NGM Bio Announces Positive Interim Results from Ongoing 24-Week Phase 2 Study Evaluating Aldafermin (NGM282) in Patients with NASH

October 7, 2019

--Treatment with aldafermin 1 mg resulted in statistically significant reductions in absolute and relative liver fat at 24 weeks compared to placebo --

-- Statistically significant improvements also observed across key non-invasive biomarkers of metabolism, inflammation and fibrosis, with favorable tolerability profile --

-- Full 24-week 1 mg Cohort 4 data, including biopsy assessments, anticipated in Q1 2020 --

-- Company to host conference call and webcast at 8:30 a.m. ET (5:30 a.m. PT) --

SOUTH SAN FRANCISCO, Calif., Oct. 07, 2019 (GLOBE NEWSWIRE) -- NGM Biopharmaceuticals, Inc. (Nasdaq: NGM), a clinical stage biotechnology company focused on developing transformative therapeutics for patients, today announced positive preliminary results from a pre-specified interim analysis of the aldafermin 1 mg 24-week Cohort 4, which is the final cohort of an adaptive Phase 2 study evaluating the efficacy, safety and tolerability of aldafermin (formerly NGM282) in patients with biopsy-confirmed non-alcoholic steatohepatitis (NASH).

The Cohort 4 interim analysis demonstrated that once-daily treatment with 1 mg of aldafermin for 24 weeks in patients with stage 2 or 3 (F2-F3) liver fibrosis resulted in a statistically significant change in the absolute liver fat content (LFC) of -7.9% (measured by magnetic resonance imaging-estimated proton density fat fraction, or MRI-PDFF), as compared to -2.0% in the placebo arm ($p<0.05$), and a statistically significant change in relative LFC of -39.6%, as compared to -5.9% in the placebo arm ($p<0.05$). As per the study protocol, results were calculated using least square (LS) mean, which is a statistical approach that adjusts for observed baseline differences. 72% of patients treated with aldafermin achieved a ≥5% absolute reduction in LFC versus 17% for placebo. Similarly, 72% of patients treated with aldafermin achieved a ≥30% relative reduction in LFC versus 17% for placebo. Of the patients treated with aldafermin, 28% achieved a normal LFC after 24 weeks, defined as ≤5% absolute LFC, versus none in the placebo arm. In addition, in assessing biomarkers of liver inflammation and injury, treatment with aldafermin resulted in clinically meaningful reductions in alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Treatment with aldafermin also resulted in a statistically significant reduction in PRO-C3, an exploratory biomarker of liver fibrogenesis, as compared to placebo.

“These 24-week findings are highly consistent with the profound impact on liver fat and key biomarkers of NASH that were reported from the three prior 12-week cohorts of this Phase 2 study,” said Stephen A. Harrison, M.D., Medical Director at Pinnacle Clinical Research, Visiting Professor of Hepatology at University of Oxford, UK and principal investigator on the study. “This interim analysis demonstrated that extended exposure to aldafermin was well tolerated with no withdrawals during the 24-week treatment period. The magnitude of effect on LFC reduction and normalization, combined with the improvement in liver enzymes, reinforce aldafermin’s potential to potently and rapidly reverse multiple aspects of NASH.”

As observed in the prior Phase 2 cohorts, patients treated with aldafermin in the Cohort 4 interim analysis experienced a mean increase of 47.6 mg/dL LDL cholesterol (LDL-C) at week 2 of treatment relative to baseline (103.5 mg/dL), which is consistent with the drug’s mechanism of action and potent FGFR4-mediated CYP7A1 inhibition. As per protocol, when elevation of LDL-C of at least 10 mg/dL was recorded, patients were directed to take an appropriate dose of rosuvastatin daily for the remainder of the study. Concomitant statin use mitigated the drug-induced LDL cholesterol rise, and the mean LDL-C level was below baseline at 24 weeks. In an assessment of other lipid biomarkers, the concurrent use of aldafermin with this statin protocol resulted in a slight increase in HDL-C and a statistically significant decrease in serum triglycerides relative to baseline.

There were no study withdrawals and no serious adverse events in the aldafermin arm of the Cohort 4 interim analysis, as compared to one withdrawal due to an adverse event and two serious adverse events in the placebo arm. The most common adverse events in the aldafermin arm, which were generally mild to moderate, were diarrhea, headache, nausea and arthralgia (joint pain).

“Aldafermin continues to be differentiated with what we believe is an industry-leading profile as a monotherapy for the potential treatment of NASH, as few drugs in development for this disease have shown meaningful metabolic, anti-inflammatory and anti-fibrotic activity,” said Hsiao D. Lieu, M.D., Senior Vice President, Chief Medical Officer of NGM. “Throughout our Phase 2 program, we’ve seen a relationship between aldafermin’s impact on biomarkers of disease and subsequent histology results. To that end, we look forward to the biopsy data readout for Cohort 4, which will further inform planning activities for our Phase 3 study.”

Topline results of the full Cohort 4, which will include an assessment of 24 weeks of treatment on liver histology, are anticipated in the first quarter of 2020.

“We’re pleased with these interim findings, as they represent another milestone in our advancement of aldafermin as an important potential treatment option to address the unmet needs of patients suffering from NASH,” said David J. Woodhouse, Ph.D., Chief Executive Officer of NGM. “This new data set adds to the comprehensive body of clinical evidence supporting the potential commercial profile of aldafermin and its promise as a cornerstone treatment for advanced NASH patients.”

Cohort 4 Study Design

Cohort 4 is an ongoing multi-center, double-blind, randomized, placebo-controlled Phase 2 study evaluating the efficacy, safety and tolerability of 1 mg daily subcutaneous injections of aldafermin over 24 weeks of treatment. The study enrolled 78 patients with biopsy-confirmed NASH with F2-F3 liver fibrosis. The primary endpoint is the treatment effect on absolute changes in LFC as measured by MRI-PDFF compared to placebo. Secondary and exploratory endpoints include relative changes in LFC, biomarkers of liver function and effect on liver histology. The interim analysis of non-invasive measures of efficacy, including LFC, liver transaminases and exploratory fibrosis biomarkers, was conducted when 38 patients completed 24 weeks of treatment.

Preliminary Cohort 4 Interim Analysis Findings

Summary of 24-Week Interim Analysis		
Non-Invasive Measures of NASH (LS mean change from baseline at W24)	**Placebo (n=13)**	**Aldafermin 1 mg (n=25)**
Absolute LFC (%)	-2.0	-7.9*
Relative LFC (%)	-5.9	-39.6*
Patients achieving ≥5% absolute LFC reduction (%)	17	72**
Patients achieving ≥30% relative LFC reduction (%)	17	72**
Patients with normalized (≤5%) LFC (%)	0	28
ALT, relative change (%)	-2	-39**
AST, relative change (%)	-4	-23
PRO-C3, relative change (%) (Exploratory biomarker of fibrogenesis)	+5	-24*
ELF+ score (Exploratory biomarker of fibrosis)	+0.1	-0.2

*p<0.05; **p<0.01, versus placebo (LS mean)
+ ELF = Enhanced liver fibrosis

Background on Comprehensive Phase 2 Aldafermin NASH Program

Phase 2 Study

The adaptive Phase 2 aldafermin study includes four 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;
- **Cohort 2:** a 12-week, single-blind expansion study that assessed the efficacy and safety of aldafermin 0.3 mg, 1 mg and 3 mg once daily, with the 3 mg cohort including histology endpoints;
- **Cohort 3:** a 12-week, single-blind expansion study that assessed the efficacy and safety of aldafermin 1 mg once daily, including histology endpoints; and
- **Cohort 4:** a 24-week, multi-center, double-blind, randomized, placebo-controlled study that is assessing the efficacy and safety of aldafermin 1 mg once daily, including 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 component of steatosis, lobular inflammation and hepatocellular ballooning), presence of liver fibrosis and ≥8% LFC by MRI-PDFF. Cohorts 1, 2 and 3 enrolled F1-F3 liver fibrosis patients, and Cohort 4 enrolled F2-F3 liver fibrosis patients. 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.

Phase 2b ALPINE Studies

NGM is conducting the Phase 2b ALPINE 2/3 clinical study evaluating aldafermin in patients with biopsy-confirmed NASH and F2-F3 liver fibrosis. This 24-week study is expected to enroll approximately 150 patients and will assess the efficacy, safety and tolerability of 0.3 mg, 1 mg and 3 mg of aldafermin compared to placebo. NGM is also in the planning stages for the Phase 2b ALPINE 4 study, which will evaluate aldafermin in NASH patients with well-compensated cirrhosis.

Conference Call / Webcast Details

The company will host a conference call and webcast with slide presentation at 8:30 a.m. ET (5:30 a.m. PT) this morning. The live conference call details are as follows: domestic (844) 873-0551; international (602) 563-8472; and Passcode: 7077749. To access the live webcast and slides, please visit the “Investors & Media” section of NGM’s website at https://ir.ngmbio.com/. The webcast will be archived for 30 days. Archived conference call details are as follows: domestic (855) 859-2056; international (404) 537-3406; and Passcode: 7077749. The archived conference call will be available for 30 days.

About Aldafermin (NGM282)

Aldafermin is an engineered variant of the human hormone FGF19 that is dosed once daily as a subcutaneous injection and is being developed to reduce liver fat content, improve liver function and reverse fibrosis by targeting multiple pathogenic pathways of liver disease. NGM has generated robust preclinical and clinical evidence supporting the ability of aldafermin to resolve disease and reverse fibrosis in NASH patients. This wholly owned therapeutic has been evaluated in multiple Phase 2 studies in primary biliary cholangitis, primary sclerosing cholangitis, type 2 diabetes and NASH.

About NGM Biopharmaceuticals, Inc.

NGM is a clinical stage biopharmaceutical company focused on developing novel therapeutics based on a scientific understanding of key biological pathways underlying cardio-metabolic, liver, oncologic and ophthalmic diseases. The company leverages its biology-centric drug discovery approach to uncover novel mechanisms of action and generate proprietary insights that enable it to move rapidly into proof-of-concept studies and deliver potential first-in-class medicines to patients. NGM aspires to operate one of the most productive research and development engines in the biopharmaceutical industry, with multiple programs in clinical development. Visit http://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 “may,” “will,” “expect,” “anticipate,” “look forward to,” “estimate,” “intend” 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 timing, enrollment and results of Phase 2 clinical studies of aldafermin, and the safety, tolerability and potential 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 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, 2019 and other filings 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.

Investor Contact:

Sylvia Wheeler
swheeler@wheelhouselsa.com
ir@ngmbio.com

Media Contact:

Liz Melone
media@ngmbio.com