

NEWLINK GENETICS INVESTOR DAY

Building a Leading Immuno-Oncology Company

> Nasdaq: NLNK July 14, 2015



Forward-Looking Disclaimer

These slides accompany an oral presentation by NewLink Genetics Corporation, which contains forward-looking statements. The Company's actual results may differ materially from those suggested here. Additional information concerning factors that could cause such a difference is contained in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2014 and other prior and subsequent regulatory filings.

NASDAQ: NLNK



NewLink Genetics

Building a Leading Immuno-Oncology Company

- Industry-leading advanced pipeline across multiple cancer types with 7 product candidates in clinical development from Phase 1 to Phase 3
- Unique HyperAcute[®] Immunotherapies that suggest clinical activity associated with potent anti-cancer immune responses
- Multiple small molecules targeting the key IDO checkpoint blockade
- Well-positioned to execute on our vision of combining checkpoint blockade inhibitors and cancer vaccines
- Potential to have the first product with an FDA approval for the adjuvant treatment of patients with surgically resected pancreatic cancer
- Founding scientific and business leadership with proven expertise in drug discovery, manufacturing, clinical development, and commercialization
- Proven success in substantial strategic collaborations
- \$200+ million in cash with the potential for near-term catalysts
- Opportunity in infectious diseases



Today's Agenda



NewLink's Immuno-Oncology Programs Charles J. Link, Jr., M.D., Chairman, CEO and CSO



Clinical Strategy and Algenpantucel-L Update Nicholas N. Vahanian, M.D., President and CMO



Algenpantucel-L Manufacturing and Readiness Gary Potter, V.P., Manufacturing



Algenpantucel-L Commercialization Readiness Brian Wiley, V.P., Business Development



Today's Agenda



Advancing Our Clinical Pipeline Eugene Kennedy, M.D., V.P., Clinical and Medical Affairs



Discovering New Immuno-Oncology Products Mario Mautino, Ph.D., V.P., Drug Discovery and IP Officer



Financial Update/Milestones/Infectious Disease Program Jack Henneman, CFO



Concluding Remarks and Q&A Charles J. Link, Jr., M.D., Chairman, CEO and CSO



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Building a Leading Immuno-Oncology Company

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Leading Pipeline in Immuno-Oncology

HyperAcute Immunotherapy Clinical Development Program

HyperAcute Immunotherapy

AGENT	TARGET DISEASE	DESIGN DETAILS	Phase1	Phase 2	Phase 3
	Pancreatic cancer (resected)	IMPRESS: algenpantucel-L + standard of care; randomized	ENROLLMENT COMPLETE		
Algenpantucel-L	Pancreatic cancer (borderline resectable or locally advanced unresectable)	PILLAR: algenpantucel-L + chemotherapy; randomized	ENROLLING		
Tergenpumatucel-L	NSCLC (advanced or metastatic)	Tergenpumatucel-L vs docetaxel and controlled for follow-on chemotherapy; phase 2b; randomized	ENROLLING		
Dorgenmeltucel-L	Melanoma (advanced)	Dorgenmeltucel-L + ipilimumab or PD-1 inhibitors; randomized	ENROLLING		
HyperAcute Prostate	Prostate cancer (castrate-resistant)	HyperAcute Prostate: single agent, dose escalation	ENROLLED		
HyperAcute Renal	Renal cancer (advanced)	HyperAcute Renal; single agent, dose escalation	ENROLLING		



Leading Pipeline in Immuno-Oncology

IDO Pathway Inhibitor Clinical Development Program

IDO Pathway Inhibitor Platform

AGENT	TARGET DISEASE	DESIGN DETAILS	Phase1 Phase 2 Ph		Phase 3
	Breast cancer (metastatic)	Indoximod + taxane; randomized	ENROLLING		
	Prostate cancer (metastatic, castrate-resistant)	Indoximod following sipuleucel-T; randomized	ENROLLING		
Indoximod	Pancreatic cancer (metastatic)	Indoximod + gemcitabine and nab-paclitaxel; phase 1b/2	ENROLLING		
	Melanoma (advanced)	Indoximod + ipilimumab or PD-1 inhibitors; phase 2	ENROLLING		
	Glioblastoma multiforme	Indoximod + temozolomide; phase 2	ENROLLING		
GDC-0919	Solid tumors	GDC-0919			
	Solid tumors	GDC-0919 + PD-L1 inhibitor or anti-OX40	Partnered with Genentech, Inc.		



Accelerating Our HyperAcute and IDO Pathway Inhibitor Pipeline

- Industry-leading pipeline, 7 products advancing in clinical trials
- HyperAcute Immunotherapy
 - Pancreatic: Algenpantucel-L Phase 3 studies ongoing
 - IMPRESS data expected in 2016
 - PILLAR enrollment completion expected in 2H15
 - Preparing for commercialization
 - Additional HyperAcute programs advancing in Phase 1 and 2
- IDO Pathway Inhibitors
 - Programs advancing across multiple cancers breast, glioblastoma, non-small-cell lung, melanoma, and pancreatic

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Immuno-Oncology

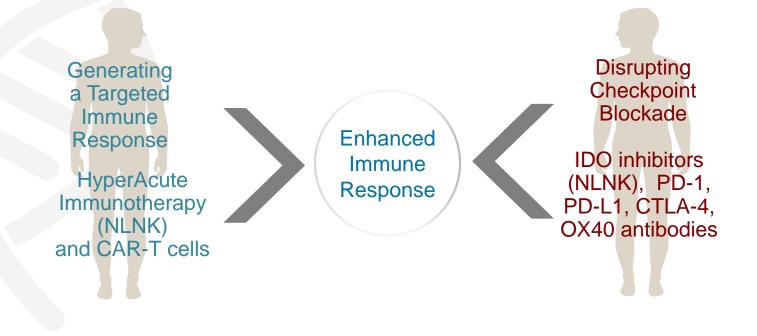
The Problem

- How do tumors in patients avoid immune destruction?
 - Weak immunity to tumors because they are derived from self
 - Tumors have active defense through active checkpoint blockade of the immune response

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Immuno-Oncology The Solution

- The emerging scientific and clinical consensus is that patients in the future will require both approaches:
 - Generating a targeted immune response
 - Disrupting checkpoint blockade





Immuno-Oncology Validation of Vaccines

Bristol-Myers Squibb Signs Exclusive Agreement with Bavarian Nordic for PROSTVAC®, a Prostate-Specific Antigen-Targeting Cancer Immunotherapy

Bavarian Nordic to receive up to \$975 million, inclusive of \$60 million upfront and potential exercise payment; potential development, regulatory and commercialization milestone payments; additional tiered double-digit royalties on future sales

Category: Partnering News, R&D News

Wednesday, March 4, 2015 1:30 am EST

KVISTGAARD, Denmark & NEW YORK--(BUSINESS WIRE)--Bavarian Nordic (OMX:BAVA) (OTC:BVNRY) and Bristol-Myers Squibb Company (NYSE:BMY) announced today an agreement that provides Bristol-Myers Squibb an exclusive option to license and commercialize PROSTVAC[®], Bavarian Nordic's investigational Phase 3 prostate-specific antigen (PSA) -targeting cancer immunotherapy in development for the treatment of asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer (mCRPC).

Under terms of the agreement, Bavarian Nordic will receive an upfront payment of \$60 million. Bristol-Myers Squibb can exercise the option in its sole discretion within a designated

"While additional treatment options have become available, metastatic castrationresistant prostate cancer remains largely incurable"

time after data is available from the ongoing Phase 3 trial. Bavarian Nordic would be entitled to a payment of \$80 million upon exercise of the option plus additional incremental payments starting at \$50 million, but with a potential to exceed \$230 million should the median overall survival benefit of PROSTVAC exceed the efficacy seen in Phase 2 results. Furthermore, Bavarian Nordic could receive regulatory milestone payments of \$110 million, up to \$495 million in sales milestones as well as tiered double-digit royalties on future sales of PROSTVAC. The parties have also agreed to enter into a supply contract, under which Bavarian Nordic will undertake the future commercial manufacturing of PROSTVAC.

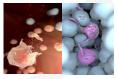
An investigator sponsored Phase 2 study is currently in the planning stages to investigate the combination of Bristol-Myers Squibb's YERVOY (ipilimumab) and PROSTVAC. The companies have also entered into an agreement by which they may conduct one or more exploratory combination studies of PROSTVAC and agents from



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Building a Leading Immuno-Oncology Company

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HyperAcute Immunotherapy

Derived from Unexpected Clinical Observation

- Experimental gene transfer trial failed to show any gene transfer
- However, clinical responses observed including four responses and one complete response (5/11 patients)
- Thought-provoking, yet puzzling positive responses were investigated
 - Infusion of mouse cells into peritoneal cavity triggered an immune response
 - Acute inflammation led to changes in immunological composition of tumor environment
 - Unusual tumor regressions were traced back to certain characteristics of infused mouse cells
 - Investigations confirmed that hyperacute rejection could explain the clinical responses

Pre-Treatment



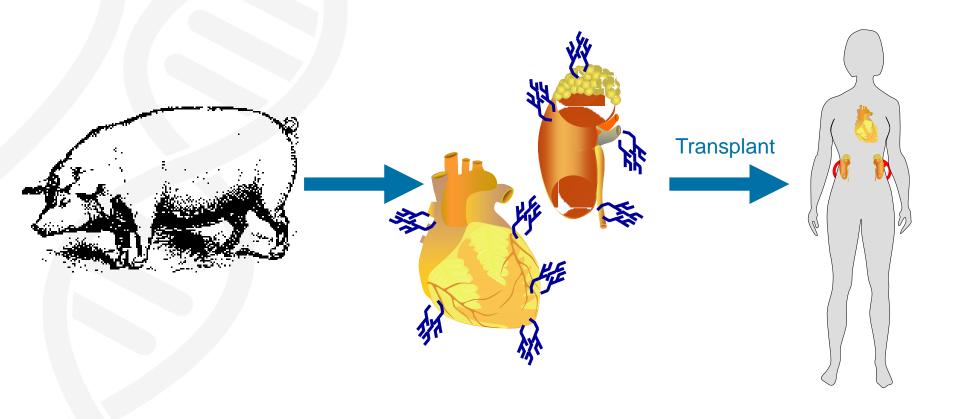
Post-Treatment





Hyperacute Rejection

Xenotransplantation Produces Hyperacute Transplant Rejection

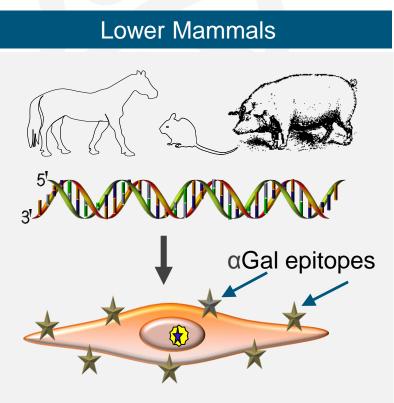


Anti-aGal antibodies are responsible for hyperacute rejection of xenotransplants

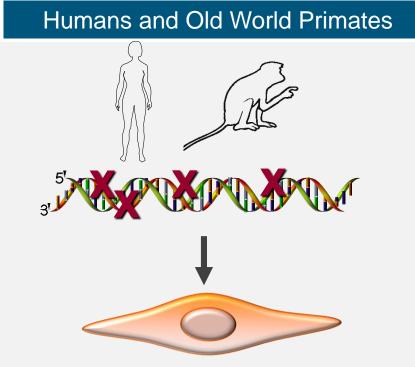


Scientific Basis for Mechanism of Action

α-1,3-Galactosyltransferase Gene



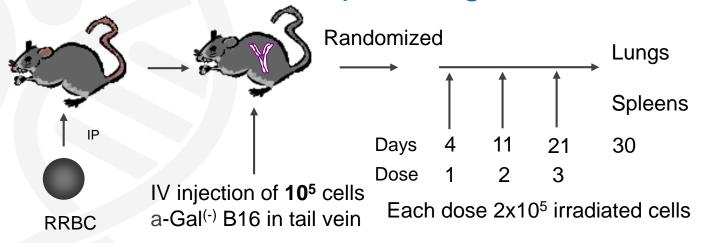
- αGal epitopes modify cell surface proteins and lipids in lower mammals
- Animal viruses express αGal epitopes



- Humans' and old world primates' cell-surface proteins are <u>NOT</u> modified with a-Gal epitope
- Anti-αGal antibodies are among the most abundant in an adult human (1-2% of total)



Effective Treatment of Preexisting Melanoma with Whole Cell Vaccines Expressing α Gal





Group 1 (control) B16.NeoR α-Gal⁽⁻⁾ Vaccine, n=6



Group 2 (active) B16. α -Gal⁽⁺⁾ Vaccine, n=7

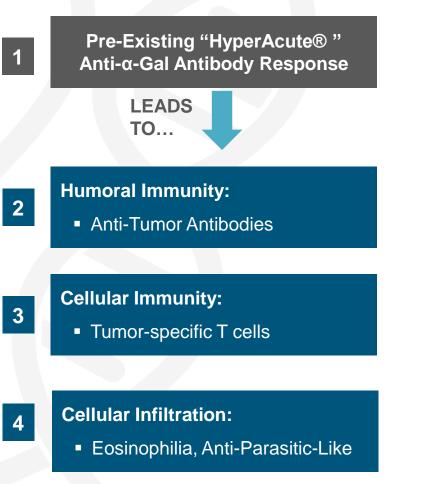
Rossi GR et al, Cancer Res 2005; 65: (22)

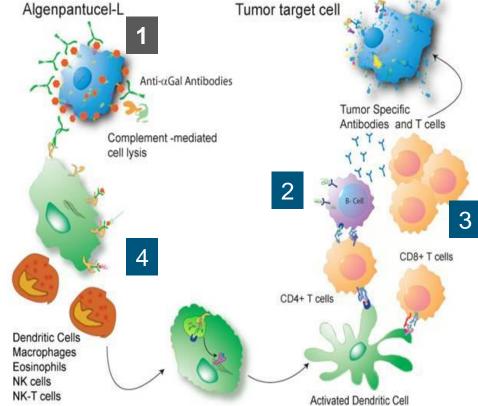
HyperAcute immunotherapy mediates tumor rejection in metastatic melanoma model



HyperAcute Immunotherapy

Educating the Immune System to Attack Cancer







HyperAcute Immunotherapy in Patients



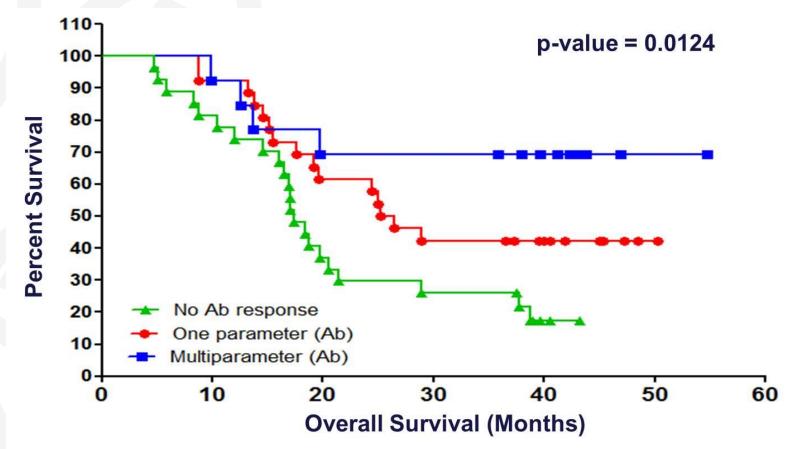
Hardacre, J. et al, JCO, Vol 30, No 15_suppl (May 20 supplement), ASCO 2012: Abstract 4049

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Algenpantucel-L

Phase 2 Results in Resected Pancreatic Cancer

Assessed Parameters: anti-MSLN Ab, anti-CEA Ab and/or anti- α GAL Ab



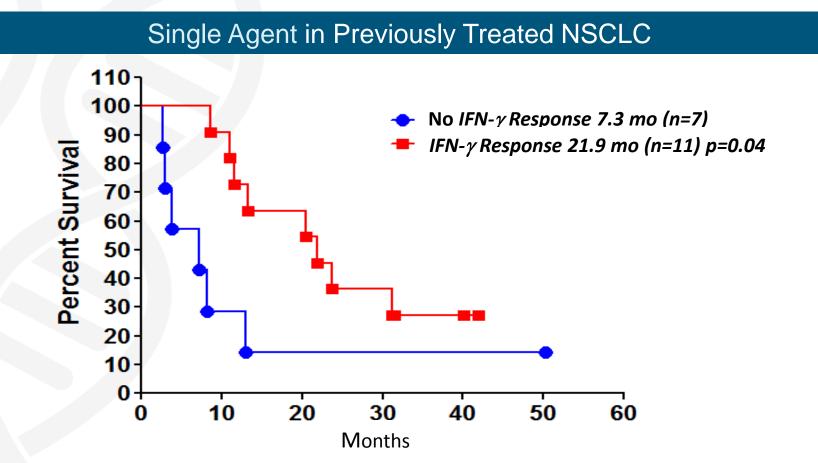
Rocha Lima, C. et al, JCO, Vol 31,_suppl (May 15 supplement), ASCO 2013: Oral Abstract 3007

Antibody Elevation Correlates With Improved Overall Survival



Tergenpumatucel-L

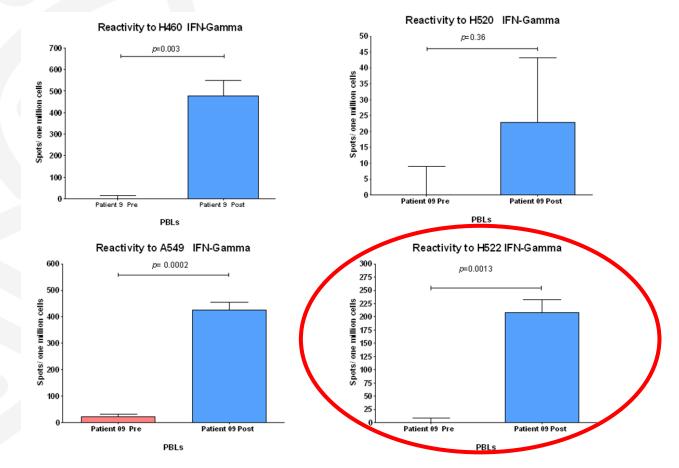
Phase 2: Survival Correlates with Immune Response



Morris, J.C. et al, JCO, Vol 30, No 15_suppl (May 20 supplement), ASCO 2012: Abstract 2571



Tergenpumatucel-L Phase 2: Evidence of Epitope Spread in Lung Cancer



Morris, J.C. et al, JCO, Vol 30, No 15_suppl (May 20 supplement), ASCO 2012: Abstract 2571

Patient's immune system can recognize lung cancer after treatment with tergenpumatucel-L



Dorgenmeltucel-L Phase 2 Clinical Response in Metastatic Melanoma

Pre-TrialWeek 6Week 9Post-TrialImage: Distribution of the second se

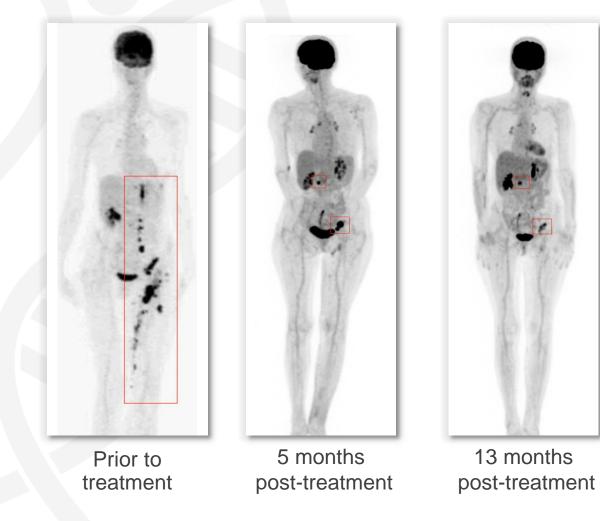
Riker, A.I.. et al, JCO, Vol 30, No 15_suppl (May 20 supplement), ASCO 2012: Abstract e19008

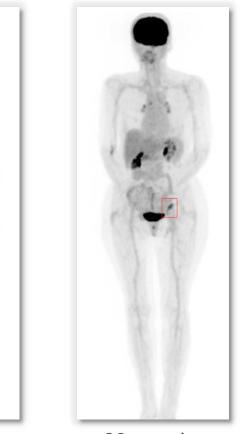
Vitiligo correlated with durable response



Dorgenmeltucel-L

Phase 2: Complete Response in Metastatic Melanoma





29 months post-treatment

Riker, A.I.. et al, JCO, Vol 30, No 15_suppl (May 20 supplement), ASCO 2012: Abstract e19008



Dorgenmeltucel-L

Vitiligo and Disease Regression in Metastatic Melanoma



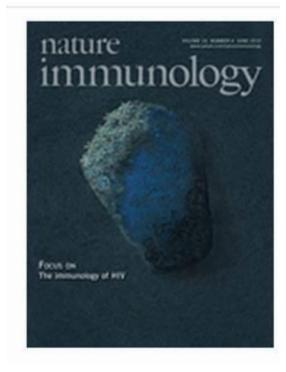


Eosinophils Play an Important Role in Immuno-Oncology

- Eosinophils are key to the anti-parasitic immune response
- Similarities between cancer and parasitic infections
- Eosinophil infiltration in tumors is a positive prognostic factor

Eosinophils orchestrate cancer rejection by normalizing tumor vessels and enhancing infiltration of CD8(+) T cells

<u>By: Carretero R</u>, <u>Sektioglu IM</u>, <u>Garbi N</u>, <u>Salgado</u> <u>OC</u>, <u>Beckhove P</u>, <u>Hämmerling GJ</u>





HyperAcute Immunotherapy Is Highly Differentiated From Other Cancer Vaccines

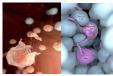
- Technology derived from serendipitous observation in the clinic that led to unexpected anti-tumor responses
- Hyperacute mechanism based on potent anti-αGal antibodies that protect humans from zoonotic infection
- Metabolically active, whole-cell immunotherapy with multiple antigens
- Does not require tissue from patient (allogeneic)
- Multi-faceted immune response: antibodies, T cells and eosinophils



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Checkpoint Inhibitors

Disrupting Tumor Evasion of Immune System

- We need mechanisms to turn off the immune system
 - Among them, enzymes such as IDO (Indoleamine 2,3 Dioxygenase) that turn off the activity of T cells
 - The mammalian placenta, for example, is packed with IDO to protect the fetus from the mother's immune system
- Cancer hijacks those mechanisms to escape the immune response
- The system is complex shutting down one checkpoint can stimulate the response from others
 - Combination with checkpoint antibodies (PD-1, PD-L1, CTLA-4, OX40)





Immun

Breakthrough of the Yes

T cells on the attack

Immunotherapy

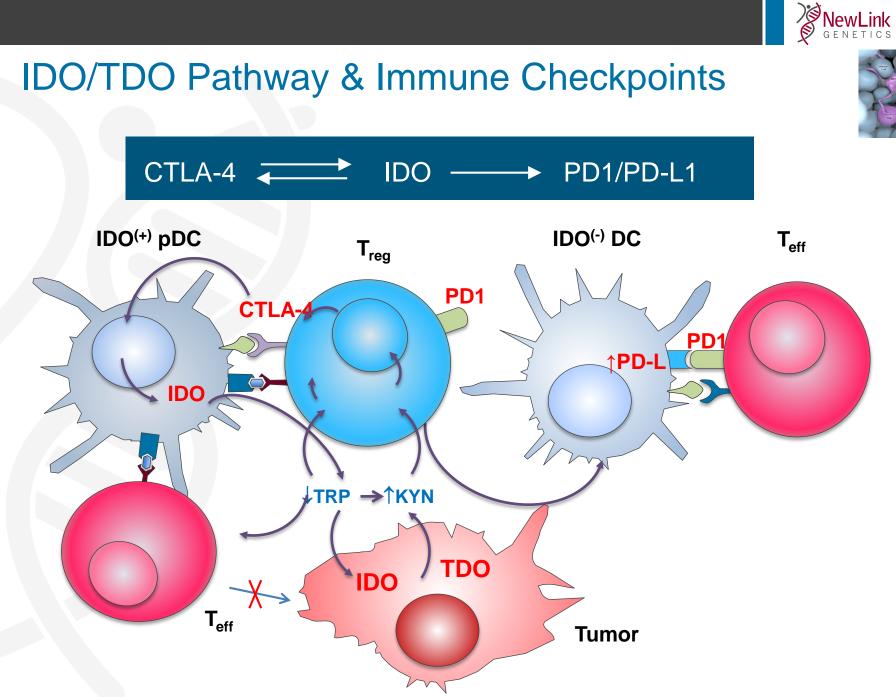
Cancer

Research

Key Academic Collaborations and Partnerships Well-Respected Publications on IDO

- Alexander J Muller, James B DuHadaway, P Scott Donover, Erika Sutanto-Ward, George C Prendergast, Inhibition of indoleamine 2,3-dioxygenase, an immunoregulatory target of the cancer suppression gene *Bin1*, potentiates cancer chemotherapy. *Nature Medicine* **11**, 312 - 319 (2005).
- Alexander J Muller, James B DuHadaway, Daniel Jaller, Peter Curtis, Richard Metz, George C Prendergast, Immunotherapeutic suppression of IDO and tumor growth with ethyl pyruvate. *Cancer Res.*, **70(5)**, 1845-1853 (2010).
- Richard Metz, James B DuHadaway, Uma Kamasani, Lisa Laury-Kleintop, Alexander J Muller, George C Prendergast, Novel tryptophan catabolic enzyme IDO2 is the preferred biochemical target of the antitumor indoleamine 2,3-dioxygenase inhibitory compound D-1-methyl-tryptophan. *Cancer Res.* 67(15), (2007).
- Alexander J Muller, George C Prendergast, Marrying Immunotherapy with Chemotherapy: why say IDO? Cancer Res. 65(15), (2005).
- Minghui Li, Aaron R Bolduc, Nasrul Hoda, Denise N Gamble, Sarah-Bianca Dolisca, Anna K Bolduc, Kelly Hoang, Clair Ashley, David McCall, Amyn M Rojiani, Bernard L Maria, Olivier Rixe, Tobey J MacDonald, Peter S Heeger, Andrew L Mellor, David H Munn, Theodore S Johnson, The indoleamine 2,3-dioxygenase pathway controls complement-dependent enhancement of chemo-radiation therapy against murine glioblastoma. *J Immunother Cancer*, 2:21 (2014).
- Richard Metz, Courtney Smith, James B DuHadaway, Phillip Chandler, Babak Baban, Laruen M F Merlo, Elizabeth Pigott, Martin P Keough, Sonja Rust, Andrew L Mellor, Laura Mandik-Nayak, Alexander J Muller, George C Prendergast, IDO2 is critical for IDO1-mediated T-cell regulation and exerts a non-redundant function in inflammation. *Int Immunol* 26(7), 357-367 (2014).
- David H Munn, Min Zhou, John T Attwood, Igor Bondarev, Simon J Conway, Brendan Marshall, Corrie Brown, Andrew L Mellor, Prevention of allogeneic fetal rejection by tryptophan catabolism. *Science* 21, 1191-1193 (1998).







Leading Pipeline in Immuno-Oncology NewLink Genetics IDO Pathway Inhibitors

IDO Pathway Inhibitor Platform

AGENT	TARGET DISEASE	DESIGN DETAILS	Phase1	Phase 2	Phase 3
	Breast cancer (metastatic)	Indoximod + taxane; randomized	ENROLLING		
	Prostate cancer (metastatic, castrate-resistant)	Indoximod following sipuleucel-T; randomized	ENROLLING		
Indoximod	Pancreatic cancer (metastatic)	Indoximod + gemcitabine and nab-paclitaxel; phase 1b/2	ENROLLING		
	Melanoma (advanced)	Indoximod + ipilimumab or PD-1 inhibitors; phase 2	ENROLLING		
	Glioblastoma multiforme	Indoximod + temozolomide; phase 2	ENROLLING		
GDC-0919	Solid tumors	GDC-0919			
	Solid tumors	GDC-0919 + PD-L1 inhibitor or anti-OX40	 Partnered with Genentech, Inc 		

Now moving into combination studies



Indoleamine 2,3-Dioxygenase (IDO) Pathway A Key Immune Checkpoint Target

Regulates Innate and Adaptive Immune Response

- Is counter-regulatory (induced by inflammation)
- Inhibits effector T cells, activates suppressive Tregs
- Can create peripheral tolerance de novo

Dominant Regulatory Role

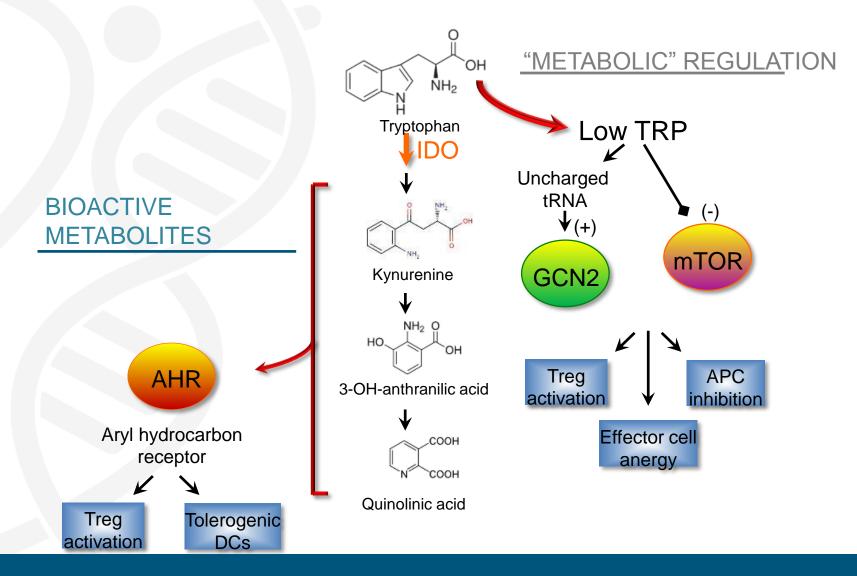
- Maternal tolerance; autoimmune disorders; transplant tolerance
- Tumor-induced immunosuppression

Overexpressed in Cancer

- Within tumor cells to directly suppress T cells
- Within antigen-presenting cells resulting in peripheral tolerance to tumor-associated antigens



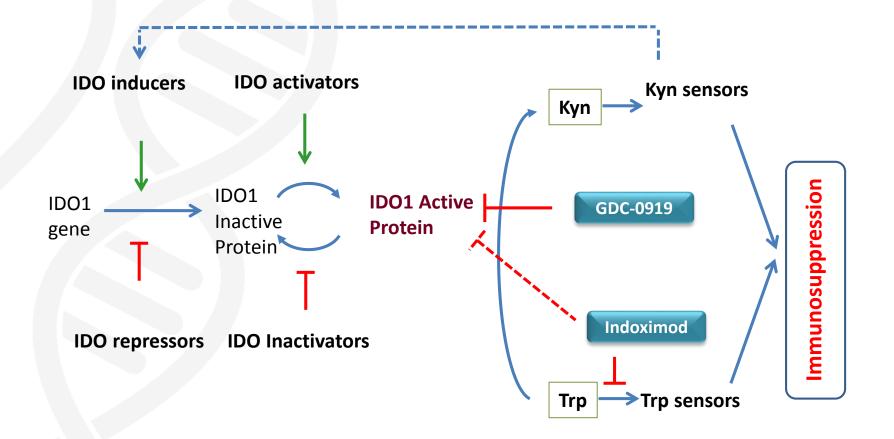
IDO Biochemical Pathway



Low tryptophan causes immune suppression



IDO Pathway and Immunosuppression



Two IDO pathway inhibitors with distinct mechanisms of action



IDO Can Be a Prognostic Marker

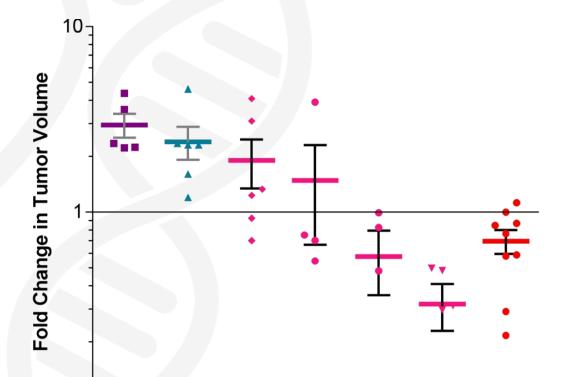
AML	(Chamuleau et al., 2008; Corm et al., 2009)	
Colorectal	(Brandacher et al., 2006) (Ferdinande et al., 2012)	100 June 100
Prostate	(Watkins et al., 2011)	
Endometrial	(Ino et al., 2006)	
Ovarian	(Okamoto et al., 2005)	
Cervical	(Inaba et al., 2010)	0 5 10 15
Glioblastoma	(Wainwright et al., 2012)	Overall survival in years from diagnosis
Melanoma (response to ipilimumab)	(Munn et al., 2004; Speeckaert et al., 2012) (Hamid et al., 2011)	Chamuleau, et al. Haematologica 200
Breast	(Mansfield et al., 2009)	

Increased IDO predicts poor survival



Indoximod + Chemotherapy Cancer Model

Enhanced Activity with Taxane in Breast Cancer Model



- Vehicle
- Paclitaxel
- Paclitaxel + 1MT 2 days po
- Paclitaxel + 1MT 3 days po
- Paclitaxel + 1MT 4 days po**
- Paclitaxel + 1MT 5 days po**
- Paclitaxel + 1MT pellets

**1 full regression

autochthonous MMTV-neu breast cancer model

1MT is mixture of D-1MT (indoximod) and L-1MT

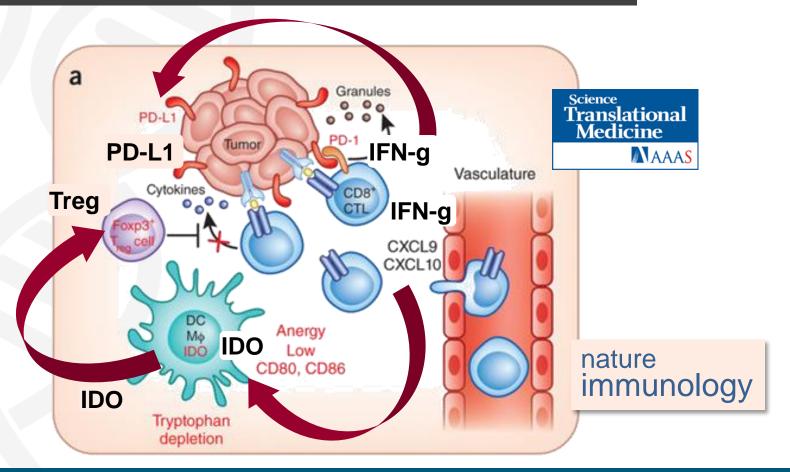
Hou, et al, Cancer Research 2007; 67: (2) 793

IDO blockade can enhance chemotherapy



IDO and Counter-Regulation

Up-Regulation of PD-L1, IDO, and Tregs in the Melanoma Tumor Microenvironment Is Driven by CD8+ T Cells Stefani Spranger, et al ... Thomas F. Gajewski (2013)



Cytotoxic T cells induce IDO



Tumor Indoleamine 2,3-Dioxygenase (IDO) Inhibits CD19-CAR T Cells and is Downregulated by Lymphodepleting Drugs

by Soranobu Ninomiya, Neeharika Narala, Leslie Huye, Shigeki Yagyu, Barbara Savoldo, Gianpietro Dotti, Helen E. Heslop, Malcolm K. Brenner, Cliona M. Rooney, and Carlos A. Ramos

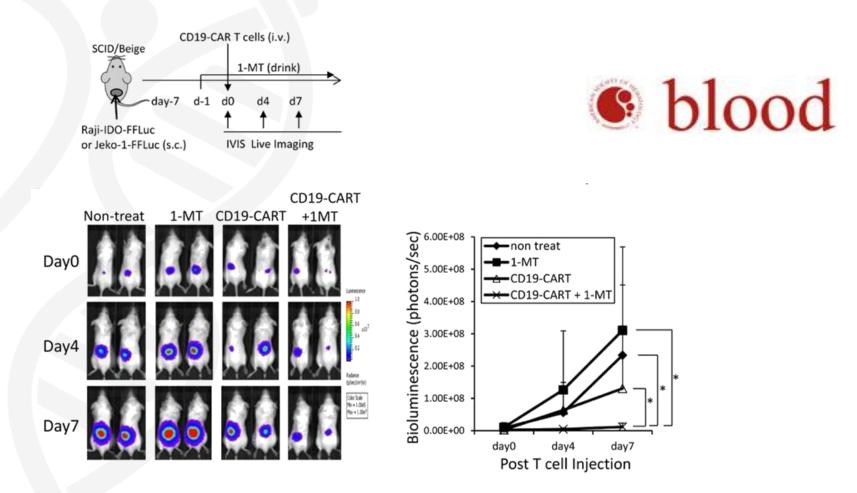
> Blood Volume 125(25):3905-3916 June 18, 2015



IDO plus CAR-T combinations are promising



CAR-T Cell Anti-Tumor Activity Is Limited By IDO



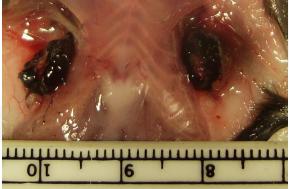
Soranobu Ninomiya et al. Blood 2015;125:3905-3916

Indoximod enhances activity of CAR-T cells

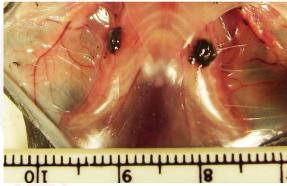


GDC-0919 and Indoximod Anti-Tumor Activity Potent Single Agent and Combination Effect

Control



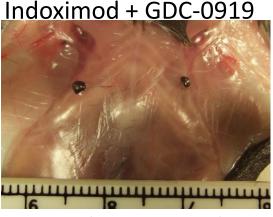
GCD-0919



65-82% reduction tumor volume



65% reduction tumor volume



92-98% reduction tumor volume



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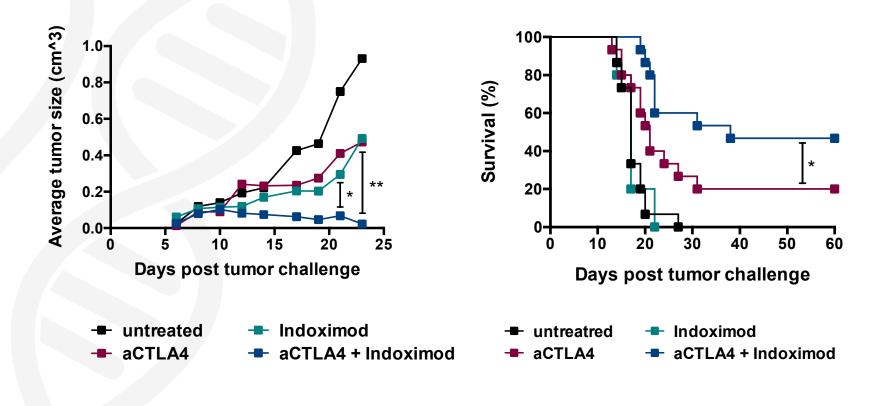


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Indoximod Plus CTLA-4 Blockade

Tumor Regression and Survival Improvement



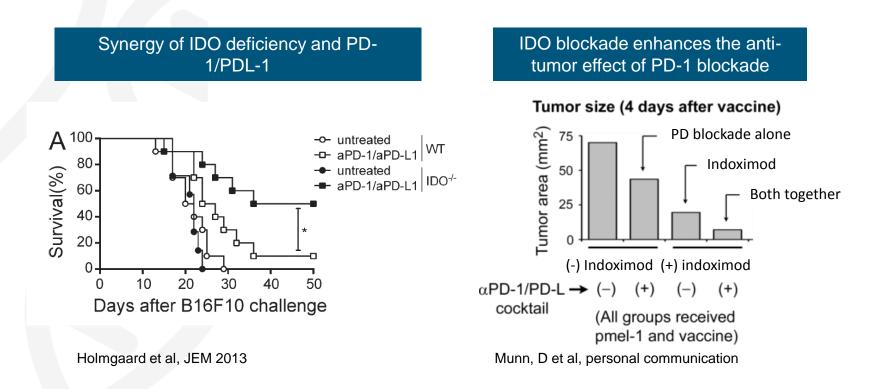
Holmgaard et al, JEM 2013

Dual checkpoint blockade is more effective than single



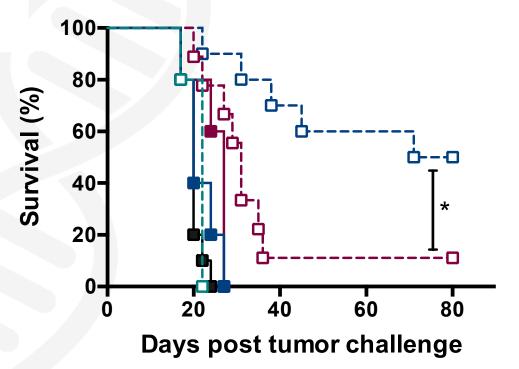
IDO Inhibition Plus Anti PD-1/PDL-1

Synergy in Preclinical Models





Indoximod Plus CTLA-4 Blockade Plus Vaccine Survival Improvement



- untreated
 aCTLA4
- aCTLA4 + Indoximod
- -D- Vaccine + Indoximod
- -o- Vaccine + aCTLA4
- -D- Vaccine + aCTLA4 + Indoximod

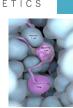
Holmgaard et al, JEM 2013

Immune-refractory tumors can respond to whole cell vaccine plus checkpoint blockade

Genentech Alliance

Validation of NewLink's Approach

- Exclusive worldwide license agreement for NewLink Genetics IDO and TDO inhibitors except indoximod, including clinical asset GDC-0919
- \$150 million upfront payment; >\$1 billion in potential milestones and royalties
- Research collaboration agreement
 - Genentech funds FTEs at NewLink Genetics
 - Research focuses on discovery of novel TDO inhibitors, dual IDO/TDO inhibitors, and the use of GDC-0919 in combination with TDO inhibitors and/or other immune checkpoint inhibitors
 - Joint Research Committee oversees research activities
- Clinical development
 - Joint Development Committee oversees clinical development activities
 - Clinical plans to combine GDC-0919 with MPDL3280A (anti-PDL1) and other checkpoint inhibitors







Clinical Strategy and Algenpantucel-L Update Nicholas N. Vahanian, M.D., President and CMO



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- Well-positioned to execute on our vision of combining checkpoint blockade inhibitors and cancer vaccines



- Potential to have the first product with an FDA approval for the adjuvant treatment for patients with surgically resected pancreatic cancer
- Founding scientific and business leadership with proven expertise in drug discovery, manufacturing, clinical development, and commercialization
- Proven success in substantial strategic collaborations
- \$200+ million in cash with the potential for near-term catalysts
- Opportunity in infectious diseases

Ongoing Clinical Trials in Pancreatic Cancer

HyperAcute Immunotherapy

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AGENT	TARGET DISEASE	DESIGN DETAILS	Phase1	Phase 2	Phase 3			
Algenpantucel-L	Pancreatic cancer (resected)	IMPRESS: algenpantucel-L + standard of care; randomized	ENROLLMENT COMPLETE					
	Pancreatic cancer (borderline resectable or locally advanced unresectable)	PILLAR: algenpantucel-L + chemotherapy; randomized	ENROLLING					







Why Target Surgically Resected Pancreatic Cancer?

- High short-term risk of recurrence and death despite surgical resection
- Minimal residual disease
- Patients must be healthy enough to undergo major surgery
- No FDA-approved drug for adjuvant treatment
- Orphan indication

Significant unmet medical need in pancreatic cancer

NewLink Genetics

About Pancreatic Cancer

- Approximately 48,960 new cases of pancreatic cancer will occur in 2015 in the U.S., resulting in 40,560 deaths*
- Pancreatic cancer has the lowest survival rate of all cancers**
 - 1-year survival rate of all stages combined is 26%
 - 5-year survival rate of all stages combined is 6%
- Treatment options vary by stage, but primarily include
 - Surgical resection
 - Chemotherapy
 - Gemcitabine
 - Gemcitabine + nab-paclitaxel
 - FOLFIRINOX
 - Erlotinib
- An estimated 15,000 patients are eligible for resection and an additional 10,000 patients have locally advanced disease***

*American Cancer Society **National Cancer Institute ***SEER data





Phase 2 Trial in Resected Pancreatic Cancer

- Evaluated in patients (n=69) who have had cancer surgically resected
- Combined with current standard chemotherapy and radiation, which is routinely administered to reduce risk of cancer returning
- Algenpantucel-L given every 2 weeks for 6 months
- High dose (300 million cells) and low dose (100 million cells)
- This study demonstrated 96% one-year survival in high dose group, 81% one-year disease-free survival in high-dose group

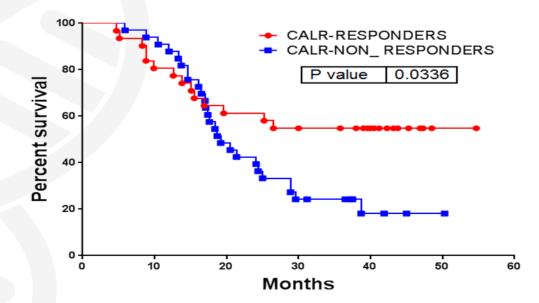
Rocha Lima, C. et al, JCO, Vol 31,_suppl (May 15 supplement), ASCO 2013: Oral Abstract 3007

Encouraging Phase 2 results led to Phase 3 under SPA





Phase 2 Results in Resected Pancreatic Cancer



Anti-CALR Ab	Increased Ab	No Increase	Total
Number Patients	31	33	64
OS (months)	>35	19.2	P < 0.04 (log rank test)
30 month survival	55%	21%	P <0.01 (Fisher's exact test)

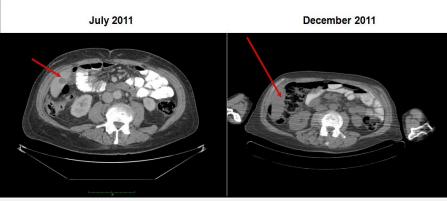
Rossi, G.R. et al, ASCO 2014: Highlights Selected. Poster 3029

Anti-CALR Antibody Elevation Correlates with Improved Overall Survival

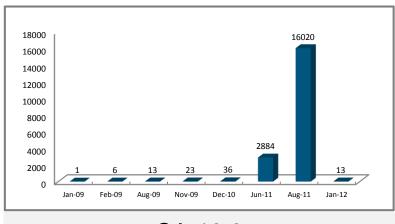


Phase 2: Additional Clinical Observations in Resected Pancreatic Cancer

- Recall skin reactions can occur
 1-2 years after last vaccination
- 70% of the patients showed eosinophilia, with 30% lasting over a year
- Long-term survivor with pulmonary metastases and persistent eosinophilia > 1 year
- Three patients with recurrent disease had complete response to second-line salvage treatment



Regression of Liver Metastasis



IMPRESS Trial

Algenpantucel-L Phase 3 Registration Trial

- Randomized two-arm study of immunotherapy added to standard adjuvant treatment versus standard treatment alone
- 722 patients with surgically removed cancers enrolled in 70+ U.S. sites from May 2010 to September 2013
- Protocol under SPA with FDA, also orphan drug and fast track status
- Statistical method employed is a log rank analysis powered at 80% to detect approximately a 20% difference in overall survival
- Algenpantucel-L given at high dose used in Phase 2 study (300 million cells) for a longer treatment period: every two weeks for six months, then monthly for an additional six months
- Stratified for nodal status, radiotherapy administration and CA19-9
- The characteristics of the patients enrolled in the IMPRESS study are consistent with patient populations enrolled in previous U.S. multiinstitutional trials in pancreatic cancer



IMPRESS Trial

Data Analyses



- The study was fully enrolled in September 2013
- The second interim analysis showed an estimated median overall survival of 28.5 months* from the time of randomization for both cohorts blended together
- We estimate that overall survival in the control arm, even allowing for advances in the SOC, should be in the low twenties following surgery
- These initial data from the Phase 3 trial have given us confidence to proceed with commercialization plans



IMPRESS Patient Characteristics

Consistent with Previously Reported Large U.S. Studies



Characteristics	RTOG 9704 ¹ (n=221)	IMPRESS (n=722)
Age (Median)	61	65
Gender (Male)	53	52
Tumor Location		
Head	85%	80%
Body/Tail	15%	20%
CA19-9 ≥180	9% ²	9%
Tumor Grade (Poor/Undifferentiated)	30%	35%
Nodal Status (N+)	68%	70%
Tumor Size (≥3.0 cm)	59%	55%
High Risk (N+ and/or ≥2.5 cm)	NA	92%

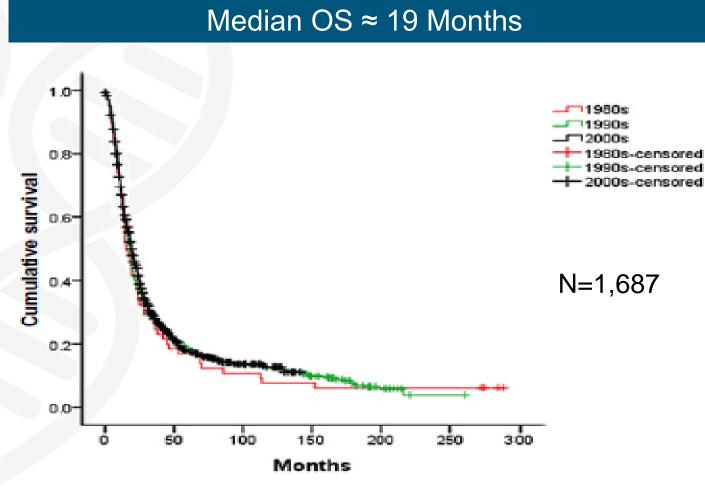
¹ Regine et al, JAMA 2008; 299(9): 1019-1026

²Berger, A et al, Int J Radiation Oncol Biol Phys, Vol 84, No 3 pp e291-297, 2012 (N=385)

Patient population similar to other large U.S. studies of post-resection patients



Survival in Resected Pancreatic Cancer



He, J, Et al, HPB, Volume 16, Issue 1, January 2014

No change in outcomes for over three decades

PILLAR: Second Phase 3 Trial

Locally Advanced Pancreatic Cancer

- Launched October 2012 (FPI, Q113)
- Open label, two-arm, randomized study (n=280)
- FOLFIRINOX or nab-paclitaxel +/- algenpantucel-L
- Algenpantucel-L: 300 million cells Q2 weeks up to 18 doses
- Overall survival is the primary endpoint
- Includes borderline or locally advanced unresectable patients
- Open to enrollment

Positive results might more than double the treatable patient population







Algenpantucel-L Manufacturing and Readiness Gary Potter, V.P., Manufacturing



Algenpantucel-L Manufacturing

Experienced Staff

- Clinical and commercial manufacturing
- Cell characterization development
- Cell culture process development
- Quality assurance
- Quality control
- Facilities and engineering





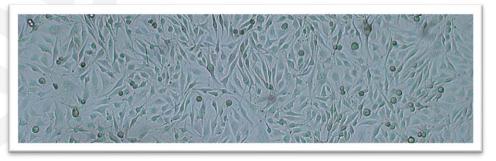


ENETICS

Algenpantucel-L Manufacturing

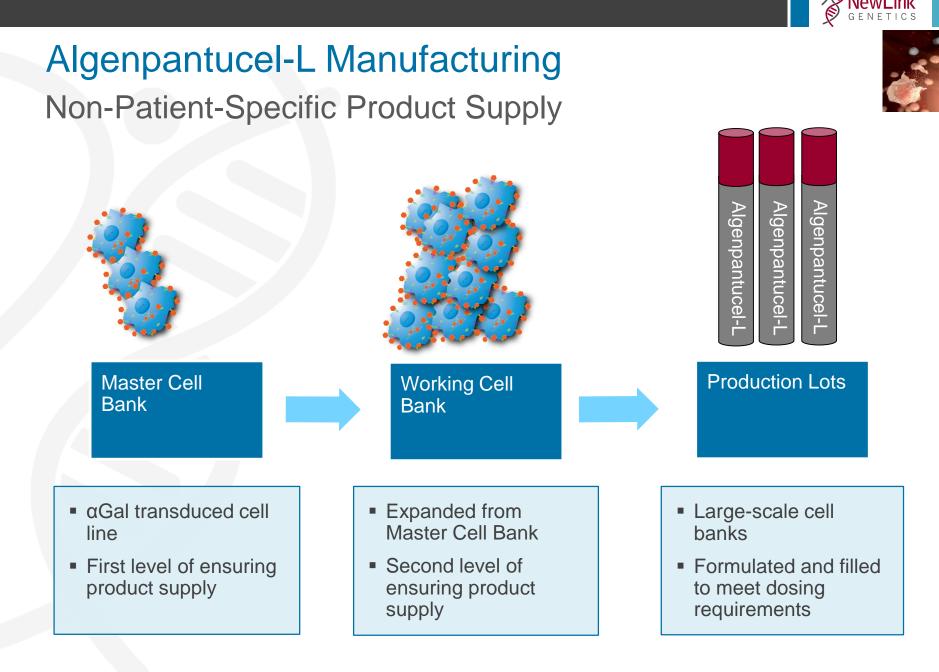
Standard Manufacturing Techniques and Materials

- Non-patient-specific product
- Platform process for all HyperAcute cell lines
- Well-established cell culture processes using
 - Traditional tissue culture techniques
 - Cell expansion, harvest, form/fill
 - Liquid nitrogen storage stability
 - Single-use materials
 - Standardized safety testing





Manufacturing platform applicable to all HyperAcute Immunotherapy



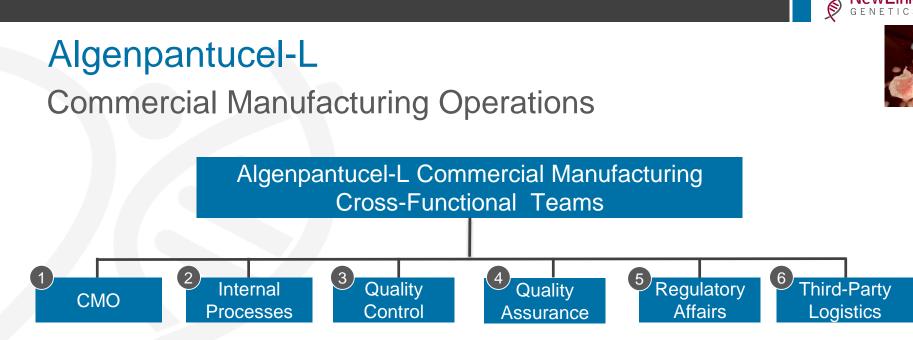
Algenpantucel-L Manufacturing

Cell Characterization and Potency

- Cell Characterization
 - Well developed Proprietary process
 - Quality Attributes
 - Cell growth patterns
 - Unique genetic signatures
 - Genetic stability and Identity
- Potency
 - Complex matrix of assays related the proposed mechanism of action
 - Based on clinical immunological and efficacy studies
 - Cell integrity studies
 - Expression of cell surface aGal
 - Multiple families of cell surface markers
 - Biologic Assays

15 years of developing cell characterization methods





- CMO
 - Expanded capacity, commercial-ready systems, maintain internal clinical capacity
- Regulatory Affairs
 - Orphan Drug Status, Special Protocol Assessment (SPA), Fast Track Designation for expedited BLA approval (rolling submission)
 - Working with industry-leading organizations





Algenpantucel-L Commercialization Readiness Brian Wiley, V.P., Business Development



Algenpantucel-L Commercial Opportunity

Potential to Showcase Substantial Innovation

Assuming success:

- First FDA approval for patients with resected pancreatic cancer
- First FDA approved allogeneic whole cell cancer vaccine
- Improvement in overall survival
- Minimal significant adverse events
- Strong rationale for combination with emerging therapies

Establish NewLink Genetics as leader in immuno-oncology

Resectable Pancreatic Cancer

Eligible for Resection Based on Stage I/II Disease

Global Market and Prognosis

- Nearly 50K patients annually in U.S. + EU5 + Japan
- Resection rates vary by country & region
- Five-year survival is 10-15% (all stage I/II)
- Stage IIB five year survival <8%</p>

U.S. Market Opportunity

- No FDA-approved drugs for adjuvant treatment
- >15K stage I/II patients diagnosed annually (resection eligible)
- ≈ 8-9K patients eligible for adjuvant treatment
- Gemcitabine is currently the accepted standard

Decision Resources 2013, Global Data 2014 and internal research

Untapped emerging market with significant unmet need







Building on a Strong Foundation

Over 90 HyperAcute Clinical Sites in the U.S.



Significant experience to learn from and leverage



Key Near Term Objectives

Increase Awareness and Strengthen Foundation

- Healthcare professionals
- Key opinion leaders
- Payers (Medicare and private)
- Patients and caregivers (patient advocacy)

Educate and engage key stakeholders



NewLink Genetics Awareness Campaign Establishing a Leadership Position in Immuno-Oncology





ASCO Annual Meeting 2015

Pancreatic Cancer Action Network Partnership NewLink Genetics' Commitment to Patients





NewLink Genetics Supports the Fight Against Pancreatic Cancer at PurpleStride 2015 Events in Austin, Los Angeles and Des Moines

AMES, Iowa, April 24, 2015 -- <u>NewLink Genetics Corporation</u> (NASDAQ: NLNK), a biopharmaceutical company focused on bringing novel immuno-oncology medicines to patients with cancer globally, is proud to support the Pancreatic Cancer Action Network's PurpleStride 5K Run and Family-Friendly Walks in Austin, Los Angeles and Des Moines as a Gold Sponsor.

"Pancreatic cancer is one of the leading causes of cancer-related deaths due in part to its rapid advancement and lack of early diagnostic tools to enable early detection. We are pleased to further our on ongoing support for the Pancreatic Cancer Action Network to raise awareness and funds to support the fight against pancreatic cancer, which this year alone will claim the lives of more than 40,000 Americans," said Charles J. Link, Jr., M.D., Chairman and Chief Executive Officer of NewLink Genetics.

NewLink Genetics employees, friends and families will participate in all three walks, with each team aiming to recruit 20 members.

PurpleStride Austin - May 2, 2015

NewLink Genetics recently opened a new office in Austin focused on commercialization efforts, and the team is looking forward to giving back to the Austin community. <u>Click here</u> to join the NewLink Genetics Austin team or support the team with a donation.

PurpleStride Los Angeles - May 2, 2015

Click here to join the NewLink Genetics Los Angeles team or support with a donation.

PurpleStride Iowa - September 26, 2015

Additional details about the event being held in Des Moines will be provided closer to the event in NewLink Genetics' home state of Iowa.

About Pancreatic Cancer

According to the Pancreatic Cancer Action Network, pancreatic cancer is currently the fourthleading cause of cancer-related deaths in the United States, and it is anticipated to become the second by 2020. It is one of the deadliest cancers, with a five-year survival rate that is just seven percent. In 2015, it is estimated that nearly 49,000 Americans will be diagnosed with pancreatic cancer and approximately 40,500 will die from the disease. Surgical removal of the tumor is





Advancing our Clinical Pipeline Eugene Kennedy, VP, Clinical and Medical Affairs



HyperAcute Immunotherapies Beyond Algenpantucel-L

HyperAcute Immunotherapy

AGENT	TARGET DISEASE	DESIGN DETAILS	Phase1	Phase 2	Phase 3
	Pancreatic cancer (resected)	IMPRESS: algenpantucel-L + standard of care; randomized			
Algenpantucel-L	Pancreatic cancer (borderline resectable or locally advanced unresectable)	PILLAR: algenpantucel-L + chemotherapy; randomized	ENROLLING		
Tergenpumatucel-L	NSCLC (advanced or metastatic)	Tergenpumatucel-L vs docetaxel and controlled for follow-on chemotherapy; phase 2b; randomized	ENROLLING		
Dorgenmeltucel-L	Melanoma (advanced)	Dorgenmeltucel-L + ipilimumab or PD-1 inhibitors; randomized	ENROLLING		
HyperAcute Prostate	Prostate cancer (castrate-resistant)	HyperAcute Prostate: single agent, dose escalation	ENROLLED		
HyperAcute Renal	Renal cancer (advanced)	HyperAcute Renal; single agent, dose escalation	ENROLLING		

Phase 1/2 Clinical Development in Lung Cancer

- Consists of three separate allogeneic lung cancer cell lines
 - Includes large cell, squamous cell, and adenocarcinoma cell types
 - Modified to express alpha-gal carbohydrate
- Evaluated in a Phase 1/2 clinical trial
 - Phase 1 portion established the safety profile and dosing of tergenpumatucel
 - Phase 2 study enrolled patients with advanced, treatment refractory NSCLC
 - Patients received a total of 8 treatments at a dose of 300 million cells per treatment
- 28 patients were evaluable from Phase 2 study





Phase 2 Survival Data in Non-Small Cell Lung Cancer

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Endpoint	Historical Data Supportive Care (SC) Alone	Historical Data Docetaxel + SC	<u>Single Agent</u> Tergenpumatucel-L
Median Survival	4.6 months	<8 months	11.3 months
1 Year Survival	11%	37%	46%

Morris, J.C. et al, JCO, Vol 30, No 15_suppl (May 20 supplement), ASCO 2012: Abstract 2571

Survival that compares favorably with standard treatment options

Phase 2 Chemo-Sensitization Response Data

Response rate to third- or fourth-line chemotherapy after treatment with tergenpumatucel-L in non-small cell lung cancer

Response	Patients (n)	Rate (%)
Partial Response	5	31%
Stable Disease	4	25%
Progressive Disease	7	44%

Morris, J.C. et al, ASCO 2013: Abstract 8094

Higher than expected response rates observed in patients with prior HyperAcute Immunotherapy







Clinical Development in Lung Cancer: Phase 2b

- Randomized study of up to 240 patients with Stage IIIb/IV NSCLC
 - Compares tergenpumatucel-L with docetaxel in second line
 - Designed to evaluate two dosing schedules for tergenpumatucel-L
- Primary endpoint: overall survival
 - Designed to evaluate effects of follow on chemotherapy
 - Capture potential chemosensitization

Aim is to establish the efficacy of tergenpumatucel-L



Clinical Development in Lung Cancer: Second Phase 2b

- A Phase 2b study will evaluate patients with stage IIIB/IV advanced non-small-cell lung cancer
- Tergenpumatucel-L combined with indoximod and docetaxel in previously treated patients
- 59 patient study, endpoint is progression free survival
- This study is expected to enroll the first patient in 2015
- Gets to the heart of NewLink's focus on developing combination therapies with a variety of mechanistic approaches

Bring together for first time NewLink's own approaches to immuno-oncology



Dorgenmeltucel-L

Clinical Development in Melanoma

- 25 patient study
- Administered weekly 150M cell dose X 12 weeks
- Pegylated interferon co-administered at dose below the threshold that is expected to produce results by itself
 - High risk stage III, resected (n=9)
 - Stage IV (n=16, 4 of which were resected)
- 2 of 12 patients with measurable disease experienced a complete response
 - 4/25 patients developed vitiligo

Preliminary evidence of efficacy seen through clinical responses

Dorgenmeltucel-L

Clinical Development in Metastatic Melanoma



Development of vitiligo after treatment with dorgenmeltucel-L



)



Dorgenmeltucel-L

Clinical Development in Melanoma: Phase 2b

- Trial evaluates the combination of dorgenmeltucel-L with checkpoint inhibitors
 - 100 patient randomized trial of ipilimumab, nivolumab, or pembrolizumab with or without dorgenmeltucel-L
 - Enrolling patients with advanced melanoma
 - Endpoints include safety, progression free survival, and response rates
 - Trial currently enrolling

Opportunity to evaluate the combination of HyperAcute Immunotherapy with current standard of care checkpoint inhibitors

HyperAcute Renal Clinical Development in R

Clinical Development in Renal Cell Cancer: Phase 1

- HyperAcute Renal Immunotherapy consists of equal doses of each of two allogeneic renal cell cancer cell lines engineered to express the αGal gene
- Phase 1 study designed to demonstrate safety of HyperAcute Renal
 - Dose finding study, two cohorts
- Endpoint: safety
 - Secondary endpoints immunological correlates, progression free survival
- Currently enrolling

Intended to evaluate HyperAcute Immunotherapy platform in a cancer type known to be immuno-responsive – groundwork for combinations





IDO Pathway Inhibitor Pipeline

IDO Pathway Inhibitor Platform

AGENT	TARGET DISEASE	DESIGN DETAILS	Phase1	Phase 2	Phase 3
	Breast cancer (metastatic)	Indoximod + taxane; randomized	ENROLLING		
	Prostate cancer (metastatic, castrate-resistant)	Indoximod following sipuleucel-T; randomized	ENROLLING		
Indoximod	Pancreatic cancer (metastatic)	Indoximod + gemcitabine and nab-paclitaxel; phase 1b/2	ENROLLING		
	Melanoma (advanced)	Indoximod + ipilimumab or PD-1 inhibitors; phase 2	ENROLLING		
	Glioblastoma multiforme	Indoximod + temozolomide; phase 2	ENROLLING		
	Solid tumors	GDC-0919	Partnered with Genentech, Inc.		
GDC-0919	Solid tumors	GDC-0919 + PD-L1 inhibitor or anti-OX40			itech, Inc.

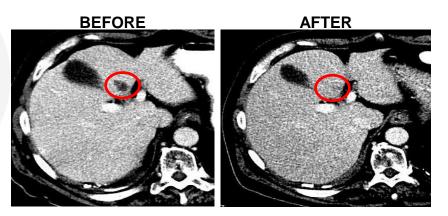
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NewLink



Key Phase 1 Safety Study Results

- Fatigue, anorexia and nausea most common adverse events
- Safety and dosing for Phase 2 studies established
- Possible clinical benefit demonstrated
 - − Five patients with stable disease for \geq 6 months
- Multiple mixed responses including regression of visceral metastases



Soliman, H. et al, JCO, Vol 30, No 15,_suppl (May 20 supplement), ASCO 2012: Abstract 2501

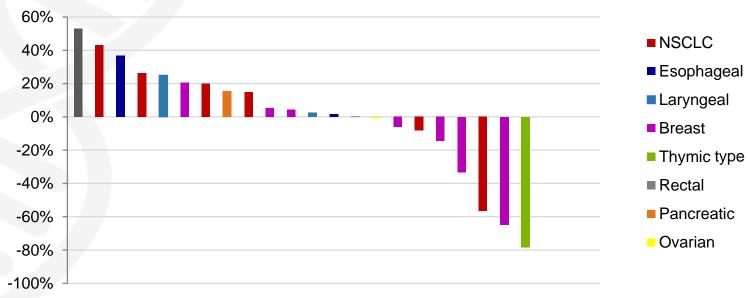
Well-tolerated without dose-limiting toxicity, preliminary suggestion of efficacy



Indoximod + Docetaxel Combination

Phase 1b Efficacy Results

- 18% (4/22) partial response rate (2 breast, 1 lung, 1 thymic)
- 41% (9/22) rate of stable disease



Fold Change in Tumor Volume

Encouraging responses in heavily pre-treated patients



Clinical Development in Breast Cancer

NLG2101 – 1 st line Metastatic Breast Cancer		
Primary Endpoint	Progression free survival	
Key Secondary Clinical End- Points	Overall survivalObjective response rates	
Trial Design	Phase 2 randomized, double blindIn combination with taxane chemotherapy	
Trial Size	154 patients	
Status	 Currently enrolling Intention to present preliminary data at medical meeting in 2015 	

Largest randomized indoximod trial to date



Clinical Development in Glioblastoma Multiforme

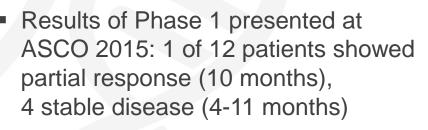
Primary EndpointProgression free survivalKey Secondary Clinical End- Points• Objective response rate • Overall survivalTrial Design• Phase 2 single arm trial • In combination with temozolomide in temozolomide refractory patients • Three subgroups, temozolomide refractory, bevicizumab refractory and radiotherapy-eligible patientsTrial Size• 93 patientsStatus• Currently enrolling • Phase 1b presented ASCO 2015 • Associated pediatric trial expected to start in 2015	NLG2102- Refrac	tory GBM
Clinical End- PointsOverall survivalImage: Phase 2 single arm trial 	Primary Endpoint	 Progression free survival
Trial Design• In combination with temozolomide in temozolomide refractory patients • Three subgroups, temozolomide refractory, bevicizumab refractory and radiotherapy-eligible patientsTrial Size• 93 patientsStatus• Currently enrolling • Phase 1b presented ASCO 2015	Clinical End-	
 Currently enrolling Phase 1b presented ASCO 2015 	Trial Design	 In combination with temozolomide in temozolomide refractory patients Three subgroups, temozolomide refractory, bevicizumab
Status Phase 1b presented ASCO 2015	Trial Size	 93 patients
	Status	Phase 1b presented ASCO 2015

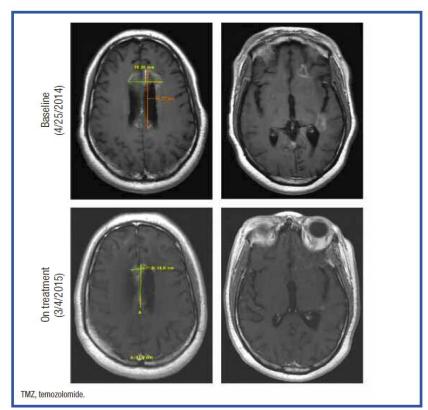
Intended to determine efficacy of the combination therapy of indoximod with temozolomide in refractory patients

Clinical Development in Glioblastoma Multiforme

Results of Phase 1 presented at partial response (10 months), 4 stable disease (4-11 months)

Intended to determine efficacy of the combination therapy of indoximod with temozolomide









Clinical Development in Melanoma

NLG2103 – Advanced Melanoma		
Primary Endpoint	 Progression free survival 	
Key Secondary Clinical End-Points	 Overall survival Correlative scientific studies Safety 	
Trial Design	Phase 2 single arm studyIndoximod in combinations with checkpoint inhibitors	
Trial Size	 38 patients 	
Status	 Enrolling Phase 1b results to be presented at ESMO/ECC 2015 	

Study underway of combination of indoximod with CTLA-4 and PD-1 inhibitors in melanoma



Clinical Development in Pancreatic Cancer

NLG2104 – 1 st line Metastatic Pancreatic Cancer		
Primary Endpoint	 Overall survival 	
Key Secondary Clinical End-Points	Objective response rateProgression free survival	
Trial Design	 Phase 2 single arm study Indoximod in combination with gemcitabine and nab-paclitaxel 	
Trial Size	 80 patients 	
Status	 Enrolling 	

Initial study of combination of indoximod with standard of care in metastatic pancreatic cancer



NewLink Genetics

Genentech's Update on GDC-0919 at ASCO*

- Pre-clinical data for GDC-0919 demonstrates
 - Plasma kynurenine levels decrease
 - Regulatory T-cells decrease
 - T effector cells show increased proliferation and CTL function
 - Enhanced anti-tumor efficacy when combined with anti-PDL1 and anti-CTLA4
- IDO inhibition with anti-PDL1 or anti-OX40 in preclinical models show benefit

GDC-0919

Ongoing Clinical Trials

- Phase I study of GDC-0919 results to be presented in conjunction with Genentech at ESMO/ECC in September 2015 in Vienna
- A Phase Ib, open-label, dose-escalation study of the safety and pharmacology of GDC-0919 in combination with PD-L1 inhibitor (MPDL3280A) in patients with advanced solid tumors targeted for 2015 initiation
- Additional combination study planned with anti-OX40

Combinations of GDC-0919 and other checkpoint inhibitors entering the clinic



Combination Immunotherapy Trials

The Future of Immuno-Oncology

- Combination therapies will be necessary to build upon initial successes seen in immuno-oncology
- NLG0304 dorgenmeltucel-L (HyperAcute Melanoma) plus checkpoint inhibitors ipilimumab, nivolumab, or pembrolizumab
- NLG2103 indoximod in combination with checkpoint inhibitors for advanced melanoma
- NLG0401 tergenmeltucel-L (HyperAcute Lung) plus indoximod for patients with advanced NSCLC

Combination therapies of cancer vaccines and checkpoint inhibitors could significantly expand the effectiveness of immuno-oncology





Discovering New Immuno-Oncology Products Mario Mautino, Ph.D., V.P., Drug Discovery and IP Officer

Drug Discovery Programs

Proven Team Producing Strong Pipeline

- Same team that discovered GDC-0919
- Team is working closely with Genentech as experts in IDO pathways









Drug Discovery Programs

Pharmacological Pathways in Immune Suppression

IDO/TDO pathway inhibitors

- Indoximod (2005 present)
 - Licensed from Georgia Regents University
 - Mechanism of action different from direct enzymatic inhibitors of IDO1
 - Currently in multiple clinical trials
 - Working to expand patent protection
- NLG-919/GDC-0919 (2008 present)
 - Developed through internal drug discovery efforts
 - Development partnered with Genentech (4Q14)
 - Mechanism of action: direct enzymatic inhibitor of IDO1

Two functionally different IDO/TDO pathway inhibitors



Overview of Drug Discovery Programs

Genentech Research Collaboration

- IDO/TDO pathway inhibitors
 - Tryptophan-2,3-dioxygenase (TDO) inhibitors
 - Dual IDO/TDO inhibitors
- Joint research committee established
 - Molecules being designed and tested at both NewLink and Genentech
 - Building and expanding our medicinal chemistry capacity and expertise

Genentech collaboration allows NewLink to expand drug discovery effort



Overview of Drug Discovery Programs

Growing capacity for drug discovery program

- Future drug discovery
 - Expanded capacity in lab space, number of chemists, instrumentation and expertise
 - State-of-the-art computer modeling
 - Discovery and/or validation of new targets functionally linked to immune suppression and immune checkpoint inhibitors
 - In-licensing opportunities

Actively growing discovery pipeline





Financial Update/Milestones/Infectious Disease Program Jack Henneman, CFO



NewLink Genetics

Building a Leading Immuno-Oncology Company

- Industry-leading advanced pipeline across multiple cancer types with 7 product candidates in clinical development from Phase 1 to Phase 3
- Unique HyperAcute Immunotherapies that suggest clinical activity associated with potent anti-cancer immune responses
- Multiple small molecules targeting the key IDO checkpoint blockade
- Well-positioned to execute on our vision of combining checkpoint blockade inhibitors and cancer vaccines
- Potential to have the first product with an FDA approval for the adjuvant treatment of patients with surgically resected pancreatic cancer
- Founding scientific and business leadership with proven expertise in drug discovery, manufacturing, clinical development, and commercialization
- Proven success in substantial strategic collaborations



- \$200+ million in cash with potential for near-term catalysts
- Opportunity in infectious diseases



Financial Position (as of March 31, 2015)

Cash and equivalents	\$206.6 million
Debt	~\$1.5 million
YE 2015 Cash	~\$160 million
Shares Outstanding	28.5 million
Market Capitalization	~\$1.5 billion*

Infectious Disease Program

Ebola Vaccine

- Novel recombinant viral vector (vesicular stomatitis virus, rVSV) developed by the Public Health Agency of Canada
- 100% protective after one dose in lethal monkey challenge model
- 100% of human subjects develop strong immune response after just one dose
- Clinical data published in New England Journal of Medicine April 1, 2015
- Manufactured multiple GMP lots meeting global requirements
- Program being supported by Merck in an agreement signed in November 2014 - \$50 million of payments through July 2015
- NewLink Genetics has established an experienced infectious disease clinical development team





NewLink Genetics

Near-Term Catalysts, 2015 - 2017

- Algenpantucel-L: results of IMPRESS in 2016, validation of HyperAcute Immunotherapy platform and commercial pathway
- Validation of IDO pathway inhibitor program (indoximod) across multiple cancer studies
- Partnership clinical advancements with Genentech/Roche (GDC-0919 clinical milestones)
- New combination trials with multiple checkpoint inhibitors and HyperAcute Immunotherapy
- Potential evidence of efficacy of the Ebola vaccine candidate from clinical trials in Africa

Significant value-creating news flow in next 24 months





Concluding Remarks and Q&A Charles J. Link, Jr., M.D., Chairman, CEO and CSO



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