



KEROS
THERAPEUTICS

Corporate Update

June 2024



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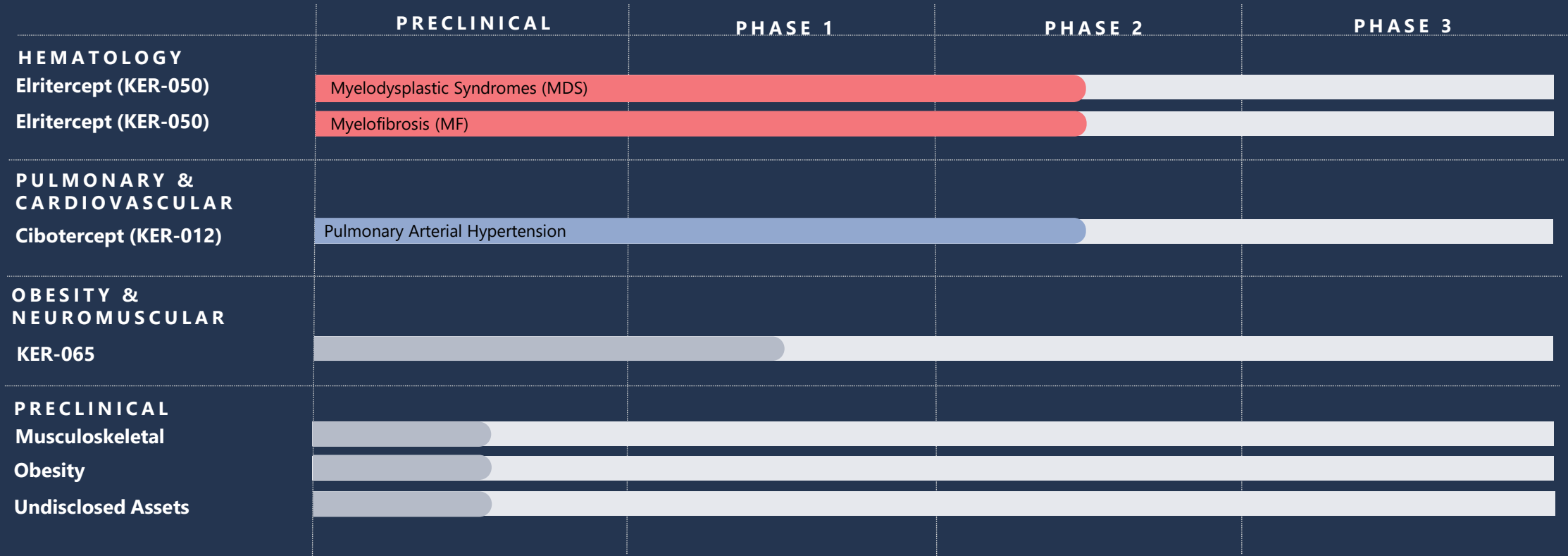
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Focused on Transforming the Lives of a Wide Range of Patients with Disorders Linked to Dysfunctional TGF-β Superfamily Signaling

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

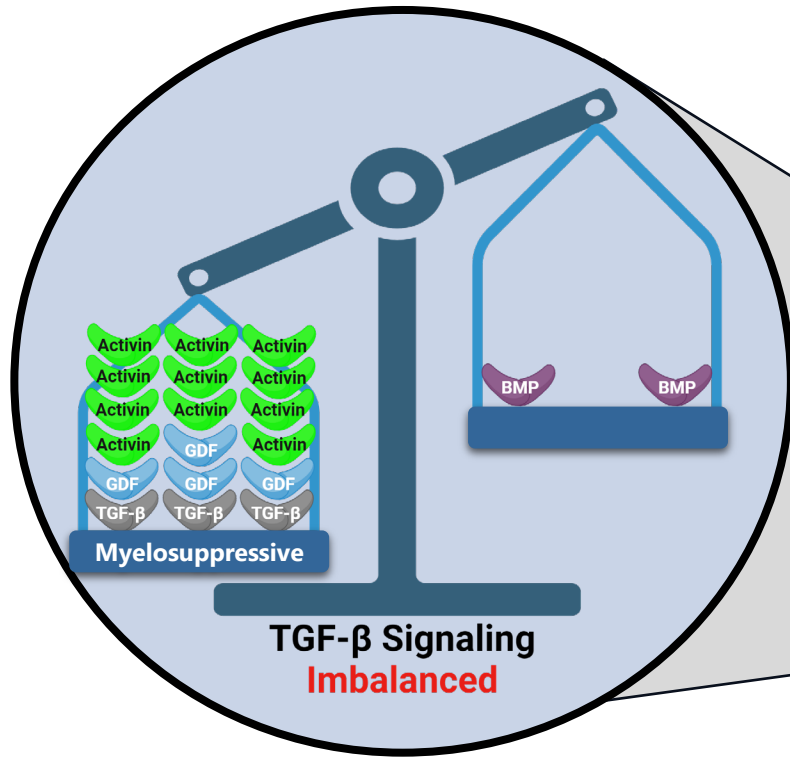
We believe our product candidates have the potential to unlock the full therapeutic benefits of modulating the TGF-β superfamily and provide disease-modifying benefit to patients





Hematology

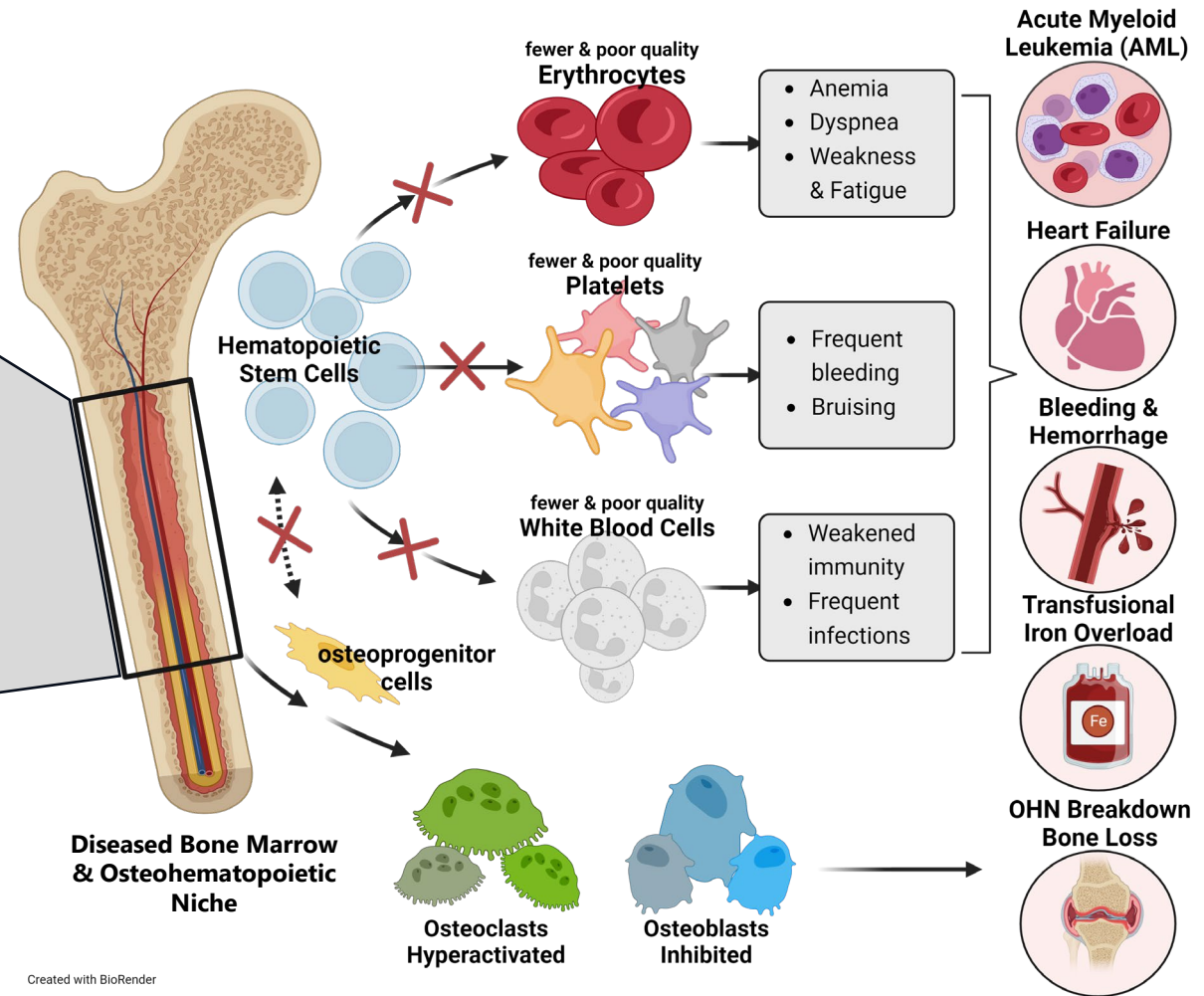
Imbalanced TGF- β Signaling in Bone Marrow Results in Ineffective Hematopoiesis and Poor Outcomes in Both MDS and MF^{1,2,3}



Inhibition of Activin A may restore effective hematopoiesis and improve outcomes

Ineffective Hematopoiesis

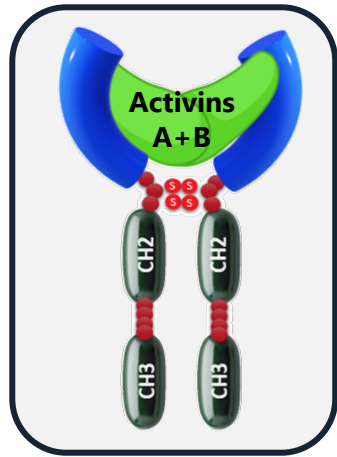
Poor Outcomes



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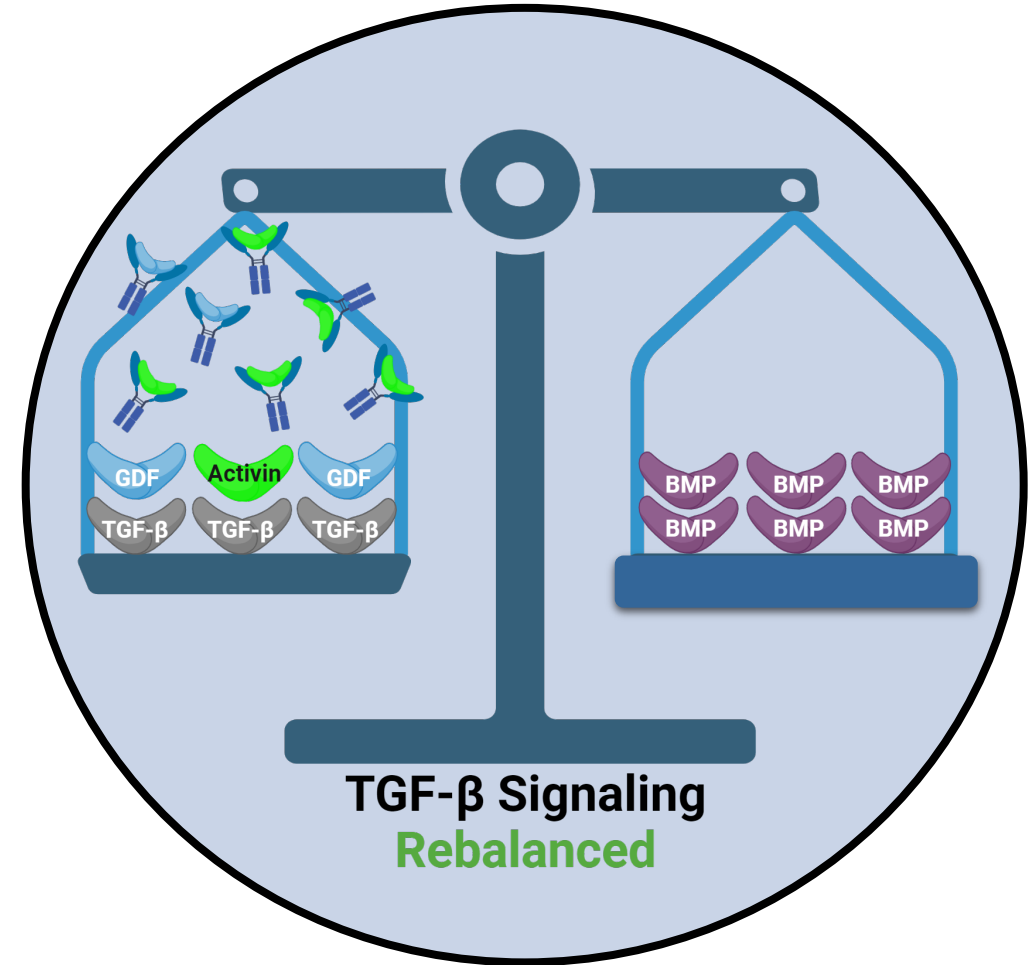
1. Verma A, et al. J Clin Inv 2020; 2. Portale F, et al., Haematologica. 2019, 3. Rambaldi B., et al, Ann Hematol. 2021
 BMP = bone morphogenetic protein; GDF = growth differentiation factor;; OHN = osteohematopoietic niche






Elritercept is Designed to Target Bone Marrow Disorders of Ineffective Hematopoiesis Including MDS and MF



Elritercept (KER-050)

- Designed to inhibit select TGF-beta superfamily ligands, including **Activin A**, which has been associated with ineffective hematopoiesis, inflammation, and driving disease pathogenesis and progression^{1,2,3}



Domain	Potential Effect
 Erythropoiesis	ALL stages of differentiation and maturation ⁴
 Thrombopoiesis	ALL stages of differentiation and maturation ⁵
 Bone	Increased bone formation ⁴ ; potential to improve the osteohematopoietic niche (OHN)
 Iron Metabolism	Improved iron utilization ⁶
 Cardiovascular	Ameliorated cardiac strain ⁶

1. Verma A, et al. J Clin Inv 2020; 2. Portale F, et al., Haematologica. 2019; 3. Phillips, D et al. Cytokine Growth factor Rev. 2009; 4. Moses et al. American Society of Hematology. 2022; 5. Moses et al. Gordon Research Conference: Cell Biology of Megakaryocytes and Platelets. 2023 6. Chee et al. American Society of Hematology. 2023



Elritercept (KER-050)

**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.

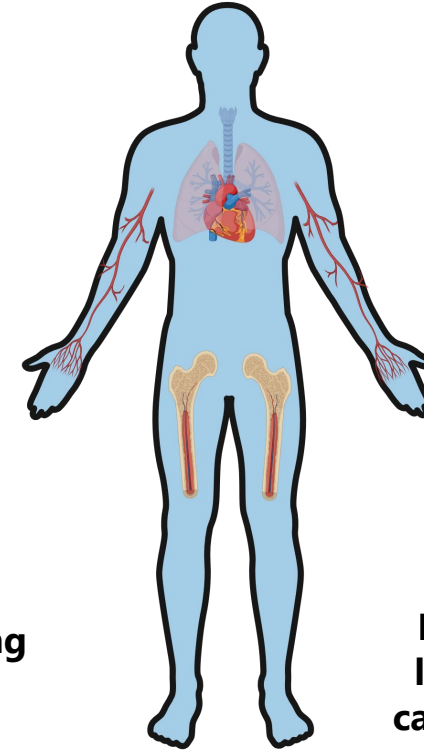


Scope

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.

QoL = quality of life

Impact of MDS



Cytopenias including severe anemia

Progressive disease leading to AML and cardiovascular disease

Created with BioRender

Severe fatigue and decreased QoL

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

Part 2 Dose Confirmation Cohorts

Patients in all Part 2 Cohorts initiate treatment at RP2D	A. LTB/HTB, RS+ N=30
	B. LTB/HTB, Non-RS, N=30
	C. NT, RS+ and Non-RS, N=10
	D. CMML-0, N=10
	E. LTB/HTB, with IO and IC, RS+ and Non-RS, N=15
	F. LTB/HTB, with IO, no IC, RS+ and Non-RS, N=15

Pretreatment
Period
8 weeks

Treatment Period
24 cycles, 96 weeks

Follow-up
Period
8 weeks

Response data are presented for the modified intent to treat 24-week population (mITT₂₄) that includes RP2D patients with at least 24 weeks of KER-050 treatment or who have discontinued (n=81)

Elritercept administered subcutaneously once every four weeks (Q4W)

Primary Objective:

- Assess safety and tolerability of elritercept

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 red blood cell (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 Cut-off Date:

- Part 1 Extension Ongoing
- RP2D: 3.75 mg/kg with the ability to titrate to 5 mg/kg Q4W
- RP2D experienced patients: N=87
 - 7 (8.0%) patients received < 3 doses
 - 46 (52.9%) patients were ongoing and remained on treatment
 - Median duration of treatment = Approx. 42 weeks (Range = 1 to 145 weeks)
 - 39 (44.8%) patients received ≥ 12 doses

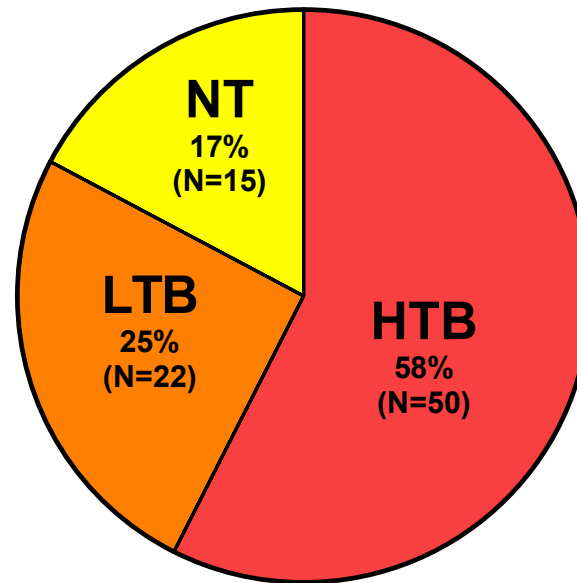
Data are presented as of a data cut-off date of April 3, 2024.

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; IPSS-R = Revised International Prognostic Scoring System

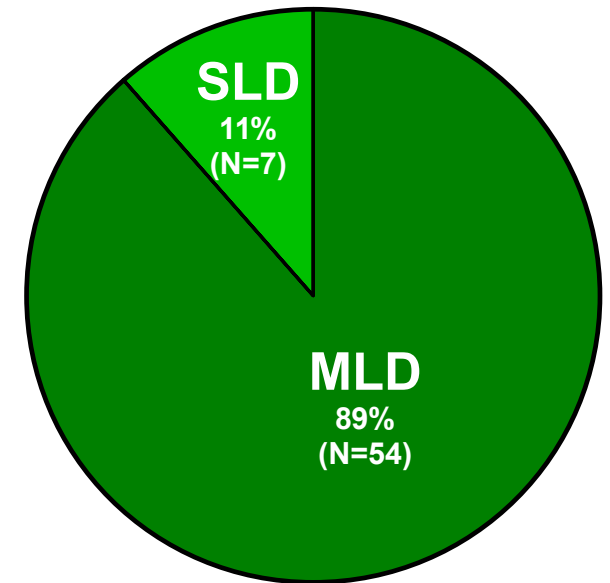
Trial Enrolled Hard-to-Treat Patients with High Disease Burden

Baseline Characteristic	RP2D (N=87)
Median Age, years (range)	74 (53-89)
Sex, n (%) male	55 (63.2)
Ring Sideroblasts Status, n (%)	
RS+	60 (69.0)
Non-RS	27 (31.0)
Prior ESA, n (%)	24 (27.6)
EPO, U/L*	
n	78
Mean (SD)	401.6 (692.1)
Median (IQR)	127.8 (50.6,309.7)
Thrombocytopenia, n (%) (platelets < 150 x 10 ⁹ /L)	21 (24.1)

Baseline Transfusion Burden



Baseline Dysplasia Category**



Data are presented as of a data cut-off date of April 3, 2024.

*9 RP2D patients had missing baseline EPO; **Excludes 26 RP2D patients with unknown dysplasia category

EPO = erythropoietin; SLD = single lineage dysplasia; MLD = multi lineage dysplasia; SD = standard deviation; IQR = interquartile range

Elritercept was Generally Well-Tolerated

- **Most frequent TEAEs (≥ in 15% of patients) regardless of causality were:**
 - Diarrhea (24; 27.6%)
 - Fatigue (22; 25.3%)
 - Dyspnea (18; 20.7%)
 - Dizziness (17; 19.5%)
 - COVID-19 & Nausea (16, 18.4%)
 - Anemia (15; 17.2%)
- **Majority of TEAEs were mild (Grade 1) to moderate (Grade 2)**
- **4 treatment-related TESAEs of injection site reaction (Grade 2), dyspnea (Grade 3), syncope (Grade 3) and gastric neoplasm (Grade 3) occurred in 1 patient each**
 - Gastric neoplasm, dyspnea and syncope were assessed as not related to study treatment by the Sponsor due to underlying comorbidities
- **Fatal TESAEs (cardiac failure, MI and sudden death) occurred in 3 (3.4%) patients; both were assessed as unrelated by the PI and the Sponsor**
- **No patients progressed to AML**

Category	RP2D (N=87) n (%)
Any TEAE	85 (97.7)
Any treatment-related TEAE*	37 (42.5)
Any TESAЕ	38 (43.7)
Any treatment-related TESAЕ	4 (4.6)
Any TEAE leading to death	3 (3.4)
Any TEAE leading to KER-050 discontinuation*	13 (14.9)

*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, sudden death, lymphocytic leukemia, COPD and 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 cut-off date of April 3, 2024.

AML = acute myeloid leukemia; COPD = chronic obstructive pulmonary disease; MI = myocardial infarction; NSCLC = non-small cell lung cancer; TEAE = treatment emergent adverse event; TESAЕ = treatment emergent serious adverse event

Hematologic Responses Observed in Broad Array of Patients Treated with Elritercept (Weeks 0 to 24)

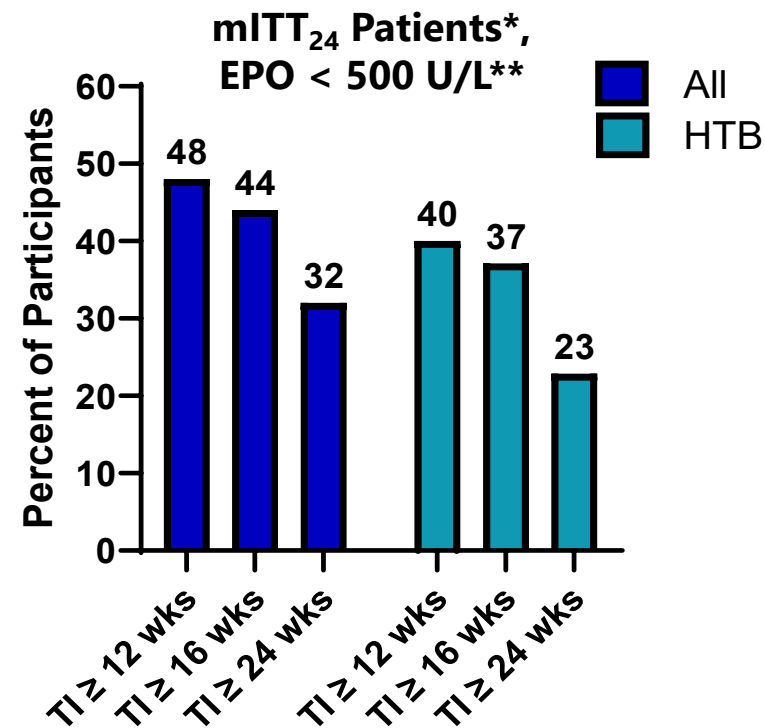
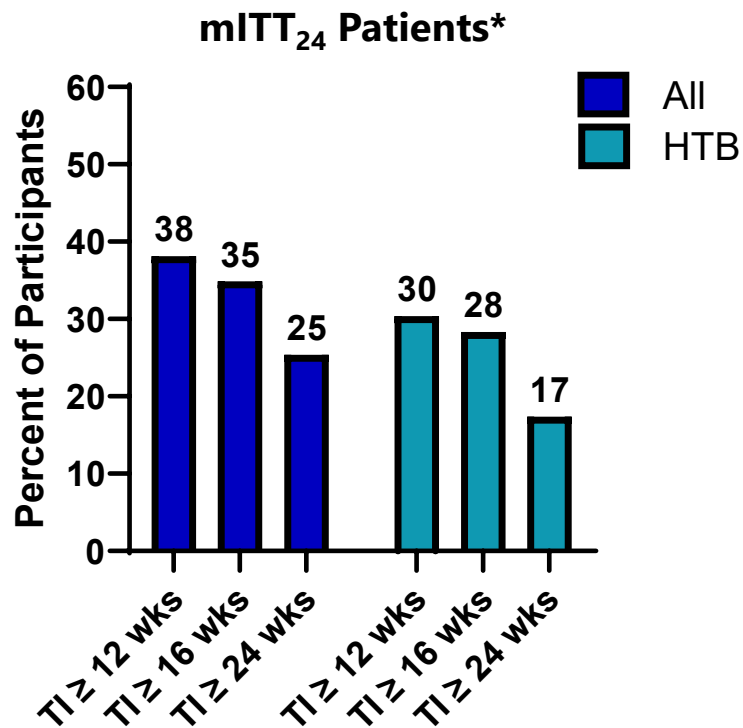
Responders/N (%)	mITT ₂₄ ^a		mITT ₂₄ + EPO < 500 U/L ^b	
	All (N=81)	HTB (N=46)	All (N=66)	HTB (N=35)
Overall Response^c	45/81 (55.6)	23/46 (50.0)	40/66 (60.6)	20/35 (57.1)
Modified IWG 2006 HI-E^d	40/81 (49.4)	22/46 (47.8)	35/66 (53)	19/35 (54.3)
RS+	33/57 (57.9)	19/33 (57.6)	29/51 (56.9)	16/29 (55.2)
non-RS	7/24 (29.2)	3/13 (23.1)	6/15 (40)	3/6 (50)
TI ≥8 weeks^e	26/63 (41.3)	16/46 (34.8)	25/50 (50.0)	15/35 (42.9)
RS+	22/45 (48.9)	13/33 (39.4)	21/40 (52.5)	12/29 (41.4)
non-RS	4/18 (22.2)	3/13 (23.1)	4/10 (40)	3/6 (50)

Response rates in mITT₂₄ patients with HTB were similar to those observed in the overall mITT₂₄ population, with higher rates observed in the EPO < 500 U/L population particularly in non-RS patients. These data support the potential for elritercept to treat a broad array of patients with LR-MDS

Data are presented as of a data cut-off date of April 3, 2024.

a. Includes data for weeks 0-24 in mITT₂₄ patients; b. Includes data for Weeks 0-24 in mITT₂₄ patients with baseline EPO < 500 U/L, excluding one patient with del5q MDS; c. Defined as achieving modified IWG 2006 HI-E and/or TI; d. Modified IWG 2006 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; e. TI-evaluable patients received at least 2 RBC units in the 8-week pre-treatment period. TI = transfusion independence

Observed Rates of TI Support Durability of Response with Elritercept Treatment (Weeks 0 to 48)



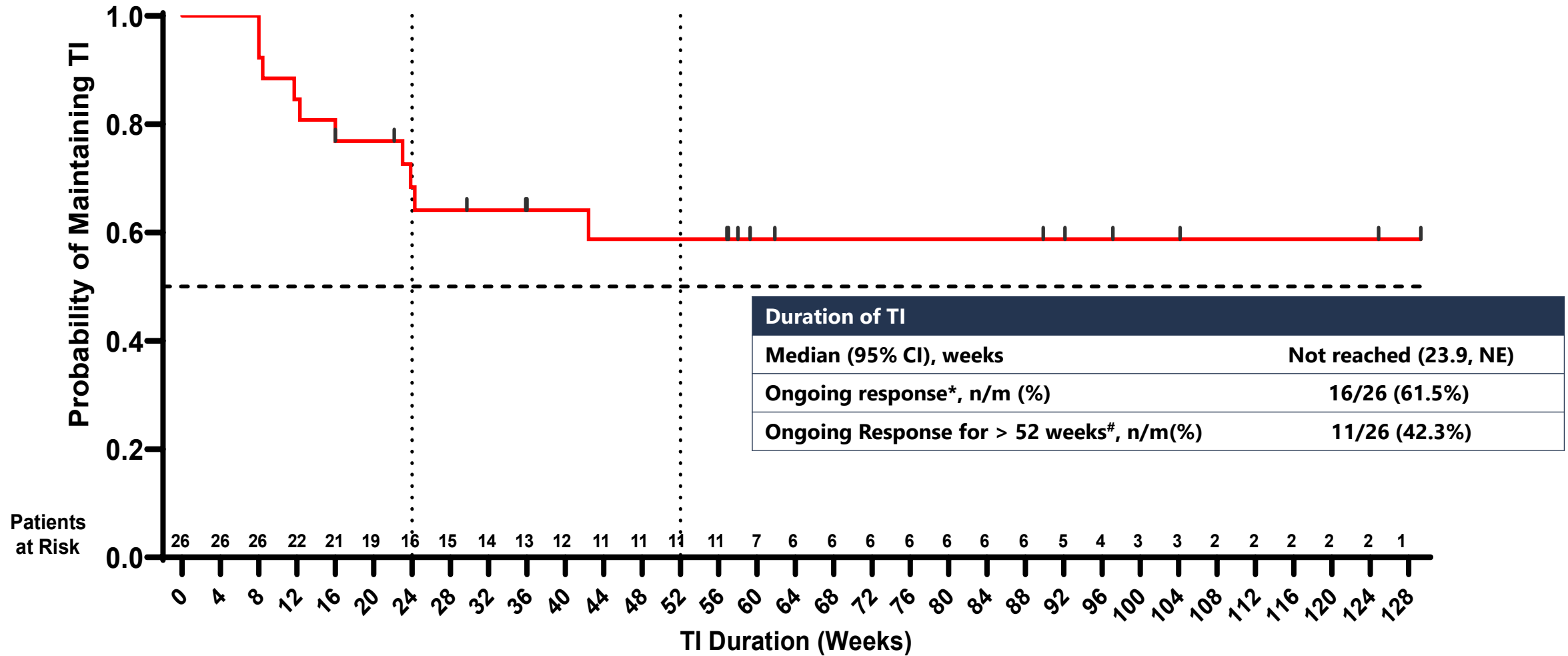
Elritercept treatment resulted in durable TI, including in patients with HTB, with relatively higher TI rates seen in patients with baseline EPO < 500 U/L

Data are presented as of a data cut-off date of April 3, 2024.

*During Weeks 0-48; **Excludes 1 patient with del5q MDS

Durable TI Responses Observed with Elritercept Treatment

Longest TI interval in mITT₂₄ participants who achieved TI ≥ 8 weeks from baseline through Week 24**



Data are presented as of a data cut-off date of April 3, 2024.

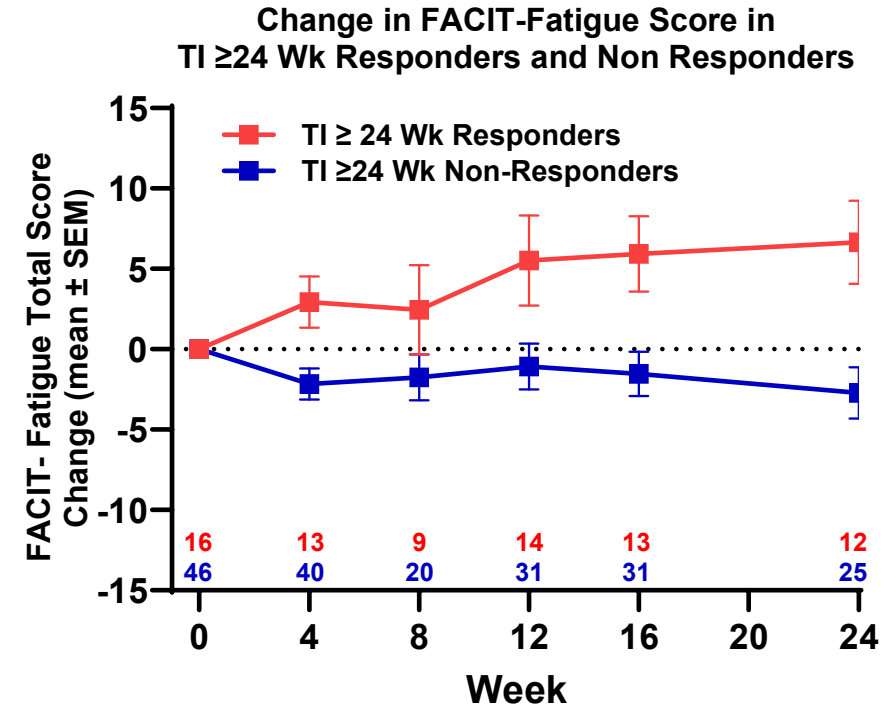
*Patients with ongoing TI response (i.e. without transfusion event) at time of cut-off are censored and denoted by vertical lines; ** RBC transfusions for elective surgery were recorded but were not counted towards baseline requirement or efficacy assessment;

#6/11 (54.5%) participants with ongoing TI for > 52 weeks were HTB, including patients who had received up to 11 RBC units/8 weeks at baseline.

NE= not evaluable; CI = confidence interval

Transfusion Dependent Patients Receiving Elritercept Achieved Clinically Meaningful and Durable Improvements in FACIT-Fatigue Score

- 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 MDS³
 - Prolonged transfusion dependence is associated with significantly worse HRQOL and shorter overall survival³
 - Evidence suggests that worse fatigue is associated with reduced survival in MDS⁴
 - 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}



Clinically meaningful improvement in fatigue defined as at least a 3-point increase in FACIT-Fatigue score

TI Response Duration	Change from Baseline in FACIT-Fatigue Score at Week 24, mean (SEM)		Mean Difference, Responder vs Non-Responder
	Responder	Non-Responder	
TI ≥24 weeks	6.6 (2.6), n=12	-2.7 (1.6), n=25	9.4

Data are presented as of a data cut-off date of April 3, 2024.

Includes data for mITT₂₄ 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;

SEM = standard error of the mean

Summary of Elritercept Data in MDS

- In the ongoing Phase 2 clinical trial of elritercept in LR-MDS, the majority of patients enrolled had HTB or MLD indicating **a difficult-to-treat trial population**
- Elritercept 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}
- **Hematologic responses were observed in 56%** and **TI ≥ 8 weeks was achieved in 41% of patients**, including those with RS+ and non-RS disease
- **Durable TI responses** were observed in a broad range of patients with LR-MDS, including those with HTB, and the **median duration of response** was not reached as of the data cut-off date
- Analysis of patients with EPO < 500 U/L revealed **improved erythroid responses** across the trial population, including **in patients with HTB and/or non-RS disease**
- Patients who achieved TI showed **clinically meaningful improvements in FACIT-Fatigue scores** indicating potential for elritercept to improve **quality of life** in patients with LR-MDS

Collectively, these Phase 2 data show potential for elritercept to provide clinical benefit to a broad difficult-to-treat patient population, supporting initiation of a Phase 3 registrational trial in LR-MDS

Data are presented as of a data cut-off date of April 3, 2024.

¹ Giagounidis et al. EHA 2023; ² Diez-Campelo et al. ASH 2023

Current 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 HTB patients achieved 8-week transfusion independence with Reblozyl® versus 4% with placebo¹
- In 2nd line setting, a medical reviewer of luspatercept noted "patient reported outcome (PRO) data showed no improvement in quality of life for patients who received luspatercept or who responded to luspatercept."²

Telomerase Inhibitor

- RYTELO™ (imetelstat) approved in 2nd line HTB MDS patients
- RYTELO™ approved in patients who have not responded to or have lost response to or are ineligible for ESAs

Unmet need remains for safe and durable treatments for anemia and for treatments that address the multifaceted pathophysiology of MDS

1. Fenaux P, et al. New Eng J Med 2020; 382:140-151; 2. Luspatercept FDA Summary Basis of Approval Medical Review Page 11 4/3/2020.

Data from Third-Party Placebo-Controlled Clinical Trial in Second-Line Lower-Risk MDS Demonstrate Need for Additional Treatment Options

	MEDALIST Trial¹ (Luspatercept Phase 3)*	
	Study Enrolled RS+ Patients Only	
	Luspatercept	Placebo
8-wk TI	38%	13%
8-wk TI in HTB patients ≥ 4 RBC units/ 8 weeks	20%	4%
Median Duration of TI in 8-week TI responders	30.6 weeks	13.6 weeks

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

*TI for 8 weeks or longer during weeks 1 through 24 in patients with baseline transfusion burden of ≥2 units/8 weeks; no EPO cap

Phase 2 Data Supports Potential for Elritercept to Achieve a Deep and Durable Efficacy Profile Differentiating from Treatment Landscape

	Elritercept Phase 2 Data (miTT ₂₄ EPO _{≤500})*	
	Study Enrolling RS+ and Non-RS Patients	
8-wk TI	50%	} Deep Response in Difficult to Treat Patients
8-wk TI in HTB patients (≥ 4 RBC units / 8 weeks)	42.9%	
24-wk TI over 48 weeks	32%	
Median Duration of TI in 8-week TI responders (RS and non-RS)	Not yet reached as of April 3, '24 52-week TI: 59% in 8-week TI responders	} Strong Durability of Response

Data are presented as of a data cut-off date of April 3, 2024.

*miTT₂₄ in patients with baseline transfusion burden of ≥2 units/8 weeks; EPO ≤500

Phase 3 Registrational Trial in MDS

Received positive feedback from the U.S. Food and Drug Administration (FDA), which resulted in **general alignment on the design and endpoints for the proposed pivotal, Phase 3, placebo-controlled, clinical trial** in patients with LR-MDS.

Planned Trial Population

- Very low-, low-, or intermediate risk MDS
- Anemic patients requiring transfusion
- Both RS+ and non-RS patients
- ESA naïve, intolerant or experienced; no prior Reblozyl® experience
- Baseline serum EPO level cap

Planned Endpoints

- Primary Endpoint: TI at 8 weeks within the first 24 weeks
- A key secondary outcome will be 24-week TI over 48 weeks

Plan to host investor call in the second half of 2024 to provide additional details on the Phase 3 design



Elritercept (KER-050)



**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. Anemia is prevalent in MF (one study reported anemia in 64% of patients beyond 1 year of diagnosis¹) and is associated with reduced quality of life and reduced survival.²



Current Treatments

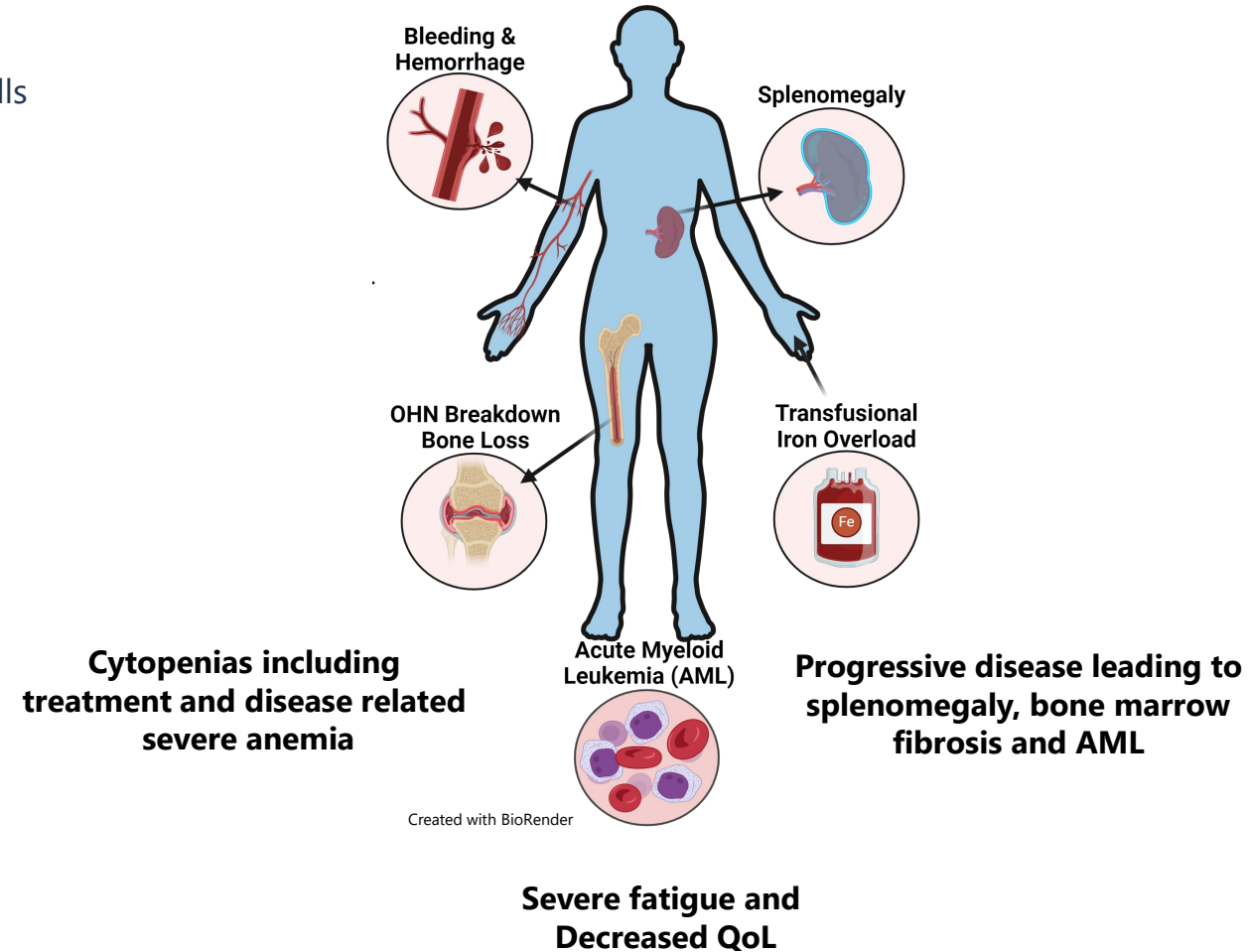
Currently, there are limited therapeutic options to address the MF-associated cytopenias. Patients not only often experience multiple disease-associated, but also treatment-emergent, cytopenias, including anemia and thrombocytopenia



Scope

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

MF Outcomes



1. Tefferi A, et al. Mayo Clin Proc. 2012; 2. Passamonti F, et al., Crit Rev Oncol Hematol. 2022

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



Primary MF, Post-ET or Post-PV MF with Anemia

Part 1: Dose Escalation 0.75 mg/kg to 4.5 mg/kg

Monotherapy:
JAK inhibitor relapsed, refractory, intolerant or ineligible

Combination with Ruxolitinib:
Prior ruxolitinib treatment \geq 8 weeks with stable dose \geq 4 weeks

Part 2: Dose Expansion RP2D

Monotherapy:
JAK inhibitor relapsed, refractory, intolerant or ineligible

Combination with Ruxolitinib:
Prior ruxolitinib treatment \geq 8 weeks with stable dose \geq 4 weeks

Key Eligibility	Objectives and Endpoints	Trial Status
<ul style="list-style-type: none"> Transfusion dependent (TD): average of ≥ 6 RBC units/12 weeks with ≥ 1 transfusion within 28 days prior to treatment Non-transfusion dependent (Non-TD): baseline hemoglobin < 10 g/dL, with or without transfusions Baseline platelet count $\geq 25 \times 10^9/L$ 	<ul style="list-style-type: none"> Primary: To evaluate safety and tolerability of elritercept as monotherapy or in combination with ruxolitinib in patients with MF Secondary/Exploratory: To evaluate effects of elritercept with or without ruxolitinib on: <ul style="list-style-type: none"> Anemia, spleen volume, symptom score, exploratory biomarkers 	<ul style="list-style-type: none"> Data presented as of a data cut-off date of April 3, 2024 Dose escalation complete RP2D identified as 3.75 mg/kg with option to up-titrate to 5 mg/kg Q4W Part 2 Dose Expansion open and enrolling Total of 54 patients enrolled

Post-ET = post-essential thrombocythemia; Post-PV= post polycythemia vera

Trial Enrolled a Population with High Disease Burden

Parameter	Monotherapy (N=23)	Combination (N=31)	Total (N=54)
Age, years, median (range)	71.0 (60 - 85)	72.0 (45 - 86)	72.0 (45 - 86)
Male (%)	16 (69.6)	18 (58.1)	34 (63.0)
DIPSS risk, n (%)			
Intermediate -1	4 (17.4)	2 (6.5)	6 (11.1)
Intermediate-2	14 (60.9)	18 (58.1)	32 (59.3)
High	5 (21.7)	11 (35.5)	16 (29.6)
Mutation, n (%)			
JAK2	12 (52.2)	18 (58.1)	30 (55.6)
CALR	2 (8.7)	7 (22.6)	9 (16.7)
MPL	4 (17.4)	2 (6.5)	6 (11.1)
Triple-negative	3 (13.0)	0	3 (5.6)
Prior JAK Inhibitor, n (%)	10 (43.5)	31 (100)	41 (75.9)
Transfusion Status			
TD*, n (%)	7 (30)	10 (32)	17 (31)
RBC U/12 wks, median (range)	10 (6 - 25)	10 (6 - 15)	10 (6 - 25)
Non-TD*, n (%)	16 (70)	21 (68)	37 (69)
RBC U/12 wks, median (range)	2 (0 - 9)	3 (0 - 5)	3 (0 - 9)
Hgb (g/dL), median (range)	8.18 (7.2 - 10.1)	8.08 (5.8 - 9.4)	8.10 (5.4 - 10.1)
Platelets, x10 ⁹ /L, median (range)	112.0 (27 - 561)	139.0 (42 - 311)	128.2 (27 - 561)
<150 x 10 ⁹ /L, n (%)	14 (60.6)	18 (58.1)	32 (59.3)
<50 x 10 ⁹ /L, n (%)	9 (39.1)	3 (9.7)	12 (22.2)
Received platelet transfusions, n (%)	5 (21.8)	0	5 (9.3)
Spleen volume, cm ³ , median (range)	968.4 (138 - 2650)	920.6 (270 - 6962)	937.4 (138 - 6962)
≥ 450 cm ³ , n(%)**	16 (76.2)	19 (76)	35 (76.1)
Missing	2 (8.7)	6 (19.4)	8 (14.8)
MF-SAF-TSS, total, median (range)	16 (0 - 56)	12 (0 - 55)	14 (0 - 56)
≥ 10, n(%)	20 (87.0)	21 (67.7)	41 (75.9)

Anemic Population
Heavily transfused population with 67% of participants receiving ≥ 3 RBC U/12 wks

Thrombocytopenia
More severe thrombocytopenia in monotherapy arm

Splenomegaly
76% evaluable for spleen response (spleen volume ≥ 450 cm³), including participants receiving ruxolitinib

Symptomatic
76% evaluable for symptom response (based on total MF-SAF-TSS ≥ 10***), including participants receiving ruxolitinib

Data are presented as of a data cut-off date of April 3, 2024.

CALR = calreticulin; DIPSS = dynamic international prognostic scoring system; JAK2 = Janus kinase 2; MPL = myeloproliferative leukemia protein gene; MF-SAF-TSS = myelofibrosis-symptom assessment form- total symptom score (version 4.0, 7-item)
*Transfusion dependent is based on IWG 2013 criteria (Tefferi et al. Blood. 2013) and is defined as receiving ≥6 RBC units in the 12 weeks prior to first dose with at least one transfusion event in the 4 weeks preceding first dose **Percentage based on participants with non-missing baseline value ***3 additional participants (1 monotherapy, 2 combination) met criteria for being symptom response evaluable based on having at least two symptoms with an average score ≥ 3.

Elritercept Was Generally Well-Tolerated in Patients with Significant Disease Burden

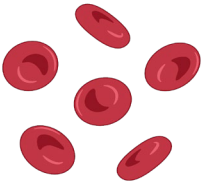




- **Most frequent TEAEs ($\geq 15\%$ of patients in both arms) regardless of causality:**
 - Thrombocytopenia (10, 18.5%)
 - Monotherapy: 7, 30.4%
 - Combination: 3, 9.7%
 - Diarrhea (9, 16.7%)
 - Monotherapy: 3, 13%
 - Combination: 6, 19.4%
- **In Part 1 Dose Escalation, 1 patient (monotherapy arm, 1.5 mg/kg dose) experienced a dose limiting toxicity (DLT) of hemoglobin increase ≥ 2 g/dL, which met protocol criteria for dose reduction and was not associated with AEs**
- **3 patients experienced Grade ≥ 3 TEAEs considered to be related to elritercept by the investigator**
 - Platelet count decreased
 - Hypertension
 - Thrombocytopenia
- **Four TEAEs leading to death, all deemed unrelated to study therapy**
 - Pneumonia aspiration
 - Multiple organ dysfunction
 - Transformation to AML
 - Cerebrovascular accident

Category, n (%)	Monotherapy (N=23)	Combination (N=31)	Total (N=54)
Exposure			
Median Duration, weeks (range)	24.1 (6-120)	23.7 (0-82)	23.9 (0-120)
Ongoing, n (%)	10 (43.5)*	21 (67.7)*	31 (57.4)*
Median Ruxolitinib Dose on C1D1, mg/day (range)	N/A	20 (10-50)	
Safety			
Any TEAE	23 (100)	25 (80.6)	48 (88.9)
TESAEs	10 (43.5)	11 (35.5)	21 (38.9)
Elritercept-Related TEAE	8 (34.8)	11 (35.5)	19 (35.2)
Ruxolitinib-Related TEAE	N/A	9 (29.0)	9 (16.7)
Elritercept-Related TEAE of Gr ≥ 3	0	3 (9.7)	3 (5.6)
Ruxolitinib-Related TEAE of Gr ≥ 3	N/A	0	0
TEAE Leading to Elritercept Discontinuation	6 (26.1)	3 (9.7)	9 (16.7)
TEAE Leading to Ruxolitinib Discontinuation	N/A	2 (6.5)	2 (3.7)
TEAE Leading to Death	2 (8.7)	2 (6.5)	4 (7.4)

Data are presented as of a data cut-off date of April 3, 2024

*As of the data cut-off date, 12/13 (92% of Part 2 patients were ongoing, median exposure of 7.5 and 7.1 weeks for monotherapy and combination arms, respectively

Data Support Potential for Elritercept to Address Multiple Aspects of MF

Hematopoiesis	Spleen Size	Symptoms
<ul style="list-style-type: none"> Observed increases in markers of erythropoiesis were generally greater at higher doses Increases in Hgb were observed in both monotherapy and combination arms Reductions in transfusion burden observed in both arms further support potential to address ruxolitinib associated anemia as well as anemia due to underlying MF. In evaluable* patients receiving 3mg/kg of elritercept or higher in combination with ruxolitinib 5/11 (45.5%) achieved T1 Improvements in platelet count were observed in patients with baseline thrombocytopenia particularly those treated with elritercept plus ruxolitinib 	<ul style="list-style-type: none"> 9/17 (53%) evaluable patients (2/8 mono, 7/9 combo) showed some reduction in spleen size at Week 24 <ul style="list-style-type: none"> Evaluable patients had baseline spleen size $\geq 450 \text{ cm}^3$ and a Week 24 spleen volume assessment 3/9 (33%) had reductions $\geq 35\%$ Among the 7 evaluable patients in the combination arm who showed reductions in spleen size at Week 24, 6 occurred without ruxolitinib dose increase. 	<ul style="list-style-type: none"> Some reduction in symptom score observed in 13/20 (65%) evaluable patients at Week 24 Evaluable patients had MF-SAF-TSS ≥ 10 or had at least 2 symptoms with an average score \geq at baseline and a week 24 assessment 3 patients had reductions $\geq 50\%$ including 2 in monotherapy and 1 in combination arm
 	 	

Data are presented as of a data cut-off date of April 3, 2024.

*Patients were included in the analysis if they received ≥ 3 RBC U/12 weeks at baseline;

Summary of Elritercept in Myelofibrosis

- The ongoing Phase 2 RESTORE trial of elritercept in MF has **enrolled a broad population of patients with high disease burden**
- Elritercept was **generally well-tolerated** in patients with MF, both as monotherapy and in combination with ruxolitinib
- Potential for elritercept to **address ineffective hematopoiesis in MF** is supported by observed **increases in hemoglobin, reduction in transfusion, and preservation or improvement of platelet counts**
- Observed effects on spleen volume reduction support potential for **elritercept to improve splenomegaly**, particularly in combination with ruxolitinib
- Potential for elritercept to **improve symptoms** is supported by observed reductions in total symptom score
- Enrollment in Part 2 of RESTORE trial is **ongoing at the RP2D of 3.75 mg/kg** with titration to 5 mg/kg to further study effects of elritercept in participants with MF

Improvements in hemoglobin, transfusion burden, spleen volume, and total symptom scores were observed in both monotherapy and combination arms, including at dose levels below the RP2D, supporting potential for elritercept to provide clinically meaningful benefits to patients with MF



Cibotercept (KER-012)

Investigational Treatment for Pulmonary Arterial Hypertension (PAH) and for Cardiovascular Disorders

Ongoing Phase 2, Randomized, Double-blind, Placebo-Controlled Clinical Trial to Evaluate the Safety and Efficacy of KER-012 in Combination with Background Therapy in Adult Participants with Pulmonary Hypertension

Cibotercept (KER-012)

- Cibotercept is a **modified** activin receptor IIB ligand trap designed to **preferentially inhibit select ligands** to potentially rebalance TGF- β superfamily signaling **without a dose-limiting increase in RBCs**
- Completed a randomized, double-blind, placebo-controlled, two-part Phase 1 clinical trial to evaluate single and multiple ascending doses of cibotercept in healthy volunteers
 - **No clinically meaningful changes in Hgb / RBCs observed** ^{1,2}
 - We believe PD data support potential for **maximal target engagement with doses being evaluated in the ongoing Phase 2 clinical trial** (TROPOS) ^{1,2}
- Ongoing TROPOS trial is a randomized, double-blind, placebo-controlled, global Phase 2 clinical trial to evaluate KER-012 in combination with background therapy in adult patients with PAH
- **Expect to complete enrollment in Q4 2024**

Cibotercept (KER-012) Open Label Biomarker Phase 2 Clinical Trial

- As part of its ongoing portfolio management activities, Keros has decided to **early terminate** its open-label Phase 2 biomarker clinical trial of cibotercept in patients with chronic heart failure with preserved ejection fraction (HFpEF) and in such patients with reduced ejection fraction (HFrEF)
- **To date, we have not enrolled any patients in this trial**
- **The planned early termination is not on the basis of any safety concerns**



KER-065: *Obesity*

- ▶ **We believe preclinical data suggests KER-065 has the potential to improve body composition by increasing muscle mass and decreasing fat mass alone or in combination with glucagon-like peptide-1 (GLP-1) receptor agonists**
- ▶ **By targeting activin A, KER-065 has the potential to directly reduce inflammation and fibrosis, the processes resulting in the development of cardiometabolic diseases**
- ▶ **Potential for infrequent subcutaneous dosing**

KER-065

- KER-065 is a **novel ligand trap** designed to bind to and inhibit TGF- β ligands, **including myostatin (GDF8) and activin A**
- **Currently being evaluated in an ongoing Phase 1 clinical trial in healthy volunteers**
 - Primary Objectives: to **evaluate safety, tolerability and pharmacokinetics** of single and multiple ascending doses of KER-065
 - Exploratory Objectives: assess the pharmacodynamic effect on bone, adipose tissue, muscle, cardiac tissue and fibrosis
- Trial Subjects:
 - Healthy volunteers (males 18-55 years of age)
 - Body Mass Index:
 - SAD: 18.5 – 30
 - **MAD: 27 – 33**
- Based on the Safety Review Committee's recommendation, we have initiated the third dose cohort in the SAD portion at 5 mg/kg and have begun dosing the first MAD cohort of this trial at 2 mg/kg every four weeks. We continue to expect to report initial data from this trial in the first quarter of 2025

We believe this trial has the potential to provide biologic proof-of-concept to support initiation of a Phase 2 proof-of-concept clinical trial in patients with obesity

Anticipated Key Milestones

KER-050

- Announce additional data from Part 2 of Phase 2 MDS trial Q4 2024
- Announce additional data from Phase 2 MF trial Q4 2024

KER-012

- Complete enrollment in Phase 2 TROPOS Trial Q4 2024

KER-065

- Announce data from Phase 1 healthy volunteer trial Q1 2025



KEROS
THERAPEUTICS

Q&A

