NGM Bio Announces Initiation of Phase 1/1b Clinical Trial of NGM831 for the Treatment of Patients with Advanced Solid Tumors

March 31, 2022

- Dose-escalation and dose-expansion trial evaluating potential of NGM831, an ILT3 antagonist antibody product candidate, as a monotherapy and in combination with KEYTRUDA® (pembrolizumab) initiated and expected to enroll up to approximately 80 patients
- NGM831 is the second of three programs comprising NGM Bio's wholly-owned myeloid reprogramming and checkpoint inhibition portfolio to enter the clinic
- NGM831, NGM707 and NGM438 are engineered to release myeloid checkpoints and reprogram myeloid cells to enhance anti-tumor immunity
- NGM Bio is currently enrolling patients in a Phase 1/2 trial of NGM707 and plans to initiate first-in-human trial of NGM438 in the second quarter of 2022

SOUTH SAN FRANCISCO, Calif., March 31, 2022 (GLOBE NEWSWIRE) -- NGM Biopharmaceuticals, Inc. (NGM Bio) (Nasdaq: NGM), a biotechnology company focused on discovering and developing transformative therapeutics for patients, today announced it has dosed the first patient in a Phase 1/1b clinical trial of NGM831 for the treatment of patients with advanced solid tumors. NGM831 is an antagonist antibody product candidate designed to block the interaction of ILT3 (also known as LILRB4) with fibronectin, a key component of the tumor stroma, as well as other cognate ligands. ILT3 is one of several receptors belonging to the LILR family that may play a central role in establishing an immune suppressive state in the tumor microenvironment. NGM831 is the second of three programs in NGM Bio's wholly-owned myeloid reprogramming and checkpoint inhibition portfolio to enter the clinic. All three programs in the portfolio, which also includes NGM707 and NGM438, are engineered to target various LILR suppressive receptors with the goal of releasing myeloid checkpoints and reprogramming myeloid cells to enhance anti-tumor immunity.

"We are proud to be among the leaders in developing an emerging class of molecules designed to inhibit myeloid checkpoints of the anti-tumor immune response. We believe this new, exciting frontier in checkpoint inhibition has the potential to enable the more effective treatment of multiple cancers, many of which elude current checkpoint inhibition approaches," said David J. Woodhouse, Ph.D., Chief Executive Officer at NGM Bio. "NGM831's entry into the clinic is another important milestone in our myeloid and stromal checkpoint development strategy. By mid-2022, we expect all three programs, which are directed at multiple and distinct targets, to be in the clinic."

NGM707, a dual ILT2/ILT4 antagonist antibody, is currently enrolling patients in an ongoing Phase 1/2 trial for the treatment of patients with advanced solid tumors and is expected to enroll approximately 180 patients. NGM438, a LAIR1 antagonist antibody, is anticipated to enter the clinic in the second quarter of 2022. NGM Bio plans to implement a robust biomarker strategy across the NGM707, NGM831 and NGM438 clinical development programs to help inform target patient populations for each product candidate.

Manish R. Sharma, M.D., Associate Director of Clinical Research at START Midwest (Grand Rapids, MI), commented, "While immunotherapy has transformed the treatment of certain types of cancer, a significant percentage of patients remain non-responders, with very poor outcomes. The biology underpinning myeloid checkpoint inhibition with the stromal component is intriguing, as the preclinical data suggest that myeloid checkpoint inhibition deepens T cell responses and reverses resistance mediated by the stromal component. I look forward to enrolling patients in the NGM831 Phase 1/1b trial and seeing how the science and preclinical findings translate in the clinic in both a monotherapy and combination setting."

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

About the NGM831 Phase 1/1b Trial Design

The Phase 1/1b open-label, multicenter, multi-dose, dose-escalation and dose-expansion trial is designed to determine the safety, pharmacokinetics and pharmacodynamics of NGM831 when given alone and in combination with KEYTRUDA® to patients with advanced solid tumors, and to evaluate preliminary antitumor activity. The trial expects to enroll adult patients with multiple tumor types, including pancreatic cancer, breast cancer, mesothelioma, gastric cancer, NSCLC, cervical and endocervical cancer, biliary duct cancer (cholangiocarcinoma), SCCHN, bladder urothelial cancer, CRC, esophageal cancer, ovarian cancer, RCC, prostate cancer, and melanoma (skin cutaneous).

The Phase 1 portion of the trial will include a monotherapy dose escalation (Part 1a) to determine the recommended Phase 2 dose (RP2D). The Phase 1b portion of the trial will include a combination dose finding with pembrolizumab to determine the RP2D.

For additional information about the trial, please click here to visit the listing on clinicaltrials.gov.

About NGM Bio's Myeloid Reprogramming and Checkpoint Inhibition Portfolio, including NGM831

NGM Bio is a leader in research elucidating the central role that myeloid cells play in creating a suppressive environment around many solid tumors that restricts antitumor immunity. Myeloid cells often represent the most abundant tumor-associated immune cells and in some tumors, myeloid cells alone account for more than half of the tumor mass[1]. Through systematic screening, NGM Bio identified the suppressive receptors that are most highly enriched in myeloid cells, including four members of the LILR family: ILT2, ILT3, ILT4 and LAIR1. These receptors may play a central role in establishing the immune suppressive state of the tumor microenvironment[2-5].

ILT3 is a fibronectin-binding inhibitory immune receptor that receives signals from the extracellular matrix to directly promote myeloid cell suppression.[6] ILT3 is expressed on a variety of immune cells including tumor-associated myeloid cells, with particularly high expression on tolerogenic dendritic cells, myeloid-derived suppressor cells and M2 macrophages, and high ILT3 expression is associated with poor survival.[7,8] Moreover, fibronectin has been shown to be upregulated in multiple cancers and associated with tumor progression.[9,10] For tumors in which both ILT3 and fibronectin are upregulated, the ILT3-fibronectin pathway may act as a stromal checkpoint to repress myeloid cell function and inhibit anti-tumor immunity. By inhibiting ILT3's interactions with fibronectin and its other ligands, we believe NGM831 has the potential to mobilize a patient's own immune system to fight tumors by shifting myeloid cells from a suppressive state to a stimulatory state and promoting anti-tumor activity. NGM Bio's scientists have made discoveries related to this pathway, including the discovery of fibronectin as ILT3's functional ligand, as described in a publication in *Cancer Immunology Research*, a journal of the American Association for Cancer Research[6].

NGM Bio has one additional oncology program, NGM120, an anti-GFRAL antagonist antibody, currently in a Phase 2 trial for the treatment of patients with metastatic pancreatic cancer.

Abbreviations (in Alphabetical Order)
CRC=colorectal cancer; GFRAL=Glial Cell-Derived Neurotrophic Factor Receptor Alpha-Like; ILT2=Immunoglobin-Like Transcript 2; ILT3=Immunoglobin-Like Transcript 3; ILT4=Immunoglobin-Like Transcript 4; LILR= Leukocyte Immunoglobin-Like Receptor [ILT2 = LILRB1, ILT3=LILRB4, ILT4=LILRB2]; LAIR1=Leukocyte-Associated Immunoglobulin-Like Receptor 1; NSCLC=non-small cell lung cancer; RCC= renal cell carcinoma; and SCCHN=squamous cell carcinoma of the head and neck.

About NGM Biopharmaceuticals, Inc.

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," "anticipates," "preliminary," "enable," "believed," "designed," "engineered to," "suggesting," "suggest," "look forward," "see," "potentially," "potential," "promise," "goal," "planned," "plans," "aspire," "aim" 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 to enable the more effective treatment of multiple cancers; NGM Bio's belief that releasing myeloid checkpoints and reprogramming myeloid cells can enhance anti-tumor immunity and the potential of its product candidates to harness that biology; the role of ILT3 in establishing an immune suppressive state; NGM831's potential to block the interaction of ILT3 with fibronectin and to mobilize a patient's own immune systems to fight tumors by shifting myeloid cells from a suppressive state to a stimulatory state; the design of NGM Bio's clinical trials; the planned commencement of a Phase 1 clinical trial of NGM438 and the anticipated timing thereof; the ability to enroll patients in and related timing for the Phase 1 clinical trial of NGM831; the availability and anticipated timing of data from the Phase 1a trial of NGM707 and expected enrollment; NGM Bio's plans to implement a robust biomarker strategy across the NGM707, NGM831 and NGM438 clinical development programs to help inform target patient populations for each product candidate; 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 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 quarter and year ended December 31, 2021 filed with the United States Securities and Exchange Commission (SEC) on March 1, 2022 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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