Geron Announces New Data to be Presented at Upcoming ASH Annual Meeting Highlighting the Potential of RYTELO™ (imetelstat) in Myeloid Hematologic Malignancies

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- New analyses from the IMerge clinical trial suggest that imetelstat demonstrates clinical activity in patients with lower-risk MDS with transfusion-dependent anemia regardless of prior therapy
- Early safety results from the dose escalation phase of the Phase 1 IMproveMF study suggest potential for the tolerability of combination therapy with imetelstat and ruxolitinib in a frontline myelofibrosis patient population

FOSTER CITY, Calif.--(BUSINESS WIRE)-- Geron Corporation (Nasdaq: GERN), a commercial-stage biopharmaceutical company aiming to change lives by changing the course of blood cancer, today announced the publication of abstracts containing new data highlighting the potential of RYTELO™ (imetelstat), a first-in-class telomerase inhibitor, in myeloid hematologic malignancies. Six abstracts have been accepted for presentation at the 66 th American Society of Hematology (ASH) Annual Meeting taking place from December 7-10, 2024, in San Diego, California and virtually.

“We look forward to collaborating with our trial investigators to present meaningful data updates across the imetelstat pipeline, which we believe continue to highlight telomerase inhibition as an important and powerful approach to treating myeloid hematologic malignancies,” said Faye Feller, M.D., Executive Vice President, Chief Medical Officer of Geron.

Lower-Risk Myelodysplastic Syndromes (LR-MDS)

Abstract #352: “Effect of Prior Treatments on the Clinical Activity of Imetelstat in Transfusion-Dependent Patients with Erythropoiesis-Stimulating Agent, Relapsed or Refractory/Ineligible Lower-Risk Myelodysplastic Syndromes”

Oral presentation on Saturday, December 7, 2024 at 4:45 p.m. PT by Uwe Platzbecker, M.D., Department of Hematology, Cellular Therapy, Hemostaseology and Infectious Diseases, Leipzig University Hospital, Leipzig,

Germany

This abstract evaluates the effect of prior treatments on the clinical activity of imetelstat in patients with red blood cell (RBC) transfusion-dependent (TD) LR-MDS in an analysis of imetelstat-treated patients pooled from the IMerge Phase 2, Phase 3 and QTc studies (N=226). The results suggest that imetelstat demonstrates RBC-transfusion-related clinical activity and increases in hemoglobin in these patients regardless of prior therapies, although there are limited data on outcomes in later lines of treatment.

“There are very few treatment options today for patients with lower-risk MDS who have symptomatic anemia and are transfusion dependent, which often results in patients having to cycle through available therapies. By pooling data across the IMerge clinical trial, we sought to understand the potential of treatment with imetelstat for these patients regardless of their prior treatment. Although we have small numbers in some cases, these data have important clinical implications, suggesting that these patients experienced a RBC-transfusion related clinical benefit and improvements in hemoglobin with imetelstat regardless of their prior treatment,” said Dr. Platzbecker.

Therapy received prior to imetelstat treatment*	≥8-week RBC-TI	≥24-week RBC-TI	RBC Transfusion Reduction of ≥4 U/8 weeks	Hb Rise of ≥1.5 g/dL for ≥8 weeks	HI-E (IWG 2018)
ESA (n=204)	40%	28%	64%	33%	43%
Luspatercept (n=35)	29%	20%	69%	29%	26%
Lenalidomide (n=26)	23%	12%	54%	19%	31%
HMA (n=22)	14%	9%	50%	14%	18%

*Prior treatment was not mutually exclusive; patients may have received more than one prior therapy.
RBC-TI, red blood cell-transfusion independence; HI-E, hematologic improvement-erythroid; IWG, International Working Group; Hb, hemoglobin; ESA, erythropoiesis-stimulating agent; HMA, hypomethylating agent.

Additionally, in imetelstat-treated patients ineligible for ESA therapy (n=22) treated in the front-line, 36% and 14% achieved ≥8-week and ≥24-week RBC-TI, respectively, 41% met HI-E, 64% had a transfusion reduction of ≥4 U/8 weeks, and 2% had a Hb rise of ≥1.5 g/dL for ≥8 weeks.

Abstract #4590: “Initial Results from the QTc Substudy of the IMerge Phase 3 Trial Demonstrate Clinically Meaningful Efficacy, Manageable Safety, and Absence of Proarrhythmic Risk in Patients with Lower-Risk Myelodysplastic Syndromes Who Received Prior Therapies Beyond Erythropoiesis Stimulating Agents”

Poster presentation on Monday, December 9, 2024 from 6:00 p.m. - 8 p.m. PT by Rami S. Komrokji, M.D., Vice Chair, Malignant Hematology Department, Moffitt Cancer Center

This abstract reports the first efficacy and safety results from the ventricular repolarization IMerge QTc substudy

conducted per FDA guidance. This substudy differed from the IMerge Phase 3 trial in its crossover design, by allowing prior lenalidomide and HMA therapy besides ESAs and by allowing lower-risk MDS patients with the del(5q) mutation. As of the data cutoff on May 10, 2024, no clinically meaningful effects of imetelstat on cardiac repolarization or other ECG parameters were observed. In the 51 total imetelstat-treated patients (35 randomized and 16 crossover), the median treatment duration was 29.3 weeks and the median (95% CI) duration of RBC-TI among ≥8-week RBC-TI responders was 52.6 weeks (40.9-non estimable). Subgroup analyses showed ≥8-week RBC-TI rates of 30% (7/23) and 50% (14/28) in patients with and without prior luspatercept, 38% (5/13) and 42% (16/38) in patients with and without prior lenalidomide, and 21% (3/14) and 49% (18/37) in patients with and without prior HMA use, respectively. No new safety signals emerged, and in the total imetelstat-treated population, Grade 3/4 neutropenia and thrombocytopenia by laboratory evaluation occurred in 65% (33/51) and 49% (25/51) of patients, respectively, of which most cases resolved to Grade ≤2 within four weeks; incidence was similar to the overall Phase 3 imetelstat-treated population. In this QTc substudy, efficacy and safety of imetelstat were comparable to that shown in the overall population of the IMerge Phase 3 trial, and notably, responses to imetelstat were seen in patients receiving prior treatments including luspatercept, lenalidomide, and HMAs.

Abstract #3210: “Correlation of Patient-Reported Outcomes with Red Blood Cell Transfusion Reduction and Rise in Hemoglobin in Patients with Lower-Risk Myelodysplastic Syndromes in the IMerge Trial”

> Poster presentation on Sunday, December 8, 2024 from 6:00 p.m. - 8 p.m. PT by Mikkael Sekeres, MD, University of Miami Health System and Sylvester Comprehensive Cancer Center

This abstract reports on post-hoc analyses of the patient-reported outcome (PRO) population from the IMerge Phase 3 clinical trial (N=175; 118 treated with imetelstat and 57 treated with placebo). PROs were assessed with validated Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue, Functional Assessment of Cancer Therapy-Anemia (FACT-An), and the Quality of Life in Myelodysplasia Scale (QUALMS) questionnaires. In the ring sideroblast positive (RS+) and RS negative (RS-) groups, respectively, sustained, meaningful improvement in fatigue was achieved by 55% and 43% of imetelstat-treated patients; differences (95% CI) versus placebo appeared to favor imetelstat (9% [−12, 29] for RS+ and 13% [−15, 36] for RS−). Similarly, in patients with prior transfusion burdens of 4-6 U/8 weeks or >6 U/8 weeks, respectively, sustained improvement in fatigue was achieved by 44% and 57% of imetelstat-treated patients; differences (95% CI) versus placebo appeared to favor imetelstat (8% [−15, 29] for 4-6 U/8 weeks and 11% [−13, 34] for >6 U/8 weeks). Similar to the RBC-TI response and improvement in fatigue association, for imetelstat-treated patients with versus in those without a ≥1.5-g/dL increase in hemoglobin lasting ≥8 weeks, improvements in fatigue were seen in 70% (28/40) versus 40% of patients, respectively (31/78; nominal P-value=.003); in those with versus in those without transfusion reduction of ≥4 U/8 weeks, improvements were seen in 69% (49/71) versus 21% of patients (10/47; nominal P-value <.001). The QUALMS and FACT-An analyses suggested that imetelstat maintained QOL and anemia symptoms, while placebo recipients experienced worsening QOL and

anemia symptoms.

“Low quality of life can be one of the most devastating and burdensome impacts of living with lower-risk MDS, particularly when patients are anemic and transfusion-dependent. The sustained improvement in fatigue and maintenance of quality of life and anemia symptoms with imetelstat shown in these post-hoc analyses are meaningful and very encouraging as we aim to improve outcomes for these patients,” Dr. Platzbecker continued.

Myelofibrosis (MF)

Abstract #998: “Trial Update from IMproveMF, an Ongoing, Open-Label, Dose-Escalation and -Expansion, Phase 1/1B Trial to Evaluate the Safety, Pharmacokinetics, and Clinical Activity of the Novel Combination of Imetelstat with Ruxolitinib in Patients with Intermediate-1, Intermediate-2, or High-Risk Myelofibrosis (MF)”

> Oral presentation on Monday, December 9, 2024 at 4:45 p.m. PT by John Mascarenhas, M.D., Professor of Medicine at the Icahn School of Medicine at Mount Sinai

This abstract reports the first safety results from the dose escalation Part 1 of the Phase 1/1B IMproveMF clinical trial, in which 13 patients were enrolled as of July 10, 2024. At least three patients received each dose level of imetelstat and doses of ruxolitinib were individualized per patient. No dose limiting toxicities (DLTs) were observed, and adverse events were consistent with those observed in other clinical trials of imetelstat. Imetelstat and ruxolitinib pharmacokinetic profiles in the combination study were similar to previous monotherapy studies. These early results show potential for the tolerability of the combination of imetelstat and ruxolitinib in this frontline MF patient population.

“These early results support the potential tolerability of imetelstat as a combination therapy and could have significant implications for future development efforts,” continued Dr. Feller.

Acute Myeloid Leukemia (AML) and Higher-Risk Myelodysplastic Syndromes (HR-MDS)

Abstract #3222: “A Phase II Study Evaluating the Efficacy and Safety of Imetelstat in Patients with Advanced Myelodysplastic Neoplasms or AML Failing HMA-Based Therapy - Interim Analysis Results of the IMpress Study”

> Poster presentation on Sunday, December 8, 2024 from 6:00 p.m. - 8 p.m. PT by Uwe Platzbecker, M.D.

This abstract, submitted by Geron collaborators, provides an interim analysis from the Phase 2 IMpress trial, led by the European Myelodysplastic Neoplasms Cooperative Group (EMSCO), which is evaluating imetelstat in patients with HR-MDS or AML, refractory, relapsing or intolerant to either azacitidine or decitabine, or venetoclax plus

azacitidine. Between June and October 2023, 23 patients (6 HR-MDS, 17 AML) received at least one dose of imetelstat with an average of 2.8 doses administered per patient. In this first part of the trial, none of the 23 treated patients reached the primary endpoint visit, which was scheduled after 4 cycles of treatment. Sixteen of these 23 patients reached the preliminary disease assessment visit after two cycles of imetelstat; one patient showed a response in hematologic improvements in the erythroid and platelet lineages (HI-E and HI-P), 7 patients had stable disease and 8 patients had progressive disease. Short-term transient improvement in hematological values was observed in individual cases. In patients on the LR-MDS dosing schedule of every four weeks, imetelstat showed some antiproliferative effects, including a decline in blasts and leukocytes. Overall, no new safety signals occurred beyond those already known for imetelstat. A total of 30 serious adverse events (SAEs) occurred in 18 patients of which 21 SAEs required hospitalizations. Based on the observations in this first cohort, the protocol was amended to a more frequent dosing schedule for a second cohort of patients being enrolled and treated with this modified schedule starting in August 2024.

Abstract #52: “Overcoming Ven/Aza Resistance Through Imetelstat-Mediated Lipophagy in Acute Myeloid Leukemia”

> Oral presentation on Saturday, December 7, 2024 at 10:15 a.m. PT by Claudia Bruedigam, Team Head, Leukaemia Metabolism Laboratory, QIMR Berghofer Medical Research Institute, Queensland, Australia

This abstract, submitted by Geron collaborators, shares pre-clinical data identifying imetelstat-mediated, ferroptosis-associated lipidomic alterations in AML cells that correlate with imetelstat treatment responses in vivo. These mechanistic insights may be leveraged to develop an optimized therapeutic strategy using imetelstat to target venetoclax/azacitidine resistant AML subclones.

About RYTELO™ (imetelstat)

RYTELO™ (imetelstat) is an FDA-approved oligonucleotide telomerase inhibitor for the treatment of adult patients with low-to-intermediate-1 risk myelodysplastic syndromes (LR-MDS) with transfusion-dependent anemia requiring four or more red blood cell units over eight weeks who have not responded to or have lost response to or are ineligible for erythropoiesis-stimulating agents (ESAs). It is indicated to be administered as an intravenous infusion over two hours every four weeks.

RYTELO is a first-in-class treatment that works by inhibiting telomerase enzymatic activity. Telomeres are protective caps at the end of chromosomes that naturally shorten each time a cell divides. In LR-MDS, abnormal bone marrow cells often express the enzyme telomerase, which rebuilds those telomeres, allowing for uncontrolled cell division. Developed and exclusively owned by Geron, RYTELO is the first and only telomerase inhibitor approved by the U.S. Food and Drug Administration.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Thrombocytopenia

RYTELO can cause thrombocytopenia based on laboratory values. In the clinical trial, new or worsening Grade 3 or 4 decreased platelets occurred in 65% of patients with MDS treated with RYTELO.

Monitor patients with thrombocytopenia for bleeding. Monitor complete blood cell counts prior to initiation of RYTELO, weekly for the first two cycles, prior to each cycle thereafter, and as clinically indicated. Administer platelet transfusions as appropriate. Delay the next cycle and resume at the same or reduced dose, or discontinue as recommended.

Neutropenia

RYTELO can cause neutropenia based on laboratory values. In the clinical trial, new or worsening Grade 3 or 4 decreased neutrophils occurred in 72% of patients with MDS treated with RYTELO.

Monitor patients with Grade 3 or 4 neutropenia for infections, including sepsis. Monitor complete blood cell counts prior to initiation of RYTELO, weekly for the first two cycles, prior to each cycle thereafter, and as clinically indicated. Administer growth factors and anti-infective therapies for treatment or prophylaxis as appropriate. Delay the next cycle and resume at the same or reduced dose, or discontinue as recommended.

Infusion-Related Reactions

RYTELO can cause infusion-related reactions. In the clinical trial, infusion-related reactions occurred in 8% of patients with MDS treated with RYTELO; Grade 3 or 4 infusion-related reactions occurred in 1.7%, including hypertensive crisis (0.8%). The most common infusion-related reaction was headache (4.2%). Infusion-related reactions usually occur during or shortly after the end of the infusion.

Premedicate patients at least 30 minutes prior to infusion with diphenhydramine and hydrocortisone as recommended and monitor patients for one hour following the infusion as recommended. Manage symptoms of infusion-related reactions with supportive care and infusion interruptions, decrease infusion rate, or permanently discontinue as recommended.

Embryo-Fetal Toxicity

RYTELO can cause embryo-fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with RYTELO and for 1 week after the last dose.

ADVERSE REACTIONS

Serious adverse reactions occurred in 32% of patients who received RYTELO. Serious adverse reactions in >2% of patients included sepsis (4.2%) and fracture (3.4%), cardiac failure (2.5%), and hemorrhage (2.5%). Fatal adverse reactions occurred in 0.8% of patients who received RYTELO, including sepsis (0.8%).

Most common adverse reactions (≥10% with a difference between arms of >5% compared to placebo), including laboratory abnormalities, were decreased platelets, decreased white blood cells, decreased neutrophils, increased AST, increased alkaline phosphatase, increased ALT, fatigue, prolonged partial thromboplastin time, arthralgia/myalgia, COVID-19 infections, and headache.

Please see RYTELO (imetelstat) full Prescribing Information, including Medication Guide, available at **https://pi.geron.com/products/US/pi/rytelo_pi.pdf**.

About Geron

Geron is a commercial-stage biopharmaceutical company aiming to change lives by changing the course of blood cancer. Our first-in-class telomerase inhibitor RYTELO™ (imetelstat) is approved in the United States for the treatment of certain adult patients with lower-risk myelodysplastic syndromes (LR-MDS) with transfusion-dependent anemia. We are also conducting a pivotal Phase 3 clinical trial of imetelstat in JAK-inhibitor relapsed/refractory myelofibrosis (R/R MF), as well as studies in other hematologic malignancies. Inhibiting telomerase activity, which is increased in malignant stem and progenitor cells in the bone marrow, aims to potentially reduce proliferation and induce death of malignant cells. To learn more, visit **www.geron.com** or follow us on **LinkedIn**.

Use of Forward-Looking Statements

Except for the historical information contained herein, this press release contains forward-looking statements made pursuant to the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. Investors are cautioned that such statements, include, without limitation, those regarding: (i) Geron’s plans to collaborate with trial investigators across the imetelstat pipeline and its belief in telomerase inhibition as an important and powerful approach to treating myeloid hematologic malignancies; (ii) results from an analysis of imetelstat-treated patients pooled from the IMerge Phase 2, Phase 3 and QTc studies that suggests that patients with lower-risk MDS who have

symptomatic anemia and are transfusion dependent experience a clinical benefit with imetelstat regardless of their prior treatment; (iii) observation of sustained improvement in fatigue and maintenance of quality of life and anemia symptoms with imetelstat shown in post-hoc analyses that are meaningful and encouraging; (iv) the potential tolerability of imetelstat as a combination therapy; and (v) other statements that are not historical facts, constitute forward-looking statements. These forward-looking statements involve risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. These risks and uncertainties, include, without limitation, risks and uncertainties related to: (a) whether Geron is successful in commercializing RYTELO (imetelstat) for the treatment of certain patients with LR-MDS with transfusion dependent anemia; (b) whether Geron overcomes potential delays and other adverse impacts caused by enrollment, clinical, safety, efficacy, technical, scientific, intellectual property, manufacturing and regulatory challenges in order to have the financial resources for and meet expected timelines and planned milestones; (c) whether regulatory authorities permit the further development of imetelstat on a timely basis, or at all, without any clinical holds; (d) whether any future safety or efficacy results of imetelstat treatment cause the benefit-risk profile of imetelstat to become unacceptable; (e) whether imetelstat actually demonstrates disease-modifying activity in patients and the ability to target the malignant stem and progenitor cells of the underlying disease; (f) that Geron may seek to raise substantial additional capital in order to continue the development and commercialization of imetelstat; (g) whether Geron meets its post-marketing requirements and commitments in the U.S. for RYTELO for the treatment of patients with LR-MDS with transfusion dependent anemia; (h) whether there are failures or delays in manufacturing or supplying sufficient quantities of imetelstat or other clinical trial materials that impact commercialization of RYTELO for the treatment of patients with LR-MDS with transfusion dependent anemia or the continuation of the IMpactMF trial; (i) that the projected timing for the interim and final analyses of the IMpactMF trial may vary depending on actual enrollment and death rates in the trial; and (j) whether the EMA will approve RYTELO for the treatment of patients with LR-MDS with transfusion dependent anemia and whether the FDA and EMA will approve imetelstat for other indications on the timelines expected, or at all. Additional information on the above risks and uncertainties and additional risks, uncertainties and factors that could cause actual results to differ materially from those in the forward-looking statements are contained in Geron's filings and periodic reports filed with the Securities and Exchange Commission under the heading "Risk Factors" and elsewhere in such filings and reports, including Geron's quarterly report on Form 10-Q for the quarter ended June 30, 2024, and subsequent filings and reports by Geron. Undue reliance should not be placed on forward-looking statements, which speak only as of the date they are made, and the facts and assumptions underlying the forward-looking statements may change. Except as required by law, Geron disclaims any obligation to update these forward-looking statements to reflect future information, events, or circumstances.

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