a powerful research and development expertise, and moreover an efficient, high-quality manufacturing on a global scale. Although TEVA considered as the world's leading provider of generic pharmaceuticals, it has world-leading position in innovative treatments for different therapeutic areas; In 1996 TEVA's first major new drug, Copaxone® for the treatment of Multiple Sclerosis (MS), was approved by the FDA. TEVA invests in a series of acquisitions that extend its global reach in the US and Europe. TEVA's exceptional integration of generics and specialty R&D enables her to generate a robust pipeline of high-value medicines, with an emphasis on complex and branded generics.
Role and Commitment of key persons (including supervisors)	Dr. Hila Epstein-Barash (Head of NTE development unit at Teva Kfar Saba). Research, training and supervision. GMP, Regulation requirements, drug development, formulation development (10%).
Key Research Facilities, Infrastructure and Equipment	TEVA brings technical knowledge, technology and support for moving a drug from the academia to the market. As a large pharmaceutical company, TEVA has the ability to mentor and support academia representatives and guide them through all challenging process of moving drug from concept to the clinic: regulatory requirements, working under GMP conditions, valid analytical methods and preclinical and clinical demands. GMP manufacturing, Pilot manufacturing, Pharma labs, Analytic lab, regulation, in vitro models to predict in vivo activity. TEVA has all infrastructure necessary to conduct these tasks.
Status of Research Premises	Dr. Epstein-Barash Group is part of Teva Kfar Saba R&D. The group has its own space and equipment. Moreover, the group also has access to other Department within Teva Kfar Saba and across the whole TEVA location. The group works with close collaboration with other groups within TEVA and with other small companies (start-ups).
Previous Involvement in Research and Training Programmes	TEVA has a strong track record in training students from academia which most of them latter incorporate as partially or full time employees. TEVA has several programs within Israel and Europe (TEVA ULM Germany), which involve student training, mentoring, scholarships and collaborations (from first degree to PhD and Postdocs). TEVA is involved in organizing seminars, training events like "breaking the silo for women in industry" and strongly encourages women to achieve high level degrees. Pharma academic, involved with Israeli universities to connect and teach academia about the Pharma world, and prepare/provide tools for students to receive a job outside academia.
Current Involvement in Research and Training Programmes	TEVA is currently coordinating a neuro collaboration between industry and academia as well as providing tools for academic students to integrate within the industry. TEVA has several collaborations with Germany location and has a Global Technology Center which collaborates with more than 5 different universities in Europe. TEVA has also an internship program for students (3/6 months stays) to have visiting students from Europe as interns. The group is active in several programs including "breaking the silo" with high school students.
Relevant Publications and/or Research / Innovation Product	[1] Epstein H, Iris Shichor, Kwon A, Hall S, Lawler M, Langer R, Kohane D. Prolonged duration local anesthesia with minimal toxicity. **PNAS,** 106(17), 7125-7130 (2009). [2] Epstein H, Orbey G, Borden M, Langer R, Kohane D. Ultrasound enhanced controlled release from hydrogel encapsulating liposomes and microbubbles. **Biomaterials**, 31(19), 5208-5217 (2010). [3] Epstein H, Gutman D, Cohen-Sela E, Haber E, Koroukhov N, Elmalak O, Danenberg HD, Golomb G. Preparation of Alendronate Liposomes for Enhanced Stability and Bioactivity: In Vitro and In Vivo Characterization. **AAPS J.,** 10(4), 505-515 (2008). [4] Epstein-Barash H, Stefanescu C, Kohane A. An in situ cross-linking hybrid hydrogel for controlled release of proteins. **Acta Biomater.** 8(5), 1703-1709 (2012). [5] Gilleron J, Querbes W, Zeigerer A, Borodovsky A, Marsico G, Schubert U, Manygoats K, Seifert S, Andree C, Stöter M, Epstein-Barash H, Zhang L, Koteliansky V, Fitzgerald K, Fava E, Bickle M, Kalaidzidis Y, Akinc A, Maier M, Zerial M. Image-based analysis of lipid nanoparticle-mediated siRNA delivery, intracellular trafficking and endosomal escape. **Nat Biotechnol**., 31(7), 638-646 (2013).

Beneficiary Legal Name: Tagworks Pharmaceuticals BV (TAG)	
General Description	Tagworks Pharmaceuticals BV, a Philips Research spin out, is developing a unique approach towards antibody-based imaging and therapy. Tagworks' technology enables the actuation of tagged antibodies through selective bio-orthogonal chemical manipulation in vivo, improving the efficacy of established approaches such as Radioimmuno-imaging and –therapy and Antibody-Drug Conjugates.
Role and Commitment of key persons (including supervisors)	Dr. Marc Robillard (CEO). Research, training and supervision (20%). Dr. Raffaella Rossin (Research Manager). Research and training (10%).
Key Research Facilities, Infrastructure and Equipment	Tagworks is based at the Radboud University Medical Center in Nijmegen in the Nuclear Medicine department, where Tagworks is a third-party guest. Tagworks has access to all preclinical research laboratories of the Nuclear Medicine department, which include protein chemistry, molecular and cell biology, radiochemistry, and small animal imaging labs, as well as a small animal hotel.
Status of Research Premises	Tagworks pays Radboud UMC a bench fee to be able to use the laboratories. There is a contract in place that ensures that Tagworks can work independently at Radboud with full control over foreground IP and the kind of research that is conducted.
Previous Involvement in Research and Training Programmes	Dr. Robillard has been involved in training several students in the industrial environment, including 4 internships bachelor students, 7 internships of Master students, 1 permanent PhD student and 1 visiting PhD student.
Current Involvement in Research and Training Programmes	Tagworks is a partner in the PRISAR project (Preclinical Intra-Operative Image-Guided Surgery and Post-Operative Radiotherapy of Tumours) under the H2020 Marie Curie program MSCA-RISE-2014.
Relevant Publications and/or Research / Innovation Product	[1] Rossin, van Duijnhoven, Hoeve, Janssen, Kleijn, Hoeben, Versteegen, Robillard. Triggered drug release from an antibody-drug conjugate using fast "Click-to-release" chemistry in mice. **Bioconj. Chem***.,* 27(7), 1697-1706 (2016). [2] van Duijnhoven, Rossin, van den Bosch, Wheatcroft, Hudson, Robillard. Diabody pretargeting with click chemistry in vivo. **J.Nucl.Med.**, 56(9), 1422-1428 (2015). [3] Versteegen, Rossin, Hoeve, Janssen, Robillard. Click to release: Instantaneous doxorubicin elimination upon tetrazine ligation. **Angew. Chem. Int. Ed.** 52, 14112–14116 (2013). [4] Rossin, van den Bosch, Hoeve, Carvelli, Versteegen, Lub, Robillard. Highly reactive trans-cyclooctene tags with improved stability for Diels-Alder chemistry in living systems. **Bioconjug. Chem.**, 24(7), 1210–1217 (2013). [5] Rossin, Verkerk, van den Bosch, Vulders, Verel, Lub, Robillard. In Vivo Chemistry for Pretargeted Tumor Imaging in Live Mice. **Angew. Chem. Int. Ed***.,* 49, 3375-3378 (2010).

Beneficiary Legal Name: Biogelx Limited (BGX)	
General Description	Biogelx Ltd is a biomaterials company that develops and supplies tuneable, cell-matched hydrogels. These allow cell biologists to control and manipulate cell behaviour in laboratory-based, cell culture applications. Biogelx operate in the life sciences sector, specifically, cell-based technology markets. The Company is currently most active in the 3D cell culture market, where biologists are seeking new technologies to improve the growth environment of their cells in the laboratory. The Company offers a research-grade product to this customer base. Additionally, the Company is increasingly active in the cell-based assays market, where the pharmaceutical industry dominates. This industry has identified the need to incorporate innovative cell culture technologies to improve laboratory-based drug screening, with the incentive to greatly improve the efficiency of drug development pipeline. Biogelx is also undertaking R&D associated with designing peptide hydrogels suitable for cell and drug delivery *in vivo*. This is relevant to the regenerative medicine and cell therapy markets.
Role and Commitment of key persons (including supervisors)	Dr. Laura Goldie (Research Chemist). Research, training and supervision. Peptide synthesis, hydrogel design (20%). Dr. Michael Connolly (Senior Product Development Scientist). Research and training. Hydrogel synthesis support (5%). Dr. Eleanore Irvine (Business Development Manager). Project management support including commercial perspective (5%).
Key Research Facilities, Infrastructure and Equipment	Key activities at Biogelx include peptide synthesis of gelator starting materials, hydrogel design/preparation and hydrogel characterisation. These activities are fundamental to the Company's R&D, where new gelators targeting specific cell applications are investigated. Biogelx is based at BioCity Scotland, which provides ready access to facilities suitable for both R&D activities relating to new hydrogels development, in addition to the production of the company's research grade/in vitro hydrogel product line currently on the market. These high-quality laboratory facilities provide the capacity for laboratory scale 'wet chemistry processes' for production of peptide starting materials (key equipment involved including fume hoods, bench space, analytical instrumentation) right through to hydrogel production and lyophilisation (key equipment involved being homogeniser, analytical instrumentation, rheometer, freeze drier). Access to cell biology capabilities within Biocity Scotland is also possible if required.
Status of Research Premises	Biogelx rent laboratory and office space at Biocity Scotland. These research premises are wholly independent from other beneficiaries and partner organisations in the consortium.
Previous Involvement in Research and Training Programmes	Biogelx possess experience in training students, having played host to 5 Masters students (from fields such as chemistry and Stratified Medicine and Pharmacological Innovation) to date.
Current Involvement in Research and Training Programmes	Biogelx is currently supporting a BBSRC DTP PhD student at the University of Manchester, in the Faculty of Medicinal and Human Sciences. This involves providing in-kind support, training, and placement opportunities.
Relevant Publications and/or Research / Innovation Product	Publication demonstrating how the stiffness of Biogelx technology can dictate stem cell fate: E.V. Alakpa, V. Jayawarna, A. Lampel, K.V. Burgess, C.C. West, S.C.J. Bakker, S. Roy, N. Javid, S. Fleming, D.A. Lamprou, J. Yang, A. Miller, A.J. Urquhart, P.W.J.M. Frederix, N.T. Hunt, B.Péault, R.V. Ulijn and M.J. Dalby. Tunable Supramolecular Hydrogels for Selection of Lineage-Guiding Metabolites in Stem Cell Cultures. **Chem**., 1, 298-319 (2016). Press release associated with above paper: https://www.sciencedaily.com/releases/2016/07/160727140037.htm#.V5mGgiuX_ME.linkedin

Partner Organisation Legal Name: Cancer Research UK (CRUK)	
General description	Cancer Research UK is the world's leading cancer charity dedicated to saving lives through research. Our vision is to bring forward the day when all cancers are cured. Our ambition is to accelerate progress and see three-quarters of people surviving cancer by 2034 by improving how we prevent, diagnose and treat cancer. As well as funding research into more than 200 types of cancer, we also develop evidence-based policy to inform government decisions related to cancer and communicate our views to key decision makers.
Key Persons and Expertise	Fionnuala Ratcliffe is Research Engagement Manager at Cancer Research UK. She leads the dissemination of research progress and results at two world-class cancer research centres in London; CRUK Barts Centre and CRUK UCL Centre. She runs a programme of engagement activities both on-site and externally at events and festivals, and delivers communications and engagement training to CRUK-funded researchers in London.
Key Research Facilities, Infrastructure and Equipment	Cancer Research UK's headquarters are in Angel, London. However, we fund research across the country, including a network of 13 CRUK-Centres consisting of partnerships between universities and local NHS trusts. We also fund 5 institutes across the country.
Previous and Current Involvement in Research and Training Programmes	Our local research engagement managers regularly deliver training on public engagement and communications to researchers working in centres where CRUK funds research. In the past, our team has hosted interns for 3-month placements as part of the wider CRUK internship scheme. On these placements, the intern was trained in the field of science engagement and communication in a medical research setting. CRUK currently delivers public engagement training to new researchers in locations across the country, including the Francis Crick Institute, Imperial, and Manchester.
Relevant Publications and/or Research / Innovation Product	CRUK has several publications for both scientists and general public, including for example Cancer Statistics (http://publications.cancerresearchuk.org/cancerstats), healthy lifestyle resources (http://publications.cancerresearchuk.org/preventionhealthylifestyles) and cancer patient resources (http://publications.cancerresearchuk.org/patientinfo).

Partner Organisation Legal Name: Fundación ESADE (ESADE)	
General description	ESADE is one of the world's most prestigious academic institutions. ESADE programs cover the entire professional cycle (from recent graduate to experienced professional). The business management teaching and research at ESADE is internationally renowned. ESADE offers courses in Management Studies that rely upon various academicians, institutions and research centres, and groups, who focus on entrepreneurship, innovation, leadership and governance, management, skills and knowledge, business social responsibility, economic law, branding, etc. ESADE has pioneered research in creativity and learning, innovation, entrepreneurial skills and management practices
Key Persons and Expertise	Jordi Vinaixa is Professor in the Dept. of Strategy and General Management and Academic Director for the Institute for Entrepreneurial Initiative at ESADE. For 4 years, he was Program Director of the MSc in Innovation and Entrepreneurship and has been an instrumental player in the KIC-Innoenergy training programmes at ESADE since its start in 2010, and continues to coordinate the short training courses on entrepreneurship with KIC Innoenergy.
Key Research Facilities, Infrastructure and Equipment	ESADE has a campus in Barcelona campus and a newest campus in Sant Cugat that offers state-of-the-art learning facilities covering around 46.000 m^2 and houses the Business School, most of ESADE's research institutes, ESADECREAPOLIS and the student residence halls. The libraries are equipped to support learning, teaching, research and continuous training in the ESADE community by acquiring and managing the most appropriate resources and information sources.
Previous and Current Involvement in Research and Training Programmes	ESADE has solid experience in EU-funded research with participation in over 25 EC funded projects, and has previously provided professional training courses for ESRs in ITNs. Additionally, ESADE is a key player in the EIT KIC-Innoenergy programme, where we provide educational courses for KIC masters and PhD students, specific training and support for innovation projects and entrepreneurs, and perform R&D work on innovative management tools
Relevant Publications and/or Research / Innovation Product	The ESADE Institute for Entrepreneurship researches and publishes on the following topics: 1) Company creation, growth and financing (venture capital, F&F, private equity, business angels, etc.), including Entrepreneurial spirit in family firms, 2) Creativity and innovation, 3) Corporate entrepreneurship, social entrepreneurship and Educating young people to become entrepreneurs

Partner Organisation Legal Name: Universitat Autònoma de Barcelona (UAB)	
General Description	**The Observatory for Equality** in the Universitat Autònoma de Barcelona is a university organization created by the Governing Council of the UAB to act as a specialist support for the design and evaluation of equality policies. It began its activity in 2005 (agreement 3/2006 of Governing Council of UAB), and in 2008 extended its field of action to those collectives that could be subjected to unfavourable conditions for reasons of disability or social or economic situations. One of the tasks entrusted to the Observatory is to elaborate proposals for action plans. The UAB has elaborated three actions plans from 2008 to 2016.
Key persons and Expertise	Prof. Joana Gallego, Director of the Observatory, is expert in Gender Studies. Co-director of the Master in Gender and Communication. Dr. Laura Duarte has PhD in Sociology, specialised in gender inequalities in promotion within the academic career, in elaborating indicators to diagnose sexism at the university. Dr. Maribel Ponferrada has PhD in Social Anthropology. Expert in gender perspective, gender dimension in research, gender bias in science.
Key Research Facilities, Infrastructure and Equipment	In order to carry out its assigned tasks, the Observatory possesses the personal and material means required. From among the university's academic personnel, the Governing Team designates the person who is responsible for the supervision of activities, and guarantees a workspace, assistance from specialist personnel and a budget allocation to fund its daily operations.
Previous and Current Involvement in Research and Training Programmes	FP7 Project "EGERA - Effective Gender Equality in Research and in Academia" (2014-2017), funded by the European Commission. Agreement num. 612413. RDI Project "Academic career. RDI. Spanish Women's Institute". 2008-2009. Exp. 003/7 RDI Project "Care and Provision". RDI. Spanish Women's Institute. 2005-2008. Ref. I+D+I Exp. Nº 79/04 EGERA Gender Sensitive Research Workshops (http://www.uab.cat/web/the-observatory-/egera-ue-fp7-1345697880330.html). The Observatory organises training activities in gender studies addressed to UAB students every year (http://www.uab.cat/web/l-observatori/estudiants/tallers-amb-reconeixement-de-credits-ects-1345685927557.html).
Relevant Publications and/or Research / Innovation Product	Observatori per a la Igualtat (2008). "Gender bias and inequalities in the assessment of academic careers. Proceedings of the I International Congress on Gender Bias and inequalities in the assessment of academic careers". Bellaterra, Spain. Rifà-Valls, M.; Ponferrada, M.; Duarte, L. (2014). Report on Mapping & Critical assessment of existing tools for including gender in research. EGERA reports.

6. Ethics Issues

THERACAT proposes the development of new anticancer therapies based on bio-orthogonal catalysis. The high benefit followed in this project requires the use of human cells and animal testing, since in the field of biologically active materials there is the lack of alternative strategies to evaluate their therapeutic potential as well as *in vitro* and *in vivo* performance. Thus, all participants of the project are aware that this proposal will have ethical issues associated and are committed to ensure that all planned activities and experiments are in conformance with national and EU legislation, regulations and ethical standards. All fundamental ethical codes will be respected, periodically assessed and performed following the basic ethical principles described in the "Charter of Fundamental Rights" of the European Union (2000/C 364/01, 2010/C 83/02). All necessary authorisations will be provided before the start of the project.

Human cells/tissues

The samples of human origin to be used in this project are cells that are commercially available from ATCC in partnership with LGC standards. In particular, human cells that are planned to be used in the THERACAT project are detailed below:

IBEC, TUE:

- PC-3 (ATCC® CRL-1435™): http://www.lgcstandards-atcc.org/products/all/CRL-1435.aspx?geo_country=es#generalinformation
- HeLa (ATCC® CCL-2™): http://www.lgcstandards-atcc.org/products/all/CCL-2.aspx?geo_country=es
- LNCaP (ATCC® CRL-1740™): http://www.lgcstandards-atcc.org/Products/All/CRL-1740.aspx
- MCF7 (ATCC® HTB-22™): https://www.lgcstandards-atcc.org/Products/All/HTB-22.aspx?geo_country=es

BAS:

- MCF7 (ATCC® HTB-22™): https://www.lgcstandards-atcc.org/Products/All/HTB-22.aspx?geo_country=es
- NCI-H460 [H460] (ATCC® HTB-177™): https://www.lgcstandards-atcc.org/Products/All/HTB-177.aspx
- HCT 116 (ATCC® CCL-247™): https://www.lgcstandards-atcc.org/Products/All/CCL-247.aspx

EDI, BGX:

- PC-3 (ATCC® CRL-1435™): http://www.lgcstandards-atcc.org/products/all/CRL-1435.aspx?geo_country=es#generalinformation
- HeLa (ATCC® CCL-2™): http://www.lgcstandards-atcc.org/products/all/CCL-2.aspx?geo_country=es
- LNCaP (ATCC® CRL-1740™): http://www.lgcstandards-atcc.org/Products/All/CRL-1740.aspx
- MCF7 (ATCC® HTB-22™): https://www.lgcstandards-atcc.org/Products/All/HTB-22.aspx?geo_country=es
- A549 (ATCC® CCL-185™): https://www.lgcstandards-atcc.org/Products/All/CCL-185.aspx
- A375 (ATCC® CRL-1619™): https://www.lgcstandards-atcc.org/Products/All/CRL-1619.aspx

TAU:

- MDA-MB-231 (ATCC® HTB-26™): https://www.atcc.org/Products/All/HTB-26.aspx
- A375 (ATCC® CRL-1619™): https://www.lgcstandards-atcc.org/Products/All/CRL-1619.aspx

TAG:

- LS 174T (ATCC® CL-188™): https://www.lgcstandards-atcc.org/Products/All/CL-188.aspx
- Capan-1 (ATCC® HTB-79™): https://www.lgcstandards-atcc.org/Products/All/HTB-79.aspx
- OVCAR3 (ATCC® HTB-161™): https://www.lgcstandards-atcc.org/Products/All/HTB-161.aspx

The project does not plan to use human embryonic stem cells, human cloning, or procedures where humans could be involved at all.

Animals

TAU: Mice are the standard animal model by which we evaluate tumour progression following full evaluation of the tumour cells in culture (i.e. in vitro). In order to monitor the migration of tumour cells in the bloodstream and follow-up their invasion and extravasation from the blood vessels into a new metastatic niche, we label the cells fluorescently and use non-invasive intravital imaging which significantly decrease the number of animals required for each study. However, in order to detect and study the effect of the new compounds on tumour-host interactions that govern processes studied in this project such as angiogenesis, metastases formation and interactions with the supporting microenvironment, animals are required and cannot be replaced by any in vitro model.

In this project, we proposed to design and physico-chemico-biological characterisation of new nanomedicines. In order to study the pharmacokinetics of these new nanomedicines synthesized during the project and evaluate and determine their effect on the tumour itself and its supporting stroma including angiogenic blood vessels formed as well as cancer-associated fibroblasts and immune cells that come from the host (i.e. the animal bearing the tumour), it is necessary to use animals that provide the physiological (and pathological) environment of the whole organism.

The specific strains of mice that will be used correlate with the tumour type and source of the cells. For example, for human tumours inoculated in mice, we will use either SCID or nu/nu mice, whereas for murine tumours, we will use C57BL/6 or BALB/c mice depending on the specific tumour type.

Since experiments on animals are indispensable to follow tumour progression and develop strategies to reduce the effects of disease progression, the experimental design and the experimental procedures are customized to avoid or at least to minimize pain, distress and other suffering for the animals' sake. All animal handling, imaging, euthanasia and discarding will be performed according to institutional guidelines (TAU IACUC).

Small animal studies: This study covers basic fundamental biological questions and is also translational ('applied') by nature, and therefore, it requires a large number of mice. In general, the procedures that will be carried out will include the inoculation of a variety of human tumour cells in a total of 700 SCID and athymic nude immunodeficient mice that will be implanted with, and another 700 mice that will be treated by all compounds and vehicles synthesized during this project, at 3 escalating doses in order to determine toxicity and biodistribution in diseased and non-disease-bearing mice. This is an important point, as we would like to use clinically-relevant tumour models including human xenografts, and thus it is necessary to use this type of immunodeficient mice.

Two hundred BALB/c and 200 C57Bl wild-type mice will be implanted with syngeneic murine tumour models, and treated with our novel polymeric nanomedicines. It is paramount to establish a tumour model in immune-competent mice, since we know that the host including mainly the tumour stroma and microenvironment with associated inflammation, have a central role in tumour progression and metastases.

Power calculation cannot be performed at this stage as the different compounds and cell types will be collected during the term of the project and therefore, the numbers are not available yet.

The anticipated impact of these experiments when completed is to shed light on fundamental cancer biology phenomenon, i.e. tumour progression and metastases and how it is affected by different compounds. Our multidisciplinary approach will offer new nanomedicines with a higher therapeutic efficiency and reduced side-effects. An additional potential outcome would be to obtain an alternative preventive therapy for patients with high risk of outbreak of metastases or for those with minimal residual disease.

***Practical considerations*:** The actual group size for the animal studies (n=6 to 10 animals) will depend on the magnitude of the probe signal or drug effect and the inter-animal variability. After completion of *in vivo* imaging and pharmacological experiments, all animals will be euthanized and tissues will be harvested for HPLC analysis (to determine PK), histological and immuno-histochemical analysis. All not-harvested tissues or post-analysis samples will be discarded according to institutional procedures. Research will be carried out with due concern for the environment, in particular the disposal of all chemical waste generated during the course of the program.

In accordance with Directive 2010/63/EU, in particular Article 33 ("Care and accommodation"), we will ensure that, as far as the care and accommodation of animals is concerned (a) all animals will be provided with accommodation, an environment, food, water and care which are appropriate to their health and well-being; (b) any restrictions on the extent to which an animal can satisfy its physiological and ethological needs will be kept to a minimum; (c) the environmental conditions in which animals are bred, kept or used will be checked daily; (d) arrangements will be made to ensure that any defect or avoidable pain, suffering, distress or lasting harm discovered is eliminated as quickly as possible; and (e) animals are transported under appropriate conditions.

All imaging protocols and procedures will be performed under anaesthesia for immobilization and will induce no pain. Animals will be monitored for levels of health and overall well-being. Any signs of discomfort greater than the disease provoked (body weight loss >15%; tumour volume > 20% of body weight) will trigger removal of the animal from the respective session. All animals will be regularly monitored for body weight, changes in behaviour and signs of any discomfort. All animals will be housed in our animal facility which is under the supervision of two qualified veterinarians. Mice will be given *ad libitum* access to food and water. Bedding is replaced regularly on a 3-weekly basis.

All animal handling, imaging, euthanasia and discarding will be performed according to institutional guidelines. **Relevant EU legislation and directives to follow are:** Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010; Directive 2003/65/EC of the European Parliament and of the Council of 22 July 2003 amending Council; Directive 86/609/EEC on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes; Directive 86/609/EEC of 24 November 1986 on the protection of Animals used for Experimental and other Scientific Purposes.

To comply with the principles of replacement, reduction and refinement, we will follow the rules of **humane animal experimentation**.

Replacement: Imaging probes and therapeutic molecules will be first evaluated biochemically in the test tube and in cell culture experiments. Following the *in vitro* experiments, we will test our newly-synthesized compounds in live animals. The use of animal models is an essential step to develop application procedures that will be applied prospectively in humans.

Reduction: Although our research requires a large number of mice, we intend to reduce the number of mice used in each experiment by several ways:

1. Experiments that are performed in parallel will use the same control group.

2. Experiments will be carried out using non-invasive imaging techniques, i.e. animals can be used in longitudinal studies for monitoring disease progression. This will significantly reduce the number of animals required for the study and enhance the statistical robustness of the experiment. These includes fluorescence-probe labelling of injected cells (by infection or transfection with GFP, mCherry or luciferase) and by using fluorescent probes and fluorescently-labelled polymers. The non-invasive imaging by fluorescence and bioluminescence devices (CRI Maestro and Biospace Photon Imager or IVIS SpectrumCT, respectively) will allow us to significantly reduce the number of mice needed for follow-up of disease progression since we are following-up on the same mouse in each group reducing the variability of the experiment. In addition, there is no need for extra mice for each time point- all experiments are terminated at the end point. Similarly, pharmacokinetic and biodistribution studies of the synthesized probes, new compounds and polymers are imaged using spectral analysis which allows for unmixing of different fluorophores. This means that we can image simultaneously at one wavelength ("colour") the pathological site and at another wavelength- the labelled polymer, compound and/or probe. Pharmacokinetics and biodistribution studies are enabled in this way without performing any unnecessary surgical procedure and resecting the mice at the different time points, but rather imaging them non-invasively until the terminal end point.

3. For each *in vivo* experiment, emphasis will be placed on the amount of information that we can receive from the experiment performed. For example, in each experiment, we will obtain as many measurements as possible in order to reduce the number of similar/parallel experiments that need to be performed. This will include measurements of body weight and follow-up of fluorescence signal to determine disease volume. Moreover, following experiment termination, we will take measurements of necrosis, hypoxia, microvessel density, proliferation and apoptosis, and specific markers for IHC in only one experiment. Standardization of

experiments and service of highly skilled staff will further contribute to a significant reduction in the number of animals.

Refinement: Animals will be housed in SPF animal facility and cared by veterinarians and experts in animal welfare ensuring the highest possible standard of treatment and care practices. Animal care unit has a humane end-point policy and any animal displaying signs of suffering will be immediately euthanized. Animals will be euthanized by cervical dislocation at the first cervical vertebra according to IACUC. For imaging studies, mice will be anaesthetized using isoflurane in medical oxygen.

All procedures will comply with the European Commission Recommendation of 07/02/2008 on a Code of Conduct for Responsible Nanosciences and Nanotechnologies Research.

In THERACAT, NU/NU mouse xenograft model of human A375 or MDA-MB-231 cancer cell will be used. A375 cells will be inoculated intradermally under ketamine (100 mg/kg) and xylazine (12 mg/kg) anaesthesia. MDA-MB-231 cells will be inoculated intramammary under ketamine (100 mg/kg) and xylazine (12 mg/kg) anaesthesia.

NU/NU mice bearing A375 tumours will be treated when tumour size will reach 50 mm^3; MDA-MB-231 tumour-bearing NU/NU mice will be treated when tumour size will reach 50 mm^3. Controls or nanomaterials will be administered by tail vein injection or intraperitonealy. Animals will be euthanized according to the protocol either right after imaging procedure, or at defined endpoint.

Alternatively, for syngeneic mouse models of cancer in immunocompetent mice, we will use murine 4T1 mammary carcinoma in Balb/c mice and B16F10 murine melanoma in C57/BL6 mice.

B16F10 cells will be inoculated intradermally under ketamine (100 mg/kg) and xylazine (12 mg/kg) anaesthesia. 4T1 cells will be inoculated intramammary under ketamine (100 mg/kg) and xylazine (12 mg/kg) anaesthesia.

C57/BL6 mice bearing B16F10 tumours will be treated when tumour size will reach 50 mm^3; 4T1 tumour-bearing Balb/c mice will be treated when tumour size will reach 50 mm^3. Controls or nanomaterials will be administered by tail vein injection or intraperitoneally. Animals will be euthanized according to the protocol either right after imaging procedure, or at defined endpoint.

TAG: The use of animals for research in The Netherlands is regulated by the Dutch Experiments on Animals Act national law “Wet op de Dierproeven (Stb 1977, 76); Revised Experiments on Animals Act (Stb 1997, 003); Revised Experiments on Animals Act (Stb 2003, 399); http://wetten.overheid.nl/BWBR0003081/geldigheidsdatum_29-07-2010

All animal experiments have to be approved by the Animal Welfare Committee of the Radboud University. This Animal Welfare Committee is acknowledged by Dutch law and has the responsibility to provide permits for animal experiments. The committee will evaluate beforehand if the scientific and societal interests weigh up to the use and discomfort of animals. This (ethical) review is done according to the previously notes Dutch law on animal experiments.

All animals are observed daily for general assessment of health by the Central Animal Facility staff. Sick animals are reported to the institutional veterinarian and responsible researcher. In case of severe discomfort also the Animal Welfare Body will be informed.
Food and water, and environmental parameters are observed daily by the Central Animal Facility staff. Husbandry logs are documented daily.

In THERACAT, Balb/c nude mouse xenograft models of above listed cancer cells will be used. Mice will be inoculated s.c. with cells under halothane anaesthesia. Mouse studies (biodistribution, imaging, or therapy) will commence when the tumours reach 50–100 mm3 size. Compounds will typically be administered by tail vein infusion.

7. Letters of Commitment

CANCER RESEARCH UK

Cancer Research UK
Angel Building
407 St John Street
London EC1V 4AD
United Kingdom

020 7242 0200
cruk.org

London, 9 January 2017

To whom it may concern,

Letter of Commitment

To whom it may concern,

Through this letter, Andrew Waldron as Director of Legal (Research) of Cancer Research UK confirms his commitment to participate as Partner Organisation in the project entitled "Bio-orthogonal catalysis for cancer therapy", coordinated by Dr. Lorenzo Albertazzi (call MSCA-ITN-2017, action MSCA-ITN-ETN, within the framework of the Marie Skłodowska-Curie Actions).

Cancer Research UK will contribute to the training of the ESRs organising a training course entitled "How to Communicate To and Engage the Public". This training has been carefully designed with the aim of ensuring ESRs in the programme are able to communicate to the general public the network purposes and results.

In addition Cancer Research UK will receive a secondment from student ESR6 for three months, and will also actively contribute to disseminate the network results and implications in close collaboration with all network members through charitable events and social media, among others.

Please do not hesitate to contact me if you need further information.

Sincerely,

Andrew Waldron

Director of Legal (Research)

Av. Pedralbes, 60-62
E-08034 Barcelona
Tel. +34 932 806 162
Fax +34 932 048 105
www.esade.edu

Barcelona, 20th December 2016

ESADE

Dr. Lòrenzò Albertazzi
Nanòscòpy fòr Nanòmedicine Gròup
Institute fòr Biòengineering òf Catalònia
C/Baldiri Reixac 15-21, pl.1
08028 BARCELONA (Spain)

Dear Prof. Albertazzi,

RE: Participation as Partner Organisation in the project "Bio-orthogonal catalysis for cancer therapy".

I am writing this letter to confirm that ESADE Business School wishes to participate as a Partner Organisation in the project entitled "Bio-orthogonal catalysis for cancer therapy", coordinated by Dr. Lorenzo Albertazzi (call MSCA-ITN-2017, action MSCA-ITN-ETN, within the framework of the Marie Skłodowska-Curie Actions).

ESADE offers courses in Management Studies that rely upon various academics, research centres, and groups, with expertise in entrepreneurship, innovation, leadership and governance, management, skills and knowledge, business social responsibility, economic law, branding, etc. ESADE has pioneered research in creativity and learning, innovation, entrepreneurial skills and management practices.

Jordi Vinaixa is Professor in the Department of Strategy and General Management and Academic and member of ESADE's Institute for Entrepreneurship (EEI). For 4 years he was Program Director of the MSc in Innovation and Entrepreneurship and has been an instrumental player in the KIC-Innoenergy training programmes at ESADE since its start in 2010, and continues to coordinate the short training courses on entrepreneurship with KIC Innoenergy.

ESADE has solid experience in EU-funded research with participation in over 30 EC funded projects, and has previously provided professional training courses for ESRs in ITNs. Additionally ESADE is a key player in the EIT KIC-Innoenergy programme, where we provide educational courses for KIC masters and PhD students, specific training and support for innovation projects and entrepreneurs, and perform R&D work on innovative management tools.

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Av. Pedralbes, 60-62
E-08034 Barcelona
Tel. +34 932 806 162
Fax +34 932 048 105
www.esade.edu

Members of ESADE's Institute for Entrepreneurship research and publish on the following topics:

ESADE

1) Company creation, growth and financing (venture capital, F&F, private equity, business angels, etc.),
2) Entrepreneurial spirit in family firms,
3) Creativity and innovation,
4) Internationalization processes, strategic alliances and born global enterprises,
5) Corporate entrepreneurship, social entrepreneurship
6) Educating young people to become entrepreneurs

ESADE will provide ESRs with training through the "Introductory Crash Course in Entrepreneurship" covering skills such as:

- Entrepreneurship
- Strategy and innovation
- Marketing for scientific/technology entrepreneurs
- Entrepreneurial finance
- Managing entrepreneurial team
- Managing intellectual property rights (IPR)

We are confident that the ESRs will acquire new competences and skills that will benefit their future career, enhance their career development plan and improve their chances for future employment in innovation and entrepreneurship.

Best regards,

T. Ysa

Tamyko Ysa
Vice-Dean of Research
ESADE Business & Law Schools
www.esade.edu

UAB
Universitat Autònoma de Barcelona

Observatori per a la Igualtat

Edifici A - A/2026 - Campus de la UAB - 08193 Bellaterra (Cerdanyola del Vallès) - Barcelona - Spain
Tel. +34 93 581 29 29 - Fax +34 93 581 31 64
observatori.igualtat@uab.cat
www.uab.cat/observatori-igualtat/

Letter of Commitment

Bellaterra, 22th December 2016

To whom it may concern,

Through this letter, Dr. Armand Sanchez as Vice-rector for Research and Transference and acting as legal representative of the Universitat Autònoma de Barcelona (UAB) confirms his commitment to participate as Partner Organisation in the project entitled "Bio-orthogonal catalysis for cancer therapy", coordinated by Dr. Lorenzo Albertazzi (call MSCA-ITN-2017, action MSCA-ITN-ETN, within the framework of the Marie Skłodowska-Curie Actions).

UAB-Observatory for Equality, whose responsible is Dr. Joana Gallego, will contribute to the training of the ESRs organising a training course entitled "Gender equality and gender dimension in research". This training has been carefully designed with the aim to provide the knowledge and skills to address gender inequalities in the academic career and to incorporate gender as a dimension in the research process. Moreover, UAB-Observatory for Equality will be part of the Recruitment Committee, being actively involved in its duties and aiming at the promotion of a gender balanced selection of candidates. UAB-Observatory for Equality will also promote the inclusion of the gender dimension in the research content throughout the project.

Please do not hesitate to contact me for further information.

Sincerely,

UAB Universitat Autònoma de Barcelona
Armand Sánchez Bonastre
Vicerector de Recerca i de Transferència

Universitat Autònoma de Barcelona
Observatori per a la Igualtat

Dr. Armand Sanchez
Vice-rector for Research and Transference

Dr. Joana Gallego
Director of the Observatory for Equality

END PAGE

MARIE SKŁODOWSKA-CURIE ACTIONS

Innovative Training Networks (ITN)
Call: H2020-MSCA-ITN-2017

PART B

THERACAT

Bio-orthogonal catalysis for cancer therapy

This proposal is to be evaluated as:

ETN

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