NGM Bio Initiates Expansion of Ongoing Phase 1b Proof-of-Concept Study of NGM120 in Patients with Metastatic Pancreatic Cancer

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--Placebo-controlled study to evaluate potential of NGM120, a novel inhibitor of GDF15/GFRAL pathway, to treat cancer and cancer-related cachexia--

--Cachexia, a wasting syndrome, is a common co-morbidity of cancer and associated with shortened survival--

--Expansion follows completion of enrollment in open-label dose-escalation safety portion of Phase 1a/1b study in patients with select advanced solid tumors and metastatic pancreatic cancer--

--NGM120 program builds on discoveries by NGM scientists related to GDF15 pathway biology, including identifying its cognate receptor, GFRAL--

SOUTH SAN FRANCISCO, Calif., March 02, 2021 (GLOBE NEWSWIRE) -- NGM Biopharmaceuticals, Inc. (Nasdaq: NGM), a biotechnology company focused on discovering and developing transformative therapeutics for patients, today announced it has dosed the first patient in an expansion of its ongoing Phase 1b proof-of-concept study of NGM120 in patients with metastatic pancreatic cancer. NGM120 is an antagonistic antibody that binds glial cell-derived neurotrophic factor receptor alpha-like (GFRAL) and inhibits growth differentiation factor 15 (GDF15) signaling. This placebo-controlled study will evaluate the effect of NGM120 on both cancer and cancer-related cachexia. Cachexia is the uncontrolled wasting of both skeletal muscle and fat linked to many cancers. It is estimated to affect 60% to 80% of advanced cancer patients and to be responsible for approximately 30% of all cancer deaths[1]. This proof-of-concept expansion represents a pre-planned progression of an ongoing Phase 1a/1b dose-finding clinical trial NGM is conducting in patients with select advanced solid tumors and metastatic pancreatic cancer.

NGM is a leader in research elucidating the central role of the GDF15/GFRAL pathway in promoting tumor-associated appetite regulation, metabolic regulation and immune modulation. Through systematic screening of human secreted factors in preclinical models, NGM identified that GDF15 expression has the ability to promote an outsized effect in weight loss. Evidence has also shown that serum levels of GDF15 are elevated in patients with a number of tumor types, including non-small cell lung cancer, melanoma, pancreatic, prostate, colorectal, gastric, esophageal and ovarian cancer, and are associated with a worse prognosis in multiple cancers.

As published in *Nature*, NGM was the first to identify GDF15's cognate receptor, GFRAL, and the associated signaling pathway [2]. This discovery enabled the development of NGM120, a proprietary inhibitory antibody binding to GFRAL that is designed to block the effects of elevated GDF15 levels. In preclinical studies, NGM has demonstrated that blocking the interaction between GDF15 and GFRAL both reduces tumor-associated weight loss and slows tumor growth. In a murine pancreatic tumor model, treatment with NGM120s, an anti-GFRAL antibody similar to NGM120, resulted in greater tumor shrinkage as well as improved survival versus the control arm. In a murine cancer cachexia model, NGM120s rapidly reversed tumor-induced weight loss. In addition, in a murine model of chemotherapy-induced weight loss, administration of NGM120s preserved lean mass and muscle function in animals treated with cisplatin, while treatment with cisplatin alone resulted in greater than 20% weight loss.

"We are pleased to advance NGM120 into a placebo-controlled, Phase 1b expansion in patients with metastatic pancreatic cancer. Patients with this aggressive disease are in particularly dire need of therapeutic solutions to fight their disease and enhance their quality of life," said Alex DePaoli, M.D., Senior Vice President, Chief Translational Officer at NGM. "Our approach of targeting the GDF15 receptor, GFRAL, gives NGM120 a novel profile in the GDF15 inhibition space and enables us to evaluate NGM120 as a potential treatment for both cancer-related cachexia and the underlying cancer."

About the Design of the NGM120 Phase 1b Expansion

In February 2020, NGM initiated a Phase 1a/1b multi-site, open-label, dose-escalation clinical study to evaluate the safety, tolerability and pharmacokinetics of NGM120 as a monotherapy in patients with select advanced solid tumors (Cohort 1) and in combination with gemcitabine and Abraxane® (paclitaxel protein bound) in patients with metastatic pancreatic cancer (Cohort 2). Entry criteria included elevated serum levels of GDF15. Cohorts 1 and 2 are fully enrolled.

The Phase 1b expansion portion of the study will evaluate the safety, tolerability and efficacy of NGM120 as a first-line treatment in 60 patients with metastatic pancreatic cancer. Entry criteria includes elevated serum GDF15 levels. The study is a randomized, single-blind (sponsor unblinded), placebo-controlled, multi-center trial. Patients will be randomized 1:1 to receive either NGM120 or placebo monthly in combination with the first-line standard of care, gemcitabine and Abraxane. The study will have both cancer and cachexia endpoints, including overall response rate (ORR), progression-free survival (PFS), overall survival (OS), body weight change, lean body mass change, patient reported outcomes and functional status changes.

About NGM120

NGM120 is an antagonistic antibody that binds glial cell-derived neurotrophic factor receptor alpha-like (GFRAL) and inhibits growth differentiation factor 15 (GDF15) signaling. NGM scientists have made several important discoveries related to GDF15, including identification of its cognate receptor, GFRAL. GFRAL is expressed in a specific region of the hindbrain, partially outside the blood brain barrier, and is believed to initiate signaling through multiple pathways, including the autonomic nervous system. NGM120 binds with high affinity to GFRAL to prevent the formation of the GDF15 co-receptor complex and its mediated signaling.

About Cachexia

Cachexia is a wasting syndrome common in cancer patients, and a frequent co-morbidity of the disease. Cachexia is associated with increased hospitalization and shortened survival compared to cancer patients who do not exhibit the syndrome. While cachexia can occur in all types of cancer, particularly high incidence rates are observed in pancreatic, gastric, colorectal and esophageal cancers, as well as non-small cell lung cancer. There are no FDA-approved therapies for cachexia.

About NGM Biopharmaceuticals, Inc.

NGM is a biopharmaceutical company focused on discovering and developing novel therapeutics based on scientific understanding of key biological pathways underlying liver and metabolic diseases, retinal diseases and oncology. We leverage our biology-centric drug discovery approach to uncover novel mechanisms of action and generate proprietary insights that enable us to move rapidly into proof-of-concept studies and deliver potential first-in-class medicines to patients. At NGM, we aspire to operate one of the most productive research and development engines in the biopharmaceutical industry, with multiple programs in clinical development. 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 “build,” “plans,” “designed to,” “continue,” “potential” 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 the design, timing, enrollment and potential results of NGM’s Phase 1a/1b clinical trial of NGM120, including the Phase 1b expansion in patients with metastatic pancreatic cancer; the potential of NGM120 as a novel treatment for cachexia and the underlying cancer, as well as its potential to enhance patient quality of life; and the therapeutic effects and benefits of NGM120 and the role of the GDF15/GFRAL pathway. Because such statements deal with future events and are based on NGM’s current expectations, they are subject to various risks and uncertainties, and actual results, performance or achievements of NGM 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 enrolling or completing clinical studies, the risk that the results obtained to date in NGM’s clinical trials may not be indicative of results obtained in subsequent pivotal or other late-stage trials, and the risk that NGM’s ongoing or future clinical studies in humans may show that NGM120 is not a tolerable and effective treatment for cachexia and underlying cancers; the ongoing COVID-19 pandemic, which has adversely affected, and could materially and adversely affect in the future, our business and operations; the time-consuming and uncertain regulatory approval process; NGM’s reliance on third-party manufacturers; the sufficiency of NGM’s cash, cash equivalents and short-term marketable securities and need for additional capital; and other risks and uncertainties affecting NGM and its development programs, as well as those discussed in the sections titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Risk Factors” in our quarterly report on Form 10-Q for the quarter ended September 30, 2020, the section titled “Risk Factors” in exhibit 99.1 to our current report on Form 8-K filed with the United States Securities and Exchange Commission (SEC) on January 6, 2021 and future filings and reports that NGM makes from time to time with the SEC. Except as required by law, NGM 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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1 = Haehlinget al, J. Cachexia Sarcopenia Muscle, 2010
2 = Hsu et. al., Nature 2017