NGM Bio to Present Late-Breaking Preclinical Research at 2022 AACR Annual Meeting Supporting Development of its Myeloid Reprogramming Portfolio

April 8, 2022

- ILT2, ILT4, ILT3 and LAIR1 are myeloid checkpoints that may play a central role in establishing an immune-suppressive state in the tumor microenvironment
- NGM707, NGM831 and NGM438 are all engineered to release myeloid checkpoints and reprogram myeloid cells to reverse immune suppression and enhance immune response in tumors
- NGM707 and NGM831 are currently in the clinic, and NGM438 is anticipated to enter the clinic this quarter

SOUTH SAN FRANCISCO, Calif., April 08, 2022 (GLOBE NEWSWIRE) -- NGM Biopharmaceuticals, Inc. (NGM Bio) (Nasdaq: NGM), a biotechnology company focused on discovering and developing transformative therapeutics for patients, provided additional detail today on two late-breaking poster presentations it will give on Wednesday, April 13, 2022, at the American Association for Cancer Research (AACR) Annual Meeting. NGM Bio will also give an oral presentation on April 10, 2022 at the AACR meeting featuring preclinical data for the lead program in its myeloid checkpoint inhibitor portfolio, NGM707, a dual ITL2/ILT4 antagonist antibody.

The late-breaking presentations will feature preclinical data supporting the development of NGM831, an ILT3 antagonist antibody product candidate, and NGM438, a LAIR1 antagonist product candidate. ILT3 (also known as LILRB4) and LAIR1 are members of the LILR family of receptors, which may play a central role in establishing an immune-suppressive state in the tumor microenvironment. NGM831 and NGM438 are engineered to target these receptors, respectively, with the goal of releasing myeloid checkpoints and reprogramming myeloid cells to enhance anti-tumor immunity.

“We’re delighted to feature all three programs in our myeloid reprogramming portfolio at AACR 2022, enabling our team to share the extensive research that supports the development of these three therapeutic candidates,” said Dan Kaplan, Ph.D., Head of Translational Immuno-Oncology at NGM Bio. “NGM831, NGM438 and NGM707 target distinct LILR receptors, each suspected of playing a key role in driving immune suppression in the tumor microenvironment. With all three programs anticipated to be in the clinic by the end of this quarter, we look forward to seeing how our preclinical findings may translate into potential benefit for patients in their fight against cancer.”

A Phase 1/2 clinical trial of NGM707 is currently underway and will evaluate NGM707 as a monotherapy and in combination with KEYTRUDA® (pembrolizumab) in patients with advanced solid tumors. An initial data readout from the Phase 1a monotherapy dose escalation portion of this trial is expected in the second half of 2022.

NGM Bio recently announced the initiation of a Phase 1/1b clinical trial evaluating NGM831 as a monotherapy and in combination with KEYTRUDA in patients with advanced solid tumors. NGM438 is anticipated to enter the clinic later this quarter.

About the NGM831 Late-Breaking Poster Presentation:
“Preclinical characterization of NGM831, an ILT3 antagonist antibody for the treatment of solid tumors”
Abstract #: 7874
Poster Session 18, Late-Breaking Research: Immunology 2, April 13, 2022; 9:00 AM – 12:30 PM

NGM831 is an antagonist antibody product candidate being developed by NGM Bio for the treatment of advanced solid tumors designed to block the interaction of ILT3 with fibronectin, a key component of the tumor stroma, as well as other cognate ligands. In August 2021, NGM published a paper in *Cancer Immunology Research*, a journal of the American Association for Cancer Research, describing the company’s discovery that fibronectin, an extracellular matrix protein that forms a fibrillar network within the tumor stroma, is a functional ligand for ILT3. The fibronectin-ILT3 interaction serves as a stromal checkpoint through which the extracellular matrix actively promotes myeloid cell suppression in the tumor microenvironment.

Per the AACR abstract, in preclinical studies NGM831 demonstrated the ability to bind human and primate ILT3 with high affinity and specificity, and to block the interaction of ILT3 with both of its reported ligands: fibronectin and ApoE. In a gene expression profiling experiment, treatment of tolerogenic dendritic cells with NGM831 in the presence of fibronectin decreased their expression of inhibitory and ‘scavenger’ receptors, as well as classical markers of an immune-suppressive myeloid cell phenotype, and increased the expression of genes involved in antigen presentation. These results suggest that the immune cells were remodeled to a more stimulatory phenotype. Consistent with these observations, treating tolerogenic cells with NGM831 increased their production of pro-inflammatory cytokines and increased the production of chemokines capable of recruiting immune cells to sites of inflammation. In addition, NGM831 acted synergistically with KEYTRUDA to increase the ability of dendritic cells to stimulate T cell activation. Taken together, these results demonstrate that NGM831 blocked fibronectin-mediated immunosuppression and promoted myeloid cell reprogramming.

About the NGM438 Late-Breaking Poster Presentation:
“Preclinical development of NGM438, a novel anti-LAIR1 antagonist monoclonal antibody for the treatment of collagen-rich solid tumors”
Abstract #219
Poster Session 18, Late-Breaking Research: Immunology 2, April 13, 2022; 9:00 AM – 12:30 PM

NGM438 is an antagonist antibody product candidate being developed by NGM Bio to inhibit LAIR1 for the treatment of advanced solid tumors. LAIR1 is a collagen-binding inhibitory receptor expressed on immune cells that is implicated in immune suppression. LAIR1 and collagens are upregulated in

multiple cancer types where collagens are produced by activated stromal cells and are associated with poor responses to checkpoint inhibitors. For such tumors, formation of collagen:LAIR1 complexes may act as a stromal checkpoint to suppress productive immune responses in the tumor microenvironment.

Per the AACR abstract, NGM Bio's preclinical research demonstrated that LAIR1 was expressed on circulating and intratumoral immune cells of cancer patients, and LAIR1-expressing cells were commonly found in collagen-rich tumor stroma. NGM438 reversed collagen-induced immune suppression in myeloid cells and promoted T cell responses to anti-PD1 mAbs in immune cell-based functional assays. Additionally, LAIR1 antagonism, in combination with anti-PD1 mAbs, led to significant tumor growth inhibition in a preclinical model resistant to either treatment alone. Taken together, these results suggest that NGM438 may inhibit LAIR1-mediated collagen-driven immune suppression alone and in combination with checkpoint inhibition.

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Abbreviations (in Alphabetical Order)
Anti-PD1 mAbs=Anti-Programmed Cell Death Protein 1 Monoclonal Antibody; ApoE=Apolipoprotein E; ILT2=Immunoglobulin-Like Transcript 2; ILT3=Immunoglobulin-Like Transcript 3; ILT4=Immunoglobulin-Like Transcript 4; LAIR1=Leukocyte-Associated Immunoglobulin-Like Receptor 1; LILR= Leukocyte Immunoglobulin-Like Receptor [ILT2 = LILRB1, ILT3=LILRB4, ILT4=LILRB2].

About NGM Bio
NGM Bio is focused on discovering and developing novel, life-changing medicines for people whose health and lives have been disrupted by disease. The company's biology-centric drug discovery approach aims to seamlessly integrate interrogation of complex disease-associated biology and protein engineering expertise to unlock proprietary insights that are leveraged to generate promising product candidates and enable their rapid advancement into proof-of-concept studies. As explorers on the frontier of life-changing science, NGM Bio aspires to operate one of the most productive research and development engines in the biopharmaceutical industry. All therapeutic candidates in the NGM Bio pipeline have been generated by its in-house discovery engine, with a disease-agnostic mindset, always led by biology and motivated by unmet patient need. Today, the company has seven disclosed programs, including four in Phase 2 or 2b studies, across three therapeutic areas: cancer, retinal diseases and liver and metabolic diseases. Visit us at www.ngmbio.com for more information.

Forward-Looking Statements
Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "will," "may," "expected," "anticipated," "implicated," "designed," "engineered to," "suspected," "suggest," "look forward," "potential," "promising," "goal," "aspires," "aims" and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These statements include those related to: NGM Bio's product candidates, including the potential of NGM Bio's oncology product candidates, NGM07, NGM831 and NGM438, to release myeloid checkpoints and reprogram myeloid cells to drive immune response in tumors and what these product candidates are designed and engineered to achieve, including enhancing anti-tumor immunity; the role of ILT3 and LAIR1 in establishing an immune-suppressive state in the tumor microenvironment; potential outcomes suggested by preclinical findings regarding NGM831 and NGM438; the ability to enroll patients in and the availability and anticipated timing of data from the Phase 1a study of NGM707; the planned commencement of a first-in-human clinical trial of NGM438 and the anticipated timing thereof; NGM Bio's aspiration to operate one of the most productive research and development engines in the biopharmaceutical industry and other statements that are not historical fact. Because such statements deal with future events and are based on NGM Bio's current expectations, they are subject to various risks and uncertainties, and actual results, performance or achievements of NGM Bio could differ materially from those described in or implied by the statements in this press release. These forward-looking statements are subject to risks and uncertainties, including, without limitation, risks and uncertainties associated with the costly and time-consuming pharmaceutical product development process and the uncertainty of clinical success, including risks related to failure or delays in successfully initiating, enrolling, reporting data from or completing clinical studies, as well as the risks that results obtained in preclinical or clinical trials to date may not be indicative of results obtained in ongoing or future trials and that NGM Bio's product candidates may otherwise not be tolerable and effective treatments in their planned indications; NGM Bio's ability to maintain its amended collaboration with Merck, including the risk that if Merck were to breach or terminate the amended collaboration or Merck's development funding obligations, NGM Bio would not obtain all of the anticipated financial and other benefits of the amended collaboration, and the development and/or commercialization of NGM Bio's product candidates within the scope of the amended collaboration could be delayed, perhaps substantially; the ongoing COVID-19 pandemic, which has adversely affected, and could materially and adversely affect in the future, NGM Bio's business and operations, including NGM Bio's ability to timely supply, initiate, enroll and complete its ongoing and future clinical trials; the time-consuming and uncertain regulatory approval process; NGM Bio's reliance on third-party manufacturers for its product candidates and the risks inherent in manufacturing and testing pharmaceutical products; the sufficiency of NGM Bio's cash resources, including to fund its wholly-owned programs, and NGM Bio's need for additional capital; and other risks and uncertainties affecting NGM Bio and its development programs, including those discussed in the section titled "Risk Factors" in NGM Bio's annual report on Form 10-K for the year ended December 31, 2021 filed with the United States Securities and Exchange Commission (SEC) on March 1, 2021 and future filings and reports that NGM Bio makes from time to time with the SEC. Except as required by law, NGM Bio assumes no obligation to update these forward-looking statements, or to update the reasons if actual results differ materially from those anticipated in the forward-looking statements.

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