Neoleukin Therapeutics Presents Preclinical Data for NL-201 and De Novo Protein Design Technology at American Association for Cancer Research (AACR) Virtual Annual Meeting II

June 22, 2020

- NL-201 demonstrates durable antitumor activity in animal tumor models -
- NL-201 and targeted variants improve outcomes when combined with CAR-T cells in vivo -
- Conditional activation of de novo proteins using split molecule technology may increase therapeutic index -
- Company to host Investor R&D Showcase Tuesday, June 23 at 3:30 p.m. PT / 6:30 p.m. ET -

SEATTLE, June 22, 2020 (GLOBE NEWSWIRE) -- Neoleukin Therapeutics, Inc., “Neoleukin” (NASDAQ:NLTX), a biopharmaceutical company utilizing sophisticated computational methods to design *de novo* protein therapeutics, today announced the presentation of preclinical data on its lead immunotherapy candidate NL-201, an IL-2 and IL-15 agonist, and applications of its *de novo* protein design platform at the American Association for Cancer Research (AACR) Virtual Annual Meeting II.

“The preclinical research presented by our research team and our academic collaborators offers compelling evidence to support advancing NL-201 into clinical trials and demonstrates exciting future opportunities for *de novo* proteins. Key findings include the potent stimulation and expansion of key cancer-killing cells by NL-201, robust and durable antitumor activity across many tumor types, and encouraging immunogenicity data in non-human primates,” said Jonathan Drachman, M.D., Chief Executive Officer of Neoleukin. “In addition, our approach to conditional activation demonstrates that *de novo* proteins can be split into two inactive pieces that regain the ability to bind receptors when co-located in the tumor microenvironment. This represents a next-generation technology designed to significantly widen the therapeutic index for potent immune activators.”

NL-201 is a *de novo* receptor agonist of the IL-2 and IL-15 receptors, designed to expand cancer-fighting CD8 T cells and natural killer (NK) cells without any bias toward cells expressing the alpha receptor subunit (CD25). New data highlights the ability of NL-201 to stimulate and expand CD8+ and NK cells at very low doses with minimal impact on immunosuppressive regulatory T cells. Treatment with NL-201 in animal models was well-tolerated and induced durable, anti-tumor immunity. Additionally, minimal immunogenicity was reported following five weekly doses of NL-201 in non-human primates.

Details of the presentations are as follows:

Pre-clinical development of NL-201: A *de novo* α-independent IL-2/IL-15 agonist

Presenter: Carl Walkey, Ph.D., Neoleukin Therapeutics

Abstract 4518
Poster Presentation

- NL-201 is more potent on CD8 effector cells and NK cells from 10 healthy volunteers than IL-2 (~3-10X) and has reduced impact on immunosuppressive Treg cells (~33X). This results in a marked increase in relative immune cell activation, especially at low concentrations where IL-2 is often immunosuppressive.

- NL-201 is well tolerated and promotes durable anti-tumor activity in preclinical models. After two doses of NL-201, 6 of 15 (or 40%) mice bearing CT26 tumors were tumor-free, while all untreated mice, or mice treated with anti-PD-1 or anti-PD-L1 checkpoint inhibitors succumbed to tumor outgrowth. When mice were re-challenged with fresh CT-26 tumor cells, none of the NL-201-treated mice re-grew tumors, demonstrating durable antitumor immunity.

- NL-201 demonstrates robust single-agent activity in multiple tumor models. NL-201 inhibited tumor growth across a diverse panel of 12 syngeneic murine tumor models.

- NL-201 shows minimal immunogenicity in non human primates.
  Five weekly doses of NL-201 led to infrequent, low titer anti-drug antibodies (ADAs) in non-human primates. Overall, 22 of 26 animals had no detectable ADAs; among the four NHPs with low or moderate ADAs, the tolerability and pharmacodynamic activation of lymphocytes appeared to be unaffected after the final dose.

- All IND-enabling activities remain on track to support a planned IND for NL-201 before the end of 2020.

Conditionally active *de novo* IL-2 cytokine mimetics for targeted immunotherapy: *de novo* split technology

Presenter: Alfredo Quijano-Rubio**,** University of Washington School of Medicine, Institute for Protein Design

Abstract 1075
Minisymposium Presentation: Tuesday, June 23, 2020, 9 a.m. to 11 a.m. Eastern Time

- NEO-2/15 can be divided into two pieces, neither of which bind to the IL-2 receptor subunits.

- When combined, the fragments can restore receptor binding activity.
- If both pieces are fused to antigen-specific binding proteins, IL-2 receptor activation will only occur when the targets for both pieces are present on tumor cells.
- This split approach to conditional activation results in widening of the therapeutic index in animal models.
- Split technology, made possible by the designed stability of *de novo* proteins, offers an opportunity to create next-generation therapeutics with enhanced safety and specificity.

Engineered variants of Neo-2/15 potently expand CAR-T cells and promote antitumor activity in lymphoma and solid tumor mouse models

Presenter: Isabel Leung, Ph.D., Fred Hutchinson Cancer Research Center, Division of Clinical Research

Abstract 2222
Poster Presentation

- NL-201 robustly expands CAR-T cells and promotes antitumor activity in both solid and lymphoma tumor models.
- NL-201 promotes CD8:Treg ratio of ~1,000 in the tumor vs. ~20 with IL-2.
- Targeted delivery of NEO-2/15 to transduced CAR-T cells achieves 100% disease control.
- NL-201 and targeted variants may be effective at increasing CAR-T cell number and improving outcomes.

Accessing Presentations

Presentations and full session details can be found at www.aacr.org and the “Science/Publications” section of the Neoleukin website www.neoleukin.com.

Webcast Event

Neoleukin will host a virtual Investor R&D Showcase Tuesday, June 23, 2020 at 3:30 p.m. Pacific Time / 6:30 p.m. Eastern Time, which will include a review of AACR presentations and discussion by guest speakers.

The live webcast event will include video and slide presentations and can be accessed from the investors section of the Neoleukin website at http://investor.neoleukin.com/events. An archived replay will also be available on the company website for at least 30 days following the event.

About Neoleukin Therapeutics, Inc.

Neoleukin is a biopharmaceutical company creating next generation immunotherapies for cancer, inflammation and autoimmunity using *de novo* protein design technology. Neoleukin uses sophisticated computational methods to design proteins that demonstrate specific pharmaceutical properties that provide potentially superior therapeutic benefit over native proteins. Neoleukin’s lead product candidate, NL-201, is a combined IL-2 and IL-15 agonist designed to improve tolerability and activity by eliminating the alpha receptor binding interface. For more information, please visit the Neoleukin website: www.neoleukin.com.

Safe Harbor / Forward-Looking Statements

This press release contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, including, but not limited to, planned development activities and timelines, use and adequacy of cash reserves and the potential benefits of the company’s product candidates and platform. Forward-looking statements can be identified by words such as: "anticipate," "intend," "plan," "goal," "seek," "believe," "project," "estimate," "expect," "strategy," "future," "likely," "may," "should," "will" and similar references to future periods. Examples of such forward-looking statements include but are not limited to statements regarding the therapeutic properties and potential of the company’s *de novo* protein design technology. These statements are subject to numerous risks and uncertainties, including risks and uncertainties related to the company’s cash forecasts, the company’s ability to advance its product candidates, the receipt and timing of potential regulatory submissions, designations, approvals and commercialization of product candidates, the timing and results of preclinical and clinical trials, the timing of announcements and updates relating to the company’s clinical trials and related data market conditions and further impacts of COVID-19, that could cause actual results to differ materially from what Neoleukin expects. Further information on potential risk factors that could affect Neoleukin’s business and its financial results are detailed under the heading “Risk Factors” in documents the company files from time to time with the Securities and Exchange Commission (SEC), and other reports as filed with the SEC. Neoleukin undertakes no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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