OTSP:

Projects must:

- Involve use of patient samples treated with programmatic MSD agents (pembrolizumab and belzutifan) and/or other approved agents
- 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

2023 Areas of Interest for Oncology Translational Studies Program

Special Note: Diversity & Inclusion

We seek to foster diverse and inclusive representation within the individual Areas of Interest for each tumor type, and so encourage study proposal submissions across our program which:

- Specifically focus on the outcome disparities in underrepresented populations
- Are led by non-academic programs/institutions
- Are conducted in under-represented regions or countries

2023 Biology Components

The OTSP Committee is interested in proposals studying immunology and/or biology in relation to one (or more) areas of interest:

- Characterization of intra-tumoral myeloid-lineage populations, including neutrophils, in the context of response or resistance to pembrolizumab
- Characterization of intra-tumoral immune cell populations in the context of response or resistance to pembrolizumab. May include NK(T) cells, gamma delta T cells, or other unconventional T cell populations.
- Analysis of PD-1/PD-L1 function in tumor biology
- Mechanisms of immune cell trafficking and exclusion from tumors
- Mechanisms of tumor cell and immune cell interactions
- Mechanisms of T cell activation and exhaustion
- Mechanism of myeloid cell-mediated immune system activation or suppression
- Mechanisms of immune checkpoints in antigen presentation
- Role of CD4+ T helper cell populations
- Immune cell architecture of the tumor environment
- Mechanisms of response and resistance to approved antibody-drug conjugates (ADCs) or standard of care chemotherapy agents directed towards inhibiting microtubule function or acting through DNA-damage or structural modification inhibition either alone or in combination with pembrolizumab

2023 Belzutifan Areas of Interest

Analyses of HIF2A inhibition in the context of tumor biology including mechanisms of response and resistance:

- Effect of tumor genetic and biological interactions between tumor signaling pathways and HIF2A biology and inhibition
- Effect of HIF2A inhibition on the tumor immune response
- Mechanisms of tumor resistance to HIF2A inhibition
- Mechanisms of tumor response to HIF2A inhibition
- Mechanisms of interaction between inhibition of HIF2A and standard of care treatment

2023 Circulating tumor (ctDNA) Study Guidelines:

ctDNA-related areas of potential interest:

- Retrospective temporal analyses of ctDNA as a surrogate for monitoring of minimal residual disease burden in the neoadjuvant, adjuvant setting, or metastatic setting
- Retrospective temporal analyses of ctDNA quantification as a predictor of treatment response or progression
- ctDNA as a tool to investigate tumor genetics, biology, or clonal evolution
- ctDNA as a tool to investigate mechanisms of response or resistance
- Note:
  - Studies using ctDNA assays for prospective clinical trial enrolment will require additional discussion
  - Studies where ctDNA assays are intended for use for on-treatment patient clinical decision making are discouraged
  - Studies using non-commercial ctDNA assays will require additional discussion

General Considerations

Proposals in all cancer indications are welcome.

- Submissions employing longitudinal patient sampling are strongly encouraged
- For solid tumor proposals, submissions that utilize tissue-based analyses are preferred over those utilizing blood-based tests
- For all proposals, submissions that prioritize analysis of previously collected patient samples are preferred
- Patient selection or clinical decision making using experimental biomarker assays or technology that are not regulatory agency-approved are discouraged and will require additional discussion
- Studies that include any tumor/personalized vaccines, CART-T, or other cellular therapies will only be considered if within the support guidance for the program
- 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
- Pediatric studies
- Studies aimed at studying or modulating the microbiome
- Studies that are purely conducted in *in vitro* or *in vivo* mouse models
- Multi-omic biomarker identification and validation

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