INTELLECTUAL PROPERTY ASSIGNMENT AND ROYALTY AGREEMENT

Agreement made effective as of this 12 day of May 2017 (the "**Effective Date**").

BETWEEN: **SOCPRA SCIENCES SANTÉ ET HUMAINES S.E.C.**, operating under the name of TransferTech Sherbrooke, a limited partnership constituted under the *Civil Code of Québec*, having its principal place of business at Pavillon Irénée-Pinard, 2500, boul de l'Université, bur B6-3012, Sherbrooke, (Québec,) J1K 2R1, acting through its general partner **GESTION SOCPRA SCIENCES SANTÉ ET HUMAINES INC.**, a legal person duly incorporated the *Business Corporation Act (Québec)*, represented by Luc Paquet, President and CEO, duly authorized for the purposes hereof as he so declares by signing;

(hereinafter referred to as **"TTS"**)

AND: **ACCUM THERAPEUTICS INC.**, a legal person constituted under the *Canada Business Corporation Act*, having its head office at 2616, Equestrian road, St-Lazare, Québec, J7T 2A1, represented by Michel Delisle President, duly authorized for the purposes hereof as he so declares by signing;

(hereinafter referred to as **"ACCUM"**)

AND: **JEFFREY VICTOR LEYTON**, Professor at the Université de Sherbrooke, residing at 2249 rue des Cascades, Sherbrooke, (Québec) J1J 1R8;

(hereinafter referred to as the **"Inventor"**)

AND: **MICHEL DELISLE**, businessman, residing at 341 James Shaw, Beaconsfield, (Quebec), H9W 6G6;

(hereinafter referred to as **"Delisle"**)

(hereinafter collectively referred to as the "**Parties**")

WHEREAS The Inventor has developed, in connection with its activities at the Université de Sherbrooke (the "**University**"), the Invention known as "*Novel Immunoconjugates with cholic acid nuclear localization sequence peptide and uses thereof*" (provisional patent application No. 62/308457) and any and all related intellectual property, as more fully described in Schedule 1;

WHEREAS According to a technology transfer agreement agreed upon between the University and TTS effective August 25th, 2015, the University has assigned to TTS all its rights, titles and interests in the Intellectual Property (as defined hereunder) and TTS has received the exclusive right to commercialize same

and to enter into agreements with commercial entities with respect thereto, including the right to enter into this Agreement;

WHEREAS TTS has filed a provisional patent application (Application No. 62/308457) claiming certain elements of the Invention;

WHEREAS The Parties now wish to enter into this agreement (the "**Agreement**").

NOW THEREFORE, the Parties agree as follows:

1. DEFINITIONS

1.1 In this Agreement and all other documents relating or referring hereto, unless the context requires otherwise, the following words, terms and expressions have the meanings indicated:

1.1.1 **Affiliate** means any business controlled by or controlling another person. For the purposes and without limiting the generality hereof, a person is deemed to control another if such person owns or controls, directly or indirectly, more than fifty percent (50%) of the capital stock or units, in the case of a partnership (as that term is defined in the *Civil Code of Québec*), thereof. "Affiliate" also includes any person related to another, within the meaning given to "related person" in subsection 251(2) of the Canada Income Tax Act;

1.1.2 **Closing** means the completion of a $1,000,000 financing in cash in favour of ACCUM. The new issuance of shares related to the financing must be approved by an unanimous decision of the Board;

1.1.3 **Closing Date** means such as may be agreed to in writing by the Parties for the Closing of the transactions contemplated in this Agreement but no later than July 31, 2017;

1.1.4 **Confidential Information** means any information proprietary to a Party, whether or not reduced to writing or other tangible medium of expression, and whether or not patented, patentable, capable of trade secret protection or protected as an unpublished or published work under applicable copyright laws. "Confidential Information" includes, without limitation, information relating to Intellectual Property and to business plans, financial matters, products, services, manufacturing processes and methods, costs, sources of supply, strategic marketing plans, customer lists, sales, profits, pricing methods, personnel and business relationships. "Confidential Information" does not include any information that: (i) was already known to the receiving Party prior to its relationship with the disclosing Party, as established by written records; (ii) becomes generally available to the public other than as a result of the receiving Party's breach of this Agreement; (iii) is furnished to the receiving Party by a third party who is lawfully in possession of, and who lawfully conveys, such information; or (iv) is subsequently developed by the receiving Party independently of the information received from the disclosing Party, as established by the receiving Party's written records. For purposes of this definition, the phrase "receiving Party" includes any Affiliate of the receiving Party;

Any combination of the information which comprises part of the Confidential Information

shall not be deemed public merely because individual parts of that information were within the public domain, within the prior possession of the receiving Party, or were so received by the receiving Party unless the combination itself was in the public domain, in the prior possession of the receiving Party, or were so received by the receiving Party;

1.1.5 **Consideration** has the meaning ascribed to it under section 5 hereunder;

1.1.6 **Intellectual Property** means any and all intellectual property rights in and to the Technology, worldwide, whether or not such rights are legally protected or registered and includes, without limitation, copyrights, patents (including the Patent), trademarks, industrial designs and trade-secrets;

1.1.7 **Invention** means the results of the research work developed by Jeffrey Victor Leyton which has been disclosed by the Inventor and which are described and claimed in the patent application listed in Schedule 1 hereto, and includes any issuance, new application, continuation, continuation-in-part and division which may result from such patent(s) or patent application(s);

1.1.8 **License** means the license granted under subsection 4 hereunder;

1.1.9 **Net Sales Price** means the total sum invoiced by ACCUM or ACCUM's Affiliates for Products sold to customers in bona fide arms length transactions (excluding any transaction between ACCUM and any of its Affiliates). Permitted deductions from Net Sales Price are taxes of the nature of sales purchase or value added tax, recognised industry trade discounts, the invoice value charged by ACCUM for Products returned under justifiable complaint as well as discounts relating to payment arrangements or volume targets;

1.1.10 **New Invention** means any fixes, patches, enhancements, developments, modifications, updates, additions and improvements made to the Technology that provide function similar to the original technology (i.e. endosome escape and nuclear localization) by the Inventor at University. This also includes any results of the research work developed by Jeffrey Victor Leyton that could modulate / enhance the activity of antibody drug conjugates (ADC), whether or not such New Invention may be protected by patent or other intellectual property rights;

1.1.11 **New Invention Notice** has the meaning ascribed to it under subsection 3.1 hereto;

1.1.12 **Offered Price** has the meaning ascribed to it under subsection 3.4 hereto;

1.1.13 **Option** has the meaning ascribed to it under subsection 3.2 hereto;

1.1.14 **Patent** means provisional patent application No. 62/308457, as further described in Schedule 1;

1.1.15 **Product** means any good, material or service incorporating or exploiting, in whole or in part, the Technology, or which could not be developed, used, manufactured or commercialized without using or infringing, in whole or in part, at least one of the claims

contained in such Patent;

1.1.16 **Rights** has the meaning ascribed to it under subsection 3.2 hereto;

1.1.17 **Royalties** has the meaning ascribed to it under subsection 5.3 hereunder;

1.1.18 **Technology** means the Invention, as well as the drawings, software, technical information, documents, research notes, inventions, patterns, prototypes, models, processes, formulas, recipes, products, samples, files, diagrams, plans, specifications, algorithms and methods related thereto owned or controlled by TTS, the whole as more fully described in Schedules 1 and 2, as well as the New Inventions acquired by ACCUM in accordance with the provisions of section 3, as the case may be; and

1.1.19 **University** has the meaning ascribed to it in the Recitals.

1.2 **Currency**. Unless otherwise indicated, all dollar amounts referred to in this Agreement are in Canadian funds.

1.3 **Tender**. Any tender of documents or money hereunder may be made upon the counsel and money may be tendered by bank draft or by certified check.

1.4 **Number and Gender**. Where the context requires, words imparting the singular shall include the plural and vice versa, and words imparting gender shall include all genders.

1.5 **Headings**. Headings contained in this Agreement are included solely for convenience, are not intended to be full or accurate descriptions of the content thereof and shall not be considered part of this Agreement or affect the construction or interpretation of any provision hereof.

1.6 **Schedules**. The Schedules to this Agreement shall be construed with and be considered an integral part of this Agreement to the same extent as if the same had been set forth verbatim herein. The following Schedules are attached hereto:

Schedule "1" Provisional Patent application;

Schedule "2" Description of the Technology;

Schedule "3" Proposed Research Contract.

2. ASSIGNMENT

2.1 Subject to the terms and conditions of this Agreement and in consideration of the payments and other considerations stipulated in section 5 hereunder, TTS hereby grants, conveys and assigns to ACCUM the Technology and the Intellectual Property as of the Effective Date.

2.2 Starting on the Effective Date, TTS accepts to cease any and all use and exploitation of the Technology and the Intellectual Property, and accepts to cause the University and the Inventor to cease any and all use and exploitation, of the Intellectual Property, except as otherwise allowed hereunder, including under subsection 4.1.

2.3 ACCUM must prosecute, maintain, protect and defend the Intellectual Property and the Technology, including the Patent, in order to preserve their value in accordance with the decisions of the Board (4 members out of 5 including the Inventor). A breach thereof shall constitute a material breach of ACCUM herehunder.

3. OPTION TO ACQUIRE NEW INVENTIONS

3.1 TTS shall notify ACCUM of the creation of any New Invention within a maximum of thirty (30) days following the same and shall provide ACCUM with a thorough description of same (each, a "**New Invention Notice**").

3.2 TTS hereby irrevocably grants to ACCUM the exclusive option (the "**Option**") to acquire all right, title and interest (including, without limitation, patent and copyright and other intellectual property rights thereto) in and to any New Invention at the Offered Price (the "**Rights**").

3.3 New Inventions shall be deemed constituting Confidential Information and shall not be published or otherwise disclosed by any of the parties, unless ACCUM doesn't exercises its Option under subsection Erreur ! Source du renvoi introuvable. above and subsection 3.4, or ACCUM's offer is refused by TTS. Notwithstanding the foregoing, University, the Inventor and TTS may file patent applications at any time in connection with any New Inventions.

3.4 ACCUM may exercise the Option at any time within thirty (30) days following a New Invention Notice by delivering notice to ACCUM if its intent to exercise the Option and the price (which may include without limitation, lump sums, royalties, milestones payments, etc.) it proposes to pay in consideration of the exercise of same (the "**Offered Price**").

3.5 Upon the acceptance of the Offered Price by TTS, all Rights in and to the New Invention shall be irrevocably and absolutely assigned, granted and conveyed to ACCUM without further formality. ACCUM and TTS agree that, in the event the Option is exercised, this document shall constitute a valid assignment, grant and conveyance of the Rights in and to the New Invention. If, however, ACCUM determines that further documents are required or desired to evidence or effect such assignment, grant and conveyance, TTS and the Inventor shall execute such further documents within ten (10) days of request by ACCUM.

3.6 Should TTS refuse the Offered Price, or should ACCUM fail to exercise its Option within the prescribed delay at subsection 3.4, the Option will be deemed irrevocably lapsed for such New Invention and ACCUM will have no rights or access thereto. For the sake of clarity, TTS's refusal of the Offered Price or ACCUM's failure to exercise its Option in relation to any given New Invention does not prevent ACCUM from exercising its Option rights in and to any other New Invention.

3.7 Notwithstanding the above, if ACCUM fails to identify any commercial application and develop at least one Product for each New Invention acquired by ACCUM within the three (3) years following the acceptance of the Offered Price by TTS, the provisions of section 7 hereto shall apply to such New Invention.

4. LICENSE

4.1 ACCUM hereby grants TTS, the University and the Inventor a royalty-free, non-transferable license without the right to sub-license to use the Intellectual Property and the Technology for non-commercial, academic, research and teaching purposes. Notwithstanding the foregoing, should such use by the University interfere, in ACCUM's discretionary opinion, with ACCUM's rights to protect, use, commercialize or otherwise exploit the Technology, ACCUM shall be entitled to require TTS and the University to postpone any publication or to otherwise maintain as confidential any research results or information pertaining to the Technology.

5. CONSIDERATION AND ROYALTY

5.1 At the Effective Date and in consideration for the Assignment, ACCUM will issue, as consideration, to each of TTS, the Inventor and Delisle, one third of its share-capital (the "**Consideration**").

5.2 At the Closing Date, and in addition to the Consideration, ACCUM will pay TTS an amount of $25,000 (the "**Lump Sum**").

5.3 In addition to the Consideration and the Lump Sum and until the expiry of the last patent rights issued on the basis of the Patent, ACCUM will pay to TTS a royalty of five percent (5%), calculated on the Net Sales Price of Products sold by ACCUM or any of its Affiliates (collectively, the "**ACCUM Group**") to any entity which is not a member of the ACCUM Group (the "**Royalties**"). The Royalties shall be calculated on a 12-month basis starting on the Closing Date (each, a "**Reference Year**"), and shall be paid by ACCUM to TTS within 90 days following the expiry of each Reference Year.

5.4 In addition to the Consideration, the Lump Sum and the Royalties, ACCUM shall enter into the following agreements within one (1) month of the Effective Date:

5.4.1 A research contract with the l'Université de Sherbrooke to pursue the development of the Technology described in Schedule 1 and 2.

5.4.2 A donation to the Fondation de l'Université de Sherbrooke, which will be specifically oriented toward research performed in the Inventors laboratory.

5.4.3 A research contract with University Pierre et Marie Curie to perform all studies described in Schedule 3, which experiment can be modified by the Advisory Committee.

5.5 ACCUM shall pay interest on any unpaid and outstanding amount, calculated at the prime business rate of the Bank of Canada, plus three percent (3 %), payable and compounded monthly. Interest shall run as of the date on which the payment becomes due until the date on which payment is received.

5.6 All applicable taxes will be invoiced by TTS and shall be paid by ACCUM.

6. ASSIGNMENT DOCUMENTATION

6.1 On the Closing Date, TTS and ACCUM will sign all the necessary documents to have the Patent and any additional registered Intellectual Property, as the case may be, transferred to ACCUM. Within ten (10) days from the receipt by TTS and the Inventor of the Consideration set forth in section 5 of this Agreement, TTS's patent agents will file such assignments with the relevant intellectual property offices and will provide ACCUM with confirmation of these actions by written notice. The costs relating to the transfers, including the cost of preparing and drafting legal documents and other forms, as well as the cost of registering the transfer, shall be paid by ACCUM.

6.2 In addition to the documents referred to in the above subsection, TTS shall provide to ACCUM, a full set of the records and documents relating to the Technology, including the complete documentation related to the Patent and its transfer.

6.3 ACCUM shall be solely responsible, as of the Closing Date hereof, for all future costs relating to obtaining and maintaining the rights forming part of the Intellectual Property including, without limitation, all Patent costs.

7. REMITTANCE TO TTS

7.1 Should ACCUM fail to sign a reasonable partnership agreement for the Intellectual Property or the Technology with a Biotech / Pharmaceutical corporation and to develop at least one Product within five (5) years following the Effective Date, TTS may terminate this Agreement upon written notice to ACCUM. Furthermore, the Intellectual Property and the Technology shall be assigned and transferred by ACCUM to TTS upon simple written request of TTS.

7.2 The consideration for such transfers shall be nominal.

7.3 The provisions of section 6 shall apply in favour of TTS with the required adaptations and all costs associated with such transfers, including official costs and legal fees, shall be borne exclusively by TTS.

8. BOARD OF DIRECTORS

8.1 At Effective Date, ACCUM's shareholders will create a board of director composed of three people: 1) Luc Paquet from TTS 2) Jeffrey Leyton, inventor 3) a member representing the investors (the "Board"). Two other people will be appointed within one year of the Closing by unanimous decision of the Board members. In addition to other legal powers, the Board will have the power to decide all experiments needed to be done by ACCUM in the upcoming years as well as the required financing to realize such experiments and the issuance of new shares or convertible titles of ACCUM.

9. CONFIDENTIALITY

9.1 The Parties acknowledge that they may access each other's Confidential Information during the performance of this Agreement.

9.2 Each Party agrees:

9.2.1 to use Confidential Information solely for the purposes referred to herein, unless it has received the prior written consent of the Party to whom the Confidential Information belongs;

9.2.2 not to disclose the other Party's Confidential Information or allow it to be disclosed to any third party. In addition, each Party agrees to limit the disclosure of Confidential Information of the other Party within its own organization to those employees, directors, officers or agents who specifically need to know it for the purposes hereof. Any person required to have access to or to hold Confidential Information of the other Party shall first sign a confidentiality agreement, the substance of which is satisfactory to the Party to whom such Confidential Information belongs; and

9.2.3 to deal with Confidential Information in the same manner and with the same care as it would its own Confidential Information, including all reasonable care required.

9.3 The obligations of the Parties under this article shall remain in effect in perpetuity.

9.4 The Parties agree that the terms and conditions of this Agreement are confidential.

9.5 Notwithstanding the foregoing, the Parties may disclose the terms and conditions hereof to its current or potential investors or its financial partners as well as its accountants, attorneys and other professional advisers; however, ACCUM, its current or potential investors or its financial partners as well as its accountants, attorneys and other professional advisers may not disclose Confidential Information of TTS or of the Inventor without entering first into confidentiality agreements with such third parties, the substance of which should be satisfactory to TTS and the Inventor.

10. PUBLICITY

10.1 The Parties shall not issue a press release or any publication disclosing the terms and conditions of this Agreement without the prior written consent of the other Party.

11. RESEARCH COLLABORATION

11.1 ACCUM shall give special consideration to the University for any research and development work it wishes to have carried out outside its own organization in order to ensure the development of the Technology and New Inventions, to the extent that the University is able to perform such work at a cost, within a time and according to a level of expertise which is equivalent to or more beneficial than the terms ACCUM could obtain from another supplier.

11.2 The terms of such collaboration shall be the subject of a research contract before any work begins at the University, on terms currently in effect at the University covering all direct and indirect costs of the work.

12. WARRANTY AND INDEMNIFICATION

12.1 Except for the representations made by TTS under section 13, TTS does not bind itself and makes no representation or warranty of any kind whatsoever with respect to the Intellectual Property and the Technology. Without limiting the generality of the foregoing, TTS makes no representation or warranty of any kind whatsoever with respect to the usefulness, quality or marketability of the Intellectual Property and the Technology, or the effect which may result from their use or that the development of applications relating to the Intellectual Property and the Technology is complete. Without limiting the generality of the foregoing, TTS does not guarantee the validity of the Patent, the Technology, or the Intellectual Property and makes no representation with respect to their scope and validity. TTS shall not be liable for the warranties, representations, undertakings or any other obligations given or assumed by ACCUM toward any party whomsoever with respect to the manufacturing, promotion, distribution, use or sale of any product and services or any other activity relating thereto or to any of the Intellectual Property or the Technology.

12.2 ACCUM agrees to indemnify and hold harmless TTS, its directors, officers, employees and representatives with respect to any claim or legal proceeding taken against them, as well as the judgements resulting therefrom relating to any damage, loss, cost and expense (including reasonable costs incurred by advisers and attorneys) which they may have incurred as a result of or arising further to or in connection with the use of any of the Intellectual Property and the Technology, by the ACCUM Group or its licensees.

13. REPRESENTATIONS AND UNDERTAKINGS OF TTS

13.1 TTS is a duly incorporated and organized legal person in good standing under the laws governing its existence and operations.

13.2 TTS has full power, capacity and authority and all necessary licences, permits and consents to enter into and to perform its obligations under this Agreement.

13.3 TTS's execution, delivery, and performance of this Agreement does not and shall not constitute a violation of any judgment or decision or a default under any material contract, including under the *Entente relative à la valorisation d'une création* entered into by TTS and the Inventor on January 25, 2016.

13.4 TTS holds all rights in and to the Technology which are necessary to grant the rights described herein and has complied with all notices that may have been issued from time to time by the Commissioner of Patents and the Intellectual Property Offices.

13.5 TTS has paid to the relevant authorities the regulatory interim taxes or other fees payable in order to maintain the rights granted by the patent applications or patents protecting the Invention.

13.6 TTS is the sole owner of the Invention and the sole holder of the related Patent. TTS has complied with all substantial and formal requirements of the *Patent Act* regarding the application for delivery of the related patent. To TTS's knowledge, the patent application does not contain any false claim. The Patent is not subject to any purchase option in favour of any person whatsoever.

13.7 TTS has not granted any license regarding the Patent or the Technology and has not taken any undertaking toward a third party which may deter ACCUM from entering into this Agreement.

13.8 TTS represents and warrants that there is no pending or threatened legal proceedings initiated by any third party regarding the Intellectual Property or the Technology and that the Technology does not, to its knowledge, infringe any third party's intellectual property.

13.9 Should the Patent be the subject of any administrative judiciary proceedings or office action, TTS undertakes to collaborate with ACCUM to prepare the required evidence to ensure the validity of the Patent and of the exclusive rights acquired on the latter by ACCUM.

13.10 To TTS's knowledge, the information provided by TTS to the other Parties prior to or simultaneously with the signing of the Agreement is true, accurate and complete; it has not failed to disclose any information about the Invention, the Technology, its status or its activities which would deter the other Parties, acting reasonably, from entering into the Agreement or which would vary the terms and conditions thereof.

14. REPRESENTATIONS AND WARRANTIES OF ACCUM

14.1 ACCUM is duly incorporated and organized legal person in good standing under the laws governing its existence and operations. ACCUM has the ability and power to own its property, carry on business as it currently does and fulfil its obligations which may result

herefrom, where applicable. ACCUM holds all authorizations required by the federal, provincial or other authorities to carry on business.

14.2 Without having to list each section hereof, ACCUM represents that it will comply with each and every undertaking hereunder and will cause, as applicable, that all its Affiliates or subcontractors who have access to TTS's Confidential Information respect the relevant portions of this Agreement.

14.3 ACCUM undertakes not to do, or cause, help or assist anybody to do, whether directly or indirectly, anything which may, in any manner whatsoever, imperil or infringe the validity of the Patent.

14.4 The information provided by ACCUM to the other Parties prior to or simultaneously with the signing of the Agreement is true, accurate and complete.

15. MEDIATION AND ARBITRATION

15.1 Any disagreement between the Parties with respect to the interpretation, application or administration hereof or any failure of the Parties to agree when an agreement is necessary, generally referred to herein as a "Dispute", shall be decided in accordance with the terms of this section, to the exclusion of any recourse before the courts.

15.2 Except as provided otherwise in this Agreement, the Parties shall make every reasonable effort to settle any Dispute quickly and amicably by mediation or otherwise. If no settlement can be reached within 90 days, each party has the right to proceed as described in subsection 15.3.

15.3 All Disputes arising out of or in connection with the present contract shall be finally settled in accordance with the Code of Civil Procedure (Québec) by a single arbitrator appointed by consent of the Parties. The place of arbitration will be Sherbrooke, Canada.

15.4 Notwithstanding the foregoing, recourse to the courts shall be allowed for conservatory measures (such as a seizure before judgement) and injunctury relief, where applicable, and to have any arbitration award homologated and enforced.

16. FORCE MAJEURE

No party hereto shall be considered in default in the performance of its obligations if such performance is delayed, hindered or prevented due to force majeure, as this notion is defined under section 1470 of the Civil Code of Quebec.

17. GOVERNING LAW

This Agreement shall be interpreted in accordance with the law applicable in the Province of Quebec without having reference to its choice of law principals.

18. ENTIRE AGREEMENT

This Agreement, including the Schedules, together with the agreements and other documents to be delivered pursuant hereto, constitute the entire agreement between the Parties pertaining to the subject matter hereof and supersedes all prior agreements, understandings, negotiations and discussions, whether oral or written, of the Parties and there are no warranties, representations or other agreements between the Parties in connection with the subject matter hereof except as specifically set forth herein and therein. This Agreement may not be amended or modified in any respect except by written instrument signed by all Parties.

19. SURVIVABILITY

All provisions of this Agreement which are by their nature intended to survive the expiration or termination of this Agreement will survive such expiration or termination, including the following sections which shall expressly survive termination hereof for any reason: sections 9, 10, 12, 13, 14 and 15.

20. TERMINATION

20.1 Should the Patent be declared invalid by a court of competent jurisdiction, the Parties shall immediately initiate negotiations regarding the calculation of Royalties and the purchase option provided at subsections 5.3 and 5.4 above. In the event no agreement is reached by the Parties within thirty (30) days following the invalidation of the Patent, the matter should be brought to arbitration in accordance with Subsection 15.3.

20.2 The Agreement shall automatically terminate if the Closing is not completed by ACCUM for any reason whatsoever by **July 31st, 2017** at the latest (the "Closing Date"), or if the agreements referred to in Section 5.4 are not executed within the prescribed delay, unless otherwise extended in writing by the mutual agreement of all Parties.

20.3 In the event of a material breach, the non-breaching Party may terminate the Agreement, in whole or in part, by giving thirty (30) days written notice to the breaching Party specifically identifying the breach, unless the breach is cured by the breaching Party within the thirty (30) day period.

20.4 It is understood by the Parties that upon termination of this Agreement the provisions of section 7 shall apply and accordingly all the Intellectual Property, the Patent, the Technology and any New Inventions acquired by ACCUM shall be automatically transferred by ACCUM to TTS at a nominal value and at ACCUM costs.

21. NOTICE

21.1 To be valid and binding upon the Parties, any notice required under any provision of the Agreement shall be given in writing at the following addresses:

For TTS:

SOCPRA SCIENCES SANTÉ ET HUMAINES S.E.C.
To: Luc Paquet, Ph.D.
Pavillon Irénée-Pinard
2500, boul de l'Université, Bur. B6-3012,
Sherbrooke, Québec, J1K 2R1
Email: info@Transfertech.ca

For ACCUM:
To: Michel Delisle
2616, Equestrian road, St-Lazare, Québec, J7T 2A1
michelrdelisle@me.com

For: Jeffrey Victor Leyton,
2249 rue des Cascades, Sherbrooke, (Québec) J1J 1R8
Email: Jeffrey.Leyton@usherbrooke.ca

For: Michel Delisle
2616, Equestrian road, St-Lazare, Québec, J7T 2A1
michelrdelisle@me.com

21.2 Any change of address by either Party shall be the subject of a written notice sent to the other Party by email.

21.3 Any notice shall be sent to the address indicated above or to any other address indicated following a change made in accordance with the foregoing paragraph.

21.4 Any notice shall be deemed to be received upon receipt, when properly addressed, if sent by registered mail, upon documented proof of its receipt; if sent by fax, with an electronic receipt; or if sent by e-mail, with virtual acknowledgement of receipt.

22. MISCELLANEOUS

22.1 The preamble and appendices form an integral part hereof.

22.2 The Parties hereby confirm that they are entering into the Agreement as independent contractors and that nothing in the Agreement should be interpreted or construed in such a manner as to create a partnership, joint venture or mandate of any kind between them.

22.3 The Parties shall, with reasonable dispatch, upon receipt of a written and reasonable request to such effect, sign such ancillary documents or instruments, cause such meetings to be held, resolutions passed and by-laws enacted, exercise their voting rights and other powers, and do

and perform and cause to be done or performed any other act as may be required to ensure the full performance of and give full effect to the Agreement.

22.4 The failure by either Party to exercise its rights resulting from the non-compliance or breach hereof and the acceptance of payment shall not be considered a waiver of rights. No provision hereof shall be deemed to have been waived by a Party unless such Party has set forth such waiver in writing.

22.5 The declaration that any provision hereof or its application is null and void shall not affect the validity of the other provisions hereof and the Parties shall remain bound.

22.6 The Agreement shall be binding upon and of benefit to the Parties and their legal representatives.

22.7 This Agreement may only be amended by a document written and signed by all the Parties hereto.

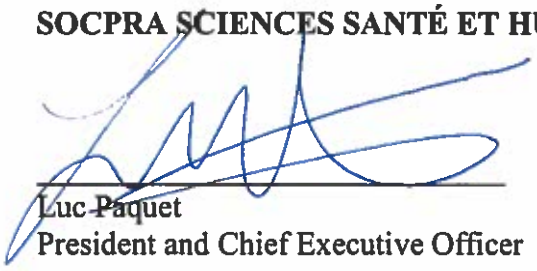
22.8 The Agreement may be signed in several counterparts, and, as the case may be, each of them when so signed shall be deemed to be an original. Such counterparts shall, however, represent one and the same document.

22.9 The Parties acknowledge that they have requested and agreed that this Agreement and all documents, notices, correspondence and legal proceedings consequent upon, ancillary or relating directly or indirectly thereto forming part hereof or resulting herefrom be drawn up in English. *Les Parties reconnaissent qu'elles ont exigé et consenti à ce que le présent contrat ainsi que toute procédure, avis et autre document s'y rapportant, directement ou indirectement soient rédigés en anglais.*

[SIGNATURES ON FOLLOWING PAGE]

IN WITNESS WHEREOF, the Parties have signed this Agreement,

SOCPRA SCIENCES SANTÉ ET HUMAINES S.E.C.



Luc Paquet
President and Chief Executive Officer

ACCUM THERAPEUTICS INC.

_____
Michel Delisle
President

_____
JEFFREY VICTOR LEYTON

_____
MICHEL DELISLE

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Michel Delisle
President

JEFFREY VICTOR LEYTON

MICHEL DELISLE

SCHEDULE 1

PATENT

TTS file: 32-8-1

US provisional patent application number: 62/308457
Title: Conjugates enhancing total cellular accumulation
Inventor(s): Victor Jeffrey Leyton and Simon Beaudoin
Filing date: 2016-03-15

SCHEDULE 2

DESCRIPTION OF THE TECHNOLOGY

TECHNOLOGY DESCRIPTION

We have developed and successfully tested in cell culture and in limited animal studies a proprietary patented technology we call CellAccumulator (**ACCUM**) that allows for universal modification of ADCs.

What are the core features of our proprietary ACCUM technology?

The universal cornerstone for intracellular drug accumulation by ADCs relies on efficient intracellular accumulation and placement of the delivered drug inside the target cancer cells. ADCs bound to cancer-antigens on the cell surface are internalized and trapped inside cellular structures (endosomes) and trafficked to lysosomes where ADCs are degraded and the chemotherapeutic is released inside the cell. The accumulation of the chemotherapeutic inside the tumor cell is directly correlated with cancer cytotoxic potency. Basically, our competitive edge compared to other ADC companies is the efficient and unique transport-mobilization system ACCUM provides when it is linked to the mAb (**Figure 2**).

Figure 2. ACCUM-modified ADCs increase drug accumulation and tumor cell killing

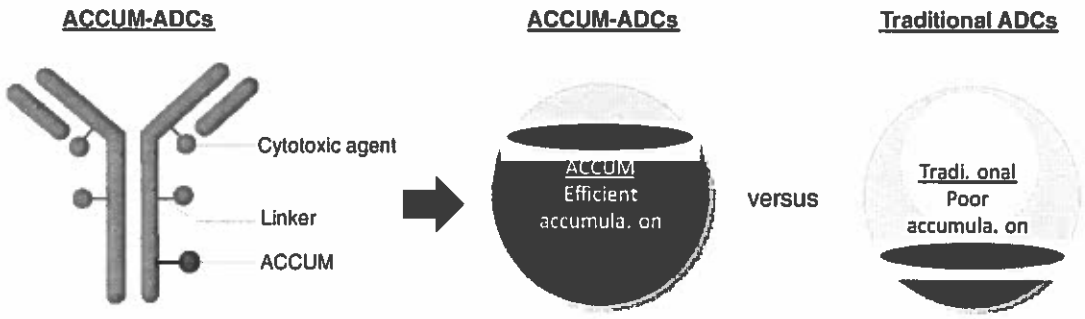

Figure 2. ADCs modified with ACCUM increase drug accumulation and therefore improve tumor cell killing.

ACCUM improves cytotoxic potency in the following manners:

- Facilitates ADC penetration without hampering its specificity
- Engages an alternative more efficient trafficking system
- Releases the chemotherapeutic in a more precise location within the cells that is less vulnerable to cancer cell mechanisms that export drugs causing reduced accumulation

These three unique features provide ACCUM-modified ADCs with superior increased chemotherapy accumulation (**Figure 2**) and cytotoxic potency. **Therefore, ACCUM is a revolutionary technology.**

TECHNICAL PROOF-OF-CONCEPT ACHIEVEMENTS

Accum modified Kadcyla with ACCUM and demonstrated:

- In extensive *in vitro* assays, ACCUM-Kadcyla remarkably out performs Kadcyla in tumor cell killing potency
- In limited *in vivo* studies, ACCUM-Kadcyla is stable in circulation, targets tumors, and is non-toxic

SCHEDULE 3

Proposed research contract with University Pierre et Marie Curie

Studies for *in vivo* proof-of-concept: Evaluation of the *ACCUM*-Kadcyla efficacy in HER2+ breast patient-derived xenograft models

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Scientific project leader at University of Sherbrooke:

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SUMMARY

The Antibody Delivery Lab (ADL) is a dynamic biopharmaceutical laboratory lead lead by Dr. Jeff Leyton and based in Sherbrooke, Québec. ADL is at the forefront of research and development focusing on the delivery of therapeutic and diagnostic molecules by antibodies to tumors.

The innovation of ADL, based on a specific technology we call CellAccumulator (***ACCUM***), allows for uncomplicated modification of a powerful new class of anti-cancer drugs known as antibody-drug conjugates (ADCs), and that our preliminary data suggests could provide for increased tumor killing and long-lasting disease-free survival for patients with cancer. ADCs are monoclonal antibodies (mAbs) that are designed to selectively deliver cytotoxic agents to cancer cells. Due to their excellent efficacy and desirable side effect profiles, the pharmaceutical industry and the medical field have accepted ADCs as a new class of anticancer medication. In 2011 a milestone was achieved with the approval of brentuximab vedotin (Adcetris ®) for the treatment of lymphoma. This was soon followed in 2013 with the approval of trastuzumab emtansine (Kadcyla ®) for the treatment of breast cancer. There are currently an estimated 22 unique ADCs in clinical phase 1 studies and 12 ADCs in phase 2 and 3. Many pharmaceutical and biotechnology companies have recognized the trend and have committed to the discovery and development of ADC anticancer drugs. These efforts have enriched the research and the pipelines, which will benefit millions of cancer patients. Accordingly, the market outlook for ADCs is estimated to climb past $10 Billion by 2020.

Dr. Leyton has worked in the antibody conjugate engineering and design in order to improve delivery to tumors for the past 15 years previously at world-renowned institutions UCLA and University of Toronto. Hence, ADLs approach includes a well-experienced researcher that understands the important challenges to improve ADC effectiveness. *ACCUM* is an innovative response to improve ADC efficacy as well as develop next-generation ADCs for new indications that are untouched by current ADCs. The completed R&D studies have already demonstrated the **technical proof of its concept** in initial *in vitro* and *in vivo* models.

AN INNOVATIVE APPROACH

ADCs suffer from a central dilemma that *ACCUM* successfully addresses:

Unfortunately, within the current pipeline of soon-to-market ADCs, 15 have been discontinued from development, seemingly after early clinical studies showed poor therapeutic effectiveness. To solve these problems, the current innovation strategies are blindly focused with discovering small molecules with increase cytotoxic potency and the chemical design of drug-mAb attachment linkers to better deliver cytotoxins inside tumor cells. However, these strategies don't address the central dilemma plaquing ADCs and preventing them from becoming widespread cancer medicines.

ADCs are subjugated to delivering the drug via the **endosomal-lysosomal pathway** and this pathway is very inefficient for effectively accumulating the delivered drugs to evoke a sustained therapeutic response. This is because cancer cells can reroute ADCs back outside the cell and prevent the delivery of the payload. In addition, when the payload is released it is near the cell surface where cancer cells expressing drug efflux pumps quickly capture the drugs and export them back outside the cell. Hence, cancer cells reduce the drug cellular concentration as a central mechanism to resist ADC treatment, and cause patient relapse followed soon by death.

The innovative approach of ADL relies on the concept of developing technologies that enable ADCs to control their intracellular trafficking once internalized inside target tumor cells. ***ACCUM*** advances ADC effectiveness by enabling control of intracellular trafficking in the following manners: **1)** it enables ADCs to escape endosomal-lysosomal pathway; **2)** it efficiently routes ADCs to the nucleus; **3)** the combination of escape and nuclear routing results in increased cellular accumulation and increased cytotoxicity. Using a multitude of biochemical methods *ACCUM* has been validated for its ability to attach to ADCs, its routing mechanism, and its ability to enhance cellular drug accumulation selectively in cancer cells. **More importantly, *ACCUM* demonstrated it can improve the cytotoxic effectiveness of Kadcyla (Fig. 1).** *ACCUM* modification does not perturb T-DM1 affinity, specificity or cause aggregation. The IC_{50} of *ACCUM*-Kadcyla was increased 100-, 50-, and 10-fold relative to Kadcyla in SKBR3 (Herceptin-sensitive), OE19, and JIMT1 (Herceptin-resistant) cells, respectively. Cytotoxicity in MCF7 (HER2-negative) cells was equivalent for *ACCUM*-Kadcyla and Kadcyla (5% at 1 µg/mL). *In vivo* acute and embryonic toxicity was not observed using the chicken chorioallantoic membrane assay. The favourable effectiveness of *ACCUM*-T-DM1 suggests our strategy of empowered intracellular drug delivery for ADCs offers an innovative and effective approach to drug accumulation and cytotoxicity, while maintaining low toxicity.

The potential widespread effect on the ADC industry and market requires careful cultivation of ACCUM. The current strategy of ADL focuses on two major themes:

- **Research and Development of the platform technology *ACCUM* in pre-clinical models of human breast cancer using the current ADC Kadcyla as the critical benchmark.**

This will provide license opportunities with big pharmaceutical companies, ("Big Pharma") who will pursue the development and commercialization of their proprietary ADCs in combination with *ACCUM*.

- **Technology extended to other cancers.**

The *ACCUM* technological platform will lead to partnership co-development with pharmaceutical industry or the development of ADCs using antibodies exclusive to ADL/Marie Curie.

OBJECTIVES

ADLs objectives are to design *ACCUM*-Kadcyla and demonstrate it can:

- Out perform Kadcyla for anti-tumor effectiveness in mice implanted with patient-derived xenograft (PDX) breast cancer tumors.
- Have low toxicity to healthy organs
- Propel the development, in parallel, of novel *ACCUM*-ADCs that would offer ADL/Marie Curie other cancer indications (colon cancer, brain cancer, etc…).

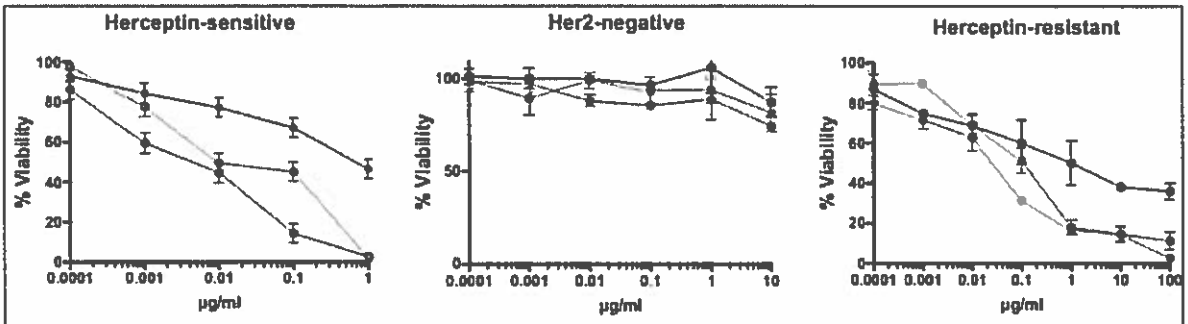

Figure 1. *ACCUM*-Kadcyla (T-DM1) modified with either 10 (green) or 20 (red) *ACCUM* per T-DM1 has remarkable increased cytotoxic effectiveness over T-DM1 (black) and has very little non-specific toxicity in Her2-negative cells. *ACCUM*-T-DM1 is 100-200-fold more cytotoxic than T-DM1 in the Herceptin-sensitive breast cancer cell line SKBR3. *ACCUM*-T-DM1 is 50-100-fold more cytotoxic than T-DM1 in Herceptin-resistant cancer cell lines.

Aims:

1. Determine the toxicity of *ACCUM*-Kadcyla and the maximum tolerated dose (MTD)
2. Determine anti-tumor effectiveness in PDX models of human Her2-positive breast cancers
3. Determine survival in mice-bearing PDX tumors

Materials and Methods:

Description of the models

The PDX models were derived from patient tumors taken during surgery at the Paris Hospital. Tumors were implanted into Nude mice and evaluated for growth of a tumor lesion. HER2 expression status was determined by immunohistochemistry (IHC) status in both patient tumors and mouse xenografts. HER2 positiviy was determined with a cutoff value set of 60% positively stained invasive cells (Vincent-Salomon et al. Histopathology. 2003). Expression of HER2 was similar in the corresponding PDX tumors (Marangoni et al. 2007; Reyal et al. 2012). ACCUM-Kadcyla will be tested in various PDX models that are Herceptin-sensitive, -resistant, or HER2 negative (Table 1).

Table: PDX models of Breast Cancer

PDX model	*Publication name*	*Histology*	*IHC*	*Neo-adjuvant treatment*	*PDX Response to Transtuzumab*

BC111	*HBCx-5*	*Invasive ductal carcinoma Grade 3*	*ER+, HER2+*	*post-neoajuvant (AC)*	*Resistant**
BC151	*HBCx-12A*	*Invasive ductal carcinoma Grade 3*	*ER-, PR-, HER2+*	*No*	*Responder**
BC911	*HBCx-73*	*Invasive ductal carcinoma Grade 3*	*ER-, PR-, HER2+*	*post-neoajuvant (Navelbine + Trastuzumab)*	*Resistant*
BC138	*HBCx-8*	*Invasive ductal carcinoma Grade 3*	*Triple-negative*	*no*	-

*published in Marangoni et al. CCR 2007

Animals and housing

Swiss nude mice, 6 to 8 weeks old, from Charles River Lab and maintained at Institut Curie, in EOPS conditions will be used. Mice will be housed in group cages of 8 mice each, at the animal quarters of the Institut Curie. UV-sterilized food and 0.22 µm filtrated water will be provided ad libitum.

Inclusion criteria and randomization

Only healthy mice weighing at least 18 g will be included in the study. At the step of transplantation, tumor fragments will be randomly distributed in mice: mice are identified by a number. Due to hetergeneity in tumor take and tumor latency (period between engraftment and tumor growth), 10 mice will be engrafted to include 8 xenografts in each treatment arm.

Tumor implantation method

Tumors are maintained by serial transplantations. For each xenograft, mice will receive subcutaneous grafts of human breast cancer fragments originated from a previous passage. Fragments for this assay will originate from at least 1 donor bearing the previous tumor passage and sacrificed when the tumor reached 12 to 15 mm of diameter. All the mice of the same experiment will be implanted the same day. Tumor bearing donor mice will be sacrificed by CO2. The tumor will be aseptically excised. Tumors will be deposited in a Petri dish containing a culture medium and dissected carefully to remove the fibrous capsule usually surrounding the tumor. Necrotic tumors will be rejected. Tumor tissue will be maintained in culture medium during the transplantation procedure. Tumors will be minced into small fragments of approximately 2-3 mm using a sterile scalpel and transplanted directly into the interscapular fat pad of 8- to 12-week-old female Swiss nude mice, under anesthesia.

Humane Endpoints

Humane endpoints are carefully implemented with attentive surveillance of clinical signs. For that, mice will be daily observed for monitoring of deterioration in clinical condition. Animal weight will twice weekly monitored, consistent or rapid body weight loss reaching 20% at any time or 15% in 3 days is an endpoint. Cachexia/ muscle atrophy, persistent hypothermia, breathing difficulties, anaemia, paralysis, ulcerative lesions will also lead to experiment end. Tumour burden will be also monitored (using calliper measurement), and will not exceed 10% of the host animal's normal body weight. Other clinical signs include chronic diarrhea or constipation for more than 48 hours, sizable abdominal enlargement or ascites, prolonged bleeding from any orifice, self-mutilation.

1. *ACCUM*-Kadcyla toxicity and MTD

Pharmacokinetic and MTD studies will be performed at the Université de Sherbrooke, Quebec, Canada.

Female Nude mice (obtained from Charles River Laboratories) will be administered Kadcyla and *ACCUM*-Kadcyla as a single i.v. bolus tail-vein injection on day 1 at a starting dose of 5 mg/kg. Body weights will be measured at predose, on day 1 and daily for 21 days. In addition, serial blood sampling will be taken from the saphenous vein and collected in EDTA and heparin coated microtainers. Complete blood count and liver enzyme levels will be monitored for hematopoietic and hepato toxicity, respectively.

Acceptability criteria: The *ACCUM*-Kadcyla dose that will be used in the efficacy studies will be the highest dose in the tolerability study that results in 10% or less mean body weight loss at the end of 21 days of treatment.

Table: Toxicity studies at ADL

Group	Treatment	Dose (mg/kg/day)	Schedule	Mice
1	Kadcyla	5 mg/kg IV	Day 1	5
2	*ACCUM*-Kadcyla	5 mg/kg IV	Day 1	5
3	*ACCUM*-Kadcyla	15 mg/kg IV	Day 1	5
4	*ACCUM*-Kadcyla	25 mg/kg IV	Day 1	5
Total				**20**

A small toxicity study will be repeated at Insitut Curie to ensure toxicity is the same in the strain of Nude mice (Swiss nude) that will be used for efficacy studies. The MTD determined by ADL will be administered. Kadcyla will be injected at the standard 5 mg/kg.

2. Tumor growth inhibition (TGI) and survival effectiveness

The PDX models of human breast cancer will be *i*) Her2+ Herceptin-sensitive; *ii*) Her2+ Herceptin resistant; and *iii*) triple negative subcutaneous tumors in female nude mice. The Her2 status, type of breast cancer, tumor stage, and prior

treatment is known for each PDX model. The treatment groups, dosing schedule and injection route are defined as follows:

Table: Treatment efficacy study

Group	Treatment	Dose (mg/kg/day)	Schedule	# Mice
1	untreated			6
2	Isotype Control (Rituximab)	5 mg/kg IV	Weekly	8
3	Herceptin	15 mg/kg IV	Weekly	8
4	Kadcyla	5 mg/kg IV	Weekly	8
5	*ACCUM*-Kadcyla	5 mg/kg IV	Weekly	8
6	Kadcyla	15 mg/kg IV	Weekly	8
7	*ACCUM*-Kadcyla	15 mg/kg IV	Weekly	8
Total n° animals /PDX				**54**
Total n° animals for 3 HER2+ PDX				**162**

Each treatment arm will include 8 mice. Tumor sizes will be measured twice per week. For treatment efficacy studies, the experiments will be stopped 6 weeks after the beginning of treatment, or when individual mice have tumors that reach 1400 mm^3. Tumors will be excised at the end of experiments and cut into halves. One half of each tumor will be formalin-fixed and the other half will be snap frozen in liquid nitrogen. Tissue blocks and vials of frozen tumor can be sent to. Tumor samples will be collected from treated animals at the end of the study. The analysis of biological mechanisms will depend on results obtained in the efficacy studies and will be performed if … and Institut Curie agree on that point (a study amendment will be eventually added to include biological studies).

In addition, a small parallel experiment will be performed in a triple-negative PDX models as negative control:

Group	Treatment	Dose (mg/kg/day)	Schedule	Mice included	Mice engrafted
1	Control	Vehicle		8	10
4	*ACCUM*-Kadcyla	MTD	15 mg/kg IV	8	10
Total n° animals				**16**	**20**

Analysis of treated tumors: To be discussed: WB/IHC of different markers could be performed

3. Survival effectiveness

Studies will be perform in similar fashion to Aim 2, however, mice will be evaluated for survival.
Kaplan–Meier plots of event-free survival will be generated from efficacy experiments and analyzed with GraphPad Prism software using the log-rank Mantel-Cox test. The duration of event-free survival will be defined as time to tumour progression beyond 1000 mm3 or beyond quadrupling of tumor volume from the initial tumor volume (RTV=4).

Evaluation methodology

All raw data will be handwritten in a book and transferred into a computer database.

Tumor sizes: will be measured twice per week using a calliper. Two perpendicular diameters (a and b) will be registered. Then individual tumor volumes will be calculated as:
$a \times b^2 / 2$ in mm^3, where *a* is the largest diameter and *b* is perpendicular to *a*.

Relative tumor volume (RTV): will be calculated, as the ratio of the volume at time t divided by the initial volume at Day 0 and multiplied by 100 [$RTV_t=(V_t/V_0)x100$]. These data allow to rapidly evaluate the lack of growth when the RTV is equal to or lower than 100% (tumor regression). Curves of mean of RTV in treated and control groups as a fonction of time will be presented in the report.

Optimal growth inhibition: will be calculated as the ratio of RTV (x 100) in the treated group divided by the RTV in the controls.

Growth delay: will be calculated as the time in days necessary to reach a relative tumor volume (RTV)
Percent (%) Tumor Volume: Percent tumor volume of the difference at time *t* of mice as compared to their initial tumor volume at Day 0 and median per group will be calculated. $\%TV_t=[(TV_t - TV_0)/TV_0]x100$.

Other parameters: Weights of individual mice will be measured twice per week when tumors are measured. Percent weight of the difference at time *t* of mice as compared to their initial weight at Day 0 and means per group will be calculated. $\%BW_t=[(BW_t - BW_0)/BW_0]x100$.

Statistics

The start of treatment will be designated as Day 0 for each study. All statistical tests will be performed using Statview® software. The following parameters will be compared:

- Log-transformed tumor volume, RTV and % Tumor Volume

- optimal growth inhibition

- growth delay

- % body weight

Statistical analysis of the efficacy of the treatments for each experiment will be determined by Repeated Measures Analysis of Variance (RM-ANOVA) on log-transformed tumor volume followed by post-hoc multiple pairwise comparisons using Fisher's *t*-Test when treatment effects are significant ($p < 0.05$) in the RM-ANOVA. % Body Weight will be analysed similarly.

TGD (Tumor growth delay) values will be calculated based on the numbers of days to event. Event is the tumor quadrupling time (RTV=4). For each individual mouse a TGD value will be calculated by dividing the time to event for that mouse by the median time to event in the respective control group. Median times to event will be estimated based on the Kaplan–Meier event-free survival distribution. The exact log-rank test, as implemented using GraphPad Prism will be used to compare event-free survival distributions between treatment and control groups.

Time plan

Target date for the initiation of the study is august 2017 with experiments first conducted in ADL for MTD and then at Marie Curie for efficacy. The study will be considered as completed at issuance of the draft report (estimated date of completion 10 months after initiation of the study).

Starting date: protocol signature.
Draft report issue: 2 months after study completion

Required informations for investigated compounds

Trastuzumab and Rituximab will be provided by Institut Curie.
T-DM1 (KADCYLA) and ACCUM-Kadcyla will be provided by Jeffrey Leyton, Université de Sherbrooke, Quebec, Canada.

Code :

Form :

Molecular weight :

Supplier :

Appearance :.

Batch number :

Storage :

Reconstitution for in vivo experiment :

Safety instruction :.

Inactivation and destruction:

Dosage and route of administration :.

Administrative clauses

Protocol amendment

For any intended deviation from the protocol, an amendment to the protocol will be prepared and inserted in the final report. The amendment will be reviewed, approved, signed and dated by both the principal investigator and the study monitor. It will be maintained with the protocol.

Unintended deviations from the protocol will be registered in the laboratory notebook of the scientist who deviates from the protocol and reported in the final report.

Ethical approval

Studies will be performed in compliance with the recommendations of the French Ethical Committee and under the supervision of authorized investigators.

Archiving

The material related to this study will be archived at Institut Curie for 3 years after completion of the study.

The material to be archived includes:

- a copy of the research agreement
- a copy of the study protocol and amendments
- a copy of the quotation of the study
- a copy of the purchase approval form
- a copy of the pages of the laboratory notebooks related to the study
- the original raw data
- the derived data
- a copy of the final version of the report

STUDY COST (Institut Curie part, including direct and indirect costs)

Part of the Study	Cost (€)
Toxicity part	6000
Efficacy studies : - 3 HER2+ PDX - 1 TN PDX	 150 000 20 000
Total cost	176 000

Timelines:

Period 1(Canada) : Construction, biochemical, and in vitro quality control of ACCUM-Kadcyla. In vivo PK studies. Anti-tumor studies using cell lines like skbr3 and JIMt1.

Period 2: Toxicity and MTD (Canada)

Period 3: Toxicy study in Swiss nude mice and efficacy studies (tumor growth inhibition and survival)

Part of the Study	Timelines
Toxicity part (France)	Months 1-2
Efficacy part (France)	Months 2-10