Gilvetmab Product Grant Program

Detailed Description
Cycle 3

Section I. Product Grant Opportunity Description

Purpose

The overarching purpose of the Merck Animal Health Gilvetmab Product Grant Program ("Program") is to provide support for well-planned research projects aimed at advancing the science of immune checkpoint inhibitor therapy in veterinary medicine. Specifically, the Program invites applications for projects that seek to advance the understanding of the role gilvetmab plays across cancers, and the factors that may predict a patient's likelihood of benefitting from treatment. Projects supported by the Program must be grounded in immune checkpoint inhibitor literature from human or veterinary medicine. Investigations could include, but are not limited to, use of gilvetmab for different cancer indications, adjunct therapies, and biomarkers.

Background

Immune checkpoint inhibition has shown remarkable potential in human medicine to facilitate complete responses in cancer patients with extended duration of effect even in the setting of late-stage metastatic disease. However, this effect, while documented to occur across multiple human cancer types, is neither universal nor predictable. Gilvetmab is the first USDA conditionally licensed immune checkpoint inhibitor to be commercially available for treatment of dogs with stage I, II, or III mast cell tumor or stage II or III melanoma. As with immune checkpoint inhibition in human medicine, there remain a great deal of questions regarding the potential role for gilvetmab across cancers and the circumstances which can help to predict favorable response to immune checkpoint inhibition. Potential key areas of research include,

without limitation, tumor characteristics that increase objective response rate with use of immune checkpoint inhibitors, patient biomarkers for favorable response to treatment, combination of immune checkpoint inhibitors with other therapeutic agents, addressing primary and adaptive tumor resistance mechanisms, and methods of altering the tumor microenvironment to be more favorable to immune checkpoint inhibitor therapy.

Section II. Award Information

Instrument

Grant: A support mechanism providing product (gilvetmab) to an eligible entity to carry out an approved project or activity. The Gilvetmab Product Grant Program provides product (gilvetmab) only and does not provide funding for the approved project or activity.

Application Types Allowed

- New
- Resubmission
- Projects that involve the clinical use of gilvetmab in canines.
- Projects conducted in the United States of America, excluding its territories and possessions.

Excluded Applications

- Applications that are purely non-clinical in nature or seeking active pharmaceutical ingredient only will not be reviewed.

Criteria for Successful Grant Applications

To enhance the likelihood of success, applicants should consider the following criteria when developing their proposals:

1. Addressing Practical Questions: Successful grants will focus on practical, clinically relevant questions in veterinary oncology. Pilot studies, proof-of-concept, and proof-of-principle studies that have readily measurable outcomes and are

designed to gather information are encouraged. Studies that can demonstrate immediate applicability of their findings to clinical practice will be prioritized.

2. Strong Background Evidence: Proposals should provide robust background evidence supporting the research question. This evidence can be drawn from existing studies in human medicine or related fields, illustrating the relevance and potential impact of the investigation.
3. Feasibility of Case Accrual: Applications that clearly outline a strategy for the expedient accrual of cases will be favored. Demonstrating a well-thought-out plan for recruiting participants is essential for timely completion of the study.
4. Timely Completion: Projects must be designed to be completed within a two-year timeframe. Clear timelines and milestones should be included in the proposal to showcase the feasibility of the research.
5. Secured Funding Sources: Priority will be given to projects that have already identified and secured necessary funding sources. This demonstrates a commitment to the research and enhances the project's sustainability.

By aligning proposals with these criteria, applicants can increase their chances of receiving support through the Program.

Terms and Conditions of the Award

Program award recipients are required to adhere to the following terms and conditions to ensure the integrity and success of their research projects. Failure to adhere to these terms and conditions may result in revocation of the grant:

1. Funding Verification: Recipients must demonstrate that they have secured adequate funding to initiate their study within six months of award receipt. Shipment of gilvetmab to the investigator is contingent upon demonstration of funding. This ensures that the research can proceed without financial hindrances.
2. Patient Enrollment Timeline: Recipients must begin enrolling patients within three months of obtaining funding. This timeline is critical for maintaining the momentum of the research.
3. Project Completion Deadline: Research projects must be completed (all patients enrolled; all data analyzed) within two years of enrolling the first patient. Adhering to this timeline is essential for timely dissemination of findings.

4. **Progress Reporting**: Recipients are required to submit progress reports every six months until the completion of their project. These reports will help monitor the project's progress and ensure accountability.
5. **Protocol Changes**: Any changes to the research protocol submitted as part of the application must be approved by Merck Animal Health through a formal protocol change request. Recipients may not implement changes without prior approval from Merck Animal Health. Failure to submit a protocol change request form may result in revocation of grant support.
6. **Adverse Event (AE) Reporting**: Recipients must agree to report all adverse events occurring within the scope of their study and associated with use of gilvetmab to Merck Animal Health at 1-800-224-5318 or uspvgilvetmab@merck.com using the provided adverse event reporting form. We request AEs be reported as soon as possible or within one business day. This is vital for ensuring participant safety and maintaining ethical standards in research.
7. **Client Informed Consent**: Recipients will be expected to provide a copy of their informed client consent form regarding extra-label use of gilvetmab where applicable. Merck Animal Health will evaluate the provided informed client consent form and will add additional language pertaining to gilvetmab as deemed necessary.
8. **Restrictions on Product Sale**: Recipients are prohibited from selling the gilvetmab provided through the Program. The product is intended solely for use in the research project outlined in the grant application.

Section III. Eligibility Information

Eligibility Criteria for Program Director(s)/Principal Investigator(s)

Eligible individuals who can serve as Program Director(s) or Principal Investigator(s) (PD(s)/PI(s)) for the Program include:

Any individual who is a veterinary medical oncologist boarded by the American College of Veterinary Internal Medicine (ACVIM) or the European College of Veterinary Internal

Medicine (ECVIM), or any board-certified veterinary specialist with demonstrable experience working with canine cancer patients is invited to collaborate with their organization to develop an application for support. This includes, but is not limited to:

- Board-Certified Veterinary Medical Oncologists
- Board-Certified Veterinary Radiation Oncologists
- Board-Certified Veterinary Surgical Oncologists

Additionally, individuals from other specialties may be eligible if they can provide acceptable evidence of experience in managing canine cancer cases. This may include:

- Board-Certified Veterinary Internal Medicine Specialists
- Board-Certified Veterinary Dermatologists

All applicants must possess the skills, knowledge, and resources necessary to effectively carry out the proposed research.

Eligible Organizations

1. Higher Education Institutions
    a. Public/State Controlled Institutions of Higher Education
    b. Private Institutions of Higher Education
2. Nonprofits Other Than Institutions of Higher Education
    a. Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
    b. Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)
3. For-Profit Organizations
    a. Small Businesses
    b. For-Profit Organizations (Other than Small Businesses)

Number of Applications

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

Location

Projects must be conducted in the United States of America, excluding its territories and possessions.

Section IV. Application and Submission Information

Content and Form of Application Submission

It is critical that applicants follow the instructions in this Program announcement. Applications that are out of compliance with these instructions may be delayed or not accepted for review.

Non-Responsive Applications

Applications with the following attributes will be deemed non-responsive and will not be reviewed.

- Applications that request active pharmaceutical ingredient (API) for purely non-clinical applications
- Applications that do not involve the canine model
- Applications that involve stage II or III canine oral melanoma (see Ongoing Clinical Trials link on the Gilvetmab Product Grant Program website for information regarding ongoing clinical trials)

Page specifications

- Single-spaced, 12-point font, 1" margins, printable on 8.5" x 11" pages; applications exceeding specified page limitations will not be considered.

Instructions for Application Submission

To apply for this product grant opportunity, applicants must prepare and submit the following sections as part of their application. All documents should be typed according to the specified page limits, converted to PDF format, and submitted electronically (see below: Submission of Proposal).

Required Sections

1. **Cover Page (Limit: 1 Page)**
   Include the following information:
   - Title of the proposed study
   - Name, affiliation, email, and postal mailing address of all investigators

- Underline the name of the investigator to whom the product will be shipped
- Anticipated number of dogs to be treated
- Anticipated time frame for study completion
- Estimated cost of the study and anticipated sources of funding

2. Project/Performance Site Locations (Limit: 2 Pages)
   Identify all locations involved in the planned project, including clinics, reference laboratories, and animal facilities, if applicable.
3. Study Objectives/Scientific Hypothesis(es) (Limit: 1 Page)
   Provide a concise overview of the study objectives and hypothesis(es). Include an impact statement that outlines the significance of the research.
4. Research Plan (Limit: 5 Pages)
   Summarize the proposed project, including:
   - Background information
   - Study design
   - Justification for the number of animals needed
   - Expectations for results
   - Methods of analysis
     - Include a milestone-driven plan with clearly stated deliverables within the two-year timeframe.
5. Timeline (Limit: 2 Pages)
   Outline a maximum of 24 months for project completion from the time of first patient enrollment. Provide a timeline with a study calendar that highlights key dates and activities necessary to complete the trial and analyze the data. Note that the 24-month timeframe does not need to include publication, but preference may be given to projects that include a publication timeline.
6. References (Limit: 1 Page)
   List pertinent literature references related to the proposed study.
7. Budget (Limit: 1 Page)
   Outline expected expenditures for the project.

8. Current and Pending Support (No Page Limit)
   Include a list of any current and pending sources of funding for this project. Full funding for the project is not required at the time of application submission, but proof of such will be required prior to shipping gilvetmab to award recipients. Proof must be provided within six months of proposal acceptance. Owner-funded studies are not recommended and will only be considered if significant documentation is provided that demonstrates a historical caseload and expenditure by owners that align with the required timeframe.
9. Biographical Sketch (Limit: 2 Pages Each)
   List all personnel involved in the project and explain their roles.
10. Client Consent Form (No Page Limit)
    Include a copy of the proposed client consent form.
11. Ethical Committee Oversight (No Page Limit)
    Provide proof of ethical committee review of the proposed project (e.g., IACUC approval). For institutions without a formal IACUC, evidence of completion of a course on Good Clinical Practice (GCP) for Veterinary Clinical Trials and a signed statement of ethical treatment of animals are required.

Additional Information Concerning Required Components

1. Study Calendar

A well-structured study timeline outlines the phases of the research project, including recruitment, treatment, follow-up, and analysis. Below is an example timeline for a hypothetical research study.

Phase	Time Frame	Activities
Recruitment	Months 1-6	Enroll participants diagnosed with the target condition.
Treatment	Months 1-4	Administer the proposed treatment regimen.
Follow-Up	Months 5-9	Monitor participants for response and collect follow-up data.
Data Analysis	Months 10-12	Analyze data on treatment outcomes and biomarker changes.

2. Deliverables

Deliverables are specific outputs or results expected from the research. Here are examples of deliverables for a hypothetical study:

- Clinical Outcomes: Documented response rates (complete or partial) of participants treated with the intervention.
- Biomarker Analysis: Changes in key biomarker levels assessed through relevant samples.
- Final Report: A comprehensive report detailing the study findings, methodologies, and implications for future research.

3. Milestones

Milestones are significant points in the project timeline that indicate progress. Here are examples of milestones for a hypothetical research project:

- Milestone 1: Enrollment of all participants by the end of Month 6.
- Milestone 2: Completion of all treatments by the end of Month 10.
- Milestone 3: Completion of follow-up assessments by Month 13.
- Milestone 4: Submission of the final report by Month 18.

4. Impact Statement

A strong impact statement articulates the significance of the research and its potential benefits. Here's a general example:

Impact Statement: The proposed study aims to evaluate the effectiveness of a novel treatment for a specific medical condition that currently has limited therapeutic options. By investigating the potential benefits of this intervention, the research seeks to improve patient outcomes and enhance quality of life. Furthermore, the findings may provide valuable insights that could inform future treatment strategies for similar conditions, ultimately contributing to advancements in healthcare.

Submission Deadlines and Application Cap

Final deadlines for submission of the complete application package can be found for the relevant application cycle on the Gilvetmab Product Grant Program webpage.

To submit your completed PDF format application, please click on the "How To Submit Application" link found on the Gilvetmab Product Grant Program webpage. This link will ask you to provide your name and e-mail address and will then provide you with directions for submitting your completed application.

Applicants are encouraged to submit applications well before the due date, as each application cycle will be capped at a maximum of 25 applications that will be reviewed. Applications exceeding the cap will not be reviewed unless an earlier application is withdrawn.

Ethical Conduct

All projects are to be conducted in accordance with applicable laws and regulations, and in accordance with generally accepted standards of animal care for projects of similar type. Organizations will be required to certify that the project follows such laws, regulations, and standards.

Where applicable, evidence of approval by an institutional animal care and use committee (IACUC) will be required. For those institutions without a formal IACUC, we require evidence of completion of a course on Good Clinical Practice (GCP) for Veterinary Clinical Trials, and a signed statement of ethical treatment of animals.

Section V. Application Review Information

Review and Selection Process

Applications will be screened initially for compliance with the aforementioned application guidelines by an internal Merck Animal Health team. Compliant applications will then be reviewed by an external committee of experts (veterinary medical oncologists, surgical oncologists, and radiation oncologists) who are not affiliated with Merck Animal Health and do not have conflicts of interest (see Criteria section below). The committee will assign an overall impact score and the top scoring applications will be submitted for final selection to a committee of Merck Animal Health colleagues with expertise in clinical veterinary medicine and research and development. Merck Animal Health decisions are final and non-reviewable.

Decisions will be communicated by e-mail approximately one month after the close of the application window.

Criteria

The external committee of experts (veterinary medical oncologists, surgical oncologists, and radiation oncologists) who are not affiliated with Merck Animal Health and do not have conflicts of interest will perform the initial evaluation and assign an impact score to each proposal. The impact score will be assigned based on the 5 primary score criteria and additional score influences. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

1. Significance
    a. Does the project address an important problem or a critical barrier to progress in the field? Is the prior research that serves as the key support for the proposed project rigorous? How will successful completion of the aims change the concepts, methods, technologies, treatments, or preventative interventions that drive this field?
2. Investigator(s)
    a. Are the PD(s)/PI(s), collaborators, and other researchers well suited to the project? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise? Do the investigators have approval from all relevant and required organizations (i.e. scientific governing bodies, IACUC, etc.)?
3. Innovation
    a. Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Does the application seek to refine or improve research or clinical practice via a new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions?
4. Approach
    a. Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators included plans to address weaknesses in the rigor of prior research or therapeutic interventions that serve as the key support for the proposed project? Have the investigators presented strategies to ensure a

robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented?

5. Environment
    a. Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment, and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?
6. Additional Score Influences
    a. Clinical Research
        i. Is the study design justified and appropriate to address primary and secondary outcome variable(s) endpoints that will be clear, informative, and relevant to the hypothesis being tested? Given the methods used to assign participants and deliver interventions, is the study design adequately powered to answer the research questions(s), test the proposed hypothesis/hypotheses, and provide interpretable results? Are the study populations (size, sex, age, breed), proposed intervention arms/dose, and duration of the trial appropriate and well justified?
        ii. Are potential ethical issues adequately addressed? Is the process for obtaining informed consent appropriate? Are the plans for recruitment outreach, enrollment, retention, handling dropouts, missed visits, and losses to follow-up appropriate to ensure robust data collection? Are the planned recruitment timelines feasible and is the plan to monitor accrual adequate? Has the need for randomization (or not), masking (if appropriate), controls, and inclusion/exclusion criteria been addressed?
        iii. Is the study timeline described in detail? Is the projected timeline feasible and well justified?
    b. Data Management and Statistical Analysis
        i. Are planned analyses and statistical approach appropriate for the proposed study design and methods used to assign participants and deliver interventions? Is there a plan to complete data analysis within the proposed period of the award?

Section VI. Award Administration Information

Primary investigators of selected proposals will be informed and provided with an agreement that must be signed and returned within 30 days. The agreement includes but is not limited to the following terms:

- Award Recipients must provide proof of adequate funding to complete the proposal activities. **Proof of adequate funding is due within six months of proposal acceptance by the Program.**
- Award Recipients must agree to use the product in accordance with the appropriate oversight and record keeping (i.e. require owner consent, report adverse events to Merck Animal Health at 1-800-224-5318 or uspvgilvetmab@merck.com using the AE reporting form, as soon as possible or within one business day).
- Award Recipients must complete the proposed activities within 24 months of enrollment of first patient. If the proposed activities cannot be completed within 24 months, an extension application must be submitted and approved by Merck Animal Health.
- Award Recipients must adhere to the proposed protocol. Any proposed protocol changes must be approved by Merck Animal Health **prior to** implementation of those changes. If a change to the protocol is necessary, notification of the proposed change must be presented to Merck Animal Health with an explanation of the necessity of the change. Merck Animal Health reserves the right to deny additional provision of product depending on the nature of the change.
- Award Recipients must complete Progress Reports every six months and present the complete data to Merck Animal Health at the completion of the research project. Though encouraged, the decision to publish the data is entirely at the discretion of the Award Recipient.
- Award Recipients are prohibited from selling the provided product.

Once the agreement has been signed and all documentation (including proof of adequate funding) has been received, the product will be shipped to the Program Director/Principal Investigator at the Address indicated on the Cover Page of the application. Approximately ¼ of the total requested product amount will be provided at a time, with regular progress updates on product usage required to ensure there are no gaps in availability for the project.

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