KEROS THERAPEUTICS

Hematology Franchise: Update of Data Presented at 64th Annual Congress of the American Society of Hematology

December 12, 2022

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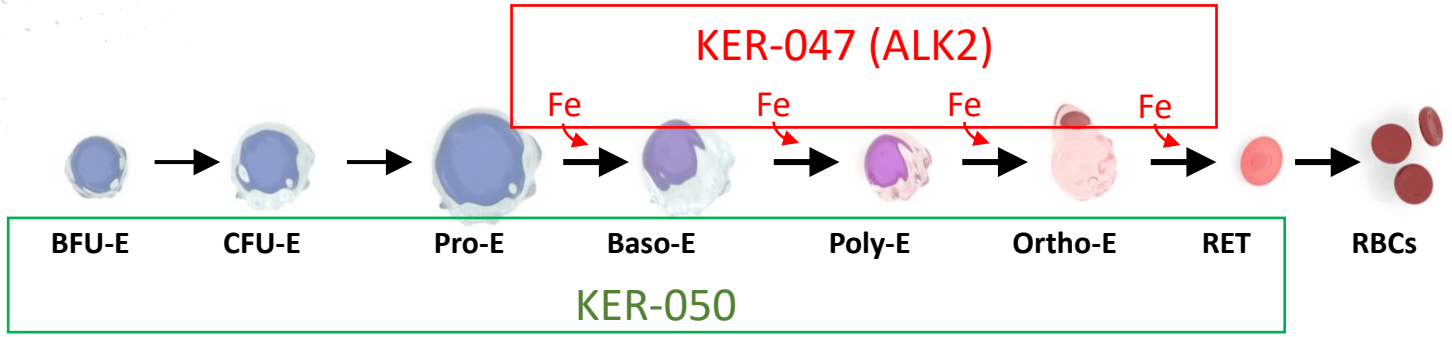
Keros is Developing Differentiated Clinical Assets in Hematological, Pulmonary, and Cardiovascular Disorders

Program	Asset	Phase of Development				Status
		Preclinical	Phase 1	Phase 2	Phase 3	
Hematology	KER-050 (therapeutic protein)			Myelodysplastic syndromes		Phase 2 clinical trial ongoing
				Myelofibrosis		Phase 2 clinical trial ongoing
	KER-047 (small molecule)			Iron-refractory iron deficiency anemia		Phase 2 clinical trial ongoing
				Functional iron deficiency anemia in MDS and MF		Completed Phase 1 clinical trial in healthy volunteers
Pulmonary and Cardiovascular	KER-012 (therapeutic protein)			Pulmonary arterial hypertension		Completed Phase 1 clinical trial in healthy volunteers
Preclinical Pipeline						

Keros' Hematology Franchise



- Production of red blood cells (RBCs), a process called erythropoiesis, requires cell division, differentiation and incorporation of iron into hemoglobin
  - A failure to produce fully mature RBCs is termed ineffective erythropoiesis
  - The synthesis of hemoglobin requires sufficient levels of iron in the bone marrow; if iron levels are too low, it can result in a failure to produce sufficient numbers of RBCs
  - Anemia is a consequence of ineffective erythropoiesis, whether due to a failure to produce erythrocytes or a failure to synthesize hemoglobin
- Keros is harnessing the powerful biology of the TGF-β superfamily to develop product candidates with the potential to address the multiple mechanisms leading to ineffective erythropoiesis
  - KER-050: Designed to inhibit signaling by activin A, activin B, GDF8 and GDF11 to promote growth and differentiation of erythroid precursors and increase platelets
  - KER-047: Designed to inhibit activin receptor like kinase (ALK-2) to inhibit hepcidin and mobilize iron for incorporation into hemoglobin

64th American Society of Hematology Annual Meeting and Exposition

Preclinical Presentations

- *"ALK2 Inhibition and a Modified Activin Receptor Type IIA Ligand Trap Co-therapy Maximized Hematologic Improvements in a Mouse Model of Anemia of Inflammation"* – Publication Number: 2338
- *"RKER-050, a Novel Activin Receptor Type II Ligand Trap, Rescued Anemia and Reduced Bone Loss in a Mouse Model of Myelodysplastic Syndromes"* – Publication Number: 4387

Clinical Presentations

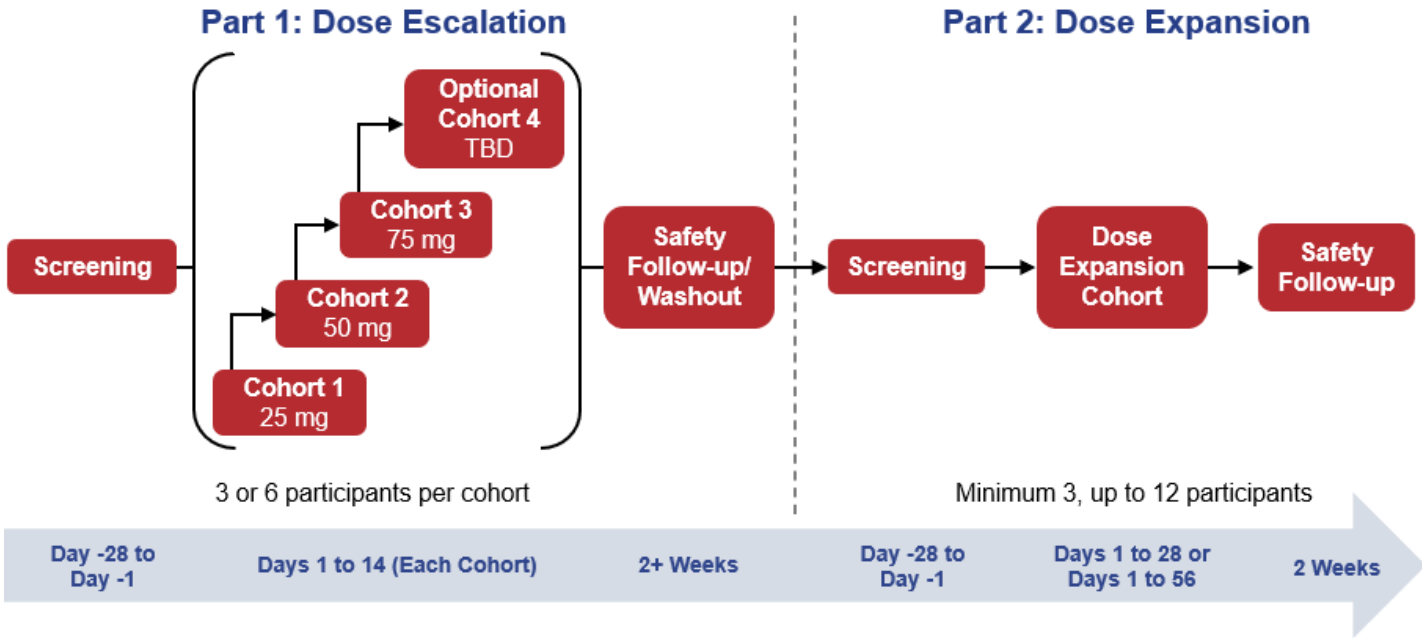
- *"Preliminary Results of a Phase 2 Clinical Trial of the ALK-2 Inhibitor KER-047 for Treatment of Iron-Refractory Iron Deficiency Anemia"* – Publication Number: 1028
- *"Effects of KER-050 on Iron Metabolism: Exploratory Analyses from an Ongoing Phase 2 Study in Patients with Myelodysplastic Syndromes"* – Publication Number: 3656
- *"Modulation of TGF-β Superfamily Signaling to Treat Myelofibrosis and Mitigate JAK Inhibitor Toxicity: A Report on the Phase 2 Study of KER-050 in Participants with Myelofibrosis"* – Publication Number: 4361

KER047-IR-201

A Phase 2 Clinical Trial Of KER-047 For The Treatment Of Patients With Iron-Refractory Iron Deficiency Anemia (IRIDA)

Phase 2 Clinical Trial of KER-047 in IRIDA

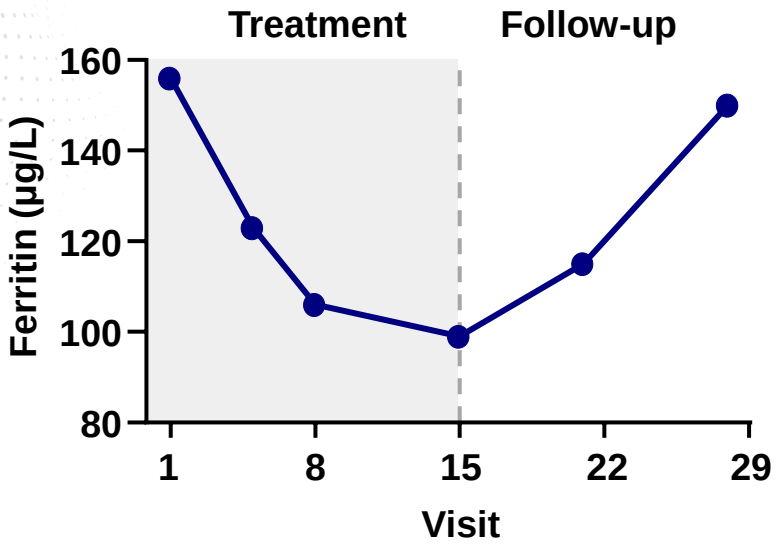
- KER-047 is a novel, oral, investigational small molecule ALK2 inhibitor
- Ongoing two-part, open-label dose-escalation and dose-expansion Phase 2 clinical trial in patients with IRIDA (an inherited form of iron deficiency anemia)
  - Participants treated once daily with KER-047 for a 2-week period followed by a 2-week washout period
  - Safety is the primary objective; secondary objectives include pharmacokinetic and pharmacodynamic analyses
- ASH Poster presentation #1028 provides an update from this ongoing Phase 2 clinical trial
  - One participant enrolled in Cohort 1 of this trial and completed 14 days treatment (KER-047 25 mg once daily) and 14-day follow-up

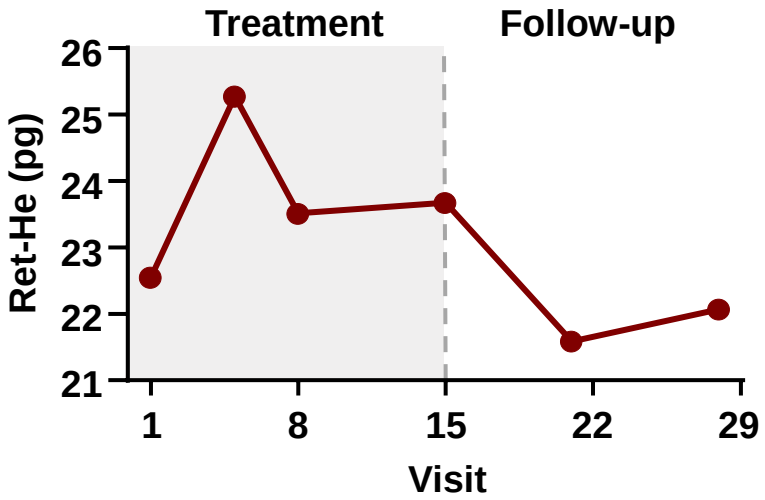


Phase 2 Clinical Trial of KER-047 in IRIDA – Preliminary Data

- A dose of 25 mg once daily was generally well tolerated in one participant enrolled thus far; no serious adverse events or dose-limiting toxicities were observed during treatment

Laboratory Results Before, During, and After Administration of KER-047 for the First Low-Dose Cohort (n=1)





- Consistent with results from our Phase 1 clinical trial of KER-047 in healthy volunteers[1], we observed decreases in hepcidin and serum ferritin as well as increases in reticulocyte hemoglobin following administration of KER-047 in one IRIDA patient

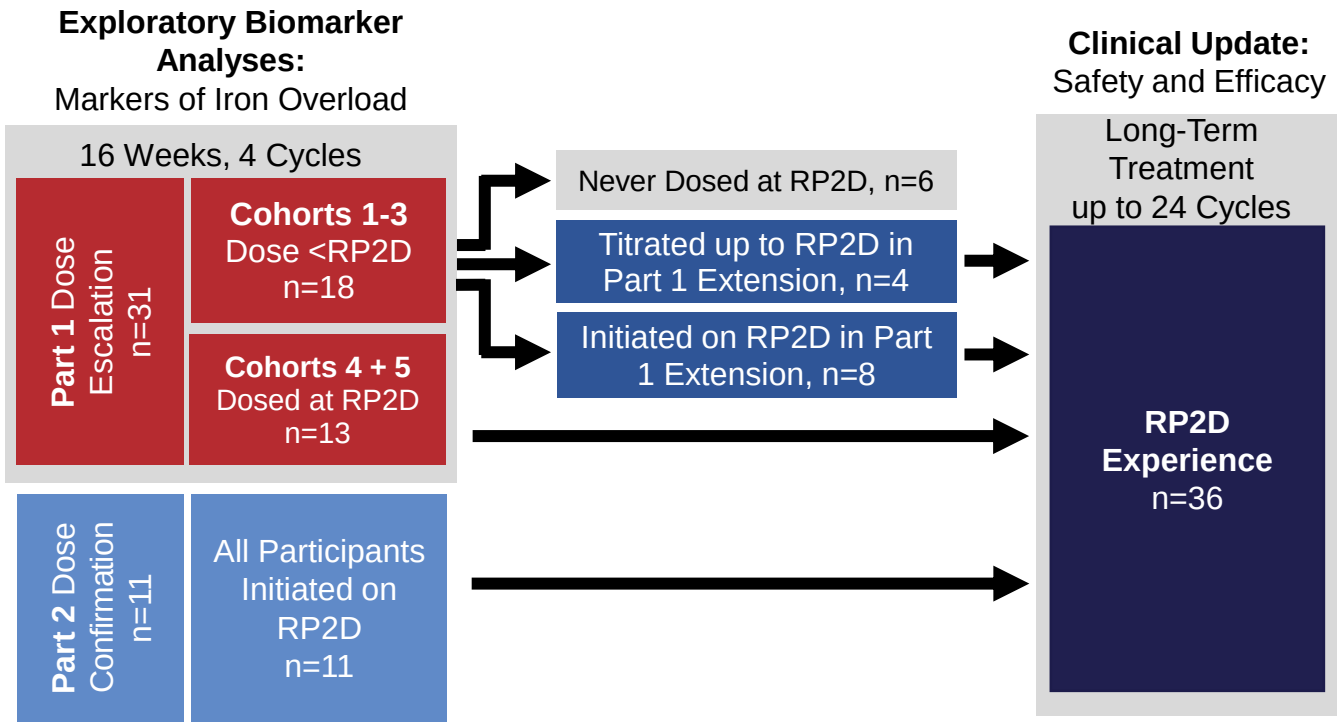
1. Ordonez C, *et al.*, 62nd American Society of Hematology Annual Meeting and Exposition

KER050-MD-201

A Phase 2 Clinical Trial Of KER-050 For The Treatment Of Anemia In Patients With Very Low, Low Or Intermediate Risk Myelodysplastic Syndromes (MDS)

Phase 2 Clinical Trial of KER-050 in MDS

- Ongoing, two-part, multicenter, open-label Phase 2 clinical trial in very low-, low- and intermediate-risk MDS patients (LR-MDS)
- KER-050 administered once every four weeks (Q4W)
- Trial objectives:
  - Part 1
    - Evaluate safety, tolerability and pharmacokinetics
    - Evaluate pharmacodynamic effects and efficacy of KER-050
  - Part 2
    - To confirm the safety, tolerability and efficacy of the dose(s) selected from Part 1
- Eligible patients in Part 1 and Part 2 may remain on treatment up to 24 cycles (2 years)
- The data from this trial included in this presentation represent available data from a cut-off date of October 1, 2022



RP2D: Recommended Part 2 dose (3.75 – 5.0 mg/kg)

Phase 2 Clinical Trial of KER-050 in MDS

Key Eligibility Criteria:

- MDS with very low-, low-, or intermediate-risk disease, as classified by the International Prognostic Scoring System-Revised (IPSS-R), including both patients that did not have ring sideroblasts (non-RS) and patients that have ring sideroblasts (RS+)
- Erythroid stimulating agents (ESA) naïve and experienced patients are eligible
- No prior treatment with azacitidine, decitabine, lenalidomide, luspatercept or sotatercept
- Anemia, categorized in one of the following three groups:
  - Non-transfused (NT): hemoglobin (Hgb) ≤10 g/dL
  - Low transfusion burden (LTB): 1-3 units of RBC/8 weeks for Hgb ≤9 g/dL
  - High transfusion burden (HTB): ≥4 units of RBC/8 weeks for Hgb ≤9 g/dL

Select Efficacy Endpoints:

- IWG 2006 Hematological improvement-erythroid (HI-E)
  - Hemoglobin increase of ≥1.5 g/dL for 8 weeks (in NT and LTB patients)
  - Reduction of ≥4 RBC units transfused over 8 weeks compared to baseline (in HTB patients)
- Transfusion independence (TI) for at least 8 weeks in patients who require ≥ 2 RBC units transfused at baseline

Demographics and Baseline Characteristics of Participants Treated at the RP2D of 3.75 to 5.0 mg/kg

Parameter	RP2D Dataset (n=36)
Age, years, median (range)	74.5 (61-88)
Male, n (%)	20 (55.6)
RS status, n (%) RS+ Non-RS	 23 (63.9) 13 (36.1)
WHO MDS classification, n (%) MDS-MLD MDS-MLD-RS MDS-SLD MDS-SLD-RS Unclassifiable/Unknown/Missing	 12 (33.3) 20 (55.6) 0 1 (2.8) 3 (8.4)
Prior ESA therapy, n (%)	6 (16.7)
Iron chelator therapy, n (%)	11 (30.6)
RBC transfusion status, units per 8 weeks NT LTB HTB 4 to <8 units ≥8 units	 10 (27.8) 6 (16.7) 20 (55.6) 11 (30.6) 9 (25.0)

MLD: Multiple lineage dysplasia
SLD: Single lineage dysplasia
WHO: World Health Organization

Data cutoff date: 1-Oct-2022

KER-050 Generally Well-Tolerated at RP2D of 3.75 to 5.0 mg/kg

Category	Participants Reporting, n (%), n=36*
Any treatment-emergent adverse event (TEAE)	33 (91.7)
Any treatment-related TEAE	11 (30.6)
Any serious TEAE	12 (33.3)
Any treatment-related serious TEAE	1 (2.8)
Any TEAE leading to death	1 (2.8)
Any TEAE leading to study drug discontinuation	4 (11.1)

- No dose-limiting toxicities and no progression to acute myeloid leukemia
- 3 TEAEs led to treatment discontinuation: injection-site reaction (related); dyspnea (unrelated); chronic obstructive pulmonary disease (unrelated)
- 1 fatal TEAE of heart failure occurred and was determined to be unrelated to study treatment
- Most common TEAEs that occurred in >5 participants were diarrhea (22.2%), fatigue (19.4%), dyspnea (16.7%), and nausea (16.7%)

*All participants who had received at least one dose of KER-050 as of the data cutoff date.

Data cutoff date: 1-Oct-2022

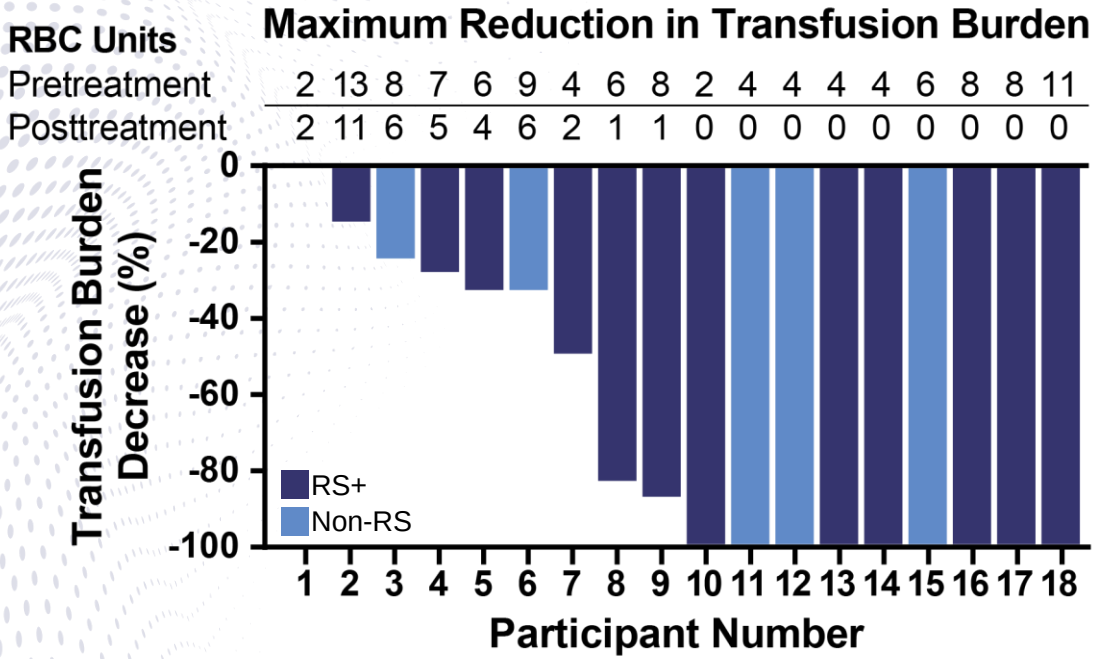
Summary of 8- and 12-Week Efficacy Endpoints in MDS Patients with RP2D Experience

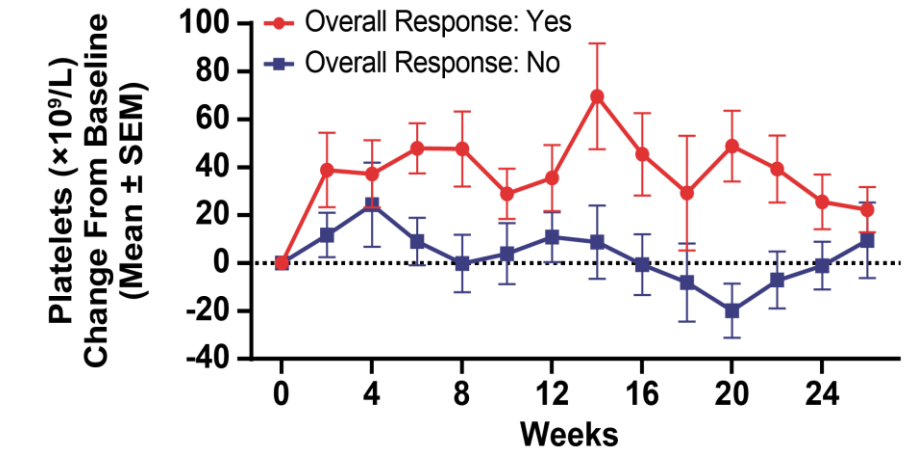
Response Summary	Response Rate, n/m (%)	
	All evaluable patients	HTB evaluable patients
Overall Erythroid Response (HI-E or TI)	15/29 (51.7%)	10/16 (62.5%)
IWG 2006 HI-E	15/29 (51.7%)	10/16 (62.5%)
TI ≥8 weeks RS+ Non-RS	9/18 (50%) 6/12 (50%) 3/6 (50%)	8/16 (50%) 5/11 (45.5%) 3/5 (60%)
TI ≥12 weeks	8/15 (53.3%)	7/14 (50%)

- Efficacy (n=29):
  - HI-E evaluable: ≥8 weeks postbaseline hemoglobin assessments (NT and LTB) or transfusion assessments (HTB)
  - TI evaluable: ≥8 (or ≥12) weeks postbaseline transfusion assessments with ≥2 units RBC transfusion at baseline
- Treatment with KER-050 at RP2D showed HI-E and TI response consistent with Part 1 dose escalation
- TI observed in both RS+ and non-RS participants regardless of transfusion burden
- Rates of TI at ≥12 weeks are consistent with the rates of TI observed at ≥8 weeks

Data cutoff date: 1-Oct-2022

KER-050 Treatment Resulted in HI-E and TI in Transfusion-Dependent Non-RS and RS+ Participants with Sustained Increase in Platelets





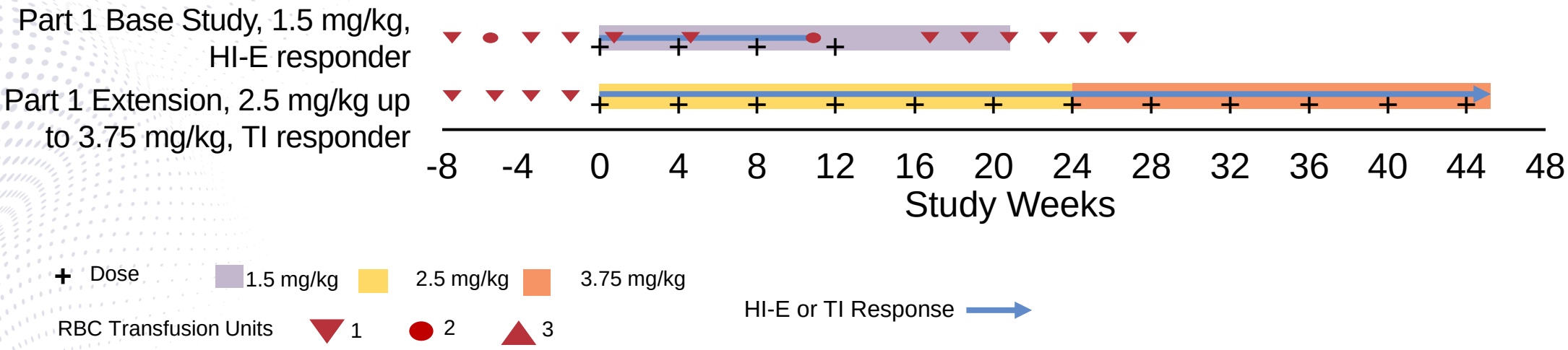
Altered visit schedules for participants re-baselined in Part 1 Extension following treatment gap contribute to fluctuating numbers across visits.

- KER-050 treatment led to improved transfusion burden in both LTB and HTB participants
- 8 out of 16 HTB participants achieved transfusion independence

- The observed increases in platelets for HI-E and TI responders suggest that KER-050 has a differentiated mechanism of action in that it potentially promotes hematopoiesis across multiple cell lineages

Data cutoff date: 1-Oct-2022

Case Study: Long-term Transfusion Independence Achieved in Participant Dosed at RP2D



Case Study: 72-year-old male, Non-RS, MDS-MLD, HTB, Concomitant Iron Chelation Therapy

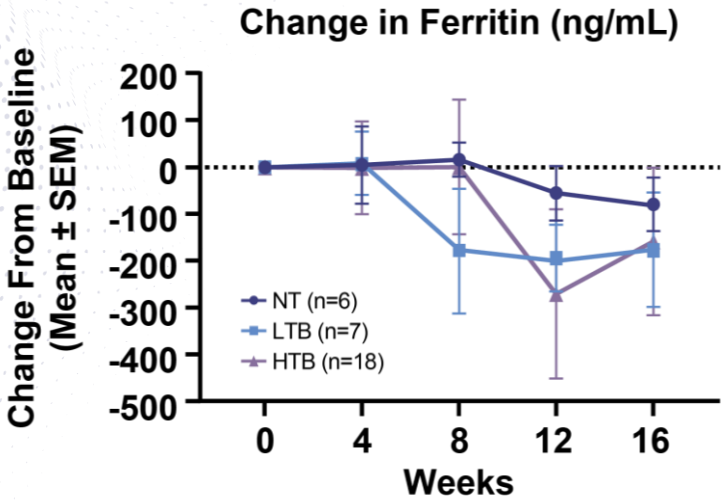
- This participant achieved an initial HI-E response (but not TI) when treated with KER-050 1.5 mg/kg in Part 1 Dose Escalation (top bar)
- The participant was rescreened and initiated Part 1 Extension (bottom bar) following a 112-day gap between the last dose in Dose Escalation and first dose in the Extension
- The participant then achieved TI upon recommencement of treatment at 2.5 mg/kg (24 weeks)
- Participant dose escalated to 3.75 mg/kg per the clinical trial protocol and remained TI as of the data cutoff date (at least 44 weeks)

Data cutoff date: 1-Oct-2022

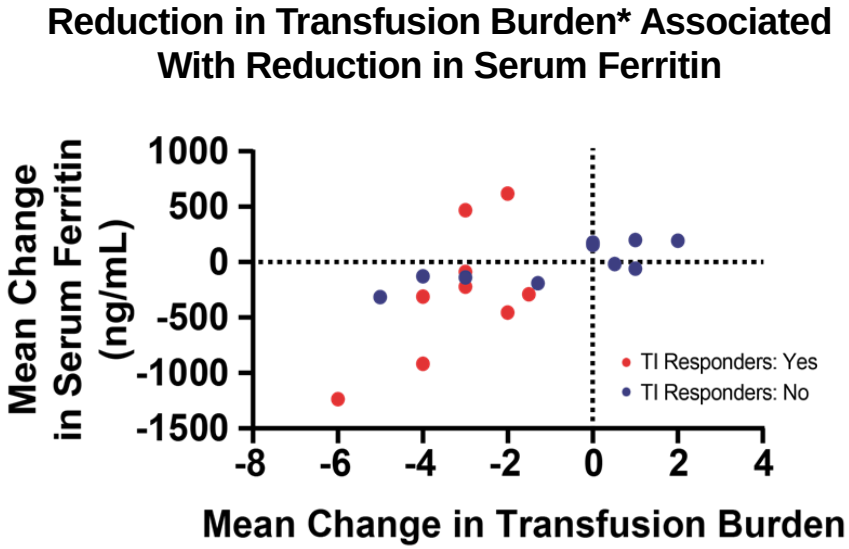
KER-050 Impact on Iron Overload

Analysis of Biomarkers from Part 1 Dose Escalation

Treatment With KER-050 Resulted in Reduction in Serum Ferritin Following 16 Weeks of Treatment (Data from Part 1 Cohorts)



- Short-term treatment with KER-050 reduced serum ferritin, which suggests reduction of iron overload, particularly in transfusion-dependent participants



- In general, reductions in transfusion burden were associated with reductions in serum ferritin, especially for participants achieving transfusion independence

These data suggest that KER-050 has the potential to reduce iron overload, a serious clinical complication impacting survival of patients with MDS

*Units per 8 weeks over 16 weeks in Part 1 Dose Escalation. TI evaluable population includes LTB and HTB participants with at least 2 units of RBC transfusion at baseline and at least 8 weeks of postbaseline transfusion records.

Data cutoff date: 1-Oct-2022

Summary: Safety and Efficacy Update From Long-Term Evaluation of Participants Receiving RP2D

- KER-050 continued to be generally well tolerated in participants receiving long-term treatment at the RP2D as of the data cutoff date
- HI-E ≥8 weeks was achieved by 51.7% of all evaluable participants and 62.5% of evaluable HTB participants
- TI ≥8 and ≥12 weeks occurred in 50% of evaluable HTB and LTB participants
  - TI responses were observed in both RS+ and non-RS participants
- Observed increases in platelets in HI-E or TI responders support the potential of KER-050 as a treatment for multilineage cytopenias
- Treatment with KER-050 resulted in biomarker changes supporting increased erythropoiesis and in observed reductions in serum ferritin

Together, these preliminary findings support the potential of KER-050 to improve hematopoiesis, reduce transfusion burden and reduce iron overload

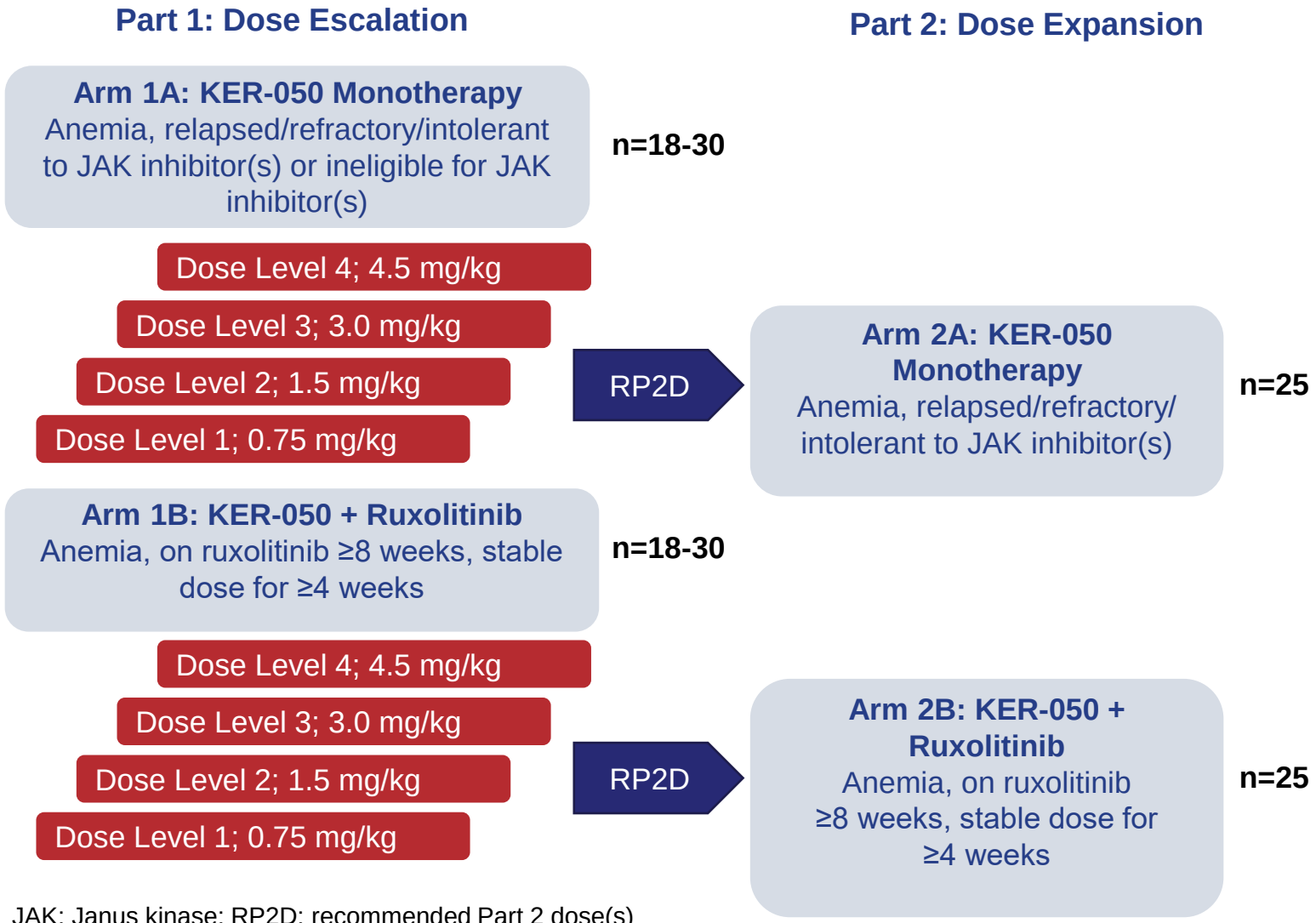
Data cutoff date: 1-Oct-2022

KER050-MF-301

A Phase 2 Open-label Study to Evaluate the Safety and Efficacy of KER-050 as Monotherapy or in Combination with Ruxolitinib in Participants with Myelofibrosis (MF)

Phase 2 Clinical Trial of KER-050 in MF

- Ongoing, two-part, open-label Phase 2 clinical trial evaluating KER-050 administered with or without ruxolitinib in participants with MF who have anemia
- Primary objective:
  - Part 1: Assess safety and tolerability of KER-050
  - Part 2: Confirm safety and tolerability of the dose(s) selected from Part 1
- Secondary objectives: Evaluate the pharmacokinetics, pharmacodynamics and efficacy of KER-050 administered with or without ruxolitinib
- The data from this trial included in this presentation represent available data from a cut-off date of October 1, 2022



JAK: Janus kinase; RP2D: recommended Part 2 dose(s)

Baseline Characteristics

Parameters	KER-050 0.75 mg/kg N=6	KER-050 0.75 mg/kg + ruxolitinib N=6	Total N=12
Median age, years (range)	72.0 (60-85)	75.5 (69-86)	75.0 (60-86)
Male sex, n (%)	3 (50.0)	6 (100.0)	9 (75.0)
RBC transfusion status			
Transfusion Dependent (TD),[a] n (%)	1 (16.7)	4 (66.7)	5 (41.7)
RBC units, mean (SD)	10.0 (NA)	9.8 (1.5)	9.8 (1.3)
Non-TD,[b] n (%)	5 (83.3)	2 (33.3)	7 (58.3)
RBC units, mean (SD)	2.2 (2.3)	4.5 (0.7)	2.9 (2.2)
Iron chelation therapy usage, n (%)			
TD, n (%)	1 (16.7)	1 (16.7)	2 (16.7)
Non-TD, n (%)	0	1 (16.7)	1 (8.3)
WHO classification diagnosis, n (%)			
Primary MF	5 (83.3)	4 (66.7)	9 (75.0)
Post-PV[c] MF	1 (16.7)	0	1 (8.3)
Post-ET[d] MF	0	2 (33.3)	2 (16.7)

[a]Defined as a participant having received ≥ 6 units transfusion for MF-related anemia in the 12 weeks preceding cycle 1 day 1 (C1D1) and at least 1 unit transfusion in the 28 days preceding C1D1.
[b]Defined as participant having received 0-5 units transfusion for MF-related anemia in the 12 weeks preceding C1D1.
[c]Post-PV: post-polycythemia vera
[d]Post-ET: post-essential thrombocythemia

Data cutoff date: 1-Oct-2022

KER-050 Was Generally Well-Tolerated as Monotherapy and in Combination with Ruxolitinib

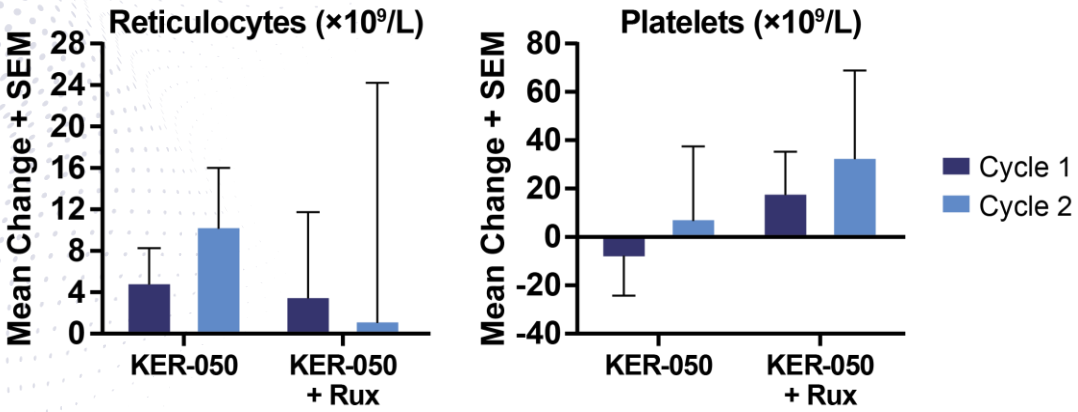
	Monotherapy KER-050 0.75 mg/kg (N=6) n (%)	Combination KER-050, 0.75 mg/kg + ruxolitinib (N=6) n (%)	Total (N=12) n (%)
TEAE, any grade	4 (66.7)	5 (83.3)	9 (75.0)
Grade 1	1 (16.7)	0	1 (8.3)
Grade 2	2 (33.3)	2 (33.3)	4 (33.3)
Grade 3	1 (16.7)	3 (50.0)	4 (33.3)
Grade 4 and 5	0	0	0
Serious TEAE	1 (16.7)	2 (33.3)	3 (25.0)
Dose-limiting toxicity	0	0	0

- No dose-limiting toxicities
- Most frequent TEAEs reported by ≥ 2 participants were diarrhea (25.0%) and fatigue, dyspnea and COVID-19 (16.7% each)
- 1 TEAE led to KER-050 dose modification: amyloidosis (unrelated)
- No TEAEs led to either study treatment or study discontinuation

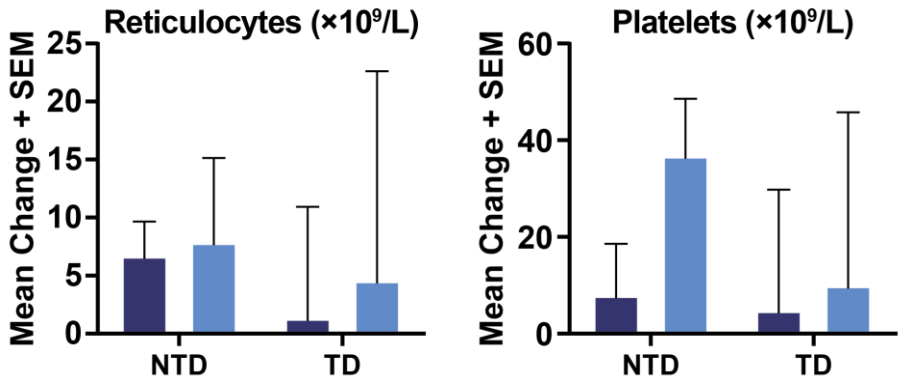
Data cutoff date: 1-Oct-2022

KER-050 Treatment Increased Reticulocytes and Platelets

Change by Study Arm



Change by Transfusion Status

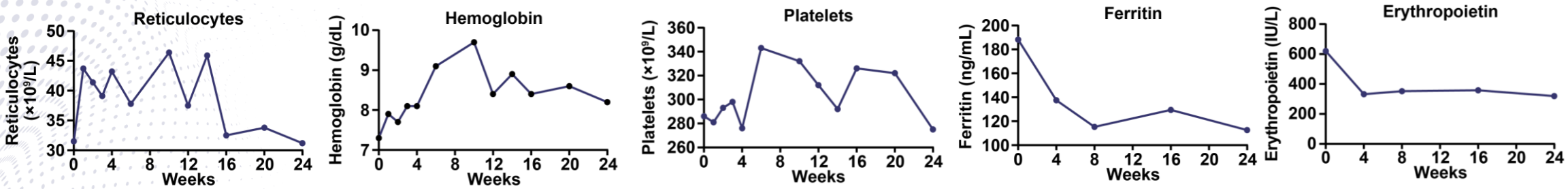


NTD: Non–transfusion dependent

- Although variability was observed, treatment with KER-050 at the lowest dose in this trial (0.75 mg/kg) resulted in increased reticulocytes and platelets on aggregate, both as monotherapy and in combination with ruxolitinib, and regardless of transfusion status
  - This is consistent with prior preclinical and clinical findings on the pharmacodynamic effect of KER-050
- These data support the potential of KER-050 to potentially promote differentiation of erythroid and megakaryocytic precursors and ameliorate anemia and thrombocytopenia in patients with MF

Data cutoff date: 1-Oct-2022

Case Study: Observed Increases in Erythropoiesis and Thrombopoiesis in Patient with KER-050 Treatment (Monotherapy)



Case Study of Participant on KER-050 Monotherapy Treatment at 0.75mg/kg Q4W

- 60-year-old non-transfusion dependent female with primary MF
- Treatment with KER-050 increased hematopoiesis
  - A robust increase in reticulocytes was observed after a single dose of KER-050, and was followed by a sustained increase in hemoglobin (≥1.5 g/dL over baseline) and corresponding decrease in ferritin and erythropoietin with continued dosing
  - An increase in platelets was also observed

Data cutoff date: 1-Oct-2022

Conclusions

- Multiple poster presentations at the 64th American Society of Hematology Annual Meeting and Exposition demonstrating continued advancement of Keros' hematology franchise
- KER-047 treatment demonstrated translation of ALK2 biology to one IRIDA patient in our ongoing Phase 2 clinical trial
- KER-050 Phase 2 Clinical Trial in MDS Patients
  - KER-050 was generally well tolerated at the recommended Part 2 dose of 3.75-5.0 mg/kg as of the data cutoff date
  - Treatment with KER-050 resulted in biomarker changes supporting increased erythropoiesis and attenuated iron overload
  - Data as of data cutoff date was consistent with responses in Part 1 dose escalation, with HI-E ≥8 weeks achieved by 51.7% of all evaluable participants and 62.5% of evaluable HTB participants
  - TI responses of ≥8 and ≥12 weeks was observed in 50% of evaluable HTB and LTB participants equally amongst both RS+ and non-RS participants as of the data cutoff date
  - Observed increases in platelets in HI-E or TI responders support the potential of KER-050 as a treatment for multilineage cytopenias
- KER-050 Phase 2 Clinical Trial in MF Patients
  - Generally well tolerated at the lowest dose as of the data cutoff date
  - Preliminary data suggests that KER-050 can potentially promote multilineage hematopoietic differentiation to ameliorate anemia and thrombocytopenia in patients with MF

Data cutoff date for MDS and MF trials: 1-Oct-2022

Q&A