NGM Bio Presents Comprehensive Findings from 24-Week Phase 2 Study (Cohort 4) of Aldafermin in Oral Plenary Presentation at The Digital International Liver Congress™ (ILC) 2020 and Announces Enrollment Completed in Phase 2b ALPINE 2/3 Study

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- *Late-breaker presentation selected as "Best of ILC"*
- *The 24-week Phase 2 study met its primary endpoint, achieving a statistically significant reduction in liver fat content (LFC), and robust fibrosis improvement and resolution of NASH, with a favorable safety profile*
- *New analysis shows 30% placebo corrected anti-fibrotic response rate among NASH patients with more advanced liver fibrosis (F3)*
- *NGM Bio anticipates Phase 2b ALPINE 2/3 study topline data readout in Q2 2021*

SOUTH SAN FRANCISCO, Calif., Aug. 29, 2020 (GLOBE NEWSWIRE) -- NGM Biopharmaceuticals, Inc. (NGM) (Nasdaq: NGM), a biotechnology company focused on discovering and developing transformative therapeutics for patients, today announced that final data from its 24-week Phase 2 study (Cohort 4) of aldafermin 1 mg in patients with non-alcoholic steatohepatitis (NASH) were featured in a late-breaker oral plenary presentation today (LBO-01) at The Digital International Liver Congress™ (ILC) 2020. The presentation included a new analysis of Cohort 4 data from NASH patients with stage 3 liver fibrosis (F3) demonstrating that 1 mg aldafermin had a potent anti-fibrotic effect in these patients with more advanced disease. NGM also announced today that it has completed enrollment in its ongoing Phase 2b ALPINE 2/3 study of 0.3 mg, 1 mg and 3 mg aldafermin versus placebo in patients with biopsy-confirmed NASH with stage 2 (F2) and F3 liver fibrosis. The primary objective of the ALPINE 2/3 study is to evaluate a dose response showing an improvement in liver fibrosis by ≥ 1 stage with no worsening of steatohepatitis at Week 24. NGM expects to report topline findings from the study in the second quarter of 2021.

Efficacy data from a new secondary analysis of patients with advanced liver fibrosis enrolled in the 24-week Phase 2 study (Cohort 4) were included in the aldafermin presentation at Digital ILC. In this patient population, 30% of patients with F3 liver fibrosis treated with aldafermin 1 mg achieved fibrosis improvement ≥1 stage without worsening of NASH compared to 0% in the placebo arm. A responder analysis conducted in patients with F3 liver fibrosis who achieved ≥30% LFC reductions showed that 46% of patients treated with aldafermin 1 mg had fibrosis improvement of ≥1 stage without worsening of NASH compared to 0% of placebo patients.

"We are delighted to present the comprehensive and promising results from the 24-week Phase 2 Cohort 4 study of aldafermin 1 mg in patients with NASH. The four successive cohorts of this Phase 2 study have enabled NGM Bio to amass a robust body of evidence that has consistently demonstrated aldafermin's potential as a transformative agent for patients with NASH and established liver fibrosis," said Stephen A. Harrison, M.D., Medical Director at Pinnacle Clinical Research, Visiting Professor of Hepatology at University of Oxford, UK and principal investigator of the study, who gave the aldafermin presentation at Digital ILC.

Phase 2 24-Week Cohort 4 Key Efficacy Findings

In February 2020, NGM announced positive preliminary topline results from the 24-week double-blind, randomized, placebo-controlled Phase 2 clinical study (Cohort 4) of aldafermin, which enrolled patients with biopsy-confirmed NASH and stage 2 and 3 (F2-F3) liver fibrosis. Cohort 4 was the final reported cohort from NGM's adaptive Phase 2 clinical study of aldafermin in NASH.

Cohort 4 was statistically powered to demonstrate the effect of 1 mg aldafermin treatment versus placebo on the primary endpoint of change in absolute LFC, which achieved statistical significance. In addition, the study assessed secondary and exploratory endpoints of liver histology and biomarkers of disease activity. The histology results revealed that treatment with aldafermin led to clinically meaningful improvements at 24 weeks versus placebo in fibrosis improvement of ≥1 stage with no worsening of NASH (38% of aldafermin-treated patients vs. 18% placebo) and in resolution of NASH with no worsening of liver fibrosis (24% of aldafermin-treated patients vs. 9% placebo). The study also demonstrated a statistically significant impact on the combined endpoint of both fibrosis improvement and resolution of NASH (22% in aldafermin-treated patients vs. 0% placebo).

Summary of Cohort 4 Histology Data[1]		
Proportion of Patients Achieving Endpoints	Aldafermin 1 mg (n=50)	Placebo (n=22)
Fibrosis improvement (≥1 stage) with no worsening of NASH[2]	38%	18%
Resolution of NASH with no worsening of liver fibrosis[3]	24%	9%
Fibrosis Improvement and resolution of NASH[4]	22%*	0%
NAS reduction of ≥2 points with no worsening of liver fibrosis	62%***	9%

*<0.05; ***p<0.001

[1] Per protocol, analyzed using the "liver histologic population," defined as the subset of enrolled patients who had valid, non-missing biopsy data at

both baseline and week 24 (n=72)

[2] Defined as patients having an improvement in liver fibrosis ≥1 stage and having no worsening of hepatocellular ballooning, no worsening of lobular inflammation and no worsening of steatosis from baseline to week 24

[3] Defined as patients having a non-alcoholic fatty liver disease (NAFLD) activity score (NAS) of 0 or 1 for lobular inflammation and 0 for hepatocellular ballooning, with no worsening of fibrosis (no progression of NASH fibrosis stage) from baseline to week 24 (as defined by Clinical Research Network criteria)

[4] Defined as patients having an improvement in liver fibrosis ≥1 stage and having a NAS of 0 or 1 for lobular inflammation and 0 for hepatocellular ballooning at week 24

"As NASH progresses, there is a critical need for a powerful, well-tolerated agent that can rapidly reverse liver fibrosis and resolve NASH to prevent the development of cirrhosis and its complications. In addition to histological efficacy data from earlier Phase 2 cohorts across the spectrum of noncirrhotic NASH, this new analysis suggests that aldafermin also has potential to be an important cornerstone of chronic therapy in more advanced NASH fibrosis," said Hsiao D. Lieu, M.D., Chief Medical Officer at NGM Bio. "These new findings, along with the existing comprehensive Phase 2 efficacy and safety data generated in over 250 NASH subjects, will help further inform and advance our ongoing planning for the aldafermin Phase 3 study."

Phase 2 24-Week Cohort 4 Key Safety and Tolerability Findings

Aldafermin had an overall adverse event profile that was similar to that of placebo, with no meaningful difference in gastrointestinal or pruritus adverse events in aldafermin compared to placebo. Serious adverse events were also similar to placebo (aldafermin 4% versus 12% placebo), with all serious adverse events determined not to be related to treatment by the site investigator. Aldafermin was generally well tolerated and there were no study withdrawals due to adverse events in the aldafermin arm as compared to one withdrawal due to an adverse event in the placebo arm.

A new analysis of lipid data presented at Digital ILC found that the statin use algorithm applied to optimize the lipid management of both aldafermin and placebo patients in Cohort 4 was associated with an overall reduction in the 10-year atherosclerotic cardiovascular disease (ASCVD) risk score for patients participating in the study. The analysis found that the 10-year ASCVD risk score declined from a baseline of 15% to 12% in patients treated with aldafermin at week 24 (compared to a decline from baseline of 12% to 11% in the placebo arm). Over the course of the study, the concomitant use of aldafermin and rosuvastatin led to a mean LDL-C decline of 19 mg/dL in the treatment group versus a mean decline of 16 mg/dL in the placebo group. As noted in the Cohort 4 publication in *Gastroenterology*, triglycerides declined 62 mg/dL in the aldafermin treatment arm vs. 29 mg/dL in placebo. Moreover, the numbers and size of lipoprotein particles did not differ between groups at the end of treatment at week 24. Additional new safety data presented from Cohort 4 showed no effect on blood pressure or heart rate in NASH patients in the treatment arm.

Phase 2 24-Week Cohort 4 Study Design

Cohort 4 was a multi-center, double-blind, randomized, placebo-controlled Phase 2 study evaluating the efficacy, safety and tolerability of 1 mg once-daily subcutaneous injections of aldafermin over 24 weeks of treatment. The study enrolled 78 patients with biopsy-confirmed NASH with F2-F3 liver fibrosis who were randomized 2:1 to receive once-daily aldafermin 1 mg (n=53) or placebo (n=25). The primary endpoint was the treatment effect on absolute LFC as measured by magnetic resonance imaging-estimated proton density fat fraction, or MRI-PDFF, compared to placebo at 24 weeks, with a ≥5% absolute LFC reduction identified as clinically meaningful. Secondary and exploratory endpoints included relative changes in LFC, biomarkers of liver function and effect on liver histology. Patients were also evaluated at week 30 following six weeks off treatment for safety and non-invasive measures.

Liver biopsies were performed at screening and at the end of 24 weeks of treatment and were read using the NASH CRN criteria by one central, independent hepatopathologist who was blinded to patient and treatment assignment. As per protocol, liver biopsy data were analyzed using the "liver histologic population," which was defined as the subset of enrolled patients who had valid, non-missing biopsy data at both baseline and week 24 (n=72). Six patients (three in the aldafermin arm and three in the placebo arm) withdrew prior to the week 24 biopsy for reasons not due to adverse events related to treatment.

Background on the Aldafermin Phase 2 Study

The adaptive Phase 2 aldafermin study included four successive cohorts:

- Cohort 1: a 12-week, multi-center, double-blind, randomized, placebo-controlled study that assessed the efficacy and safety of aldafermin 3 mg and 6 mg once daily through non-invasive measures only;
- Cohort 2: a 12-week, single-blind study that assessed the efficacy and safety of aldafermin 0.3 mg, 1 mg and 3 mg once daily, with the 3 mg dose group including histology endpoints;
- Cohort 3: a 12-week, single-blind study that assessed the efficacy and safety of aldafermin 1 mg once daily, including non-invasive and histology endpoints; and
- Cohort 4: a 24-week, multi-center, double-blind, randomized, placebo-controlled study that assessed the efficacy and safety of aldafermin 1 mg once daily, including non-invasive and histology endpoints.

Key eligibility criteria were similar across study cohorts and included adult patients with biopsy-confirmed NASH, NAS ≥4 (with at least one point in each NAS component of steatosis, lobular inflammation and hepatocellular ballooning), presence of liver fibrosis and ≥8% LFC as measured by MRI-PDFF. Cohorts 1, 2 and 3 enrolled patients with fibrosis stages F1-F3; Cohort 4 enrolled only patients with fibrosis stages F2-F3. Results from Cohort 1 were presented at the International Liver Congress™ in 2017 and published in *The Lancet* in 2018. Data from Cohorts 2 and 3 were presented at the International Liver Congress in 2018 and The Liver Meeting® in 2018 and published in *Hepatology* in 2019. Results from Cohort 4 were presented at the Digital International Liver Congress 2020 and published in *Gastroenterology* in 2020.

About Aldafermin

Aldafermin (formerly NGM282) is an engineered variant of the human hormone FGF19 that is dosed once daily as a subcutaneous injection and has generated robust preclinical and clinical evidence supporting its ability to reduce liver fat content, improve liver function, reverse fibrosis and resolve

NASH by targeting multiple pathogenic pathways of liver disease. NGM has evaluated this wholly-owned therapeutic in over 500 healthy volunteers and patients across multiple liver and metabolic diseases, including more than 200 NASH patients.

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 cancer. 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 “promising,” “suggests,” “aspire,” “advance,” “potential,” “expects,” “anticipates,” “planning” 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 potential of aldafermin as a transformative agent or a cornerstone therapy for patients with NASH and established liver fibrosis; the potential of NGM’s drug discovery approach to deliver first-in-class medicines; the continued progress of, and the timing of enrollment and results of, NGM’s clinical trials, including timing of topline results of the ALPINE 2/3 study; NGM’s ability to advance aldafermin into Phase 3 clinical development for NASH patients; and the safety, tolerability and efficacy of aldafermin. 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 aldafermin is not a tolerable and effective treatment for NASH patients; 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 for aldafermin and its other product candidates; 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 “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our quarterly report on Form 10-Q for the quarter ended June 30, 2020 and future filings and reports that NGM makes from time to time with the United States Securities and Exchange Commission. 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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