**PARTICIPATION AGREEMENT**

**THIS AGREEMENT** is made as of the Effective Date.

**BETWEEN**:

**CLINICAL TRIALS ONTARIO**
MaRS Centre, West Tower
661 University Avenue, Suite 460
Toronto, Ontario M5G 1M1
(herein **"CTO"**)

**–**and **–**

**[FULL LEGAL NAME]**
[ADDRESS]
(herein **"PARTICIPATING ORGANIZATION" OR "PO"**)

Each a "**Party**" and together, the "**Parties**"

**RECITALS:**

A. CTO is an independent not-for-profit organization supported with funding from the Government of Ontario with the mandate to provide a streamlined approach to conducting multi-centre Clinical Studies in Ontario. The CTO Streamlined Research Ethics Review System (**"CTO SRERS"**) supports the ethics review and oversight of Clinical Studies by a single qualified Research Ethics Board (**"REB"**) for studies conducted at multiple research sites in Ontario.

B. The PO wishes to participate in the CTO SRERS and shares a commitment to supporting efficient and timely ethics review for Clinical Studies while maintaining the highest ethical standards for participant protection. PO's participation in the CTO SRERS may include the PO acting as an REB Host Institution for certain Clinical Studies in accordance with this Agreement, wherein the PO may also act as a recruiting site.

(i) The PO intends to act as both a recruiting site and when qualified and invited by CTO, an REB Host Institution ☐

(ii) The PO intends to act only as a recruiting site ☐

(iii) The PO intends to act only as an REB Host Institution (when qualified and invited by CTO on a study-by-study basis) ☐

C. The purpose of this Agreement is to set out CTO's and the PO's respective rights and obligations in connection with the CTO SRERS.

**THEREFORE,** the Parties agree as follows:

## ARTICLE 1
## DEFINITIONS AND PRINCIPLES OF INTERPRETATION

### 1.1 Definitions

In this Agreement, the following words and terms have the following meanings:

(a) "**Agreement**" means this agreement including all schedules, exhibits, and all amendments or restatements as permitted, and references to "**Article**", "**Section**", "**Schedule**" or "**Exhibit**" means the specified Article, Section, Schedule or Exhibit of this Agreement;

(b) **"Clinical Study"** means a clinical study that will have its research ethics review conducted through the CTO SRERS as a result of this Agreement;

(c) **"Confidential Information**" means all information disclosed in oral, written, electronic or any other form by a Disclosing Party (including its respective employees, investigators, agents and representatives) related to this Agreement and including information that is the property of third parties;

(d) "**Effective Date**" means the date of final execution of this Agreement;

(e) **"End of Study"** means the time when all accountabilities of an REB Host Institution's REB are met and REB review and oversight is no longer required;

(f) "**FIPPA**" means the *Freedom of Information and Protection of Privacy Act* (Ontario) and any amendments thereto;

(g) "**Force Majeure Event**" has the meaning set out in Section 9.10;

(h) "**REB Host Institution**" means a PO whose REB has been qualified by CTO or its agent to assume the role of an REB of Record for the research ethics review, approval and oversight of a specific Clinical Study;

(i) "**Intellectual Property Rights**" means all rights in and to any and all intellectual and industrial property of any kind, including works protected by the law of copyright or in which copyright may subsist such as documentation, software, data and information, whether in printed, electronic, magnetic, optical or other material or tangible form, compilations of information and databases (whether or not any of same are protected by copyright); designs; trade-marks and trade names; patents, inventions, processes and discoveries; industrial designs; trade secrets; know-how; Confidential Information or other information of a confidential nature and any other works that are subject to intellectual and industrial property protection under the laws of Canada, any foreign country, or any political subdivision thereof;

(j) "**Laws and Regulations**" means all applicable laws, regulations and guidelines, including but not limited to the most current version of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans ("**TCPS**") and *Personal Health Information Protection Act* (Ontario) ("**PHIPA**") and its regulations;

(k) "**Parties**" means CTO and the PO and "**Party**" means any one of them;

(l) "**Personal Health Information**" has the same meaning as defined in PHIPA;

(m) **"Personal Information"** means any information about an identifiable individual, including Personal Health Information, that is required to be protected pursuant to PHIPA, PIPEDA or other Laws and Regulations pertaining to the protection of personal information;

(n) "**PHIPA**" means the *Personal Health Information Protection Act, 2004* (Ontario) and any amendments thereto;

(o) "**PIPEDA**" means the Personal Information Protection and Electronic Documents Act (Canada) and any amendments thereto;

(p) **"REB of Record"** means an REB that has been qualified and selected by CTO, and appointed, through a REB of Record Agreement, by a participating organization under whose auspices the Clinical Study is being conducted to serve as the primary or sole authority for the research ethics oversight in a CTO SRERS Clinical Study;

(q) **"Term"** has the meaning given to it in Section 2.1.

### 1.2 Schedules

The following are Schedules to this Agreement:

Schedule A Qualification Requirements - REB of Record
Schedule B CTO REB of Record Selection Process
Schedule C Fee Structure
Schedule D Description of CTO Stream including Security and Confidentiality
Schedule E REB of Record Agreement Template

### 1.3 Conflicts

(a) In the event of any conflict or inconsistency between the terms of this Agreement and any Schedule, the terms of this Agreement shall prevail.

## ARTICLE 2
## TERM & TERMINATION

### 2.1 Term & Termination

(a) The term of this Agreement shall commence on the Effective Date and shall terminate on April 30, 2019 with the intent to renew as mutually agreed by the Parties, and subject to earlier termination in accordance with the provisions hereof.

(b) The PO shall provide written notice to CTO of its election to terminate the Agreement not later than ninety (90) days prior to the end of the term.

(c) Despite clause 2.1(b) above, the PO must continue its obligations for all Clinical Studies until all such Clinical Studies have met their respective End of Study obligations. A PO that is also a REB Host Institution may not terminate this agreement prior to the end of its REB of Record obligations according to this Agreement and in accordance with all Laws and Regulations. A PO which is acting as a recruiting site must continue to meet its obligations and allow the REB of Record to provide ethical oversight irrespective of the date of termination of this Agreement.

## ARTICLE 3
## RESPONSIBILITIES OF PARTIES

### 3.1 CTO Responsibilities

CTO shall have the following responsibilities:

(a) administering Participation Agreements and REB of Record Agreements with participating organizations;

(b) implementing the CTO Qualification process in accordance with Schedule "A";

(c) conducting full qualification reviews every three years and annual reviews to document substantive changes, including a review of performance related to CTO Clinical Studies in accordance with Schedule "A";

(d) maintaining in a manner available to PO a current list of CTO qualified REBs;

(e) identifying and inviting a REB of Record for each Clinical Study based on established selection criteria as set out in Schedule "B";

(f) setting template and standards for submissions to REBs of Record;

(g) providing and maintaining a web-based system as described in Schedule "D" to support the CTO SRERS; and

(h) collecting REB review fees and disbursing of REB fees to the REB Host Institution in support of its REB in accordance with Schedule "C".

### 3.2 PO Responsibilities

A PO may have responsibilities only as a recruiting site for a Clinical Study and/or responsibilities as the REB Host Institution. The PO is responsible for fulfilling and complying with its obligations in this Agreement as a recruiting site and/or REB Host Institution as described below.

3.2.1 The PO shall have the following responsibilities when it acts as a recruiting or participating site:

(a) providing one point of contact (the "**PO Contact**") at the PO to manage the implementation and operation of the CTO SRERS for the PO in a timely manner and execute REB of Record Agreements in the form provided in Schedule "E";

(b) fulfilling its obligations as the PO under the REB of Record Agreement;

(c) ensuring it has institutional authorization and/or policies and procedures that permit the delegation of REB review and oversight to a CTO qualified REB;

(d) documenting, through the CTO SRERS, institutional ethical requirements; and

(e) meeting all institutional requirements related to a specific Clinical Study.

3.2.2 The PO shall have the following responsibilities when it acts as the REB Host Institution:

(a) confirming with CTO within two (2) business days of selection, acceptance or decline of role as the REB Host Institution for a specific Clinical Study;

(b) declining to act as the REB Host Institution only in reasonable situations including, but not limited to, lack of REB expertise in the area of the specific Clinical Study or inability to conduct a timely ethics review of the Clinical Study;

(c) entering into an REB of Record agreement with Ontario recruiting participating organizations, providing timely ethics review, communication, document access and reporting using the CTO SRERS;

(d) using REB fees received from CTO to support the operations of its REB;

(e) ensuring that the institutional ethical requirements of participating institutions are considered during review and implemented whenever possible; and

(f) maintaining its REB in a state of CTO qualification readiness, providing annual reports to CTO on substantive changes in accordance with Schedule "A" and allowing CTO to conduct a qualification review every three years.

## ARTICLE 4
## REPRESENTATIONS AND WARRANTIES

### 4.1 Representations and Warranties

Each party represents and warrants to the other party that it:

(a) has the full power and authority to enter into this Agreement and to observe, perform, and comply with the terms and conditions of this Agreement;

(b) shall operate in compliance with all Laws and Regulations related to any aspect of this Agreement;

(c) holds all permits, licenses, consents, Intellectual Property Rights, and authorities necessary to perform its obligations under this Agreement;

## ARTICLE 5
## INTELLECTUAL PROPERTY RIGHTS

### 5.1 Reservation of Rights

Except as expressly provided in this Agreement, no Party shall acquire any right, title or interest in or to any Intellectual Property Rights of another Party or of its licensors or subcontractors. For greater clarity, no right, title or interest in or to CTO's e-tools that support the CTO SRERS are hereby granted save a non-exclusive, royalty-free licence during the term of this Agreement to use the e-tools solely in support of fulfilling obligations under this Agreement.

## ARTICLE 6
## ACCESS TO INFORMATION/CONFIDENTIALITY

### 6.1 Confidential Information

(a) From time to time a Party (the "**Disclosing Party**") may provide to the other Party (the "**Receiving Party**") Confidential Information in accordance with its obligations pursuant to this Agreement. The Receiving Party agrees that it will not at any time, directly or indirectly, disclose the Confidential Information of the Disclosing Party to any person, other than to the Receiving Party's directors, officers, employees, and professional advisors strictly on a need-to-know basis in order for the Receiving Party to exercise its rights or perform its obligations hereunder, except as otherwise specifically authorized by the Disclosing Party.

(b) The requirement of confidentiality shall survive for a period of ten (10) years.

(c) Upon termination of the Agreement, the Receiving Party may retain one secure archival copy of the Confidential Information and otherwise shall return it, or upon written authorization of the Disclosing Party, securely destroy it and provide notice of its secure destruction.

(d) This Agreement imposes no obligation upon a Receiving Party with respect to information that:

(i) at the time of or after its disclosure is in or becomes part of the public domain, other than as a result of a breach by the undersigned of its obligations hereunder;

(ii) can be demonstrated to have been disclosed to the Receiving Party by a third party that was not bound by a confidentiality agreement or otherwise prohibited from transmitting such information by a contractual, legal or fiduciary obligation;

(iii) was independently developed by Receiving Party without benefit of the Confidential Information as demonstrated by written records; or

(iv) is required to be disclosed by any court order or applicable Laws or Regulations.

## ARTICLE 7
## INSURANCE & INDEMNITY

### 7.1 Insurance Coverage Requirements

Each Party shall maintain for the period during which the Agreement is in effect, at its own cost and expense:

(a) Professional liability insurance and comprehensive general liability insurance (including any excess liability coverage, if necessary) on an occurrence basis for third party bodily injury, personal injury and property damage, to an inclusive limit of not less than $5,000,000 per occurrence. The policy shall name the Parties to this Agreement as additional insureds but only with respect to this Agreement and shall include the following:

(i) contractual liability coverage;

(ii) a cross-liability clause;

(iii) personal injury coverage;

(iv) products and completed operations coverage; and

(v) a thirty (30) day prior written notice of cancellation, termination or material change.

(b) CTO will hold insurance to cover errors and omissions in an amount of not less than $5,000,000 per occurrence and shall name the PO as an additional insured on the policy with respect to this Agreement.

(c) Upon request, the Parties shall provide certificates of the above insurance to the requesting Party. The Parties agree to provide thirty (30) days' written notice of any changes to their policy of insurance as it affects coverage provided to a Party under this Agreement.

**7.2 Indemnities**

(a) CTO agrees to indemnify, and undertakes to defend and hold harmless, the PO, its officers, directors, investigators, employees and agents (collectively, the "**PO Indemnitees**"), from and against all losses directly resulting from:

(i) the death of or bodily injury to any third party or to any employee of the PO (or other person for whom the PO is responsible in law) to the extent caused by the negligence or wilful misconduct of CTO or any contractor of CTO in performance of its obligations under this Agreement;

(ii) the loss of or damage to the real or tangible personal property (whether owned or leased) of any third party or any of the PO Indemnitees, to the extent caused by the negligence or wilful misconduct of CTO or any subcontractor of CTO in the performance of its obligations hereunder; or

(iii) any third-party action, claim or demand directly arising as a result of CTO's failure to perform its obligations under this Agreement.

(b) The PO agrees to indemnify, and undertakes to defend and hold harmless, CTO, its officers, directors, employees and agents (collectively, the "**CTO Indemnitees**"), from and against all losses directly resulting from:

(i) the death of or bodily injury to any third party or to any employee of CTO (or other person for whom CTO is responsible in law) to the extent caused by the negligence or wilful misconduct of the PO or any contractor of the PO in performance of its obligations under this Agreement;

(ii) the loss of or damage to the real or tangible personal property, whether owned or leased, of any third party or any of the CTO Indemnitees, to the extent caused by the negligence or wilful misconduct of the PO or any subcontractor of the PO in the performance of its obligations hereunder; or

(iii) any third-party action, claim or demand directly arising as a result of PO's failure to perform its obligations under this Agreement.

(c) In the event that any Party receives notice of a legal proceeding by a third party related to a Clinical Study, it shall immediately notify the other Parties in writing.

## ARTICLE 8
## DISPUTE RESOLUTION

### 8.1 Dispute Resolution

In the event that a dispute arises related to this Agreement, the parties will initially and in good faith discuss the matter through their contacts named at Section 9.2 of this Agreement and seek a resolution. If no resolution has been reached within fifteen (15) days from the commencement of discussions, the Parties shall be free to pursue any other remedies available to them. While a dispute is being settled, the REB Host Institution is required to continue with its role as REB of Record.

### 8.2 Confidentiality

The proceedings of all negotiations, mediations and arbitrations as part of the dispute resolution process shall at all times be privately conducted. The Parties agree that all information, materials, statements, conduct, communications, negotiations, mediations, arbitrations, offers of settlement, documents, decisions, and awards of either Party, in whatever form prior to the commencement of formal legal proceedings in a court or other tribunal: (i) shall at all times be Confidential Information; (ii) shall not be offered into evidence, disclosed or used for any purpose other than the dispute resolution process under this Agreement; and (iii) will not constitute an admission or waiver of rights.

## ARTICLE 9
## GENERAL

### 9.1 Further Assurances

The Parties shall sign such further and other documents, cause such meetings to be held, cause such resolutions to be passed, exercise their vote and influence and do and perform (and cause to be done and performed) such further and other acts or things as may be necessary or desirable in order to give full effect to this Agreement and every part of it.

### 9.2 Notices

(a) All notices under this Agreement shall be in writing and shall be delivered by personal delivery/courier, fax, email or registered mail:

(i) to CTO at:

Clinical Trials Ontario
MaRS Centre, West Tower
661 University Avenue, Suite 460
Toronto, Ontario M5G 1M1

Attention: Susan Marlin, President and CEO

(ii) to the PO at:

[ADDRESS]

[FAX]

Attention: [NAME, TITLE]

(b) The notice shall be deemed to have been delivered on the day of personal delivery, on the day received by fax (as evidenced by a transmission confirmation) or by e-mail, or on the fifth day following mailing.

### 9.3 Governing Law

This Agreement shall be governed by, and construed and interpreted in accordance with, the laws in force in the Province of Ontario and shall be treated in all respects as an Ontario contract.

### 9.4 Severability

Each of the provisions contained in this Agreement are distinct and severable. Any declaration by a court of competent jurisdiction of the invalidity or unenforceability of any provision or part of a provision will not affect the validity or enforceability of any other provision of this Agreement.

### 9.5 Waiver

No delay or omission by a Party to exercise any right or power it has under this Agreement shall impair or be construed as a waiver of such right or power. A waiver by any Party of any breach or covenant shall not be construed to be a waiver of any succeeding breach or any other covenant. All waivers must be in writing and signed by the Party waiving its rights.

### 9.6 Counterparts

This Agreement may be executed in any number of counterparts, each of which shall be deemed an original and all of which, taken together, shall constitute one and the same instrument. Delivery by facsimile or email of any executed counterpart of this Agreement shall be equally as effective as delivery of a manually executed counterpart thereof.

### 9.7 Entire Agreement

This Agreement, including the Schedules hereto, constitutes the entire agreement between the Parties with respect to the subject matter hereof and cancels and supersedes any prior understandings and agreements between the Parties. There are no representations, warranties, forms, conditions, undertakings or collateral agreements, express, implied or statutory between the Parties other than as expressly set forth in this

Agreement. Except as otherwise explicitly set out herein, this Agreement may only be amended by a written document signed by the Parties.

### 9.8 Relationship of Parties

In connection with this Agreement, each Party is an independent contractor. This Agreement does not and shall not be deemed to create a joint venture, partnership, fiduciary or agency relationship between the Parties for any purpose. With respect to its own personnel, each Party is independently responsible for all obligations incumbent upon an employer.

### 9.9 Assignment

This Agreement will be binding upon and will enure to the benefit of the Parties and their respective successors and permitted assigns. No Party shall assign this Agreement or any part hereof or any benefit or interest herein without the prior approval of the other Party.

### 9.10 Force Majeure

No Party shall be liable for any delays in the performance of any of its obligations hereunder due to causes beyond its reasonable control ("**Force Majeure Event**"), including, but not limited to, fire, strike, war, riots, acts of terrorism and/or of a public enemy, acts of any civil or military authority, acts of God, floods, unusually severe weather, epidemics, pandemics or quarantine restrictions, public utility failure or service fluctuation, judicial action and acts and failures to act by governmental authorities.

### 9.11 Survival

Notwithstanding the expiration or earlier termination of this Agreement for any reason, the following Articles and sections of this Agreement shall survive any such termination or expiration: Articles 2.1(c), 3, 5.1, 6, 7 and 9.3.

**IN WITNESS WHEREOF** the Parties have executed this Agreement as of the last signature below.

**CLINICAL TRIALS ONTARIO**

By: _____
Susan Marlin, President and CEO

Date: _____

**[PARTICIPATING ORGANIZATION]**

By: _____
[NAME, TITLE]

Date: _____

By: _____
[NAME, TITLE]

Date: _____

## SCHEDULE A

## QUALIFICATION REQUIREMENTS

Qualification requirements are detailed in the CTO REB Qualification Manual. The Manual is available at www.ctontario.ca and is incorporated herein by reference.

## SCHEDULE B

## CTO REB OF RECORD SELECTION PROCESS

The selection criteria for choosing an REB of Record is available at www.ctontario.ca and is incorporated herein by reference.

## SCHEDULE C

## FEE STRUCTURE

The fee structure for the REB of Record review is available at www.ctontario.ca and is incorporated herein by reference. CTO will provide notification to PO of any change in the fee structure sixty (60) days in advance of such change taking effect.

**SCHEDULE D**

**Description of CTO Stream including Security and Confidentiality**

## About CTO Stream

CTO Stream is web-based management system that allows for the electronic submission of applications and documents for research ethics review and oversight by an REB of Record of a Clinical Study using the CTO Streamlined Research Ethics Review System ("**SRERS"**).

### Access to CTO Stream

CTO Stream requires a computer/tablet/mobile device, web browser and secure internet access. CTO Stream supports access through Internet Explorer, Firefox, Google Chrome and Safari. Users are encouraged to use the latest version of their web browser and browser support is subject to ongoing support by the browser manufacturer. For more information on supported browser versions, please access CTO Stream policies and procedures available at www.ctostream.ca. Separate portals are maintained with different URLs for Clinical Study applicants and the Research Ethics Boards to access CTO Stream.

### Secure User Authentication

All users are required to enter a username and password to access the system. The system uses strong passwords of 6 characters or more using capital and lowercase letters and numbers. User accounts are tied to levels of access according to user roles to ensure a controlled and secure environment. In order to obtain a username and password, individuals must electronically agree to the confidentiality clauses as stipulated by CTO.

### Communications and Notifications

In order to maintain the security and confidentiality of the information within the system, no confidential information (as detailed below) is transmitted via e-mail or any other insecure method of communication. Users may receive e-mails to their designated e-mail account containing a link to the information contained within CTO Stream. Users must then log in to CTO Stream to access the information.

### Security of Data Transmission

All data transferred between the user's device and CTO Stream is encrypted using SSL. The software is hosted in a secure data centre in the United Kingdom. System

protection is provided through a combination of physical security at the data centre, network security via firewalls, and security measures within the application itself. Backend access, to either the database or the file system, is only available to authorized system administrators.

Data Storage and Backup

CTO Stream data is kept for the maximum period required by Laws and Regulations applicable to the Clinical Study. Full data back-up and disaster recovery procedures are in place to ensure the safety, security and operation of the system. More information on these procedures is available upon requests directed to CTO.

**Confidential information within CTO Stream**

CTO Stream contains two (2) types of information that may be deemed confidential: information specific to the Clinical Study and REB information.

**Clinical Study Information** includes responses to the questions contained within each application, as well as material such as the protocol, Investigator Brochure ("**IB**")/Product Monograph (**"PM"**), study budget, and written information to be provided to Clinical Study participants.

**REB Information** is categorized in the following two ways:

> **Accessible REB Information** includes letters issued by the REB (e.g., documenting the results of a review) and communication between the REB and an applicant within CTO Stream.
>
> **Restricted REB Information** includes comments by the REB in the application, meeting minutes and agenda, and any review material uploaded into CTO Stream by the REB of Record.

For greater clarity, no Personal Health Information or study participant record is intended to be shared through CTO Stream.

Access to confidential information within CTO Stream by user group

*CTO*

Clinical Study Information is formally provided to CTO when the provincial initial application is submitted for research ethics review. In addition, designated individuals

at CTO have access to all confidential information contained within CTO Stream for system administration purposes.

*REBs*

The REB of Record will have access to all Clinical Study Information and REB Information applicable to the Clinical Study for which they provide oversight. CTO will provide the REB identified as the potential REB of Record with access to the provincial initial application (and all Clinical Study Information contained within). This REB will either accept or decline to act as the REB of Record for the Clinical Study. If the REB declines to act as the REB of Record, they will no longer have access to the Clinical Study Information within CTO Stream.

*Institutions*

The provincial applicant and study staff at the provincial applicant centre have the ability to see all Clinical Study Information and Accessible REB Information contained within CTO Stream for that Clinical Study.

The centre applicant and study staff have the ability to see all Clinical Study Information and Accessible REB Information contained in provincial-level applications and applications from their centre only.

The institution's department head/department approver has the ability to see all Clinical Study Information and Accessible REB Information contained in provincial-level applications and applications from their centre only.

The institutional representative(s) of the provincial and centre applicants has the ability to see all Clinical Study Information and Accessible REB Information contained in provincial-level applications and applications from their centre only, when applicable.

*Sponsors*

Individual representatives of the Sponsor will have access to Clinical Study Information and only Accessible REB Information associated with applications via the sharing functionality, as granted by the provincial applicant/study staff and/or centre applicant/study staff. The sharing functionality is described in 'Sharing of confidential information within CTO Stream', below.

<u>Sharing of confidential information within CTO Stream</u>

CTO Stream allows for the secure collaboration with any registered user both within the applicant's institution and also with registered users at other institutions and organizations. In order to allow for multiple study staff members to access the Clinical Study application, the creator of the project must share the Clinical Study application.

This process is facilitated by the share functionality in CTO Stream. This functionality will keep a record of every user who has been given share access and will be crucial to ensure that investigators have access to provincial documentation when completing centre REB applications.

Individuals with whom an application has been shared will have access to the Clinical Study Information and Accessible REB Information contained on that application. The provincial applicant and study staff has the ability to share any application within CTO Stream with another user who has an account with CTO. The centre applicant and study staff has the ability to share any centre application within CTO Stream with another user who has an account with CTO.

Requests for access to confidential information

Requests for access to Restricted REB Information (e.g., for purposes of inspection/audit) must go to the REB of Record for consideration.

Requests for access to Clinical Study Information or Accessible REB Information by individuals outside of the permissions noted above should be directed to CTO.

**SCHEDULE E**

**REB OF RECORD STUDY AGREEMENT**

**CTO Study ID Number:**

**Agreement Between:**

| **("Participating Institution"):** |
|---|
| **Address for direction of legal notices under this agreement:**<br>**Address:**<br>**Attention:** |

**And**

| **("REB Host Institution"):** |
|---|
| **Address for direction of legal notices under this agreement:**<br>**Address:**<br>**Attention:** |

**And**

| **Participating Institution Principal Investigator Name:**<br>**("Participating Institution PI")** |
|---|
| **Address:** |
| **Phone:**<br>**Fax:**<br>**Email:** |

Collectively, the "**Parties**"

This Agreement is effective as of the date of last signature below (the "**Effective Date**").

| **Study Title (**the **"Study"):** |
|---|
| |

**Preamble**

The institutions which are party to this Agreement have each entered into a Participation Agreement with Clinical Trials Ontario ("**CTO**") agreeing to participate in CTO's Streamlined Research Ethics Review System ("**CTO SRERS**"). The REB Host Institution's Research Ethics Board ("**REB**") has been qualified by CTO such that the REB Host Institution's REB is eligible to act as a delegated REB of Record responsible for ethics review and oversight of multi-centre clinical studies under the CTO SRERS. The REB Host Institution's REB has been selected by CTO to act as the single REB for the Study.

This inter-institutional agreement ("**Agreement**") sets out the terms and conditions for Participating Institution's delegation of research ethics review, approval and oversight to the REB Host Institution's REB for the Study.

CTO is an independent not-for-profit organization established by the Government of Ontario with the mandate to provide a streamlined approach to conducting multi-centre clinical trials in Ontario while ensuring the highest ethical standards for participant protection. CTO is not a party to this Agreement and provides administrative support only to parties for their review and execution of this Agreement.

The parties hereby agree as follows:

**1. REB of Record**

1.1 The Participating Institution retains REB Host Institution, and REB Host Institution agrees to act, as the Research Ethics Board of Record ("**REB of Record**") for the Participating Institution in respect of the Study.

1.2 Participating Institution and REB Host Institution agree that the REB of Record may approve, reject, propose modifications to, put on hold or terminate the Study at its sole discretion ("**REB of Record Determinations**").

1.3 In agreeing that its REB shall act as the REB of Record, REB Host Institution agrees that REB of Record shall act:

(i) in accordance with its responsibilities set out in the attached Schedule 1, including but not limited to the REB Host Institution's Participation Agreement with CTO; and

(ii) in compliance with all applicable Laws and Regulations and guidelines, including but not limited to the most current version of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans ("**TCPS**") and *Personal Health Information Protection Act* (Ontario) ("**PHIPA**") and its applicable regulations. ("**Applicable Laws and Regulations**").

1.4 REB Host Institution acknowledges that the documents and information that it receives from the Participating Institution are subject to strict confidentiality obligations pursuant to agreements between or among Participating

Institution, Participating Institution PI, and the Study sponsor ("**Sponsor Agreements**"). REB Host Institution and its agents shall maintain in confidence all documents and information received from the Participating Institution and/or Participating Institution PI and shall not disclose them to third parties without prior written permission of the sponsor and/or Participating Institution and Participating Institution PI as applicable. In the event that the REB Host Institution (a) reasonably believes that information or documents obtained from the Participating Institution and/or Participating Institution PI must be disclosed in the interest of protecting the safety of Study participants, or (b) REB Host Institution is required by law, regulation or court order to disclose information or documents obtained from the Participating Institution, then the REB Host Institution shall, before making any such disclosure, notify the Participating Institution and Participating Institution PI so that the REB Host Institution, Participating Institution and Participating Institution PI may collectively determine how disclosure may be made without breach of Sponsor Agreements. The obligations contained in this paragraph shall survive completion or earlier termination of this Agreement.

1.5 In the event of an on-site assessment or involvement in resolving a Study participants' complaint by the REB Host Institution, Participating Institution and Participating Institution PI may be required in accordance with Schedule 1 to provide direct access to Study participants' Personal Health Information or records thereof (as that term is defined under PHIPA) that are in the direct or indirect control of the Participating Institution and/or Participating Institution PI ("**Participants' Records**"). Should that occur, REB Host Institution will hold the Participants' Records in confidence, use them solely for the purpose of carrying out its duties under this Agreement, and will not copy or remove said records or transfer any information contained in them to anyone other than employees and agents of REB Host Institution with a need to know, without the prior written consent of Participating Institution or in accordance with Applicable Laws and Regulations.

1.6 REB Host Institution represents and warrants that REB Host Institution's REB operates and is constituted in accordance with all Applicable Laws and Regulations, is registered as an Institutional Review Board ("**IRB**") with the U.S. Office for Human Research Protections, has been qualified by CTO, is appropriately constituted, and is in compliance with the standard operating procedures upon which the CTO qualification was based.

## 2. Obligations of the Participating Institution and Participating Institution PI

The Participating Institution and Participating Institution PI agree to comply with all REB of Record Determinations with respect to the Study, and each with respect to its/his/her own role to conduct the Study in accordance with all Applicable Laws and Regulations and in accordance with its/his/her responsibilities set out in the attached Schedule 1.

## 3. Relationship of the Parties

The Participating Institution, the Participating Institution PI, and REB Host Institution are and at all times shall remain independent of each other and are not and shall not represent themselves as being a principal, agent, joint venture, partner or employee of the other(s). No representations shall be made or actions taken by a Party which could establish or imply any apparent relationship of agency, joint venture, partnership or employment with another, and other than expressly provided under this Agreement, no party shall be bound in any manner whatsoever by any agreements, warranties or representations of another party.

## 4. Assignment

Neither this Agreement nor any of the rights or obligations of any party may be assigned without prior written consent of the other parties to this Agreement.

## 5. Term and Termination

5.1 This Agreement remains in place from the Effective Date until all accountabilities of REB Host Institution's REB are met and REB review and oversight is no longer required.

5.2(a) Any party may terminate this Agreement immediately following thirty (30) days written notice of a material breach of this Agreement which is not cured within such thirty (30) day notice period.

(b) The Participating Institution may terminate this Agreement immediately following sixty (60) days written notice to the REB Host Institution of non-compliance with CTO qualification standards if such non-compliance is not cured with the sixty (60) day notice period.

## 6. Insurance and Indemnity

6.1 Except as otherwise provided in this Agreement:

(i) The Participating Institution agrees to indemnify, and undertakes to defend and hold harmless, the REB Host Institution and its REB members, for third party claims to the extent arising out of the negligent or intentional acts or omissions of the Participating Institution in performance of its obligations under this Agreement, except to the extent that such liability arises out of the negligent or intentional acts or omissions of the REB Host Institution and its REB members.

(ii) REB Host Institution agrees to indemnify, and undertakes to defend and hold harmless, the Participating Institution and Participating Institution PI for third party claims to the extent arising out of the negligent or intentional acts or omissions of the REB Host Institution or its REB members in performance of its obligations under this Agreement, except to the extent

that such liability arises out of the negligent or intentional acts or omissions of the Participating Institution and Participating Institution PI.

6.2 During the term of this Agreement and for the duration of the obligations surviving expiration or premature termination of this Agreement, each institutional party shall maintain a policy or policies of commercial general liability and healthcare professional liability insurance with limits of not less than five million dollars ($5,000,000) per occurrence and ten million dollars ($10,000,000) in aggregate.

6.3 The Participating Institution PI shall maintain membership in the Canadian Medical Protective Association ("**CMPA**"), as appropriate, for the duration of the Study.

6.4 Each party shall provide evidence of insurance or CMPA membership, as applicable, upon written request of another, and shall provide to the others thirty (30) days prior written notice of modification, cancellation or non-renewal of its coverage.

6.5 Except as a component of third party claims, no Party shall be liable to another for any indirect or consequential damages.

## 7. Dispute Resolution

In the event that a dispute arises related to this Agreement, the Parties will initially and in good faith discuss the matter through their contacts named at the beginning of the Agreement and seek a resolution. If no resolution has been reached within fifteen (15) days from the commencement of discussions, the Parties shall be free to pursue any other remedies available to them and will notify CTO of the dispute. In the event that any Party receives notice of a legal proceeding by a third party against it that is related to the Study, it shall immediately notify the other Parties in writing through its contacts named at the beginning of the Agreement. While a dispute is being settled, the REB Host Institution REB is required to continue with its role as REB of Record.

## 8. Governing Law

This Agreement shall be governed by, and construed and interpreted in accordance with, the laws in force in the Province of Ontario and shall be treated in all respects as an Ontario contract.

## 9. Severability

If any provision of this Agreement is determined to be invalid or unenforceable in whole or in part, such invalidity or unenforceability shall attach to such provision and the remainder of the Agreement shall continue in full force and effect; and the parties shall in good faith negotiate a substitute for any provision declared unenforceable, which shall most nearly approximate the intent of the parties in

entering into this Agreement.

**10. Signatures**

By signing, the signatories agree that a signed photocopy or electronic version (e.g., *.pdf or facsimile) of this Agreement is as valid as an original. This Agreement may be signed in counterparts, each of which is to be considered an original, and taken together as one and the same document. A copy of this Agreement executed in counterpart shall be provided by each party to the other parties.

**Participating Institution**

Name: _____ Title: _____

Signature: _____ Date: _____

Authorized Signing Officer
("I have authority to bind the Participating Institution")

**REB Host Institution**

Name: _____ Title: _____

Signature: _____ Date: _____

Authorized Signing Officer
("I have authority to bind REB Host Institution")

**Participating Institution Principal Investigator:**

Name: _____

Signature: _____

Date: _____

**Witness:**

Name: _____

Signature: _____

Date: _____

***All counterparts of this fully executed Agreement should be kept on file at REB Host Institution, Participating Institution, and in the Participating Institution PI's essential Study documents file.***

## SCHEDULE 1

**Division of Responsibilities among REB Host Institution, Participating Institution and Participating Institution PI**

**I. <u>The Responsibilities of REB HOST INSTITUTION</u>:**

1. Abide by the terms and conditions of its Participation Agreement with CTO with respect to the CTO SRERS for ethics review and oversight of multi-participating institution Studies.

2. Maintain its registration as an IRB with the U.S. Office for Human Research Protections, and with CTO.

3. Mandate its REB to review and consider the provincial application materials submitted by the provincial applicant for Ontario and correspond with the provincial applicant regarding any issues or recommended changes to the Study, and make a decision about approval of the Study and handle any appeals in accordance with its standard appeals process.

4. Mandate its REB to be familiar with the CTO list of Participating Institution-specific informed consent language/preferences and other relevant local context and requirements.

5. Mandate its REB to conduct the ethics review of the Centre application materials submitted by each Participating Institution PI and correspond with the Participating Institution and Participating Institution PI regarding any issues or recommended changes to the Participating Institution's materials.

6. Mandate its REB to ensure an ongoing review plan is in place with respect to the Study, which includes an annual review (or more frequently at the discretion of its REB) of the approved Study, a review of all study-wide (provincial) amendments and reportable events (e.g., DSMB reports; global safety updates) and all centre-specific reportable events (e.g., adverse events, protocol deviations) submitted in accordance with REB standard operation procedures and the Study protocol and review of and decision regarding approval of any protocol amendments/modifications to the Study submitted to REB Host Institution's REB by the provincial applicant and/or Participating Institution PI, as applicable.

7. Mandate its REB to maintain all materials related to the Clinical Study submitted for review by the provincial or centre applicant and all materials related to the review of the Clinical Study by the REB.* This includes, but is not limited to, application forms, associated materials (such as study protocols, informed consent forms), all communication between the REB and applicants (including correspondence relaying the results of its deliberations such as REB review letters), meeting agenda and minutes.

8. Maintain written REB Host Institution's REB policies and procedures and membership roster, and make such documents accessible to designated Participating Institution and Participating Institution PI staff members.

9. Mandate its REB to adhere to the requirements of the Participating Institution's Federalwide Assurance (**FWA**) and CTO qualification standards and Applicable Laws.

10. Mandate its REB to immediately notify the Participating Institution and Participating Institution PI in writing if REB approval of the Study is placed on hold or terminated by REB Host Institution REB.*

11. Mandate its REB to notify in writing, and cooperate with, the Participating Institution and the Participating Institution PI concerning any significant Study-related communication received by REB Host Institution REB that has not been received by the Participating Institution or Participating Institution PI, including, but not limited to Study participant complaints, protocol deviations and privacy breaches.

**II. <u>The Responsibilities of the Participating Institution</u>:**

1. The Participating Institution shall inform REB Host Institution of the appropriate Participating Institution representative to be copied on key correspondence (including but not limited to notification of approvals) from REB Host Institution in addition to the Participating Institution PI.*

2. The Participating Institution shall maintain a FWA.

3. The Participating Institution shall administratively assess and approve the Study. The Participating Institution shall not approve the Study unless:

    i. the Participating Institution PI has access to the resources necessary to conduct the Study;

    ii. the Participating Institution PI has completed Participating Institution mandatory clinical research training and if a physician, has been credentialed by the Participating Institution or its hospital's Medical Affairs Committee;

    iii. it has entered into appropriate contractual agreements with funders, sponsors and/or other institutions in which Study budget has been reviewed and financial conflict of interest has been addressed.

4. The Participating Institution will notify Participating Institution PI if it is unable to approve a Study. The Participating Institution will notify REB Host Institution's REB and Participating Institution PI if it suspends or terminates institutional approval for a Study.* For greater certainty, although REB Host Institution may approve the ethical aspects of the Study, the final decision to conduct the Study at the Participating Institution rests with the Participating Institution.

**III. <u>The Responsibilities of the Participating Institution PI</u>:**

1. Participating Institution PI agrees to conduct the Study in accordance with the REB approved Study protocol and in compliance with all Applicable Laws and Participating Institution and REB policies, procedures, and requirements.

Participating Institution PI further agrees to assume full responsibility for the scientific and ethical conduct of the Study at the Participating Institution. Participating Institution PI certifies that they will comply with all REB determinations with respect to the Study and obtain REB approval and all applicable Participating Institution authorizations prior to commencing the Study.

2. Participating Institution PI shall ensure they, as well as all research team members (which may include sub-investigators) at Participating Institution, are appropriately qualified and experienced and will undergo appropriate training to fulfill their respective roles in this Study. Participating Institution PI shall promptly report to the Participating Institution and REB any information that would indicate that their qualifications or those of any of the research team are no longer appropriate to the Study.

3. Using CTO Stream, Participating Institution PI shall (i) review REB materials submitted by the provincial applicant, (ii) certify all local information submitted to the REB is complete, current and an accurate description of the conduct of the Study at the Participating Institution, (iii) ensure all REB approved provincial changes are implemented at the Participating Institution when relevant, (iv) certify that they and the members of the research team will adhere to the current protocol and consent form as approved by the REB and any conditions placed on the REB approval, and (v) promptly report to the REB all local reportable events as required by protocol and/or the REB, including but not limited to local unexpected serious adverse events, protocol deviations and any new information that may adversely affect the safety of the participants or significantly affect the conduct of the Study.

4. The Participating Institution PI shall ensure that privacy breaches and communication or findings that would be relevant to the conduct or REB oversight of the Clinical Study shall be promptly reported to the Participating Institution in accordance with Participating Institution policies and procedures and to the REB.

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* Managed through CTO Stream