NGM Bio Announces New Clinical Data from Ongoing Trial of NGM707 in Advanced Solid Tumors and Outlines Evolved Strategy for Aldafermin and NGM120 to Focus on Rare Conditions with Significant Unmet Need

January 9, 2024

- Encouraging findings in heavily pretreated patients in multiple solid tumor indications, including MSS colorectal cancer (CRC), in ongoing Phase 1 Part 1b study evaluating NGM707, a dual ILT2/ILT4 antagonist antibody, in combination with KEYTRUDA® (pembrolizumab)

- Aldafermin, an engineered FGF19 analog, has been granted Orphan Drug Designation by the FDA for the treatment of primary sclerosing cholangitis (PSC), a rare liver disease
    - Initiating design of a potential registrational trial of aldafermin in PSC and in discussion with the FDA on utilizing proposed surrogate endpoints with the goal of obtaining accelerated approval
    - Large body of clinical data, including from NGM Bio's prior Phase 2 study in PSC, supports aldafermin's differentiated potential to address the bile acid dysregulation underpinning PSC

- NGM120, a GDF15/GFRAL antagonist, has strong biologic rationale for the treatment of hyperemesis gravidarum
    - Discussing design of an acceptable toxicology package to support clinical trials in hyperemesis gravidarum patients in ongoing dialogue with the FDA
    - Recent evidence suggests this rare, devastating condition is linked to higher levels of, and greater sensitivity to, GDF15 during pregnancy
    - NGM Bio is a long-time pioneer in elucidating GDF15 biology, including identifying its cognate receptor, GFRAL

SOUTH SAN FRANCISCO, Calif., Jan. 09, 2024 (GLOBE NEWSWIRE) -- NGM Biopharmaceuticals, Inc. (NGM Bio) (Nasdaq: NGM), a biotechnology company focused on discovering and developing transformative therapeutics for patients, today announced encouraging new data from an ongoing Phase 1 Part 1b study evaluating NGM707, a dual ILT2/ILT4 antagonist antibody product candidate, in combination with KEYTRUDA® (pembrolizumab). NGM Bio also outlined its strategy to evolve clinical development of its product candidates aldafermin and NGM120 to focus on rare conditions characterized by significant unmet need.

"Our priorities for 2024 center on directing our efforts and investing our resources as efficiently and effectively as possible toward select development activities that we believe have the greatest potential to deliver nearer-term impact and value creation while being fully aligned with our mission to deliver life-changing medicines for patients with significant unmet needs," said David J. Woodhouse, PhD, Chief Executive Officer at NGM Bio.

Dr. Woodhouse continued, "Our focus on the combination of NGM707 and pembrolizumab stems from encouraging responses observed in heavily pretreated patients with very advanced disease, including MSS CRC, that has been largely unresponsive to anti-PD-1/L1 monotherapy. Our interest and efforts in aldafermin in PSC are based on data that we believe supports aldafermin's differentiated potential as an engineered FGF19 analog to address the bile acid dysregulation underpinning this rare liver disease, including our prior Phase 2 study in PSC, as well as our positive clinical study in NASH F4 patients and data from other PSC trials supporting the use of biomarkers of fibrosis, such as ELF, to predict clinical outcomes. Finally, our potential exploration of NGM120, a GDF15/GFRAL antagonist, in a proof-of-concept study for the treatment of hyperemesis gravidarum is rooted in our decade-long efforts advancing the understanding of GDF15 biology and exploring its therapeutic application in a number of disease areas. Recent landmark genetic research confirmed the link between this rare, devastating condition experienced during pregnancy to higher levels of GDF15. Given our deep expertise in GDF15 biology, we believe we are well positioned to potentially pursue this indication for NGM120. As we concurrently pursue these important development efforts, exploring partnering opportunities across our full product candidate and research portfolio, all wholly owned by NGM, remains an important priority for us in 2024."

Key Pipeline Updates

NGM707 in Advanced Solid Tumors

- Announced encouraging new findings from the Phase 1 Part 1b dose escalation cohort of the ongoing Phase 1/2 trial evaluating NGM707 in combination with pembrolizumab for the treatment of patients with advanced or metastatic solid tumors. The combination of NGM707 and pembrolizumab was generally well tolerated at all four dose levels of NGM707. The maximum tolerated dose was not reached.

- The Phase 1 Part 1b cohort enrolled 46 patients as of a November 6, 2023 data-cutoff. Of 37 response-evaluable patients (those completing at least one on-treatment scan), there were four confirmed partial responses (PRs) across multiple indications, including one pathological complete response (CR), and 12 stable disease (SD) (11% overall response rate [ORR] and 43% disease control rate [DCR]). The pathological CR patient had significant target lesion reduction that

allowed subsequent surgical resection of all gross residual disease, resulting in a confirmed pathological CR with no active tumor cells and ctDNA below detection. Three of the four responders had active liver metastases at baseline; patients with liver metastases, which are associated with immune suppression and lower survival rates, tend to have a reduced response to immunotherapy.

- Eight of the 37 response-evaluable patients had MSS CRC; two of these MSS CRC patients were among the confirmed PRs, including the patient with a pathological CR, and two had SD (25% ORR and 50% DCR). Anti-PD-1/L1 monotherapies have shown low or no benefit in MSS CRC patients.

- NGM Bio is completing enrollment in the Phase 1 Part 1b cohort and anticipates providing an update in mid-2024 on the completed cohort and subsequent next steps, including the potential for additional cohorts, which may include MSS CRC patients.

Aldafermin in Primary Sclerosing Cholangitis (PSC)

- Announced planned further development of aldafermin for the treatment of PSC, a rare liver disease that irreparably damages the bile ducts, leading to bile acid dysregulation, which, ultimately, results in serious liver damage. There are currently no FDA-approved therapies for PSC. NGM Bio recently met with the FDA regarding the design of a potential registrational trial, including the utilization of proposed surrogate primary endpoints. NGM Bio plans to continue working with the FDA to reach agreement on a trial design in the coming months, with the goal of initiating trial enrollment by the end of 2024, contingent upon reaching agreement with the FDA on trial design and additional capital availability.

- NGM Bio's decision to pursue the potential further clinical development of aldafermin as a treatment for PSC was informed by a large body of clinical data. Over 800 patients across multiple indications have been treated with aldafermin, which has repeatedly demonstrated powerful bile acid suppression in patients with PSC and NASH, and thus, NGM Bio believes aldafermin has the differentiated potential to directly address the underlying biology of PSC. NGM Bio previously reported data from a randomized, double-blind, placebo-controlled Phase 2 study of aldafermin for the treatment of PSC. While that Phase 2 study did not meet its primary endpoint of statistically significant change in alkaline phosphatase, an exploratory biomarker of PSC disease progression, from baseline to week 12, aldafermin demonstrated both statistically significant improvements in biomarkers of hepatic injury and fibrosis, as well as statistically significant reductions in biomarkers of bile acid synthesis and serum bile acids, consistent with past studies of aldafermin in other liver diseases. The Phase 2 study met the secondary endpoints and was generally well tolerated by patients.

NGM120 in Hyperemesis Gravidarum

- Announced potential development of NGM120 for the treatment of hyperemesis gravidarum (referred to colloquially as hyperemesis), subject to the outcome of ongoing discussions with the FDA. Hyperemesis, a rare, serious condition that affects approximately 100,000 – 150,000 women in the United States each year during pregnancy, is characterized by intractable nausea and vomiting, which then results in dehydration, weight loss and malnutrition. Hyperemesis has a significant physical and psychosocial impact on patients and leads to overall higher rates of fetal loss, preeclampsia, preterm birth, low birth weight and fetal malnutrition. Hyperemesis is the second leading cause of hospitalization in pregnancy (second to preterm labor) and typically recurs in subsequent pregnancies. There are currently no FDA-approved therapies for this condition.

- Research published by an international team that included Marlena Fejzo, Ph.D., Clinical Assistant Professor of Population and Public Health Sciences in the Center for Genetic Epidemiology at the University of Southern California, and Sir Stephen O'Rahilly, M.D. FRS FMedSci, Professor of Clinical Biochemistry and Medicine at the University of Cambridge, found that GDF15 levels increase steadily in early pregnancy and are higher in women who experience nausea and vomiting in pregnancy and hyperemesis. The research uncovered that women with GDF15 genetic variants associated with lower levels of GDF15 in a non-pregnant state are predisposed to hyperemesis. NGM120, a GFRAL antagonist antibody, is designed to block GDF15 signaling and, thereby, may have therapeutic benefit for treating patients suffering from hyperemesis. Dr. Fejzo, who experienced hyperemesis in her own pregnancies and subsequently dedicated her professional life to uncovering the biology underpinning the condition, is serving as an advisor to NGM Bio.

Key 2023 Highlights

Solid Tumor Oncology

- Continued enrollment in a Phase 1 Part 1b cohort of the ongoing Phase 1/2 trial evaluating NGM707 in combination with pembrolizumab for the treatment of patients with advanced or metastatic solid tumors. This cohort is anticipated to complete enrollment in the first half of 2024.

- Completed enrollment in Phase 1 Part 1b cohorts of Phase 1/1b trials evaluating NGM831 and NGM438, respectively, in combination with pembrolizumab in patients with solid tumors. NGM831 is an ILT3 antagonist antibody product candidate, and NGM438 is a LAIR1 antagonist antibody product candidate.

- Initiated an ongoing Phase 1 Part 1c dose finding cohort evaluating the triplet combination of NGM831, NGM438 and pembrolizumab. This cohort is anticipated to complete enrollment in the first half of 2024.

- Completed a Phase 2 randomized, single-blind (investigator-blinded), placebo-controlled, multi-center expansion trial of NGM120 in combination with gemcitabine and Nab-paclitaxel as a first-line treatment in patients with metastatic pancreatic cancer (referred to as the PINNACLES trial). NGM120 was well tolerated in the trial. A clear signal of response was not detected, and further development of NGM120 in oncology has been paused.

Liver and Metabolic Diseases

- Presented positive, comprehensive results from the Phase 2b ALPINE 4 trial of aldafermin in patients with compensated cirrhosis (liver fibrosis stage 4 or F4) due to NASH at AASLD The Liver Meeting® in November 2023. ALPINE 4 met its primary endpoint, with aldafermin 3 mg demonstrating a statistically significant reduction in ELF score compared to placebo at 48 weeks of treatment. Although ALPINE 4 was not statistically powered for the secondary endpoint of histological fibrosis improvement of ≥1-stage (NASH Clinical Research Network, or CRN, criteria), a dose-dependent trend in fibrosis improvement was observed.

- Announced positive data from a Phase 2 investigator-sponsored trial of aldafermin for the treatment of patients with diarrhea-predominant irritable bowel syndrome (IBS-D) and bile acid malabsorption (BAM) in May 2023 at Digestive Disease Week 2023. Aldafermin demonstrated statistically significant reductions in serum 7αC4 (a marker of bile acid synthesis) and fecal bile acids versus placebo in patients with idiopathic BAM with IBS-D.

Key 2024 Priorities and Anticipated Milestones

- Complete enrollment in the Phase 1 Part 1b cohort evaluating the combination of NGM707 and pembrolizumab; provide an update in mid-2024.

- Continue discussions with the FDA on the design of a potential registrational trial of aldafermin for the treatment of PSC and provide an update in the first half of 2024; plan to initiate enrollment by the end of 2024, contingent upon reaching agreement with the FDA on trial design and additional capital availability.

- Plan to initiate a reproductive toxicology study of NGM120 for the treatment of hyperemesis in 2024, subject to ongoing discussions with the FDA.

- Continue exploring partnering opportunities across the full NGM Bio product candidate and research portfolio. NGM Bio may further develop other product candidates in its pipeline, pending partnering and/or the availability of additional capital.

NGM Bio plans to post an updated corporate presentation on the Investor Relations section of NGM Bio's website at www.ir.ngmbio.com.

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. NGM Bio'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. All therapeutic candidates in the NGM Bio pipeline have been generated by its in-house discovery engine, always led by biology and motivated by unmet patient need. Visit us at www.ngmbio.com for more information.

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

Abbreviations (in Alphabetical Order)

F4=Fibrosis stage 4; ILT2=Immunoglobin-Like Transcript 2; ILT3=Immunoglobin-Like Transcript 3; ILT4=Immunoglobin-Like Transcript 4; LAIR1=Leukocyte-Associated Immunoglobulin-Like Receptor 1; MSS=Microsatellite stable; NASH=nonalcoholic steatohepatitis

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 "support", "aims," "anticipates," "believe," "may," "plans," "potential," "promising," "proposed" 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 evolved strategy for aldafermin and NGM120 and focus on rare conditions with unmet needs, and NGM Bio's belief that this strategy has the greatest potential to deliver nearer-term impact and value creation; discussions with the FDA regarding the design of a potential registrational trial of aldafermin in PSC, including the proposed use of surrogate endpoints for potential accelerated approval; NGM Bio's belief that the large body of clinical data supports aldafermin's differentiated potential to

address the bile acid dysregulation underpinning PSC; the potential of aldafermin as an engineered FGF19 analog to address the bile acid dysregulation underpinning PSC; the potential of biomarkers of fibrosis, like ELF, to predict clinical outcome in patients with PSC; the potential of NGM120 to treat hyperemesis; NGM Bio's potential exploration of NGM120 in a planned proof-of-concept study for the treatment of hyperemesis, including ongoing discussions with the FDA on an acceptable toxicology package; the therapeutic potential of, potential indications for and/or planned and continued development of the product candidates in NGM Bio's pipeline, including NGM707, aldafermin, NGM120, NGM831 and NGM438; the planned timing of initiation, enrollment, data readouts and results of NGM Bio's clinical trials; NGM Bio's continued pipeline development, including identification and engagement of third-party partners for potential future business development arrangements ("BD Arrangements") to determine further development of programs across the full NGM Bio product candidate and research portfolio; 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 shift in NGM Bio's strategy and investor perception thereof; the costly and time-consuming pharmaceutical product development process and the uncertainty of clinical success; 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 future trials and that interim topline and preliminary results of clinical trials may change as more participant data becomes available and are subject to audit and verification procedures, which could result in material changes in the final data and such interim topline and preliminary results may not be predictive of final results or results obtained in future trials; the lack of regulatory clarity regarding acceptable surrogate endpoints for PSC and related development uncertainty; the vulnerable patient population experiencing hyperemesis and risks associated with clinical trials on such patient population; uncertainties inherent in the preclinical development process of NGM120 in hyperemesis, including that NGM120 in hyperemesis may never reach clinical development; NGM Bio's ability to identify, attract and engage third-party partners for BD Arrangements; 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 and anticipated cash runway, including the risk that NGM Bio could utilize its available capital resources sooner than it currently expects, and its need for additional capital to pursue further development of its product candidates, including the additional capital necessary for NGM Bio to pursue further development of aldafermin in PSC and NGM120 in hyperemesis; macroeconomic conditions (such as the impacts of global geopolitical conflict, global economic slowdown, increased inflation, high interest rates and recent and potential future bank failures); 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 filed with the United States Securities and Exchange Commission ("SEC") on November 2, 2023 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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