Imara Announces Primary Endpoint Change in the Ardent Phase 2b Clinical Trial of Tovinontrine (IMR-687) in Sickle Cell Disease

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Primary endpoint to be changed to annualized rate of VOCs following written U.S. Food and Drug Administration recommendation

No change to conduct or size of trial planned; Ardent trial remains on track for interim analysis of VOC rates in first quarter of 2022

BOSTON, Nov. 22, 2021 (GLOBE NEWSWIRE) -- Imara Inc. (Nasdaq: IMRA), a clinical-stage biopharmaceutical company dedicated to developing and commercializing novel therapeutics to treat patients suffering from rare inherited genetic disorders of hemoglobin and other serious diseases, today announced a change to the primary endpoint for the Ardent clinical trial, a Phase 2b study of tovinontrine (IMR-687) in patients with sickle cell disease (SCD), based on the recommendation of the U.S. Food and Drug Administration (FDA).

Imara requested feedback from the FDA on the draft statistical analysis plan (SAP) for the Ardent trial in which fetal hemoglobin (HbF) response was the primary endpoint and annualized rate of vaso-occlusive crises (VOCs) was the key secondary endpoint. In reviewing the Ardent draft SAP and prior to any database lock for analysis, the FDA recommended that Imara change the primary endpoint to be annualized rate of VOCs. HbF response will continue to be evaluated as a key secondary endpoint. The endpoint revisions do not affect the conduct of the trial or operational aspects of the study. As part of its recommendation, the FDA suggested further interactions regarding the revised SAP and engagement on the potential of the current program for regulatory decision-making.

“We welcome the FDA’s recommendations and are in the process of changing the primary endpoint of the Ardent trial to be annualized rate of VOCs and moving HbF response to be a key secondary endpoint,” said Rahul Ballal, Ph.D., President and Chief Executive Officer of Imara. “A reduction in VOC rate is an established approval endpoint, and we are engaging the FDA further on this and related topics, including possible streamlined paths to registration.”

Dr. Ballal continued, “In light of this endpoint revision, the previously planned fourth quarter interim analysis will no longer occur. That interim analysis had been designed to have a focus on safety and pharmacodynamic biomarkers, including HbF, but did not include a review of VOCs. The first review of data from the Ardent trial, including annualized VOC rate, will be conducted when all subjects have completed assessment at Week 24 or terminated early, and is planned for the first quarter of 2022, subject to our upcoming discussions with the FDA. Final data analysis from the Ardent trial remains on track for the second half of 2022. In June 2021, we reported promising data from our Phase 2a and open label extension clinical trials in SCD that demonstrated reduced annualized rates of VOCs in patients treated with tovinontrine versus placebo. We expect to present updated 12-month VOC data from our ongoing Phase 2a open label extension clinical trial at the American Society of Hematology Annual Meeting in December 2021.”

About the Ardent Phase 2b Clinical Trial
The Ardent Phase 2b clinical trial is a fully-enrolled, global, randomized, double-blind, placebo-controlled, multicenter study with approximately 115 adult patients with sickle cell disease (SCD) enrolled. The planned primary efficacy objective will be to evaluate the annualized rate of vaso-occlusive crises (VOCs) in patients dosed with tovinontrine (IMR-687) as compared to placebo. A key secondary endpoint will be to evaluate the proportion of all patients with fetal hemoglobin (HbF) response, defined as an absolute increase from baseline of at least 3% in HbF, as compared to placebo. Additional endpoints include the evaluation of the effect of tovinontrine versus placebo on other VOC-related outcome measures, HbF-associated biomarkers, markers of red blood cell hemolysis, white blood cell adhesion markers and quality of life measures over the course of a one-year treatment period. For more information about the Ardent trial visit ClinicalTrials.gov here.

The FDA has granted Orphan Drug, Fast Track and Rare Pediatric Disease designations and the European Commission has granted Orphan Drug designation for tovinontrine for the treatment of SCD.

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 several 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 Sickle Cell Disease
Sickle cell disease (SCD), a hemoglobinopathy, is a rare inherited red blood cell disorder. The disease causes structural abnormalities in hemoglobin that cause red blood cells to become inflexible and elongated, ultimately blocking blood flow to organs, which can lead to vaso-occlusive crises (VOCs). SCD is characterized by debilitating pain, progressive multi-organ damage and early death. The global prevalence of SCD is estimated to be approximately 4.4 million patients, including an estimated 100,000 patients in the United States and 134,000 patients in the European Union.

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 Company's plans to change the primary and secondary endpoints for the Ardent Phase 2b clinical trial of tovinontrine (IMR-687), (ii) the timing for reporting of additional data from the Ardent Phase 2b and open label extension clinical trials of tovinontrine in patients with sickle cell disease and (iii) the Company's planned discussions with the FDA regarding the regulatory pathway for tovinontrine. 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 Ardent Phase 2b and open label extension clinical trials of tovinontrine in sickle cell disease; 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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