NewLink Genetics Describes the Differentiated Mechanism of Action of Indoximod in AACR Poster Presentation

April 17, 2018

AMES, Iowa--(BUSINESS WIRE)--Apr. 17, 2018-- NewLink Genetics Corporation (NASDAQ:NLNK) today presented a poster entitled *"Indoximod modulates AhR-driven transcription of genes that control immune function*" in the Immunomodulatory Agents and Interventions session at the American Association for Cancer Research (AACR) 2018 Annual Meeting in Chicago.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20180417005885/en/

(Graphic: Business Wire)

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"The data demonstrate that indoximod has a unique mechanism of action, remarkably differentiated from IDO enzymatic inhibitors. This different mechanism may contribute to antitumor immune responses in the IDO pathway and through activity independent of IDO," said Charles J. Link, Jr., M.D., Chairman and Chief Executive Officer.

The data suggest that indoximod regulates the differentiation of helper T cells toward an immuno-stimulatory helper function and downregulates genes that control the differentiation of T cells into immuno-suppressive regulatory T cells (Tregs) in an AhR dependent manner. This leads to an increase in the ratio of helper T cells to Tregs. Additionally, it was shown that indoximod reduces the level of IDO protein in dendritic cells *in vitro*, leading to increased stimulation of CD8 T cell proliferation and reduced production of kynurenine. Moreover, indoximod stimulation of mTOR in T cells appears to increase the proliferation of effector T cells in an IDO and TDO-independent manner. Through this mechanism, indoximod may be able overcome the effects of Trp degradation mediated by both IDO and TDO. Thus, in addition to opposing immunosuppression mediated by the IDO pathway, indoximod may drive antitumor immune responses independent from IDO.

In summary, indoximod has immunostimulatory effects involving 4 main cell types: $CD8^+$ T cells, T helper cells, T regulatory cells, and dendritic cells. Indoximod appears to function through three main mechanisms to inhibit the IDO pathway:

- Reversing the effects of low tryptophan by increasing proliferation of effector T cells
- Increasing the ratio of T helper to T regulatory cells by both favoring differentiation of activated CD4 T cells into helper T cells and directly reprogramming T regulatory cells into helper T cells
- Downregulating IDO expression in dendritic cells

About Indoximod

Indoximod is an investigational, orally available small molecule targeting the IDO pathway. The IDO pathway is a key immuno-oncology target involved in regulating the tumor microenvironment and immune escape. Indoximod is being evaluated in combination with treatment regimens including anti-PD-1/PD-L1 agents, cancer vaccines, radiation and chemotherapy across solid and liquid tumors.

About NewLink Genetics Corporation

NewLink Genetics is a late-stage biopharmaceutical company focusing on discovering, developing and commercializing 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.

Editor's Note: Please see infographic on Indoximod Mechanism of Action

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements of NewLink Genetics that involve substantial risks and uncertainties.All statements, other than statements of historical fact, contained in this press release are forward-looking statements, within the meaning of The Private Securities Litigation Reform Act of 1995. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "target," "potential," "will," "could," "should," "seek" 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 aboutresults 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; 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 Genetics' views as of the date of this press release. NewLink Genetics 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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