Updated etavopivat Phase 1 trial results presented in two 2021 ASH Annual Meeting Oral Sessions

Etavopivat was well tolerated with a safety profile consistent with underlying sickle cell disease

Clinical data in 15 patients dosed for up to 12 weeks showed sustained increase in hemoglobin and improvement in biomarkers of hemolysis and red blood cell health

Decreasing vaso-occlusive crisis trend observed during the 12 week treatment period compared to 12 months prior to trial entry

Etavopivat was well tolerated, consistent with safety profile of underlying SCD

Etavopivat multimodal mechanism of action improved biomarkers of RBC health and SCD in exploratory analyses

Significant and sustained improvement in anemia and RBC health

Etavopivat administered for up to 12 weeks reduced anemia by significantly raising and sustaining hemoglobin levels. A hemoglobin increase >1 g/dL was experienced by 73.3 percent (11/15) of patients (p<0.0001), with a maximal mean increase of 1.5 g/dL.

Etavopivat therapy also significantly increased the lifespan of RBCs and decreased hemolysis, as measured by three biomarkers that together indicate enhanced survival of RBCs. Durability of these improvements was sustained throughout the 12 weeks of treatment: absolute reticulocyte count (ARC, p<0.05), indirect bilirubin (p<0.0001), and lactate dehydrogenase (p<0.05).

Etavopivat was well tolerated, consistent with safety profile of underlying SCD

The primary endpoint of the Phase 1 trial was the incidence, frequency, and severity of adverse events (AEs). In the 12-week open-label extension, most AEs were grades 1 and 2. Two patients reported three serious grade 3 AEs on treatment, including a VOC following a COVID-19 infection unrelated to treatment, and a previously reported deep vein thrombosis. During the four weeks post-treatment, three patients reported four serious AEs, all grade 3 and considered unrelated to etavopivat, including VOC, syncope, and acute chest syndrome and VOC following a respiratory infection.

Etavopivat multimodal mechanism of action improved biomarkers of RBC health and SCD in exploratory analyses

Findings from exploratory analyses showed improvements in RBC health and function as measured by biomarkers of SCD during 12 weeks of etavopivat therapy.

Etavopivat’s multimodal mechanism of action via PKR activation resulted in increased adenosine triphosphate (ATP), and decreased 2,3-diphosphoglycerate (2,3 DPG), which was sustained during 12 weeks of etavopivat treatment. Four weeks post-treatment, ATP and DPG levels gradually returned to pre-treatment levels, suggesting the potential durability of etavopivat on RBC health may persist for 1-4 weeks following the treatment period.

Surrogate marker results showed etavopivat normalized the affinity of hemoglobin for oxygen, resulting in improved oxygen release in the peripheral tissues and reducing RBC sickling. Further analysis after two weeks of etavopivat treatment support improved RBC membrane health, with increased levels of two enzymes important to reducing oxidative stress in sickled RBCs: superoxide dismutase activity (SOD, p<0.05) and glutathione reductase activity (GSH, p<0.001), as well as significantly repairing membrane damage, as measured by phosphatidylserine (PS, p<0.01). Additionally, up to 12 weeks of etavopivat showed promising trends in reducing systemic biomarkers of inflammation and coagulation. Significant decreases were observed.
in TNF-alpha (p<0.001), prothrombin 1.2 (p<0.05), and D-dimer (p<0.01). In addition, improved oxygen delivery was observed as measured by significant decreases in erythropoietin levels (p<0.05).

**Oral Presentations Details**

- **Abstract 147091**: Activation of Pyruvate Kinase-R with Etavopivat (FT-4202) Is Well Tolerated, Improves Anemia, and Decreases Intravascular Hemolysis in Patients with Sickle Cell Disease Treated for up to 12 Weeks. Session 114 on Saturday, Dec. 11, at 9:45 a.m. ET. Presenter: R. Clark Brown, M.D., Ph.D.

- **Abstract 147078**: Etavopivat, an Allosteric Activator of Pyruvate Kinase-R, Improves Sickle RBC Functional Health and Survival and Reduces Systemic Markers of Inflammation and Hypercoagulability in Patients with Sickle Cell Disease: An Analysis of Exploratory Studies in a Phase 1 Study. Session: 114 on Saturday, Dec. 11, at 10:00 a.m. ET. Presenter: Theodosia A. Kalfa, M.D., Ph.D.


**Forma Webcast**

Forma is hosting a webcast Monday, Dec. 13 at 8:00 a.m. ET to discuss these etavopivat results being presented at the ASH Annual Meeting. The webcast can be accessed in the “News & Investors” section of Forma’s website at [www.formatherapeutics.com](http://www.formatherapeutics.com).

**Ongoing Hibiscus Trial**

Forma is enrolling patients aged 12 to 65 years 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 etavopivat in this patient population. The study is enrolling participants in France, Spain, and the United States. For more information, please visit [clinicaltrials.gov/NCT04624659](https://clinicaltrials.gov/NCT04624659).

**About Sickle Cell Disease**

Sickle cell disease (SCD) is a chronic and progressive inherited disorder associated with a decrease in the health and lifespan of red blood cells (RBCs). Individuals living with SCD have RBCs that are crescent shaped, rendering them inflexible, fragile, and unable to effectively deliver oxygen. The health of these sickle RBCs is impaired and characterized by reduced cellular energy, poor deformability, decreased membrane repair, and increased adhesion.

SCD affects approximately 100,000 people in the United States, as well as approximately 30,000 in France, Germany, Italy, Spain, and the United Kingdom. SCD can cause serious health problems, including anemia, fatigue, episodes of pain known as vaso-occlusive crises (VOCs), and chronic, progressive end-organ damage. Despite recent advances in treatment, most patients with SCD still suffer from pain crises, lifelong disability, reduced quality of life, and decreased survival.

**About Etavopivat**

Etavopivat is an investigational, once-daily, selective pyruvate kinase-R (PKR) activator designed to be a disease-modifying therapy with the potential to improve RBC health and transform the lives of people living with SCD. Employing a multimodal approach, etavopivat works by activating the RBCs’ natural PKR activity to decrease levels of the metabolite 2,3-DPG, allowing sickle hemoglobin to hold on to oxygen longer, resulting in decreased polymerization, hemolysis, and sickling. Etavopivat-mediated PKR activation also increases adenosine triphosphate (ATP) levels, to improve RBC function, which can lead to improved deformability, capacity for membrane repair, RBC health, and lifespan. Together, these effects are anticipated to improve the health of sickle RBCs and lead to a reduction in anemia, hemolysis, vaso-occlusive crises, and end organ damage.

The need for new SCD treatment options is recognized broadly, and the U.S. Food and Drug Administration (FDA) has granted etavopivat Fast Track, Rare Pediatric Disease and Orphan Drug designations. Additionally, etavopivat was granted 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](http://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: future plans for etavopivat, including expectations regarding timing, trial enrollment, success and data announcements of our current ongoing clinical trials; initial results for the etavopivat open label extension cohort of our Phase 1 clinical trial; therapeutic potential, clinical benefits, mechanisms of action as well as tolerability and safety of our product candidates; upcoming milestones and planned additional trials for the company’s product candidates; presentation of data at upcoming scientific conferences; and the potential impact of COVID-19 on patient retention and enrollment, future operations, clinical trials or investigational new drug (IND) applications. 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 impact of the COVID-19 pandemic on the company’s business, operations, patient enrollment and retention, strategy, goals and anticipated milestones; the therapeutic potential of etavopivat; the timing and completion of our Phase 1 clinical study in etavopivat and final audit and quality controlled verification of initial data and related analyses; the timing associated with the initiation or continuation of any trials and success of ongoing clinical trials of etavopivat; our ability to execute on our strategy; 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 our product candidates may not be successfully developed and commercialized; regulatory developments in the United States and foreign countries; our ability to protect and maintain our intellectual property position; the impact of COVID-19 our supply chain and production as well as global economies and financial markets; and our ability to fund operations; as well as those risks and uncertainties set forth more fully under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, to be filed with the U.S. Securities and Exchange Commission (SEC) and subsequent filings with the SEC. 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 our views as of any subsequent date.

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