

Harnessing intracellular mechanisms

How would you propose leveraging intracellular mechanisms to expand the druggable target landscape by using innovative approaches?

Answers to this question including a proposal for collaboration can only be considered if they arrive no later than January 18, 2026, 11:59 pm PST.

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What is the context of the problem that we would like to solve?

Despite significant advances in drug discovery, a large portion of the proteome remains inaccessible to conventional small molecules or biologics, which adds to the challenge of addressing high unmet medical need in various indications. These "undruggable" targets often play critical roles in disease biology and comprise transcription factors, scaffold proteins, and components of intracellular trafficking systems.

Recent developments in targeted protein degradation or modulation (e.g., PROTACs, molecular glues or biomolecular condensates) have demonstrated the potential of hijacking endogenous cellular machinery to overcome these limitations. Building on this paradigm, we aim to explore novel strategies that leverage cellular processes to modulate protein function, localization, or stability in a selective and programmable manner.

Several interesting new approaches have recently emerged that allow targeting previously "undruggable" targets. Although already integrated into ongoing pharmaceutical research and development efforts and therefore out of scope of the current call, they provide good examples for what kind of novel approaches we are looking for in this call:

- **Advanced degradation strategies**, such as PROTACs and molecular glues, that hijack the ubiquitin-proteasome system to eliminate cytosolic targets.^{1,2,3}
- **Modulation of biomolecular condensates** that tether or sequester specific proteins to modulate their activity or interactions.⁴

By using novel approaches beyond the ones mentioned above, which intracellular mechanisms would you propose exploit and how would you approach it to expand the druggable target landscape?

What potential solutions could be in scope?

We seek to **explore and exploit intrinsic cellular processes** to enable therapeutic intervention against targets traditionally considered undruggable.

We call for proposals that explore:

- Novel approaches that enable selective targeting of previously inaccessible proteins or cellular pathways.
- Explore mechanisms to modulate nuclear translocation of transcription factors or other regulatory proteins—either by inhibition, activation, or redirection.
- Strategies to modulate organelle-specific trafficking, such as mitochondrial import, lysosomal routing, or ER-associated degradation.
- Modulation of biomolecular condensates.
- Concepts that expand the druggable proteome and genome by leveraging spatial and temporal control over protein localization and activity.

What potential solutions would be out of scope?

The following will be considered out of scope:

- Degraders such as PROTACs, Molecular glues, RIPTACs, LYTACs, X-TACs
- RNAi technologies, CRISPR/CAS, RNA glues
- Unselective inhibition of cellular processes
- Gene therapy, viral therapy, cell therapy
- Cellular processes that are druggable by current options

What benefits do we offer to you in exchange for having submitted a solution?

If your project is selected, you will have the opportunity to directly collaborate with Boehringer Ingelheim's Discovery Research Expert Panel, comprising of multi-sciences experts such as medicinal chemistry, drug discovery sciences and pharmacology for various disease areas who will support you in technology enablement.

Successful proposals will be rewarded with tailored and scalable funding packages and, if IP is involved, appropriate business options along well-defined parameters.

We predict that eligible solutions may come from scientists with very different backgrounds, ranging from academia, start-ups, biotech, or even larger enterprises such as pharmaceutical or digital life science companies.

Winning proposals should therefore expect appropriate funding that will help them to bring their conceptual idea and/or discovery (invention) to the next relevant inflection point within the next one to two years.

The following inflexion point is in scope: Establishment of a technology with in-vitro proof of concept. Explicitly out of scope are IND related drug development packages that are not related to technology validation. Depending on the complexity and maturity of a proposed solution, it may require different budget terms that would be negotiated with the selected partners in good faith. If applicable, respective business options will be negotiated with winning proposals.

Depending on the status of the project and applicability, we also offer a range of possibilities to support the winner besides funding. Examples include access to high-quality molecules, execution of pharmacokinetics studies, and collaboration with experts in relevant fields.

In case a project proposal has reached sufficient maturity to build on existing – or reasonably soon to be filed – IP, licensing, options to licensing agreements, or similar business collaborations could be considered as well. Upon a successful outcome, we may engage in a long-term collaboration with the selected winner.

We are particularly interested in finding mutually agreeable solutions concerning each partner's rights and obligations (including intellectual property rights). Furthermore, winners will be encouraged to publish their findings in accordance with the collaboration agreement, which will be negotiated in good faith. We hope that this represents a great opportunity for your innovative ideas and solutions to gain recognition in the scientific community.

For some winners, it may be beneficial to announce their partnership with Boehringer Ingelheim. Depending on the conditions of the agreement and mutual needs, we would be open to such an arrangement.

What are the key success criteria on which we base our selection for the best answer?

Our scientific review will address the following key success criteria for selecting winning proposals:

The proposed solution must be based on a compelling scientific hypothesis and address the in-scope and out-of-scope criteria of this call.

Outlining the technical feasibility, and potentially existing data or previous publications that support feasibility / experience with outlined technology, based on existing and established models, is expected.

Ideally, the proposed solution is backed up by relevant (preliminary) data providing mechanistic insights (such as target engagement) and demonstrating functional modulation (e.g. ability to hijack endogenous cellular machinery addressing a specific gene product). It should be based on established and existing methods, assays, and involve tools, reagents, or data that are accessible.

A mitigation plan should be included to overcome the anticipated hurdles that also includes a contingency plan in case one approach may not lead to the desired outcome.

Your exact funding request should be outlined in your proposal based on a well-thought-through project. The project should be structured in milestones and planned with key decision points (clear Go/No-Go criteria). Please note that the funding should cover bringing your conceptual idea and/or discovery (invention) to the next relevant inflexion point within the next two years.

The submission should include information on potential conflicting intellectual property rights of third parties and freedom to operate.

The access to relevant infrastructure to implement the proposed solution is a prerequisite of a collaboration with Boehringer Ingelheim.

The ability to reach tangible results within a timeframe of approximately two years to reach the next decision point is mandatory.

What information should be included in your answer submission?

Please use our answer submission template to provide a 2–3-page non-confidential proposal (available for download on the following [site](#)).

If confidential data exists that would strengthen the proposal, please indicate that information is available to share under a Confidential Disclosure Agreement (CDA). If we find the non-confidential concept proposal sufficiently interesting, we will execute a CDA for confidential discussions.

Anticipated Project Phases or Project Plan

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| Phase 1 | Please complete your submission by January 18, 2026, 11:59 pm PST at the very latest. |
| Phase 2 | Our review of all proposals will be completed by mid-March 2026 and scientists will be informed after that. |
| Phase 3 | Start of discussions for the collaboration agreement in Q2/2026. |

Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS “[Harnessing intracellular mechanisms](#)” on opnMe.
- Alternatively, you may click the “Get Submission Template” banner to access the material transfer template.
- Follow the instructions to upload your submission document (requires login or registration).
- The upload allows you to attach additional application files if desired.
- You will be able to access your final submitted collaboration proposal in your personal dashboard and follow its review status.
- Please also visit the [FAQ](#) section on opnMe.com to learn more about our opn2EXPERTS program.

References

1. Nalawansha D. A., Crews C. M. PROTACs: An Emerging Therapeutic Modality in Precision Medicine *Cell Chem Biol.* **2020**, 27(8):998-1014. [DOI: 10.1016/j.chembiol.2020.07.020](#), [PubMed](#).
2. Li K., Crews C. M. PROTACs: past, present and future *Chem Soc Rev.* **2022**, 51(12):5214-5236. [DOI: 10.1039/d2cs00193d](#), [PubMed](#).

3. Li Q., Kang C. Targeting RNA-binding proteins with small molecules: Perspectives, pitfalls and bifunctional molecules *FEBS Lett.* **2023**, 597(16):2031-2047. [DOI: 10.1002/1873-3468.14710](https://doi.org/10.1002/1873-3468.14710), [PubMed](#).
4. Mitrea D. M., Mittasch M., Gomes B. F., Klein I. A., Murcko M. A. Modulating biomolecular condensates: a novel approach to drug discovery *Nat Rev Drug Discov.* **2022**, 21(11):841-862. [DOI: 10.1038/s41573-022-00505-4](https://doi.org/10.1038/s41573-022-00505-4), [PubMed](#).