Gilvetmab Product Grant Program

Detailed Description

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 with gilvetmab. 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

Funding Instrument

Grant: A support mechanism providing product to an eligible entity to carry out an approved project or activity.

Application Types Allowed

- New
- Resubmission

Award Project Period

A maximum of 24 months is allowed for completion of the research project. If it becomes evident that the project will not be completed in the allotted time, submission of an extension application will be required.

Special Considerations

1. Product grant recipients will be expected to provide a copy of their informed client consent form regarding extra-label use of gilvetmab where applicable or may use the Merck Animal Health provided client consent form. Merck Animal Health will evaluate the provided informed client consent form and add additional language pertaining to gilvetmab as deemed necessary.
2. Product grant recipients will be expected 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 using the provided adverse event reporting form.
3. Product grant recipients will be expected to provide a Progress Report on their project activities to Merck Animal Health every 6 months, and a final complete presentation of the data at the completion of the project.

Section III. Eligibility Information

Eligible Individuals (Program Director/Principal Investigator)

Any individual(s) who is a veterinary oncologist boarded by the ACVIM or ECVIM with the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s) (PD(s)/PI(s)) is invited to work with his/her organization to develop an application for support.

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.

Ethical Conduct

All projects are to be conducted in accordance with applicable law and regulations, and in accordance with generally accepted standards of animal care for projects of similar type. Organizations will be required to certify that it 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 IV. Application and Submission Information

Content and Form of Application Submission

It is critical that applicants follow the instructions in the product grant opportunity 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 non-clinical applications
- Applications that are purely preclinical in nature
- Applications that do not involve the canine model
- Applications that involve stage III canine oral melanoma (see Ongoing Clinical Trial link on the Gilvetmab Product Grant Program website for information regarding ongoing clinical trials)

Page Limitations

All page limitations must be followed as described. Applications exceeding specified page limitations will not be considered.

Instructions for Application Submission

The following sections are required for preparing an application to this product grant opportunity. The application should be typed following the page specifications (see below: Page specifications), converted to PDF format, and submitted electronically (see below: Submission of Proposal).

- **Cover page (limit 1 page)**: Title of proposed study; name, affiliation, email, and postal mailing address of all investigators; underline name of investigator to whom product

would be shipped; anticipated number of dogs to be treated; anticipated time frame to study completion; estimated cost of study and anticipated sources of funding.

- **Project/Performance Site Locations (limit 2 pages):** The project/performance site locations should include identification of all locations that will be involved in the planned project, including clinics, reference laboratories used, and animal facilities if applicable.
- **Study Objectives/Scientific Hypothesis(es) (limit 1 page):** Concise overview of study objectives and hypothesis(es). Please also provide an impact statement.
- **Research Plan (limit 5 pages):** Summary of proposed project including background; study design; reason for numbers of animals needed; expectations for results; methods of analysis. Please include a milestone-driven plan and stated deliverables within the two year time period.
- **Timeline (limit 2 pages):** A maximum of 24 months from the time of receipt of product is allowed for completion of each research project. Provide a timeline denoting key dates and activities necessary to complete the research, including a study calendar. The 24-month timeframe does not need to include publication, but preference may be given to those projects detailing a timeline for publication.
- **References (limit 1 page):** Pertinent related literature references
- **Budget (limit 1 page):** Outline expected expenditures
- **Current and Pending Support (no page limit):** Include a list of any current and pending sources of funding and/or additional grants requested for this project. For pending funding, please supply a timeline of when acquisition of the funding is anticipated. Product will not be shipped until proof of adequate funding to complete the research proposal is supplied. Owner-funded studies will be considered; however the panel encourages mindfulness of the ability to accrue patients within the required timeframe, and may give preference to those studies that can demonstrate comparable historical caseload and expenditure by owners.
- **Biographical sketch (limit 2 pages each):** List all personnel and explain their role on the proposed project.
- **Client consent form (no page limit):** Copy of proposed client consent form.
- **Ethical Committee Oversight (no page limit):** Provide proof of ethical committee review of the proposed project (e.g., IACUC approval). 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.

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

Supplementary Required Documentation

In addition to the application, supplementary required documentation includes:

- Proof of adequate funding to cover projected expenses
    - Acquisition of full funding is not required at the time of application submission but will be required prior to shipping of product to accepted proposals. Proof must be provided within 12 months of proposal acceptance.

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 be automatically rolled over into the next application cycle unless otherwise noted.

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 including but 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 12 months of proposal acceptance by the Program.
- Award Recipients who receive a grant for any extra label use 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).
- Award Recipients must complete the proposed activities within 24 months of product receipt. If the proposed activities cannot be completed within 24 months, an extension application must be submitted.
- Award Recipients must adhere to the proposed protocol. If a change to the proposed protocol is necessary, notification of this 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 6 months and present the complete data to Merck Animal Health at the completion of the grant period. Though encouraged, decision to publish the data is entirely at the discretion of the Award Recipient.
- Award Recipients must agree that they will not sell 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 and Address indicated on the Cover Page of the application. Approximately ¼ of the 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.

INDICATION This product contains gilvetmab, a caninized monoclonal antibody against canine programmed cell death receptor-1. For the treatment of dogs with mast cell tumors or melanomas. This product has demonstrated a reasonable expectation of efficacy and a preliminary safety profile in reducing the solid tumor burden in dogs with stage I, II, and III mast cell tumors or dogs with stage II and III melanomas. This product license is Conditional; safety, efficacy, and potency have not been fully evaluated. For more information regarding safety, see productdata.aphis.usda.gov.

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