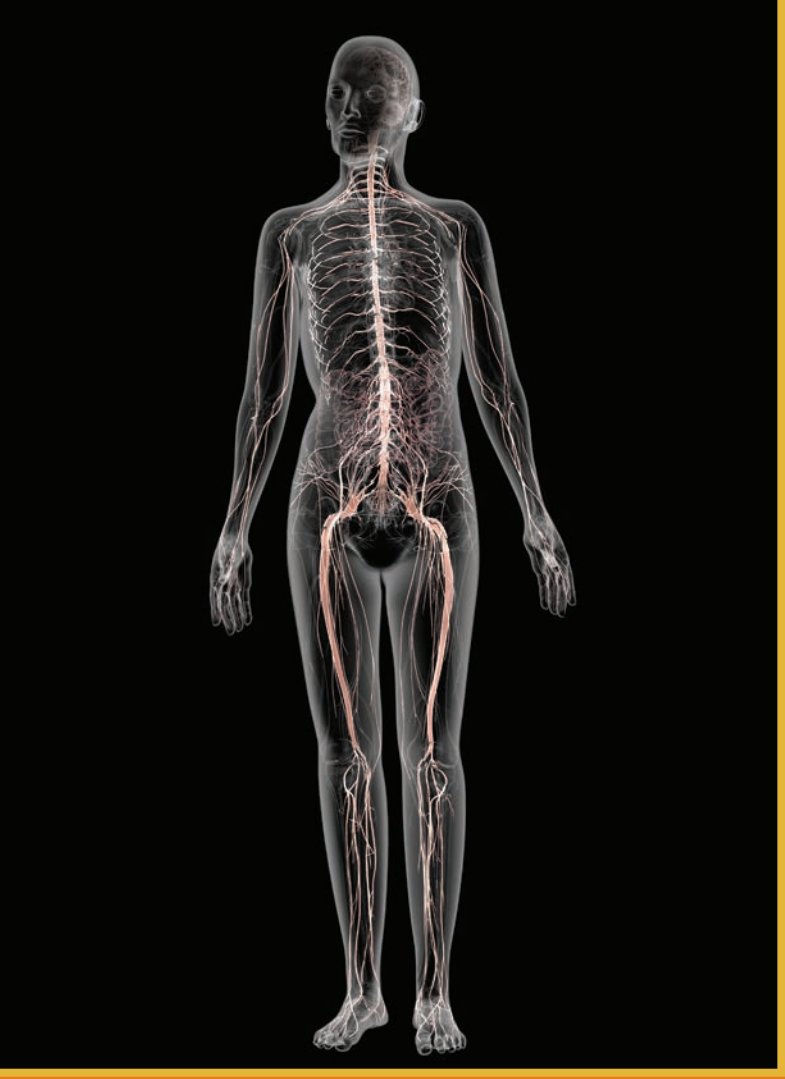
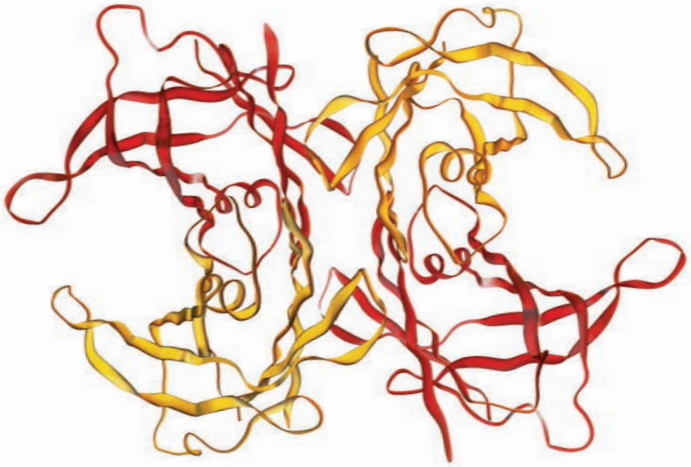






Application Guide

2016 Global Awards in Transthyretin (TTR) Amyloidosis Research Research

A Competitive Grants Program Supported by Pfizer

www.aspireresearch.org

ASPIRE

Advancing Science Through Pfizer – Investigator Research Exchange

Pfizer

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2016 Global ASPIRE TTR Amyloidosis Competitive Research Grant Awards

Advancing Science through Pfizer - Investigator Research Exchange (ASPIRE)

A Competitive Grant Program Sponsored by Pfizer

Mission

The mission of the Global ASPIRE TTR amyloidosis program is to support research in basic science and broad clinical research through a competitive grants program that advances medical knowledge in the understanding, diagnosis and treatment of TTR amyloidosis. **In-scope research submissions along the entire clinical spectrum of TTR amyloidosis (from TTR familial amyloid polyneuropathy (TTR-FAP) to TTR cardiomyopathy) and including mixed phenotypes are**

Background

Although recent developments have been made in the diagnosis and treatment of TTR amyloidosis, more research is needed. The goal of the 2016 GLOBAL ASPIRE TTR amyloidosis program is to further improve our understanding of the epidemiology, basic science and early diagnosis and treatment of TTR amyloidosis. Specifically, the program aims to advance Pfizer's understanding of the basic science and clinical knowledge of TTR amyloidosis through the submission of innovative proposals focused on (a) epidemiologic evaluations for TTR amyloidosis; (b) approaches for early diagnosis (e.g. multidisciplinary strategies, new diagnostic algorithms, , non-invasive diagnostic techniques, risk factors for disease penetrance, natural history studies); (c) the evaluation of patients with TTR amyloidosis presenting with a mixed phenotype including studies of patients with nonV30M mutations; (d) analyses of long-term efficacy and safety of tafamidis in the real world clinical setting; and/or (e) research that advances the basic science of amyloid formation and deposition.

Request for Proposals

Pfizer invites investigators to apply for the 2016 GLOBAL ASPIRE Awards in TTR amyloidosis through submission of innovative research proposals designed to enhance our ability to understand the epidemiology, basic science early diagnosis and treatment of patients with TTR amyloidosis.

2016 Research Topic: Epidemiology, Basic Science and Early Diagnosis and Treatment of Patients with TTR Amyloidosis.

Key Dates

Application deadline: May 9, 2016 (by 11:59pm EST in the United States)
Notification of awards recipients and award acceptance: July, 2016
Award expected to start by: October/November 2016*
Completion of award: Research must be completed within 12 months of start date.

**Contracts not executed by December 30, 2016 may risk loss of funding*

Eligibility *(Applicants must meet the following requirements)*

1. Eligibility

To be eligible for a GLOBAL ASPIRE TTR-FAP award, applicants must

- Have a professional degree (MD, PhD, PharmD or equivalent)
- Be affiliated with a host institution in the United States, Europe, Latin America or Asia Pacific region
- Have a mentor or senior investigator participate as a co-investigator if within 5 years of receipt of the terminal degree (i.e. applies to junior investigators only).

Note: Members of the 2016 External Review Committee and 2015 ASPIRE awardees are <u>not</u> eligible to apply or serve as mentors or collaborating investigators on applications from other investigators (this includes applications from junior investigators).

2. Research Requirements

Pfizer is interested in supporting research proposals that advance our understanding of the epidemiology, basic science and early diagnosis and treatment of TTR amyloidosis through research focused in the following areas:

- Epidemiologic evaluations for TTR amyloidosis
  - Global or regionally-focused evaluations

- Approaches for the early diagnosis of patients. Examples could include:
  - Multidisciplinary approaches
  - New diagnostic algorithms
  - Imaging studies
  - Non-invasive diagnostic techniques
  - Autonomic markers of TTR-FAP disease progression
  - Risk factors for disease penetrance
  - Markers of disease progression and natural history studies
  - Genetic screening programs for families
  - Genetic counseling patient support tools

- Evaluation of patients with TTR amyloidosis presenting with a mixed phenotype (e.g. polyneuropathy and cardiomyopathy) and including studies of patients with nonV30M mutations
  - Case Control and Cross-Sectional Studies
    - Includes examination of phenotype and genotype relationships
  - Evaluating Existing Databases for:
    - Clinical or treatment information
    - Phenotype or genomic factors

- Retrospective analyses of the long-term efficacy and safety of tafamidis in the clinical setting for the management of TTR-FAP
  - Impact on disease progression and quality of life
    - Includes prospective or retrospective evaluations based on the tafamidis real world experience in clinical practice
    - Note: Pfizer will not supply formulated study drug
- Mechanistic studies to advance the basic science of amyloid formation and deposition

3. Research Expectations

Within the specified areas of research interest, investigators are expected to:

- Generate data to better understand important diagnostic and clinical management issues relevant to treating patients with TTR amyloidosis.
- Proposals may include post-hoc exploratory analyses and well-designed retrospective or prospective analyses to generate and/or test hypotheses or studies to validate new assessments.
- Be able to complete the research within 12 months of start date.
- Present and/or publish the results of the study.

Evaluations may include standardized assessments as well as surrogate markers that may define or predict clinical response and to identify novel diagnostic strategies. **See website FAQ's for additional guidance on topics that fall outside the scope of this program.**

4. Other Funding

No other government, non-governmental, or industry-sponsored projects may cover the same work scope as the grant application to the ASPIRE Program. However, a ASPIRE Program grant may be related to other funding from foundations or government agencies, as long as there is no direct overlap. It is the responsibility of the applicant to justify the novelty of the proposal and provide evidence that the application does not overlap with any current or pending funding.

Once awarded, an ASPIRE grant cannot be amended upwards with additional funding support from Pfizer (via the standard IIR process or separate competitive grant program), nor can additional drug support above and beyond what is sufficient to complete the original study as reviewed and approved by the external review committee be provided. If supplemental funding is required, it must be secured from sources outside of Pfizer. Similarly, an ongoing Pfizer supported standard IIR cannot apply for supplemental funding via a Pfizer supported competitive grant program. ASPIRE awards cannot be provided to studies that are already in progress.

Application

Applications are to be submitted to Pfizer through an online submission website. Visit **www.aspireresearch.org** and click:

- "2016 TTR Amyloidosis Global Awards"
- Open the "Apply" tab on the top of the page
- Click on link **"To Apply for a 2016 ASPIRE Award Click Here"**
- When you select, "To apply for a 2016 ASPIRE Award Click Here", you will be routed to Pfizer's global investigator-initiated research website: **www.iirsubmission.pfizer.com**
- Click on "Submit an IIR Request" and follow the online instructions.

NEW USERS: If this is your first time visiting the portal you must first "Create an Account".

- Select "Create account"
- Complete:
  - User name
  - Email
  - Password
    - Press Continue to "Log In" and provide relevant details
- Complete:
  - User Profile
  - Investigator and Organization Profile
    - By completing these now, it will pre-populate this same information in the profile and will be available for subsequent submissions

ESTABLISHED USERS

- Log In
  - User name
  - Password

SUBMISSION

- Select "Create New Proposal"
- **PFIZER POLICY on Submission of an Investigator Initiated Research Proposal**
  - Check that you have read and agree to policy
  - Under: "Please select any option from below"
    - **Select** IIR (Investigator Initiated Research) Program
    - **Click** on "initiate submission"

GENERAL

- Are you applying to a Competitive Grants Program
  - Select "Yes"
  - A dropdown list appears and select:
    - "2016 GLOBAL ASPIRE TTR Amyloidosis"
- Study title (no more than 250 characters)
  - All text fields are limited, so a character count is given on all text fields
  - Add a descriptive study title of your proposal
  - At Primary Pfizer Therapeutic Area
    - Select "Rare Disease" from dropdown
    - Secondary Pfizer Therapeutic Area not required

STUDY DETAILS (all text fields limited at 3000 characters)

- **Brief Study Synopsis**
  - Provide an abstract outlining your overall research proposal (limit 250 words)
- **Brief Study Rationale**
  - Provide a brief description of the objectives and relevance of the proposed research in advancing the medical knowledge of the diagnosis of patients with TTR amyloidosis.
- **High Level Primary Endpoint**
  - Provide a brief description of the primary endpoint for the study proposal

UPLOAD STUDY PROTOCOL (12-page max limit), DESCRIPTION OF RESOURCES AND BUDGET AS A SINGLE DOCUMENT. DO NOT SUBMIT MULTIPLE DOCUMENTS. READ CAREFULLY BELOW FOR HOW TO PREPARE THIS SECTION OF YOUR APPLICATION.

- General Notes about Study Protocol Requirements and Organization
  - The content for this portion of the application should be organized as detailed below and is mandatory.
  - The study protocol itself must not exceed 12 pages: minimum 12 pt. font with 1' margins around (not including references or itemized budget). **Study protocols that exceed this 12 page limit will not be reviewed.**
  - Following the study protocol, include these sections in the same document which are not part of the 12-page limit noted above: Reference list, Description of the Overall Research Environment, Qualifications to Conduct the Proposed Research, Study Budget.
  - **All protocols are to be organized as noted below. Please do not deviate from this outline in preparing your study protocol and accompanying information and review the instructions carefully. A protocol submission template is provided here. Use of this protocol template is required to ensure your submission is fully compliant with the study protocol requirements and organization.**

PREPARING THE STUDY PROTOCOL: LIST THE TITLE OF YOUR APPLICATION AT THE TOP OF THE FIRST PAGE, THEN ORGANIZE THE PROTOCOL AS FOLLOWS:

(1) BACKGROUND:

(a) Objectives

(i) We suggest about 4 paragraphs to discuss the objectives of your proposed research

(b) Specific Aims and Hypotheses

(i) List each separate Specific Aim and how the hypothesis for that aim will be tested

(2) RELEVANCE OF PROPOSED STUDY TO PROGRAM MISSION (up to 3 brief paragraphs suggested)

(3) PRELIMINARY DATA IN SUPPORT OF THE PROPOSAL (up to 2 pages suggested or longer if needed)

(a) Review data generated by your or your collaborator's laboratories or clinical programs that support the proposed research and specific aims

(4) METHODS: a general schema for preparing this section of your application follows. Some sections may not apply to your research. All applicable sections should be included and other appropriate sections added as applicable to your proposal. Any figures and tables must be included in the body of the text.

(a) Experimental Design

(i) Population to be tested, sample size and recruitment plan

1. Inclusion criteria
2. Exclusion criteria

(b) Study Procedures

(i) State specifically how each Specific Aim will be accomplished by providing a detailed review of the methods for the proposed research.

1. What type of study design will be used (e.g. open label prospective study, cross-sectional study, retrospective chart review, etc).
2. State how the primary and secondary outcomes measures will be collected (e.g. discuss the dependent measures to be used)
   a. Review all outcome measures and their collection in sufficient detail to allow the review committee to determine whether the measures and schedule for collection of them is sufficient to allow for meaningful conclusions to be drawn from the proposed research.
3. Provide justification for the involvement of human subjects.

(c) Data Analysis Plan: Discuss all endpoints and outcome measures and specifically how these data will be managed.

(i) Include sample size and power calculations

(ii) Discuss how any variability and bias will be controlled as applicable

(iii) Describe the actual statistical methods to be employed

(iv) Review the anticipated results

(5) Milestones and Study Timeline

(a) Briefly describe (1 paragraph), or use a table to illustrate, how the specific aims will be completed within 12-months of funding. Indicating the timing for any training of investigators and research personnel, subject recruitment, laboratory assessments, data analysis and manuscript preparation. These are just examples. Your timeline should include details for achieving all milestones relevant to your proposed research.

(6) Potential Limitations and Considerations

(a) In a few paragraphs, discuss possible issues to obtaining the primary outcome measure(s) and management plans should they not be feasible. Other limitations, depending on the research proposed, could include managing delays in subject recruitment, underestimating sample sizes needed, or unforeseen issues with study methodologies proposed.

(b) The purpose of this section is to demonstrate to the review committee that you have planned for potential hurdles in completing the proposed research.

ii) At the end of the study protocol, include the following mandatory items. These are excluded from the 12-page maximum page count for the study protocol but must be included as part of the same document (i.e. 1 file should contain all of the information above for your study protocol plus the sections noted below).

(1) Reference List for any literature sited in the study protocol.

(2) Description of the Overall Research Environment.

(a) As the external reviews are blinded, please do not identify the name of the institution, research laboratory or related facilities in place to support the proposed research. Rather, briefly describe the overall resources available to you in support of the proposed research. If you have collaborators on the proposed research, include similar descriptions for any resources their collaboration brings to the research.

(3) Qualifications to conduct the proposed research

(a) Prepare a paragraph for the committee explaining what uniquely qualifies you (and your collaborators, if applicable) to conduct the proposed research. Please do not identify yourself or your collaborators in describing your unique qualifications to conduct the research as these reviews are blinded.

(i) Junior investigators should include some discussion of how mentors or collaborators involved can help to ensure the successful completion of the proposed work.

(4) STUDY BUDGET. ***All budgets must be detailed in USD. Applications containing budgets in other currencies will be returned.*** Please reach out to your local Pfizer medical colleague if you need assistance preparing your budget in USD. **Include the following in your budget:**

(a) Direct Costs

(i) Examples include labor and study costs such as: Personnel, Procedural Costs such as subject payments, relevant laboratory supplies or tests, Non-Procedural costs such as database programming,

(b) Indirect Costs

(i) Examples are: Additional study expenses such as costs for publication, IRB/IEC review fees, supplies, software license fees, and travel.

(ii) Note: Pfizer does not pay overhead on indirect costs.

(c) Overhead Costs

(i) These are the costs to your institution for the support of your study that are to be based on your Direct Costs and must be capped at 28% per Pfizer policy. **Applications listing overhead in excess of 28% will not be considered. Please be sure to consult with your local University/Institution to ensure they will agree to this overhead rate before submitting your application.**

(d) Total Budget: Direct + Indirect + Overhead; not to exceed USD$75,000

(e) Overlap

(i) If applicable, list any other research support with a description of overlap but do not identify yourself or collaborators when creating this list. Otherwise state: NO OTHER RESEARCH SUPPORT OR OVERLAP.

LEGAL, SAFETY, REGULATORY

- Complete section identifying relationships and responsibilities

PRIMARY SITE INFORMATION

- If completed user and investigator profile, this is automatically populated, if not COMPLETE section

UPLOAD

- CV (no more than 3 pages or if NIH biosketch, no more than 4 pages) for Principal Investigator and any collaborators.
  - Remove any personal information from CV (such as your home contact information, birth date, tax ID number or medical license number. Your business contact information should be the only contact information on your CV)
  - Note, any identifying information will be redacted before sharing with the external review committee to preserve the blind nature of the reviews; however we are required to have a complete CV for you and your collaborators on file for our records.
  - **Please combine all CVs into one document in either Word or PDF format. DO NOT UPLOAD MULTIPLE FILES.**

APPLICATION DEADLINE: May 9, 2016.

Applications must be received by 11:59pm EST on May 9, 2016. **LATE OR DRAFT SUBMISSIONS WILL NOT BE ACCEPTED UNDER ANY CIRCUMSTANCES. YOU MUST COMPLETELY SUBMIT YOUR APPLICATION BY THE MAY 9th DEADLINE TO HAVE YOUR GRANT APPLICATION CONSIDERED.** ADDENDA, supplemental materials, changes, or updates will not be accepted after the deadline. For further information please visit **www.aspireresearch.org**

Submit questions to **questions.aspireresearch-TTR-Amyloidosis@pfizer.com**

Criteria for Selection – Independent, External Review Committee

The ASPIRE applications will be reviewed by an independent, external review committee comprised of medical and scientific experts. **All reviews will be conducted on a blinded basis. Applicant identifying information will be redacted from submissions as required to protect and ensure the integrity of the blinded review process.** Grants will be awarded based upon:

- Scientific merit of the research proposal
- Qualifications of the applicant
- Relevance of proposed research to the program's mission
- Evidence of the applicant's commitment to an academic research career
- Evidence of a suitable research environment

Pfizer anticipates awarding 4 grants for the 2016 program.

Please note that Pfizer will perform an internal review of each submission to ensure it is within the scope of the program, and to verify that the principal investigator is cleared to conduct research (i.e. not appearing on any debarment list in countries where such lists exist).

Conditions of the Award

Each award is subject to the following conditions.

A. Financial Administration

The ASPIRE Program grant **will be awarded to the host institution on behalf of the Awardee. Pfizer is funding research awards ranging from $25,000 USD to a maximum of $75,000 USD each. Budgets for the program must be submitted in USD and all grants will be paid in USD. Pfizer anticipates awarding 4 grants for the 2016 program.** The amount of each award includes direct costs (labor and study costs), institutional overhead costs capped at 28% per Pfizer policy, and indirect costs (additional expenses such as publication, software license fees, and travel costs). Pfizer does not pay overhead on indirect costs. Each payment will be made in installments according to milestones, with a maximum of 70% of the funding delivered at the beginning of the project. The last installment will be made when the final results of the study are available. **Final budgets of those studies awarded a grant will be reviewed for fair market value in accordance with local policies and procedures before the contracting process begins. A signed, executed contract must be returned prior to disbursement of funds.**

** Contracts that are unable to be executed by December 30, 2016 are subject to loss of funding.*

B. Use of ASPIRE Program Funding

Funds from the ASPIRE Program may be used to support the Applicant's salary and fringe benefits, technical salaries, and supplies.

C. Financial Record Keeping

A separate financial record must be maintained by the Awardee.

D. ASPIRE Program Awards Progress and Final Reports

The Awardee must submit a final report on study results to the ASPIRE within 12 months of study start

Reprints of articles, published or in press, should be included with all reports.

From time to time, the ASPIRE Program may ask prior Awardees for information on study progress.

E. Required Documents if Proposal is Selected for Funding

Required additional documentation if your proposal is selected for funding by the review committee (further guidance will be provided):

- Two copies of the Signed Research Agreement, which Pfizer will provide
- IRB or Ethics Committee approval documentation, if applicable
- IND documentation from local regulatory authorities, as applicable per local regulations
- W-9 form for your institution (U.S. only)

F. Publications

Awardees are expected to present their findings at scientific meetings or to publish them in scientific journals. All publications that result from a project supported by the ASPIRE Program must carry the following acknowledgment: *"This research was supported by the Advancing Science through Pfizer–Investigator Research Exchange program, a competitive grants program supported by Pfizer, to (name of Awardee)."*

Awardees will provide to the ASPIRE Program the opportunity to view manuscripts or abstracts 60 days prior to submission for publication or other public disclosure.

G. Patents and Licensing

If the conduct of the research results in any invention or discovery by the Awardee that relates to a Pfizer product, the Awardee will grant to Pfizer a perpetual, royalty-free worldwide, non-exclusive license to each such invention.

H. Stipulations

1. Should the Awardee discontinue the research project or leave the designated host institution, the ASPIRE program must be notified without delay.

2. The ASPIRE Award may be transferred to another institution at the sole discretion of the ASPIRE Program, acting on the recommendation of the Review Committee. If a transfer is requested, letters from the Awardee and the new institution must be submitted to the ASPIRE Program at least 3 months before the date of the proposed transfer.

3. If the host institution or the Awardee wishes to terminate the award before its completion, an agreement between the host institution and the ASPIRE Program will be arranged. Termination will be made with the understanding that all unexpended funds will be returned to the ASPIRE Program and any unpaid balance of the award will be cancelled.

I. Serious Adverse Events (SAE) Reporting (As Applicable)

For All Studies Using a Pfizer Product and/or Device:

Reporting of Serious Adverse Events. Within 24 hours of first awareness of the event (immediately if the event is fatal or life-threatening), Principal Investigator will report to Pfizer by facsimile any Serious Adverse Event ("SAE," as defined below) for which reporting is required under this provision (as described below). Such SAEs are to be reported for (1) Study subjects who are assigned or, in the case of a blinded Study, possibly assigned to receive the Pfizer Product or (2) individuals otherwise exposed to the Pfizer Product as described below. Principal Investigator should report SAEs as soon as they are determined to meet the definition, even if complete information is not yet available.

a. Reporting Forms. Principal Investigator will report SAEs using one of the following forms: (1) a reporting form approved by the local regulatory authority, (2) a CIOMS form, (3) a Pfizer-provided *Investigator-Initiated Research Serious Adverse Event Form*, or (4) any other form prospectively approved by Pfizer. The Reportable Event Fax Cover Sheet provided by Pfizer must also be included with each SAE submitted.

b. SAE Definition. An SAE is any adverse event, without regard to causality, that is life-threatening (i.e., causes an immediate risk of death) or that results in any of the following outcomes: death; in-patient hospitalization or prolongation of existing hospitalization; persistent or significant disability or incapacity (ie, substantial disruption of the ability to conduct normal life functions); or a congenital anomaly or birth defect. Any other medical event that, in the medical judgment of the Principal Investigator, may jeopardize the subject or may require medical or surgical intervention to prevent one of the outcomes listed above is also considered an SAE. A planned medical or surgical procedure is not, in itself, an SAE.

c. Exposure During Pregnancy, Exposure During Lactation, Occupational Exposure, and Lack Of Effect. Even though there may not be an associated SAE, exposure to the Pfizer Product during pregnancy, exposure to the Pfizer Product during lactation, and occupational exposure to the Pfizer Product are reportable, and lack of effect of the Pfizer Product may also be reportable. These requirements are further explained in the training material provided by Pfizer (see Pfizer-Provided Training, below). As used in this Agreement, the term SAE will be understood to include exposure during pregnancy, exposure during lactation, occupational exposure, and reportable instances of lack of effect.

d. Hy's Law Cases. Cases of potential drug-induced liver injury as assessed by laboratory test values ("Hy's Law Cases") are also reportable to Pfizer. If a Study subject develops abnormal values in aspartate transaminase

(AST) or alanine transaminase or both, concurrent with abnormal elevations in total bilirubin and no other known cause of liver injury, that event would be classified as a Hy's Law Case. This reporting requirement is further explained in the training material provided by Pfizer (see Pfizer-Provided Training, below). As used in this Agreement, the term SAE will be understood to also include Hy's Law Cases.

e. Exclusions from SAE Reporting Requirements. Specifically excluded from the reporting requirements for SAEs under this provision is any SAE identified in the Protocol as anticipated to occur in the Study population at some frequency independent of drug exposure, unless the Principal Investigator assesses such an event as related to the Pfizer Product.

f. SAE Reporting Period. The SAEs that are subject to this reporting provision are those that occur from after the first dose of the Pfizer Product through 28 calendar days after the last administration of the Pfizer Product, or longer if so specified in the Protocol. In addition, if Principal Investigator becomes aware of an SAE occurring any time after the administration of the last dose of the Pfizer Product, Principal Investigator should report that SAE to Pfizer if the Principal Investigator suspects a causal relationship between the Pfizer Product and the SAE.

g. Follow-Up Information. Principal Investigator will assist Pfizer in investigating any SAE and will provide any follow-up information reasonably requested by Pfizer.

h. Regulatory Reporting. Reporting an SAE to Pfizer does not relieve Principal Investigator of responsibility for reporting it to appropriate regulatory authorities, if such reporting is required.

i. Pfizer-Provided Training. Pfizer will make available training material that provides information about the SAE reporting requirements for IIR studies. Principal Investigator will review this material and share it with any Study staff engaged in the reporting of SAEs.

In addition, for any non-interventional study with sites in the EU, the following requirements also apply:

Reporting of Non-Serious Adverse Events. Certain Non-Serious Adverse Events ("NS-AEs," as defined below) must also be reported to Pfizer. The NS-AEs that are reportable to Pfizer are those that (1) were specified in the Protocol as being reportable and (2) occur during the NS-AE reporting period (as defined below). Within 24 hours of first awareness of the event, Principal Investigator will report to Pfizer by facsimile any such NS-AE. Principal Investigator should report these NS-AEs as soon as they are determined to meet the definition and reportability criteria, even if complete information is not yet available.

1. Reporting Forms. Principal Investigator will report NS-AEs on one of the following forms: (1) a reporting form approved by the local regulatory authority, (2) a CIOMS form, (3) a Pfizer-provided I*nvestigator-Initiated Research Non-Interventional Study Adverse Event Report Form*, or (4) any other form prospectively approved by Pfizer. The Reportable Event Fax Cover Sheet provided by Pfizer must also be included with each NS-AE submitted.

2. AE and NS-AE Definitions. An Adverse Event ("AE") is any untoward medical occurrence in a Study subject receiving the Pfizer Product or an individual otherwise exposed to the Pfizer Product, without regard to whether there is a causal relationship between the Pfizer Product and the medical occurrence. A Non-Serious AE ("NS-AE") is any AE that does not meet the definition of an SAE (see Section b above, SAE Definition). For this Study, only NS-AEs identified in the Study Protocol as reportable must be submitted to Pfizer.

3. NS-AE Reporting Period. Unless the Protocol specifies a longer period, the NS-AEs that are subject to this reporting provision are those that occur from after the first dose of the Pfizer Product or the Study subject's enrollment in the Study (whichever is later) through 28 calendar days after the last administration of the Pfizer Product or the subject's last Study visit (whichever is earlier).

4. Follow-Up Information. Institution will assist Pfizer in investigating any NS-AE if Pfizer considers it necessary and will provide any follow-up information reasonably requested by Pfizer.

5. Regulatory Reporting. Reporting an NS-AE to Pfizer does not relieve Institution of responsibility for reporting it to appropriate regulatory authorities, if such reporting is required.

6. Pfizer-Provided NS-AE Training. Further information about the NS-AE reporting requirements for non-interventional IIR studies conducted within the European Union is provided in the Pfizer-provided training referenced in section i above. Principal Investigator will review this material and share it with any Study staff engaged in the reporting of NS-AEs.