Forma Therapeutics Announces Positive FT-4202 600 mg Multiple Ascending Dose Cohort Data Supporting the Doses Being Evaluated in Phase 2/3 Registrational Trial, Called the Hibiscus Study

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Blinded data from the 600 mg dose cohort support the doses (400 mg v 200 mg v placebo) being evaluated in the Hibiscus Study currently enrolling people living with sickle cell disease (SCD)

Doubling the dose of FT-4202 to 600 mg daily for 14 days compared to the previous 300 mg cohort was well-tolerated with no dose-limiting toxicities or treatment-related adverse events observed

Improvements in hematologic (hemoglobin and reticulocytes) and hemolytic (bilirubin and LDH) parameters were comparable to that observed with 300 mg dose, with best response typically at the end of the 14-day treatment period

Across 300 mg and 600 mg cohorts, 10 of 14 (71%) patients on FT-4202 for 14 days achieved a hemoglobin increase ≥ 1 g/dL from baseline

WATERTOWN, Mass.--(BUSINESS WIRE)--Mar. 30, 2021-- Forma Therapeutics Holdings, Inc. (Nasdaq: FMTX), a clinical-stage biopharmaceutical company focused on rare hematologic diseases and cancers, today announced new data from its ongoing randomized, placebo-controlled, multi-center Phase 1 trial of FT-4202 in patients with sickle cell disease (SCD) that further support the development of this novel investigational agent, a selective red blood cell (RBC) pyruvate kinase-R (PKR) activator, as a potential disease-modifying therapy. Data previously presented at the 2020 American Society of Hematology (ASH) Annual Meeting were based on the first cohort of patients in the Phase 1 trial dosed with 300 mg of FT-4202 or placebo once daily for 14 days and a 7-day follow up period. The new findings include an analysis of the blinded data from the second cohort of patients randomly assigned to receive 600 mg of FT-4202 or placebo once daily for 14 days and a 7-day follow up period.

“We are excited to see the favorable safety and tolerability profile of FT-4202 at a 600 mg dose, coupled with the overlap of pharmacodynamic activity and biologic effects across the 300 and 600 mg doses, supporting the evaluation of safety and efficacy at an upper range of 400 mg in our Phase 2/3 trial,” said Patrick Kelly, M.D., chief medical officer of Forma. “These results after only 14 days of treatment support the potential of FT-4202 to treat the underlying pathophysiology of the disease by increasing hemoglobin and reducing hemolysis, which may reduce the number and severity of vaso-occlusive crises SCD patients may experience annually.”

Aggregate findings from the placebo-controlled cohorts of the Phase 1 trial demonstrated 10 of 14 patients (71%) who received FT-4202 achieved a hemoglobin increase of greater than or equal to 1 g/dL from baseline with once-daily dosing of FT-4202 during 14 days of treatment. Based on a trend toward increasing response over the treatment period, the potential exists for additional benefit when dosing beyond 14 days; this is being explored in the ongoing open label extension, which is dosing patients at 400 mg daily for 12 weeks.

The data also showed activation of PKR by FT-4202 increased sickle RBC survival and reduced intravascular hemolysis in patients with SCD based on a reduction in reticulocytes, bilirubin and LDH levels.

Change in hematologic and hemolytic parameters at end of 14-day treatment as compared to baseline in FT-4202-treated patients (median change)

Dose Cohort	**Hb ≥ 1 g/dL**	**Reticulocytes ↓**	**LDH ↓**	**Bilirubin ↓**
300 mg	6/7 (1.2 g/dL)	7/7 (-60%)	6/7 (-36%)	7/7 (-35%)
600 mg	4/7 (1.0 g/dL)	7/7 (-45%)	4/7 (-5%)	7/7 (-41%)
Combined	**10/14 (1.2 g/dL)**	**14/14 (-57%)**	**10/14 (-20%)**	**14/14 (-37%)**

While the data from the 600 mg cohort of patients remain blinded, initial analysis of the cohort suggests FT-4202 has a similar safety and tolerability profile as the 300 mg cohort, despite the doubling of the dose. No dose-limiting toxicities or treatment-related adverse events (AE) were reported, and the overall AE profile of the 600 mg cohort was consistent with the 300 mg cohort.

Unblinded 600 mg cohort data are expected to be reported at an upcoming medical conference in Summer 2021, in addition to initial results from the ongoing open label extension.

Ongoing Trials

The blinded, randomized, placebo-controlled portion of the ongoing Phase 1 study is now complete. People with SCD are now directly enrolling into the 12-week open label cohort receiving 400 mg of FT-4202 daily.

Forma is currently enrolling adults and adolescents with SCD into the Hibiscus Study, a registrational Phase 2/3 randomized, placebo-controlled, double-blind, multicenter trial to further evaluate the safety and efficacy of FT-4202 in this patient population. For more information, please visit

clinicaltrials.gov/NCT04624659.

About Sickle Cell Disease

SCD is one of the most common single-gene disorders and is estimated to affect approximately 100,000 people in the United States, as well as approximately 30,000 in France, Germany, Italy, Spain and the United Kingdom. The National Institutes of Health (NIH) reports that prevalence is estimated at more than 20 million individuals globally. From 2010 to 2050, the annual number of newborns with SCD is expected to rise globally by approximately one-third.[1] Despite recent advances in treatment, most patients with SCD still suffer from pain crises, lifelong disability, significant morbidity and reduced quality of life.

About FT-4202

FT-4202 is a novel investigational selective red blood cell (RBC) pyruvate kinase-R (PKR) activator designed to be a disease-modifying therapy for the treatment of sickle cell disease (SCD). Employing a multimodal approach, FT-4202 is designed to work upstream by activating the RBCs' natural PKR activity to decrease 2,3-DPG levels, which leads hemoglobin to hold on to oxygen molecules longer to reduce RBC sickling. The downstream activity of FT-4202 is designed to increase ATP levels, the fuel that provides energy to cells, to improve RBC health and survival. Together, these effects are anticipated to increase hemoglobin levels and decrease painful vaso-occlusive crises. In preclinical safety studies, FT-4202 did not inhibit aromatase activity or affect steroidogenesis, important biological processes responsible for sexual development. FT-4202 has been granted Fast Track, Rare Pediatric Disease and Orphan Drug designations from the U.S. Food and Drug Administration (FDA), and Orphan Drug Designation from the European Commission based on a positive opinion from the Committee for Orphan Medicinal Products of the European Medicines Agency for the treatment of patients with SCD.

About Forma Therapeutics

Forma Therapeutics is a clinical-stage biopharmaceutical company focused on the research, development and commercialization of novel therapeutics to transform the lives of patients with rare hematologic diseases and cancers. Our R&D engine combines deep biology insight, chemistry expertise and clinical development capabilities to create drug candidates with differentiated mechanisms of action focused on indications with high unmet need. Our work has generated a broad proprietary portfolio of programs with the potential to provide profound patient benefit. For more information, please visit www.FormaTherapeutics.com or follow us on Twitter @FORMAInc and LinkedIn.

Forward-looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, express or implied statements regarding our beliefs and expectations regarding: our ability to complete our ongoing clinical trials for FT-4202, including their timing and success, our expectations of the therapeutic benefits related to FT-4202, whether positive interim results from a clinical study are predictive of the results of ongoing or future clinical studies, our presentation of additional data at upcoming scientific conferences, and other preclinical data in 2021, our expectations around our future regulatory filings and our growth as a company. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, those risks and uncertainties associated with the following: the therapeutic potential of FT-4202, and the timing and success of ongoing clinical trials of FT-4202; positive results from a clinical study may not necessarily be predictive of the results of future or ongoing clinical studies; any one or more of Forma's product candidates may not be successfully developed and commercialized; and other risks identified in our SEC filings, including those risks discussed under the heading "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, as well as other risks detailed in our subsequent filings with the SEC. We caution you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. We disclaim any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this press release represent our views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. We explicitly disclaim any obligation to update any forward-looking statements.

[1] Piel, F. B., Hay, S. I., Gupta, S., Weatherall, D. J., & Williams, T. N. (2013). Global burden of sickle cell anaemia in children under five, 2010-2015: Modelling based on demographics, excess mortality, and interventions. PLOS Medicine, 10(7). Retrieved from link.

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