

## CONSULTANT SERVICES AGREEMENT

**THIS AGREEMENT** is dated effective September 18, 2020 (the "**Effective Date**").

**BETWEEN:**

**DEFENCE THERAPEUTICS INC.**, a company  
incorporated under the laws of the Province of British  
Columbia;

(the "**Corporation**")

**AND:**

**AXIOM SERVICES INC.**, a company  
incorporated pursuant to the laws of the Province  
of Québec;

(the "**Consultant**")

**WHEREAS:**

- (A) The Corporation is a pre-clinical stage biopharmaceutical company engaged in the business of research and development of novel drug delivery systems focusing on enhancing delivery of tumor-specific therapeutic drugs;
- (B) Consultant has the expertise and qualifications required to perform the Services (as defined herein) contemplated by this Agreement; and
- (C) the Corporation wishes to retain Consultant to perform such services, and Consultant wishes to be retained to perform such services, on the terms and conditions set out in this Agreement.

**NOW THEREFORE THIS AGREEMENT WITNESSES THAT** in consideration of the mutual covenants and agreements contained in this Agreement and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties agree as follows:

**1. Term**

- 1.1 This Consultant Services Agreement (the "**Agreement**") commences on September 17, 2020 and, unless terminated earlier in accordance with its terms, will expire on the earlier of: (i) the completion of all work and reporting as set out

in Schedule A: Study Proposal (the "**Study**"), and September 17, 2021 (the "**Term**").

- 1.2 For the avoidance of doubt, this Agreement terminates and replaces any existing services agreement ("**Existing Agreement**") between the parties.
- 1.3 The parties by mutual agreement in writing, at least 30 days prior to the expiry of the Term, may agree to renew the consultant services relationship by executing a new agreement.

## **2. Consultant's Obligations**

- 2.1 The Consultant will provide the Corporation with all the services (the "**Services**") required to complete the Study:
  - (a) with all due care and skill and to the best of the Consultant's knowledge and expertise;
  - (b) in compliance with all applicable laws;
  - (c) in a manner consistent with the best interests of the Corporation;
  - (d) in accordance with the terms of this Agreement; and
  - (e) devoting such time and attention as may be necessary for the proper performance of the Services.
- 2.2 The Consultant will, as and when required by the Corporation, report to the Corporation in the form required by the Corporation on the status and progress of the Services.
- 2.3 If the Corporation provides or allows the Consultant to use the Corporation's materials or equipment in connection with the provision of the Services, the Consultant:
  - (a) is responsible for the materials and equipment (including any loss or damage to it) for as long as the equipment is in the possession or control of the Consultant; and
  - (b) must promptly return the materials and equipment once the Services for which the material and equipment was being used have been completed.

- 2.4 The Consultant must not bind, and must ensure that its employees, agents and contractors do not bind, the Corporation or any of its Related Corporations (as defined herein) in contract or otherwise.
- 2.5 The Consultant will provide the Services at a location, place and time which Consultant deems appropriate, which may include working on the premises of the Corporation or a Related Corporation from time to time.

### **3. Key Personnel**

- 3.1 The Consultant must ensure that the Services are performed by the Key Personnel (as defined herein).
- 3.2 The Consultant may only change the Key Personnel with the prior written approval of the Corporation. The Corporation may withhold this approval in its absolute discretion.
- 3.3 The Consultant must ensure that all Key Personnel:
- (a) use their best efforts to do all things necessary to give full effect to this Agreement;
  - (b) refrain from doing anything that may hinder performance of this Agreement;
  - (c) act in accordance with this Agreement;
  - (d) act with all due care and skill and to the best of their knowledge and expertise;
  - (e) act in accordance with any directions given by any person nominated by the Corporation from time to time;
  - (f) act in compliance with all applicable laws;
  - (g) act in a manner consistent with the Corporation's best interests; and
  - (h) execute a Confidentiality and Intellectual Property Agreement ("CIPA") as set out in Schedule C on commencement of their involvement in the Services (and the Consultant will provide an executed copy of each CIPA to the Corporation).

### **4. Fees**

- 4.1 Subject to the Consultant providing the Services in accordance with this Agreement to the satisfaction of the Corporation, the Corporation will pay the Consultant a fee of up to \$110,675 (the "**Fee**") in accordance with the payment provisions set out in Section 4.2.
- 4.2 Fee due and owing to Consultant shall be payable as follows:
- (a) \$33,203 upon execution of this Agreement; and
  - (b) an additional \$33,202, subject to, and upon, completion of 3 aims in the Study. The work on the last 2 aims should begin when the Corporation is ready from which the total payable to the Consultant for those 2 aims will be \$44,270 representing \$22,135 per aim. Half will be payable when the work will begin on each aim and the balance upon completion of the 2 remaining aims in the study;
  - (c) Consultant will provide invoice with a statement of Services provided, and such other information as the Corporation may reasonably request, and the Corporation will pay the invoice within fifteen (15) days of receipt, by wire transfer of funds to Consultant's bank account, or by cheque, at the Corporation's discretion
- 4.3 Consultant agrees to pay and be responsible for all customary corporate source deductions payable by Consultant in connection with the performance of the Services. The Fees shall exclude all sales, value-added, excise, or other taxes or duties payable in respect of this Agreement, and the Corporation will pay and be responsible for all such taxes or duties provided that Consultant shall add same to any invoice provided to the Corporation. Any additional reimbursable expenses that may be claimed by the Consultant must be charged to the Corporation at the net invoiced cost, in accordance with Section 5.
- 4.4 All references to money in this Agreement shall mean the lawful money of Canada, except as otherwise indicated.
- 4.5 Consultant must keep complete, true, and accurate books of account and records of its performance of the Services for a period of at least three (3) years after the expiration of the Term. The Corporation may, at its expense and on reasonable prior notice, have such records audited by an independent certified public accountant reasonably acceptable to Consultant no more than once per calendar year for the purpose of verifying the payments made hereunder. The accountant shall enter into a confidentiality agreement with Consultant upon request and will disclose to the Corporation only information to verify the payments made. Any overpayments or underpayments revealed by the audit will be paid or refunded by

the applicable party within thirty (30) days after the accountant's report. If the audit reveals that the Corporation has overpaid by more than five percent (5%) of the amount due, Consultant shall pay for the cost of the audit.

- 4.6 Despite any other provision of this Agreement, the Consultant will not be entitled to any payment in respect of any period:
- (a) where the Consultant is required to provide the Services but does not do so; or
  - (b) for which the Consultant has not produced an invoice which complies with the obligations under Section 4.2.

## **5. Expenses**

- 5.1 The Corporation will pay for or reimburse the Consultant for the Consultant's reasonable expenses incurred in providing the Services and all the costs of the Study, subject to:
- (a) the Corporation approving the incurring of these expenses in advance (which approval may be withheld by the Corporation in its sole discretion);
  - (b) the Consultant providing an invoice for expenses on a calendar monthly basis;
  - (c) the Consultant providing the appropriate receipts and tax invoices; and
  - (d) the Consultant complying with any additional and reasonable requirements of the Corporation in relation to the expenses.

## **6. Insurance**

- 6.1 The Consultant must maintain, at Consultant's own expense, all necessary statutory insurances required in connection with the Services, including all necessary statutory workers compensation insurance for the Key Personnel. The Corporation will not provide any form of insurance for the benefit of the Consultant or Key Personnel in connection with the Services. The Consultant expressly agrees to assume any and all liability that may arise from any occupational accident or hazardous disease that any Key Personnel might suffer while performing the Services.

6.2 The Corporation may at any time require the Consultant to provide written proof of any insurance the Consultant is required to take out in accordance with this Agreement.

**7. Confidential Information and Intellectual Property**

7.1 The Consultant must:

- (a) keep the Confidential Information confidential, except where disclosure is permitted under Section 7.2(b); and
- (b) take whatever measures are reasonably necessary to preserve such confidentiality, including:
  - (i) take all steps necessary to safeguard the confidentiality of the Confidential Information and in no event use less than a reasonable degree of care;
  - (ii) complying with all security measures established to safeguard Confidential Information from access or unauthorized use;
  - (iii) keeping Confidential Information under the Consultant's control;
  - (iv) immediately notifying the Corporation if the Consultant, or any Key Personnel, suspects or is aware Confidential Information is being used, copied or disclosed without authorization,

and must ensure all Key Personnel do the same.

7.2 The Consultant may:

- (a) only use Confidential Information (as defined herein) for the sole purpose of providing the Services to the Corporation; and
- (b) disclose Confidential Information:
  - (i) only to persons who have signed an agreement to keep confidential the Confidential Information in a form approved by the Corporation and either:
    - (A) have a need to know (and only to the extent that each has a need to know); or

- (B) have been approved by the Corporation;
  - (ii) that the Consultant is required by law to disclose (and only to the extent so required provided it promptly notifies the Corporation to allow intervention by the Corporation, cooperates to contest or minimize the scope of disclosure, including application for a protective order, at the Corporation's expense, and limits such disclosure to the party entitled to receive Confidential Information and the scope of the legal requirement).
- 7.3 The Consultant must provide assistance reasonably requested by the Corporation in relation to any proceedings the Corporation may take against any person for unauthorized use, copying or disclosure of Confidential Information.
- 7.4 The Consultant will:
  - (a) promptly disclose in writing to the Corporation particulars of all Inventions which are Developed Materials;
  - (b) deliver to the Corporation, as and when required by the Corporation, all source materials relating to any Developed Materials; and
  - (c) from time to time, upon request by the Corporation, also provide reasonable particulars of all other Developed Materials.
- 7.5 All right, title and interest of the Consultant throughout the world in any Intellectual Property Rights (as defined herein) in any Developed Material will, as between the Corporation and the Consultant, become the property of the Corporation as absolute legal and beneficial owner without any additional payment to the Consultant for it, and the Consultant hereby agrees to assign and does assign all such right, title, and interest throughout the world to the Corporation.
- 7.6 The Consultant must, at the request and expense of Corporation and without delay, prepare, execute and deliver such instruments and do such other acts and things as may, in the opinion of the Corporation, be necessary or desirable to perfect the assignment set forth in Section 7.5, to enable the Corporation or its nominee to obtain protection of any Intellectual Property Rights in the Developed Materials in such parts of the world as may be specified by the Corporation or its nominee and to enable the Corporation to exploit and enforce any Intellectual Property Rights in the Developed Materials.

7.7 The Consultant grants to the Corporation and each of its Related Corporations (or will promptly procure the grant to the Corporation and each of its Related Corporations) a perpetual, world-wide, irrevocable, royalty-free, transferable, non-exclusive licence to:

- (a) modify, test, copy and use the Proprietary Material (as defined herein), but only to the extent necessary to allow the Corporation or the relevant Related Corporation to modify, test, exploit, copy and use the Developed Material; and
- (b) grant sublicences of the rights referred to in Section 7.7(a), but only to the extent necessary to allow sublicensees to provide services to the Corporation or the relevant Related Corporation or to perform work on the Corporation's or the relevant Related Corporation's behalf.

7.8 The Consultant acknowledges the Consultant and Key Personnel may have Moral Rights in works which the Consultant has created or may create in connection with the Services (the "**Works**"). In so far as the Consultant is able, the Consultant waives the Consultant's Moral Rights (as defined herein) in respect of the Works and shall obtain such a waiver from all authors of the Works in favour of the Corporation and each of its Related Corporations and successors and assigns. The Consultant voluntarily and unconditionally consents to the Corporation or any of its Related Corporations, and to any persons authorized by the Corporation, doing, or omitting to do, with respect to the Works, any act, including but not limited to:

- (a) reproducing, publishing, communicating, performing or adapting a Work without attributing its authorship to the Consultant;
- (b) altering a Work in anyway, whether or not the alteration is prejudicial to the Consultant's honour or reputation;
- (c) dealing in any way with a Work which has been substantially altered, or a reproduction of a Work which has been substantially altered, as the Consultant's unaltered Work,

which would otherwise infringe the Consultant's Moral Rights in one or more of the Works.

7.9 The Consultant must surrender to the Corporation or, at the Corporation's option destroy, at any time on demand all materials of any kind embodying any Confidential Information or Intellectual Property Rights relating to the business or any product or service of the Corporation or one of its Related Corporations in the

Consultant's possession or under the Consultant's control. No unauthorized copy or other record of such materials will be made or retained by the Consultant.

- 7.10 The Consultant represents and warrants to the Corporation that:
- (a) the Developed Materials are wholly original with the Consultant and do not incorporate any Intellectual Property Rights of Consultant unrelated to this Agreement or any third party (including any open-source software);
  - (b) the performance or implementation of the Services and the use of the Developed Materials by the Corporation or any of its Related Corporations does not and will not infringe the Intellectual Property Rights of any person; and
  - (c) the Consultant has full power and authority to enter into this Agreement.
- 7.11 The Consultant agrees and acknowledges that the obligations in this clause 7 also apply in their entirety to the Existing Agreement.

## **8. Termination**

- 8.1 This Agreement will terminate at the expiry of the Term, unless renewed by the parties, as set forth in Section 1.3 of this Agreement.
- 8.2 The Corporation may terminate this Agreement at any time by providing 30 days written notice to the Consultant. In such case, the Corporation will pay the Consultant, subject to and in accordance with the invoicing and payment obligations set out in this Agreement, a pro-rata amount of Fees for Services performed in accordance with this Agreement to the satisfaction of the Corporation but not yet invoiced.
- 8.3 Notwithstanding any other provision of this Agreement, the Corporation may at its sole discretion terminate this Agreement at any time with immediate effect if at any time:
- (a) the Consultant is unable for any reason to provide the Services for a period or periods aggregating at least 2 weeks;
  - (b) the Consultant fails or neglects to efficiently and diligently comply with the terms of this Agreement or is guilty of any material or persistent breach or non-observance of any provision of this Agreement; or

- (c) the Consultant is guilty of any other conduct calculated or likely to affect prejudicially the interests of the Corporation.
- 8.4 On termination of this Agreement, the Consultant must return all property of the Corporation (including documents recording any information belonging to the Corporation or containing or recording Confidential Information).
- 8.5 During the period of 24 months after termination of this Agreement, the Consultant must not:
  - (a) solicit, canvass, approach or accept any approach from or deal with any person who was, during the term of this Agreement, a customer of the Corporation or its Related Corporations with a view to obtaining the custom of that person for any competitor;
  - (b) interfere with the relationship between the Corporation or its Related Corporations, and their respective customers, employees, or suppliers; or
  - (c) induce or assist in the inducement of any employee of the Corporation to leave their employment.
- 8.6 The Corporation may require the Consultant to provide evidence confirming to the satisfaction of the Corporation that the Consultant is not in breach of Section 8.5. The Consultant acknowledges that each restriction specified in Section 8.5 is in the circumstances reasonable and necessary to protect the Corporation's legitimate interests.
- 8.7 Sections 7.1 to 7.11 inclusive, 8.5, 8.6, 9.2, 11.4 and 11.8 survive the termination of this Agreement.
- 8.8 After the termination of this Agreement, the Consultant and Key Personnel will not represent themselves as being in any way connected with the Corporation. Provided the Corporation has paid the Consultant the amounts required to be paid under this Agreement, the Consultant will not claim any damages, compensation, loss or any other amount from the Corporation for any reason whatsoever, including for termination of this Agreement and/or any infrastructure or expenses incurred by the Consultant in rendering the Services to the Corporation under this Agreement.
- 9. No employment relationship**
- 9.1 The Consultant acknowledges that the Consultant provides the Services to the Corporation as an independent contractor, and that nothing in this Agreement constitutes a relationship of employer and employee, principal and agent,

partnership or joint venture between the Corporation and the Consultant. The relationship between the Corporation and the Consultant is of a principal to principal and on an arm's length basis. The Consultant further acknowledges and agrees that none of the Key Personnel are or will become an employee of the Corporation or any of its Related Corporations as a consequence of this Agreement or as a result of having been involved in the provision of the Services.

9.2 The Consultant indemnifies the Corporation and each of its Related Corporations from any and all expenses, losses, damages and costs (including legal and court costs and whether incurred by or awarded against the Corporation or a Related Corporation):

- (a) arising out of any claim or demand against the Corporation or any Related Corporation by any person (including the Consultant): under which it is alleged that any Key Personnel are employees of the Corporation or any of its Related Corporations; or in respect of any employment-related payment, right or entitlement sought by any current or former Key Personnel in connection with the Services, including, without limitation, vacation, sick or any other form of leave; pension contributions; hours of work; overtime; notice of termination; severance or redundancy payments or rights; or any other payment, right or entitlement afforded to an employee under applicable law in Canada;
- (b) that the Corporation or any Related Corporation incurs in connection with any act or omission by the Consultant in breach of: this Agreement, including a breach of any of the warranties set forth in this Agreement; or a duty the Consultant has to the Corporation or a Related Corporation; and
- (c) arising out of:
  - (i) any damage, injury or loss caused by or resulting from any negligent act or omission of the Consultant or any Key Personnel; and
  - (ii) all injury, loss or damage sustained by the Consultant or any Key Personnel incurred while performing the Services unless the injury, loss or damage was caused by any negligent act or omission of the Corporation or a Related Corporation.

## **10. No Conflicts**

10.1 The Consultant and Key Personnel will not provide any services to, or accept employment from, another person if in the opinion of the Corporation doing so

will adversely affect the Consultant's ability to provide the Services in accordance with this Agreement (which will be determined at the Corporation's sole discretion). The Consultant and Key Personnel must notify the Corporation before agreeing to provide services to, or accept employment from, another person.

- 10.2 During this term of this Agreement the Consultant and Key Personnel must not engage in any business or activity that is the same or similar to part or parts of the business carried on by the Corporation or any of its Related Corporations, except for academic purposes and his involvement with IntelliStem Tehnologies.

## 11. **Miscellaneous**

- 11.1 The Consultant warrants that:

- (a) the Consultant has the necessary knowledge, experience, equipment, financial means and human resources to provide the Services that the Corporation requires in an independent manner;
- (b) the Consultant has disclosed to the Corporation information about any possible prohibitions or restrictions on the Consultant from providing the Services set out in this Agreement;
- (c) other than what the Consultant has disclosed to the Corporation, the Consultant is not prohibited from or restricted in providing the Services to the Corporation;
- (d) the credentials and information provided by the Consultant to the Corporation touching upon the Consultant's qualifications and ability to perform the Services are true and correct; and
- (e) the Consultant will not use the names, logos, or any other marks owned by or associated with the Corporation for marketing or advertising purposes, or on any form of publicity (including, if applicable, the Consultant's website, or in any of the Consultant's other promotional materials) or refer to the existence of this Agreement in press releases or advertising without prior written consent from the Corporation.

- 11.2 In providing the Services:

- (a) the Consultant shall use its own equipment, materials and resources, unless otherwise provided by the Corporation, and will provide the Services hereunder in the place of the Consultant's choice; however, the Corporation may request the Key Personnel, when so needed, to perform

his/her duties in any other place, even if such place is located abroad, including without limitation the Corporation's facilities and/or the Corporation's customers' facilities;

- (b) the Consultant must observe all rules and regulations in connection with workplace safety and security and the use of the Corporation's equipment and/or materials, if applicable, as well as the Corporation's administrative guidelines, with the understanding that this will not imply under any circumstance that the Consultant is subordinated to, or an employee of, the Corporation;
  - (c) the Corporation agrees that it will not control nor direct the details, manner or means by which the Consultant provides the Services.
- 11.3 The Corporation may assign part or all of its rights or obligations arising out of this Agreement with immediate effect by giving notice to the Consultant. The Consultant may not assign nor subcontract the Consultant's rights and obligations under this Agreement except with the express prior written permission of the Corporation.
- 11.4 The Consultant has complied with all applicable laws regarding business permits and licenses that may be required to carry out the Services to be performed under this Agreement.
- 11.5 Except where specifically provided under this Agreement, the Consultant will be liable for all taxes and charges on amounts payable under this Agreement.
- 11.6 The Corporation excludes any liability to the Consultant for consequential damage including, but not limited to, lost profits suffered by the Consultant arising (whether under tort, equity, contract, statute or otherwise) in connection with this Agreement. The Corporation's total liability to the Consultant for damages arising in connection with this Agreement (whether under tort, equity, contract, statute or otherwise), when aggregated, is limited to the total Fees payable by the Corporation under this Agreement. This clause does not exclude or limit the application of any statutory provision where to do so would:
- (a) contravene that statute; or
  - (b) cause any part of this clause to be void.
- 11.7 This Agreement constitutes the entire agreement between the parties as to its subject matter and supersedes all prior understandings or agreements between the parties.

- 11.8 The Consultant must keep this Agreement confidential and may not disclose it to any other person other than for the purposes of obtaining professional legal or accounting advice or as required by law.
- 11.9 A party giving notice under this Agreement must do so in writing. A notice given in accordance with this Section 11.9 is taken to be received:
- (a) if hand delivered, on delivery;
  - (b) if sent by prepaid post, 3 business days after the date of posting;
  - (c) if sent by facsimile, when the sender's facsimile system generates a message confirming successful transmission of the total number of pages of the notice unless, within 8 business hours after that transmission, the recipient informs the sender that it has not received the entire notice.
- 11.10 This Agreement is governed by the laws of the Province of British Columbia. Part or all of any clause of this Agreement that is illegal will be severed from this Agreement and the remaining provisions of this Agreement continue in force.

## 12. Definitions

12.1 In this Agreement:

**"Confidential Information"** means all confidential information or information otherwise having value in the Corporation's or any of its Related Corporations' business, including but not limited to:

- (a) financial information concerning the Corporation or a Related Corporation;
- (b) trade secrets of the Corporation or a Related Corporation;
- (c) know-how and Intellectual Property Rights of the Corporation or a Related Corporation;
- (d) information relating to the business affairs, accounts, work, marketing plans, sales plans, records and research of the Corporation or a Related Corporation;
- (e) information relating to the customers and suppliers of the Corporation or a Related Corporation;

- (f) databases, software and subroutines, object code and Source Code Materials belonging to or used by the Corporation or a Related Corporation; and
- (g) the Developed Material,

of which the Consultant or any Key Personnel becomes aware or generates (both before and after the day this Agreement is signed) in the course of or in connection with providing the Services but does not include information which becomes public knowledge other than as a breach of confidentiality by the Consultant or any Key Personnel or information which was known to the Consultant prior to the commencement of the Services and which the Consultant was not obliged to keep confidential.

**"Key Personnel"** means the employees of the Consultant who are listed in Schedule B.

**"Developed Material"** means all materials (in any form), Inventions, subroutines, computer programs including all source and object codes, compilers, libraries and developer tools, and any manuals, descriptions, data files, resource files and other such materials relating thereto, hardware, models, designs, drawings, plans, reports, proposals, documents, equipment, compilations, products, studies, devices, prototypes, hardware, software, information and data stored by any means, created or developed by the Consultant, the Key Personnel or any other person involved in the performance of the Services, (either alone or with any other person) in the course of providing or in connection with the Services.

**"Intellectual Property Rights"** means all intellectual property rights including without limitation:

- (a) copyright, patent, industrial design, and trademark rights and the right to have confidential information kept confidential; and
- (b) any application or right to apply for registration of any of those rights.

**"Inventions"** include without limitation: inventions; discoveries; designs; formulas; works of authorship; trade secrets; technology; circuit layouts; algorithms; computer programs; ideas; processes; techniques; concepts; methodologies; procedures; protocols; formulae; know-how; and data, and any improvements to any of these items, in all cases whether or not patentable.

**"Moral Rights"** means:

- (a) the right of integrity of authorship (that is not to have a work subjected to derogatory treatment);
- (b) the right of attribution of authorship of a work by name or pseudonym and the right to remain anonymous; and
- (c) the right not to have authorship of a work falsely attributed

and any other similar right capable of protection under the laws of any applicable jurisdiction.

**“Proprietary Material** means any products, materials, tools processes and methodologies other than the Developed Material which is:

- (a) used by the Consultant, the Key Personnel, or any other person involved in the performance of the Services, to develop the results of the Services; or
- (b) incorporated into or supplied as part of the Services or the materials generated by the Consultant in the course of or in connection with providing the Services

whether owned by the Consultant or a third party (other than the Corporation or any of its Related Corporations).

**“Related Corporation** means any subsidiary parent branch or affiliate of the Corporation and any of their respective subsidiaries, parents, branches or affiliates and includes any successors or assigns of any such Related Corporation.

## **DEFENCE THERAPEUTICS INC.**

Per: Sébastien Plouffe  
Sébastien Plouffe

## **AXIOM SERVICES INC.**

Per: Mouth Rafei  
Mouth Rafei

**SCHEDULE A**

**Discovery and Development of Novel Vaccines Using  
The *Accum* Technology**

Study Proposal  
04/09/2020

Prepared and Approved by:  
Simon Beaudoin, PhD  
Mouth Rafei, PhD

Experiment Performed by:  
**DEFENCE THERAPEUTICS**  
(Represented by Sebastien Plouffe, CEO)  
**WASSC Technology inc**  
(Represented by Dr Simon Beaudoin, CEO-CSO)  
**AXIOM Services inc**  
(Represented by Dr Mouth Rafei, CEO)

**PROBLEM TO BE INVESTIGATED**

Vaccines exist in different forms. These include cell, protein, DNA/RNA or live attenuated formulations. The main component driving vaccine efficacy is the stable formation of peptides (fragments derived from a given protein) by the major histocompatibility (MHC) complex I or MHCII at the surface of antigen presenting cells (APCs) such as dendritic cells (DCs). As result, responding CD8 or CD4 T cells bind to peptide-MHCI/MHCII complexes respectively leading to the generation of a cytotoxic or humoral response. Therefore protective vaccines depend heavily on efficient presentation of peptide-MHCI/II to responding T cells.

In contrast to peptide MHCII generation, which requires lysosomal machinery (specialized types of vesicles), the generation of peptide-MHCI complexes depends on endocytosed antigens to be degraded by cytosolic proteasome complexes. ***In many situations however, entrapment and non-specific degradation of endocytosed antigens (protein, mRNA or DNA) occurs consequently resulting in poor MHCII antigen processing and presentation. It is therefore logical to stipulate that enhanced endosome-to-cytosol transport of antigen increases the formation of immunogenic MHCII-peptide complexes.***

## **TECHNOLOGY**

The *Accum* technology is known to induce endosomal escape of endocytosed antigens, increasing therefore cytosolic and nuclear accumulation of proteins and/or antibody-drug conjugates (ADC). Thus, this strategy could be easily adapted to increase protein-based vaccine efficacy. More specifically, the *Accum* moiety, which is composed of a Nuclear-Localization-Signal (NLS) linked to a bile acid moiety (eg cholic acid), induces the rupture of endosomal membranes through the production of ceramide. Such endosomal rupture allows proteins and ADCs to bypass endosomal entrapment and recycling leading to increases intracellular accumulation for degradation. ***Accordingly, we hypothesise that bypassing endosomal entrapment of vaccine materials using the Accum moiety will stimulate the production and presentation of peptide-MHCI complexes by APCs consequently enhancing the triggered immune response.***

## **OBJECTIVES**

The *Accum* technology will be tested using two different methods. As a first step, the *Accum* moiety will be chemically linked to immunogenic proteins and tested as a classical vaccine formulation. In the second stage of the project, ADCs treated with the *Accum* moiety will be used to pulse DCs and tested for its efficacy as a cancer cell vaccine.

### **OBJECTIVE 1: The discovery and testing of new peptide-based vaccines using the Accum technology**

Three different protein-based vaccines will be tested using the *Accum* Technology. Since the Ovalbumin (OVA) protein is a gold standard in studying concepts such as immunogenicity and vaccine formulations, OVA will be first used as a proof-of-concept.

Once the first proof-of-concept study is completed using OVA, we will start approaching several companies having a clinical COVID-19 vaccine program to establish collaborations. Selected companies were sorted according to their antigen type:

Protein-based vaccine companies include:

- Novavax (S protein, <https://novavax.com/>)
- Sanofi/GSK (S protein)
- Vaxine Pty (S protein, <http://vaxine.net/>)
- Medigen (S-2P protein, <https://www.medigene.com/home>)

mRNA-based vaccine companies include:

- Moderna (<https://www.modernatx.com/>)
- BioNTech (<https://biontech.de/>)
- CureVac (<https://www.curevac.com/en/about-us/>)

DNA-based vaccine companies are:

- Scancell (<https://www.scancell.co.uk/home>)
- DioSynVax (<https://diosvax.com/>)
- Immunomic Therapeutics (<https://www.immunomix.com/>)

Finally, the IL-13R $\alpha$ 2 is an interesting tumor-specific antigen (TSA) currently tested in the clinic to target catastrophic illnesses such as glioblastoma and metastatic breast cancer. Thus, the use of the *Accum* technology to identify immunogenic peptides derived from this protein would enable the development of novel and immunogenic IL-13R $\alpha$ 2-derived peptide vaccines.

### **OBJECTIVE 2: Using the *Accum* technology in DC-based vaccines**

Cell-based therapies, including DC vaccination, have recently gained a lot of interest due to major advancements in the field of cancer immunotherapies. It consists of exposing *ex vivo* generated DCs to immunogenic peptides/proteins prior to their infusion back to patients. Since endosomal entrapment of endocytosed proteins can greatly limit the potency of pulsed DCs, we believe that combining the *Accum* strategy to a given TSA (example IL13R $\alpha$ 2 and/or HER2) could greatly enhance the potency of the vaccine.

### **TEAM**

Dr Moutih Rafei is an expert in cellular and molecular immunology with immunotherapeutics, cell therapy and lymphocyte biology focus. He is an innovative scientist continuously proposing and implementing new therapeutic strategies while fostering external collaborations based on emerging human disease understanding.

Dr Simon Beaudoin is an innovative expert in biochemistry and cellular biology in different pathologies such as cancer and neurodegeneration disease. He has an expertise in biological-chemical conjugation, chemistry synthesis, drug formulation and in the development of targeting therapy such as ADC.

### **Detailed AIMS for objectives 1 and 2.**

### **PROJECT 1: The discovery and testing of new peptide-based vaccines using the *Accum* technology**

**AIM 1: Proof-of-Concept using OVA**

- A) Identification of immunogenic MHC I peptides capable of inducing Cytotoxic-T cells based-responses vaccine (50 000\$ per vaccine candidate project \_3 – 4 months) \_Mouse\_
- B) Identification of immunogenic MHC II peptides capable of inducing high antibody titer (50 000\$ per vaccine candidate project \_3 - 4 months) \_Mouse\_
- C) Demonstrating efficacy of the vaccine *in vivo* (400 000 - 625 000\$ per vaccine candidate project\_6 - 12months) \_Mouse\_

**AIM 2: Development of a COVID-19 vaccine**

- A) Identification of immunogenic MHC I peptides capable of inducing Cytotoxic-T cells based-responses vaccine (50 000\$ per vaccine candidate project \_3 – 4 months) \_Mouse\_
- B) Identification of immunogenic MHC II peptides capable of inducing high antibody titer (50 000\$ per vaccine candidate project \_3 - 4 months) \_Mouse\_
- C) Demonstrating efficacy of the vaccine *in vivo* (400 000 - 625 000\$ per vaccine candidate project\_6 - 12months) \_Mouse\_
- D) Idem with human specimen

**AIM 3: Development of a cancer vaccine based on HER2 or IL-13R $\alpha$ 2**

- A) Identification of immunogenic MHC I peptides and development of an *in vitro* antigen presentation assay (150 000\$ 4 – 6 months)
- B) Identification of immunogenic MHC I peptides and development of an *in vitro* antigen presentation assay (150 000\$ 4 – 6 months)
- C) Demonstrating efficacy of the vaccine *in vivo* using HLA.A2 transgenic mice or humanized mice undergoing human hematopoietic stem cell transplantation (400 000 - 625 000\$ per vaccine candidate project\_6 - 12months) (risky AIM)

**PROJECT 2: Using the *Accum* technology in DC-based vaccines**

**AIM 1: Proof-of-Concept using OVA**

- A) Testing the antigen presentation capacity of pulsed DCs (50 000\$ - 3 - 4 months) \_Mouse\_
- B) Evaluating the potency of the vaccine in autologous setting *in vivo* (120 000\$ \_3 - 4 months) \_Mouse\_
- C) Testing the vaccine in allogeneic settings *in vivo* (120 000\$ - 6 - 12months) \_Mouse\_

**AIM 2: Developing a DC cancer vaccine (HER2 or IL-13R $\alpha$ 2)**

- A) Testing the antigen presentation capacity of pulsed DCs (60 000\$\_3 - 4 months) \_Mouse\_
- B) Evaluating the potency of the vaccine in autologous setting *in vivo* (120 000\$ - 200 000\$\_3 - 4 months) \_Mouse\_
- C) Testing the vaccine in allogeneic settings *in vivo* (120 000\$ - 200 000\$\_6 - 12months) \_Mouse\_

**SCHEDULE B**

**Key Personnel**

The Key Personnel are:

Mouth Rafei  
Simon Beaudouin