Imara Announces Interim Analysis Data from Forte Phase 2b Clinical Trial of Tovinontrine (IMR-687) in Transfusion-Dependent Subjects with Beta-thalassemia

November 16, 2021

Positive trend observed in transfusion-dependent subjects treated with higher dose tovinontrine for reduced transfusion burden

Tovinontrine was generally well-tolerated in this patient population

BOSTON, Nov. 16, 2021 (GLOBE NEWSWIRE) -- Imara Inc. (Nasdaq: IMRA), a clinical-stage biopharmaceutical company dedicated to developing and commercializing novel therapeutics to treat subjects suffering from rare inherited genetic disorders of hemoglobin and other serious diseases, today announced data from a pre-specified interim analysis from its ongoing Forte Phase 2b clinical trial of tovinontrine (IMR-687) in transfusion-dependent subjects (TDT) with beta-thalassemia.

“Today’s announcement of the first clinical data exploring tovinontrine’s potential in transfusion-dependent patients with beta-thalassemia marks an important milestone for Imara and patients with beta-thalassemia seeking oral therapies,” said Rahul Ballal, Ph.D., President and Chief Executive Officer of Imara. “We are encouraged by the positive trend for transfusion burden reduction at the higher dose of tovinontrine. Furthermore, we are pleased that the interim data continue to demonstrate a favorable safety and tolerability profile at doses of tovinontrine up to 400 mg once daily. We look forward to a key efficacy analysis, which we expect will occur in the first quarter of 2022, with more subjects treated through 24 weeks. In addition, we are continuing to advance enrollment in the non-transfusion-dependent (NTDT) cohort of the trial and expect to report initial NTDT data in the first half of 2022.”

Highlights of the Forte Phase 2b Interim Analysis
Subjects in the Forte trial were randomized to either a lower dose group (200 mg or 300 mg), higher dose group (300 mg or 400 mg), or placebo, utilizing a pre-defined weight gate. Of the 43 TDT subjects in this interim dataset, 35 completed at least 12 weeks of treatment and were in the analysis population for transfusion burden. Safety data through week 24 from higher and lower dose groups were pooled for this interim analysis to prevent unblinding of the study. The median baseline transfusion burden in each of the higher dose tovinontrine and placebo groups was 7.5 red blood cell (RBC) units/12 weeks. Furthermore, 54% of the subjects in the analysis population (19/35) had the more severe β^0/β^0 genotype.

Interim data from the Forte study demonstrated tovinontrine was well-tolerated, with the most frequent adverse events (≥10% of subjects in pooled tovinontrine dose groups) being nausea, headache and dizziness. Four (9.3%) subjects discontinued due to adverse events considered at least possibly related to study drug.

The proportion of subjects who had a ≥33% reduction in transfusion burden (of at least 2 units) in any 12-week interval as compared to the 12-week interval prior to randomization was greater in the higher dose tovinontrine group (7/8) versus placebo, despite an unexpectedly high response rate in the placebo group (8/12). Lower dose tovinontrine did not show a higher response rate when compared to the placebo group. No substantial differences between groups were observed in transfusion burden response rate using a fixed interval (weeks 13-24). Red blood cell markers are not evaluable in these regularly transfused subjects. Additional data will be presented as part of a key efficacy analysis expected in the first quarter of 2022.

About the Forte Phase 2b Clinical Trial
The Forte study is a 9-month, global, randomized, double-blind, placebo-controlled, multicenter Phase 2b clinical trial evaluating the safety and tolerability of tovinontrine (IMR-687) in approximately 120 adult subjects with beta-thalassemia. Patient randomization is stratified by transfusion-dependent thalassemia (TDT) or non-transfusion-dependent thalassemia (NTDT). The primary objective of the study is safety and tolerability. For TDT subjects, the clinical trial is evaluating the effect of tovinontrine versus placebo in reducing transfusion burden. For NTDT subjects, the clinical trial is evaluating the effect of tovinontrine versus placebo on fetal hemoglobin as well as total hemoglobin. For more information about the Forte trial visit https://www.clinicaltrials.gov/ct2/show/NCT04411082.

The U.S. Food and Drug Administration (FDA) has granted Orphan Drug, Fast Track and Rare Pediatric Disease designations for tovinontrine for the treatment of beta-thalassemia.

About Tovinontrine (IMR-687)
Tovinontrine is a highly selective and potent small molecule inhibitor of phosphodiesterase-9 (PDE9). PDE9 selectively degrades cyclic guanosine monophosphate (cGMP), an active signaling molecule that plays a role in vascular biology and hemoglobin production in red blood cells. Lower levels of cGMP are found in people with sickle cell disease (SCD) and beta-thalassemia and are associated with reduced blood flow, increased inflammation, greater cell adhesion and reduced nitric oxide mediated vasodilation. Blocking PDE9 acts to increase cGMP levels, which is associated with a number of benefits including the potential reactivation of fetal hemoglobin (HbF), a natural hemoglobin produced during fetal development. Increased levels of HbF in RBCs have been demonstrated to improve symptomology and substantially lower disease burden in both patients with SCD and patients with beta-thalassemia.

About Beta-Thalassemia
Beta-thalassemia, a hemoglobinopathy, is a rare inherited red blood cell disorder. The disease can lead to severe anemia, splenomegaly, skeletal abnormalities and iron overload leading to organ failure and early death. The prevalence of beta-thalassemia globally is estimated to be approximately 288,000, with an incidence of 60,000 births per year, and it is especially prevalent in northern Africa, South Asia, Southeast Asia, the Mediterranean region and the Middle East. The total combined prevalence of beta thalassemia in the European Union and United States is estimated to be approximately 19,000 patients.

About Imara

Imara Inc. is a clinical-stage biotechnology company dedicated to developing and commercializing novel therapeutics to treat patients suffering from rare inherited genetic disorders of hemoglobin and other serious diseases. Imara is advancing tovinontrine (IMR-687), a highly selective, potent small molecule inhibitor of PDE9 that is an oral, potentially disease-modifying treatment currently in clinical development for sickle cell disease and beta-thalassemia and preclinical development for heart failure with preserved ejection fraction, or HFpEF. Imara is also advancing IMR-261, an oral activator of nuclear factor erythroid 2–related factor 2, or Nrf2. For more information, please visit www.imaratx.com.

Cautionary Note Regarding Forward-Looking Statements

Statements in this press release about future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute "forward-looking statements" within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements relating to (i) the timing for reporting of additional data from the Company's Forte Phase 2b clinical trials of tovinontrine (IMR-687) in patients with beta-thalassemia and (ii) the Company's beliefs regarding the strength of its clinical data, the therapeutic potential of tovinontrine and advancement of its development programs. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the impact of extraordinary external events, such as the risks and uncertainties resulting from the impact of the COVID-19 pandemic on the Company's business, operations, strategy, goals and anticipated milestones, including its ongoing and planned research activities and ability to readout data from the Forte Phase 2b clinical trial of tovinontrine in beta-thalassemia; the Company's ability to advance the development of tovinontrine under the timelines it projects in current and future clinical trials, demonstrate in any current and future clinical trials the requisite safety and efficacy of tovinontrine; and other factors discussed in the "Risk Factors" section of the Company's most recent Quarterly Report on Form 10-Q, which is on file with the Securities and Exchange Commission and in other filings that the Company makes with the Securities and Exchange Commission in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and the Company expressly disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

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