Imara Announces Results of Interim Analyses of Tovinontrine (IMR-687) Phase 2b Clinical Trials in Sickle Cell Disease and Beta-Thalassemia

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Interim results in Ardent trial for sickle cell disease showed no significant difference in median annualized rate of vaso-occlusive crises in high-dose group versus placebo in an intent-to-treat population

Interim results in Forte trial for beta-thalassemia demonstrated no meaningful benefit in transfusion burden or improvement in most disease-related biomarkers

Tovinontrine was generally well-tolerated across studies

Both Phase 2b clinical trials and further development of tovinontrine in sickle cell and beta-thalassemia to be discontinued

BOSTON, April 05, 2022 (GLOBE NEWSWIRE) -- Imara Inc. (Nasdaq: IMRA) today announced results from interim analyses of its Ardent Phase 2b clinical trial of tovinontrine (IMR-687) in patients with sickle cell disease (SCD) and Forte Phase 2b clinical trial of tovinontrine in patients with beta-thalassemia. Imara also announced that because of the data generated by these interim analyses, the company will discontinue the Ardent and Forte trials as well as the further development of tovinontrine in sickle cell disease and beta-thalassemia.

“We are disappointed in the outcome of both of the interim analyses in our Phase 2b studies for sickle cell disease and beta-thalassemia, and particularly that the Ardent trial interim analysis did not replicate our previously observed positive vaso-occlusive crisis data,” said Rahul Ballal, Ph.D., President and Chief Executive Officer of Imara. “We plan to discontinue both studies during the second quarter. As we do this, we remain deeply grateful to the patients, investigators and their teams for their participation in these trials and to the extended Imara team for their role and dedication in generating the comprehensive interim results."

Dr. Ballal continued, "Moving forward, we plan to consider our strategic options, including development of tovinontrine in heart failure with preserved ejection fraction (HFpEF) as well IMR-261 clinical development plans.”

Ardent Phase 2b Sickle Cell Disease Interim Analysis:
The interim analysis for the Ardent trial was conducted when all participants completed the week 24 assessment or terminated early. The intent-to-treat (ITT) population was used for the primary efficacy analysis, which is a comparison of the median annualized vaso-occlusive crisis (VOC) rate between the high dose tovinontrine group (n=47, once daily oral dose of 300 mg or 400 mg based on patient weight) and placebo group (n=32).

Safety was analyzed across all participants enrolled in the Ardent trial, including the high dose, low dose (n=33, 200 mg or 300 mg once daily oral dose based on patient weight) and placebo groups. Data from the interim analysis demonstrated that tovinontrine was generally well-tolerated, with the most frequent adverse events (≥10% of participants in any treatment group) considered at least possibly related to study drug by the investigator being nausea, headache, dizziness and vomiting. Four (3.6%) participants discontinued prior to week 24 due to adverse events.

The median annualized VOC rate in the placebo group was 2.02 VOCs per year and was 1.89 VOCs per year in the high dose tovinontrine group, for a treatment difference of 0.13 VOCs per year, or 6.4%. Based on the minimal decrease observed in VOCs with the high dose and low VOC rate in the placebo arm, Imara enacted an addendum to the statistical analysis plan for the trial and noted trends of VOC benefit with tovinontrine. The median annualized rate of VOCs in the low dose tovinontrine group was zero, as compared to 2.02 in the placebo group, and as compared to placebo, the low dose tovinontrine group experienced an increase in median time to first VOC and a higher proportion of participants who were VOC-free. A trend for lower median annualized rate of VOCs was also observed for participants in the high and low dose tovinontrine groups on monotherapy (not on background hydroxyurea) as compared to placebo. Although these additional data are encouraging, none were statistically significant. In addition, no meaningful difference was observed in fetal hemoglobin (HbF) response in either the high or low dose tovinontrine groups as compared to placebo. Collectively, the overall additional data did not materially increase the likelihood of success for this trial.

Forte Phase 2b Beta-thalassemia Interim Analysis:
The Forte trial interim analysis evaluated safety and biomarker data for both transfusion-dependent thalassemia (TDT) and non-transfusion-dependent thalassemia (NTDT) cohorts, as well as data on transfusion burden reduction in the TDT cohort. In both cohorts, tovinontrine was well-tolerated, with the most frequent adverse events (≥10% of participants in any treatment group) considered at least possibly related to study drug by the investigator being nausea and headache. One NTDT and eight TDT participants (3.3% and 10.8%, respectively) discontinued study drug due to adverse events.

Participants in the TDT cohort of the Forte trial were randomized to either placebo (n=20), low dose (n=25, 200 mg or 300 mg) or high dose (n=29, 300 mg or 400 mg). No meaningful benefit was observed in transfusion burden in either tovinontrine group when compared to placebo. Participants in the NTDT cohort of the Forte trial were randomized to either placebo (n=7), low-dose group (n=8, 200 mg or 300 mg), or high-dose group (n=14, 300 mg or 400 mg). No meaningful improvements were observed in most disease-related biomarkers, including total hemoglobin (Hb).

About the Ardent Phase 2b Clinical Trial
The Ardent study was a randomized, double-blind, placebo-controlled, multicenter Phase 2b study in adult patients with sickle cell disease (SCD) randomized to either placebo, low-dose tovinontrine (200 mg or 300 mg) or high-dose tovinontrine (300 mg or 400 mg). The primary efficacy endpoint was annualized rate of VOCs in participants dosed with high dose tovinontrine as compared to placebo. The key secondary endpoints were time to first VOC and proportion of participants with fetal hemoglobin (HbF) response, defined as an absolute increase from baseline of at least 3% in HbF in the high dose group vs placebo.

About the Forte Phase 2b Clinical Trial
The Forte study was a randomized, double-blind, placebo-controlled, multicenter Phase 2b clinical trial evaluating the safety and tolerability of

tovinontrine in adult patients with beta-thalassemia. Patient randomization was stratified by transfusion-dependent thalassemia (TDT) or non-transfusion-dependent thalassemia (NTDT). The primary objective of the study was safety and tolerability. For TDT participants, the clinical trial also evaluated the effect of tovinontrine versus placebo in reducing transfusion burden. For NTDT participants, the clinical trial also evaluated the effect of tovinontrine versus placebo on fetal hemoglobin as well as total hemoglobin.

About Tovinontrine (IMR-687)
Tovinontrine is a highly selective and potent small molecule inhibitor of phosphodiesterase-9 (PDE9). Tovinontrine has a multimodal mechanism of action that acts on red blood cells, white blood cells, adhesion molecules and blood vessels. PDE9 selectively degrades cyclic guanosine monophosphate (cGMP), an active signaling molecule that plays a role in vascular biology.

About Imara
Imara Inc. is a clinical-stage biotechnology company dedicated to developing and commercializing novel therapeutics to treat patients suffering from serious diseases. Imara is considering development plans for tovinontrine in heart failure with preserved ejection fraction (HFpEF), as well as for 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 the Company’s plans to discontinue the Ardent and Forte clinical trials of tovinontrine and the Company’s future strategy, prospects and plans, including for tovinontrine in HFpEF and for IMR-261. 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; the risk that the Company may not be able to successfully implement its strategic plans; the Company’s ability to advance the development of its product candidates under the timelines it projects in current and future clinical trials and to demonstrate in any current and future clinical trials the requisite safety and efficacy of such product candidates; and other factors discussed in the “Risk Factors” section of the Company’s most recent Annual Report on Form 10-K, 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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