

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K/A

(Amendment No. 1)

(Mark One)

- ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2002

or

- TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Commission File Number 0-15006

AVANT IMMUNOTHERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction
of incorporation or organization)

13-3191702

(I.R.S. Employer
Identification No.)

119 Fourth Avenue, Needham, Massachusetts
(Address of principal executive offices)

02494
(Zip Code)

Registrant's telephone number, including area code: (781) 433-0771

Securities registered pursuant to Section 12(b) of the Act: **None**

Securities registered pursuant to Section 12(g) of the Act:
Common Stock, par value \$.001

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is an accelerated filer (as defined in Exchange Act Rule 12b-2). Yes No

The aggregate market value of common stock held by non-affiliates as of June 28, 2002 was \$67,713,408 (excludes shares held by directors and executive officers). Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, direct or indirect, to direct or cause the actions of the management or policies of the registrant, or that such person is controlled by or under common control with the registrant. The number of shares of common stock outstanding at September 5, 2003 was: 64,700,534 shares.

EXPLANATORY NOTE

This Amendment No. 1 to the Annual Report on Form 10-K of Avant Immunotherapeutics, Inc. for the fiscal year ended December 31, 2002, is being filed solely for the purpose to add Exhibits 10.20 – 10.28 and 23.1 and to revise the exhibit index in Item 15 "Exhibits, Financial Statement Schedules, and Reports on Form 8-K".

PART IV

Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES, AND REPORTS ON FORM 8-K

(A) The following documents are filed as part of this Form 10-K:

(3) Exhibits:

No.	Description	Page No.
2.1	Agreement and Plan of Merger, dated as of November 20, 2000, by and among AVANT, AVANT Acquisition Corp., and Megan Health, Inc.	Incorporated by reference to Exhibit 2.1 of the Company's Current Report on Form 8-K filed December 12, 2000
2.2	First Amendment to Agreement and Plan of Merger, dated as of November 20, 2000, by and among AVANT, AVANT Acquisition Corp., and Megan Health, Inc.	Incorporated by reference to Exhibit 2.2 of the Company's Current Report on Form 8-K filed December 12, 2000
3.1	Third Restated Certificate of Incorporation of the Company	Incorporated by reference to Exhibit 3.1 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215), filed July 16, 1998
3.2	Certificate of Amendment of Third Restated Certificate of Incorporation of the Company	Incorporated by reference to Exhibit 3.1 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215), filed July 16, 1998
3.3	Certificate of Designation for Series C-1 Junior Participating Cumulative Preferred Stock	Incorporated by reference to Exhibit 3.1 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215), filed July 16, 1998
3.4	Second Certificate of Amendment of Third Restated Certificate of Incorporation of the Company	Incorporated by reference to Exhibit 3.2 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215), filed July 16, 1998
3.5	Amended and Restated By-Laws of the Company as of November 10, 1994	Incorporated by reference to Exhibit 3.3 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215), filed July 16, 1998
3.6	Third Certificate of Amendment of Third Restated Certificate of Incorporation of the Company	Incorporated by reference to Exhibit 3.1 of the Company's Quarterly Report on Form 10-Q, filed May 10, 2002
4.1	Shareholder Rights Agreement dated November 10, 1994 between the Company and State Street Bank and Trust Company as Rights Agent	Incorporated by reference to Exhibit 4.1 of the Company's Annual Report on Form 10-K filed March 28, 2000
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4.2	Amendment to Shareholder Rights Agreement between State Street Bank and Trust Company and AVANT Immunotherapeutics, Inc. dated as of December 17, 2001	Incorporated by reference to Exhibit 4.2 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2001
10.1	AVANT Immunotherapeutics, Inc. 1994 Employee Stock Purchase Plan	Incorporated by reference to Exhibit 10.1 of the Company's Registration Statement on Form S-8 filed June 8, 1994
10.2	Megan Health, Inc. Stock Option Plan	Incorporated by reference to Exhibit 4.6 of the Company's Registration Statement on Form S-8 (Reg. No. 333- 52796), filed December 27, 2000
10.3	AVANT Immunotherapeutics, Inc. 1999 Stock Option and Incentive Plan	Incorporated by reference to Exhibit A to the Company's Proxy Statement on Schedule 14A filed on April 1, 1999
10.4	Virus Research Institute, Inc. 1992 Equity Incentive Plan as amended and restated	Incorporated by reference to Exhibit 10.4 of the Company's Annual Report on Form 10-K filed March 28, 2000
10.5	Performance Plan of the Company	Incorporated by reference to Exhibit 10.5 of the Company's Annual Report on Form 10-K filed March 28, 2000
10.6	Form of Agreement relating to Change of Control	Incorporated by reference to Exhibit 10.6 of the Company's Annual Report on Form 10-K filed March 28, 2000
10.7	Amended and Restated Employment Agreement between the Company and Una S. Ryan, Ph.D. dated August 20, 1998	Incorporated by reference to Exhibit 10.8 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 1998
10.8	Commercial Lease Agreement of May 1, 1996 between the Company and Fourth Avenue Ventures Limited Partnership	Incorporated by reference to Exhibit 10.11 of the Company's quarterly report on Form 10-Q/A for the quarterly period ended June 30, 1996 (File No. 0-15006)
10.9	Extension of Lease Agreement of May 1, 1997 between the Company and DIV Needham 53 LLC (successor in interest to Fourth Avenue	Incorporated by reference to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2001

Ventures Limited Partnership) dated as of August 23, 2001

10.10	Option Agreement by and between the Company and Novartis Pharma AG dated as of October 31, 1997, portions of which are subject to a request for confidential treatment	Incorporated by reference to Exhibit 10.16 of the Company's Quarterly Report on Form 10-Q/A for the quarterly period ended September 30, 1997
10.11	Settlement Agreement between the Company and Forest City 38 Sidney Street, Inc.; Forest City Management, Inc.; and Forest City Enterprises, Inc.	Incorporated by reference to Exhibit 10.15 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 1997
10.12	Agreement between Lonza Biologics plc and the Company dated as of April 19, 2000, portions of which are subject to confidential treatment	Incorporated by reference to Exhibit 10.11 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2000
10.13	Stock Purchase Agreement dated December 1, 2000 by and between the Company and Pfizer Inc	Incorporated by reference to Exhibit 10.12 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2000

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10.14	License and Royalty Agreement by and between Pfizer Inc, the Company and Megan Health, Inc. dated as of December 1, 2000, portions of which are subject to confidential treatment	Incorporated by reference to Exhibit 10.13 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2000
10.15	Amendment to License and Royalty Agreement by and between Pfizer Inc., the Company and Megan Health, Inc. dated as of December 1, 2000, portions of which are subject to confidential treatment	Incorporated by reference to Exhibit 10.14 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2000
10.16	Collaborative Research and Development Agreement by and between Pfizer Inc. and Megan Health, Inc. dated as of December 1, 2000, portions of which are subject to confidential treatment	Incorporated by reference to Exhibit 10.15 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2000
10.17	Exclusive License Agreement between AVANT Immunotherapeutics, Inc. and DynPort Vaccine Company, LLC dated as of October 10, 2001, portions of which are subject to a request for confidential treatment	Incorporated by reference to Exhibit 10.17 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2001
10.18	First Amendment to AVANT Immunotherapeutics, Inc. 1999 Stock Option and Incentive Plan	Incorporated by reference to Exhibit 10.18 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2001
10.19	First Amendment to Amended and Restated Employment Agreement between the Company and Una S. Ryan, Ph.D. dated as of December 23, 2002	Previously filed with the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2002
10.20	License Agreement between Virus Research Institute, Inc. and SmithKline Beecham PLC dated as of December 1, 1997, portions of which are subject to confidential treatment	Incorporated by reference to Exhibit 10.20 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 1999
10.21	Amendment Agreement, dated January 9, 2003, between the Company and SmithKline Beecham PLC	Filed herewith
10.22	License Agreement, dated as of January 31, 2003, by and between the Company and Elan Drug Delivery Limited	Filed herewith
10.23	License and Clinical Trials Agreement, effective as of February 27, 1995, between Virus Research Institute, Inc. and the James N. Gamble Institute of Medical Research	Filed herewith
10.24	License Agreement, dated as of May 1, 1992, by and between the President and Fellows of Harvard College and Virus Research Institute, Inc.	Filed herewith
10.25	Amendment to License Agreement, dated July 23, 1993, by and between the President and Fellows of Harvard College and Virus Research Institute, Inc.	Filed herewith
10.26	Amendment to License Agreement, dated as of August 2, 2000, by and between the President and Fellows of Harvard College and the Company	Filed herewith

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10.27	PHS Patent License Agreement–Nonexclusive, dated March 25, 1998, by and between the National Institutes of Health and Virus Research Institute, Inc.	Filed herewith
10.28	License Agreement, dated as of November 25, 1988, by and among The Johns Hopkins University, Brigham and Women’s Hospital and the Company f/k/a T Cell Sciences, Inc.	Filed herewith
21.0	List of Subsidiaries	Incorporated by reference to Exhibit 21.0 of the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2001
23.0	Consent of Independent Accountants	Previously filed with the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2002
23.1	Consent of L.E.K. Consulting LLC	Filed herewith
31.1	Certification of President and Chief Executive Officer	Filed herewith
31.2	Certification of Senior Vice President and Chief Financial Officer	Filed herewith

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this amendment to be signed on its behalf by the undersigned, thereunto duly authorized.

AVANT IMMUNOTHERAPEUTICS, INC.

Date: September 12, 2003

By: /s/ Una S. Ryan
 Una S. Ryan
 President and Chief Executive Officer

Amendment Agreement

This Amendment Agreement is made this 9th day of January 2003 ("Effective Date") by and between:

- (1) **AVANT IMMUNOTHERAPEUTICS INC**, having a place of business at 119 Fourth Avenue, Needham, MA 02494-2725, United States of America ("AVANT"); and
- (2) **SMITHKLINE BEECHAM PLC**, having its registered office at 980 Great West Road, Brentford, Middlesex TW8 9GS, United Kingdom ("GSK").

Whereas:

- (A) AVANT (as legal successor of Virus Research Institute, Inc.) and GSK entered in to a License Agreement dated 1 December 1997 (the "Agreement") relating to the field of Rotavirus.
- (B) As a result of, amongst other things, increased requirements of regulatory authorities for clinical safety data, the initiation of a Phase III clinical study under an IND in the US, and therefore payment of the second milestone fee, has been delayed.
- (C) Whereas GSK is proposing to undertake a Phase III clinical study in Latin America.
- (D) The parties hereto ("Parties") wish to amend the Agreement on the terms set out in this Amendment Agreement.

Therefore, the Parties have agreed for good and valuable consideration, receipt of which is hereby acknowledged:

1. Paragraph 5.01 shall be deleted and replaced by the following:

"5.01 Subject to the provisions of Paragraph 5.02 below and the further provisions of this Paragraph 5.01, LICENSEE will, in accordance with LICENSEE's reasonable business and scientific judgement, exercise its reasonable efforts and diligence in developing VACCINE.

Only in the event that:

- (a) a competitor vaccine product against rotavirus is registered in one or more MAJOR MARKETS (each a "RELEVANT MAJOR MARKET"): and
- (b) LICENSEE has significant Phase IV data (as defined below) from countries that are not MAJOR MARKETS to support applications for

governmental approvals to market VACCINE in the RELEVANT MAJOR MARKET(S),

shall LICENSEE be obliged to use its reasonable efforts and diligence to undertake investigations and actions required to obtain appropriate governmental approvals to market VACCINE in the RELEVANT MAJOR MARKET(S) and to commercialise VACCINE in those RELEVANT MAJOR MARKET(S) in which such governmental approval is obtained. For the purpose of this Paragraph 5.01 (b), "significant Phase IV data" shall mean post-marketing safety data on 2 million vaccinees with respect to the VACCINE so as to allow a proper assessment of the Intussusception risk associated with the VACCINE.

All such activity shall be undertaken at LICENSEE's expense. At LICENSEE's request and expense, LICENSOR shall supply LICENSEE with reasonable technical assistance in undertaking such investigations and actions."

2. GSK hereby agrees to pay AVANT US\$1 million within 30 days of the Effective Date of this Agreement. Such payment shall be considered as in lieu of the "second milestone fee" of US 1million provided for in Paragraph 5.02(c) and such fee shall be considered made in full. For the avoidance of doubt the proposed Phase III clinical study to be undertaken by GSK in Latin America shall not be considered to be the pivotal Phase III study as referred to in Paragraphs 5.02 (c) and (d).

3. Paragraph 19.01 shall be deleted and replaced with the following:

"19.01 Any notice required or permitted under this Agreement shall be sent by certified mail, return receipt requested, postage pre-paid to the following addresses of the parties:

if to LICENSOR:

AVANT Immunotherapeutics, Inc.,
119 Fourth Avenue
Needham, MA 02494-2725,
USA
Attention: President

with a copy to:

Leon R. Yankwich
Yankwich and Associates
201 Broadway
Cambridge, MA 02139

if to LICENSEE:

SmithKline Beecham PLC.
980 Great West Road
Brentford
Middlesex TW8 9GS
United Kingdom
Attention: General Counsel

with a copy to:
GlaxoSmithKline Biologicals Manufacturing S.A.
rue de l'Institut 89
1330 Rixensart, Belgium
Attention: President

4. All other provisions of the Agreement shall remain unchanged and in full force and effect.

IN WITNESS WHEREOF, the parties, through their authorised officers, have executed this Amendment Agreement on the date above written.

AVANT IMMUNOTHERAPEUTICS INC

BY: /s/ Dr. Una S. Ryan, O.B.E.
Dr. Una S. Ryan, O.B.E.
President and C.E.O.

SMITHKLINE BEECHAM PLC,

BY: /s/ Moncef Slaoui
Moncef Slaoui
Attorney in fact

LICENSE AGREEMENT

THIS AGREEMENT, effective this 31st day of January, 2003, (“the Effective Date”) is entered into by AVANT IMMUNOTHERAPEUTICS, INC., (“AVANT” or “LICENSEE” herein) a Delaware corporation having its principal place of business at 119 Fourth Avenue, Needham, MA 02494, and ELAN DRUG DELIVERY LIMITED (“ELAN” or “LICENSOR” herein) an English corporation having its registered office at 1 Mere Way, Ruddington, Nottingham NG11 6JS, England.

WHEREAS, LICENSOR has or stands to acquire by assignment from UPT Asset Holdings, LLC certain PATENT RIGHTS (as defined below) pertaining to methods for preserving or stabilizing active ingredients as described in patent applications, granted or otherwise, listed in Schedule A attached hereto (“Elan Patent Applications”); in patent applications, granted or otherwise, listed in Schedule B attached hereto (“Related UPT Applications”); and in patent applications, granted or otherwise, listed in Schedule C attached hereto (“Elan Stabilization Patents”), in respect of which it is prepared to grant a license to LICENSEE pursuant to the terms set forth herein.

WHEREAS, LICENSEE wishes to acquire a license under PATENT RIGHTS of LICENSOR.

WHEREAS, LICENSEE stands to acquire by asset transfer from UPT Asset Holdings, LLC certain intellectual property rights listed in Schedule D (the “Transferred Patent Applications”), in respect of which it is prepared to covenant not to assert said intellectual property rights against LICENSOR and entities associated with it, as recited below.

WHEREAS, LICENSOR wishes to secure such a covenant of non-assertion from LICENSEE with respect to the Transferred Patent Applications.

NOW, THEREFORE, in consideration of the mutual covenants, payment and understandings set forth herein and in a Deed of Assignment of Patents and Patent Applications between UPT Asset Holdings, LLC, OCM Principal Opportunities Fund, L.P. and ELAN, and an Asset Purchase Agreement between OCM Principal Opportunities Fund, L.P., UPT Asset Holdings, LLC and AVANT, both executed on even date herewith, LICENSOR and LICENSEE hereby agree as follows:

1. Definitions.

As used herein, the following terms shall have the meanings set forth below:

1.1 PATENT RIGHTS means any subject matter that is encompassed by a claim of an APPLICATION or any division, continuation, continuation in part, reissue, substitute, and extension thereof, or any patent issuing therefrom, and any foreign counterparts of any of

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the foregoing (except for those counterparts included within the Transferred Patent Applications or otherwise not prosecuted or maintained by Elan).

1.2 APPLICATION means any of the patents or patent applications listed in Schedule A (attached hereto), Schedule B (attached hereto), or Schedule C (attached hereto), and any divisions, continuations, reissues, substitutes, and extensions thereof.

1.3 LICENSED TERRITORY means worldwide.

1.4 LICENSED PRODUCT means a product encompassed by PATENT RIGHTS or produced using a process encompassed by PATENT RIGHTS.

1.5 LICENSED PROCESS means any method encompassed by PATENT RIGHTS.

1.6 AFFILIATE means any legal entity (such as a corporation, partnership, or limited liability company) that controls or is controlled by AVANT or by ELAN. For the purposes of this definition, the term “control” means (i) beneficial ownership of at least fifty percent (50%) of the voting securities of a corporation or other business organization with voting securities or (ii) a fifty percent (50%) or greater interest in the net assets or profits of a partnership or other business organization without voting securities.

1.7 AVANT FIELD means all stabilization processes, drying processes and methods of formulation, including but not limited to those involving freeze-drying and/or spray-drying and/or supercritical fluid, and/or preservation and/or delivery of:

- (A) vaccines for oral administration for delivery to the gastrointestinal tract (excluding buccal and/or sublingual and/or inhalation routes of administration) or for intravaginal administration, including but not limited to (i) bacterial vaccines and vectors, and (ii) viral vaccines and vectors; and
- (B) vaccines for administration to animals (i) via the drinking water, and/or (ii) as a coarse spray, and/or (iii) in the form of eye drops;
- (C) vaccines for administration to avian species by any means;

and the vaccines referred to in clauses (A) and (B) and (C) of this paragraph thus stabilized and/or preserved and/or to be delivered.

The AVANT FIELD shall exclude:

- (1) the use of Hydrophobically Derivatized Carbohydrates (“HDCs”) (as defined in patent publication WO 96/03978 (international application no. PCT/GB95/01861), “Elan’s Solidose Patent”) where such HDCs are part of either (i) a vaccine formulation administered in solid form or (ii) a vaccine formulation administered in liquid form where the HDCs are not in solution; and
- (2) the ELAN FIELD as described below.

1.8 ELAN FIELD means all stabilization processes, drying processes and methods of formulation, including but not limited to those involving freeze-drying and/or spray-drying and/or supercritical fluid, and/or preservation and/or delivery of:

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- (A) vaccines and/or active pharmaceutical ingredients for administration (i) by injection, including but not limited to intra-epidermal, intra-dermal, sub-cutaneous, intra-muscular and intra-peritoneal administration; (ii) into, onto and/or across the skin, including but not limited to intra-epidermal, intra-dermal, sub-cutaneous, intra-muscular and intra-peritoneal administration; (iii) to and/or via the nasal cavity and/or pulmonary tract; and/or (iv) by buccal and/or sub-lingual routes of administration (excluding oral administration for delivery to the gastrointestinal tract);
- (B) blood factors including but not limited to Factor VIII;
- (C) blood cells including but not limited to platelets;
- (D) materials used in connection with the diagnosis of disease and/or genetic disorders;
- (E) materials used in connection with the measurement of glucose in blood, plasma, serum and/or interstitial fluid; and
- (F) materials used in connection with the in vitro analysis of human specimens and predictive medicine in pharmacogenomics

and the vaccines and/or ingredients, blood factors, blood cells, and/or other materials thus stabilized and/or preserved and/or to be delivered. The ELAN FIELD shall exclude the AVANT FIELD.

2. Grant of Rights.

2.1 License Grant.

LICENSOR hereby grants to LICENSEE:

- (1) a worldwide, royalty-free, exclusive license in the AVANT FIELD under Elan Patent Applications and Related UPT Applications to make, have made, use, sell, offer to sell, have sold, and import LICENSED PRODUCTS and to practice LICENSED PROCESSES;
- (2) a worldwide, royalty-free, non-exclusive license under Elan Patent Applications and Related UPT Applications in all fields of use excluding the ELAN FIELD to make, have made, use, sell, offer to sell, have sold, and import LICENSED PRODUCTS and to practice LICENSED PROCESSES;
- (3) a worldwide, royalty-free, non-exclusive license in the AVANT FIELD under Elan Stabilization Patents to make, have made, use, sell, offer to sell, have sold, and import LICENSED PRODUCTS and to practice LICENSED PROCESSES;
- (4) a worldwide, royalty-free license under Elan Patent Applications (Schedule A) and Related UPT Applications (Schedule B), for the benefit of Stratagene, as licensee from Universal Preservation Technologies, Inc. ("UPT") in the field described in the Exclusive License Agreement dated March 1, 2002, and as amended, by and between UPT and Stratagene ("the Stratagene License Agreement", copy attached as Schedule E) to make, have made, use, sell, offer to sell, have sold, and import Licensed Products as such term is defined in the Stratagene License Agreement.

LICENSOR further agrees that subsequent to October 24, 2002, no additional or further licenses under the Elan Patent Applications or the Related UPT Applications have been or

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will be granted by LICENSOR with respect to the manufacture, use, sale, offer for sale, and importation of Licensed Products (as such term is defined in the Stratagene License Agreement) within the Licensed Field (as such term is defined in the Stratagene License Agreement).

LICENSEE acknowledges that, through the Asset Purchase Agreement, LICENSEE shall be assigned the Development and License Agreement entered into between American Home Products Corporation, acting through its Fort Dodge Animal Health division ("FDAH"), and Universal Preservation Technologies("UPT") dated August 25, 1998, which agreement granted a license from UPT to FDAH of certain UPT patents and patent applications now being assigned to Elan pursuant to the Deed of Assignment and licensed to Avant pursuant to this LICENSE AGREEMENT. The field of said FDAH-UPT agreement is limited to avian vaccines and does not extend to vaccines for administration to humans.

LICENSEE further acknowledges and agrees that, except as specifically provided above, no other license is granted or implied under PATENT RIGHTS or any other patent rights, and agrees not to practice PATENT RIGHTS outside of the license grant pursuant to Section 2.1(1) to (4) inclusive

2.2 Sublicenses.

Except as set forth with respect to the existing Stratagene licensee in this subsection, LICENSEE may sublicense, directly or indirectly, through multiple tiers, the rights and licenses granted to LICENSEE in accordance with Section 2.1. LICENSEE shall give written notice of each sublicense to LICENSOR promptly, and any such sublicense shall include terms of confidentiality at least as strict as those set forth in Section 6 below. The rights of Stratagene to sublicense the rights granted hereunder shall be governed by the Stratagene License Agreement (Schedule E).

LICENSEE shall be liable for all acts and omissions of its sub-licensees which, if committed by LICENSEE, would constitute a breach of any of the covenants or obligations of LICENSEE in this LICENSE AGREEMENT.

2.3 Retained Rights. Except as set forth in Sections 2.1 and 2.2 above, LICENSOR shall retain all other rights in PATENT RIGHTS.

3. Consideration for Grant of Rights.

3.1 In consideration of the license of the PATENT RIGHTS hereunder, upon execution of this LICENSE AGREEMENT, LICENSEE agrees to pay LICENSOR the non-refundable sum of Five Hundred Thousand U.S. Dollars (US\$500,000.00). No further royalties, payments, or other consideration will be exchanged between the parties in connection with the execution of this LICENSE AGREEMENT.

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The foregoing sum shall not be subject to any future performance obligations of LICENSOR to LICENSEE and shall not be applicable against future services provided by LICENSOR to LICENSEE. The terms of this Clause 3 are independent and distinct from the other terms of this Agreement. For the avoidance of doubt, the foregoing shall be without prejudice to LICENSOR'S other obligations under this LICENSE AGREEMENT which are assumed in consideration of LICENSEE'S other obligations hereunder.

4. Licensee Obligations.

4.1 Indemnification.

(a) Indemnity. LICENSEE or its permitted sublicensees or any party acting on its behalf, shall indemnify, defend, and hold harmless ELAN and its directors, officers, employees, and agents and their respective successors, heirs and assigns (the "Indemnitees"), against any liability, damage, loss, or expense (including reasonable attorneys fees and expenses of litigation) incurred by or imposed upon any of the Indemnitees in connection with any claims, suits, actions, demands or judgments arising out of any theory of liability (including without limitation actions in the form of tort, warranty, or strict liability and regardless of whether such action has any factual basis) concerning any product, process, or service that is made, used, sold, offered for sale, or imported pursuant to any right or license granted under this LICENSE AGREEMENT; provided, however, that such indemnification shall not apply to any liability, damage, loss, or expense to the extent directly attributable to the gross negligence or wilful misconduct of the Indemnitees. LICENSEE'S indemnification obligations shall specifically extend to any such claim, suit, action or demand brought by a third party alleging that the making, using, selling, offering for sale or importing of a LICENSED PRODUCT infringes any intellectual property rights of a third party.

(b) Procedures. The Indemnitees agree to provide LICENSEE with prompt written notice of any claim, suit, action, demand, or judgment for which indemnification is sought under this LICENSE AGREEMENT, but any delay in notification shall relieve LICENSEE of its liability to indemnify hereunder only to the extent that LICENSEE is actually prejudiced thereby. LICENSEE agrees, at its own expense, to provide attorneys reasonably acceptable to the Indemnitees to defend against any such claim. The Indemnitees shall cooperate fully with LICENSEE in such defense and will permit LICENSEE to conduct and control such defense and the disposition of such claim, suit, or action (including all decisions relative to litigation, appeal, and settlement); provided, however, that any Indemnitee shall have the right to retain its own counsel, at its own expense, if representation of such Indemnitee by the counsel retained by LICENSEE is deemed inappropriate because of perceived or potential conflicts in the interests of such Indemnitee and any other party represented by such counsel. LICENSEE agrees to keep the Indemnitees informed of the progress in the defense and disposition of such claim and to consult with the Indemnitees with regard to any proposed settlement. In defending against such claim, suit, action, demand or judgment, LICENSEE shall not take any position adverse to the validity of the PATENT RIGHTS without the prior written consent of LICENSOR, which shall not be unreasonably refused.

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4.2. Use of ELAN Name. LICENSEE and its AFFILIATES shall not use the name "Elan" or "Elan Drug Delivery Limited" or any variation of those names in connection with the marketing or sale of any LICENSED PRODUCTS without the prior written consent of ELAN.

4.3. Marking of LICENSED PRODUCTS. To the extent commercially feasible and consistent with prevailing business practices, LICENSEE shall mark, and shall cause its AFFILIATES to mark, all LICENSED PRODUCTS that are manufactured or sold under this LICENSE AGREEMENT with the number of each issued patent under the PATENT RIGHTS that applies to such LICENSED PRODUCT.

4.4. Orange Book Submission. LICENSEE shall submit to the Food & Drug Administration, or other relevant agency, documents necessary to include in the Orange Book, or similar publication, each issued patent under the PATENT RIGHTS that applies to a LICENSED PRODUCT sold by LICENSEE.

4.5. Compliance with Law. LICENSEE shall comply with, and shall ensure that its AFFILIATES comply with, all local, state, and federal laws and regulations relating to the development, manufacture, use, and sale of LICENSED PRODUCTS.

4.6. Non-Assertion. LICENSEE covenants and agrees not to assert outside the AVANT FIELD the Transferred Patent Applications and/or any patents issuing from any of the Transferred Patent Applications and/or any patents which are subsequently abandoned by LICENSOR and taken over by LICENSEE pursuant to the provisions of this LICENSE AGREEMENT, against ELAN, its AFFILIATES, successors, customers, and/or licensees (both current and future). If LICENSEE assigns or licenses (except with respect to the Stratagene licensee mentioned above) or otherwise disposes of all or any of the patents or patent rights referred to in this Section 4.6, such assignment or license shall include a comparable non-assertion provision.

5. Patents and Infringement.

5.1. Responsibility for PATENT RIGHTS. In connection with LICENSOR'S prosecution of APPLICATIONS, LICENSOR shall, subject to subsection 5.3 below, use commercially reasonable efforts to obtain claims in the AVANT FIELD. Limited to the extent related to the AVANT FIELD, LICENSOR shall generally keep LICENSEE informed about significant prosecution activities relating to the Elan Patent Applications and the Related UPT Applications and give LICENSEE personnel reasonable access to patent personnel of LICENSOR involved in or knowledgeable of such prosecution activities, with instructions to cooperate with LICENSEE as to matters relating to the Elan Patent Applications and Related UPT Applications and licenses granted pursuant to this LICENSE AGREEMENT.

5.2. Cooperation. If requested by the LICENSOR, the LICENSEE shall cooperate fully with the LICENSOR in the preparation, filing, prosecution, and maintenance of all PATENT RIGHTS. In the same manner, LICENSOR shall cooperate fully with LICENSEE

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as reasonably necessary in preparation, filing, prosecution, and maintenance of applications added to Transferred Patent Applications subsequent to the Effective Date pursuant to Section 5.3 below. Such cooperation includes, without limitation, (i) promptly executing all papers and instruments or requiring employees of LICENSOR or LICENSEE to execute such papers and instruments as reasonable and appropriate so as to enable LICENSOR or LICENSEE to file, prosecute, and maintain such PATENT RIGHTS in any country; and (ii) promptly informing the other party of matters that may affect the preparation, filing, prosecution, or maintenance of any such PATENT RIGHTS (such as becoming aware of an additional inventor who is not listed as an inventor in a patent application).

5.3. Abandonment. LICENSOR shall have the right, but not the obligation, to continue to prosecute and maintain the APPLICATIONS and any patents issuing therefrom. In the event that LICENSOR desires to abandon any patent or APPLICATION within the Elan Patent Applications (Schedule A) or the Related UPT Applications (Schedule B), LICENSOR shall, strictly subject to its other third party obligations:

(i) notify LICENSEE in advance and in a timely manner with respect to upcoming deadlines where LICENSOR is not intending to take steps to meet the deadline; and

(ii) give LICENSEE the opportunity to take over the prosecution and/or maintenance, at its own expense, of any such patent or APPLICATION. In the event that LICENSOR elects not to continue prosecuting or maintaining an APPLICATION or any patent issuing therefrom in any jurisdiction, LICENSOR shall notify LICENSEE, and, subject to any third party agreements existing as of the date hereof, LICENSEE shall have the option to prosecute and/or maintain, at its own expense, such APPLICATION or patent in such jurisdictions. LICENSOR agrees, subject to any third party agreements existing as of the date thereof, to assign to LICENSEE any such APPLICATION that LICENSEE elects to prosecute and/or maintain after LICENSOR'S decision to abandon. LICENSOR agrees, upon LICENSEE'S request, and at LICENSEE'S expense, to execute all legal documents required for preparation, filing, prosecution, and maintenance of any APPLICATION or patent issuing therefrom for which LICENSEE has taken over prosecution and/or maintenance responsibility. Any APPLICATION or patent transferred in accordance with this Section 5.3 from LICENSOR or LICENSEE shall be regarded as a patent or patent right belonging to the Transferred Patent Applications, and following such transfer such patents or patent rights shall be treated under this LICENSE AGREEMENT in accordance with the provisions herein relating to the Transferred Patent Applications (including but not limited to Section 4.6).

5.4. Infringement.

(a) Notification of Infringement. Each party agrees to provide written notice to the other party promptly after becoming aware of any infringement of the PATENT RIGHTS, save that the LICENSOR shall be under no obligation to provide such notice to the LICENSEE in relation to any infringement in the ELAN FIELD.

(b) LICENSEE Right to Enforce. LICENSEE, as the exclusive licensee in accordance with Section 2.1(1) in the AVANT FIELD, shall have the right, under its own control and at its own expense, to bring suit against any third party for infringement in the AVANT FIELD of the Related UPT Applications and the Elan Patent Applications. Prior to

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commencing any such action, LICENSEE shall consult with LICENSOR and shall consider the views of LICENSOR regarding the advisability of the proposed action and its effect on the public interest. LICENSEE shall not enter into any settlement, consent judgment, or other voluntary final disposition of any infringement action under this Subsection 5.4(b) without the prior written consent of LICENSOR, which consent shall not be unreasonably withheld or delayed. LICENSEE shall not take any position adverse to the validity of the Related UPT Applications or the Elan Patent Applications without first consulting with LICENSOR. Any recovery obtained in an action under this Subsection 5.4(b) shall be distributed as follows: (i) LICENSEE shall be reimbursed for any expenses incurred in bringing and prosecuting the action, (ii) LICENSOR shall be reimbursed for any non-reimbursed expenses (see Subsection 5.4(f) below), and (iii) from any remaining recovery, LICENSEE shall receive seventy-five percent (75%) and LICENSOR shall receive twenty-five percent (25%).

(c) LICENSOR Right to Enforce. In the event that LICENSEE elects not to exercise its right of enforcement under Subsection 5.4(b) or fails to initiate an infringement action within nine months after it first becomes aware of the basis for such action, LICENSOR shall have the right to bring suit against any third party for infringement within the AVANT FIELD, under its sole control and at its sole expense, and any recovery obtained shall be distributed as follows: (i) LICENSOR shall be reimbursed for any expenses incurred in bringing and prosecuting the action, (ii) LICENSEE shall be reimbursed for any non-reimbursed expenses (see Subsection 5.4(f) below) and (iii) from any remaining recovery, LICENSOR shall receive one hundred percent (100%). LICENSOR shall have the sole right to bring suit under PATENT RIGHTS against a third party for infringement in the ELAN FIELD, or to answer and defend a declaratory judgement action involving any PATENT RIGHTS, and any recovery obtained in such an action by LICENSOR shall be the sole property of LICENSOR. LICENSOR shall have the unilateral right to enter into any settlement, consent judgment, or other voluntary final disposition of an infringement action under this Subsection 5.4(c), except that as part of such settlement, consent judgment, or other voluntary final disposition, LICENSOR shall not take a position adverse to the validity of the Related UPT Applications or the Elan Patent Applications without prior written consent of LICENSEE which shall not be unreasonably refused.

(d) LICENSEE Second Right to Enforce. LICENSOR shall have the right, under its own control and at its own expense, to bring suit against any third party for infringement of PATENT RIGHTS outside the AVANT FIELD and outside the ELAN FIELD, and recovery obtained in such an action by LICENSOR shall be the sole property of LICENSOR. LICENSOR shall have the unilateral right to enter into any settlement, consent judgment, or other voluntary final disposition of an infringement action under this Subsection 5.4(d), except that, as part of such settlement, consent judgment, or other voluntary final disposition, LICENSOR shall not take a position adverse to the validity of the Related UPT Applications or the Elan Patent Applications without prior written consent of LICENSEE which shall not be unreasonably refused. In the event that LICENSOR elects not to exercise its right of enforcement under this Subsection 5.4(d) with respect to Related UPT Applications or Elan Patent Applications or fails to initiate an infringement action within nine months after it first becomes aware of the basis for such action under the Related UPT

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Applications or Elan Patent Applications, subject to third party rights existing as of the date hereof, LICENSEE shall have the right to bring suit against any third party for infringement, under its sole control and at its sole expense; provided however, that LICENSEE shall not take any position adverse to the validity of the Related UPT Applications or Elan Patent Applications without prior written consent of LICENSOR which shall not be unreasonably refused. Any recovery for a suit brought by LICENSEE pursuant to this Subsection 5.4(d) shall be distributed as follows: (i) LICENSEE shall be reimbursed for any expenses incurred in bringing and prosecuting the action, (ii) LICENSOR shall be reimbursed for any non-reimbursed expenses (see Subsection 5.4(f) below), and (iii) from any remaining recovery, LICENSEE shall receive one hundred percent (100%).

(e) LICENSEE shall have the sole right to bring suit under Transferred Patent Applications against a third party for infringement, or to answer and defend a declaratory judgement action involving any Transferred Patent Applications, and any recovery obtained in such an action by LICENSEE shall be the sole property of LICENSEE. LICENSEE shall have the unilateral right to enter into any settlement, consent judgment, or other voluntary final disposition of an infringement action under this Subsection 5.4(e).

(f) Cooperation. Each party agrees to cooperate fully in any action brought under this Section 5.4 that is controlled by the other party, provided that the controlling party reimburses the cooperating party promptly for any costs and expenses incurred by the cooperating party in connection with providing such assistance.

6. Confidential Information; Publications; Publicity.

6.1. Confidential Information.

(a) Designation. Confidential Information that is disclosed pursuant to this LICENSE AGREEMENT in writing shall be marked with a legend indicating its confidential status (such as “Confidential” or “Proprietary”). Confidential Information that is disclosed pursuant to this LICENSE AGREEMENT orally or visually shall be documented in a written notice prepared by the Disclosing Party and delivered to the Receiving Party within thirty (30) days of the date of disclosure; such notice shall summarize the Confidential Information disclosed to the Receiving Party and reference the time and place of disclosure.

(b) Obligations. For a period of five (5) years after disclosure of any portion of Confidential Information, the Receiving Party shall (i) maintain such Confidential Information in strict confidence, except that the Receiving Party may disclose or permit the disclosure of any Confidential Information to its directors, officers, employees, consultants, and advisors who are obligated to maintain the confidential nature of such Confidential Information and who have a need to know such Confidential Information; (ii) use such Confidential Information solely for the purposes of this LICENSE AGREEMENT; and (iii) allow its directors, officers, employees, consultants, and advisors to reproduce the Confidential Information only to the extent necessary for the purposes of this LICENSE AGREEMENT, with all such reproductions being also considered Confidential Information.

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(c) Exceptions. The obligations of the Receiving Party under Subsection 6.1(b) above shall not apply to any Confidential Information to the extent that the Receiving Party can demonstrate that such Confidential Information (i) was in the public domain prior to the time of its disclosure to the Receiving Party; (ii) entered the public domain after the time of its disclosure to the Receiving Party through means other than an unauthorized disclosure resulting from an act or omission by the Receiving Party; (iii) was independently developed or discovered by the Receiving Party without use of or reference to the Confidential Information; (iv) is or was disclosed to the Receiving Party at any time, whether prior to or after the time of its disclosure under this LICENSE AGREEMENT, by a third party having no fiduciary relationship with the Disclosing Party and having no obligation of confidentiality with respect to such Confidential Information; or (v) is required to be disclosed to comply with applicable laws or regulations, or with a court or administrative order, provided that the Disclosing Party receives reasonable prior written notice of such disclosure and the Receiving Party cooperates in legal efforts to limit such disclosure.

(d) Ownership and Return. The Receiving Party acknowledges that the Disclosing Party (or any third party entrusting its own information to the Disclosing Party) retains a proprietary interest in its Confidential Information in the possession of the Receiving Party. Upon the expiration or termination of this LICENSE AGREEMENT, and at the request of the Disclosing Party, the Receiving Party shall return to the Disclosing Party all originals, copies, and summaries of documents, materials, and other tangible manifestations of Confidential Information in the possession or control of the Receiving Party, except that the Receiving Party may retain one copy of the Confidential Information in the possession of its legal counsel solely for the purpose of monitoring its obligations under this LICENSE AGREEMENT.

6.2. Publications. Both parties and their employees will be free to publicly disclose (through journals, lectures, or otherwise) the results of any research relating to the subject matter of the PATENT RIGHTS.

6.3. Publicity Restrictions.

(a) The specific terms of this LICENSE AGREEMENT are confidential and shall not be disclosed to a third party without the prior written approval of the other party, except that either party may disclose this LICENSE AGREEMENT (1) to its AFFILIATES and professional advisers or in connection with the sale or proposed sale of all or substantially all of the assets related to the subject matter of this LICENSE AGREEMENT; and (2) in any prospective, offering memorandum, or other document or filing required by applicable securities laws or other applicable law or regulation. To the extent disclosure of this LICENSE AGREEMENT, or the terms thereof, is required by law, the disclosing party shall take all reasonable steps necessary to preserve the continued confidentiality of this LICENSE AGREEMENT.

(b) Except as set forth above in Subsection 6.3(a), neither party will, without the prior written consent of the other party, issue any press release or promotional

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material or make any other public announcement or furnish any public statement to any person concerning this LICENSE AGREEMENT.

7. Term and Termination.

7.1. Term. This LICENSE AGREEMENT shall commence on the Effective Date and shall remain in effect on a country by country basis until the expiration of the last to expire of any patent issuing from the APPLICATIONS in that country.

7.2. Voluntary Termination by LICENSEE. LICENSEE shall have the right to terminate this LICENSE AGREEMENT, for any reason, upon ninety (90) days prior written notice to LICENSOR. In the event that LICENSEE terminates this LICENSE AGREEMENT under this Section 7.2., all licensed rights granted to LICENSEE, including those granted for the benefit of Stratagene, shall revert to LICENSOR. Voluntary termination by LICENSEE under this Section 7.2 shall not reverse any assignment of PATENT RIGHTS that has occurred pursuant to Section 5.3 above.

7.3. Termination for Default. In the event that either party commits a material breach of its obligations under this LICENSE AGREEMENT and fails to cure that breach within sixty (60) days after receiving written notice thereof, the other party may initiate executive discussions regarding resolution of the breach. If these good-faith discussions fail to yield a resolution of the breach within another sixty (60) day period, the other party may terminate this LICENSE AGREEMENT upon written notice to the party in breach.

7.4. Termination by LICENSOR. In the event that LICENSEE institutes legal action against LICENSOR challenging the validity, ownership or scope of the PATENT RIGHTS, LICENSOR shall be entitled to terminate this LICENSE AGREEMENT by written notice, with respect to the PATENT RIGHTS so challenged.

7.5. Force Majeure. Neither party will be responsible for delays resulting from causes beyond the reasonable control of such party, including without limitation, fire, explosion, flood, war, strike, or riot, provided that the nonperforming party uses commercially reasonable efforts to avoid or remove such causes of nonperformance and continues performance under this LICENSE AGREEMENT with reasonable dispatch whenever such causes are removed.

7.6. Effect of Termination. The following provisions shall survive the expiration or termination of this LICENSE AGREEMENT: Articles 1 and 8; Sections 4.1, 4.4, 4.5, 4.6, 6.1, 6.3, and 7.6. Upon the early termination of this LICENSE AGREEMENT, LICENSEE and its AFFILIATES may complete and sell any work-in-progress and inventory of LICENSED PRODUCTS that exist as of the effective date of termination, provided that LICENSEE and its AFFILIATES complete and sell all work-in-progress and inventory of LICENSED PRODUCTS within one year after the effective date of termination. Upon the termination of this LICENSE AGREEMENT pursuant to the terms and conditions herein, LICENSEE and its AFFILIATES shall stop using all LICENSED PRODUCTS and stop

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practicing LICENSED PROCESSES except as permitted in the preceding sentence; and any sublicense granted hereunder shall automatically terminate.

8. Dispute Resolution.

In the event of any dispute arising out of or relating to this LICENSE AGREEMENT, the affected party shall notify the other party, and the parties shall attempt in good faith to resolve the matter within thirty (30) days after the date of such notice (the "Notice Date"). Any disputes not resolved by good faith discussions shall be referred to senior executives of each party, who shall meet at a mutually acceptable time and location within sixty (60) days after the Notice Date and attempt to negotiate a settlement. In the absence of settlement the parties shall have the liberty to resort to the courts under the jurisdiction of the State of New York.

9. Miscellaneous.

9.1. Representations and Warranties.

(a) LICENSOR represents and warrants that it is owner of the entire right, title, and interest in the Elan Patent Applications and the Elan Stabilization Patents and that it has authority to grant the rights and licenses set forth in this LICENSE AGREEMENT. LICENSOR MAKES NO OTHER WARRANTIES CONCERNING THE PATENT RIGHTS, INCLUDING WITHOUT LIMITATION ANY EXPRESS OR IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. Specifically, LICENSOR makes no warranty or representation (i) regarding the validity or scope of the PATENT RIGHTS, (ii) that the exploitation of the PATENT RIGHTS or manufacture, use, sale, offer for sale, or importation of any LICENSED PRODUCT will not infringe any patents or other intellectual property rights of a third party, and (iii) that any third party is not currently infringing or will not infringe the PATENT RIGHTS.

(b) LICENSEE represents and warrants that it is prepared to receive and, upon the execution of an Asset Purchase Agreement of even date between OCM Principal Opportunities Fund, L.P., UPT Asset Holdings, LLC and Avant, will receive the entire right, title, and interest in the Transferred Patent Applications and that it has authority to grant the rights and covenants set forth in this LICENSE AGREEMENT. LICENSEE MAKES NO OTHER WARRANTIES CONCERNING THE TRANSFERRED PATENT APPLICATIONS, INCLUDING WITHOUT LIMITATION ANY EXPRESS OR IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. Specifically, LICENSEE makes no warranty or representation (i) regarding the validity or scope of the Transferred Patent Applications, (ii) that the exploitation of the Transferred Patent Applications or manufacture, use, sale, offer for sale, or importation of any products thereunder will not infringe any patents or other intellectual property rights of a third party, and (iii) that any third party is not currently infringing or will not infringe patent rights encompassed by the Transferred Patent Applications.

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9.2. Counterparts. This LICENSE AGREEMENT may be executed in one or more counterparts, each of which shall be deemed an original, and all of which together shall be deemed to be one and the same instrument.

9.3. Headings. All headings are for convenience only and shall not affect the meaning of any provision of this LICENSE AGREEMENT.

9.4. Binding Effect. This LICENSE AGREEMENT shall be binding upon and inure to the benefit of the parties and their respective successors and assigns.

9.5. Assignment. This LICENSE AGREEMENT may not be assigned by LICENSEE without the prior written consent of LICENSOR, except that either party may assign this LICENSE AGREEMENT without consent of the other party to an AFFILIATE or to a successor in connection with the merger, consolidation, or sale of all or substantially all of its assets or that portion of its business to which this LICENSE AGREEMENT relates.

9.6. Amendment and Waiver. This LICENSE AGREEMENT may be amended, supplemented, or otherwise modified only by means of a written instrument signed by both parties. Any waiver of any rights or failure to act in a specific instance shall relate only to such instance and shall not be construed as an agreement to waive any rights or fail to act in any other instance, whether or not similar.

9.7. Governing Law. This LICENSE AGREEMENT shall be governed by and construed in accordance with the laws of the State of New York irrespective of any conflicts of law principles.

9.8. Notice. Any notices required or permitted under this LICENSE AGREEMENT shall be in writing, shall specifically refer to this LICENSE AGREEMENT, and shall be sent by hand, recognized international courier, confirmed facsimile transmission, or registered or certified mail, to the following addresses or facsimile numbers of the parties:

If to LICENSEE:

Una S. Ryan, Ph.D.

President and CEO
AVANT Immunotherapeutics, Inc.
119 Fourth Avenue
Needham, MA 02494
U.S.A.

Tel: (781) 433-0771
Fax: (781) 433-0262

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If to LICENSOR:

Mr Rajan Uppal
Senior Vice President
Elan Drug Delivery Limited
1 Mere Way
Ruddington
Nottingham NG11 6JS
England

Tel: (+44) (0)115-974 7474
Fax: (+44) (0)115-974 8420

All notices under this LICENSE AGREEMENT shall be deemed effective upon receipt. A party may change its contact information immediately upon written notice to the other party in the manner provided in this Section.

9.9. Severability. In the event that any provision of this LICENSE AGREEMENT shall be held invalid or unenforceable for any reason, such invalidity or unenforceability shall not affect any other provision of this LICENSE AGREEMENT, and the parties shall negotiate in good faith to modify the LICENSE AGREEMENT to preserve (to the extent possible) their original intent. If the parties fail to reach a modified agreement within sixty (60) days after the relevant provision is held invalid or unenforceable, then the dispute shall be resolved in accordance with the procedures set forth in Article 8.

9.10. Entire Agreement. This LICENSE AGREEMENT constitutes the entire agreement between the parties with respect to its subject matter and supersedes all prior agreements or understandings between the parties relating to its subject matter.

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IN WITNESS WHEREOF, the parties have caused this LICENSE AGREEMENT to be executed by their duly authorized representatives as of the date first written above.

AVANT IMMUNOTHERAPEUTICS, INC.

ELAN DRUG DELIVERY LTD.

By: /s/ Una S. Ryan, Ph.D.
Name: Una S. Ryan, Ph.D.
Title: President and CEO

By: /s/ Rajan Uppal
Name: Rajan Uppal
Title: Director

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ATTACHMENTS:

- [Schedule A:](#) [Elan Patent Applications](#)
- [Schedule B:](#) [Related UPT Applications](#)
- [Schedule C:](#) [Elan Stabilization Patents](#)
- [Schedule D:](#) [Transferred Patent Applications](#)
- [Schedule E:](#) [copy of the Stratagene License Agreement and the amendment thereto](#)

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Schedule A. **Elan Patent Applications**
As of December 20, 2002

Foamed Glass Matrices

a)	European Patent Office		Appl. No. 96917569.4	(7 Jun 96)
b)	United States		Appl. No. 08/923783	(7 Jun 95)
c)	Israel	Pat. No. 122482 (30 Jan 00)	Appl. No. 122482	(7 Jun 96)
d)	Mexico		Appl. No. 9709716	(7 Jun 96)
e)	Norway		Appl. No. 975773	(7 Jun 96)
f)	Japan		Appl. No. 500235/97	(7 Jun 96)
g)	Poland		Appl. No. P323902	(7 Jun 96)
h)	Canada		Appl. No. 2223438	(7 Jun 96)
i)	China		Appl. No. 96194617.2	(7 Jun 96)
j)	Australia	Pat. No. 713599 (23 Mar 00)	Appl. No. 60098/96	(7 Jun 96)
k)	New Zealand	Pat. No. 309841 (8 Feb 00)	Appl. No. 309841	(7 Jun 96)
l)	ARIPO	Pat. No. AP852 (30 Jun 00)	Appl. No. AP/P/97/01151	(7 Jun 96)
m)	Brazil		Appl. No. PI9609188.6	(7 Jun 96)
n)	Singapore	Pat. No. 51104 (19 Dec 00)	Appl. No. 9705893-7	(7 Jun 96)
o)	Slovak Republic		Appl. No. PV 1675/97	(7 Jun 96)
p)	Czech Republic		Appl. No. PV 3912-97	(7 Jun 96)

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as well as any substitutes, divisionals, continuations, continuations-in-part, or reissue applications that claim priority to any of the above patents or patent applications, and any foreign counterparts of any of the foregoing.

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Schedule B. Related UPT Applications

As of December 20, 2002

1) Preservation by Foam Formation (patent in interference)

a)	United States	Pat. No. 5,766,520(16 June 98)	Appl. No. 08/785,473	(17 Jan 97)
b)	Australia	Pat. No. 714328 (6 April 00)	Appl. No. 36606/97	(14 July 97)
c)	Brazil		Appl. No. PI9711808-7	(14 July 97)
d)	Canada		Appl. No. 2260233	(14 July 97)
e)	China		Appl. No. 97196422.X	(14 July 97)
f)	Czech Republic		Appl. No. PV79-99	(14 July 97)
g)	Eurasian Regional	Pat. No. 001138 (17 July 00)	Appl. No. 199900268/26	(14 July 97)
h)	European Regional		Appl. No. 97933415.8	(14 July 97)
i)	Hungary		Appl. No. P9903917	(14 July 97)
j)	Israel	Pat. No. 127971 (16 Dec 01)	Appl. No. 127971	(14 July 97)
k)	Japan		Appl. No. 506201/1998	(14 July 97)
l)	Korea		Appl. No. 1019997000253	(14 July 97)
m)	Mexico		Appl. No. 990592	(14 July 97)
n)	Norway		Appl. No. P990158	(14 July 97)
o)	New Zealand	Pat. No. 333738 (11 Jan 01)	Appl. No. 333738	(14 July 97)
p)	Poland		Appl. No. P331174	(14 July 97)
q)	Singapore	Pat. No. 61161 (24 May 01)	Appl. No. 9900222-2	(14 July 97)
r)	Turkey	Pat. No. 199900127 (21 Dec 99)	Appl. No. 99/00127	(14 July 97)
s)	Ukraine		Appl. No. 99-02-0968/N	(14 July 97)

2) Scalable Long-Term Shelf Preservation (CIP of Foam patent)

a)	United States		Appl. No. 08/979,458	(26 Nov 97)
b)	Canada		Appl. No. 2312233	(26 Nov 97)
c)	Chile		Appl. No. 2859-98	(25 Nov 97)
d)	China		Appl. No. 97182498.3	(26 Nov 97)
e)	European Regional		Appl. No. 97948550.5	(26 Nov 97)

f)	India		Appl. No. 2064/CAL/98	(23 Nov 97)
g)	Japan		Appl. No. 522213/2000	(26 Nov 97)
h)	Mexico		Appl. No. 5123	(26 Nov 97)
i)	Russia		Appl. No. 2000112399/20	(26 Nov 97)
j)	Saudi Arabia		Appl. No. 99191193	(11 Mar 99)
k)	Thailand		Appl. No. 047344	(24 Nov 97)

3) Industrial Scale Barrier Technology For Preservation

a)	United States	Pat. No. 6,306,345 (23 Oct 01)	Appl. No. 09/306,137	(6 May 99)
b)	Canada		Appl. No. 2360032	(5 Jan 00)
c)	European Regional		Appl. No. 00903099.0	(5 Jan 00)
d)	Japan		Appl. No. 2000-592394	(5 Jan 00)

4) Industrial Scale Barrier Technology For Preservation (CIP)

a)	United States		Appl. No. 09/589,381	(7 Jun 00)
b)	PCT		Appl. No. US00/19667	(19 Jul 00)

5) Vacuum Control System for Foam Drying Apparatus

a)	United States		Appl. No. 09/869,886	(5 Jul 01)
b)	Canada		Appl. No. 2360112	(5 Jan 00)
c)	European Regional		Appl. No. 00903104.8	(5 Jan 00)
d)	Japan		Appl. No. 2000-592581	(5 Jan 00)

6) Long-Term Shelf Preservation by Vitrification

a)	United States		Appl. No. 09/734,970	(17 Jan 97)
b)	Canada		Appl. No. 2256333	(28 May 97)
c)	European Regional		Appl. No. 97927769.6	(28 May 97)
d)	Japan		Appl. No. 542857/1997	(28 May 97)

7) Formulation of Preservation Mixtures (α -methyl glucose)

a)	United States		Appl. No. 09/721,609	(22 Nov 00)
b)	Australia		Appl. No. 17986/01	(22 Nov 00)
c)	Brazil		Appl. No. PI0015738-4	(22 Nov 00)
d)	Canada		Appl. No.	(22 Nov 00)
e)	China		Appl. No. 00817902.6	(22 Nov 00)
f)	Czech Republic		Appl. No. PV2002-1835	(22 Nov 00)
g)	European Regional		Appl. No. 00980766.0	(22 Nov 00)
h)	Hungary		Appl. No. P9903917	(22 Nov 00)
i)	Israel		Appl. No. 149778	(22 Nov 00)
j)	India		Appl. No. INPCT0200779	(22 Nov 00)
k)	Japan		Appl. No. 2001-539285	(22 Nov 00)
l)	Korea		Appl. No. 1020027006561	(22 Nov 00)
m)	Mexico		Appl. No. 2002005115	(22 Nov 00)
n)	New Zealand		Appl. No. 519367	(22 Nov 00)
o)	Singapore		Appl. No. 200202945-2	(22 Nov 00)

8) Preservation and Formulation in Hydrophobic Carriers

a)	United States		Appl. No. 10/130,840	(20 May 02)
b)	PCT		Appl. No. US00/32071	(22 Nov 00)

9) Preservation of Bacterial Cells (Modified Fermentation)

a)	United States		Appl. No. 10/089,003	(22 Mar 02)
b)	Canada		Appl. No. 2382061	(21 Aug 00)
c)	European Regional		Appl. No. 00969011.6	(21 Aug 00)

10) Methods of Forming a Humidity Barrier (Notice of Allowance 10/22/02)

a)	United States		Appl. No. 09/694,630	(23 Oct 00)
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11) Loading And Unloading Of Permeating Protectants For Cryopreservation

a)	United States		Appl. No. 09/194,397	(4 Mar 99)
b)	Canada		Appl. No. 2256714	(29 May 97)
c)	European Regional		Appl. No. 97928712.5	(29 May 97)
d)	Japan		Appl. No. 542954/1997	(29 May 97)

12) Vitrification Solutions for Cryopreservation

a)	United States	Appl. No. 09/254,563	(5 Mar 99)
b)	European Regional	Appl. No. 97940831.7	(5 Sep 97)
c)	Israel	Appl. No. 128855	(5 Sep 97)
d)	Japan	Appl. No. 512916/1998	(5 Sep 97)

as well as any substitutes, divisionals, continuations, continuations-in-part, or reissue applications that claim priority to any of the above patents or patent applications, and any foreign counterparts of any of the foregoing.

Schedule C. Elan Stabilization Patents

As of December 23, 2002

<u>Client Reference</u>	<u>Country</u>	<u>Application Number</u>	<u>Application Date</u>	<u>Publication No.</u>	<u>Grant Date</u>
QS1	Australia	61363/86	09/07/1986	591160	
QS1	Austria	86904281.2	09/07/1986	EP0229810	16/10/91
QS1	Belgium	86904281.2	09/07/1986	EP0229810	16/10/91
QS1	Canada	531500	09/03/1987	1307485	
QS1	Denmark	1207/87	09/07/1986	170173	
QS1	France	86904281.2	09/07/1986	EP0229810	16/10/91
QS1	Germany	86904281.2	09/07/1986	EP0229810	16/10/91
QS1	Italy	86904281.2	09/07/1986	EP0229810	16/10/91
QS1	Japan	503940/61	09/07/1986	2140344	
QS1	Luxembourg	86904281.2	09/07/1986	EP0229810	16/10/91
QS1	Netherlands	86904281.2	09/07/1986	EP0229810	16/10/91
QS1	Sweden	86904281.2	09/07/1986	EP0229810	16/10/91
QS1	Switzerland	86904281.2	09/07/1986	EP0229810	16/10/91
QS1	UK	8704890.6	09/07/1986	2187191	
QS1	United States of America	026695	09/07/1986	4981319	
QS2	Argentina	313044	20/01/1989	240255	
QS2	Austria	89901874.1	18/01/1989	EP0357709	29/09/93
QS2	Belgium	89901874.1	18/01/1989	EP0357709	29/09/93
QS2	Canada	588875	23/01/1989	1333562	
QS2	Czechoslovakia	PV 402-89	20/01/1989	276472	
QS2	France	89901874.1	18/01/1989	EP0357709	29/09/93
QS2	Germany	89901874.1	18/01/1989	EP0357709	29/09/93
QS2	Italy	89901874.1	18/01/1989	EP0357709	29/09/93
QS2	Japan	1-501732	18/01/1989	2135928	
QS2	Luxembourg	89901874.1	18/01/1989	EP0357709	29/09/93
QS2	Netherlands	89901874.1	18/01/1989	EP0357709	29/09/93
QS2	Spain	8900206	20/01/1989	8900206	
QS2	Sweden	89901874.1	18/01/1989	EP0357709	29/09/93
QS2	Switzerland	89901874.1	18/01/1989	EP0357709	29/09/93
QS2	UK	89901874.1	18/01/1989	EP0357709	29/09/93
QS2	United States of America	07/411473	18/01/1989	5149653	
QS12	European Patent Office	97947793.2	05-Dec-97		
QS12	United States of America	08/985343	35768	6468782	

QS12	India	932/Del/2002	05-Dec-97		
QS12	South Africa	97/10974	05-Dec-97		31-Mar-99
QS12	Australia	54034/98	05-Dec-97		12-Oct-00
QS12	Canada	2272821	05-Dec-97		
QS12	China	97180328.5	05-Dec-97		
QS12	Japan	10-525367	05-Dec-97		
QS12.1	United States of America	10/215060	04-Dec-97		
QD1	European Patent Office	95927856.5	04-Aug-95		
QD1	United States of America	08/349029	02-Dec-94	6290991	18-Sep-01
QD1	Australia	71864/98	04-Aug-95		28-Oct-99
QD1.1	United States of America	09/628380	02-Dec-94	6331310	18-Dec-01
QD1.2	United States of America	09/945180	02-Dec-94		
QD1.1 (Glaxo)	United States of America	10/280468	02-Dec-94		
QD1/2	Poland	P318898	04-Aug-95		
QD1/2	Japan	506345/96	04-Aug-95		

QD1/2.1	European Patent Office	01116638.6	04-Aug-95	
QD2	European Patent Office	01116637.8	04-Aug-95	
QD2	Brazil	PI1100784.2	12-May-97	
QD2	Romania	97-00293	13-Feb-97	
QD2	United States of America	09/755737	04-Aug-95	
QD2	Czech Republic	PV 476/97	04-Aug-95	
QD2	Australia	31851/95	04-Aug-95	01-Oct-98
QD2	Canada	2197982	04-Aug-95	
QD2	China	95195496.2	04-Aug-95	
QD2	Estonia	P19970006-2	04-Aug-95	19-Feb-02
QD2	Finland	970867	04-Aug-95	
QD2	Hungary	P9800694	04-Aug-95	
QD2	New Zealand		04-Aug-95	290896
QD2	Norway	P971688	04-Aug-95	
QD2	Russian Federation	97103529	04-Aug-95	10-Jan-02
QD2	Singapore	9700739.7	04-Aug-95	22-Feb-99
QD2	Mexico	97134	04-Aug-95	
QD2	Slovak Republic	PV 277/97	04-Aug-95	

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QPA5	European Patent Office	94921046.2	19-Jul-94	EP063947	
QPA5	Austria	94921046.2	19-Jul-94		
QPA5	Belgium	94921046.2	19-Jul-94		
QPA5	Switzerland	94921046.2	19-Jul-94		
QPA5	Germany	94921046.2	19-Jul-94		
QPA5	Denmark	94921046.2	19-Jul-94		
QPA5	Spain	94921046.2	19-Jul-94		
QPA5	France	94921046.2	19-Jul-94		
QPA5	Greece	94921046.2	19-Jul-94		
QPA5	Ireland	94921046.2	19-Jul-94		
QPA5	Italy	94921046.2	19-Jul-94		
QPA5	Luxembourg	94921046.2	19-Jul-94		
QPA5	Monaco	94921046.2	19-Jul-94		
QPA5	Netherlands	94921046.2	19-Jul-94		
QPA5	Portugal	94921046.2	19-Jul-94		
QPA5	Sweden	94921046.2	19-Jul-94		
QPA5	Australia	71920/94	19-Jul-94		02-Jul-98
QPA5	United States of America	08/397270	19-Jul-94	5728574	17-Mar-98
QPA2	United Kingdom	Not Yet Known	19-Dec-02		

as well as any substitutes, divisionals, continuations, continuations-in-part, or reissue applications that claim priority to any of the above patents or patent applications, and any foreign counterparts of any of the foregoing.

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Schedule D. Transferred Patent Applications
As of December 20, 2002

1) Bulk Drying and Bubble Nucleation

a)	United States	Appl. No. 10/274,719	(18 Oct 02)
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2) Preservation of Competent Bacteria

a)	PCT	Appl. No. US02/14552	(7 May 02)
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3) Scalable Long-Term Shelf Preservation

a)	Australia	Appl. No. 54596/98	(26 Nov 97)
b)	Korea	Appln. No. 1020007005794	(26 Nov 97)
c)	South Africa	Pat. No. 98/10789 (29 Sep 99)	Appl. No. 98/10789 (25 Nov 98)

as well as any substitutes, divisionals, continuations, continuations-in-part, or reissue applications that claim priority to any of the above patent applications, and any foreign counterparts of any of the foregoing.

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Schedule E. [Stratagene License Agreement plus amendment document]

LICENSE AND CLINICAL TRIALS AGREEMENT

Agreement (“AGREEMENT”), effective as of February 27, 1995 (“Effective Date”) between VIRUS RESEARCH INSTITUTE, INC., a Delaware corporation, with its principal place of business at 61 Moulton Street, Cambridge, Massachusetts 02138 (hereinafter referred to as “VRI”) and the JAMES N. GAMBLE INSTITUTE OF MEDICAL RESEARCH, an Ohio non-profit corporation, with its principal place of business at 2141 Auburn Avenue, Cincinnati, Ohio 45219 (hereinafter referred to as “GAMBLE”).

WITNESSETH:

WHEREAS, GAMBLE is the owner of certain rights in technology as defined herein; and

WHEREAS, GAMBLE desires to have such rights utilized to promote the public interest by granting a license thereunder;

WHEREAS, VRI is engaged in the development, production, marketing and sale of products similar to the technology which is the subject of this AGREEMENT and has the strategic commitment to facilitate the transfer of such technology for the public interest; and

WHEREAS, VRI desires to obtain a license to said rights upon the terms and conditions hereinafter set forth;

WHEREAS, VRI desires to utilize GAMBLE’s services with respect to the conduct of certain of the clinical trials and laboratory services needed to obtain FDA approval for GAMBLE’S rotavirus vaccines.

NOW THEREFORE, in consideration of the mutual covenants herein contained and intending to be legally bound hereby, the parties hereto agree as follows:

1. DEFINITIONS

1.1 “Invention(s)” shall mean rotavirus vaccines, developed from rotavirus strain 89-12, including that which was safety tested by Lou Potash, Ph.D. of PRI/DynCorp for GAMBLE and received by GAMBLE on 12/2/93 or modification of rotavirus strain 89-12 generated by natural or site-directed mutagenesis, that stimulate neutralizing antibody to multiple serotypes of human rotavirus, and methods for vaccinating humans against rotavirus illness caused by rotaviruses of different serotypes using rotavirus strain 89-12 and for expanding the titers and memory of the cells that express the pre-existing neutralizing antibodies induced following primary vaccination against rotavirus disease using solely rotavirus strain 89-12. The Invention(s) include inactivated vaccines using rotavirus strain 89-12.

1.2 “Technical Information” shall mean vaccine production information and the results of the safety and identity testing conducted by Lou Potash, Ph.D., of PRI/DynCorp and received by GAMBLE on 12/2/93 and information regarding the history, culture, adaptation and attenuation of rotavirus strain 89-12; and scientific, technical and medical information related to 89-12, generated by or on behalf of GAMBLE or obtained from Dr. Potash as part of the quality assurance process during the term of this AGREEMENT.

1.3 “Patent Rights” shall mean any current or future United States or foreign patent applications which are set forth in Appendix A attached hereto and arising from Inventions owned by or assigned to GAMBLE, together with any divisions and continuations (related to rotavirus strain 89-12) continuations-in-part (related solely to rotavirus strain 89-12 and improvements thereto), patents issuing thereon and reissues thereof and extensions thereof; provided that in the case of future patent applications and patents, inclusion in Patent Rights shall be subject to reimbursement by VRI to GAMBLE of the cost of Research and Development with respect thereto. Nothing in this Agreement gives VRI rights to Improvements in a vaccine which does not employ rotavirus strain 89-12.

1.4 “Licensed Products” shall mean any product which is covered in whole or in part by a Valid Claim in the Patent Rights and/or which incorporates or utilizes to a significant degree Technical Information.

1.5 “Licensed Process” shall mean any process which is covered in whole or in part by a Valid Claim in the Patent Rights and/or which incorporates or utilizes to a significant degree Technical Information.

1.6 “Territory” shall mean the entire world.

1.7 “Net Sales” shall mean the gross revenue received by VRI, its Affiliates from the sales of Licensed Products or Licensed Processes to independent third parties less:

- (a) Transportation charges or allowances separately stated and invoiced;
- (b) Trade, quantity, cash, rebates or other allowances and discounts and brokers’, distributors’, or agents’ commissions actually allowed and taken;
- (c) Credits or allowances made or given on account of rejects or returns;
- (d) Medicare and Medicaid disallowed reimbursements;
- (e) Taxes levied on and/or other governmental charges made as to production, sale, transportation, delivery or use and paid by or on behalf of Licensee.

Licensed Products shall be considered “sold” when invoiced.

1.8 "Sublicensee" shall mean any corporation, partnership or business organization which is not an Affiliate to which VRI grants a license to enable said party to sell Licensed Products or utilize Licensed Processes.

1.9 "Affiliate" shall mean any corporation or other business entity controlled by, controlling, or under common control with VRI. For this purpose "control" means direct or indirect beneficial ownership of at least fifty percent (50%) interest in the income or stock of such corporation or other business.

1.10 "Valid Claim" shall mean a claim of an issued patent or pending patent application which has not been pending for more than five (5) years from the relevant U.S. priority date, January 3, 1992, which has not lapsed or become abandoned or been declared invalid or unenforceable by a court of competent jurisdiction or an administrative agency from which no appeal can be or is taken.

2. GRANT

2.1 GAMBLE hereby grants to VRI the exclusive right and license under Patent Rights and Technical Information to make, have made, use, lease, have leased, sell, and have sold the Licensed Products and to practice the Licensed Processes in the Territory for the term of this AGREEMENT unless this AGREEMENT is sooner terminated according to the terms hereof. VRI shall have the right to extend the grant set forth in this Section 2.1 to its Affiliates.

2.2 Notwithstanding the provision of Section 2.1, GAMBLE shall retain the right to make, use and practice the Invention(s) and the Technical Information for its own non-commercial, research purposes. GAMBLE shall have the right to convey to other non-profit organizations at no charge other than shipping fees, the Invention(s) and Technical Information for use in non-commercial, basic research, provided that such organizations have entered into agreements in substantially the form attached as Appendix B.

2.3 VRI agrees that any Licensed Products subject to obligations under Public Laws 96-517 or 98-620 and which are intended for sale in the United States shall be manufactured substantially in the United States. In the event that VRI determines that compliance with the foregoing obligation is commercially impracticable, GAMBLE agrees that it will cooperate with VRI in attempting to obtain from the U.S. Government a waiver of such obligation.

2.4 (a) VRI will have the right, subject to the terms of this AGREEMENT, to enter into sublicensing agreements with any other entity (other than an Affiliate to whom the license may be extended in accordance with Section 2.1) for the rights, privileges and licenses granted hereunder.

(b) VRI agrees that any sublicenses granted by it shall provide that the obligations to GAMBLE contained in the following provisions of this AGREEMENT shall be binding upon the Sublicensee: Sections 2.4 (c), 8 and 10. VRI further agrees to attach a copies of such provisions to each sublicense agreement.

(c) VRI agrees to forward to GAMBLE a copy of any and all fully executed sublicense agreements within thirty (30) days of execution thereof, and further agrees to forward to GAMBLE annually a copy of such reports received by VRI from its Sublicensee during the preceding twelve (12) month period under the sublicenses as shall be pertinent to a royalty accounting under said sublicense agreements. VRI may delete from copies of sublicense

agreements provided to GAMBLE hereunder commercial, research and development, manufacturing, financial and other provisions unrelated to VRI's or the Sublicensee's obligations to GAMBLE.

(d) In the event that this AGREEMENT is terminated prior to its normal expiration, any sublicense granted by VRI shall remain in full force and effect from and after that date as a direct license between GAMBLE and the Sublicensee, to the extent that the royalty obligations of VRI in individual countries have not ceased pursuant to the terms of this AGREEMENT and the Sublicensee's agreement to be bound by the terms and conditions set forth in this AGREEMENT.

2.5 (a) In addition to the license granted herein, GAMBLE grants to VRI an exclusive option to obtain a world-wide, exclusive royalty-bearing license to any improvement(s) on the Invention(s) that (i) are not subject to prior commitments to other parties; (ii) relate to the diagnosis, treatment and/or prevention of human rotavirus illnesses employing strain 89-12; (iii) which are not specifically included in the Invention(s) or Patent Rights; and (iv) provide a significant commercial advantage, herein collectively ("Improvements").

(b) Such option shall extend for a period of sixty (60) days from the date VRI receives written notice from GAMBLE disclosing such Improvement. During such sixty (60) day period, GAMBLE shall reasonably make available to VRI any other information in its possession or control which would be useful to VRI in evaluating the improvement. In the event VRI decides to exercise its option, VRI shall do so by notifying GAMBLE in writing during such sixty (60) day period. Upon exercise of VRI's option, GAMBLE and VRI shall enter into a license agreement containing substantially the same provisions as the applicable provisions of this AGREEMENT except for the initial license fee which shall be at least an amount sufficient to reimburse GAMBLE for its costs relating to the development of the Improvement, plus GAMBLE's actual patent costs relating thereto.

(c) The written notice to GAMBLE of VRI's exercise of its option hereunder shall include instructions to GAMBLE as to whether VRI wishes GAMBLE to have a patent application prepared and filed with respect to any such improvement. VRI shall pay for all patent costs relating to any Improvement to which VRI exercises its option.

(d) In the event that VRI does not exercise its option hereunder or if the parties have not entered into a license agreement as described in Section 2.5 (b)(1) above at the close of sixty (60) days from VRI's notice of exercise, GAMBLE shall be free to offer a license for the Improvement on terms of its own choosing to a third party, provided the terms are not more favorable than those terms offered to VRI. VRI will grant a sublicense under Patent Rights to such third party, if required, royalty-free, to permit such party to develop and sell such Improvement.

2.6 As soon as reasonably possible following the Effective Date of this AGREEMENT, but in no event later than thirty (30) days after the Effective Date, GAMBLE shall provide to VRI copies of all Technical Information directly relating to the Invention(s) in its possession and control on the Effective Date. In addition, GAMBLE shall transfer to VRI all supplies of rotavirus strain 89-12 and the master and working cellbanks except as may be

necessary for GAMBLE to conduct such basic research as may be agreed upon by the parties. Upon termination of this AGREEMENT, as a result of a breach by VRI or by VRI pursuant to Section 7.4, VRI shall return all Technical Information to GAMBLE.

3. CLINICAL TRIALS AND DUE DILIGENCE

3.1 (a) GAMBLE and VRI will cooperate with one another to complete all pre-clinical studies necessary for the continued support of the Investigational New Drug application (“IND”) filed with the U.S. Food and Drug Administration (FDA) and for foreign equivalents filed with respect to a Licensed Product. VRI shall consult with GAMBLE, shall provide GAMBLE with drafts of the regulatory submission prior to its filing, and shall not unreasonably refuse to comply with any request by GAMBLE for any changes thereto, but all regulatory filings shall be submitted in the name of VRI and VRI shall have the final authority with respect to their content. GAMBLE shall cooperate with VRI in responding to any comments of the FDA with respect to its regulatory filing.

(b) Following approval under FDA regulations that clinical trials may commence under the IND for which approval has been granted, GAMBLE, recognizing the need for expeditious handling of all matters for which GAMBLE is responsible herein, agrees that GAMBLE will use reasonable efforts to promptly conduct the clinical trials and necessary laboratory work provided for in the IND, subject to the following:

- (1) In consultation with and subject to the approval of VRI, GAMBLE will use reasonable efforts to design and draft the protocols with respect to Phase I clinical trials;
- (2) In consultation with, and subject to the approval of VRI, GAMBLE will use reasonable efforts to design and draft the protocols with respect to Phase II clinical trials;
- (3) GAMBLE will use reasonable efforts to conduct the initial Phase II clinical trials and, subject to consultation with and the approval of VRI, conduct and/or participate in confirmatory or other Phase II clinical trials, together with all laboratory work, as required;
- (4) if other sites are required in connection with Phase II clinical trials, VRI will consult with GAMBLE regarding the use and selection of other sites and GAMBLE will use reasonable efforts to assist VRI in selecting such additional sites;
- (5) GAMBLE and VRI will use reasonable efforts to jointly design and draft protocols for Phase III clinical trials and GAMBLE may, at GAMBLE’s option, participate as one of multiple centers for the clinical trials; Dependent upon FDA requirements, GAMBLE will use reasonable efforts to conduct all laboratory work required therefore; provided, however, that if GAMBLE’s laboratory capabilities are not sufficient for the central lab work required for Phase III clinical trials, GAMBLE will use reasonable efforts to assist VRI in selecting and approving an appropriate central

laboratory and will use reasonable efforts to supervise that laboratory in its performance of such work;

- (6) promptly after completion of the above-described clinical trials, GAMBLE will cooperate with VRI in preparation and submission to the FDA of an appropriate application for approval with respect to the Licensed Product (PLA/NDA) and in the submission of regulatory filings in foreign countries;
- (7) if the PLA/NDA is not approved, GAMBLE will cooperate with VRI at VRI’s expense in taking any further action required to obtain its approval;
- (8) GAMBLE will use reasonable efforts to conduct all trials with the prior approval and ongoing review of all appropriate and necessary review authorities and in accordance with applicable federal, state and local laws and regulations and will provide VRI with written evidence of review and approval of each trial by the appropriate Institutional Review Board prior to the initiation of each trial and of that Board’s continuing review and approval of each trial whenever it is reviewed, but at least once per year;
- (9) GAMBLE will furnish VRI with the data resulting from the clinical trials within a reasonable time after completion of each trial, provided that GAMBLE will permit representatives of VRI to examine GAMBLE’s facilities, validate case reports against original data in its files and monitor work performed, at reasonable times and in a reasonable manner at mutually agreed upon times during the term of this AGREEMENT, to determine the adequacy of the facilities and whether the clinical trials are being conducted in compliance with the protocol and relevant FDA regulations;
- (10) GAMBLE will retain original records of the clinical trials conducted by GAMBLE including the original of all volunteer consent forms in strict accordance with all federal regulations.
- (11) GAMBLE shall compile clinical trial data and provide copies of the complete data set to VRI in a timely manner. GAMBLE will cooperate with VRI in the analysis of the clinical data.
- (12) GAMBLE is conducting the adult and child phases of the Phase I clinical trials described in the protocols entitled “Reactivity and Immunogenicity of Live, Attenuated Rotavirus Vaccine Candidate Strain 89-12.” and attached as Appendix C, and will make reasonable efforts to conduct the infant phase of the Phase I clinical trial, and Phase II and Phase III clinical trials.

(13) Gilbert M. Schiff, M.D. shall be responsible for supervising the adult clinical trials at GAMBLE and shall be designated as "Principal Adult Investigator." David I. Bernstein, M.D. shall be responsible for supervising the pediatric clinical trials at GAMBLE and shall be designated as "Principal Pediatric Investigator." In the event that either such investigator is disabled or no longer employed at GAMBLE,

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then GAMBLE shall have the right to appoint another such investigator, subject to approval by VRI which shall not be unreasonably withheld.

(14) GAMBLE and VRI agree to conduct the clinical trials according to the protocols. However, if at any future date, changes in the protocol appear desirable, such changes may be made through prior written mutual agreement between GAMBLE and VRI. The clinical trials may be suspended or terminated, as appropriate, at any time by GAMBLE if in the reasonable medical judgment of either: the Principal Adult or Pediatric Investigator, or responsible institutional review board(s) or in the medical and/or regulatory judgment of VRI the health or safety of patients will be adversely affected and it is appropriate to do so. Any action taken by GAMBLE or its investigators or employees based on any such medical judgment shall not be deemed a breach of this AGREEMENT.

(15) GAMBLE agrees that the rights and welfare of the human subjects shall be protected in accordance with the protocols and all applicable federal and state laws. GAMBLE shall be responsible for obtaining appropriate institutional review board approval for the protocols and any subsequent changes to the protocols, and for obtaining informed consent of each human subject participating in the protocols. GAMBLE shall retain records of the clinical trials including the original of all volunteer consent forms in accordance with all federal regulations.

(16) In order to maintain subject confidentiality, no information relative to subject name or address shall be provided to VRI. All patient information will be identified in code. Any audits conducted by VRI shall be undertaken in conjunction with GAMBLE in order to ensure confidentiality.

(17) VRI shall promptly advise GAMBLE of adverse reactions or side effects relating to clinical trials which may become known to VRI and, similarly GAMBLE shall promptly advise VRI of adverse reactions or side effects relating to clinical trials which may become known to GAMBLE.

(c) If GAMBLE fails to perform any of its obligations under this Section 3.1 and any such failure is not cured following sixty (60) days written notice to GAMBLE, VRI may terminate GAMBLE's services relating to the obligations in the relevant Section (Sections 3.1(b) (1-17)) of this Section and VRI shall thereafter have the right to hire a third party contractor at VRI's expense to perform and control the performance of such services. Termination of services provided herein in Sections 3.1(b) (1-17) shall not affect the rights and obligations of GAMBLE under any other Section. Upon termination of GAMBLE's services for the foregoing reasons VRI will be obligated to pay GAMBLE for all pre-approved costs of the studies incurred by GAMBLE and not capable of cancellation. Such payment will be made within 30 days of submission of billing by GAMBLE to VRI. At VRI's request, GAMBLE will assist VRI in selecting and approving such third party contractors to perform functions described in this Section 3.1.

(d) Notwithstanding the foregoing, VRI, as sponsor of the development program may terminate GAMBLE services in conducting clinical trials for commercial reasons

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at any time with 30 days' notice subject to VRI's payment of all non-cancelable, pre-approved costs within 30 days of GAMBLE's billing to VRI.

3.2 VRI agrees to pay GAMBLE for all fees and expenses that GAMBLE expects to reasonably incur in conducting the trials described in Section 3.1 above, provided that the amounts of such fees and costs have been approved by VRI in writing in advance. VRI agrees to pay 40% of the approved budget for each study in phase I, II and III upon initiation of each study and the remaining 60% at agreed upon milestones during the course of each study, so that full payment for each study is made by the conclusion of that study. Irrespective of the amount advanced, VRI shall pay all costs incurred by GAMBLE in conducting the trials described in Section 3.1, provided such expenses have been approved in advance by VRI. If the monies advanced by VRI exceed expenses for a study, GAMBLE shall refund the difference. VRI shall have the trials monitored by its own staff or outside contractors at its election and shall have the data resulting from the studies compiled and analyzed. VRI shall have any such VRI staff or outside contractors execute a confidentiality agreement, prior to such staff or outside contractors involvement in the clinical trials.

3.3 GAMBLE and/or its investigators will have the right to publish the results of the clinical trials described in Section 3.1 above and performed by GAMBLE, provided that VRI is provided with a preprint and/or abstract of any proposed publication at least forty-five (45) days in advance of submission of the proposed publication. In the event that, as a result of reviewing such abstract or preprint, VRI determines that such publication would result in disclosure of an Invention as to which VRI has rights under Sections 2.1, 2.4 and/or 2.5 hereof or includes any VRI Confidential Information (as hereinafter defined), GAMBLE agrees to delay publication for a sufficient period to enable a patent application to be filed with respect thereto at VRI's expense and delete VRI confidential information, VRI acknowledges and agrees that GAMBLE and/or its investigators will be entitled to appropriate credit, and to be included as co-authors for those directly involved in the study, in accordance with prevailing scientific standards.

3.4 In lieu of VRI paying minimum royalties and subject to obtaining FDA or foreign regulatory approval for the 89-12 rotavirus vaccine VRI agrees to use reasonable efforts to bring one or more Licensed Products to the marketplace through a program of development, production, distribution, and marketing consistent with sound and reasonable business practices and judgments. VRI agrees to provide GAMBLE annually with a business development plan (which will include strategy, major milestones for clinical development, FDA registration, commercialization, and financial performance data) for the upcoming fiscal year, the first plan due no later than one hundred eighty (180) days from the Effective Date hereof and each subsequent plan due no later than December 31 in subsequent years. In the event GAMBLE believes VRI is not exerting reasonable efforts GAMBLE shall advise VRI and state the efforts which it believes would meet this requirement. If VRI disagrees the parties will attempt to resolve the matter by good faith discussions. If they still cannot agree the matter shall be submitted to arbitration pursuant to Section 12 to determine the efforts to be exerted by VRI. After the arbitration decision, in the event VRI fails to exert the efforts required by the arbitration, GAMBLE shall have the right to terminate this AGREEMENT upon giving VRI thirty (30) days prior written notice and the opportunity to cure within said thirty (30) days or alternatively VRI may resume minimum royalty payments in lieu of preparation of a business

plan and using reasonable efforts; however, in such event, resumption of payment of minimum royalties under this Section 3.4 does not entitle VRI to an exclusive license agreement.

4. PAYMENTS

4.1 (a) VRI agrees to pay GAMBLE in partial consideration for the license granted hereunder a licensing fee in the total amount of \$50,000 payable in two equal installments, as follows:

(1)	upon signing of this AGREEMENT	\$	25,000
(2)	upon filing of the PLA/NDA for a Licensed Product with the FDA	\$	25,000

4.2 (a) VRI shall pay the following running royalties to GAMBLE during the term of this AGREEMENT as set forth below:

(1) Five percent (5%) on the Net Sales by VRI or its Affiliates of Licensed Products or any use of Licensed Processes in the United States (other than sales to Sublicensees for resale) where the manufacture, use or sale of such Licensed Products or any use of such Licensed Processes is covered by a Valid Claim of Patent Rights; or four percent (4%) on such Net Sales in countries other than the United States (other than sales to Sublicensees for resale) where the manufacture, use or sale of Licensed Products or any use of Licensed Processes is covered by a Valid Claim of Patent Rights in the country of sale; or one percent (1%) of Net Sales for five (5) years from first commercial sale in a country, on a country by country basis, on any other sales by VRI or its Affiliates of Licensed Products (other than sales to Sublicensees for resale) where no Patent Rights have been nor are intended to be filed with respect to such products; or two percent (2%) of Net Sales of Licensed Products sold to the United States Government or sold to State or other agencies at equivalent prices to those established for sale to the United States Government.

(2) From any royalties received from its Sublicensees, VRI shall pay GAMBLE thirty (30%) of royalties received by VRI from a Sublicensee for sale of Licensed Products. Reporting and payment of such royalties shall be made in accordance with the provisions of Section 5.

(3) If royalties for Licensed Products or Licensed Processes covered by a Valid Claim of Patent Rights cease to be paid because a patent application has been pending for more than five (5) years from the relevant U.S. priority date, then a royalty of 1% of Net Sales will be payable until the end of the fifth year on the market in that country. No royalty will be payable following the fifth anniversary of first marketing in that country unless a valid and enforceable patent subsequently issues. If a valid and enforceable patent issues royalties will be payable from the date of issue until the expiry of said valid and enforceable patent at the full applicable royalty rate for that country as set forth in Section 4.2(1).

4.3 (a) Subject to Section 3.4. During the exclusive period of the AGREEMENT, VRI shall pay a minimum annual royalty commencing on the expiration of calendar year 1999 and continuing through calendar year 2003, as follows:

1999	\$	100,000
2000	\$	200,000
2001	\$	300,000
2002	\$	400,000
2003	\$	500,000

(b) If the royalties earned and paid to GAMBLE pursuant to Section 4.2(a) for any of the above calendar years are not at least equal to the applicable minimum royalties, VRI shall have the right to pay any difference between such minimum royalty amounts and the royalties paid to GAMBLE in full satisfaction of such obligation under this Section 4.3, which payment, if any, shall be made with the quarterly royalty payment due for the last quarter of the applicable calendar year. Waiver of any minimum royalty payment by GAMBLE shall not be construed as a waiver of any such subsequent payment. If VRI fails to make any such minimum royalty payment, GAMBLE shall have the right, at its option, to convert the License for the Licensed Products and Licensed Processes under Section 2.1 to a non-exclusive license. Royalty rates for non-exclusive licenses shall be fifty percent (50%) of the exclusive rates set forth in Section 4.2(a).

4.4 (a) In the event that a Licensed Product under this AGREEMENT is sold in any country in a combination package or kit containing other active products not licensed hereunder, the Net Sales in each such country for purposes of determining royalty payments on the combination package, shall be calculated using one of the following methods:

(1) By multiplying the net selling price of that combination package by the fraction $A/A+B$, where A is the net selling price in such country during the royalty-paying period in question, of the Licensed Product sold separately or Licensed Process used separately, and B is the net selling price in such country during the royalty period in question, of the other active products sold separately or used separately.

(2) In the event that no such separate sales are made of the Licensed Product or any of the active products in such combination package in such country during the royalty-paying period in question, Net Sales for the purposes of determining royalty payments, shall be calculated by dividing the net selling price in such country of the combination package by the number of functions performed by the combination package sold where such package contains active agents or other proprietary technology other than those licensed under this AGREEMENT.

4.5 Payment of royalties specified in Section 4.2(a) shall be made by VRI to GAMBLE within sixty (60) days after March 31, June 30, September 30 and December 31 each year during the term of this AGREEMENT covering the quantity of Licensed Products sold or Licensed Processes used by VRI during the preceding calendar quarter. The last such payment shall be made within sixty (60) days after termination or expiration of this AGREEMENT.

4.6 All payments to be made under this Section shall be paid in United States dollars at such a place and in such a way, as GAMBLE may reasonably designate, without deduction of exchange, collection or other charges. Conversion of foreign currency to U.S. dollars shall be made at the conversion rate published by the Bank of Boston on the last day of the calendar quarter with respect to which payments are due.

4.7 Only a single royalty shall be paid with respect to any Licensed Product or Licensed Process, under Section 4.2(a) irrespective of the number of Valid Claims of Patent Rights utilized.

4.8 In the event that VRI is required to pay royalties to one or more third parties under patents other than Patent Rights in order to make, use, sell or have sold Licensed Products or Licensed Processes, VRI shall be entitled to a credit against royalties due GAMBLE under Section 4.2(a) in an amount equal to fifty percent (50%) of the royalties paid to such third parties. However, in no event shall royalties payable to GAMBLE under Section 4.2(a) hereunder be reduced by more than forty percent (40%).

4.9 If the transfer of or the conversion into the United States dollar equivalent of any remittance due hereunder is not lawful or permissible in any country, such remittance shall be made thereof in the currency of the country to the credit and account of GAMBLE or its nominee in any commercial bank located in that country. Prompt notice shall be given to GAMBLE and GAMBLE may provide a nominee if so desired.

4.10 If VRI exercises its option for the rights to improvements, VRI shall reimburse GAMBLE for the cost of the development program to make such Improvements.

5. REPORTS AND RECORDS

5.1 VRI shall maintain true books of account containing an accurate record of all data necessary for the determination of the amounts payable under Section 4 hereof. Said records shall be kept at VRI's principal place of business or the principal place of business of the appropriate division of VRI to which this AGREEMENT relates. Said records shall be available for inspection by a certified public accountant selected and paid by GAMBLE once each year during regular business hours and for six (6) years thereafter following the end of the calendar year to which they pertain in order for GAMBLE to ascertain the correctness of any report and/or payment made under this AGREEMENT. The provision of this Section 5.1 shall survive termination of this AGREEMENT.

5.2 (a) Commencing with the calendar quarter in which Net Sales first occurs, sixty (60) days after March 31, June 30, September 30 and December 31, of each year in which this AGREEMENT is in effect, VRI shall deliver to GAMBLE full, true and accurate reports of its activities and those of its Sublicensee(s), if any, relating to this AGREEMENT during the preceding three month period. These reports shall include at least the following:

- (1) Gross Sales for Licensed Products or Licensed Processes;
 - (2) Net Sales for Licensed Products or Licensed Processes;
-
- (3) Expenses, defined in Section 1.7, used to calculate Net Sales;
 - (4) Calculation of royalties due based on Net Sales;
 - (5) Any adjustments to amounts due pursuant to this AGREEMENT; and
 - (6) Amounts due to GAMBLE for the applicable quarters.

5.3 With each such report, VRI shall pay to GAMBLE the royalties due and payable as provided for in Section 4.5. If no royalties are due under Section 4.2(a), VRI shall so report.

6. PATENT PROSECUTION AND INFRINGEMENT

6.1 GAMBLE shall apply for and maintain during the term of this AGREEMENT any Patent Rights in the United States and in the European Union, Australia, Brazil, Canada, Japan and South Korea, and Mexico. The prosecution, filing and maintenance of all patents, with the exception of fee payments, shall be the primary responsibility of GAMBLE, using patent counsel selected by GAMBLE and reasonably acceptable to VRI, provided, however, that VRI shall be given a reasonable opportunity to advise GAMBLE on such matters, particularly as they pertain to patent prosecution in foreign countries, and GAMBLE shall furnish to VRI copies of any documents relevant to such prosecution, filing and maintenance in sufficient time in advance for VRI or its patent counsel to comment thereon. VRI shall pay all reasonable patent fees and costs, including reasonable counsel fees, incurred by GAMBLE pursuant to this Section.

6.2 VRI has reimbursed GAMBLE the sum of \$24,277, representing 50% of foreign phase filing costs for the countries and listed in Section 6.1. VRI shall reimburse GAMBLE the sum of \$78,558 upon VRI signing this AGREEMENT for the remaining 50% of the foreign phase filing costs and for its U.S. patent fees and costs arising from the Patent Rights invoiced by patent counsel to GAMBLE prior to October 10, 1994. All fees and costs incurred by GAMBLE after the Effective Date relating to the filing, prosecution and maintenance of all Patent Rights shall be paid by VRI within 30 days of receipt of invoice from GAMBLE. The foregoing notwithstanding, VRI shall will have the right to discontinue payment of any such fees or costs with respect to the Patent Rights in any particular country or countries, if after a good faith assessment of the cost of patent filing, the enforceability of intellectual property rights and the commercial value of the market, in a specific country, VRI believes that making such payments would not be commercially practical. VRI shall provide timely notice of VRI's intention not to pay a fees so, if GAMBLE desires, GAMBLE may pay such fee.

6.3 If at any time during the term of this AGREEMENT, VRI furnishes to GAMBLE reasonably convincing written evidence of an infringement of a patent included in the Patent Rights which adversely and substantially affects the commercial operations of VRI under the license granted hereunder, GAMBLE shall have the right, but not the obligation, to prosecute, at its own expense any such infringement and shall have the right for such

purpose to join VRI as a party plaintiff at GAMBLE's expense. VRI independently shall have the right to join any such suit or action brought by GAMBLE and, in such event, shall pay one-half of the cost of such suit or action from the date of joining. Provided that VRI has joined in the action and shared the costs

thereof as stated in the preceding sentence, no settlement, consent judgment or other voluntary final disposition of the suit may be entered into without the consent of VRI, which consent will not unreasonably be withheld. Any recovery or damages derived from such action shall first be used to reimburse GAMBLE for all legal expenses relating to such action. If VRI has not joined the action, GAMBLE is entitled to all recovery or damages still remaining; however, if VRI has joined the action, any recovery or damages still remaining shall be applied toward (i) reimbursement of GAMBLE for the amount of royalties not received by GAMBLE from the infringing party as a result of such infringement, and (ii) compensation of VRI for its lost profits or a reasonable royalty on the sales of the infringer, whichever is applicable; provided, however that if such remaining amount of recovery or damages is insufficient to compensate GAMBLE fully for such royalties and to compensate VRI fully for such lost profits or reasonable royalty, then such amount of recovery or damages still remaining shall be apportioned pro rata between GAMBLE and VRI in proportion to (a) the amount of royalties not received by GAMBLE from the infringing party as a result of such infringement, as compared with (b) VRI's lost profits or reasonable royalty on the sales of the infringer. Any recovery or damages still remaining after the above-mentioned applications shall be distributed two-thirds (2/3) to GAMBLE and one-third (1/3) to VRI.

6.4 If after said three (3) months, GAMBLE fails to cause such infringement to terminate or to bring a suit or action to compel termination, VRI shall have the right, but not the obligation, to prosecute, at its own expense any such infringement and shall have the right for such purpose to join GAMBLE as a party plaintiff at VRI's expense. GAMBLE independently shall have the right to join any such suit or action brought by VRI and, in such event, shall pay one-half of the cost of such suit or action from the date of joining. Provided that GAMBLE has joined in the action and shared the costs thereof as stated in the preceding sentence, no settlement, consent judgment or other voluntary final disposition of the suit may be entered into without the consent of GAMBLE, which consent will not unreasonably be withheld. Any recovery or damages derived from such action shall first be used to reimburse VRI (and GAMBLE if it joined in the action) for all legal expenses relating to such action. If GAMBLE has not joined the action, VRI is entitled to all recovery or damages still remaining; however, if GAMBLE has joined the action, any recovery or damages still remaining shall be applied toward (i) reimbursement of GAMBLE for the amount of royalties not received by GAMBLE from the infringing party as a result of such infringement, and (ii) compensation of VRI for its lost profits or a reasonable royalty on the sales of the infringer, whichever is applicable; provided, however that if such remaining amount of recovery or damages is insufficient to compensate GAMBLE fully for such royalties and to compensate VRI fully for such lost profits or reasonable royalty, then such amount of recovery or damages still remaining shall be apportioned pro rata between GAMBLE and VRI in proportion to (a) the amount of royalties not received by GAMBLE from the infringing party as a result of such infringement, as compared with (b) VRI's lost profits or reasonable royalty on the sales of the infringer. Any recovery or damages still remaining after the above-mentioned applications shall be distributed two-thirds (2/3) to GAMBLE and one-third (1/3) to VRI.

6.5 In any infringement suit that either party may institute to enforce the Patent Rights pursuant to this AGREEMENT, the other party hereto shall, cooperate in all respects and, to the extent possible, have its employees testify when requested and make available relevant records, papers, information, samples and the like.

6.6 In the event that a declaratory judgment action alleging invalidity or non-infringement of any of the Patent Rights shall be brought against VRI, GAMBLE, at its sole option shall have the right, within sixty (60) days after GAMBLE receives notice from VRI of such action, to intervene and participate in action at its own expense.

7. TERM AND TERMINATION

7.1 Unless earlier terminated as provided herein, this AGREEMENT shall remain in full force and effect for the life of the last to expire patent issued under the Patent Rights. Upon expiration, VRI shall have a fully paid-up, non-cancelable license.

7.2 Subject to Section 16, if VRI shall cease to carry on its business, this AGREEMENT shall terminate ninety (90) days after VRI ceases to do business, unless, within ninety (90) days VRI has identified a qualified successor licensee reasonably acceptable to GAMBLE willing to assume the obligation of VRI hereunder, in which case the assignment of this AGREEMENT to such successor licensee shall be subject to the written assumption by such successor of VRI's obligations hereunder and to the written approval of GAMBLE, which shall not be unreasonably withheld.

7.3 Should VRI fail to pay GAMBLE such royalties other than minimum royalties as are due and payable hereunder, GAMBLE shall have the right to terminate this AGREEMENT on thirty (30) days written notice, or to convert this AGREEMENT from an exclusive to a non-exclusive license upon expiration of the thirty (30) day period.

7.4 VRI shall have the right to terminate this AGREEMENT at any time upon six (6) months written notice to GAMBLE, and upon payment of all amounts due GAMBLE through the effective date of termination. If this AGREEMENT is terminated, VRI will provide GAMBLE with information and data necessary for GAMBLE to pursue the development of Licensed Products or Licensed Processes and a right to reference VRI's regulatory filings with the FDA.

7.5 Upon any material breach or default of this AGREEMENT by VRI or GAMBLE, the non-breaching party shall have the right to terminate this AGREEMENT and the rights, privileges and license hereunder granted upon ninety (90) days written notice to the other party. Such termination shall become effective immediately at the conclusion of such notice period unless the breaching party shall have cured any such breach or default prior to the expiration of the ninety (90) day period.

7.6 Upon termination of this AGREEMENT for any reason, nothing herein shall be construed to release either party from any obligation that matured prior to the effective date of such termination. VRI and any Sublicensee thereof may, after the effective date of such termination, sell all Licensed Products which are in inventory at the time of termination, and complete and sell Licensed Products which VRI can clearly demonstrate were in the process of manufacture at the time of such termination, provided that VRI shall pay to GAMBLE the royalties thereon as required by Section 4 of this AGREEMENT and shall submit the reports required by Section 5 hereof on the sales of Licensed Products.

8. INDEMNIFICATION AND INSURANCE

8.1 VRI shall defend, indemnify and hold harmless GAMBLE and its trustees, officers, medical and professional staff, employees, and agents and their respective successors, heirs and assigns, against all losses, damages, expenses, including attorney's fees and against any claims, suits, actions, demands or judgments brought against any one or more of them, arising out of any theory of product liability (including, but not limited to, actions in the form of tort, warranty, or strict liability) or negligence concerning any product, process or service made, used or sold pursuant to any right or license granted under this AGREEMENT. VRI shall have the right to control the defense settlement and/or compromise of any such claims or actions.

8.2 VRI's obligations under Section 8.1 above shall not apply to any liability, damage, loss or expense to the extent that it is directly attributable to the negligence or intentional misconduct of GAMBLE or of any of its trustees, officers, medical and professional staff, employees, agents or their respective successors, heirs or assigns.

8.3 VRI shall add, at VRI's expense, GAMBLE as an additional insured on VRI's clinical trial insurance policy, which provides limits of liability of \$2,000,000 per incident and aggregate, effective upon the Effective Date of this AGREEMENT, to provide insurance coverage for GAMBLE for the clinical trials.

8.4 VRI, at VRI's expense, shall maintain policies of comprehensive general liability insurance and will obtain product liability insurance in amounts not less than \$1,000,000 per incident and \$2,000,000 annual aggregate and shall add GAMBLE as an additional insured on VRI's policy, which provides such limits of liability. Such insurance shall provide (i) product liability coverage, (ii) negligence, and (iii) broad form contractual liability coverage, for VRI's indemnification under Section 8.1 of this AGREEMENT. The minimum amounts of insurance coverage required under these provisions shall not be construed to create a limit of VRI's liability with respect to VRI's indemnification obligation under Section 8.1 of this AGREEMENT. VRI shall maintain such comprehensive general liability insurance and product liability insurance beyond the expiration or termination of this AGREEMENT and for a reasonable period after the termination of the clinical trials, which in no event shall be less than fifteen (15) years after the clinical trials.

8.5 This Section 8 shall survive expiration or termination of this AGREEMENT.

9. REPRESENTATIONS

9.1 Subject to any prior rights of the U.S. government, GAMBLE represents that patent applications or patents included in the Patent Rights have been assigned to it and that GAMBLE has the authority and power to issue licenses under said Patent Rights and that GAMBLE has the right to disclose Technical Information to VRI and to enter into and perform this AGREEMENT.

9.2 GAMBLE does not warrant the validity of the Patent Rights licensed hereunder and makes no representation whatsoever with regard to the scope of the Patent Rights or that such Patent Rights may be exploited by VRI, its Affiliates, or Sublicensees without infringing

other patents, except that GAMBLE represents that as of the Effective Date it is not aware of any patent or patent application not a part of the Patent Rights licensed hereunder that would be infringed by the exercise by VRI, its Affiliates or Sublicensees, of the rights granted to them hereunder.

10. CONFIDENTIALITY

10.1 Confidential Information. As used in this AGREEMENT, "Confidential Information" means all information transmitted by a party hereto or obtained by a party hereto in connection with the performance of the clinical trials and other services described in Section 3 hereof or of any such other services to be provided by the parties as described herein, subject to the exceptions specified below. "Confidential Information" means information of any type, not generally known, about the business, processes, services, products, suppliers, customers, clients or plans of GAMBLE or VRI ("the parties hereto") of any client of the parties hereto (regardless of whether the parties hereto have executed a confidentiality agreement with such customer), which is used or useful in the conduct of business of the parties hereto, or which confers or tends to confer a competitive advantage over one who does not possess such information. Such information includes, but is not limited to, information relating to trade secrets, Technical Information, patent applications, know-how, research, development, design, engineering, quality control or service techniques, information about existing, new or envisioned products, processes or services and their development, performance, scientific, engineering or technical information, laboratory notebooks, notes, computer programs, source codes, object codes, software manuals, sketches, drawings, reports, formulae, gels, slides, sequences, biological materials living or otherwise, photographs, negatives, prototypes, models, correspondence, and other documents and things, and information relating to purchasing, sales, marketing, licensing, contracts with third parties, and pricing, whether or not in writing and whether or not labeled or identified as confidential or proprietary. Confidential Information may be disclosed in writing or orally or may be obtained by observation or inspection. All data, materials, information, and records developed by a party hereto in the course of performing this AGREEMENT shall be considered Confidential Information. However, Confidential Information shall not include information that a party hereto can demonstrate: (i) is in or enters the public domain through no fault of such party; (ii) is disclosed to a party hereto by a third party entitled to disclose it; (iii) was known to a party hereto before the date of this AGREEMENT; or (iv) is required by law to be disclosed, provided reasonable advance notice of such requirement is given to a party hereto before such disclosure.

10.2 Confidentiality. Without prior written consent, the parties hereto will not disclose the other party's Confidential Information to any third party other than employees, agents or others of the parties hereto who must necessarily be informed thereof, but only if and to the extent that any such person has a need for such information. A party hereto will only use Confidential Information for the purpose of fulfilling its obligations under this AGREEMENT. The parties hereto agree that they will take such reasonable steps as may be necessary to prevent the disclosure or use of any such materials by their officers, employees or agents except as provided herein, including but not limited to obtaining and enforcing appropriate confidentiality agreements with such persons. All obligations of confidentiality and nondisclosure set forth in this AGREEMENT shall survive the termination or expiration of this AGREEMENT.

10.3 The parties agree that clinical trial data generated by GAMBLE under the terms of the AGREEMENT will not be published by VRI prior to its publication by GAMBLE's principal investigators. To the extent not published, the results of the clinical trials will be held in confidence by GAMBLE. Subject to the foregoing, VRI will have the unrestricted right to use or disclose such clinical trial data.

11. NOTICES

11.1 Reports, notices and other communications from VRI to GAMBLE as provided hereunder shall be sent by certified mail to:

James N. Gamble Institute of Medical Research
2141 Auburn Avenue
Cincinnati, OH 45219
Attention: President

or other individuals or addresses as shall hereafter be furnished by written notice to VRI.

11.2 Reports, notices and other communications from GAMBLE to VRI as provided hereunder shall be sent to by certified mail to:

Virus Research Institute, Inc.
61 Moulton Street
Cambridge, MA 02138
Attention: President

or other individuals or addresses as shall hereafter be furnished by written notice to GAMBLE.

12. ARBITRATION

12.1 (a) Any controversy, dispute or claim arising out of, or relating to, any provisions, the interpretation or the performance of this AGREEMENT or any breach thereof which cannot otherwise be resolved by good faith negotiations between the parties shall be resolved by final and binding arbitration under the rules of the American Arbitration Association, or the Patent Arbitration Rules, if applicable, which are in effect as of the Effective Date of this AGREEMENT. In the event that VRI initiates, requests and/or files for arbitration, the arbitration shall be conducted in Cincinnati, Ohio. In the event that GAMBLE initiates, requests and/or files for arbitration, the arbitration shall be conducted in Boston, Massachusetts.

(b) The arbitration shall be subject to the following terms:

(1) The number of arbitrators shall be three (3).

(2) The arbitrators shall be independent, impartial third parties having no direct or indirect personal or financial relationship to any of the parties to the dispute, who has have agreed to accept the appointment as arbitrator on the terms set out in this Section 12.1.

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(3) The arbitrators shall be active or retired attorneys, law professors, or judicial officers with at least five (5) years experience in general commercial matters and a familiarity with the laws governing proprietary rights in intellectual property and in particular patent law.

(4) The arbitrators shall be selected as follows:

(i) Each party shall submit a description of the matter to be arbitrated to the American Arbitration Association at the appropriate Regional Office in Cincinnati, Ohio or Boston, Massachusetts, depending upon where the arbitration is to be held. Said Association shall submit to the parties a list of the arbitrators available to arbitrate any dispute between them. Thereafter, each party shall select, in numerical order, those persons on said list acceptable as arbitrators and return the same to the Association. The first three arbitrators acceptable to both parties shall be deemed the selected arbitrators with respect to the dispute then at issue under this AGREEMENT. In the event of a failure to select three mutually agreeable arbitrators, the Association shall be requested to submit as many subsequent lists of arbitrators as shall be necessary to effect a mutual selection.

(ii) If the method of selection set out in Section 12.1(b)(4)(a) fails for any reason, then either party may petition any state or federal court in Massachusetts or Ohio having jurisdiction for appointment of the arbitrators in accordance with applicable law, provided that the arbitrators must satisfy the requirements of Sections 12.1(b)(2) and 12.1(b)(3) above and be acceptable to each party hereto.

(5) The arbitrators shall announce the award in writing accompanied by written findings explaining the facts determined in support of the award, and any relevant conclusions of law.

(6) Unless otherwise provided in this Section 12.1 or extended by agreement of the parties, each party shall submit an initial request for designation of arbitrators within thirty (30) days after any request for arbitration, the dispute shall be submitted to the arbitrators within sixty (60) days after the arbitrators are selected, and a decision shall be rendered within thirty (30) days after the dispute is submitted.

(7) The fees of the arbitrators and any other costs and fees associated with the arbitration shall be paid in accordance with the decision of the arbitrators.

(8) The arbitrators shall have no power to add to, subtract from, or modify any of the terms or conditions of this AGREEMENT. Any award rendered in such arbitration may be enforced by either party in either the courts of the Commonwealth of Massachusetts

12.2 Notwithstanding the foregoing, nothing in this Section shall be construed to waive any rights or timely performance of any obligations existing under this AGREEMENT.

13. RESTRICTIONS ON USE OF NAMES

VRI shall not use the names of GAMBLE, its related entities and its employees, or any adaptations thereof in any advertising, promotional or sales literature, without the prior written consent of GAMBLE; provided however, that VRI (a) may refer to publications by employees of GAMBLE in the scientific literature or (b) may state that a license from GAMBLE has been granted as herein provided.

14. INDEPENDENT CONTRACTOR

For the purpose of this AGREEMENT and all services to be provided hereunder, both parties shall be, and shall be deemed to be, independent contractors and not agents or employees of the other. Neither party shall have authority to make any statements, representations or commitments or any kind, or to take any action, that will be binding on the other party.

15. SEVERABILITY

If any one or more of the provisions of this AGREEMENT shall be held to be invalid, illegal or unenforceable, the validity, legality or enforceability of the remaining provisions of this AGREEMENT shall not in any way be affected or impaired thereby.

16. NON-ASSIGNABILITY

Neither this AGREEMENT nor any part hereof shall be assignable by either party without the express written consent of the other provided that either VRI or GAMBLE may assign this AGREEMENT in connection with the merger, consolidation or sale of substantially all of its assets or the sale of that portion of its business to which the Inventions relate or as set forth in Section 7.2 and further provided that neither party shall unreasonably withhold its consent to any other assignment by the other party to an assignee which can reasonably demonstrate its qualifications to carry out the obligations of VRI or GAMBLE hereunder. Any other attempted assignment without such consent shall be void.

17. ENTIRE AGREEMENT

This instrument contains the entire AGREEMENT between the parties hereto. No verbal agreement, conversation or representation between any officers, agents, or employees of the parties hereto either before or after the execution of this AGREEMENT shall affect or modify any of the terms or obligations herein contained.

18. MODIFICATIONS IN WRITING

No change, modification, extension, termination or waiver of this AGREEMENT, or any of the provisions herein contained, shall be valid unless made in writing and signed by a duly authorized representative of each party.

19. GOVERNING LAW

The validity and interpretation of this AGREEMENT and the legal relations of the parties to it shall be governed by the laws of the State of Ohio.

20. CAPTIONS

The captions are provided for convenience and are not to be used in construing this AGREEMENT.

21. PATENT MARKING

VRI agrees to mark and have marked all Licensed Products sold by it under the license granted herein, if practical, with the word "Patent" or "Patents" and the number of the patent or patents applicable thereto.

IN WITNESS WHEREOF, the parties hereto have caused this AGREEMENT to be executed in quadruplicate by their duly authorized representatives as of the date first above written.

JAMES N. GAMBLE INSTITUTE
(GAMBLE)

VIRUS RESEARCH INSTITUTE, INC.
(VRI)

By: /s/ Gilbert M. Schiff 2/24/95
Gilbert M. Schiff, M.D.

By: /s/ William A. Packer
William A. Packer

WITNESSED BY:

WITNESSED BY:

/s/ [signature illegible]

/s/ [signature illegible]

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APPENDIX A**LIST OF PATENT APPLICATIONS INCLUDED IN THE PATENT RIGHTS**

- 1.) U.S. Serial No. 07/614,310, filed November 16, 1990, entitled "Human Rotaviruses, Vaccines and Methods," and invented by Richard L. Ward.
- 2.) U.S. Serial No. 07/816,974, filed January 3, 1992, entitled "Human Rotaviruses, Vaccines and Methods," and invented by Richard L. Ward (Division of U.S. Serial No. 07/614,310).
- 3.) Serial No. PCT/U.S. 91/08191, filed November 4, 1990, entitled "Human Rotaviruses, Vaccines and Methods," and invented by Richard L. Ward.

U.S. Patent Application Serial Number	08/143975
U.S. Patent Application Serial Number	08/114114
Brazilian Patent Application Serial Number	9106982
European Patent Application Serial Number	92900590.8
Mexican Patent Application Serial Number	9303196
Australian Application Serial Number	90603/91
Canadian Application Serial Number	2096315
S. Korean Application Serial Number	93701493
Japanese Application Serial Number	501860/92

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APPENDIX B**MATERIALS TRANSFER AGREEMENT**

THIS AGREEMENT entered the _____ day of _____, 19____, by and between the James N. Gamble Institute of Medical Research ("Provider"), a non-profit corporation having a place of business at 2141 Auburn Ave., Cincinnati, Ohio 45219 and ("Recipient"), a corporation having a place of business at _____

1. Subject to availability Provider agrees to provide the following material to recipient: ***. Such material and any related biological material or associated know-how and data that will be received by Recipient from Provider, and any substance that is replicated or derived therefrom are covered by this Agreement. All such materials shall hereinafter be referred to as the "Material(s)."
2. The Materials will be used by Recipient in connection with the research described in Appendix A and only for non-commercial purposes. The Materials shall not be used in research that is subject to consulting or licensing obligations to another institution, corporation or business entity, unless written permission is obtained in advance from Provider.
3. Recipient shall not distribute, release or disclose the Materials to any other person or entity and shall ensure that no one will be allowed to take or send the Materials to any other location, unless written permission is obtained in advance from Provider. Recipient agrees to maintain the confidentiality of any propriety information of Provider regarding the Materials.
4. The Materials are supplied solely for scientific research purposes, for use in animals and/or in vitro. **THE MATERIALS SHALL NOT BE USED IN HUMANS.**
5. No right or license is granted under the Agreement either expressly or by implication. It is understood that any and all proprietary rights, including but not limited to patent rights, in and to the Materials shall be and remain in Provider.
6. Recipient agrees to provide Provider with an advance copy at least thirty (30) days in advance of any written submission (abstract or paper) or oral presentation that makes reference to the Materials. If in the opinion of Provider any such publication describes a patentable development, Provider shall have an opportunity to request that Recipient delay the submission or public presentation until after a U.S. patent application has been filed. In no event shall the delay be unreasonable. If a publication does result from work using the Materials, Recipient agrees to acknowledge Provider and/or give credit to Provider's scientists, as scientifically appropriate, based on any direct contribution they may have made to the work.
7. Recipient agrees not to sequence or clone any Material provided by Provider without the written permission of Provider.

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8. In the event that use of the Material results in an invention, improvement, substance, or information whether or not patentable and patents, if any, which result therefrom ("Developed Technology"), Recipient agrees to disclose promptly to Provider all such inventions, improvements or

substances.

9. Recipient shall assign all right, title and interest in and to Developed Technology to Provider. Recipient agrees to cooperate and assist Provider in obtaining patent protection for Developed Technology.
10. Recipient agrees to execute, acknowledge and deliver all such further papers as may be necessary to perform its obligation under this Agreement
11. Recipient acknowledges that the Materials are provided WITHOUT WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR ANY OTHER WARRANTY, EXPRESS OR IMPLIED. PROVIDER MAKES NO REPRESENTATION THAT THE USE OF THE MATERIALS WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK OR OTHER PROPRIETARY RIGHT.
12. In no event shall Provider be liable for any use of the Materials by Recipient. Recipient hereby agrees to defend, indemnify and hold harmless Provider, its officers, directors, trustees, employees and agents from any loss, claim, damage, expense or liability, of whatsoever kind or nature (including attorney's fees), which may arise from or in connection with this Agreement or the use, handling or storage of the Materials.
13. Recipient shall report to Provider a summary of the results of Recipient's work utilizing the Materials.
14. Upon the request of Provider, Recipient shall promptly return to Provider the Materials furnished to Recipient under this Agreement.
15. Recipient agrees to comply with all government and National Institutes of Health regulations and guidelines which are applicable to the Recipient's use of the Materials.
16. This Agreement is not assignable, whether by operation of law or otherwise, without the prior written consent of Provider.

IN WITNESS WHEREOF, the parties, intending to be legally bound, have caused this Agreement to be executed by their respective duly authorized representatives.

RECIPIENT'S INVESTIGATOR

AUTHORIZED REPRESENTATIVE FOR RECIPIENT

By: _____

By: _____

Typed Name

Typed Name

Title

Title

PROVIDER'S INVESTIGATOR

AUTHORIZED REPRESENTATIVE FOR PROVIDER

By: _____

By: _____

Typed Name

Typed Name

Title

Title

APPENDIX C

PROTOCOL

REACTIVITY AND IMMUNOGENICITY OF LIVE, ATTENUATED

ROTAVIRUS VACCINE CANDIDATE 89-12

A copy of the protocol will be attached to the execution copy of this AGREEMENT

LICENSE AGREEMENT

This Agreement is made and entered into between the President and Fellows of Harvard College (hereinafter HARVARD) having offices at the Office for Technology and Trademark Licensing, 124 Mt. Auburn Street, Suite 440, Cambridge, Massachusetts, 02138 and Virus Research Institute (hereinafter LICENSEE), a corporation of Cambridge, MA, having offices at 61 Moulton Street, Cambridge, MA 02139.

Whereas HARVARD and The General Hospital Corporation (GENERAL) doing business as Massachusetts General Hospital are or will be the Owners by assignment, of the entire right, title and interest in the following United States patent applications, and in the foreign patent applications corresponding thereto, and in the inventions described and claimed therein and any patents issuing thereon, and whereas GENERAL and HARVARD have agreed to cooperate in the patent and license administration of such patent applications:

U.S.S.N. 629,602 - "Improved Vaccines"; filed December 18, 1990; Inventors: John Mekalanos and Samuel Miller.

U.S.S.N. 629,102 - "Vibrio Cholerae Strains Defective in irgA Expression and Cholera Vaccines Derived Therefrom"; filed December 18, 1990; Inventors: John Mekalanos and Stephen Calderwood.

U.S.S.N. 000,000 - "Doubly-Attenuated Strain of Vibrio Cholerae to Deliver Heterologous Antigens for Vaccination" to be filed in 1992; Inventors: John Mekalanos and Stephen Calderwood (serial number and filing date to be inserted when available);

Whereas GENERAL has agreed HARVARD is its sole licensing agent for these jointly owned patent applications; and

Whereas HARVARD is the Owner by assignment of the entire right, title and interest in the following United States Patents or Patent Applications and in the foreign patent applications corresponding thereto, and in the inventions described and contained therein:

U.S.S.N. 043,907 - "Cholera Vaccines"; filed April 29, 1987 and its CIP USSN 5,098,998, filed April 29, 1988; Inventors: John Mekalanos and Ronald Taylor.

U.S. 4,882,278 - "Non-Toxic Vibrio Cholera Mutants"; issued November 21, 1989; Inventor: John Mekalanos.

U.S.S.N 000,000 - "Peruvian Strain of Cholera Vaccine"; to be filed in 1992; Inventor: John Mekalanos (serial number and filing date to be inserted when available); and

Whereas HARVARD and GENERAL are the Owners by assignment from the inventors of the BIOLOGICAL MATERIAL as defined in Appendix B and have the right to license the BIOLOGICAL MATERIAL; and

Whereas HARVARD and the GENERAL are committed to a policy that ideas or creative works produced at HARVARD and the GENERAL should be used for the greatest possible public benefit; and

Whereas HARVARD accordingly believes that every reasonable incentive should be provided for the prompt introduction of such ideas into public use, all in a manner consistent with the public interest; and

Whereas LICENSEE is desirous of obtaining an exclusive worldwide license in order to practice the above referenced inventions covered by PATENT RIGHTS and to use the BIOLOGICAL MATERIAL in the United States and in certain foreign countries, and to manufacture, use and sell in the commercial market the products made in accordance therewith; and

Whereas HARVARD is desirous of granting such a license to LICENSEE in accordance with the terms of this Agreement. Now therefore, in consideration of the foregoing premises, the parties agree as follows:

ARTICLE I - DEFINITIONS

1.1 PATENT RIGHTS shall mean any and all United States patents or patent applications listed above and attached hereto in Appendix A, the inventions described and claimed therein, and any divisions, continuations, continuations-inpart directed to subject matter specifically described in the application and patents listed in Appendix A, patents issuing thereon or reissues thereof; and any and all foreign patents and patent applications corresponding thereto; which will be automatically incorporated in and added to this Agreement and shall periodically be added to Appendix A and made a part thereof. To the extent HARVARD's obligations to third parties permit, PATENT RIGHTS shall also include all IMPROVEMENT INVENTIONS. IMPROVEMENT INVENTIONS shall mean any inventions or discoveries that enhance, substitute for, or are useful with the products, procedures or processes described in PATENT RIGHTS to the extent they are (i) dominated by any claims of a pending and/or issued patent or patent application which is then included in the PATENT RIGHTS, and HARVARD's ownership interest in any United States or foreign patents and patent application thereon, and (ii) made (i.e., conceived and reduced to practice) by Dr. John Mekalanos solely or jointly with others directly supervised in his laboratory at Harvard Medical School. IMPROVEMENT INVENTIONS shall not include inventions assignable to GENERAL

1.2 LICENSED PRODUCTS shall mean products covered in whole or in part by an issued, unexpired claim or a pending claim contained in PATENT RIGHTS which has not been declared invalid by a court of competent jurisdiction.

1.3 LICENSED PROCESSES shall mean processes covered in whole or in part by an issued, unexpired claim or a pending claim contained in PATENT RIGHTS which has not been declared invalid by a court of competent jurisdiction.

1.4 NET SALES shall mean the amount billed or invoiced on sales of LICENSED PRODUCTS less:

(a) Customary trade, quantity or cash discounts and non-affiliated brokers' or agents' commissions actually allowed and taken;

(b) Amounts repaid or credited by reason of rejection or return; and/or

(c) To the extent separately stated on purchase orders, invoices or other documents of sale, taxes levied on and/or other governmental charges made as to production, sale, transportation, delivery or use and paid by or on behalf of LICENSEE.

1.5 AFFILIATES shall mean any company, corporation, or business (i) in which LICENSEE directly or indirectly owns or controls at least fifty percent (50%) of the voting stock, or (ii) which directly or indirectly owns or controls at least fifty percent (50%) of the voting stock of LICENSEE or (iii) the majority ownership of which is directly or indirectly under common control with LICENSEE.

1.6 BIOLOGICAL MATERIAL shall mean the materials supplied by HARVARD and GENERAL (identified in Appendix B).

1.7 TECHNOLOGY shall mean any and all information or PATENT RIGHTS, or BIOLOGICAL MATERIAL supplied by HARVARD and GENERAL to LICENSEE.

ARTICLE II - GRANT

2.1 For the term of this Agreement, HARVARD hereby grants to LICENSEE and LICENSEE accepts, subject to the terms and conditions hereof, a worldwide license under PATENT RIGHTS and a worldwide license to use the BIOLOGICAL MATERIAL, to make and have made, to use and have used, to sell and have sold the LICENSED PRODUCTS, and to practice the LICENSED PROCESSES. Such license shall include the right to grant sublicenses. In order to provide LICENSEE with a period of exclusivity, HARVARD agrees it will not grant licenses to others except as required under Paragraph 2.2 (a) or as permitted in paragraph 2.2 (b). LICENSEE agrees during the period of exclusivity of this license in the United States that any LICENSED PRODUCT produced for sale in the United States will be manufactured substantially in the United States.

2.2 The granting and acceptance of this license is subject to the following conditions:

(a) HARVARD's "Statement of Policy in Regard to Inventions, Patents and Copyrights" dated March 17, 1986, Public Law 96-517, Public Law 98-620 and HARVARD's and GENERAL'S obligations under agreements with other sponsors of research. Any right granted in this Agreement greater than that permitted under Public Law 96-517 or Public Law 98-620 shall be subject to modification as may be required to conform to the provisions of that statute.

(b) HARVARD's and GENERAL's right to make and to use and to grant non-exclusive licenses to make and to use, for academic research purposes only and for GENERAL's

internal inpatient care purposes and not for any commercial purpose, the subject matter described and claimed in PATENT RIGHTS, or the BIOLOGICAL MATERIAL.

(c) LICENSEE shall use reasonable effort to effect introduction of the LICENSED PRODUCTS into the commercial market as soon as practicable, consistent with sound and reasonable business practices and judgment; thereafter, until the expiration of this Agreement, LICENSEE shall endeavor to keep LICENSED PRODUCTS reasonably available to the public.

(d) HARVARD shall have the right to terminate or render non-exclusive any license granted hereunder if in HARVARD's reasonable judgement, LICENSEE:

(i) has not, within five years from the date of this Agreement, commenced clinical trials of a LICENSED PRODUCT or LICENSED PROCESS in the country or countries where licensed; and/or

(ii) is not, within one year of the date of this Agreement, demonstrably engaged in on-going research, development, or marketing or licensing programs as appropriate, directed toward commercial use of the LICENSED PRODUCT or LICENSED PROCESSES.

In making this determination HARVARD shall take into account the normal course of such programs conducted with sound and reasonable business practices and judgment and shall take into account the reports provided hereunder by LICENSEE.

(e) All sublicenses granted by LICENSEE hereunder shall include a requirement that the sublicensee use its good faith efforts to bring the subject matter of the sublicense into commercial use as quickly as is reasonably possible consistent with sound and reasonable business practices and judgement and shall bind the sublicensee to meet LICENSEE's obligations to HARVARD under this Agreement. Royalties charged for sublicenses by LICENSEE shall not be in excess of normal trade practice. Copies of all sublicense agreements shall be provided to HARVARD.

(f) In the event that LICENSEE is in default of its obligations under Section 2.2 (c) or (e) or Article III, and such default remains unresolved following notice as provided in Section 8.2 or LICENSEE fails to meet the milestones specified in Section 2.2 (d) and HARVARD does not thereafter exercise its right to terminate this license, and LICENSEE is thereafter unable or unwilling to grant sublicenses, either as suggested by HARVARD or a potential sublicensee or otherwise, HARVARD may directly license such potential sublicensee unless LICENSEE reasonably satisfies HARVARD that such sublicense would be contrary to sound and reasonable business practice, and that the granting of such sublicense would not materially increase the availability to the public of products manufactured under this license.

(g) HARVARD shall have the right to terminate this Agreement if LICENSEE does not have commitments for a minimum of one million dollars (\$1,000,000) of investment capital within six (6) months of the signing of this Agreement, and three million dollars (\$3,000,000) of total funding within thirty-six (36) months of the signing of this Agreement.

2.3 HARVARD hereby grants to LICENSEE the right to extend the licenses granted or to be granted in paragraph 2.1 to an AFFILIATE subject to the terms and conditions hereof.

2.4 All rights reserved to the United States Government and others under Public Law 96-517 and 98-620 shall remain and shall in no way be affected by this Agreement.

ARTICLE III - ROYALTIES

3.1 LICENSEE shall pay to HARVARD a non-refundable license fee in the sum of \$200,000 in two equal installments, the first upon execution of this Agreement, and the second six months after the signing of this Agreement.

3.2 LICENSEE shall pay HARVARD, during the term of the license granted in Section 2.1, a royalty of four percent (4%) of the NET SALES of all LICENSED PRODUCTS sold by LICENSEE and its AFFILIATES or sublicensees to commercial organizations, and two percent (2%) of the NET SALES of all LICENSED PRODUCTS sold by LICENSEE and its AFFILIATES or sublicensees to non-profit or government agencies. In the case of sublicensees, LICENSEE shall also pay to HARVARD twenty-five percent (25%) of non-royalty sublicense income (e.g., license issue fees, license maintenance fees, etc.) from commercial organizations, and ten percent (10%) of all such income from government or non-profit organizations. If this license is converted to a non-exclusive one and if other non-exclusive licenses are granted, this royalty shall not exceed the royalty being paid by other licensees during the term of the non-exclusive license. On sales between LICENSEE and its AFFILIATES or sublicensees for resale, the royalty shall be paid on the resale.

3.3 HARVARD shall have the right to terminate or render non-exclusive this license in the event that LICENSEE does not pay to HARVARD at least the following amounts in license maintenance fees and/or minimum royalties:

First calendar year	-\$	10,000
Next calendar year	-\$	15,000
Next calendar year and each year thereafter.	-\$	20,000

In the event that actual royalties are not at least equal to the above amounts for the specified periods, LICENSEE shall have the right to pay any difference between such minimum amounts and the actual royalties paid in satisfaction of its obligations under this Section 3.3.

3.4 In the event that LICENSEE is required to pay royalties to one or more third parties under patents other than PATENT RIGHTS covering LICENSED PRODUCTS or LICENSED PROCESSES, LICENSEE shall be entitled to a credit against royalties due HARVARD in an amount equal to fifty percent (50%) of royalties paid to such third parties, provided that in no event shall the royalties otherwise due HARVARD be reduced by more than one-half.

3.5 In the event that the royalties paid to HARVARD are so significant a factor in the return realized by LICENSEE as to diminish LICENSEE's capability to respond to competitive pressures in the market, HARVARD agrees to consider a reasonable reduction in the royalty paid to HARVARD as to each LICENSED PRODUCT for the period during which such market

condition exists. Factors determining the size of the reduction will include profit margin on LICENSED PRODUCTS and on analogous products, prices of competitive products, total prior sales by LICENSEE, and LICENSEE's expenditures on LICENSED PRODUCT development.

ARTICLE IV - REPORTING

4.1 Prior to signing this Agreement, LICENSEE has provided to HARVARD a written research and development plan under which LICENSEE intends to bring the subject matter of the licenses granted hereunder into commercial use upon execution of this Agreement. Such plan includes projections of sales and proposed marketing efforts.

4.2 LICENSEE shall provide written annual reports within sixty (60) days after June 30 of each calendar year which shall include but not be limited to: reports of progress on research and development, regulatory approvals, manufacturing, sublicensing, marketing and sales during the preceding twelve (12) months as well as plans for the coming year. If progress differs from that anticipated in the plan provided under Section 4.1, LICENSEE shall explain the reasons for the difference and propose a modified plan for HARVARD's review and approval. LICENSEE shall also provide any reasonable additional data HARVARD requires to evaluate LICENSEE's performance.

4.3 LICENSEE shall report to HARVARD the date of first sale of LICENSED PRODUCTS (or results of LICENSED PROCESSES) in each country within thirty (30) days of occurrence.

4.4 Commencing with the calendar year half in which Net Sales first occur, LICENSEE agrees to submit to HARVARD within sixty (60) days after the calendar half years ending June 30 and December 31, reports setting forth for the preceding six (6) month period the amount of the LICENSED PRODUCTS sold by LICENSEE, its AFFILIATES and sublicensees in each country, the NET SALES thereof, and the amount of royalty due thereon and with each such royalty any non-royalty sublicense income and pay the amount of royalty due. Such report shall be certified as correct by an officer of LICENSEE and shall include a detailed listing of all deductions from NET SALES, sublicensee income or from royalties as specified herein. Such report shall also specify which PATENT RIGHTS are used in or by each LICENSED PRODUCT generating royalty income. If no royalties are due to HARVARD for any reporting period, the written report shall so state. If royalties for any calendar year do not equal or exceed the minimum royalties established in paragraph 3.3, LICENSEE shall include the balance of the minimum royalty with the payment for the half year ending December 31. All royalties due hereunder shall be payable in United States dollars. Conversion of foreign currency to U.S. dollars shall be made at the conversion rate existing in the United States on the, last business day in the reporting period as reported in the Wall Street Journal. All such reports shall be maintained in confidence by HARVARD, except as required by law, including Public Law 96-517 and 98-620.

4.5 If by law, regulation, of fiscal policy of a particular country, conversion into United States dollars or transfer of funds of a convertible currency to the United States is restricted or forbidden, LICENSEE shall give HARVARD prompt notice in writing and shall pay the royalty and other amounts due through such means or methods as are lawful in such country

as HARVARD may reasonably designate. Failing the designation by HARVARD of such lawful means or methods within thirty (30) days after such notice is given to HARVARD, LICENSEE shall deposit such royalty payment in local currency to the credit of HARVARD in a recognized banking institution designated by HARVARD, or if none is designated by HARVARD within the thirty (30) day period described above, in a recognized banking institution selected by LICENSEE and identified in a written notice to HARVARD by LICENSEE, and such deposit shall fulfill all obligations of LICENSEE to HARVARD with respect to such royalties.

ARTICLE V - RECORD KEEPING

5.1 LICENSEE shall keep, and shall require its AFFILIATES and sublicensees to keep accurate and correct records of LICENSED PRODUCTS made, used or sold under this Agreement, appropriate to determine the amount of royalties due hereunder to HARVARD. Such records shall be retained for at least three (3) years following a given reporting period. They shall be available during normal business hours for inspection at the expense of HARVARD by HARVARD's Internal Audit Department or by a Certified Public Accountant selected by HARVARD and approved by LICENSEE for the sole purpose of verifying reports and payments hereunder. Such accountant shall not disclose to HARVARD any information other than information relating to accuracy of reports and payments made under this Agreement. In the event that any such inspection shows an under reporting and underpayment in excess of five percent (5%) for any twelve (12) month period, then LICENSEE shall pay the cost of such examination.

ARTICLE VI - DOMESTIC AND FOREIGN PATENT FILING AND MAINTENANCE

6.1 LICENSEE shall reimburse HARVARD for all reasonable expenses HARVARD and GENERAL have incurred and shall incur for the preparation, filing, prosecution and maintenance of PATENT RIGHTS for which HARVARD or GENERAL has not been, and is not eligible to be reimbursed by any third party. HARVARD and GENERAL shall take responsibility for the preparation, filing, prosecution and maintenance of any and all patent applications and patents included in PATENT RIGHTS using patent counsel reasonably acceptable to LICENSEE, provided however that HARVARD and GENERAL shall first consult with LICENSEE as to the preparation, filing, prosecution and maintenance of such patent applications and patents and shall furnish to LICENSEE copies of documents relevant to any such preparation, filing, prosecution or maintenance.

6.2 HARVARD, GENERAL, and LICENSEE shall cooperate fully in the preparation, filing, prosecution and maintenance of PATENT RIGHTS and of all patents and patent applications licensed to LICENSEE hereunder, executing all papers and instruments or requiring members of HARVARD and GENERAL to execute such papers and instruments so as to enable HARVARD and GENERAL to apply for, to prosecute and to maintain patent applications and patents in HARVARD's and/or GENERAL's name in any country. Each party shall provide to the other prompt notice as to all matters which come to its attention and which may affect the preparation, filing, prosecution or maintenance of any such patent applications or patents.

6.3 If LICENSEE elects not to pay the expenses of a patent application or patent included within PATENT RIGHTS in a particular country, LICENSEE shall notify HARVARD

not less than sixty (60) days prior to such action and shall thereby surrender its rights under such patent or patent application in such country. LICENSEE agrees that it shall not exercise this right for the purpose of avoiding the payment of royalties otherwise due in such country.

ARTICLE VII - INFRINGEMENT

7.1 With respect to any PATENT RIGHTS under which LICENSEE is exclusively licensed pursuant to this Agreement, LICENSEE or its sublicensee shall have the right to prosecute in its own name and at its own expense any infringement of such patent, so long as such license is exclusive at the time of the commencement of such action. HARVARD agrees to notify LICENSEE promptly of each infringement of such patents of which HARVARD is or becomes aware. Before LICENSEE or its sublicensees commences an action with respect to any infringement of such patents, LICENSEE shall give careful consideration to the views of HARVARD and to potential effects on the public interest in making its decision whether or not to sue and in the case of a LICENSEE sublicensee, shall report such views to the sublicensee.

7.2 If LICENSEE or its sublicensee elects to commence an action as described above and HARVARD and/or GENERAL is a legally indispensable party to such action, HARVARD and/or GENERAL shall have the right to assign to LICENSEE all of HARVARD's and/or GENERAL's right, title and interest in each patent which is a part of the PATENT RIGHTS and is the subject of such action (subject to all HARVARD's and/or GENERAL's obligations to the government and others having rights in such patent). In the event that HARVARD and/or GENERAL makes such an assignment, such assignment shall be irrevocable, and such action by LICENSEE on that patent or patents shall thereafter be brought or continued without HARVARD and/or GENERAL as a party, if HARVARD and/or GENERAL is no longer an indispensable party. Notwithstanding any such assignment to LICENSEE by HARVARD and/or GENERAL and regardless of whether HARVARD and/or GENERAL is or is not an indispensable party, HARVARD and/or GENERAL shall cooperate fully with LICENSEE, at LICENSEE's expense, in connection with any such action. In the event that any patent is assigned to LICENSEE by HARVARD and/or GENERAL, pursuant to this paragraph, such assignment shall require LICENSEE to continue to meet its obligations under this Agreement as if the assigned patent or patent application were still licensed to LICENSEE.

7.3 If LICENSEE or its sublicensee elects to commence an action as described above, LICENSEE may reduce, by up to 50%, the royalty due to HARVARD earned under the patent subject to suit by the amount of the expenses and costs of such action, including attorney fees. In the event that such expenses and costs exceed the amount of royalties withheld by LICENSEE for any calendar year, LICENSEE may to that extent reduce the royalties due to HARVARD from LICENSEE in succeeding calendar years, but never by more than 50% of the royalty due in any one year.

7.4 Recoveries or reimbursements from such action shall first be applied to reimburse LICENSEE and HARVARD and GENERAL for litigation costs not paid from royalties (if any) and then to reimburse HARVARD for royalties withheld. Any remaining recoveries or reimbursements shall be

7.5 In the event that LICENSEE and its sublicensee, if any, elect not to exercise their right to prosecute an infringement of the PATENT RIGHTS pursuant to the above paragraphs, HARVARD and/or GENERAL may do so at its own expense, controlling such action and retaining all recoveries therefrom.

ARTICLE VIII - TERMINATION OF AGREEMENT

8.1 This Agreement, unless extended or terminated as provided herein, shall remain in effect for the life of the last to expire of PATENT RIGHTS licensed hereunder.

8.2 In the event that one party to this Agreement shall be in default in the performance of any obligations under this Agreement, and if the default has not been remedied within ninety (90) days after the date of notice in writing of such default, the party giving such notice may terminate this Agreement by written notice.

8.3 In the event that LICENSEE shall cease to carry on its business, HARVARD shall have the right to terminate this entire Agreement by giving LICENSEE written notice of such termination.

8.4 Any sublicenses granted by LICENSEE under this Agreement shall provide for termination or assignment to HARVARD, at the option of HARVARD, of LICENSEE's interest therein upon termination of this Agreement.

8.5 LICENSEE shall have the right to terminate this Agreement by giving thirty (30) days advance written notice to HARVARD to that effect. Upon termination, a final report shall be submitted and any royalty payments and unreimbursed patent expenses due to HARVARD become immediately payable.

8.6 Sections 8.5, 9.2, 9.3 and 9.4 of this Agreement shall survive termination.

ARTICLE IX - GENERAL

9.1 HARVARD represents and warrants that the entire right, title, and interest in the patent applications or patents comprising the PATENT RIGHTS have been or will be assigned to it and/or GENERAL and that HARVARD has the authority to issue the licenses under said PATENT RIGHTS set forth herein. HARVARD does not warrant the validity of the PATENT RIGHTS licensed hereunder and makes no representations whatsoever with regard to the scope of the licensed PATENT RIGHTS or that such PATENT RIGHTS may be exploited by LICENSEE, an AFFILIATE, or sublicensee without infringing other patents.

9.2 EXCEPT AS PROVIDED IN SECTION 9.1, HARVARD EXPRESSLY DISCLAIMS ANY AND ALL IMPLIED OR EXPRESS WARRANTIES AND MAKES NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS OF THE TECHNOLOGY, LICENSED PROCESSES OR LICENSED PRODUCTS CONTEMPLATED BY THIS AGREEMENT.

9.3 (a) LICENSEE shall indemnify, defend and hold harmless HARVARD and GENERAL and their directors, governing board members, trustees, officers, faculty, medical and

professional staff, employees, students, and agents and their respective successors, heirs and assigns (the "Indemnitees"), against any liability, damage, loss or expenses (including reasonable attorneys' fees and expenses of litigation) incurred by or imposed upon the Indemnitees or any one of them in connection with any claims, suits, actions, demands or judgments arising out of any theory of product liability (including, but not limited to, actions in the form of tort, warranty, or strict liability) concerning any product, process or service used or sold pursuant to any right or license granted under this Agreement. LICENSEE's indemnification under this Section shall apply to any liability, damage, loss or expense whether or not it is attributable to the negligent activities of the Indemnitees.

(b) LICENSEE agrees, at its own expense, to provide attorneys reasonably acceptable to HARVARD to defend against any actions brought or filed against any party indemnified hereunder with respect to the subject of indemnity contained herein, whether or not such actions are rightfully brought.

(c) At such time as any such product, process, service is being commercially distributed or sold (other than for the purpose of obtaining regulatory approvals) by LICENSEE or by a sublicensee, AFFILIATE or agent of LICENSEE, LICENSEE shall, at its sole cost and expense, procure and maintain comprehensive general liability insurance in amounts not less \$2,000,000 per incident and \$2,000,000 annual aggregate and naming the Indemnitees as additional insureds. During clinical trials of any such product, process or service, LICENSEE shall, at its sole cost and expense, procure and maintain comprehensive general liability insurance in such equal or lesser amount as HARVARD shall require, naming the Indemnitees as additional insureds. Such comprehensive general liability insurance shall provide (i) product liability coverage and (ii) broad form contractual liability coverage for LICENSEE's indemnification under this Agreement. If LICENSEE elects to self-insure all or part of the limits described above (including deductibles or retentions which are in excess of \$250,000 annual aggregate) such self-insurance program must be acceptable to HARVARD and the Risk Management Foundation of the Harvard Medical Institutions, Inc. The minimum amounts of insurance coverage required shall not be construed to create a limit of LICENSEE's liability with respect to its indemnification under this Agreement.

(d) LICENSEE shall provide HARVARD with written evidence of such insurance upon request of HARVARD. LICENSEE shall provide HARVARD with written notice at least fifteen (15) days prior to the cancellation, non-renewal or material change in such insurance; if LICENSEE does not obtain replacement insurance providing comparable coverage within such fifteen (15) day period, HARVARD shall have the right to terminate this Agreement effective at the end of such fifteen (15) day period without notice or any additional waiting periods.

(e) LICENSEE shall maintain such comprehensive general liability insurance beyond the expiration or termination of this Agreement during (i) the period that any product, process, or service, relating to, or developed pursuant to, this Agreement is being commercially distributed or sold by LICENSEE or by a sublicensee, AFFILIATE or agent of LICENSEE and (ii) a reasonable period after the period referred to in (e) (i) above which in no event shall be less than fifteen (15) years.

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9.4 LICENSEE shall not use HARVARD's or GENERAL'S name or any adaptation of it in any advertising, promotional or sales literature without the prior written assent of HARVARD or GENERAL, as the case may be.

9.5 Without the prior written approval of HARVARD, the entire license granted pursuant to this Agreement shall not be transferred by LICENSEE to any party other than to a successor to the business interest of LICENSEE relating to the PATENT RIGHTS. This Agreement shall be binding upon the successors, legal representatives and assignees of HARVARD and LICENSEE.

9.6 The interpretation and application of the provisions of this Agreement shall be governed by the laws of the Commonwealth of Massachusetts.

9.7 LICENSEE agrees to comply with all applicable laws and regulations. In particular, it is understood and acknowledged that the transfer of certain commodities and technical data is subject to United States laws and regulations controlling the export of such commodities and technical data, including all Export Administration Regulations of the United States Department of Commerce. These laws and regulations, among other things, prohibit or require a license for the export of certain types of technical data to certain specified countries. LICENSEE hereby agrees and gives written assurance that it will comply with all United States laws and regulations controlling the export of commodities and technical data, that it will be solely responsible for any violation of such by LICENSEE or its AFFILIATES or sublicensees, and that it will defend and hold HARVARD and GENERAL harmless in the event of any legal action of any nature occasioned by such violation.

9.8 Written notices required to be given under this Agreement shall be addressed as follows:

If to HARVARD: Office of Technology and Trademark
Licensing
Harvard University
124 Mt. Auburn Street
Suite 440
Cambridge, MA 02138

CC: Office of Technology Licensing and Industry
Sponsored Research
333 Longwood Ave.
Boston, MA 02115

Director
Office of Technology Affairs
Massachusetts General Hospital
13th Street, Building 149
Charlestown, MA 02129

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If to LICENSEE: Virus Research Institute
61 Moulton Street
Cambridge, MA 02139
Attn: John Littlechild, President

or such other address as either party may request in writing.

9.9 Should a court of competent jurisdiction later consider any provision of this Agreement to be invalid, illegal, or unenforceable, it shall be considered severed from this Agreement. All other provisions, rights and obligations shall continue without regard to the severed provision, provided that the remaining provisions of this Agreement are in accordance with the intention of the parties.

9.10 In the event of any controversy or claim arising out of or relating to any provision of this Agreement or the breach thereof, the parties shall try to settle such conflicts amicably between themselves. Subject to the limitation stated in the final sentence of this section, any such conflict which the parties are unable to resolve shall be settled through arbitration conducted in accordance with the rules of the American Arbitration Association. The demand for arbitration shall be filed within a reasonable time after the controversy or claim has arisen, and in no event after the date upon which institution of legal proceedings based on such controversy or claim would be barred by the applicable statute of limitation. Such arbitration shall be held in Boston, Massachusetts. The award through arbitration shall be final and binding. Either party may enter any such award in a court having jurisdiction or may make application to such court for judicial acceptance of the award and an order of enforcement, as the case may be. Notwithstanding the foregoing, either party may, without recourse to arbitration, assert against the other party a third-party claim or cross-claim in any action brought by a third party, to which the subject matter of this Agreement may be relevant.

9.11 This Agreement constitutes the entire understanding between the parties and neither party shall be obligated by any condition or representation other than those expressly stated herein or as may be subsequently agreed to by the parties hereto in writing.

IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be executed by their duly authorized representatives.

The effective date of this Agreement is May 1st, 1992

PRESIDENT AND FELLOWS OF
HARVARD COLLEGE

By: /s/ Joyce Brinton
Name and Title: Joyce Brinton
Director, Office for Technology and
Trademark Licensing, Harvard
University

Virus Research Institute

By: /s/ John Littlechild
Name and Title: President

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APPENDIX A

U.S.S.N. 629,602 - "Improved Vaccines"; filed December 18, 1990; Inventors: John Mekalanos and Samuel Miller.

U.S.S.N. 629,102 - "Vibrio Cholerae Strains Defective in irgA Expression and Cholera Vaccines Derived Therefrom"; filed December 18, 1990; Inventors: John Mekalanos and Stephen Calderwood.

U.S.S.N. 000,000 - "Doubly-Attenuated Strain of Vibrio Cholerae to Deliver Heterologous Antigens for Vaccination" to be filed in 1992; Inventors: John Mekalanos and Stephen Calderwood (serial number and filing date to be inserted when available).

U.S.S.N. 043,907 - "Cholera Vaccines"; filed April 29, 1987 and its CIP USSN 5,098,998, filed April 29, 1988; Inventors John Mekalanos and Ronald Taylor.

U.S. 4,882,278 - "Non-Toxic Vibrio Cholera Mutants"; issued November 21, 1989; Inventor: John Mekalanos.

U.S.S.N. 000,000 - "Peruvian Strain of Cholera Vaccine"; to be filed in 1992; Inventor: John Mekalanos (serial number and filing date to be inserted when available).

APPENDIX B

Biological Materials

1. All strain and plasmid inventions described in the following patents, patent applications and unfiled patent applications.
 - a. U.S. Patent No. 4,882,278
 - b. U.S. Patent Application Serial No. 629,602
 - c. U.S. Patent Application Serial No. 629,102
 - d. U.S. Patent Application Serial No. 043,907
 - e. Unfiled Patent Application entitled "Doubly-Attenuated Strain of Vibrio Cholerae to Deliver Heterologous Antigens for Vaccination"
 - f. Unfiled Patent Application entitled "Cholera Vaccine Strains derived from a 1992 Peruvian Isolate of Vibrio Cholerae and other El Tor Strains"
2. The following, recently constructed Vibrio Cholerae Strains
 - a. Peru 1,2,3,4 and 5; each derived from wild-type C6709
 - b. Bang 1,2,3,4 and 5; each derived from wild-type P27459
 - c. Bah 1,2,3,4 and 5; each derived from wild-type E7946

d. Any additional *Vibrio Cholerae* strains derived from items 2(a) - 2(c) above.

3. All progeny, mutants, derivatives and replications of the biological materials in sections 1 and 2 above which are developed by Dr. John Mekalanos solely or jointly with others directly supervised in his laboratory at Harvard Medical School, but only to the extent that Harvard is able to license such biological materials consistent with its obligations to third parties.
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AMENDMENT TO LICENSE AGREEMENT

This amendment is entered into between the President and Fellows of Harvard College (hereinafter HARVARD) having offices at the Office for Technology and Trademark Licensing, 124 Mt. Auburn Street, Suite 440, Cambridge, Massachusetts, 02138 and Virus Research Institute (hereinafter LICENSEE), a corporation, having offices at 61 Moulton Street, Cambridge, MA 02139.

WHEREAS HARVARD and LICENSEE have entered into a License Agreement effective as of May 1, 1992 with respect to certain patents and technology directed to cholerae (the "License Agreement");

WHEREAS the parties desire to amend such License Agreement.

NOW THEREFORE, in consideration of the foregoing premises, and the mutual promises and other good and valuable consideration, the parties agree as follows:

1. Section 1.4 of the License Agreement is deleted in its entirety and rewritten as follows:

—"NET SALES" means the total received by LICENSEE from sale of LICENSED PRODUCTS less transportation charges and insurance, sales taxes, use taxes, excise taxes, value added taxes, customs duties or other imports, to the extent itemized on invoice, normal and customary quantity and cash discounts (to the extent allowed), allowances and credits on account of rejection or return of LICENSED PRODUCTS. In the event that a LICENSED PRODUCT includes, a component which has therapeutic and/or prophylactic activity ("Active Component(s)") covered by a PATENT RIGHT (Patented Component(s)) and Active Components not covered by a PATENT RIGHT (Unpatented Component(s)) (such PRODUCT being a Combined Product), then NET SALES shall be the amount which is normally received by LICENSEE from a sale of the Patented Component(s) when sold separately in an arm's length transaction with an unaffiliated third party. If the Patented Component(s) are not sold separately, then NET SALES upon which royalty is paid shall be the NET SALES of the Combined Product multiplied by a fraction, the numerator of which is the cost for

producing the Patented Components and the denominator of which is the cost for producing the Combined Product.

2. Add the following Section 1.6 to the License Agreement.

—1.6 The term "SUBLICENSEE" shall mean any non-AFFILIATE third party licensed by LICENSEE to make, have made, use or sell any product or use any process under PATENT RIGHTS.

3. Paragraphs 2.2(c), 2.2(d), 2.2(e) and 2.2(f) of the License Agreement are deleted in the entirety.
4. Paragraph 2.2(g) of the License Agreement is renumbered as Paragraph 2.2(c).
5. The following paragraph is added to the License Agreement as Paragraph 2.5.

—2.5 LICENSEE has provided HARVARD with a development plan for developing and obtaining regulatory approval of the LICENSED PRODUCT selected by LICENSEE, which development plan includes milestones.

LICENSEE shall exert reasonable efforts under the circumstances to achieve such milestones. In the event LICENSEE subsequently indicates in writing to HARVARD that such milestones cannot be met or fails to meet such milestones, LICENSEE shall promptly notify HARVARD, and LICENSEE and HARVARD shall promptly enter into good faith negotiations to reconsider such milestones. In the event that the parties cannot agree to the milestones within sixty (60) days after beginning good faith negotiations, the matter shall be submitted to arbitration to determine the milestones and the time period therefor which should be met pursuant to this Section. The arbitrator in setting and determining milestones shall consider the state of technology; the efforts exerted by LICENSEE, the business circumstances of LICENSEE and the public interest objectives to HARVARD'S licensing program; and technical and regulatory problems. Thereafter, LICENSEE shall exert reasonable efforts to achieve such milestones.

In the event that LICENSEE cannot meet the milestones set by arbitration because of technological or regulatory problems, HARVARD shall not unreasonably deny an extension of time to meet the milestones, upon a showing by LICENSEE that it has made good faith reasonable efforts to meet the milestones.

If LICENSEE (i) fails to meet the milestones established by agreement of the parties and (ii) fails to obtain extensions of such milestones established by arbitration and (iii) LICENSEE has not exerted good faith reasonable efforts to meet such milestones, as its sole and exclusive remedy HARVARD shall have the right to terminate or convert the licenses to non-exclusive licenses by providing to LICENSEE sixty (60) days prior written notice.

Notwithstanding anything else to the contrary, in the event that LICENSEE and/or its AFFILIATE(s) and/or SUBLICENSEE(s) have expended at least two hundred fifty thousand dollars (\$250,000) in research and developing a LICENSED PRODUCT and LICENSEE intends to continue development of a LICENSED PRODUCT, the rights and licenses granted hereunder shall not terminate and shall be converted to a non-exclusive right and license, and further provided that LICENSEE or a SUBLICENSEE or an entity on its behalf spends at least one hundred thousand dollars (\$100,000) per year in pursuing development of PRODUCT for commercial sale.

LICENSEE shall ensure that for any PRODUCT being developed or commercialized by a SUBLICENSEE, such SUBLICENSEE shall assume the obligations imposed on LICENSEE under this paragraph.

The efforts of an AFFILIATE, SUBLICENSEE or collaborator of LICENSEE shall be considered as efforts of LICENSEE.-

6. Rewrite Paragraph 3.2 of the License Agreement in its entirety to read as follows:

—3.2 LICENSEE shall pay HARVARD, during the term of the license granted in Section 2.1, (1) a royalty of four percent (4%) of the NET SALES of the LICENSED PRODUCTS sold by LICENSEE and its AFFILIATES to commercial organizations, and two percent (2%) of the NET SALES of the LICENSED PRODUCTS sold by LICENSEE and its AFFILIATES to non-profit or government agencies, or (ii) twenty-five percent (25%) of royalties received by LICENSEE or its AFFILIATES from a SUBLICENSEE for all LICENSED PRODUCTS covered by a PATENT RIGHT licensed to LICENSEE, and twenty-five percent (25%) of upfront license and license maintenance fees received from a SUBLICENSEE for a license under PATENT RIGHTS, in the case where the SUBLICENSEE is a commercial organization, and ten percent (10%) of such royalties and fees where the SUBLICENSEE, is a government or non-profit organization.-

7. Delete Paragraph 4.1 of the License Agreement in its entirety.

8. Rewrite Paragraph 4.2 of the License Agreement in its entirety to read as follows:

—4.2 LICENSEE shall provide written annual reports within sixty (60) days after June 30 of each calendar year which shall include but not be limited to: reports of progress on research and development, regulatory approvals, manufacturing, sublicensing, marketing and sales during the preceding twelve (12) months as well as plans for the coming year.-

9. Rewrite Paragraph 8.4 of the License Agreement in its entirety to read as follows:

—8.4 In the event that the licenses granted to LICENSEE under this Agreement are terminated, any granted sub-licenses shall remain in full force and effect as a

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direct license from HARVARD to the SUBLICENSEE, provided that the SUBLICENSEE is not then in breach of its sub-license agreement and the SUBLICENSEE agrees to be bound (as a licensee) to HARVARD (as a licensor) under the terms and conditions of the sub-license agreement.-

10. In Paragraph 9.3(a) of the License Agreement, delete the last sentence in its entirety.

11. Delete Paragraphs 9.3(b), 9.3(c), 9.3(d) and 9.3(e) of the License Agreement and in lieu thereof insert the following:

(b) LICENSEE'S indemnification under (a) above shall not apply to any liability, damage, loss or expense to the extent to apply to any liability, damage, loss or expense to the extent that it is attributable to the negligent activities or willful misconduct of the Indemnitees.

(c) HARVARD shall notify LICENSEE promptly of any claim or threatened claim under this Paragraph 9.3 and shall fully cooperate with all reasonable requests of LICENSEE with respect thereto.

(d) LICENSEE agrees, at its own expense, to provide attorneys reasonably acceptable to HARVARD to defend against any actions brought or filed against any party indemnified hereunder with respect to the subject of indemnity contained herein, whether or not such actions are rightfully brought and LICENSEE shall have the right to control the defense, settlement or compromise of any such claim or action.

(e) At such time as any PRODUCT is being commercially distributed or sold (other than for research purposes or for the purpose of obtaining regulatory approvals) by LICENSEE, or by an AFFILIATE, SUBLICENSEE or agent of LICENSEE (hereunder "Other Seller"), LICENSEE shall itself or in the alternative shall ensure that Other Seller either (1) at its sole cost and expense, procure (s) and maintain (s) comprehensive general liability insurance in amounts not less than \$2,000,000 per incident and \$2,000,000 annual aggregate and naming the Indemnitees as additional insureds or (ii) pay(s) for the procurement and maintenance by HARVARD of insurance in the amounts and in the form set forth in this paragraph. Such comprehensive general liability insurance shall provide (I) product liability coverage and (ii) broad form contractual liability coverage for LICENSEE'S Indemnification under Paragraph 9.3(a) of this Agreement. LICENSEE shall ensure that if LICENSEE or the Other Seller elects to self-insure all or part of the limits described above (including deductibles or retentions which are in excess of \$250,000 annual aggregate) such self-insurance program must be acceptable to HARVARD and the Risk Management Foundation. The minimum amounts of insurance coverage required under this Paragraph 9.3(c) shall not be construed to create a limit of LICENSEE'S liability with respect to its indemnification under Paragraph 9.3(a) of this Agreement. At such time, or at any time, LICENSEE can request that HARVARD ascertain

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whether Risk Management Foundation has in effect Uniform Indemnification and Insurance Provisions more favorable than those of this Agreement, in which event LICENSEE and HARVARD shall amend this Agreement to include such more favorable provisions.

(f) LICENSEE shall provide HARVARD with written evidence of such insurance upon request of HARVARD. LICENSEE shall provide HARVARD with written notice of at least thirty (30) days prior to the cancellation, non-renewal or material change in such insurance; if LICENSEE does not obtain replacement insurance providing comparable coverage within such thirty (30) days period,

HARVARD shall have the right to terminate this Agreement effective at the end of such thirty (30) day period by written notice to LICENSEE.

(g) LICENSEE shall itself maintain, or shall ensure that Other Seller maintains or that payments are made for the maintenance by HARVARD of, as the case may be, such comprehensive general liability insurance beyond the expiration or termination of this Agreement during (i) the period that any LICENSED PRODUCT is being commercially distributed or sold (other than for research purposes or the purpose of obtaining regulatory approvals) by Other Seller and (ii) a reasonable period after the period referred to in (g) (1) above which shall in no event be less than ten (10) years. The obligations of (g) (ii) above can be satisfied by the purchase of insurance by LICENSEE or a third party which covers claims resulting from occurrences during such period of (g) (ii) above for LICENSED PRODUCT commercially distributed or sold by LICENSEE or Other Seller during the period referred to in (g) (i) above.

12. Except as modified herein, the License Agreement and the terms, conditions and obligations thereof remain in full force and effect as originally written.

IN WITNESS WHEREOF, the parties hereto intending to be bound have set their hands and seal effective as of the date first above written.

PRESIDENT AND FELLOWS OF
HARVARD COLLEGE

VIRUS RESEARCH INSTITUTE

By: /s/ Joyce Brinton

Name: Joyce Brinton
Title : Director
Office for Technology and
Trademark Licensing
Harvard University

Date: 7/9/93

By: /s/ William A. Packer

Name: William A. Packer
Title: President

Date: 7/23/93

AMENDMENT TO LICENSE AGREEMENT

This amendment is entered into affective as of August 2, 2000 between the President and Fellows of Harvard College (hereinafter HARVARD) having offices at 25 Shattuck Street, Suite 414, Boston, MA 02115 and AVANT Immunotherapeutics, Inc. (hereinafter LICENSEE) having offices at 119 Fourth Avenue, Needham, Massachusetts 02494.

WHEREAS HARVARD and Virus Research Institute ("VRI") entered into a license agreement effective as of May 1, 1992, and amended as of April 30, 1993, with respect to certain patents and technology directed to cholerae and salmonella (the "License Agreement"); and

WHEREAS licensee has succeeded to VRI's rights and obligations under the License Agreement; and

WHEREAS the Parties desire to amend the License Agreement.

NOW THEREFORE, in consideration of the foregoing premises, and the mutual promises and other good and valuable consideration, the parties agree as follows:

1. Section 6.3 of the License Agreement shall be amended by adding the following sentence at the end of such section:

In the event such surrendered PATENT RIGHTS are subject to a sublicense granted by LICENSEE, LICENSEE shall assign LICENSEE'S interest therein upon termination of the Agreement, subject to HARVARD'S consent, which shall not be unreasonably withheld or delayed. In the event HARVARD shall reject such assignment, the sublicense shall be terminated.

2. Section 8.4 of the License Agreement is deleted in its entirety and replaced with the following:

Any sublicenses granted by LICENSEE under this Agreement shall provide (i) that LICENSEE shall assign LICENSEE'S interest therein upon termination of the Agreement, subject to HARVARD'S consent, which shall not be unreasonably withheld or delayed, and (ii) that, in the event HARVARD shall reject such assignment, the sublicense shall be terminated.

3. Except as modified herein, the License Agreement and the terms, conditions and obligations thereof remain in full force and effect as originally written.

PRESIDENT AND FELLOWS OF
HARVARD COLLEGE

AVANT IMMUNOTHERAPEUTICS, INC.

By: /s/ Jeffrey Labovitz

Name: Jeffrey Labovitz, Ph.D.
Title: Director, Office of Technology
Licensing & Industry
Sponsored Research
Date: 8/29/2000

By: /s/ Fritz Casselman

Name: Fritz Casselman
Title: Senior Vice President,
Strategy and Corporate
Development
Date: 8/24/2000

PUBLIC HEALTH SERVICE

PATENT LICENSE AGREEMENT –NONEXCLUSIVE

COVER PAGE

For Office of Technology Transfer/NIH internal use only:

Patent License Number:

Serial Numbers of Licensed Patents:

U.S. Patent Number 5,591,631, USSN
08/082,849 and SN 60/025,270

Licensee:

Virus Research Institute

CRADA Number (if applicable):

none

Additional Remarks:

none

This Patent License Agreement, hereinafter referred to as the “Agreement,” consists of this Cover Page, an attached agreement, a Signature Page, Appendix A (Patent or Patent Application), Appendix B (Fields of Use and Territory), Appendix C (Royalties), Appendix D (Modifications) and Appendix E (Benchmarks). This Cover Page serves to identify the Parties to this Agreement as follows:

1. The National Institutes of Health (“NIH”) or the Centers for Disease Control (“CDC”), hereinafter singly or collectively referred to as “PHS,” agencies of the United States Public Health Service within the Department of Health and Human Services (“DHHS”); and
2. The person, corporation, or institution identified above and/or on the Signature Page, having offices at the address indicated on the Signature Page, hereinafter referred to as “Licensee.”

PHS PATENT LICENSE AGREEMENT–NONEXCLUSIVE

PHS and Licensee agree as follows:

1. BACKGROUND

1.01 In the course of conducting biomedical and behavioral research, PHS investigators made inventions that may have commercial applicability.

1.02 By assignment of rights from PHS employees and other inventors, DHHS, on behalf of the United States Government, owns intellectual property rights claimed in any United States and foreign patent applications or patents corresponding to the assigned inventions. DHHS also owns any tangible embodiments of these inventions actually reduced to practice by PHS.

1.03 The Assistant Secretary for Health of DHHS has delegated to PHS the authority to enter into this Agreement for the licensing of the rights to these inventions under 35 U.S.C. §§ 200-212, the Federal Technology Transfer Act of 1986, 15 U.S.C. § 3710a, and/or the regulations governing the licensing of Government-owned inventions, 37 CFR Part 404.

1.04 PHS desires to transfer these inventions to the private sector through commercialization licenses to facilitate the commercial development of products and processes for public use and benefit.

1.05 Licensee desires to acquire commercialization rights to certain of these inventions in order to develop processes, methods, or marketable products for public use and benefit.

2. DEFINITIONS

2.01 “Licensed Patent Rights” shall mean:

- a) U.S. patent applications and patents listed in Appendix A, all divisions and continuations of these applications, all patents issuing from such applications, divisions, and continuations, and any reissues, reexaminations, and extensions of all such patents;
- b) to the extent that the following contain one or more claims directed to the invention or inventions disclosed or claimed in a) above: i) continuations-in-part of a) above; ii) all divisions and continuations of these continuations-in-part; iii) all patents issuing from such continuations-in-part, divisions, and continuations; and iv) any reissues, reexaminations, and extensions of all such patents;
- c) to the extent that the following contain one or more claims directed to the invention or inventions disclosed or claimed in a) above: all counterpart

foreign applications and patents to a) and b) above, including those listed in Appendix A.

Licensed Patent Rights shall *not* include b) or c) above to the extent that they contain one or more claims directed to new matter which is not the subject matter of a claim in a) above.

2.02 “Licensed Product(s)” means tangible materials which, in the course of manufacture, use, or sale would, in the absence of this Agreement, infringe one or more granted claims of the Licensed Patent Rights that have not been held invalid or unenforceable by an unappealed or unappealable

judgment or decision of a court of competent jurisdiction or an administrative agency.

2.03 "Licensed Process(es)" means processes which, in the course of being practiced would, in the absence of this Agreement, infringe one or more granted claims of the Licensed Patent Rights that have not been held invalid or unenforceable by an unappealed or unappealable judgment or decision of a court of competent jurisdiction or of an administrative agency.

2.04 "Licensed Territory" means the geographical area identified in Appendix B.

2.05 "Net Sales" means the total gross receipts for sales of Licensed Products or practice of Licensed Processes by or on behalf of Licensee and from leasing, renting, or otherwise making Licensed Products available to others without sale or other dispositions, whether invoiced or not, less returns and allowances actually granted, packing costs, insurance costs, freight out, taxes or excise duties imposed on the transaction (if separately invoiced), rebates, disallowed reimbursements, and wholesaler and cash discounts in amounts customary in the trade. No deductions shall be made for commissions paid to individuals, whether they be with independent sales agencies or regularly employed by Licensee and on its payroll, or for the cost of collections.

2.06 "First Commercial Sale" means the initial transfer by or on behalf of Licensee of Licensed Products or the initial practice of a Licensed Process in exchange for cash or some equivalent to which value can be assigned for the purpose of determining Net Sales.

2.07 "Government" means the government of the United States of America.

2.08 "Licensed Fields of Use" means the fields of use identified in Appendix B.

3. GRANT OF RIGHTS

3.01 PHS hereby grants and Licensee accepts, subject to the terms and conditions of this Agreement, a nonexclusive license to Licensee under the Licensed Patent Rights in the Licensed Territory to make and have made, to use and have used, to sell and have sold, to import and have imported, and to offer for sale any Licensed Products in the Licensed Fields of Use and to practice and have practiced any Licensed Processes in the Licensed Fields of Use.

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3.02 This Agreement confers no license or rights by implication, estoppel, or otherwise under any patent applications or patents of PHS other than the Licensed Patent Rights regardless of whether such patents are dominant or subordinate to Licensed Patent Rights.

3.03 Upon written approval by PHS, which approval will not be unreasonably withheld, nor will a decision on approval be unduly delayed beyond ninety (90) days from receipt of a written request from Licensee, Licensee may enter into sublicensing agreements under the Licensed Patent Rights in which the Licensed Patent Rights are licensed to a third party who also receives a license under technology and/or in patent rights in addition to the Licensed Patent Rights as to which Licensee has proprietary rights.

3.04 Licensee agrees that any sublicenses granted by it shall provide that the obligations to PHS of Paragraphs 4.01, 6.01, 8.01, 8.02, 10.05, and 11.07-11.10 of this Agreement shall be binding upon the sublicensee as if it were a party to this Agreement. Licensee further agrees to attach copies of these Paragraphs to all sublicense agreements.

3.05 Any sublicenses granted by Licensee shall provide for the termination of the sublicense, or the conversion to a license directly between such sublicensees and PHS, at the option of the sublicensee, upon termination of this Agreement under Article 11. Such conversion is contingent upon acceptance by the sublicensee of the remaining provisions of this Agreement.

3.06 Licensee agrees to forward to PHS a copy of each fully executed sublicense agreement postmarked within sixty (60) days of the execution of such agreement.

4. STATUTORY AND PHS REQUIREMENTS AND RESERVED GOVERNMENT RIGHTS

4.01 Licensee agrees that products used or sold in the United States embodying Licensed Products or produced through use of Licensed Processes shall be manufactured substantially in the United States, unless a written waiver is obtained in advance from PHS.

5. ROYALTIES AND REIMBURSEMENT

5.01 Licensee agrees to pay to PHS a noncreditable, nonrefundable license issue royalty as set forth in Appendix C within thirty (30) days from the date that this Agreement becomes effective.

5.02 Licensee agrees to pay to PHS a nonrefundable minimum annual royalty as set forth in Appendix C. The minimum annual royalty is due and payable on January 1 of each calendar year and may be credited against any earned royalties due for sales made in that year. The minimum annual royalty for the first calendar year of this Agreement is due and payable within thirty (30) days from the effective date of this Agreement and may be prorated according to the fraction of the calendar year remaining between the effective date of this Agreement and the next subsequent January 1.

5.03 Licensee agrees to pay PHS benchmark royalties as set forth in Appendix C.

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5.04 Licensee agrees to pay PHS earned royalties as set forth in Appendix C.

5.05 A claim of a patent licensed under this Agreement shall cease to fall within the Licensed Patent Rights for the purpose of computing the minimum annual royalty and earned royalty payments in any given country on the earliest of the dates that a) the claim has been abandoned but not continued,

b) the patent expires, c) the patent is no longer maintained by the Government, or d) all claims of the Licensed Patent Rights have been held to be invalid or unenforceable by an unappealed or unappealable decision of a court of competent jurisdiction or administrative agency.

5.06 No multiple royalties shall be payable because any Licensed Products or Licensed Processes are covered by more than one of the Licensed Patent Rights.

5.07 On sales of Licensed Products by Licensee in other than an arm's-length transaction, the value of the Net Sales attributed under this Article 5 to such a transaction shall be that which would have been received in an arm's-length transaction, based on sales of like quantity and quality products on or about the time of such transaction.

5.08 As an additional royalty, Licensee agrees to pay PHS, an amount equivalent to all patent expenses previously incurred by PHS in the preparation, filing, prosecution, and maintenance of Licensed Patent Rights, the amount of Seventy-five Thousand Dollars (\$75,000.00). PHS will bill Licensee for past patent prosecution costs of Seventy-five Thousand Dollars (\$75,000.00) in five equal installments of Fifteen Thousand Dollars (\$15,000.00) on the first, second, third, fourth, and fifth anniversary of this Agreement unless PHS has executed additional nonexclusive licenses to the Licensed Patent Rights before these dates under which circumstances these payments will be divided equally among all nonexclusive commercialization licensees of record as of the date the statement and request for payment is sent by PHS to Licensee. Licensee further agrees to pay PHS annually, within sixty (60) days of PHS's submission of a statement and request for payment, a royalty amount equivalent to all such future patent expenses incurred during the previous calendar year divided equally among all nonexclusive commercialization licensees of record as of the date the statement and request for payment are sent by PHS to Licensee. Fifty percent (50%) of the cumulative amount of the payments due under this Paragraph 5.08 may be credited against royalties due under Paragraph 5.03; however, the net royalty payment in any calendar year may not be lower than the minimum annual royalty specified in Appendix C. Licensee may elect to surrender its rights in any country of the Licensed Territory under any Licensed Patent Rights upon sixty (60) days' written notice to PHS and owe no payment obligation under this Paragraph for subsequent patent-related expenses incurred in that country. PHS intends that all non-exclusive licensees of the Licensed Patent Rights shall contribute equally for the expenses of patent prosecution of the Licensed Patent Rights. In order that Licensee, as the first licensee of these Licensed Patent Rights, pays an equal share of the costs of patent prosecution to that paid by subsequent licensee(s) of these Licensed Patent Rights, PHS will adjust payments for patent prosecution of the Licensed Patent Rights among the licensees at the time such payments become due.

5.09 PHS intends that the royalty terms of all other licenses under Licensed Patent Rights in the identical Licensed Fields of Use will be essentially similar to the terms of this Agreement. During the term of this Agreement, PHS will advise Licensee as to those royalty

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terms in other agreements under Licensed Patent Rights in the Licensed Fields of Use in the Licensed Territory signed after the effective date of this Agreement that are different from this Agreement as to Minimum Annual Royalty or Earned Royalty or the basis on which these royalties are computed. During the term of this Agreement, Licensee may determine whether such package of royalty terms are more favorable than those granted under this Agreement, and shall be entitled upon written notice to PHS, within sixty (60) days after receipt from PHS of the different royalty terms, to have this Agreement amended to substitute this package of royalty terms as of the date upon which more favorable royalty terms become effective.

6. RECORD KEEPING

6.01 Licensee agrees to keep accurate and correct records of Licensed Products made, used, or sold and Licensed Processes practiced under this Agreement appropriate to determine the amount of royalties due PHS. Such records shall be retained for at least five (5) years following a given reporting period. They shall be available during normal business hours for inspection at the expense of PHS by an accountant or other designated auditor selected by PHS for the sole purpose of verifying reports and payments hereunder. The accountant or auditor shall only disclose to PHS information relating to the accuracy of reports and payments made under this Agreement. If an inspection shows an underreporting or underpayment in excess of five percent (5%) for any twelve (12) month period, then Licensee shall reimburse PHS for the cost of the inspection at the time Licensee pays the unreported royalties, including any late charges as required by Paragraph 7.06 of this Agreement. All payments required under this Paragraph shall be due within thirty (30) days of the date PHS provides Licensee notice of the payment due.

7. REPORTS ON PROGRESS, SALES, AND PAYMENTS

7.01 Prior to signing this Agreement, Licensee has provided to PHS a written commercialization plan ("Commercial Development Plan") under which Licensee intends to bring the subject matter of the Licensed Patent Rights into commercial use. The Commercial Development Plan is hereby incorporated by reference into this Agreement.

7.02 Licensee shall provide written annual reports on its product development progress or efforts to commercialize under the Commercial Development Plan for each of the Licensed Fields of Use within sixty (60) days after December 31 of each calendar year. These progress reports shall include, but not be limited to: progress on research and development, status of applications for regulatory approvals, manufacturing, marketing, and sales during the preceding calendar year, as well as plans for the present calendar year. Licensee agrees to provide any additional data reasonably required by PHS to evaluate Licensee's performance.

7.03 Licensee shall report to PHS the date of the First Commercial Sale in each country in the Licensed Territory within thirty (30) days of such occurrence.

7.04 Licensee shall submit to PHS within sixty (60) days after each calendar half-year ending June 30 and December 31 a royalty report setting forth for the preceding half-year period the amount of the Licensed Products sold or Licensed Processes practiced by or on behalf of Licensee in each country within the Licensed Territory, the Net Sales, and the amount of royalty

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accordingly due. With each such royalty report, Licensee shall submit payment of the earned royalties due. If no earned royalties are due to PHS for any reporting period, the written report shall so state. The royalty report shall be certified as correct by an authorized officer of Licensee and shall include a detailed listing of all deductions made under Paragraph 2.05 to determine Net Sales made under Article 5 to determine royalties due.

7.05 Royalties due under Article 5 shall be paid in U.S. dollars. For conversion of foreign currency to U.S. dollars, the conversion rate shall be the rate quoted in *The Wall Street Journal* on the day that the payment is due. All checks and bank drafts shall be drawn on United States banks and shall be payable to NIH/Patent Licensing at the address shown on the Signature Page below. Any loss of exchange, value, taxes, or other expenses incurred in the transfer or conversion to U.S. dollars shall be paid entirely by Licensee. All royalty payments due under this Agreement shall be mailed to the following address: NIH, P.O. Box 360120, Pittsburgh, Pennsylvania 15251-6120. The royalty report required by paragraph 7.04 of this Agreement shall accompany each such payment and a copy of such report shall also be mailed to PHS at its address for notices indicated on the Signature Page of this Agreement.

7.06 Late charges will be applied to any overdue payments as required by the U.S. Department of Treasury in the Treasury Fiscal Requirements Manual, Section 8025.40. The payment of such late charges shall not prevent PHS from exercising any other rights it may have as a consequence of the lateness of any payment.

7.07 All plans and reports required by this Article 7 and marked "confidential" by Licensee shall be treated by PHS as commercial and financial information obtained from a person, and as privileged and confidential and, to the extent permitted by law, shall not be subject to disclosure under the Freedom of Information Act, 5 U.S.C. § 552.

8. PERFORMANCE

8.01 Consistent with sound and reasonable business practices and judgment, Licensee shall use its reasonable best efforts to introduce the Licensed Products into the commercial market or apply the Licensed Processes to commercial use as soon as practicable. "Reasonable best efforts" for the purpose of this provision shall include, but not be limited to, adherence to the Commercial Development Plan and Benchmarks in Appendix E. However, the failure of Licensee to meet a Benchmark does not solely establish that Licensee has not met the requirements under this section.

8.02 Upon the First Commercial Sale, until the expiration of this Agreement, Licensee shall use its reasonable best efforts to keep Licensed Products and Licensed Processes reasonably accessible to the public.

9. INFRINGEMENT AND PATENT ENFORCEMENT

9.01 PHS and Licensee agree to notify each other promptly of each infringement or possible infringement, as well as any facts which may affect the validity, scope, or enforceability of the Licensed Patent Rights of which either Party becomes aware.

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9.02 If PHS has been unable to eliminate a substantial infringement within one (1) year of written notification to the Office of Technology Transfer from Licensee of the existence of a substantial infringement and has not instituted infringement litigation, Licensee shall be excused from the payment of the minimum annual royalty and earned royalties in any country in which the substantial infringement continues to occur. Thereafter, when the substantial infringement has ceased or an infringement suit has been initiated, PHS shall so notify the Licensee in writing, at which time Licensee's obligation to pay such royalties shall resume as of the date of such notification.

9.03 In the event that a declaratory judgment action alleging invalidity of any of the Licensed Patent Rights shall be brought against PHS, PHS agrees to notify Licensee that an action alleging invalidity has been brought. PHS does not represent that it will commence legal action to defend against a declaratory action alleging invalidity. Licensee shall take no action to compel the Government either to initiate or to join in any such declaratory judgment action. Should the Government be made a party to any such suit by motion or any other action of Licensee, Licensee shall reimburse the Government for any costs, expenses, or fees which the Government incurs as a result of its defending against such motion or other action taken in response to the motion. Upon Licensee's payment of all costs incurred by the Government as a result of Licensee's joinder motion or other action, these actions by Licensee will not be considered a default in the performance of any material obligation under this Agreement.

10. NEGATION OF WARRANTIES AND INDEMNIFICATION

10.01 PHS offers no warranties other than those specified in Article 1.

10.02 PHS does not warrant the validity of the Licensed Patent Rights and makes no representations whatsoever with regard to the scope of the Licensed Patent Rights, or that the Licensed Patent Rights may be exploited without infringing other patents or other intellectual property rights of third parties.

10.03 PHS MAKES NO WARRANTIES, EXPRESSED OR IMPLIED, OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OF ANY SUBJECT MATTER DEFINED BY THE CLAIMS OF THE LICENSED PATENT RIGHTS.

10.04 PHS does not represent that it will commence legal actions against third parties infringing the Licensed Patent Rights.

10.05 Licensee shall indemnify and hold PHS, its employees, students, fellows, agents, and consultants harmless from and against all liability, demands, damages, expenses, and losses, including but not limited to death, personal injury, illness, or property damage in connection with or arising out of a) the use by or on behalf of Licensee or its directors, employees, or third parties of any Licensed Patent Rights, or b) the design, manufacture, distribution, or use of any Licensed Products, Licensed Processes, or other products or processes developed in connection with or arising out of the Licensed Patent Rights. Licensee agrees to maintain a liability insurance program consistent with sound business practice.

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11. TERMINATION AND MODIFICATION OF RIGHTS

11.01 This Agreement is effective when signed by all parties and shall extend to the expiration of the last to expire of the Licensed Patent Rights unless sooner terminated as provided in this Article 11.

11.02 In the event that Licensee is in default in the performance of any material obligations under this Agreement, and if the default has not been remedied within ninety (90) days after the date of notice in writing of such default, PHS may terminate this Agreement by written notice.

11.03 At least thirty (30) days prior to filing a petition in bankruptcy, Licensee must inform PHS in writing of its intention to file the petition in bankruptcy or of a third party's intention to file an involuntary petition in bankruptcy.

11.04 In the event that Licensee becomes insolvent, files a petition in bankruptcy, has such a petition filed against it, determines to file a petition in bankruptcy, or receives notice of a third party's intention to file an involuntary petition in bankruptcy, Licensee shall immediately notify PHS in writing. Furthermore, PHS shall have the right to terminate this Agreement by giving Licensee written notice. Termination of this Agreement is effective upon Licensee's receipt of the written notice.

11.05 Licensee shall have a unilateral right to terminate this Agreement and/or its rights in any country by giving PHS sixty (60) days' written notice to that effect.

11.06 PHS shall specifically have the right to terminate or modify, at its option, this Agreement, if PHS determines that the Licensee: 1) is not executing the Commercial Development Plan submitted with its request for a license and the Licensee cannot otherwise demonstrate to PHS's satisfaction that the Licensee has taken, or can be expected to take within a reasonable time, effective steps to achieve practical application of the Licensed Products or Licensed Processes; 2) has willfully made a false statement of, or willfully omitted, a material fact in the license application or in any report required by the license agreement; 3) has committed a substantial breach of a covenant or agreement contained in the license; 4) cannot reasonably satisfy unmet health and safety needs; or 5) cannot reasonably justify a failure to comply with the domestic production requirement of Paragraph 4.01 unless waived. In making this determination, PHS will take into account the normal course of such commercial development programs conducted with sound and reasonable business practices and judgment and the annual reports submitted by Licensee under Paragraph 7.02. Prior to invoking this right, PHS shall give written notice to Licensee providing Licensee specific notice of, and a ninety (90) day opportunity to respond to, PHS's concerns as to the previous items 1) to 5). If Licensee fails to remedy the deficiencies specified in the notice provided by PHS with respect to the previous items 1) to 5) or fails to initiate corrective action to PHS's satisfaction, PHS may terminate this Agreement.

11.07 PHS reserves the right according to 35 U.S.C. § 209(f)(4) to terminate or modify this Agreement if it is determined that such action is necessary to meet requirements for public

use specified by Federal regulations issued after the date of the license and such requirements are not reasonably satisfied by Licensee.

11.08 Within thirty (30) days of receipt of written notice of PHS's unilateral decision to terminate this Agreement, Licensee may, consistent with the provisions of 37 CFR § 404.11, appeal the decision by written submission to the Director of NIH or designee. The decision of the NIH Director or designee shall be the final agency decision. Licensee may thereafter exercise any and all administrative or judicial remedies that may be available.

11.09 Within ninety (90) days of termination of this Agreement under this Article 11 or expiration under Paragraph 11.01, a final report shall be submitted by Licensee. Any royalty payments and unreimbursed patent expenses due to PHS become immediately due and payable upon termination or expiration of this Agreement, and Licensee shall return all Licensed Products or other materials included within the Licensed Patent Rights to PHS or provide PHS with certification of their destruction.

11.10 Paragraphs 6.01, 7.05-7.07, 10.01, 10.03, 10.05, and 11.08 of this Agreement shall survive termination of this Agreement.

12. GENERAL PROVISIONS

12.01 Neither Party may waive or release any of its rights or interests in this Agreement except in writing. The failure of the Government to assert a right hereunder or to insist upon compliance with any term or condition of this Agreement shall not constitute a waiver of that right by the Government or excuse a similar subsequent failure to perform any such term or condition by Licensee.

12.02 This Agreement constitutes the entire agreement between the Parties relating to the subject matter of the Licensed Patent Rights, and all prior negotiations, representations, agreements, and understandings are merged into, extinguished by, and completely expressed by this Agreement.

12.03 The provisions of this Agreement are severable, and in the event that any provision of this Agreement shall be determined to be invalid or unenforceable under any controlling body of law, such determination shall not in any way affect the validity or enforceability of the remaining provisions of this Agreement.

12.04 If either Party desires a modification to this Agreement, the Parties shall, upon reasonable notice of the proposed modification by the Party desiring the change, confer in good faith to determine the desirability of such modification. No modification will be effective until a written amendment is signed by the signatories to this Agreement or their designees.

12.05 The construction, validity, performance, and effect of this Agreement shall be governed by Federal law as applied by the Federal courts in the District of Columbia.

12.06 All notices required or permitted by this Agreement shall be given by prepaid, first class, registered or certified mail properly addressed to the other Party at the address

designated on the following Signature Page, or to such other address as may be designated in writing by such other Party, and shall be effective as of the date of the postmark of such notice.

12.07 This Agreement shall not be assigned by Licensee except a) with the prior written consent of PHS; orb) as part of a sale or transfer of substantially the entire business of Licensee relating to operations which concern this Agreement including but not limited to asset sales, stock sales, mergers and consolidations. Licensee shall notify PHS within ten (10) days of any assignment of this Agreement by Licensee.

12.08 Licensee agrees in its use of any PHS-supplied materials to comply with all applicable statutes, regulations, and guidelines, including Public Health Service and National Institutes of Health regulations and guidelines. Licensee agrees not to use the materials for research involving human subjects or clinical trials in the United States without complying with 21 CFR Part 50 and 45 CFR Part 46. Licensee agrees not to use the materials for research involving human subjects or clinical trials outside of the United States without notifying PHS, in writing, of such research or trials and complying with the applicable regulations of the appropriate national control authorities. Written notification to PHS of research involving human subjects or clinical trials outside of the United States shall be given no later than sixty (60) days prior to commencement of such research or trials.

12.09 Licensee acknowledges that it is subject to and agrees to abide by the United States laws and regulations (including the Export Administration Act of 1979 and Arms Export Control Act) controlling the export of technical data, computer software, laboratory prototypes, biological material, and other commodities. The transfer of such items may require a license from the cognizant agency of the U.S. Government or written assurances by Licensee that it shall not export such items to certain foreign countries without prior approval of such agency. PHS neither represents that a license is or is not required or that, if required, it shall be issued.

12.10 Licensee agrees to mark the Licensed Products or their packaging sold in the United States with all applicable U.S. patent numbers and similarly to indicate "Patent Pending" status. All Licensed Products manufactured in, shipped to, or sold in other countries shall be marked in such a manner as to preserve PHS patent rights in such countries.

12.11 By entering into this Agreement, PHS does not directly or indirectly endorse any product or service provided, or to be provided, by Licensee whether directly or indirectly related to this Agreement. Licensee shall not state or imply that this Agreement is an endorsement by the Government, PHS, any other Government organizational unit, or any Government employee. Additionally, Licensee shall not use the names of PHS, NIH, or CDC or their employees in any advertising, promotional, or sales literature without the prior written consent of PHS.

12.12 The Parties agree to attempt to settle amicably any controversy or claim arising under this Agreement or a breach of this Agreement, except for appeals of modification or termination decisions provided for in Article 11. Licensee agrees first to appeal any such unsettled claims or controversies to the Director of NIH, or designee, whose decision shall be considered the final agency decision. Thereafter, Licensee may exercise any administrative or judicial remedies that may be available.

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12.13 Nothing relating to the grant of a license, nor the grant itself, shall be construed to confer upon any person any immunity from or defenses under the antitrust laws or from a charge of patent misuse, and the acquisition and use of rights pursuant to 37 CFR Part 404 shall not be immunized from the operation of state or Federal law by reason of the source of the grant.

SIGNATURES BEGIN ON NEXT PAGE

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PHS PATENT LICENSE AGREEMENT –NONEXCLUSIVE

SIGNATURE PAGE

FOR PHS:

by: /s/ Barbara McGarey
Barbara McGarey, J.D.
Deputy Director, Office of Technology Transfer
National Institutes of Health

3/25/98
Date

Mailing Address for Notices:

Office of Technology Transfer
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, Maryland 20852

FOR Licensee (Upon information and belief, the undersigned expressly certifies or affirms that the contents of any statements of Licensee made or referred to in this document are truthful and accurate.):

Licensee

by: /s/ William A. Packer
Signature of Authorized Official

3/4/98
Date

William A. Packer
Printed Name

President/CFO

Title

Mailing Address for Notices:

61 Moulton Street

Cambridge, MA 02138

APPENDIX A - Patent or Patent Application

PATENT OR PATENT APPLICATION:

U.S. Patent Number 5,591,631 (USSN 08/021,601), entitled, "Anthrax Toxin Fusion Proteins And Related Methods", Leppla et al., filed February 12, 1993, issued, January 7, 1997.

U.S. Patent Application Serial Number 08/082,849 (CIP of 08/021,601), entitled, "Anthrax Toxin Fusion Proteins And Related Methods", Leppla et al., filed June 25, 1993.

Patent Application Serial Number 60/025,270, entitled, "Targeting Antigens To The MHC Class I Processing Pathway With An Anthrax Toxin Fusion Protein", Klimpel et al., filed September 17, 1996.

APPENDIX B - Licensed Fields of Use and Territory

LICENSED TERRITORY:

Worldwide

LICENSED FIELDS OF USE:

Vaccines and immunotherapeutics for the prevention or treatment of human and animal diseases.

APPENDIX C - Royalties

ROYALTIES:

Licensee agrees to pay to PHS a noncreditable, nonrefundable license issue royalty in the amount of Ten Thousand Dollars (\$10,000.00) due within thirty (30) days of the date of execution of this Agreement.

Licensee agrees to pay to PHS a nonrefundable minimum annual royalty in the amount of One Thousand Dollars (\$1,000.00) for the first Five (5) years of this Agreement, and Five Thousand Dollars (\$5,000.00), thereafter.

Licensee agrees to pay PHS earned royalties on Net Sales as follows:

1. One Percent (1%) on Net Sales of Licensed Products made, have made, used, or sold by Licensee or its Affiliates and
2. In the case where Licensee grants a sublicense under the Licensed Patent Rights with respect to a Licensed Product which includes a proprietary antigen of Licensee, One Percent (1%) on Net Sales of Licensed Products made, have made, used, or sold by sublicensees or Ten Percent (10%) of the earned royalties received by Licensee from its sublicensees on Net Sales of Licensed Products, whichever is greater and
3. In the case where Licensee grants a sublicense other than those of paragraph 2 above, Ten Percent (10%) of the earned royalties received by Licensee from its sublicensees on Net Sales of Licensed Products.

Licensee agrees to pay PHS a noncreditable, nonrefundable sublicensing royalty in the amount of Twenty Thousand Dollars (\$20,000) for each sublicense.

Licensee agrees to pay PHS benchmark royalties as follows:

Fifteen Thousand Dollars (\$15,000.00) at the initiation of the first Phase III study for Licensed Product(s) for the first indication in cancer and for the first indication in infectious disease.

Twenty-five Thousand Dollars (\$25,000) upon filing of the first PLA for Licensed Product(s) for the first indication in cancer and for the first indication in infectious disease.

One Hundred Thousand Dollars (\$100,000.00) upon the First Commercial Sale of the first Licensed Product(s) for the first indication in cancer and for the first indication in infectious disease.

APPENDIX D - Modifications

PHS and Licensee agree to the following modifications to the Articles and Paragraphs of this Agreement:

none

APPENDIX E - Benchmarks

Cancer Vaccines

Evaluation of Anthrax-Toxoid (AT) delivery system for efficiency in generating immune responses directed against tumor tissues in a mouse model system.	12/1/98
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Application of the AT delivery system to two murine tumor models.	12/1/99
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DNA Delivery Systems

Evaluation of the AT system for efficiency of DNA expression.	12/1/98
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Testing of AT system for generating immune responses for <i>Listeria monocytogenes</i> .	12/1/98
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Testing of a human pathogen as a DNA vaccine target.	12/1/99
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Persistent Viral Infections

Application of the AT system to the (Latent <i>Cytomegalovirus</i>) LCMV model in mice.	12/1/98
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Therapy of immunodeficiency virus (SHIV) infected Rhesus macaques and hepatitis B infected non-human primates using the AT system.	12/1/99
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Clinical Development

Phase I Clinical Trials	12/1/2000
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Phase II Clinical Trials	12/1/2001
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Manufacturing Activities	12/1/2003
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Phase III Clinical Trials and preparation of Registration File.	12/1/2005
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FDA Review	12/1/2006
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Product Approval & Marketing	12/1/2007
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LICENSE AGREEMENT

This Agreement, effective as of November 25, 1988 (“EFFECTIVE DATE”) is between The Johns Hopkins University, (JHU), a not-for-profit corporation of the State of Maryland, having a principal place of business at 720 Rutland Avenue, Baltimore, Maryland 21205 and Brigham and Women’s Hospital (BWH), a corporation of the State of Massachusetts, having a principal place of business at 75 Francis Street, Boston Massachusetts 02115 (JHU and BWH hereinafter referred to as “Licensor”) and T Cell Sciences, Inc. a Delaware Corporation, having a principal place of business at 840 Memorial Drive, Cambridge, MA 02139 (hereinafter the “Company”).

WITNESSETH;

WHEREAS, as a center for research and education, Licensor is interested in licensing PATENT RIGHTS (hereinafter defined) in a manner that will benefit the public by facilitating the distribution of useful products, but is without capacity to commercially develop, manufacture, and distribute any such product; and

WHEREAS, a valuable invention in the field of the human C3b/C4b receptor (CRI) was developed during the course of work funded by the United States Government and the Government has certain rights therein; and

WHEREAS, Licensor has acquired through assignment all right, title, and interest in said valuable invention from the Department of Health and Human Services (hereinafter “DHHS”); and

WHEREAS, Company as a leader in the development and use of T cell materials, has such capacity, and desires to commercially develop, manufacture, use and distribute such products throughout the world; and

WHEREAS, JHU and BWH entered into an agreement (attached as Exhibit A) with an effective date of June 28, 1988;

NOW, THEREFORE, the parties agree as follows:

ARTICLE 1 - DEFINITIONS

1.1 PATENT RIGHTS shall mean the U.S. Patent Application Serial No. 176,532 filed on April 1, 1988 in the names of Drs. Douglas T. Fearon, Lloyd B. Klickstein, and Winnie W. Wong, assigned to The Johns Hopkins University and The Brigham and Women’s Hospital entitled “The Human C3b/C4b Receptor (CR1)” (hereinafter the “Patent Application”) and the invention disclosed and claimed therein, all continuations, continuations in part, divisions, and reissues thereto, and any corresponding foreign patent applications that may be filed in the future

at the Company’s request and expense and any patents issuing thereon, all of which are more fully set forth in Appendix A attached hereto and made part of this Agreement.

1.2 LICENSED PRODUCTS shall mean all products for therapeutic purposes, the manufacture, use or sale of which, except for this Agreement, would constitute infringement of one or more pending claims of a patent application contained within PATENT RIGHTS or one or more valid and unexpired claims of an issued patent contained within PATENT RIGHTS. LICENSED PRODUCTS shall not include such products for research, diagnostic, or medical device purposes and Licensor shall be free to license such products for such purposes to third parties, subject, however, to the requirement that the Company shall have the option of first refusal to negotiate for an exclusive license on reasonable terms to use such products for research, diagnostic, or medical device purposes.

1.3 LICENSED PROCESSES shall mean all methods and/or processes for therapeutic purposes which are covered by any claim of one or more PATENT RIGHTS.

1.4 NET SALES shall mean selling price received by Company and/or Affiliated Company from the sale of LICENSED PRODUCTS, less trade and quantity discounts allowed, transportation and handling charges, credits for claims or allowances, refunds, returns and recalls, and less taxes and other governmental charges levied on or measured by sales whether absorbed by Company or the customer. For purposes of this definition, LICENSED PRODUCTS shall be considered sold when billed out to customers, other than Licensee’s AFFILIATED COMPANY or sublicensee. In the event that Company and/or AFFILIATED COMPANY sells a LICENSED PRODUCT in combination with other active ingredients or components which are not LICENSED PRODUCTS (“Other Items”), the NET SALES for purposes of royalty payments on the combination shall be calculated as follows:

(a) If all LICENSED PRODUCTS, and Other Items contained in the combination are available separately, the NET SALES for purposes of royalty payments will be calculated by multiplying the NET SALES of the combination by the fraction $A/A+B$, where A is the invoiced price of all LICENSED PRODUCTS in the combination, and B is the invoiced price of all Other Items in the combination.

(b) If the combination includes Other Items which are not sold separately (but all LICENSED PRODUCTS contained in the combination are available separately), the NET SALES for purposes of royalty payments will be calculated by multiplying the NET SALES of the combination by A/C , where A is as defined above and C is the invoiced price of the combination.

(c) If neither the LICENSED PRODUCTS nor the Other Items contained in the combination are sold separately, the NET SALES for such combination shall be NET SALES of such combination as defined in the first sentence of this Paragraph 1.4. However, the royalty rates paid on such combination NET SALES, as described in Paragraph 4.4 (2%, 3%, and 4%), shall be reduced by fifty percent (50%). In no event shall the royalty rates be reduced by greater than fifty percent (50%). The term “Other Items” is not intended to include carriers, excipients or the like used in formulating a pharmaceutical product.

1.5 NET ROYALTIES shall mean all royalties actually received by the Company or its AFFILIATED COMPANIES, including the receipt of lump sums as advances against royalties, from nonaffiliated sublicensees in connection with the sublicensing of any LICENSED PRODUCTS and LICENSED PROCESSES under the PATENT RIGHTS.

1.6 AFFILIATED COMPANY shall mean any corporation, company, partnership, joint venture or other entity which controls, is controlled or under common control with the Company or Licensor, as the case may be. For the purposes of this Section 1.6, control shall mean the direct or indirect ownership of at least fifty percent (50%) or if less than fifty percent (50%), the maximum percentage as allowed by applicable law of (a) the stock shares entitled to vote for the election of directors; or (b) ownership interest.

1.7 RESEARCH PHASE of product development shall mean laboratory research efforts up to and including the completion of protein expression studies, undertaken by Company and/or AFFILIATED COMPANY, for the purpose of commercializing LICENSED PRODUCTS.

ARTICLE 2 - GRANTS

2.1 Subject to the terms and conditions of this Agreement, Licensor hereby grants to the Company an exclusive license to make, have made, use, and sell the LICENSED PRODUCTS, and to use the LICENSED PROCESSES in the United States and worldwide under the PATENT RIGHTS and to sublicense others under LICENSED PRODUCTS, LICENSED PROCESSES and PATENT RIGHTS subject to section 2.2 and limitations imposed on Licensor's right to grant such license by 35 USC 200-211 and the regulations promulgated thereunder.

2.2 Licensor retains the right under the PATENT RIGHTS to make, provide and use the LICENSED PRODUCTS and LICENSED PROCESSES for its own not-for-profit use. For purposes of this Section 2.2, Licensor shall include but not be limited to JHU, The Johns Hopkins Health System and BWH.

ARTICLE 3 - PATENT INFRINGEMENT

3.1 Company shall have the right to enforce any patent within PATENT RIGHTS against any infringement or alleged infringement thereof, and shall at all times keep Licensor informed as to the status thereof. Company may, in its sole judgment and its own expense, institute suit against any such infringer or alleged infringer and control, settle, and defend such suit in a manner consistent with the terms and provisions hereof and recover, for its account, any damages, awards, or settlements resulting therefrom, subject to Section 3.3. This right to sue for infringement shall not be used in an arbitrary or capricious manner. Licensor shall reasonably cooperate in any such litigation at Company's expense.

3.2 If Company elects not to enforce any patent within PATENT RIGHTS, then it shall so notify Licensor in writing, and Licensor may, in its sole judgment and at its own expense, do so and control, settle, and defend such suit in a manner consistent with the terms and

provisions hereof, and recover, for its own account, any damages, awards or settlements resulting therefrom.

3.3 Any recovery by Company under Section 3.1 shall be deemed to reflect loss of commercial sales, and Company shall pay Licensor a royalty in accordance with this license agreement on said recovery. Company may, in calculating any royalty due Licensor on said recovery, deduct reasonable expenses of litigation actually incurred and not reimbursed, provided, however, that in no event shall such royalty due Licensor be reduced by more than fifty percent (50%).

ARTICLE 4 - PAYMENTS

4.1 The Company shall pay to Licensor, within thirty (30) days of the execution of this agreement by both parties, the sum of Fifteen Thousand Dollars (\$15,000.00).

4.2 The Company shall pay to Licensor minimum annual royalties at the end of each calendar year beginning after the first commercial sale by the Company and/or AFFILIATED COMPANY and/or sublicensee thereof of a LICENSED PRODUCT (hereinafter "Royalty Year") as follows:

At the end of the first Royalty Year:	Twenty-five Thousand Dollars (\$25,000.00)
At the end of the second Royalty Year:	Fifty Thousand Dollars (\$50,000.00)
At the end of the third Royalty Year:	Seventy-five Thousand Dollars (\$75,000.00)
At the end of the fourth and subsequent Royalty Years:	One Hundred Thousand Dollars (\$100,000.00)

Said minimum annual royalties shall be paid to Licensor within thirty (30) days after the end of each Royalty Year. Said minimum annual royalties shall be credited against running royalties as defined by Section 4.4.

4.3 The Company shall use all reasonable efforts to effect the lawful commercial sale of a LICENSED PRODUCT in each country in which such LICENSED PRODUCT is licensed hereunder as soon as is commercially practicable, consistent with the Company's sound and reasonable business practices and judgment. The Company or AFFILIATED COMPANY or a sublicensee thereof shall identify a LICENSED PRODUCT within twenty-four (24) months of the date of execution of this Agreement by both parties and file an IND with the Food and Drug Administration (FDA) within five (5) years of the date of execution of this Agreement by both parties and make a first commercial sale of a LICENSED PRODUCT within ten (10) years of the

date of execution of this Agreement by both parties. If the Company or AFFILIATED COMPANY or a sublicensee has not identified a LICENSED PRODUCT or filed an IND within said time periods, Licensor shall have the right to terminate this Agreement. If the Company, an AFFILIATED COMPANY, or a sublicensee thereof has not achieved a first commercial sale of a LICENSED PRODUCT by the end of the ninth year from the date of execution of this Agreement by both parties, the Company shall begin payment of a minimum annual royalty of \$10,000 per year until the first commercial sale has occurred, at which time the Company shall begin payment of the minimum annual royalties pursuant to Section 4.2. If the Company or AFFILIATED COMPANY or a sublicensee has not achieved a first commercial sale of a Licensed product by the end of the tenth year of the effective date of this Agreement, Licensor shall have the right to terminate this Agreement. This tenth year milestone may be extended for such length of time as the first commercial sale is delayed by reason of a delay in receiving the required governmental approval for such sale in excess of one hundred twenty (120) days from the time application for such approval is made. If the license grant is terminated, all right shall revert to Licensor.

4.4 The Company shall pay to Licensor, as a royalty, for each LICENSED PRODUCT sold by the Company and AFFILIATED COMPANIES thereof, two percent (2%) of the first fifty million dollars (\$50,000,000) of NET SALES, three percent (3%) of the next fifty million dollars (\$50,000,000) of NET SALES, and four percent (4%) of all the NET SALES over one hundred million dollars (\$100,000,000) for the term of this Agreement. However, if no patent has issued with respect to the PATENT RIGHTS by December 31, 1992, the applicable royalty rate, pursuant to this Section 4.4, shall be reduced by fifty percent (50%) unless the Patent Application is involved in an interference or subject to a secrecy order from the U.S. Patent and Trademark office, in which cases the full royalty rate shall apply. If the royalty rate is reduced by fifty percent (50%) as provided by this Section and a patent subsequently issues, the full royalty rate shall be payable as of the issue date of the patent. After a patent issues, the full royalty rate shall again apply.

4.5 In the event that the Company grants sublicenses to any third party that is not an AFFILIATED COMPANY to make, have made, use, and sell the LICENSED PRODUCTS and/or to use the LICENSED PROCESSES anywhere in the world under the PATENT RIGHTS at anytime during the term of this Agreement, then for each such sublicense the Company agrees to pay Licensor NET ROYALTIES at the rates set forth below in the NET ROYALTY rate schedule. Such NET ROYALTIES shall be paid to Licensor whether or not a patent issues with respect to the PATENT RIGHTS.

NET ROYALTY RATE SCHEDULE

On all of the NET ROYALTIES collected by the Company or its AFFILIATED COMPANIES (including dollar equivalents in foreign funds) during each calendar year during the term of this agreement,

(1) if Company or AFFILIATED COMPANY does not complete, within its internal laboratories, the RESEARCH PHASE of product development, the royalty rate shall be 50%, or

(2) if Company or AFFILIATED COMPANY does complete, within its internal laboratories, the RESEARCH PHASE of product development, the royalty rate shall be 25%.

4.6 If, in the Company's reasonable judgment, it is necessary to have one or more royalty-bearing licenses from third parties in order to fully exercise the rights granted by Licensor hereunder, then the applicable royalty rate set forth in section 4.4 shall be reduced by one percent (1%) for each percent of royalty the Company would be required to pay under such licenses from third parties, but in no case will the royalty otherwise due Licensor be reduced by more than fifty percent (50%).

4.7 No multiple royalties shall be payable on NET SALES of any LICENSED PRODUCT by virtue of such LICENSED PRODUCT being covered by a claim or claims of more than one patent or patent application within PATENT RIGHTS.

4.8 In the event that the Company and Licensor jointly own a patent or patent application within PATENT RIGHTS by virtue of co-inventorship between personnel of Licensor and one or more employees of the Company, (i) the applicable minimum annual royalties as set forth in Sections 4.2 and 4.3 hereof, which become due by virtue of the sale of a LICENSED PRODUCT covered solely by one or more claims of such a jointly owned patent or patent application shall be reduced by fifty percent (50%); and (ii) the applicable royalty rates, as set forth in Sections 4.4 and 4.5 hereof, based on NET SALES of a LICENSED PRODUCT covered solely by one or more claims of such a jointly owned patent or patent application shall be reduced by fifty percent (50%). However, where such LICENSED PRODUCT is also covered by a claim of a patent or patent application within PATENT RIGHTS which is owned solely by Licensor, the applicable royalty reduction of this Section shall not apply.

4.9 The Company shall provide within thirty (30) days of the end of each June and December after execution of this Agreement by both parties a written report to Licensor of the amount of LICENSED PRODUCT sold, the total NET SALES of such LICENSED PRODUCT, the royalties due to Licensor as a result thereof, the amount of NET ROYALTIES received from nonaffiliated sublicensees pursuant to Section 4.5, and royalties due to Licensor pursuant to Section 4.5. Payment of any such royalties due shall accompany such report. Until the Company has achieved a first commercial sale of a LICENSED PRODUCT, each report shall include a full written report on the progress of the Company's efforts towards such first commercial sale.

4.10 The Company shall make and retain, for a period of three (3) years following the period of such report, true and accurate records, files and books of account containing all the data reasonably required for the full computation and verification of sales and other information required in section 4.9. Such books and records shall be satisfactory to Licensor and in accordance with generally accepted accounting principles consistently applied. The Company shall permit the reasonable inspection and copying of such records, files and books of account by Licensor during regular business hours upon ten (10) business days' written notice to the company. Such inspection shall not be made more than once each calendar year. All reasonable costs of such inspection and copying shall be paid by Licensor, provided that if any such inspection shall reveal that an error has been made in the amount of any payment in amount equal to 15% or more of such payment, such costs shall be borne by the Company.

ARTICLE 5 - PATENT RIGHTS AND CONFIDENTIAL INFORMATION

5.1 Licensor represents that Appendix A contains an accurate and complete listing and description of the Patent Application and issued patents included within PATENT RIGHTS. Appendix A shall be periodically updated.

5.2 Licensor warrants that, except to the extent specifically set forth in Article 6, Licensor has the right to grant the rights and licenses granted therein to the Company free and clear of all liens and encumbrances.

5.3 Title to all patent and patent applications included within PATENT RIGHTS, in which no employees of the Company are co-inventors, shall reside in Licensor. All patent applications included within PATENT RIGHTS in which no employees of the Company are co-inventors shall be assigned to Licensor. Inventions which arise from joint inventorship between personnel of Licensor and one or more employees of the Company shall be assigned to both Licensor and the Company. Throughout the term of the Agreement, the Company shall have the right, but shall not be obligated, to file United States and/or foreign patent applications included within PATENT RIGHTS; to prosecute and defend such applications against third party oppositions; and upon grant of any Letters Patent included within PATENT RIGHTS to maintain such Letters Patent in force, and the Company shall be licensed under such patents or patent applications. In carrying out the filing and prosecution of applications and maintenance of Letters Patents in which no employees of the Company are coinventors, due care shall at all times be taken to reasonably safeguard the interests of Licensor as assignee, and Licensor shall have the right of final decision on all actions taken in such filing, prosecution, and maintenance, which decision shall not be unreasonable in view of the Company's interests as licensee. All the costs of such filing, prosecution, and maintenance for PATENT RIGHTS in which Licensor is the sole assignee shall be billed directly to JHU, and reimbursed in full by the Company within thirty (30) days of receipt. At the time of billing, a duplicate copy of such bill shall be sent directly to the Company, so as to keep it informed of incurred costs. Costs for filing, prosecution, and maintenance of PATENT RIGHTS which are jointly owned by Licensor and the Company shall be billed directly to the Company and paid by Company. For PATENT RIGHTS which are either solely owned by Licensor or jointly owned by Licensor and Company:

(a) the patent attorney will timely send copies of all correspondence to and from the various patent offices to both parties and shall give both parties an opportunity to comment thereon.

(b) Company, at its own expense, shall have the right, but shall not be obligated, to file United States and/or foreign patent applications included within the PATENT RIGHTS; to prosecute and defend such applications against third party oppositions; and upon grant of any Letters Patent included within the PATENT RIGHTS, to maintain such Letters Patent in force.

(c) if the Company elects not to file or prosecute such applications or maintain such Letters Patent., the Company. shall so notify Licensor, in which event Licensor shall have the right to file or prosecute such applications and to maintain such Letters Patent entirely at its own expense, and the Company shall not be licensed thereunder.

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5.4 The Company agrees that the investigators and researchers of Licensor shall have the right to publish any results relating to the invention disclosed within PATENT RIGHTS. The Company shall be provided with an advance copy of any such proposed publication. At the Company's request, the Licensor agrees to delay submission for publication to permit the filing of patent application(s) but in no event shall such delay exceed sixty (60) days from the time the Company receives the advance copy of the proposed publication.

5.5 During the term of this Agreement, Licensor and the Company may disclose to each other information which each considers to be confidential (hereinafter "CONFIDENTIAL INFORMATION"). All written CONFIDENTIAL INFORMATION shall be marked as confidential by the party providing the information at the time it is provided. All CONFIDENTIAL INFORMATION which is verbally disclosed shall be subject to the obligations of this Section 5.5 only upon written communication of its confidential nature prior to or within 20 days after the time of its disclosure. Upon the acceptance of the disclosure of the CONFIDENTIAL INFORMATION, each party agrees to employ all reasonable efforts to maintain the CONFIDENTIAL INFORMATION secret and confidential, such efforts to be no less than the degree of care employed by each party to preserve and safeguard the party's own CONFIDENTIAL INFORMATION. The Company and Licensor each agrees to treat as confidential and to use only in the conduct of its business all CONFIDENTIAL INFORMATION disclosed to it by the other party except insofar as this Agreement authorizes the use of such CONFIDENTIAL INFORMATION other purposes. The Company and Licensor each agree not to disclose any of the CONFIDENTIAL INFORMATION received from the other party to any third party who has not agreed to keep it confidential. The company and/or Licensor shall be relieved from their respective obligations under this Section 5.5 with regard to any part of the CONFIDENTIAL INFORMATION:

(a) that can be demonstrated to have been in the public domain or publicly known and readily available to the trade or the public prior to the date of the disclosure; or

(b) that can be demonstrated, in writing, to have been in the possession of the party seeking release, or readily available to such party from another source without binder of secrecy, provided however, that such source is not under obligation of secrecy to the other party; or

(c) that becomes part of the public domain or known to the trade or public by publication or otherwise, not due to any unauthorized act by the party seeking release.

The Company's and Licensor's respective obligations under this Section 5.5 shall extend for a period of five (5) years from the EFFECTIVE DATE hereof; or (b) three (3) years from the date of termination, whichever occurs later.

ARTICLE 6 - DHHS

6.1 Pursuant to 35 USC 202, Licensor elected to take all right, title, and interest in the invention forming the basis of the PATENT APPLICATION.

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6.2 The Company hereby specifically agrees to cooperate with Licensor in abiding by the terms and conditions imposed on Licensor pursuant to 35 USC 200-211 and the regulations promulgated thereunder. If a conflict arises between the terms of this agreement and said federal statutes and regulations, said federal statutes and regulations shall prevail.

6.3 Licensor warrants that it has complied with and will continue to comply with all duties and obligations running from Licensor to the Government pursuant to 35 USC 200-211 and the regulations promulgated thereunder.

6.4 Licensor warrants that it has the right to grant the exclusive licenses granted under this Agreement for the life of any U.S. or foreign patent that might issue with respect to the PATENT APPLICATION.

ARTICLE 7 - TERM AND TERMINATION

7.1 This Agreement shall be effective on the date that the last party executes this Agreement. It shall expire on the date of expiration of the last to expire patent issued within PATENT RIGHTS, or if no patent ultimately issues, fifteen (15) years after the first commercial sale of a LICENSED PRODUCT.

7.2 The Company may terminate this Agreement at any time by written notice to Licensor. Upon termination, all rights revert back to Licensor.

7.3 Upon breach or default of any of the terms and conditions of this Agreement, the defaulting party shall be given notice of such default in writing and a period of thirty (30) days after receipt of such notice to correct the breach or default. If the default or breach is not corrected within said thirty (30) day period, the party not in default shall have the right to terminate this Agreement.

7.4 Nonpayment of the royalties required under Article 4 and nonreimbursement of costs required under Article 5 hereinabove shall be a breach of this Agreement in accordance with the provisions of Section 7.3 hereinabove and Licensor shall have the right to terminate this Agreement if said breach is not corrected within thirty (30) days. Termination shall not affect right to recover unpaid royalties and nonreimbursed patent costs.

7.5 In the event (a) either party shall become insolvent or shall suspend business or shall file a voluntary petition or answer admitting the jurisdiction of the Court and the material allegations of or shall consent to an involuntary petition pursuant to or purporting to be pursuant to any reorganization or insolvency law of any jurisdiction or shall make an assignment for the benefit of creditors, or shall apply for or consent to the appointment of a receiver or trustee of a substantial part of its property, and (b) no AFFILIATED COMPANY shall undertake to assume its obligations under the provisions of this Agreement within ninety (90) days from the date on which the party becomes so disabled, then to the extent permitted by law, the other party may thereafter immediately terminate this Agreement by giving written notice of termination to the disabled party. This Agreement shall terminate upon receipt of such notice, except with respect to all accrued and unpaid royalties and sales.

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7.6 Sections 3.3, 4.10, 5.5, 7.4, 7.6, 8.5, 8.6, 8.8 8.9 of this Agreement shall survive the termination of this Agreement.

ARTICLE 8 - MISCELLANEOUS.

8.1 All notices pertaining to extension, termination, and amendment to this Agreement shall be in writing and sent certified mail, return receipt requested, to the parties at the following addresses or such other addresses as such party shall have furnished in writing to the other party in accordance with this Section 8.1:

ASSOCIATE DEAN FOR RESEARCH
The Johns Hopkins University.
School of Medicine
720 Rutland Avenue
Baltimore, Maryland 21205

Ms. Susan E. Dubé
Vice President
Brigham and Women's Hospital
75 Francis Street
Boston Massachusetts 02115

T CELL SCIENCES, INC.
840 Memorial Drive
Cambridge, MA 02139
Attention: Chairman and Chief Executive Officer

8.2 All progress reports, royalty and other payments, and any other related correspondence shall be in writing and sent certified mail, return receipt requested, by TCS to:

Assistant Dean for Technology Licensing
The Johns Hopkins University
School of Medicine
720 Rutland Avenue
Baltimore, Maryland 21205

JHU shall provide copies of said reports and correspondence to BWH.

8.3 The Company may assign this Agreement in whole or in part to a party (i) acquiring substantially all of its business relating to LICENSED PRODUCTS and/or LICENSED PROCESSES; (ii) to any AFFILIATED COMPANY; or (iii) to any other party provided Licensor approves the assignment

By /s/ Ms. Susan E. Dubé

Name Ms. Susan E. Dubé

Title Vice President

Date 12/7/88

T CELL SCIENCES, INC.

By /s/ Patrick C. Kung

Name Patrick C. Kung

Title Executive Vice President

Date 11/30/88

I have read and agree with the terms of this Agreement.

By /s/ Douglas T. Fearson
Douglas T. Fearson

Date December 14, 1988

By /s/ Lloyd B. Klickstein
Lloyd B. Klickstein

Date December 8, 1988

By /s/ Winnie W. Wong
Winnie W. Wong

Date December 9, 1988

APPENDIX A

(TO BE UPDATED PERIODICALLY)

U.S. Patent Application Serial Number 176,532 filed on April 1, 1988

EXHIBIT A

AGREEMENT

THIS AGREEMENT is made between THE JOHNS HOPKINS UNIVERSITY, having a place of business at 720 Rutland Avenue, Baltimore, Maryland 21205 (hereinafter referred to as "JHU") and BRIGHAM AND WOMAN'S HOSPITAL, having a place of business at 75 Francis Street, Boston, Massachusetts 02115 (hereinafter referred to as "BRIGHAM AND WOMAN'S"); and

WITNESSETH THAT:

WHEREAS, Douglas T. Fearon of JHU, Lloyd B. Klickstein of JHU and BRIGHAM AND WOMAN'S and Winnie W. Wong of BRIGHAM AND WOMAN'S have jointly invented "The Human C3b/C4b Receptor (CRT)" (hereinafter referred to as "INVENTION").

WHEREAS, a United States patent application on the INVENTION was filed on April 1, 1988 and was accorded Serial Number 176,532.

WHEREAS, said United States patent application shall be assigned jointly to JHU and BRIGHAM AND WOMAN'S, each of which shall have an equal and undivided half interest in said INVENTION disclosed and claimed therein, as well as any patent issuing thereon.

WHEREAS, JHU and BRIGHAM AND WOMAN'S wish to act jointly in offering options on licenses and licenses to others under the patent rights pertaining to said INVENTION.

WHEREAS, JHU and BRIGHAM AND WOMAN'S wish to provide for the handling and division of the monies received from any licensee under said patent rights.

NOW, THEREFORE, in consideration of the premises and of the mutual covenants and agreements contained herein and of other good and valuable considerations, the parties have agreed and do hereby agree as follows:

1. Licensing of said INVENTION shall only be by mutual agreement. Neither party shall independently grant a license to a third party without agreement from the other party. JHU shall take the lead in identifying potential licensees and negotiating a license agreement.

2. Foreign patent applications shall be filed at the mutual discretion of JHU and BRIGHAM AND WOMAN'S.

3. Expenses related to administering the INVENTION and obtaining, defending, maintaining and licensing patents issuing thereon shall be equally divided between JHU and BRIGHAM AND WOMAN'S.

4. Royalties and other income received pursuant to options on licenses and licenses under the patent rights of said INVENTION shall be equally divided between JHU and BRIGHAM AND WOMAN'S.

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5. This Agreement shall terminate with the expiration of the last to expire patent issued on said INVENTION, or on abandonment of all patent applications on the INVENTION, provided such abandonment is by mutual consent.

All notices and communications hereunder shall be forwarded to:

David A. Blake, Ph.D.
Associate Dean for Research
The Johns Hopkins University
School of Medicine
720 Rutland Avenue
Baltimore, MD 21205

Ms. Susan Dubé
Vice President
Brigham and Woman's Hospital
75 Francis Street
Boston, Massachusetts 02115

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IN WITNESS WHEREOF, JHU and BRIGHAM AND WOMAN'S have caused this Agreement to be duly executed as indicated below.

WITNESS:

/s/ Carol S. Grap

Date: 6/28/88

THE JOHNS HOPKINS UNIVERSITY

By: /s/ David A. Blake

David A. Blake, Ph.D.
Associate Dean for Research

WITNESS:

/s/ [signature illegible]

Date: 6/24/88

BRIGHAM AND WOMAN'S HOSPITAL

By: /s/ Susan Dubé

Susan Dubé
Vice President

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Consent of L.E.K. Consulting LLC

We hereby consent to the incorporation by reference in the Registration Statements on Forms S-8 (File Nos. 333-52796, 333-34780, 33-80036, 33-80050 and 333-62017) and the Registration Statements on Forms S-3 (File Nos. 333-64704, 333-43204, 333-52736, 33-64021, 333-08607, 333-56755, 333-64761 and 333-89341), of Avant Immunotherapeutics, Inc. f/k/a/ TCell Sciences, Inc. (the "Company") of the summarization of our report to the Company, dated June 7, 2002, that is contained on page 6 in the last sentence of Section C.2. of Item 1 of this Annual Report on Form 10-K.

/s/ L.E.K. Consulting LLC

/s/ Michael Clabault

C.O.O. for L.E.K. Consulting LLC

Boston, Massachusetts
September 8, 2003

Certification

I, Una S. Ryan, certify that:

1. I have reviewed this amendment no. 1 to the annual report on Form 10-K/A of AVANT Immunotherapeutics, Inc.; and
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report.

Date: September 12, 2003

/s/ Una S. Ryan

Name: Una S. Ryan
Title: President and Chief Executive Officer

Certification

I, Avery W. Catlin, certify that:

1. I have reviewed this amendment no. 1 to the annual report on Form 10-K/A of AVANT Immunotherapeutics, Inc.; and
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report.

Date: September 12, 2003

/s/ Avery W. Catlin

Name: Avery W. Catlin
Title: Chief Financial Officer
