COLLABORATIVE AGREEMENT

on the establishment of a Max Planck Partner Group

between

Max-Planck-Gesellschaft zur Förderung der Wissenschaften e.V.
Hofgartenstraße 8, 80539 München, Germany

represented by the Managing Director at the Max Planck Institute of Molecular Physiology, Otto-Hahn-Str. 11, 44227 Dortmund, Germany, Prof. Dr. Stefan Raunser

(hereinafter referred to as **"MPI-DO"**)

Fundación Para el Progreso de la Química (FUNDAQUIM)
1614 Isidoro de María Street, 11800, Montevideo, Department of Montevideo, represented in this act by Dr. Eduardo Dellacasa and Dr. Gustavo Seoane, in their capacity as Secretary and Member of the Board of Directors

(hereinafter referred to as "FUNDAQUIM")

and

Universidad de la República de Uruguay
Av. 18 de Julio 1968, 11200 Montevideo, Departamento de Montevideo, Uruguay

represented by The Rector Héctor Cancela, who delegates the signature to the President of the International Relations Service (SRI) of Udelar, Gonzalo Vicci Gianotti, according to resolution 370/2025 del 21 de julio de 2025.

(hereinafter referred to as **"UdelaR"**)

(MPI-DO, FUNDAQUIM and UdelaR individually hereinafter also referred to as a **"Partner"** and collectively as the **"Partners"**)

PREAMBLE

Whereas, the Max-Planck-Gesellschaft zur Förderung der Wissenschaften e.V. is an independent, non-governmental and non-profit German research organization, founded on February 26, 1948, and is the successor organization to the Kaiser Wilhelm Society, which was established in 1911. Currently more than 80 research institutes belong to MPG, performing basic research in the natural sciences, life sciences, social sciences and humanities (hereinafter referred to as **"Max Planck Institutes"**).

Whereas, MPI-DO is a Max Planck Institute belonging to the Max-Planck-Gesellschaft zur Förderung der Wissenschaften e.V. and is legally not independent.

Whereas, FUNDAQUIM is a legal entity whose purpose is to stimulate the creation, application and dissemination of knowledge in all disciplines cultivated at the Faculty of Chemistry of UdelaR, as well as to promote the relationship with the productive system and society in general and that it is linked to the Faculty of Chemistry of UdelaR through an agreement in which both agreed on the possibility of one of them entrusting the other with the administration of academic and technical activities of common interest.

Whereas, UdelaR is is the largest and oldest University of Uruguay, which has the legal nature of a public legal entity and is organized as an Autonomous Entity co-governed in accordance with the provisions of Articles 202 and 203 of the Constitution of the Republic and Law 12.549, Organic Law of the University of the Republic.

Whereas, the Max-Planck-Gesellschaft zur Förderung der Wissenschaften e.V. established a Max Planck Partner Group Program as a highly competitive and person-centered program with the aim of creating career paths for outstanding young researchers who have spent a research residency at a Max Planck Institute and are returning to their home country.

Whereas, Dr. Laura Florencia Posada Trindade has spent a research residency at MPI-DO as PostDoc from September 15, 2022 until November 30, 2023 and is going back to her home country as of December 11, 2023.

Whereas, in order to safeguard the continuity of scientific collaboration to the mutual benefit, the Department of Structural Biochemistry at the MPI-DO headed by Prof. Dr. Stefan Raunser and Dr. Laura Florencia Posada intend to perform common scientific research activities.

Now, therefore, the Partners wish to enter into the following collaborative agreement on the establishment of a Max Planck Partner Group at UdelaR (hereinafter referred to as the **"Agreement"**) on the terms and conditions set out below.

SECTION 1

SUBJECT MATTER OF AGREEMENT

1.1 The Partners agree to establish the Max Planck Partner Group at UdelaR (hereinafter referred to as **"Partner Group"**) as further specified in Section 2 below. The Partner Group shall be headed by Dr. Laura Florencia Posada (hereinafter referred to as **"Partner Group Leader"**).

1.2 The Department of Structural Biochemistry at the MPI-DO and the Partner Group intend to conduct fundamental new research as further specified in Section 3 below.

1.3 MPI-DO agrees to provide a financial contribution in order to perform the collaborative research program as further specified in Section 4 below. The expenditure of the financial contribution is at the full discretion of the Partner Group Leader.

1.4 The Partner Group is established for a five (5) year period. A further extension beyond this five (5) year period is not possible.

1.5 Nothing in this Agreement shall be regarded as creating a joint venture, partnership, agency, employment relationship, franchise relationship or taxable entity between the Partners, nor shall either Partner have the right, power or authority to create any obligations or duties, express or implied, on behalf of the other Partner hereto, it being understood that the Partners are independent vis-à-vis one another.

SECTION 2

PARTNER GROUP

2.1 The Partner Group shall be hosted and accommodated at UdelaR in Facultad de Química, Av. Gral. Flores 2124, 11800 Montevideo, Departamento de Montevideo, Uruguay. UdelaR agrees to provide adequate scientific and technical facilities, infrastructure, rooms and administrative services for the Partner Group and to ensure the adequate integration of the Partner Group at UdelaR.

2.2 The Partner Group Leader will be engaged at UdelaR. UdelaR ensures that the Partner Group Leader will comply with the corresponding obligations arising from this Agreement.

2.3 Apart from the Partner Group Leader, the Partner Group shall comprise further members, such as postdoctoral researchers, doctoral students, and technicians (hereinafter referred to as **"Partner Group Members"**) to be engaged at UdelaR. UdelaR ensures that each Partner Group Member will comply with the corresponding obligations arising from this Agreement.

2.4 UdelaR shall appoint and dismiss the Partner Group Members in consultation with the Partner Group Leader and according to the applicable contractual stipulations and the regulations in force at UdelaR.

SECTION 3

COLLABORATIVE RESEARCH ACTIVITIES

3.1 The Department of Structural Biochemistry at the MPI-DO and the Partner Group intend to perform collaborative research activities according to the collaborative research program outlined in Appendix 1 (hereinafter referred to as **"Research Activities"**).

3.2 The Partners agree that Appendix 1 shall be binding, but may be adapted from time to time to reflect developments in the sphere of research. Any such adaptation shall become binding through the medium of records signed by both Partners.

3.3 Contact person with regard to the Research Activities from part of MPI-DO is the Director at the Department of Structural Biochemistry, Prof. Dr. Stefan Raunser. Contact person with regard to the Research Activities from part of UdelaR is the Partner Group Leader. It is not possible to change the person of the Associate Group Leader, notwithstanding the fact that Udelar states that the functional relationship may vary or be terminated in accordance with the provisions of the regulations in force at Udelar. If for any reasons a change in the contact person of MPI-DO should be reasonably required, the Partners shall endeavor to identify an appropriate substitute within a reasonable timeframe upon consultation with each other.

3.4 To the extent necessary for the performance of the Research Activities, the Partners shall grant each other access to their respective research infrastructure. In the event of mutual use of the research infrastructure, the Partners shall observe the principle of balance. For the avoidance of doubt, the Partners will not charge any overhead.

3.5 The Partners shall keep each other continually informed about their generated experiences, knowledge, and know-how in an appropriate manner obtained in the course of the Research Activities.

3.6 At the end of the Research Activities, the Partners shall prepare a pertinent written scientific report in close coordination with each other. The Partners shall ensure that preparation and completion of the report are not unreasonably delayed.

SECTION 4

MPG's FINANCIAL CONTRIBUTION

4.1 In order to exclusively perform the Research Activities, the Partners mutually agree that MPI-DO provides a financial contribution in the amount of annually up to EUR 20.000,00 (in words: twenty thousand euros) plus any applicable value added tax.

4.2 The financial contribution shall be made by means of a transfer to the FUNDAQUIM account that UdelaR shall indicate, so that FUNDAQUIM may administer the funds. FUNDAQUIM shall invoice MPI-DO in accordance with best accounting practices at the following address:

invoice-moph@gv.mpg.de

For the avoidance of doubt, such invoice may also be an advance invoice (*Vorabrechnung*) listing the intended use of the transferred financial contribution. At the minimum, at the end of each calendar year, UdelaR shall provide a final invoice that proves the use of the transferred financial contribution. All invoices shall include the mandatory information according to section 14 of the German Value Added Tax Act (*Umsatzsteuergesetz*).

4.3 MPI-DO's financial contribution according to Section 4.1 shall be primarily used to cover personnel costs for Partner Group Members, travel costs, costs for workshops as well as running lab costs such as costs relating to lab technicians and lab supplies/consumables. Subsequently, MPI-DO's financial contribution according to Section 4.1 may be partially used for the purchase of minor scientific equipment for the Research Activities with a value not exceeding EUR 4.000,00 (in words: four thousand euros). MPI-DO's financial contribution according to Section 4.1 may not be

used for salaries of permanent staff or salary increments. In particular, UdelaR will not charge any overhead costs.

SECTION 5

CONFIDENTIALITY

5.1 The Partners undertake to hold in confidence any and all documents marked as secret and any other secret information which the Partners have made available to one another in a manner that clearly indicates their confidential nature ("Confidential Information") only for the purpose of pursuing Research Activities and to handle Confidential Information with care, keeping it in a manner appropriate to its confidential nature and not to disclose such information to any third party. In particular, the Partners undertake to distribute Confidential Information among MPI-DO's staff members and Project Group Members only on a need-to-know-basis, and it must be guaranteed that said people undertake to keep them under confidentiality.

5.2 The obligation of confidentiality shall not apply if

5.2.a) the information is or has become of public nature without breach of this confidentiality obligation,

5.2.b) a Partner gives written authorization for publication of certain Confidential Information,

5.2.c) the Confidential Information is communicated to the other Partner without any breach of obligation by a third party,

5.2.d) the Confidential Information was developed independently by the other Partner without any disclosure of such, or

5.2.e) the Confidential Information was already known by the other Partner prior to disclosure, or

5.2.f) the Partner is obligated to disclose the Confidential Information in order to comply with applicable laws or regulations or with a court or administrative order or is covered by the second article of the Organic Law of the Universidad de la República,.

5.3 The obligation of confidentiality shall survive termination of this Agreement but apply no longer than three (3) years following the Expiry Date.

SECTION 6

BACKGROUND INTELLECTUAL PROPERTY and WORK RESULTS

6.1 **"Background Intellectual Property"** within the meaning of this Agreement shall mean any intellectual property owned or controlled by either of the Partners prior to commencement of or developed independently from the Research Activities to be performed under this Agreement, and which the owning Partner contributes or uses in the course of performing the Research Activities as listed in Appendix 1.

6.2 All Background Intellectual Property used in connection with the Research Activities shall remain the property of the Partner introducing the same. Each Partner acknowledges and confirms that nothing contained in this Agreement shall give it any right, title or interest in or to the Background Intellectual Property of the other Partner save as explicitly granted by this Agreement.

6.3 **"Work Results"** within the meaning of this Agreement shall mean any generated research results, whether fit for protection or not, and any research data collected in performance of the Research Activities.

6.4 Any Work Results generated solely by staff members of MPI-DO shall solely belong to MPI-DO. Any Work Results generated solely by the Partner Group Leader and / or the Partner Group Members shall solely belong to UdelaR. Jointly generated Work Results shall jointly belong to MPI-DO and UdelaR. Their share in the jointly generated Work Results shall be determined in accordance with the significance of the contribution to the jointly generated Work Result, and shall be regulated on a specific agreement between the Parties. Neither MPI-DO nor UdelaR may assign any of its rights in the jointly generated Work Result without the prior consent of the other Partner, regardless of the name under which a protective right is registered. Should either Partner wish to abandon its share in a jointly generated Work Result, it shall first offer such right to the other Partner.

6.5 For the duration of this Agreement the Partners grant each other a no-charge, non-transferable, non-sublicensable and non-exclusive right to use their Background Intellectual Property if and to the extent to which this is necessary for the successful performance of the Research Activities and subject to any legal restrictions or limits, including those imposed by the rights of third parties.

6.6 For the duration of this Agreement the Partners grant each other a no-charge, non-transferable, non-sublicensable and non-exclusive right of use in their respective Work Results and in their share in jointly owned Work Results if and to the extent to which this is necessary for the successful performance of the Research Activities.

6.7 Each Partner shall be entitled to use the Work Results generated under this Agreement free of any charge, unrestricted and unlimited solely for their own scientific purposes (research, teaching and outreach). For any further desired use of the Work Results, the Partners shall enter into a separate pertinent agreement.

SECTION 7
PUBLICATIONS

7.1 The Work Results as defined above in Section 6.3 are intended for publication.

7.2 In principle, the Partners shall jointly publish the Work Results.

7.3 In case of sole publication of Work Results by either Partner, the written consent of the other Partner shall be obtained prior to publication. Publication shall not be denied without just cause. The publishing Partner shall provide the other Partner with a copy of the planned publication not less than thirty (30) days prior to the planned publication, giving the other Partner the opportunity to review and submit substantiated comments to indicate what modifications are required to protect its confidential information. If, after thirty (30) days, no objection has been raised by the receiving Partner, consent to publication shall be deemed to be granted.

7.4 In all cases, including any case of joint publication, the Partners shall acknowledge the contribution of the other Partner in accordance with customary international practice.

SECTION 8

LIABILITY

8.1 To the extent legally possible, the Partners shall be liable to each other only with regard to willful intent (*Vorsatz*) and gross negligence (*grobe Fahrlässigkeit*).

8.2 To the extent legally possible, any liability for consequential damages shall be excluded.

8.3 The Partners shall be liable without limitation to each other for damages (i) resulting from injury to life or bodily harm, (ii) with regard to the assumption of guarantees, (iii) in the event of a Partner's primary essential obligations (*Kardinalpflichten*), i.e. the fulfilment of such obligations form the basic foundation of the Agreement and the Partner regularly relies on and may rely on their performance.

SECTION 9

DATA PROTECTION

9.1 The Partners shall comply with the applicable data protection regulations as amended from time to time, such as but not limited to the Regulation [EU] 2016/679 *(General Data Protection Regulation, GDPR)* as well as the Federal Data Protection Act *(Bundesdatenschutzgesetz, BDSG)* and the applicable State Data Protection Act *(Landesdatenschutzgesetz, LDSG)*. If personal data are subject of the Research Activities to be performed under this Agreement, the Partners shall conclude a pertinent separate written agreement with regard to data protection.

9.2 In the event that a Partner becomes aware of mandatory laws imposing additional or deviating requirements or restrictions regarding the collection and/or use of research data, or an administrative order or court order is issued by a competent body in that regard, such Partner shall promptly notify the other Partner. The Partners shall then cooperate in order to effectively continue performing the Research Activities within the scope of this Agreement by, inter alia, obtaining necessary approvals.

SECTION 10

DURATION AND TERMINATION

10.1 This Agreement shall become effective on November 1st, 2025 (**"Effective Date"**) for a period of five (5) years and expire on October 30th 2030 (**"Expiry Date"**). A further extension is not possible.

10.2 Either Partner may terminate this Agreement prior to the end of term according to Section 10.1 above with six (6) months' written notice.

10.3 If the Partner Group Leader leaves UdelaR, MPI-DO is entitled to immediately terminate the Agreement. The Agreement may also be terminated by either Partner in case the Partners fail to agree on an appropriate substitute to the contact person within three (3) months according to Section 3.3 above, or in case the Research Activities cannot be completed due to mandatory approval or certificate documents within two (2) months after the necessity of such an approval or certification has been identified.

10.4 In case the Agreement is terminated, the Partners will amicably resolve the details of termination. Section 5.3 shall apply analogously.

10.5 Sections 5, 7.3 and 7.4 and such provisions of this Agreement that according to their content are intended to be in effect for longer, shall survive termination.

SECTION 11

APPLICABLE LAW AND DISPUTE RESOLUTION

11.1 This Agreement shall be governed by laws of the Federal Republic of Germany.

11.2 All Research Activities under this Agreement shall be conducted in compliance with all applicable laws, regulations and guidelines of the country and institution in which the Research Activities are conducted, including but not limited to the "Rules of Good Scientific Practice" adopted by the Senate of the Max-Planck--Gesellschaft zur Förderung der Wissenschaften e.V. on November 24, 2000, and amended on March 20, 2009 and the "Guidelines and Rules of the Max Planck Society on a Responsible Approach to Freedom of Research and Research Risks" in their version as of March 17, 2017. The Partners agree that they must provide any and all necessary materials to the scientists conducting the Research Activities such as but not limited to the Partner Group Members for them to be able to comply with this regulation.

11.3 Any dispute arising from the interpretation or implementation of this Agreement will be resolved amicably and expeditiously by consultation or negotiation between the Partners or such means as they may mutually decide.

11.4 If the Partners fail to settle the differences, the Partners agree to arbitrate the dispute according to the WIPO arbitration rules. Seat of arbitration shall be Geneva, Switzerland. The language of arbitration shall be English. The Partners shall each nominate one (1) member to this arbitration board. These two (2) designated members will then name a third arbitrator to function as chairperson. The arbitration board sets the regulations for the proceedings and makes decisions in accordance with international codes of practice. The decisions of the arbitration board will be accepted by the Partners as binding and final.

SECTION 12

EXPORT CONTROL

12.1 Each Partner shall comply with applicable national and international laws and regulations, in particular the applicable export control regulations and sanction programs.

12.2 UdelaR shall implement effective measures to ensure compliance with the UN- and EU-anti-terrorism regulations as well as with any applicable official sanctions lists and to ensure that their respective employees, subcontractors and other partners, involved in this Agreement, are not companies, organizations or persons on the respective sanctions lists.

12.3 UdelaR shall not use any Work Results, generated in performance of the Research Activities, or services under this Agreement directly or indirectly for nuclear, chemical or biological weapons-related activities, or missile activities, nor supply them to military or for military purposes, or for human rights violations.

12.4 The Partners understand that Work Results, generated in performance of the Research Activities, goods (including software and technology) or services may be subject to export control laws and regulations or depend on governmental approval. UdelaR shall inform the MPI-DO in writing of such export control classification identification. Each Partner shall use its best efforts to obtain, if possible before the Agreement comes into force, all approvals requested for this Agreement. Each Partner is also prohibited from re-exporting goods or technology received under this Agreement to Russia or Belarus or re-exporting them for use in Russia or in Belarus. Any violation of the aforementioned prohibition shall constitute a material breach of an essential element of this Agreement, and the Partner shall be entitled to seek appropriate remedies, including, but not limited to termination of this Agreement. If the government of either Partner denies, fails to grant, or revokes any import or export authorizations necessary for the performance of this Agreement, that Partner shall immediately notify the other Partner and neither Partner shall be responsible for performance or payment under this Agreement for directly or indirectly affected activities.

After the coming into force of the Agreement, the Partners shall inform each other, as soon as the information is available, of any new conditions or limitations of the license approval(s) which may affect the Research Activities under this Agreement, specifying any detail and information which may be useful to understand and evaluate the new situation and related consequences. The conditions of the Agreement may be

renegotiated in order to decide the consequences such modifications may have on the Agreement.

12.5 The Partners shall not be obligated to fulfill this Agreement if such fulfillment is prevented by any impediments arising out of national or international foreign trade or customs requirements or any embargoes or other sanctions.

12.6 Each Partner shall indemnify and hold the other Partner harmless from and against any and all liability, claims, proceedings, actions, fines, losses, costs, expenses and damages arising out of, connected with or resulting from the Partner infringing (by act or omission).

SECTION 13

FINAL PROVISIONS

13.1 This Agreement supersedes all previous agreements between the Partners with regard to the subject matter of this Agreement and regulates in full the relationship between the Partners with respect to the subject matter of this Agreement.

13.2 This Agreement may be amended upon mutual consent of the Partners. Any changes shall be in writing; this shall also apply to a change of the written form requirement itself.

13.3 Appendices to this Agreement shall form an integral part of this Agreement.

13.4 In the event that one or more terms of this Agreement are or become invalid, the Partners shall be obliged to replace the invalid terms with other valid provisions which so closely approach the invalid terms as to permit of a reasonable presumption that the Partners might also have entered into the Agreement had it originally contained this clause. Should it not be possible to arrive at such a provision, the fact that one or more terms of this Agreement are invalid shall not affect the validity of the Agreement as a whole, unless the invalid terms are of such material importance to the Agreement that it may be reasonably presumed that the Partners would not have entered into the Agreement had it not contained the invalid terms.

[signatures on the following page]

[signature page]

For **Max-Planck-Gesellschaft zur Förderung der Wissenschaften e.V.**

_____

Prof. Dr. Stefan Raunser
Managing Director at the MPI-DO

Digitally signed by Prof. Dr. Stefan Raunser
DN: cn=Prof. Dr. Stefan Raunser, o=Max Planck Institute of Molecular Physiology, ou=Department of Structural Biochemistry, email=stefan.raunser@mpi-dortmund.mpg.de, c=DE
Date: 2025.11.24 13:05:04 +01'00'

Date: _____

For **Fundación para el Progreso de la Química**

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Dr. Gustavo Seoane
Member of the Board of Directors

Gustavo Augusto Seoane Muniz
19/11/2025

Date: _____

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Prof. Dr. Eduardo Dellacassa
Secretary

Date: _____

For **Universidad de la República de Uruguay**

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Gonzalo Vicci Gianotti
President of International Relations
Date: _____

ALVARO WASHINGTON MOMBRÚ RODRÍGUEZ

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Appendix 1 – Collaborative Research Program

Project Title of the Partner Group:

Dithiolane containing cyclic peptides as cell-permeable p-PROTACs to target RBM39

Field of research:

Medicinal chemistry, chemical biology

Brief summary describing research activities and objectives:

This research activities aim to design, synthesize, and select cyclic peptides capable of binding RNA-binding motif protein 39 (RBM39), a promising anti-cancer target. By incorporating a dithiolane heterocycle into an amino acid, we will enhance the peptides' cell permeability and facilitate cyclization through Native Chemical Ligation. E3-ligase ligands will then be attached to create peptide-based PROTACs, which will be characterized and optimized using chemical and structural biology tools.

Research Goal

The goal of this collaborative project is to develop cell-permeable, dithiolane-containing cyclic peptides as peptidic PROTACs (p-PROTACs) targeting RBM39, a splicing factor overexpressed in various cancers. By incorporating dithiolane heterocycles and engineering RBM39-binding motifs into cyclic peptides, we aim to overcome current limitations in cell permeability and selective degradation of RBM39 via E3 ligases such as VHL or CRBN, bypassing the DCAF15 dependency of current SPLAM-based therapies.

Tasks to be Performed by the Partners

School of Chemistry, UdelaR – Medicinal Chemistry Laboratory (Partner Group)

- Design and synthesis of cyclic peptides containing dithiolane units using solid-phase peptide synthesis (SPPS) and native chemical ligation (NCL).
- Construction of peptide libraries targeting RBM39's RRM domains, especially the UHM-ULM interface.
- *In vitro* screening and binding studies using immobilized recombinant RBM39 and mass spectrometry-based identification.
- Linker engineering and peptide-E3 ligase conjugation, including the attachment of VHL and CRBN ligands to optimized peptides.

- Preliminary evaluation of antitumoral activity using cancer cell viability assays.

Max Planck Institute of Molecular Physiology (MPI Dortmund)

- Chemical biology support including use of NanoClick assays to evaluate cell permeability of candidate peptides.
- Biological validation including western blotting for RBM39 degradation and ubiquitin-proteasome dependency using proteasome inhibitors.
- Structural biology support via cryo-EM to visualize the ternary complex (RBM39–p-PROTAC–E3 ligase) for structure-based optimization.
- Student training and knowledge transfer, including internships for UdelaR students in MPI labs.

Respective Contributions of the Partners

- UdelaR contributes its core expertise in synthetic and peptide chemistry, especially cyclization strategies using dithiolane-containing amino acids, and generates the core peptide libraries and chemical tools.
- MPI Dortmund contributes its expertise in chemical biology, cell-based assays, and structural biology, enabling the functional and mechanistic evaluation of the compounds and structural validation of the ternary complexes.

Scheduling

The project is planned over a 5-year period, with the following tentative timeline:

1st Year:

- Setup of laboratory conditions and procurement of necessary reagents and materials.
- Optimization of solid-phase peptide synthesis (SPPS) and native chemical ligation (NCL) methodologies for cyclic peptide generation with dithiolane-containing amino acids.
- Design and synthesis of a small initial cyclohexapeptides library incorporating the Trp-Asp motif and variations at other positions.
- Establishment of recombinant RBM39 immobilization protocols for peptide screening.
- Initial binding studies using MS-based identification to isolate preliminary hits.

2nd Year:

- Resynthesis and validation of peptide hits from Year 1 library.
- Structural-activity relationship (SAR) analysis to refine binding peptide features.
- Introduction of click handles to the peptides for permeability studies.
- First permeability assays using NanoClick, in collaboration with the 't Hart lab.
- Design and synthesis of RBM39-binding peptides fused to E3 ligase ligands (VHL, CRBN) via variable linkers.

3rd Year:

- Functional screening of p-PROTACs in cancer cell lines (NSCLC, TNBC, CRC).
- Optimization of linker length
- Western blot analysis to confirm RBM39 degradation and establish E3 ligase expression in each cell line.
- Use of proteasome inhibitors (e.g., bortezomib) to verify ubiquitin-proteasome pathway involvement.
- Evaluation of peptide stability *in vitro* and in cellular extracts.
- Permeability assays of the p-PROTACS using NanoClick, in collaboration with the 't Hart lab.

4th year

- Structural biology support via cryo-EM to visualize the ternary complex (RBM39–p-PROTAC–E3 ligase) for structure-based optimization
- Final optimization of lead compounds for improved stability, permeability, and selectivity.

5th year

- Integration of all data to establish proof-of-concept for RBM39-targeted degradation.
- Preparation of manuscripts and patents.

Background Intellectual Property

School of Chemistry, UdelaR has prior expertise and published methodology on peptide cyclization using native chemical ligation and solid phase peptide synthesis, which forms part of the synthetic approach.

MPI Dortmund brings proprietary tools and methods for NanoClick assays, cell-based degradation validation, and access to high-end cryo-EM facilities.

Both partners retain ownership of their respective background IP. Any foreground IP arising from the collaboration will be managed under a jointly agreed IP policy, ensuring proper attribution and exploitation rights.