NewLink Genetics Presents Phase 1 Data Supporting Significantly Higher Exposure with Indoximod Prodrug, NLG802, and Biomarker Data from Two Phase 2 Trials Illustrating Indoximod's Impact on the Tumor Microenvironment at SITC 2018

November 9, 2018

AMES, Iowa, Nov. 09, 2018 (GLOBE NEWSWIRE) -- NewLink Genetics Corporation (NASDAQ:NLNK) announced that data from three separate trials are being presented at the Society for Immunotherapy of Cancer (SITC) Annual Meeting in Washington D.C. Data from a Phase 1a clinical trial of NLG802, a prodrug of indoximod, as well as biomarker data from two Phase 2 studies of indoximod in combination therapy are being presented in poster sessions today and tomorrow, November 9th and 10th, from 8:00AM to 8:00PM ET. These posters with full data sets are provided on the company's website in the " Posters & Presentations" section under the "Investors & Media" tab.

"We are delighted to be able to present these data supporting both activity of indoximod within the tumor microenvironment and the higher exposure levels obtained by indoximod prodrug, NLG802, supporting the potential for these drugs to elicit therapeutic responses and improve the lives of patients with cancer," said Charles J. Link, Jr, MD, Chairman and Chief Executive Officer.

Phase 1 Clinical Trial of NLG802, Indoximod Prodrug with Enhanced Pharmacokinetic Properties

Preliminary data from a Phase 1a study of NLG802, a prodrug of indoximod, are being presented today by Olivier Rixe, MD, PhD, Professor of Medicine, University of New Mexico Comprehensive Cancer Center, Albuquerque, NM in a poster session (P331). Co-author, Eugene Kennedy, MD, Chief Medical Officer, NewLink Genetics, will be present Friday, November 9th, 12:45-2:15PM and 6:30-8:00PM, to discuss these data.

NLG802 is being evaluated in an ongoing standard 3+3 dose escalation Phase 1a study in patients with recurrent advanced solid malignancies. The purpose of this trial is to assess the safety, maximum tolerated dose, and pharmacokinetic properties of this drug candidate. As of October 3rd, the cutoff date for these data, 11 patients were enrolled in this study in three separate dose cohorts, 180 mg BID, 363 mg BID, and 726 mg BID.

Key findings from these preliminary data:

- NLG802, was well tolerated, with no unexpected safety signals.
- At the time of analysis, neither maximum tolerated dose (MTD), nor maximum biologically achievable dose (MBAD) had been reached.
- NLG802 produced 4-fold increase in C_{MAX} and AUC after a single dose, and a 4–5.5 fold increases in C_{MAX} and AUC after continuous BID dosing compared with the molar equivalent of indoximod dosing.

The Immunogenic Impact of Indoximod on the Tumor Microenvironment of Patients with Advanced Melanoma

Biopsy data from a Phase 2 study of indoximod plus checkpoint inhibition from patients with advanced melanoma are being presented today by Jiayi Yu, PhD, Senior Scientist, NewLink Genetics, in a poster session (P142). The author will be present Saturday, November 10th, 12:20-1:50PM and 7:00-8:30PM to discuss these data.

In this study, patients with unresectable advanced melanoma underwent pretreatment tumor biopsy followed by a repeat biopsy after cycle 3 of indoximod plus pembrolizumab. Fourteen pairs of tumor specimens (6 patients with objective response and 8 non-responders) underwent RNA sequencing analysis and immunofluorescence staining to assess immune activity in the tumor microenvironment (TME), to define changes in the tumor genomic profile and gene expression. Baseline samples from the trial were used for predictive biomarker assessment (N = 38).

Key findings from these biopsy data:

- Compared to published studies, these biopsy data suggested indoximod exclusively contributed to immunologic and metabolic changes in the TME.
- Indoximod in combination therapy may contribute to immunologic and metabolic changes in a different manner than anti-PD-1 alone.
- Decreased IDO1 in $Ki67^-$ cells supports indoximod's mechanism of action (MOA).
- Patients with high IDO expression showed a trend towards both higher rate of response to treatment and longer progression-free survival (PFS), results which were independent of PD-L1 expression.

Previously published results from this Phase 2 study of indoximod plus pembrolizumab for patients with advanced melanoma may be found on the company's website under " Posters & Publications" in the "Investors & Media" section.

Effects of indoximod plus gemcitabine/nab-paclitaxel on tumor microenvironment of patients with metastatic pancreas cancer

Biopsy data from a Phase 2 study of indoximod plus chemotherapy for patients with metastatic pancreatic cancer are being presented today by Jiayi Yu, PhD, Senior Scientist, NewLink Genetics, in a poster session (P706). Co-author, Gabriela Rossi, PhD, Vice President, Biologics Development, NewLink Genetics, will be present Saturday, November 10th, 12:20-1:50PM and 7:00-8:30PM to discuss these data.

In this study, treatment-naïve patients with metastatic pancreatic cancer underwent pre-treatment tumor biopsy with a repeat biopsy on week 8. Sixteen pairs of tumor specimens (8 patients with objective response, and 8 non-responders) underwent RNA sequencing analysis and immunohistochemistry (IHC) staining to assess immune activity in the tumor microenvironment.

Key findings from these biopsy data indicate that indoximod plus standard-of-care (SOC) chemotherapy:

- Tumor samples observed to have increased recruitment of intratumoral T cells.
- Increased recruitment of innate immune cells (NK cells) in responding patients.
- Downregulated Treg population and IDO expression in the TME.
- Increased both innate and adaptive immune responses in TME of these patients, supporting indoximod's MOA.

Previously published results from this Phase 2 study of indoximod plus gemcitabine/nab-paclitaxel for patients with metastatic pancreatic cancer may be found on the company's website under " Posters & Publications" in the "Investors & Media" section.

About Indoximod

Indoximod is an investigational, orally available small molecule targeting the IDO pathway. The IDO pathway is a key immuno-oncology target, suppressing immune response and allowing for immune escape by degrading tryptophan with the resultant production of kynurenine. Indoximod reverses the immunosuppressive effects of low tryptophan and high kynurenine through mechanisms that include modulation of the AhR-driven transcription of genes that control immune function. This results in increased proliferation of effector T cells, increased differentiation into helper T cells rather than regulatory T cells, and downregulation of IDO expression in dendritic cells. Indoximod is being evaluated in combination with treatment regimens including chemotherapy, radiation, checkpoint blockade and cancer vaccines across multiple indications including recurrent pediatric brain tumors, DIPG, and AML.

About NLG802

NLG802 is a prodrug of indoximod. NLG802 has been shown in preclinical trials to increase bioavailability and exposure to indoximod above the levels achievable by direct administration of indoximod. NLG802 is currently being evaluated in clinical trials.

About NewLink Genetics Corporation

NewLink Genetics is a clinical stage biopharmaceutical company focusing on developing novel immuno-oncology product candidates to improve the lives of patients with cancer. NewLink Genetics' IDO pathway inhibitors are designed to harness multiple components of the immune system to combat cancer. For more information, please visit www.NewLinkGenetics.com and follow us on Twitter @NLNKGenetics.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements of NewLink that involve substantial risks and uncertainties. All statements contained in this press release are forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The words "guidance," "upcoming," "will," "plan," "intend," "anticipate," "approximate," "expect," or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among others, statements about NewLink Genetics' financial guidance for 2018; results of its clinical trials for product candidates; its timing of release of data from ongoing clinical studies; its plans related to moving additional indications into clinical development; NewLink Genetics' future financial performance, results of operations, cash position and sufficiency of capital resources to fund its operating requirements; the effects of its organizational realignment; and any other statements other than statements of historical fact. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that NewLink makes due to a number of important factors, including those risks discussed in "Risk Factors" and elsewhere in NewLink Genetics' Annual Report on Form 10-K for the year ended December 31, 2017 and other reports filed with the U.S. Securities and Exchange Commission (SEC). The forward-looking statements in this press release represent NewLink's views as of the date of this press release. NewLink anticipates that subsequent events and developments will cause its views to change. However, while it may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. You should, therefore, not rely on these forward-looking statements as representing NewLink Genetics' views as of any date subsequent to the date of this press release.

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