



NGM Bio Announces Positive Preliminary Topline Liver Histology and Biomarker Data from 24-Week Phase 2 Study (Cohort 4) of Aldafermin in NASH Patients, Including Statistically Significant Achievement of Composite Endpoint of Both Fibrosis Improvement and Resolution of NASH versus Placebo

February 24, 2020

--Clinically meaningful response rates of 38% of patients treated with aldafermin having liver fibrosis improvement of ≥ 1 stage and 24% of patients achieving resolution of NASH at 24 weeks--

--22% of aldafermin-treated patients versus 0% placebo achieved composite endpoint of both fibrosis improvement and resolution of NASH, a statistically significant result--

--Data support aldafermin's differentiation in the NASH development landscape as a potential potent monotherapy that rapidly improves and sustains liver health with a favorable tolerability profile--

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

SOUTH SAN FRANCISCO, Calif., Feb. 24, 2020 (GLOBE NEWSWIRE) -- NGM Biopharmaceuticals, Inc. (Nasdaq: NGM), a biotechnology company focused on developing transformative therapeutics for patients, today announced positive preliminary topline results from the 24-week double-blind, randomized, placebo-controlled cohort (Cohort 4) of an adaptive Phase 2 study evaluating the efficacy, safety and tolerability of 1 mg aldafermin in patients with biopsy-confirmed non-alcoholic steatohepatitis (NASH) with stage 2 or 3 liver fibrosis (F2-F3). Aldafermin (formerly NGM282), NGM's lead wholly-owned drug candidate, is an engineered variant of the human hormone FGF19 being developed as a once-daily treatment for patients with NASH. Cohort 4 was powered to demonstrate the effect of aldafermin treatment versus placebo on the primary endpoint of change in absolute liver fat content (LFC), which achieved statistical significance. In addition, the study assessed secondary and exploratory endpoints of liver histology and biomarkers of disease activity, many of which also achieved statistical significance.

The histology results revealed that treatment with aldafermin led to clinically meaningful improvements at 24 weeks versus placebo in fibrosis and in resolution of NASH. Treatment with aldafermin 1 mg resulted in a fibrosis improvement of ≥ 1 stage with no worsening of NASH in 38% of patients compared to 18% in the placebo arm. 24% of patients in the aldafermin treatment arm achieved the endpoint of resolution of NASH with no worsening of liver fibrosis as compared to 9% of placebo patients. Of note, 22% of patients in the aldafermin treatment arm versus 0% in the placebo arm achieved the composite endpoint of both fibrosis improvement and resolution of NASH, which was statistically significant. [Draft guidance](#) by the U.S. Food and Drug Administration (FDA) indicates that each of these is an acceptable endpoint for potential accelerated approval in a future pivotal trial.

Patients treated with aldafermin also demonstrated statistically significant improvements in each of the non-alcoholic fatty liver disease (NAFLD) activity score (NAS) components: steatosis, lobular inflammation and hepatocellular ballooning. In addition, a statistically significant proportion of patients in the aldafermin treatment arm (62%) experienced a two-point improvement in total NAS without worsening of fibrosis, compared to the placebo arm (9%).

"To my knowledge, aldafermin is the first drug to demonstrate a robust, statistically significant effect of greater than 20% of patients achieving the FDA composite regulatory endpoint of fibrosis improvement and resolution of NASH versus placebo, as well as show an impressive impact on both of these endpoints independently," 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. "These preliminary results are remarkable and show that aldafermin's rapid and profound effect across all histological measures of NASH previously seen at 12 weeks is sustained, and also suggest that extended treatment may lead to further improvement in liver health. Moreover, these data further strengthen aldafermin's potential as a transformative monotherapy for NASH patients with established fibrosis."

Aldafermin was generally well tolerated with no study withdrawals due to adverse events as compared to one withdrawal due to an adverse event in the placebo arm. The most common adverse events (>10% in either treatment arm) in the study (diarrhea, headache, abdominal distension, nausea, fatigue, diabetes mellitus and peripheral edema) were primarily mild to moderate and occurred with comparable frequency in both the aldafermin and placebo arms. None of the reported serious adverse events (two in the aldafermin arm and three in the placebo arm) was deemed related to treatment by the site investigator.

Hsiao D. Lieu, M.D., Senior Vice President and Chief Medical Officer of NGM, said, "We're very pleased with these data, as they are consistent with the comprehensive body of efficacy and tolerability data generated in over 200 aldafermin-treated NASH patients across our multi-cohort Phase 2 aldafermin program. Given that aldafermin has a promising effect on fibrosis and NASH resolution and is well tolerated, we believe this drug could be a central tool in the future treatment landscape of NASH. We look forward to furthering our Phase 2b clinical development program and advancing aldafermin into pivotal studies."

NGM's ongoing Phase 2b ALPINE 2/3 clinical study is designed to assess the efficacy, safety and tolerability of 0.3 mg, 1 mg and 3 mg of aldafermin compared to placebo in patients with biopsy-confirmed NASH and F2-F3 liver fibrosis. NGM expects to enroll approximately 150 patients in the ALPINE 2/3 study, with data expected in the first half of 2021. In addition, NGM plans to initiate the Phase 2b ALPINE 4 study, which is designed to evaluate aldafermin in NASH patients with F4 liver fibrosis and well-compensated cirrhosis, in the first half of 2020.

“I want to thank our team, all of the investigators, clinical site staff and, most importantly, the patients, whose participation and dedication enabled this important and highly informative Phase 2 clinical exploration of aldafermin,” said David J. Woodhouse, Ph.D., Chief Executive Officer at NGM. “We are committed to delivering powerful new therapies to address some of today’s most widespread and difficult medical challenges. The successful completion of this Phase 2 study brings us a critical step closer to achieving that goal for NASH patients.”

Phase 2 24-Week Cohort 4 Study Design

Cohort 4 is 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.

Patient liver biopsies were performed at baseline 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.

Phase 2 24-Week Cohort 4 Findings

Summary of Cohort 4 Preliminary 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 <u>and</u> resolution of NASH ⁴	22%*	0%
NAS reduction of ≥2 points with no worsening of liver fibrosis	62%***	9%

* p < 0.05; *** p < 0.0001

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 NAS of 0 or 1 for lobular inflammation and 0 for hepatocellular ballooning, with no worsening of fibrosis (no progression of NASH CRN fibrosis stage) from baseline to week 24

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

Non-Invasive Biomarker Data

The study achieved its primary endpoint, demonstrating a statistically significant absolute least square (LS) mean reduction in LFC of 8% and a statistically significant LS mean relative reduction in LFC of 39% in the treatment arm, as compared to reductions of 3% and 13%, respectively, in the placebo arm, as measured by MRI-PDFF. A statistically significant proportion of patients (68%) treated with aldafermin achieved a ≥5% absolute reduction in LFC compared to placebo (24%). Similarly, a statistically significant proportion of patients treated with aldafermin (66%) achieved a ≥30% relative reduction in LFC compared to placebo (29%).

Statistically significant improvements were also observed in the aldafermin treatment arm versus placebo related to biomarkers of liver inflammation and injury (alanine aminotransferase, or ALT, and aspartate aminotransferase, or AST) and PRO-C3. Consistent with the previously announced interim analysis data from this cohort, the reductions in key biomarkers to near normal levels were observed as early as week 2 and sustained through week 24.

As observed in the prior Phase 2 cohorts, the Cohort 4 findings revealed that patients treated with 1 mg of aldafermin experienced a mean increase of 45 mg/dL LDL cholesterol (LDL-C) at week 2 of treatment relative to baseline. This increase is consistent with the drug’s mechanism of action and potent FGFR4-mediated CYP7A1 inhibition. Under the protocol, patients in both the placebo and aldafermin arms who experienced an increase in mean levels of LDL-C of at least 10 mg/dL at week 2 of treatment were directed to take rosuvastatin daily during the treatment period. LDL-C was effectively managed with concomitant statin use, and LDL-C levels for both placebo and aldafermin arms were nearly identical at approximately 77 mg/dL at week 24. In addition, mean serum triglyceride levels were significantly reduced in patients treated with aldafermin versus placebo as early as week 2 and sustained through week 24.

NGM plans to present additional efficacy and tolerability findings of the Phase 2 Cohort 4 data at an upcoming medical meeting.

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 expansion 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 expansion study that assessed the efficacy and safety of aldafermin 1 mg once daily, including non-invasive and histology endpoints; and
- **Cohort 4 (reported today):** 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 $\geq 8\%$ LFC as measured by MRI-PDFF. Cohorts 1, 2 and 3 enrolled F1-F3 liver fibrosis patients. Cohort 4 enrolled only 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 and published in *Hepatology* in 2019.

Conference Call / Webcast Details

NGM 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: 2466937. 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: 2466937. The archived conference call will be available for 30 days.

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 approximately 475 subjects across healthy volunteer studies and studies in primary biliary cholangitis, primary sclerosing cholangitis, type 2 diabetes and NASH.

About NGM Biopharmaceuticals, Inc.

NGM is a 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 <https://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 "preliminary," "believe," "could," "designed," "expect," "future," "look forward to," "plans," "potential," "suggest," "would," 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 safety, tolerability and potential efficacy of aldafermin, including impact on liver health and potential as a monotherapy; the therapeutic potential, effect and differentiation of aldafermin; potential benefits of extended treatment with aldafermin and its potential role in the future treatment landscape for NASH; NGM's expectations as to the endpoints that would potentially be supportive of accelerated approval; NGM furthering its aldafermin development program and advancing aldafermin into pivotal studies; the design, initiation, enrollment and availability of data for NGM's clinical trials and the timing thereof; and other statements that are not historical fact. 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 forward-looking statements in this press release. These risks and uncertainties include, 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 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 time-consuming and uncertain regulatory approval process; NGM's reliance on third-party manufacturers for aldafermin; the sufficiency of NGM's cash resources and need for additional capital; and other risks and uncertainties affecting NGM and its development programs, including those described under the caption "Risk Factors" in NGM's quarterly report on Form 10-Q for the quarter ended September 30, 2019 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.

Investor Contact:

Alexandra Santos
asantos@wheelhouselsa.com
ir@ngmbio.com

Media Contact:

Liz Melone
media@ngmbio.com