# Oncology Translational Studies Program

Below you will find our updated Areas of Interest (AOI) for the upcoming MSD Oncology Translational Studies Program (OTSP) 2025 submission cycle and the Pre-Clinical Investigator Studies Program. Please be aware that this is a highly competitive process. To help to prepare a successful proposal, we are providing the following guidance:

- Please contact your local Research Medical Scientific Director (RMSD, US only) or country-specific Global Medical Affairs Field Medical liaison for guidance that may pertain to your specific proposal prior to its submission to ensure that your proposal falls within the scope and interest of the Oncology Translational Studies Program and AOIs.
- Carefully review the AOIs below. Proposals that are not designed to encompass at least one AOI may be rejected without further review. Occasionally, we receive proposals not included in the AOIs that represent innovative biology and are ultimately of great interest. If you believe this may apply to your proposal, please review with your RMSD or appropriate country-specific liaison for additional programmatic assessment by the appropriate MSD team and by the OTSP review committee.
- The MSD Investigator-Initiated Studies Program (IISP) is large with numerous approved studies. Please check www.clinicaltrials.gov to ensure studies like your proposed proposal are not already approved or ongoing. You may also discuss what may be possibly in development with your RMSD or country specific liaison.
- Please include documentary evidence of successful and timely accrual to and publication of results from investigators' studies in similar indications where possible. Operational deliverability is carefully considered in the assessment process.
- Pembrolizumab may be available for combination with assets available in the program provided there is a strong rationale for the combination.
- Combinations of available assets with non-MSD agents may be of interest for clinical trials. Please confirm with your country-specific liaison if the combination agent is of programmatic interest. These requests will also be reviewed by the OTSP review committee. In such cases, it is the responsibility of the investigator to procure approval for supply of third-party agents, and matching funding, where possible, which should be demonstrated with a formal letter of support. Proposals lacking such documentation may be rejected. If the agents are approved by health authorities or considered standard of care by country-specific guidelines and the agent is obtained through routine care, then no letter is required.
- The program encourages young investigators to be involved in conducting studies under the guidance of a mentor. In such cases, please specifically mention in the proposal form the intent for a mentored study. Include CVs of both investigator and mentor as well as a detailed letter from the mentor describing the mentoring plan and how this study will help the investigator meet his/her career objectives.
- Please note that only specified MSD investigational agents identified in these areas of interest are available for use in the IIS program.
- The program requests that investigators specify how they will include traditionally underrepresented minorities/ethnic groups and thus ensure diversity in enrollment.

Beginning January 29, 2025, the Oncology Translational Studies Program (OTSP) Committee will accept proposal applications in response to our current AOIs. For this review cycle, we require that all applicants complete and submit a full proposal by March 21, 2025. For investigators outside of the US, please contact your MSD country representative for requirements and timelines. Please note that we will not be able to accept sacituzumab tirumotecan proposals from China, Hong Kong, Taiwan or Macau.

***SUBMISSION PROCESS FOR US INVESTIGATORS*:**

There are three required components for the application:

- Proposal – please complete the proposal template prior to entering the proposal details directly into Visiontracker. All required fields must be completed as outlined in the Application Guide. Please upload the completed proposal template as well.
  - For Submission Type, please select Proposal
  - For Type of Support, please select the appropriate support (Product Only, Funding Only or Funding and Product)
- Investigator CV – please upload a current CV (updated within the last two years) as an attachment to your application in Visiontracker
- Feasibility Worksheet – please complete the form and upload as an attachment to your application in Visiontracker. Completion of this worksheet is required for all proposal submissions.

Proposals are evaluated through a competitive grant review process that will be conducted by the Oncology OTSP committee, with award recipient selection in 2025. Decisions will be made based on scientific merit, innovation, and strategic fit within the AOI. Please review the areas of interest carefully and abide by the timelines as outlined below.

**OTSP:**

Projects must:

- Involve use of patient samples treated with programmatic MSD agents (sacituzumab tirumotecan, zilovertamab vedotin and/or bomedemstat) and/or other approved/standard of care agents as per the areas of interest
- Have primary translational or co-primary translational/clinical endpoints
- Be innovative, focused, and hypothesis driven
- Have mature hypotheses supported by existing data (e.g., preclinical, epidemiologic, etc.)
- Be adequately powered for evaluation of the primary hypothesis

**Special Note: Diversity & Inclusion**

We seek to foster diverse and inclusive representation and patient engagement within the individual Areas of Interest for each tumor type. We encourage study proposals across our Program which, in addition to demonstrating scientific merit, also take into consideration the following:

- Outcome disparities in underrepresented populations
- Inclusion of non-academic programs/institutions
- Involvement of under-represented regions or countries

## 2025 AREAS OF INTEREST FOR ONCOLOGY TRANSLATIONAL STUDIES PROGRAM

**It is strongly encouraged to collect and analyze samples at confirmed radiological/clinical progression or at the end of treatment. Please note that IISP proposals competing with or duplicating any Company registration trial cannot be supported.**

**Antibody Drug Conjugates:**

- Mechanisms of response and/or resistance to approved, standard-of-care antibody-drug conjugates (ADCs) alone and/or in combination with pembrolizumab or other SOC chemotherapies.

**Sacituzumab tirumotecan (sac-TMT):**

- Mechanisms of response and/or resistance to sac-TMT either alone or in combination with pembrolizumab or other standard-of-care agents.
- Mechanisms to overcome resistance to sac-TMT either alone or in combination with pembrolizumab or other standard-of-care agents.
- Evaluate/understand the distribution of Sac-TMT at a tissue level
- Evaluate/understand the processing of Sac-TMT within tissues

**Zilovertamab Vedotin (ZV):**

- Mechanisms of resistance to ZV
- Evaluate/understand the distribution of ZV at a tissue level
- Evaluate/understand the processing of ZV within tissues

Conditions of interest:

- High Grade Lymphomas
- Follicular Lymphoma
- Marginal Zone Lymphoma
- T cell and NK cell Lymphoma

**Bomedemstat:**

- Mechanisms of resistance to bomedemstat including clonal evolution
- Identification of malignant cell epigenetic or transcriptional changes associated with bomedemstat treatment.
- Interaction between key tumor driver mutations and LSD-1 pathway biology and inhibition

Note: Potential combination partners for clinical trials should have published toxicity data that can be used to guide trial design and potentially predict expected toxicities. Proposals including combinations for which there are no safety data should include an appropriate safety run-in component.
Conditions of interest:

- myeloproliferative neoplasms (accelerated phase (AP) or blast phase (BP))
- myelofibrosis (when in combination with JAK inhibitors or other "rational combination partners")
- pre-fibrotic myelofibrosis
- Polycythemia vera (when in combination with hepcidin mimetics)
- chronic myeloid leukemia
- chronic myelomonocytic leukemia
- chronic eosinophilic leukemia
- chronic neutrophilic leukemia

**ctDNA-related areas:**

- Retrospective temporal analyses of ctDNA for monitoring of minimal residual disease burden in the neoadjuvant or adjuvant setting.
- ctDNA as a tool to investigate tumor genetics, biology, or evolution.

Note: Samples should be collected from patients who have received treatment with one of our company's drugs included in the OTSP program. It is not recommended to conduct studies that involve the use of ctDNA assays for prospective clinical trial enrollment or for on-treatment patient clinical decision making. Furthermore, studies utilizing non-commercial ctDNA assays are also discouraged.

## 2025 AREAS OF INTEREST FOR PRE-CLINICAL OTSP

**Sacituzumab tirumotecan (sac-TMT):**

- In vitro treatment with Sac-TMT to study biomarkers associated with response and/or resistance
- Use of established preclinical mouse/patient-derived xenograft (PDX) models to gain insights into possible mechanisms of response and/or resistance to Sac-TMT
- Use of preclinical mouse/patient-derived xenograft (PDX) models, to identify combination partners, to overcome the resistance to Sac-TMT

**MK-1084:**

- Characterize target engagement related to and/or elucidate novel biological mechanisms of resistance (intrinsic or acquired) to MK-1084, especially those that could inform future patient selection strategies or combination approaches
- Identify additive and/or antagonistic mechanisms of action between MK-1084 and novel combination partners. There is particular interest in antibody-drug conjugates, tumor-intrinsic targeted therapies, and immunomodulatory agents
- Identify diagnostic strategies to identify potential combination partners

**Bomedemstat:**

- Sickle cell disease:
  - Explorations of the relationship between LSD1 inhibition and hemoglobin F production
  - Identification of biologic/genetic variations related to RNA regulation and correlation with hemoglobin F production
  - Identification of prognostic molecular/biologic markers that may serve to identify patients who are more likely to respond and predict response to bomedemstat treatment
- Myeloproliferative neoplasms:
  - Identify additive/synergistic and/or inhibitory/antagonistic mechanisms of action between bomedemstat and combination partners

Note : Studies in solid tumors are not of interest at this time.

Conditions of interest:

- myeloproliferative neoplasms (accelerated phase (AP) or blast phase (BP))
- myelofibrosis (when in combination with JAK inhibitors or other "rational combination partners")
- pre-fibrotic myelofibrosis
- Polycythemia vera (when in combination with hepcidin mimetics)
- chronic myeloid leukemia
- chronic myelomonocytic leukemia
- chronic eosinophilic leukemia
- chronic neutrophilic leukemia

**Nemtabrutinib:**

- Establish novel mechanisms of intrinsic and/or acquired resistance to nemtabrutinib that occur independent or concurrent with previously described mutations
- Evaluate hematological or non-hematological disease states beyond CLL/SLL and mantle cell lymphoma that may be susceptible to treatment with nemtabrutinib, either as a single agent or in novel combinations
- Identify additive and or antagonistic mechanisms of action between nemtabrutinib and novel combination partners

**Zilovertamab Vedotin:**

- Studies investigating drug internalization and payload processing

**General Considerations:**

We advised you to consult with your field-based team to discuss tumor types that are of interest.

- Submissions employing longitudinal patient sampling, including trials conducted in the neoadjuvant setting, are strongly encouraged.
- Patient selection or clinical decision making using experimental biomarker assays or technology that are not regulatory agency-approved will require additional discussion.
- Submissions focused on the following areas are discouraged:
    - Pipeline compounds not approved for investigator studies
    - Technology development, implementation, or validation
    - Therapeutic agents for combination studies that:
        - Have shown no monotherapy activity in phase I or II studies
        - Do not have a phase II recommended dose or an established safety profile
        - Are repurposed agents from non-oncology therapeutic areas
    - Phase I studies
    - Tumor vaccines
    - CART-T or other cellular therapies
    - Pediatric studies
    - Studies aimed at studying or modulating the microbiome
    - Biomarker identification or validation

**Expectations of the OTSP and Pre-Clinical studies program are as follows:**
Data sharing is an intrinsic requirement for studies funded under the OTSP program. Expectations regarding types of programmatic requests for data will be provided.

Data Tiers