

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

Current Report
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (date of earliest event reported): January 22, 2015

LION BIOTECHNOLOGIES, INC.
(Exact Name of Registrant as Specified in Charter)

NEVADA
(State of Incorporation)

000-53127
(Commission File Number)

75-3254381
(I.R.S. Employer Identification No.)

21900 Burbank Blvd., Third Floor, Woodland Hills, California
(Address of Principal Executive Offices)

91367
(Zip Code)

(818) 992-3126
(Registrant's Telephone Number, Including Area Code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425).
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12).
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)).
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c)).

Item 1.01 Entry into a Material Definitive Agreement

On August 5, 2011, Lion Biotechnologies (“we” or “us,”) entered into a Cooperative Research and Development Agreement (“CRADA”) with the National Institutes of Health and the National Cancer Institute (NCI), pursuant to which we are currently supporting the *in vitro* development of improved methods for the generation and selection of autologous tumor infiltrating lymphocytes (TIL), are developing approaches for large-scale production of TIL, and intend to conduct clinical trials using these improved methods of generating TIL for the treatment of metastatic melanoma. On January 22, 2015, we executed an amendment (the “Amendment”) to the CRADA to include four new indications. As amended, in addition to metastatic melanoma, the CRADA now also includes the development of TIL therapy for the treatment of patients with bladder, lung, triple-negative breast, and HPV-associated cancers. Under the Amendment, the NCI also has agreed to provide us with samples of all tumors covered by the Amendment for performing studies related to improving TIL selection and/or TIL scale-out production and process development.

To fund the NCI’s expanded development efforts and support, the annual payments we are required to make to the NCI have increased from \$1 million to \$2 million, to be paid in quarterly installments of \$500,000. The first quarterly installment of a prorated amount is due within thirty (30) days of the effective date of the Amendment.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Filed as part of this report is the exhibit listed on the accompanying Index to Exhibits, which information is incorporated herein by reference.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this Report to be signed on its behalf by the undersigned hereunto duly authorized.

LION BIOTECHNOLOGIES, INC.

Date: January 26, 2015

By: /s/ Michael Handelman
Michael Handelman, Chief Financial Officer

EXHIBIT INDEX

Exhibit No.	Description
10.1	Cooperative Research and Development Agreement for the Development and Evaluation of the NCI Proprietary Adoptive Cell Transfer Immunotherapy Using Tumor Infiltrating Lymphocytes in Patients with Metastatic Melanoma, Bladder, Lung, Triple-negative Breast, and HPV-associated Cancers, Utilizing Lion Biotechnologies, Inc.'s Business Development Expertise in Adoptive Cell Transfer Immunotherapy, executed by Lion Biotechnologies, Inc. on January 22, 2015.

Amendment #1**Cooperative Research and Development Agreement # 02734****“Cooperative Research and Development Agreement for the Development and Evaluation of the NCI Proprietary Adoptive Cell Transfer Immunotherapy Using Tumor Infiltrating Lymphocytes in Patients with Metastatic Melanoma, Utilizing Genesis Biopharma’s Business Development Expertise in Adoptive Cell Transfer Immunotherapy”**

The purpose of this amendment is to change certain terms of the above-referenced Cooperative Research and Development Agreement (CRADA). These changes are reflected below, and except for these changes, all other provisions of the original CRADA remain in full force and effect. Two originals of this amendment are provided for execution; one is to remain with the National Cancer Institute and the other is to remain with the Collaborator.

- 1) The Collaborator’s name is revised from Genesis Biopharma, Inc. to Lion Biotechnologies, Inc., with accompanying address corrections; the Collaborator Principal Investigator (PI) is revised from Anthony J. Cataldo to Elma S. Hawkins, Ph.D., M.B.A.
- 2) Appendix A - TIL (tumor infiltrating lymphocytes) for the following cancer indications are added to the Appendix A Research Plan: bladder, lung, triple-negative breast, and HPV-associated cancers. Appendix A is also amended for the NCI Surgery Branch to send fresh melanoma, bladder, lung, triple-negative breast, and HPV-associated cancer tumor specimens collected under NCI protocol 03-C-0277 entitled “Cell Harvest and Preparation for Surgery Branch Adoptive Cell Therapy Protocols” to Lion or its agents for performing studies of improved TIL selection and/or for studies related to TIL scale-out production and process development.
- 3) Appendix B the Collaborator’s yearly funding is increased to \$2,000,000.00 per year, with quarterly payments of \$500,000.00 (except for the first payment which is \$250,000 prorated from the amendment execution date to 2/4/15). Appendix B is also amended to add the NCI Surgery Branch’s contribution of melanoma, bladder, lung, triple-negative breast, and HPV-associated cancer specimens to Lion or its agents for studies under this CRADA.
- 5) Appendix C — Section 8.8 and a definition for “Multi-Party Data” is added, along with accompanying revisions to Section 7.2 and 7.6 licensing provisions; Section 13.9 is revised to add language relating to the use of Collaborator’s agents, contractors or consultants.

SIGNATURES BEGIN ON THE NEXT PAGE

ACCEPTED AND AGREED TO:

For the National Cancer Institute

/s/ JAMES H. DOROSHOW
James H. Doroshow, M.D.
Deputy Director for Clinical and Translational
Research, NCI

1/16/2015
Date

For Collaborator:

/s/ ELMA S. HAWKINS
Elma S. Hawkins, Ph.D., M.B.A.
Chief Executive Officer

1/22/2015
Date

PUBLIC HEALTH SERVICE

**COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT
FOR INTRAMURAL-PHS CLINICAL RESEARCH**

This Agreement is based on the model Cooperative Research and Development Agreement (“CRADA”) adopted by the U.S. Public Health Service (“PHS”) Technology Transfer Policy Board for use by components of the National Institutes of Health (“NIH”), the Centers for Disease Control and Prevention (“CDC”), and the Food and Drug Administration (“FDA”), which are agencies of the PHS within the Department of Health and Human Services (“HHS”).

This Cover Page identifies the Parties to this CRADA:

The U.S. Department of Health and Human Services, as represented by the
National Cancer Institute
an Institute, Center, or Division (hereinafter referred to as the “IC”) of the
National Institutes of Health

and

Lion Biotechnologies, Inc.
hereinafter referred to as the “**Collaborator**”,
having offices at **21900 Burbank Blvd., 3rd Floor, Woodland Hills, CA 91367**
created and operating under the laws of Nevada.

CONTACTS INFORMATION PAGE

CRADA Notices

For ICD:

Technology Transfer Center, NCI
6120 Executive Blvd., Suite 450
Rockville, MD 20852
Tel. 301-496-0477
Fax: 301-402-2117

For Collaborator:

Lion Biotechnologies, Inc.
21900 Burbank Blvd., 3rd Floor
Woodland Hills, CA 91367
Tel. 818-992-3126
www.lionbio.com

Patenting and Licensing

For ICD:

Division Director, Division of Technology
Development and Transfer
NIH Office of Technology Transfer
6011 Executive Boulevard, Suite 325
Rockville, Maryland 20852-3804
Tel: 301-496-7057
Fax: 301-402-0220

For Collaborator (if separate from above):

Peter D. Ho, Ph.D., M.B.A.
Director, Business Development
Lion Biotechnologies, Inc.
21900 Burbank Blvd., 3rd Floor
Woodland Hills, CA 91367
Tel. 818-992-3126

Delivery of Materials Identified In Appendix B (if any)

For ICD:

Steven A. Rosenberg, M.D., Ph.D.
Surgery Branch, NCI
10 Center Drive, MSC 1201
Bldg. 10, CRC Room 3-3940
Bethesda, MD 20892-1201
Tel. 301-496-4164
Fax: 301-402-1738

For Collaborator:

Elma S. Hawkins, Ph.D., M.B.A.
Clinical Development
Lion Biotechnologies, Inc.
21900 Burbank Blvd., 3rd Floor
Woodland Hills, CA 91367
Tel. 646-775-4817

SUMMARY PAGE

EITHER PARTY MAY, WITHOUT FURTHER CONSULTATION OR PERMISSION,
RELEASE THIS SUMMARY PAGE TO THE PUBLIC.

TITLE OF CRADA: Cooperative Research and Development Agreement for the Development and Evaluation of the NCI Proprietary Adoptive Cell Transfer Immunotherapy Using Tumor Infiltrating Lymphocytes in Patients with Metastatic Melanoma, Bladder, Lung, Triple-negative Breast, and HPV-associated Cancers, Utilizing Lion Biotechnologies' Business Development Expertise in Adoptive Cell Transfer Immunotherapy

PHS [IC] Component: National Cancer Institute

IC CRADA Principal Investigator: Steven A. Rosenberg, M.D., Ph.D.

Collaborator: Lion Biotechnologies, Inc.

Collaborator CRADA Principal Investigator: Elma S. Hawkins, Ph.D., M.B.A.

Term of CRADA: Five (5) years from the Effective Date

ABSTRACT OF THE RESEARCH PLAN:

The principal goal of this CRADA is to develop and evaluate effective adoptive cell transfer-based immunotherapies (ACT) using Tumor Infiltrating Lymphocytes (TIL), where the ACT/TIL therapy approach is proprietary to the NCI, for the treatment of patients with metastatic melanoma, bladder, lung, triple-negative breast, and HPV-associated cancers, utilizing the business development expertise and resources of Lion Biotechnologies, Inc., Specifically this CRADA will (1) support the *in vitro* development of improved methods for the large scale generation and selection of TIL with anti-tumor reactivity from patients with metastatic melanoma, bladder, lung, triple-negative breast, and HPV-associated cancers, based on ACT therapies developed by and proprietary to the NCI Surgery Branch, to be used for large scale production of TIL for the ACT treatment of patients with these cancers; (2) develop these approaches for large scale TIL generation that are in accord with Good Manufacturing Practice (GMP) procedures suitable for use in treating patients with metastatic melanoma, bladder, lung, triple-negative breast, and HPV-associated cancers; and (3) develop clinical trials using these improved methods of large scale TIL generation as well as improved patient preparative regimens with the goal of commercializing the ACT/TIL therapy approach for treating patients with metastatic melanoma, bladder, lung, triple-negative breast, and HPV-associated cancers.

**PUBLIC HEALTH SERVICE
COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT**

FOR INTRAMURAL-PHS CLINICAL RESEARCH

APPENDIX A

RESEARCH PLAN

Title of CRADA

Cooperative Research and Development Agreement for the Development and Evaluation of the NCI Proprietary Adoptive Cell Transfer Immunotherapy Using Tumor Infiltrating Lymphocytes in Patients with Metastatic Melanoma, Bladder, Lung, Triple-negative Breast, and HPV-associated Cancers, Utilizing Lion Biotechnologies, Inc.'s Business Development Expertise in Adoptive Cell Transfer Immunotherapy

NCI Principal Investigator

Steven A. Rosenberg, M.D., Ph.D.
Chief, Surgery Branch
Center for Cancer Research (CCR)
National Cancer Institute (NCI)

Collaborator Principal Investigator

Elma S. Hawkins, Ph.D., M.B.A.
Chief Operating Officer, Clinical Development
Lion Biotechnologies, Inc.

Term of CRADA

Five (5) years from the date of the final CRADA signature.

GOALS OF THIS CRADA

The principal goal of this CRADA is to develop and evaluate effective adoptive cell transfer-based immunotherapies (ACT) using Tumor Infiltrating Lymphocytes (TIL), where the ACT/TIL therapy approach is proprietary to the NCI, for the treatment of patients with metastatic melanoma, bladder, lung, triple-negative breast, and HPV (Human Papilloma Virus)-associated cancers, utilizing the business development expertise and resources of Lion Biotechnologies, Inc., Specifically this CRADA will (1) support the *in vitro* development of improved methods for the large scale generation and selection of TIL with anti-tumor reactivity from patients with metastatic melanoma, bladder, lung, triple-negative breast, and HPV-associated cancers, based on ACT therapies developed by and proprietary to the NCI Surgery Branch, to be used for large scale production of TIL for the ACT treatment of patients with these cancers; (2) develop these approaches for large scale TIL generation that are in accord with Good Manufacturing Practice (GMP) procedures suitable for use in treating patients with metastatic melanoma, bladder, lung, triple-negative breast, and HPV-associated cancers; and (3) develop clinical trials using these improved methods of large scale TIL generation as well as improved patient preparative regimens with the goal of commercializing the ACT/TIL therapy approach for treating patients with metastatic melanoma, bladder, lung, triple-negative breast, and HPV-associated cancers. The scope of this CRADA, including any *in vitro* and *in vivo* testing conducted by Dr. Steven A. Rosenberg and members of the NCI Surgery Branch within the CCR is strictly limited to the development of TIL as a single agent therapy in conjunction with commercially available reagents routinely used for ACT therapy (aldesleukin (IL-2), other chemotherapeutic agents) in treating patients with metastatic melanoma, bladder, lung, triple-negative breast, and HPV-associated cancers, utilizing Lion's expertise in the large scale production of adoptive cell transfer immunotherapies. Additional research or clinical activities involving current or prospective NCI Surgery Branch adoptive immunotherapy protocols are outside the scope of this CRADA unless and until the Parties mutually agree to these studies which shall be added by written amendment to this CRADA.

EXPERTISE OF THE PARTIES

Dr. Steven A. Rosenberg has extensive experience in the development and application of his proprietary adoptive cell-based therapies (ACT) for patients with cancer. His laboratory has developed *in vitro* techniques for generating anti-tumor T cells obtained from patient tumors (TIL) under conditions suitable for subsequent infusion. Dr. Rosenberg and his colleagues in the NCI Surgery Branch have extensive experience in the development of cell-based reagents and the conduct of clinical trials utilizing these cells in immunotherapeutic protocols.

Lion Biotechnologies, Inc. has assembled a team of senior level scientists and clinicians who have experience in the application of cell-based immunotherapies to help guide the commercial development of ACT therapy for the treatment of metastatic melanoma, bladder, lung, triple-negative breast, and HPV-associated cancers, as specified in "Goals of this CRADA" ("Goals") based on the NCI Surgery Branch proprietary technologies for TIL preparation and administration of ACT to patients. Lion is developing GMP facilities to perform this work emphasizing the development and evaluation of improved techniques for TIL generation that meet GMP standards as well as to conduct clinical trials of ACT/TIL therapy designed to meet the standards of the FDA to achieve approval for the commercialization of this treatment approach. Thus the combination of the scientific and clinical expertise of the NCI Surgery Branch with the scientific and clinical expertise of Lion, and availability of Lion's GMP production facilities, represents an ideal opportunity that can lead to the commercialization of the ACT/TIL treatment approach for patients with those cancers as specified in "Goals", making these treatments more widely available to patients in need.

The NCI Surgery Branch and Lion thus have complementary expertise and facilities that can develop technologies and clinical treatment approaches that have the potential to improve cell transfer therapy and make it more widely available to patients through commercialization by Lion.

EXPERIMENTAL PLAN

The experimental details that follow are approximate and may be changed upon mutual agreement of the NCI and Collaborator. Any change in the scope of this CRADA will be by mutual consent and written Amendment to the CRADA.

I. Develop improved methods for the generation and selection of TIL with anti-tumor reactivity from patients with metastatic melanoma, bladder, lung, triple-negative breast, and HPV-associated cancers, as specified in "Goals", based on adoptive cell transfer therapies proprietary to and developed by the NCI Surgery Branch, for use in the large scale production of TIL for this ACT treatment of these cancers.

Simplified and better methods for TIL selection and growth are needed to supplement current NCI Surgery Branch efforts in order to expand ACT/TIL therapy to greater numbers of patients with those cancers as specified in "Goals". Studies of improved methods for TIL selection will be investigated by the NCI Surgery Branch and Lion. This will include use of *in vitro* assays of specificity that are based on specific blocking of Class I MHC (Major Histocompatibility Complex) molecules that can provide evidence for the specific recognition of autologous tumor and use of sensitive assays of the upregulation of molecules such as 4-1-BB or others on the lymphocyte cell surface. Such studies in the NCI Surgery Branch may also include the separation of phenotypically different lymphocyte subsets present in TIL such as central memory, effector memory and terminally differentiated effector cells. NCI Surgery Branch studies in mice have shown that lymphocyte subsets such as central memory cells can be more effective in the adoptive immunotherapy of experimental tumors and this needs to be studied in humans with those cancers as specified in "Goals." In addition, NCI Surgery Branch may send fresh melanoma, bladder, lung, triple-negative breast, and HPV-associated cancer specimens from NCI protocol 03-C-0277 entitled "Cell Harvest and Preparation for Surgery Branch Adoptive Cell Therapy Protocols" to Lion or its agents to develop techniques for growing TIL and for performing assays involving criteria which are designed to improve TIL selection. Assays will be performed on the growing TIL to evaluate their recognition of autologous tumor cells assessed by gamma interferon release in overnight co-culture with tumor and to evaluate the phenotypic expression of cell surface markers on TIL such as CD62L, CD45RO, CD45RA and CD127. Such studies would form the basis for TIL selection and generation for use in the large scale production of TIL for the treatment of patients with those cancers as specified in "Goals."

II. Develop approaches to large scale TIL generation that are in accord with Good Manufacturing Practice (GMP) procedures suitable for their use in treating patients with metastatic melanoma, bladder, lung, triple-negative breast, and HPV-associated cancers, as specified in "Goals"

The selection and growth of autologous TIL from patients with those cancers as specified in “Goals” is a vital part of the successful use of this approach. Prior NCI Surgery Branch methods for TIL growth involved extensive *in vitro* testing using multiple cell lines and fresh tissue samples as well as the growth of cells in up to 40 2-liter culture bags using large amounts of medium to treat each patient. Under this CRADA, studies will be conducted of improved methods for the generation of the large numbers of TIL necessary for patient treatment. These studies will explore the use of alternate culture vessels including those that involve the use of gas permeable membranes. The NCI Surgery Branch has begun some of these studies but extensive additional studies are required to optimize cell growth including the determination of the best concentrations of feeder cells, timing of media change and concentrations of growth factors such as IL-2 (commercially available). These studies will be conducted by the NCI Surgery Branch with advice, input and expertise provided by Lion. In addition, the NCI Surgery Branch may send tumor samples from those cancers as specified in “Goals” which were collected from NCI protocol 03-C-0277 to Lion or its agents for studies including scale-out for the methods of expansion of individualized lymphocyte treatments, assays for product and in-process performance, and harmonization assays for centralized process development and determination of TIL product consistency. Additionally, biological reagents and materials may be sent to Lion or its agents for the development of qualifying assays and process development related to scale-out of the TIL expansion process. Techniques thus described will need to be adapted to meet the GMP requirements of the Food and Drug Administration for infusion into patients. This may require modification of the procedures developed in the NCI Surgery Branch. Lion and the NCI Surgery Branch will work together to develop Standard Operating Procedures (SOP) for large scale TIL growth, selection and testing that meet the approval of the FDA. Joint meetings with the FDA will be required to define the exact format and criteria need to meet FDA approval.

III. Develop clinical trials using these improved methods of large scale TIL generation as well as improved patient preparative regimens to treat patients with metastatic melanoma, bladder, lung, triple-negative breast and HPV-associated cancers, as specified in “Goals”

Clinical trials will be designed and implemented to evaluate the clinical effectiveness of ACT/TIL therapy resulting from large scale techniques in patients with those cancers as specified in “Goals”, based on the proprietary NCI Surgery Branch technology and approaches developed in the first two parts of this Experimental Plan. Lion and the NCI Surgery Branch will work together to develop multiinstitutional clinical trials evaluating the clinical effectiveness of the administration of autologous TIL generated using Lion technology to patients with those cancers as specified in “Goals” that can potentially be used as licensing trials for FDA approval. The NCI Surgery Branch does not have a suitable GMP facility that will meet FDA standards for the conduct of such a trial. Exploratory pilot trials may be necessary prior to beginning a licensing trial and these may be conducted in the Surgery Branch alone or in conjunction with other multicenter sites associated with Lion. The development and conduct of licensing trials will require the GMP expertise of Lion and the extensive experience of the NCI Surgery Branch working together. TIL for these trials will be produced on a large scale by Lion at a central facility for distribution to participating multicenter sites (including the NCI Surgery Branch). An IND with the FDA will be filed by Lion which will serve as the Coordinating Center for such trials. The goal of such trials will be to generate data to support the approval by the FDA of this ACT/TIL therapy approach. *In vitro* testing of patient samples from such trials will evaluate the activity and persistence level of the transferred cells in the circulation of treated patients and will be conducted by the NCI Surgery Branch both for any pilot trials that are performed as well as for the large multiinstitutional trials that are planned.

DESCRIPTION OF THE CONTRIBUTIONS AND RESPONSIBILITIES OF THE PARTIES

Surgery Branch, NCI

- Develop and test new improved and simplified *in vitro* methods for the selection and growth of TIL with anti-tumor activity for large scale preparations that can be used in clinical cell transfer studies. As described in the Experimental Plan above, this will include evaluation of new growth techniques, culture vessels, and tests
- Perform *in vitro* studies of the immunologic parameters surrounding the new cell transfer clinical protocol(s) by analyzing the phenotypic and functional properties of the transferred cells and their persistence in the patient following adoptive transfer in all clinical trials conducted under this CRADA, as outlined in Section III above.

Lion

- Develop, implement and evaluate GMP procedures for the large scale production of TIL suitable for infusion into patients with metastatic melanoma, bladder, lung, triple-negative breast, and HPV-associated cancers as specified in "Goals."
- Conduct studies including scale-out for the methods of expansion of individualized lymphocyte treatments, assays for product and in-process performance, and harmonization assays for centralized process development and determination of TIL product consistency. Additional studies may be conducted for the development of qualifying assays and process development related to scale-out of the TIL expansion process.
- Consult with the FDA to determine the appropriate clinical trial design necessary to secure approval for the commercial development of TIL therapy for patients with those cancers as specified in "Goals" and sponsor the IND for these new clinical protocols Serve as the coordinating center for the multicenter licensing clinical trials.
- Supply TIL in sufficient quantities to the NCI Surgery Branch and other multicenter sites to complete the planned clinical trials (including the licensing trial) needed for FDA approval of ACT/TIL. Support the establishment of a central facility for the processing and provision of TIL for the studies under this CRADA.

Surgery Branch, NCI and Lion

- Develop SOP for large scale TIL growth, selection and testing to support the FDA approval of the ACT/TIL therapy approach. Attend joint meetings with the FDA to define the exact format and criteria needed in the clinical trial(s) to obtain FDA approval.

Develop, conduct and evaluate multiinstitutional clinical trials (to include the NCI Surgery Branch as a clinical trial site) for patients with metastatic melanoma, bladder, lung, triple-negative breast and HPV-associated cancers (as specified in "Goals") treated with TIL that can be used as licensing trials required for FDA approval and subsequent commercialization of ACT/TIL.
- Conduct assays to be used in the selection of appropriate cells (based on both functional and phenotypic criteria) to optimize the effectiveness of the adoptive transfer.
- Exchange information and expertise to further the successful development of TIL therapy for patients with those cancers as specified in "Goals."

RELATED NCI AND COLLABORATOR AGREEMENTS: NONE

RELATED INTELLECTUAL PROPERTY AND BUSINESS/SCIENTIFIC EXPERTISE OF THE PARTIES

NCI Surgery Branch

- 1) PCT/US03/27873 entitled "Immunotherapy with *In Vitro*-Selected Antigen-specific Lymphocytes After Nonmyeloablative Lymphodepleting Chemotherapy", filed 9/5/03. Inventors: Mark E. Dudley, Steven A. Rosenberg, John R. Wunderlich. This is inclusive of all U.S. continuing applications and divisionals, and foreign applications.
- 2) USSN 12/869,390 entitled "Adoptive Cell Therapy with Young T Cells", filed 8/26/10. Inventors: Mark E. Dudley and Steven A. Rosenberg. This is inclusive of all U.S. continuing applications and divisionals.
- 3) PCT/US12/02974 entitled "Methods of Growing Tumor Infiltrating Lymphocytes in Gas-Permeable Containers", filed 3/20/12. Inventors: Steven A. Rosenberg, Mark E. Dudley, et al.. This is inclusive of all U.S. continuing applications and divisionals, and foreign applications.

4) PCT/US14/046478 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells", filed 7/14/2014. Inventors: Christian S. Hinrichs and Steven A. Rosenberg. This is inclusive of all U.S. continuing applications and divisionals.

Lion Biotechnologies, Inc.

Lion has applied to NIH for a license to NIH owned intellectual property under the license applications A-079-2014 and A-286-2014; Lion has a license to NIH-owned intellectual property under license L-129-2011/0. Collaborator desires to license NIH owned intellectual property that includes the patents describing the NCI proprietary ACT/TIL therapy approach to be developed under this CRADA.

Lion Biotechnologies, Inc. is a publicly traded biotechnology company developing therapies for the treatment of cancer. Lion's lead therapeutic candidate will be an autologous cell therapy product using tumor infiltrating lymphocytes for the treatment of metastatic melanoma, bladder, lung, triple-negative breast and HPV-associated cancers as specified in "Goals", to be developed under this CRADA. Lion has a partnership with a major manufacturer for the provision of TIL for clinical trials to be conducted under this CRADA as well as post-regulatory approval. The manufacturing facility is cGMP certified and inspected by FDA.

**PUBLIC HEALTH SERVICE
COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT
FOR INTRAMURAL-PHS CLINICAL RESEARCH**

APPENDIX B

**STAFFING, FUNDING AND MATERIALS/EQUIPMENT CONTRIBUTIONS
OF THE PARTIES**

Staffing Contributions:

IC will provide scientific staff and other support necessary to conduct the research and other activities described in the Research Plan. IC's scientific staff will include IC's CRADA Principal Investigator and technical staff.

IC estimates that 3-5 person-years of effort per year will be required to complete the CRADA research.

Collaborator will provide scientific staff and other support necessary to conduct the research and other activities described in the Research Plan. Collaborator's scientific staff will include Collaborator's Principal Investigator and technical staff.

Collaborator estimates that 3-5 person-years of effort per year will be required to complete the CRADA research.

Funding Contributions:

Collaborator agrees to provide funds in the amount of \$2,000,000.00 per year of the CRADA for IC to use to acquire technical, statistical, and administrative support for the research activities, as well as to pay for supplies and travel expenses. Collaborator will provide funds in the amount of \$500,000.00 on a quarterly basis. The first quarterly installment of a prorated amount of \$250,000.00 from the Amendment execution date to February 4, 2015 will be due within thirty (30) days of the Effective Date of the Amendment. Each subsequent installment will be due within thirty (30) days of each quarterly anniversary of the CRADA Effective Date. Collaborator agrees that IC can allocate the funding between the various categories in support of the CRADA research as IC's CRADA PI sees fit.

CRADA PAYMENTS:

Collaborator will make checks payable to the National Cancer Institute and will reference the CRADA number 02734 and title "CRADA for the Development and Evaluation of the NCI Proprietary Adoptive Cell Transfer Immunotherapy Using Tumor Infiltrating Lymphocytes in Patients with Metastatic Melanoma, Bladder, Lung, Triple-negative Breast and HPV-associated Cancers Utilizing Lion Biotechnologies, Inc.'s Business Development Expertise in Adoptive Cell Transfer Immunotherapy" on each check, and will send them via trackable mail or courier to:

CRADA Funds Coordinator
Technology Transfer Center, NCI
6120 Executive Blvd., Suite 450
Rockville, MD 20852

CRADA Travel Payments:

Travel arrangements for all Government staff will be made in accordance with the Federal Travel Rules and Regulations, whether arranged by IC and funded using either appropriated funds or CRADA funds, or arranged and funded directly by Collaborator.

Materials/Equipment Contributions:

IC will provide the following IC Materials for use under this CRADA:

Test Article:	None
IC Materials:	Fresh melanoma, bladder cancer, lung cancer, triple- negative breast cancer, and HPV-associated cancer tumor specimens collected under NCI protocol 03-C-0277 entitled "Cell Harvest and Preparation for Surgery Branch Adoptive Cell Therapy Protocols"
Capital Equipment:	None

Collaborator will provide the following Collaborator Materials and/or capital equipment for use under this CRADA:

Test Article:	Autologous Tumor Infiltrating Lymphocytes (TIL) grown and processed under GMP conditions, suitable for use in clinical trials under this CRADA.
Collaborator Materials:	None
Capital Equipment:	None

If either Party decides to provide additional Materials for use under this CRADA, those materials will be transferred under a cover letter that identifies them and states that they are being provided under the terms of the CRADA.

**PUBLIC HEALTH SERVICE
COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT
FOR INTRAMURAL-PHS CLINICAL RESEARCH**

APPENDIX C

MODIFICATIONS TO THE MODEL CRADA

Add the Definition of “Multi-Party Data” in Article 2 to read as follows:

“Multi-Party Data” means data from studies sponsored by IC pursuant to Clinical Trial Agreements (CTA) or CRADAs, where such data are collected under Protocols involving combinations of investigational agents supplied from more than one CTA or CRADA collaborator. “Multi-Party Data” also means data from studies where such data are collected pursuant to research involving combinations of proprietary materials from more than one collaborator as documented in more than one agreement.

Amend Section 7.2 to read as follows:

7.2 Collaborator’s License Option to CRADA Subject Inventions. With respect to Government rights to any CRADA Subject Invention made solely by an IC employee(s) or made jointly by an IC employee(s) and a Collaborator employee(s) for which a Patent Application was filed, PHS hereby grants to Collaborator an exclusive option to elect an exclusive or nonexclusive or co-exclusive, if applicable, commercialization license. The option to elect a co-exclusive license shall apply when a CRADA Subject Invention is also an Invention made under another agreement resulting from mutually agreed upon studies, as described in Section 8.8 (regarding Multi-Party Data Rights)], and the field of use of this co-exclusive license shall be limited to the use of the combination of the Test Article with another agent(s) commensurate with the scope of the Research Plan. The license will be substantially in the form of the appropriate model PHS license agreement and will fairly reflect the nature of the CRADA Subject Invention, the relative contributions of the Parties to the CRADA Subject Invention and the CRADA, a plan for the development and marketing of the CRADA Subject Invention, the risks incurred by Collaborator, and the costs of subsequent research and development needed to bring the CRADA Subject Invention to the marketplace. The field of use of the license will not exceed the scope of the Research Plan.

Amend Section 7.6 to read as follows:

7.6 **Third Party License.** Pursuant to 15 U.S.C. § 3710a(b)(1)(B), if PHS grants Collaborator an exclusive license or co-exclusive license to a CRADA Subject Invention made solely by an IC employee or jointly with a Collaborator employee, the Government will retain the right to require Collaborator to grant to a responsible applicant a nonexclusive, partially exclusive, or exclusive sublicense to use the CRADA Subject Invention in Collaborator's licensed field of use on terms that are reasonable under the circumstances; or, if Collaborator fails to grant a license, to grant a license itself. The exercise of these rights by the Government will only be in exceptional circumstances and only if the Government determines (i) the action is necessary to meet health or safety needs that are not reasonably satisfied by Collaborator, (ii) the action is necessary to meet requirements for public use specified by federal regulations, and such requirements are not reasonably satisfied by Collaborator; or (iii) Collaborator has failed to comply with an agreement containing provisions described in 15 U.S.C. § 3710a(c)(4)(B). The determination made by the Government under this Paragraph is subject to administrative appeal and judicial review under 35 U.S.C. § 203(b).

Section 7.8 "Joint CRADA Subject Inventions Not Exclusively Licensed by Collaborator" is deleted in its entirety.

Add Section 8.8 as follows:

8.8 **Multi-Party Data Rights.** For mutually agreed upon clinical Protocol(s) where Test Article is used in combination with another investigational agent supplied to IC pursuant to a CTA or CRADA between IC and an entity not a Party to this CRADA (hereinafter referred to as "Third Party"), or for non-clinical study(ies) where research involving combinations of proprietary materials from more than one collaborator as documented in more than one agreement, the access and use of Multi-Party Data by the Collaborator and Third Party shall be co-exclusive as follows:

- 8.8.1 IC will provide both Collaborator and Third Party with notice regarding the existence and nature of the agreements governing the use of the Test Article and Third Party's investigational agent, the design of the proposed combination Protocol(s) or non-clinical study(ies), and the existence of any obligations that might restrict IC's participation in the proposed combination Protocols or non-clinical study(ies).
- 8.8.2 Collaborator shall agree to permit use of the Multi-Party Data from these trials by Third Party to the extent necessary to allow Third Party to develop, obtain regulatory approval for, or commercialize its own investigational agent(s). However, this provision will not apply unless Third Party also agrees to Collaborator's reciprocal use of Multi-Party Data.
- 8.8.3 Collaborator and Third Party must agree in writing prior to the commencement of the combination Protocol(s) or non-clinical study(ies) that each will use the Multi-Party Data solely for the development, regulatory approval, and commercialization of its own investigational agent(s).

8.84 The sharing of Multi-Party Data does not alter the ownership of the Multi-Party Data or obligations of IC, Collaborator and Third Party to keep Confidential Information owned by any other Party or Parties confidential.

Amend the Definition of “Independent Contractors” in Article 13.9 to read as follows:

13.9 **Independent Contractors.** The relationship of the Parties to this CRADA is that of independent contractors and not agents of each other or joint venturers or partners. Each Party shall maintain sole and exclusive control over its personnel and operations. If Collaborator elects to perform any portion of the Research Plan through an agent, contractor or consultant, Collaborator agrees to incorporate into such contracts all provisions necessary to ensure that the work of such agents, contractors or consultants is governed by the terms of the CRADA, including, but not limited to a provision for the assignment of inventions of the agent, contractor or consultant to the Collaborator.