# MASTER CLINICAL STUDY AGREEMENT

This MASTER CLINICAL STUDY AGREEMENT (the "**Master Agreement**") is made effective as of March 16, 2015 (the "**Effective Date**") by and between

1. AstraZeneca LP/AstraZeneca Pharmaceuticals LP, a Delaware limited partnership with offices at 1800 Concord Pike, Wilmington, Delaware 19803, including their affiliates and their respective successors, transferees and permitted assigns, (hereinafter"**AstraZeneca**" or "**Sponsor**"),

2. The University of Texas Health Science Center at San Antonio, The University of Texas Health Science Center at Houston, The University of Texas Health Science Center at Tyler, The University of Texas Medical Branch at Galveston, The University of Texas Southwestern Medical Center, and The University of Texas at Austin, each a member institution of The University of Texas System ("**System**") which is located at 201 West 7th Street, Austin, Texas 78701 (each an "**Institution**") and each with an office and place of business as set forth on Appendix 4 hereto (each a "**Study Site**"); and

3. Each of AstraZeneca (or Sponsor) and Institution shall be referred to as "Party" or "Parties" throughout this Master Agreement.

4. For purposes of this Master Agreement, each Party acknowledges and agrees that the other Party or any of its Affiliates may perform any of such other Party's obligations under this Master Agreement and will be entitled to all rights as provided under this Master Agreement. Each Party further acknowledges and agrees that the other Party or any of its Affiliates may contract for a Study by executing a Study Addendum with Institution under this Agreement. For purposes hereof, Affiliate shall mean any business entity that, directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with a Party. With respect to AstraZeneca, the term Affiliate shall also include, but not be limited to, any business entity that is controlled by or under common control with AstraZeneca PLC. For purposes of this definition only, "control," means (a) to possess, directly or indirectly, the power to direct the management or policies of a corporation or business whether through ownership of voting securities, or by contract relating to voting rights or corporate governance or otherwise, or (b) to own, directly or indirectly, fifty percent (50%) or more of the outstanding voting securities or other ownership interest of such corporation or business (which for a limited partnership shall mean control of the general partner). In addition, third party licensors or contractors of AstraZeneca shall also be deemed Affiliates.

## Background

(a) WHEREAS, AstraZeneca intends to conduct one or more clinical studies with the Institution regarding an AstraZeneca Test Drug and the Institution desires to participate in such clinical studies;

(b) WHEREAS, clinical studies are to be written and funded by AstraZeneca and carried out by Institution, under the terms and conditions specified herein;

(c) WHEREAS, the Institution has appropriate facilities and personnel necessary to conduct such clinical studies and will procure the services of a Principal Investigator; and

(d) WHEREAS, as of the Effective Date, this Master Clinical Study Agreement amends and restates a certain "Master Clinical Study Agreement" dated December 22, 2005, between Institution and AstraZeneca (the "**Universal Master**") and is intended to amend and restate in its entirety the terms, conditions, and provisions of the Universal Master. Accordingly, as of the Effective Date, this Master Clinical Study Agreement supersedes and replaces the Universal Master and will govern and control all Studies undertaken by the Parties from and after the Effective Date. Any Study which began under the Universal Master and which is still in progress as of the Effective Date will continue to be governed by the Universal Master.

**Agreement**

NOW THEREFORE, in consideration of the mutual covenants contained in this Master Agreement, the Parties agree as follows:

**1. DEFINITIONS**

Unless otherwise specifically provided in this Master Agreement, capitalized terms shall have the meaning set forth in Appendix 1.

**2. CONDUCT OF THE STUDY**

**2.1** This Master Agreement pertains to the conduct of one or more clinical studies that are mutually agreed upon and undertaken under this Master Agreement. Each such clinical study will be detailed in a Clinical Study Addendum ("**Addendum**"; substantially in the form as set forth in Appendix 2) to this Master Agreement and referred to as a "**Study**". Each Study shall be identified by a Study code. For sake of clarity, "Study" and "clinical trial" may be used interchangeably throughout this document. Until the Parties have agreed to a Study and signed the applicable Addendum, neither Party shall have any obligations with respect to such a Study. AstraZeneca shall be the sponsor of each Study and any reference to "Sponsor" in the Master Agreement, Appendix or Addendum shall be reference to AstraZeneca.

**2.2** AstraZeneca and Institution shall direct its Principal Investigator to conduct each Study in accordance with this Master Agreement, the Protocol, any Addendum, the Investigator's Brochure, and/or other prescribing information, Study manuals, as each may be amended, and in compliance with all Applicable Laws, any condition required by a Regulatory Authority and/or an Institutional Review Board ("**IRB**"). The Institution shall direct its Principal Investigator to follow all guidelines and instructions reasonably provided by AstraZeneca.

**2.3** The specific requirements for any Study shall be set forth in the Addendum issued for a Study under the terms of this Master Agreement. The Addendum shall be in substantially the form attached hereto as

Appendix 2, and shall include the information noted thereon, including the referenced attachments. Other terms and conditions shall be as set forth in this Master Agreement. The Institution will request its Principal Investigator for each Study to acknowledge in writing the terms of the Addendum, as evidenced by the signature of the Principal Investigator on the Addendum.

**2.4** Study Subject Safety. Institution and AstraZeneca shall promptly notify each other of any significant new findings developed during a Study and thereafter that may (i) adversely affect the safety, well-being, or medical care of Study Subjects, (ii) affect the willingness of a Study subject to continue participation in the Study, (iii) influence the conduct of the Study, or (iv) alter the IRB's continuing approval of the Study. Institution shall promptly notify the IRB of any such events. When Study subject safety or medical care could be directly affected by Study results, Institution shall be free to provide the Study results to Study subject in accordance with IRB policy. AstraZeneca agrees to monitor Study data and will provide to Institution urgent safety information in accordance with International Conference on Harmonization ("**ICH**") E6 Guidelines (section 5.17) and FDA IND regulations (CFR § 312.32) and shall provide routine annual Study update reports.

**2.5** Contract Research Organizations. AstraZeneca may retain one or more contract research organizations ("**CRO[s]**") to assist AstraZeneca in managing and monitoring a Study. The Institution acknowledges AstraZeneca's right to assign or transfer, in whole or in part, without consent of the Institution, any of its rights or obligations under an Addendum to any such CRO(s). Notwithstanding such assignment, AstraZeneca shall retain responsibility for the performance of its obligations under this Master Agreement. The Institution shall permit such CRO(s) to perform any or all of AstraZeneca's obligations, or exercise any or all of AstraZeneca's rights, under this Master Agreement. AstraZeneca shall direct its CRO(s) to use this Master Agreement as their guide when negotiating with Institution.

**2.6** Nothing in this Master Agreement will limit or prohibit Institution or any of its personnel, including the Principal Investigators, from conducting any research or from performing research for or with any entity or person, including any other outside sponsors, provided, however, that such research: (i) is conducted independently; (ii) is performed in a manner that does not interfere or prevent the performance of clinical trials under this Master Agreement; (iii) is conducted without violating the confidentiality provisions of this Master Agreement; and (iv) such third parties will not gain any rights to any results, discoveries or inventions arising from any clinical trial under this Master Agreement. Furthermore, AstraZeneca will not gain any rights via this Master Agreement to any such other research. AstraZeneca acknowledges that this provision is intended to preserve the academic freedom and integrity of Institution and its faculty and to ensure that Institution and its faculty are not regarded as exclusive researchers for AstraZeneca.

## 3. PRINCIPAL INVESTIGATOR AND INSTITUTION

**3.1** AstraZeneca understands and agrees that the Principle Investigator is not a Party to this Master Agreement; only the Principle Investigator's Institution is the Party to this Master Agreement. As such, Institution shall notify the Principal Investigator of his/her following obligations and responsibilities: The Principal Investigator shall be responsible on a day-to-day basis for the conduct of a Study, including

responsibility for training the Study Site Staff and supervising their work. Defined terms can be found in Appendix 1.

**3.2 Institution will ensure that the Principal Investigator shall:**

**3.2.1** prior to the commencement of a Study, provide AstraZeneca with evidence of his/her qualifications through a current curriculum vitae and other relevant documentation related to his/her qualifications, an executed investigator statement on U.S. Food and Drug Administration ("**FDA**") Form 1572, and a list of appropriately qualified Study Site Staff and, as applicable, their curricula vitae. Such list shall be kept up to date during a Study;

**3.2.2** obtain and maintain all approvals from the relevant IRB (including approval of the Informed Consent Materials) necessary to conduct a Study and keep AstraZeneca fully apprised on the progress of such submissions and provide written documentation of such approval(s) to AstraZeneca;

**3.2.3** ensure that any amendments (agreed in writing by the Parties) to the Protocol are approved by the relevant IRB and Regulatory Authority (if applicable) prior to implementation of such amendments;

**3.2.4** ensure that Informed Consent to participate in a Study is obtained from each Subject and maintained in accordance with a Study Protocol and documented in a form approved by AstraZeneca, the relevant IRB, and, if applicable, the relevant Regulatory Authority;

**3.2.5** notify AstraZeneca, the Institution and the relevant IRB of any serious adverse event that occurs during the course of a Study in accordance with the Protocol and Applicable Laws;

**3.2.6** ensure that all Medical Records of all Subjects are kept and maintained in accordance with Applicable Law and Case Report Forms ("**CRF**") instructions;

**3.2.7** ensure that CRFs are completed within the agreed time period as instructed by AstraZeneca;

**3.2.8** allow and, if requested, be available at Study related monitoring, AstraZeneca audits, IRB review, Regulatory Authority inspections, and provide direct access to Study Documentation and Subject Medical Records as soon as reasonably possible upon request by AstraZeneca, Regulatory Authority, IRB or other party designated by AstraZeneca. Subject Medical Records shall remain the property of the Institution;

**3.2.9** notify AstraZeneca within five (5) business days if Institution or the Principal Investigator is contacted by a Regulatory Authority with respect to a Study, unless prevented from doing so by Applicable Laws. The Principal Investigator shall provide AstraZeneca with copies of all pertinent information and documentation issued by any Regulatory Authority and any proposed

response. No response shall contain any false or misleading information with respect to a Study, the AstraZeneca Test Drug or AstraZeneca. AstraZeneca shall be present at and participate in any inspection or regulatory action with respect to a Study and review and comment in advance any responses that pertain to a Study;

**3.2.10** be available for AstraZeneca to perform work outlined in a Study at least until Site Closure;

**3.2.11** (a) assist AstraZeneca in the preparation and submission of investigational new drug applications, new drug applications, any other premarket or marketing applications relating to a Study or the AstraZeneca Test Drug, and any amendments or supplements to the foregoing, (b) attend meetings with the FDA and other regulatory or governmental authorities regarding such applications and the associated approvals and (c) provide such other reasonable and cooperation assistance as AstraZeneca may request in connection with regulatory matters relating to a Study or the AstraZeneca Test Drug, at the request and expense of AstraZeneca;

**3.2.12** ensure that any Study Site Staff complies with the parts of this Master Agreement that relate to their duties in a Study;

**3.2.13** agree that AstraZeneca may publicize the existence of a Study in an attempt to recruit Subjects ("**Recruitment**") provided that the Principal Investigator obtains AstraZeneca's prior written consent and obtains IRB(s) prior approval to any such Recruitment activities and materials in respect of a Study; and

**3.2.14** provide to AstraZeneca promptly, at AstraZeneca's request, financial disclosure statements in compliance with 21 C.F.R. Part 54, in the form required by AstraZeneca and executed by the Principal Investigator and any sub-investigators, and such other financial information as AstraZeneca may reasonably request. During the term of a Study and for a period of one (1) year thereafter, the Principal Investigator and any sub-investigators shall promptly notify AstraZeneca of any changes to such financial information.

**3.3 The Institution shall:**

**3.3.1** give AstraZeneca written notice at such time as it becomes aware that the Principal Investigator plans to leave the Institution or shall be unable to complete a Study. The Institution shall, in consultation with AstraZeneca, use reasonable efforts to promptly nominate a replacement for the Principal Investigator for such study;

**3.3.2** retain and store complete, current, accurate, organized and legible Study Documentation in a manner acceptable for the collection of data for submission to, or review by, a Regulatory Authority and in full compliance with the Protocol and all Applicable Laws, and shall ensure that no Study Documentation is destroyed for fifteen (15) years after the completion by Institution and Principal Investigator of all obligations in the conduct of a Study or the early termination of a Study; and

**3.3.3** ensure that no Study Documentation is destroyed without the prior written approval of AstraZeneca.

## 4. REPRESENTATIONS, CERTIFICATIONS AND PROMISES

**4.1** The Institution (and the Principal Investigator wherein to the extent that such representations, certifications and promises relate to the Principal Investigator, s/he acknowledges) represents, certifies and promises and the Principal Investigator acknowledges to AstraZeneca:

**4.1.1** that they will conduct a Study within the agreed time schedule set forth in each Addendum and in the way set forth in the Protocol and in this Master Agreement and each Addendum;

**4.1.2** Principal Investigator has not engaged in conduct that has resulted or may result in a felony conviction or that may cause Principal Investigator to be regarded as unsuitable to perform a Study or that may otherwise adversely affect AstraZeneca's reputation;

**4.1.3** Institution and the Principal Investigator have, at all times during the course of a Study, the appropriate licenses, approvals and certifications necessary to safely, adequately and lawfully perform a Study in accordance with good clinical practice, FDA requirements and all Applicable Laws and have no notice of any investigations that would jeopardize such licenses, approvals or certifications;

**4.1.4** Neither the Institution, nor the Principal Investigator, nor any member of a Study Site Staff has (a) any conflicting obligations, financial interest or other interest in the outcome of a Study, or (b) entered into any contract that might interfere with the performance of a Study or that might impair the acceptance of the resulting data by the FDA, or create a conflict of interest;

**4.1.5** Principal Investigator is, at all times during the course of a Study, qualified by training and experience with appropriate expertise to conduct a Study;

**4.1.6** Neither the Institution, nor the Principal Investigator nor any other person assisting in a Study is restricted or prohibited by any ethics or other law or regulation from entering into or otherwise receiving any benefit under this Master Agreement because of his or her role as a government employee or service provider;

**4.1.7** The Institution and the Principal Investigator acknowledge that they have been selected to conduct a Study and/or attend Study Meetings because of their experience, expertise and resources and not, in any way, as an inducement to, or in return for, past, present or future prescribing, purchasing, recommending, using, obtaining preferential formulary status for or dispensing any AstraZeneca product;

**4.1.8** If during the term of this Master Agreement or within two (2) years of the termination of this Master Agreement, Principal Investigator is a member of a committee that sets formularies or develops clinical guidelines, Principal Investigator will disclose to such committee the existence and nature of this Master Agreement and will follow the procedures set forth by the committee. Principal Investigator further agrees to fully comply with all applicable disclosure obligations relating to Principal Investigator's relationship with AstraZeneca that may be externally imposed on Principal Investigator based on the requirements of any Institution, medical committee or other medical or scientific organization with which Principal Investigator is affiliated;

**4.1.9** Debarment. Institution has not used, and shall not use the services of any person, including the Principal Investigator, who (i) is excluded, debarred, suspended or otherwise ineligible to participate in federal health care, procurement, or non-procurement programs; (ii) has been convicted of a criminal offense that requires exclusion from a federal health care program or (iii) is otherwise disqualified or suspended from performing a Study or subject to any restrictions or sanctions by the FDA or any other governmental or regulatory authority or professional body with respect to the performance of a Study (a "**Debarred Person**");

**4.1.9.1** Institution will immediately notify AstraZeneca in writing if any person who assists in performing a Study becomes a Debarred Person, or if any pending or threatened action, suit, claim, investigation, or other legal or administrative proceeding may result in a person performing under this Master Agreement becoming a Debarred Person. Institution agrees that any Debarred Person, or person proposed to be Debarred, shall be immediately prohibited from performing services under this Master Agreement; and

**4.1.10** Institution and/or Principal Investigator shall immediately notify AstraZeneca in writing of any breach of the foregoing or if any representation, certification or promise made in the foregoing ceases to be accurate.

## 5. STUDY SITE

The Institution and the Principal Investigator shall conduct a Study at the Study Site identified in the applicable Addendum, or such other Study Sites as the Parties may agree in writing and as shall be listed on FDA Form 1572.

## 6. MATERIALS

**6.1** AstraZeneca, or AstraZeneca's delegate, may provide the Institution and the Principal Investigator with the Materials set forth in applicable Addendum. Subject to Institution's right to publish the results as referenced in Article 13 below, AstraZeneca shall own all right in and to the Materials (irrespective of whether or not set forth above), unless otherwise agreed to by AstraZeneca in writing. The Materials supplied may only be accessed and used by the Institution, the Principal Investigator and the Study Site Staff to the extent required for the conduct of a Study and only for the purposes described in the Protocol,

unless otherwise agreed by the Parties in writing. Nothing herein, however, shall prevent Institution from using Study results for internal ordinary patient care, research and educational purposes, subject to the provisions of this Master Agreement, including Confidentiality. To the extent AstraZeneca supplies computers, Institution agrees that no software may be installed unless the Parties agree in writing that such software is required to conduct a Study.

**6.2** The Principal Investigator is responsible for maintenance of the Materials and AstraZeneca will assist the Principal Investigator in maintaining the Materials in good working order at AstraZeneca's expense.

**6.3** At Site Closure, the termination or expiration of this Master Agreement, or at AstraZeneca's earlier request, the Institution shall promptly return to AstraZeneca any Materials as indicated above unless the Parties agree that the Institution or the Principal Investigator shall acquire the Materials. Any acquisition of Materials shall be the subject of a separate agreement between the relevant Parties and must be done at fair market value. Institution's failure to return Materials will be managed as set forth in Section 9.8.

## 7. SUBJECT ENROLLMENT

**7.1** The Principal Investigator shall enroll Subjects in a Study in accordance with the applicable Addendum for such Study. The Subject enrollment period for a Study may be extended or shortened and the number of Subjects that the Institution may enroll in a Study may be changed, at AstraZeneca's sole discretion.

**7.1.1** Principal Investigator shall ensure that no Subjects are enrolled in a Study before prior written approval has been given by AstraZeneca;

**7.2** The Institution acknowledges that if a Study to be conducted under this Master Agreement and applicable Addendum is part of a Multi-Center Study, it agrees that when the enrollment goal for the Multi-Center Study as a whole is reached, enrollment will be closed at all sites, including at the Institution, regardless of whether the Institution or any other site has reached its individual enrollment goal for such a Study.

**7.3** AstraZeneca representative and Principal Investigator (or delegate) will discuss enrollment of the first recruited Subject to confirm that the Subject fulfills all inclusion criteria stated in the Protocol, and does not meet any exclusion or withdrawal criteria stated therein.

## 8. INVESTIGATIONAL PRODUCT

**8.1** Investigational Product shall only be used for the conduct of a Study and strictly in accordance with the related Protocol and all Applicable Laws. AstraZeneca shall:

**8.1.1** provide the Principal Investigator with all current and relevant information regarding the Investigational Product; and

**8.1.2** provide Institution with all amounts of Investigational Product required for completion of a Study.

**8.2** All Investigational Products supplied to the Institution for each Study shall remain the exclusive property of AstraZeneca until administered or dispensed to Subjects during the course of a Study. Upon termination of this Master Agreement, the Institution shall, at AstraZeneca's expense, handle any quantities of unused Investigational Product, in accordance with AstraZeneca's written instructions. The Institution shall maintain complete and accurate records relating to the disposition of Investigational Product supplied to the Institution.

## 9. COMPENSATION

**9.1** For the services to be rendered under this Master Agreement, AstraZeneca shall pay the Institution in accordance with each applicable Addendum. The Parties acknowledge that the amounts to be paid by AstraZeneca under this Master Agreement and each applicable Addendum are reasonable compensation, representing the fair market value, for the work performed by the Institution, the Principal Investigator and the Study Site Staff and that neither of the Institution, the Principal Investigator or the Study Site Staff have received any other compensation or inducement in connection with this Master Agreement or their participation in a Study.

**9.2** Any amounts paid by AstraZeneca to the Institution under this Master Agreement and applicable Addendum for services that have not been performed or expenses that have not been incurred shall promptly be refunded to AstraZeneca upon the expiration or termination of this Master Agreement or earlier at the request of AstraZeneca.

**9.3** The Institution shall not submit claims to, or otherwise seek reimbursement from, Medicare, Medicaid or any other third party payor, whether public or private, for any costs covered by payments made or goods or services provided by AstraZeneca under this Master Agreement and applicable Addendum, including Protocol procedures detailed in Schedule A attached thereto.

**9.4** All amounts payable by AstraZeneca to the Institution pursuant to this Master Agreement and applicable Addendum shall not be reduced on account of any taxes unless required by Applicable Laws. The Institution alone shall be responsible for paying any and all taxes (other than withholding taxes required by Applicable Laws to be paid by AstraZeneca) levied on account of, or measured in whole or in part by reference to, any payments it receives. AstraZeneca shall deduct or withhold from the amounts payable any taxes that it is required by Applicable Laws to deduct or withhold.

**9.5** All payments made by AstraZeneca under this Master Agreement and applicable Addendum are inclusive of sales and use taxes. AstraZeneca shall pay all sales and use taxes at the applicable rate, where applicable.

**9.6** Attendance at Study Meetings, Reimbursement for Accommodation Expenses, and Disclosure Requirements. Principal Investigator and/or Study Site Staff may be invited by or on behalf of AstraZeneca, to attend and participate in Study Meetings. To the extent that Principal Investigator and/or Study Site Staff attend a Study Meeting, the Parties agree that there will be no additional compensation for attendance or participation at such Study Meeting. If the Principal Investigator or Institution is

retained by AstraZeneca to perform services at a Study Meeting, the terms and obligations of such services will be subject to a separate agreement.

**9.6.1** Consistent with the Pharmaceutical Research and Manufacturers of America Code on Interactions with Healthcare Professionals ("**PhRMA Code**") and AstraZeneca's Global Policy on External Interactions available at www.astrazeneca.com, AstraZeneca may provide modest hotel accommodations, meals and transportation to and from a Study Meeting and reimbursement for other reasonable and modest expenses incurred (collectively, "**Accommodation**") to Principal Investigator and/or Study Site Staff who attend Study Meetings. AstraZeneca will not provide Accommodation to individuals who do not attend Study Meetings or to spouses or guests of Principal Investigator and/or Study Site Staff. Attendance at Study Meetings is restricted to Principal Investigator and/or Study Site Staff only.

**9.6.2** Accommodations will be arranged and paid for by the AstraZeneca vendor handling a Study Meeting logistics. Any additional Accommodation expenses incurred by Principal Investigator and/or Study Site Staff must comply with the AstraZeneca Expense Guidelines in Appendix 3, and the reimbursement requirements set forth in the applicable Addendum.

**9.7** U. S. Sunshine Act Requirements**.** All funds paid to a Covered Recipient under this Master Agreement must be in U.S. currency. Institution acknowledges and agrees that any direct or indirect Payments or Transfers of Value to Covered Recipients are subject to transparency reporting requirements, including disclosure on AstraZeneca's website. AstraZeneca's report shall identify the Principal Investigator and shall include payments to Institution hereunder as research payments attributable to Institution. Transfers of Value for research-related expenses (e.g., transportation, lodging, meals) may be attributed to the respective individual. Institution shall not contract with or make any Payment or Transfer of Value to a Covered Recipient on behalf of AstraZeneca without AstraZeneca's prior written approval, except as otherwise contemplated herein. Documentation concerning Payments or Transfers of Value to a Covered Recipient must be maintained by Institution for five (5) years. Notwithstanding the foregoing, Institution shall use reasonable efforts to assist AstraZeneca in obtaining information in the event that any reporting details are missing from AstraZeneca's records.

**9.8** AstraZeneca reserves the right to deduct from the final payment, the fair market value of any Materials not used or returned to AstraZeneca at Site Closure, or upon termination or expiration of the Master Agreement the applicable Addendum, or at AstraZeneca's earlier request. In the event such deduction occurs, and thereafter Institution returns the Materials, AstraZeneca shall pay Institution the fair market value of the returned Materials as of the date of receipt by AstraZeneca.

## 10. INTELLECTUAL PROPERTY

**10.1** Institution shall, and shall cause the Principal Investigator and the Study Site Staff to, make prompt and full disclosure to AstraZeneca of all AstraZeneca IP. Institution agrees that AstraZeneca shall own all rights and title in and to all AstraZeneca IP. Institution hereby assigns and transfers, and shall cause the Principal Investigator and the Study Site Staff to assign and transfer, without additional consideration, to

AstraZeneca (or its nominated designee) all their rights and title in and to the AstraZeneca IP throughout the world. AstraZeneca hereby grants Institution a non-exclusive, perpetual, royalty-free license, without the right to grant sub-licenses, to use the Study Documentation, study data and results,and know-how generated in the performance of this Master Agreement for its own (i) internal research and/or patient care and/or (ii) educational purposes and/or (iii) Subject care purposes, provided that the restrictions with regards to Confidential Information and Publication as set forth in Articles 11 and 13 respectively are observed and adhered to. For the avoidance of doubt this grant does not include any rights to use AstraZeneca Test Drug Inventions.

**10.1.1** Upon the request and at the sole expense and exclusive control of AstraZeneca, Institution shall, and shall cause the Principal Investigator and the Study Site Staff to, execute any instruments or testify as AstraZeneca deems reasonably necessary for AstraZeneca to obtain patents or otherwise to protect AstraZeneca's interest in AstraZeneca IP.

**10.1.2** To the extent that research is legally conducted at Institution outside of this Master Agreement and unrelated to the Study with commercially available AstraZeneca Test Drug, then the results or inventions relating thereto shall not be deemed AstraZeneca IP hereunder.

**10.2** Institution shall, and shall cause the Principal Investigator and the Study Site Staff to, make prompt and full disclosure to AstraZeneca of all Institution IP. Institution shall own all rights and title in and to all Institution IP. Institution hereby grants to AstraZeneca a non-exclusive, world-wide, perpetual, royalty-free license, with the right to grant sub-licenses, to use the Institution IP to the extent required to use and exploit the AstraZeneca Test Drug and the AstraZeneca IP.

**10.3** Each Party shall retain all rights in its respective Background Intellectual Property. Unless otherwise provided for in the Addendum, this Master Agreement is not intended to and shall not infer any license grant or assignment, whether expressed or implied, with regard to such Background Intellectual Property, except that Institution is authorized to use the AstraZeneca Test Drug or Investigational Product for purposes of the research described in the related Protocol and approved under this Master Agreement or as expressly agreed in writing by AstraZeneca.

**10.4** Government-funded Activities. The Institution and Principal Investigator acknowledge and agree that the activities they are to conduct under this Master Agreement will fall outside the scope of their planned and committed activities under any government-funded projects they have undertaken ("**Government-funded Activities**") and will not diminish or distract from their performance of Government-funded Activities. In the event that any AstraZeneca Test Drug Invention made hereunder is determined to have been conceived or first reduced to practice in the performance of Government-funded Activities, the Institution and the Principal Investigator agree to take all steps reasonably necessary in order to obtain for AstraZeneca, to the maximum extent possible, the rights in such AstraZeneca Test Drug Invention contemplated by Sections 10.1 through 10.3 (without limitation of any other remedies available to AstraZeneca hereunder or under Applicable Laws).

## 11. CONFIDENTIAL INFORMATION

**11.1** At all times during the term of the applicable Addendum issued under this Master Agreement and for a period of seven (7) years following termination or expiration thereof, and subject to Institution's publication rights as set forth in Article 13, each Party (the "**Receiving Party**") shall, and shall cause its officers, directors and other employees and agents to, keep confidential and not publish or otherwise disclose and not use, directly or indirectly, for any purpose, any Confidential Information provided to it by the other Party (the "**Disclosing Party**"), except with the other Party's prior written consent or to the extent such disclosure or use is expressly permitted by the terms of this Master Agreement and applicable Addendum. Any data and information referred to as AstraZeneca IP shall be deemed Confidential Information provided by AstraZeneca and any Confidential data and information referred to as Institution IP shall be deemed Confidential Information of the Institution irrespective of where such data and information was developed or generated. The Receiving Party shall restrict the dissemination of Confidential Information to only those persons within its organization who have a need to know, and shall ensure that they are aware of the obligation of confidentiality required by this Master Agreement and are similarly bound. The Receiving Party shall use at least the same care and discretion in maintaining the confidentiality of the Confidential Information as it uses with its most sensitive confidential information. The Receiving Party shall notify the Disclosing Party promptly upon discovery of any loss or compromise of the Confidential Information. Upon the termination or expiration of the applicable Addendum under this Master Agreement or upon a Party's earlier request, the Parties shall promptly return to the other Party all of its respective Confidential Information, provided that each Party shall have the right to retain, subject to the terms of this Master Agreement, any Study Documentation to the extent required by Applicable Laws. For the sake of clarity, all of this Article 11 (Confidential Information) is subject to Institution's publication rights as set forth in Article 13 (Publication of Results).

**11.2** The obligations of confidentiality in Section 11.1 shall not extend to any Confidential Information that: (a) is or comes into the public domain without breach of this Master Agreement, (b) is received by Receiving Party from a third party without any obligation of confidentiality and without breach of this Master Agreement, (c) Receiving Party can prove was already in its possession without any limitation on use or disclosure prior to the Effective Date, or (d) is independently developed by Institution. For the avoidance of doubt, in the event that AstraZeneca lists or discloses any information relating to the AstraZeneca Test Drug or a Study in a clinical trial registry(ies) or clinical results database(s), any aspects or details of Confidential Information concerning the AstraZeneca Test Drug or a Study that are not listed or disclosed in such registry(ies) or database(s) shall not be deemed to be or become part of the public domain.

**11.3** Notwithstanding any other provision of this Master Agreement, Institution will be entitled to disclose Confidential Information if such disclosure:

(i) Is communicated to the Institution's scientific and/or institutional review committees with respect to a Study, provided, however, that that members of such committees are obligated to maintain the confidentiality of the information consistent with the terms hereof;

(ii) Is required by Applicable Laws (including statute, rule, regulation, order, or other legal compulsion) or proper legal, governmental, or other competent authority, but to the extent

reasonably possible the Receiving Party will notify the Disclosing Party of the required disclosure with as much advance notice as reasonably possible and sufficiently in advance of such disclosure so that the Disclosing Party may seek a protective order or other appropriate protection with respect to such disclosure, which the Receiving Party will fully comply with;

(iii) Is necessary in order to seek or enforce a patent on Institution IP or Secondary Research IP, provided, however, that Institution will disclose Confidential Information only to the extent necessary and will take steps to request protection of the Confidential Information where possible or if such disclosure cannot be protected, AstraZeneca shall be given the advanced opportunity and reasonable time to seek a protective order or other appropriate protection with respect to its Confidential Information, including the filing of U.S. or foreign patents;

(iv) Relates to the AstraZeneca Test Drug or a Study and is required in order to obtain consent from patients or Subjects who may wish to enroll in a Study, but information will be disclosed only to the extent necessary and Confidential Information will not be disclosed by telephone or to any individuals who are not eligible candidates for a Study; or

(v) Is Confidential Information contained in Institution IP or Secondary Research IP and such disclosure is necessary in order to license the Institution IP or Secondary Research IP, provided, however, that Institution shall not disclose such Confidential Information to the extent that it was disclosed to Institution by AstraZeneca and Institution will only disclose such other Confidential Information after AstraZeneca has been given the advanced opportunity and reasonable time to seek a protective order or other appropriate protection with respect to its Confidential Information, including the filing of U.S. or foreign patents.

(vi) Is Confidential Information which needs to be disclosed to the protect the Study Subject's health and well-being.

**11.4** If Receiving Party is legally required to disclose Confidential Information, both Parties will endeavor to agree to a mutually satisfactory means to disclose such information. Nothing contained herein shall prohibit the Parties from immediately disclosing results of a Study to the extent necessary to prevent or mitigate a serious health hazard; provided, however, that the Disclosing Party shall notify the Receiving Party prior to making such a disclosure and immediately after it has made such a disclosure.

**11.5** External Discussions**.** Neither the Institution nor the Principal Investigator shall discuss a Study or the AstraZeneca Test Drug with any financial, securities or industry analyst or with the press or media.

**11.6** The Parties agree to maintain the Confidential Information in a secure facility, taking commercially reasonable steps to protect the information from unauthorized use, access and disclosure.

**11.7** Notwithstanding any other provision of this Master Agreement, if either Party obtains any health or medical information on any Study Subject, the Party will, pursuant to the requirements of law and subject to the provisions of the Informed Consent form, hold in confidence the identity of the Subject and the health/medical information and will comply with Applicable Laws regarding the confidentiality of such information.

**11.8** Institution can use the Intellectual Property, inventions, data, and results from a Study for its own non-commercial, internal research and educational purposes only and may publish the data and results of any Study only as provided in and subject to the provisions of this Master Agreement.

## 12. PERSONAL DATA AND BIOLOGICAL MATERIALS

**12.1** Each Party shall be responsible for its own processing of Personal Data and shall ensure that any Personal Data relating to a Subject, the Principal Investigator and/or the Study Site Staff, is collected, stored, used, disclosed and transferred in accordance with all applicable national, federal, state, or local privacy laws and with the Protocol and Informed Consents that are or will be obtained from Subjects. Principal Investigator shall be responsible for obtaining and providing AstraZeneca with written Informed Consent from each Study Site Staff for the collection, use and disclosure of their Personal Data. Institution will provide to AstraZeneca written notice within forty-eight (48) hours of all security incidents that involve, or which Institution reasonably believes involve, the unauthorized access, use or disclosure of Personal Data. Such notice shall summarize in reasonable detail the impact of the breach or unauthorized use or disclosure of, or access to, Personal Data and the corrective action taken or to be taken by Institution, including, without limitation, providing notices to individuals whose Personal Data may have been affected, whether or not such notice may be required by law.

**12.2** Biological Materials. If Institution collects or obtains Biological Materials (including but not limited to blood and body tissues and any other material containing human cells) during the course of a Protocol, then:

**12.2.1** Institution will comply with the terms of the Protocol in collecting and retaining the Biological Materials as specified in the Protocol, and shall preserve those Biological Materials under appropriate conditions for the term specified in the Study Addendum and Applicable Laws, but in any event, for a period no shorter than three (3) years from the end of the active conduct of the Protocol. Institution shall notify Study Subjects in the Informed Consent forms for all Protocols that research that exceeds or differs from the research specified in the Protocol, including genetic research, may be done, consistent with law, on Subjects' Biological Materials by either Institution or its designees ("**Secondary Research**") or by AstraZeneca or its designees. Institution shall not provide Study Subjects an opportunity to opt out of the possibility that their Biological Materials may be used, consistent with law, for Secondary Research by AstraZeneca or its designees that exceeds or differs from a Protocol, other than by opting out of a Protocol altogether, in recognition of the impracticability of AstraZeneca's consistently respecting such an "opt-out" choice. Except for the terms of this Section 12.2, any Secondary Research conducted by Institution or its designees will not be subject to this Master Agreement.

**12.2.2** Institution may collect, obtain, and/or reserve additional quantities of Biological Materials (i.e., exceeding that which is required to be collected, obtained and/or reserved for the Protocol) for purposes of testing or use in Secondary Research, including pharmacokinetic, pharmacogenomics, and biomarker testing and research, only if (a) such collection and testing complies with all applicable laws, regulations and acceptable clinical trial practices, including, but not limited to,

patient privacy and Informed Consent laws, and (b) such collection is done with prior written notice to AstraZeneca of the nature and types of additional collections to be undertaken in connection with such Secondary Research at the time of developing the Protocols and any amendments thereto for such Secondary Research, (c) such collection and/or reservation does not in fact jeopardize or interfere with the Protocol or the Institution's adherence to the Protocol (including enrollment and timetable) and collection of specimens in the Protocol, and (d) such additional Biological Materials are not allowed by Institution to be used or accessed by persons unaffiliated with Institution, unless either (i) such person(s) agrees in writing for the benefit of AstraZeneca to be bound by the terms of this Section 12.2 and AstraZeneca is notified of and provided with copies of such agreements, or (ii) AstraZeneca has agreed to such use or access in writing beforehand which shall not be unreasonably withheld.

**12.2.3** Subject to the rights, ownership or access granted to AstraZeneca either under this Master Agreement or under specific Protocols, as between AstraZeneca and Institution, Institution will be the owner of all Biological Materials, except for those that are specified in Protocols or Addendums to be provided to AstraZeneca or its designees.

**12.2.4** At least three (3) months before undertaking any Secondary Research, Institution will inform AstraZeneca of such research so that AstraZeneca can review and provide to Institution comments upon the Secondary Research or upon the research proposal. Subject to the rights granted to AstraZeneca hereunder or as otherwise agreed, Institution will be the owner of all data and results arising from its own Secondary Research. Institution agrees to provide the results of its Secondary Research to AstraZeneca promptly after that Secondary Research has been completed or terminated or has been inactive for a period of one (1) year, whichever is earlier. Institution further agrees to provide on a confidential basis interim results of its Secondary Research as reasonably requested in writing by AstraZeneca. AstraZeneca's comments on the Institution's Secondary Research, and its receipt of data or results pursuant to this Section 12.2, shall not obligate AstraZeneca to make any additional payments to Institution or otherwise to assist Institution in the conduct of the Institution's Secondary Research, and AstraZeneca shall not be deemed a "sponsor" or a "sponsor-investigator" (as those terms are defined for purposes of Title 21 of the Code of Federal Regulations, including but not limited to 21 C.F.R. §§ 50.3, 56.102, and 312.3) with respect to any of Institution's Secondary Research. Institution will have the right to publish the results and data from its Secondary Research but will not publish such results and data until four (4) months after providing those results and data to AstraZeneca so that AstraZeneca may review and comment upon the results and data. AstraZeneca will treat those results and data as Confidential Information and will not disclose the results or data until they have been published by Institution. Notwithstanding the foregoing, AstraZeneca may release the results and data to governmental authorities including the FDA, to respond to governmental inquiries or to provide information in relation to a product or compound under regulatory review. Further, to the extent required, Institution grants to AstraZeneca a world-wide, perpetual, non-exclusive, royalty-free license to refer to or recommend the use of the results and data, including those results that constitute a diagnostic product, in AstraZeneca's labeling, promotional or regulatory material for any compound marketed by AstraZeneca.

**12.2.5** Institution agrees, to the extent that it now or hereafter has the right to do so, that if it or any of its employees or researchers publish the results or data of its Secondary Research, AstraZeneca is granted an irrevocable, royalty-free license to make and distribute copies of such publication under any copyright privileges that the Institution and/or Principal Investigator, researchers, or employees may have. The license and rights granted to AstraZeneca in this Section 12.2.5, however, are subject to and subordinate to any rights of any publisher with respect to a publication, and Institution and its employees will not be required to forego any opportunity to publish if, in connection with any such publication, they are unable to retain the foregoing rights on behalf of AstraZeneca.

**12.2.6** Except as otherwise agreed by Institution and AstraZeneca, Institution will own all inventions, discoveries, know-how, results, methods and data recorded in any form, including Background IP, that are conceived, reduced to practice, created, developed or otherwise made solely by Institution as a result of the use of Biological Materials during the course of the Institution's Secondary Research ("**Secondary Research IP**") subject only to the following: Within one (1) month of determining that any significant Secondary Research IP has been developed, Institution will inform AstraZeneca in writing on a confidential basis of such Secondary Research IP, and will respond to reasonable inquiries and requests from AstraZeneca relating thereto.

**12.2.7** Notwithstanding any other provision of this Master Agreement, the provisions of Sections 12.2.2(d), 12.2.4, 12.2.5, and 12.2.6 will not apply to Secondary Research with Biological Materials that are distributed by Institution to researchers under an anonymized system imposed, arranged, and policed by Institution the effect of which is to deny those researchers all knowledge of the source of the Biological Materials as being from Subjects in a Study funded or sponsored by AstraZeneca, and that also shall deny those researchers knowledge of the presence in the Biological Materials, or the effect on those Biological Materials, of any agent or compound that has been provided to Institution by AstraZeneca ("**Unannotated Secondary Research**"). Institution shall arrange such a system to assure that researchers engaged in Unannotated Secondary Research are denied any and all access to any link that would identify Biological Materials as being associated with a Study funded or sponsored by, or as containing or being affected by a Study agent provided by AstraZeneca. Institution shall inform AstraZeneca immediately and in detail of any failure by Institution to adhere to the terms of this Section 12.2.7. Institution also will answer all reasonable inquiries from AstraZeneca as to how such a system to implement the requirements of this Section 12.2.7 has been arranged and is being enforced. The requirements of this Section 12.2.7 shall survive the end or termination of this Master Agreement.

**12.3** Each Party shall ensure that the security, integrity and quality of the Biological Materials is maintained at all times. Each Party shall be responsible for maintaining its own chain of custody to allow traceability and management of the Biological Materials.

## 13. PUBLICATION OF RESULTS

**13.1** Rights and Procedures. In the exercise of the rights of academic freedom of an educational institution and its faculty, Institution, the Principal Investigator, and any additional authors, shall have the right, consistent with academic standards and subject to this Section, to publish in scientific or other journals, or to present at professional conferences or other meetings, the Multi-Center Study results. At least thirty (30) days prior to submission of any material for publication or presentation, Institution and/or Principal Investigator shall provide AstraZeneca with such material for its review for Confidential Information. AstraZeneca shall have thirty (30) days to respond to Institution and/or Principal Investigator with any comments in order to protect AstraZeneca's Confidential Information. If requested in writing by AstraZeneca, Institution and/or Principal Investigator shall withhold material from submission for publication or presentation for an additional sixty (60) days from the date of AstraZeneca's request to allow for the filing of a patent application or the taking of such measures as AstraZeneca deems appropriate to establish and preserve its proprietary rights in any Confidential Information in the material being submitted for publication or presentation. Institution and/or Principal Investigator agree that scientific lead-time is a key element of the value of the research activities and further agree that premature publication of any Multi-Center Study results before all research activities are completed and the data is pooled and analyzed could be misleading. Therefore, Institution and/or Principal Investigator agree not to publish or present the Multi-Center Study results until the completion of all research activities, and, if such research activities are part of broader research effort conducted at multiple Study Sites, until all data is compiled from all Study Sites, but in no event shall Institution's and/or Principal Investigator's right to publish be delayed after the expiration of eighteen (18) months from completion of Institution's performance of the Study. No publication or presentation with respect to the research activities shall be made unless and until any information determined to be Confidential Information (as defined in Article 11 above) has been removed; provided, however, that certain Confidential Information which supports the conclusions of the research shall be allowed to be included in such publications and/or presentations.

**13.1.1** Additionally, any (i) analyses performed by Principal Investigator using data from any single-center Study, (ii) analyses performed by Principal Investigator using any Multi-Center Study data (or Study Site data), or (iii) analyses that have been disclosed in a publication or presentation authorized pursuant to this Article 13 or pursuant to another clinical study agreement under the Multi-Center Study (but not the underlying data from any single-center Study or the Multi-Center Study Data (including the Study Site data), as the case may be), shall not be deemed Confidential Information for purposes of this Article 13.

**13.2** AstraZeneca Rights. Institution and/or Principal Investigator hereby grant to AstraZeneca and its Affiliates an irrevocable, perpetual royalty-free license to make and distribute copies of any publication of the Multi-Center Study results. AstraZeneca and its Affiliates also shall have the right to publish independently the Multi-Center Study results provided that due acknowledgement is made for the intellectual contribution made by Institution and Principal Investigator in accordance with standard scientific practice.

**13.3** Responsibilities of Authors. Institution and/or Principal Investigator agree to comply with the International Committee of Medical Journal Editors criteria regarding authorship (available at: http://www.icmje.org/ethical_1author.html) and to disclose any relationship with AstraZeneca and any potential conflicts of interest, including any financial or personal relationships that might be perceived to bias their work. In so doing, Institution and/or Principal Investigator agree to disclose in any manuscript, journal submission or elsewhere, as appropriate or required, any potential conflict of interest, including any financial or personal relationship with AstraZeneca, the names of any individuals who have provided medical writing or editorial support for the publication, and all funding sources for the publication and any related study. Institution and/or Principal Investigator further agree to provide any additional disclosure required by any medical or scientific institution, medical committee or other medical or scientific organization with which they are affiliated.

**13.3.1** Authorship and Final Contents. Subject to the foregoing, the authorship and final contents, including scientific conclusions and professional judgments, of any paper submitted about a Study, as the case may be, by the Principal Investigator shall be determined by the Principal Investigator in his/her sole discretion.

**13.4** Publications support. If appropriate, and requested by Institution and/or Principal Investigator, AstraZeneca may provide medical writing, editorial and logistical support for a publication. Regardless of whether AstraZeneca provides editorial support, Institution and/or Principal Investigator remain responsible and have final approval for any publication. All medical writing, editorial and logistical support provided by a third party must be undertaken in accordance with the requirements set forth in the AstraZeneca policy titled AstraZeneca Policy for Scientific, Technical & Medical Publications. Such requirements include, but are not limited to:

a) AstraZeneca, not the third party, will make initial contact with other potential authors;
b) All authors must approve the general content and direction of the publication before it is written;
c) The third party writers will make no attempt to influence the opinions of authors;
d) All authors must approve the final version of the publication before it is submitted to a journal;
e) The third party will not be the contact for the target journal; and
f) Contributions of the third party will be openly acknowledged in any resulting publication in line with their level of contribution.

**13.5** Without limitation to any other right of AstraZeneca hereunder, the Institution and the Principal Investigator acknowledge and agree that AstraZeneca as Sponsor will register a Study and, when available, post the Multi-Center Study results in accordance with AstraZeneca internal policy on one or more publicly-accessible trial registries and websites (including the publicly-funded website http://www.clinicaltrials.gov/ and on its own website http://www.astrazenecaclinicaltrials.com). The Institution and the Principal Investigator should not undertake registration or posting of results to avoid duplication of entries. AstraZeneca personnel must comply with local/national law and/or regulations which require registration of Study information to a publicly-accessible registry other than those named above. Where the Institution and the Principal Investigator wish to use a publicly-accessible website on a voluntary basis (e.g. a university/hospital website) the information related to the Protocol must not exceed the information AstraZeneca has already posted and it should be sufficient to provide a hyperlink to the trial when registered on http://www.clinicaltrials.gov/.

## 14. USE OF NAME

Subject to Applicable Laws, neither the Institution, the Principal Investigator, nor AstraZeneca shall mention or otherwise use the name, trademark, trade name or logo of the other Party in any publication, press release or promotional material with respect to a Study without the prior written approval of such Party; provided, however, that AstraZeneca shall have the right to identify the Institution as the site at which a Study is being conducted and the responsible Principal Investigator and Study Site Staff and to use the Institution and Principal Investigator's name in any AstraZeneca Study recruitment activities and provided, further, that Institution and Principal Investigator will have the right to identify and acknowledge AstraZeneca as the sponsor of the Study.

## 15. INDEMNITY, REIMBURSEMENT OF MEDICAL EXPENSES AND INSURANCE

**15.1** AstraZeneca Responsibility. AstraZeneca agrees to defend and indemnify System, Institution, their Regents, officers, agents, employees and the Principal Investigator ("**Institutional Indemnified Parties**"), and hold them harmless from and against any liability, claim, loss, damages and expense (including lawyers' fees and costs of suit) (collectively, "**Losses**") incurred by them in connection with any and all suits, investigations, claims or demands made or brought:

**15.1.1** by or on behalf of Subjects against the Institution or the Principal Investigator for bodily or personal injury to Subjects, to the extent arising out of or relating to (i) the administration of Investigational Product in accordance with this Master Agreement, the applicable Protocol, the applicable Addendum and any other written instructions of AstraZeneca, or (ii) the performance of any test or procedure that is required by the applicable Protocol to which the Subjects would not have been exposed but for their participation in the applicable Study, or

**15.1.2** by third parties against any Institutional Indemnified Party to the extent resulting from the commercial use by AstraZeneca of the data and results collected, prepared, developed, or generated by the Institution in conducting a Study pursuant to this Master Agreement and the Protocol, provided that in each case Institution and Principal Investigator (i) have used reasonable

medical judgment in the conduct of the Study (including the enrollment of Subjects for which participation in the Study is medically appropriate), (ii) otherwise acted in conformity with generally accepted standards of the medical community in which it practices, and (iii) fully complied with all Applicable Laws and all ethical and professional standards relating to the protection of human subjects, including with respect to ensuring all appropriate IRB approval and oversight, obtaining effective Informed Consent (for AstraZeneca to use the above referenced data as provided in the Protocol and the Investigator's Brochure), and maintaining patient privacy. It is understood that AstraZeneca will not enter into any settlement which contains an admission of fault on behalf of the Institution without Institution's written consent.

**15.2** AstraZeneca's obligation to indemnify under Section 15.1 will not apply to the extent that such claims or proceedings:

**15.2.1** arise out of or relate to the negligence, willful misconduct or wrongful act or omission of the Institution, the Principal Investigator or any Study Site Staff; or

**15.2.2** arise out of or relate to the Principal Investigator's or the Institution's failure to report promptly to AstraZeneca any Subject Adverse Event or Serious Adverse Event (as both such terms are defined in the applicable Protocol); or

**15.2.3** arise as a result of Institution's or Principal Investigator's compromise or settlement of any such claim without the written consent of AstraZeneca.

**15.3** Institution Responsibility. To the extent authorized under the Constitution and laws of the State of Texas, Institution shall hold harmless AstraZeneca from any and all Losses caused by:

**15.3.1** the alleged negligence or negligence or alleged willful misconduct or willful misconduct of Institution, Principal Investigator or Study Site Staff in performing their obligations under this Master Agreement; or

**15.3.2** the failure of Institution, Principal Investigator or Study Site Staff, to comply with the provisions of this Master Agreement, the applicable Protocol, any written instructions of AstraZeneca concerning a Study or any Applicable Laws;

**15.3.3** provided, however, that Institution shall not hold AstraZeneca harmless from claims arising out of the negligence of AstraZeneca, its offers, agents, or any person or entity not subject to Institution supervision or control. Institution shall perform its obligations under this Master Agreement through its officers, agents or persons or entities which are subject to Institution's supervision or control.

**15.4** Reimbursement of Medical Expenses. Notwithstanding Section 15.1, AstraZeneca shall be responsible for the reasonable and necessary medical expenses incurred by the Institution for the treatment of any bodily or personal injury that is a direct result of (a) the administration of the AstraZeneca Test Drug in accordance with this Master Agreement, the applicable Protocol, the applicable Addendum and any other

written instructions of AstraZeneca, or (b) any performance of any test or procedure that is required by the applicable Protocol to which the Subjects would not have been exposed but for their participation in a Study if (i) the Institutional Indemnified Parties have complied with this Master Agreement, the applicable Protocol, the applicable Addendum and any written instructions of AstraZeneca concerning such a Study, (ii) all the requirements of Informed Consent have been complied with in accordance with Articles 3.2.2 and 3.2.4, and (iii) the injury was not a result of the negligence or willful misconduct of an Institutional Indemnified Party. AstraZeneca will not provide compensation for lost wages or for any other damages, expenses or Losses, or for medical expenses that have been covered by a Subject's medical or other insurance.

**15.5** AstraZeneca maintains liability insurance in sufficient limits to cover the indemnification obligations in this Master Agreement. Institution agrees to maintain adequate insurance or financial resources sufficient to cover the indemnification obligations of this Master Agreement and each Addendum. Institution, as a member institution of System, is an agency of the State of Texas and is self-insured pursuant to The University of Texas System Professional Medical Malpractice Self-Insurance Plan, under authority of Section 59.01, Texas Education Code.

**15.6** Termination or expiration of this Master Agreement and/or a Study shall not affect AstraZeneca's obligations to the Institutional Indemnified Parties with respect to any Loss or expense resulting from the conduct of the applicable Study prior to termination of the applicable Study, to the extent that such Loss or expense would otherwise be covered by this Article 15.

**15.7** Notice and Assumption of Defense. The Party desiring indemnification under this Article 15 (the "**Indemnified Party**") shall promptly provide the other Party (the "**Indemnifying Party**") with written notice of the possibility of a Loss upon learning of any events that could give rise to such Loss or the receipt of any claim, suit, demand or notice with respect thereto, whichever is earlier. The Indemnifying Party shall not be responsible for any Loss, or any increase in any Loss, resulting from any delay by the Indemnified Party in providing such notice. Subject to the statutory duties of the Texas Attorney General, the Indemnified Party shall allow the Indemnifying Party to assume the defense of any such Loss, including the right to select counsel of its choosing and the right to compromise or settle any Loss, provided that the Indemnifying Party shall not make any settlement admitting fault or incur any liability of the part of an Indemnified Party without its written consent, such consent not to be unreasonably withheld. Subject to the statutory duties of the Texas Attorney General, if the Indemnifying Party is required to defend any Loss, the Indemnified Party shall, and shall cause its employees and agents to, cooperate fully in the defense thereof and furnish such records, information and testimony, provide such witnesses and attend such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested by the Indemnifying Party in connection therewith. In no event shall the Indemnified Party compromise, settle or otherwise admit any liability with respect to any Loss subject to indemnification under this Master Agreement without the prior written consent of the Indemnifying Party (such consent not to be unreasonably withheld or delayed).

**15.8** No Acknowledgment of Liability. The assumption of the defense of a Loss by the Indemnifying Party shall not be construed as an acknowledgment that such Party is liable to indemnify any Indemnified Party

in respect of the Loss, nor shall it constitute a waiver by the Indemnifying Party of any defenses it may assert against the Indemnified Party's claim for indemnification. If it is ultimately determined that the Indemnifying Party is not obligated to indemnify, defend or hold harmless the Indemnified Party from and against the Loss, the Indemnified Party shall reimburse the Indemnifying Party for any and all costs and expenses or other Losses incurred by the Indemnifying Party in its defense of the Loss with respect to such Indemnified Party.

## 16. TERM AND TERMINATION

**16.1** This Master Agreement commences on the Effective Date and will remain in effect until the end of five (5) calendar years thereafter, provided, however, that with respect to any Study entered into prior to such expiration, this Master Agreement shall remain in effect until the expiration or earlier termination of such Study or the date that the final data has been provided to AstraZeneca following Site Closure as required in the applicable Addendum and related Protocol, subject at all times to the Parties' right to terminate this Master Agreement or any Study as provided in this Article 16. The Addendum shall be effective upon date of the last signature and shall continue until the earlier of the date that the required final data has been provided to AstraZeneca following Site Closure or the date that the Addendum is terminated in accordance with this Article 16.

**16.2** Either Party may terminate this Master Agreement, the Addendum or one or more of the Studies with immediate effect at any time upon written notice if the other Party is:

**16.2.1** in breach of any material obligations under the Master Agreement, the Addendum or the Protocol (including a failure without just cause to meet a timeline) and fails to remedy such breach, where it is capable of cure, within fifteen (15) days of written notice from the other Party specifying the breach and requiring its cure; or

**16.2.2** declared insolvent or has an administrator or receiver appointed over all or parts of its assets or cease or threatens to cease to carry on its business.

**16.3** A Party may terminate one or more of the Studies with immediate effect upon written notice to the other Party, if it on reasonable grounds believes such a Study(ies) should cease in the interest of the health, safety or well-being of Subjects.

**16.4** AstraZeneca may terminate one or more of the Studies upon notice to the Institution if the Principal Investigator is no longer able (for whatever reason) to act as principal investigator of such a Study(ies) and no replacement mutually acceptable to AstraZeneca and the Institution has been found. If Institution does not enroll a Subject into a Study within sixty (60) days from Investigator's receipt of written approval by AstraZeneca according to clause 7.1.1, the applicable Addendum may be immediately terminated by AstraZeneca.

**16.5** In addition to Sections 16.2, 16.3 and 16.4, AstraZeneca may terminate or suspend one or more Studies and/or terminate this Master Agreement or applicable Addendum immediately for any reason whatsoever upon written notice to the Institution and the Principal Investigator.

**16.6** This Master Agreement, an Addendum or one or more of the Studies may be terminated by the Institution, on written notice to AstraZeneca, if a Study(ies) is/are suspended or terminated and not recommenced within ninety (90) days. Further, this Master Agreement, an Addendum or one of more Studies may be terminated by the Institution if AstraZeneca makes changes to a Study that are not required by Applicable Laws and not agreed to by the Institution and such changes materially increase the cost of performance of a Study(ies) by the Institution.

**16.7** Upon notice of termination of this Master Agreement or an Addendum, and to the extent that one or more of the Studies are also terminated, the Institution shall, and shall cause the Principal Investigator to, immediately cease enrollment of Subjects into such a Study(ies), and at the election of AstraZeneca, shall: (a) terminate a Study with respect to the enrolled Subjects in an orderly and prompt manner and pursuant to consultation with AstraZeneca's clinical monitor, including any required follow-up treatment with previously enrolled Subjects, or (b) transfer the enrolled Subjects to another clinical site in accordance with AstraZeneca's instructions. AstraZeneca or its designee shall have the right to assume full control of the terminated Study and the Institution shall promptly provide to AstraZeneca all Study Documentation (except such documents as are required to be maintained by Institution pursuant to Applicable Laws), AstraZeneca's Confidential Information and any Materials provided by or on behalf of AstraZeneca in connection with a Study and provide such other assistance as is necessary to ensure a smooth and orderly transition of a Study with no disruption of the applicable Protocol.

**16.8** Upon expiration or early termination of this Master Agreement, an Addendum or one or more of the Studies (except in the case of termination of this Master Agreement or applicable Addendum hereto as a result of an uncured breach of this Master Agreement by the Institution), AstraZeneca shall, upon receipt of invoices and other supporting documentation, pay to the Institution in accordance with each applicable Addendum for such Study(ies) all costs incurred and falling due for payment up to the date of termination and all non-cancelable costs committed before receipt of notice of termination, provided that such commitments are reasonable and necessarily incurred by the Institution for the performance of such Study(ies) prior to the date of termination and agreed with AstraZeneca.

**16.9** Within thirty (30) days after the termination of this Master Agreement, an Addendum, and to the extent that one or more of the Studies are also terminated, the Institution shall deliver to AstraZeneca in writing a final accounting of all Subjects that participated in applicable Studies, the Subject visits completed in accordance with the applicable Protocols during the term of this Master Agreement or applicable Addendum, and all reasonable direct costs incurred in connection with any transfer of the Study(ies). Within thirty (30) days of delivery or receipt of the final accounting, either the Institution shall refund to AstraZeneca any excess amounts paid by AstraZeneca or AstraZeneca shall pay any additional amounts owed to the Institution, as the case may be. AstraZeneca or its designee shall have the right for a period of one (1) year after the payment of any transfer costs to audit the Institution's books and records with respect to such accounting.

**17. INDEPENDENT CONTRACTOR**

In undertaking to perform its, his or her respective services hereunder, the Institution and the Principal Investigator and the Study Site Staff are doing so as independent contractors in relation to AstraZeneca, and not as employees or agents of AstraZeneca.

**18. ASSIGNMENT**

No Party shall assign this Master Agreement or any of its, his or her rights or obligations hereunder without the prior written consent of the other Party, except that each Party may assign this Master Agreement and its rights and obligations hereunder to any successor in interest (whether by merger, acquisition, asset purchase or otherwise) to all or substantially all of the business to which this Master Agreement relates. Notwithstanding the foregoing, AstraZeneca may assign this Master Agreement and its rights and obligations hereunder (a) in connection with the transfer, whether by license or otherwise, or sale of all or substantially all of its rights to the AstraZeneca Test Drug, (b) to any of its Affiliates, or (c) subject to Section 2.4, to any external service providers such as Clinical Research Organizations retained to assist AstraZeneca in managing and monitoring a Study. AstraZeneca shall have the right to perform any and all of its obligations and exercise any of its rights under this Master Agreement through any of its Affiliates.

**19. GOVERNING LAW**

The Parties respectfully agree to remain silent on Governing Law.

**20. NOTICES**

Any notice, request or other communication permitted or required under this Master Agreement shall be in writing, shall refer specifically to this Master Agreement and shall be deemed given only if hand delivered or sent by an internationally recognized overnight delivery service, costs prepaid, or by facsimile (with transmission confirmed), addressed to the Parties at:

**If to AstraZeneca, to:**
Address: 1800 Concord Pike
Wilmington, DE 19850-5438
Facsimile: 302-885-0020
Attention: SM&M- Contracts

With a copy to:
Address: 1800 Concord Pike
Wilmington, DE 19850-5438
Facsimile: 302-886-1578
Attention: General Counsel

**If to Institution, to:**
See Appendix 4

or to such other address as the Party to whom notice is to be given may have provided to the other Parties in accordance with this Section 20. Such notice shall be deemed to have been given as of the date delivered by hand, or on the second business day (at the place of delivery) after deposit with an internationally recognized overnight delivery service, whichever is the earlier.

**21. SURVIVAL**

The respective rights and obligations of the Parties set forth in Articles 3 (Principal Investigator and Institution), 4 (Representations, Certifications, and Promises), 6 (Materials), 7 (Subject Enrollment), 8 (Investigational Product), 9 (Compensation), 10 (Intellectual Property), 11 (Confidential Information), 12 (Personal Data and Biological Materials), 13 (Publication of Results), 14 (Use of Name), 15 (Indemnity, Reimbursement of Medical Expenses and Insurance), 16 (Term and Termination), 19 (Governing Law), 20 (Notices), 21 (Survival), 22 (Entire Agreement and Amendment), 26 (Privacy and HIPAA), and 31 (State Agency Limitations) shall survive the expiration or termination of this Master Agreement to the extent necessary to preserve such rights and obligations.

**22. ENTIRE AGREEMENT AND AMENDMENT**

This Master Agreement together with the Appendices hereto, any and all Addenda and attachments thereto, and the Confidentiality Agreement constitute the entire agreement among the Parties hereto with respect to the subject matter of this Master Agreement and supersede all prior agreements, whether written or oral, with respect to the subject matter of this Master Agreement. Any amendment or modification to this Master Agreement or an Addendum must be in writing and signed by authorized representatives of each Party.

**23. COUNTERPARTS**

This Master Agreement may be executed in two or more counterpart copies, each of which shall be deemed an original, and shall together be deemed to constitute one and the same instrument.

**24. ELECTRONIC SIGNATURE**

The Parties agree that execution of this Master Agreement by industry standard electronic signature software and or by exchanging PDF signatures shall have the same legal force and effect as the exchange of original signatures, and that in any proceeding arising under or relating to this Master Agreement, each Party hereby waives any right to raise any defense or waiver based upon execution of this Master Agreement by means of such electronic signatures or maintenance of the executed agreement electronically.

**25. SEVERABILITY**

If any provision of this Master Agreement is held to be illegal, invalid, or unenforceable in whole or in part for any reason, the remaining provisions shall continue in full force and effect, and the Parties shall substitute a legal, valid, and enforceable provision with terms similar to such provision as may be possible and reasonably acceptable to the Parties.

**26. PRIVACY AND HIPAA.**

**26.1** Institution represents, certifies and covenants that it is a “Covered Entity” under the provisions of the Health Insurance Portability and Accountability Act of 1996 and any regulations and guidance promulgated thereunder (“**HIPAA**”). Institution shall handle all Study Documentation in accordance with HIPAA requirements and all other Applicable Laws and shall ensure that it obtains from each subject a

valid authorization that complies with HIPAA and is, in form and substance, acceptable to AstraZeneca, in order for Institution to provide AstraZeneca with the Study Documentation and to satisfy its other obligations under this Master Agreement with respect to Study Documentation.

**26.2** Institution acknowledges and agrees that no component of AstraZeneca or any of its Affiliates that will be performing any of AstraZeneca's obligations under this Master Agreement is a "Covered Entity" or a "Business Associate," as those terms are defined by HIPAA.

**27. AMENDMENT**

Any amendment or modification to this Master Agreement must be in writing and signed by authorized representatives of each Party.

**28. WAIVER**

A Party's failure to enforce, at any time or for a period of time, any provision of this Master Agreement, or to exercise any right or remedy shall not constitute a waiver of that provision, right or remedy or prevent such Party from enforcing any or all provisions of this Master Agreement and exercising rights or remedies. To be effective, any waiver must be in writing.

**29. INCONSISTENCY**

In the event of any inconsistency or conflict between the text of this Master Agreement and the text of the final, IRB-approved and AstraZeneca-approved Protocol, the final Protocol shall control with respect to the conduct of the Study and the treatment of Subjects in connection therewith; in all other respects (including but not limited to, Articles 13 and 15), the terms of this Master Agreement shall prevail. If either Party believes that there is a conflict described in either of the preceding sentences, such Party shall promptly notify the other Party of the nature of such conflict.

**30. CONSTRUCTION**

Except where the context requires otherwise, whenever used the singular includes the plural, the plural includes the singular, the use of any gender is applicable to all genders, the word "or" has the inclusive meaning represented by the phrase "and/or" and the term "including" or "includes" means including, without limiting the generality of any description preceding such term. Whenever this Master Agreement refers to a number of days, unless otherwise specified, such number refers to calendar days. The headings of this Master Agreement are for convenience of reference only and do not define, describe, extend or limit the scope or intent of this Master Agreement or the scope or intent of any provision contained in this Master Agreement. A reference in this Master Agreement to an Article, Section, or Appendix is to the referenced Article, Section, or Appendix of this Master Agreement. The wording of this Master Agreement shall be deemed to be the wording mutually chosen by the Parties and no rule of strict construction shall be applied.

**31. STATE AGENCY LIMITATIONS**

Institution is an agency of the State of Texas and, under the Constitution and laws of the State of Texas, possesses certain rights and privileges, is subject to certain limitations and restrictions, and only has such authority as is granted to it under the Constitution and laws of the State of Texas. Notwithstanding any

provision hereof, nothing in this Master Agreement is intended to be, nor will it be construed to be, a waiver of the sovereign immunity of the State of Texas or a prospective waiver or restriction on any of the rights, remedies, claims, and privileges of the State of Texas. Moreover, notwithstanding the generality or specificity of any provision hereof, the provisions of this Master Agreement as they pertain to Institution are enforceable only to the extent authorized by the Constitution and laws of the State of Texas.

**REST OF PAGE INTENTIONALLY LEFT BLANK**

**THIS MASTER AGREEMENT IS EXECUTED** by the authorized representatives of AstraZeneca and the Institution as of the dates indicated below.

SIGNED for and on behalf of

**AstraZeneca Pharmaceuticals LP and AstraZeneca LP**

DocuSigned by:
Rogge, Debra
68A0A2648F10422...

Signature

Name: Rogge, Debra

Title: Clinical Research Manager

Date: 27 March 2015

SIGNED for and on behalf of

**The University of Texas at Austin**

Signature

Name: DAVID HAWKINS

Title: ASSOCIATE DIRECTOR, OSP

Date: 3.24.2015

SIGNED for and on behalf of

**The University of Texas Health Science Center at Houston**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at San Antonio**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at Tyler**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Medical Branch at Galveston**

Signature

Name:

Title:

Date:

**THIS MASTER AGREEMENT IS EXECUTED** by the authorized representatives of AstraZeneca and the Institution as of the dates indicated below.

SIGNED for and on behalf of

**AstraZeneca Pharmaceuticals LP and AstraZeneca LP**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas at Austin**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at Houston**

Karen S. Niemeier
Director, Contracts
Sponsored Projects Administration

Digitally signed by karen.niemeier@uth.tmc.edu
DN: cn=karen.niemeier@uth.tmc.edu
Date: 2015.03.20 11:25:45 -05'00'

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at San Antonio**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at Tyler**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Medical Branch at Galveston**

Signature

Name:

Title:

Date:

**THIS MASTER AGREEMENT IS EXECUTED** by the authorized representatives of AstraZeneca and the Institution as of the dates indicated below.

SIGNED for and on behalf of

**AstraZeneca Pharmaceuticals LP and AstraZeneca LP**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas at Austin**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at Houston**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at San Antonio**

Signature

Name: Chris G. Green, CPA

Title: Director, Office of Sponsored Programs

Date: 20 March 2015

SIGNED for and on behalf of

**The University of Texas Health Science Center at Tyler**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Medical Branch at Galveston**

Signature

Name:

Title:

Date:

**THIS MASTER AGREEMENT IS EXECUTED** by the authorized representatives of AstraZeneca and the Institution as of the dates indicated below.

SIGNED for and on behalf of

**AstraZeneca Pharmaceuticals LP and AstraZeneca LP**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas at Austin**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at Houston**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at San Antonio**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at Tyler**

Signature

Name: David Anderson

Title: Director, Pre-Award Services

Date: March 25, 2015

SIGNED for and on behalf of

**The University of Texas Medical Branch at Galveston**

Signature

Name:

Title:

Date:

**THIS MASTER AGREEMENT IS EXECUTED** by the authorized representatives of AstraZeneca and the Institution as of the dates indicated below.

SIGNED for and on behalf of

**AstraZeneca Pharmaceuticals LP and AstraZeneca LP**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas at Austin**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at Houston**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at San Antonio**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Health Science Center at Tyler**

Signature

Name:

Title:

Date:

SIGNED for and on behalf of

**The University of Texas Medical Branch at Galveston**

Angela Cook

Signature

Name: ANGELA COOK

Title: DIRECTOR OFFICE OF CLINICAL RESEARCH

Date: 23-MAR-2015

SIGNED for and on behalf of

**The University of Texas Southwestern Medical Center**

Signature

Name: Angela R. Charboneau Wishon, J.D.

Title: Vice President for Research Administration

Date: 3-20-2015

## Appendix 1 – Definitions

"**Applicable Laws**" means all applicable laws, rules, and regulations, including without limitation, Regulatory Authority rules and guidelines relating to the conduct of a Study, including GCP (as defined below), and the Health Insurance Portability and Accountability Act of 1996 and any regulations and official guidance promulgated thereunder **("HIPAA")**, as amended by the Health Information Technology for Economic and Clinical Health ("HITECH") Act.

"**AstraZeneca IP**" means Study Documentation and all Intellectual Property in and to any AstraZeneca Test Drug Invention.

"**AstraZeneca Test Drug**" means the AstraZeneca medicinal product being studied or tested in a Study.

"**AstraZeneca Test Drug Invention**" means all inventions relating to the AstraZeneca Test Drug including, without limitation, new indications or uses thereof, that are conceived, generated or otherwise made by the Institution, the Principal Investigator or any Study Site Staff (other than AstraZeneca) whether solely or jointly with others, under or in connection with a Study. For the avoidance of doubt, AstraZeneca Test Drug Inventions also include any inventions relating (a) to the AstraZeneca Test Drug's metabolic activity, pharmacological activity, side effects, drug metabolism, mechanism of action, safety, or drug interactions, or (b) to biomarkers, assays, diagnostic methods or diagnostic products, which may be used to predict patient response or resistance to the AstraZeneca Test Drug or be used in any way to select patients for treatment with the AstraZeneca Test Drug.

"**Background Intellectual Property**" means any Intellectual Property that was owned or controlled, directly or indirectly, by a Party prior to the Effective Date.

"**Biological Materials**" means any human biological materials, including but not limited to blood, body tissue, plasma and any other material containing human cells.

"**Case Report Form**" or "**CRF**" means a printed document ("**pCRF**"), optical or electronic document ("**eCRF**") or database designed to record all of the information, to be reported to AstraZeneca on each Study Subject, as required by the Protocol.

**"Clinical Research Organization"** or "**CRO**" means a person or an organization contracted by AstraZeneca to perform one or more of AstraZeneca's study-related duties and functions. The CRO for a Study, if applicable, will be provided in each respective Clinical Study Addendum.

"**Clinical Study Addendum**" or "**Addendum**" means an addition to this Master Agreement by which the Parties agree to conduct a Study on an AstraZeneca Test Drug under the terms and conditions of this Master Agreement, and which will be sufficiently specific to describe, including but not limited to, the planned Subject enrollment, time frames, Materials, and compensation related to such a Study.

"**Confidential Information**" means any data and information related to the terms of this Master Agreement, a Study (including the AstraZeneca Test Drug and Study Documentation), any Background Intellectual Property, AstraZeneca IP and Institution IP, that is provided by either Party or otherwise developed or generated in connection with the discussions and negotiations pertaining to, or in the course of performing, this Master Agreement and any Addendum hereto.

"**Confidentiality Agreement**" means the confidentiality agreement entered into by and between the Institution and/or the Principal Investigator and AstraZeneca relating to a Study.

"**Covered Recipient**" means any physician licensed to practice in the U.S. and any U.S. teaching hospital.

"**FDA**" means the U.S. Food and Drug Administration.

"**Good Clinical Practice**" or "**GCP**" shall have the meaning defined by the ICH Harmonised Tripartite Guideline for Good Clinical Practice, at all times in its most recent version.

"**Indirect Taxes**" means value added taxes ("VAT"), sales taxes or similar taxes.

"**Informed Consent**" has the meaning set forth by GCP.

"**Informed Consent Materials**" means the information to be provided to potential Subjects in a Study to secure their Informed Consent, including information about any compensation being provided to Subjects for their participation in a Study, and HIPAA authorization.

"**Institution**" means the Institution including all employees, Study Site Staff, executives, officers, directors, contractors and agents of the Institution.

"**Institution IP**" means all Intellectual Property other than the AstraZeneca IP that is conceived, generated or otherwise made by the Institution, the Principal Investigator or any Study Site Staff (other than AstraZeneca) under or in connection with a Study.

"**Institutional Review Board**" or "**IRB**" means an independent body, institutional, regional, national or supranational committee or review board, whose responsibility it is to ensure the protection of rights, safety and well-being of human subjects in a clinical study and responsible for, among other things, reviewing and approving/providing opinion on, the Protocol and amendments, subject recruitment materials, methods and Informed Consent Materials.

"**Intellectual Property**" means any and all rights in and to ideas, formula, trade secrets, inventions, discoveries, know-how, data, databases, documentation, reports, materials, writings, designs, computer software, processes, principles, methods, techniques and other information, including patents, trademarks, service marks, trade names, registered designs, design rights, copyrights and any rights or property similar to any of the foregoing in any part of the world, whether registered, or not, together with the right to apply

for the registration of any such rights created or generated in performance of this Master Agreement or a specific Clinical Study Addendum.

"**Investigational Product**" means the AstraZeneca Test Drug, placebo, and/or comparator drug, which is to be administered in a Study according to the Protocol.

"**Investigator's Brochure**" means the compilation of all relevant clinical and non-clinical information and data on the Investigational Product.

"**Materials**" means any equipment, materials (excluding Investigational Product), documents, data, software and information supplied by or on behalf of, or purchased at the expense of, AstraZeneca, in connection with a Study.

"**Medical Records**" means medical information revealed by a patient or discovered by a physician in connection with the treatment of a patient.

"**Multi-Center Study**" means a Study conducted by several investigators according to a single Protocol at more than one Study Site.

"**Party**" means each of AstraZeneca and Institution, and "**Parties**" means AstraZeneca and Institution collectively.

"**Payment or Transfer of Value**" is any payment or transfer of value as defined in the U.S. Physician Payment Sunshine Act (42 USC 1320(e)(10)), and implementing regulations (42 CFR 403.900 et seq.), and includes compensation, reimbursement for expenses, meals, travel, medical journal reprints, Study drug, Study supplies and medical writing and publications assistance.

"**Personal Data**" means any information and data that is directly or indirectly referable to a human being.

"**Principal Investigator**" means each person identified in an Addendum to this Master Agreement as the principal investigator for a Study (with respect to such Study the "Principal Investigator") to lead and co-ordinate a Study on behalf of Institution, or any other person as may be agreed by the Parties as a replacement.

"**Protocol**" means the clinical study protocol for a Study identified in an Addendum to this Master Agreement, which describes such a Study, including all amendments thereto as the Parties may from time to time agree in writing.

"**Regulatory Authority**" means any national, supranational or other governmental or regulatory body which has power to regulate the conduct of a Study at the Study Site or to inspect the Study site.

"**Secondary Research**" means research that exceeds or differs from the research specified in the Protocol, including genetic research.

"**Secondary Research IP**" means all Intellectual Property that is conceived, reduced to practice, created, developed, generated or otherwise made solely by a Party during the course of that Party's Secondary Research.

"**Site Closure**" means the date of receipt by the Principal Investigator of the site closure visit report from AstraZeneca.

"**Study**" means each clinical study identified in an Addendum to this Master Agreement and that is described in the applicable Protocol.

"**Study Documentation**" means all records, accounts, notes, reports, data, and IRB communications (submission approval and progress reports) collected, generated or used in connection with a Study, whether in written, electronic, optical or other form, including all recorded original observations and notations of clinical activities such as CRFs and all other reports and records necessary for the evaluation and reconstruction of a Study.

"**Study Meeting"** means meetings regarding a Study to which Principal Investigator and/or Study Site Staff are invited by or on behalf of AstraZeneca, including, but not limited to, investigator, study coordinator and/or results meetings.

"**Study Site**" means the facilities set out in Article 5 of this Master Agreement and the applicable Addendum.

"**Study Site Staff**" means all those students, employees, agents or others who are engaged by the Institution in the conduct of a Study, including any sub-investigator.

"**Subject**" means a person recruited to participate in a Study.

"**Unannotated Secondary Research**" means research that exceeds or differs from the research specified in the Protocol, including genetic research, under which an anonymized system has been imposed which denies researchers all knowledge that would identify biological specimens as being associated with Subjects in a Study funded or sponsored by, or containing or being affected by any agent or compound provided to Institution by, AstraZeneca.

**APPENDIX 2**
**CLINICAL STUDY ADDENDUM**

This Clinical Study Addendum is issued under that Master Clinical Study Agreement between AstraZeneca LP and AstraZeneca Pharmaceuticals LP and <<Institution>> dated << >> (the "**Master Agreement**"). This Clinical Study Addendum ("**Addendum**"), together with the Master Agreement, governs the conduct of the clinical study identified on the cover page (the "**Study**") and sets forth AstraZeneca's financial support of the Study. Unless otherwise specifically provided in this Addendum, capitalized terms shall have the meaning set forth in the Master Agreement.

The Master Agreement is hereby incorporated herein by reference and shall govern the performance of the Parties' duties under this Addendum, except for Articles 18 (Assignment) and 22 (Entire Agreement) thereof. To the extent that the provisions of the Master Agreement refer to an Addendum, such references shall be deemed to be references to this Clinical Study Addendum.

The Study to be performed is entitled "_____", No. "_____" and is set forth in the Protocol, as the same may be amended by AstraZeneca from time to time. For purposes of this Addendum, the Study Drug for the Study is defined as _____.

The services to be performed by Institution under the direction of _____, an employee of Institution, but not a Party to the Master Agreement, acting as Principal Investigator for the Study, including any Subject enrollment requirements, are set forth below:

**1. STUDY CONDUCT**

Institution and Principal Investigator shall conduct the Study in accordance with this Addendum, the Master Agreement, and the Protocol referenced above and incorporated by reference herein and any amendment(s) thereto, the Investigator's Brochure and/or prescribing information, Study manuals as each may be amended, and in compliance with all Applicable Laws, and any condition required by a Regulatory Authority and/or an IEC.

**2. ENROLLMENT AND COMPENSATION**

**I. ENROLLMENT**

PATIENT ENROLLMENT OPENING DATE: Estimated to be _____

PATIENT ENROLLMENT CLOSING DATE: Estimated to be _____

MINIMUM/MAXIMUM ENROLLMENT: Approximately _____ per site

Institution acknowledges that the Study is part of a [multi-center] clinical trial, and agrees that when the enrollment goal for the clinical trial as a whole is reached (randomization of approximately

_____ Subjects), enrollment will be closed at all sites, including Institution, regardless of whether Institution or any other site has reached its individual enrollment goal.

## II. IRB FEES

If using a central IRB, AstraZeneca will reimburse reasonable IRB fees for the initial IRB review directly to the central IRB. If a local IRB is used, AstraZeneca will reimburse Institution for reasonable IRB fees for the initial IRB review, not to exceed $ _____, upon receipt of documentation of IRB review and receipt of an invoice from the IRB. AstraZeneca will reimburse Institution or Central IRB for annual IRB review and/or Protocol amendments, as necessary. (See Section VIII, Invoices, below).

## III. ADMINISTRATIVE FEE $ _____

Upon receipt and approval of all regulatory documents and this signed Addendum, Institution shall forward to AstraZeneca an itemized invoice documenting work completed and costs incurred for up to $ _____ to cover Institution's administrative start-up costs. Administrative start-up fees may include the following:

Protocol Review
Determine potential number of eligible subjects
Regulatory Documentation
IRB Submission, copies and amendments
Informed Consent Document

## IV. PER SUBJECT PAYMENT $ _____

Per Subject payment shall be made for **evaluable, eligible** Subjects only. An eligible Subject is one from whom Informed Consent has been obtained, who meets the inclusion/exclusion requirements of the Protocol, and who was enrolled by Institution. An evaluable Subject is one for whom all CRFs have been completed in accordance with the Protocol, who has completed the appropriate Study procedures as set forth in the Protocol, and undergone the evaluations required by the Protocol for assessment of efficacy and safety. A completed CRF is one that is *[electronically]* signed by Principal Investigator when required and contains all complete, verified information in accordance with the procedures as stated in the Protocol. Per Subject payment includes all Subject-related costs such as compensation for Protocol procedures as described in Schedule A, attached hereto, (excluding procedures identified by Institution as Standard of Care in Schedule A) *[and subject compensation,]* as well as non-Subject costs such as overhead expenses and administration costs.

AstraZeneca shall pay to Institution, on a _____ *[bi-weekly, monthly, bi-monthly, quarterly]* basis throughout the term of a Study beginning in approximately _____, the Per Subject payment according to the following schedule:

**[Insert table]**

Final payment for a Study will be made after all evaluable, eligible, enrolled Subjects have completed all procedures for a Study as set forth in the Protocol, all [*electronic*] CRFs have been completed and verified against original supporting source documentation, all outstanding data queries have been resolved and returned, close-out audits (visits) have been completed, Investigator's final report has been received by AstraZeneca, and all Materials have been returned to AstraZeneca, or AstraZeneca's agent, pursuant to Article 6 of the Master Agreement.

## V. SCREEN FAILURES

## VI. DISCONTINUED SUBJECTS

If a Subject discontinues participation in a Study, or this Addendum is terminated, only those costs incurred up until the date of discontinuation or termination will be paid, according to the above-referenced Per Subject payment schedule, provided that all CRFs have been completed by Institution and subsequently reviewed by AstraZeneca. If a Subject discontinues between visits and does not complete each of the Study visits, Institution will be paid only for visits that the Subject completes. Partial visits will not be paid. Payment will be made on a _____ *[bi-weekly, monthly, bi-monthly, quarterly]* basis throughout the term of a Study, beginning in approximately_____.

## VII. ADVERTISING AND RECRUITMENT FEES

Advertising and recruitment fees shall be reimbursed to Institution not to exceed $_____.00 in the aggregate, upon receipt of satisfactory invoice(s) by AstraZeneca. (See Section VIII, Invoices, below). **The content and form of the advertisement/recruitment method and materials MUST be pre-approved by both AstraZeneca and the Institution's IRB prior to being published/carried out and prior to reimbursement for an advertising/recruiting fee.** Proposed advertisements and recruitment methods should be submitted to:

AstraZeneca LP/AstraZeneca Pharmaceuticals LP
[Address]
Attention:

## VIII. INVOICES

Invoices should be submitted to:_____ and include a Study Code Number, _____, and name of Study Drug, _____.

## IX. PAYEE

All payments required hereunder, with exception for reimbursement of accommodation expenses incurred by permitted attendees at Study Meetings under Section XI below, if applicable, shall be made payable to _____, and mailed to:

[Name of Institution]

[Address]
Attention:

## X. CONDITIONS OF PAYMENT

AstraZeneca shall have no obligation to reimburse Institution for authorized expenses that are not invoiced pursuant to Section VIII above within ninety (90) days after the date that Institution incurred such expenses. In addition, Institution will have thirty (30) days from the receipt of the final Study payment to dispute any claimed payment discrepancies occurring during the course of a Study.

## XI. REIMBURSEMENT FOR ACCOMMODATION EXPENSES AT STUDY MEETINGS

Reimbursement of expenses incurred while attending Study Meetings can only be paid after this Addendum is fully executed. There are 2 options for reimbursement:

Option 1: Reimbursement to the payee named in Section IX above.

Option 2: Direct reimbursement to the attendee who has incurred the expense. The attendee will receive instructions for reimbursement in a Study Meeting packet.

The Pass-Through and Expense Reimbursement Guidelines in Appendix 3 must be followed under both options.

## 3. MATERIALS PROVIDED BY ASTRAZENECA

During the course of this Study, pursuant to Article 6 of the Master Agreement, AstraZeneca, or AstraZeneca's designee, may provide Materials to Institution for use by Institution/Principal Investigator during the Study.

Equipment: [list equipment]

Other materials: [list other materials]

## 4. BACKGROUND INTELLECTUAL PROPERTY

Each Party shall retain all rights in its respective Background Intellectual Property. The Master Agreement and this Addendum are not intended to and shall not infer any license grant or assignment, whether expressed or implied, with regard to such Background Intellectual Property.

## 5. SOURCE DATA, RECORDS AND STORAGE

Institution shall ensure that source data, CRFs and Subject medical records are handled, kept and maintained in accordance with the Master Agreement, the Protocol and Applicable Law.

## 6. EFFECTIVE DATE

This Addendum commences on the last date of signature below and will remain in effect until the final data has been provided to AstraZeneca following Site Closure or earlier termination of this Addendum in accordance with Section 16 (Termination) of the Master Agreement. This Addendum may be extended upon mutual agreement of the Parties.

## 7. SURVIVAL

The respective rights and obligations of the Parties set forth in Articles 20 (Notices), 22 (Entire Agreement), and 21 (Survival) of the Master Agreement, shall survive the expiration or termination of this Addendum.

## 8. NOTICES

Notices relating to this Addendum shall be delivered in accordance with Article 20 of the Master Agreement, but shall be addressed as follows:

**AstraZeneca**

Name: Clinical Agreement and Grant Management
Address: 1800 Concord Pike
Wilmington, DE 19850-5438
Facsimile: 302-885-9962

**With Copy to:**

Name: General Counsel
Address: 1800 Concord Pike
Wilmington, DE 19850-5438
Facsimile: 302-886-1578

**Institution**

Name: << >>
Address: << >>

Facsimile: << >>

**Principal Investigator**

Name: << >>
Address: << >>

Facsimile: << >>

## 9. ENTIRE AGREEMENT

This Addendum, including the terms of the Master Agreement, constitutes the entire agreement among the Parties hereto with respect to the Study performed under this Addendum.

## 10. INSTITUTION RESPONSIBILITIES

Institution shall be responsible for the performance of the obligations of Principal Investigator and Study Site Staff as set out in this Addendum and the Master Agreement. Institution shall cause its employees, executives, officers, directors, faculty and other authorized agents, including Principal Investigator and Study Site Staff, to comply with and adhere to the terms of the Master Agreement and this Addendum and to conduct the Study in accordance with the terms of the Master Agreement and this Addendum.

## 11. ELECTRONIC SIGNATURE

The Parties agree that execution of this Addendum by industry standard electronic signature software and or by exchanging PDF signatures shall have the same legal force and effect as the exchange of original signatures, and that in any proceeding arising under or relating to this Addendum, each Party hereby waives any right to raise any defense or waiver based upon execution of this Addendum by means of such electronic signatures or maintenance of the executed agreement electronically.

THIS CLINICAL STUDY ADDENDUM IS EXECUTED by the authorized representatives of AstraZeneca and Institution as of the dates indicated below.

| | |
|---|---|
| SIGNED for and on behalf of<br>**AstraZeneca LP/AstraZeneca Pharmaceuticals LP** | SIGNED for and on behalf of<br>**<<Name of Institution>>** |
| Signature | Signature |
| Name: | Name: |
| Title: | Title: |
| Date: | Date: |

I confirm that I have received a copy of the Master Agreement under which this Clinical Study Addendum is issued, and that I have read and understood the Master Agreement and this Clinical Study Addendum. I agree to be bound by and to comply with the terms of the Master Agreement as they relate to my activities as Principal Investigator and to this Clinical Study Addendum, including, but not limited to, Article 11 (Confidential Information) of the Master Agreement. Principal Investigator undertakes to comply with the obligations that this Clinical Study Addendum and the Master Agreement imposes on him/her.

READ AND ACKNOWLEDGED by
**Principal Investigator**

Signature

Name:

Title: Principal Investigator

Date:

*Schedule A to Appendix 2*

**Protocol Procedures Covered in Appendix 2**

*[Attach Protocol Study Plan or Protocol procedure spreadsheet with prices and Standard of Care Procedures identified]*

## Appendix 3 Accommodation Expenses at Study Meetings
## Expense Reimbursement Guidelines

This attachment provides guidance on Expense Reimbursements that can be charged back to AstraZeneca. Note that for expenses due to the University's employee, AstraZeneca shall pay the employee such costs directly, or for Covered Recipients (US physicians and teaching hospitals), AstraZenecawill require detailed allocation as set forth set forth in *AstraZeneca's Data Requirements for Payments and Transfers of Value to Covered Recipients,* available at http://www.astrazeneca-us.com/astrazeneca-purchasing-general-terms-and-conditions.

**Travel Expenses**
All travel expenditures must be modest. Service providers are expected to use AstraZeneca's designated travel management company unless a more favorable rate can be obtained from another corporate travel agency. If a more favorable rate can be obtained, AstraZeneca will reimburse service providers for travel-related expenses as outlined below.

**Air/Rail Travel**
Travelers must use Economy/Coach Class for all flights and rail tickets. Business Class airfare is not reimbursable unless the trip involves an overseas flight of greater than six hours in duration. Service providers are expected to use cost savings measures whenever possible including the use of non-refundable fares and advance travel arrangements.

**Ground Transportation**
Travelers should use the most economical means of ground transportation. Luxury limousines, black car services, and watercraft vehicles are not reimbursable. Car rentals should only be used when other means of transportation are unavailable, more costly, or impractical. Compact or mid-sized cars should be selected whenever possible.
For travel by personal car, mileage will be reimbursed at the prevailing rate as noted by applicable government (e.g., IRS) guidelines.

**Short-Term Lodging (Less than 30 days)**
Travelers must select standard accommodations at reasonably priced mid-market hotels or motels. Unless prior approval is obtained, AstraZeneca will not reimburse for lodging expenses at up-market or luxury hotels (Ritz, Four Seasons, etc.).

**Long-Term Lodging (30 days or More)**
Service providers on assignment for four nights a week for a period of 30 days or more are required to use long-term lodging arrangements approved by the AstraZeneca project manager.

**Travel Duration**
If a scheduled trip needs to be extended, the traveler should notify the project manager for approval. If a scheduled trip is completed early, the traveler should return no later than the next business day. Travelers will not be reimbursed for incurred expenses thereafter.

**Non-Travel /Category Specific Expense Reimbursement**

The service provider must work with the AstraZeneca project manager to complete a category-specific budget worksheet. Examples of category-specific expenses are:

- Consulting and Professional Services
- Advertising Agencies
- Professional Education
- Business Insight
- Public Relations
- Clinical

**Non-Reimbursable Expenses**

- The following expenses will not be reimbursed:

| | | |
|---|---|---|
| Overhead allocations | Administration fees | Traffic/parking violations |
| Child care fees | Personal phone calls | Life insurance |
| Health club fees | Pay TV entertainment | Loss of personal property |
| Late fees on credit cards | Air phone usage | Dry cleaning/laundry |
| Personal property insurance | Indirect expenses | Unsubstantiated expenses |
| On-site administration/ secretarial fees | Mark-ups | |

**Expense Audits**

Intentionally left blank.

**Appendix 4**
**Administrative Contact Person and Address for Each Institution**

| | |
|---|---|
| David Hawkins<br>Associate Director<br>Office of Sponsored Projects<br>**The University of Texas at Austin**<br>North Office Bldg., Suite 5.300<br>Austin, TX 78712<br><br>Phone: 512-471-6424<br>Fax: 512-471-6564<br><br>Tax ID: 74-6000203 | Angela R. Charboneau Wishon, J.D.<br>Vice President for Research Administration<br>**The University of Texas Southwestern Medical Center**<br>5323 Harry Hines Blvd.<br>Dallas, Texas 75390-9105<br><br>Phone: 214-648-6449<br>Fax: 214-648-4474<br><br>Tax ID: 75-6002868 |
| Chris Green<br>Director, Office of Sponsored Programs<br>**The University of Texas Health Science Center at San Antonio**<br>7703 Floyd Curl Dr., Mail Code 7828<br>San Antonio, TX 78229-3900<br><br>Phone: 210-567-2340<br>Fax: 210-567-8107<br><br>Tax ID: 74-1586031 | Karen Niemeier<br>Director, Contracts<br>**The University of Texas Health Science Center at Houston**<br>7000 Fannin Street, Suite 1006<br>Houston, TX 77030<br>Phone: 713-500-3999<br>Fax: 713-383-3746<br><br>Tax ID: 74-1761309 |
| David Anderson<br>Director, Office of Pre-Award Services<br>**The University of Texas Health Science Center at Tyler**<br>11937 U.S. Hwy. 271<br>Tyler, TX 75708-3154<br><br>Phone: 903-877-7486<br>Fax: 903-877-7558<br><br>Tax ID: 75-6001354 | Angela Cook<br>Director, Office of Clinical Research<br>**The University of Texas Medical Branch at Galveston**<br>301 University Boulevard<br>Galveston, TX 77555-0158<br><br>Phone: 409-772-1978<br>Fax: 409-772-1968<br><br>Tax ID: 74-6000949 |