Imara Reports Phase 2a Clinical Trial Results of IMR-687 in Adult Patients with Sickle Cell Disease

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Promising reductions in rate of VOCs/SCPCs observed in monotherapy IMR-687 treated patients vs. placebo

Biomarker data from both monotherapy IMR-687 and combination IMR-687+HU groups show improvement in markers of hemolysis with variable HbF results

Reductions in hsCRP and NTproBNP in monotherapy IMR-687 treated patients suggest potential for lowering inflammation and cardiac stress in SCD

IMR-687 was well tolerated as a monotherapy and in combination with hydroxyurea

Additional data from Phase 2a open label extension trial and interim results from Ardent and Forte Phase 2b clinical trials expected in 2021

BOSTON, Jan. 06, 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 (Hb), today reported results from its Phase 2a clinical trial of IMR-687 in adult patients with sickle cell disease (SCD).

“I am encouraged by the incremental data from this readout, especially in light of the COVID-19 pandemic challenges,” said Biree Andemariam, M.D., Associate Professor at UConn School of Medicine, Director of the New England Sickle Cell Institute at UConn Health and lead investigator for the Phase 2a trial. “This includes a favorable safety profile of IMR-687, lower rate of VOCs/SCPCs and VOC-related hospitalizations in the Population A1 monotherapy arm and improvements in several biomarker results across both the monotherapy and combination groups. I am also pleased by the reductions in hsCRP and NT-proBNP in the Population A1 monotherapy arm. Both are clinically utilized biomarkers of inflammation and cardiac stress, respectively, and suggest that higher doses of IMR-687 may have novel anti-inflammatory and cardiovascular benefits in sickle cell disease.”

“I would like to thank the patients, sickle cell disease community, and healthcare providers for their participation in this trial, particularly because the COVID-19 pandemic reduced access to clinical centers,” said Rahul Ballal, Ph.D., President and Chief Executive Officer of Imara. “These incremental Phase 2a results start an important year of data readouts at Imara. In the first quarter of 2021, we plan to report updates from our Phase 2a open label extension trial, including results on 10-15 patients. In the second half of 2021, we expect to report interim data from our ongoing higher dose Ardent and Forte Phase 2b clinical trials in sickle cell disease and beta-thalassemia, respectively.”

The Phase 2a clinical trial included a total of 93 treated patients across four different sub-studies and was designed to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and clinical outcomes of escalating doses of IMR-687 administered once daily for 16 to 24 weeks, either as a monotherapy or in combination with hydroxyurea (HU). Overall, the data from the Phase 2a clinical trial demonstrated that IMR-687 was well tolerated as a monotherapy and in combination with HU at all dose levels. There were no observed clinically significant shifts in vital signs or electrocardiogram data, including no hypotension or neutropenia in either the monotherapy or combination arms. Interim data on patients from Populations A and B were previously disclosed, with results from the A1 and B1 populations being reported for the first time.

Monotherapy Sub-studies (A/A1):
*Population A (n=40)***:** Patients received either placebo or IMR-687 at once-daily doses of 50 mg or 100 mg through 12 weeks and then higher doses of 100 mg or 200 mg, respectively, through an additional 12 weeks (24 weeks total).

Population A1 (n=18): Patients received either placebo or IMR-687 at a once-daily dose of 100 mg through 4 weeks and then 200 mg through an additional 20 weeks (24 weeks total).

Combination Sub-studies (B/B1):
Population B (n=21): Patients received either placebo or IMR-687 once-daily at 50 mg on top of a stable dose of standard of care HU, with escalation after 4 weeks to 100 mg for an additional 12 weeks (16 weeks total).

Population B1 (n=14): Patients received either placebo or IMR-687 once-daily at 50 mg on top of a stable dose of standard of care HU, with escalation after 4 weeks to 100 mg for an additional 20 weeks (24 weeks total).

Population A1 (monotherapy)
The most frequent adverse events in the IMR-687 treatment arm included sickle cell anemia with crisis, nausea, headache and back pain and were generally consistent with those observed at two previously reported interim analyses. A 25% lower rate of vaso-occlusive crises/sickle cell-related pain crises (VOCs/SCPCs), as part of the safety analysis, was observed in the IMR-687 treatment group when compared to placebo. 58% of patients (7 of 12, 9 events total) experienced at least one VOC/SCPC in the IMR-687 treatment group as compared to 83% (5 of 6, 14 events total) in the placebo population. Furthermore, the rate of VOC-related hospitalizations was lower in the IMR-687 treatment group when compared to placebo. 33% of patients (4 of 12) experienced one VOC-related hospitalization in the IMR-687 treatment group as compared to 66% (4 of 6) in the placebo population.

Biomarker results showed no meaningful changes in F-cells, fetal hemoglobin (HbF) levels, or Hb levels from baseline through week 24. However, a dose-dependent increase in HbF (1.3% absolute increase) was seen when patients dose escalated from 100 mg to 200 mg, starting after 4 weeks and through 24 weeks. One of seven evaluable patients (14%) in Population A1 recorded an absolute increase in HbF percentage from baseline of greater than 1% (increase of 3.2%). Markers of hemolysis that include percent reticulocytes, absolute reticulocyte count, indirect bilirubin and LDH all improved from baseline in a dose dependent manner, with the greatest improvement occurring when patients were on the 200 mg dose. This trend similarly occurred with high sensitivity C-reactive protein (hsCRP) and amino-terminal pro-brain type natriuretic peptide (NT-proBNP) values. Placebo patients from Population A1 did not have evaluable week 24 PD biomarker results due in part to missing study visits and are therefore not included in the table below. A summary of the mean results from the IMR-687 treatment arm are as follows:

Measure	Baseline Value	Week 24 Value	Percent Change from Baseline to Week 24
HbF percentage (%)	8.8	8.7	-1.1%
F-cell percentage (%)	28.1	28.5	1.4%
Hb (g/dL)	8.8	8.6	-2.3%
Markers of Hemolysis			
Percent reticulocytes (%)	10.4	7.4	-28.8%
Absolute reticulocyte count ($\times 10^9$/L)	296	240	-18.9%
Indirect bilirubin (µmol/L)	61.4	44.0	-28.3%
LDH (IU/L)	397	346	-12.8%
Markers of Inflammation & Cardiac Stress			
hsCRP (mg/L)	10.4	2.5	-75.9%
NTproBNP (ng/L)	685	414	-39.6%

Population B1 (combination therapy)
The most frequent adverse events in the IMR-687+HU treatment arm included headache, sickle cell anemia with crisis and nausea and were generally consistent with those observed in Population A1. There were no meaningful differences in VOCs/SCPCs or VOC related hospitalizations, between the IMR-687+HU and HU+placebo groups.

Biomarker results in IMR-687+HU treated patients showed an overall increase in F-cells and HbF levels from baseline to week 24, while Hb levels did not meaningfully change. Three of the eight evaluable subjects (33%) had absolute increases in HbF percentage of greater than 1%, with a mean absolute increase in HbF percentage of 4.3% in that subset of patients. Dose dependent improvements in several markers of hemolysis were observed from baseline through week 24, with the greatest improvement occurring when patients were on the 100 mg dose. hsCRP and NT-proBNP values through week 24 slightly increased from baseline. There was a single placebo patient from Population B1, as other patients did not have evaluable week 24 PD biomarker data due in part to missing study visits. Therefore, this single patient is not included in the table below. A summary of the mean results from the IMR-687+HU treatment arm are as follows:

Measure	Baseline Value	Week 24 Value	Percent Change from Baseline to Week 24
HbF percentage (%)	18.6	19.8	6.5%
F-cell percentage (%)	58.8	61.4	4.4%
Hb (g/dL)	9.5	9.4	-1.1%
Markers of Hemolysis			
Reticulocytes (%)	7.5	5.3	-29.3%
Absolute reticulocyte count ($\times 10^9$/L)	185	137	-25.9%
Indirect bilirubin (µmol/L)	34.9	37.9	8.6%
LDH (IU/L)	351	340	-3.1%
Markers of Inflammation & Cardiac Stress			
hsCRP (mg/L)	11.5	12.5	8.7%
NTproBNP (ng/L)	284	317	11.6%

Population A/B (monotherapy, combination therapy)
Imara previously reported interim results within Populations A and B. Subsequently, four additional patients completed 24 weeks of dosing in the Population A monotherapy arm. A completers analysis in this group showed that the high dose of IMR-687 (100 mg/200 mg) resulted in a relative increase in F-cell percentage of 13.3% from baseline (p=0.025) and a mean absolute increase in HbF percentage from baseline of 0.9%. Three of the eight evaluable subjects (38%) in Population A recorded absolute HbF percentage increases of greater than 1%, with a mean absolute increase in HbF percentage of 3.1% in that subset of patients.

In Population B, we examined the PK of IMR-687+HU as compared to HU alone. The PK data in the second interim analysis indicated that treatment with IMR-687+HU did not result in changes in HU PK.

Imara anticipates that it will present additional study details at a future medical meeting.

About IMR-687

IMR-687 is a highly selective and potent small molecule inhibitor of PDE9. PDE9 uniquely degrades cyclic guanosine monophosphate (cGMP), an active signaling molecule that plays a role in vascular biology. Lower levels of cGMP are often found in people with sickle cell disease and beta-thalassemia and are associated with impaired blood flow, increased inflammation, greater cell adhesion and reduced nitric oxide-mediated vasodilation.

Blocking PDE9 acts to increase cGMP levels, which are associated with reactivation of fetal hemoglobin, or HbF, a natural hemoglobin produced during fetal development. Increased levels of HbF in red blood cells have been demonstrated to improve symptomology and lower disease burden in patients with sickle cell disease and patients with beta-thalassemia.

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. Imara is currently advancing IMR-687, a highly selective, potent small molecule inhibitor of PDE9 that

is an oral, once-a-day, potentially disease-modifying treatment for sickle cell disease and beta-thalassemia. IMR-687 is being designed to have a multimodal mechanism of action that acts on red blood cells, white blood cells, adhesion mediators and other cell types. 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 (i) plan to release additional data on the Phase 2a clinical trial of IMR-687 in patients with sickle cell disease, (ii) content of, and timing with respect to, the reporting of data from the open label extension clinical trial evaluating IMR-687 in patients with sickle cell disease, (iii) clinical trial design and timing with respect to reporting of data from the Ardent and Forte Phase 2b clinical trials in patients with sickle cell disease and beta-thalassemia and (iv) the Company's beliefs regarding the strength of its clinical data, the tolerability and therapeutic potential of IMR-687 and advancement of its clinical program. 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 conduct and readout data from its ongoing clinical trials of IMR-687; the Company's ability to advance the development of IMR-687 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 IMR-687, replicate scientific and non-clinical data in both subsequent case report readouts and in clinical trials 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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