KEROS THERAPEUTICS

Hematology Franchise:

Update at 65th Annual Congress of the American Society of Hematology

December 2023

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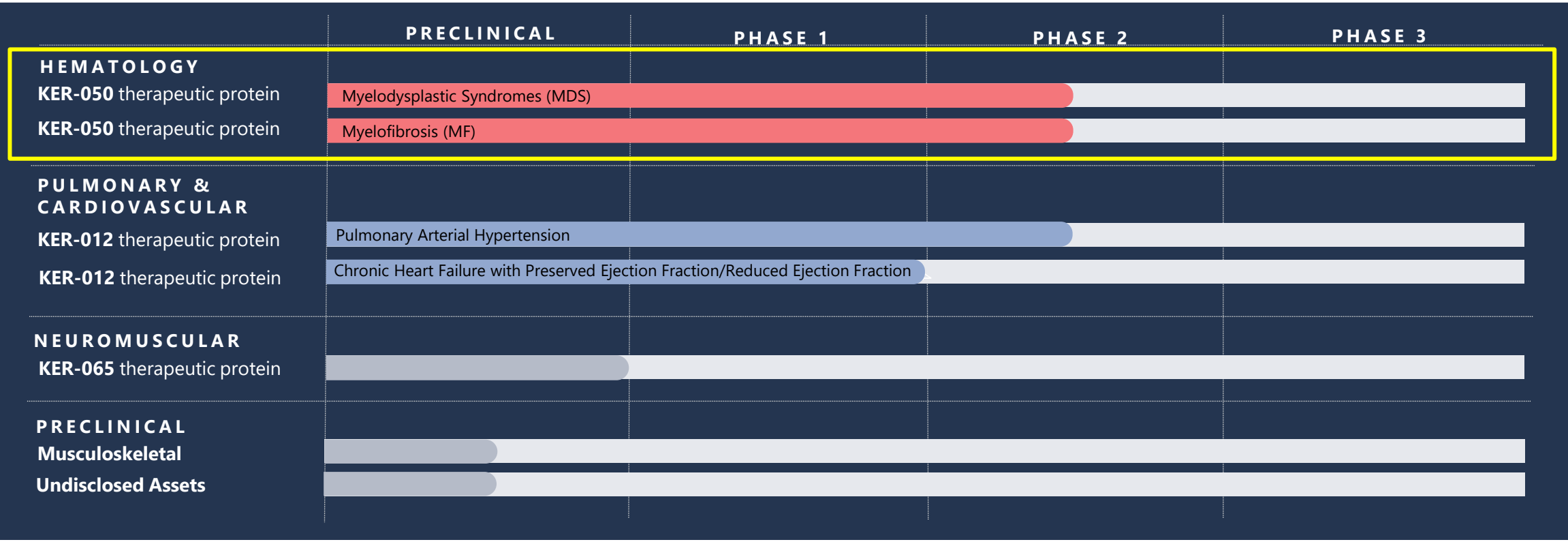
Focused on Transforming the Lives of a Wide Range of Patients with Disorders Linked to Dysfunctional TGF-β Superfamily Signaling

Keros is a clinical-stage biopharmaceutical company
Developing potentially differentiated product candidates designed to alter transforming growth factor-beta (TGF-β) signaling and target pathways critical for the growth, repair and maintenance of a number of tissue and organ systems

We believe our product candidates have the potential to unlock the full therapeutic benefits of modulating the TGF-β superfamily and provide disease-modifying benefit to patients



65th American Society of Hematology Annual Meeting and Exposition

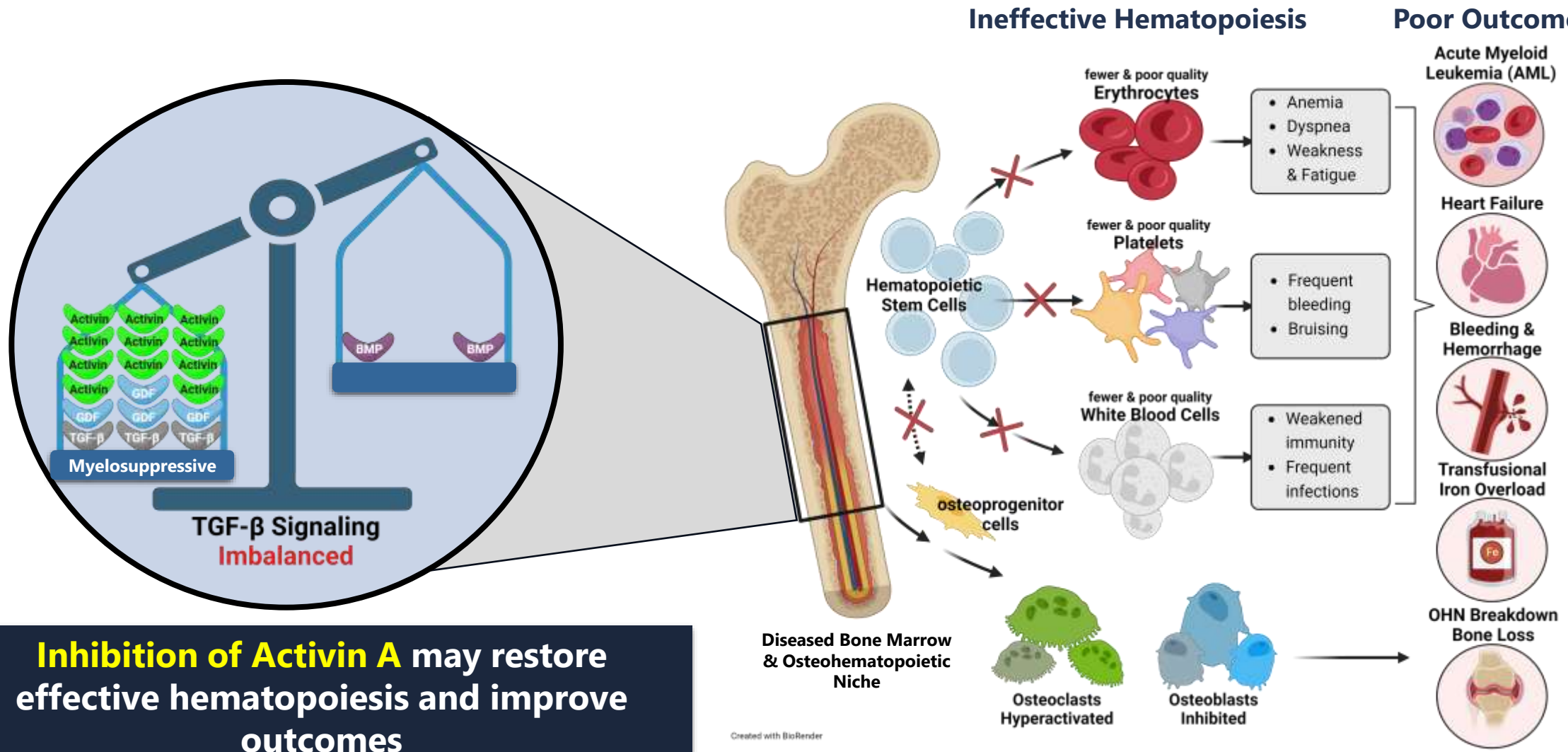
Clinical Presentations

- "*Durable Clinical Benefit with KER-050 treatment: Findings From an Ongoing Phase 2 Study in participants with Lower-Risk MDS*" – Publication Number: 196
- *"KER-050 Treatment Reduced Iron Overload and Increased Bone Specific Alkaline Phosphatase in participants with Lower-Risk MDS Supporting Potential to Restore Balance to the Osteohematopoietic Niche"* – Publication Number: 1089
- *"Modulation of TGF-β Superfamily Signaling By KER-050 Demonstrated Potential to Treat Myelofibrosis and Mitigate Ruxolitinib-Associated Cytopenia"* – Publication Number: 3185

Preclinical Presentations

- *"RKER-050, A Modified Activin Receptor Type IIA Ligand Trap, Promoted Erythropoiesis in a Murine Model of Myelofibrosis"* – Publication Number: 4524
- *"RKER-216 Reversed Microcytic Anemia in a Mouse Model of Iron Refractory Iron Deficiency Anemia"* – Publication Number: 2466

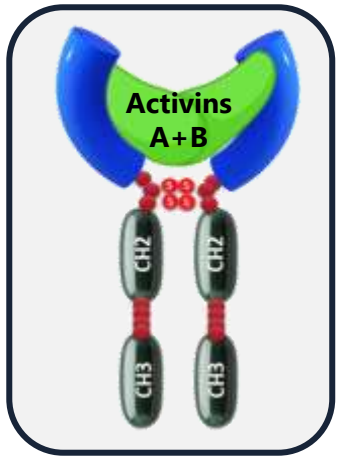
Imbalanced TGF-β Signaling in Bone Marrow Results in Ineffective Hematopoiesis and Poor Outcomes in Both MDS and MF[1,2,3]



Inhibition of Activin A may restore effective hematopoiesis and improve outcomes

1. Verma A, et al. J Clin Inv 2020; 2. Portale F, et al., Haematologica. 2019, 3. Rambaldi B., et al, Ann Hematol. 2021
BMP = bone morphogenetic protein; GDF = growth differentiation factor; TGF-β = transforming growth factor-β

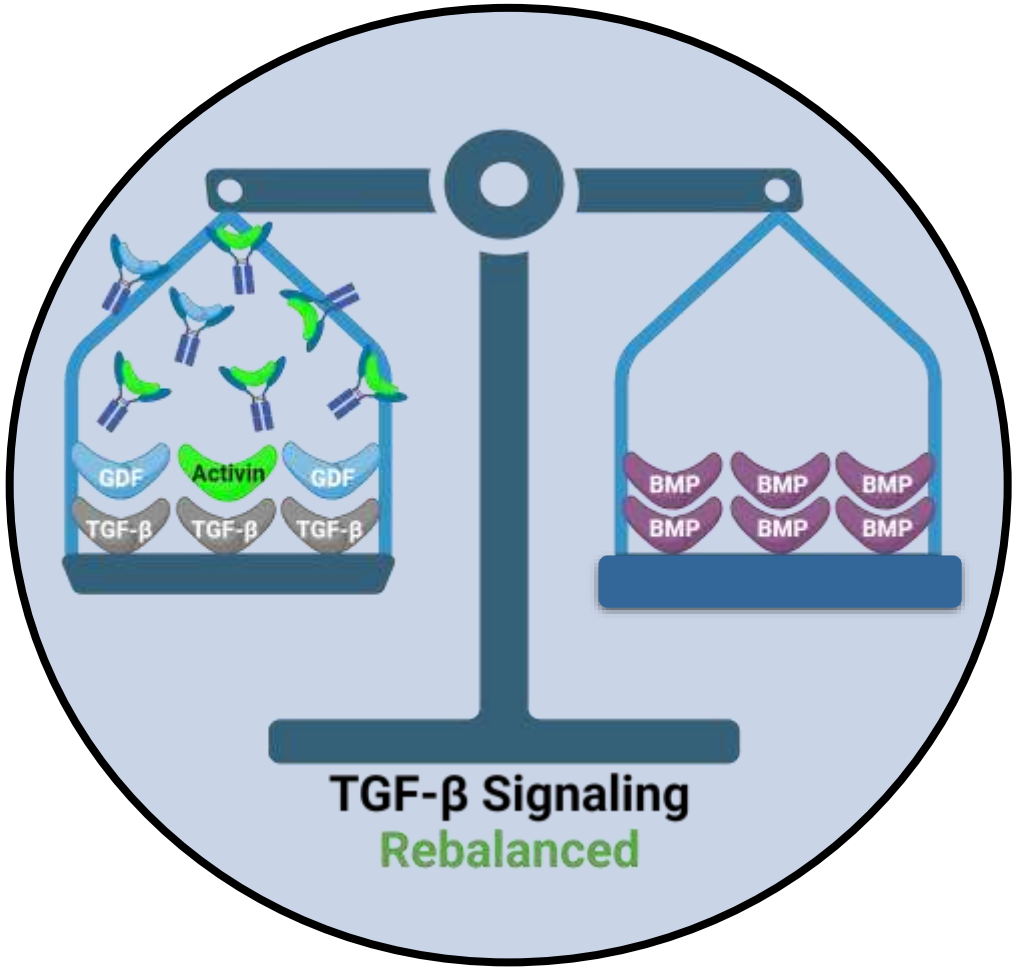
KER-050 is Designed to Target Bone Marrow Disorders of Ineffective Hematopoiesis Including MDS and MF



KER-050 (elritercept)

- **Designed to inhibit select TGF-beta ligands, including Activin A, which has been associated with driving disease pathogenesis and progression**

Domain	Effect
Erythropoiesis	ALL stages of differentiation and maturation
Thrombopoiesis	ALL stages of differentiation and maturation
Bone	Increased bone formation
Iron Metabolism	Improved iron utilization



KER-050 (Elritercept)

Investigational Treatment for Anemia and Thrombocytopenia in Patients with Myelodysplastic Syndromes

Ongoing Phase 2 Clinical Trial of KER-050 for the Treatment of Anemia in Patients with Very Low-, Low- or Intermediate-Risk Myelodysplastic Syndromes

Myelodysplastic Syndromes (MDS)

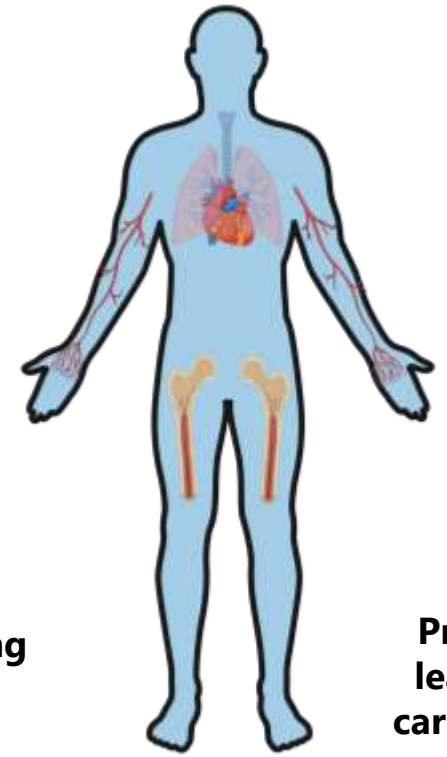
MDS
MDS is a collection of bone marrow disorders characterized by ineffective hematopoiesis and peripheral cytopenias.

Clinical Consequences
The clinical consequences of MDS include anemia, bleeding, iron overload, cardiovascular disease and progression to acute myeloid leukemia (AML).

Survival Ranges
Median survival ranges from approximately nine years for very low-risk patients to less than a year for high-risk patients.

Scope
In the United States, there are 60,000 to 170,000 patients living with MDS and 15,000 to 20,000 new cases of MDS reported each year.

Impact of MDS



Cytopenias including severe anemia

Progressive disease leading to AML and cardiovascular disease

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Severe fatigue and decreased QoL

QoL = quality of life

Current Treatment Landscape for Treatment of Anemia in Lower Risk MDS

RBC Transfusions

- RBC transfusions provide symptomatic relief of anemia
- Transfusion dependency is associated with iron overload, further exacerbating damage to the bone marrow and increasing risk of AML progression and cardiovascular disease
- Prolonged transfusion dependence is associated with shorter overall survival

Erythroid Stimulating Agents

- ESAs are currently first line treatment of choice but response is limited in patients with endogenous erythropoietin levels (>200 U/L) and high transfusion burden (≥4 units of RBC/8 weeks)

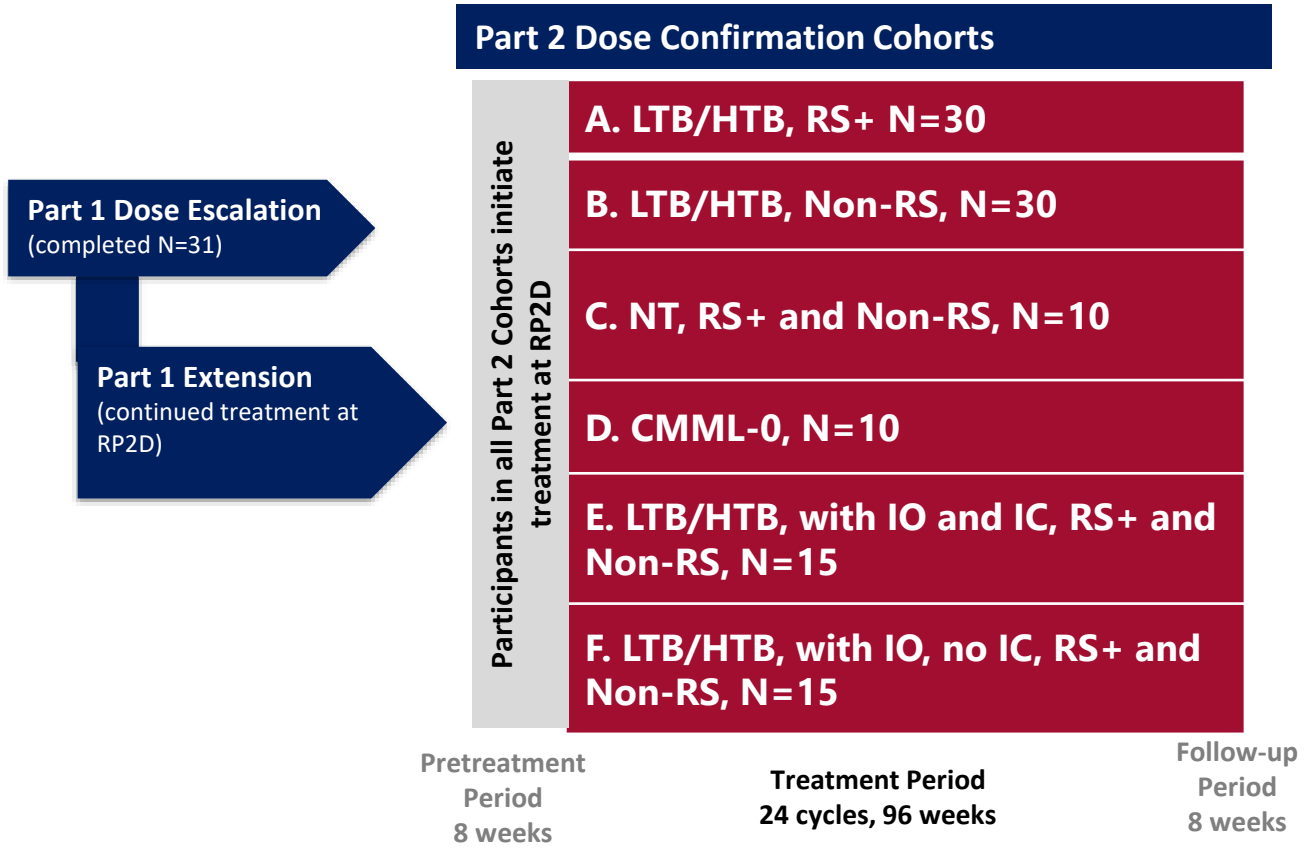
Erythroid Maturation Agent

- Reblozyl approved in 1st and 2nd line MDS
- In second line treatment, only 20% of high transfusion burden (HTB) patients achieved 8-week transfusion independence with Reblozyl® versus 4% with placebo[1]
- In 2nd line setting, "patient reported outcome (PRO) data showed no improvement in quality of life for patients who received luspatercept or who responded to luspatercept." *(Medical reviewer from the luspatercept FDA review document Page 11 4/3/2020)*

Unmet need remains for treatment that can address the multifaceted pathophysiology of MDS

1. Femaix P, et al. New Eng J Med 2020; 382:140-151

Ongoing Phase 2 Clinical Trial of KER-050 for the Treatment of Anemia in Patients with Very Low-, Low- or Intermediate-Risk MDS



Response data are presented for the modified intent to treat 24-week population ($mITT_{24}$) that includes RP2D participants with at least 24 weeks of KER-050 treatment or who have discontinued (n=60)

KER-050 administered subcutaneously once every four weeks (Q4W)

Primary Objective:
- Assess safety and tolerability of KER-050

Key Eligibility Criteria:
- MDS per 2016 WHO criteria, RS+ or non-RS, very-low, low, or intermediate risk disease (LR-MDS) by IPSS-R with anemia (NT, LTB, HTB)
  - CMML in Cohort D

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

Ongoing Trial – Status as of Data Cutoff Date:
- Part 1 Extension Ongoing
- RP2D: 3.75 mg/kg with the ability to titrate to 5 mg/kg Q4W
- RP2D experienced patients: N=79
  - 7 (8.9%) patients received ≤3 doses
  - 50 (63%) patients were ongoing and remained on treatment
  - Median duration of treatment = Approx. 29 weeks (Range = Approx. 4 to 114 weeks)
  - Median doses received = 7 (range 1 to 28 doses)
  - 22 (27.8%) patients received ≥12 doses

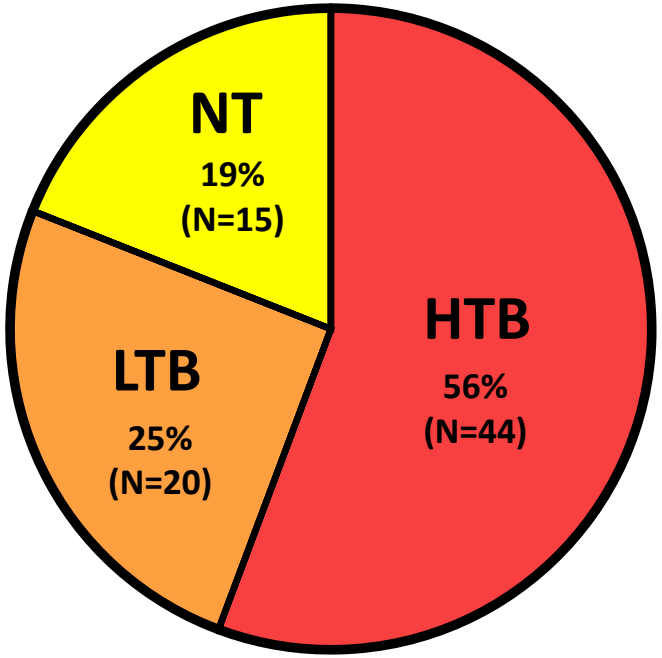
Data are presented as of a data cutoff date of September 1, 2023.

RP2D = Recommended Part 2 Dose; CMML: chronic myelomonocytic leukemia; high transfusion burden (HTB): ≥4 units of RBC/8 weeks for hemoglobin (Hgb) ≤9 g/dL; low transfusion burden (LTB): 1-3 units of RBC/8 weeks for Hgb ≤9 g/dL; non-transfused (NT): Hgb ≤10 g/dL; RS = ring sideroblasts.; IO = Iron Overload; IC = Iron Chelation

Trial Enrolled Hard-to-Treat Patients with High Disease Burden

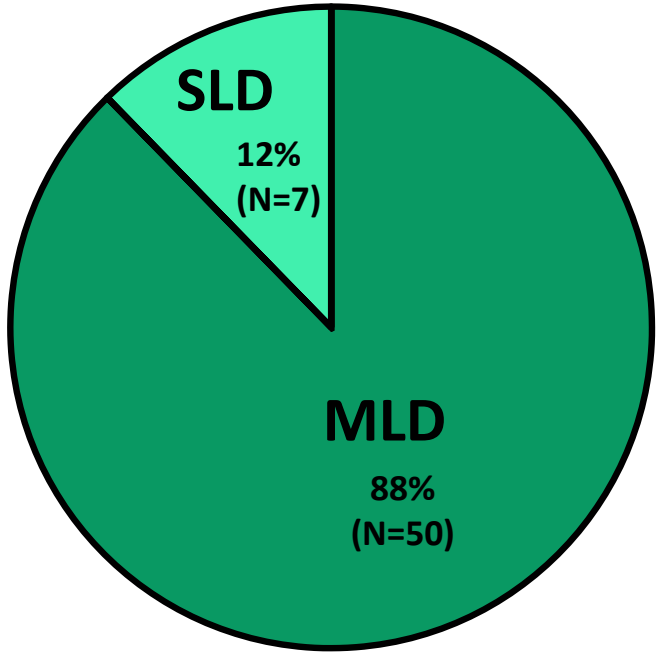
Baseline Characteristic	RP2D (N=79)
Median age, years (range)	75 (53, 89)
Sex, male, n (%)	50 (63.3)
Hemoglobin, g/dL, median (range)	8.37 (3.7, 10.5)
RS+, n (%) Non-RS, n (%)	57 (72.2) 22 (27.8)
Prior ESA, n (%)	21 (26.6)
Median baseline EPO level, U/L (range)*	127.8 (1, 4000)
Thrombocytopenia, n (%) (platelets < 150 x 10^9/L)	20 (25)

Baseline Transfusion Burden



- 44 (56%) had high transfusion burden (HTB, ≥4 RBC units/8 weeks)
- 25 (32%) heavily transfused (≥ 6 RBC units/8 weeks)

Baseline Dysplasia Category**



- 50 (88%) had multi-lineage dysplasia (MLD)

Data are presented as of a data cutoff date of September 1, 2023.
*9 RP2D patients had missing baseline EPO; **Excludes 22 RP2D participants with unknown dysplasia category
EPO= erythropoietin, SLD = single lineage dysplasia; MLD = multi lineage dysplasia

KER-050 was Generally Well-tolerated

- **Most frequent TEAEs (≥ in 15% of patients) regardless of causality were:**
  - Dyspnea or diarrhea (18; 22.8% each)
  - Fatigue (16; 20.3%)
  - Nausea (15; 19.0%)
  - Headache (12; 15.2%)
- **Most TEAEs were mild (Grade 1) to moderate (Grade 2)**
- **3 treatment-related TESAEs of injection site reaction (Grade 2), dyspnea (Grade 3), and syncope (Grade 3) occurred in 1 patient each**
  - Dyspnea and syncope were assessed as not related to study treatment by the Sponsor due to underlying co-morbidities
- **Fatal TESAEs (cardiac failure and myocardial infarction) occurred in 2 (2.5%) patients; both were assessed as unrelated by the PI and Keros**
- **No patients progressed to AML**

Category	RP2D (N=79) n (%)
Any TEAE	**74 (93.7)**
Any treatment-related TEAE	**33 (41.8)**
Any TESAE	**28 (35.4)**
Any treatment-related TESAE	**3 (3.8)**
Any TEAE leading to death	**2 (2.5)**
Any TEAE leading to KER-050 discontinuation*	**11 (13.9)**

***Treatment-related TEAEs leading to KER-050 discontinuation: injection site reaction, platelet count increased, and dyspnea**

Unrelated TEAEs leading to KER-050 discontinuation: nodular melanoma, NSCLC, MI, dementia Alzheimer's type, dyspnea, cardiac failure, and COPD & cardiac failure congestive (both in 1 patient)

Treatment-related = considered to be related to the study treatment by the treating investigator.
Number and percent of patients with events were summarized.

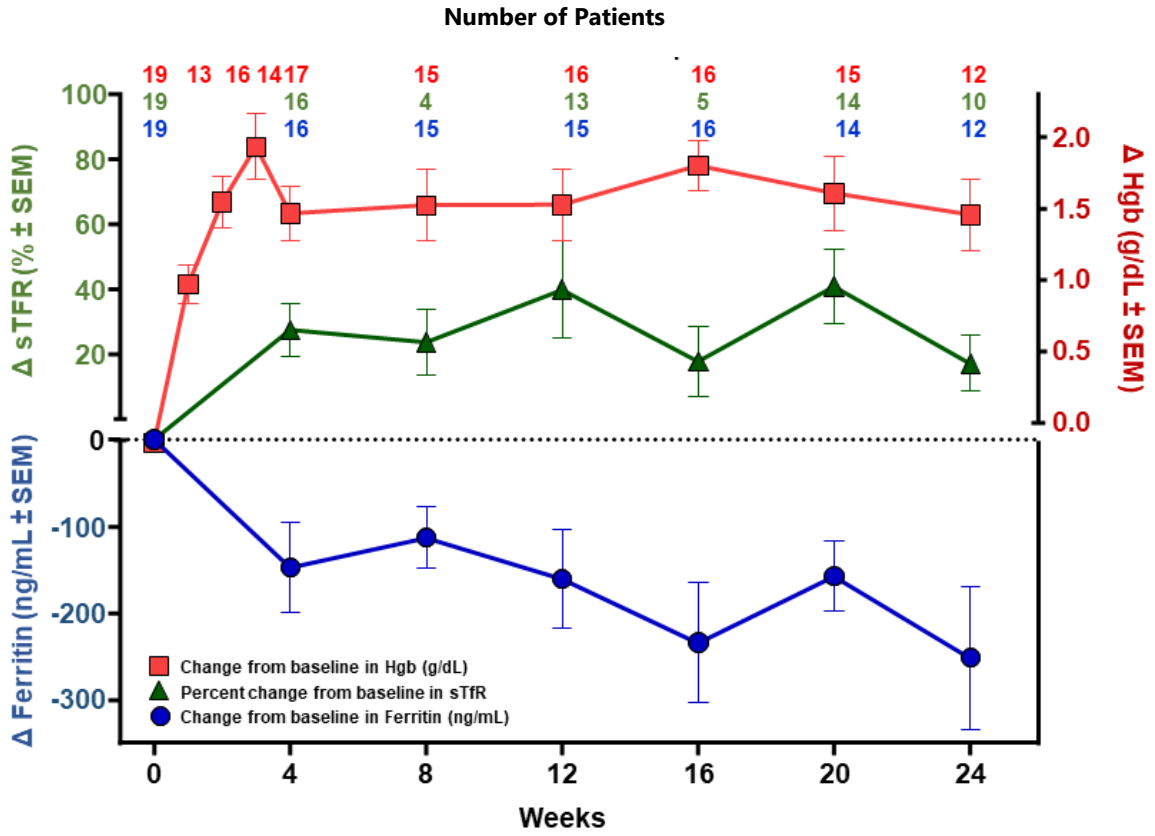
Data are presented as of a data cutoff date of September 1, 2023.
AML = acute myeloid leukemia; COPD = chronic obstructive pulmonary disease; MI = myocardial infarction; NSCLC = non-small cell lung cancer; TEAE = treatment emergent adverse event; TESAE = treatment emergent serious adverse event

KER-050 Treatment Led to Sustained Increases in Hemoglobin

- **Durable increases in hemoglobin were achieved in NT and LTB patients**
- **Increases in sTfR a marker of erythropoiesis and decreases in serum ferritin were also observed**

Collectively, suggests KER-050 resulted in durable restoration of erythropoiesis and improved iron metabolism

Observed Change in HgB, sTfR, and Ferritin



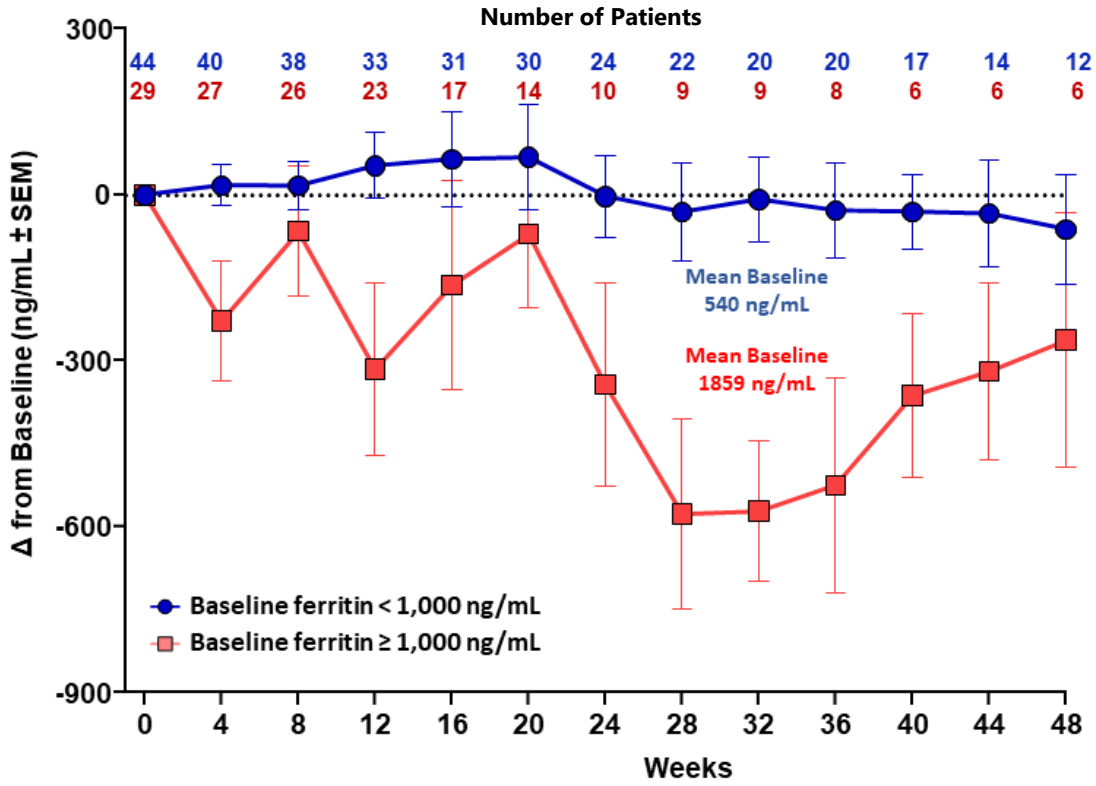
Data are presented as of a data cutoff date of September 1, 2023.
Hgb=hemoglobin; sTfR=soluble transferrin receptor

Treatment of KER-050 Led to Decreased Iron Overload Regardless of Transfusion Burden in Exploratory Analysis

- **Among the 29 patients with baseline ferritin ≥ 1,000 and post-baseline measurements:**
  - 14 (48%) showed decreases of ferritin to <1000 ng/ml while on treatment
  - 20 (69%) showed a ≥20% reduction in ferritin while on treatment
  - 2 patients, including one who was NT, discontinued iron chelator therapy due to decreases in ferritin observed while on treatment

Supports KER-050 potential to ameliorate iron overload in patients with MDS, regardless of baseline transfusion burden

Observed Change in Serum Ferritin by Baseline Ferritin

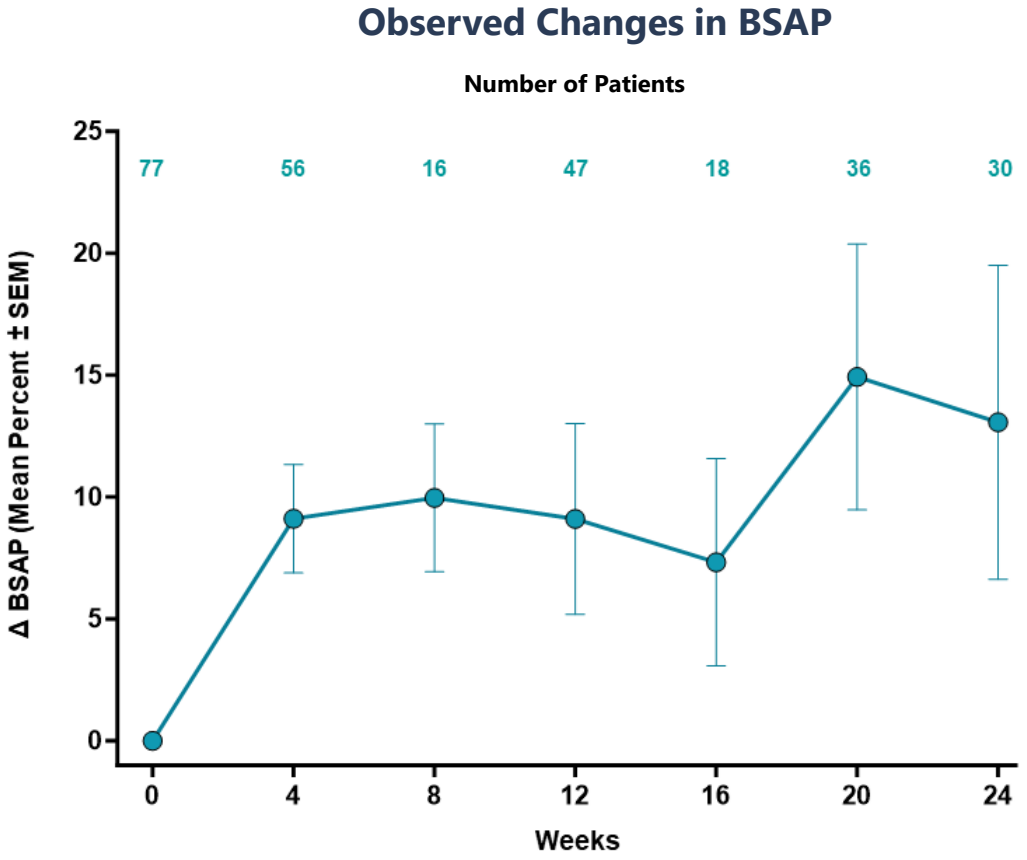


Data are presented as of a data cutoff date of September 1, 2023.
Hgb=hemoglobin; sTfR=soluble transferrin receptor

Potential of KER-050 to Restore Osteohematopoietic Environment in Exploratory Analysis

- **In MDS, disrupted crosstalk between hematopoietic stem cells and osteoprogenitors within the OHN leads to suppression of bone formation (osteogenesis) and hematopoiesis[1]**
- **BSAP (bone-specific alkaline phosphatase) is a marker of osteoblast activity**
- **Sustained increase in BSAP observed with KER-050 treatment**
  - Seen regardless of hematologic response, baseline transfusion burden, or RS status

Findings are consistent with preclinical studies and support KER-050's potential to act on multiple components of the OHN to restore a bone marrow microenvironment conducive to functional hematopoiesis



Data are presented as of a data cutoff date of September 1, 2023.
1. Moses B, et al. ASH 2022;
OHN=osteohematopoietic niche

Hematologic Responses Observed in Broad Array of Patients Treated with KER-050

Responders/N (%)	$mITT_{24}$	
	All (N=60)	HTB (N=33)
Overall Response[a,b]	**30/60 (50)**	**15/33 (45.5)**
Modified IWG 2006 HI-E[c]	**28/60 (47)**	**15/33 (45.5)**
RS+	23/40 (58)	12/23 (52.2)
non-RS	5/20 (25)	3/10 (30)
TI ≥8 weeks[d]	**18/46 (39.1)**	**11/33 (33.3)**
RS+	15/32 (46.9)	8/23 (34.8)
non-RS	3/14 (21.4)	3/10 (30)

HI-E and TI response rates in $mITT_{24}$ patients with HTB were similar to those observed in the overall $mITT_{24}$ population, supporting the potential for KER-050 to treat a broad array of patients with MDS including those with greater transfusion burden and bone marrow dysfunction

Data are presented as of a data cutoff date of September 1, 2023.

a. Includes data for weeks 0-24 in $mITT_{24}$ patients; b. Defined as achieving modified IWG 2006 HI-E and/or TI; c. Modified HI-E = mean increase in hemoglobin ≥1.5 g/dL (NT+LTB) or reduction in transfusion of ≥4 RBC units (HTB) over 8 weeks on treatment compared to 8-week pre-treatment period; d. TI-evaluable patients received at least 2 RBC units in the 8-week pre-treatment period;
$mITT_{24}$ = modified intent to treat 24-week population; TI = transfusion independence

Higher Hematologic Response Rates Observed in Patients with Baseline EPO <500 U/L

Responders/N (%)	$mITT_{24}$ EPO<500 U/L[a]	
	All (N=50)	HTB (N=26)
Overall Response[a,b]	**28/50 (56.0)**	**14/26 (53.8)**
Modified IWG 2006 HI-E[c]	**26/50 (52.0)**	**14/26 (53.8)**
RS+	21/36 (58.3)	11/20 (55)
non-RS	5/14 (35.7)	3/6 (50)
TI ≥8 weeks[d]	**17/38 (44.7)**	**10/26 (38.5)**
RS+	14/29 (48.3)	7/20 (35)
non-RS	3/9 (33.3)	3/6 (50)

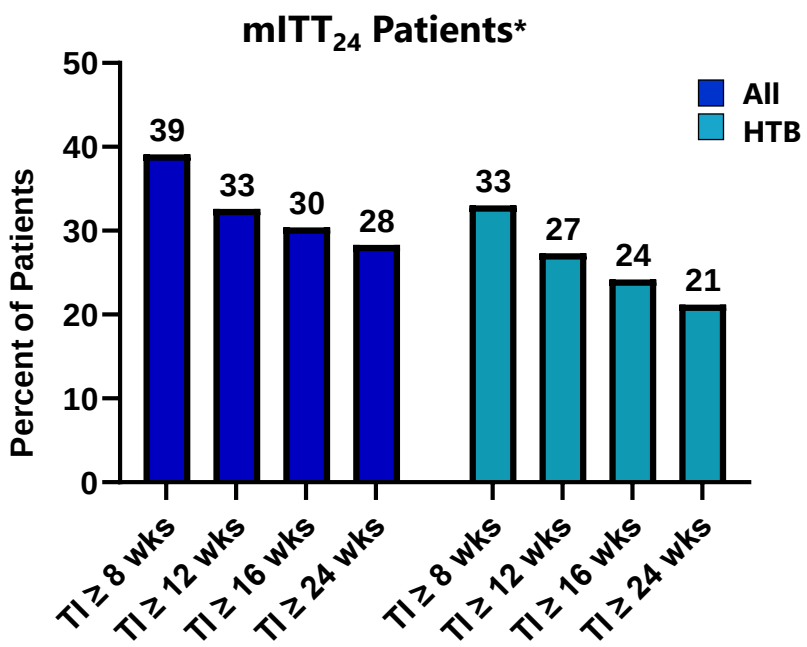
- **Studies in mainly LR-MDS patients suggest that the majority (~90%) of patients have serum EPO levels < 500 U/L[1]**
- **EPO levels ≥500 U/L are associated with lower erythroid response rates across multiple treatments[1]**
- **9 patients in the $mITT_{24}$ population had baseline EPO levels ≥ 500 U/L:**
  - 6/9 had non-RS MDS
  - 3/9 were reclassified by IPSS-M as having high or very-high risk disease

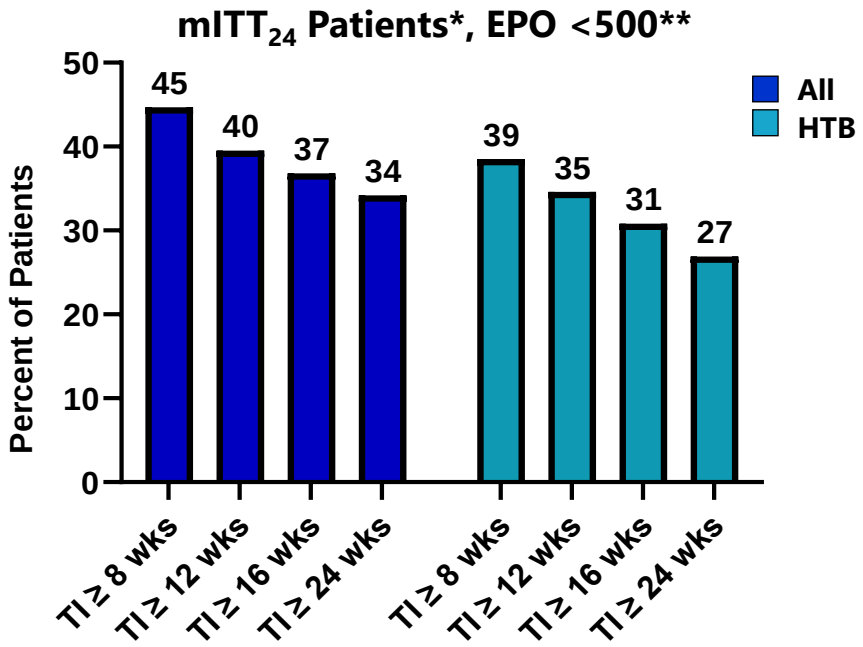
Data are presented as of a data cutoff date of September 1, 2023.

a. Includes data for weeks 0-24 in $mITT_{24}$ patients, excluding one patient with del5q MDS although their baseline EPO was <500 U/L; b. Defined as achieving modified IWG 2006 HI-E and/or TI; c. Modified HI-E = mean increase in hemoglobin ≥1.5 g/dL (NT+LTB) or reduction in transfusion of ≥4 RBC units (HTB) over 8 weeks on treatment compared to 8-week pre-treatment period; d. TI-evaluable patients received at least 2 RBC units in the 8-week pre-treatment period

1. Park, S et al. Annals of Hematology. 2020.

Observed Rates of TI for ≥24 Weeks Support Durability of Response with KER-050 Treatment

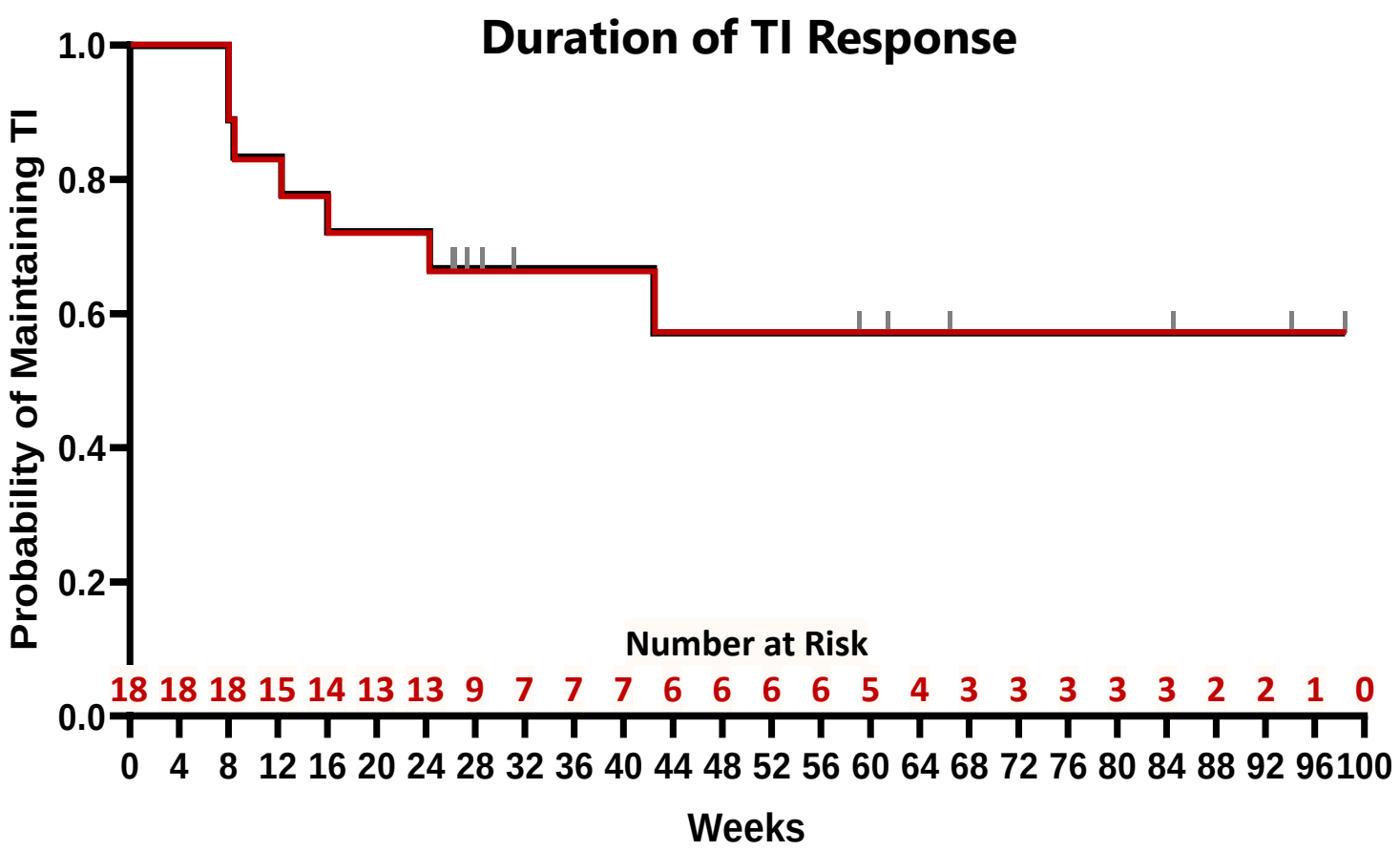




Durable TI was observed including in patients with HTB, and response rates were relatively higher in patients with baseline EPO < 500 U/L

Data are presented as of a data cutoff date of September 1, 2023.
*During Weeks 0-48; **Excludes 1 patient with del5q MDS

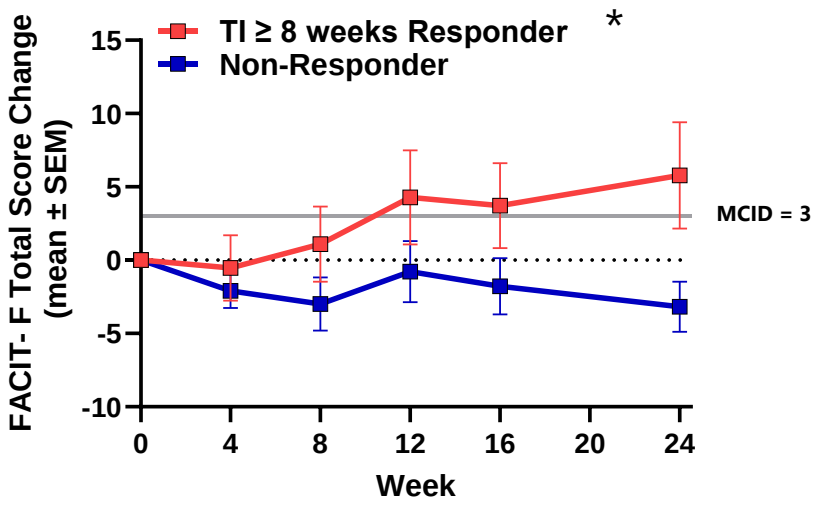
Durable TI Responses Observed with KER-050 Treatment

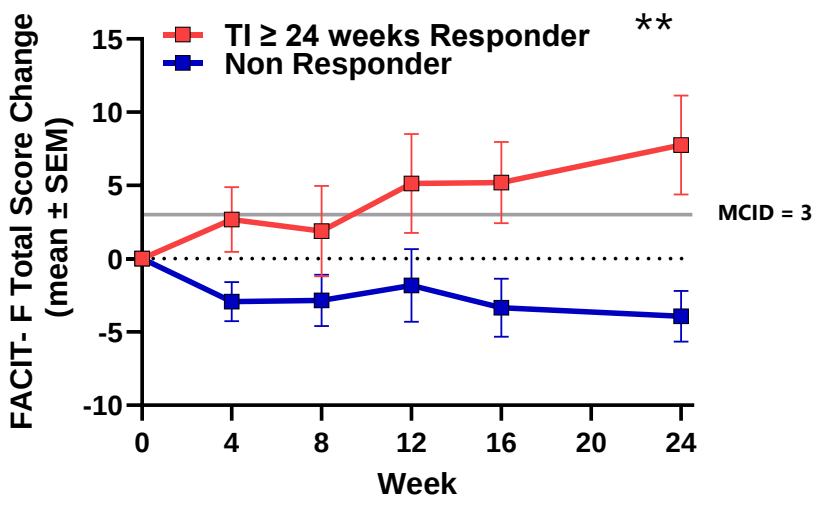


- **18 participants in the $mITT_{24}$ population had TI ≥ 8 weeks**
  - 11/18 (61.1%) had HTB
  - 13/18 (72%) had TI ≥ 24 weeks
- **11/18 (61.1%) had ongoing TI at time of data cut-off**
  - Median baseline transfusion burden: 4 RBC units/8 weeks (range 2 to 11)
  - 6/11 (54.5%) had ongoing TI for > 52 weeks including participants who had received up to 11 RBC units/8 weeks at baseline
- **Median duration of response not reached (range: 8 to 98 weeks)**

Data are presented as of a data cutoff date of September 1, 2023.
Longest TI interval through KER-050 treatment for $mITT_{24}$ patients who achieved TI≥8 weeks during weeks 0-24; Patients with ongoing response censored at time of cutoff (denoted by vertical lines)

Durable and Clinically Meaningful Improvements in FACIT-Fatigue Scores were Observed in TI Responders to KER-050





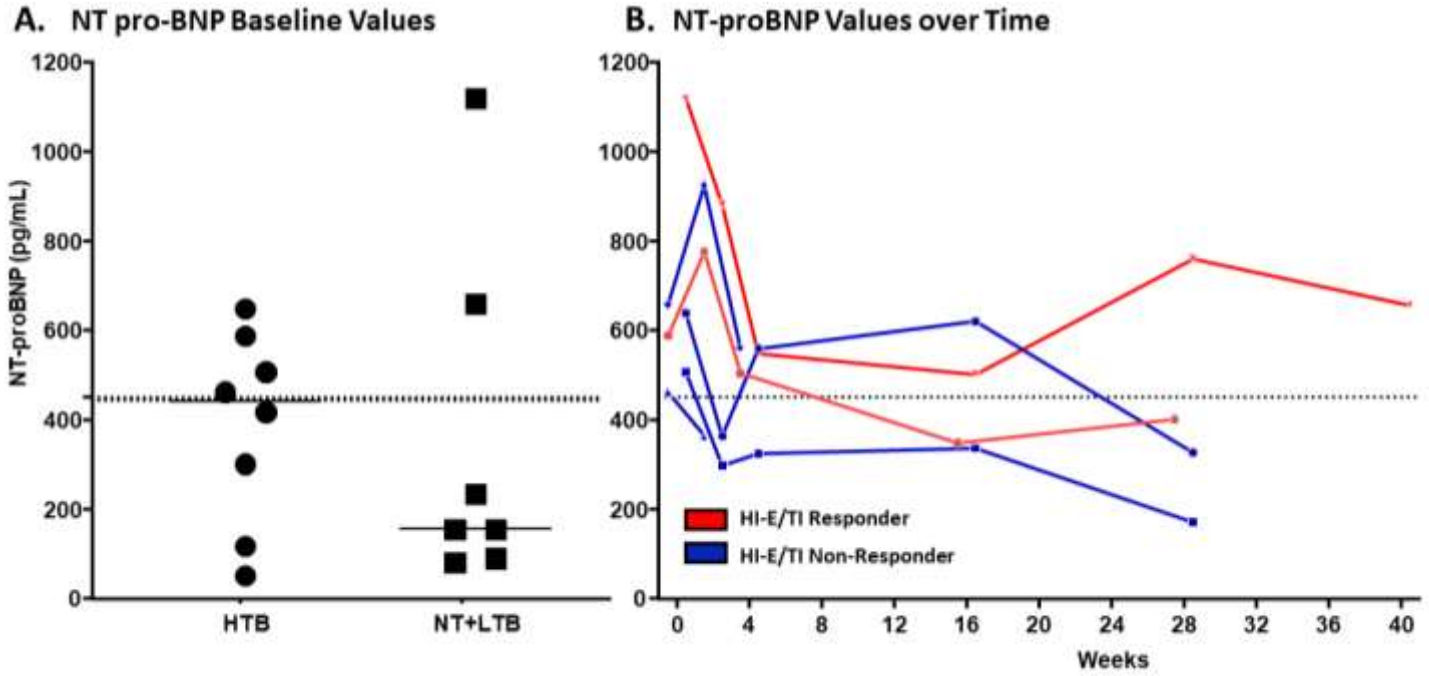
- **Health-related quality of life (HRQOL) is negatively impacted by MDS[1,2] with fatigue identified as a critically important domain to assess in patients with MDS[3]**
  - Prolonged transfusion dependence is associated with significantly worse HRQOL and shorter overall survival[3]
  - Evidence suggests that worse fatigue is associated with reduced survival in MDS[4]
  - The FACIT-Fatigue scale is a validated measure of self-reported fatigue and its impact upon daily activities and function that has been widely used in MDS studies[4,5]

Data are presented as of a data cutoff date of September 1, 2023.
*Includes data for $mITT_{24}$ patients with baseline FACIT-Fatigue scores (n = 1 missing) for TI ≥ 8 weeks Responder, assessed from Weeks 0 to 24; ** Includes data for $mITT_{24}$ patients with baseline FACIT-Fatigue scores (n = 1 missing) for TI ≥ 24 weeks Responder, assessed from Weeks 0 to 48;
1. Stauder, R et. al., Blood. 2018; 2. Pleyer, Lisa, et al., Cancers. 2023; 3. Santini V. Et al., Clin Lymphoma Myeloma Leuk. 2018; 4. Oliva EN et al., Blood. 2021; 5. Sekeres M. et al., HemaSphere. 2023;
MCID = minimally clinically important difference

Potential of KER-050 to Reduce Cardiac Stress in Exploratory Analysis

- In patients with LR-MDS, cardiovascular (CV) events represent a major cause of death possibly due to myocardial stress exacerbated by chronic anemia and iron overload in MDS[1-3]; NT-proBNP is a biomarker of myocardial stress
- Activin A has been shown to play a pathophysiologic role in CVD[4,5], and has been associated with inflammation[6], vascular and myocardial remodeling[7,8], myocardial infarction[9] and severity of HF[10]
- Decreases in NT-proBNP were observed rapidly following initiation of dosing and were sustained for the majority of individuals regardless of erythropoietic response

Observed Decreases in NT-proBNP



Suggests KER-050 may ameliorate cardiac strain directly via inhibition of activin A and indirectly by improving anemia and reducing transfusion burden

Data are presented as of a data cutoff date of September 1, 2023.

1. Madry et al, Br J Haematol 2022; 2. Oliva E, et al. Am J Blood Res 2011; 3. Gatterman N Int J Hematol 2018; 4. Yndestad A J Appl Physiol. (2009) 106:1356–64; 5. Liu H et al Arteriosclerosis,Thrombosis, and Vascular Biology. 2023;43:330–349; 6. Phillips D, et al. Cytokine Growth Factor Reviews 2009; 20(2):153-164; 7. Ryanto G, et al. Int J Mol Sci 2023; 24(4), 3332; 8. Lin JF, et al. Acta Cardiol Sin 2016; 32(4):420-427; 9.Yndestad et al Circulation. 2004;109:1379–1385; 10. Roh et al Sci Trans Med 2019; CVD=cardiovascular disease; NT-proBNP=N-terminal prohormone brain natriuretic peptide

Summary of KER-050 in MDS

- **In the ongoing Phase 2 clinical trial of KER-050 in LR-MDS, the majority of patients enrolled had HTB or MLD indicating a difficult-to-treat trial population**
- **KER-050 was generally well-tolerated as of the data cut-off date, with a safety profile consistent to that previously reported for this trial[1,2]**
- **Durable responses of transfusion independence were observed in a broad range of patients with LR-MDS, including those with HTB**
  - Analysis of patients with EPO < 500 U/L revealed improved erythroid responses across the trial population, including in patients with HTB or non-RS disease
  - Transfusion independence, increases in hemoglobin, and increases in platelets were observed, supporting the potential for KER-050 to ameliorate ineffective hematopoiesis across multiple lineages in patients with MDS
- **Patients who achieved transfusion independence showed clinically meaningful improvements in FACIT-Fatigue scores indicating potential for KER-050 to improve quality of life in patients with LR-MDS**
- **Observations from exploratory assessments of biomarkers:**
  - Sustained increases in bone specific alkaline phosphatase (BSAP) were observed with KER-050 treatment supportive of potential to improve the bone marrow microenvironment
  - Several patients presented with elevated NT-proBNP at baseline, suggestive of increased myocardial stress
    - Rapid decreases with NT-ProBNP were observed with KER-050 treatment in HI-E/TI responders and non-responders
- **Collectively, these results support advancing KER-050 into a Phase 3 registration trial in patients with LR-MDS**

[1] Giagounidis et al. EHA 2023; [2] Chee et al. ASH 2022

KER-050 (Elritercept)

RESTORE

Investigational Treatment for Anemia and Thrombocytopenia in Patients with Myelofibrosis

Ongoing Phase 2 Open-Label Clinical Trial to Evaluate the Safety and Efficacy of KER-050 as Monotherapy or in Combination with Ruxolitinib in patients with Myelofibrosis

Myelofibrosis

MF

MF is a rare cancer of the bone marrow in which the marrow is replaced by scar tissue and is not able to produce healthy blood cells

Clinical Consequences

MF is characterized by ineffective hematopoiesis, an enlarged spleen, bone marrow fibrosis and shortened survival. Both anemia and thrombocytopenia are negative prognostic indicators

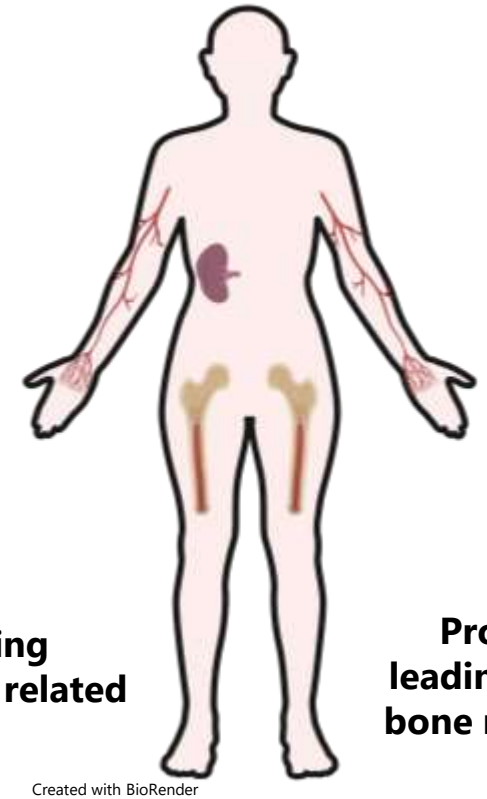
Current Treatments

Currently, there are limited therapeutic options to address the MF-associated cytopenias. Patients not only often experience multiple disease-associated, but also treatment-emergent, cytopenias, including anemia and thrombocytopenia

Scope

In the United States, there are 16,000 to 18,500 patients living with MF and approximately 3,000 newly diagnosed each year

Impact of MF



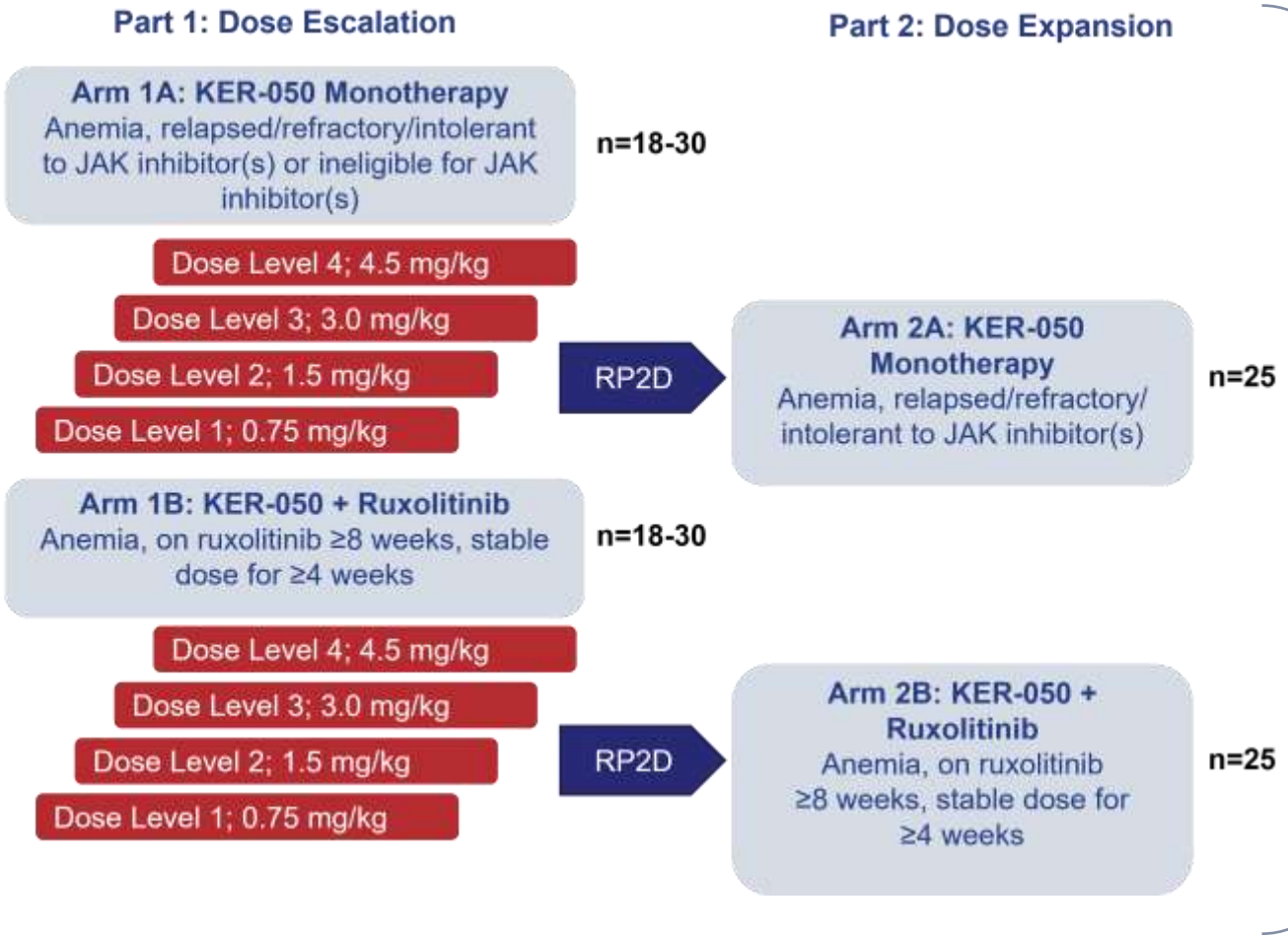
Cytopenias including treatment and disease related severe anemia

Progressive disease leading to splenomegaly, bone marrow fibrosis and AML

Created with BioRender

Severe fatigue and Decreased QoL

Ongoing Phase 2 Clinical Trial to Evaluate KER-050 as Monotherapy or in Combination with Ruxolitinib in Patients with MF



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 Endpoints include:

- Evaluate the pharmacokinetics, pharmacodynamics and efficacy of KER-050 administered with or without ruxolitinib

Following recommendation by the Safety Review Committee, dosing for Part 2 of this trial was initiated at a starting dose of 3.75 mg/kg, with an opportunity to dose escalate to 5.0 mg/kg based on individual titration rules, in both combination and monotherapy arms

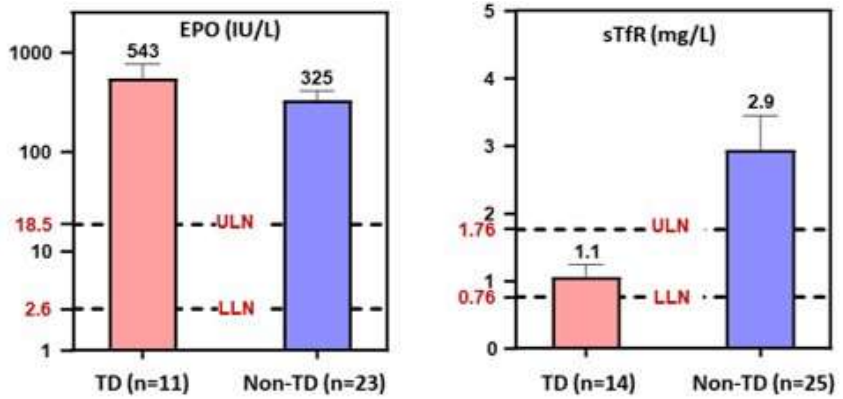
Baseline Characteristics

RESTORE

RESTORE Baseline Demographics

Characteristic	Monotherapy (N=21)	Combination (N=20)	Total (N=41)
Age, years, median (range)	72.0 (60, 85)	74.5 (45, 86)	73.0 (45, 86)
Male (%)	14 (66.7)	12 (60)	26 (63.4)
DIPSS risk category, n (%)			
Intermediate -1	4 (19.0)	1(5.0)	5 (12.2)
Intermediate-2	13 (61.9)	13 (65.0)	26 (63.4)
High	4 (19.0)	6 (30.0)	10 (24.4)
Mutation			
JAK2	10 (47.6)	10 (50.0)	20 (48.8)
CALR	2 (9.5)	5 (25.0)	7 (17.1)
MPL	3 (14.3)	2 (10.0)	5 (12.2)
Triple-negative	5 (23.8)	0	5 (12.2)
RBC U/12 wks, median (range)	4 (0, 25)	4.5 (0, 15)	4 (0, 25)
TD (≥6 RBC U/12 wks)*	10 (6, 25) [n=6]	9 (6, 15) [n=9]	10 (6, 25) [n=15]
Non-TD (<6 RBC U/12wks)	3 (0, 9) [n=15]	3 (0, 5) [n=11]	3 (0, 9) [n=26]
Hgb (g/dL), median (range)	8.18 (7.2, 10.1)	8.03 (5.4, 9.4)	8.08 (5.4, 10.1)
Reticulocytes, $x10^9$/L, median (range)	50.4 (9, 328)	70.7 (7, 173)	62.1 (7, 328)
Platelets, $x10^9$/L, median (range)	112.0 (27, 561)	158.1 (42, 243)	142.3 (27, 561)
Spleen volume, cm^3, median (range)	587.4 (138,2650) [n=16]	920.6 (357,2195) [n=17]	867.7 (138,2650) [n=33]
≥ 450 cm^3, n(%)	11 (68.8)	12 (70.6)	23 (69.7)
MF-SAF-TSS, total, median (range)	16 (0, 56)	10 (0, 36)	11 (0, 56)
≥ 10, n(%)	18 (85.7)	11 (55.0)	29 (70.7)

RESTORE Baseline Biomarkers of Erythropoiesis



- **Patients with high disease burden and severe erythropoietic dysfunction**
- **Most receiving transfusions**
  - 37% TD (IWG 2013 criteria; ≥6 RBC units/12 weeks)
  - Transfusions prevalent even among NTD (median: 3 RBC units/12 weeks)
- **Most had splenomegaly**
  - Marked splenomegaly observed in the KER-050+RUX arm, indicative of inadequate control of disease
- **TD and NTD had anemia with ↑ EPO ≈ erythropoietic dysfunction**
  - In TD, mean serum EPO was 543 IU/L and in NTD, mean EPO was 325 IU/L

Data are presented as of a data cutoff date of September 14, 2023.
IWG=International Working Group; LLN=lower limit of normal; RUX=ruxolitinib; ULN=upper limit of normal

KER-050 Was Generally Well-Tolerated in Patients with Significant Disease Burden

- **TEAEs mild to moderate**
- **Treatment-related TEAEs relatively infrequent**
  - Two had Grade 3 or higher worsening cytopenias
- **One Dose Limiting Toxicity in Part 1**
  - Increased Hgb ≥2 g/dL in dose Level 2 cohort of monotherapy arm
  - No associated AE, Hgb within normal limits
- **Three TEAEs* leading to death, all deemed unrelated to study therapy**

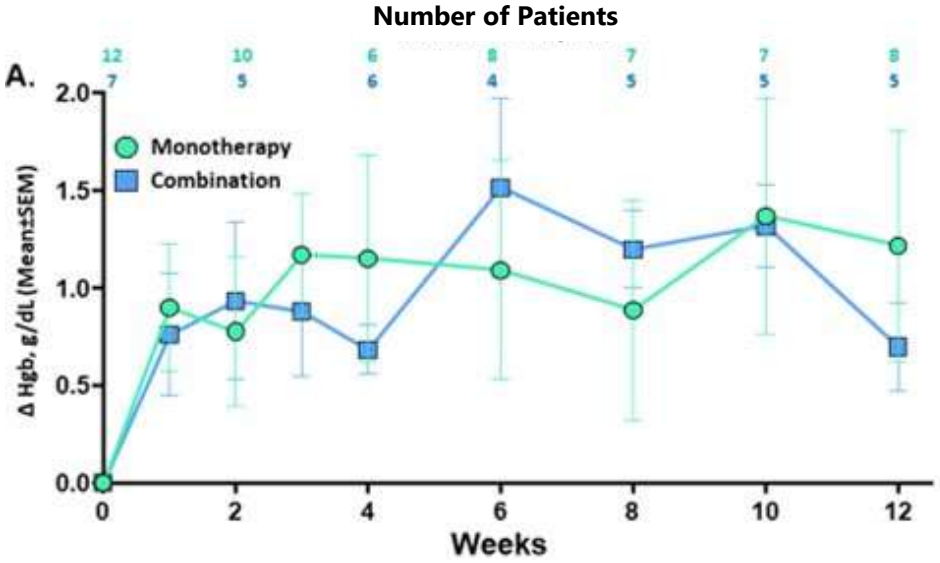
Category, n (%)	Monotherapy (N=21)	Combination (N=20)	Total (N=41)
Any TEAE	**20 (95.2)**	**19 (95.0)**	**39 (95.1)**
Most frequent TEAEs (≥10%* of participants)			
Diarrhea	3 (14.3)	6 (30.0)	9 (22.0)
Thrombocytopenia	5 (23.8)	2 (10.0)	7 (17.1)
Asthenia	5 (23.8)	1 (5.0)	6 (14.6)
Fatigue	3 (14.3)	3 (15.0)	6 (14.6)
Pyrexia	5 (23.8)	1 (5.0)	6 (14.6)
DLTs	**1 (4.8)**	**0**	**1 (2.4)**
SAEs	**7 (33.3)**	**8 (40.0)**	**15 (36.6)**
KER-050-related TEAE	**6 (28.6)**	**4 (20.0)**	**10 (24.4)**
Ruxolitinib-related TEAE	**N/A**	**6 (30.0)**	**6 (14.6)**
KER-050-related TEAE of Grade ≥ 3	**1 (4.8)**	**0**	**1 (2.4)**
Ruxolitinib-related TEAE of Grade ≥ 3	**N/A**	**1 (5.0)**	**1 (2.4)**
TEAE leading to KER-050 discontinuation	**4 (19.0)**	**3 (15.0)**	**7 (17.1)**
TEAE leading to ruxolitinib discontinuation	**N/A**	**2 (10.0)**	**2 (4.9)**
TEAE Leading to Death	**1 (4.8)**	**2 (10.0)**	**3 (7.3)**

Data are presented as of a data cutoff date of September 14, 2023.
*Transformation to AML, cerebrovascular accident and pneumonia
DLT=dose limiting toxicity

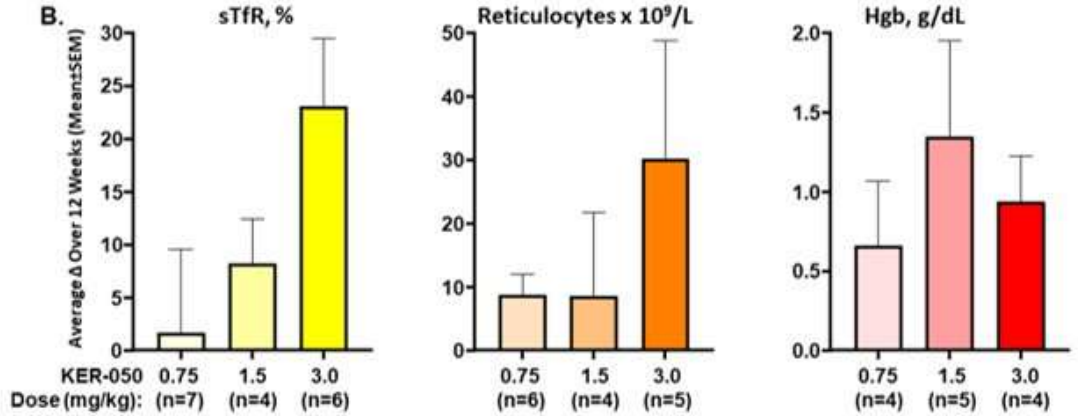
KER-050 Treatment Led to Sustained Increases in Hemoglobin

- **Biomarkers of erythropoiesis assessed in NTD RESTORE patients**
  - Sustained increases in Hgb observed over first 12 weeks of KER-050 treatment in both monotherapy and combination arms
  - Observed increases in sTfR, reticulocytes and Hgb generally higher with increasing dose levels between 0.75 to 3 mg/kg

Observed Change in Hgb



Biomarkers of Erythropoiesis

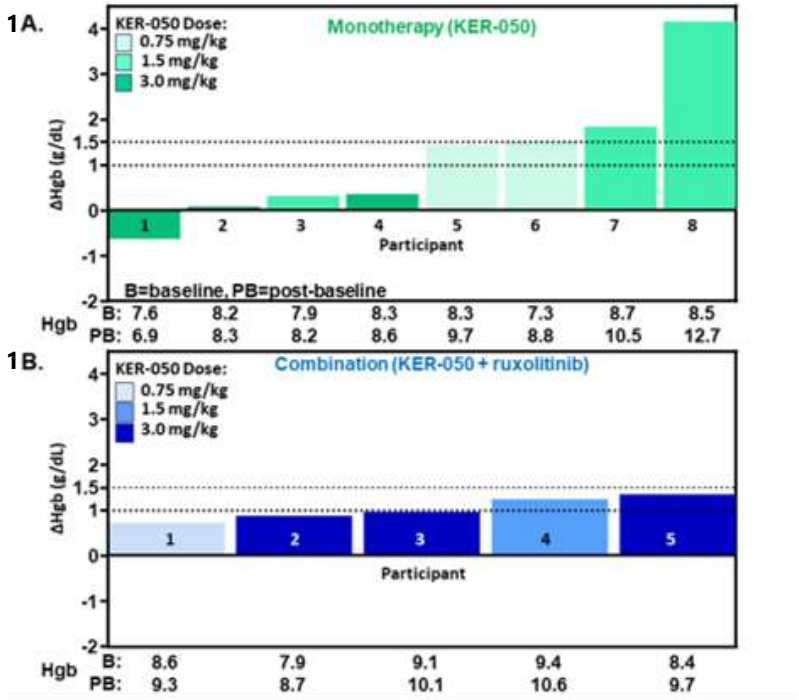


Data are presented as of a data cutoff date of September 14, 2023.

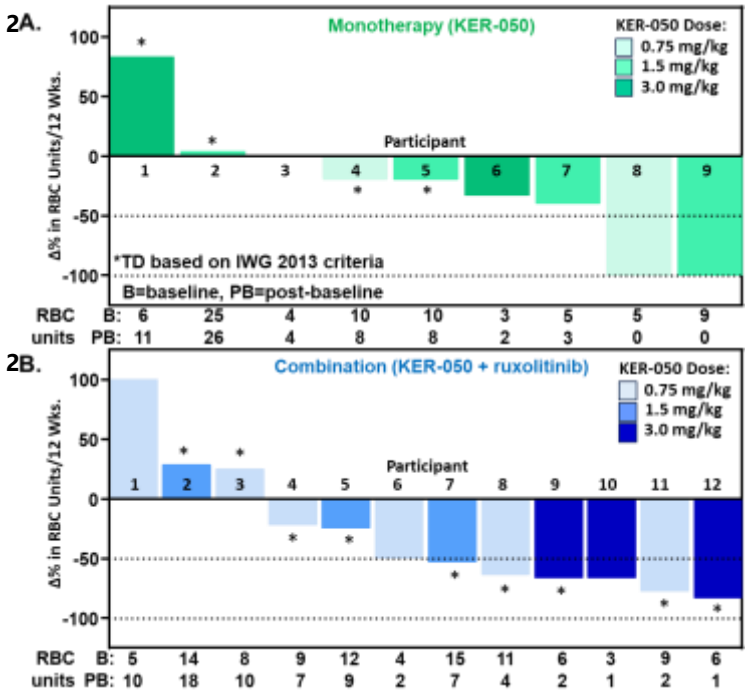
Treatment with KER-050 Led to Robust Increases in Hemoglobin and Reduction in Transfusion Burden in MF Patients

RESTORE

Observed Maximum Change in Hgb: NTD Patients



Observed Reductions in Transfusion Burden



- **Hemoglobin assessed in NTD RESTORE patients:**
  - Observed increases in Hgb in monotherapy arm suggests potential for KER-050 to address anemia due to underlying MF
  - Observed increases in Hgb in combination arm suggests potential to mitigate RUX-associated anemia

- **Changes in transfusion burden over 12 weeks assessed in patients receiving ≥ 3 units RBC/12 weeks at baseline**
- **Decreased transfusion burden occurred in most patients, notably:**
  - At 3 lowest KER-050 dose levels
  - In patients receiving up to 15 RBC units/12 weeks at baseline
- **Data support potential of KER-050 to improve anemia due to MF and RUX-associated anemia**

Data are presented as of a data cutoff date of September 14, 2023.

Preliminary Data Support Potential for KER-050 to Address Multiple Aspects of MF

Hematopoiesis	Spleen Size	Symptoms
• Observed increases in markers of erythropoiesis • Mean increases in hemoglobin and reduction in transfusion burden observed over 12 weeks • Maintenance or improvement in platelet counts observed	• Observed reduction in spleen size in 4/7 (57%) evaluable* patients (1/3 mono, 3/4 combo) at Week 24 • Median reduction (n=4) = -27.1% (range -47.5% to -11.2%) • Median change (n=7) = -11.2% (range: -47.5% to 30%)	• Observed reduction in disease symptoms in 8/12 (67%) evaluable# patients at Week 24 • Median reduction (n=8) = -16.8% (range -55.6% to -6.7%) • Median change (n=12) = -13.2% (range -55.6% to 54.5%)

Data are presented as of a data cutoff date of September 14, 2023.

*Evaluable defined as patients with baseline spleen size ≥ 450 cm^3 and a Week 24 spleen assessment

Evaluable defined as patients with at least 2 symptoms with an average score ≥ 3 or an average total score of ≥ 10 on the MF-SAF-TSS questionnaire at baseline and with a Week 24 MF-SAF-TSS assessment

Summary of KER-050 in Myelofibrosis

- **KER-050 was generally well-tolerated in RESTORE Part 1 as of the data cutoff date, including patients with high disease burden and complex comorbidities**
  - Safety review committee approved RP2D of KER-050 consistent with dose selected for Part 2 of the ongoing Phase 2 clinical trial of KER-050 in patients with lower-risk MDS
- **RESTORE data presented here support potential for KER-050 to:**
  - **Ameliorate ineffective hematopoiesis and address cytopenias (anemia and thrombocytopenia) due to MF and associated with RUX**
    - Based on observed increased markers of erythropoiesis, increased Hgb, decreased transfusion burden, maintained or increased platelets even at doses <RP2D
  - **Provide broader clinical benefit in patients with MF (decreased spleen size and improved symptoms)**

Key Takeaways

- **KER-050 is a novel ligand trap designed to inhibit select TGF-beta ligands, including Activin A, which has been associated with driving disease pathogenesis and progression**
- **Data presented at ASH from the Phase 2 trials in MDS and MF support the potential of KER-050 to ameliorate ineffective hematopoiesis, improve bone health and reduce cardiac stress**
- **In LR-MDS patients:**
  - KER-050 demonstrated durable transfusion independence, including in patients with high transfusion burden
  - Durable clinical responses were associated with improvements in patient-reported measures of fatigue
  - Exploratory biomarker data demonstrate the potential of KER-050 to reduce NT-proBNP, a measure of cardiac stress/strain, and other key biomarker data, supporting its broad potential
- **Collectively, these results support advancing KER-050 into a Phase 3 registration trial in patients with LR-MDS**
  - Keros plans to engage with regulators in H1 2024 on the design of the Phase 3 clinical trial of KER-050 in patients with LR-MDS
- **In MF:**
  - Preliminary findings from Phase 2 clinical trial in myelofibrosis demonstrate that KER-050 can ameliorate ineffective hematopoiesis and address cytopenias
  - KER-050 has the potential broader clinical benefit seen through reduction of spleen size and overall reduction in symptom score

KEROS THERAPEUTICS

Q&A