opnMe by Boehringer Ingelheim

Studying ICB resistance in lung cancer

How would you propose to develop novel models that bridge the translational gap between preclinical disease models and clinical outcomes in immune checkpoint blockade resistant lung cancer?

Answers to this question including a proposal for collaboration can only be considered if they arrive no later than October 15, 2026, 11:59 pm PST.

Boehringer Ingelheim

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

Lung cancer has one of the highest rates of incidence and mortality worldwide, making research on its mechanisms and treatments crucial. Lung cancer is a heterogenous disease composed of small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) with various driver mutations (ALK, BRAF, EGFR, HER2, KRAS, MET, etc) and differing histological representations (squamous vs non-squamous). Treatment regimens depend on these factors in addition to the tumor proportion score (TPS) of PDL1. All these factors should be considered in preclinical modeling to accurately represent patients in need.

The treatment of lung cancer has changed dramatically over the last decade, with the use of immune checkpoint blockade (ICB) inhibitors, which target the PD-1/PD-L1 axis, leading to improvement in overall survival. Nevertheless, only a proportion of patients respond, and those that develop long-term responses, frequently are met with primary or relapse with acquired resistance. Specifically in non-small cell lung cancer (NSCLC), up to 64% of patients who initially respond to ICB develop acquired resistance when an ICB is given as second-line treatment. Thus, understanding mechanisms and improved modeling for acquired resistance is critical to curing lung cancer.

As part of this call, we invite proposals to develop or apply clinically relevant models that investigate ICB acquired resistance mechanisms driven by tumor-intrinsic pathways or the immunosuppressive tumor microenvironment (TME), ultimately to identify vulnerabilities in anti-PD-1/ICB non-responder patients.

What potential solutions could be in scope?

Solutions that will lead to resistance models with an understanding of the molecular mechanisms underlying PD-1 resistance. These should be validated and will make use of the following approaches:

Building on / using innovative *in vivo* platforms reflecting biology and pathology of PD1 resistance in lung cancer

- Murine / human-based models that replace standard subcutaneous tumor models with high-fidelity platforms that recapitulate the complex, spatial architecture and mutational landscape of human lung cancer:
    - Orthotopic Models: To study organ-specific immune responses within the lung.
    - GEMMs: To model spontaneous tumor development and native immune evasion.
    - Humanized PDX: To test therapeutics against patient-derived tumor tissue within a reconstituted human immune system.
- Combination Screening: Platforms to test synergies between PD-1 blockade and novel agents (e.g., TcEs, metabolic modifiers, or myeloid-targeting therapies).

Utilizing models that reflect the multidimensional microenvironment in the disease setting (i.e., advanced cellular & tissue models (new approach methodologies (NAMs) that can model PD-1 resistance or response)

- Multicellular Systems: Use of patient-derived organoids (PDOs), lung-on-a-chip, and precision-cut lung slices (PCLS) incorporating TME.
- Human-Centric Platforms: Priority for human primary cells or iPSC-derived models (e.g., alveolar epithelium, myeloid cells) to ensure clinical relevance.
- Immune Reconstitution: Integration of autologous or HLA-matched immune populations (T-cells, NK, Myeloid) to model the evasion "battlefield."

Systems that allow validation through functional readouts & deep phenotyping

- Response Assessment: Integration of sensitive readouts for T-cell exhaustion (e.g., TOX, LAG-3), metabolic flux, and real-time cytotoxicity.
- Spatial Analysis: Use of spatial transcriptomics or multiplexed imaging to quantify immune cell infiltration and exclusion.

Proposals that have established clinically relevant resistance models or that provide preliminary evidence for a novel resistance mechanism would become prioritized.

What potential solutions would be out of scope?

- Simple subcutaneous models and in *vitro* systems
- Proposals with exclusivity rights to models created

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 the Oncology Research Team of Boehringer Ingelheim. You can expect appropriate funding for the prospective collaboration period. Your exact funding request should be outlined in your proposal. As a framework, we suggest that your funding request be structured in milestones and not exceed 300,000 euros per submitted project in total. Please note that depending on the complexity and maturity of a proposed model and the degree of validation, different budget terms could be negotiated with you.

Our collaboration agreement will provide full transparency about each partner's rights & obligations (including intellectual property rights). As part of the agreement, you will be encouraged to publish following the collaboration agreement (to be negotiated in good faith).

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

The proposal needs to be highly feasible, should be based on established and existing methods, assays, and involve tools / reagents that are either available or which can be easily produced. We expect that the project will be executed in your laboratory and takes advantage of existing technologies and assays.

We are seeking research collaboration proposals that contain:

- A well-structured research proposal that is based on already established ICB resistant lung cancer models would be preferred. Completely de novo models would be entertained but may not be achievable given time constraints.
- Any form of preliminary validation and/or the provision of relevant omics data would strengthen the proposal and would be prioritized.
- Your exact funding request should be outlined in your proposal. The project should be structured in milestones and planned with key decision points (clear Go/No-Go criteria). The funding request for the initial milestones resulting in a Go/No-Go decision should not exceed 300,000 euros per submitted project in total. Depending on the complexity and maturity of a proposed model and the degree of validation, different budget terms could be negotiated with the selected partner(s).
- Proven track record in the required field of expertise.
- Ability to implement the outlined solution as part of a scientific collaboration project with Boehringer Ingelheim including access to a wet laboratory and to conduct/carry out -omics analyses if required.
- Openness to transfer the established assay/model system to Boehringer Ingelheim's laboratories.
- Proposals that lead to a fully established model with a resistance mechanism with validation within two years will be prioritized.

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

Phase 1	Please complete your submission by **October 15, 2026 11:59 pm PST at** the very latest.
Phase 2	Our review of all proposals will be completed in early 2027 and scientists will be informed after that.
Phase 3	Start of discussions for the collaboration agreement in Q1/2027.

Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS "Studying ICB resistance in lung cancer" 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. Memon D., Schoenfeld A. J., Ye D., Fromm G., Rizvi H., Zhang X., Keddar M. R., Mathew D., Yoo K. J., Qiu J., Lihm J., Miriyala J., Sauter J. L., Luo J., Chow A., Bhanot U. K., McCarthy C., Vanderbilt C. M., Liu C., Abu-Akeel M., Plodkowski A. J., McGranahan N., Łuksza M., Greenbaum B. D., Merghoub T., Achour I., Barrett J. C., Stewart R., Beltrao P., Schreiber T. H., Minn A. J., Miller M. L., Hellmann M. D. Clinical and molecular features of acquired resistance to immunotherapy in non-small cell lung cancer *Cancer Cell*. **2024**, 42(2):209-224.e9. DOI: 10.1016/j.ccell.2023.12.013, PubMed.