Keros Therapeutics Presents Clinical Data from its Elritercept Program at the 66th American Society of Hematology Annual Meeting and Exposition

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- *Elritercept demonstrated a durable transfusion independence in lower-risk myelodysplastic syndromes, including in patients with high transfusion burden, with a median duration of response of 134.1 weeks*
- *Durable clinical responses were associated with improvements in patient-reported measures of fatigue in MDS patients early, and with continued improvement over time*
- *Data from ongoing Phase 2 clinical trial in myelofibrosis continue to demonstrate that elritercept can potentially ameliorate ineffective hematopoiesis and address cytopenias, and also provide broader clinical benefit, as supported by observed reductions in spleen volume and improved total symptom scores*

LEXINGTON, Mass., Dec. 09, 2024 (GLOBE NEWSWIRE) -- Keros Therapeutics, Inc. (“Keros” or the “Company”) (Nasdaq: KROS), a clinical-stage biopharmaceutical company focused on developing and commercializing novel therapeutics to treat a wide range of patients with disorders that are linked to dysfunctional signaling of the transforming growth factor-beta (“TGF-ß”) family of proteins, today announced that it presented additional data from its two ongoing Phase 2 clinical trials of elritercept (KER-050), one in patients with very low-, low-, or intermediate-risk myelodysplastic syndromes (“MDS”) and one in patients with myelofibrosis (“MF”), at the 66th American Society of Hematology Annual Meeting and Exposition (“ASH”), held in person in San Diego, California and virtually from December 7-10, 2024.

“The data we presented at ASH supports the differentiated profile of elritercept in both MDS and MF,” said Jasbir S. Seehra, Ph.D., Chair and Chief Executive Officer. “We look forward to commencing enrollment of our Phase 3 RENEW clinical trial evaluating elritercept in adult patients with transfusion-dependent anemia with very low-, low-, or intermediate-risk MDS soon, so that we can take the next step towards bringing this potential treatment option to patients.”

Clinical Presentations

- *Improvements in Hematological Parameters and Quality of Life (“QoL”) with Elritercept: Results from an Ongoing Phase 2 Trial in Participants with Lower-Risk MDS*

This ongoing, open-label, two-part, Phase 2 clinical trial is evaluating elritercept in patients with very low-, low-, or intermediate-risk MDS. As of August 30, 2024 (the “data cut-off date”), 95 patients had received at least one dose of elritercept at the recommended Part 2 dose (“RP2D”) (collectively, the “safety population”). Of these patients in the safety population, 87 had completed at least 24 weeks of treatment or discontinued as of the data cut-off date (collectively, the modified intent-to-treat 24-week population, or the “mITT $_{24}$ patients”). Data for hematological response and markers of hematopoiesis were presented from exploratory analyses of these mITT$_{24}$ patients. All data presented from this trial is as of the data cut-off date.

Of the 95 patients in the safety population, 60.0% (n=57) were high transfusion burden (“HTB”) while 24.2% (n=23) were low transfusion burden and 15.8% (n=15) were non-transfused (“NT”).
Elritercept was generally well-tolerated in the safety population. There were four cases of fatal treatment-emergent adverse events (“TEAEs”) in the trial that were all deemed unrelated to treatment. The most commonly reported TEAEs (in ≥15% of patients) were diarrhea, fatigue, COVID-19, dyspnea, dizziness, anemia, nausea and epistaxis. One patient had progressed to acute myeloid leukemia as of the data cutoff date.

55.2% (n=48/87) of the mITT$_{24}$ patients achieved an overall erythroid response over the first 24 weeks of treatment, which is defined as meeting either modified International Working Group 2006 Hematological improvement-erythroid (“HI-E”) or transfusion independence (“TI”) for at least eight weeks in transfusion-dependent patients who required ≥ 2 red blood cell (“RBC”) units transfused at baseline. The median duration of transfusion independence was 134.1 weeks. Due to ongoing TI responses as of the data cutoff date, the median duration of TI is expected to change as data continues to accumulate. 48.1% (n=13/27) of patients with a TI response had ongoing TI as of the data cutoff date, of which 92.3% (n=12/13) had ongoing TI for greater than 52 weeks.

Additional data from the mITT$_{24}$ patients include:

- 39.1% (n=27/69) of the TI-evaluable patients achieved TI for at least eight weeks over the first 24 weeks of treatment.
- Of the patients with HTB, 31.4% (n=16/51) achieved TI for at least eight weeks during the first 24 weeks of treatment. Eight of those 16 patients (50.0%) achieved TI for at least 24 weeks over the first 48 weeks of treatment.

- Of the TI-evaluable patients with baseline erythropoietin level less than 500 U/L, 47.3% (n=26/55) achieved TI for at least eight weeks over the first 24 weeks of treatment. Of the TI-evaluable patients with baseline erythropoietin level less than 500 U/L and HTB, 38.5% (n=15/39) achieved TI for at least eight weeks over the first 24 weeks of treatment.

The FACIT-Fatigue scale, a measure of self-reported fatigue and its impact upon daily activities and function, was utilized to assess health-related quality of life, including in a subgroup of patients (n=17) achieving TI for at least 24 weeks over the first 48 weeks of treatment. Patients in this subgroup showed clinically meaningful improvements in QoL, and meaningful improvements in FACIT-Fatigue were observed early and generally continued to improve over time in patients with more durable TI responses.

The majority of patients enrolled in this ongoing trial had HTB and/or multi-lineage dysplasia, indicating a difficult-to-treat trial population. Durable TI responses continued to be observed in a broad range of patients with lower-risk MDS, including in those with HTB, which support the potential for elritercept to ameliorate ineffective hematopoiesis across multiple lineages in patients with MDS. These Phase 2 data further support the rationale for the planned Phase 3 RENEW registrational trial of elritercept in transfusion-dependent patients with very low-, low-, and intermediate risk MDS.

- *Hematologic Improvement and Fatigue Reduction with Elritercept in Participants with Lower-Risk MDS with Non-Transfusion Dependent Anemia: New Analyses from an Ongoing Phase 2 Trial*

In a subgroup analysis of patients that were non-transfused (“NT”) at baseline, treatment with elritercept showed:

- Robust hematological responses observed with 93.3% (n=14/15) of NT patients having an increase greater than 1.0 g/dL and 86.7% (n=13/15) having an HI-E response.
- Durable HI-E responses observed with elritercept treatment with 100% (n=13/13) achieving a continuous response duration of greater than 24 weeks and 76.9% (n=10/13) achieving a cumulative response duration greater than 52 weeks.
- Sustained and durable increases in hemoglobin and soluble transferrin receptor, a marker of erythropoietic activity, were observed in NT participants.
- Overall improvement in mean platelet and neutrophil counts along with decreases in mean ferritin and hepcidin were observed after only one dose and were generally maintained through 48 weeks, demonstrating that elritercept has the potential to address ineffective hematopoiesis across multiple lineages and improve iron utilization and reduce inflammation.
- NT patients achieved meaningful improvements in FACIT-Fatigue scores, with improvements seen early, generally within the first two treatment cycles.

- *Hematological Improvement and Other Clinical Benefits of Elrtiercept as Monotherapy and in Combination with Ruxolitinib in Participants with Myelofibrosis from the Ongoing Phase 2 RESTORE Trial*

This ongoing, open-label, two-part Phase 2 clinical trial is evaluating elritercept administered with or without ruxolitinib in patients with MF who have anemia and were either currently on, failed, or ineligible for ruxolitinib at baseline. Safety data are presented for all patients that received at least one dose of elritercept (n=73) as of the August 30, 2024 data cutoff date. Evaluations of markers of hematopoiesis and anemia over 12 weeks, along with measurements of spleen volume and symptom scores (by the MF-symptom assessment form-Total Symptom Score, or “MF-SAF-TSS”) over 24 weeks, were presented for dose levels 1 through 4 in Part 1 and the RP2D, ranging from 0.75 mg/kg to 5.0 mg/kg (collectively, the “efficacy evaluable patients”). Enrollment of Part 1 of the trial, the dose escalation portion, is complete. Part 2, the dose expansion portion, is open and enrolling with an RP2D of 3.75 mg/kg with the option to up-titrate to 5.0 mg/kg. All data presented from this trial is as of the data cutoff date.

Elritercept was generally well-tolerated by the safety population. There were six cases of fatal TEAEs in the trial that were each deemed unrelated to treatment. The most commonly reported TEAEs (in ≥15% of patients) were thrombocytopenia and diarrhea. The majority of treatment-related TEAEs were mild to moderate, with 12 patients experiencing Grade 3 or higher treatment-related TEAEs of thrombocytopenia. 93.3% (n=14/15) of patients with a TEAE of thrombocytopenia had baseline platelets below 150 x 10^9/L.

Additional data from the efficacy evaluable patients include:

- Increases in hemoglobin were observed in 82.8% (n=24/29) of evaluable non-transfusion dependent patients in both arms over a 12-week period within the first 24 weeks, suggesting that elritercept has the potential to address anemia due to MF and ruxolitinib-associated anemia.
- 63.4% (n=26/41) of patients that received at least three RBC units per 12 weeks at baseline in

both arms and all dose levels tested showed reductions in transfusion burden over 12 weeks within the first 24 weeks. 24.4% (n=10/41) of the patients who showed reductions in transfusion burdens achieved TI.
    - Additionally, within the subgroup of these patients in the combination arm who received a starting dose of 3.0 mg/kg of elritercept or higher, 62.5% (n=10/16) had reductions of 50% or greater, and 37.5% (n=6/16) achieved TI.
- At week 24, reduction in spleen volume was observed in 40% (n=8/20) of patients with baseline spleen size ≥ 450 cm^3 and a week 24 spleen assessment, including three patients who had reductions of 35% or greater. Reductions in spleen volume in the combination arm generally occurred without an increase in ruxolitinib dose.
    - For evaluable patients in the combination arm with a starting dose of 3.0 mg/kg of elritercept or higher, 88% (n=7/8) had some reduction in spleen size at week 24
- At week 24, reduction in disease symptoms was observed in 66.7% (n=18/27) of patients with at least two symptoms with an average score ≥ 3 or an average total score of ≥ 10 on the MF-SAF-TSS questionnaire at baseline and a week 24 MF-SAF-TSS assessment. Five patients had reductions of at least 50%, including three in the monotherapy arm and two in the combination arm.

The data support the potential of elritercept to ameliorate ineffective hematopoiesis and address cytopenias due to MF and associated with ruxolitinib, and provide broader clinical benefit in patients, as supported by the observed reduction in spleen volume and improvement in total symptom scores.

About the Ongoing Phase 2 Clinical Trial of Elritercept in Patients with MDS (NCT04419649)

Keros is conducting an open label, two-part, multiple ascending dose Phase 2 clinical trial to evaluate elritercept in patients with very low-, low-, or intermediate-risk MDS who either have or have not previously received treatment with an erythroid stimulating agent.

The primary objective of this trial is to assess the safety and tolerability of elritercept in patients with MDS that are RS positive or non-RS. The primary objective of Part 2 of this trial is confirmation of the safety and tolerability of the RP2D (3.75 mg/kg and 5.0 mg/kg). The secondary objectives of this trial are to evaluate the pharmacokinetics, pharmacodynamics and efficacy of elritercept.

About the Ongoing Phase 2 Clinical Trial of Elritercept in Patients with MF-Associated Cytopenias (RESTORE trial; NCT05037760)

Keros is conducting an open label, two-part, multiple ascending dose Phase 2 clinical trial to evaluate elritercept as a monotherapy and in combination with ruxolitinib in patients with MF-associated cytopenias.

The primary objective of this trial is to assess the safety and tolerability of elritercept in patients with MF-associated cytopenias. The primary objective of Part 2 of this trial is confirmation of the safety and tolerability of the RP2D (3.75 mg/kg and 5.0 mg/kg). The secondary objectives of this trial are to evaluate the pharmacokinetics, pharmacodynamics and efficacy of elritercept administered with or without ruxolitinib.

About Elritercept

Elritercept is an engineered ligand trap comprised of a modified ligand-binding domain of the TGF-ß receptor known as activin receptor type IIA that is fused to the portion of the human antibody known as the Fc domain. Elritercept is being developed for the treatment of low blood cell counts, or cytopenias, including anemia and thrombocytopenia, in patients with MDS and in patients with MF.

About Keros Therapeutics, Inc.

Keros is a clinical-stage biopharmaceutical company focused on developing and commercializing novel therapeutics to treat a wide range of patients with disorders that are linked to dysfunctional signaling of the TGF-ß family of proteins. We are a leader in understanding the role of the TGF-ß family of proteins, which are master regulators of the growth, repair and maintenance of a number of tissues, including blood, bone, skeletal muscle, adipose and heart tissue. By leveraging this understanding, we have discovered and are developing protein therapeutics that have the potential to provide meaningful and potentially disease-modifying benefit to patients. Elritercept is being developed for the treatment of low blood cell counts, or cytopenias, including anemia and thrombocytopenia, in patients with MDS and in patients with MF. Cibotercept (KER-012) is being developed for the treatment of pulmonary arterial hypertension and for the treatment of cardiovascular disorders. KER-065 is being developed for the treatment of obesity and for the treatment of neuromuscular diseases.

Cautionary Note Regarding Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as “expect,” “enable,” “forward,” “potential” and “will” or similar expressions are intended to identify forward-looking statements. Examples of these forward-looking statements include statements concerning: Keros’ expectations regarding the design, objectives, timing, results and outcomes of its clinical trials for elritercept, including the Phase 2 RESTORE trial and the Phase 3 RENEW trial; the differentiated profile of elritercept in both MDS and MF; the potential of elritercept to ameliorate ineffective hematopoiesis across multiple lineages in patients with MDS, improve iron utilization, reduce inflammation and improve quality of life in patients with lower-risk MDS; and the potential of elritercept to address anemia due to MF- and ruxolitinib-associated anemia, and to provide broader clinical benefit to patients with MF. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. These risks and uncertainties include, among others: Keros’ limited operating history and historical losses; Keros’ ability to raise additional funding to complete the development and any commercialization of its product candidates; Keros’ dependence on the success of its product candidates, cibotercept, elritercept and KER-065; that Keros may be delayed in initiating, enrolling or completing any clinical trials; the risk that initial or interim results from a clinical trial may not be predictive of the final results of the trial or the results of future trials; competition from third parties that are developing products for similar uses; Keros’ ability to obtain, maintain and protect its intellectual property; and

Keros' dependence on third parties in connection with manufacturing, clinical trials and preclinical studies.

These and other risks are described more fully in Keros' filings with the Securities and Exchange Commission ("SEC"), including the "Risk Factors" section of the Company's Quarterly Report on Form 10-Q, filed with the SEC on November 6, 2024, and its other documents subsequently filed with or furnished to the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. Except to the extent required by law, Keros undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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