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

FORM 10-Q

☒ **Quarterly report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.**

For the quarterly period ended March 31, 2012.

o **Transition report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.**

For the transition period from to .

Commission File Number
001-35342

NEWLINK GENETICS CORPORATION
(Exact name of Registrant as specified in Its Charter)

Delaware	**42-1491350**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

2503 South Loop Drive
Ames, Iowa 50010
(515) 296-5555
(Address, including zip code, and telephone number, including area code, of principal executive offices)

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 o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of “large accelerated filer,” “accelerated filer” and “smaller reporting company” in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o	Accelerated filer o
Non-accelerated filer x (Do not check if a smaller reporting company)	Smaller reporting company o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No ☒

As of May 4, 2012, there were 20,672,029 shares of the registrant’s Common Stock, par value $0.01 per share, outstanding.

NEWLINK GENETICS CORPORATION

FORM 10-Q

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PART I

NewLink Genetics Corporation
(A Development Stage Enterprise)

Condensed Consolidated Balance Sheets
(unaudited)
(In thousands, except share and per share data)

	March 31, 2012	December 31, 2011
Assets		
Current assets:		
Cash and cash equivalents	$ 33,269	$ 39,490
Certificates of deposit	2,490	2,490
Prepaid expenses	292	409
State research and development credit receivable	247	202
Interest receivable	2	1
Other receivables	918	196
Total current assets	37,218	42,788
Leasehold improvements and equipment:		
Leasehold improvements	4,873	4,459
Computer equipment	744	710
Lab equipment	3,629	3,333
Total leasehold improvements and equipment	9,246	8,502
Less accumulated depreciation and amortization	(3,017)	(2,911)
Leasehold improvements and equipment, net	6,229	5,591
Total assets	$ 43,447	$ 48,379

See accompanying notes to condensed consolidated financial statements.

NewLink Genetics Corporation
(A Development Stage Enterprise)

Condensed Consolidated Balance Sheets
(unaudited)
(In thousands, except share and per share data)

	March 31, 2012	December 31, 2011
Liabilities and Equity		
Current liabilities:		
Accounts payable	$ 803	$ 1,670
Accrued expenses	1,226	1,867
Deferred rent	65	913
Notes payable to Iowa Department of Economic Development	—	6,000
Obligations under capital leases	123	121
Current portion of long term debt	93	93
Total current liabilities	2,310	10,664
Long term liabilities:		
Royalty obligation payable to Iowa Economic Development Authority	6,000	—
Notes payable to Iowa State University Research Park	524	548
Notes payable to City of Ames	300	300
Obligations under capital leases	61	94
Deferred rent	1,454	—
Total long-term liabilities	8,339	942
Total liabilities	10,649	11,606
Equity:		
Blank check preferred stock, $0.01 par value: Authorized shares — 5,000,000 at March 31, 2012, and December 31, 2011; issued and outstanding shares — 0 at March 31, 2012, and December 31, 2011	—	—
Common stock, $0.01 par value: Authorized shares — 38,833,334 at March 31, 2012, and December 31, 2011; issued and outstanding shares — 20,672,029 at March 31, 2012, and 20,591,240 at December 31, 2011	207	206
Additional paid-in capital	118,909	118,043
Deficit accumulated during the development stage	(86,318)	(81,476)
Total equity	32,798	36,773

Commitments		
Total liabilities and equity	$ 43,447	$ 48,379

See accompanying notes to condensed consolidated financial statements.

NewLink Genetics Corporation
(A Development Stage Enterprise)

Condensed Consolidated Statements of Operations
(unaudited)
(In thousands, except share and per share data)

	Three Months Ended March 31,		Cumulative from June 4, 1999 (inception) through March 31, 2012
	2012	2011	
Grant revenue	$ 471	$ 604	$ 6,188
Operating expenses:			
Research and development	3,830	3,180	64,148
General and administrative	1,458	1,316	31,293
Total operating expenses	5,288	4,496	95,441
Loss from operations	(4,817)	(3,892)	(89,253)
Other income and expense:			
Miscellaneous (expense) income	(21)	1	337
Forgiveness of debt	—	—	449
Interest income	4	4	1,757
Interest expense	(8)	(11)	(151)
Other (expense) income, net	(25)	(6)	2,392
Net loss	(4,842)	(3,898)	(86,861)
Less net loss attributable to noncontrolling interest	—	1	583
Net loss attributable to NewLink	$ (4,842)	$ (3,897)	$ (86,278)
Net loss per common share, basic and diluted	$ (0.23)	$ (1.07)	
Weighted-average common shares outstanding, basic and diluted	20,613,146	3,636,044	

See accompanying notes to condensed consolidated financial statements.

NewLink Genetics Corporation
(A Development Stage Enterprise)

Condensed Consolidated Statement of Equity (Deficit)
(unaudited)
(In thousands, except share and per share data)

	Common Stock			Deficit	
	Number of Common Shares Outstanding	Common Stock	Additional Paid-in Capital	Accumulated During the Development Stage	Total Equity (Deficit)
Balance at December 31, 2011	20,591,240	$ 206	$ 118,043	$ (81,476)	$ 36,773
Stock compensation	10,000	—	736	—	736
Exercise of stock options	70,789	1	134	—	135
Fractional shares from initial public offering	—	—	(4)	—	(4)
Net loss	—	—	—	(4,842)	(4,842)
Balance at March 31, 2012	20,672,029	$ 207	$ 118,909	$ (86,318)	$ 32,798

See accompanying notes to condensed consolidated financial statements.

NewLink Genetics Corporation
(A Development Stage Enterprise)

Condensed Consolidated Statements of Cash Flows
(unaudited)
(In thousands, except share and per share data)

	Three Months Ended March 31,		Cumulative from June 4, 1999 (inception) through March 31, 2012
	2012	2011	
Cash Flows From Development Activities			
Net loss	$ (4,842)	$ (3,898)	$ (86,861)
Adjustments to reconcile net loss to net cash used in development activities:			
Share-based compensation	736	368	6,085
Depreciation and amortization	175	174	3,136
Loss on sale of fixed assets	20	—	20
In-process research and development expenses	—	—	1,629
Forgiveness of debt	—	—	(449)
Forgiveness of notes receivable from related parties	—	—	350
Changes in operating assets and liabilities:			
Prepaid expenses	117	(418)	(292)
State research and development credit receivable	(45)	(80)	(247)
Interest due on notes receivable	(2)	8	(2)
Other receivables	(722)	65	(918)
Accounts payable	(1,042)	(137)	(602)
Accrued expenses and deferred rent	(35)	(418)	2,746
Net cash used in development activities	(5,640)	(4,336)	(75,405)
Cash Flows From Investing Activities			
Purchase of investments	—	—	(11,290)
Sale of investments	—	269	8,800
Notes receivable from related parties	—	—	(350)
Purchase of fixed assets	(709)	(48)	(7,478)
Proceeds on sale of fixed assets	50	—	50
Cash paid for OncoRx	—	—	(120)
Net cash provided by (used in) investing activities	(659)	221	(10,388)
Cash Flows From Financing Activities			
Cash received from noncontrolling interest investment	—	—	3,479
Issuance of common stock	135	—	41,295
Repurchase of common stock	(4)	—	(505)
Repayments (advances) of notes receivable for common stock	—	13	—
Proceeds from preferred stock	—	—	67,743
Proceeds from notes payable	—	—	7,759
Principal payments on debt	(23)	(23)	(392)
Payments under capital lease obligations	(30)	(31)	(317)
Net cash provided by (used in) financing activities	78	(41)	119,062
Net (decrease) increase in cash and cash equivalents	(6,221)	(4,156)	33,269

Cash and cash equivalents at beginning of period	39,490	10,572	—
Cash and cash equivalents at end of period	$ 33,269	$ 6,416	$ 33,269
Supplemental disclosure of cash flows information:			
Cash paid for interest	$ 10	$ 11	$ 114
Noncash financing and investing activities:			
Accretion on redeemable preferred stock	—	—	113
Purchased leasehold improvements and equipment in accounts payable	173	—	1,424
Common stock issued to shareholders of OncoRx as part of acquisition	—	—	1,654
Issuance of common stock dividend to Series AA preferred shareholders	—	—	6
Assets acquired under capital lease	—	—	542

See accompanying notes to condensed consolidated financial statements.

NewLink Genetics Corporation
(A Development Stage Enterprise)
Notes to Condensed Consolidated Financial Statements
(unaudited)

1. Description of Business and Development Stage Activities

On June 4, 1999, NewLink Genetics Corporation ("NewLink") was incorporated as a Delaware corporation. NewLink was formed for the purpose of developing treatments for cancer and other diseases. NewLink initiated operations in April of 2000, which primarily consist of research and development. In 2005, NewLink created a wholly owned subsidiary, BioProtection Systems Corporation ("BPS"). NewLink contributed certain licensing agreements and other intangible assets for BPS to create vaccines against potential biological terror threats. NewLink and BPS (together referred to herein as the "Company") are development stage enterprises and are devoting substantially all of their efforts toward research and development.

The Company has never earned revenue from sales of its drugs under development. The Company has, from June 4, 1999 (inception) through March 31, 2012 generated a cumulative deficit of $86.3 million. The accompanying financial statements have been prepared assuming the Company will continue as a going concern. The Company received $37.6 million as a result of the closing of the initial public offering of the Company's common stock ("IPO") on November 16, 2011, which is expected to fund operations through 2013. The generation of additional financing may be necessary for the Company to continue operations in the future. There can be no assurance, however, that such financing will be available on terms acceptable to the Company or at all.

2. Basis of Presentation

The interim financial statements have been prepared and presented by the Company in accordance with accounting principles generally accepted in the United States ("GAAP") and the rules and regulations of the Securities and Exchange Commission ("SEC"), without audit, and reflect all adjustments necessary to present fairly the Company's interim financial information.

Certain information and footnote disclosures normally included in the Company's annual financial statements prepared in accordance with GAAP have been condensed or omitted. The accompanying unaudited financial statements should be read in conjunction with the audited financial statements for the year ended December 31, 2011, included in the Company's Annual Report on Form 10-K (as amended). There were no significant changes in the Company's accounting policies or estimates since the end of fiscal 2011. The financial results for any interim period are not necessarily indicative of financial results for the full year.

3. Significant Accounting Policies

(a) Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. generally accepted accounting principles (U.S. GAAP) requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

(b) Principles of Consolidation

The consolidated financial statements include the financial statements of NewLink and BPS. All significant intercompany balances and transactions have been eliminated in consolidation.

(c) Financial Instruments and Concentrations of Credit Risk

The fair values of cash and cash equivalents, certificates of deposit, prepaid expenses, receivables, accounts payable, and accrued liabilities, which are recorded at cost, approximate fair value based on the short-term nature of these financial instruments. Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash and cash equivalents, and certificates of deposit. Cash and cash equivalents are held by financial institutions and are federally insured up to certain limits. At times, the Company's cash and cash equivalents balance exceeds the federally insured limits. To limit the credit risk, the Company invests its excess cash primarily in high quality securities such as money market funds. The fair value and carrying value of notes payable, capital lease obligations, and the royalty obligation payable was $7.1 million and $7.2 million as of March 31, 2012 and December 31, 2011, respectively.

(d) Recently Adopted Accounting Pronouncements

In June 2011, the Financial Accounting Standards Board (FASB) issued new accounting guidance which revised the manner in which companies present comprehensive income in their financial statements. The new guidance removed the presentation options previously allowed and requires companies to report components of comprehensive income as part of the consolidated statement of income or as a separate consolidated statement of comprehensive income. The revised guidance did not change the items that must be reported in other comprehensive income. The guidance was effective for the Company on January 1, 2012. Comprehensive income consists of net income and other comprehensive income (loss). Other comprehensive income (loss) refers to revenues, expenses, gains and losses that are not included in net income, but rather are recorded directly in stockholders' equity. The Company adopted this guidance on January 1, 2012. During the three months ended March 31, 2012 and 2011 there were no amounts recorded directly in stockholders' equity and therefore there was no difference between net income and comprehensive income for these two respective periods.

4. Long-Term Debt Conversion to Royalty Obligation

March 2005 Iowa Department of Economic Development Loan

In March 2005, the Company entered into a $6.0 million forgivable loan agreement with the Iowa Department of Economic Development, or the IDED. Under the agreement, in the absence of default, there were no principal or interest payments due until the completion date for the project. The balance outstanding under the loan agreement was $6.0 million as of December 31, 2011. The agreement provided the Company with financial assistance for research

and product development activities at its Iowa State University Research Park facility. Additionally, under the agreement, the Company was obligated to pay a minimum of 0.25% royalties on all gross revenues of any products the Company brings to market with a cumulative maximum royalty amount due of $3.2 million. Substantially all of the Company's assets were pledged to secure this loan.

On March 27, 2012 the Company entered into a settlement agreement with the Iowa Economic Development Authority ("IEDA") as the successor organization to IDED. Under the terms of the settlement agreement the Company agreed to pay a 0.5% royalty on future product sales up to a cap of $6.8 million in exchange for IEDA's release of the Company's job creation and project expenditure obligations and their release of the security interest in substantially all of the Company's assets. As no payments are expected in the next 12 months, the entire accrued royalty obligation of $6.0 million is considered long-term.

There were no other changes in the terms of the Company's other long-term debt agreements since December 31, 2011 as reported in the Company's Annual Report on Form 10-K as amended.

5. Common Stock Equity Incentive Plan

Share-based employee compensation expense for the three months ended March 31, 2012 and 2011 and since inception was $736,000, $368,000 and $5.8 million, respectively, and is allocated between research and development and general and administrative expenses within the consolidated statements of operations. As of March 31, 2012, the total compensation cost related to non-vested option awards not yet recognized was $5.2 million and the weighted average period over which it is expected to be recognized was 1.9 years.

The following table summarizes the stock option activity for the three months ended March 31, 2012:

	Number of options	Weighted average exercise price	Weighted average remaining contractual term (years)
Outstanding at beginning of period	3,515,051	$ 3.51	
Options granted	534,281	6.87	
Options exercised	(70,789)	1.90	
Options forfeited	(8,654)	5.91	
Options expired	—	—	
Outstanding at end of period	3,969,889	$ 3.98	7.8
Options exercisable at end of period	2,383,389	$ 2.96	7.1

As of March 31, 2012, there were an additional 597,027 shares reserved for future issuance under the Company's employee benefit plans.

During the three months ending March 31, 2012 the Company issued stock awards of 10,000 shares of common stock with a fair value of $68,700.

The following table summarizes the assumptions used to estimate the fair value of those stock options granted during the three months ended March 31, 2012 using a Black-Scholes valuation model:

Risk-free interest rate	0.9% - 1.4%
Expected dividend yield	—
Expected volatility	63.0% - 67.8%
Expected term (in years)	5.0 - 7.0
Weighted average grant-date fair value per share	$4.18

The intrinsic value of options exercised during the three months ending March 31, 2012 was $567,540. The fair value of shares available under awards that vested during the three months ending March 31, 2012 was $1.9 million.

During the three months ended March 31, 2012 and since inception 32,381 and 534,524 stock options and awards were granted to nonemployees, respectively. As a result of the issuance of these options and awards, $151,000 and $975,000 of expense was recorded in the three months ended March 31, 2012 and since inception, respectively.

6. Income Taxes

The Company incurred no income tax expense for the three months ended March 31, 2012 and 2011 or since inception. Income tax expense differs from the amount that would be expected after applying the statutory U.S. federal income tax rate primarily due to changes in the valuation allowance for deferred taxes.

The valuation allowance for deferred tax assets as of March 31, 2012 and December 31, 2011 was $19.8 million and $18.9 million, respectively. The net change in the total valuation allowance for the three months ended March 31, 2012 and 2011 was an increase of $961,000 and $1.1 million, respectively. In assessing the realizability of deferred tax assets, management considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. Management considers the scheduled reversal of deferred tax liabilities, projected taxable income, and tax planning strategies in making this assessment. Valuation allowances have been established for the entire amount of the net deferred tax assets as of March 31, 2012 and December 31, 2011, due to the uncertainty of future recoverability.

7. Net Loss per Common Share

Basic net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, without consideration of common stock equivalents. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted average number of common share equivalents outstanding for the period determined using the treasury-stock method.

For purposes of this calculation, preferred stock, stock options and warrants are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

The following table presents the computation of basic and diluted net loss per common share (in thousands, except per share data):

	Three Months Ended March 31,	
	2012	2011
Numerator		
Net loss attributable to common stockholders	$ (4,842)	$ (3,897)
Denominator		
Weighted-average common shares outstanding	20,613	3,636
Basic and diluted net loss per common share	$ (0.23)	$ (1.07)

The numerator was not adjusted for the stock dividend paid on the Company's Series AA preferred stock as the impact is not material. Potentially dilutive securities not included in the calculation of diluted net loss per common share because to do so would be anti-dilutive are as follows (in common equivalent shares):

	As of March 31,	
	2012	2011
Preferred stock (1)	—	9,870,527
Common stock options	3,969,889	2,992,810
	3,969,889	12,863,337

(1) Amounts for the Company's Series BB, C, D and E conversions are computed based on the IPO price of $7.00 per share.

8. Commitments and Contingencies

The Company substantially completed construction of approximately 14,000 square feet of additional space adjoining the Company's existing facilities in Ames, Iowa as of March 31, 2012. In connection with this expansion, the landlord provided incentives on a portion of the expansion leasehold improvement costs. The Company recorded the incentive as deferred rent and categorized the liability into short-term and long-term components as of March 31, 2012.

There were no other outstanding commitments or contingencies as of March 31, 2012.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This Quarterly Report on Form 10-Q contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, and such statements are subject to the "safe harbor" created by those sections. Forward-looking statements are based on our management's beliefs and assumptions and on information available to our management as of the date hereof. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expect," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "potential" and similar expressions intended to identify forward-looking statements. Examples of these statements include, but are not limited to, statements regarding: our plans to develop and commercialize our product candidates; our ongoing and planned preclinical studies and clinical trials, including the timing for completion of enrollment and outcome of our Phase 3 clinical trial for our HyperAcute Pancreas cancer immunotherapy; the timing of release of data from ongoing clinical studies; the timing of and our ability to obtain and maintain regulatory approvals for our product candidates; the clinical utility of our products; our plans to leverage our existing technologies to discover and develop additional product candidates; our ability to quickly and efficiently identify and develop product candidates; our commercialization, marketing and manufacturing capabilities and strategy; our intellectual property position; the potential benefits of strategic collaboration agreements and our ability to enter into strategic arrangements; our estimates regarding expenses, future revenues, capital requirements and needs for additional financing; and other risks and uncertainties, including those described in Part II, Item 1A, "Risk Factors" of this Quarterly Report and in our other periodic reports filed from time to time with the Securities and Exchange Commission, or SEC, including our Annual Report on Form 10-K for the year ended December 31, 2011. Our actual results could differ materially from those discussed in our forward-looking statements for many reasons, including those risks. You should not place undue reliance on these forward-looking statements, which apply only as of the date of this Quarterly Report on Form 10-Q. You should read this Quarterly Report on Form 10-Q completely. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

The following discussion and analysis should be read in conjunction with the unaudited financial statements and notes thereto included in Part I, Item 1 of this Quarterly Report on Form 10-Q.

Overview

We are a biopharmaceutical company focused on discovering, developing and commercializing novel immunotherapeutic products to improve cancer treatment options for patients and physicians. Our portfolio includes biologic and small-molecule immunotherapy product candidates intended to treat a wide range of oncology indications. Our lead product candidate, HyperAcute Pancreas cancer immunotherapy, or HyperAcute Pancreas, is being studied in a Phase 3 clinical trial in surgically-resected pancreatic cancer patients that is being performed under a Special Protocol Assessment, or SPA, with the United States Food and Drug Administration, or FDA. We initiated this trial based on encouraging Phase 2 data that suggests improvement in both disease-free and overall survival. We have also received Fast Track and Orphan Drug designations from the FDA for this product candidate for the adjuvant treatment of surgically-resected pancreatic cancer. We have three additional product candidates in clinical development, including our HyperAcute Lung cancer immunotherapy, or HyperAcute Lung, which is being studied in a Phase 1/2 clinical trial at the National Cancer Institute, or NCI, and our HyperAcute Melanoma cancer immunotherapy, or HyperAcute Melanoma, which is being studied in an investigator-initiated Phase 2 clinical trial. To date, our HyperAcute product candidates have been dosed in more than 300 cancer patients, either as a monotherapy or in combination with other therapies, and have demonstrated a favorable safety profile.

Our HyperAcute product candidates are based on our proprietary HyperAcute immunotherapy technology, which is designed to stimulate the human immune system. Our HyperAcute product candidates use allogeneic (non-patient specific) cells from previously established cell lines rather than cells derived from the patient. We believe our approach enables a simpler, more consistent and scalable manufacturing process than therapies based on patient specific tissues or cells. Our product candidates are designed with an objective to harness multiple components of the innate immune system to combat cancer, either as a monotherapy or in combination with current treatment regimens without incremental toxicity. We are also conducting small-molecule based research and development with an aim to produce new drugs capable of breaking the immune system's tolerance to cancer through inhibition of the indoleamine-(2,3)-dioxygenase, or IDO, pathway. We are currently studying our lead IDO pathway inhibitor product candidate, d-1-methyltryptophan, or D-1MT, in collaboration with the NCI in two Phase 1B/2 clinical trials. We believe that our immunotherapeutic technologies will enable us to discover, develop and commercialize multiple product candidates that can be used either alone or in combination to enhance or potentially replace current therapies to treat cancer with underserved patient populations and significant market potential.

BioProtection Systems Corporation, or BPS, was founded by us as a subsidiary in 2005 to research, develop and commercialize vaccines to control the spread of emerging lethal viruses and infectious diseases, improve the efficacy of existing vaccines and provide rapid-response prophylactic and therapeutic treatment for pathogens most likely to enter the human population through pandemics or even acts of bioterrorism. BPS is based upon three core technologies, each of which can be leveraged into the infectious disease or biodefense fields. The first is our HyperAcute immunotherapy technology, which is currently focused on enhancing vaccines for influenza. The second technology, based on a yellow fever virus, is in licensed from the University of California at San Francisco. The third technology is replication competent recombinant Vesicular Stomatitus Vaccine, or rVSV, an advanced vaccine technology developed for the Marburg and Ebola viruses.

We are a development stage company and have incurred significant losses since our inception. As of March 31, 2012, we had an accumulated deficit of $86.3 million. We incurred a net loss of $4.8 million, $3.9 million, and $86.3 million, for the three months ended March 31, 2012 and 2011, and since inception, respectively. We expect our losses to increase over the next several years as we advance into late-stage clinical trials and pursue regulatory approval of our product candidates. In addition, if one or more of our product candidates are approved for marketing, we will incur significant expenses for the initiation of commercialization activities.

On October 19, 2011, our board of directors approved a 2.1-for-one reverse split of the Company's common stock which became effective upon filing of a Certificate of Amendment of the Restated Certificate of Incorporation with the Secretary of State of Delaware on October 25, 2011. All share and per share amounts have been retroactively restated in the accompanying financial statements and notes for all periods presented.

Financial Overview

Revenues

From our inception through March 31, 2012, we have not generated any revenue from product sales. We have generated $6.2 million in grant revenue from our inception through March 31, 2012, which is primarily attributable to research and development being performed by our subsidiary, BioProtection Systems Corporation, or BPS, under contracts and grants with the Department of Defense, or DOD, and the National Institutes of Health, or NIH.

In the future, we may generate revenue from a variety of sources, including product sales if we develop products which are approved for sale, license fees, and milestone, research and development and royalty payments in connection with strategic collaborations or licenses of our intellectual property. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of license fees, research and development reimbursements, milestone and other payments we may receive under potential strategic collaborations, and the amount and timing of payments we may receive upon the sale of any products, if approved, to the extent any are successfully commercialized. We do not expect to generate revenue from product sales for several years, if ever. If we fail to complete the development of our product candidates in a timely manner or to obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

Research and Development Expenses

Research and development expenses consist of expenses incurred in connection with the discovery and development of our product candidates. These expenses consist primarily of:

- employee-related expenses, which include salaries, bonuses, benefits and share-based compensation;
- the cost of acquiring and manufacturing clinical trial materials;
- expenses incurred under agreements with contract research organizations, investigative sites and consultants that conduct our clinical trials and a substantial portion of our preclinical studies;
- facilities, depreciation of fixed assets and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities and equipment;
- license fees for and milestone payments related to in-licensed products and technology; and
- costs associated with non-clinical activities and regulatory approvals.

We expense research and development expenses as incurred.

Product candidates in late stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size, duration and complexity of later stage clinical trials. We plan to increase our research and development expenses for the foreseeable future as we seek to complete development of our most advanced product candidates, and to further advance our earlier-stage research and development projects. From our inception through March 31, 2012, we have incurred $64.1 million in research and development expenses. The following tables summarize our research and development expenses for the periods indicated:

Research and Development Expenses by Product
(In thousands)
(unaudited)

	Three Months Ended March 31,		Cumulative from June 4, 1999 (inception) through March 31,
	2012	2011	2012
HyperAcute immunotherapy technology	$ 2,660	$ 2,154	$ 45,805
IDO pathway inhibitor technology	795	587	11,719
Other research and development	375	439	6,624
Total research and development expenses	$ 3,830	$ 3,180	$ 64,148

Research and Development Expenses by Category
(In thousands)
(unaudited)

	Three Months Ended March 31,		Cumulative from June 4, 1999 (inception) through March 31,
	2012	2011	2012
Compensation	$ 1,909	$ 1,535	32,304
Equipment, supplies and occupancy	1,045	991	20,645
Outside clinical and other	876	654	11,199
Total research and development expenses	$ 3,830	$ 3,180	64,148

At this time, we cannot accurately estimate or know the nature, specific timing or costs necessary to complete clinical development activities for our product candidates. We are subject to the numerous risks and uncertainties associated with developing biopharmaceutical products including the uncertain cost and outcome of ongoing and planned clinical trials, the possibility that the FDA or another regulatory authority may require us to conduct clinical or non-clinical testing in addition to trials that we have planned, rapid and significant technological changes, frequent new product and service introductions and enhancements, evolving industry standards in the life sciences industry and our future need for additional capital. In addition, we currently have limited clinical data concerning the safety and efficacy of our product candidates. A change in the outcome of any of these variables with respect to the development of any of our product candidates could result in a significant change in the costs and timing of our research and development expenses.

General and Administrative Expenses

General and administrative expenses consist principally of salaries and related costs for personnel in executive, finance, business development, information technology, legal and human resources functions. Other general and administrative expenses include facility costs not otherwise associated with research and development expenses, intellectual property prosecution and defense costs and professional fees for legal, consulting, auditing and tax services.

We anticipate that our general and administrative expenses will continue to increase over the next several years for, among others, the following reasons:

- we expect our general and administrative expenses to increase as a result of increased payroll, expanded infrastructure and higher consulting, legal, auditing and tax services and investor relations costs, and director and officer insurance premiums associated with being a public company;
- we expect to incur increased general and administrative expenses to support our research and development activities, which we expect to expand as we continue to advance the clinical development of our product candidates; and
- we may also begin to incur expenses related to the planned sales and marketing of our product candidates in anticipation of commercial launch before we receive regulatory approval, if any, of a product candidate.

Interest Income and Interest Expense

Interest income consists of interest earned on our cash and cash equivalents and certificates of deposit. The primary objective of our investment policy is capital preservation. We expect our interest income to increase as we invest the net proceeds from the offering pending their use in our operations.

Interest expense consists primarily of interest, amortization of debt discount and amortization of deferred financing costs associated with our loans payable.

Tax Loss Carryforwards

The valuation allowance for deferred tax assets as of March 31, 2012 and December 31, 2011 was $19.8 million and $18.9 million, respectively. The net change in the total valuation allowance for the three months ended March 31, 2012 and 2011 was an increase of $961,000 and $1.1 million, respectively. In assessing the realizability of deferred tax assets, management considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized.

The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. Management considers the scheduled reversal of deferred tax liabilities, projected taxable income, and tax planning strategies in making this assessment. Valuation allowances have been established for the entire amount of the net deferred tax assets as of March 31, 2012 and December 31, 2011, due to the uncertainty of future recoverability.

As of March 31, 2012 and December 31, 2011, we had federal net operating loss carryforwards of $80.3 million and $76.2 million and federal research credit carryforwards of $3.0 million and $2.9 million, respectively, that expire at various dates from 2020 through 2031. Sections 382 and 383 of the Internal Revenue Code limit a corporation's ability to utilize its net operating loss carryforwards and certain other tax attributes (including research credits) to offset any future taxable income or tax if the corporation experiences a cumulative ownership change of more than 50% over any rolling three year period. State net operating loss carryforwards (and certain other tax attributes) may be similarly limited. An ownership change can therefore result in significantly greater tax liabilities than a corporation would incur in the absence of such a change and any increased liabilities could adversely affect the corporation's business, results of operations, financial condition and cash flow.

Based on a preliminary analysis, we believe that, from its inception through December 31, 2009, NewLink experienced Section 382 ownership changes in September 2001 and March 2003. These two ownership changes limit NewLink's ability to utilize its federal net operating loss carryforwards (and certain other tax attributes) that accrued prior to the 2003 ownership change. In addition, the net operating loss carryforwards (and certain other tax attributes) of our subsidiary may be limited by Sections 382 and 383 as a result of a prior ownership change of the subsidiary.

Additional analysis will be required to determine whether changes in our ownership since December 31, 2009 and/or changes in our ownership that resulted from our IPO have caused another ownership change to occur. Any such change could result in significant limitations on all of our net operating loss carryforwards and other tax attributes.

Even if another ownership change has not occurred, additional ownership changes may occur in the future as a result of events over which we will have little or no control, including purchases and sales of our equity by our 5% stockholders, the emergence of new 5% stockholders, additional equity offerings or redemptions of our stock or certain changes in the ownership of any of our 5% stockholders.

Income tax expense was $0 for the three months ended March 31, 2012 and 2011. Income tax expense differs from the amount that would be expected after applying the statutory United States federal income tax rate primarily due to changes in the valuation allowance for deferred taxes.

Critical Accounting Policies and Significant Judgments and Estimates

We have prepared our financial statements in accordance with United States generally accepted accounting principles. Our preparation of these financial statements requires us to make estimates, assumptions and judgments that affect the reported amounts of assets, liabilities, expenses and related disclosures at the date of the financial statements, as well as revenues and expenses during the reporting periods. We evaluate our estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results could therefore differ materially from these estimates under different assumptions or conditions.

Our Annual Report on Form 10-K for the year ended December 31, 2011, as amended, discusses our most critical accounting policies. Since December 31, 2011, there have been no material changes in the critical accounting policies discussed in the 2011 Annual Report.

Results of Operations

Comparison of the Three Months Ended March 31, 2012 and 2011

Revenues. Revenues for the three months ended March 31, 2012 were $471,000, decreasing from $604,000 for the same period in 2011. The decrease in revenue of $133,000 was due to reduced research by BPS under various DOD contracts and NIH grants as amended.

Research and Development Expenses. Research and development expenses for the three months ended March 31, 2012 were $3.8 million, increasing from $3.2 million for the same period in 2011. The $650,000 increase was primarily due to a $374,000 increase in personnel-related expenses accompanied by an increase of $222,000 in clinical trial expense, contract

research and other expenses and an increase of $54,000 in equipment and supplies expenses. The increase in personnel-related expense is attributable to both increases in headcount and compensation levels and the increase in clinical trial expense is primarily attributable to higher levels of patient counts enrolled in our clinical trials.

General and Administrative Expenses. General and administrative expenses for the three months ended March 31, 2012 were $1.5 million, increasing from $1.3 million for the same period in 2011. The $142,000 increase was primarily due to an increase of $141,000 in personnel expenses, accompanied by an $8,000 increase in other expenses and offset by a $7,000 decrease in equipment, supplies and occupancy expenses.

Interest Income and Expense. Interest expense for the three months ended March 31, 2012 was $8,000, compared to $11,000 for the same period in 2011. Interest income for the three months ended March 31, 2012 was $4,000, compared to $4,000 for the same period in 2011.

Other Income (Expense). Miscellaneous (expense) income, net for the three months ended March 31, 2012 was $(21,000), compared to $1,000 for the same period in 2011. Miscellaneous (expense) income, net for the three months ended March 31, 2012 was primarily attributable to a loss on the sale of fixed assets.

Liquidity and Capital Resources

We have funded our operations through our IPO proceeds, the private placement of equity securities, debt financing and interest income. As of March 31, 2012, we have received proceeds of $112.5 million from the issuance of common and convertible preferred stock and $7.8 million from debt financing. As of March 31, 2012, we had cash, cash equivalents and certificates of deposit of approximately $35.8 million. The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

Sources and Uses of Cash
(in thousands)

	Three Months Ended March 31,	
	2012	2011
Net cash used in development activities	$ (5,640)	$ (4,336)
Net cash (used in) provided by investing activities	(659)	221
Net cash provided by financing activities	78	(41)
Net decrease in cash and cash equivalents	$ (6,221)	$ (4,156)

For the three months ended March 31, 2012 and 2011, we used cash of $5.6 million and $4.3 million for our development activities, respectively. The cash used by development activities in the three months ended March 31, 2012 primarily resulted from our net loss of $4.8 million, accompanied by changes in operating assets and liabilities of $1.7 million and offset by non-cash expenses of $931,000. The cash used by development activities in the three months ended March 31, 2011 primarily resulted from our net loss of $3.9 million, accompanied by changes in operating assets and liabilities of $980,000 and offset by non-cash expenses of $542,000.

For the three months ended March 31, 2012 and 2011, our investing activities (used) provided cash of $(659,000) and $221,000 million, respectively. The cash used by investing activities in the three months ended March 31, 2012 was primarily due to the purchase of fixed assets. The cash provided by investing activities in the three months ended March 31, 2011 was primarily a result of the sale of investments.

For the three months ended March 31, 2012 and 2011, our financing activities provided (used) $78,000 and $(41,000), respectively. The cash provided by financing activities in the three months ended March 31, 2012 was primarily due to the sale and issuance of common stock of $135,000 offset by payments on long-term financing obligations of $53,000. The cash used by financing activities in the three months ended March 31, 2011 was primarily due to payments on long-term financing obligations.

Operating Capital Requirements

We anticipate that we will continue to generate significant operating losses for the next several years as we incur expenses related to the research and development of our HyperAcute immunotherapy and IDO pathway inhibitor product

candidates, build commercial capabilities and expand our corporate infrastructure. Including the funds received from our initial public offering, or IPO, we believe that we have sufficient cash and cash equivalents and certificates of deposit to fund our operations through at least the end of 2013.

We may seek to sell additional equity or debt securities or obtain a credit facility if our available cash and cash equivalents are insufficient to satisfy our liquidity requirements or if we develop additional opportunities to do so. The sale of additional equity and debt securities may result in additional dilution to our shareholders. If we raise additional funds through the issuance of debt securities or preferred stock, these securities could have rights senior to those of our common stock and could contain covenants that would restrict our operations. We may require additional capital beyond our currently forecasted amounts. Any such required additional capital may not be available on reasonable terms, if at all. If we were unable to obtain additional financing, we may be required to reduce the scope of, delay or eliminate some or all of our planned research, development and commercialization activities, which could harm our business.

Because of the numerous risks and uncertainties associated with research, development and commercialization of biopharmaceutical products, we are unable to estimate the exact amounts of our working capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the scope, progress, results and costs of clinical trials for our product candidates, and discovery and development activities related to new product candidates;
- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates;
- the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our product candidates and any products we commercialize;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- whether, and to what extent, we are required to repay our outstanding government provided loans;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation; and
- the timing, receipt and amount of sales of, or royalties on, our future products, if any.

Contractual Obligations and Commitments

Our contractual obligations are disclosed in our Annual Report on Form 10-K (as amended) filed with the SEC on March 30, 2012. In March 2005, we entered into a $6.0 million forgivable loan agreement with the Iowa Department of Economic Development, or the IDED. Under the agreement, in the absence of default, there were no principal or interest payments due until the completion date for the project. The balance outstanding under the loan agreement was $6.0 million as of December 31, 2011. The project provided us with financial assistance for research and product development activities at our Iowa State University Research Park facility. The project called for the creation of 315 jobs at the time of commercialization and retention of 35 jobs with total project expenditures of $189.9 million for clinical trials, research and development activities, building construction, equipment purchases, and other working capital needs. As of December 31, 2011, we believe we had created 36 jobs, retained 35 jobs and incurred $72.4 million of project expenditures. Additionally, under the agreement, we were obligated to pay a minimum of 0.25% royalties on all gross revenues of any products we bring to market with a cumulative maximum royalty amount due of $3.2 million. Substantially all of our assets were pledged to secure this loan.

On March 26, 2012, we entered into a settlement agreement with the Iowa Economic Development Authority, or the IEDA, which is the successor organization to the Iowa Department of Economic Development, or IDED. Under the terms of the settlement agreement the IDED forgivable loan agreement was terminated and we were thereby released from its job creation, project expenditure, royalty and other requirements in exchange for agreeing to pay a minimum of 0.50% royalties on all gross revenues of any products we bring to market with a cumulative maximum royalty amount due of $6.8 million. Additionally, under the settlement agreement, the IEDA released its security interest in our assets. The obligation to maintain our business in the State of Iowa while amounts remain outstanding is a continuing obligation under the terms of the settlement agreement.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under Securities and Exchange Commission, or SEC, rules.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risk related to changes in interest rates. As of March 31, 2012 and December 31, 2011, we had cash and cash equivalents and certificates of deposit of $35.8 million and $42.0 million, respectively, consisting of money market funds and bank certificates of deposit. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of United States interest rates, particularly because our investments are in short-term marketable securities. Our certificates of deposit are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our portfolio. We expect to have the ability to hold our certificates of deposit until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

Our long-term debt and our capital lease obligations bear interest at fixed rates. Any change in interest rates would have an immaterial (or no) impact on our financial statements.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

As required by paragraph (b) of Rules 13a-15 and 15d-15 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, an evaluation was carried out under the supervision and with the participation of our management, including our principal executive officer (Chief Executive Officer) and principal financial officer (Chief Financial Officer), of the effectiveness of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Based on that evaluation, our management, including our principal executive officer and principal financial officer, concluded that our disclosure controls and procedures were effective as of March 31, 2012 to ensure that information required to be disclosed by us in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in Securities and Exchange Commission's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

No Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting during the period covered by this Quarterly Report on Form 10-Q that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

None.

ITEM 1A. RISK FACTORS

You should consider carefully the following information about the risks described below, together with the other information contained in this Quarterly Report and in our other public filings in evaluating our business. If any of the following risks actually occurs, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline.

Those risks described below that reflect substantive changes from the risks described under Part I, Item 1A "Risk Factors" included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2011, as filed with the Securities and Exchange Commission on March 30, 2012, as amended, have been marked with an (*).

Business Risks

Risks Relating to Clinical Development and Commercialization of Our Product Candidates

Our near term prospects are highly dependent on our lead product candidate, HyperAcute Pancreas cancer immunotherapy, or HyperAcute Pancreas. If we fail to complete, or demonstrate safety and efficacy in, clinical trials, fail to obtain regulatory approval or fail to successfully commercialize HyperAcute Pancreas, our business would be harmed and the value of our securities would likely decline.

We must be evaluated in light of the uncertainties and complexities affecting a development stage biopharmaceutical company. We have not completed clinical development for any of our products. Our most advanced product candidate is HyperAcute Pancreas. The United States Food and Drug Administration, or FDA, must approve HyperAcute Pancreas before it can be marketed or sold. Our ability to obtain FDA approval of HyperAcute Pancreas depends on, among other things, completion of our Phase 3 clinical trial, whether our Phase 3 clinical trial of HyperAcute Pancreas demonstrates statistically significant achievement of the clinical trial endpoints with no significant safety issues and whether the FDA agrees that the data from our Phase 3 clinical trial of HyperAcute Pancreas is sufficient to support approval. The final results of our Phase 3 clinical trials of HyperAcute Pancreas may not meet the FDA's requirements to approve the product for marketing, and the FDA may otherwise determine that our manufacturing processes, facilities or raw materials are insufficient to warrant approval. We may need to conduct more clinical trials than we currently anticipate. Furthermore, even if we do receive FDA approval, we may not be successful in commercializing HyperAcute Pancreas. If any of these events occur, our business could be materially harmed and the value of our common stock would likely decline.

If our product candidates do not meet safety and efficacy endpoints in clinical trials, they will not receive regulatory approval, and we will be unable to market them. We have not tested any of our product candidates in controlled clinical trials.

The clinical development and regulatory approval process is expensive and time-consuming. The timing of any future product approval cannot be accurately predicted. If we fail to obtain regulatory approval for our current or future product candidates, we will be unable to market and sell them and therefore we may never be profitable.

As part of the regulatory process, we must conduct clinical trials for each product candidate to demonstrate safety and efficacy to the satisfaction of the FDA and other regulatory authorities abroad. The number and design of clinical trials that will be required varies depending on the product candidate, the condition being evaluated, the trial results and regulations applicable to any particular product candidate.

Prior clinical trial program designs and results are not necessarily predictive of future clinical trial designs or results. Initial results may not be confirmed upon full analysis of the detailed results of a trial. Product candidates in later stage clinical trials may fail to show the desired safety and efficacy despite having progressed through initial clinical trials with acceptable endpoints.

In particular, there have been no control groups in our clinical trials conducted to date. While comparisons to results from other reported clinical trials can assist in predicting the potential efficacy of our HyperAcute Pancreas product candidate, there are many factors that affect the outcome for patients in clinical trials, some of which are not apparent in published reports, and

results from two different trials cannot always be reliably compared. As a result, we are studying HyperAcute Pancreas in combination with the current standard-of-care in direct comparison to the current standard-of-care alone in the same trial and will need to show a statistically significant benefit when added to the current standard-of-care in order for HyperAcute Pancreas to be approved as a marketable drug. Patients in our Phase 3 study who do not receive HyperAcute Pancreas may not have results similar to patients studied in the other studies we have used for comparison to our Phase 2 studies. If the patients in our Phase 3 study who receive standard-of-care without HyperAcute Pancreas have results which are better than the results predicted by the other large studies, we may not demonstrate a sufficient benefit from the HyperAcute Pancreas to allow the FDA to approve it for marketing.

Our HyperAcute product candidates are based on a novel technology, which may raise development issues we may not be able to resolve, regulatory issues that could delay or prevent approval or personnel issues that may keep us from being able to develop our product candidates.

Our HyperAcute product candidates are based on our novel HyperAcute immunotherapy technology. In the course of developing this technology and these product candidates, we have encountered difficulties in the development process. There can be no assurance that additional development problems will not arise in the future which we may not be able to resolve or which may cause significant delays in development.

Regulatory approval of novel product candidates such as ours can be more expensive and take longer than for other, more well-known or extensively studied pharmaceutical or biopharmaceutical products, due to our and regulatory agencies' lack of experience with them. This may lengthen the regulatory review process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these product candidates or lead to significant post-approval limitations or restrictions. For example, the two cell lines that comprise HyperAcute Pancreas are novel and complex therapeutics that we have endeavored to better characterize so that their identity, strength, quality, purity and potency may be compared among batches created from different manufacturing methods. We currently lack the manufacturing capacity necessary for larger-scale production. If we make any changes to our current manufacturing methods or cannot design assays that satisfy the FDA's expectations regarding the equivalency of such therapeutics in the laboratory, the FDA may require us to undertake additional clinical trials.

The novel nature of our product candidates also means that fewer people are trained in or experienced with product candidates of this type, which may make it difficult to find, hire and retain capable personnel for research, development and manufacturing positions.

Our Special Protocol Assessment, or SPA, with the FDA relating to our HyperAcute Pancreas Phase 3 clinical trial does not guarantee any particular outcome from regulatory review of the trial or the product candidate, including any regulatory approval.

The protocol for our HyperAcute Pancreas Phase 3 clinical trial was reviewed by the FDA under its SPA process, which allows for FDA evaluation of a clinical trial protocol intended to form the primary basis of an efficacy claim in support of a New Drug Application, or NDA, and provides an agreement that the study design, including trial size, clinical endpoints and/or data analyses are acceptable to the FDA. However, the SPA agreement is not a guarantee of approval, the FDA retains the right to require additional Phase 3 testing and we cannot be certain that the design of, or data collected from, the HyperAcute Pancreas Phase 3 clinical trial will be adequate to demonstrate the safety and efficacy of HyperAcute Pancreas for the treatment of patients with pancreatic cancer, or otherwise be sufficient to support FDA or any foreign regulatory approval. In addition, the survival rates, duration of response and safety profile required to support FDA approval are not specified in the HyperAcute Pancreas Phase 3 clinical trial protocol and will be subject to FDA review. Although the SPA agreement calls for review of interim data at certain times prior to completion, there is no assurance that any such review, even if such interim data is positive, will result in early approval. Further, the SPA agreement is not binding on the FDA if public health concerns unrecognized at the time the SPA agreement was entered into become evident, other new scientific concerns regarding product safety or efficacy arise, or if we fail to comply with the agreed upon trial protocols. In addition, the SPA agreement may be changed by us or the FDA on written agreement of both parties, and the FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from the HyperAcute Pancreas Phase 3 clinical trial. As a result, we do not know how the FDA will interpret the parties' respective commitments under the SPA agreement, how it will interpret the data and results from the HyperAcute Pancreas Phase 3 clinical trial, or whether HyperAcute Pancreas will receive any regulatory approvals as a result of the SPA agreement or the HyperAcute Pancreas Phase 3 clinical trial. Therefore, significant uncertainty remains regarding the clinical development and regulatory approval process for HyperAcute Pancreas for the treatment of patients with pancreatic cancer.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we must focus on research programs and product candidates for the specific indications that we believe are the most scientifically and commercially promising. As a result, we have in the past determined to let certain of our development projects remain idle including by allowing Investigational New Drug applications, or INDs, to lapse into inactive status, and we may in the future decide to forego or delay pursuit of opportunities with other product candidates or other indications that later prove to have greater scientific or commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable scientific or commercial products or profitable market opportunities. In addition, we may spend valuable time and managerial and financial resources on research programs and product candidates for specific indications that ultimately do not yield any scientifically or commercially viable products. If we do not accurately evaluate the scientific and commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in situations where it would have been more advantageous for us to retain sole rights to development and commercialization.

We may face delays in completing our clinical trials, and we may not be able to complete them at all.

We have not completed all the clinical trials necessary to support an application with the FDA for approval to market any of our product candidates. Our current and future clinical trials may be delayed or terminated as a result of many factors, including:

- delays or failure in reaching agreement on acceptable clinical trial contracts or clinical trial protocols with prospective sites;
- regulators or institutional review boards may not authorize us to commence a clinical trial;
- regulators or institutional review boards may suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or concerns about patient safety;
- we may suspend or terminate our clinical trials if we believe that they expose the participating patients to unacceptable health risks;
- slower than expected patient enrollment or lack of a sufficient number of patients that meet the enrollment criteria for our clinical trials;
- patients may not complete clinical trials due to safety issues, side effects, dissatisfaction with the product candidate, or other reasons;
- difficulty in maintaining contact with patients after treatment, preventing us from collecting the data required by our study protocol;
- product candidates may demonstrate a lack of efficacy during clinical trials;
- governmental or regulatory delays, failure to obtain regulatory approval or changes in regulatory requirements, policy and guidelines;
- competition with ongoing clinical trials and scheduling conflicts with participating clinicians; and
- delays in achieving study endpoints and completing data analysis for a trial.

In addition, we rely on academic institutions, physician practices and clinical research organizations to conduct, supervise or monitor some or all aspects of clinical trials involving our product candidates. We have less control over the timing and other aspects of these clinical trials than if we conducted the monitoring and supervision entirely on our own. Third parties may not perform their responsibilities for our clinical trials on our anticipated schedule or consistent with a clinical trial protocol or applicable regulations. We also may rely on clinical research organizations to perform our data management and analysis. They may not provide these services as required or in a timely or compliant manner.

Moreover, our development costs will increase if we are required to complete additional or larger clinical trials for the HyperAcute product candidates, our lead IDO pathway inhibitor product candidate, d-1-methyltryptophan, or D-1MT, or other product candidates prior to FDA approval. If the delays or costs are significant, our financial results and ability to commercialize the HyperAcute product candidates, D-1MT or other future product candidates will be adversely affected.

If we encounter difficulties enrolling patients in our clinical trials, our clinical trials could be delayed or otherwise adversely affected.

Clinical trials for our product candidates require us to identify and enroll a large number of patients with the disease under investigation. We may not be able to enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a study, to complete our clinical trials in a timely manner. Patient enrollment is affected by factors including:

- severity of the disease under investigation;
- design of the trial protocol;
- the size of the patient population;
- eligibility criteria for the study in question;
- perceived risks and benefits of the product candidate under study;
- availability of competing therapies and clinical trials;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

In particular, the inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events for reasons that may not be related to the product candidate we are testing or, in those trials where our product candidate is being tested in combination with one or more other therapies, for reasons that may be attributable to such other therapies, but which can nevertheless negatively affect clinical trial results. In addition, we have experienced difficulties enrolling patients in certain of our smaller clinical trials due to lack of referrals and may experience similar difficulties in the future. If we have difficulty enrolling a sufficient number or diversity of patients to conduct our clinical trials as planned, we may need to delay or terminate ongoing or planned clinical trials, either of which would have an adverse effect on our business.

Regulatory authorities may not approve our product candidates even if they meet safety and efficacy endpoints in clinical trials.

We have discussions with and obtain guidance from regulatory authorities regarding certain aspects of our clinical development activities. These discussions are not binding commitments on the part of regulatory authorities. Under certain circumstances, regulatory authorities may revise or retract previous guidance during the course of our clinical activities or after the completion of our clinical trials. A regulatory authority may also disqualify a clinical trial in whole or in part from consideration in support of approval of a potential product for commercial sale or otherwise deny approval of that product. Prior to regulatory approval, a regulatory authority may elect to obtain advice from outside experts regarding scientific issues and/or marketing applications under a regulatory authority review. In the United States, these outside experts are convened through the FDA's Advisory Committee process, which would report to the FDA and make recommendations that may differ from the views of the FDA; should an Advisory Committee be convened, it would be expected to lengthen the time for obtaining regulatory approval, if such approval is obtained at all.

The FDA and other foreign regulatory agencies can delay, limit or deny marketing approval for many reasons, including:

- a product candidate may not be considered safe or effective;
- our manufacturing processes or facilities may not meet the applicable requirements; and
- changes in their approval policies or adoption of new regulations may require additional work on our part.

Any delay in, or failure to receive or maintain, approval for any of our product candidates could prevent us from ever generating meaningful revenues or achieving profitability.

Our product candidates may not be approved even if they achieve their endpoints in clinical trials. Regulatory agencies, including the FDA, or their advisors may disagree with our trial design and our interpretations of data from preclinical studies and clinical trials. Regulatory agencies may change requirements for approval even after a clinical trial design has been approved. Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

We may be required to suspend, repeat or terminate our clinical trials if they are not conducted in accordance with regulatory requirements, the results are negative or inconclusive or the trials are not well designed.

Clinical trials must be conducted in accordance with the FDA's current Good Clinical Practices, or cGCP, or other applicable foreign government guidelines and are subject to oversight by the FDA, other foreign governmental agencies and Institutional Review Boards at the medical institutions where the clinical trials are conducted. In addition, clinical trials must be conducted with product candidates produced under current Good Manufacturing Practices, or cGMP, and may require large numbers of test subjects. Clinical trials may be suspended by the FDA, other foreign governmental agencies, or us for various reasons, including:

- deficiencies in the conduct of the clinical trials, including failure to conduct the clinical trial in accordance with regulatory requirements or clinical protocols;
- deficiencies in the clinical trial operations or trial sites;
- the product candidate may have unforeseen adverse side effects;
- the time required to determine whether the product candidate is effective may be longer than expected;
- fatalities or other adverse events arising during a clinical trial due to medical problems that may not be related to clinical trial treatments;
- the product candidate may not appear to be more effective than current therapies;
- the quality or stability of the product candidate may fall below acceptable standards; or
- insufficient quantities of the product candidate to complete the trials.

In addition, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to Institutional Review Boards for reexamination, which may impact the costs, timing or successful completion of a clinical trial. Due to these and other factors, our HyperAcute product candidates, D-1MT and other product candidates could take a significantly longer time to gain regulatory approval for any additional indications than we expect or we may never gain approval for additional indications, which could reduce our revenue by delaying or terminating the commercialization of our HyperAcute product candidates, D-1MT and other product candidates for additional indications.

Our product candidates are being and will be studied in clinical trials co-sponsored by the National Cancer Institute, or NCI, and in investigator-initiated clinical trials, which means we have little control over the conduct of such trials.

Our D-1MT product candidate is being studied in two Phase 1B/2 clinical trials co-sponsored by the National Cancer Institute. We are also currently providing clinical supply of our HyperAcute Melanoma cancer immunotherapy product candidate in support of a Phase 2 investigator-initiated clinical trial. We expect to continue to supply and otherwise support similar trials in the future. However, because we are not the sponsors of these trials, we do not control the protocols, administration or conduct of these trials and, as a result, are subject to risks associated with the way these types of trials are conducted, in particular should any problems arise. These risks include difficulties or delays in communicating with investigators or administrators, procedural delays and other timing issues and difficulties or differences in interpreting data.

If we cannot demonstrate the safety of our product candidates in preclinical and/or other non-clinical studies, we will not be able to initiate or continue clinical trials or obtain approval for our product candidates.

In order to move a product candidate not yet being tested in humans into a clinical trial, we must first demonstrate in preclinical testing that the product candidate is safe. Furthermore, in order to obtain approval, we must also demonstrate safety in various preclinical and non-clinical tests. We may not have conducted or may not conduct in the future the types of preclinical and other non-clinical testing ultimately required by regulatory authorities, or future preclinical tests may indicate that our product candidates are not safe for use in humans. Preclinical testing is expensive, can take many years and have an uncertain outcome. In addition, success in initial preclinical testing does not ensure that later preclinical testing will be successful. We may experience numerous unforeseen events during, or as a result of, the preclinical testing process, which could delay or prevent our ability to develop or commercialize our product candidates, including:

- our preclinical testing may produce inconclusive or negative safety results, which may require us to conduct additional preclinical testing or to abandon product candidates that we believed to be promising;
- our product candidates may have unfavorable pharmacology, toxicology or carcinogenicity;
- our product candidates may cause undesirable side effects; and
- the FDA or other regulatory authorities may determine that additional safety testing is required.

Any such events would increase our costs and could delay or prevent our ability to commercialize our product candidates, which could adversely impact our business, financial condition and results of operations.

Even if approved, the HyperAcute product candidates, D-1MT or any other product we may commercialize and market may be later withdrawn from the market or subject to promotional limitations.

We may not be able to obtain the labeling claims necessary or desirable for the promotion of our products. We may also be required to undertake post-marketing clinical trials. If the results of such post-marketing studies are not satisfactory, the FDA or a comparable agency in a foreign country may withdraw marketing authorization or may condition continued marketing on commitments from us that may be expensive and/or time consuming to fulfill. In addition, if we or others identify adverse side

effects after any of our products are on the market, or if manufacturing problems occur, regulatory approval may be withdrawn and reformulation of our products, additional clinical trials, changes in labeling of our products and additional marketing applications may be required. Any reformulation or labeling changes may limit the marketability of our products.

We will need to develop or acquire additional capabilities in order to commercialize any product candidates that obtain FDA approval, and we may encounter unexpected costs or difficulties in doing so.

We will need to acquire additional capabilities and effectively manage our operations and facilities to successfully pursue and complete future research, development and commercialization efforts. Currently, we have no experience in preparing applications for marketing approval, commercial-scale manufacturing, managing of large-scale information technology systems or managing a large-scale distribution system. We will need to add personnel and expand our capabilities, which may strain our existing managerial, operational, regulatory compliance, financial and other resources. To do this effectively, we must:

- train, manage and motivate a growing employee base;
- accurately forecast demand for our products; and
- expand existing operational, financial and management information systems.

We plan to increase our manufacturing capacity and seek FDA approval for our production process simultaneously with seeking approval for sale of our HyperAcute Pancreas product candidate. Should we not receive timely approval of our production process, our ability to produce the immunotherapy products following regulatory approval for sale could be delayed, which would further delay the period of time when we would be able to generate revenues from the sale of such products, if we are even able to generate revenues at all.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate significant product revenue.

We do not have a sales organization and have no experience in the sales and distribution of pharmaceutical products. There are risks involved with establishing our own sales capabilities and increasing our marketing capabilities, as well as entering into arrangements with third parties to perform these services. Developing an internal sales force is expensive and time consuming and could delay any product launch. On the other hand, if we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we market and sell any products that we develop ourselves.

We may establish our own specialty sales force and/or engage other biopharmaceutical or other healthcare companies with established sales, marketing and distribution capabilities to sell, market and distribute any future products. We may not be able to establish a specialty sales force or establish sales, marketing or distribution relationships on acceptable terms. Factors that may inhibit our efforts to commercialize any future products without strategic partners or licensees include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Because the establishment of sales, marketing and distribution capabilities depends on the progress towards commercialization of our product candidates, and because of the numerous risks and uncertainties involved with establishing those capabilities, we are unable to predict when, if ever, we will establish our own sales, marketing and distribution capabilities. If we are not able to partner with third parties and are unsuccessful in recruiting sales, marketing and distribution personnel or in building the necessary infrastructure, we will have difficulty commercializing our product candidates, which would adversely affect our business and financial condition.

**** Failure to attract and retain key personnel could impede our ability to develop our products and to obtain new collaborations or other sources of funding.***

Because of the specialized scientific nature of our business, our success is highly dependent upon our ability to attract and retain qualified scientific and technical personnel, consultants and advisors. We are highly dependent on the principal members of our scientific and management staff, particularly Dr. Charles J. Link, Jr. The loss of his services might significantly delay or prevent the achievement of our research, development, and business objectives. We do not maintain key-man life insurance with respect to any of our employees, nor do we intend to secure such insurance.

We will need to recruit a significant number of additional personnel in order to achieve our operating goals. In order to pursue our product development and marketing and sales plans, we will need to hire additional qualified scientific personnel to perform research and development, as well as personnel with expertise in clinical testing, government regulation, manufacturing, marketing and sales. We also rely on consultants and advisors to assist in formulating our research and development strategy and adhering to complex regulatory requirements. We face competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities and other research institutions. There can be no assurance that we will be able to attract and retain such individuals on acceptable terms, if at all. If the personnel that have contingently agreed to join us do not join us it will be difficult or impossible for us to execute our business plan in a timely manner. Additionally, our facilities are located in Iowa, which may make attracting and retaining qualified scientific and technical personnel from outside of Iowa difficult. We have a forgivable loan totaling $300,000 as of March 31, 2012, that is contingent on us creating jobs in Iowa. If we leave Iowa or fail to create the required number of jobs in Iowa, we may be required to pay back some or all of this loan. In addition, under our settlement agreement with the Iowa Economic Development Authority, or IEDA, we are obligated to maintain specific aspects of our business substantially in the State of Iowa while amounts remain payable pursuant to the settlement agreement. The failure to attract and retain qualified personnel, consultants and advisors could have a material adverse effect on our business, financial condition and results of operations.

Risks Relating to Manufacturing Activities

We have never manufactured our product candidates at commercial scale, and there can be no assurance that such products can be manufactured in compliance with regulations at a cost or in quantities necessary to make them commercially viable.

We have no experience in commercial-scale manufacturing, the management of large-scale information technology systems or the management of a large-scale distribution system. We may develop our manufacturing capacity in part by expanding our current facilities. This activity would require substantial additional funds and we would need to hire and train significant numbers of qualified employees to staff these facilities. We may not be able to develop commercial-scale manufacturing facilities that are sufficient to produce materials for additional later-stage clinical trials or commercial use.

If we are unable to manufacture or contract for a sufficient supply of our product candidates on acceptable terms, or if we encounter delays or difficulties in the scale-up of our manufacturing processes or our relationships with other manufacturers, our preclinical and human clinical testing schedule would be delayed. This in turn would delay the submission of product candidates for regulatory approval and thereby delay the market introduction and subsequent sales of any products that receive regulatory approval, which would have a material adverse effect on our business, financial condition and results of operations. Furthermore, we or our contract manufacturers must supply all necessary documentation in support of our Biologics License Application, or BLA, or our NDA, on a timely basis and must adhere to Good Laboratory Practice, or GLP, and cGMP regulations enforced by the FDA through its facilities inspection program. If these facilities cannot pass a pre-approval plant inspection, the FDA approval of the products will not be granted.

We and our contract manufacturers are subject to significant regulation with respect to manufacturing of our products.

All entities involved in the preparation of a therapeutic drug for clinical trials or commercial sale, including our existing contract manufacturer for D-1MT and the components used in the HyperAcute product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Our facilities and quality systems and the facilities and quality systems of some or all of our third party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of the HyperAcute product candidates, D-1MT or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of the HyperAcute product candidates, D-1MT or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

We currently rely on relationships with third-party contract manufacturers, which limits our ability to control the availability of, and manufacturing costs for, our product candidates in the near-term.

We will rely upon contract manufacturers for D-1MT, and for components of the HyperAcute product candidates, for commercial sale if any are approved for sale. Problems with any of our facilities or processes, or our contract manufacturers' facilities or processes, could prevent or delay the production of adequate supplies of antigen, components or finished HyperAcute product candidates or D-1MT. This could delay or reduce commercial sales and materially harm our business. We do not currently have experience with the manufacture of products at commercial scale, and may incur substantial costs to develop the capability to manufacture products at commercial scale. Any prolonged delay or interruption in the operations of our facilities or our contract manufacturers' facilities could result in cancellation of shipments, loss of components in the process of being manufactured or a shortfall in availability of a product. A number of factors could cause interruptions, including the inability of a supplier to provide raw materials, equipment malfunctions or failures, damage to a facility due to natural disasters, changes in regulatory requirements or standards that require modifications to our manufacturing processes, action by the regulatory authorities or by us that results in the halting or slowdown of production of components or finished product due to regulatory issues, a contract manufacturer going out of business or failing to produce product as contractually required or other similar factors. Because manufacturing processes are highly complex and are subject to a lengthy regulatory approval process, alternative qualified production capacity and sufficiently trained or qualified personnel may not be available on a timely or cost-effective basis or at all. Difficulties or delays in our contract manufacturers' production of drug substances could delay our clinical trials, increase our costs, damage our reputation and cause us to lose revenue and market share if we are unable to timely meet market demand for any products that are approved for sale.

Further, if our contract manufacturers are not in compliance with regulatory requirements at any stage, including post-marketing approval, we may be fined, forced to remove a product from the market and/or experience other adverse consequences, including delays, which could materially harm our business.

We use hazardous materials in our business and must comply with environmental laws and regulations, which can be expensive.

Our research and development involves the controlled use of hazardous materials, chemicals, various active microorganisms and volatile organic compounds, and we may incur significant costs as a result of the need to comply with numerous laws and regulations. We are subject to laws and regulations enforced by the FDA, the Drug Enforcement Agency, foreign health authorities and other regulatory requirements, including the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Food, Drug and Cosmetic Act, the Resource Conservation and Recovery Act, and other current and potential federal, state, local and foreign laws and regulations governing the use, manufacture, storage, handling and disposal of our products, materials used to develop and manufacture our product candidates, and resulting waste products. Although we believe that our safety procedures for handling and disposing of such materials, and for killing any unused microorganisms before disposing of them, comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, we could be held liable for any damages that result and any such liability could exceed our resources.

We replicate all biological cells for our products internally and utilize a single manufacturing site to manufacture our clinical product candidates. Any disruption in the operations of our manufacturing facility would have a significant negative impact on our ability to manufacture products for clinical testing and would result in increased costs and losses.

We have thus far elected to replicate all biological cells for our products internally using a complex process. The disruption of our operations could result in manufacturing delays due to the inability to purchase the cell lines from outside sources. We have only one manufacturing facility in which we can manufacture clinical products. In the event of a physical catastrophe at our manufacturing or laboratory facilities, we could experience costly delays in reestablishing manufacturing capacity, due to a lack of redundancy in manufacturing capability.

Our current manufacturing facility contains highly specialized equipment and utilizes complicated production processes developed over a number of years, which would be difficult, time-consuming and costly to duplicate. Any prolonged disruption in the operations of our manufacturing facility would have a significant negative impact on our ability to manufacture products for clinical testing on our own and would cause us to seek additional third-party manufacturing contracts, thereby increasing our development costs. We may suffer losses as a result of business interruptions that exceed the coverage available under our insurance policies or any losses may be excluded under our insurance policies. Certain events, such as natural disasters, fire, political disturbances, sabotage or business accidents, which could impact our current or future facilities, could have a significant negative impact on our operations by disrupting our product development efforts until such time as we are able to repair our facility or put in place third-party contract manufacturers to assume this manufacturing role.

We recently transferred our manufacturing operation to a new facility. We have experienced bacterial and mycoplasm contaminations in lots produced at the previous facility and we destroyed the contaminated lots and certain overlapping lots. We may have contaminated lots at our new facility and we will destroy any contaminated lots that we detect.

Our facilities are located in areas where floods and tornados are known to occur, and the occurrence of a flood, tornado or other catastrophic disaster could damage our facilities and equipment, which could cause us to curtail or cease operations.

Our facilities are located in Ames, Iowa, which is susceptible to floods and tornados, and our facilities are therefore vulnerable to damage or disruption from floods and tornados. We are also vulnerable to damage from other types of disasters, such as power loss, fire and similar events. If any disaster were to occur, our ability to operate our business could be seriously impaired. We currently carry business personal property insurance in the amount of $6.25 million in the aggregate, but this policy does not cover disasters such as floods and earthquakes. We may not have adequate insurance to cover our losses resulting from disasters or other similar significant business interruptions, and we do not plan to purchase additional insurance to cover such losses due to the cost of obtaining such coverage. Any significant losses that are not recoverable under our insurance policies could seriously impair our business and financial condition.

Risks Relating to Regulation of Our Industry

The industry within which we operate and our business are subject to extensive regulation, which is costly, time consuming and may subject us to unanticipated delays.

The research, design, testing, manufacturing, labeling, marketing, distribution and advertising of biologic and pharmaceutical products such as our product candidates are subject to extensive regulation by governmental regulatory authorities in the United States and other countries. The drug development and approval process is generally lengthy, expensive and subject to unanticipated delays. Data obtained from preclinical and clinical testing are subject to varying interpretations that could delay, limit or prevent regulatory approval. In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of development and regulatory review of each submitted application for approval. To obtain approval for a product candidate, we must demonstrate to the satisfaction of the regulatory authorities that the product candidate is safe, pure, potent and effective, which typically takes several years or more depending upon the type, complexity and novelty of the product and requires the expenditure of substantial resources.

There can be no assurance that we will not encounter problems in clinical trials that would cause us or the regulatory authorities to delay or suspend clinical trials. Any such delay or suspension could have a material adverse effect on our business, financial condition and results of operations. There can be no assurance that clinical studies for any of our product candidates currently under development will be completed successfully or within any specified time period, if at all. Further, there can also be no assurance that such testing will show any product to be safe, pure, potent or effective. There can be no assurance that we will not encounter problems in clinical trials that will cause us to delay or suspend clinical trials.

Regardless of how much time and resources we devote to development of a product candidate, there can be no assurance that regulatory approval will be obtained for that product candidate. To date, the FDA has approved only one active cellular cancer immunotherapy product, even though several have been, and currently are in, clinical development. Further, even if such regulatory approval is obtained, we, our products and any contract manufacturers or commercial collaborators of ours will be subject to continual regulatory review in both the United States and other countries. Later discovery of previously unknown problems with regard to a product, distributor or manufacturer may result in restrictions, including withdrawal of the product from the market and/or disqualification or decertification of the distributor or manufacturer.

We cannot predict when, if ever, we might submit for regulatory review our product candidates currently under development. Once we submit our potential products for review, there can be no assurance that regulatory approvals for any pharmaceutical products developed by us will be granted on a timely basis, if at all.

The FDA and comparable agencies in foreign countries impose substantial requirements on the introduction of new biologic and pharmaceutical products through lengthy and detailed preclinical and clinical testing procedures, sampling activities and other costly and time-consuming compliance procedures. Clinical trials are vigorously regulated and must meet requirements for FDA review and oversight and requirements under GCP guidelines. A new drug may not be marketed in the United States until the FDA has approved it. There can be no assurance that we will not encounter delays or rejections or that the FDA will not make policy changes during the period of product development and FDA regulatory review of each submitted BLA and NDA. A delay in obtaining or failure to obtain such approvals would have a material adverse effect on our business, financial condition and results of operations. Even if regulatory approval were obtained, it would be limited as to the indicated

uses for which the product may be promoted or marketed. A marketed product, its manufacturer and the facilities in which it is manufactured are subject to continual review and periodic inspections. If marketing approval is granted, we would be required to comply with FDA requirements for manufacturing, labeling, advertising, record keeping and reporting of adverse experiences and other information. In addition, we would be required to comply with federal and state anti-kickback and other health care fraud and abuse laws that pertain to the marketing of pharmaceuticals. Failure to comply with regulatory requirements and other factors could subject us to regulatory or judicial enforcement actions, including product recalls or seizures, injunctions, withdrawal of the product from the market, civil penalties, criminal prosecution, refusals to approve new products and withdrawals of existing approvals, as well as enhanced product liability exposure, any of which could have a material adverse effect on our business, financial condition and results of operations. Sales of our products outside the United States will be subject to foreign regulatory requirements governing clinical trials, marketing approval, manufacturing and pricing. Non-compliance with these requirements could result in enforcement actions or penalties or could delay introduction of our products in certain countries.

The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement outside the United States vary greatly from country to country. The time required to obtain approvals outside the United States may differ from that required to obtain FDA approval. We may not obtain foreign regulatory approvals on a timely basis, or at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other countries or by the FDA and foreign regulatory authorities could require additional testing. Failure to comply with these regulatory requirements or obtain required approvals could impair our ability to develop foreign markets for our products and may have a material adverse effect on our results of operations and financial condition.

We are also subject to laws generally applicable to businesses, including but not limited to, federal, state and local regulations relating to wage and hour matters, employee classification, mandatory healthcare benefits, unlawful workplace discrimination and whistle-blowing. Any actual or alleged failure to comply with any regulation applicable to our business or any whistle-blowing claim, even if without merit, could result in costly litigation, regulatory action or otherwise harm our business, results of operations, financial condition, cash flow and future prospects.

The availability and amount of reimbursement for our product candidates, if approved, and the manner in which government and private payors may reimburse for our potential product, are uncertain.

In both United States and foreign markets, sales of our proposed products will depend in part on the availability of reimbursement from third-party payors such as government health administration authorities, private health insurers and other organizations. Our future levels of revenues and profitability may be affected by the continuing efforts of governmental and third party payors to contain or reduce the costs of health care. We cannot predict the effect that private sector or governmental health care reforms may have on our business, and there can be no assurance that any such reforms will not have a material adverse effect on our business, financial condition and results of operations.

In addition, in both the United States and elsewhere, sales of prescription drugs are dependent in part on the availability of reimbursement to the consumer from third-party payors, such as government and private insurance plans. Third-party payors are increasingly challenging the price and cost-effectiveness of medical products and services. Significant uncertainty exists as to the reimbursement status of newly approved health care products. There can be no assurance that our proposed products will be considered cost-effective or that adequate third-party reimbursement will be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Legislation and regulations affecting the pricing of pharmaceuticals may change before any of our proposed products are approved for marketing. Adoption of such legislation could further limit reimbursement for medical products and services. As a result, we may elect not to market future products in certain markets.

Moreover, while we are in clinical trials, we will not be reimbursed for any of our materials used during the clinical trials.

The biopharmaceutical industry is subject to significant regulation and oversight in the United States, in addition to approval of products for sale and marketing.

In addition to FDA restrictions on marketing of biopharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the biopharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes.

The federal health care program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for purchasing, leasing, ordering, or arranging for the

purchase, lease, or order of any health care item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to get a false claim paid. Recently, several pharmaceutical and other health care companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of marketing of the product for unapproved, and thus non-reimbursable, uses. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Sanctions under these federal and state laws may include civil monetary penalties, exclusion of a manufacturer’s products from reimbursement under government programs, criminal fines and imprisonment.

Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of these laws, which could have a material adverse effect on our business, financial condition and results of operations.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. We expect to face pricing pressure globally from managed care organizations, institutions and government agencies and programs, which could negatively affect the sales and profit margins for our HyperAcute product candidates, D1-MT or any other of our product candidates that are approved for marketing.

In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reduce healthcare costs. Most recently, in March 2010 the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA, was enacted, which includes measures to significantly change the way health care is financed by both governmental and private insurers. Among the provisions of the PPACA of greatest importance to the pharmaceutical and biotechnology industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- requirements to report certain financial arrangements with physicians and others, including reporting any “transfer of value” made or distributed to prescribers and other healthcare providers and reporting any investment interests held by physicians and their immediate family members during each calendar year beginning in 2012, with reporting starting in 2013;
- a licensure framework for follow-on biologic products, also known as biosimilars;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- creation of the Independent Payment Advisory Board which, beginning in 2014, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law even if Congress does not act on the recommendations; and
- establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Many of the details regarding the implementation of the PPACA are yet to be determined, and at this time, it remains unclear the full effect that the PPACA would have on our business. The regulations that are ultimately promulgated and their implementation are likely to have considerable impact on the way we conduct our business and may require us to change current strategies.

Individual states have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts,

restrictions on certain product access, and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce ultimate demand for our products or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

In addition, given recent federal and state government initiatives directed at lowering the total cost of healthcare, Congress and state legislatures will likely continue to focus on healthcare reform, the cost of prescription drugs and biologics and the reform of the Medicare and Medicaid programs. While we cannot predict the full outcome of any such legislation, it may result in decreased reimbursement for drugs and biologics, which may further exacerbate industry-wide pressure to reduce prescription drug prices. This could harm our ability to generate revenues. In addition, legislation has been introduced in Congress that, if enacted, would permit more widespread importation or re-importation of pharmaceutical products from foreign countries into the United States, including from countries where the products are sold at lower prices than in the United States. Such legislation, or similar regulatory changes, could put competitive pressure on our ability to profitably price our products, which, in turn, could adversely affect our business, results of operations, financial condition and prospects. Alternatively, in response to legislation such as this, we might elect not to seek approval for or market our products in foreign jurisdictions in order to minimize the risk of re-importation, which could also reduce the revenue we generate from our product sales. It is also possible that other legislative proposals having similar effects will be adopted.

Furthermore, regulatory authorities' assessment of the data and results required to demonstrate safety and efficacy can change over time and can be affected by many factors, such as the emergence of new information, including on other products, changing policies and agency funding, staffing and leadership. We cannot be sure whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects. For example, average review times at the FDA for marketing approval applications have fluctuated over the last ten years, and we cannot predict the review time for any of our submissions with any regulatory authorities. In addition, review times can be affected by a variety of factors, including budget and funding levels and statutory, regulatory and policy changes.

Financial Risks

**** We have a history of net losses. We expect to continue to incur increasing net losses for the foreseeable future, and we may never achieve or maintain profitability.***

We are not profitable and have incurred significant net losses in each year since our inception, including net losses of $18.1 million, $16.2 million and $10.0 million for the years ended December 31, 2011, 2010 and 2009, respectively and a net loss of $4.8 million for the three months ending March 31, 2012. As of March 31, 2012, we had an accumulated deficit of $86.4 million. Our losses have resulted principally from costs incurred in our discovery and development activities. We anticipate that our operating losses will substantially increase over the next several years as we expand our discovery, research and development activities, including the Phase 2 and Phase 3 clinical development of the HyperAcute product candidates and Phase 2 clinical development of D-1MT.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development and commercialization, we are unable to accurately predict the timing or amount of future expenses or when, or if, we will be able to achieve or maintain profitability. Currently, we have no products approved for commercial sale, and to date we have not generated any product revenue. We have financed our operations primarily through the sale of equity securities, government grants, economic development loans and capital lease and equipment financing. The size of our future net losses will depend, in part, on the rate of growth or contraction of our expenses and the level and rate of growth, if any, of our revenues. Our ability to achieve profitability is dependent on our ability, alone or with others, to complete the development of our products successfully, obtain the required regulatory approvals, manufacture and market our proposed products successfully or have such products manufactured and marketed by others and gain market acceptance for such products. There can be no assurance as to whether or when we will achieve profitability.

We will require substantial additional capital in the future. If additional capital is not available, we will have to delay, reduce or cease operations.

Development of our HyperAcute product candidates, D-1MT and any other product candidates will require substantial additional funds to conduct research, development and clinical trials necessary to bring such product candidates to market and to establish manufacturing, marketing and distribution capabilities. Our future capital requirements will depend on many factors, including, among others:

- the scope, rate of progress, results and costs of our preclinical studies, clinical trials and other research and development activities;
- the scope, rate of progress and costs of our manufacturing development and commercial manufacturing activities;
- the cost, timing and outcomes of regulatory proceedings (including FDA review of any BLA or NDA we file);
- payments required with respect to development milestones we achieve under our in-licensing agreements;
- the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;
- the costs associated with commercializing our product candidates, if they receive regulatory approval;
- the cost and timing of developing our ability to establish sales and marketing capabilities;
- competing technological efforts and market developments;
- changes in our existing research relationships;
- our ability to establish collaborative arrangements to the extent necessary;
- revenues received from any existing or future products; and
- payments received under any future strategic partnerships.

We anticipate that we will continue to generate significant losses for the next several years as we incur expenses to complete our clinical trial programs for our product candidates, build commercial capabilities, develop our pipeline and expand our corporate infrastructure. We believe that our existing cash and cash equivalents and marketable securities, will allow us to fund our operating plan through at least the end of 2013. However, our operating plan may change as a result of factors currently unknown to us.

There can be no assurance that our revenue and expense forecasts will prove to be accurate, and any change in the foregoing assumptions could require us to obtain additional financing earlier than anticipated. There is a risk of delay or failure at any stage of developing a product candidate, and the time required and costs involved in successfully accomplishing our objectives cannot be accurately predicted. Actual drug research and development costs could substantially exceed budgeted amounts, which could force us to delay, reduce the scope of or eliminate one or more of our research or development programs.

We are party to license agreements with various parties pursuant to which we have obtained licenses to certain patents, patent applications and other intellectual property related to our product candidates and product development efforts. Pursuant to most of these license agreements, we are obligated to make aggregate payments ranging from around $200,000 to $2.8 million per license (and in some cases, for each product candidate in such license) upon achievement of development and regulatory approval milestones specified in the applicable license. The timing of our achievement of these events and corresponding milestone payments to our licensors are subject to factors relating to the clinical and regulatory development and commercialization of our product candidates, many of which are beyond our control. We may become obligated to make a milestone payment when we do not have the cash on hand to make such payment, which could require us to delay our clinical trials, curtail our operations, scale back our commercialization or marketing efforts or seek funds to meet these obligations on terms unfavorable to us.

We may never be able to generate a sufficient amount of product revenue to cover our expenses. Until we do, we expect to seek additional funding through public or private equity or debt financings, collaborative relationships, capital lease transactions or other available financing transactions. However, there can be no assurance that additional financing will be available on acceptable terms, if at all, and such financings could be dilutive to existing stockholders. Moreover, in the event that additional funds are obtained through arrangements with collaborative partners, such arrangements may require us to relinquish rights to certain of our technologies, product candidates or products that we would otherwise seek to develop or commercialize ourselves.

If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our research or development programs. Our failure to obtain adequate financing when needed and on acceptable terms would have a material adverse effect on our business, financial condition and results of operations.

**** We have outstanding debt that may be accelerated as early as March 10, 2015.***

On March 26, 2012, we entered into a settlement agreement with the Iowa Economic Development Authority, or the IEDA, which is the successor organization to the IDED. Under the terms of the settlement agreement the IDED forgiveable loan agreement was terminated and we were thereby released from its job creation, project expenditure, royalty and other requirements in exchange for agreeing to pay a minimum of 0.50% royalties on all gross revenues of any products we bring to market with a cumulative maximum royalty amount due of $6.8 million. Additionally, under the settlement agreement, the IEDA released its security interest in our assets. The obligation to maintain our business in the State of Iowa while amounts remain outstanding is a continuing obligation under the terms of the settlement agreement.

In March 2010, we entered into a $400,000 forgivable loan agreement with the City of Ames, Iowa and the Ames Chamber of Commerce, in order to help finance the construction of new facilities within the Ames city limits. In the absence of a default, there are no principal or interest payments due until the expected completion date for the project, which is March 10, 2015. The project calls for us to create or retain at least 70 full-time jobs located in Ames, Iowa as of March 10, 2012 and to create or retain at least 150 full-time positions located in Ames, Iowa as of March 10, 2015. The agreement also calls for us to enter into a five-year building lease with option for extension for an additional five years of not less than 20,000 square feet within the corporate limits of the City of Ames by March 10, 2015. If, as of March 10, 2015, we have fulfilled the terms of the loan agreement, the loan will be forgiven. If on March 10, 2012 and March 10, 2015, we have failed to create or retain at least 70 full-time jobs and 150 full-time jobs in Ames, Iowa, respectively, we will be required to repay approximately $3,100 per job not created or retained following the respective date. As of December 31, 2011, we had created or retained an aggregate of 69 full-time jobs in Ames, Iowa, and prior to March 10, 2012, we had created or retained at least 70 full-time jobs in Ames, Iowa. As of March 31, 2012, $300,000 of the total $400,000 forgivable loan was advanced to us with the final $100,000 pending certification to the City of Ames regarding the creation of a threshold level of jobs. In the event of default, including failure to repay any amounts under the loan when due, we will be required to repay the note including 6.5% interest per annum beginning at the date of default.

We have not met all the job creation requirements of the City of Ames loan as of the present date. If we cannot or do not comply with these and all other requirements under this loan, we may be obligated to pay principal and interest on this loan immediately. If we are unable to meet our obligations to service our debt and fund our business, we may be forced to reduce or delay capital expenditures, seek additional debt financing or equity capital, restructure or refinance our debt or sell assets. We cannot assure you that we would be able to obtain additional financing, refinance existing debt or sell assets on satisfactory terms or at all.

Even though we have received governmental support in the past, we may not continue to receive support at the same level or at all.

We have received significant financial assistance from state and local governments, primarily in the form of forgivable loans. There can be no assurance that we will continue to receive the same level of assistance from these or other government agencies, if at all.

Through our subsidiary, BioProtection Systems Corporation, or BPS, we also have ongoing contracts and grants with the United States Department of Defense and National Institutes of Health, respectively. The termination of a United States government grant, contract or relationship as a result of our failure to satisfy any of our obligations under the grants or contracts would have a negative impact on our operations and harm our reputation and ability to procure government contracts. Additionally, there can be no assurance that we will secure comparable contracts with, or grants from, the United States government in the future.

Risks Relating to Competitive Factors

We compete in an industry characterized by extensive research and development efforts and rapid technological progress. New discoveries or commercial developments by our competitors could render our potential products obsolete or non-competitive.

New developments occur and are expected to continue to occur at a rapid pace, and there can be no assurance that discoveries or commercial developments by our competitors will not render some or all of our potential products obsolete or non-competitive, which would have a material adverse effect on our business, financial condition and results of operations.

We expect to compete with fully integrated and well-established pharmaceutical and biotechnology companies in the near and long term. Most of these companies have substantially greater financial, research and development, manufacturing and marketing experience and resources than we do and represent substantial long-term competition for us. Such companies may succeed in discovering and developing pharmaceutical products more rapidly than we do or pharmaceutical products that are safer, more effective or less costly than any that we may develop. Such companies also may be more successful than we are in production and marketing. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and established biotechnology companies. Academic institutions, governmental agencies and other public and private research organizations also conduct clinical trials, seek patent protection and establish collaborative arrangements for the development of oncology products.

We will face competition based on product efficacy and safety, the timing and scope of regulatory approvals, availability

of supply, marketing and sales capabilities, reimbursement coverage, price and patent position. There can be no assurance that our competitors will not develop safer and more effective products, commercialize products earlier than we do, or obtain patent protection or intellectual property rights that limit our ability to commercialize our products.

There can be no assurance that our issued patents or pending patent applications, if issued, will not be challenged, invalidated or circumvented or that the rights granted thereunder will provide us with proprietary protection or a competitive advantage.

**** Our competitors may develop and market products that are less expensive, more effective, safer or reach the market sooner than our product candidates, which may diminish or eliminate the commercial success of any products we may commercialize.***

The biopharmaceutical industry is highly competitive. There are many public and private biopharmaceutical companies, public and private universities and research organizations actively engaged in the discovery and research and development of products for cancer. Given the significant unmet patient need for new therapies, oncology is an area of focus for large and small companies as well as research institutions. As a result, there are and will likely continue to be extensive research and substantial financial resources invested in the discovery and development of new oncology products. In addition, there are a number of multinational pharmaceutical companies and large biotechnology companies currently marketing or pursuing the development of products or product candidates targeting the same cancer indications as our product candidates, and several large public biopharmaceutical companies have approved or are developing cancer immunotherapy products, including Dendreon Corporation, Bristol- Myers Squibb Company, GlaxoSmithKline plc, Merck & Co., Merck KGaA and Sanofi-Aventis.

There are several marketed products indicated for pancreatic cancer, including Eli Lilly and Company's Gemzar®, Astellas Pharma's Tarceva®, Teva Pharmaceutical Industries Limited's streptozocin, and fluorouracil, or 5-FU, and mitomycin which are marketed by several generic pharmaceutical firms. There are numerous marketed therapeutics indicated for NSCLC, including Roche AG's Avastin®, Eli Lilly's Alimta® and Gemzar, Astellas Pharma's Tarceva, AstraZeneca's Iressa®, and Sanofi-Aventis' Taxotere and Eloxatin, as well as generically available platinum-based chemotherapeutics (cisplatin and carboplatin) and mitotic inhibitors (paclitaxel and venorelbine). There are also several marketed therapeutics indicated for advanced melanoma, including Merck's Intron A and Novartis/Prometheus Laboratories' Proleukin®, as well as cisplatin and dacarbazine, which are available generically. Bristol- Myers Squibb's immunotherapy ipilimumab was recently approved by the FDA as was Roche/Daiichi Sankyo's drug, vemurafenid.

In addition, there are a number of companies with active clinical trials ongoing in pancreatic cancer including AB Science SA, Amgen Inc., Astellas Pharma, BioSante Pharmaceuticals, Inc., Celgene Corporation, Immunomedics, Inc., Clovis Oncology, Inc., Lorus Therapeutics Inc., Sanofi-Aventis and Threshold Pharmaceuticals, Inc., a number of companies with active clinical trials ongoing in NSCLC, including Abbott Laboratories, Amgen, Bristol-Myers Squibb, Boehringer Ingelheim, BioNumerik Pharmaceuticals, Inc., Celgene, GlaxoSmithKline, Merrimack Pharmaceuticals, Inc., NovaRx Corporation, Onyx Pharmaceuticals, Inc., Pfizer Inc. and Regeneron Pharmaceuticals, Inc., and a number of companies with active clinical trials ongoing in advanced melanoma, including Amgen, Astellas Pharma, Eli Lilly, Onyx, Roche, Synta Pharmaceuticals Corp., and Vical Inc. among other companies.

Many of our competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of drugs, obtaining FDA and other regulatory approvals, and the commercialization of those products. Accordingly, our competitors may be more successful in obtaining approval for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render our product candidates obsolete or non-competitive before we can recover the significant expenses of developing and commercializing any of our product candidates. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available.

There are many different approaches to using immunotherapies to treat cancer, including anti-idiotype, whole cell, DNA, peptide/antigen, viral, tumor lysate, shed antigens, and dendritic cell. Cancer immunotherapies are also distinguished by whether or not they are derived from autologous or allogeneic sources. Each of the various approaches to cancer immunotherapy have potential advantages and disadvantages based on factors such as their immunostimulatory mechanisms, formulation characteristics, manufacturing requirements, and treatment regimens.

We also compete with other clinical-stage companies and institutions for clinical trial participants, which could reduce our ability to recruit participants for our clinical trials. Delay in recruiting clinical trial participants could adversely affect our ability to bring a product to market prior to our competitors. Further, research and discoveries by others may result in breakthroughs that render our HyperAcute product candidates, D-1MT or our other potential products obsolete even before

they begin to generate any revenue.

In addition, our competitors may obtain patent protection or FDA approval and commercialize products more rapidly than we do, which may impact future sales of any of our products that receive marketing approval. If the FDA approves the commercial sale of any of our products, we will also be competing with respect to marketing capabilities and manufacturing efficiency, areas in which we have limited or no experience. We expect that competition among products approved for sale will be based, among other things, on product efficacy, price, safety, reliability, availability, patent protection, and sales, marketing and distribution capabilities. Our profitability and financial position will suffer if our products receive regulatory approval, but cannot compete effectively in the marketplace.

If any of our product candidates are approved and commercialized, we may face competition from generic products if the product candidate is a small molecule drug, or biosimilars if the product candidate is a biologic. The route to market for generic versions of small molecule drugs was established with the passage of the Hatch-Waxman Amendments in 1984 and for biosimilars with the passage of the PPACA in March 2010. The PPACA establishes a pathway for the FDA approval of follow-on biologics and provides 12 years of marketing exclusivity for reference products and an additional six months of exclusivity if pediatric studies are conducted. In Europe, the European Medicines Agency has issued guidelines for approving products through an abbreviated pathway, and biosimilars have been approved in Europe. If a biosimilar version of one of our potential products were approved in the United States or Europe, it could have a negative effect on sales and gross profits of the potential product and our financial condition.

Our biodefense product candidates face significant competition for United States government funding for both development and procurement of medical countermeasures for biological, chemical and nuclear threats, diagnostic testing systems and other emergency preparedness countermeasures. Competitors include Emergent BioSolutions, SIGA Technologies, AVI Biopharma, Pharmathene, Acambis, Bavarian Nordic AS, and Novartis. Academic institutions, government agencies, private research organizations and public research organizations are also conducting research and filing patents toward commercialization of products. In addition, we may not be able to compete effectively if our product candidates do not satisfy government procurement requirements with respect to biodefense products.

Our products may not be accepted in the marketplace; therefore, we may not be able to generate significant revenue, if any.

Even if the HyperAcute product candidates, D-1MT or any of our other potential products are approved for sale, physicians and the medical community may not ultimately use them or may use them only in applications more restricted than we expect. Our products, if successfully developed, will compete with a number of traditional products and immunotherapies manufactured and marketed by major pharmaceutical and other biotechnology companies. Our products will also compete with new products currently under development by such companies and others. Physicians will prescribe a product only if they determine, based on experience, clinical data, side effect profiles and other factors, that it is beneficial as compared to other products currently in use. Many other factors influence the adoption of new products, including marketing and distribution restrictions, course of treatment, adverse publicity, product pricing, the views of thought leaders in the medical community and reimbursement by government and private third party payors.

Risks Relating to Our Arrangements with Third Parties

We rely on third parties to conduct our preclinical studies and our clinical trials. If these third parties do not perform as contractually required or expected, we may not be able to obtain regulatory approval for our product candidates, or we may be delayed in doing so.

We do not have the ability to conduct preclinical studies or clinical trials independently for our product candidates. We must rely on third parties, such as contract research organizations, medical institutions, academic institutions, clinical investigators and contract laboratories, to conduct our preclinical studies and clinical trials. We are responsible for confirming that our preclinical studies are conducted in accordance with applicable regulations and that each of our clinical trials is conducted in accordance with its general investigational plan and protocol. The FDA requires us to comply with GLP for conducting and recording the results of our preclinical studies and cGCP for conducting, monitoring, recording and reporting the results of clinical trials, to assure that data and reported results are accurate and that the clinical trial participants are adequately protected. Our reliance on third parties does not relieve us of these responsibilities. If the third parties conducting our clinical trials do not perform their contractual duties or obligations, do not meet expected deadlines, fail to comply with cGCP, do not adhere to our clinical trial protocols or otherwise fail to generate reliable clinical data, we may need to enter into new arrangements with alternative third parties and our clinical trials may be more costly than expected or budgeted, extended, delayed or terminated or may need to be repeated, and we may not be able to obtain regulatory approval for or commercialize the product candidate being tested in such trials.

Further, if our contract manufacturers are not in compliance with regulatory requirements at any stage, including post-marketing approval, we may be fined, forced to remove a product from the market and/or experience other adverse consequences, including delays, which could materially harm our business.

If we fail to enter into any needed collaboration agreements for our product candidates, we may be unable to commercialize them effectively or at all.

To successfully commercialize the HyperAcute product candidates or D-1MT, we will need substantial financial resources as well as expertise and physical resources and systems. We may elect to develop some or all of these physical resources and systems and expertise ourselves or we may seek to collaborate with another company that can provide some or all of such physical resources and systems as well as financial resources and expertise. Such collaborations are complex and any potential discussions may not result in a definitive agreement for many reasons. For example, whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of our clinical trials, the potential market for the HyperAcute product candidates and D-1MT, the costs and complexities of manufacturing and delivering the HyperAcute product candidates and D-1MT to patients, the potential of competing products, the existence of uncertainty with respect to ownership or the coverage of our technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. If we were to determine that a collaboration for the HyperAcute product candidates or D-1MT is necessary and were unable to enter into such a collaboration on acceptable terms, we might elect to delay or scale back the commercialization of the HyperAcute product candidates or D-1MT in order to preserve our financial resources or to allow us adequate time to develop the required physical resources and systems and expertise ourselves.

If we enter into a collaboration agreement we consider acceptable, the collaboration may not proceed as quickly, smoothly or successfully as we plan. The risks in a collaboration agreement include the following:

- the collaborator may not apply the expected financial resources, efforts or required expertise in developing the physical resources and systems necessary to successfully commercialize the HyperAcute product candidates or D-1MT;
- the collaborator may not invest in the development of a sales and marketing force and the related infrastructure at levels that ensure that sales of the HyperAcute product candidates or D-1MT reach their full potential;
- disputes may arise between us and a collaborator that delay the commercialization or adversely affect its sales or profitability of the HyperAcute product candidates or D-1MT; or
- the collaborator may independently develop, or develop with third parties, products that could compete with the HyperAcute product candidates or D-1MT.

If we enter into one or more collaborations for our HyperAcute product candidates, D-1MT or any of our other product candidates, we will be dependent on our collaborators' performance of their responsibilities and their cooperation with us. Our collaborators may not perform their obligations under our agreements with them or otherwise cooperate with us. We cannot control whether our collaborators will devote the necessary resources to the activities contemplated by our collaborative agreements, nor can we control the timing of their performance. Our collaborators may choose to pursue existing or alternative technologies in preference to those being developed in collaboration with us. Disputes may arise between us and our collaborators that delay the development and commercialization of our product candidates that are difficult and costly to resolve, or may not be resolved. In addition, a collaborator for the HyperAcute product candidates or D-1MT may have the right to terminate the collaboration at its discretion. Any termination may require us to seek a new collaborator, which we may not be able to do on a timely basis, if at all, or require us to delay or scale back the commercialization efforts. The occurrence of any of these events could adversely affect the commercialization of the HyperAcute product candidates or D-1MT and materially harm our business and stock price by delaying the sale of any product that may be approved by the FDA, by slowing the growth of such sales, by reducing the profitability of the product and/or by adversely affecting the reputation of the product.

We rely on a single manufacturer for a key component used in the manufacture of our HyperAcute immunotherapy product candidates, which could impair our ability to manufacture and supply our products.

The manufacturing process for our HyperAcute immunotherapy product candidates has one component that we obtain from a single manufacturer. If we utilize an alternative manufacturer, we may be required to demonstrate comparability of the drug product before releasing the product for clinical use. The loss of our current supplier could result in manufacturing delays for the component substitution, and we may need to accept changes in terms or price from our existing supplier in order to avoid such delays.

We may explore strategic partnerships that may never materialize or may fail.

We may, in the future, periodically explore a variety of possible strategic partnerships in an effort to gain access to additional product candidates or resources. At the current time, we cannot predict what form such a strategic partnership might take. We are likely to face significant competition in seeking appropriate strategic partners, and these strategic partnerships can be complicated and time consuming to negotiate and document. We may not be able to negotiate strategic partnerships on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any additional strategic partnerships because of the numerous risks and uncertainties associated with establishing strategic partnerships.

If we enter into one or more strategic partnerships, we may be required to relinquish important rights to and control over the development of our product candidates or otherwise be subject to unfavorable terms.

Any future strategic partnerships we enter into could subject us to a number of risks, including:

- we may be required to undertake the expenditure of substantial operational, financial and management resources;
- we may be required to issue equity securities that would dilute our existing stockholders' percentage ownership;
- we may be required to assume substantial actual or contingent liabilities;
- we may not be able to control the amount and timing of resources that our strategic partners devote to the development or commercialization of our product candidates;
- strategic partners may delay clinical trials, provide insufficient funding, terminate a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new version of a product candidate for clinical testing;
- strategic partners may not pursue further development and commercialization of products resulting from the strategic partnering arrangement or may elect to discontinue research and development programs;
- strategic partners may not commit adequate resources to the marketing and distribution of our product candidates, limiting our potential revenues from these products;
- disputes may arise between us and our strategic partners that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management's attention and consumes resources;
- strategic partners may experience financial difficulties;
- strategic partners may not properly maintain or defend our intellectual property rights or may use our proprietary information in a manner that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- business combinations or significant changes in a strategic partner's business strategy may also adversely affect a strategic partner's willingness or ability to complete its obligations under any arrangement;
- strategic partners could decide to move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors; and
- strategic partners could terminate the arrangement or allow it to expire, which would delay the development and may increase the cost of developing our product candidates.

Risks Relating to Protecting Our Intellectual Property

If we are unable to protect our proprietary rights or to defend against infringement claims, we may not be able to compete effectively or operate profitably.

Our success will depend, in part, on our ability to obtain patents, operate without infringing the proprietary rights of others and maintain trade secrets, both in the United States and other countries. Patent matters in the biotechnology and pharmaceutical industries can be highly uncertain and involve complex legal and factual questions. Accordingly, the validity, breadth, and enforceability of our patents and the existence of potentially blocking patent rights of others cannot be predicted, either in the United States or in other countries.

There can be no assurance that we will discover or develop patentable products or processes or that patents will issue from any of the currently pending patent applications or that claims granted on issued patents will be sufficient to protect our technology or adequately cover the actual products we may actually sell. Potential competitors or other researchers in the field may have filed patent applications, been issued patents, published articles or otherwise created prior art that could restrict or block our efforts to obtain additional patents. There also can be no assurance that our issued patents or pending patent applications, if issued, will not be challenged, invalidated, rendered unenforceable or circumvented or that the rights granted hereunder will provide us with proprietary protection or competitive advantages. Our patent rights also depend on our

compliance with technology and patent licenses upon which our patent rights are based and upon the validity of assignments of patent rights from consultants and other inventors that were, or are, not employed by us.

In addition, competitors may manufacture and sell our potential products in those foreign countries where we have not filed for patent protection or where patent protection may be unavailable, not obtainable or ultimately not enforceable. In addition, even where patent protection is obtained, third party competitors may challenge our patent claims in the various patent offices, for example via opposition in the European Patent Office or reexamination or interference proceedings in the United States Patent and Trademark Office, or USPTO. The ability of such competitors to sell such products in the United States or in foreign countries where we have obtained patents is usually governed by the patent laws of the countries in which the product is sold.

We will incur significant ongoing expenses in maintaining our patent portfolio. Should we lack the funds to maintain our patent portfolio or to enforce our rights against infringers, we could be adversely impacted. Even if claims of infringement are without merit, any such action could divert the time and attention of management and impair our ability to access additional capital and/or cost us significant funds to defend.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The United States Patent and Trademark Office is currently developing regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act will not become effective until one year or 18 months after its enactment. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

We may be subject to litigation with respect to the ownership and use of intellectual property that will be costly to defend or pursue and uncertain in its outcome.

Our success also will depend, in part, on our refraining from infringing patents or otherwise violating intellectual property owned or controlled by others. Pharmaceutical companies, biotechnology companies, universities, research institutions, and others may have filed patent applications or have received, or may obtain, issued patents in the United States or elsewhere relating to aspects of our technology. It is uncertain whether the issuance of any third-party patents will require us to alter our products or processes, obtain licenses, or cease certain activities. Some third-party applications or patents may conflict with our issued patents or pending applications. Any such conflict could result in a significant reduction of the scope or value of our issued or licensed patents.

In addition, if patents issued to other companies contain blocking, dominating or conflicting claims and such claims are ultimately determined to be valid, we may be required to obtain licenses to these patents or to develop or obtain alternative non-infringing technology and cease practicing those activities, including potentially manufacturing or selling any products deemed to infringe those patents. If any licenses are required, there can be no assurance that we will be able to obtain any such licenses on commercially favorable terms, if at all, and if these licenses are not obtained, we might be prevented from pursuing the development and commercialization of certain of our potential products. Our failure to obtain a license to any technology that we may require to commercialize our products on favorable terms may have a material adverse impact on our business, financial condition and results of operations.

Litigation, which could result in substantial costs to us (even if determined in our favor), may also be necessary to enforce any patents issued or licensed to us or to determine the scope and validity of the proprietary rights of others. Under the Abbreviated New Drug Application provisions of U.S. law, after four years from the date marketing approval is granted to us by the FDA for a patented drug, a generic drug company may submit an Abbreviated New Drug Application to the FDA to obtain approval to market in the United States a generic version of the drug patented by us. If approval were given to the generic drug company, we would be required to promptly initiate patent litigation to prevent the marketing of such generic version prior to the normal expiration of the patent. There can be no assurance that our issued or licensed patents would be held valid by a court of competent jurisdiction or that any generic drug would be found to infringe our patents.

In addition, if our competitors file patent applications in the United States that claim technology also claimed by us, we

may have to participate in interference proceedings to determine priority of invention. These proceedings, if initiated by the USPTO, could result in substantial cost to us, even if the eventual outcome is favorable to us. Such proceedings can be lengthy, are costly to defend and involve complex questions of law and fact the outcomes of which are difficult to predict. An adverse outcome with respect to a third party claim or in an interference proceeding could subject us to significant liabilities, require us to license disputed rights from third parties, or require us to cease using such technology, any of which could have a material adverse effect on our business, financial condition and results of operations.

We also rely on trade secrets to protect technology, especially where patent protection is not believed to be appropriate or obtainable or where patents have not issued. We attempt to protect our proprietary technology and processes, in part, with confidentiality agreements and assignment of invention agreements with our employees and confidentiality agreements with our consultants and certain contractors. There can be no assurance that these agreements will not be breached, that we would have adequate remedies for any breach, or that our trade secrets will not otherwise become known or be independently discovered by competitors. We may fail in certain circumstances to obtain the necessary confidentiality agreements, or their scope or term may not be sufficiently broad to protect our interests.

If our trade secrets or other intellectual property become known to our competitors, it could result in a material adverse effect on our business, financial condition and results of operations. To the extent that we or our consultants or research collaborators use intellectual property owned by others in work for us, disputes may also arise as to the rights to related or resulting know-how and inventions.

Risks Relating to Our Exposure to Litigation

We are exposed to potential product liability or similar claims, and insurance against these claims may not be available to us at a reasonable rate in the future.

Our business exposes us to potential liability risks that are inherent in the testing, manufacturing and marketing of human therapeutic products. Clinical trials involve the testing of product candidates on human subjects or volunteers under a research plan, and carry a risk of liability for personal injury or death to patients due to unforeseen adverse side effects, improper administration of the product candidate, or other factors. Many of these patients are already seriously ill and are therefore particularly vulnerable to further illness or death.

We currently carry clinical trial liability insurance in the amount of $5 million in the aggregate, but there can be no assurance that we will be able to maintain such insurance or that the amount of such insurance will be adequate to cover claims. We could be materially and adversely affected if we were required to pay damages or incur defense costs in connection with a claim outside the scope of indemnity or insurance coverage, if the indemnity is not performed or enforced in accordance with its terms, or if our liability exceeds the amount of applicable insurance. In addition, there can be no assurance that insurance will continue to be available on terms acceptable to us, if at all, or that if obtained, the insurance coverage will be sufficient to cover any potential claims or liabilities. Similar risks would exist upon the commercialization or marketing of any products by us or our partners. Regardless of their merit or eventual outcome, product liability claims may result in:

- decreased demand for our product;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial volunteers;
- costs of litigation;
- distraction of management; and
- substantial monetary awards to plaintiffs.

We may become involved in securities class action litigation that could divert management's attention and adversely affect our business and could subject us to significant liabilities.

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the common stock of biopharmaceutical companies. These broad market fluctuations as well a broad range of other factors, including the realization of any of the risks described in this ''Risk Factor,'' section, may cause the market price of our common stock to decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies generally experience significant stock price volatility. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management's attention and resources, which could adversely affect our business. Any adverse determination in any such litigation or any amounts paid to settle any such actual or threatened litigation could require that we make significant payments.

Risks Related to Ownership of Our Common Stock

The market price of our common stock may be highly volatile, and could decline significantly.

The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in price in response to various factors, many of which are beyond our control, including those described elsewhere in this "Risk Factors" section and the following:

- new products, product candidates or new uses for existing products introduced or announced by our strategic partners, or our competitors, and the timing of these introductions or announcements;
- actual or anticipated results from and any delays in our clinical trials, including our Phase 3 clinical trial of our HyperAcute Pancreas product candidate, as well as results of regulatory reviews relating to the approval of our product candidates;
- variations in the level of expenses related to any of our product candidates or clinical development programs, including relating to the timing of invoices from, and other billing practices of, our clinical research organizations and clinical trial sites;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures and capital commitments;
- additions or departures of key scientific or management personnel;
- conditions or trends in the biotechnology and biopharmaceutical industries;
- actual or anticipated changes in earnings estimates, development timelines or recommendations by securities analysts; actual and anticipated fluctuations in our quarterly operating results;
- the financial projections we may provide to the public, any changes in these projections or our failure to meet these projections;
- deviations from securities analysts' estimates or the impact of other analyst ratings downgrades by any securities analysts who follow our common stock;
- other events or factors, including those resulting from war, incidents of terrorism, natural disasters or responses to these events;
- changes in accounting principles;
- discussion of us or our stock price by the financial and scientific press and in online investor communities;
- general economic and market conditions and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and
- sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock.

In addition, the stock market in general and the market for biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business and financial condition.

**** Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.***

As of April 15, 2012, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 45% of our common stock, including shares subject to outstanding options that are exercisable within 60 days after April 15, 2012. Accordingly, these stockholders are able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our Board of Directors, future issuances of our common stock or other securities, declarations of dividends on our common stock and approval of other significant corporate transactions. This concentration of ownership could have the effect of delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock. In addition, sales of shares beneficially owned by executive officers and directors and their affiliates could be viewed negatively by third parties and have a negative impact on our stock price. Moreover, we cannot assure you as to how these shares may be distributed and subsequently voted.

**** A significant portion of our total outstanding shares of common stock is restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our common stock to drop significantly, even if our business is doing well.***

Sales of a substantial number of shares of our common stock in the public market could occur in the future. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. As of December 31, 2011, sales of 15,484,459 shares of our common stock were restricted under securities laws or as a result of lock-up agreements but a large number of these shares may now be resold due to the expiration of the lock-up agreements, which occurred on May 9, 2012. Moreover, as of March 31, 2012, holders of an aggregate of 10,317,800 shares of our common stock had rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to meet compliance obligations.

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. We will be subject to the reporting requirements of the Securities Exchange Act of 1934, or the Exchange Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the Securities and Exchange Commission, or SEC, and The NASDAQ Stock Market, or NASDAQ, that impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. The Exchange Act will require, among other things, that we file annual, quarterly and current reports with respect to our business and financial condition. In addition, on July 21, 2010, the Dodd-Frank Wall Street Reform and Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation-related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas. The requirements of these rules and regulations will increase our legal and financial compliance costs, make some activities more difficult, time-consuming or costly and may also place undue strain on our personnel, systems and resources. Our management and other personnel will need to devote a substantial amount of time to these new compliance initiatives. In addition, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our Board of Directors, our board committees or as executive officers.

Failure to achieve and maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our ability to produce accurate financial statements and on our stock price.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, we will be required to publish a report by our management on our internal control over financial reporting. We have not been subject to these requirements in the past. The internal control report must contain (a) a statement of management's responsibility for establishing and maintaining adequate internal control over financial reporting, (b) a statement identifying the framework used by management to conduct the required evaluation of the effectiveness of our internal control over financial reporting, (c) management's assessment of the effectiveness of our internal control over financial reporting as of the end of our most recent fiscal year, including a statement as to whether or not internal control over financial reporting is effective, and (d) a statement that our independent registered public accounting firm has issued an attestation report on internal control over financial reporting.

To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to dedicate internal resources, engage outside consultants and adopt a detailed work plan to (a) assess and document the adequacy of internal control over financial reporting, (b) take steps to improve control processes where appropriate, (c) validate through testing that controls are functioning as documented, and (d) implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, we can provide no assurance as to our, or our independent registered public accounting firm's, conclusions with respect to the effectiveness of our internal control over financial reporting under Section 404. There is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We do not expect to pay any cash dividends for the foreseeable future. Investors may never obtain a return on their investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, our ability to pay cash dividends is currently prohibited by the terms of one of our debt financing arrangements, and any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

**** Provisions in our certificate of incorporation, our by-laws or Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.***

Provisions of our certificate of incorporation, our by-laws or Delaware law may have the effect of deterring unsolicited takeovers or delaying or preventing a change in control of our company or changes in our management, including transactions in which our stockholders might otherwise receive a premium for their shares over then current market prices. In addition, these provisions may limit the ability of stockholders to approve transactions that they may deem to be in their best interest. These provisions include:

- the division of our Board of Directors into three classes with staggered, three-year terms;
- advance notice requirements for stockholder proposals and nominations;
- the inability of stockholders to call special meetings;
- limitation on the ability of stockholders to remove directors or amend our by-laws; and
- the ability of our Board of Directors to designate the terms of and issue new series of preferred stock without stockholder approval, which could include the right to approve an acquisition or other change in our control or could be used to institute a rights plan, also known as a poison pill, that would work to dilute the stock ownership of a potential hostile acquirer, likely preventing acquisitions that have not been approved by our Board of Directors.

In addition, Section 203 of the Delaware General Corporation Law prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

The existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that you could receive a premium for your common stock in an acquisition.

Our stockholders may be diluted, and the prices of our securities may decrease, by the exercise of outstanding stock options and warrants or by future issuances of securities by us.

We may issue additional common stock, preferred stock, restricted stock units, or securities convertible into or exchangeable for our common stock. Furthermore, substantially all shares of common stock for which our outstanding stock options or warrants are exercisable are, once they have been purchased, eligible for immediate sale in the public market. The issuance of additional common stock, preferred stock, restricted stock units, or securities convertible into or exchangeable for our common stock or the exercise of stock options or warrants would dilute existing investors and could adversely affect the price of our securities. In addition, such securities may have rights senior to the rights of securities held by existing investors.

Our ability to use our net operating loss carryforwards and certain other tax attributes is limited by Sections 382 and 383 of the Internal Revenue Code.

Sections 382 and 383 of the Internal Revenue Code limit a corporation's ability to utilize its net operating loss carryforwards and certain other tax attributes (including research credits) to offset any future taxable income or tax if the corporation experiences a cumulative ownership change of more than 50% over any rolling three year period. State net operating loss carryforwards (and certain other tax attributes) may be similarly limited. An ownership change can therefore result in significantly greater tax liabilities than a corporation would incur in the absence of such a change and any increased liabilities could adversely affect the corporation's business, results of operations, financial condition and cash flow.

Based on a preliminary analysis, we believe that, from its inception through December 31, 2009, we experienced Section 382 ownership changes in September 2001 and March 2003. These two ownership changes limit our ability to utilize our federal net operating loss carryforwards (and certain other tax attributes) that accrued prior to the 2003 ownership change. In addition, the net operating loss carryforwards (and certain other tax attributes) of our subsidiary may be limited by Sections 382 and 383 as a result of a prior ownership change of the subsidiary.

Additional analysis will be required to determine whether changes in our ownership since December 31, 2009 and/or changes in our ownership that resulted from our initial public offering have caused or will cause another ownership change to occur, and the conclusions will depend on information that currently may not be available to us. Any such change could result in significant limitations on all of our net operating loss carryforwards and other tax attributes.

Additional ownership changes may occur in the future as a result of events over which we will have little or no control, including purchases and sales of our equity by our 5% stockholders, the emergence of new 5% stockholders, additional equity offerings or redemptions of our stock or certain changes in the ownership of any of our 5% stockholders.

Accounting pronouncements may impact our reported results of operations and financial position.

United States generally accepted accounting principles, or GAAP, and related implementation guidelines and interpretations can be highly complex and involve subjective judgments. Changes in these rules or their interpretation, the adoption of new pronouncements or the application of existing pronouncements to changes in our business could significantly alter our reported financial statements and results of operations.

**** If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.***

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our stock, or publishes inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price and trading volume to decline.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Recent Sales of Unregistered Securities

None.

Use of Proceeds

Our initial public offering, or IPO, of common stock was effected through a Registration Statement on Form S-1 (File No. 333-171300) that was declared effective by the Securities and Exchange Commission on November 10, 2011, which registered an aggregate of 7,130,000 shares of our common stock, including 930,000 shares that the underwriters had the option to purchase to cover over-allotments. On November 16, 2011, 6,200,000 shares of common stock were sold on our behalf at an initial public offering price of $7.00 per share, for aggregate gross proceeds of $43.4 million. The underwriters of the offering were Stifel Nicolaus & Company, Incorporated, Canaccord Genuity Inc., Robert W. Baird & Co. Incorporated and Cantor Fitzgerald & Co. Following the sale of the shares in connection with the closing of the IPO, the offering terminated.

We paid to the underwriters underwriting discounts totaling approximately $3.0 million in connection with the IPO. In addition, we incurred expenses of approximately $2.9 million in connection with the IPO, which, when added to the underwriting discounts paid by us, amount to total expenses of approximately $5.9 million. Thus, the net offering proceeds to us, after deducting underwriting discounts and offering costs were approximately $37.5 million. No offering costs were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

As of March 31, 2012, we have used approximately $6.2 million of the net proceeds from the initial public offering to fund our Phase 3 clinical trial and related development activities for HyperAcute Pancreas, clinical and related development activities for our other HyperAcute immunotherapy and IDO pathway inhibitor product candidates, other research and development activities and other working capital expenditures and general corporate purposes. We have invested the unused net proceeds from the IPO in money market funds, treasury bills and certificates of deposit. There has been no material change in our planned use of the net proceeds from the IPO as described in the final prospectus for the offering filed with the SEC pursuant to Rule 424(b).

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 4. REMOVED

ITEM 5. OTHER INFORMATION

None.

ITEM 6. EXHIBITS

The exhibits listed in the Index to Exhibits (following the signatures page of this Quarterly Report) are filed with, or incorporated by reference in, this Quarterly Report.

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 thereunto duly authorized.

Date: May 10, 2012

NEWLINK GENETICS CORPORATION

By: /s/ Charles J. Link, Jr.
Charles J. Link, Jr.
Chief Executive Officer
(Principal Executive Officer)

By: /s/ Gordon H. Link, Jr.
Gordon H. Link, Jr.
Chief Financial Officer and Secretary
(Principal Financial and Accounting Officer)

NEWLINK GENETICS CORPORATION

Index to Exhibits

Exhibit No.		Description	Incorporated by Reference				Filed Herewith
			Form	Filing Date	Exhibit Number	SEC File Number	
3.1		Amended and Restated Certificate of Incorporation of NewLink Genetics Corporation	8-K	11/18/2011	3.1	001-35342	
3.2		Amended and Restated Bylaws of NewLink Genetics Corporation	8-K	11/18/2011	3.2	001-35342	
4.1		Form of the Registrant's Common Stock Certificate	S-1/A	10/26/2011	4.1	333-171300	
4.2		Reference is made to Exhibits 3.1 and 3.2	8-K	11/18/2011	3.1,3.2	001-35342	
4.3		Amended and Restated Investor Rights Agreement by and between the Company and certain holders of the Company's capital stock dated as of December 1, 2010					X
10.1		NewLink Genetics Corporation 401(k) Prototype Plan and Trust; Effective as of January 1, 2005	8-K	3/12/2012	10.2	001-35342	
10.2		NewLink Genetics Corporation 401(k) Adoption Agreement; Effective as of January 1, 2005	8-K	3/12/2012	10.3	001-35342	
10.3		Material Modification to the NewLink Genetics Corporation 401(k) Adoption Agreement; Effective as of January 1, 2011	8-K	3/12/2012	10.4	001-35342	
10.4		Settlement Agreement with the Iowa Economic Development Authority	8-K	3/28/2012	10.1	001-35342	
10.5		2012 Target Bonus Awards	8-K	3/28/2012	10.2	001-35342	
10.6	+	Cooperative Research and Development Agreement between the Company and the National Cancer Institute					X
31.1		Certification of principal executive officer required by Rule 13a-14(a) / 15d-14(a)					X
31.2		Certification of principal financial officer required by Rule 13a-14(a) / 15d-14(a)					X
32.1	#	Section 1350 Certification					X
101.INS	‡	XBRL Instance Document					X
101.SCH	‡	XBRL Taxonomy Extension Schema Document					X
101.CAL	‡	XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	‡	XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	‡	XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	‡	XBRL Taxonomy Extension Presentation Linkbase Document					X

+ Indicates confidential treatment has been requested with respect to specific portions of this exhibit. Omitted portions have been filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

The certifications attached as Exhibit 32.1 that accompany this Quarterly Report on Form 10-Q are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of NewLink Genetics Corporation under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-Q, irrespective of any general incorporation language contained in such filing.

‡ XBRL (Extensible Business Reporting Language) information is furnished and not filed or a part of a registration statement or prospectus for purposes of sections 11 or 12 of the Securities Act of 1933, as amended, is deemed not filed for purposes of section 18 of the Securities Exchange Act of 1934, as amended, and otherwise is not subject to liability under these sections.

Exhibit 4.3

NEWLINK GENETICS CORPORATION

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT

This **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** (the "Agreement") is entered into as of the 1st day of December, 2010, by and among **NEWLINK GENETICS CORPORATION**, a Delaware corporation (the "Company") and the investors listed on *Exhibit A-1* hereto (collectively, the "Investors" and individually an "Investor") and the BPS Preferred Holders listed on *Exhibit A-2* (collectively the "BPS Preferred Holders" and individually as "BPS Preferred Holder").

RECITALS

WHEREAS, certain of the Investors are purchasing shares of the Company's Series E Preferred Stock (the "Series E Stock");

WHEREAS, the Company has entered into an Agreement and Plan of Merger ("Merger Agreement") with BioProtection Systems, Inc. ("BPS") whereby the Company will acquire the minority interest in BPS in exchange for shares of Series E Stock;

WHEREAS, the Merger Agreement provides that the holders of BPS Series A and Series B Preferred Stock ("BPS Preferred Holders") will be entitled to become parties to this Agreement;

WHEREAS, certain of the Investors (the "Prior Investors") are holders of the Company's Series A Preferred Stock (the "Series A Stock"), Series AA Preferred Stock (the "Series AA Stock"), Series AAA Preferred Stock (the "Series AAA Stock"), Series B Preferred Stock (the "Series B Stock"), the Series BB Preferred Stock (the "Series BB Stock"), the Series C Preferred Stock (the "Series C Stock") and Series D Preferred Stock (the "Series D Stock" and, together with the Series A Stock, Series AA Stock, Series AAA Stock, Series B Stock, Series BB Stock, Series C Stock and Series E Stock, the "Series Preferred");

WHEREAS, the Prior Investors and the Company are parties to an Amended and Restated Investor Rights Agreement dated as of July 15, 2009 (the "Prior Agreement");

WHEREAS, the parties to the Prior Agreement desire to terminate the Prior Agreement and accept the rights and covenants hereof in lieu of their rights and covenants under the Prior Agreement;

WHEREAS, pursuant to Section 5.6 of the Prior Agreement, the Prior Agreement may be amended or modified with respect to all parties thereto upon the written consent of the Company and the holders of at least a majority of the Registrable Securities (as defined therein), including the holders of a majority of the Series Preferred Registrable Securities (as defined therein); and

WHEREAS, in connection with the consummation of the sale of the Series E Stock (the "Preferred Stock Transactions"), the parties desire (i) to amend and restate the Prior Agreement in

its entirety with the terms set forth in this Agreement and (ii) to enter into this Agreement in order to grant registration rights, information rights and other rights to the Investors as set forth below.

NOW, THEREFORE, in consideration of these premises and for other good and valid consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto agree as follows:

SECTION 1. GENERAL.

1.1 Amendment and Restatement of Prior Agreement. The Prior Agreement is hereby amended in its entirety and restated herein. Such amendment and restatement is effective upon the execution of the Agreement by the Company and the holders of a majority in interest of the Registrable Securities (as defined in the Prior Agreement) held by the Prior Investors outstanding as of the date of this Agreement. Upon such execution, all provisions of, rights granted and covenants made in the Prior Agreement are hereby waived and released on behalf of each and every party to the Prior Agreement and superseded in their entirety and shall have no further force or effect with respect to each and every party to the Prior Agreement, including, without limitation, all rights of first refusal and any notice period associated therewith otherwise applicable to the Preferred Stock Transactions.

1.2 Definitions. As used in this Agreement the following terms shall have the following respective meanings:

(a) "Exchange Act" means the Securities Exchange Act of 1934, as amended.

(b) "Form S-3" means such form under the Securities Act as in effect on the date hereof or any successor or similar registration form under the Securities Act subsequently adopted by the SEC which permits inclusion or incorporation of substantial information by reference to other documents filed by the Company with the SEC.

(c) "Holder" means any person owning of record Registrable Securities that have not been sold to the public or any assignee of record of such Registrable Securities in accordance with Section 2.10 hereof.

(d) "Initial Offering" means the Company's first firm commitment underwritten public offering of its Common Stock registered under the Securities Act.

(e) "Register," "registered," and "registration" refer to a registration effected by preparing and filing a registration statement in compliance with the Securities Act, and the declaration or ordering of effectiveness of such registration statement or document.

(f) "Registrable Securities" means (a) Common Stock of the Company issued or issuable upon conversion of the Shares, (b) any Common Stock of the Company issued as (or issuable upon the conversion or exercise of any warrant, right or other security which is issued as)

a dividend or other distribution with respect to, or in exchange for or in replacement of, such above-described securities and (c) shares of Common Stock issued or issuable upon exercise of warrants originally issued to holders of Series AA Stock. Notwithstanding the foregoing, Registrable Securities shall not include any securities sold by a person to the public either pursuant to a registration statement or Rule 144 or sold in a private transaction in which the transferor's rights under Section 2 of this Agreement are not assigned.

(g) "Registrable Securities then outstanding" shall be the number of shares determined by calculating the total number of shares of the Company's Common Stock that are Registrable Securities and either (a) are then issued and outstanding or (b) are issuable pursuant to then exercisable or convertible securities.

(h) "Registration Expenses" shall mean all expenses incurred by the Company in complying with Sections 2.2, 2.3 and 2.4 hereof, including, without limitation, all registration and filing fees, printing expenses, fees and disbursements of counsel for the Company, reasonable fees and disbursements not to exceed fifteen thousand dollars ($15,000) of a single special counsel for the selling stockholders, blue sky fees and expenses and the expense of any special audits incident to or required by any such registration (but excluding the compensation of regular employees of the Company which shall be paid in any event by the Company).

(i) "SEC" or "Commission" means the Securities and Exchange Commission.

(j) "Securities Act" shall mean the Securities Act of 1933, as amended.

(k) "Selling Expenses" shall mean all underwriting discounts and selling commissions applicable to the sale of Registrable Securities.

(l) "Series Preferred Registrable Securities" shall mean Common Stock issued or issuable upon conversion of the Series AA Stock, Series B Stock, Series BB Stock, Series C Stock, Series D Stock, Series E Stock and Common Stock issued or issuable upon exercise of warrants originally issued to the holders of Series AA Stock.

(m) "Shares" shall mean the Company's Series E Stock, Series D Stock, Series C Stock, Series BB Stock, Series B Stock, Series AAA Stock, Series AA Stock and Series A Stock held by the Investors listed on *Exhibit A-1* hereto and the BPS Preferred Holders on *Exhibit A-2* hereto and their permitted assigns.

(n) "Special Registration Statement" shall mean (i) a registration statement relating to any employee benefit plan or (ii) with respect to any corporate reorganization or transaction under Rule 145 of the Securities Act, including any registration statements related to the resale of securities issued in such a transaction or (iii) a registration related to stock issued upon conversion of debt securities.

SECTION 2.REGISTRATION; RESTRICTIONS ON TRANSFER.

2.1 Restrictions on Transfer.

(a) Each Holder agrees not to make any disposition of all or any portion of the Shares or Registrable Securities unless and until:

(i) There is then in effect a registration statement under the Securities Act covering such proposed disposition and such disposition is made in accordance with such registration statement; or

(ii) (A) The transferee has agreed in writing to be bound by the terms of this Agreement, (B) such Holder shall have notified the Company of the proposed disposition and shall have furnished the Company with a detailed statement of the circumstances surrounding the proposed disposition, and (C) if reasonably requested by the Company, such Holder shall have furnished the Company with an opinion of counsel, reasonably satisfactory to the Company, that such disposition will not require registration of such shares under the Securities Act. It is agreed that the Company will not require opinions of counsel for transactions made pursuant to Rule 144, except in unusual circumstances. After its Initial Offering, the Company will not require the transferee to be bound by the terms of this Agreement with respect to transfers made under Rule 144.

(iii) Notwithstanding the provisions of paragraphs (i) and (ii) above, no such registration statement or opinion of counsel shall be necessary for a transfer by a Holder that is (A) a partnership transferring to its partners or former partners in accordance with partnership interests, (B) a corporation transferring to a wholly-owned subsidiary or a parent corporation that owns all of the capital stock of the Holder, (C) a limited liability company transferring to its members or former members in accordance with their interest in the limited liability company, or (D) an individual transferring to the Holder's family member or trust for the benefit of an individual Holder; *provided* that in each case the transferee will be subject to the terms of this Agreement to the same extent as if he were an original Holder hereunder.

(b) Each certificate representing Shares or Registrable Securities shall (unless otherwise permitted by the provisions of the Agreement) be stamped or otherwise imprinted with a legend substantially similar to the following (in addition to any legend required under applicable state securities laws):

> THE SHARES REPRESENTED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND THUS MAY NOT BE OFFERED FOR SALE, SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF UNLESS REGISTERED UNDER APPLICABLE FEDERAL OR STATE SECURITIES LAWS, OR UNLESS THE COMPANY IS FURNISHED WITH AN OPINION OF COUNSEL ACCEPTABLE TO IT THAT AN EXEMPTION FROM SUCH REGISTRATION IS AVAILABLE.

THE SALE, PLEDGE, HYPOTHECATION OR TRANSFER OF THE SHARES REPRESENTED BY THIS CERTIFICATE IS SUBJECT TO THE TERMS AND CONDITIONS OF A CERTAIN INVESTOR RIGHTS AGREEMENT BY AND BETWEEN THE STOCKHOLDER, THE COMPANY AND CERTAIN HOLDERS OF STOCK OF THE COMPANY. COPIES OF SUCH AGREEMENT MAY BE OBTAINED UPON WRITTEN REQUEST TO THE COMPANY.

(c) The Company shall be obligated to reissue promptly unlegended certificates at the request of any Holder thereof if the Holder shall have obtained an opinion of counsel (which counsel may be counsel to the Company) reasonably acceptable to the Company to the effect that the securities proposed to be disposed of may lawfully be so disposed of without registration, qualification or legend; provided that the second legend listed above shall be removed only at such time as the Holder of such certificate is no longer subject to any restrictions hereunder

(d) Any legend endorsed on an instrument pursuant to applicable state securities laws and the stop-transfer instructions with respect to such securities shall be removed upon receipt by the Company of an order of the appropriate blue sky authority authorizing such removal.

2.2 Demand Registration.

(a) Subject to the conditions of this Section 2.2, if the Company shall receive a written request from the Holders of at least 20% of the Series Preferred Registrable Securities (the "Initiating Holders") that the Company file a registration statement under the Securities Act covering the registration of Registrable Securities then outstanding in which the anticipated aggregate offering price, net of underwriting discounts and commissions, would exceed $20,000,000 (a "Qualified Public Offering"), then the Company shall, within thirty (30) days of the receipt thereof, give written notice of such request to all Holders, and subject to the limitations of this Section 2.2, effect, as expeditiously as reasonably possible, the registration under the Securities Act of all Registrable Securities that the Holders request to be registered.

(b) If the Initiating Holders intend to distribute the Registrable Securities covered by their request by means of an underwriting, they shall so advise the Company as a part of their request made pursuant to this Section 2.2 or any request pursuant to Section 2.4 and the Company shall include such information in the written notice referred to in Section 2.2(a) or Section 2.4(a), as applicable. In such event, the right of any Holder to include its Registrable Securities in such registration shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent provided herein. All Holders proposing to distribute their securities through such underwriting shall enter into an underwriting agreement in customary form with the underwriter or underwriters selected for such underwriting by a majority in interest of the Initiating Holders (which underwriter or underwriters shall be reasonably acceptable to the Company). Notwithstanding any other provision of this

Section 2.2 or Section 2.4, if the underwriter advises the Company that marketing factors require a limitation of the number of securities to be underwritten (including Registrable Securities) then the Company shall so advise all Holders of Registrable Securities which would otherwise be underwritten pursuant hereto, and the number of shares that may be included in the underwriting shall be allocated to the Holders of such Registrable Securities on a *pro rata* basis based on the number of Registrable Securities held by all such Holders (including the Initiating Holders). Any Registrable Securities excluded or withdrawn from such underwriting shall be withdrawn from the registration.

(c) The Company shall not be required to effect a registration pursuant to this Section 2.2:

(i) prior to one hundred eighty (180) days following the effective date of the registration statement pertaining to the Initial Offering;

(ii) after the Company has effected three (3) registrations pursuant to this Section 2.2, and such registrations have been declared or ordered effective;

(iii) if the Company shall furnish to Holders requesting a registration statement pursuant to this Section 2.2, a certificate signed by the Chairman of the Board stating that in the good faith judgment of the Board of Directors of the Company, it would be seriously detrimental to the Company and its stockholders for such registration statement to be effected at such time, in which event the Company shall have the right to defer such filing for a period of not more than one hundred twenty (120) days after receipt of the request of the Initiating Holders; *provided* that such right to delay a request shall be exercised by the Company not more than twice in any twelve (12) month period;

(iv) if within thirty (30) days of receipt of a written request from Initiating Holders pursuant to Section 2.2(a), the Company gives notice to the Holders of the Company's intention to file a registration statement for a public offering, other than pursuant to a Special Registration Statement, within ninety (90) days;

(v) if the Initiating Holders propose to dispose of shares of Registrable Securities that may be immediately registered for sale in the manner contemplated by such Holders on Form S-3 pursuant to a request made pursuant to Section 2.4 below; or

(vi) in any particular jurisdiction in which the Company would be required to qualify to do business or to execute a general consent to service of process in effecting such registration, qualification or compliance.

2.3 Piggyback Registrations. The Company shall notify all Holders of Registrable Securities in writing at least fifteen (15) days prior to the filing of any registration statement under the Securities Act for purposes of a public offering of securities of the Company (including, but not limited to, registration statements relating to secondary offerings of securities of the Company, but

excluding Special Registration Statements) and will afford each such Holder an opportunity to include in such registration statement all or part of such Registrable Securities held by such Holder. Each Holder desiring to include in any such registration statement all or any part of the Registrable Securities held by it shall, within fifteen (15) days after the above-described notice from the Company, so notify the Company in writing. Such notice shall state the intended method of disposition of the Registrable Securities by such Holder. If a Holder decides not to include all of its Registrable Securities in any registration statement thereafter filed by the Company, such Holder shall nevertheless continue to have the right to include any Registrable Securities in any subsequent registration statement or registration statements as may be filed by the Company with respect to offerings of its securities, all upon the terms and conditions set forth herein.

(a) Underwriting. If the registration statement under which the Company gives notice under this Section 2.3 is for an underwritten offering, the Company shall so advise the Holders of Registrable Securities. In such event, the right of any such Holder to be included in a registration pursuant to this Section 2.3 shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent provided herein. All Holders proposing to distribute their Registrable Securities through such underwriting shall enter into an underwriting agreement in customary form with the underwriter or underwriters selected for such underwriting by the Company. Notwithstanding any other provision of this Agreement, if the underwriter determines in good faith that marketing factors require a limitation of the number of shares to be underwritten, the number of shares that may be included in the underwriting shall be allocated, first, to the Company; second, to the Holders and the Stoddard Cancer Research Institute, its successors, transferees and assigns (the "Institute"), on a *pro rata* basis based on the total number of Registrable Securities held by the Holders and Common Stock held by the Institute; and third, to any stockholder of the Company (other than a Holder or the Institute) on a *pro rata* basis. In no event will shares of any other selling stockholder be included in such registration that would reduce the number of shares which may be included by Holders without the written consent of Holders of not less than a majority of the Registrable Securities proposed to be sold in the offering. If any Holder disapproves of the terms of any such underwriting, such Holder may elect to withdraw therefrom by written notice to the Company and the underwriter, delivered at least ten (10) business days prior to the effective date of the registration statement. Any Registrable Securities excluded or withdrawn from such underwriting shall be excluded and withdrawn from the registration. For any Holder which is a partnership, limited liability company or corporation, the partners, retired partners, members, retired members and stockholders of such Holder, or the estates and family members of any such partners or retired partners, members or retired members and any trusts for the benefit of any of the foregoing person shall be deemed to be a single "Holder," and any *pro rata* reduction with respect to such "Holder" shall be based upon the aggregate amount of shares carrying registration rights owned by all entities and individuals included in such "Holder," as defined in this sentence.

(b) Right to Terminate Registration. The Company shall have the right to terminate or withdraw any registration initiated by it under this Section 2.3 prior to the effectiveness of such registration whether or not any Holder has elected to include securities in such registration. The Registration Expenses of such withdrawn registration shall be borne by the Company in accordance with Section 2.5 hereof.

2.4 Form S-3 Registration. Subject to the conditions of this Section 2.4, if the Company shall receive a written request from the Holders of at least 20% of the Registrable Securities that the Company effect a registration on Form S-3 (or any successor to Form S-3) or any similar short-form registration statement and any related qualification or compliance with respect to all or a part of the Registrable Securities owned by such Holders, the Company will:

(a) promptly give written notice of the proposed registration, and any related qualification or compliance, to all other Holders of Registrable Securities; and

(b) as soon as practicable, effect such registration and all such qualifications and compliances as may be so requested and as would permit or facilitate the sale and distribution of all or such portion of such Holder's or Holders' Registrable Securities as are specified in such request, together with all or such portion of the Registrable Securities of any other Holder or Holders joining in such request as are specified in a written request given within fifteen (15) days after receipt of such written notice from the Company; *provided*, *however*, that the Company shall not be obligated to effect any such registration, qualification or compliance pursuant to this Section 2.4:

(i) if Form S-3 is not available for such offering by the Holders, or

(ii) if the Holders, together with the holders of any other securities of the Company entitled to inclusion in such registration, propose to sell Registrable Securities and such other securities (if any) at an aggregate price to the public of less than five hundred thousand dollars ($500,000), or

(iii) if (x) within thirty (30) days of receipt of a written request from any Holder or Holders pursuant to this Section 2.4, the Company gives notice to such Holder or Holders of the Company's intention to make a public offering of Common Stock within ninety (90) days, other than pursuant to a Special Registration Statement, or (y) the Company shall furnish to the Holders a certificate signed by the Chairman of the Board of Directors of the Company stating that in the good faith judgment of the Board of Directors of the Company, it would be seriously detrimental to the Company and its stockholders for such Form S-3 registration to be effected at such time (in which event the Company shall have the right to defer the filing of the Form S-3 registration statement for a period of not more than one hundred twenty (120) days after receipt of the request of the Holder or Holders under this Section 2.4); *provided* such right to delay a request pursuant to (x) or (y) above shall be exercised by the Company not more than twice in any twelve (12) month period, or

(iv) if the Company has**,** within the twelve (12) month period preceding the date of such request, already effected two (2) registrations on Form S-3 for the Holders pursuant to this Section 2.4, or

(v) in any particular jurisdiction in which the Company would be required to qualify to do business or to execute a general consent to service of process in effecting such registration, qualification or compliance.

(c) Subject to the foregoing, the Company shall file a Form S-3 registration statement covering the Registrable Securities and other securities so requested to be registered as soon as practicable after receipt of the requests of the Holders. Registrations effected pursuant to this Section 2.4 shall not be counted as demands for registration or registrations effected pursuant to Sections 2.2 or 2.3, respectively.

2.5 Expenses of Registration. Except as specifically provided herein, all Registration Expenses incurred in connection with any registration, qualification or compliance pursuant to Section 2.2 or any registration under Section 2.3 or Section 2.4 herein shall be borne by the Company. All Selling Expenses incurred in connection with any registrations hereunder, shall be borne by the holders of the securities so registered *pro rata* on the basis of the number of shares so registered. The Company shall not, however, be required to pay for expenses of any registration proceeding begun pursuant to Section 2.2 or 2.4, the request of which has been subsequently withdrawn by the Initiating Holders unless (a) the withdrawal is based upon material adverse information concerning the Company of which the Initiating Holders were not aware at the time of such request or such withdrawal is at the request of the Company or (b) the Holders of a majority of Registrable Securities agree to forfeit their right to one requested registration pursuant to Section 2.2 or Section 2.4, as applicable, in which event such right shall be forfeited by all Holders). If the Holders are required to pay the Registration Expenses, such expenses shall be borne by the holders of securities (including Registrable Securities) requesting such registration in proportion to the number of shares for which registration was requested. If the Company is required to pay the Registration Expenses of a withdrawn offering pursuant to clause (a) above, then the Holders shall not forfeit their rights pursuant to Section 2.2 or Section 2.4 to a demand registration.

2.6 Obligations of the Company. Whenever required to effect the registration of any Registrable Securities, the Company shall, as expeditiously as reasonably possible:

(a) Prepare and file with the SEC a registration statement with respect to such Registrable Securities and use all reasonable efforts to cause such registration statement to become effective, and, upon the request of the Holders of a majority of the Registrable Securities registered thereunder, keep such registration statement effective for up to sixty (60) days or, if earlier, until the Holder or Holders have completed the distribution related thereto; provided, however, that at any time, upon written notice to the participating Holders and for a period not to exceed sixty (60) days thereafter (the “Suspension Period”), the Company may delay the filing or effectiveness of any registration statement or suspend the use or effectiveness of any registration statement (and the Initiating Holders hereby agree not to offer or sell any Registrable Securities pursuant to such registration statement during the Suspension Period) if the Company reasonably believes that there is or may be in existence material nonpublic information or events involving the Company, the failure of which to be disclosed in the prospectus included in the registration statement could result in a Violation (as defined below). In the event that the Company shall exercise its right to delay or suspend the filing or effectiveness of a registration hereunder, the applicable time period during which the registration statement is to remain effective shall be extended by a period of time equal to the duration of the Suspension Period. The Company may extend the Suspension Period for an additional consecutive sixty (60) days with the consent of the holders of a majority of the Registrable

Securities registered under the applicable registration statement, which consent shall not be unreasonably withheld. If so directed by the Company, the Initiating Holders shall use all reasonable efforts to deliver to the Company (at the Company's expense) all copies, other than permanent file copies then in such Initiating Holders' possession, of the prospectus relating to such Registrable Securities current at the time of receipt of such notice.

(b) Prepare and file with the SEC such amendments and supplements to such registration statement and the prospectus used in connection with such registration statement as may be necessary to comply with the provisions of the Securities Act with respect to the disposition of all securities covered by such registration statement for the period set forth in paragraph (a) above.

(c) Furnish to the Holders such number of copies of a prospectus, including a preliminary prospectus, in conformity with the requirements of the Securities Act, and such other documents as they may reasonably request in order to facilitate the disposition of Registrable Securities owned by them.

(d) Use its reasonable efforts to register and qualify the securities covered by such registration statement under such other securities or Blue Sky laws of such jurisdictions as shall be reasonably requested by the Holders; *provided* that the Company shall not be required in connection therewith or as a condition thereto to qualify to do business or to file a general consent to service of process in any such states or jurisdictions.

(e) In the event of any underwritten public offering, enter into and perform its obligations under an underwriting agreement, in usual and customary form, with the managing underwriter(s) of such offering. Each Holder participating in such underwriting shall also enter into and perform its obligations under such an agreement.

(f) Notify each Holder of Registrable Securities covered by such registration statement at any time when a prospectus relating thereto is required to be delivered under the Securities Act of the happening of any event as a result of which the prospectus included in such registration statement, as then in effect, includes an untrue statement of a material fact or omits to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances then existing. The Company will use reasonable efforts to amend or supplement such prospectus in order to cause such prospectus not to include any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances then existing.

(g) Use all reasonable efforts to furnish, on the date that such Registrable Securities are delivered to the underwriters for sale, if such securities are being sold through underwriters, (i) an opinion, dated as of such date, of the counsel representing the Company for the purposes of such registration, in form and substance as is customarily given to underwriters in an underwritten public offering, addressed to the underwriters, if any, and (ii) a letter, dated as of such date, from the independent certified public accountants of the Company, in form and substance as

is customarily given by independent certified public accountants to underwriters in an underwritten public offering addressed to the underwriters.

2.7 Termination of Registration Rights. A Holder's registration rights shall expire if (a) such Holder (together with its affiliates) holds less than 1% of the Company's outstanding Common Stock (treating all shares of convertible Preferred Stock on an as converted basis) and (b) all Registrable Securities held by and issuable to such Holder (and its affiliates) may be sold under Rule 144 during any ninety (90) day period. Additionally, all registration rights granted under this Section 2 shall terminate and be of no further force and effect three (3) years after the date of the Company's Initial Offering.

2.8 Delay of Registration; Furnishing Information.

(a) No Holder shall have any right to obtain or seek an injunction restraining or otherwise delaying any such registration as the result of any controversy that might arise with respect to the interpretation or implementation of this Section 2.

(b) It shall be a condition precedent to the obligations of the Company to take any action pursuant to Section 2.2, 2.3 or 2.4 that the selling Holders shall furnish to the Company such information regarding themselves, the Registrable Securities held by them and the intended method of disposition of such securities as shall be required to effect the registration of their Registrable Securities.

(c) The Company shall have no obligation with respect to any registration requested pursuant to Section 2.2 or Section 2.4 if, due to the operation of subsection 2.2(b), the number of shares or the anticipated aggregate offering price of the Registrable Securities to be included in the registration drops below 80% of the number of shares or 80% of the anticipated aggregate offering price required to originally trigger the Company's obligation to initiate such registration as specified in Section 2.2 or Section 2.4, whichever is applicable.

2.9 Indemnification. In the event any Registrable Securities are included in a registration statement under Sections 2.2, 2.3 or 2.4:

(a) To the extent permitted by law, the Company will indemnify and hold harmless each Holder, the partners, members, officers and directors of each Holder, any underwriter (as defined in the Securities Act) for such Holder and each person, if any, who controls such Holder or underwriter within the meaning of the Securities Act or the Exchange Act, against any losses, claims, damages, or liabilities (joint or several) to which they may become subject under the Securities Act, the Exchange Act or other federal or state law, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon any of the following statements, omissions or violations (collectively a "Violation") by the Company: (i) any untrue statement or alleged untrue statement of a material fact contained in such registration statement or incorporated reference therein, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto, (ii) the omission or alleged omission to state

therein a material fact required to be stated therein, or necessary to make the statements therein not misleading, or (iii) any violation or alleged violation by the Company of the Securities Act, the Exchange Act, any state securities law or any rule or regulation promulgated under the Securities Act, the Exchange Act or any state securities law in connection with the offering covered by such registration statement; and the Company will pay as incurred to each such Holder, partner, member, officer, director, underwriter or controlling person for any legal or other expenses reasonably incurred by them in connection with investigating or defending any such loss, claim, damage, liability or action; *provided however*, that the indemnity agreement contained in this Section 2.9(a) shall not apply to amounts paid in settlement of any such loss, claim, damage, liability or action if such settlement is effected without the consent of the Company, which consent shall not be unreasonably withheld or delayed, nor shall the Company be liable in any such case for any such loss, claim, damage, liability or action to the extent that it arises out of or is based upon a Violation which occurs in reliance upon and in conformity with written information furnished expressly for use in connection with such registration by such Holder, partner, member, officer, director, underwriter or controlling person of such Holder.

(b) To the extent permitted by law, each Holder will, if Registrable Securities held by such Holder are included in the securities as to which such registration qualifications or compliance is being effected, indemnify and hold harmless the Company, each of its directors, its officers and each person, if any, who controls the Company within the meaning of the Securities Act, any underwriter and any other Holder selling securities under such registration statement or any of such other Holder's partners, directors or officers or any person who controls such Holder, against any losses, claims, damages or liabilities (joint or several) to which the Company or any such director, officer, controlling person, underwriter or other such Holder, or partner, director, officer or controlling person of such other Holder may become subject under the Securities Act, the Exchange Act or other federal or state law, insofar as such losses, claims, damages or liabilities (or actions in respect thereto) arise out of or are based upon any of the following statements: (i) any untrue statement or alleged untrue statement of a material fact contained in such registration statement or incorporated reference therein, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto, (ii) the omission or alleged omission to state therein a material fact required to be stated therein, or necessary to make the statements therein not misleading, or (iii) any violation or alleged violation by the Company of the Securities Act (collectively, a "Holder Violation"), in each case to the extent (and only to the extent) that such Holder Violation occurs in reliance upon and in conformity with written information furnished by such Holder under an instrument duly executed by such Holder and stated to be specifically for use in connection with such registration; and each such Holder will pay as incurred any legal or other expenses reasonably incurred by the Company or any such director, officer, controlling person, underwriter or other Holder, or partner, officer, director or controlling person of such other Holder in connection with investigating or defending any such loss, claim, damage, liability or action if it is judicially determined that there was such a Holder Violation; *provided, however,* that the indemnity agreement contained in this Section 2.9(b) shall not apply to amounts paid in settlement of any such loss, claim, damage, liability or action if such settlement is effected without the consent of the Holder, which consent shall not be unreasonably withheld or delayed; *provided further*, that in no event shall any indemnity under this Section 2.9 exceed the net proceeds from the offering received by such Holder.

(c) Promptly after receipt by an indemnified party under this Section 2.9 of notice of the commencement of any action (including any governmental action), such indemnified party will, if a claim in respect thereof is to be made against any indemnifying party under this Section 2.9, deliver to the indemnifying party a written notice of the commencement thereof and the indemnifying party shall have the right to participate in, and, to the extent the indemnifying party so desires, jointly with any other indemnifying party similarly noticed, to assume the defense thereof with counsel mutually satisfactory to the parties; *provided, however,* that an indemnified party shall have the right to retain its own counsel, with the fees and expenses to be paid by the indemnifying party, if representation of such indemnified party by the counsel retained by the indemnifying party would be inappropriate due to actual or potential differing interests between such indemnified party and any other party represented by such counsel in such proceeding. The failure to deliver written notice to the indemnifying party within a reasonable time of the commencement of any such action, if materially prejudicial to its ability to defend such action, shall relieve such indemnifying party of any liability to the indemnified party under this Section 2.9, but the omission so to deliver written notice to the indemnifying party will not relieve it of any liability that it may have to any indemnified party otherwise than under this Section 2.9.

(d) If the indemnification provided for in this Section 2.9 is held by a court of competent jurisdiction to be unavailable to an indemnified party with respect to any losses, claims, damages or liabilities referred to herein, the indemnifying party, in lieu of indemnifying such indemnified party thereunder, shall to the extent permitted by applicable law contribute to the amount paid or payable by such indemnified party as a result of such loss, claim, damage or liability in such proportion as is appropriate to reflect the relative fault of the indemnifying party on the one hand and of the indemnified party on the other in connection with the Violation(s) or Holder Violation(s) that resulted in such loss, claim, damage or liability, as well as any other relevant equitable considerations. The relative fault of the indemnifying party and of the indemnified party shall be determined by a court of law by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission to state a material fact relates to information supplied by the indemnifying party or by the indemnified party and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission; *provided*, that in no event shall any contribution by a Holder hereunder exceed the net proceeds from the offering received by such Holder.

(e) The obligations of the Company and Holders under this Section 2.9 shall survive completion of any offering of Registrable Securities in a registration statement and, with respect to liability arising from an offering to which this Section 2.9 would apply that is covered by a registration filed before termination of this Agreement, such termination. No indemnifying party, in the defense of any such claim or litigation, shall, except with the consent of each indemnified party, consent to entry of any judgment or enter into any settlement which does not include as an unconditional term thereof the giving by the claimant or plaintiff to such Indemnified Party of a release from all liability in respect to such claim or litigation.

2.10 Assignment of Registration Rights. The rights to cause the Company to register Registrable Securities pursuant to this Section 2 may be assigned by a Holder to a transferee or

assignee of Registrable Securities that acquires at least fifty thousand (50,000) shares of Registrable Securities (as adjusted for stock splits and combinations); *provided, however,* that (i) the transferor shall, within ten (10) days after such transfer, furnish to the Company written notice of the name and address of such transferee or assignee and the securities with respect to which such registration rights are being assigned and (ii) such transferee shall agree to be subject to all restrictions set forth in this Agreement.

2.11 Amendment of Registration Rights. Any provision of this Section 2 may be amended and the observance thereof may be waived (either generally or in a particular instance and either retroactively or prospectively), only with the written consent of the Company and the Holders of a majority of the Registrable Securities then outstanding, including the Holders of a majority of the Series Preferred Registrable Securities. Any amendment or waiver effected in accordance with this Section 2.11 shall be binding upon each Holder and the Company. By acceptance of any benefits under this Section 2, Holders of Registrable Securities hereby agree to be bound by the provisions hereunder.

2.12 Limitation on Subsequent Registration Rights. Other than as provided in Section 5.11, after the date of this Agreement, the Company shall not, without the prior written consent of the Holders of at least a majority of the Registrable Securities then outstanding, including the Holders of a majority of the Series Preferred Registrable Securities, enter into any agreement with any holder or prospective holder of any securities of the Company that would grant such holder registration rights senior to those granted to the Holders hereunder, other than the right to a Special Registration Statement.

2.13 *"Market Stand-Off"* Agreement. Each Holder hereby agrees that such Holder shall not sell, transfer, make any short sale of, grant any option for the purchase of, or enter into any hedging or similar transaction with the same economic effect as a sale, any Common Stock (or other securities) of the Company held by such Holder (other than those included in the registration) for a period specified by the representative of the underwriters of Common Stock (or other securities) of the Company not to exceed (i) one hundred eighty (180) days following the effective date of a registration statement of the Company filed under the Securities Act pursuant to the Initial Offering (or such longer period as the underwriters or the Company shall request in order to facilitate compliance with NASD Rule 2711 or NYSE Member Rule 472 or any successor or similar rule or regulation) or (ii) ninety (90 days) following the effective date of any registration statement of the Company filed pursuant to under the Securities Act, except as set forth above with respect to the Company's Initial Offering (or such longer period as the underwriters or the Company shall request in order to facilitate compliance with NASD Rule 2711 or NYSE Member Rule 472 or any successor or similar rule or regulation). Each Holder agrees to execute and deliver such other agreements as may be reasonably requested by the Company and/or the managing underwriter(s) which are consistent with the foregoing or which are necessary to give further effect thereto. In order to enforce the foregoing covenant, the Company may impose stop-transfer instructions with respect to such Common Stock (or other securities) until the end of such period. The underwriters of the Company's stock are intended third party beneficiaries of this Section 2.13 and shall have the right, power and authority to enforce the provisions hereof as though they were a party hereto.

2.14 Agreement to Furnish Information. Each Holder agrees to execute and deliver such other agreements as may be reasonably requested by the Company or the underwriter that are consistent with the Holder's obligations under Section 2.13 or that are necessary to give further effect thereto. In addition, if requested by the Company or the representative of the underwriters of Common Stock (or other securities) of the Company, each Holder shall provide, within ten (10) days of such request, such information as may be required by the Company or such representative in connection with the completion of any public offering of the Company's securities pursuant to a registration statement filed under the Securities Act. The obligations described in Section 2.13 and this Section 2.14 shall not apply to a Special Registration. The Company may impose stop-transfer instructions with respect to the shares of Common Stock (or other securities) subject to the foregoing restriction until the end of said one hundred eighty (180) day or ninety (90) day period, as applicable. Each Holder agrees that any transferee of any shares of Registrable Securities shall be bound by Sections 2.13 and 2.14. The underwriters of the Company's stock are intended third party beneficiaries of Sections 2.13 and 2.14 and shall have the right, power and authority to enforce the provisions hereof as though they were a party hereto.

2.15 Rule 144 Reporting. With a view to making available to the Holders the benefits of certain rules and regulations of the SEC which may permit the sale of the Registrable Securities to the public without registration, the Company agrees to use all reasonable efforts to:

(a) Make and keep public information available, as those terms are understood and defined in SEC Rule 144 or any similar or analogous rule promulgated under the Securities Act, at all times after the effective date of the first registration filed by the Company for an offering of its securities to the general public;

(b) File with the SEC, in a timely manner, all reports and other documents required of the Company under the Exchange Act; and

(c) So long as a Holder owns any Registrable Securities, furnish to such Holder forthwith upon request: a written statement by the Company as to its compliance with the reporting requirements of said Rule 144 of the Securities Act, and of the Exchange Act (at any time after it has become subject to such reporting requirements); a copy of the most recent annual or quarterly report of the Company; and such other reports and documents as a Holder may reasonably request in availing itself of any rule or regulation of the SEC allowing it to sell any such securities without registration.

SECTION 3. COVENANTS OF THE COMPANY.

3.1 Basic Financial Information and Reporting.

(a) The Company will maintain true books and records of account in which full and correct entries will be made of all its business transactions pursuant to a system of accounting established and administered in accordance with generally accepted accounting principles consistently applied, and will set aside on its books all such proper accruals and reserves as shall

be required under generally accepted accounting principles consistently applied.

(b) As soon as practicable after the end of each fiscal year of the Company, and in any event within one hundred twenty (120) days thereafter, to the extent requested by an Investor, the Company will furnish each Investor a balance sheet of the Company, as at the end of such fiscal year, and a statement of income and a statement of cash flows of the Company, for such year, all prepared in accordance with generally accepted accounting principles consistently applied and setting forth in each case in comparative form the figures for the previous fiscal year, all in reasonable detail. Such financial statements shall be accompanied by a report and opinion thereon by independent public accountants of national standing selected by the Company's Board of Directors.

(c) The Company will furnish each Investor, as soon as practicable after the end of the first, second and third quarterly accounting periods in each fiscal year of the Company, and in any event within forty-five (45) days thereafter, to the extent requested by such Investor, a balance sheet of the Company as of the end of each such quarterly period, and a statement of income and a statement of cash flows of the Company for such period and for the current fiscal year to date, prepared in accordance with generally accepted accounting principles, with the exception that no notes need be attached to such statements and year-end audit adjustments may not have been made.

(d) So long as an Investor (with its affiliates) owns not less than the greater of (i) 100,000 shares of Registrable Securities and (ii) 1% of the Company's outstanding capital stock (treating all outstanding Preferred Stock on an as-if-converted basis and all outstanding options or warrants on an as-if-exercised basis) (a "Major Investor"), to the extent requested by such Major Investor, the Company will furnish each such Major Investor: (i) at least thirty (30) days prior to the beginning of each fiscal year an annual budget and operating plans for such fiscal year (and as soon as available, any subsequent revisions thereto); and (ii) as soon as practicable after the end of each fiscal quarter, and in any event within twenty (20) days thereafter, a balance sheet of the Company as of the end of each such quarter, and a statement of income and a statement of cash flows of the Company for such quarter and for the current fiscal year to date, including a comparison to plan figures for such period, prepared in accordance with generally accepted accounting principles consistently applied, with the exception that no notes need be attached to such statements and year-end audit adjustments may not have been made.

3.2 Inspection Rights. Each Major Investor shall have the right to visit and inspect any of the properties of the Company or any of its subsidiaries, and to discuss the affairs, finances and accounts of the Company or any of its subsidiaries with its officers, and to review such information as is reasonably requested all at such reasonable times and as often as may be reasonably requested; *provided, however,* that the Company shall not be obligated under this Section 3.2 with respect to a competitor of the Company or with respect to information which the Board of Directors determines in good faith is confidential and should not, therefore, be disclosed.

3.3 Confidentiality of Records. Each Investor agrees to use, and to use all reasonable efforts to insure that its authorized representatives use, the same degree of care as such Investor uses to protect its own confidential information to keep confidential any information furnished to

it which the Company identifies as being confidential or proprietary (so long as such information is not in the public domain), except that such Investor may disclose such proprietary or confidential information to any partner, subsidiary or parent of such Investor for the purpose of evaluating its investment in the Company as long as such partner, subsidiary or parent is advised of the confidentiality provisions of this Section 3.3.

3.4 Reservation of Common Stock. The Company will at all times reserve and keep available, solely for issuance and delivery upon the conversion of the Preferred Stock, all Common Stock issuable from time to time upon such conversion.

3.5 Key Man Insurance. The Company will use all reasonable efforts to maintain in full force and effect term life insurance in the amount determined by the Board of Directors on the life of Charles J. Link, Jr., naming the Company as beneficiary.

3.6 Director and Officer Liability Insurance. The Company shall use all reasonable efforts to obtain and maintain director and officer insurance policy in an amount deemed appropriate by a majority of the outside directors of the Company.

3.7 Proprietary Information and Inventions Agreement. The Company shall require all employees to execute and deliver a Proprietary Information and Inventions Agreement substantially in the form attached hereto as *Exhibit B*.

3.8 Termination of Covenants. All covenants of the Company contained in Section 3 of this Agreement shall expire and terminate as to each Investor upon the earlier of (i) the closing of the Initial Offering, (ii) the closing of an Acquisition (as defined in the Company's Certificate of Incorporation) or, (iii) the closing of an Asset Transfer (as defined in the Company's Certificate of Incorporation).

SECTION 4. RIGHTS OF FIRST REFUSAL.

4.1 Subsequent Offerings. Each Major Investor who holds shares of Series Preferred (each such Major Investor shall be referred to as a "Participating Investor" for purposes of this Section 4) shall have a right of first refusal to purchase its *pro rata* share of all Equity Securities, as defined below, that the Company may, from time to time, propose to sell and issue after the date of this Agreement, other than the Equity Securities excluded by Section 4.6 hereof. Each Participating Investor's *pro rata* share is equal to the ratio of (a) the number of shares of the Company's Common Stock (including all shares of Common Stock issued or issuable upon conversion of the Shares and Common Stock issued or issuable upon conversion of warrants held by such Participating Investor, as applicable) which such Participating Investor is deemed to be a holder immediately prior to the issuance of such Equity Securities to (b) the total number of shares of the Company's outstanding Common Stock (including all shares of Common Stock issued or issuable upon conversion of the Shares or upon the exercise of any outstanding warrants or options) immediately prior to the issuance of the Equity Securities. The term "Equity Securities" shall mean (i) any Common Stock, Preferred Stock or other security of the Company, (ii) any security

convertible, with or without consideration, into any Common Stock, Preferred Stock or other security (including any option to purchase such a convertible security), (iii) any security carrying any warrant or right to subscribe to or purchase any Common Stock, Preferred Stock or other security or (iv) any such warrant or right.

4.2 Exercise of Rights. If the Company proposes to issue any Equity Securities, it shall give each Participating Investor written notice of its intention, describing the Equity Securities, the price and the terms and conditions upon which the Company proposes to issue the same. Each Participating Investor shall have fifteen (15) days from the giving of such notice to agree to purchase its *pro rata* share of the Equity Securities for the price and upon the terms and conditions specified in the notice by giving written notice to the Company and stating therein the quantity of Equity Securities to be purchased. Notwithstanding the foregoing, the Company shall not be required to offer or sell such Equity Securities to any Participating Investor who would cause the Company to be in violation of applicable federal securities laws by virtue of such offer or sale.

4.3 Issuance of Equity Securities to Other Persons. If not all of the Participating Investors elect to purchase their *pro rata* share of the Equity Securities, then the Company shall promptly notify in writing the Participating Investors who do so elect and shall offer such Participating Investors the right to acquire such unsubscribed shares. The Participating Investors shall have five (5) days after receipt of such notice to notify the Company of its election to purchase all or a portion thereof of the unsubscribed shares. If the Participating Investors fail to exercise in full the rights of first refusal, the Company shall have ninety (90) days thereafter to sell the Equity Securities in respect of which the Participating Investors' rights were not exercised, at a price and upon general terms and conditions materially no more favorable to the purchasers thereof than specified in the Company's notice to the Participating Investors pursuant to Section 4.2 hereof. If the Company has not sold such Equity Securities within ninety (90) days of the notice provided pursuant to Section 4.2, the Company shall not thereafter issue or sell any Equity Securities, without first offering such securities to the Participating Investors in the manner provided above.

4.4 Termination and Waiver of Rights of First Refusal. The rights of first refusal established by this Section 4 shall not apply to, and shall terminate upon the earlier of (i) the effective date of the registration statement pertaining to the Company's Initial Offering or (ii) the closing of an Acquisition or Asset Transfer. The rights of first refusal established by this Section 4 may be amended, or any provision waived with the written consent of Participating Investors holding a majority of the Registrable Securities held by all Participating Investors or as permitted by Section 5.6.

4.5 Transfer of Rights of First Refusal. The rights of first refusal of each Participating Investor under this Section 4 may be transferred to the same parties, subject to the same restrictions as any transfer of registration rights pursuant to Section 2.10.

4.6 Excluded Securities. The rights of first refusal established by this Section 4 shall have no application to any of the following Equity Securities:

(a) options, warrants or other rights to purchase shares of Common Stock reserved from time to time for issuance under the Company's equity incentive plans approved by the Board, and the Common Stock issued pursuant to such options, warrants or other rights to employees, officers or directors of, or consultants or advisors to, the Company or any subsidiary pursuant to stock purchase or stock option plans or other arrangements that are approved by a majority of the Board;

(b) stock issued or issuable pursuant to any rights or agreements outstanding as of the date of this Agreement or options, warrants or convertible securities outstanding as of the date of this Agreement; and stock issued pursuant to any such rights, agreements, options, warrants or convertible securities granted after the date of this Agreement as long as the rights of first refusal established by this Section 4 were complied with, waived, or were inapplicable pursuant to any provision of this Section 4.6 with respect to the initial sale or grant by the Company of such rights, agreements, options, warrants or convertible securities;

(c) any Equity Securities issued for consideration other than cash pursuant to a merger, consolidation, strategic alliance, acquisition or similar business combination or for the acquisition of one or more assets or for the provision of services to or for the benefit of the Company;

(d) shares of Common Stock issued in connection with any stock split, stock dividend or recapitalization by the Company;

(e) shares of Common Stock issued upon conversion of shares of the Company's Preferred Stock;

(f) Any Equity Securities issued in connection with strategic transactions involving the Company and other entities, including (i) joint ventures, manufacturing, marketing or distribution arrangements or (ii) technology transfer or development arrangements.

(g) any Equity Securities issued pursuant to any equipment leasing, real property leasing or loan arrangement, or debt financing from a bank or similar financial or lending institution;

(h) any Equity Securities that are issued by the Company pursuant to a registration statement filed under the Securities Act;

(i) any Series E Stock issued pursuant to the Preferred Stock Transactions.

SECTION 5. MISCELLANEOUS.

5.1 Governing Law. This Agreement and all disputes arising out of or relating to this Agreement shall be governed by and construed under the laws of the State of Delaware as applied to agreements among Delaware residents entered into and to be performed entirely within Delaware without reference to any conflict-of-laws principle that would cause the application of the law of any other jurisdiction. ANY LAWSUIT OR OTHER LEGAL ACTION ARISING FROM OR

RELATING TO ANY PROVISION OF THIS AGREEMENT OR THE SUBJECT MATTER HEREOF MUST BE BROUGHT IN A FEDERAL OR STATE COURT LOCATED IN DES MOINES, IOWA (AND MAY NOT BE BROUGHT IN ANY OTHER COURT OR FORUM) AND THE PARTIES HEREBY SUBMIT TO THE JURISDICTION OF, AND WAIVE ANY OBJECTION TO THE LAYING OF VENUE IN, ANY SUCH COURT.

5.2 Survival. The representations, warranties, covenants, and agreements made herein shall survive any investigation made by any Holder and the closing of the transactions contemplated hereby. All statements as to factual matters contained in any certificate or other instrument delivered by or on behalf of the Company pursuant hereto in connection with the transactions contemplated hereby shall be deemed to be representations and warranties by the Company hereunder solely as of the date of such certificate or instrument.

5.3 Successors and Assigns. Except as otherwise expressly provided herein, the provisions hereof shall inure to the benefit of, and be binding upon, the successors, assigns, heirs, executors, and administrators of the parties hereto and shall inure to the benefit of and be enforceable by each person who shall be a holder of Registrable Securities from time to time; *provided* that such party has agreed in writing to be bound by the terms of this Agreement. Prior to the receipt by the Company of adequate written notice of the transfer of any Registrable Securities specifying the full name and address of the transferee, the Company may deem and treat the person listed as the holder of such shares in its records as the absolute owner and holder of such shares for all purposes, including the payment of dividends or any redemption price.

5.4 Entire Agreement. This Agreement, the Exhibits and Schedules hereto, and the other documents delivered pursuant hereto or in connection herewith constitute the full and entire understanding and agreement between the parties with regard to the subjects hereof and no party shall be liable or bound to any other in any manner by any representations, warranties, covenants and agreements except as specifically set forth herein and therein.

5.5 Severability. In the event one or more of the provisions of this Agreement should, for any reason, be held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect any other provisions of this Agreement, and this Agreement shall be construed as if such invalid, illegal or unenforceable provision had never been contained herein.

5.6 Amendment and Waiver.

(a) Except as otherwise expressly provided, this Agreement may be amended or modified only upon the written consent of the Company and the holders of at least a majority of the Registrable Securities, including the holders of a majority of the Series Preferred Registrable Securities.

(b) Except as otherwise expressly provided, the obligations of the Company and the rights of the Holders under this Agreement may be waived only with the written consent of the Company and the holders of at least a majority of the Registrable Securities, including the holders

of a majority of the Series Preferred Registrable Securities.

(c) For the purposes of determining the number of Holders or Investors entitled to vote or exercise any rights hereunder, the Company shall be entitled to rely solely on the list of record holders of its stock as maintained by or on behalf of the Company.

5.7 Delays or Omissions. It is agreed that no delay or omission to exercise any right, power, or remedy accruing to any Holder, upon any breach, default or noncompliance of the Company under this Agreement shall impair any such right, power, or remedy, nor shall it be construed to be a waiver of any such breach, default or noncompliance, or any acquiescence therein, or of any similar breach, default or noncompliance thereafter occurring. It is further agreed that any waiver, permit, consent, or approval of any kind or character on any Holder's part of any breach, default or noncompliance under the Agreement or any waiver on such Holder's part of any provisions or conditions of this Agreement must be in writing and shall be effective only to the extent specifically set forth in such writing. All remedies, either under this Agreement, by law, or otherwise afforded to Holders, shall be cumulative and not alternative.

5.8 Notices. All notices required or permitted hereunder shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient; if not, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent to the party to be notified at the address as set forth on the signature pages hereof or *Exhibit A* hereto or at such other address as such party may designate by ten (10) days advance written notice to the other parties hereto.

5.9 Attorneys' Fees. In the event that any suit or action is instituted to enforce any provision in this Agreement, the prevailing party in such dispute shall be entitled to recover from the losing party all fees, costs and expenses of enforcing any right of such prevailing party under or with respect to this Agreement, including without limitation, such reasonable fees and expenses of attorneys and accountants, which shall include, without limitation, all fees, costs and expenses of appeals.

5.10 Titles and Subtitles. The titles of the sections and subsections of this Agreement are for convenience of reference only and are not to be considered in construing this Agreement.

5.11 Additional Investors. Notwithstanding anything to the contrary contained herein, if the Company shall issue additional shares of its Series Preferred, any purchaser of such shares of Series Preferred may become a party to this Agreement by executing and delivering an additional counterpart signature page to this Agreement and shall be deemed an "Investor," a "Holder" and a party hereunder. Notwithstanding anything to the contrary contained herein, if the Company shall issue Equity Securities in accordance with Section 4.6 (c), (f) or (g) of this Agreement, any purchaser of such Equity Securities may become a party to this Agreement by executing and delivering an

additional counterpart signature page to this Agreement and shall be deemed an "Investor," a "Holder" and a party hereunder.

5.12 Counterparts. This Agreement may be executed in any number of counterparts, each of which shall be an original, but all of which together shall constitute one instrument.

5.13 Aggregation of Stock. All shares of Registrable Securities held or acquired by affiliated entities or persons or persons or entities under common management or control shall be aggregated together for the purpose of determining the availability of any rights under this Agreement.

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IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: /s/ Charles J. Link, Jr. **By:** _____

(signature)

Name: Charles J. Link, Jr. **Name:** _____

(please print)

Title: Chief Executive Officer **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION Stine Seed Farm, Inc.
(entity name, if applicable)

By: _____ **By:** /s/ Jerald L. Reichling
(signature)

Name: _____ **Name:** Jerald L. Reichling
(please print)

Title: _____ **Title:** CFO
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section 5.6 of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION Iowa Capital Corporation
(entity name, if applicable)

By: _____ **By:** /s/ Terry L Sullivan
(signature)

Name: _____ **Name:** Terry L. Sullivan
(please print)

Title: _____ **Title:** Vice President
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION James S. Cownie IRA, Bankers Trust Cust.
(entity name, if applicable)

By: _____ **By:** /s/Mindy Nussbaum-Bell, Bankers Trust
(signature)

Name: _____ **Name:** Mindy Nussbaum-Bell
(please print)

Title: _____ **Title:** Vice President
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION NLG Investors, LLC
(entity name, if applicable)

By: _____ **By:** /s/ James T. Campney
(signature)

Name: _____ **Name:** James T. Campney
(please print)

Title: _____ **Title:** Manager
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION NLG "Series C", LLC
(entity name, if applicable)

By: _____ **By:** /s/ James T. Campney
(signature)

Name: _____ **Name:** James T. Campney
(please print)

Title: _____ **Title:** Manager
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION James T. Campney Roth IRA
(entity name, if applicable)

By: _____ **By:** /s/ James T. Campney
(signature)

Name: _____ **Name:** James T. Campney
(please print)

Title: _____ **Title:** Manager
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION Tonto Investments, LLC
(entity name, if applicable)

By: _____ **By:** /s/ James T. Campney
(signature)

Name: _____ **Name:** James T. Campney
(please print)

Title: _____ **Title:** Manager
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: _____ **By:** /s/ Brian P. Waller

(signature)

Name: _____ **Name:** Brian P. Waller

(please print)

Title: _____ **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION Brian and Sheila Waller Foundation
(entity name, if applicable)

By: _____ **By:** /s/ Brian P. Waller
(signature)

Name: _____ **Name:** Brian P. Waller
(please print)

Title: _____ **Title:** _____
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION Insurance Finance Corp.
(entity name, if applicable)

By: _____ **By:** /s/ Brian P. Waller
(signature)

Name: _____ **Name:** Brian P. Waller
(please print)

Title: _____ **Title:** _____
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION Charles D. Jons IRA
(entity name, if applicable)

By: _____ **By:** /s/Charles D. Jons
(signature)

Name: _____ **Name:** Charles D. Jons
(please print)

Title: _____ **Title:** Owner
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: _____ **By:** /s/Richard O. Jacobson

(signature)

Name: _____ **Name:** Richard O. Jacobson

(please print)

Title: _____ **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: _____ **By:** /s/ Charles Link, Jr.

(signature)

Name: _____ **Name:** Charles Link, Jr.

(please print)

Title: _____ **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION Sedgwick Fund, LLC
(entity name, if applicable)

By: _____ **By:** /s/ Russell Novak
(signature)

Name: _____ **Name:** Russell Novak
(please print)

Title: _____ **Title:** Member
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION RGPC Investors LLC – Series B
(entity name, if applicable)

By: _____ **By:** /s/ Matthew Busick
(signature)

Name: _____ **Name:** Matthew Busick
(please print)

Title: _____ **Title:** Manager
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: _____ **By:** /s/ Glenda F. Millard

(signature)

Name: _____ **Name:** Glenda F. Millard

(please print)

Title: _____ **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: _____ **By:** /s/ Michelle Link Smith

(signature)

Name: _____ **Name:** Michelle Link Smith

(please print)

Title: _____ **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: _____ **By:** /s/ Kenneth L. Pollack

(signature)

Name: _____ **Name:** Kenneth L. Pollack

(please print)

Title: _____ **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION Daniel L. Krieger Rev. Trust dtd 3/21/00
(entity name, if applicable)

By: _____ **By:** /s/ Daniel L. Krieger
(signature)

Name: _____ **Name:** Daniel L. Krieger
(please print)

Title: _____ **Title:** Co-Trustee
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: _____ **By:** /s/ Johnny Danos

(signature)

Name: _____ **Name:** Johnny Danos

(please print)

Title: _____ **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION Central Iowa Hospital Corporation
(entity name, if applicable)

By: _____ **By:** /s/ Joseph F. Corfits, Jr.
(signature)

Name: _____ **Name:** Joseph F. Corfits, Jr.
(please print)

Title: _____ **Title:** Chief Financial Officer
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION Iowa First Capital Fund II
(entity name, if applicable)

By: _____ **By:** /s/ Mark Drish
(signature)

Name: _____ **Name:** Mark Drish
(please print)

Title: _____ **Title:** Member
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION JSC Trust
(entity name, if applicable)

By: _____ **By:** /s/ James S. Cownie
(signature)

Name: _____ **Name:** James S. Cownie
(please print)

Title: _____ **Title:** Trustee
(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: _____ **By:** /s/ Richard Derner, DPM

(signature)

Name: _____ **Name:** Richard Derner, DPM

(please print)

Title: _____ **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: _____ **By:** /s/ Bradley K. Hiatt, D.O.

(signature)

Name: _____ **Name:** Bradley K. Hiatt, D.O.

(please print)

Title: _____ **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: _____ **By:** /s/ Dennis D. Kommer

(signature)

Name: _____ **Name:** Dennis D. Kommer

(please print)

Title: _____ **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: _____ **By:** /s/ Hasmig S. Link

(signature)

Name: _____ **Name:** Hasmig S. Link

(please print)

Title: _____ **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

IN WITNESS WHEREOF, the parties hereto have executed this **AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT** as of the date set forth in the first paragraph hereof.

COMPANY: **INVESTOR:**

NEWLINK GENETICS CORPORATION __

(entity name, if applicable)

By: _____ **By:** /s/Nicholas Vahanian

(signature)

Name: _____ **Name:** Nicholas Vahanian

(please print)

Title: _____ **Title:** _____

(if applicable)

Execution of this Amended and Restated Investor Rights Agreement constitutes consent to the amendment and restatement of the Prior Agreement as provided under Section ___ of the Prior Agreement

EXHIBIT A-1

SCHEDULE OF INVESTORS

130 Dotson LLC
2-C's Partnership, LLP
A. Severin Johnson
Adams Partners
Alan Gillman J. Gillman Trust
Allen and Cindy Sabbag
Alphonse Cardamone
Ameriprise Trust Company FBO Matthew D. Busick IRA Acct. 56164239-8-021
Ameriprise Trust Company FBO Tim Pratt IRA Acct. 14361208-3-021
Ameriprise Trust Company FBO Todd Janus IRA Acct. 18974543-3-021
Ames Seed Capital, LLC
Anthony Pontarelli
Banker's Trust Company, N.A., Custodian of the
James S. Cownie IRA dated 11/18/02
Bball Properties, LLC
Blake Waller
Blue Sky Properties, LLC
Bob Shreck
Brad Fortune
Bradley K. Hiatt
Brian & Sheila Waller Foundation
Brian P. Waller
Broad Street Investment Co., Inc.
Bruce Anderson
Bryan Lamb
C. Edward and Michele Brown
Carl Langren
Carl Langren IMG MPP Plan Custodial Account
Carl Schweser
Carolyn L. Jons, Trustee of the Jons Children's Trust dated June 25, 2010
Central Iowa Hospital Corporation
Chad Tramp
Charles and Carolyn Jons Trust
Charles D. Berger
Charles D. Jons Roth IRA
Charles DePena
Charles E. Gillman Dec'l of Trust dated 5/13/92
Charles Jons IRA

Charles Jons SEP IRA
Charles Link
Charles P. Hammersmith, Jr.
Charles Waller
Chelsea McMillen
Chicagoland Investors, LLC
Citigroup Global Markets Inc. Cust. For William Caldbeck IRA
Connie Wimer Trust
Cornerstone Government Affairs
Craig P. Mickelson
Dale & Mary Parker Revocable Trust dated April, 22 1993
Dale and Mary Parker Irrevocable Trust FBO Monica Parker
Dale and Mary Parker Irrevocable Trust FBO Emily Parker
Dale and Mary Parker Irrevocable Trust FBO Kelly Parker
Dale and Mary Parker Irrevocable Trust FBO Natalie Parker
Dale Howard
Dale Robert Parker
Dan Sibthorp
Dan Wunschel
Daniel & Robin Rubenstein Family Trust
Daniel B. and Florence E. Green Foundation
Daniel L. Krieger Revocable Trust dtd 3-21-2000
David and Catherine Bird
David J. Lies
David L. Lacey
David Lundquist
David Lundquist Revocable Trust, dated November 19, 2002, David J. Lundquist, Trustee
Dayton Park LLC
Dean E. Hunziker
Delaware Charter GTY Trust FBO Keith Putbrese IRA Acct# 88678253
Delaware Charter Gty Trust Tr Elizabeth J. Schellhardt IRA A/C 5730-5378
Delaware Charter GTY Trust Tr FBO Elizabeth K. Flynn
Delaware Charter GTY Trust Tr FBO John Kaufman Beneficiary Trust
Delaware Charter Gty Trust Tr Scott Campney Roth IRA 8890-1345
Delaware Charter Gty. Trust Tr. James T. Campney Roth IRA A/C 88901342
Denise Redenius
Dennis D. Kommer
Des Moines Anesthesiologists, PC PSP, FBO Michael Hurt u/a 01/01/1974, Michael Hurt, Trustee
Diane Harms
Doug Vander Weide
Douglas D. Truckenmiller Indiv. Retirement Account, Dain Rausher Custodian
Douglas S. Draper

Douglas S. Hackett and Neala S. Hackett, Joint Tenants
Dr. Mark Westberg
Eastern Iowa Angel Investors, LLC
Eby, William H.
Edwin M. Garrison
Elan Hadar
Eleventh Generation LP
Elizabeth J. Schellhardt
Elizabeth Kaufman Flynn
Entrust Midwest LLC FBO Zane Smith IRA 6221
Entrust Midwest, LLC FBO Brad Lair, Acct. #OS7382
Erben A. Hunziker Revocable Trust
Eric & Arlene Coles
Erickson Family, L.C.
Ernest Talarico
Errol P. Eernisse Revocable Trust, Errol P. Eernisse Trustee
FBO Joseph A. Bisignano, IRA
Fidelity Management Trust Company FBO Johnny Danos Roth IRA #647-121703
Fidelity Management Trust Company FBO Kenneth Pollack Roth IRA #647-093203
Frederick E. Miller
Garondah Partners
Gene A. Johnson
Gerald W. Paul
Gilbert Carl Schweser
Glenda Millard
Gopika Myneni, M.D.
Gregory L. O'Hara
Hal Moon - Linda Moon
Hansen, Charles R.
Harold Darren Leavitt
Harry I. Laibstain
Harv & Lois Vanderweide
Heath & Kimberly Hinkhouse
Heidi and Ronald Pachura
Horizon Trust & Investment, Custodian, Catherine Pesek Bird IRA
Hyland Heights Apartments LLC
I Wistar Morris III
Insurance Finance Corporation
Iowa Capital Corporation
Iowa Commitment Fund, LP
Iowa First Capital Fund II LP
Iowa First Capital Fund, LP

Iowa Radiology, P.C.
IRA FBO John Krohn Pershing LLC as Custodian
Ira J. Kaufman
J. Andrew Axel
James and Teresa Larson Revocable Trust
James B. Fogt
James Carmichael Lodge
James S. Cownie IRA, Bankers Trust Co. N.A. Custodian
James S. Petro
James T. Campney
Jamie Harold Shaffer
January Associates
Jay Lawrence Goldfarb
Jayson Lansink
Jeanne Temple
Jeff Carpenter
Jeffrey R. Rode
Jennifer A. Berger
Jerry D. Smith
Jim Sibthorp
John Ahrold
John J. Sabl
John Kaufman
John Langeland
John Livingston
John R. Baur & Judith A. Baur
John Rizzi, M.D.
John S. Schellhardt
Johnny Danos
Johnny Danos Revocable Trust
Jon & Mary Lageschulte
Jon E. & Bonnie K. Hunziker
Jon Lageschulte
Jons Grandchildren's Trust dated June 25, 2010, Carolyn L. Jons, Trustee
Jordon P. Grossman
Joseph Bisignano
Joseph F. Caputo
Joseph K. Haggerty
Joseph Lucas
Joshua Butkus
JSC Trust
Julie Ann Wrigley 1999 Revocable Trust

Julie Schweser
Karl Dresdner
Kaufman Investors Limited Partnership
Keith A. Barnes
Kelly E. Berger
Kelly Scott Parker
Kenneth L. Pollack
Kevin F. Cestone
Kevin J. Grimm
Kim and Debra Clayton
Kim Hinkhouse
Kitty Shean Conover 2008 Revocable Trust u/a/d December 26, 2008
Lankenau Hospital Foundation
Larry Morris
Laurie M. Kuestner & Thomas A. Burleson
Lee V. Livingston
Lee V. Livingston, Patricia G. Livingston JTWROS
Leonard A. Foxman Living Trust
LIMR Development, Inc.
Lisa Weary
LLH Partnership
LLJ, Inc.
Loran J. Schiltz 1999 Revocable Trust
Loran J. Schiltz Family Trust, Dated 2/26/06
Loran J. Schiltz Marital Trust, Dated 2/26/06
M.E. and Ann S. Tharp
Marc Jalbert
Marc S. Gillotti & Sarah L. Kincaid
Margaret H. Hunziker Revocable Trust
Mario D'Agostino
Mark & Ann Meyer
Mark Speck
Mark Waller
Martha H. Morris
Mary D'Agostino
Mary Pat Burns
Matthew Helgeson
Melvin Katten
Merdix Family Living Trust
Merle Lansink
Mesirow Financial Inc Cust Audrey Kaufman IRA A/C 5292-3377
Mesirow Financial Inc Cust Elizabeth J. Schellhardt IRA Acct 5730-5378

Mesirow Financial Inc Cust Elizabeth K. Duberman Beneficiary IRA Acct 6299-2311
Mesirow Financial Inc Cust James Campney ROTH IRA Acct 8890-1342
Mesirow Financial Inc Cust John Kaufman Beneficiary IRA Acct 7493-1210
Mesirow Financial Inc Cust Keith Putbrese SEP IRA Acct 8867-8253
Mesirow Financial Inc Cust Scott Campney ROTH IRA Acct 8890-1345
Mesirow Financial Inc Cust Thomas F. Baldacci IRA Acct 1628-1122
Mesirow Financial, Inc., custodian FBO Joseph Vendetti IRA #8882-0327
Michael & Kris Dee
Michael Antonio Coppola
Michael C. Hubbell Art. III Trust FBO
Michael C. Hubbell and Descendants dated 11/23/03
Michael Hopson
Michael Lee
Michael Magee
Michael P. & Bobbye J. McMurray
Michael P. Balkin
Michelle Link Smith
Midwest Oilseeds, Inc.
Mike Kemery
Millennium Trust Co LLC Custodian FBO Karl P. Dresdner
Millennium Trust Co., LLC Cust FBO Nancy J. Cass, IRA #90DN63013
Millennium Trust Company, LLC Cust. FBO RGPC Investors LLC Series B, # 173463H11
MOHA Profit Sharing Plan FBO Loren D. Brown
MOHA Profit Sharing Plan FBO Mark Westberg
Morgan Stanley DW Inc Cust for Joseph A Bisignano IRA Rollover DTD 2/8/92
MSSB C/F Joseph A. Bisignano Roth IRA dated 10/04/10
Nathan Hostetter
National Financial Service, LLC FBO Todd Janus IRA
NewLink Investors II, L.C.
NewLink Investors, LC
Nicholas Vahanian
Nickolas J. Henderson 2007 Grantor Retained Annuity Trust
Nicole M. Berger
Nile Wayne McDonald
NLG Investors, LLC
NLG Series "C", LLC
Norman F. Siegel as Trustee of the Norman F. Siegel Living Trust Dated July 26, 2005
Northwest Financial Corp
Perlman Family LLC
Peter D'Agostino
Piper Jaffray Cust FBO Timothy P. Woods
R. Douglas Fisher
Ramon Flick

Raymond James & Assoc Inc CSDN FBO Allen Sabbag IRA
RGPC Investors LLC-Series B
Richard Derner
Richard L. Prey
Richard O. Jacobson
Richard O. Jacobson, as Trustee of the Richard O. Jacobson Trust under agreement dated November 9, 2007
Rob Marshall
Robert A. Dee Family Trust, Dated 6/19/1985
Robert A. Dee GST Family Trust, Dated 6/19/1985
Robert and Lynn Sibthorp
Robert and Sharon Dee Residual Trust 1985
Robert D'Agostino
Robert J. Powers
Robert McCardle
Robert Pinkert
Robert Reid Shreck Living Trust, Robert R. Shreck, Trustee
Robert W. & Karen L. Shirk
Ron & Marion Helgeson
Ron McMillen
Ronald Peterson
Roy Molina
Russell Novak
S Enterprises, LLC
Sallerson Family L.P.
Saluri, Joseph B.
Sandra Zutowt
Sarah Alexander
SCAPJAK, L.P.
Schweser Capital, LLC
Scott H. Lang
Sean McMurray
Sedgwick Fund, LLC
Sharon P.Dee Revocable Trust, Dated 6/18/1985
Sheila and Frank Caputo
Sheila L. Waller
SLS Westcoast Trust
Spot On Investments
Stacy Kaufman Tabachnik
Stephen Cerrone
Stephen Feltz
Stephen Kaufman
Stephen T. Beasley

Steve C. Stahly
Steven Gene Goldfarb
Steven P. Stahly
Steven Perlman and Elizabeth Perlman
Stine Seed Farm, Inc
Stoddard Cancer Research Center, a d.b.a. of Central Iowa Health System
Ted Foxman
Ted Foxman Family Trust
Terry L. Rich, Schwab & Co., Custodial IRA Rollover
Terry Rich
The Cotswold Foundation
Thomas A. Raffin
Thomas Baldacci IRA
Thomas Burleson & Laurie Kuestner
Thomas G. Schellhardt
Tim G. Osborne
Timothy E. & Ewa J. Pratt, Joint Tenants with rights of survivorship
Timothy L. Neugent
Traci Simons
Trustees of NGMEO Profit Sharing Plan FBO G R Neumann
UBS Financial Services CDN FBO Douglas D. Truckenmiller IRA
UBS Financial Services Inc CON FBO Timothy Woods
Vince D'Agostino
W.J. Latham, Jr. & Jana S. Latham, JTW full ROS and not as tenants in common
William C. Black & Maria E. Blanco
William C. Jacobson
William E. Caldbeck IRA, Wells Fargo
Wolfson Family LLC
Zachary Hostetter

EXHIBIT A-2

SCHEDULE BPS PREFERRED HOLDERS

Cherie Lynn Shreck Living Trust
R. Douglas Fisher
R. Douglas and Pamela D. Fisher
David J. Lundquist
Schweser Capital, L.L.C.
Ronald J. Peterson and Judy M. Peterson
Steven G. Patterson Traditional IRA
Piper Jaffray as Custodian FBO Douglas D. Truckenmiller IRA
Morgan Stanley DW Inc. Cust for Joseph A Bisignano IRA Rollover
John R. Baur and Judith A. Baur
LBS-I, LLC
Errol P. Eernisse Revocable Trust, Errol P Eernisse Trustee
Piper Jaffray as Custodian FBO R. Douglas Fisher IRA
Ames Seed Capital, L.L.C.
BPS Group, LLC
Carl Langren IMG MPP Plan Custodial Account
AJH Investment, LLC
Michael Arneson
BPS Investors, LLC
Dale Parker
Steve C. Stahly and Marcia Stahly
Richard L. Prey
CJS Farms, LP
UBS Financial Services CDN FBO Douglas D. Truckenmiller IRA
David Lundquist Revocable Trust, dated November 19, 2002, David J. Lundquist, Trustee
Dale and Mary Parker Revocable Trust dated April 22, 1993
UBS Financial Srvice CDN FBO R. Douglas Fisher IRA
Stifel Nicolaus Custodian for R. Douglas Fisher IRA
END-IRA, Inc. FBO Marc Jalbert, IRA
Iowa Capital Corporation
Bruce Anderson
Iowa Commitment Fund, LP
Karl Dresdner
Shane Hackett
Thomas Burleson & Laurie Kuestner
BPS Investments, LLC

EXHIBIT B

FORM OF PROPRIETARY INFORMATION AND INVENTIONS AGREEMENT

NEWLINK GENETICS CORPORATION

EMPLOYEE PROPRIETARY INFORMATION, INVENTIONS, NON-COMPETITION, AND NON-SOLICITATION AGREEMENT

This Employee Proprietary Information, Inventions, Non-competition, and Non-solicitation Agreement (this "Agreement") is made in consideration for my employment or continued employment by **NEWLINK GENETICS CORPORATION** or any of its subsidiaries (the "Company"), and the compensation now and hereafter paid to me. I hereby agree as follows:

1. NONDISCLOSURE.

1.1 Recognition of Company's Rights; Nondisclosure. At all times during my employment and thereafter, I will hold in strictest confidence and will not disclose, use, lecture upon or publish any of the Company's Proprietary Information (defined below), except as such disclosure, use or publication may be required in connection with my work for the Company, or unless an officer of the Company expressly authorizes such in writing. I will obtain Company's written approval before publishing or submitting for publication any material (written, verbal, or otherwise) that relates to my work at Company and/or incorporates any Proprietary Information. I hereby assign to the Company any rights I may have or acquire in such Proprietary Information and recognize that all Proprietary Information shall be the sole property of the Company and its assigns.

1.2 Proprietary Information. The term "**Proprietary Information**" shall mean any and all confidential and/or proprietary knowledge, data or information of the Company. By way of illustration but not limitation, "Proprietary Information" includes (a) tangible and intangible information relating to antibodies and other biological materials, cell lines, samples of assay components, media and/or cell lines and procedures and formulations for producing any such assay components, media and/or cell lines, formulations, products, processes, know-how, designs, formulas, methods, developmental or experimental work, clinical data, improvements, discoveries, plans for research, new products, marketing and selling, business plans, budgets and unpublished financial statements, licenses, prices and costs, suppliers and customers, and information regarding the skills and compensation of other employees of the Company; (b) trade secrets, inventions, mask works, ideas, processes, formulas, source and object codes, data, programs, other works of authorship, know-how, improvements, discoveries, developments, designs and techniques (hereinafter collectively referred to as "Inventions"); (c) information regarding plans for research, development, new products, marketing and selling, business plans, budgets and unpublished financial statements, licenses, prices and costs, suppliers and customers; and (d) information regarding the skills and compensation of other employees of the Company. Notwithstanding the foregoing, it is understood that, at all such times, I am free to use information which is generally known in the trade or industry, which is not gained as result of a breach of this Agreement, and my own, skill, knowledge, know-how and experience to whatever extent and in whichever way I wish.

1.3 Third Party Information. I understand, in addition, that the Company has received and in the future will receive from third parties confidential or proprietary information ("Third Party Information") subject to a duty on the Company's part to maintain the confidentiality of such information and to use it only for certain limited purposes. During the term of my employment and thereafter, I will hold Third Party Information in the strictest confidence and will not disclose to anyone (other than Company personnel who need to know such information in connection with their work for the Company) or use, except in connection with my work for the Company, Third Party Information unless expressly authorized by an officer of the Company in writing.

1.4 No Improper Use of Information of Prior Employers and Others. During my employment by the Company I will not improperly use or disclose any confidential information or trade secrets, if any, of any former employer or any other person to whom I have an obligation of confidentiality, and I will not bring onto the premises of the Company any unpublished documents or any property belonging to any

former employer or any other person to whom I have an obligation of confidentiality unless consented to in writing by that former employer or person. I will use in the performance of my duties only information which is generally known and used by persons with training and experience comparable to my own, which is common knowledge in the industry or otherwise legally in the public domain, or which is otherwise provided or developed by the Company.

2. ASSIGNMENT OF INVENTIONS.

2.1 Proprietary Rights. The term "**Proprietary Rights" s**hall mean all trade secret, patent, copyright, mask work and other intellectual property rights throughout the world.

2.2 Prior Inventions. Inventions, if any, patented or unpatented, which I made prior to the commencement of my employment with the Company are excluded from the scope of this Agreement. To preclude any possible uncertainty, I have set forth on *Exhibit A* (Previous Inventions) attached hereto a complete list of all Inventions that I have, alone or jointly with others, conceived, developed or reduced to practice or caused to be conceived, developed or reduced to practice prior to the commencement of my employment with the Company, that I consider to be my property or the property of third parties and that I wish to have excluded from the scope of this Agreement (collectively referred to as "Prior Inventions"). If disclosure of any such Prior Invention would cause me to violate any prior confidentiality agreement, I understand that I am not to list such Prior Inventions in Exhibit A but am only to disclose a cursory name for each such invention, a listing of the party(ies) to whom it belongs and the fact that full disclosure as to such inventions has not been made for that reason. A space is provided on Exhibit A for such purpose. If no such disclosure is attached, I represent that there are no Prior Inventions. If, in the course of my employment with the Company, I incorporate a Prior Invention into a Company product, process or machine, the Company is hereby granted and shall have a nonexclusive, royalty-free, irrevocable, perpetual, worldwide license (with rights to sublicense through multiple tiers of sublicensees) to make, have made, modify, use and sell such Prior Invention. Notwithstanding the foregoing, I agree that I will not incorporate, or permit to be incorporated, Prior Inventions in any Company Inventions without the Company's prior written consent.

2.3 Assignment of Inventions. Subject to Sections 2.4, and 2.6, I hereby assign and agree to assign in the future (when any such Inventions or Proprietary Rights are first reduced to practice or first fixed in a tangible medium, as applicable) to the Company all my right, title and interest in and to any and all Inventions (and all Proprietary Rights with respect thereto) whether or not patentable or registrable under copyright or similar statutes, made or conceived or reduced to practice or learned by me, either alone or jointly with others, during the period of my employment with the Company. Inventions assigned to the Company, or to a third party as directed by the Company pursuant to this Section 2, are hereinafter referred to as "Company Inventions."

2.4 Nonassignable Inventions. I recognize that, in the event of a specifically applicable state law, regulation, rule, or public policy ("Specific Inventions Law"), this Agreement will not be deemed to require assignment of any invention which qualifies fully for protection under a Specific Inventions Law by virtue of the fact that any such invention was, for example, developed entirely on my own time without using the Company's equipment, supplies, facilities, or trade secrets and neither related to the Company's actual or anticipated business, research or development, nor resulted from work performed by me for the Company. In the absence of a Specific Inventions Law, the preceding sentence will not apply.

2.5 Obligation to Keep Company Informed. During the period of my employment and for six months after the last day of my employment with the Company, I will promptly disclose to the Company fully and in writing all Inventions authored, conceived or reduced to practice by me, either alone or jointly with others. In addition, I will promptly disclose to the Company all patent applications filed by me or on my behalf within a year after termination of employment. At the time of each such disclosure, I will advise the Company in writing of any Inventions that I believe fully qualify for protection under the provisions of a Specific Inventions Law; and I will at that time provide to the Company in writing all evidence necessary to substantiate that belief. The Company will keep in confidence and will not use for any purpose or disclose to third parties without my consent any confidential information disclosed in writing to the Company pursuant to this Agreement relating to Inventions that qualify fully for protection under a Specific Inventions Law. I will preserve the confidentiality of any Invention that does not fully qualify for protection under a Specific Inventions Law.

2.6 Government or Third Party. I also agree to assign all my right, title and interest in and to any particular Company Invention to a third party, including without limitation the United States, as directed by the Company.

2.7 Works for Hire. I acknowledge that all original works of authorship which are made by me (solely or jointly with others) within the scope of my employment at the Company and which are protectable by copyright are "works made for hire," pursuant to United States Copyright Act (17 U.S.C., Section 101).

2.8 Enforcement of Proprietary Rights. I will assist the Company in every proper way to obtain, and from time to time enforce, United States and foreign Proprietary Rights relating to Company Inventions in any and all countries. To that end I will execute, verify and deliver such documents and perform such other acts (including appearances as a witness) as the Company may reasonably request for use in applying for, obtaining, perfecting, evidencing, sustaining and enforcing such Proprietary Rights and the assignment thereof. In addition, I will execute, verify and deliver assignments of such Proprietary Rights to the Company or its designee. My obligation to assist the Company with respect to Proprietary Rights relating to such Company Inventions in any and all countries shall continue beyond the termination of my employment, but the Company shall compensate me at a reasonable rate after my termination for the time actually spent by me at the Company's request on such assistance.

In the event the Company is unable for any reason, after reasonable effort, to secure my signature on any document needed in connection with the actions specified in the preceding paragraph, I hereby irrevocably designate and appoint the Company and its duly authorized officers and agents as my agent and attorney in fact, which appointment is coupled with an interest, to act for and in my behalf to execute, verify and file any such documents and to do all other lawfully permitted acts to further the purposes of the preceding paragraph with the same legal force and effect as if executed by me. I hereby waive and quitclaim to the Company any and all claims, of any nature whatsoever, which I now or may hereafter have for infringement of any Proprietary Rights assigned hereunder to the Company.

3. NO CONFLICTS OR SOLICITATION. I acknowledge that during my employment I will have access to and knowledge of Proprietary Information. To protect the Company's Proprietary Information, I agree that during the period of my employment by the Company I will not, without the Company's express written consent, engage in any other employment or business activity directly related to the business in which the Company is now involved or becomes involved, nor will I engage in any other activities which conflict with my obligations to the Company. For the period of my employment by the Company and continuing until one year after my last day of employment with the Company, I will not (a) directly or indirectly induce any employee of the Company to terminate or negatively alter his or her relationship with the Company, (b) solicit the business of any client or customer of the Company (other than on behalf of the Company) or (c) induce any supplier, vendor, consultant or independent contractor of the Company to terminate or negatively alter his, her or its relationship with the Company. If any restriction set forth in this Section is found by any court of competent jurisdiction to be unenforceable because it extends for too long a period of time or over too great a range of activities or in too broad a geographic area, it shall be interpreted to extend only over the maximum period of time, range of activities or geographic area as to which it may be enforceable.

4. COVENANT NOT TO COMPETE. I acknowledge that during my employment I will have access to and knowledge of Proprietary Information. To protect the Company's Proprietary Information, I agree that during my employment with the Company whether full-time or half-time and for a period of one year after my last day of employment with the Company, I will not directly or indirectly engage in (whether as an employee, consultant, proprietor, partner, director or otherwise), or have any ownership interest in, or participate in the financing, operation, management or control of, any person, firm, corporation or business that engages in a "Restricted Business" in a "Restricted Territory" (as defined below). It is agreed that ownership of (i) no more than one percent (1%) of the outstanding voting stock of a publicly traded corporation, or (ii) any stock I presently own shall not constitute a violation of this provision.

4.1 Reasonable. I agree and acknowledge that the time limitation on the restrictions in this paragraph, combined with the geographic scope, is reasonable. I also acknowledge and agree that this paragraph is reasonably necessary for the protection of Company's Proprietary Information as defined in paragraph 1.2 herein, that through

my employment I shall receive adequate consideration for any loss of opportunity associated with the provisions herein, and that these provisions provide a reasonable way of protecting Company's business value which will be imparted to me. If any restriction set forth in this paragraph 4 is found by any court of competent jurisdiction to be unenforceable because it extends for too long a period of time or over too great a range of activities or in too broad a geographic area, it shall be interpreted to extend only over the maximum period of time, range of activities or geographic area as to which it may be enforceable.

4.2 As used herein, the terms:

(i) "Restricted Business" shall mean any business engaged in areas similar to those the Company is pursuing, including but not limited to research, development and/or commercialization of (1) one or more products for the treatment of cancer through the use of ex vivo derived cellular cancer vaccines, immunotherapy vaccines or IDO inhibitors, (2) one or more products directed to any of the bioterrorism or infectious disease targets that the Company or any subsidiary (including BioProtection Systems Corporation) is researching or developing, or is preparing to research or develop, during the term of your employment by the Company or (3) any other technology that is potentially competitive with any technology that the Company or any subsidiary is researching or developing, or is preparing to research or develop, during the term of your employment by the Company. The term "Restricted Business" includes an individual or entity that is engaged in or preparing to directly or indirectly engage in the research, development and/or commercialization of any of activities set forth in the preceding sentence.

(ii) "Restricted Territory" shall mean any state, county, or locality in the United States in which the Company conducts business and any other country, city, state, jurisdiction, or territory in which the Company does business.

5. RECORDS. I agree to keep and maintain adequate and current records (in the form of notes, sketches, drawings and in any other form that may be required by the Company) of all Proprietary Information developed by me and all Company Inventions made by me during the period of my employment at the Company, which records shall be available to and remain the sole property of the Company at all times.

6. NO CONFLICTING OBLIGATION. I represent that my performance of all the terms of this Agreement and as an employee of the Company does not and will not breach any agreement to keep in confidence information acquired by me in confidence or in trust prior to my employment by the Company. I have not entered into, and I agree I will not enter into, any agreement either written or oral in conflict herewith.

7. RETURN OF COMPANY MATERIALS. When I leave the employ of the Company, I will deliver to the Company any and all drawings, notes, memoranda, specifications, devices, formulas, and documents, together with all copies thereof, and any other material containing or disclosing any Company Inventions, Third Party Information or Proprietary Information of the Company. I further agree that any property situated on the Company's premises and owned by the Company, including disks and other storage media, filing cabinets or other work areas, is subject to inspection by Company personnel at any time with or without notice.

8. LEGAL AND EQUITABLE REMEDIES. Because my services are personal and unique and because I may have access to and become acquainted with the Proprietary Information of the Company, the Company shall have the right to enforce this Agreement and any of its provisions by injunction, specific performance or other equitable relief, without bond and without prejudice to any other rights and remedies that the Company may have for a breach of this Agreement.

9. NOTICES. Any notices required or permitted hereunder shall be given to the appropriate party at the address specified below or at such other address as the party shall specify in writing. Such notice shall be deemed given upon personal delivery to the appropriate address or if sent by certified or registered mail, three days after the date of mailing.

10. NOTIFICATION OF NEW EMPLOYER. In the event that I leave the employ of the Company, I hereby consent to the notification of my new employer of my rights and obligations under this Agreement.

11. GENERAL PROVISIONS.

11.1 Governing Law; Consent to Personal Jurisdiction and Exclusive Forum. This Agreement will be governed by and construed according to the laws of the State of Iowa as such laws are applied to agreements entered into and to be performed entirely within Iowa between Iowa residents. I hereby expressly understand and consent that my employment is a transaction of business in the State of Iowa and constitutes the minimum contacts necessary to make me subject to the personal jurisdiction of the federal courts located in the State of Iowa, and the state courts located in the County of Story, Iowa, for any lawsuit filed against me by Company arising from or related to this Agreement. I agree and acknowledge that any controversy arising out of or relating to this Agreement or the breach thereof, or any claim or action to enforce this Agreement or portion thereof, or any controversy or claim requiring interpretation of this Agreement must be brought in a forum located within the State of Iowa. No such action may be brought in any forum outside the State of Iowa. Any action brought in contravention of this paragraph by one party is subject to dismissal at any time and at any stage of the proceedings by the other, and no action taken by the other in defending, counter claiming or appealing shall be construed as a waiver of this right to immediate dismissal. A party bringing an action in contravention of this paragraph shall be liable to the other party for the costs, expenses and attorney's fees incurred in successfully dismissing the action or successfully transferring the action to the federal courts located in the State of Iowa, or the state courts located in the County of Story, Iowa.

11.2 Severability. In case any one or more of the provisions contained in this Agreement shall, for any reason, be held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability shall not affect the other provisions of this Agreement, and this Agreement shall be construed as if such invalid, illegal or unenforceable provision had never been contained herein. If moreover, any one or more of the provisions contained in this Agreement shall for any reason be held to be excessively broad as to duration, geographical scope, activity or subject, it shall be construed by limiting and reducing it, so as to be enforceable to the extent compatible with the applicable law as it shall then appear.

11.3 Successors and Assigns. This Agreement will be binding upon my heirs, executors, administrators and other legal representatives and will be for the benefit of the Company, its successors, and its assigns.

11.4 Survival. The provisions of this Agreement shall survive the termination of my employment and the assignment of this Agreement by the Company to any successor in interest or other assignee.

11.5 Employment. I agree and understand that my employment is at-will which means I or the company each have the right to terminate my employment at will, with or without advanced notice and with or without cause. I further agree and understand that nothing in this Agreement shall confer any right with respect to continuation of employment by the Company, nor shall it interfere in any way with my right or the Company's right to terminate my employment at any time, with or without cause.

11.6 Waiver. No waiver by the Company of any breach of this Agreement shall be a waiver of any preceding or succeeding breach. No waiver by the Company of any right under this Agreement shall be construed as a waiver of any other right. The Company shall not be required to give notice to enforce strict adherence to all terms of this Agreement.

11.7 Entire Agreement. The obligations pursuant to Sections 1 through 4 and Sections 6 and 7 (including all subparts) of this Agreement shall apply to any time during which I was previously employed, or am in the future employed, by the Company as a consultant if no other agreement governs nondisclosure and assignment of inventions during such period. This Agreement is the final, complete and exclusive agreement of the parties with respect to the subject matter hereof and supersedes and merges all prior discussions between us. No modification of or amendment to this Agreement, nor any waiver of any rights under this Agreement, will be effective unless in writing and signed by the party to be charged. Any subsequent change or changes in my duties, salary or compensation will not affect the validity or scope of this Agreement

This Agreement shall be effective as of the first day of my employment with the Company, namely: _____ ___, _____.

I HAVE READ THIS AGREEMENT CAREFULLY AND UNDERSTAND ITS TERMS. I HAVE COMPLETELY FILLED OUT EXHIBIT A TO THIS AGREEMENT.

Dated:_____

_____

Signature

_____

Printed Name

ACCEPTED AND AGREED TO:

_____

EXHIBIT A

TO: NewLink Genetics Corporation

FROM: _____

DATE: _____

SUBJECT: Previous Inventions

1. Except as listed in Section 2 below, the following is a complete list of all inventions or improvements relevant to the subject matter of my employment by **NewLink Genetics Corporation** that have been made or conceived or first reduced to practice by me alone or jointly with others prior to my engagement by the Company:

☐ No inventions or improvements.

☐ See below:

_____

_____

_____

☐ Additional sheets attached.

2. Due to a prior confidentiality agreement, I cannot complete the disclosure under Section 1 above with respect to inventions or improvements generally listed below, the proprietary rights and duty of confidentiality with respect to which I owe to the following party(ies):

Invention or Improvement	**Party(ies)**	**Relationship**
1. _____	_____	_____
2. _____	_____	_____
3. _____	_____	_____

☐ Additional sheets attached.

Exhibit 10.6

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

PUBLIC HEALTH SERVICE

COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT FOR EXTRAMURAL-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
National Cancer Institute
an Institute or Center (hereinafter referred to as the "IC") of the
National Institutes of Health

and

Newlink Genetics Corporation,
hereinafter referred to as the "Collaborator,"
having offices at 2503 South Loop Drive, Suite 5100, Ames, Iowa 50010,
created and operating under the laws of Delaware.

COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT
FOR EXTRAMURAL-PHS CLINICAL RESEARCH

Article 1. Introduction

This CRADA between IC and Collaborator will be effective when signed by the Parties, which are identified on both the Cover Page and the Signature Page (page 35). The official contacts for the Parties are identified on the Contacts Information Page (page 36). Publicly available information regarding this CRADA appears on the Summary Page (page 37). The research and development activities that will be undertaken by IC, IC's contractors or grantees, and Collaborator in the course of this CRADA are detailed in the Research Plan, attached as Appendix A. The staffing, funding, and materials contributions of the Parties are set forth in Appendix B. An example of typical terms for a Material Transfer Agreement ("MTA") for the transfer of Investigational Agent from NCI to NCI Extramural Investigators is attached as Appendix C. The original CRADA Letter of Intent (LOI) and its extensions executed between the NCI and Collaborator, which are superseded by this CRADA, are attached as Appendix D (solely for reference). For this Agreement, IC means National Cancer Institute (NCI). Since CTEP and DCTD (defined below) within the NCI are responsible for the Research Plan, IC, NCI, DCTD and CTEP may be used interchangeably in this Agreement when a specific program is responsible for an activity.

Article 2. Definitions

The capitalized terms listed in this Article will have the meanings indicated below when used throughout the CRADA. To the extent a definition of a term as provided in this Article is inconsistent with a corresponding definition in the applicable sections of either the United States Code (U.S.C.) or the Code of Federal Regulations (C.F.R.), the definition in the U.S.C. or C.F.R. will control.

"**Adverse Event**" or "**AE**" means any untoward medical occurrence in a Human Subject administered Investigational Agent associated with the use of a drug, whether or not considered drug related, as defined under 21 C.F.R §312.32. See also FDA Good Clinical Practice Guideline (International Conference on Harmonisation (ICH) E6: "Good Clinical Practice: Consolidated Guidance, 62 Federal Register 25, 691 (1997)).

"**Affiliate**" means any corporation or other business entity controlled by, controlling, or under common control with Collaborator at any time during the term of the CRADA. For this purpose, "control" means direct or indirect

beneficial ownership of at least fifty percent (50%) of the voting stock or at least fifty percent (50%) interest in the income of the corporation or other business entity.

"**Annual Report**" means the report of progress of an IND-associated investigation that the Sponsor must submit to the FDA within sixty (60) days of the anniversary of the effective date of the IND (pursuant to 21 C.F.R. § 312.33).

"**Background Invention**" means an Invention conceived and first actually reduced to practice before the Effective Date.

"**Biomarker**" means a biological marker that can be used to guide therapeutic administration of a drug including but not limited to: (i) to predict whether or not a patient is likely to be sensitive or resistant to treatment with a certain therapeutic agent; or (ii) to guide any aspect of clinical practice (e.g. dosing, safety, efficacy and response).

"**Clinical Investigator**" means, in accordance with 21 C.F.R. § 312.3, an individual who actually conducts a clinical investigation, that is, who directs the administration or dispensation of Investigational Agent to a subject, and who assumes responsibility for studying Human Subjects, for recording and ensuring the integrity of research data, and for protecting the welfare and safety of Human Subjects.

"**Clinical Research Site(s)**" means the site(s) at which the Protocol(s) described in the Research Plan will be performed.

"**Collaborator Materials**" means all tangible materials (a) that are not first produced in the performance of the Research Plan under this CRADA, and (b) that are owned or controlled by Collaborator and used in the performance of the Research Plan. The term "Collaborator Materials" does not include "Investigational Agent" (defined below).

"**Confidential Information**" means confidential scientific, business, financial information of a Party (including any confidential information of a third party that is in a Party's possession), or Identifiable Private Information, provided that Confidential Information does not include:

(a) information that is publicly known or that is available from public sources;

(b) information that has been made available by its owner to others without a confidentiality obligation;

(c) information that is already known by the receiving Party, or information that is independently created or compiled by the receiving Party without reference to or use of the provided information; or

(d) information regarding potential hazards or cautionary warnings associated with the production, handling, or use of Investigational Agent, which is the subject of the Research Plan.

"**Contract**" means a Funding Agreement that is a mechanism that provides that the contractor perform for the benefit of the Government, with an expectation of completion of the stated research goals and the delivery of a report, data, materials or other product. Generally, Contracts are administered under the Federal Acquisition Regulations (FAR) codified at Title 48 C.F.R., Chapter 1 or the Health Services Acquisition Regulations (HSAR) codified at Title 48 C.F.R., Chapter 3.

"**Cooperative Agreement**" means a Funding Agreement that is a species of a Grant, whereby the funding Federal agency intends to be substantially involved in carrying out the research program.

"**Cooperative Research and Development Agreement**" or "**CRADA**" means this Agreement, entered into pursuant to the Federal Technology Transfer Act of 1986, as amended (15 U.S.C. §§ 3710a *et seq*.), and Executive Order 12591 of April 10, 1987.

"**CRADA Collaborator Principal Investigator(s)**" or "**CRADA Collaborator PI(s)**" means the person(s) who will be responsible for the scientific and technical conduct of the Research Plan on behalf of the CRADA Collaborator.

"**CRADA Data**" means information developed by or on behalf of the Parties in the performance of the Research Plan under this CRADA, excluding Raw Data.

"**CRADA Materials**" means all tangible materials first produced in the performance of the Research Plan under this CRADA, *other than* CRADA Data, Collaborator Materials or Investigational Agent. CRADA Materials do not include specimens collected from Human Subjects.

"**CRADA Patent**" means any Patent claiming or covering any CRADA Subject Invention.

"**CRADA Patent Application**" means a Patent Application having claims that cover a CRADA Subject Invention.

"**CRADA Subject Invention**" means any Invention made by either Party or both Parties jointly, conceived or first actually reduced to practice in the performance of the Research Plan.

"**CTA**" means Clinical Trial Agreement.

"**CTEP**" means the Cancer Therapy Evaluation Program, DCTD, NCI, a program within NCI which plans, assesses and coordinates all aspects of clinical trials including extramural clinical research programs, internal resources, treatment methods and effectiveness, and compilation and exchange of data.

"**DCTD**" means Division of Cancer Treatment and Diagnosis, NCI.

"**DCTD Clinical Support Assays**" or "**DCTD CSA**" means assays aimed at enhancing the understanding of the mechanism of action of Investigational Agent and its targets and optimizing DCTD's clinical development program. DCTD's work may include such activities as the development of assays to detect target modulation, biomarker studies, and pharmacodynamic analyses performed in conjunction with the NCI-sponsored clinical studies. These studies will be performed by DCTD employees and contractors who are obligated to assign any and all intellectual property to PHS. Although DCTD Clinical Support Assays are non-clinical in nature, for the purpose of this CRADA they are treated separately from Non-Clinical Studies (defined below) as the approval process and oversight for DCTD Clinical Support Assays and Non-Clinical Studies are different.

"**Drug Master File**" or "**DMF**" is described in 21 C.F.R. Part 314.420. A DMF is a submission to the FDA that may be used to provide confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of one or more human drugs.

"**Effective Date**" means May 23, 2007, the date that this CRADA is deemed to commence effectiveness (which is the date of the last signature of the Parties executing the original CRADA Letter of Intent (LOI) between the Parties).

"**Funding Agreement**" means a Contract, Grant, or Cooperative Agreement entered into between a Federal agency and another party for the performance of experimental, developmental or research work funded in whole or in part by the Federal Government.

"**Government**" means the Government of the United States of America.

"**Grant**" means a Funding Agreement that is an award of financial assistance that may be provided for support of basic research in a specific field of interest to the

funding Federal agency.

"**Human Subject**" means, in accordance with the definition in 45 C.F.R. § 46.102(f), a living individual about whom an investigator conducting research obtains:

(a) data through intervention or interaction with the individual; or

(b) Identifiable Private Information.

"**IC Materials**" means all tangible materials (a) that are not first produced in the performance of the Research Plan under this CRADA, and (b) that are owned or controlled by IC and used in the performance of the Research Plan.

"**IND**" means an "**Investigational New Drug Application**," filed in accordance with 21 C.F.R. Part 312 under which clinical investigation of an experimental drug or biologic (Investigational Agent) is performed in Human Subjects in the United States or intended to support a United States licensing action.

"**Identifiable Private Information**" or "**IPI**" means private information concerning a particular Human Subject from which the identity of such Human Subject is or may readily be ascertained. Regulations defining and governing this information include 45 C.F.R. Part 46 and 21 C.F.R. Part 50.

"**Institutional Review Board**" or "**IRB**" means, in accordance with 45 C.F.R. Part 46, 21 C.F.R. part 56, and other applicable regulations, an independent body comprising medical, scientific, and nonscientific members, whose responsibility is to ensure the protection of the rights, safety, and well-being of the Human Subjects involved in a study.

"**Invention**" means any invention or discovery that is or may be patentable or otherwise protected under Title 35 of the United States Code, or any novel variety of plant which is or may be protectable under the Plant Variety Protection Act, 7 U.S.C. §§ 2321 *et seq*.

"**Investigational Agent**" means, for purposes of this CRADA, and in accordance with 21 C.F.R. § 312.3 , the drug candidate 1-methyl-D-tryptophan (also known as 1MT, or NSC721782), which is provided by or on behalf of Collaborator.

"**Investigator's Brochure**" means, in accordance with the definition in 21 C.F.R. § 312.23(a)(5), a document containing information about the Investigational Agent, including animal screening, preclinical toxicology, and detailed pharmaceutical data, including a description of possible risks and side effects to be anticipated on the basis of prior experience with the drug or related drugs, and

precautions, such as additional monitoring, to be taken as part of the investigational use of the drug.

"**Licensee**" means any licensee (or sublicensee) of Collaborator or its Affiliate of products containing Investigational Agent.

"**Multi-Party Data**" means data from studies sponsored by NCI pursuant to CTAs or CRADAs, where such data are collected under Protocols and Non-Clinical Studies involving combinations of investigational agents supplied from more than one CTA or CRADA collaborator.

"**NCI Extramural Investigator**" means an investigator who is not an NCI employee and who is supported by NCI Funding Agreements.

"**NCI Intramural Investigator**" means an investigator who is an NCI employee.

"**NCI Investigator**" includes any of NCI Intramural Investigator, NCI Extramural Investigator, Non-Clinical Investigator or an investigator who conducts the DCTD Clinical Support Assays.

"**NIH CRADA Extramural Investigator/Officer(s)**" means the extramural staff who are responsible for the conduct and/or management of the CRADA on behalf of the NIH IC. In the case of this CRADA, the NIH CRADA Extramural Investigator is Dr. Howard Streicher and the NIH CRADA Extramural Officer is Dr. Jeffrey Abrams.

"**Non-Clinical Investigator**" means any individual who conducts, directs, or assumes responsibility for Non-Clinical Studies. Non-Clinical Investigators will include NCI intramural and extramural investigators.

"**Non-Clinical Studies**" means exploratory *in vitro*, *in vivo*, and *ex vivo* studies using defined biological models including cell lines, xenograft models, circulating tumor cells, normal tissue, blood and any of its components and shall include ancillary correlative studies, proof-of-mechanism and proof-of-principle assays, development of imaging techniques, and evaluation of target linkage. Non-Clinical Studies may include studies using human materials derived from clinical trials (such as primary, metastatic, or circulating tumor cells), normal tissue, blood and any of its components). This defined term shall be limited to studies under this CRADA. Non-Clinical Studies can be performed by Clinical Investigators or Non-Clinical Investigators. Non-Clinical Studies under this CRADA shall not include DCTD Clinical Support Assays.

"**Patent**" means any patent claiming or covering any invention that is issued in the

United States patent, or in any other country or jurisdiction, and including any corresponding grant(s) of similar rights by a non-U.S. government in place of a patent.

"**Patent Application**" means an application for patent protection for an Invention with the United States Patent and Trademark Office ("U.S.P.T.O.") or the corresponding patent-issuing authority of another nation.

"**Placebo**" means an inactive substance identical in appearance to the material being tested that is used to distinguish between drug action and suggestive effect of the material under study.

"**Protocol**" means the formal, detailed description of a study to be performed as provided for in the Research Plan. It describes the objective(s), design, methodology, statistical considerations, and organization of a trial. For the purposes of this CRADA, the term, Protocol, for clinical research involving Human Subjects, includes any and all associated documents, including informed consent forms, to be provided to Human Subjects and potential participants in the study.

"**Protocol Review Committee**" (or "**PRC**") means the CTEP/DCTD committee that reviews and approves studies involving NCI investigational agents and/or activities supported by NCI.

"**Raw Data**" means the primary quantitative and empirical data first collected from experiments and clinical trials conducted within the scope of this CRADA. Raw Data includes case report forms and/or source documents.

"**Research Plan**" means the statement in Appendix A of the respective commitments of the Parties. The Research Plan should describe the provisions for sponsoring the IND, clinical and safety monitoring, and data management.

"**Sponsor**" means, in accordance with the definition in 21 C.F.R. § 312.3, an organization or individual who assumes legal responsibility for supervising or overseeing clinical trials with Investigational Agents, and is sometimes referred to as the IND holder.

"**Steering Committee**" means the team whose composition and responsibilities with regard to the research performed under this CRADA are described in Appendix A.

"**Summary Data**" means any extract or summary of the Raw Data, generated either by or, on behalf of, IC or by, or on behalf of, Collaborator. Summary Data

may include extracts or summaries that incorporate IPI.

"**Unauthorized Use**" means any unauthorized modifications to the Investigational Agent or the conduct of any unauthorized research using the Investigational Agent.

Article 3. Cooperative Research and Development

3.1 **Performance of CRADA Activities**. The research and development activities to be carried out under this CRADA will be performed by the Parties identified on the Cover Page, as well as IC's contractors or grantees as described in the Research Plan. However, IC's contractors or grantees are not Parties to the CRADA, and this CRADA does not grant to Collaborator any rights to Inventions made by IC's contractors or grantees except to the extent that IC obtains rights to any such CRADA Subject Inventions. The NIH CRADA Extramural Investigator/Officer(s) and CRADA Collaborator PI(s) will be responsible for coordinating the scientific and technical conduct of this project on behalf of their employers. Any Collaborator employees who will work at IC facilities will be required to sign a Guest Researcher or Special Volunteer Agreement appropriately modified in view of the terms of this CRADA.

3.2 **Research Plan**. The Parties recognize that the Research Plan describes the collaborative activities they will undertake and that interim research goals set forth in the Research Plan are good faith guidelines. Should events occur that require modification of these goals, then by mutual agreement the Parties can modify them through an amendment, according to Paragraph 13.6.

3.3 **Use and Disposition of Collaborator Materials and IC Materials**. The Parties agree to use Collaborator Materials and IC Materials only in accordance with the Research Plan and Protocol(s), not to transfer these materials to third parties except in accordance with the Research Plan and Protocol(s) or as approved by the owning or providing Party, and, upon expiration or termination of the CRADA, to dispose of these materials as directed by the owning or providing Party.

3.4 **Third-Party Rights in Collaborator's CRADA Subject Inventions**. If Collaborator has received (or will receive) support of any kind from a third party in exchange for granting such third party rights in any of Collaborator's CRADA Subject Inventions, Collaborator agrees to ensure that its obligations to the third party are both consistent with Articles 6 through 8 and subordinate to Sections 7.1, 7.4, 7.5, 7.6, 7.7 and 7.8 of this CRADA.

3.5 **Disclosures to IC**. Prior to execution of this CRADA, Collaborator agrees to disclose to IC all instances in which outstanding royalties are due from

Collaborator under a PHS license agreement, and in which Collaborator had a PHS license terminated in accordance with 37 C.F.R. § 404.10. These disclosures will be treated as Confidential Information upon request by Collaborator in accordance with the definition in Article 2 and Paragraphs 8.3 and 8.4.

3.6 Clinical Investigator Responsibilities. The Clinical Investigator will be required to submit, or to arrange for submission of, each Protocol associated with this CRADA to all appropriate IRBs, and for ensuring that the IRBs are notified of the role of Collaborator in the research. In addition to the Protocol, all documents associated with the Protocol, including informational documents and advertisements relating to the Protocol, must be reviewed and approved by the appropriate IRB(s) before starting the research at each Clinical Research Site. The research will be done in strict accordance with the Protocol(s) and no substantive changes in a finalized Protocol will be made unless mutually agreed upon, in writing, by the Parties. Research will not commence (or will continue unchanged, if already in progress) until each substantive change to a Protocol, including those required by either the FDA or the IRB, has been integrated in a way acceptable to the Parties, submitted to the FDA (if applicable) and approved by the appropriate IRBs.

3.7 Investigational New Drug Applications.

3.7.1 DCTD, NCI, as provided in the Research Plan, has prepared and submitted an IND(s) covering the clinical research on the Investigational Agent conducted in accordance with the Protocol(s) under the CRADA LOI and to be conducted under this CRADA, and all Clinical Investigators participating in such DCTD-sponsored clinical trials must have completed registration documents on file (1572 forms) with CTEP. The DCTD hereby agrees to permit Collaborator and its Affiliates and Licensees to review, cross-reference and use the IND(s) in conducting Collaborator (and/or such Licensee's) sponsored clinical trials and in Collaborator's (and/or such Licensee's) fulfilling all of the requirements necessary for obtaining FDA approval (and/or equivalent regulatory approvals in other countries or jurisdictions) to market Investigational Agent as an anti-cancer agent, which rights survive termination of this CRADA. Upon Collaborator's request, DCTD will make all necessary filings with the FDA during the term of this CRADA to allow Collaborator (and its Licensees) such rights of cross-reference, and, if requested by Collaborator, shall provide Collaborator a letter acknowledging such rights of cross-reference, which Collaborator (and its Licensees) may use in regulatory filings with similar regulatory agencies in other countries.

3.7.2 To support the DCTD IND(s) submitted under Section 3.7.1, Collaborator agrees to provide DCTD such background data and information in Collaborator's possession and control as necessary to support the IND(s). Collaborator further agrees to provide a letter of cross-reference to all pertinent regulatory filings by Collaborator relating to Investigational Agent, including an IND and/or DMF sponsored by Collaborator, as required by DCTD to file or support the DCTD IND(s) in order to conduct clinical trials under the CRADA. Collaborator's employees will be reasonably available to respond to inquiries from the FDA regarding information and data contained in the Collaborator's IND, DMF, other filings, or other information and data provided to DCTD by the Collaborator pursuant to this Article 3. If CTEP or DCTD has provided information or data for use in, or to assist Collaborator in, its IND filing, CTEP or DCTD (as applicable) will provide a copy of its letter of cross reference to its INDs and respond to inquiries related to information provided by DCTD, and will permit Collaborator's (and its Licensee's) uses of the DCTD IND(s) in clinical development and seeking regulatory approval of Investigational Agent (or any product containing Investigational Agent).

3.7.3 If Collaborator supplies Confidential Information to DCTD in support of an IND filed by DCTD, this information will be protected in accordance with the corresponding confidentiality provisions of Article 8.

3.7.4 Collaborator may sponsor its own clinical trials and hold its own INDs covering Investigational Agent for studies performed outside the scope of this CRADA. These studies, however, should not adversely affect the ability to accomplish the goal of the Research Plan, for example, by competing for the same study population, and Collaborator shall use reasonable efforts to avoid such adverse effects. All data from those clinical trials are proprietary to Collaborator for purposes of this CRADA. To the extent consistent with Collaborator's other business and contractual obligations, Collaborator will use reasonable efforts to permit DCTD to review and use such data for regulatory purposes for DCTD-sponsored clinical trials which are under the CRADA.

3.7.5 In the event that Canadian institutions are participating on DCTD-sponsored clinical trials, Collaborator will need to assist in the submission of the regulatory documents to the Canadian Health Products and Food Branch to allow for such participation. This may include a letter of cross-reference to an existing Clinical Trials Application or a DMF, including

supporting documentation on the production of the Investigational Agent. The forms and procedures for preparing Canadian Clinical Trials Application are available at http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/form/index-eng.php.

3.7.6 In the event that other international Clinical Research Sites are participating on the NCI-sponsored protocols, NCI will provide copies, with Collaborator's approval, of the Investigational Agent IBs and Certificates of Analysis to the international Clinical Research Sites to support the regulatory filings. Collaborator will assist the international Clinical Research Sites with the submission of other necessary regulatory documents to allow for such participation. The international Clinical Research Sites will work directly with the Collaborator to obtain the necessary regulatory documents.

3.8 Investigational Agent Information and Supply.

3.8.1 Collaborator agrees to provide DCTD without charge and on a schedule that will reasonably ensure adequate and timely performance of the research under the mutually approved clinical Protocols, a sufficient quantity of formulated and acceptably labeled, clinical-grade Investigational Agent (and, to the extent required by the Protocols, Placebo) to complete the clinical trial(s) agreed to and approved under this CRADA, subject to Article 12.3 of this CRADA. Collaborator represents that it believes it has access to the sufficient supply of Investigational Agent to complete the mutually approved clinical Protocols, as documented by the signed drug approval forms, which will not be affected by (1) early termination of this CRADA by either Party, unless for DCTD's uncured breach of this CRADA, or (2) Collaborator termination of its Investigational Agent developmental activities, unless such termination is for safety concerns, or for material efficacy issues as determined by mutual agreement of DCTD and Collaborator with each Party acting reasonably. Investigational Agent should be suitable for shipment to all countries and sites participating in DCTD-sponsored clinical trials on Investigational Agent. DCTD does not maintain country specific Investigational Agent supplies. Collaborator will provide a Certificate of Analysis to DCTD for each lot of the Investigational Agent provided. It is understood that DCTD shall take responsibility for and reasonable steps to maintain appropriate records and assure appropriate supply, handling, storage, distribution and usage of these materials in accordance with the terms of this Agreement, the Protocol(s) and any applicable laws and regulations relating thereto.

3.8.2 Collaborator agrees to use reasonable efforts to maintain sufficient inventory to ensure adequate and timely supply of Investigational Agent as required under the mutually agreed upon Protocol(s). DCTD will provide updated forecasts of amounts of Investigational Agent anticipated for ongoing and anticipated studies. Collaborator further agrees to provide draft Investigational Agent labels to the NCI Pharmaceutical Management Branch (PMB) for review and agrees to reasonable labeling revisions to comply with DCTD label guidelines. NCI NSC (National Service Center) numbers will be required to be on the label of Investigational Agent for all DCTD-sponsored clinical trials.

3.8.3 Furthermore, Collaborator agrees to provide **[*]** a reasonable amount, not to exceed **[*]** of the quantity of Investigational Agent supplied by Collaborator to DCTD for clinical studies under this CRADA, of Investigational Agent or unformulated analytical grade Investigational Agent or metabolites, if available, to DCTD as needed to supply to NCI Investigators for the development of mutually agreed upon Non-Clinical Studies (such as analytical assays and ancillary correlative studies conducted in conjunction with DCTD-sponsored Protocols), to the extent such assays or studies are approved by the PRC and Collaborator and are covered by the Research Plan. These studies will be approved by the Collaborator and PRC and conducted according to the mutually approved clinical Protocols.

3.8.4 Collaborator agrees to allow reasonable amounts of Investigational Agent to be distributed to NCI Investigators for conduct of mutually-agreeable Non-Clinical Studies designed to enhance the basic understanding and development of Investigational Agent. These may include non-clinical studies designed to support clinical trials in **[*]**; non-clinical **[*]** studies to provide data in support of a clinical trial and other pertinent requests. Each study will be proposed by the NCI Investigator and will be approved by both the NCI and Collaborator. All NCI Extramural Investigators will sign Material Transfer Agreements (MTAs) substantially in the form attached hereto as Appendix C that acknowledge the proprietary nature of the Investigational Agent to Collaborator and include appropriate intellectual property and publication provisions.

3.8.5 Collaborator agrees to provide a reasonable amount, not to exceed **[*]** of the quantity of Investigational Agent supplied by Collaborator to DCTD for clinical studies under this CRADA, of Investigational Agent to DCTD as required for DCTD to conduct DCTD Clinical Support Assays aimed at enhancing the understanding of the mechanism of action of Investigational

Agent and its targets and optimizing its clinical development program.

3.8.6 Collaborator agrees to provide to the PMB the Investigator's Brochure (IB) on Investigational Agent to be used to support the clinical trials to be conducted under this CRADA, and all subsequent revisions/editions thereto. In addition to being filed to the CTEP IND, the IB will be on file in the PMB and will be distributed to all investigators participating on a clinical trial using the Investigational Agent under the Protocol(s). Distribution will be accompanied by a statement about the confidentiality of the document and it is anticipated that distribution will be electronic. All electronic distribution will be done using Adobe Acrobat PDF. Any IB received by the PMB that is not in this format will be converted before distribution. Hard copy IBs should be sent to IB Coordinator, Pharmaceutical Management Branch, CTEP, DCTD, NCI, 6130 Executive Blvd, Room 7149, Rockville, MD 20852. Electronic versions should be emailed to the IB Coordinator at IBCoordinator@mail.nih.gov.

3.9 Investigational Agent Delivery and Usage. Collaborator will ship the Investigational Agent and, if required, Placebo to NCI or its designee (e.g, the NCI clinical repository) in containers marked in accordance with 21 C.F.R. § 312.6. NCI agrees that the Clinical Investigators will keep appropriate records and take reasonable steps to ensure that the Investigational Agent is used in accordance with the Protocol(s) and applicable FDA regulations. In addition, NCI agrees that the Investigational Agent (and all Confidential Information supplied by Collaborator relating to the Investigational Agent) will be used solely for the conduct of the CRADA Research Plan. Furthermore, NCI agrees that no analysis or modification of the Investigational Agent will be performed without Collaborator's prior written consent. At the completion of the Research Plan, any unused quantity of Investigational Agent will be returned to Collaborator or disposed as directed by Collaborator. The contact person for NCI will be Mr. Charles Hall, Chief, Pharmaceutical Management Branch (Telephone Number 301-496-5725) and the Collaborator contact will be Dr. Nick Vahanian (Telephone Number (515) 598-2922).

3.10 Auditing and Monitoring.

3.10.1 DCTD, NCI will be primarily responsible for monitoring Clinical Research Sites and for assuring the quality of all clinical data, unless otherwise stated in the Research Plan. Auditing will comply with the DCTD guidelines as described on the CTEP website at: http://ctep.info.nih.gov/branches/ctmb/clinicalTrials/monitoring.htm.

NCI shall ensure that all clinical trials are conducted in accordance with the FDA Good Clinical Practices (GCP).

3.10.2 Subject to the restrictions in Article 8 concerning IPI, and with reasonable advance notice and at reasonable times, IC will permit Collaborator or its designee(s) to access Clinical Research Sites and to audit the conduct of the research at times convenient to Clinical Research Sites and the data generated, and to obtain updates on ongoing clinical trials. Collaborator also will have the right to (by making arrangements with IC) to review and audit all source documents containing Raw Data, at the completion of a Protocol and at Collaborator's expense, to the extent reasonably necessary to verify compliance with FDA Good Clinical Practice and the Protocol(s) or for exercising Collaborator's data access rights under this CRADA, or otherwise to comply with applicable laws or regulations.

3.10.3 NCI shall ensure that Collaborator shall be provided copies of all CRADA Data and Raw Data generated under this CRADA which are in its possession and control, for use as provided in the terms of this Agreement. Further, Collaborator shall have the right to audit appropriate records at the Clinical Research Sites to ensure complete transfer of and access to all such data and results.

3.11 FDA Meetings/Communications. All formal meetings with the FDA concerning any clinical trial within the scope of the Research Plan will be discussed by Collaborator and IC in advance. Each Party reserves the right to take part in setting the agenda for, to attend, and to participate in these meetings. The Sponsor will provide the other Party with copies of FDA meeting minutes, all transmittal letters for IND submissions, IND safety reports, formal questions and responses that have been submitted to the FDA, Annual Reports, and official FDA correspondence, pertaining either to the INDs under this CRADA or to the Clinical Investigators on Protocols performed in accordance with the Research Plan, except to the extent that those documents contain the proprietary information of a third party or dissemination is prohibited by law.

3.12 Steering Committee and CRADA Research. The Parties agree to establish a Steering Committee comprising at least the NIH CRADA Extramural Investigator/officer(s) and Collaborator CRADA PIs to conduct and monitor the proposed and ongoing clinical studies and non-clinical research of the Investigational Agent in accordance with the CRADA Research Plan. Members of the Steering Committee shall continue to remain employed by their respective employers under their

respective terms of employment.

In addition to the Steering Committee a project team comprising NCI and Collaborator scientific members for the purpose of discussing the DCTD Clinical Support Assays may be assembled. This Project Team will be a collaborative body to approve projects described under “Respective Contributions of the Parties” in the Research Plan of Appendix A of this CRADA which outlines the DCTD Clinical Support Assays. Manuscripts and presentations related to these studies will be handled in accordance with Article 8.7 of this CRADA.

Additional CRADA information, including Steering Committee meeting reports, Protocol Review Committee records, clinical Protocols, IND and general regulatory information, and non-clinical and clinical data in NCI’s possession and control shall remain on file with NCI.

Article 4. Reports

4.1 **Interim Research Plan Reports**. The NIH CRADA Extramural Investigator/Officer(s) and CRADA Collaborator PI(s) should exchange information regularly about progress under the Research Plan, in writing on a regular basis. This exchange may be accomplished through meeting minutes, detailed correspondence, circulation of draft manuscripts, Steering Committee reports, copies of Annual Reports and any other reports updating the progress of the CRADA research. However, the Parties must exchange updated Investigator’s Brochure, formulation and preclinical data, and toxicology findings (whether or not generated under the Research Plan), as they become available, to support the clinical studies with Investigational Agent under the CRADA.

4.2 **Final Research Plan Reports**. The Parties will exchange final reports of all their results under the Research Plan within six (6) months after the expiration or termination of this CRADA. These reports will set forth the technical progress made; any publications arising from the research; and the existence of invention disclosures of potential CRADA Subject Inventions and/or any corresponding CRADA Patent Applications. Abstracts and publications provided to CTEP by investigators and further provided by CTEP to Collaborator will fulfill this final report obligation. With respect to clinical studies, a copy of the IND(s) Annual Report will also fulfill this reporting obligation.

4.3 **Fiscal Reports**. If Collaborator has agreed to provide funding to IC under this CRADA and upon the request of Collaborator, then concurrent with the exchange of final Research Plan reports according to Paragraph 4.2, IC will submit to Collaborator a statement of all costs incurred by IC for the CRADA. If the

CRADA has been terminated, IC will specify any costs incurred before the date of termination for which IC has not received funds from Collaborator, as well as for all reasonable termination costs including the cost of returning Collaborator property or removal of abandoned Collaborator property, for which Collaborator will be responsible.

4.4 **Safety Reports**. DCTD shall report all serious and unexpected possible, probable and definite Adverse Events to FDA in accordance with the reporting obligations of 21 CFR 312.32 and will, within 24 hours of notification to FDA, forward all such reports to Collaborator. All other Adverse Event reports received by DCTD shall be reported to the FDA consistent with 21 CFR 312.32 and 312.33. In the event that Collaborator informs the FDA of any serious and/or unexpected Adverse Events relating to Investigational Agent, Collaborator must notify the NCI at the same time by sending the reports to CTEPSupportAE@tech-res.com. NCI will then notify the Clinical Investigator(s) conducting studies under DCTD-sponsored Protocols, if appropriate.

4.5 **Annual Reports**. DCTD will provide Collaborator a copy of the Annual Report concurrently with the submission of the Annual Report to the FDA. Collaborator will provide DCTD with a copy of its Annual Report to the FDA if Collaborator is sponsoring studies of Investigational Agent under its own IND. All such disclosed Annual Reports will be kept confidential by receiving Party in accordance with Article 8.

Article 5. Staffing, Financial, and Materials Obligations

5.1 **IC and Collaborator Contributions**. The contributions of any staff, funds, materials, and equipment by the Parties are set forth in Appendix B. The Federal Technology Transfer Act of 1986, 15 U.S.C. § 3710a(d)(1) prohibits IC from providing funds to Collaborator for any activities under this CRADA.

5.2 **IC Staffing**. No IC employees will devote 100% of their effort or time to the activities under this CRADA. IC will not use funds provided by Collaborator under this CRADA for IC personnel to pay the salary of any permanent IC employee. Although personnel hired by IC using CRADA funds will focus principally on CRADA research and development activities under the Research Plan, Collaborator acknowledges that these personnel may nonetheless make contributions to other research and development activities independent of this CRADA, and such activities will be outside the scope of this CRADA.

5.3 **Collaborator Funding**. Collaborator acknowledges that Government funds

received by Collaborator from an agency of the Department of Health and Human Services may not be used to fund IC under this CRADA. Collaborator has agreed to provide funds to IC solely as provided in Appendix B. Each Party will maintain separate and distinct current accounts, records, and other evidence supporting its financial obligations under this CRADA and, upon written request, will provide the other Party a Fiscal Report according to Paragraph 4.3, which delineates all payments made and all obligated expenses, along with the Final Research Report described in Paragraph 4.2.

5.4 **Capital Equipment**. Collaborator's commitment, if any, to provide IC with capital equipment to enable the research and development activities under the Research Plan appears in Appendix B. If Collaborator transfers to IC the capital equipment or provides funds for IC to purchase it, then IC will own the equipment. If Collaborator loans capital equipment to IC for use during the CRADA, Collaborator will be responsible for paying all costs and fees associated with the transport, installation, maintenance, repair, removal, or disposal of the equipment, and IC will not be liable for any damage to the equipment.

Article 6. Intellectual Property

6.1 **Ownership of CRADA Subject Inventions, CRADA Data, and CRADA Materials**. Subject to the Government license described in Paragraph 7.5, the sharing requirements of Paragraph 8.1 and the regulatory filing requirements of Paragraph 8.2, the producing Party will retain sole ownership of and title to all CRADA Subject Inventions, all copies of CRADA Data, and all CRADA Materials produced solely by its employee(s). The Parties will own jointly all CRADA Subject Inventions invented jointly and all CRADA Materials developed jointly by the Parties. Each Party will retain the right to use, exploit and license its interest in the invention (without consent of or accounting to the other Party) with the understanding that both Parties will endeavor to cooperate in any licensing strategy for such Joint Inventions. A PHS contractor's or grantee's rights in data it generates will not be affected by this CRADA, except to the extent that PHS (including any agency or department thereof) obtains rights to any inventions or information developed or made by such contractor or grantee in performing work under the Research Plan or the Protocol. The Parties acknowledge that certain IC contractors who may perform DCTD Clinical Support Assays are obligated to assign any and all intellectual property to NIH related to Investigational Agent provided under this CRADA.

6.2 **Reporting**. The Parties will promptly report to each other in writing each CRADA Subject Invention reported by their respective personnel, and any

CRADA Patent Applications filed thereon, resulting from the conduct of the Research Plan or any other research or development activities under this CRADA. Each Party will report all CRADA Subject Inventions to the other Party in sufficient detail to determine inventorship, which will be determined in accordance with U.S. patent law, These reports will be treated as Confidential Information in accordance with Article 8. Formal reports will be made by and to the Patenting and Licensing Offices identified on the Contacts Information Page herein.

6.3 **Filing of CRADA Patent Applications**. Each Party will solely control and make decisions regarding the filing of CRADA Patent Applications on the CRADA Subject Inventions made solely by its employee(s), and will notify the other Party in advance of filing. Collaborator will have the first opportunity to file CRADA Patent Applications on joint CRADA Subject Inventions and will notify PHS of its decision within **[*]** days of a joint Invention being reported by the Parties in writing or at least **[*]** days before any patent filing deadline, whichever occurs sooner. If Collaborator does not notify PHS of its decision on a particular joint CRADA Subject Invention within the above time period or notifies PHS of its decision not to file a CRADA Patent Application covering such joint inventions, then PHS has the right to file a CRADA Patent Application on the joint CRADA Subject Invention. Neither Party will be obligated to file a CRADA Patent Application. Collaborator will place the following statement in any CRADA Patent Application it files on a CRADA Subject Invention: “This invention was created in the performance of a Cooperative Research and Development Agreement with the **National Institutes of Health**, an Agency of the Department of Health and Human Services. The Government of the United States has certain rights in this invention.” If either Party files a CRADA Patent Application on a joint CRADA Subject Invention, then the filing Party will include a statement within the Patent Application that clearly identifies the Parties and states that the joint CRADA Subject Invention was made under this CRADA.

6.4 **CRADA Patent Expenses**. Unless agreed otherwise, the Party filing a CRADA Patent Application will pay all preparation and filing expenses, prosecution fees, issuance fees, post issuance fees, patent maintenance fees, annuities, interference expenses, and attorneys’ fees for that CRADA Patent Application and any resulting Patent(s). If a license to any CRADA Subject Invention is granted to Collaborator, then Collaborator will be responsible for all out-of-pocket expenses and fees, past and future, in connection with the preparation, filing, prosecution, and maintenance of any CRADA Patent Applications and Patents claiming the CRADA Subject Inventions exclusively licensed to Collaborator and will be responsible for a pro-rated share, divided equally among all licensees, of those out-of-pocket expenses and fees for CRADA Subject Inventions non-exclusively

licensed to Collaborator. Collaborator may waive its exclusive option or license rights at any time, and incur no subsequent financial obligation for those CRADA Patent Application(s) or Patent(s).

6.5 Prosecution of CRADA Patent Applications. The Party filing a CRADA Patent Application will provide the non-filing Party with a copy of any patent office official communication relating to prosecution of the CRADA Patent Application within thirty (30) days of transmission of the communication. Each Party will also provide the other Party with the power to inspect and make copies of all documents retained in the applicable CRADA Patent Application or CRADA Patent file. The Parties agree to consult with each other regarding the prosecution of CRADA Patent Applications directed to jointly owned CRADA Subject Inventions. If Collaborator elects to file and prosecute CRADA Patent Applications on jointly owned CRADA Subject Inventions, then Collaborator agrees to use the U.S.P.T.O. Customer Number Practice and/or grant PHS a power(s) of attorney (or equivalent) necessary to assure PHS access to its intellectual property rights in these CRADA Patent Applications. PHS and Collaborator will cooperate with each other to obtain necessary signatures on CRADA Patent Applications, assignments, or other documents.

Article 7. Licensing

7.1 Background Inventions. Other than as specifically stated in the following sentence, nothing in this CRADA will be construed to grant any rights in one Party's Background Invention(s) to the other Party, and such other Party obtains no such rights. Each Party hereby grants the other Party the limited, non-exclusive, royalty-free license under such granting Party's Background Invention(s) solely to the extent necessary for such other Party to conduct its research and development activities as described in the Research Plan. The field of use of such licenses will not exceed the scope of the Research Plan.

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 CRADA Patent Application has been filed, PHS hereby offers to the Collaborator the following options and grants:

7.2(a). For any such CRADA Subject Inventions that would be described in CRADA Patent Applications that claim the use and/or the composition of the Investigational Agent(s), PHS hereby grants to Collaborator: (i) an option to elect

and obtain a royalty-free ([*] which will be pro-rated and divided equally among all licensees), worldwide, non-exclusive license for commercial purposes with the right to sublicense to Affiliates or collaborators working on behalf of Collaborator for Collaborator's development purposes; (ii) a time limited option to negotiate an exclusive, or co-exclusive, if applicable, world-wide, royalty bearing license for commercial purposes, including the right to grant sublicenses, on terms to be negotiated in good faith by the Collaborator(s) and PHS; and (iii) at Collaborator's request, a paid-up, nonexclusive, royalty-free, world-wide license for research purposes only. NIH retains the right to make and use any Inventions covered by this Paragraph 7.2(a) for all non-profit research, including for educational purposes and to permit other educational and non-profit institutions to do so.

7.2(b). For CRADA Subject Inventions pursuant to research under this CRADA not covered under Paragraph 7.2(a), including those that use non-publicly available CRADA Data or specimens from patients treated with Investigational Agent under the CRADA, (including specimens obtained from NCI CTEP-funded tissue banks) PHS hereby grants to Collaborator: (i) a paid-up nonexclusive, nontransferable, royalty-free, world-wide license for research purposes only; and (ii) a nonexclusive, royalty-free, world-wide license to: (a) disclose such Inventions to a regulatory authority when seeking marketing authorization of the Investigational Agent, and (b) disclose such Inventions on a product insert or other promotional material regarding the Investigational Agent after having obtained marketing authorization from a regulatory authority. Notwithstanding the above, PHS is under no obligation to file a CRADA Patent Application or maintain patent prosecution for any such Inventions.

7.2(c). In addition, for Inventions made by NIH' s Intramural Investigator(s) or any other employees or agents of IC, which are or may be patentable or otherwise protectable, as a result of research utilizing the Investigational Agent(s), unreleased or non-publicly available CRADA Data or Investigational Agent-treated specimens outside the scope of approval granted by the NCI CTEP (Unauthorized Inventions): PHS agrees, at Collaborator's request, to grant to Collaborator a royalty-free ([*] which will be pro-rated and divided equally among all licensees) exclusive or co-exclusive commercial license to Unauthorized Inventions. NIH will retain a nonexclusive, nontransferable, irrevocable, paid-up license from the Collaborator to practice the invention or have the invention practiced throughout the world by or on behalf of the Government.

7.2(d). In addition to the license options to CRADA Subject Invention(s) contained in Paragraphs 7.2(b) and 7.2(c) above, PHS hereby grants to Collaborator an exclusive option to CRADA Subject Inventions to elect an

exclusive or nonexclusive commercialization license to such Inventions. The field of use of this license option will not exceed the scope of the Research Plan.

7.3 **Exercise of Collaborator's License Option**. To exercise the option(s) or grant(s) set forth in Paragraph 7.2, Collaborator must submit a written notice to the PHS Patenting and Licensing Contact identified on the Contacts Information Page (and provide a copy to the IC Contact for CRADA Notices) within **[*]** after either (i) Collaborator receives written notice from PHS that a CRADA Patent Application has been filed or (ii) the date on which Collaborator files a CRADA Patent Application. The written notice exercising the option(s) will include a completed "Application for License to Public Health Service Inventions" and will initiate a negotiation period that expires **[*]** after the date of exercise of the option. If PHS has not responded in writing to the last proposal by Collaborator within this **[*]**, the negotiation period will be extended to expire one (1) month after PHS so responds, during which month Collaborator may accept in writing the final license proposal of PHS. If PHS and Collaborator fail to reach agreement within **[*]**, (or such additional period as described above) on the terms for an exclusive license for a particular Paragraph 7.2(a) Invention, then for a period of **[*]** thereafter PHS agrees not to offer to license the Paragraph 7.2(a) Invention to any third party on materially better terms than those last offered to Collaborator without first offering such terms to Collaborator, in which case Collaborator will have a period of **[*]** in which to accept or reject the offer. In the absence of Collaborator's exercise of the option with respect to a CRADA Subject Invention, or upon election of a nonexclusive license to such Invention, PHS will be free to license the CRADA Subject Invention to others. These time periods may be extended at the sole discretion of PHS upon good cause shown in writing by Collaborator.

7.4 **Government License in IC Sole CRADA Subject Inventions and Joint CRADA Subject Inventions**. Pursuant to and subject to the terms of 15 U.S.C. § 3710a(b)(1)(A), for CRADA Subject Inventions owned solely by IC or jointly by IC and Collaborator, and licensed pursuant to the option of Paragraph 7.2, Collaborator grants to the Government a nonexclusive, nontransferable, irrevocable, paid-up license to practice the CRADA Subject Invention or have the CRADA Subject Invention practiced throughout the world by or on behalf of the Government. In the exercise of this license, the Government will not publicly disclose trade secrets or commercial or financial information that is privileged or confidential within the meaning of 5 U.S.C. § 552(b)(4) or which would be considered privileged or confidential if it had been obtained from a non-federal party.

7.5 **Government License in Collaborator Sole CRADA Subject Inventions**.

Pursuant to and subject to the terms of 15 U.S.C. § 3710a(b)(2), for CRADA Subject Inventions made solely by an employee of Collaborator, Collaborator grants to the Government a nonexclusive, nontransferable, irrevocable, paid-up license to practice the CRADA Subject Invention or have the CRADA Subject Invention practiced throughout the world by or on behalf of the Government for research or other Government purposes.

7.6 **Third Party License**. Pursuant to and subject to the terms of 15 U.S.C. § 3710a(b)(1)(B), if PHS grants Collaborator an exclusive, 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 does not grant such a license to the extent required under the above code section, to grant such 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).

7.7 **Third-Party Rights In IC Sole CRADA Subject Inventions**. For a CRADA Subject Invention conceived prior to the Effective Date solely by an IC employee that is first actually reduced to practice after the Effective Date in the performance of the Research Plan, the option offered to Collaborator in Paragraph 7.2 may be restricted if, prior to the Effective Date, PHS had filed a CRADA Patent Application and has either offered or granted a license in the CRADA Subject Invention to a third party. Collaborator nonetheless retains the right to apply for a license to any such CRADA Subject Invention in accordance with the terms and procedures of 35 U.S.C. § 209 and 37 C.F.R. Part 404.

7.8 **Joint CRADA Subject Inventions Not Exclusively Licensed by Collaborator**. If Collaborator does not acquire an exclusive commercialization license in a joint CRADA Subject Invention in all fields of use then, for those fields of use not exclusively licensed to Collaborator, each Party will have the right to use the joint CRADA Subject Invention and to license its use to others, and each Party will cooperate with the other, as necessary, to fulfill international licensing

requirements. The Parties may agree to a joint licensing approach for any such remaining fields of use.

Article 8. Rights of Access and Publication

8.1 **Right of Access to CRADA Data and CRADA Materials**. IC and Collaborator agree to exchange all CRADA Data and to share all CRADA Materials. If the CRADA is terminated, both Parties agree to provide CRADA Materials in quantities needed to complete the Research Plan. Such provision will occur before the termination date of the CRADA or sooner, if required by the Research Plan. If Collaborator possesses any human biological specimens from clinical trials under the CRADA, the specimens must be handled as described in the Protocol or as otherwise directed by IC before the termination date of the CRADA.

8.2 Use of CRADA Data and CRADA Materials. The Parties will be free to utilize CRADA Data and CRADA Materials internally for their own purposes, consistent with their obligations under this CRADA. IC may share CRADA Data or CRADA Materials with any contractors, grantees, or agents it has engaged to conduct the Research Plan, provided the obligations of this Article 8.2 are simultaneously conveyed. Collaborator may share CRADA Data or CRADA Materials with any contractors, Affiliates, development partners, licensees or agents it has engaged to conduct the Research Plan, and with any of its Licensees, provided the obligations of this Article 8.2 are simultaneously conveyed. For clarity, such Collaborator development partners also include entities (including Licensees) that Collaborator (or its Affiliate) engages to further develop and/or commercialize Investigational Agent or product containing Investigational Agent, or with whom it has contracted to further research, develop or commercialize the Investigational Agent or such a product. Collaborator shall not transfer any confidential CRADA Data provided by IC to any third party other than as permitted in this section without the written permission of the NCI (such permission not to be unreasonably withheld). Following NCI's permission, Collaborator and such third party shall enter into a Confidential Disclosure Agreement with confidentiality terms at least as stringent as those set forth herein. Collaborator can then transfer the data to such third party.

8.2.1 **CRADA Data and Raw Data**.
Collaborator and IC will use reasonable efforts to keep CRADA Data and Raw Data confidential until published. To the extent permitted by law, each Party (or it authorized collaborators and partners as described in Article 8.2 above) will have the right to use any and all CRADA Data and Raw Data (subject to Article 8.10) in and for any regulatory filing or related CRADA

Subject Inventions filing by or on behalf of the Party.

8.2.2 **CRADA Materials**.
Collaborator and IC will use reasonable efforts to keep descriptions of CRADA Materials confidential until published. Collaborator acknowledges that the basic research mission of PHS includes sharing with third parties for further research those research resources made in whole or in part with NIH funding. Consistent with this mission and the tenets articulated in "Sharing of Biomedical Research Resources: Principles and Guidelines for Recipients of NIH Research Grants and Contracts," December 1999, available at http://ott.od.nih.gov/NewPages/RTguide_final.html, following publication either Party may make available to third parties for further research those CRADA Materials made jointly by both PHS and Collaborator.

Notwithstanding the above, if those joint CRADA Materials are the subject of a pending CRADA Patent Application or a CRADA Patent, or were created using a patent-pending or patented material or technology, the Parties may agree to restrict distribution or freely distribute them. Either Party may distribute those CRADA Materials made solely by the other Party only upon written consent from that other Party or that other Party's designee.

8.3 Confidential Information. Each Party agrees to limit its disclosure of Confidential Information to the amount necessary to carry out the Research Plan, and otherwise to perform the rights and obligations under this Agreement, and will place a confidentiality notice on all this information. A Party orally disclosing Confidential Information to the other Party will summarize the disclosure in writing and provide it to the other Party within fifteen (15) days of the disclosure. Each Party receiving Confidential Information agrees to use it only for the purposes described in the Research Plan. Either Party may object to the designation of information as Confidential Information by the other Party.

8.4 Protection of Confidential Information. Confidential Information of a Party will not be disclosed, copied, reproduced or otherwise made available by the other Party to any other person or entity without the consent of the owning or providing Party except as required by a court or administrative body of competent jurisdiction, or federal law or regulation. Each Party agrees to use reasonable efforts to maintain the confidentiality of Confidential Information of the other Party, which will in no instance be less effort than the Party uses to protect its own Confidential Information. Each Party agrees that a Party receiving Confidential

Information will not be liable for the disclosure of that portion of the Confidential Information which, after notice to and consultation with the disclosing Party, the receiving Party determines may not be lawfully withheld, provided the disclosing Party has been given a reasonable opportunity to seek a court order to enjoin disclosure.

8.5 **Human Subject Protection**. The research to be conducted under this CRADA involves Human Subjects or human tissues within the meaning of 45 C.F.R. Part 46, and all research to be performed under this CRADA will conform to applicable federal laws and regulations. Additional information is available from the HHS Office for Human Research Protections (http://www.hhs.gov/ohrp/).

8.6 **Duration of Confidentiality Obligation**. The obligation to maintain the confidentiality of Confidential Information will expire at the earlier of the date when the information is no longer Confidential Information as defined in Article 2 or **[*]** after the expiration or termination date of this CRADA, except for IPI, for which the obligation to maintain confidentiality will extend indefinitely. Collaborator may request an extension to this term when necessary to protect Confidential Information relating to products not yet commercialized.

8.7 **Publication**. The Parties are encouraged to make publicly available the results of their activities under the Research Plan. However, Collaborator will not publish or publically disclose any CRADA Data provided by NCI or by NCI Investigators under the CRADA without NCI's permission. Before Collaborator, NCI or NCI Investigator submits a paper or abstract for publication disclosing a CRADA Subject Invention, CRADA Data, or CRADA Materials, the other Party will have thirty (30) days to review proposed manuscripts and three (3) days to review proposed abstracts to assure that Confidential Information is protected. Either Party may request in writing that such a proposed publication be delayed for up to thirty (30) additional days as necessary to file a CRADA Patent Application. Manuscripts to be submitted for publication by NCI Investigators will be sent to NCI's Regulatory Affairs Branch [NCICTEPpubs@mail.nih.gov] for forwarding to Collaborator for review as soon as they are received and in compliance with the timelines outlined above. Abstracts to be presented by NCI Investigators will be sent to NCI's Regulatory Affairs Branch [NCICTEPpubs@mail.nih.gov] for forwarding to Collaborator as soon as they are received, preferably no less than three (3) days prior to submission, but prior to presentation or publication, to allow for review by Collaborator as above and for preservation of U.S. or foreign patent rights. No Collaborator Confidential Information will be published by NCI or by any Clinical Investigator without Collaborator's consent, such consent not to be unreasonably withheld.

8.8 Clinical Investigators' Research and Non-Clinical Investigators' Development Activities. In pursuing the development of Investigational Agent pursuant to this CRADA, NCI may utilize contractors and Extramural Investigators that are not NCI employees for part or all of the completion of this Research Plan, which may cover Non-Clinical Studies and clinical studies, through Funding Agreements and MTAs. Participation in DCTD-sponsored clinical trials by these investigators shall be determined after competitive solicitation and review of Protocol Letters of Intent (LOIs) and study Protocols by CTEP, NCI. All Funding Agreements and MTAs for the conduct of extramural Non-Clinical Studies and clinical trials will include the Intellectual Property Option to Collaborator (including any updates) offering Collaborator first rights of negotiation to extramural Inventions (web site: http://ctep.cancer.gov/industryCollaborations2/intellectual_property.htm). Although this CRADA does not grant to Collaborator any rights to Inventions made or Raw Data generated by NCI's contractors or grantees (except to the extent that the IC contractors who may perform DCTD Clinical Support Assays are obligated to assign any intellectual property to NIH related to Investigational Agent provided under this CRADA), as they are not parties to this CRADA, NCI agrees that:

8.8.1 With regard to Collaborator's Confidential Information, NCI will require all the NCI Investigators to agree to confidentiality provisions at least as restrictive as those provided in this CRADA, and subject to Collaborator's use of CRADA Data and Raw Data for obtaining regulatory approval for marketing Investigational Agent.

8.8.2 If Collaborator wants access to Raw Data or any other data in the possession of the NCI Investigators working with Investigational Agent under a Funding Agreement or MTAs, Collaborator must first contact the Regulatory Affairs Branch (RAB), CTEP, NCI [Telephone 301-496-7912; anshers@mail.nih.gov]. Subsequent to authorization by RAB, Collaborator may directly contact the NCI Investigators. Collaborator will bear any costs associated with Raw Data provided in formats customized for Collaborator, which costs will be paid by Collaborator directly to the NCI Investigators.

8.8.3 If Collaborator does not continue to use commercially reasonable efforts to conduct the development or (if regulatory approval is obtained) commercialization of Investigational Agent without the transfer of its development or (if applicable) commercialization efforts to another party within ninety (90) days of discontinuation of all such efforts, NCI has the right to make CRADA Data and Raw Data in NCI's possession or control available to a third party. NCI will provide prior written notice to Collaborator of such disclosure.

8.9 **Multi-Party Data Rights**. For clinical Protocol(s) and Non-Clinical Study(ies) where Investigational Agent is used in combination with another investigational agent supplied to NCI pursuant to a CTA or CRADA between NCI and an entity not a Party to this CRADA (hereinafter referred to as "Third Party"), the access and use of Multi-Party Data by the Collaborator and Third Party shall be co-exclusive as follows:

8.9.1 NCI will provide both Collaborator and Third Party with notice regarding the existence and nature of the agreements governing their collaborations with NIH, the design of the proposed combination Protocol(s) or Non-Clinical Study(ies), and the existence of any obligations that might restrict NCI's participation in the proposed combination Protocols or Non-Clinical Study(ies).

8.9.2 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.

8.9.3 Collaborator and Third Party must agree in writing, by signing the drug approval forms for clinical Protocols, 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).

8.10 **Access, review and receipt of Identifiable Private Information**. Collaborator access to and review of Identifiable Private Information shall be only for on-site quality auditing. Collaborator will receive Identifiable Private Information only if necessary for purposes of satisfying FDA or other health authorities' reporting requirements, and for internal research purposes, directly related to obtaining regulatory approval of Investigational Agent. Collaborator is prohibited from access, review, receipt, or use of such information for other purposes. All IRB approved Protocols and informed consent documents related to this research project will clearly describe this practice. If the Collaborator will have access to Identifiable Private Information, the Protocol and the informed consent must clearly state (i) the existence of the Collaborator; (ii) the Collaborator's access to Identifiable Private Information, if any; and (iii) the extent to which confidentiality will be maintained. For clinical Protocol(s) involving a third party, the other party's access, review, receipt, or use of Identifiable Private Information shall be subject to the same limitations as described in this Article 8.10.

Article 9. Representations and Warranties

9.1 Representations of IC. IC hereby represents to Collaborator that:

9.1.1 IC has the requisite power and authority to enter into this CRADA and to perform according to its terms, and that IC's official signing this CRADA has authority to do so.

9.1.2 To the best of its knowledge and belief, neither IC nor any of its personnel involved in this CRADA is presently subject to debarment or suspension by any agency of the Government which would directly affect its performance of the CRADA. Should IC or any of its personnel involved in this CRADA be debarred or suspended during the term of this CRADA, IC will notify Collaborator within thirty (30) days of receipt of final notice.

9.2 Representations and Warranties of Collaborator. Collaborator hereby represents and warrants to IC as of the Effective Date that:

9.2.1 Collaborator has the requisite power and authority to enter into this CRADA and to perform according to its terms, and that Collaborator's official signing this CRADA has authority to do so.

9.2.2 To the best of its knowledge and belief, neither Collaborator nor any of its personnel involved in this CRADA, including Affiliates, agents, and contractors are presently subject to debarment or suspension by any agency of the Government. Should Collaborator or any of its personnel involved in this CRADA be debarred or suspended during the term of this CRADA, Collaborator will notify IC within thirty (30) days of receipt of final notice.

9.2.3 Subject to Paragraph 12.3, and if and to the extent Collaborator has agreed to provide funding under Appendix B, Collaborator is financially able to satisfy these obligations in a timely manner.

9.2.4 The Investigational Agent provided by Collaborator under this CRADA has or will have been produced in accordance with the FDA's current Good Manufacturing Practice set out in 21 C.F.R. §§ 210-211, and ICH Q7, and meets or will meet the specifications cited in the Certificate of Analysis and Investigator's Brochure provided.

Article 10. Expiration and Termination

10.1 **Expiration**. This CRADA will expire on the last date of the term set forth on the Summary Page. In no case will the term of this CRADA extend beyond the term indicated on the Summary Page unless it is extended in writing in accordance with Paragraph 13.6.

10.2 **Termination by Mutual Consent**. IC and Collaborator may terminate this CRADA at any time by mutual written consent.

10.3 **Unilateral Termination**. Either IC or Collaborator may unilaterally terminate this CRADA at any time by providing written notice at least sixty (60) days before the desired termination date. IC may, at its option, retain funds transferred to IC before unilateral termination by Collaborator for use in completing the Research Plan. If Collaborator terminates this Agreement before the completion of all approved or active Protocol(s), then Collaborator will supply enough Investigational Agent (and Placebo, if applicable) to complete these Protocol(s) unless termination is for safety concerns.

10.4 **Funding for IC Personnel**. If Collaborator has agreed to provide funding for IC personnel and this CRADA is mutually or unilaterally terminated by Collaborator before its expiration, then Collaborator agrees that funds for that purpose will be available to IC for a period of six (6) months after the termination date or until the expiration date of the CRADA, whichever occurs sooner. If there are insufficient funds to cover this expense, Collaborator agrees to pay the difference.

10.5 **New Commitments**. Neither Party will incur new expenses related to this CRADA after expiration, mutual termination, or a notice of a unilateral termination, and each Party will, to the extent feasible, cancel all outstanding commitments and contracts by the termination date. Collaborator acknowledges that IC will have the authority to retain and expend any funds provided by the Collaborator during the term of this CRADA (if any) for up to **[*]** subsequent to the expiration or termination date to cover any unpaid costs obligated during the term of the CRADA in undertaking the activities set forth in the Research Plan.

10.6 **Collaborator Failure to Continue Development**. If Collaborator permanently ceases the further development of the Investigational Agent (other than due to safety or) without the license or other transfer of its active development efforts, assets, and obligations to a third party within **[*]** of such discontinuation, Collaborator agrees that IC may request the right to continue developing the Investigational Agent. In such event, Collaborator agrees (subject to its other contractual obligations) to transfer to IC such information in its possession and control as is necessary to enable IC to contract for the manufacture of the

Investigational Agent and, unless discontinued for reasons relating to safety as determined by the data safety monitoring board, to provide the Investigational Agent (and Placebo, if any) in Collaborator's inventory to IC for the completion of ongoing and approved clinical studies.

The foregoing is subject to the following: it is understood that in no event shall Collaborator have any obligation to grant rights or to assist IC, and that Collaborator is under no obligation in any event to assist IC in any manufacture or use of Investigational Agent.

Article 11. Disputes

11.1 **Settlement**. Any dispute arising under this CRADA which is not disposed of by agreement of the NIH CRADA Extramural Investigator/Officer(s) and CRADA Collaborator PI(s) will be submitted jointly to the signatories of this CRADA. If the signatories, or their designees, are unable to jointly resolve the dispute within thirty (30) days after notification thereof, the Assistant Secretary for Health (or his/her designee or successor) will propose a resolution. Nothing in this Paragraph will prevent any Party from pursuing any additional administrative remedies that may be available and, after exhaustion of such administrative remedies, pursuing all available judicial remedies.

11.2 **Continuation of Work**. Pending the resolution of any dispute or claim pursuant to this Article 11, the Parties each agree that performance of all of its obligations will be pursued diligently, using reasonable, good faith efforts, except to the extent that breach by a Party of its obligations under this Agreement impairs the ability of the other Party to perform its obligations.

Article 12. Liability

12.1 **NO WARRANTIES**. EXCEPT AS SPECIFICALLY STATED IN ARTICLE 9, THE PARTIES MAKE NO EXPRESS OR IMPLIED WARRANTY AS TO ANY MATTER WHATSOEVER, INCLUDING THE CONDITIONS OF THE RESEARCH OR ANY INVENTION OR MATERIAL, WHETHER TANGIBLE OR INTANGIBLE, MADE OR DEVELOPED UNDER OR OUTSIDE THE SCOPE OF THIS CRADA, OR THE OWNERSHIP, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE OF THE RESEARCH OR ANY INVENTION OR MATERIAL, OR THAT A TECHNOLOGY UTILIZED BY A PARTY IN THE PERFORMANCE OF THE RESEARCH PLAN DOES NOT INFRINGE ANY THIRD-PARTY PATENT RIGHTS.

12.2 Indemnification and Liability.
No indemnification for any loss, claim, damage, or liability is intended or provided by either Party under this CRADA. Each Party shall be liable for any loss, claim, damage, or liability that said Party incurs as a result of said Party's activities under this CRADA, except that IC, as an agency of the Government, assumes liability only to the extent provided under the Federal Tort Claims Act , 28 U.S.C. Chapter 171.

12.3 ***Force Majeure***. Neither Party will be liable for any unforeseeable event beyond its reasonable control and not caused by its own fault or negligence, which causes the Party to be unable to perform its obligations under this CRADA, and which it has been unable to overcome by the exercise of due diligence. If a *force majeure* event occurs, the Party unable to perform will promptly notify the other Party. It will use its best efforts to resume performance as quickly as possible and will suspend performance only for such period of time as is necessary as a result of the *force majeure* event.

12.4 Neither Party will be liable to the other Party under this Agreement for any indirect, consequential, special, punitive or exemplary damages, regardless of the cause or the theory of liability, and regardless if a Party was aware of the risk of such damages.

Article 13. Miscellaneous

13.1 Governing Law. The construction, validity, performance and effect of this CRADA will be governed by U.S. federal law, as applied by the federal courts in the District of Columbia. If any provision in this CRADA conflicts with or is inconsistent with any U.S. federal law or regulation, then the U.S. federal law or regulation will preempt that provision.

13.2 Compliance with Law. IC and Collaborator agree that they will comply with, and advise any contractors, grantees, or agents they have engaged to conduct the Research Plan to comply with, all applicable Executive Orders, statutes, and HHS regulations relating to research on human subjects (45 C.F.R. Part 46, 21 C.F.R. Parts 50 and 56) and relating to the appropriate care and use of laboratory animals (7 U.S.C. §§ 2131 *et seq.*; 9 C.F.R. Part 1, Subchapter A). IC and Collaborator will advise any contractors, grantees, or agents they have engaged to conduct clinical trials for this CRADA that they must comply with all applicable federal regulations for the protection of Human Subjects, which may include the Standards for Privacy of Individually Identifiable Health Information set forth in 45 C.F.R. Part 164 and Corporate Integrity Policy. Collaborator agrees to ensure

that its employees, contractors, and agents who might have access to a “select agent or toxin” (as that term is defined in 42 C.F.R. §§ 73.4-73.5) transferred from IC is properly licensed to receive the “select agent or toxin.”

13.3 **Waivers**, None of the provisions of this CRADA will be considered waived by any Party unless a waiver is given in writing to the other Party. The failure of a Party to insist upon strict performance of any of the terms and conditions hereof, or failure or delay to exercise any rights provided herein or by law, will not be deemed a waiver of any rights of any Party.

13.4 **Headings**. Titles and headings of the articles and paragraphs of this CRADA are for convenient reference only, do not form a part of this CRADA, and will in no way affect its interpretation.

13.5 **Severability**. The illegality or invalidity of any provisions of this CRADA will not impair, affect, or invalidate the other provisions of this CRADA.

13.6 **Amendments**. Minor, immaterial modifications to the Research Plan may be made by the mutual written consent of the NIH CRADA Extramural Investigator/Officer(s) and CRADA Collaborator PI(s). Substantial or material changes to the Research Plan (Appendix A of this CRADA) and any changes to the CRADA including extensions of the term will become effective only upon a written amendment signed by the signatories to this CRADA or by their representatives duly authorized to execute an amendment. A change will be considered substantial if it directly expands the range of the potential CRADA Subject Inventions, alters the scope or field of any license option governed by Article 7, or requires a significant increase in the contribution of resources by either Party.

13.7 **Assignment**. Neither this CRADA nor any rights or obligations of any Party hereunder shall be assigned or otherwise transferred by either Party without the prior written consent of the other Party, *except* as provided below. The Collaborator acknowledges the applicability of 41 U.S.C. § 15, the Anti Assignment Act, to this Agreement. The Parties agree that the identity of the Collaborator is material to the performance of this CRADA and that the duties under this CRADA are nondelegable. However, Collaborator may assign this Agreement, and its respective rights and transfer its respective duties, without any consent to either: (a) its Affiliate, or (b) its successor in interest pursuant to the acquisition, merger or consolidation of Collaborator with another business entity, *provided that* if Collaborator assigns this Agreement, and its respective rights and transfers its respective duties to its successor in interest pursuant to the acquisition, merger or consolidation of Collaborator with another business entity, NIH may

immediately terminate this Agreement on written notice to Collaborator, provided such notice is given by NIH within 30 days of such assignment, at its reasonable discretion. In the event Collaborator assigns this Agreement pursuant to the foregoing, Collaborator shall immediately give NIH written notice of the assignment and the name of the assignee.

13.8 **Notices**. All notices pertaining to or required by this CRADA will be in writing, signed by an authorized representative of the notifying Party, and delivered by first class, registered, or certified mail, or by an express/overnight commercial delivery service, prepaid and properly addressed to the other Party at the address designated on the Contacts Information Page, or to any other address designated in writing by the other Party. Notices will be considered timely if received on or before the established deadline date or sent on or before the deadline date as verifiable by U.S. Postal Service postmark or dated receipt from a commercial carrier. Notices regarding the exercise of license options will be made pursuant to Paragraph 7.3. Either Party may change its address by notice given to the other Party in the manner set forth above.

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 will maintain sole and exclusive control over its personnel and operations. If Collaborator elects to perform any portion of the Research Plan through a contractor or consultant, Collaborator agrees to incorporate into such contract all provisions necessary to ensure that the work of such contractor or consultant is governed by the terms of the CRADA, including, but not limited to a provision for the assignment of inventions of the contractor or consultant to the Collaborator.

In conducting a portion of the CRADA research, it may be necessary for NCI to utilize the services of NCI's contractors or subcontractors. As described in Article 8.8, certain contractors perform under Funding Agreements and MTAs, which include an Intellectual Property Option to Collaborator offering Collaborator first rights of negotiation to extramural Inventions (web site: http://ctep.cancer.gov/industryCollaborations2/intellectual_property.htm).

Other NCI contractors or subcontractors, including those performing the DCTD Clinical Support Assays, are subject to a Determination of Exceptional Circumstances (35 U.S.C. § 202(a)(ii)), through which their rights in Inventions made using the Investigational Agent are assigned to the Government. Such Inventions are then subject to the terms of this CRADA.

13.10 Use of Name; Press Releases. By entering into this CRADA, the Government does not directly or indirectly endorse any product or service that is or will be provided, whether directly or indirectly related to either this CRADA or to any patent or other intellectual-property license or agreement that implements this CRADA by Collaborator, its successors, assignees, or licensees. Collaborator will not in any way state or imply that the Government or any of its organizational units or employees endorses any product or services. Each Party agrees to provide proposed press releases that reference or rely upon the work under this CRADA to the other Party for review and comment at least five (5) business days before publication. Either Party may disclose the Title and Abstract of the CRADA to the public without the approval of the other Party, and Collaborator may disclose this CRADA and all related documents to the extent such disclosure is required by securities laws or regulations or other applicable law or court order, provided that Collaborator shall use reasonable efforts to obtain such confidential treatment of proprietary or confidential aspects of the CRADA as are available under applicable law.

13.11 Reasonable Consent. Whenever a Party's consent or permission is required under this CRADA, its consent or permission will not be unreasonably withheld.

13.12 Export Controls. Collaborator agrees to comply with U.S. export law and regulations, including 21 U.S.C. 382 and 21 CFR Part 312.110. If Collaborator has a need to transfer any CRADA Materials made in whole or in part by IC, or IC Materials, or IC's Confidential Information to a person located in a country other than the United States, to an Affiliate organized under the laws of a country other than the United States, or to an employee of Collaborator in the United States who is not a citizen or permanent resident of the United States, Collaborator will acquire any and all necessary export licenses and other appropriate authorizations.

13.13 Entire Agreement. This CRADA (including all Appendixes attached hereto, which are deemed incorporated into and part of this Agreement) constitutes the entire agreement between the Parties concerning the subject matter of this CRADA and supersedes any prior understanding or written or oral agreement, including the original Letter of Intent for CRADA #02166 which was executed between NCI and Newlink on May 23, 2007 and its eight (8) amendments to extend the term of the CRADA Letter of Intent to May 23, 2012, through eight amendments executed by NCI and Newlink. The original CRADA Letter of Intent and its amendments are attached with this CRADA as Appendix D.

13.14 Survivability. The provisions of Paragraphs 3.3, 3.4, 3.7.1, 3.7.2 (last sentence), 3.7.3, 4.2, 4.4, 4.5, 5.4, 6.1-9.1, 10.3-10.6, 11.1, 11.2, 12.1-12.3, 13.1-13.3, 13.7,

13.10, 13.13 and 13.14 will survive the expiration or early termination of this CRADA.

SIGNATURES BEGIN ON THE NEXT PAGE

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

SIGNATURE PAGE

ACCEPTED AND AGREED

BY EXECUTING THIS AGREEMENT, EACH PARTY REPRESENTS THAT ALL STATEMENTS MADE HEREIN ARE TRUE, COMPLETE, AND ACCURATE TO THE BEST OF ITS KNOWLEDGE. COLLABORATOR ACKNOWLEDGES THAT IT MAY BE SUBJECT TO CRIMINAL, CIVIL, OR ADMINISTRATIVE PENALTIES FOR KNOWINGLY MAKING A FALSE, FICTITIOUS, OR FRAUDULENT STATEMENT OR CLAIM.

FOR IC:

/s/ James H. Doroshow
James H. Doroshow, M.D.
Deputy Director, National Cancer Institute

3/8/2012
Date

FOR COLLABORATOR:

/s/Nicholas N. Vahanian
Signature

Typed Name: Nicholas N. Vahanian, M.D.
Title: President and Chief Medical Officer

3/27/2012
Date

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

CONTACTS INFORMATION PAGE

CRADA Notices

For IC:
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Regulatory Affairs Branch
Cancer Therapy Evaluation
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Rockville, MD 20852
Tel. 301-496-7912
Fax: 301-402-1584

For Collaborator:
Nicholas N. Vahanian, M.D.
President and Chief Medical Officer
2503 S. Loop Drive
Bldg. 5, Suite 5100
Ames, IA 50010-8646
Tel: 515-598-2922 (office)
Fax: 515-296-5557

Patenting and Licensing

For IC:
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):

Delivery of Materials Identified In Appendix B (if any)

For IC:
N/A

For Collaborator:
N/A

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

SUMMARY PAGE

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

TITLE OF CRADA: Clinical Development of NewLink Genetics' 1-Methyl-[d]-Tryptophan, an indoleamine 2,3-dioxygenase (IDO) Inhibitor, as an Anti-Cancer Agent

PHS [IC] Component:	National Cancer Institute
NIH CRADA Extramural Investigator/Officer(s):	Drs. Howard Streicher and Jeffrey Abrams
Collaborator:	NewLink Genetics Corporation
CRADA Collaborator Principal Investigators:	Drs. Charles Link and Nicholas Vahanian
Term of CRADA:	Nine (9) years from the Effective Date

ABSTRACT OF THE RESEARCH PLAN:

NewLink Genetics Corporation and the National Cancer Institute have entered into a Cooperative Research and Development Agreement ("CRADA") under which they will collaborate on the non-clinical and clinical development of 1-methyl-D-tryptophan (also known as 1MT), an indoleamine 2,3-dioxygenase (IDO) inhibitor, as an anti-cancer agent.

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

APPENDIX A: RESEARCH PLAN

Title of CRADA

Clinical Development of NewLink Genetics Corporation's 1-Methyl-[d]-Tryptophan, an indoleamine 2,3-dioxygenase (IDO) Inhibitor, as an Anti-Cancer Agent

NIH CRADA Extramural Investigator/Officer(s)
Dr. Howard Streicher
Dr. Jeffrey Abrams

CRADA Collaborator Principal Investigators
Dr. Charles Link
Dr. Nicholas Vahanian

Term of CRADA
Nine (9) years from the Effective Date

1. RESEARCH GOAL OF CRADA

The overall goal of this CRADA is to collaborate with NewLink Genetics Corporation (hereafter NewLink or Collaborator) on the clinical development of 1-methyl-D-tryptophan (also known as 1MT, NSC721782, or Investigational Agent) for the treatment of cancers that overexpress indoleamine 2,3-dioxygenase (IDO) and other cancers in which IDO plays a critical immunological role.

2. SCIENTIFIC BACKGROUND

The enzyme IDO catalyzes tryptophan degradation. IDO can be a potent effector of immunosuppression and of tolerance induction in certain settings; for example, expression of IDO in the placenta maintains maternal tolerance towards the fetus. Tumors create a state of immunologic unresponsiveness (tolerance) toward their own antigens, which allows tumors to escape the host's immune system. This also imposes a barrier to effective anti-tumor immunotherapy. One molecular mechanism contributing to this tolerance is expression of the immunosuppressive enzyme IDO, leading to inhibition of T-cell response. Expression of IDO by human and mouse antigen-presenting cells inhibits T cell mediated immune responses *in vitro* and *in vivo*. Tumor cells transfected with IDO become immunosuppressive *in vivo*, and expression of IDO has been reported in tumor cells from a variety of human tumors. IDO is also expressed by a population of host antigen-presenting cells (dendritic cells) found in tumor-draining lymph nodes of melanoma, breast cancer, and a variety of other tumors, which may act to create tolerance to tumor antigens. Therefore, IDO may be a primary molecular target for cancer immunotherapy and inhibition of the IDO pathway may assist in breaking tumor tolerance.

Studies have shown that the small-molecule 1MT possesses immune-enhancing activity by inhibiting IDO in a variety of animal models. 1MT can inhibit IDO enzyme activity *in vitro* and can prevent IDO-mediated immunosuppression *in vivo*. 1MT has also been shown to be synergistic with a number of commonly used chemotherapeutic agents. Thus, 1MT may potentially be used as a novel immune modulator in cancer immunotherapy.

3. BACKGROUND AND CONTRIBUTIONS OF THE PARTIES

NewLink is a biopharmaceutical company applying proprietary techniques in cancer biology to produce new diagnostic and therapeutic agents for cancer patients.

A CRADA Letter of Intent (LOI) between NCI and Newlink was executed in May 2007 to permit pre-clinical and clinical development of 1MT. Copies of the original CRADA LOI and its amendments are attached in this CRADA as Appendix D. Under the CRADA LOI, DCTD, NCI completed **[*]** and **[*]** using 1MT, and manufactured the clinical formulation of 1MT to support DCTD-sponsored clinical trials. DCTD also filed a DCTD-sponsored IND for 1MT and initiated phase 1 clinical trials using 1MT. The following clinical trials were initiated under the CRADA LOI and are currently ongoing and will be completed under this CRADA:

P8784: A Phase 1 Study of 1-Methyl-D-tryptophan (NSC-721782; IND # 78060) in Combination with Docetaxel in Metastatic Solid Tumors, and

P8045: A Phase 1 Study of 1-Methyl-D-Tryptophan in Patients with Advanced Malignancies.

4. DESCRIPTION OF THE CRADA RESEARCH PLAN

The Division of Cancer Treatment and Diagnosis (DCTD), NCI and Collaborator are interested in the evaluation of Investigational Agent in a clinical development program that includes various tumor types. DCTD will sponsor Investigational Agent phase 1 and phase 2 clinical trials that will help determine the safety, efficacy and the potential spectrum of Investigational Agent anti-tumor activity. DCTD and Collaborator are also interested in evaluating Investigational Agent in combination with other novel investigational agents.

DCTD may also support intramural and extramural Non-Clinical Studies that focus on identifying assays for monitoring the biologic activity of Investigational Agent, as well as studies for combination of Investigational Agent with other investigational targeted agents. These Non-Clinical Studies are aimed to support the clinical trials that will be conducted under the CRADA, and might involve convening a meeting of scientific experts and ultimately sponsoring core laboratories with expertise in the performance of appropriate assays with patient material.

In addition, DCTD may also support assay development via internal mechanisms (DCTD Clinical Support Assays). These assays (described in Section 5(C)1 below) will be conducted

using internal NCI resources and are intended to further the clinical development of Investigational Agent and provide information regarding targets and assay development to the broader research community.

5. RESPECTIVE CONTRIBUTIONS OF THE PARTIES

A. Joint Responsibilities

1. Steering Committee and Communication Plan

A Steering Committee may be employed by the Parties to exchange information and data and to discuss and to plan the proposed and ongoing clinical research. The Steering Committee shall be composed of the CRADA Principal Investigators from both Parties. In addition , other NCI and Collaborator staff with expertise in toxicology, pharmacology, pharmaceutical development, project management and other disciplines as pertinent to the current development stage of the Investigational Agent at the time of the meeting will be participating members. Both Parties shall report regularly to the Steering Committee on the progress of the clinical research and development efforts covered by this CRADA, will review the current progress, and will make any required decisions. The routes of communication, format of written minutes, etc. will be determined at the Steering Committee meetings and will be driven by the needs of the project.

The Steering Committee will function under the oversight of Co-Chairs, one from NCI and one from the Collaborator. NCI's Steering Committee Co-Chair will be appointed by the DCTD Division Director and report to the DCTD Division Director or his or her designee. Steering Committee meeting minutes summarizing all key decisions and issues under discussion will be provided to all the Steering Committee members and to the DCTD Division Director within **[*]** of each meeting. All Steering Committee decisions will be made **[*]**.

In addition to the Steering Committee a project team comprising NCI and Collaborator scientific members for the purpose of discussing the DCTD Clinical Support Assays may be assembled. This project team will be a collaborative body to approve projects described in Section 5C1 which outlines the DCTD Clinical Support Assays. This project team will be a collaborative body charged with the planning and successful execution of experimental objectives. It is intended that study areas approved by the project team will be broad enough in scope to allow all necessary experiments to realize the goal of said research without further approval from the project team. Submission of new projects/areas of inquiry will be addressed by the project team within **[*]** of receipt. Disagreements between DCTD and Collaborator will be discussed by the Steering Committee and/or project team who may recommend a course of action. In the event that project team is unable to reach consensus, it will be the Division Director's responsibility

to resolve any impasse. The Division Director will confer with representatives of the Collaborator before making any decision. Project teams will meet quarterly, or more often if necessitated by results or submission of a new projects/area of inquiry.

2. The DCTD and Collaborator may explore the clinical utility of Investigational Agent for various cancers. As sensitive tumor types are identified, it will be important to develop combinations of Investigational Agent and other active anti-cancer agents and to compare Investigational Agent and Investigational Agent combinations with standard therapy for these tumor types. Adjuvant studies may be important in diseases where Investigational Agent has activity and where there is a high risk of recurrence following initial primary therapy.

3. Both Parties shall collaborate in the collection and analysis of data generated under the Research Plan.

4. Both Parties will work closely together to ensure that the clinical studies move forward expeditiously.

5. The Parties acknowledge that **[*]** means any **[*]** that is either readily usable as a **[*]** or is **[*]** that will be useful to **[*]** in developing **[*]** (rather than useful **[*]** or **[*]**). A **[*]** may simultaneously be a **[*]** and be the essence of a **[*]**, or **[*]** (or an integral component of such **[*]**). For the purposes of this CRADA, **[*]** shall include, but not be limited to, **[*]**. If NewLink elects to request a **[*]** that is a **[*]**, such **[*]** will ensure, as appropriate for the circumstances, that (a) the **[*]** will undertake to make the **[*]** on a **[*]** to **[*]** for **[*]** under **[*]**, such **[*]**, or (b) **[*]** the right to make the **[*]** on a **[*]** to **[*]** for **[*]** purposes under **[[*]**.

B. Collaborator Responsibilities

1. Collaborator, **[*]**, will supply formulated Investigational Agent for the ongoing clinical trials identified in Section 3 of this Apendix A and supportive Non-Clinical Studies as provided under the CRADA. Collaborator may elect to produce bulk 1MT and formulated 1MT through contractors other than established **[*]** contractors in order to obtain the most competitive pricing. Collaborator will then be responsible for subsequent payment of such contractors, and **[*]** will have no obligations with respect to such contractors. If Collaborator elects to perform any portion of this CRADA Research Plan through a contractor or consultant, Collaborator shall incorporate into such contracts all provisions necessary to ensure that the work of the contractor or consultant is governed by the terms of the CRADA, including, but not limited to, a provision for the assignment of inventions of the contractor or consultant to Collaborator; such inventions shall be deemed **[*]** of Collaborator. In addition, Collaborator will ensure that any contractor or consultant is obligated to maintain **[*]** Confidential Information regarding 1MT manufacturing and

formulation in confidence at least to the extent provided for by the terms of the CRADA.

Collaborator's supply of Investigation Agent includes and unless otherwise agreed between the Parties shall be limited to the following :

- Provision of appropriately packaged and labeled Investigational Agent for NCI-sponsored clinical studies initiated under this CRADA.

- Supply of Investigational Agent, or unformulated analytical grade Investigational Agent or metabolites, if available, to DCTD for DCTD to provide to NCI Intramural Investigators and NCI Extramural Investigators for the development of analytical assays or ancillary correlative studies conducted in conjunction with clinical Protocol Letters of Intent (LOIs) that are approved by the DCTD's Protocol Review Committee and Collaborator under this CRADA.

- Supply of Investigational Agent for distribution to NCI Intramural Investigators and NCI Extramural Investigators for Non-Clinical Studies designed to enhance the basic understanding and development of Investigational Agent as provided for in Section 3.8.4. These will include non-clinical studies designed to support clinical trials in **[*]**; non-clinical **[*]** studies to provide data in support of a clinical trial; and other pertinent requests.

- Provision of Investigational Agent for DCTD Clinical Support Assays as described in Section 5(C)1 of this Appendix A.

2. Collaborator will provide resources for data collection and management, beyond that normally carried out by the DCTD as set forth in the CRADA for CTEP-sponsored studies, if Collaborator desires such data collection and management. This would include the collection of the data required to submit an NDA to the FDA.

3. Collaborator intends and will use reasonable efforts to prepare and submit an NDA to the FDA expeditiously when justified by clinical studies, with the object of obtaining pharmaceutical regulatory approval for the commercial marketing of Investigational Agent.

4. Collaborator may sponsor its own clinical trials and carry out its own non-clinical studies using Investigational Agent, Such Collaborator-sponsored trials and studies are outside the scope of this CRADA. For these clinical trials and studies, Collaborator will maintain possession and control of the clinical trial and study results. Collaborator will permit DCTD to review and use the results for DCTD-

sponsored clinical trials which are under the CRADA.

C. DCTD Responsibilities

I. DCTD may develop and conduct DCTD Clinical Support Assays on Investigational Agent to enhance understanding of the Investigational Agent's molecular target and mechanism of action (MoA) and to optimize the clinical development program of Investigational Agent. DCTD's work may include activities such as the development of assays to detect target modulation; studies of biomarkers; and the conduct of pharmacodynamic (PD) assays in conjunction with DCTD-sponsored clinical studies. These studies, performed in conjunction with the Pharmacodynamic Assay Development and Implementation Section (PADIS) and the National Clinical Target Validation Laboratories at the NCI, are intended to create research tools that will be accessible to the broader research community through appropriate agreements. Specifically, these studies will comprise:

a. *In vitro* and *in vivo* MoA studies (including profiling compound for activity in the NCI 60 cell-line panel, COMBO plates, and in vivo hollow fiber assays against human tumor cell lines).

b. *In vitro* and *in vivo* PD studies.

c. Efficacy studies in support of the PD studies in (b).

d. Development of Standard Operating Procedure-driven PD assays suitable for early phase clinical trials.

All DCTD Clinical Support Assays shall be conducted under the scope of this Research Plan. Manuscripts and inventions resulting from these studies will be handled in accordance with the terms of the CRADA.

2. The DCTD, as sponsor, has submitted to the FDA an Investigational New Drug Application (IND) for Investigational Agent.

3. The DCTD will collaborate with Collaborator for Investigational Agent development under this CRADA, and will assist Collaborator in all aspects of the regulatory approval process.

4. The DCTD will solicit Protocol Letters of Intent (LOI) from the investigators in the DCTD's clinical trials network for (1) clinical research and (2) non-clinical research.

The Protocol Review Committee (PRC), of the DCTD, will:

- Evaluate the rationale of each LOI received at the DCTD;
- Review the LOIs for study design, including dose, schedule and comparison groups, if relevant, in order to address any pertinent scientific questions;
- Examine the characteristics of the patient population to be studied;
- Assess the feasibility of the projected accrual, including the ability of each investigator to accrue the appropriate patient population in a timely manner;
- Review competing studies of the investigator in the specified disease(s);
- Provide investigator(s) with consensus review(s) of the PRC's evaluation to be used to revise the Protocol;
- Provide a copy of the consensus review to Collaborator. All CTEP approved clinical Protocol LOIs will be sent to Collaborator. Collaborator will provide NCI with the approval or disapproval within **[*]** of receiving the CTEP approved clinical Protocol LOIs by signing and returning the drug approval form. Only LOIs that have been approved by both the PRC and Collaborator will lead to the submission of full study protocols.

The Protocols received from investigators in response to the approved LOIs will be reviewed and evaluated by the PRC. The PRC will:

- Evaluate each Protocol from the agent, disease, statistical and regulatory perspectives in order to ensure that the study design that was approved by the PRC at the LOI stage is carried out;
- Provide each clinical research Protocol received by DCTD to Collaborator for review and comment approximately **[*]** before it is reviewed by the PRC of CTEP, Comments from Collaborator received by CTEP before the Protocol Review Committee meeting will be discussed by CTEP, will be given due consideration, and incorporated in the Protocol, absent good cause. Comments from either Collaborator or the CTEP staff that are agreed upon in the PRC meeting will be formatted as a consensus review, which will be returned to the investigator for necessary and/or suggested changes before the Protocol can be given final approval and submitted to the FDA. In addition, the PRC will review any correlative laboratory studies, solicited from

investigators, to address cellular pharmacological and/or pharmacokinetics questions as necessary.

- Forward a copy of any final Protocol to Collaborator following its submission to FDA.

5. Investigational Drug Steering Committee (IDSC)

The NCI Clinical Trials Working Group has mandated the formation of the Investigational Drug Steering Committee (IDSC). The IDSC is designed to provide DCTD with broad external scientific and clinical input for the design and prioritization of phase 1 and phase 2 trials with agents for which CTEP sponsors an IND. Membership of the IDSC includes the principal investigators of phase 1 U01 grants and phase 2 N01 contracts, representatives from the NCI Cooperative Groups, NCI staff members, and additional representatives with expertise in biostatistics, correlative science technologies, radiation oncology, etc., as well as patient advocates and community oncologists, as needed. Experts with specific expertise will be included as ad hoc members for consideration of specific agents. Periodically the IDSC will assess, from a strategic perspective, CTEP investigational agent development plans, agent portfolios, and LOIs submitted by investigators to determine whether the clinical development plan for an agent should be modified. When requested by CTEP, the IDSC will provide input on LOIs to assist in CTEP decision-making. All participating members will be vetted for conflict of interest and are under confidentiality agreements with DCTD.

The IDSC is described in greater detail on p. 23 of the report of the Cancer Trials Working Group of National Cancer Advisory Board (http://integratedtrials.nci.nih.gov/ict/CTWG_report June2005.pdf)

6. The DCTD will evaluate each of the active studies as they progress to ensure that the appropriate questions are being addressed and to ensure that the studies are modified as required based on the developing data. The DCTD will utilize its existing procedures and mechanisms to follow the clinical studies to ensure that all studies meet the pertinent FDA regulations.

6. RELATED INTELLECTUAL PROPERTY AND OTHER RELATED AGREEMENTS OF THE PARTIES

NCI Patents and Patents Applications:
None

Collaborator Patents and Patents Applications:

NewLink has obtained a worldwide, exclusive license to the following patents covering therapeutic uses of 1MT as **[*]** for **[*]** from the University of Georgia. 1MT is disclosed and claimed in the following representative patents. There are other issued patents and patent applications in the US, Europe and other countries not listed under this section.

[*]

[*]

[*]

Related Agreements between Parties:

At the time of execution of this CRADA, there are no active Confidential Disclosure Agreements (CDAs), Material Transfer Agreements and Clinical Trial Agreements between the Parties.

There are no active Cooperative Research and Development Agreements (CRADAs) between NCI and Newlink. The Letter of Intent for CRADA #02166 was executed on May 23, 2007 (expiration date of November 23, 2007). The term of the LOI has been extended to May 23, 2012 through eight (8) amendments executed by NCI and Newlink.

APPENDIX B

Financial and Staffing Contributions of the Parties

For NIH:

The NCI will conduct clinical, and Non-Clinical Studies of Investigational Agent under its intramural and extramural research program and DCTD Clinical Support Assays as described in Appendix A. The NCI estimates that **[*]** of effort will be dedicated to its participation in the Non-Clinical Studies, DCTD Clinical Support Assays, clinical studies, Steering Committee meetings, updates to its IND, compiling data, and drug management and monitoring in support of the clinical trials. PHS shall, in addition to its Principal Investigators provide sufficient staffing to execute and fulfill the obligations of the CRADA.

NCI will provide **[*]** to Collaborator for collaborative research and development pursuant to this CRADA, inasmuch as financial contributions by the U.S. government to non-Federal parties under a CRADA is prohibited under the Federal Technology Transfer Act of 1986 (15 U.S.C. 3710a(d)(1)).

For Collaborator:

Personnel:

Collaborator intends to commit **[*]**of effort to permit the timely execution of the studies implemented under this CRADA. More specifically, this staffing shall include Collaborator full-time employees, consultants to the company, external contract agencies and contract research organizations. If Collaborator elects to perform any portion of the Research Plan through a contractor or consultant, Collaborator agrees to incorporate into such contract all provisions necessary to ensure that the work of such contractors or consultants is governed by the terms of the CRADA, including, but not limited to, the provision for the assignment of inventions of the contractor or consultant to Collaborator.

Clinical Data Collection Support Funding Directly to Contractors:

CTEP/DCTD utilizes the contract services of two companies for assistance in the monitoring of DCTD-sponsored clinical trials. Collaborator will be responsible for making arrangements directly with the appropriate DCTD contractors to receive reports from DCTD-sponsored trials. This will include quarterly reports, adverse event reports and summary reports. The contractor for the **[*]** studies will provide these reports electronically in a format compatible with Collaborator's database. The NCI **[*]** contractor will also provide reports directly to Collaborator. Contact information for each of the DCTD contractors will be provided as needed. Any arrangement which involves the collection of more than the summarized data (Summary Data) provided annually to the DCTD will be at the expense of **[*]**. Collaborator will make

payment arrangements as necessary directly with such contractor(s).

Collaborator will have access to CRADA Data and Raw Data or any other information that is in the possession of NCI Extramural Investigators, as provided for in the CRADA. The information will be provided as specified in the CRADA, or otherwise according to a mutually agreed upon plan between the NCI, the Collaborator, and the NCI Extramural Investigator(s), and only in accordance with the guidelines and policies of the responsible Data Monitoring Committee. Collaborator will be responsible for the costs associated with any **[*]**, such as a request that **[*]** in **[*]** which is **[*]** than **[*]**. Should Collaborator choose to review copies of patient case report forms, such a review will be at Collaborator's expense and occur after notification and agreement of the NCI Extramural Investigators and only after all patient identifiers have been removed.

Funding to NCI:

(1) Collaborator agrees to provide funding to support the development of the Investigational Agent by NCI under this CRADA, as follows: The funds will be used to support preclinical studies, formulation and production of the Investigational Agent and support costs associated with the clinical trials under the CRADA, including those initiated under the CRADA LOI. The total amount of such Collaborator funding is $500,000, which amount shall be payable in **[*]** if the following milestone events are achieved during the term of the CRADA, as follows: **[*]**.

(2) CTEP/DCTD utilizes contract services for assistance in carrying out its responsibilities as a sponsor of clinical trials. In support of such services as provided in the CRADA, Collaborator agrees to pay NCI $**[*]**, within **[*]** days of the date of execution of the full CRADA. In addition, Collaborator agrees to provide $**[*]** per year, commencing January 1, 2013, to supplement the CTEP/DCTD support contract costs and other reasonable and necessary expenses incurred by NCI in carrying out its responsibilities under this CRADA.

(3) Collaborator, at its sole discretion, may also provide up to $**[*]** during the term of the CRADA to support analytical assays, those focusing on identifying new assays for monitoring the biological activity of Investigational Agent and correlative studies associated with clinical Protocols which are approved by both Parties and made a part of the Research Plan. Such funds may be used for but are not limited to, costs of **[*]**, including sample acquisition, storage and shipping costs.

(4) Collaborator, at its sole discretion, may provide direct support, under the 348 travel mechanism, for the travel and lodging costs for attendance of NCI staff at selected scientific or development meetings. Both Collaborator and NCI must agree that the activities would be appropriate under this Agreement and acceptance of Collaborator's support of NCI's participation in the activities will be contingent upon appropriate NCI approval. Travel costs for such travel are also limited by the Federal Travel Rules and Regulations for all government staff whether paid for by government funds or Collaborators.

Any additional funding will not be added to this CRADA without an appropriate written executed Amendment pursuant to Article 13.6.

No funds provided under this CRADA by Collaborator will be used by NCI to pay the salary of full-time tenured federal employees.

Payment Information:

Checks for monies payable directly to the NCI should be made payable to the National Cancer Institute and addressed to:

Regulatory Affairs Branch
Attn: Dr. Sherry Ansher
National Cancer Institute
6130 Executive Blvd., Suite 7111
Rockville, MD 20852

All checks should be marked with a clear reference to the NCI CRADA Number and Title: CRADA #2166, “Clinical Development of NewLink Genetics Corporation’s 1-Methyl-[d]-Tryptophan, an indoleamine 2,3-dioxygenase (IDO) Inhibitor, as an Anti-Cancer Agent.”
Should NCI require electronic deposit of any monies payable under this CRADA NCI agrees to provide Collaborator with the appropriate account information.

Materials/Equipment Contributions:

NCI will not provide IC Materials for use under this CRADA and Collaborator will not provide Collaborator Materials for use under this CRADA. If NCI decides to provide IC Materials for use under this CRADA, or if Collaborator decides to provide Collaborator 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. Collaborator will not provide capital equipment for use under this CRADA.

MATERIAL TRANSFER AGREEMENT

Provider: Division of Cancer Treatment and Diagnosis, National Cancer Institute

Recipient: University School of Medicine

Recipient's Investigator: Dr. John Doe, Ph.D., as an employee of the University School of Medicine

1. Provider agrees to transfer to Recipient's Investigator the following Research Material:

1.0 mg of Agent X (NSC 00000), an agent proprietary to Company A, Inc. (Collaborator)

2. THIS RESEARCH MATERIAL MAY NOT BE USED IN HUMANS. The Research Material will only be used for research purposes by Recipient's Investigator in his/her laboratory, for the Research Project described below, under suitable containment conditions. This Research Material will not be used by for-profit recipients for screening, production or sale, for which a commercialization license may be required. Recipient agrees to comply with all Federal rules and regulations applicable to the Research Project and the handling of the Research Material.

2(a). Is Research Material of human origin?

_____ Yes
____No

2(b). If yes in 2(a), was Research Material collected according to 45 CFR Part 46, "Protection of Human Subjects"?

_____ Yes (Please provide Assurance Number:_____)
_____ No
_____ Not Applicable

3. This Research Material will be used by Recipient's Investigator solely in connection with the following research project ("Research Project") described with specificity as follows (use an attachment page if necessary):

This Research Material will be used for preclinical studies investigating the effects of the Research Material in a cancer cell line.

3(a). Are any materials used in the Research Project of human origin?

_____ Yes
_____ No

3(b). If yes in 3(a), were human-origin materials collected according to 45 CFR Part 46,

"Protection of Human Subjects"?

_____ Yes (Please provide Assurance Number:_____)
_____ No
_____ Not Applicable

4. (a). To the extent permitted by law, Recipient agrees to treat in confidence, for a period of **[*]** from the date of its disclosure, any of Provider's or Collaborator's written information about this Research Material that is stamped "CONFIDENTIAL," except for information that was previously known to Recipient or that is or becomes publicly available or which is disclosed to Recipient without a confidentiality obligation. Any **[*]** to Recipient shall be identified as being CONFIDENTIAL by written notice delivered to Recipient within **[*]** after the date of **[*]**.

4. (b). Recipient may publish or otherwise publicly disclose the results of the Research Project, however Collaborator will have **[*]** to review proposed manuscripts and **[*]** to review proposed abstracts to assure that CONFIDENTIAL Information is protected, except when a shortened time period under court order or the Freedom of Information Act pertains. Collaborator may request in writing that a proposed publication be delayed for up to **[*]** additional days as necessary to file a Patent Application. Manuscripts to be submitted for publication by Recipient's Investigators will be sent to NCI's Regulatory Affairs Branch [NCICTEPpubs@mail.nih.gov] for forwarding to Collaborator for review as soon as they are received and in compliance with the timelines outlined above. Abstracts to be presented by Recipient's Investigators will be sent to NCI's Regulatory Affairs Branch [NCICTEPpubs@mail.nih.gov] for forwarding to Collaborator as soon as they are received, preferably no less than three days prior to submission, but prior to presentation or publication, to allow for preservation of U.S. or foreign patent rights. In all oral presentations or written publications concerning the Research Project, Recipient will acknowledge Provider's or Collaborator's contribution of this Research Material unless requested otherwise.

5. This Research Material is proprietary to Collaborator. Collaborator has agreed to allow NCI to make their proprietary compound available for this Research Project. Recipient's Investigator agrees to retain control over this Research Material and further agrees not to transfer the Research Material to other people not under her or his direct supervision without advance written approval of Provider. When the Research Project is completed, the Research Material will be disposed of, if directed by Provider.

6. This Research Material is provided as a service to the research community. **[*]** Provider **[*]** that the **[*]** will not **[*]** or **[*]** of **[*]**.

7. Recipient shall retain title to any patent or other intellectual property rights in inventions made by its employees in the course of the Research Project. Recipient agrees not to claim, infer, or imply endorsement by the Government of the United States of America (hereinafter referred to as "Government") of the Research Project, the institution or personnel conducting the Research Project or any resulting product(s). Unless prohibited by law from doing so, Recipient agrees to hold the Government harmless and to indemnify the Government for all liabilities, demands, damages, expenses and losses arising out of Recipient's use for any purpose of the Research Material.

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

8. The undersigned Provider and Recipient expressly certify and affirm that the contents of any statements made herein are truthful and accurate.

9. This MTA shall be construed in accordance with Federal law as applied by the Federal courts in the District of Columbia.

10. Results of the Research Project shall be provided to the Provider. Publications shall be provided to Provider and Collaborator as described in Article 4.

11. Recipient ("Institution") agrees to notify Provider and Collaborator upon the filing of any patent applications related to research with this Research Material under this Agreement and abide by the following terms of the Intellectual Property Option to Collaborator:

Institution agrees to promptly notify the Provider (NCI) and Collaborator in writing of any inventions, discoveries or innovations made by the Recipient's Investigator or any other employees or agents of Institution, whether patentable or not, which are conceived or first actually reduced to practice pursuant to the Research Project.

For inventions described in patent disclosures that claim the use and/or the composition of the Research Material(s) (Section A Inventions), Institution agrees to grant to Collaborator(s): (i) a royalty-free, worldwide, non-exclusive license for commercial purposes with the right to sub license to affiliates or collaborators working on behalf of Collaborator for Collaborator's development purposes; and (ii) a time limited first option to negotiate an exclusive, or co-exclusive, if applicable, world-wide, royalty bearing license for commercial purposes, including the right to grant sub licenses, subject to any rights of the Government of the United States of America, on terms to be negotiated in good faith by the Collaborator(s) and Institution. If Collaborator accepts the non-exclusive commercial license, the Collaborator agrees to pay **[*]** which will be pro-rated and divided equally among all licensees. If Collaborator obtains an exclusive commercial license, in addition to any other agreed upon licensing arrangements such as royalties and due diligence requirements, the Collaborator agrees to pay **[*]**. Collaborator(s) will notify Institution, in writing, if it is interested in obtaining a commercial license to any Section A Invention within **[*]** of Collaborator's receipt of a patent application or **[*]** of receipt of an invention report notification of such a Section A Invention. In the event that Collaborator fails to so notify Institution, or elects not to obtain an exclusive license, then Collaborator's option expires with respect to that Section A Invention, and Institution will be free to dispose of its interests in accordance with its policies. If Institution and Collaborator fail to reach agreement within **[*]**, (or such additional period as Collaborator and Institution may agree) on the terms for an exclusive license for a particular Section A Invention, then for a period of **[*]** thereafter Institution agrees not to offer to license the Section A Invention to any third party on materially better terms than those last offered to Collaborator without first offering such terms to Collaborator, in which case Collaborator will have a period of **[*]** in which to accept or reject the offer. If Collaborator elects to negotiate an exclusive commercial license to a Section A Invention, then Institution agrees to file and prosecute patent application(s) diligently and in a timely manner and to give Collaborator an opportunity to comment on the preparation and filing of any such patent application(s). Notwithstanding the above, Institution is under no obligation to file or maintain patent prosecution for any Section A Invention.

For those inventions not covered by Section A, but are nevertheless conceived or first actually reduced to practice pursuant to the Research Project and to those inventions that are conceived or first actually reduced to practice pursuant to the Research Project that use non-publicly available clinical data or specimens from patients treated with the NCI-provided Research Material (including specimens obtained from NCI DCTD-funded tissue banks) (Section 13 Inventions), Institution agrees to grant the following to the collaborator: (i) a paid-up nonexclusive nontransferable, royalty-free, world-wide license to all Section B Inventions for research purposes only; and (ii) a nonexclusive, royalty-free, world-wide license to (a) disclose Section B Inventions to a regulatory authority when seeking marketing authorization of the Research Material and (b) disclose Section B Inventions on a product insert or other promotional material regarding the Research Material after having obtained marketing authorization from a regulatory authority. Notwithstanding the above, Institution is under no obligation to file or maintain patent prosecution for any Section B Invention.

For all Section A and Section B Inventions, regardless of Collaborator's decision to seek a commercial license, Institution agrees to grant Collaborator a paid-up, nonexclusive, royalty-free, world-wide license for research purposes only. Institution retains the right to make and use any Section A Invention for all non-profit research, including for educational purposes and to permit other educational and non-profit institutions to do so.

Institution agrees, at Collaborator's request and expense, to grant to Collaborator a royalty-free exclusive or co-exclusive license to inventions made by Institution's Investigator(s) or any other employees or agents of Institution, which are or may be patentable or otherwise protectable, as a result of research utilizing the Research Material(s) outside the scope of the NCI DCTD Research Project (Unauthorized Inventions). Institution will retain a non-exclusive, non-sub-licensable royalty free license to practice the invention for research use purposes.

Institution agrees to promptly notify NCI DCTD (NCICTEPpubs@mail.nih.gov) and Collaborator(s) in writing of any Section A Inventions, Section B Inventions, and Unauthorized Inventions upon the earlier of: (i) any submission of any invention disclosure to Institution of a Section A, Section B, or Unauthorized Invention, or (ii) the filing of any patent applications of a Section A, Section B, or Unauthorized Invention. Institution agrees to provide a copy of either the invention disclosure or the patent application to the Collaborator and to NCI DCTD which will treat it in accordance with 37 CFR Part 401. These requirements do not replace any applicable reporting requirements under the Bayh-Dole Act, 35 USC 200-212, and implementing regulations at 37 CFR Part 401.

12. This Agreement shall terminate two (2) years from the date of the last signature below.

Signatures Begin on Next Page

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

SIGNATURES

RECIPIENT

Date — John Doe, Ph.D.

Date — Authorized Signature for Recipient and Title

Recipient's Official and Mailing Address:

John Doe, Ph.D.
Associate Professor
Department of Biochemistry
University School of Medicine
City, State, Zip
Phone:

NATIONAL CANCER INSTITUTE

Sherry Ansher, Ph.D.
Associate Chief, Agreement Coordination Group
Date

Jason Cristofaro, J.D., Ph.D.
Date — CTEP Alternate Technology Development Coordinator

Please address all correspondence related to this agreement to Sally Hausman at the following address by express mail:

Sally Hausman
Senior Specialist, Research and Development Agreements
Regulatory Affairs Branch
Cancer Therapy Evaluation Program
Executive Plaza North, Suite 7111
6130 Executive Blvd.
Rockville, MD 20852-7181

Any false or misleading statements made, presented, or submitted to the Government, including any relevant omissions, under this Agreement and during the course of negotiation of this

Agreement are subject to all applicable civil and criminal statutes including Federal statutes 31 U.S.C. §§ 3801-3812 (civil liability) and 18 U.S.C. § 1001 (criminal liability including fine(s) and/or imprisonment).

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DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

National Institutes of Health
National Cancer Institute
Technology Transfer Center
Executive Plaza South, Room 450
6120 Executive Blvd. MSC 7182
Bethesda MD 20892-7182
(301) 496-0477
(301) 402-2117 Fax

COPY

May 7, 2007

Dr. Charles Link
NewLink Genetics Corporation
Suite 3900
2901 South Loop Drive
Ames, IA 50010 USA

Re: Letter of Intent for a Cooperative Research and Development Agreement #02166
NCI Principal Investigators: Drs. Sherry S. Ansher, Lee Jia and Howard Streicher Collaborator Investigators: Drs. Charles Link and Nicholas Vahanian
Title: Preclinical and Clinical Development of 1-Methyl [d]-tryptophan as an Anticancer Agent

Dear Dr. Link:

It is my understanding that a cooperative research and development project between the parties referenced below is being considered. Accordingly, until the formal Cooperative Research and Development Agreement (CRADA) is reviewed by the CRADA Subcommittee and approved by the Director, National Cancer Institute (NCI), this Letter is offered to permit the joint research to commence. However, in the case of human clinical trials which are a part of the subject CRADA, the parties agree that all such trials which may begin prior to the execution of the formal CRADA shall be preceded by the appropriate regulatory approvals (U.S. Food and Drug Administration IND approval or international equivalents thereof).

It is acknowledged by the parties below that cooperative research pursuant to the Research Plan, attached as Appendix A, will be conducted informally by the NCI Principal Investigators and Collaborator pending formal approval of the CRADA. It is further acknowledged that patentable inventions may be made by NCI employees and employees of the Collaborator. Pursuant to its authority under the Federal Technology Transfer Act of 1986, as amended, NCI agrees that should this CRADA be approved, it will have retroactive effect to the date that the last party has

executed this Letter for any inventions that may be made under this Research Plan. NCI further agrees that should this CRADA be approved it will have retroactive effect to the date that the last party has executed this Letter for confidentiality obligations specified in the NIH Model CRADA. The Model CRADA for Extramural-PHS Clinical Research (2005) provisions for the protection of proprietary information are incorporated in this Letter by reference and are considered controlling during the period of informal joint research. These provisions include, but are not limited to Articles 2.0 and 8. The Model CRADA for Extramural-PHS Clinical Research (2005) is attached as Appendix B and the CTEP Exceptions or Modifications to this CRADA (6/27/06) is attached as Appendix C.

You understand, however, that this Letter is not a commitment on the part of either party to enter into a CRADA. Further, this Letter is effective for a term not to exceed six (6) months. The six month term may be extended, provided the CRADA is under active negotiation and the collaborative research is continuing. Assuming that the necessary approvals are forthcoming, we look forward to a successful collaboration.

Sincerely,

/s/ Kathleen Carroll for
Karen Maurey, M.S.
Chief, Technology Transfer Center, NCI

AGREED AND ACCEPTED:

National Cancer Institute **NewLink Genetics Corporation**

/s/Anna D. Barker /s/ Charles Link
Anna D. Barker, Ph.D.
Deputy Director

05/14/07 05/23/07
Date Date

Attachments: Appendix A - Letter of Intent Research Plan
Appendix B - Model CRADA for Extramural-PHS Clinical Research (2005)

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Appendix C - CTEP Exceptions or Modifications to this CRADA (6/27/06)

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Appendix A

Letter of Intent Research Plan

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APPENDIX A: LETTER OF INTENT RESEARCH PLAN

Pre-Clinical and Clinical Development of 1-Methyl-[d]-Tryptophan as an Anti-Cancer Agent

National Cancer Institute (NCI) Investigators:
Dr. Sherry Ansher
Dr. Lee Jia
Dr. Howard Streicher

NewLink Genetics Corporation Investigators:
Dr. Charles Link
Dr. Nicholas Vahanian

Term of Proposed CRADA:
Four (4) years from the date of CRADA execution

1. RESEARCH GOALS OF PROPOSED CRADA

The overall goal of this proposed CRADA is to collaborate with NewLink Genetics Corporation (hereafter NewLink) on the pre-clinical and clinical development of 1-methyl-D-tryptophan (also known as 1MT, NSC721782, or Investigational Agent) for the treatment of cancers that overexpress indoleamine 2,3-dioxygenase (IDO) and other cancers in which IDO plays a critical immunological role.

The Division of Cancer Treatment and Diagnosis (DCTD), NCI and NewLink will both provide resources and expertise for the pre-clinical development of 1MT and will work together towards the successful clinical development of 1MT as a safe and effective novel pharmaceutical compound. The DCTD will provide expertise in designing, implementing and monitoring Phase 0, Phase 1 and Phase 2 clinical trials through its intramural and extramural clinical trials network. Additionally, the DCTD will work jointly with NewLink to obtain all the necessary regulatory approval by the U.S. Food and Drug Administration (FDA) for 1MT as an anti-cancer agent. NewLink will provide expertise in the development, formulation and production of 1MT. The Parties will work together in the design, implementation and monitoring of the clinical trials planned under this CRADA as well as all regulatory aspects and New Drug Application (NDA) filings as necessary for marketing approval for 1MT as an anti-cancer agent.

2. SCIENTIFIC BACKGROUND

The enzyme IDO catalyzes tryptophan degradation. IDO can be a potent effector of immunosuppression and of tolerance induction in certain settings; for example, expression of IDO in the placenta maintains maternal tolerance towards the fetus. Tumors create a state of immunologic unresponsiveness (tolerance) toward their own antigens, which allows tumors

to escape the host's immune system. This also imposes a barrier to effective anti-tumor immunotherapy. One molecular mechanism contributing to this tolerance is expression of the immunosuppressive enzyme IDO, leading to inhibition of T-cell response.

Expression of IDO by human and mouse antigen-presenting cells inhibits T cell mediated immune responses *in vitro* and *in vivo*. Tumor cells transfected with IDO become immunosuppressive *in vivo*, and expression of IDO has been reported in tumor cells from a variety of human tumors. IDO is also expressed by a population of host antigen-presenting cells (dendritic cells) found in tumor-draining lymph nodes of melanoma, breast cancer, and a variety of other tumors, which may act to create tolerance to tumor antigens. Therefore, IDO may be a primary molecular target for cancer immunotherapy and inhibition of the IDO pathway may assist in breaking tumor tolerance.

Studies have shown that the small-molecule 1MT possesses immune-enhancing activity by inhibiting IDO in a variety of animal models. 1MT can inhibit IDO enzyme activity *in vitro* and can prevent IDO-mediated immunosuppression *in vivo*. 1MT has also been shown to be synergistic with a number of commonly used chemotherapeutic agents. Thus, 1MT may potentially be used as a novel immune modulator in cancer immunotherapy.

3. PRE-CLINICAL DEVELOPMENT OF 1MT

1MT was originally submitted to the NCI's Rapid Access to Intervention Development (RAID) program by Dr. David Munn, Medical College of Georgia, and Dr. Scott Antonia, H. Lee Moffitt Cancer Center, and the application was approved by NCI in April 2001. Based upon promising *in vitro* and *in vivo* data, 1MT was then reviewed by the NCI's Drug Development Group (DDG) and was approved by the DDG in December 2003 for further pre-clinical development at DDG level IIA. In January 2006 the DDG approved 1MT at level IIB/III to start IND-directed toxicology studies and to subsequently enter into NCI sponsored clinical trials. In October 2005, University of Georgia granted NewLink a worldwide, exclusive license to patents covering therapeutic uses of 1MT as an immunomodulator for any and all medical applications.

The following sections summarize the pre-clinical studies conducted by the NCI prior to this CRADA Letter of Intent.

[*]

4. BACKGROUND OF THE COLLABORATOR

NewLink is a biopharmaceutical company applying innovative techniques in cancer biology to produce new diagnostic and therapeutic agents for cancer patients. NewLink is privately held and was incorporated in June 1999. The core of NewLink is a Cancer Vaccine Development Division that exists to accelerate the deployment of oncology pharmaceuticals, including HyperAcute™ Vaccines, into clinical testing and commercialization. NewLink has

recently acquired a worldwide, exclusive license to patents covering therapeutic uses of 1MT as **[*]** for **[*]**, and its OncoRx Division undertakes the development 1MT. 1MT is envisioned as **[*]** and as an adjuvant therapy for use in combination with immuno-modulating therapies for the purpose of enhancing the effects of the immuno-modulating therapy. NewLink expects to start 1MT Phase 1 and Phase 2 clinical trials in **[*]**, subject to the filing of one or more NewLink-sponsored INDs to support such studies.

5. DETAILED DESCRIPTION OF THE RESEARCH PLAN

The Division of Cancer Treatment and Diagnosis (DCTD), NCI and NewLink are interested in the evaluation of 1MT in a pre-clinical and clinical development program that includes various tumor types that over-express IDO and other cancers in which IDO plays a critical immunological role. The pre-clinical work will include IND-directed toxicology studies and formulation studies. In addition, if NCI deems it necessary, NCI may conduct pre-clinical research aimed at enhancing the understanding of the mechanism of action of 1MT and its targets and optimizing its clinical development program. NCI's work may also include such activities as the development of assays to detect target modulation, biomarker studies, and pharmacodynamic analyses performed in conjunction with the DCTD-sponsored clinical studies. DCTD will sponsor 1MT Phase 0, Phase 1 and Phase 2 clinical trials that will help determine the safety, efficacy and the potential spectrum of 1MT's anti-tumor activity. DCTD and NewLink are also interested in evaluating 1MT in combination with other novel investigational agents or cancer therapeutics such as vaccines, chemotherapy and radiation therapy in clinical trials.

6. RESPECTIVE CONTRIBUTIONS OF THE PARTIES

A. Joint Responsibilities

1. Steering Committee and Communication Plan

A Steering Committee will be employed by the Parties to exchange information and data and to discuss and to plan the proposed and ongoing clinical research. The Steering Committee shall be composed of the CRADA Principal Investigators from NCI and NewLink. In addition, other NCI and NewLink staff with expertise in toxicology, pharmacology, pharmaceutical development, project management and other disciplines as pertinent to the current development stage of the Investigational Agent at the time of a meeting may participate in the meetings of the Steering Committee. Both Parties shall report regularly to the Steering Committee on the progress of the clinical research and development efforts covered by this CRADA, will review the current progress, and will make any required decisions. The routes of communication, format of written minutes, etc. will be determined at the Steering Committee meetings and will be driven by the needs of the project. The Parties have been meeting regularly prior to the execution of this CRADA Letter of Intent, and will continue to do so.

The Steering Committee will function under the oversight of Co-Chairs, one from NCI and one from the Collaborator. NCI's Steering Committee Co-Chair will be appointed by the DCTD Division Director and report to the DCTD Division Director or his or her designee. Steering Committee meeting minutes summarizing all key decisions and issues under discussion will be provided to all the Steering Committee members and to the DCTD Division Director within **[*]** of each meeting. Steering Committee decisions will be made **[*]**.

2. DCTD's preclinical and ancillary studies shall be conducted **[*]**, as per **[*]**.

3. The DCTD and NewLink will explore the clinical utility of 1MT for various cancers. As sensitive tumor types are identified, it will be important to develop combinations of 1MT and other active anti-cancer agents and to compare 1MT and 1MT combinations with standard therapy for these tumor types. Adjuvant studies may be important in diseases where 1MT has activity and where there is a high risk of recurrence following initial primary therapy.

4. Both Parties shall collaborate in the collection and analysis of data generated under the Research Plan.

5. Both Parties will work closely together to ensure that the pre-clinical and clinical studies move forward expeditiously.

6. Subject to the obligations of the Parties to maintain the data under this CRADA as confidential and proprietary, the Parties may publicly disclose the results of their research under the circumstances set forth in the model CRADA.

7. When pre-clinical studies and/or a CRADA clinical protocol involves either **[*]** or involves **[*]**, the NCI, NewLink **[*]** will jointly determine a reasonable and appropriate mechanism for intellectual property and data access and sharing prior to initiation of the pre-clinical studies and/or the clinical trial.

8. For activities conducted pursuant to this CRADA in the United States of America, both Parties agree to comply with all appropriate DHHS regulations relating to Human Subjects Use, all U.S. Department of Agriculture regulations, and all Public Health Service policies relating to the use and care of laboratory animals. For activities conducted pursuant to this CRADA outside of the United States of America, both Parties shall conduct such in accordance with GLPs and all applicable rules, regulations and statutes, both local and national, governing such activity in that country.

9. The Parties acknowledge that **[*]** means any **[*]** that is either readily usable as a **[*]** or is **[*]** that will be useful to **[*]** in developing **[*]** (rather than useful **[*]** or **[*]**). A **[*]** may simultaneously be a **[*]** and be the essence of a **[*]**, or **[*]** (or an integral component of such **[*]**). For the purposes of this CRADA, **[*]** shall include, but not be limited to, a **[*]**. If NewLink elects to request **[*]** that is a **[*]**, such **[*]** will ensure, as appropriate for

the circumstances, that (a) the [*] will undertake to make the [*] on a [*] to [*] for [*] under [*], such [*], or (b) [*] the right to make the [*] on a [*] to [*] for [*] purposes under [*].

B. NewLink Responsibilities

1. Following execution of the CRADA, NewLink will provide [*] funding for pre-clinical studies including the IND-directed toxicity studies and formulation studies which will be conducted by [*]. The exact amount of funding and the payment schedule will be agreed upon and addressed in an Appendix B to the executed CRADA.

2. Following CRADA execution, NewLink will be responsible for the [*] cost of GMP-grade 1MT in current [*] inventories manufactured to support pre-clinical studies, NCI-sponsored [*] clinical trials, and NewLink-sponsored [*] clinical trials. The exact amount of funding and the payment schedule will be agreed upon and addressed in an Appendix B to the executed CRADA.

   If additional formulated 1MT is required for clinical studies under this CRADA Research Plan, NewLink will be responsible for the provision and costs of such extra supply of formulated and acceptably labeled 1MT. NewLink may elect to produce bulk 1MT and formulated 1MT through contractors other than established [*] contractors in order to obtain the most competitive pricing. NewLink will then be responsible for subsequent payment of such contractors, and [*] will have no obligations with respect to such contractors. If NewLink elects to perform any portion of this CRADA Research Plan through a contractor or consultant, NewLink shall incorporate into such contracts all provisions necessary to ensure that the work of the contractor or consultant is governed by the terms of the CRADA, including, but not limited to, a provision for the assignment of inventions of the contractor or consultant to NewLink; such inventions shall be deemed [*] of NewLink. In addition, NewLink will ensure that any contractor or consultant is obligated to maintain [*] Confidential Information regarding 1MT manufacturing and formulation in confidence at least to the extent provided for by the terms of the CRADA.

   Following the use of [*] supplies of 1MT, NewLink will provide 1MT to [*] for use by [*] in [*] studies, studies designed to [*] of 1MT, and other studies relevant to the development of 1MT as provided in the Research Plan.

3. NewLink will prepare and submit to the FDA an Investigational New Drug Application (IND) for NewLink sponsored clinical studies of 1MT, which will cross-reference the DCTD IND.

4. NewLink agrees to permit DCTD to supply formulated 1MT for all clinical trials set forth in this CRADA. This includes:

   - Provision of appropriately packaged and labeled 1MT for all NCI-sponsored clinical

studies;

- Supply of 1MT for compassionate use, as described in the NCI Investigator Handbook; and

- Supply of 1MT for, and any resources necessary for the management of, Group C distribution, as described in the NCI Investigator Handbook. Group C distribution shall be initiated if such action is justified by clinical results and is feasible based on adequate 1MT supply, such that NewLink's NDA efforts are not negatively impacted.

NewLink agrees to supply 1MT, or to provide unformulated analytical grade 1MT or metabolites, if available, to DCTD for DCTD to provide to DCTD intramural and extramural investigators for the development of analytical assays or ancillary correlative studies conducted in conjunction with DCTD-approved protocols. NewLink also agrees to provide 1MT for distribution for pre-clinical studies designed to enhance the basic understanding and development of 1MT. These will include pre-clinical studies designed to support clinical trials in **[*]**; pre-clinical **[*]** studies to provide data in support of a clinical trial; and other pertinent requests.

5. Upon CRADA execution, NewLink will provide resources for data collection and management, beyond that normally carried out by the DCTD as set forth in the CRADA for CTEP-sponsored studies, if NewLink desires such data collection and management. This would include the collection of the data required to submit an NDA to the FDA.

6. Upon CRADA execution, NewLink may provide funds for partial support of the DCTD-sponsored clinical trials and IND.

7. Upon CRADA execution, NewLink will provide funds for travel by DCTD staff to attend meetings sponsored by NewLink concerning 1MT clinical trials, such funds not to exceed **[*]** per year of the term of the CRADA.

8. NewLink intends and will use reasonable efforts to prepare and submit an NDA to the FDA expeditiously when justified by clinical studies, with the object of obtaining pharmaceutical regulatory approval for the commercial marketing of 1MT.

9. NewLink may sponsor its own clinical trials using 1MT. Such Collaborator-sponsored trials are outside the scope of this CRADA. For these clinical trials, NewLink will maintain possession and control of the clinical trial results. NewLink will permit DCTD to review and use the results for DCTD-sponsored clinical trials which are under the CRADA.

10. NewLink will update DCTD on the progress of its preclinical studies of 1MT to help ensure optimal experimental designs and avoid duplication.

C. NCI Responsibilities

I. Division of Cancer Treatment and Diagnosis, NCI

1. DCTD will develop and implement its preclinical/pharmacodynamic program for 1MT. DCTD also may conduct **[*]** studies to **[*]** 1MT. DCTD will update Collaborator regarding progress and findings to help ensure optimal experimental designs and avoid duplication.

2. DCTD will conduct **[*]** studies in **[*]**, and **[*]** studies using existing supplies of 1MT. As stated in B(l) above, upon execution of the CRADA, NewLink will be responsible for partial costs associated with such studies.

3. DCTD will provide GMP-grade 1MT for **[*]** Phase 0 clinical studies, initial **[*]** Phase 1 clinical studies, and **[*]** Phase 1 clinical trials. As stated in **[*]**, upon execution of the CRADA, **[*]** will be responsible for the costs associated with the drug production for such clinical studies.

4. The DCTD, as sponsor, will prepare and submit to the FDA an IND for 1MT for NCI-sponsored clinical studies. DCTD will permit NewLink to participate in DCTD's IND preparation process.

5. The DCTD will collaborate solely with NewLink for 1MT development, and will assist NewLink in all aspects of the regulatory approval process, so long as NewLink is pursuing clinical development of 1MT.

6. To the extent permitted by law, the DCTD will maintain the DCTD-sponsored IND, including protocols and other supporting information relative to 1MT as an anti-cancer agent in DCTD's possession and control, as proprietary and confidential, and make it available exclusively to NewLink. The DCTD will permit NewLink to review, cross-reference and use the IND in conducting clinical trials and in fulfilling all of the requirements necessary for obtaining FDA approval to market 1MT as an anti-cancer agent.

7. To the extent permitted by law, the DCTD will maintain the clinical data, results and raw data from all new studies developed under this proposed CRADA in its possession and control, as proprietary and confidential, and make them available exclusively to NewLink for use in obtaining approval for the commercial marketing of 1MT as an anti-cancer agent, so long as NewLink is pursuing commercial development for 1MT.

8. The DCTD will solicit protocol Letters of Intent (LOI) from the investigators in the DCTD's clinical trials network as appropriate.

The Protocol Review Committee (PRC), of the DCTD, will:

- Evaluate the rationale of each LOI received at the DCTD;

- Review the LOIs for study design, including dose, schedule and comparison groups, if relevant, in order to address any pertinent scientific questions;

- Examine the characteristics of the patient population to be studied;

- Assess the feasibility of the projected accrual, including the ability of each investigator to accrue the appropriate patient population in a timely manner;

- Review competing studies of the investigator in the specified disease(s);

- Provide investigator(s) with consensus review(s) of the PRC's evaluation to be used to revise the protocol;

- Provide a copy of the consensus review to NewLink. All CTEP approved clinical LOIs will be sent by NCI to NewLink. NewLink will provide NCI with its approval or disapproval within **[*]** of receiving the CTEP approved clinical LOIs. Only LOIs that have been approved by both the PRC and NewLink will lead to the submission of full study protocols.

The protocols received from investigators in response to the fully approved LOIs will be reviewed and evaluated by the PRC and by NewLink. The PRC will:

- Evaluate each protocol from agent, disease, statistical and regulatory perspectives in order to ensure that the study design that was approved by the PRC at the LOI stage is carried out.

- Provide each clinical research protocol received by DCTD to NewLink for review and comment approximately **[*]** before it is reviewed by the PRC of CTEP. Comments from NewLink received by CTEP before the PRC meeting will be discussed by the PRC, will be given due consideration, and will be incorporated into the protocol, absent good cause. Comments from either NewLink or the CTEP staff that are agreed upon in the PRC meeting will be formatted as a consensus review, which is returned to the investigator for necessary and/or suggested changes before the protocol can be given final approval and submitted to the FDA. In addition, the PRC will review any correlative laboratory studies, solicited from investigators, to address cellular pharmacological and/or pharmacokinetics questions as necessary.

9. The DCTD will evaluate each of the active studies as they progress to ensure that the appropriate questions are being addressed and to ensure that the studies are modified as required based on the developing data. The DCTD will utilize its existing procedures and mechanisms to follow the clinical studies to ensure that all studies meet the pertinent FDA regulations.

II. Experimental Immunology Branch, Center for Cancer Research, NCI

[*] studies such as **[*]** in **[*]** will be conducted in the Experimental Immunology Branch under the direction of Dr. Gene Shearer.

7. Intellectual Property of the Parties:

NCI Patents and Patent Applications: **[*]**

NewLink has obtained a worldwide, exclusive license to the following patents covering **[*]** for **[*]** from the University of Georgia.

[*]

In addition, a number of patent applications corresponding to the above patent applications and patents have been filed in countries other than the U.S.

Appendix B

NIH Model CRADA for Extramural-PHS Clinical Research (version 2005)

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

PUBLIC HEALTH SERVICE

COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT FOR EXTRAMURAL-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
[Insert the full name of the ICD]
an Institute, Center, or Division (hereinafter referred to as the "ICD") of the
[INSERT as appropriate: NIH, CDC, or FDA]

and

[Insert Collaborator's official name],
hereinafter referred to as the "Collaborator",
having offices at **[Insert Collaborator's address**],
created and operating under the laws of **[Insert State of Incorporation]**.

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT FOR EXTRAMURAL-PHS CLINICAL RESEARCH

Article 1. Introduction

This CRADA between ICD and Collaborator will be effective when signed by the Parties, which are identified on both the Cover Page and the Signature Page (page 22). The official contacts for the Parties are identified on the Contacts Information Page (page 23). Publicly available information regarding this CRADA appears on the Summary Page (page 24). The research and development activities that will be undertaken by ICD, ICD's contractors or grantees, and Collaborator in the course of this CRADA are detailed in the Research Plan, attached as Appendix A. The staffing, funding, and materials contributions of the Parties are set forth in Appendix B. Any changes to the model CRADA are set forth in Appendix C.

Article 2. Definitions

The terms listed in this Article will carry the meanings indicated throughout the CRADA. To the extent a definition of a term as provided in this Article is inconsistent with a corresponding definition in the applicable sections of either the United States Code (U.S.C.) or the Code of Federal Regulations (C.F.R.), the definition in the U.S.C. or C.F.R. will control.

"**Adverse Drug Experience**" or "**ADE**" means an Adverse Event associated with the use of the Test Article, that is, an event where there is a reasonable possibility that the Test Article may have caused the event (a relationship between the Test Article and the event cannot be ruled out), in accordance with the definitions of 21 C.F.R. Part 310, 305, or 312, or other applicable regulations.

"**Adverse Event**" or "**AE**" means any untoward medical occurrence in a Human Subject administered Test Article. An AE does not necessarily have a causal relationship with the Test Article, that is, it can be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of the Test Article, whether or not it is related to it. See FDA Good Clinical Practice Guideline (International Conference on Harmonisation (ICH) E6: "Good Clinical Practice: Consolidated Guidance, 62 Federal Register 25, 691 (1997)).

"**Affiliate**" means any corporation or other business entity controlled by, controlling, or under common control with Collaborator at any time during the term of the CRADA. For this purpose, "control" means direct or indirect beneficial ownership of at least fifty percent (50%) of the voting stock or at least fifty percent (50%) interest in the income of the corporation or other business entity.

"**Annual Report**" means the report of progress of an IND-associated investigation that the Sponsor must submit to the FDA within sixty (60) days of the anniversary of the effective date of the IND (pursuant to 21 C.F.R. § 312.33).

"**Background Invention**" means an Invention conceived and first actually reduced to practice before the Effective Date.

"**Clinical Data in ICD's Possession and Control**" means all Raw Data that ICD employees create directly; and all copies of Raw Data and Summary Data that ICD obtains from Clinical Investigators or contractors performing CRADA activities.

"**Clinical Investigator**" means, in accordance with 21 C.F.R. § 312.3, an individual who actually conducts a clinical investigation, that is, who directs the administration or dispensation of Test Article to a subject, and who assumes responsibility for studying Human Subjects, for recording and ensuring the integrity of research data, and for protecting the welfare and safety of Human Subjects.

"**Clinical Research Site(s)**" means the site(s) at which the Protocol(s) described in the Research Plan will be performed.

"**Collaborator Materials**" means all tangible materials not first produced in the performance of this CRADA that are owned or controlled by Collaborator and used in the performance of the Research Plan. The term "Collaborator Materials" does not include "Test Article" (defined below).

"**Confidential Information**" means confidential scientific, business, financial information, or Identifiable Private Information provided that Confidential Information does not include:

(a) information that is publicly known or that is available from public sources;
(b) information that has been made available by its owner to others without a confidentiality obligation;
(c) information that is already known by the receiving Party, or information that is independently created or compiled by the receiving Party without reference to or use of the provided information; or
(d) information that relates to potential hazards or cautionary warnings associated with the production, handling, or use of the subject matter of the Research Plan.

"**Cooperative Research and Development Agreement**" or "**CRADA**" means this Agreement, entered into pursuant to the Federal Technology Transfer Act of 1986, as amended (15 U.S.C. §§ 3710a et seq.), and Executive Order 12591 of April 10, 1987.

"**CRADA Data**" means information developed by or on behalf of the Parties in the performance of the Research Plan, excluding Raw Data.

"**CRADA Materials**" means all tangible materials first produced in the performance of the Research Plan other than CRADA Data.

"**CRADA Principal Investigator(s)**" or "**CRADA PI(s)**" means the person(s) designated by the Parties who will be responsible for the scientific and technical conduct of the Research Plan.

"**CRADA Subject Invention**" means any Invention of either or both Parties, conceived or first actually reduced to practice in the performance of the Research Plan.

"**Drug Master File**" or "**DMF**" is described in 21 C.F.R. Part 314.420. A DMF is a submission to the FDA that may be used to provide confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of one or more human drugs.

"**Effective Date**" means the date of the last signature of the Parties executing this Agreement.

"**Government**" means the Government of the United States of America.

"**Human Subject**" means, in accordance with the definition in 45 C.F.R. § 46.102(f), a living individual about whom an investigator conducting research obtains:

(a) data through intervention or interaction with the individual; or
(b) Identifiable Private Information.

"**ICD Materials**" means all tangible materials not first produced in the performance of this CRADA that are owned or controlled by ICD and used in the performance of the Research Plan.

"**IND**" means an "Investigational New Drug Application," filed in accordance with 21 C.F.R. Part 312 under which clinical investigation of an experimental drug or biologic (Test Article) is performed in Human Subjects in the United States or intended to support a United States licensing action.

"**Identifiable Private Information**" or "**IPI**" about a Human Subject means private information from which the identity of the subject is or may readily be ascertained. Regulations defining and governing this information include 45 C.F.R. Part 46 and 21 C.F.R. Part 50.

"**Institutional Review Board**" or "**IRB**" means, in accordance with 45 C.F.R. Part 46, 21 C.F.R. part 56, and other applicable regulations, an independent body comprising medical, scientific, and nonscientific members, whose responsibility is to ensure the protection of the rights, safety, and well-being of the Human Subjects involved in a study.

"**Invention**" means any invention or discovery that is or may be patentable or otherwise protected under Title 35 of the United States Code, or any novel variety of plant which is

or may be protectable under the Plant Variety Protection Act, 7 U.S.C. §§ 2321 et seq.

"**Investigator's Brochure**" means, in accordance with the definition in 21 C.F.R. § 312.23(a)(5), a document containing information about the Test Article, including animal screening, preclinical toxicology, and detailed pharmaceutical data, including a description of possible risks and side effects to be anticipated on the basis of prior experience with the drug or related drugs, and precautions, such as additional monitoring, to be taken as part of the investigational use of the drug.

"**Patent Application**" means an application for patent protection for a CRADA Subject Invention with the United States Patent and Trademark Office ("U.S.P.T.O.") or the corresponding patent-issuing authority of another nation.

"**Patent**" means any issued United States patent, any international counterpart(s), and any corresponding grant(s) by a non-U.S. government in place of a patent.

"**Placebo**" means an inactive substance identical in appearance to the material being tested that is used to distinguish between drug action and suggestive effect of the material under study.

"**Protocol**" means the formal, detailed description of a study to be performed as provided for in the Research Plan. It describes the objective(s), design, methodology, statistical considerations, and organization of a trial. For the purposes of this CRADA, the term, Protocol, for clinical research involving Human Subjects, includes any and all associated documents, including informed consent forms, to be provided to Human Subjects and potential participants in the study.

"**Raw Data**" means the primary quantitative and empirical data first collected from experiments and clinical trials conducted within the scope of this CRADA.

"**Research Plan**" means the statement in Appendix A of the respective research and development commitments of the Parties. The Research Plan should describe the provisions for sponsoring the IND, clinical and safety monitoring, and data management.

"**Sponsor**" means, in accordance with the definition in 21 C.F.R. § 312.3, an organization or individual who assumes legal responsibility for supervising or overseeing clinical trials with Test Articles, and is sometimes referred to as the IND holder.

"**Steering Committee**" means the research and development team whose composition and responsibilities with regard to the research performed under this CRADA are described in Appendix A.

"**Summary Data**" means any extract or summary of the Raw Data, generated either by or, on behalf of, ICD or by, or on behalf of, Collaborator. Summary Data may include

extracts or summaries that incorporate IPI.

"**Test Article**" means, in accordance with 21 C.F.R. § 50.3(j), any drug (including a biological product), medical device, food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food, Drug, and Cosmetic Act that is intended for administration to humans or animals, including a drug or biologic as identified in the Research Plan and Appendix B, that is used within the scope of the Research Plan. The Test Article may also be referred to as Investigational Agent, Study Material, or Study Product.

Article 3. Cooperative Research and Development

3.1 **Performance of Research and Development.** The research and development activities to be carried out under this CRADA will be performed by the Parties identified on the Cover Page, as well as ICD's contractors or grantees as described in the Research Plan. However, ICD's contractors or grantees are not Parties to the CRADA, and this CRADA does not grant to Collaborator any rights to Inventions made by ICD's contractors or grantees. The CRADA PIs will be responsible for coordinating the scientific and technical conduct of this project on behalf of their employers. Any Collaborator employees who will work at ICD facilities will be required to sign a Guest Researcher or Special Volunteer Agreement appropriately modified in view of the terms of this CRADA.

3.2 **Research Plan.** The Parties recognize that the Research Plan describes the collaborative research and development activities they will undertake and that interim research goals set forth in the Research Plan are good faith guidelines. Should events occur that require modification of these goals, then by mutual agreement the Parties can modify them through an amendment, according to Paragraph 13.6.

3.3 **Use and Disposition of Collaborator Materials and ICD Materials.** The Parties agree to use Collaborator Materials and ICD Materials only in accordance with the Research Plan and Protocol(s), not to transfer these materials to third parties except in accordance with the Research Plan and Protocol(s) or as approved by the owning or providing Party, and, upon expiration or termination of the CRADA, to dispose of these materials as directed by the owning or providing Party.

3.4 **Third-Party Rights in Collaborator's CRADA Subject Inventions.** If Collaborator has received (or will receive) support of any kind from a third party in exchange for rights in any of Collaborator's CRADA Subject Inventions, Collaborator agrees to ensure that its obligations to the third party are both consistent with Articles 6 through 8 and subordinate to Article 7 of this CRADA.

3.5 **Disclosures to ICD.** Prior to execution of this CRADA, Collaborator agrees to disclose to ICD all instances in which outstanding royalties are due under a PHS license agreement and in which Collaborator had a PHS license terminated in accordance with 37 C.F.R. § 404.10. These

disclosures will be treated as Confidential Information upon request by Collaborator in accordance with Paragraphs 2.4, 8.3, and 8.4.

3.6 **Clinical Investigator Responsibilities.** The Clinical Investigator will be required to submit, or to arrange for submission of, each Protocol associated with this CRADA to all appropriate IRBs, and for ensuring that the IRBs are notified of the role of Collaborator in the research. In addition to the Protocol all associated documents, including informational documents and advertisements, must be reviewed and approved by the appropriate IRB(s) before starting the research at each Clinical Research Site. The research will be done in strict accordance with the Protocol(s) and no substantive changes in a finalized Protocol will be made unless mutually agreed upon, in writing, by the Parties. Research will not commence (or will continue unchanged, if already in progress) until each substantive change to a Protocol, including those required by either the FDA or the IRB, has been integrated in a way acceptable to the Parties, submitted to the FDA (if applicable) and approved by the appropriate IRBs.

3.7 **Investigational Applications.**

3.7.1 If an IND is required either ICD or Collaborator, as indicated in the Research Plan, will submit an IND and all Clinical Investigators must have completed registration documents on file (1572 forms).

3.7.2 If ICD elects to file its own IND, Collaborator agrees to provide ICD background data and information necessary to support the IND. Collaborator further agrees to provide a letter of cross-reference to all pertinent regulatory filings sponsored by Collaborator. Collaborator's employees will be reasonably available to respond to inquiries from the FDA regarding information and data contained in the Collaborator's IND, DMF, other filings, or other information and data provided to ICD by the Collaborator pursuant to this Article 3. If ICD has provided information or data to assist Collaborator in its IND filing, ICD will provide a letter of cross reference to its IND and respond to inquiries related to information provided by ICD, as applicable.

3.7.3 If Collaborator supplies Confidential Information to ICD in support of an IND filed by ICD, this information will be protected in accordance with the corresponding confidentiality provisions of Article 8.

3.7.4 Collaborator may sponsor its own clinical trials and hold its own IND for studies performed outside the scope of this CRADA. These studies, however, should not adversely affect the ability to accomplish the goal of the Research Plan, for example, by competing for the same study population. All data from those clinical trials are proprietary to Collaborator for purposes of this CRADA.

3.8 **Test Article Information and Supply.** Collaborator agrees to provide ICD without charge and on a schedule that will ensure adequate and timely performance of the research, a sufficient quantity of formulated and acceptably labeled, clinical-grade Test Article (and, as

required by the Protocol(s), Placebo) to complete the clinical trial(s) agreed to and approved under this CRADA. Collaborator will provide a Certificate of Analysis to ICD for each lot of the Test Article provided.

3.9 **Test Article Delivery and Usage.** Collaborator will ship the Test Article and, if required, Placebo to ICD or its designee in containers marked in accordance with 21 C.F.R. § 312.6. ICD agrees that the Clinical Investigators will keep appropriate records and take reasonable steps to ensure that the Test Article is used in accordance with the Protocol(s) and applicable FDA regulations. In addition, ICD agrees that the Test Article (and all Confidential Information supplied by Collaborator relating to the Test Article) will be used solely for the conduct of the CRADA research and development activities. Furthermore, ICD agrees that no analysis or modification of the Test Article will be performed without Collaborator's prior written consent. At the completion of the Research Plan, any unused quantity of Test Article will be returned to Collaborator or disposed as directed by Collaborator. Pharmacy contacts at ICD or its designee will be determined by ICD and communicated to Collaborator.

3.10 **Monitoring.**

3.10.1 The Sponsor or its designee will be primarily responsible for monitoring clinical sites and for assuring the quality of all clinical data, unless otherwise stated in the Research Plan. Monitoring will comply with FDA Good Clinical Practice (International Conference on Harmonisation (ICH) E6: "Good Clinical Practice: Consolidated Guidance; 62 Federal Register 25, 691 (1997)). The other Party may also perform quality assurance oversight. The monitor will communicate significant Protocol violations and submit documentation of monitoring outcomes on Protocol insufficiencies to the other Party in a timely manner.

3.10.2 Subject to the restrictions in Article 8 concerning IPI, and with reasonable advance notice and at reasonable times, ICD will permit Collaborator or its designee(s) access to clinical site(s) to monitor the conduct of the research, as well as to audit source documents containing Raw Data, to the extent necessary to verify compliance with FDA Good Clinical Practice and the Protocol(s).

3.11 **FDA Meetings/Communications.** All meetings with the FDA concerning any clinical trial within the scope of the Research Plan will be discussed by Collaborator and ICD in advance. Each Party reserves the right to take part in setting the agenda for, to attend, and to participate in these meetings. The Sponsor will provide the other Party with copies of FDA meeting minutes, all transmittal letters for IND submissions, IND safety reports, formal questions and responses that have been submitted to the FDA, Annual Reports, and official FDA correspondence, pertaining either to the INDs under this CRADA or to the Clinical Investigators on Protocols performed in accordance with the Research Plan, except to the extent that those documents contain the proprietary information of a third party or dissemination is prohibited by law.

Article 4. Reports

4.1 **Interim Research and Development Reports.** The CRADA PIs should exchange information regularly, in writing. This exchange may be accomplished through meeting minutes, detailed correspondence, circulation of draft manuscripts, Steering Committee reports, copies of Annual Reports and any other reports updating the progress of the CRADA research. However, the Parties must exchange updated Investigator's Brochure, formulation and preclinical data, and toxicology findings, as they become available.

4.2 **Final Research and Development Reports.** The Parties will exchange final reports of their results within six (6) months after the expiration or termination of this CRADA. These reports will set forth the technical progress made; any publications arising from the research; and the existence of invention disclosures of potential CRADA Subject Inventions and/or any corresponding Patent Applications.

4.3 **Fiscal Reports.** If Collaborator has agreed to provide funding to ICD under this CRADA and upon the request of Collaborator, then concurrent with the exchange of final research and development reports according to Paragraph 4.2, ICD will submit to Collaborator a statement of all costs incurred by ICD for the CRADA. If the CRADA has been terminated, ICD will specify any costs incurred before the date of termination for which ICD has not received funds from Collaborator, as well as for all reasonable termination costs including the cost of returning Collaborator property or removal of abandoned Collaborator property, for which Collaborator will be responsible.

4.4 **Safety Reports.** In accordance with FDA requirements, the Sponsor will establish and maintain records and submit safety reports to the FDA, as required by 21 C.F.R. § 312.32 and 21 C.F.R. 812.150(b)(1), or other applicable regulations. In the conduct of research under this CRADA, the Parties will comply with specific ICD guidelines and policies for reporting ADEs and AEs, as well as procedures specified in the Protocol(s). The Sponsor must provide the other Party with copies of all Safety Reports concurrently with their submission to the FDA, and with any other information affecting the safety of Human Subjects in research conducted under this CRADA.

4.5 **Annual Reports.** The Sponsor will provide the other Party a copy of the Annual Report concurrently with the submission of the Annual Report to the FDA. Annual Reports will be kept confidential in accordance with Article 8,

Article 5. Staffing, Financial, and Materials Obligations

5.1 **ICD and Collaborator Contributions.** The contributions of any staff, funds, materials, and equipment by the Parties are set forth in Appendix B. The Federal Technology Transfer Act of 1986, 15 U.S.C. § 3710a(d)(1) prohibits ICD from providing funds to Collaborator for any research and development activities under this CRADA.

5.2 **ICD Staffing.** No ICD employees will devote 100% of their effort or time to the research and development activities under this CRADA. ICD will not use funds provided by Collaborator

under this CRADA for ICD personnel to pay the salary of any permanent ICD employee. Although personnel hired by ICD using CRADA funds will focus principally on CRADA research and development activities, Collaborator acknowledges that these personnel may nonetheless make contributions to other research and development activities, and the activities will be outside the scope of this CRADA.

5.3 **Collaborator Funding.** Collaborator acknowledges that Government funds received by Collaborator from an agency of the Department of Health and Human Services may not be used to fund ICD under this CRADA. If Collaborator has agreed to provide funds to ICD then the payment schedule appears in Appendix B and Collaborator will make payments according to that schedule. If Collaborator fails to make any scheduled payment, ICD will not be obligated to perform any of the research and development activities specified herein or to take any other action required by this CRADA until the funds are received. ICD will use these funds exclusively for the purposes of this CRADA. Each Party will maintain separate and distinct current accounts, records, and other evidence supporting its financial obligations under this CRADA and, upon written request, will provide the other Party a Fiscal Report according to Paragraph 4.3, which delineates all payments made and all obligated expenses, along with the Final Research Report described in Paragraph 4.2.

5.4 **Capital Equipment.** Collaborator's commitment, if any, to provide ICD with capital equipment to enable the research and development activities under the Research Plan appears in Appendix B. If Collaborator transfers to ICD the capital equipment or provides funds for ICD to purchase it, then ICD will own the equipment. If Collaborator loans capital equipment to ICD for use during the CRADA, Collaborator will be responsible for paying all costs and fees associated with the transport, installation, maintenance, repair, removal, or disposal of the equipment, and ICD will not be liable for any damage to the equipment.

Article 6. Intellectual Property

6.1 **Ownership of CRADA Subject Inventions, CRADA Data, and CRADA Materials.** Subject to the Government license described in Paragraph 7.5, the sharing requirements of Paragraph 8.1 and the regulatory filing requirements of Paragraph 8.2, the producing Party will retain sole ownership of and title to all CRADA Subject Inventions, all copies of CRADA Data, and all CRADA Materials produced solely by its employee(s). The Parties will own jointly all CRADA Subject Inventions invented jointly and all CRADA Materials developed jointly. A PHS contractor's or grantee's rights in data it generates will not be affected by this CRADA.

6.2 **Reporting.** The Parties will promptly report to each other in writing each CRADA Subject Invention reported by their respective personnel, and any Patent Applications filed thereon, resulting from the research and development activities conducted under this CRADA. Each Party will report all CRADA Subject Inventions to the other Party in sufficient detail to determine inventorship, which will be determined in accordance with U.S. patent law. These reports will be treated as Confidential Information in accordance with Article 8. Formal reports will be made by and to the Patenting and Licensing Offices identified on the Contacts

Information Page herein.

6.3 **Filing of Patent Applications.** Each Party will make timely decisions regarding the filing of Patent Applications on the CRADA Subject Inventions made solely by its employee(s), and will notify the other Party in advance of filing. Collaborator will have the first opportunity to file a Patent Application on joint CRADA Subject Inventions and will notify PHS of its decision within sixty (60) days of an Invention being reported or at least thirty (30) days before any patent filing deadline, whichever occurs sooner. If Collaborator fails to notify PHS of its decision within that time period or notifies PHS of its decision not to file a Patent Application, then PHS has the right to file a Patent Application on the joint CRADA Subject Invention, Neither Party will be obligated to file a Patent Application. Collaborator will place the following statement in any Patent Application it files on a CRADA Subject Invention: "This invention was created in the performance of a Cooperative Research and Development Agreement with the **[INSERT into Agency's model as appropriate: National Institutes of Health, Food and Drug Administration, Centers for Disease Control and Prevention],** an Agency of the Department of Health and Human Services. The Government of the United States has certain rights in this invention." If either Party files a Patent Application on a joint CRADA Subject Invention, then the filing Party will include a statement within the Patent Application that clearly identifies the Parties and states that the joint CRADA Subject Invention was made under this CRADA.

6.4 **Patent Expenses.** Unless agreed otherwise, the Party filing a Patent Application will pay all preparation and filing expenses, prosecution fees, issuance fees, post issuance fees, patent maintenance fees, annuities, interference expenses, and attorneys' fees for that Patent Application and any resulting Patent(s). If a license to any CRADA Subject Invention is granted to Collaborator, then Collaborator will be responsible for all expenses and fees, past and future, in connection with the preparation, filing, prosecution, and maintenance of any Patent Applications and Patents claiming exclusively licensed CRADA Subject Inventions and will be responsible for a pro-rated share, divided equally among all licensees, of those expenses and fees for non-exclusively licensed CRADA Subject Inventions. Collaborator may waive its exclusive option rights at any time, and incur no subsequent financial obligation for those Patent Application(s) or Patent(s).

6.5 **Prosecution of Patent Applications.** The Party filing a Patent Application will provide the non-filing Party with a copy of any official communication relating to prosecution of the Patent Application within thirty (30) days of transmission of the communication. Each Party will also provide the other Party with the power to inspect and make copies of all documents retained in the applicable Patent Application or Patent file. The Parties agree to consult with each other regarding the prosecution of Patent Applications directed to joint CRADA Subject Inventions. If Collaborator elects to file and prosecute Patent Applications on joint CRADA Subject Inventions, then Collaborator agrees to use the U.S.P.T.O. Customer Number Practice and/or grant PHS a power(s) of attorney (or equivalent) necessary to assure PHS access to its intellectual property rights in these Patent Applications. PHS and Collaborator will cooperate with each other to obtain necessary signatures on Patent Applications, assignments, or other documents.

Article 7. Licensing

7.1 **Background Inventions.** Other than as specifically stated in this Article 7, nothing in this CRADA will be construed to grant any rights in one Party's Background Invention(s) to the other Party, except to the extent necessary for the Parties to conduct the research and development activities described in the Research Plan.

7.2 **Collaborator's License Option to CRADA Subject Inventions.** With respect to Government rights to any CRADA Subject Invention made solely by an ICD employee(s) or made jointly by an ICD 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 commercialization license. 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.

7.3 **Exercise of Collaborator's License Option.** To exercise the option of Paragraph 7.2 Collaborator must submit a written notice to the PHS Patenting and Licensing Contact identified on the Contacts Information Page (and provide a copy to the ICD Contact for CRADA Notices) within three (3) months after either (i) Collaborator receives written notice from PHS that the Patent Application has been filed or (ii) the date on which Collaborator files the Patent Application. The written notice exercising this option will include a completed "Application for License to Public Health Service Inventions" and will initiate a negotiation period that expires nine (9) months after the exercise of the option. If PHS has not responded in writing to the last proposal by Collaborator within this nine (9) month period, the negotiation period will be extended to expire one (1) month after PHS so responds, during which month Collaborator may accept in writing the final license proposal of PHS. In the absence of Collaborator's exercise of the option, or upon election of a nonexclusive license, PHS will be free to license the CRADA Subject Invention to others. These time periods may be extended at the sole discretion of PHS upon good cause shown in writing by Collaborator.

7.4 **Government License in ICD Sole CRADA Subject Inventions and Joint CRADA Subject Inventions.** Pursuant to 15 U.S.C. § 3710a(b)(1)(A), for CRADA Subject Inventions owned solely by ICD or jointly by ICD and Collaborator, and licensed pursuant to the option of Paragraph 7.2, Collaborator grants to the Government a nonexclusive, nontransferable, irrevocable, paid-up license to practice the CRADA Subject Invention or have the CRADA Subject Invention practiced throughout the world by or on behalf of the Government. In the exercise of this license, the Government will not publicly disclose trade secrets or commercial or financial information that is privileged or confidential within the meaning of 5 U.S.C. § 552(b)(4) or which would be considered privileged or confidential if it had been obtained from a non-federal party.

7.5 **Government License in Collaborator Sole CRADA Subject Inventions.** Pursuant to 15 U.S.C. § 3710a(b)(2), for CRADA Subject Inventions made solely by an employee of Collaborator, Collaborator grants to the Government a nonexclusive, nontransferable, irrevocable, paid-up license to practice the CRADA Subject Invention or have the CRADA Subject Invention practiced throughout the world by or on behalf of the Government for research or other Government purposes.

7.6 **Third Party License.** Pursuant to 15 U.S.C. § 3710a(b)(1)(B), if PHS grants Collaborator an exclusive license to a CRADA Subject Invention made solely by an ICD 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(2).

7.7 **Third-Party Rights In ICD Sole CRADA Subject Inventions.** For a CRADA Subject Invention conceived prior to the Effective Date solely by an ICD employee that is first actually reduced to practice after the Effective Date in the performance of the Research Plan, the option offered to Collaborator in Paragraph 7.2 may be restricted if, prior to the Effective Date, PHS had filed a Patent Application and has either offered or granted a license in the CRADA Subject Invention to a third party. Collaborator nonetheless retains the right to apply for a license to any such CRADA Subject Invention in accordance with the terms and procedures of 35 U.S.C. § 209 and 37 C.F.R. Part 404.

7.8 **Joint CRADA Subject Inventions Not Exclusively Licensed by Collaborator.** If Collaborator does not acquire an exclusive commercialization license in a joint CRADA Subject Invention in all fields of use then, for those fields of use not exclusively licensed to Collaborator, each Party will have the right to use the joint CRADA Subject Invention and to license its use to others, and each Party will cooperate with the other, as necessary, to fulfill international licensing requirements. The Parties may agree to a joint licensing approach for any remaining fields of use.

Article 8. Rights of Access and Publication

8.1 **Right of Access to CRADA Data and CRADA Materials.** ICD and Collaborator agree to exchange all CRADA Data and to share all CRADA Materials. If the CRADA is terminated, both Parties agree to provide CRADA Materials in quantities needed to complete the Research Plan. Such provision will occur before the termination date of the CRADA or sooner, if required

by the Research Plan. If Collaborator possesses any human biological specimens from clinical trials under the CRADA, the specimens must be handled as described in the Protocol or as otherwise directed by ICD before the termination date of the CRADA.

8.2 **Use of CRADA Data and CRADA Materials.** The Parties will be free to utilize CRADA Data and CRADA Materials internally for their own purposes, consistent with their obligations under this CRADA. ICD may share CRADA Data or CRADA Materials with any contractors, grantees, or agents it has engaged to conduct the CRADA research and development activities, provided the obligations of this Article 8.2 are simultaneously conveyed. Collaborator may share CRADA Data or CRADA Materials with any contractors, Affiliates, or agents it has engaged to conduct the CRADA research and development activities, provided the obligations of this Article 8.2 are simultaneously conveyed.

8.2.1 **CRADA Data.**
Collaborator and ICD will use reasonable efforts to keep CRADA Data confidential until published or until corresponding Patent Applications are filed. To the extent permitted by law, each Party will have the right to use any and all CRADA Data in and for any regulatory filing by or on behalf of the Party.

8.2.2 **CRADA Materials.**
Collaborator and ICD will use reasonable efforts to keep descriptions of CRADA Materials confidential until published or until corresponding Patent Applications are filed. Collaborator acknowledges that the basic research mission of PHS includes sharing with third parties for further research those research resources made in whole or in part with NIH funding. Consistent with this mission and the tenets articulated in “Sharing of Biomedical Research Resources: Principles and Guidelines for Recipients of NIH Research Grants and Contracts,” December 1999, available at http://ott.od.nih.gov/NewPages/RTguide_final.html, following publication either Party may make available to third parties for further research those CRADA Materials made jointly by both PHS and Collaborator. Notwithstanding the above, if those joint CRADA Materials are the subject of a pending Patent Application or a Patent, or were created using a patent-pending or patented material or technology, the Parties may agree to restrict distribution or freely distribute them. Either Party may distribute those CRADA Materials made solely by the other Party only upon written consent from that other Party or that other Party’s designee.

8.3 **Confidential Information.** Each Party agrees to limit its disclosure of Confidential Information to the amount necessary to carry out the Research Plan, and will place a confidentiality notice on all this information. A Party orally disclosing Confidential Information to the other Party will summarize the disclosure in writing and provide it to the other Party within fifteen (15) days of the disclosure. Each Party receiving Confidential Information agrees to use it only for the purposes described in the Research Plan. Either Party may object to the designation of information as Confidential Information by the other Party.

8.4 **Protection of Confidential Information.** Confidential Information will not be disclosed, copied, reproduced or otherwise made available to any other person or entity without the consent of the owning or providing Party except as required by a court or administrative body of competent jurisdiction, or federal law or regulation. Each Party agrees to use reasonable efforts to maintain the confidentiality of Confidential Information, which will in no instance be less effort than the Party uses to protect its own Confidential Information. Each Party agrees that a Party receiving Confidential Information will not be liable for the disclosure of that portion of the Confidential Information which, after notice to and consultation with the disclosing Party, the receiving Party determines may not be lawfully withheld, provided the disclosing Party has been given a reasonable opportunity to seek a court order to enjoin disclosure.

8.5 **Human Subject Protection.** The research to be conducted under this CRADA involves Human Subjects or human tissues within the meaning of 45 C.F.R. Part 46, and all research to be performed under this CRADA will conform to applicable federal laws and regulations. Additional information is available from the HHS Office for Human Research Protections (http://www.hhs.gov/ohrp/).

8.6 **Duration of Confidentiality Obligation.** The obligation to maintain the confidentiality of Confidential Information will expire at the earlier of the date when the information is no longer Confidential Information as defined in Paragraph 2.4 or three (3) years after the expiration or termination date of this CRADA, except for IPI, for which the obligation to maintain confidentiality will extend indefinitely. Collaborator may request an extension to this term when necessary to protect Confidential Information relating to products not yet commercialized.

8.7 **Publication.** The Parties are encouraged to make publicly available the results of their research and development activities. Before either Party submits a paper or abstract for publication or otherwise intends to publicly disclose information about a CRADA Subject Invention, CRADA Data, or CRADA Materials, the other Party will have thirty (30) days to review proposed manuscripts and three (3) days to review proposed abstracts to assure that Confidential Information is protected. Either Party may request in writing that the proposed publication or other disclosure be delayed for up to thirty (30) additional days as necessary to file a Patent Application.

8.8 **Clinical Investigators' Research and Development Activities.** Although this CRADA does not grant to Collaborator any rights to Inventions made or Raw Data generated by ICD's contractors or grantees, as they are not parties to this CRADA, ICD agrees that:

8.8.1 Subject to the other provisions of Article 8 of this CRADA, ICD will maintain, to the extent permitted by law, all Clinical Data in ICD's Possession and Control as Confidential Information, and make them available to Collaborator for its own use and for exclusive use in obtaining regulatory approval for the commercial marketing of Test Article and related CRADA Subject Inventions.

8.8.2 With regard to Collaborator's Confidential Information, ICD will require the

Clinical Investigators to agree to confidentiality provisions at least as restrictive as those provided in this CRADA and to Collaborator's use of data in accordance with Paragraph 8.8.1 for obtaining regulatory approval for marketing Test Article.

8.8.3 If Collaborator wants access to Raw Data or any other data in the possession of the Clinical Investigators working with Test Article, Collaborator must first contact the CRADA PI. Collaborator will bear any costs associated with Raw Data provided in formats customized for Collaborator.

8.8.4 Collaborator's right to access Clinical Data in ICD's Possession and Control under Paragraph 8.8 is dependent upon Collaborator's continued development and commercialization of Investigational Agent. If Collaborator fails to continue development or commercialization of Investigational Agent without the transfer of its development efforts to another party within ninety (90) days of discontinuation, ICD has the right to make Clinical Data in ICD's Possession and Control available to a third party.

Article 9. Representations and Warranties

9.1 **Representations of ICD**. ICD hereby represents to Collaborator that:

9.1.1 ICD has the requisite power and authority to enter into this CRADA and to perform according to its terms, and that ICD's official signing this CRADA has authority to do so.

9.1.2 To the best of its knowledge and belief, neither ICD nor any of its personnel involved in this CRADA is presently subject to debarment or suspension by any agency of the Government which would directly affect its performance of the CRADA. Should ICD or any of its personnel involved in this CRADA be debarred or suspended during the term of this CRADA, ICD will notify Collaborator within thirty (30) days of receipt of final notice.

9.2 **Representations and Warranties of Collaborator.** Collaborator hereby represents and warrants to ICD that:

9.2.1 Collaborator has the requisite power and authority to enter into this CRADA and to perform according to its terms, and that Collaborator's official signing this CRADA has authority to do so.

9.2.2 Neither Collaborator nor any of its personnel involved in this CRADA, including Affiliates, agents, and contractors are presently subject to debarment or suspension by any agency of the Government. Should Collaborator or any of its personnel involved in this CRADA be debarred or suspended during the term of this CRADA, Collaborator will notify ICD within thirty (30) days of receipt of final notice.

9.2.3 Subject to Paragraph 12.3, and if and to the extent Collaborator has agreed to provide funding under Appendix B, Collaborator is financially able to satisfy these

obligations in a timely manner.

9.2.4 The Test Article provided has been produced in accordance with the FDA's current Good Manufacturing Practice set out in 21 C.F.R. §§ 210-211, and ICH QA7, and meets the specifications cited in the Certificate of Analysis and Investigator's Brochure provided.

Article 10. Expiration and Termination

10.1 **Expiration.** This CRADA will expire on the last date of the term set forth on the Summary Page. In no case will the term of this CRADA extend beyond the term indicated on the Summary Page unless it is extended in writing in accordance with Paragraph 13.6.

10.2 **Termination by Mutual Consent.** ICD and Collaborator may terminate this CRADA at any time by mutual written consent.

10.3 **Unilateral Termination.** Either ICD or Collaborator may unilaterally terminate this CRADA at any time by providing written notice at least sixty (60) days before the desired termination date. ICD may, at its option, retain funds transferred to ICD before unilateral termination by Collaborator for use in completing the Research Plan. If Collaborator terminates this Agreement before the completion of all approved or active Protocol(s), then Collaborator will supply enough Test Article (and Placebo, if applicable) to complete these Protocol(s) unless termination is for safety concerns.

10.4 **Funding for ICD Personnel.** If Collaborator has agreed to provide funding for ICD personnel and this CRADA is mutually or unilaterally terminated by Collaborator before its expiration, then Collaborator agrees that funds for that purpose will be available to ICD for a period of six (6) months after the termination date or until the expiration date of the CRADA, whichever occurs sooner. If there are insufficient funds to cover this expense, Collaborator agrees to pay the difference.

10.5 **New Commitments.** Neither Party will incur new expenses related to this CRADA after expiration, mutual termination, or a notice of a unilateral termination and will, to the extent feasible, cancel all outstanding commitments and contracts by the termination date. Collaborator acknowledges that ICD will have the authority to retain and expend any funds for up to one (1) year subsequent to the expiration or termination date to cover any unpaid costs obligated during the term of the CRADA in undertaking the research and development activities set forth in the Research Plan.

10.6 **Collaborator Failure to Continue Development.** If Collaborator suspends development of the Test Article without the transfer of its active development efforts, assets, and obligations to a third party within ninety (90) days of discontinuation, Collaborator agrees that ICD may continue developing the Test Article. In that event, the following will apply:

10.6.1 Collaborator agrees to transfer to ICD all information necessary to enable ICD to contract for the manufacture of the Test Article and, unless abandoned for reasons relating to safety as determined by the data safety monitoring board, to provide the Test Article (and Placebo, if any) in Collaborator's inventory to ICD.

10.6.2 Further, Collaborator hereby grants to ICD a nonexclusive, irrevocable, world-wide, paid-up license to practice, or have practiced for or on behalf of the Government, any Background Invention that Collaborator may currently have or will obtain on the Test Article, its manufacture, or on any method of using the Test Article for the indication(s) described in the Research Plan, including the right to sublicense to third parties.

Article 11. Disputes

11.1 **Settlement.** Any dispute arising under this CRADA which is not disposed of by agreement of the CRADA Principal Investigators will be submitted jointly to the signatories of this CRADA. If the signatories, or their designees, are unable to jointly resolve the dispute within thirty (30) days after notification thereof, the Assistant Secretary for Health (or his/her designee or successor) will propose a resolution. Nothing in this Paragraph will prevent any Party from pursuing any additional administrative remedies that may be available and, after exhaustion of such administrative remedies, pursuing all available judicial remedies.

11.2 **Continuation of Work.** Pending the resolution of any dispute or claim pursuant to this Article 11, the Parties agree that performance of all obligations will be pursued diligently.

Article 12. Liability

12.1 **NO WARRANTIES.** EXCEPT AS SPECIFICALLY STATED IN ARTICLE 9, THE PARTIES MAKE NO EXPRESS OR IMPLIED WARRANTY AS TO ANY MATTER WHATSOEVER, INCLUDING THE CONDITIONS OF THE RESEARCH OR ANY INVENTION OR MATERIAL, WHETHER TANGIBLE OR INTANGIBLE, MADE OR DEVELOPED UNDER OR OUTSIDE THE SCOPE OF THIS CRADA, OR THE OWNERSHIP, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE OF THE RESEARCH OR ANY INVENTION OR MATERIAL, OR THAT A TECHNOLOGY UTILIZED BY A PARTY IN THE PERFORMANCE OF THE RESEARCH PLAN DOES NOT INFRINGE ANY THIRD-PARTY PATENT RIGHTS.

12.2 **Indemnification and Liability.** Collaborator agrees to hold the Government harmless and to indemnify the Government for all liabilities, demands, damages, expenses and losses arising out of the use by Collaborator for any purpose of the CRADA Data, CRADA Materials or CRADA Subject Inventions produced in whole or part by ICD employees under this CRADA, unless due to the negligence or willful misconduct of ICD, its employees, or agents. The Government has no statutory authority to indemnify Collaborator. Each Party otherwise will be liable for any claims or damages it incurs in connection with this CRADA, except that ICD, as an agency of the Government, assumes liability only to the extent provided under the Federal

Tort Claims Act , 28 U.S.C. Chapter 171.

12.3 ***Force Majeure.*** Neither Party will be liable for any unforeseeable event beyond its reasonable control and not caused by its own fault or negligence, which causes the Party to be unable to perform its obligations under this CRADA, and which it has been unable to overcome by the exercise of due diligence. If a *force majeure* event occurs, the Party unable to perform will promptly notify the other Party. It will use its best efforts to resume performance as quickly as possible and will suspend performance only for such period of time as is necessary as a result of the *force majeure* event.

Article 13. Miscellaneous

13.1 **Governing Law.** The construction, validity, performance and effect of this CRADA will be governed by U.S. federal law, as applied by the federal courts in the District of Columbia. If any provision in this CRADA conflicts with or is inconsistent with any U.S. federal law or regulation, then the U.S. federal law or regulation will preempt that provision.

13.2 **Compliance with Law.** ICD and Collaborator agree that they will comply with, and advise any contractors, grantees, or agents they have engaged to conduct the CRADA research and development activities to comply with, all applicable Executive Orders, statutes, and HHS regulations relating to research on human subjects (45 C.F.R. Part 46, 21 C.F.R. Parts 50 and 56) and relating to the appropriate care and use of laboratory animals (7 U.S.C. §§ 2131 et seq.; 9 C.F.R. Part 1, Subchapter A). ICD and Collaborator will advise any contractors, grantees, or agents they have engaged to conduct clinical trials for this CRADA that they must comply with all applicable federal regulations for the protection of Human Subjects, which may include the Standards for Privacy of Individually Identifiable Health Information set forth in 45 C.F.R. Part 164. Collaborator agrees to ensure that its employees, contractors, and agents who might have access to a “select agent or toxin” (as that term is defined in 42 C.F.R. §§ 73.4-73.5) transferred from ICD is properly licensed to receive the “select agent or toxin.”

13.3 **Waivers.** None of the provisions of this CRADA will be considered waived by any Party unless a waiver is given in writing to the other Party. The failure of a Party to insist upon strict performance of any of the terms and conditions hereof, or failure or delay to exercise any rights provided herein or by law, will not be deemed a waiver of any rights of any Party.

13.4 **Headings.** Titles and headings of the articles and paragraphs of this CRADA are for convenient reference only, do not form a part of this CRADA, and will in no way affect its interpretation.

13.5 **Severability.** The illegality or invalidity of any provisions of this CRADA will not impair, affect, or invalidate the other provisions of this CRADA.

13.6 **Amendments.** Minor modifications to the Research Plan may be made by the mutual written consent of the CRADA Principal Investigators. Substantial changes to the CRADA,

extensions of the term, or any changes to Appendix C will become effective only upon a written amendment signed by the signatories to this CRADA or by their representatives duly authorized to execute an amendment. A change will be considered substantial if it directly expands the range of the potential CRADA Subject Inventions, alters the scope or field of any license option governed by Article 7, or requires a significant increase in the contribution of resources by either Party.

13.7 **Assignment.** Neither this CRADA nor any rights or obligations of any Party hereunder will be assigned or otherwise transferred by either Party without the prior written consent of the other Party. This CRADA will be binding upon and inure to the benefit of the Parties and their respective successors and permitted assigns.

13.8 **Notices.** All notices pertaining to or required by this CRADA will be in writing, signed by an authorized representative of the notifying Party, and delivered by first class, registered, or certified mail, or by an express/overnight commercial delivery service, prepaid and properly addressed to the other Party at the address designated on the Contacts Information Page, or to any other address designated in writing by the other Party. Notices will be considered timely if received on or before the established deadline date or sent on or before the deadline date as verifiable by U.S. Postal Service postmark or dated receipt from a commercial carrier. Notices regarding the exercise of license options will be made pursuant to Paragraph 7.3. Either Party may change its address by notice given to the other Party in the manner set forth above.

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 will maintain sole and exclusive control over its personnel and operations.

13.10 **Use of Name; Press Releases.** By entering into this CRADA, the Government does not directly or indirectly endorse any product or service that is or will be provided, whether directly or indirectly related to either this CRADA or to any patent or other intellectual-property license or agreement that implements this CRADA by Collaborator, its successors, assignees, or licensees. Collaborator will not in any way state or imply that the Government or any of its organizational units or employees endorses any product or services. Each Party agrees to provide proposed press releases that reference or rely upon the work under this CRADA to the other Party for review and comment at least five (5) business days before publication. Either Party may disclose the Title and Abstract of the CRADA to the public without the approval of the other Party.

13.11 **Reasonable Consent.** Whenever a Party’s consent or permission is required under this CRADA, its consent or permission will not be unreasonably withheld.

13.12 **Export Controls.** Collaborator agrees to comply with U.S. export law and regulations. If Collaborator has a need to transfer any CRADA Materials made in whole or in part by ICD, or ICD Materials, or ICD’s Confidential Information to a person located in a country other than the United States, to an Affiliate organized under the laws of a country other than the United States,

or to an employee of Collaborator in the United States who is not a citizen or permanent resident of the United States, Collaborator will acquire any and all necessary export licenses and other appropriate authorizations.

13.13 **Entire Agreement.** This CRADA constitutes the entire agreement between the Parties concerning the subject matter of this CRADA and supersedes any prior understanding or written or oral agreement.

13.14 **Survivability.** The provisions of Paragraphs 3.3, 3.4, 3.8, 4.2, 4.3, 5.3, 5.4, 6.1-9.2, 10.3-10.6, 11.1, 11.2, 12.1-12.3, 13.1-13.3, 13.7, 13.10 and 13.14 will survive the expiration or early termination of this CRADA.

SIGNATURES BEGIN ON THE NEXT PAGE

SIGNATURE PAGE

ACCEPTED AND AGREED

BY EXECUTING THIS AGREEMENT, EACH PARTY REPRESENTS THAT ALL STATEMENTS MADE HEREIN ARE TRUE, COMPLETE, AND ACCURATE TO THE BEST OF ITS KNOWLEDGE. COLLABORATOR ACKNOWLEDGES THAT IT MAY BE SUBJECT TO CRIMINAL, CIVIL, OR ADMINISTRATIVE PENALTIES FOR KNOWINGLY MAKING A FALSE, FICTITIOUS, OR FRAUDULENT STATEMENT OR CLAIM.

FOR ICD:

Signature Date

Typed Name:
Title:

FOR COLLABORATOR:

Signature Date

Typed Name:
Title:

CONTACTS INFORMATION PAGE

CRADA Notices

For ICD:

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For Collaborator:

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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):

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Delivery of Materials Identified In Appendix B (if any)

For ICD:

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For Collaborator:

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ICD Project Officer for Extramural Investigators

Name: __
Branch: __
Address: __
Telephone: __

SUMMARY PAGE

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

TITLE OF CRADA: __

__

PHS [ICD] Component: __
ICD CRADA Principal Investigator: __

Collaborator: __
Collaborator CRADA Principal Investigator: __

Term of CRADA: _____ (__) years from the Effective Date

ABSTRACT OF THE RESEARCH PLAN:

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[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Appendix C

CTEP Exceptions or Modifications to this CRADA (6/26/06)

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Appendix C

Exceptions or Modifications to this CRADA

Additions and deletions within Articles of the extramural clinical trial CRADA appear as underline and strikeout, respectively.

"**Test Article**" means, in accordance with 21 C.F.R. § 50.3(j), any drug (including a biological product), medical device, food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food, Drug, and Cosmetic Act that is intended for administration to humans or animals, including a drug or biologic as identified in the Research Plan and Appendix B, that is used within the scope of the Research Plan. The Test Article may also be referred to as Investigational Agent, Study Material, or Study Product. For this Agreement, Investigational Agent means xxxxxxxxxxxx.

Add the following new sections to the **Article 2. Definitions:**

"**Contract**" means a Funding Agreement that is a research and development mechanism that provides that the contractor perform for the benefit of the Government, with an expectation of completion of the stated research goals and the delivery of a report, data, materials or other product. Generally, Contracts are administered under the Federal Acquisition Regulations (FAR) codified at Title 48 C.F.R., Chapter 1 or the Health Services Acquisition Regulations (HSAR) codified at Title 48 C.F.R., Chapter 3.

"**Cooperative Agreement**" means a Funding Agreement that is a species of a Grant, whereby the funding Federal agency intends to be substantially involved in carrying out the research program.

"**CTA**" means Clinical Trial Agreement.

"**CTEP**" means the Cancer Therapy Evaluation Program, DCTD, NCI, a program within NCI which plans, assesses and coordinates all aspects of clinical trials including extramural clinical research programs, internal resources, treatment methods and effectiveness, and compilation and exchange of data.

"**DTP**" means Developmental Therapeutics Program, DCTD, NCI, the program within the NCI which coordinates preclinical development of agents to be evaluated in DCTD-sponsored clinical trials.

"**DCTD**" means Division of Cancer Treatment and Diagnosis, NCI.

"**FDA**" means U.S. Food and Drug Administration.

"**Funding Agreement**" means a Contract, Grant, or Cooperative Agreement entered into

between a Federal agency and another party for the performance of experimental, developmental or research work funded in whole or in part by the Federal Government.

"**Grant**" means a Funding Agreement that is an award of financial assistance which may be provided for support of basic research in a specific field of interest to the funding Federal agency.

"**Multi-Party Data**" means clinical data from clinical studies sponsored by NCI pursuant to CTAs or CRADAs, where such data are collected under protocols involving combinations of investigational agents from more than one CTA or CRADA collaborator.

"**Protocol Review Committee**" (or "**PRC**") means the CTEP/DCTD committee that reviews and approves studies involving NCI investigational agents and/or activities supported by NCI.

3.7 **Investigational New Drug Applications.**

3.7.1 ~~If an IND is required either ICD or Collaborator,~~ DCTD, NCI, as indicated in the Research Plan, will prepare and submit an IND and all Clinical Investigators participating in DCTD-sponsored clinical trials must have completed registration documents on file (1572 forms) with CTEP.

3.7.2 ~~If ICD elects to file its own IND,~~ To support the DCTD IND, Collaborator agrees to provide ~~ICD~~ DCTD background data and information necessary to support the IND. Collaborator further agrees to provide a letter of cross-reference to all pertinent regulatory filings including an IND and/or DMF sponsored by Collaborator. Collaborator's employees will be reasonably available to respond to inquiries from the FDA regarding information and data contained in the Collaborator's IND, DMF, other filings, or other information and data provided to ~~ICD~~ DCTD by the Collaborator pursuant to this Article 3. If ~~ICD~~ DCTD has provided information or data to assist Collaborator in its IND filing, ~~ICD~~ DCTD will provide a letter of cross reference to its IND and respond to inquiries related to information provided by ~~ICD~~ DCTD, as applicable.

3.7.3 If Collaborator supplies Confidential Information to ~~ICD~~ DCTD in support of an IND filed by ~~ICD~~ DCTD, this information will be protected in accordance with the corresponding confidentiality provisions of Article 8.

3.7.4 Collaborator may sponsor its own clinical trials and hold its own IND for studies performed outside the scope of this CRADA. These studies, however, should not adversely affect the ability to accomplish the goal of the Research Plan, for example, by competing for the same study population. All data from those clinical trials are proprietary to Collaborator for purposes of this CRADA.

3.7.5 In the event that Canadian institutions are participating on DCTD-sponsored

clinical trials, Collaborator will need to assist in the submission of the regulatory documents to the Canadian Health Products and Food Branch to allow for such participation. This may include a letter of cross-reference to an existing Clinical Trials Application (CTA) or a DMF, including supporting documentation on the production of the Investigational Agent. The forms and procedures for preparing Canadian CTAs are available at http://www.hc-sc.gc.ca/hpfb-dgpsa/index_e.html.

3.8 **~~Test Article~~ Investigational Agent Information and Supply**. Collaborator agrees to provide ~~ICD~~ DCTD without charge and on a schedule that will ensure adequate and timely performance of the research, a sufficient quantity of formulated and acceptably labeled, clinical-grade ~~Test Article~~ Investigational Agent (and, as required by the Protocol(s), Placebo) to complete the clinical trial(s) agreed to and approved under this CRADA. Collaborator will provide a Certificate of Analysis to ~~ICD~~ DCTD for each lot of the ~~Test Article~~ Investigational Agent provided. It is understood that DCTD shall take responsibility for and reasonable steps to maintain appropriate records and assure appropriate supply, handling storage, distribution and usage of these materials in accordance with the terms of this Agreement, the Protocol(s) and any applicable laws and regulations relating thereto.

Collaborator agrees to supply sufficient inventory to ensure adequate and timely supply of Investigational Agent for mutually agreed upon Protocol(s). DCTD will provide updated forecasts of amounts of Investigational Agent anticipated for ongoing and anticipated studies. Collaborator further agrees to provide draft Investigational Agent labels to the NCI Pharmaceutical Management Branch (PMB) for review and agrees to reasonable labeling revisions to comply with DCTD label guidelines. NCI NSC (National Service Center) numbers will be required to be on the label of Investigational Agent for all DCTD-sponsored clinical trials.

Furthermore, Collaborator agrees to provide without charge Investigational Agent or unformulated analytical grade Investigational Agent or metabolites, if available, to DCTD to supply to NCI investigators for the development of mutually agreed upon analytical assays, ancillary correlative studies and pre-clinical studies conducted in conjunction with DCTD-sponsored protocols.

Collaborator agrees to allow Investigational Agent to be distributed to NCI investigators for mutually agreeable preclinical studies designed to enhance the basic understanding and development of Investigational Agent. These will include preclinical studies designed to support clinical trials in pediatric patients; preclinical combination studies to provide data in support of a clinical trial and other pertinent requests. All NCI investigators will sign Material Transfer Agreements (MTAs) that acknowledge the proprietary nature of the Investigational Agent to Collaborator and include intellectual property and publication provisions consistent with those in this Agreement and for clinical trials.

For many investigational agents for which NCI collaborates in development, NCI will undertake non-clinical studies to enhance the understanding of the mechanism of action of the investigational agent and its targets such as, but not limited to, the development of assays to detect target modulation, biomarker studies, and pharmacodynamics in conjunction with the conduct of clinical studies

sponsored by DCTD. Collaborator agrees to provide Investigational Agent to DCTD for these non-clinical studies. A general plan for the non-clinical studies of the Investigational Agent will be established by the Steering Committee. Manuscripts and presentations related to non-clinical studies will be handled in accordance with Article 8.7 of this CRADA.

Collaborator agrees to provide to the PMB the Investigator's Brochure (IB) for Investigational Agent and all subsequent revisions/editions. In addition to being filed to the CTEP IND, the IB will be on file in the PMB and will be distributed to all investigators participating on a clinical trial using the Investigational Agent. Distribution will be accompanied by a statement about the confidentiality of the document and it is anticipated that distribution will be electronic. All electronic distribution will be done using Adobe Acrobat PDF. Any IB received by the PMB that is not in this format will be converted before distribution. Hard copy IBs should be sent to IB Coordinator, Pharmaceutical Management Branch, CTEP, DCTD, NCI, 6130 Executive Blvd, Room 7149, Rockville, MD 20852. Electronic versions should be emailed to the IB Coordinator at IBCoordinator@mail.nih.gov.

3.9 ~~**Test Article**~~ **Investigational Agent Delivery and Usage**. Collaborator will ship the ~~Test Article~~ Investigational Agent and, if required, Placebo to ~~ICD~~ NCI or its designee in containers marked in accordance with 21 C.F.R. § 312.6. ~~ICD~~ NCI agrees that the Clinical Investigators will keep appropriate records and take reasonable steps to ensure that the ~~Test Article~~ Investigational Agent is used in accordance with the Protocol(s) and applicable FDA regulations. In addition, ~~ICD~~ NCI agrees that the ~~Test Article~~ Investigational Agent (and all Confidential Information supplied by Collaborator relating to the ~~Test Article~~ Investigational Agent) will be used solely for the conduct of the CRADA research and development activities. Furthermore, ~~ICD~~ NCI agrees that no analysis or modification of the ~~Test Article~~ Investigational Agent will be performed without Collaborator's prior written consent. At the completion of the Research Plan, any unused quantity of ~~Test Article~~ Investigational Agent will be returned to Collaborator or disposed as directed by Collaborator. ~~Pharmacy contacts at ICD or its designee will be determined by ICD and communicated to Collaborator.~~ The contact person. for NCI will be Mr. Charles Hall, Chief, Pharmaceutical Management Branch (Telephone Number 301-496-5725) and the Collaborator contact will be XXXXXX (Telephone Number XXXXX).

3.10 **Monitoring.**

3.10.1 ~~The Sponsor or its designee~~ DCTD, NCI will be primarily responsible for monitoring clinical sites and for assuring the quality of all clinical data, unless otherwise stated in the Research Plan. Monitoring will comply with FDA Good Clinical Practice (International Conference on Harmonisation (ICH) E6: "Good Clinical Practice: Consolidated Guidance; 62 Federal Register 25, 691 (1997)). ~~The other Party may also perform quality assurance oversight. The monitor will communicate significant Protocol violations and submit documentation of monitoring outcomes on Protocol insufficiencies to the other Party in a timely manner.~~

[*] = Certain confidential information contained in this document, marked by brackets, is filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

3.10.2 Subject to the restrictions in Article 8 concerning IPI, and with reasonable advance notice and at reasonable times, ~~ICD~~ DCTD will permit Collaborator or its designee(s) access to clinical site(s) to monitor the conduct of the research, as well as to audit source documents containing Raw Data, to the extent necessary to verify compliance with FDA Good Clinical Practice and the Protocol(s).

3.11 **FDA Meetings/Communications**. All formal meetings with the FDA concerning any clinical trial within the scope of the Research Plan will be discussed by Collaborator and ICD in advance. Each Party reserves the right to take part in setting the agenda for, to attend, and to participate in these meetings. The Sponsor will provide the other Party with copies of FDA meeting minutes, all transmittal letters for IND submissions, IND safety reports, formal questions and responses that have been submitted to the FDA, Annual Reports, and official FDA correspondence, pertaining either to the INDs under this CRADA or to the Clinical Investigators on Protocols performed in accordance with the Research Plan, except to the extent that those documents contain the proprietary information of a third party or dissemination is prohibited by law.

Add a new **Article 3.12** as follows:

3.12 **Steering Committee and CRADA Research**. The Parties agree to establish a Steering Committee comprising at least the CRADA Principal Investigators to conduct and monitor the research of the Investigational Agent in accordance with the CRADA Research Plan. Members of the Steering Committee shall continue to remain employed by their respective employers under their respective terms of employment.

Investigational Agent's development under the CRADA Research Plan shall be a collaborative undertaking by Collaborator and NCI. Details of this development beyond those set forth in the CRADA Research Plan shall be formulated and/or discussed in Steering Committee meeting(s) before implementation of large-scale or resource intensive studies. The clinical development plans formulated by the Steering Committee shall be implemented either intramurally at the NCI or extramurally under NCI-sponsored Funding Agreements.

Additional CRADA information, including Steering Committee meeting reports, Protocol Review Committee records, clinical trial protocols, Institutional Review Board approval information, IND and general regulatory information, and preclinical and clinical data in NCI's possession and control shall remain on file with NCI.

Add a new **Article 3.13** as follows:

3.13 **Clinical Protocols.** Clinical protocol Letters of Intent (LOI) or concepts for each study within the scope of the CRADA Research Plan will be solicited by CTEP from selected intramural and extramural Clinical Investigators. Clinical protocols from each DCTD- and Collaborator-approved LOI or concept will describe in detail the research to be conducted at each center and must be submitted to the Protocol Review Committee (PRC) for review and

approval prior to implementation. Each clinical protocol received by NCI will be forwarded electronically to Collaborator for review and comment approximately two weeks before it is reviewed by the PRC. Comments from Collaborator received by CTEP before the PRC meeting will be discussed by the PRC, will be given due consideration, and will be incorporated into the protocol, absent good cause. Comments from either Collaborator or the CTEP staff that are agreed upon in the PRC meeting will be formatted as a consensus review, which is returned to the Clinical Investigator for necessary and/or suggested changes before the protocol can be given final approval and submitted to the FDA. A copy of the final approved protocol will be forwarded to Collaborator within 24 to 48 hours of its submission to the FDA.

4.2 **Final Research and Development Reports.** The Parties will exchange final reports of their results within six (6) months after the expiration or termination of this CRADA. These reports will set forth the technical progress made; any publications arising from the research; and the existence of invention disclosures of potential CRADA Subject Inventions and/or any corresponding Patent Applications. Abstracts and publications provided to CTEP by investigators and further provided by CTEP to Collaborator will fulfill this final report obligation.

4.4 **Safety Reports.** ~~In accordance with FDA requirements, the Sponsor will establish and maintain records and submit safety reports to the FDA, as required by 21 C.F.R. § 312.32 and 21 C.F.R. 812.150(b)(1), or other applicable regulations. In the conduct of research under this CRADA, the Parties will comply with specific ICD guidelines and policies for reporting ADEs and AEs, as well as procedures specified in the Protocol(s). The Sponsor must provide the other Party with copies of all Safety Reports concurrently with their submission to the FDA, and with any other information affecting the safety of Human Subjects in research conducted under this CRADA.~~ DCTD shall report all serious and/or unexpected Adverse Events to FDA in accordance with the reporting obligations of 21 CFR 312.32 and will, within 24 to 48 hours of notification to FDA, forward all such reports to Collaborator. All other Adverse Event reports received by DCTD shall be reported to the FDA consistent with 21 CFR 312.32 and 312.33. In the event that Collaborator informs the FDA of any serious and/or unexpected Adverse Events, Collaborator must notify the NCI at the same time by sending the reports to CTEPSupportAE@tech-res.com. NCI will then notify the Clinical Investigator(s) conducting studies under DCTD-sponsored protocols, if appropriate.

4.5 **Annual Reports.** ~~The Sponsor~~ DCTD will provide ~~the other Party~~ Collaborator a copy of the Annual Report concurrently with the submission of the Annual Report to the FDA. Annual Reports will be kept confidential in accordance with Article 8. Collaborator will provide DCTD with a copy of its Annual Report to the FDA if Collaborator is sponsoring studies of Investigational Agent under its own IND.

7.2 **Collaborator's License Option to CRADA Subject Inventions.** With respect to Government rights to any CRADA Subject Invention made solely by an ICD employee(s) or made jointly by an ICD 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 co-exclusive, if applicable, or nonexclusive commercialization license. The option

to elect a co-exclusive license shall apply when a CRADA Subject Invention is also a CRADA Subject Invention under another CRADA resulting from mutually agreed upon studies as described in Article 8.9 and the field of use of this co-exclusive license shall be to the use of the combination of the Investigational Agent 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.

7.6 **Third Party License.** Pursuant to 15 U.S.C. § 3710a(b)(1)(B), if PHS grants Collaborator an exclusive, or co-exclusive, license to a CRADA Subject Invention made solely by an ICD 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(2).

8.7 **Publication.** The Parties are encouraged to make publicly available the results of their research and development activities. Before ~~either Party~~ Collaborator or NCI submits a paper or abstract for publication ~~or otherwise intends to publicly disclose information~~ about a CRADA Subject Invention, CRADA Data, or CRADA Materials, the other Party will have thirty (30) days to review proposed manuscripts and three (3) days to review proposed abstracts to assure that Confidential Information is protected. Either Party may request in writing that ~~the~~ a proposed publication ~~or other disclosure~~ be delayed for up to thirty (30) additional days as necessary to file a Patent Application. Manuscripts to be submitted for publication by NCI investigators will be sent to NCI's Regulatory Affairs Branch [anshers@mail.nih.gov] for forwarding to Collaborator for review as soon as they are received and in compliance with the timelines outlined above. Abstracts to be presented by NCI investigators will be sent to NCI's Regulatory Affairs Branch [anshers@mail.nih.gov] for forwarding to Collaborator as soon as they are received, preferably no less than three days prior to submission, but prior to presentation or publication, to allow for preservation of U.S. or foreign patent rights.

8.8 **Clinical Investigators' Research and Development Activities.** In pursuing the development of Investigational Agent pursuant to this CRADA, NCI may utilize contractors and

extramural investigators that are not NCI employees for part or all of the completion of this Research Plan, which may cover pre-clinical, non-clinical and clinical studies, through Funding Agreements. Participation in DCTD-sponsored clinical trials by these investigators shall be determined after competitive solicitation and review of Protocol Letters of Intent (LOIs) and study protocols by CTEP, NCI. All Funding Agreements for the conduct of extramural clinical trials will include the Intellectual Property Option to Collaborator Terms of Award Addition offering Collaborator first rights of negotiation to extramural inventions (web site: http://ctep.cancer.gov/industry). Although this CRADA does not grant to Collaborator any rights to Inventions made or Raw Data generated by ~~ICD's~~ NCI's contractors or grantees, as they are not parties to this CRADA, ~~ICD~~ NCI agrees that:

8.8.1 Subject to the other provisions of Article 8 of this CRADA, ~~ICD~~ NCI will maintain, to the extent permitted by law, all Clinical Data in ~~ICD's~~ NCI's Possession and Control as Confidential Information, and make them available to Collaborator for its own use and for exclusive use in obtaining regulatory approval for the commercial marketing of ~~Test Article~~ Investigational Agent and related CRADA Subject Inventions. Similarly, NCI will also maintain, to the extent permitted by law, all data generated in preclinical and non-clinical studies that are in NCI's possession and control as Confidential Information, and make them available to Collaborator for its own use and for exclusive use in obtaining regulatory approval for the commercial marketing of Investigational Agent and related CRADA Subject Inventions. Collaborator will not publish any such data provided under the CRADA without NCI's permission. Accordingly, said data shall not be transferable by Collaborator to any third party, except to Collaborator affiliates and development partners, without the written permission of the NCI. Following NCI's permission, the third party shall enter into a Confidential Disclosure Agreement with the NCI and Collaborator, if requested by NCI, before any data can be transferred.

8.8.2 With regard to Collaborator's Confidential Information, ~~ICD~~ NCI will require the Clinical Investigators to agree to confidentiality provisions at least as restrictive as those provided in this CRADA and to Collaborator's use of data in accordance with Paragraph 8.8.1 for obtaining regulatory approval for marketing ~~Test Article~~ Investigational Agent.

8.8.3 If Collaborator wants access to Raw Data or any other data in the possession of the Clinical Investigators working with ~~Test Article~~ Investigational Agent under a Funding Agreement or other agreements, Collaborator must first contact the ~~CRADA PI~~ Regulatory Affairs Branch (RAB), CTEP, NCI [Telephone 301-496-7912; anshers@mail.nih.gov]. Subsequent to authorization by RAB, Collaborator may directly contact the Clinical Investigators. Collaborator will bear any costs associated with Raw Data provided in formats customized for Collaborator, which costs will be paid by Collaborator directly to the Clinical Investigators.

8.8.4 Collaborator's right to access Clinical Data in ~~ICD's~~ NCI's Possession and Control under Paragraph 8.8 is dependent upon Collaborator's continued development and commercialization of Investigational Agent, If Collaborator fails to continue

development or commercialization of Investigational Agent without the transfer of its development efforts to another party within ninety (90) days of discontinuation, ~~ICD~~ NCI has the right to make Clinical Data in ~~ICD's~~ NCI's Possession and Control available to a third party.

Add a new **Article 8.9** as follows:

8.9 **Multi-Party Data Rights.** For clinical protocol(s) where Investigational Agent is used in combination with another investigational agent supplied to NCI pursuant to a CTA or CRADA between NCI and an entity not a Party to this CRADA [hereinafter referred to as "Third Party"], the access and use of Multi-Party Data by the Collaborator and Third Party shall be co-exclusive as follows:

8.9.1 NCI will provide both Collaborator and Third Party with notice regarding the existence and nature of the agreements governing their collaborations with NIH, the design of the proposed combination protocol(s), and the existence of any obligations that might restrict NCI's participation in the proposed Combination protocols.

8.9.2 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.

8.9.3 Collaborator and Third Party must agree in writing prior to the commencement of the combination trial(s) that each will use the Multi-Party Data solely for the development, regulatory approval, and commercialization of its own investigational agent(s).

Add a new **Article 8.10** as follows:

8.10 **Access, review and receipt of Identifiable Private Information.** Collaborator access to and review of Identifiable Private Information shall be only for on-site quality auditing. Collaborator will receive Identifiable Private Information only if necessary for purposes of satisfying FDA or other health authorities' reporting requirements, and for internal research purposes, directly related to obtaining regulatory approval of Investigational Agent. Collaborator is prohibited from access, review, receipt, or use of such information for other purposes. All IRB approved protocols and informed consent documents related to this research project will clearly describe this practice. If the Collaborator will have access to Identifiable Private Information, the protocol and the informed consent must clearly state (i) the existence of the Collaborator; (ii) the Collaborator's access to Identifiable Private Information, if any; and (iii) the extent to which confidentiality will be maintained. For clinical protocol(s) involving a third party, the other party's access, review, receipt, or use of Identifiable Private Information shall be

subject to the same limitations as described in this Article 8.10.

10.6 **Collaborator Failure to Continue Development.** If Collaborator suspends development of the ~~Test Article~~ Investigational Agent without the transfer of its active development efforts, assets, and obligations to a third party within ninety (90) days of discontinuation, Collaborator agrees that ICD may continue developing the ~~Test Article~~ Investigational Agent. In that event, the following will apply:

10.6.1 Collaborator agrees to transfer to ICD all information necessary to enable ICD to contract for the manufacture of the ~~Test Article~~ Investigational Agent and, unless abandoned for reasons relating to safety as determined by the data safety monitoring board, to provide the ~~Test Article~~ Investigational Agent (and Placebo, if any) in Collaborator's inventory to ICD or arrange for an independent contractor to manufacture and provide Investigational Agent to NCI for two years or until the completion of ongoing mutually agreed to studies.

10.6.2 Further, Collaborator hereby grants to ICD a nonexclusive, irrevocable, world-wide, paid-up license to practice, or have practiced for or on behalf of the Government, any Background Invention that Collaborator may currently have or will obtain on the ~~Test Article~~ Investigational Agent, its manufacture, or on any method of using the ~~Test Article~~ Investigational Agent for the indication(s) described in the Research Plan, including the right to sublicense to third parties.

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 will maintain sole and exclusive control over its personnel and operations. If Collaborator elects to perform any portion of the Research Plan through a contractor or consultant, Collaborator agrees to incorporate into such contract all provisions necessary to ensure that the work of such contractor or consultants is governed by the terms of the CRADA, including, but not limited to a provision for the assignment of inventions of the contractor or consultant to the Collaborator.

13.12 **Export Controls.** Collaborator agrees to comply with U.S. export law and regulations, including 21 U.S.C. 382 and 21 CFR Part 312.110. If Collaborator has a need to transfer any CRADA Materials made in whole or in part by ICD, or ICD Materials, or ICD's Confidential Information to a person located in a country other than the United States, to an Affiliate organized under the laws of a country other than the United States, or to an employee of Collaborator in the United States who is not a citizen or permanent resident of the United States, Collaborator will acquire any and all necessary export licenses and other appropriate authorizations.

13.14 **Survivability**. The provisions of Paragraphs [3.3, 3.4, 3.8, 4.2, 4.3, 4.4, 5.3, 5.4, 6.1-9.2, 10.3-10.6, 11.1, 11.2, 12.1-12.3, 13.1-13.3, 13.7, 13.10 and 13.14] will survive the expiration or early termination of this CRADA.

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AMENDMENT #1

To Letter of Intent for Proposed CRADA #2166

"Pre-Clinical and Clinical Development of 1-Methyl-[d]-Tryptophan as an Anti-Cancer Agent"

The purpose of this amendment is to change certain terms of the Letter of Intent (LOI) for the proposed Cooperative Research and Development Agreement (CRADA) entitled "Pre-Clinical and Clinical Development of 1-Methyl-[d]-Tryptophan as an Anti-Cancer Agent." These changes are reflected below, and except for these changes, all other provisions of the original CRADA LOI remain in full force and effect. Two originals of this amendment are provided for execution; one is to remain with the National Cancer Institute (NCI) and the other copy is to remain with the Collaborator.

1. Upon final signature, the term of this CRADA Letter of Intent is extended for six months from November 23, 2007 to May 23, 2008.

2. Dr. Lee Jia is removed as an NCI Principal Investigator. The NCI Principal Investigators are Dr. Sherry Ansher and Dr. Howard Streicher.

ACCEPTED AND AGREED TO:

For the National Cancer Institute:

/s/Anna D. Barker 01/08/08
Anna D. Barker, Ph.D. Date
Deputy Director, NCI

For NewLink Genetics Corporation:

/s/Charles Link 1/17/08
Date

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AMENDMENT #2

To Letter of Intent for Proposed CRADA #2166

"Pre-Clinical and Clinical Development of 1-Methyl-[d]-Tryptophan as an Anti-Cancer Agent"

The purpose of this amendment is to change certain terms of the Letter of Intent (LOI) for the proposed Cooperative Research and Development Agreement (CRADA) entitled "Pre-Clinical and Clinical Development of 1-Methyl-[d]-Tryptophan as an Anti-Cancer Agent." These changes are reflected below, and except for these changes, all other provisions of the original CRADA LOI remain in full force and effect. Two originals of this amendment are provided for execution; one is to remain with the National Cancer Institute (NCI) and the other copy is to remain with the Collaborator.

1. Upon final signature, the term of this CRADA Letter of Intent is extended for six months from May 23, 2008 to November 23, 2008.

2. Drs. Jeffrey Abrams and James Zwiebel are added as NCI Principal Investigators. The NCI Principal Investigators are Dr. Jeffrey Abrams, Dr. Sherry Ansher, Dr. James Zwiebel and Dr. Howard Streicher.

ACCEPTED AND AGREED TO:

For the National Cancer Institute:

/s/Anna D. Barker 06/24/08
Anna D. Barker, Ph.D. Date
Deputy Director, NCI

For NewLink Genetics Corporation:

/s/Nicholas Vahanian 7/7/2008
Date

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AMENDMENT #3

To Letter of Intent for Proposed CRADA #2166

“Preclinical and Clinical Development of 1-Methyl [d]-Tryptophan as an Anticancer Agent”

The purpose of this Amendment is to change certain terms of the Letter of Intent (LOI) for the proposed Cooperative Research and Development Agreement (CRADA) entitled “Preclinical and Clinical Development of 1-Methyl [d]-Tryptophan as an Anticancer Agent.” These changes are reflected below, and except for these changes, all other provisions of the original CRADA LOI remain in full force and effect. Two originals of this Amendment are provided for execution; one is to remain with the National Cancer Institute (NCI) and the other original is to remain with the Collaborator.

Upon final signature, the term of the CRADA Letter of Intent is extended for six months from November 23, 2008 to May 23, 2009.

ACCEPTED AND AGREED TO:

For the National Cancer Institute:

/s/Anna D. Barker 03/16/09
Anna D. Barker, Ph.D. Date
Deputy Director, NCI

For NewLink Genetics Corporation:

/s/Nicholas Vahanian 03/24/09
Name: Nicholas Vahanian Date
Title: COO

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AMENDMENT #4

To Letter of Intent for Proposed CRADA #2166

"Preclinical and Clinical Development of 1-Methyl [d]-Tryptophan as an Anticancer Agent"

The purpose of this Amendment is to change certain terms of the Letter of Intent (LOI) for the proposed Cooperative Research and Development Agreement (CRADA) entitled "Preclinical and Clinical Development of 1-Methyl [d]-Tryptophan as an Anticancer Agent." These changes are reflected below, and except for these changes, all other provisions of the original CRADA LOI remain in full force and effect. Two originals of this Amendment are provided for execution; one is to remain with the National Cancer Institute (NCI) and the other original is to remain with the Collaborator.

Upon final signature, the term of the CRADA Letter of Intent is extended for six months from May 23, 2009 to November 23, 2009.

ACCEPTED AND AGREED TO:

For the National Cancer Institute:

/s/Anna D. Barker 10/16/09
Anna D. Barker, Ph.D. Date
Deputy Director, NCI

For NewLink Genetics Corporation:

/s/Nicholas Vahanian 10/28/09
Nicholas Vahanian Date
Chief Operating Officer

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AMENDMENT #5

To Letter of Intent for Proposed CRADA #2166

"Preclinical and Clinical Development of 1-Methyl [d]-Tryptophan as an Anticancer Agent"

The purpose of this Amendment is to change certain terms of the Letter of Intent (LOI) for the proposed Cooperative Research and Development Agreement (CRADA) entitled "Preclinical and Clinical Development of 1-Methyl [d]-Tryptophan as an Anticancer Agent." These changes are reflected below, and except for these changes, all other provisions of the original CRADA LOI remain in full force and effect. Two originals of this Amendment are provided for execution; one is to remain with the National Cancer Institute (NCI) and the other original is to remain with the Collaborator.

Upon final signature, the term of the CRADA Letter of Intent is extended for six months from November 23, 2009 to May 23, 2010.

ACCEPTED AND AGREED TO:

For the National Cancer Institute:

/s/ Anna D. Barker 11/04/09
Anna D. Barker, Ph.D. Date
Deputy Director, NCI

For NewLink Genetics Corporation:

/s/ Nicholas N. Vahanian 12/16/09
Nicholas Vahanian, M.D. Date
Chief Operating Officer

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AMENDMENT #6

To Letter of Intent for Proposed CRADA #2166

"Preclinical and Clinical Development of 1-Methyl [d]-Tryptophan as an Anticancer Agent"

The purpose of this Amendment is to change certain terms of the Letter of Intent (LOI) for the proposed Cooperative Research and Development Agreement (CRADA) entitled "Preclinical and Clinical Development of 1-Methyl [d]-Tryptophan as an Anticancer Agent." These changes are reflected below, and except for these changes, all other provisions of the original CRADA LOI remain in full force and effect. Two originals of this Amendment are provided for execution; one is to remain with the National Cancer Institute (NCI) and the other original is to remain with the Collaborator.

Upon final signature, the term of the CRADA Letter of Intent is extended for six months from May 23, 2010 to November 23, 2010.

ACCEPTED AND AGREED TO:

For the National Cancer Institute:

/s/ Anna D. Barker 6/24/10
Anna D. Barker, Ph.D. Date
Deputy Director, NCI

For NewLink Genetics Corporation:

/s/ Nicholas Vahanian 6/29/10

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Nicholas Vahanian, M.D. Date
Chief Operating Officer

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AMENDMENT #7

To Letter of Intent for Proposed CRADA #2166

"Preclinical and Clinical Development of 1-Methyl [d]-Tryptophan as an Anticancer Agent"

The purpose of this Amendment is to change certain terms of the Letter of Intent (LOI) for the proposed Cooperative Research and Development Agreement (CRADA) entitled "Preclinical and Clinical Development of 1-Methyl [d]-Tryptophan as an Anticancer Agent." These changes are reflected below, and except for these changes, all other provisions of the original CRADA LOI remain in full force and effect. Two originals of this Amendment are provided for execution; one is to remain with the National Cancer Institute (NCI) and the other original is to remain with the Collaborator.

Upon final signature, the term of the CRADA Letter of Intent is extended for six months from November 23, 2010 to, May 23, 2011.

ACCEPTED AND AGREED TO:

For the National Cancer Institute:

/s/ Douglas R. Lowy 11/26/10
Douglas R. Lowy, M.D. Date
Deputy Director, NCI

For NewLink Genetics Corporation:

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/s/ Nicholas Vahanian 1/12/10
Nicholas Vahanian, M.D. Date
Chief Operating Officer

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AMENDMENT #8

To Letter of Intent for Proposed CRADA #02166

"Preclinical and Clinical Development of 1-Methyl-[d]-Tryptophan as an Anti-Cancer Agent"

The purpose of this amendment is to change certain terms of the Letter of Intent (LOI) for the proposed Cooperative Research and Development Agreement (CRADA) entitled "Preclinical and Clinical Development of 1-Methyl-[d]-Tryptophan as an Anti-Cancer Agent". These changes are reflected below, and except for these changes, all other provisions of the original CRADA LOI remain in full force and effect. Two originals of this amendment are provided for execution; one is to remain with the National Cancer Institute (NCI) and the other copy is to remain with the Collaborator.

Upon final signature, the term of the CRADA Letter of Intent is retroactively extended for one year from May 23, 2011 to, May 23, 2012.

AGREED AND ACCEPTED:

For the National Cancer Instute:

/s/ Douglas R. Lowy, M.D.
Douglas R. Lowy, M.D.
Deputy Director, NCI

5/26/2011
Date

For NewLink Genetics Corporation:

6/2/2011
Date

/s/ Nicholas Vahanian, M.D.
Nicholas Vahanian, M.D.
Chief Operating Officer

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EXHIBIT 31.1

CERTIFICATION

I, Charles J. Link, Jr., certify that:

1. I have reviewed this quarterly report on Form 10-Q of NewLink Genetics Corporation;

2. Based on my knowledge, this 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 report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   c. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 10, 2012

By: /s/ Charles J. Link, Jr.
Charles J. Link, Jr.
Chief Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATION

I, Gordon H. Link, Jr., certify that:

1. I have reviewed this quarterly report on Form 10-Q of NewLink Genetics Corporation;

2. Based on my knowledge, this 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 report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   c. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 10, 2012

By: /s/ Gordon H. Link, Jr.
Gordon H. Link, Jr.
Chief Financial Officer and Secretary
(Principal Financial and Accounting Officer)

EXHIBIT 32.1

CERTIFICATION

Pursuant to the requirements set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. § 1350), Charles J. Link, Jr., Chief Executive Officer of NewLink Genetics Corporation (the "Company"), and Gordon H. Link, Jr., Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Quarterly Report on Form 10-Q for the period ended March 31, 2012, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: May 10, 2012

By: /s/ Charles J. Link, Jr.
Charles J. Link, Jr.
Chief Executive Officer
(Principal Executive Officer)

By: /s/ Gordon H. Link, Jr.
Gordon H. Link, Jr.
Chief Financial Officer and Secretary
(Principal Financial and Accounting Officer)

A signed original of this written statement has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its Staff upon request. This certification "accompanies" the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.