oral presentation provides first look at new program, IMR-261, a novel, oral, clinic-ready nuclear factor erythroid 2-related factor 2 (Nrf2) activator

SCD Townes mouse model demonstrates IMR-261 activation of Nrf2 increases HbF and F-cells, reduces VOCs and reduces markers of adhesion and hemolysis

Beta-thalassemia mouse model shows IMR-261 increases hemoglobin and improves ineffective erythropoiesis

BOSTON, Dec. 14, 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 the presentation of data from its nuclear factor erythroid 2-related factor 2 (Nrf2) activator program, IMR-261, at the American Society of Hematology (ASH) Annual Meeting, held December 11-14, 2021.

“I am excited by these preclinical data demonstrating the beneficial effect of IMR-261 in mouse models of sickle cell disease and beta-thalassemia,” said Dr. Betty Pace, Professor of Pediatrics at Augusta University and Director of the Comprehensive Sickle Cell Program Telehealth Center. “Induction of fetal hemoglobin is an effective strategy to ameliorate the pathophysiology of sickle cell disease, and the direct mechanistic role of Nrf2 in fetal hemoglobin reactivation has been established by my lab and other researchers. Nrf2-mediated protection against oxidative stress further highlights the therapeutic potential of IMR-261 for the treatment of hemoglobin disorders and potentially more broadly.”

Preclinical studies evaluated the impact of IMR-261 using in-vitro cell cultures and in-vivo mouse models of sickle cell disease (SCD) and beta-thalassemia. In CD34+ cells from sickle cell and healthy donors, high dose IMR-261 reactivated HbF by approximately 7-fold versus placebo, whereas lower dose IMR-261 reactivated HbF by approximately 4-fold versus placebo. Furthermore, an approximately 3-fold increase in F-cells was seen in both high dose and low dose groups when compared to placebo. In the Townes mouse model of SCD, high dose IMR-261 reactivated HbF by approximately 2.2-fold when compared to placebo (8.3 ng/ml versus 3.7 ng/ml). In addition, high dose IMR-687 significantly decreased select markers of hemolysis and increased hemoglobin (Hb) by approximately 1.1 g/dL when compared to placebo (8.7 g/dL versus 7.6 g/dL).

In a separate experiment in Townes SCD mice that assessed VOC reduction after administration of TNF-alpha, IMR-261 significantly reduced the presence of red blood cells on occluded vessels when compared to placebo. IMR-261 was also tested in a mouse model of beta-thalassemia (HbS(α-th1/α-th1)) and showed significant increases in Hb and reductions in ineffective erythropoiesis at the high dose.

“We are pleased to report robust data with IMR-261 in validated preclinical models of SCD and beta-thalassemia,” said Rahul Ballal, Ph.D., President and Chief Executive Officer of Imara. “IMR-261 also has the potential to work across several areas beyond hemoglobin disorders and we are exploring diseases of iron overload to further expand our portfolio reach. It is exciting to have this clinical-ready asset and we look forward to providing further updates on study plans in 2022.”

IMR-261, formerly known as CXA-10, was previously evaluated by Complexa, Inc. in Phase 2 clinical trials for focal segmental glomerulosclerosis (FSGS) and pulmonary arterial hypertension (PAH). Independent medical literature suggests potential promise in a broad array of RBC diseases, including hemoglobin disorders and iron overload diseases.

**Presentation at the American Society of Hematology (ASH) Annual Meeting:**

**Title:** IMR-261, a Novel Oral Nrf2 Activator, Induces Fetal Hemoglobin in Human Erythroblasts, Reduces VOCs, and Ameliorates Ineffective Erythropoiesis in Experimental Mouse Models of Sickle Cell Disease and Beta-Thalassemia

**Abstract:** 853

**Presenter:** Thiago Trovati Maciel, Ph.D., INSERM, France

The presentation will be available on the Investors section of the [Imara website](https://www.imara.com).

**About IMR-261**
IMR-261 (formerly CXA-10) is an activator of nuclear factor erythroid 2–related factor 2, or Nrf2. Nrf2 coordinates the expression of antioxidant genes in response to oxidative stress, regulates inflammation, inhibits the NF-kB pathway, and reactivates fetal hemoglobin, or HbF. In preclinical sickle cell disease models, IMR-261 significantly increased HbF and F-cells, improved hemolytic markers, and decreased vaso-occlusive crises. In a preclinical beta-thalassemia model, IMR-261 increased hemoglobin and enabled RBC maturation. Imara has initiated work on drug product manufacturing for IMR-261, as it explores potential clinical development paths.

**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.imarax.com](http://www.imarax.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 potential clinical development plans for IMR-261 and beliefs regarding the therapeutic potential of 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, including its ongoing and planned research and development activities; 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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