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Gilead Oncology Request for Proposal (RFP) Program

Advancing Research in Lung (NSCLC), Upper Gastrointestinal (GI), and Gynecological (GYN) Cancers

Through the Medical Affairs Collaborative Study Programs, Gilead supports the research efforts of academic institutions, clinical investigators, and research networks to evaluate the best approaches for advancing oncology development. Proposals are evaluated based on the validity of the scientific question, the relevance of the data gap, and the originality of the research inquiry, ensuring that it does not duplicate existing work or research. This Request for Proposal (RFP) Program is focused on research to advance development in lung (specifically NSCLC), upper gastrointestinal (GI), and gynecological (GYN) cancers.

Non-small cell lung cancer (NSCLC), the leading cause of cancer deaths globally, presents with heterogeneous patients, burdensome symptoms, low quality of life (QOL), and poor prognosis, especially when diagnosed at a metastatic stage, which occurs in over half of cases, leading to significantly diminished survival prospects.^{13,14} Results from the ARC-7 study¹ (NCT04262856), presented at the ASCO Annual meeting in 2022, indicate sustained improvement in progression-free survival (PFS) and overall response rate (ORR) with the combination of domvanalimab (Dom) and zimberelimab (Zim) compared to zimberelimab alone in first-line metastatic NSCLC with PD-L1 TPS $\geq 50\%$ and without EGFR/ALK mutations. The study demonstrates the potential efficacy of the Fc-silent anti-TIGIT / anti-PD-1 combination and no unexpected safety signals, supporting ongoing Phase 3 registrational studies for Dom and Zim in NSCLC. Additionally, Gilead has several studies including IMMU-132-01 (NCT01631552)⁹ and EVOKE-02 (NCT05186974)¹⁰, which demonstrated promising activity for Sacituzumab Govitecan (SG) in non-small cell lung cancer (NSCLC), both as monotherapy and in combination with pembrolizumab. Although the phase 3 study EVOKE-01 (NCT05089734)¹¹ did not meet its primary endpoint of overall survival (OS) in NSCLC patients post-platinum chemotherapy and PD-L1 therapy, there was a numerical improvement in OS favoring SG over docetaxel in the intention-to-treat (ITT) population, with an improvement in OS among patients who did not respond to their last PD-L1 containing regimen. These findings support the ongoing phase 3 EVOKE-03 (NCT05609968)¹² study of SG in combination with pembrolizumab in first-line metastatic NSCLC (mNSCLC) and continued interest in potential role of SG in lung cancers.

Upper GI cancers, including esophageal, gastroesophageal junction, and gastric carcinoma, represent a significant area of unmet medical need with high recurrence rates for resectable disease, and a 5-year survival rate of 7%⁸. While the addition of anti-PD-1 therapies to chemotherapy has shown some improvement in outcomes in the first-line setting, a substantial proportion of patients fail to achieve a satisfactory response to immunotherapy plus chemotherapy, and for responders, relapses still occur. Initial results from the ARC-21/EDGE Gastric study² (NCT05329766) presented at ASCO Virtual Plenary in 2023 showed that combining Dom and Zim with FOLFOX chemotherapy in upper GI cancer resulted in promising objective response rates and early progression-free survival, with a safety profile comparable to anti-PD-1 + FOLFOX regimen.⁴ These findings contribute to the support for the Phase 3 STAR-221 study³ (NCT05568095) in first-line upper GI cancer treatment.

Gynecologic cancers, including endometrial, ovarian, and cervical cancers, are multiple areas of high enduring unmet need that are expected to persist despite active development across tumors. Gilead has a diverse portfolio with encouraging results in GYN with sacituzumab govitecan (SG) as a potential cornerstone, supported by the Phase 2 studies TROPiCS-03⁵ (NCT03964727), EVER-132-003⁶ (NCT05119907), and an investigator-sponsored trial of SG in endometrial cancer (NCT04251416)¹⁵. These

studies have demonstrated encouraging efficacy in pretreated patients with advanced metastatic endometrial and recurrent/metastatic cervical cancer and no new safety signals, SG.⁷

Through the 2024 GILEAD Oncology RFP Program, Gilead will evaluate and potentially support collaborative research proposals that address the following areas of interest for sacituzumab govitecan, domvanalimab, and zimberelimab where data gaps exist and seek to the answer the following open research questions:

NSCLC Research Questions of Interest

- Outcomes of SG (with or without novel combinations) in:
 - NSCLC patients with actionable genomic alterations
 - Unresectable and 1L NSCLC
 - NSCLC patients with clinical/biological characteristics of interest (e.g., elderly, brain metastases, ECOG>1)
- Understanding use of ctDNA to identify high risk patients and/or to determine need for adjuvant treatment
- Understand optimal treatment sequencing in neoadjuvant/adjuvant setting in context of evolving treatment landscape
- Biomarker expression, evolution throughout disease course of therapy in NSCLC
- Outcomes of Dom + Zim in:
 - 1L NSCLC patients who have received IO in early stage NSCLC
 - Subgroups of 1L NSCLC (e.g. elderly, brain metastases, ECOG>1, unfit for platinum doublet)
- Efficacy and safety of new MOA combinations with Dom + Zim
- Identification of predictive biomarkers associated with greater benefit from Dom + Zim

Upper GI Research Questions of Interest:

- Outcomes of Dom + Zim in:
 - Patients with FGFR2B+ and CLDN18.2+ Upper GI cancers
 - Combination with alternative chemo backbones to FOLFOX or CAPOX in upper GI cancers (1L or earlier setting)
 - 1L metastatic upper GI cancer patients who have received adjuvant or perioperative IO
 - Neoadjuvant or perioperative upper GI cancers
 - Squamous cell carcinomas in upper GI
- Use of ctDNA to determine the need for treatment of early-stage Upper GI cancers
- Understand overlap of biomarker expression across upper GI tumors (e.g., PDL1, Claudin 18.2, FGFR2)
- Understand optimal treatment sequencing in upper GI in the context of the evolving treatment landscape
- Efficacy and safety of new MOA combinations with Dom + Zim (e.g., aFGFR, aCLDN18.2)
- Identification of predictive biomarkers associated with greater benefit from Dom + Zim

GYN Research Questions of Interest:

- Outcomes of SG in:
 - Earlier metastatic lines of endometrial cancer (e.g. higher risk)
- Novel combinations with SG (e.g., IO, ADCs, TIGIT) in GYN cancers
- Translational data, expression of biomarkers (including overlap with Trop-2 expression) to define better understanding of GYN cancers (endometrial, ovarian, and cervical)

Proposals should include (where appropriate) descriptions of:

- Prospective/Interventional signal seeking or proof-of-concept clinical trials
- Incorporation of patient involvement in study planning and study design/protocols
- Multi-center proposals will be prioritized
- Incorporation of biomarker / translational work including sample collection and objectives for research

- Clear scientific objectives and endpoints, based on sound scientific hypotheses
- Appropriate, defined, and specific data collection/evaluation methods
- Incorporation of clear plan for clinical trial diversity and methods for capturing the patient voice
- Defined and clear timelines for start-up, enrollment and publications
- Consideration of working with junior investigators as part of the study team who are underrepresented in scientific research and medicine

Key Dates & Program Specifics

Review Process & Key Dates

- Letter of Intent (LOI) must be submitted via [G.Optics](#) between **May 30 to July 31, 2024**
- All proposals should be discussed with your local Gilead Medical Affairs contact before submission into [G.Optics](#).

Any questions about the 2024 GILEAD Oncology RFP Program or application process can be submitted to your local Gilead Medical Affairs contact (e.g. MSL) or OncologyRFP@gilead.com.

All those who have submitted an LOI will be informed of the outcome of the LOI review by October 18, 2024. Certain applicants will be invited to submit a full application, including a detailed budget.

The timelines for submission and review of full applications are as follows:

- **November 15, 2024:** Deadline for receipt of full application
- **By end of December, 2024:** Notice of full application outcome

Full applications must be completed in [G.Optics](#) following approval to submit

Review Process

LOI will be rigorously reviewed by a Gilead internal committee. Each complete LOI that meets program requirements will be assigned to a reviewer. Each reviewer will assess and score the LOI according to the below criteria:

- How well the proposal addresses the RFP Program
- The potential impact of the study
- The strength of the objectives/study design
- Sustainability/scalability of the proposal/intervention
- The site and study team's ability to recruit the proposed study population

Budget Considerations

All Letters of Intent (LOIs) submitted in response to this RFP must adhere to a maximum budget of \$2,500,000 USD. Proposals exceeding this budget cap will not be considered for funding. Additionally, proposed budgets should reflect fair market value for a typical study of this nature.

No Guarantee of Funding

Gilead reserves the right to approve or decline any application at its sole discretion. Submission of an LOI or a full application does not guarantee funding. Applications are reviewed by an internal review committee.

No Inducement or Reward

Gilead approval of awards does not take into account the past, present, or future volume or value of any business or referrals between the parties. Awards are not being given, directly or indirectly, as an inducement or reward with respect to the past or potential future purchase, utilization, recommendation or formulary placement of any Gilead product. Further, except for the use of the Gilead product in approved award/research, the awardee is not required to purchase, order, recommend or prescribe to any patients any products manufactured by or available through Gilead.

About Gilead Sciences

Gilead Sciences, Inc. is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases worldwide. Gilead has operations in more than 30 countries worldwide, with headquarters in Foster City, California.

About Sacituzumab Govitecan (Trodelvy)

Trodelvy® (sacituzumab govitecan-hziy) is a first-in-class Trop-2-directed antibody-drug conjugate. Trop-2 is a cell surface antigen highly expressed in multiple tumor types, including in more than 90% of breast, bladder and lung cancers. Trodelvy is intentionally designed with a proprietary hydrolyzable linker attached to SN-38, a topoisomerase I inhibitor payload. This unique combination delivers potent activity to both Trop-2 expressing cells and the tumor microenvironment through a bystander effect.

Trodelvy is approved in almost 50 countries, with multiple additional regulatory reviews underway worldwide, for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease.

Trodelvy is also approved to treat certain patients with pre-treated HR+/HER2- metastatic breast cancer in Australia, Brazil, Canada, the European Union, Israel, United Arab Emirates and the United States. In the U.S., Trodelvy has an accelerated approval for treatment of certain patients with second-line metastatic urothelial cancer; see below for full indication statements.

Trodelvy is being explored for potential investigational use in other TNBC, HR+/HER2- and metastatic UC populations, as well as a range of tumor types where Trop-2 is highly expressed, including metastatic non-small cell lung cancer (NSCLC), head and neck cancer, gynecological cancer, and gastrointestinal cancers.

About Domvanalimab

Domvanalimab is the first and most clinically advanced Fc-silent investigational monoclonal antibody that is specifically designed with Fc-silent properties to block and bind to the T-cell immunoreceptor with Ig and ITIM domains (TIGIT), a checkpoint receptor on immune cells that acts as a brake on the anticancer immune response. By binding to TIGIT with Fc-silent properties, domvanalimab works to free up immune-activating pathways and activate immune cells to attack and kill cancer cells without depleting the peripheral regulatory T cells important in avoiding immune-related toxicity.

Combined inhibition of both TIGIT and programmed cell death protein-1 (PD-1) has been understood to significantly enhance immune cell activation, as these checkpoint receptors play distinct, complementary roles in anti-tumor activity. Domvanalimab is being evaluated in combination with anti-PD-1 monoclonal antibodies as well as other investigational cancer immunotherapies, including PD-1 inhibitor zimberelimab in multiple ongoing and planned early and late-stage clinical studies in various tumor types.

About Zimberelimab

Zimberelimab is an investigational anti-programmed cell death protein-1 (PD-1) monoclonal antibody that binds PD-1, with the goal of restoring the antitumor activity of T cells. A.

Zimberelimab is being evaluated in the U.S. and globally as a foundational PD-1 treatment option in multiple ongoing and planned early and late-stage clinical studies in combination with other immunotherapies, including investigational Fc-silent anti-TIGIT monoclonal antibody domvanalimab.

Zimberelimab is currently approved in China as the first and only anti-PD-1 antibody to treat recurrent or metastatic cervical cancer, and for the treatment of relapsed or refractory classical Hodgkin's lymphoma. Zimberelimab is not approved for any use in the U.S.

References:

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