Areas of Interest for Nemtabrutinib (MK-1026): Hematological malignancies

We are currently accepting proposals for the Hematology-Oncology Investigator-Initiated Studies Program (IISP). This is a highly competitive review process; decisions are based on scientific/clinical merit, strategic fit, and feasibility.

The following guidance is provided to ensure a successful proposal:

- Please consult your local Research Medical Scientific Director (RMSD, US) or country Global Medical Affairs Field Medical liaison for proposal-specific guidance before submission to confirm alignment with IISP scope and interests.
- Carefully review the AoIs. Proposals that do not address at least one AoI may be rejected without further review. In rare cases, proposals outside the AoIs may be considered if they present compelling, innovative biology. If you believe this applies, please consult your RMSD or MSD Country Representative for programmatic assessment.
- Please review www.clinicaltrials.gov to ensure your study is not already approved or ongoing and consult your RMSD or MSD Country Representative regarding studies in development. Proposals duplicating or competing with Nemtabrutinib MK-1026 registration trials will not be supported.
- Letter of Support are required for use of third-party funding or agent unless the agents is approved by health authorities or obtained as standard of care.
- Less experienced investigators are encouraged to work with a mentor prior to IISP submission. If a mentor is involved, please provide their CV and a detailed letter outlining the mentoring plan.
- Safety-only primary endpoint proposals are out of scope.
- Only MSD investigational agents specified in these AoIs are available for IIS use.
- The Program requests that investigators specify how they will support diversity in enrollment, including but not restricted to traditionally underrepresented minorities/ethnic groups.

<u>General Considerations:</u>

We advise 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 IISP
  - 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 unless specifically noted in the Areas of Interest

- Pediatric studies
- Studies aimed at studying or modulating the microbiome
- Biomarker identification or validation

Note for all translational projects: It is strongly encouraged to collect and analyze samples at confirmed radiological/clinical progression or at the end of treatment.

All studies with translational primary or co-primary endpoints must:

- Use patient samples treated with programmatic MSD agents and/or approved or standard-of-care agents per the AoI.
- Have primary translational or co-primary translational/clinical endpoints
- Be innovative, focused, and hypothesis-driven, with mature hypotheses supported by existing data (e.g., preclinical or epidemiologic).
- Be adequately powered for evaluation of the primary hypothesis
- Data share per the guidance provided: Translational Data Tiers
  - Note: Prior to submission, please ensure your institutional or local policies allow data sharing as per the Data Tiers linked above for any study with primary/co-primary translational endpoints.

Nemtabrutinib Clinical AoIs for 2026:

Primary interest: Studies in specific lymphomas (DLBCL, Follicular Lymphoma, Marginal Zone Lymphoma, and Waldenstrom's Macroglobulinemia). This includes in the post-transplant setting and in relation to the occurrence of GVHD.

Secondary interest: Studies in CLL/SLL, MCL and Richter's Transformation. The program remains interested in innovative concepts for these diseases, but it is strongly recommended that investigators discuss their concepts with the field or country team before submission.

Both the primary and secondary areas of interest listed above include:

1. Studies with standard-of-care combinations, or other novel therapies (eg, CAR-T, BCL2 inhibitors, polyspecific antibodies, ADCs)
2. Studies addressing sequencing of therapies (e.g., nemta either prior to or followed by other BTK inhibitors or BTK degraders)

Notes:

- The following are currently not of interest in 2026: Primary CNS lymphoma, autoimmune conditions, solid tumors.
- Potential combination partners for clinical trials MUST have published toxicity data that can be used to guide trial design and potentially predict expected toxicities.
- Consideration should be given on whether to include an appropriate safety run-in component which assesses toxicity of a small initial group of patients with a single, uniform dosing regimen. Dose finding/dose escalation is not of interest.

SUBMISSION PROCESS FOR US INVESTIGATORS:

Non-US investigators should contact their MSD country representative for requirements and timelines.

Please comply with the timelines outlined below when submitting applications.

The following are **required** components for the application:

- Proposal – please complete the Submission Form 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 Submission Form as well.
  - For Application Type, please select either Clinical Research or Non-Clinical Research based on the provided descriptions.
  - Your Submission Type will be 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 (less than 2 years old - must be dated within the document) as an attachment in Visiontracker
- Detailed budget (if funding is requested) – please provide an appropriate budget per the guidance provided in the submission form.

Expectations of the Nemtabrutinib MK-1026 Review Cycle:

Data sharing is an intrinsic requirement for translational studies. Expectations regarding types of programmatic requests for data will be provided.

Data Tiers