COLLABORATIVE RESEARCH AGREEMENT FOR THE RESEARCH PROJECT

« Development of protein- and cell-based vaccines using the Accum™ technology »

(hereinafter referred to as the « **Agreement** »)

BETWEEN: **UNIVERSITÉ DE MONTRÉAL**, a legal person duly constituted by virtue of the *Law constituting in incorporation the University of Montreal* having its main office at 2900 Édouard-Montpetit, Montréal, Québec, H3T 1J4, hereby represented by its Acting Director-Contracts and Partnerships, Martine Haviernick, duly authorized as she so declares,

(hereinafter referred to as « **UdeM** »)

AND: **DEFENCE THERAPEUTICS INC.**, a legal person duly constituted under the laws of the Province of British Columbia, having its main office at 1680 - 200 Burrard Street, Vancouver, BC, V6C 3L6, hereby represented by Sébastien Plouffe, President and CEO, duly authorized as he so declares,

(hereinafter referred to as « **Defence Therapeutics** »)

(UdeM and Defence Therapeutics are hereinafter referred to individually as a « **Party** » and collectively as « **Parties** »).

RECITALS

WHEREAS Defence Therapeutics is a biotechnology company engaged in the business of research and development focusing on vaccine development and on enhancing delivery of tumor-specific therapeutic drugs;

WHEREAS Defence Therapeutic as developed a new technology enable to enhance immune response (« **Accum™** »), as described in Appendix B thereafter, that needs to be validated with *in vitro* and *in vivo* studies;

WHEREAS UdeM and Defence Therapeutics wish to collaborate to carry out a collaborative research project entitled « Development of protein- and cell-based vaccines using the Accum™ technology » (the « **Project** »);

WHEREAS Defence Therapeutics has agreed to make a cash contribution equivalent to fifty-four thousand six hundred and eight Canadian dollars and forty cents ($54,608.40 CA) including 40% of overhead cost for the execution of the Project;

WHEREAS during the course of the Project it is expected that, amongst other things, intellectual property and related matters as well as publication issues may arise;

WHEREAS the Parties under this Agreement wish to establish and define their respective rights, obligations and interests with respect to the Project;

THE PARTIES AGREE AS FOLLOWS:

Article 1 - Definitions

As used herein, the following terms shall have the following meanings:

1.1 « **Agreement** » shall mean this Collaborative Research Agreement.

1.2 « **Background Intellectual Property** » shall mean any and all Intellectual Property rights and any other information, whether or not patentable, created, obtained, conceived or made by one Party before or outside its performance in the Project.

1.3 « **Confidential Information** » shall mean all information which is confidential and which is disclosed to a Receiving Party by a Disclosing Party under this Agreement. In order to be considered as Confidential Information, information disclosed by the Disclosing Party in writing or electronically must be designated as « Confidential » at the time of disclosure and must include a disclosure date. Confidential Information disclosed by the Disclosing Party visually or orally must be stated to be as such at the time of disclosure and shall be confirmed in writing within fifteen (15) days from the date of disclosure and marked with the word « Confidential », dated and delivered to the Receiving Party.

1.4 « **Disclosing Party** » shall mean a Party that discloses Confidential Information to the other Party under this Agreement.

1.5 « **Intellectual Property** » means, without limitation, all technologies, research results, software, documentation, drawings, specifications, user manuals, materials, compounds, procedures, databases and any related works; all inventions, devices, discoveries, concepts, algorithms, formulae, processes, techniques, systems and improvements, whether registered or unregistered.

1.6 « **Material** » shall mean all tangible research materials that Defence Therapeutics transfers to UdeM for use in the Project and which are listed in Appendix B thereafter.

1.7 « **Methods** » shall mean any and all method, including Protocol, or improvement to method or Protocol, developed by UdeM in the course of the Project and related know-how thereof.

1.8 « **Project** » shall mean the research project as more fully described in Appendix A hereof.

1.9 « **Project Intellectual Property** » shall mean all Intellectual Property that is created, obtained, conceived or made in performing the Project and includes Results and the Final Report, if completed.

1.10 « **Protocol** » shall mean the protocol developed by UdeM and used in furtherance of the Project as more fully described in Appendix A hereof.

1.11 « **Receiving Party** » shall mean a Party that receives Confidential Information from the other Party under this Agreement.

1.12 « **Results** » shall mean all results created in carrying out the Project, excluding the Methods.

Article 2 – Purpose of the Agreement and Term of the Agreement

2.1 UdeM, in collaboration with Defence Therapeutics, undertakes to carry out the Project, as described in Appendix A, the whole in accordance with the provisions provided under this Agreement.

2.2 Notwithstanding the date of its execution by the Parties, the Agreement shall become effective on December 1st, 2020 (the « **Effective Date** ») and shall expire on December 31st, 2021 (the « **Expiration Date** ») unless terminated sooner in accordance with the provisions of Article 10.

2.3 After expiry or termination of the Agreement, the provisions of Article 6 (Confidentiality) shall remain in force for three (3) years and Articles 7 (Intellectual Property, Copyrights, and Reserved Rights), Article 8 (Publications) and Article 11 (Liability, Indemnification, Disclaimer of Warranty and Non-Endorsement) shall remain in force indefinitely.

Article 3 – Principal Investigator and technical representative of Defence Therapeutics

3.1 The Project shall be performed under the responsibility of Dr Moutih Rafei, Associate Professor at the Department of Pharmacology and Physiology of UdeM (hereinafter referred to as « **Principal Investigator** »).

3.2 Principal Investigator will be responsible for the scientific content of the Project.

3.3 In the event that the Principal Investigator becomes unable or unwilling to continue its work for the Project, and a mutually acceptable substitute is not available, each Party shall have the option to terminate the Agreement in accordance with the provisions set forth in Article 10.

3.4 The technical representative of Defence Therapeutics will be Dr. Simon Beaudoin, Chief Technical Scientific Officer.

Article 4 – Cash contribution to the Project, Payment schedule, Defence Therapeutics' Obligation and Use of Material

4.1 Defence Therapeutics shall pay to UdeM the total amount of fifty-four thousand six hundred and eight Canadian dollars and forty cents ($54,608.40 CA) including forty (40%) percent of overhead cost for the execution of the Project (hereinafter the « **Cash Contribution** »). The Cash Contribution shall be paid according to the following schedule:

a) Twenty-seven thousand three hundred and four Canadian dollars and twenty cents ($27,304.20 CA) becomes payable upon the execution of the Agreement and is due within thirty (30) days following the receipt of an invoice from UdeM;

b) Thirteen thousand six hundred and fifty-two Canadian dollars and ten cents ($13,652.10 CA) becomes payable six (6) months after the Effective Date and is due within thirty (30) days following the receipt of an invoice from UdeM;

c) Thirteen thousand six hundred and fifty-two Canadian dollars and ten cents ($13,652.10 CA) becomes payable upon receipt of the Final Report and is due within thirty (30) days following the receipt of an invoice from UdeM.

4.2 Extra costs and additional work: UdeM shall not be required to perform any tasks that would result in costs in excess of the Cash Contribution from Defence Therapeutics or that are not described in Appendix A.

4.3 For any Material sent to UdeM, Defence Therapeutics will provide UdeM with all known safety information related to the use of the Material.

4.4 The Material shall be used solely for the purpose of the Project as described in Appendix A hereunder. Any new use of the Material must be agreed upon in writing by the Parties and reflected by way of a modification to the Agreement in accordance with Section 12.4.

Article 5 – Reports and Final Report

5.1 UdeM will prepare and send to Defence Therapeutics a final report on or before the Expiration Date (« **Final Report** »).

5.2 The Final Report shall present (i) the Results (ii) all patent applications, if applicable, and (iii) a financial report for the Project. If Defence Therapeutics considers that the report is incomplete, it shall send its comments in writing to UdeM no later than thirty (30) days following the receipt of the Final Report by explaining the reasons why it considers the Final

Report incomplete. Then the Parties shall agree on (i) additions to make to the Final Report and (ii) the extension to the term of the Agreement to allow UdeM to make such additions to the Final Report. However, if Defence Therapeutics does not send written comments to UdeM within thirty (30) days upon receipt of the Final Report, the Final Report shall be considered complete, satisfactory and accepted by Defence Therapeutics.

Article 6 – Confidentiality

6.1 A Party may, from time to time, disclose to the other Party Confidential Information in connection with the Project. Unless being requested to disclose any Confidential Information because of a legal obligation or a court order, or having the prior written consent of the Disclosing Party, each Party agrees to hold in confidence any Confidential Information of the Disclosing Party and not to use the Disclosing Party's Confidential Information for any purpose except in furtherance of the Project.

6.2 The obligation of confidentiality shall not, however, apply to information which:

6.2.1 was known to the Receiving Party prior the time of disclosure by the Disclosing Party, as, if requested, can be demonstrated by competent written evidence;

6.2.2 is in, or becomes part of, the public domain other than by breach of this Agreement by the Receiving Party;

6.2.3 is legally provided to the Receiving Party in good faith by a third party at arm's length; and

6.2.4 is independently developed by students, employees or agents of the Receiving Party, who did not access or use the Confidential Information of the Disclosing Party, as demonstrated by competent proof.

6.3 Each Party shall be entitled to disclose the Confidential Information to the extent it is required to disclose it under applicable laws or regulations or by an order by a court or government agency having competent jurisdiction; provided, however, that the Receiving Party shall give the Disclosing Party reasonable prior notice of such disclosure requirement and shall afford the Disclosing Party a reasonable opportunity to oppose, limit or secure confidential treatment for such required disclosure before disclosing such Confidential Information and, to the extent possible, make any required disclosure in consultation with the Disclosing Party.

6.4 The provisions of this Article 6 shall remain in force for a period of three (3) years after the expiry or termination of the Agreement.

6.5 **Project IP Disclosure**: None of the Parties will publicly disclose the Project Intellectual Property except as permitted under this Section. UdeM may disclose Project Intellectual Property in connection with publications under Article 8. Defence Therapeutics may disclose Project Intellectual Property in connection with an application for protection of Project

Intellectual Property (e.g., patent application) under Article 7 and as necessary or useful to exploit its rights in Project Intellectual Property as set forth in this Agreement, provided that Defence Therapeutics shall not make any such disclosure in a manner that would have a material adverse effect on the ability of the Principal Investigator to publish Project Intellectual Property under Article 8.

Article 7 - Intellectual Property, Copyrights and Reserved Rights

7.1 Each Party owns all rights, and interest in and to its Background Intellectual Property and no licenses are granted with respect to its Background Intellectual Property in this Agreement, whether by implication, estoppel or otherwise. Each Party hereby grants to the other Party a non-exclusive right of use of its Background Intellectual Property which it, through its researchers, has introduced into the Project which is otherwise unencumbered for the sole purpose of realizing the Project, for the term of the Agreement. The list of elements of Background Intellectual Property used in the scope of the Project is attached as Appendix B. If, during the Project, an undeclared Background Intellectual Property is to be used, the Parties shall be informed promptly and an amendment to the Agreement shall be executed in order to update the Appendix B.

7.2 Subject to Sections 7.4 and 7.5, UdeM hereby irrevocably and automatically assigns to Defence Therapeutics all right, title and interest in and to all Project Intellectual Property arising from the Project immediately upon creation thereof. Defence Therapeutic will have sole responsibility and control for securing any available protection (e.g., patent applications) for Project Intellectual Property at its sole expense.

7.3 Material is to be and shall remain the exclusive property of Defence Therapeutics.

7.4 UdeM may make improvements related to the Methods used to perform the Project. If Intellectual Property is created in respect of one of the Methods, it will belong entirely to UdeM (the « **UdeM Intellectual Property**»).

7.5 **Copyrights**. All students, trainees, postdoctoral fellows (hereinafter referred collectively as « **Students** ») involved in the research activities of the Project shall retain copyright in respect of their master's theses or doctoral theses and, in the cases of trainees and postdoctoral fellows, of their training period report. All researchers and Students involved in the research activities of the Project shall retain copyright in respect of all presentations, conferences and all publications regarding the Project.

7.6 **Reserved Rights**. Subject to Article 6 (Confidentiality) and Article 8 (Publications) and notwithstanding any grant of rights in the Agreement, Defence Therapeutics hereby grants to UdeM, as of the date any Project Intellectual Property is created, developed, improved or modified or reduced to practice, a non-exclusive, royalty-free, perpetual license to use Project Intellectual Property solely for its internal non-commercial research, educational purposes and publication under terms and conditions that will not interfere with efforts to commercialize the Project Intellectual Property. UdeM hereby grants to Defence Therapeutics, as of the date any

UdeM Intellectual Property is created, developed, improved or modified or reduced to practice, a non-exclusive, royalty-free, perpetual license to use UdeM Intellectual Property solely for its internal non-commercial research.

Article 8 - Publications

8.1 The Parties recognise that under UdeM's rules and policies, the Project Intellectual Property, including Results, must be publishable and agrees that the Principal Investigator, or any member of its research team, shall be permitted to present at symposia or meetings, and shall be permitted to publish the Results and Project Intellectual Property (the « **Proposed Disclosure** ») provided, however, that Defence Therapeutics shall first receive a copy of any Proposed Disclosure at least thirty (30) days prior to the submission of such Proposed Disclosure. If Defence Therapeutics does not object, with a written notice, to the Proposed Disclosure fifteen (15) days following the receipt of the Proposed Disclosure (the « **Review Period** »), UdeM will be free to proceed with the Proposed Disclosure. The Parties understand that the only reasons for which Defence Therapeutics may object to a Proposed Disclosure are the followings: (i) the presence of Defence Therapeutics' Confidential Information in the Proposed Disclosure; and (ii) the presence of patentable Project Intellectual Property in the Proposed Disclosure.

8.2 During the Review Period, in the event that the Proposed Disclosure includes Defence Therapeutics' Confidential Information, Defence Therapeutics may request in writing that UdeM removes from the Proposed Disclosure all Defence Therapeutics' Confidential Information.

8.3 During the Review Period, Defence Therapeutics can object, by a written notice to such Proposed Disclosure if it contains patentable or otherwise protectable Project Intellectual Property. If this case happens, Defence Therapeutics may request that the Proposed Disclosure be postponed, and UdeM shall postpone, for a maximum of three (3) months after the receipt of the Proposed Disclosure (the « **Patent Delay** ») in order to file patent application directed to the patentable subject matter contained in the Proposed Disclosure.

8.4 Subject to confidentiality obligations of Article 6, no Proposed Disclosure may be postponed for longer than three (3) months following the receipt by Defence Therapeutics of the Proposed Disclosure.

8.5 Notwithstanding anything otherwise contained in this Agreement, the Parties acknowledge that the defense of a student's thesis shall not be postponed on the grounds that it contains patentable matter but the concerned Party may request that such defense be made in confidence if it is to be made during the Patent Delay.

8.6 Article 9 - Default

For the purposes hereof, a Party shall be in default if any of the following events occurs:

9.1 if a Party commits a material breach of any of the terms or conditions of this Agreement, and fails to remedy such breach within thirty (30) days after receipt of written notice from the other Party stating the material breach and demanding that such material breach be remedied.

9.2 if it violates the law so that compromising the performance of the Agreement or could in any way harm the reputation, integrity or position of the other Party, or tarnish its image;

9.3 if it ceases to exist, discontinues its activities for more than six (6) months, or assigns a material portion of its assets to a third party; or

9.4 if it becomes insolvent or bankrupt or makes a proposal under the *Bankruptcy Act* or the *Companies' Creditors Arrangement Act* or liquidates its assets.

Article 10 - Termination

10.1 If a Party is in default under Section 9.1 above, the Agreement shall terminate as of right on the deadline stated in the notice of default.

10.2 If a Party is in default under any of Sections 9.2, 9.3 or 9.4 above, the Agreement shall terminate as of right on the date the default occurs.

10.3 Each Party may terminate this Agreement immediately upon written notice to the other Party in the event that the Parties cannot agree on a replacement on Principal Investigator under Section 3.3.

10.4 Any termination shall have the following consequences:

10.4.1 if termination is sought by the UdeM under Article 3.3 or Article 9, UdeM shall complete all of the work planned to be done prior to the date of such written notice based on the Project schedule presented in Appendix A;

10.4.2 Defence Therapeutics shall pay all amounts that it owes to UdeM, including all costs incurred by the UdeM up to the termination date and any amounts that UdeM has committed to pay prior to the termination date, less any amounts Defence Therapeutics may have overpaid to UdeM;

10.4.3 UdeM shall send to Defence Therapeutics the report referred to in Article 5 on the portion of the Project that was completed up to the termination date;

10.4.4 the Parties shall retain all of the rights to which they are entitled hereunder in connection with the Project Intellectual Property, Methods and Results existing as at the termination date; and

10.4.5 the Receiving Party shall, at the instruction of the Disclosing Party either return or destroy all tangible manifestations of the Disclosing Party's Confidential Information and all Disclosing Party's Materials, where applicable, except that each Party may retain one copy of Confidential Information in its secure archives to monitor its obligations

under this Agreement and no Party shall have an obligation to delete Confidential Information stored in routine computer backup archives.

Article 11 – Liability, Indemnification, Disclaimer of Warranty and Non-Endorsement

11.1 Liability and Indemnification

Each Party (the « **Responsible Party** ») shall indemnify and save harmless the other Party, its directors, officers, agents and employees (collectively, the « **Indemnified Party** ») from any and all damages, liabilities, claims, losses or costs sustained by the Indemnified Party (the « **Damages** ») caused by the fault, including negligence or wilful misconduct of the Responsible Party, including the persons or property who are under the Responsible Party's control, pursuant to its default to comply with its obligations under the terms of this Agreement or under the law, unless the Damages are caused by the fault of the Indemnified Party, including any person or property who are under the Indemnified Party's control, or by a breach by the Indemnified Party of its obligations hereunder or of its legal obligations. A Party requiring indemnification shall give a prompt notice of the concerned claim to the Responsible Party, and provide all reasonable assistance in order to the Responsible Party to produce a defence or settle the claim.

11.2 Disclaimer of Warranty

Each Party to this Agreement acknowledges that any and all Project Intellectual Property, including information, Background Intellectual Property, Methods and other tangible and intangible materials that it may receive pursuant to this Agreement are to be used with caution and prudence, since all of their characteristics are not known. Each Party disclaims all liability for any damages however arising from the other Party's use of such Project Intellectual Property and/or Background Intellectual Property and/or Methods. Each Party further acknowledges that such Project Intellectual Property, information, Background Intellectual Property, Methods and other tangible or intangible materials are provided without warranty of merchantability or fitness for a particular purpose or any other warranty of any sort, express or implied, and that the provider makes no representations that the use of the same will not infringe any patent or other proprietary right.

11.3 Non-Endorsement

The realization of the Project by the UdeM does not constitute an endorsement of the products and services of Defence Therapeutics on behalf of UdeM and consequently, any summary, publication, presentation, reproduction or other type of dissemination of the report, as referred to in Article 5, or any other report or the Results, resulting from this Agreement by Defence Therapeutics shall not mention the participation of UdeM, its employees or representatives including the names of the Principal Investigator without the prior written consent of the UdeM as stated in Section 12.5 thereafter.

Article 12 - General Provisions

12.1 The Recitals, the Appendix A - « Description of the Project and Budget » and the Appendix B - « Description of Background Intellectual Property » hereto form part of the Agreement.

12.2 **Successors and Assigns.** This Agreement can be assigned or transferred only with the prior written approval of the Parties. The case arising, the rights and obligations of the Parties in virtue of this Agreement also bind their successor and assignees.

12.3 **Relationship between the Parties.** Each of the Parties recognizes and agrees that the relationship created by this Agreement shall be that of independent contractor without the authority to assume nor create any obligation in the other's name, either expressly or implicitly, except that which is strictly and expressly provided for in this Agreement. Each Party also recognizes and agrees that it has no authority to bind the other Party in any way, nor to incur the other's liability.

12.4 **Entire Agreement; Modifications.** This Agreement embodies the entire understanding of the Parties and supersedes any other agreement or understanding between the Parties relating to the subject matter hereof. There are no additional or supplemental agreements related to the subject matter hereof. Modifications to the Agreement will not be binding unless made in writing and signed by the Parties.

12.5 **Name of the Parties.** No Party shall have the right to use the name, logo or any trademarks, or the name of one of the members or employees, of the other Party for any purpose without their prior written consent. Notwithstanding the foregoing, UdeM may disclose the existence of this Agreement, including the name of the Principal Investigator, other Party's name, the nature and the term of the Agreement in any statement of fact routinely disclosed as part of UdeM's responsibility for openness as a non-profit, educational institution or as required by law.

12.6 **Notices.** Any demand, notice or other communication hereunder shall be deemed made if given by registered or certified envelope, postage prepaid, and addressed to the Party to receive such demand, notice, or other communication at the address given below, or such other address as may hereafter be designated by notice in writing:

If to UdeM:

Martine Haviernick
Acting Director – Contracts and Partnerships
Bureau Recherche-Développement-Valorisation (BRDV)
Université de Montréal
Ph: 514-343-6111 ext 36883
e-mail: martine.haviernick@umontreal.ca

If by courier:

Université de Montréal
Bureau Recherche-Développement-Valorisation (BRDV)

3744, Jean-Brillant, bureau 6320
Montréal (Québec)
H3T 1P1

If by regular mail: Université de Montréal
Pavillon 3744 Jean-Brillant
Bureau Recherche-Développement-Valorisation (BRDV)
C.P. 6128, Succursale Centre-ville
Montréal (Québec)
H3C 3J7

Defence Therapeutics Inc.: Sebastien Plouffe
President and CEO
1680 - 200 Burrard Street
Vancouver, BC, V6C 3L6
Ph.: (514) 947 – 2272
Email: info@defencetherapeutics.com

12.7 **Waiver.** No failure on the part of either Party to exercise, and no delay in exercising, any right or remedy hereunder shall operate as a waiver hereof, nor shall any single or partial exercise of any right or remedy hereunder preclude any other or a future exercise thereof or the exercise of any other right or remedy granted hereby or by any related document or by law.

12.8 **Severability.** If, for any reason, any provision of this Agreement is determined to be invalid or unenforceable in whole or in part, such invalidity or unenforceability shall not affect the remaining terms and provision of this Agreement and the remainder of the Agreement shall be enforced to the fullest extent.

12.9 **Governing Law.** This Agreement shall be governed by the laws of Québec and by the laws of Canada applicable therein and any dispute arising from the Agreement shall be decided by the courts of Québec in the district of Montréal.

12.10 **Electronic Signatures.** The Parties agree that any xerographically or electronically reproduced copy of this fully-executed Agreement will have the same legal force and effect as any copy bearing original signatures of the Parties.

IN WITNESS WHEREOF, the Parties have executed the Agreement as of the Effective Date.

UNIVERSITÉ DE MONTRÉAL

By: Martine Haviernick
Signature numérique de Martine Haviernick
Date : 2020.12.14 14:52:38 -05'00'

Martine Haviernick
Acting Director-Contracts and Partnerships

DEFENCE THERAPEUTICS INC.

By: _____
Sébastien Plouffe
President and CEO

Principal Investigator's Declaration

I, undersigned, Moutih Rafei, Associate Professor at the Department of Pharmacology and Physiology of the Université de Montréal, declare:

1- I have read this Collaborative Research Agreement;

2- I am the Principal Investigator designated in this Collaborative Research Agreement;

3- I shall abide by all provisions contained in the Collaborative Research Agreement that concern me;

4- I undertake to disclose promptly in writing to the Office of Research Services and Development (BRDV) of Université de Montréal all inventions, discoveries, improvements or achievements related directly to the Project and which are Methods and that have been developed, created or obtained in the framework of its realization thereof;

5- I hereby, assign to the Université de Montréal all rights that I could hold on all inventions, discoveries, improvements or achievements related directly to the Project and designed, developed, created or obtained in the framework of its realization so that the Université de Montréal can meet its obligations under the Collaborative Research Agreement;

6- I shall have all the researchers and other personnel from Université de Montréal informed of their obligations under this Collaborative Research Agreement and take all reasonable measures to have them act accordingly;

7- If necessary, I undertake to obtain all applicable certificate and (or) authorization for the Project, including those which require the use of humans, animals or involve biological or environmental risks;

8- I agree to sign any documents and take any action that could reasonably be required by the Université de Montréal to implement the provisions of this representation.

I have signed in MONTREAL,

Moutih Rafei
Associate Professor

08/12/2020
Date

Appendix A

Description of the Project and Budget

List of experiments for Defense Therapeutics Inc.

Defense Therapeutics Inc. has recently acquired a technology, which consists of modifying a given antigen for enhanced uptake and access to the cytoplasm of cells. As a result, captured antigens can be efficiently processed by the proteasomal machinery leading to the generation of potent and effective immune response. To validate this hypothesis, a series of *in vitro* and *in vivo* studies will be proposed in the herein contract for the upcoming year.

➢ **Antigen Presentation Assays (*in vitro* studies)**

Our laboratory has established and optimized the use of *ex vivo* generated dendritic cells (DCs) for antigen presentation. As such, the first set of experiment consists of testing various ovalbumin (OVA) formulations using the Accum^{TM} technology at various ratios (50X, 25X and 10X). The idea would be to treat DCs with the Accum-OVA or naked OVA then co-culture pulsed DCs with CD8 T lymphocytes derived from the spleen of OT-I transgenic mice (specific to the OVA-derived peptide SIINFEKL). The final outcome consists of conducting an ELISA to quantify IFN-gamma levels. In addition, analysis of SIINFEKL/H2-K^{b} presence on the surface of DCs will be assessed by flow-cytometry. This would demonstrate how potent is the technology at presenting immunogenic peptides.

Reagents needed:

- Antigen with the formulation (to be provided by the Defense Therapeutics Inc.)
- Reagents to generate DCs (Mice, recombinant GM-CSF - $1,500.00 CA)
- IFN-gamma ELISA ($750.00 CA)
- OT-I mice ($256.00/unit x 5 = $1,280.00 CA)
- Antibody for flow-cytometry ($356.00 CA)
- Flow-cytometry use ($60.00/hr x 5 hrs = $300.00 CA)

Total cost for this set of experiment: $4,186.00 CA

➢ **Autologous Prophylactic Vaccination (*in vivo* studies)**

To confirm the *in vitro* data, animal vaccination will be conducted to demonstrate potent activation of the immune system. Two sets of studies will be needed for this purpose.

In the first set, wild-type C57BL/6 mice (n=10/group) will be immunized with Accum-OVA-pulsed DCs using various doses (10^5, 10^4, 10^3 and 10^2 cells/dose) and routes (sub-cutaneously versus intraperitoneally). Immunization will be conducted on days 0 and 14. One week following the second immunization, animals will be challenged with 5 x 10^5 EG.7 tumor cells (OVA-expressing lymphoma cells). Tumor growth and survival will be then followed until reaching endpoints (tumor ulceration and/or tumor volume reaching >1000 mm^3). The condition leading to the best protective effect will be used thereafter.

Reagents needed:

- Antigen with the formulation (to be provided by the Defense Therapeutics Inc.)

- Reagents to generate DCs (Mice and recombinant GM-CSF - $1,500.00 CA)
- C57BL/6 mice ($34.00/unit x 100 = $3,400.00 CA)

Total cost for this set of experiment: $4,900.00 CA

Following the identification of the best dosing and routing, characterization of the immune response generated by the vaccine will be conducted. For this purpose, wild-type C57BL/6 mice will be vaccinated as detailed above but using a single dose and one route (to be determined). Two weeks following the second immunization, all spleens will be isolated and re-stimulated *in vitro* to trigger the secretion of various chemokines and cytokines. Three days later, the supernatants derived from activated splenocytes will be analyzed by luminex to screen for more than 30 cytokines/chemokines.

Reagents needed:
- Antigen with the formulation (to be provided by the Defense Therapeutics Inc.)
- Reagents to generate DCs (Mice and recombinant GM-CSF - $1,500.00 CA)
- C57BL/6 mice ($34.00/unit x 30 = $1,020.00 CA)
- Luminex analysis ($2,850.00 CA)

Total cost for this set of experiment: $5,370.00 CA

➢ **Allogeneic Prophylactic Vaccination (*in vivo* studies)**

The design of an effective vaccine does not only entail eliciting potent immunity, but it has also to be highly translatable to the clinic and appropriate for manufacturing. Therefore, the ideal DC-based vaccine would have to be "universal", which means derived from genetically distinct or mismatched subjects (allogeneic). For this purpose, DCs will be generated from Balb/c mice then used to vaccinate C57BL/6 mice ($H2^d \rightarrow H2^b$). Vaccinated animals will be then challenged as previously detailed and tumor growth will be followed thereafter using the same parameters explained above. Once completed, the immune response triggered by allogeneic vaccination will be characterized as done with the autologous vaccine).

Reagents needed:
- Antigen with the formulation (to be provided by the Defense Therapeutics Inc.)
- Reagents to generate DCs (Mice and recombinant GM-CSF - $1,500.00 CA)
- Balb/c mice ($34.00/unit x 10 = $340.00 CA)
- C57BL/6 mice ($34.00/unit x 40 = $1,360.00 CA)
- Luminex analysis ($2,850.00 CA)

Total cost for this set of experiment: $6,050.00 CA

Highly qualified personnel (HQP) salary

A PhD student will dedicate 50% of his time to work on the *in vitro* and *in vivo* studies related to the vaccine project. A stipend of $10,000.00 CA will be required to cover his salary for the entire year.

General laboratory reagents

The cost related to the purchase of molecular biology reagents, chemicals, cell culture media and plastic ware is estimated to be $5,000.00 CA.

Publications

We anticipate that the results generated by this study would lead to at least 1 publication in a peer-reviewed journal. The cost associated nowadays to publish in an open-access journal is $3,500.0 CA.

Total cost of the Project: $39,006.00 CA + $15,602.40 CA (40% overheads) = $54,608.40 CA

Gantt Chart for the Project:

				Schedule													
				2020		2021											
				No	De	Ja	Fe	Ma	Ap	Ma	Ju	Jul	Au	Se	Oc	No	De
	Studies	**Member in charge**	**Duration**														
1	*In vitro* studies	PI/PhD student*	2 months														
2	Autologous vaccination (dosing and routing)	PI/PhD student	3 months														
3	Immune response characterization	PI/PhD student	2 months														
4	Allogeneic vaccination	PI/PhD student	6 months														

*PI = Principal Investigator as defined in Section 3.1 of this Agreement

Appendix B

Description of Background Intellectual Property

UdeM's Background Intellectual Property:

- Know-how and knowledge of Principal Investigator's lab, including but not limited to, the use of dendritic cells (DCs) for antigen presentation
- Protocol described in Appendix A

Defence Therapeutics' Background Intellectual Property:

All proprietary rights provided under applicable law relating to the Accum Technology, which includes but not limited to, patents in Canada (patent no CA3017950Al), the United States (patent no US20190077879A1), Japan (patent no JP20195 I 2545A), Israel (patent no IL26 1 765D0), Australia (patent no AU2017233725AI), and Europe (patent no EP3430060Al).

Material that will be sent to UdeM in furtherance of the Project:

- 100 mg of Antigen with the formulation