KEROS THERAPEUTICS

Corporate Presentation

August 2024

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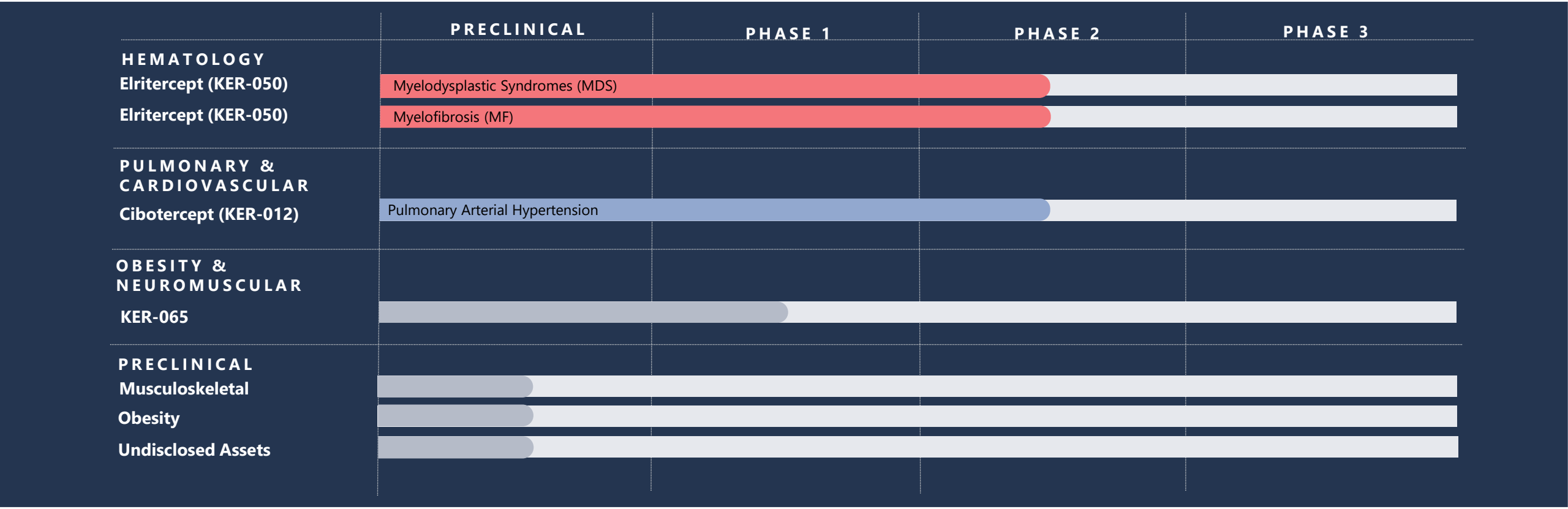
Focused on Transforming the Lives of a Wide Range of Patients with Disorders Linked to Dysfunctional TGF-β Superfamily Signaling

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

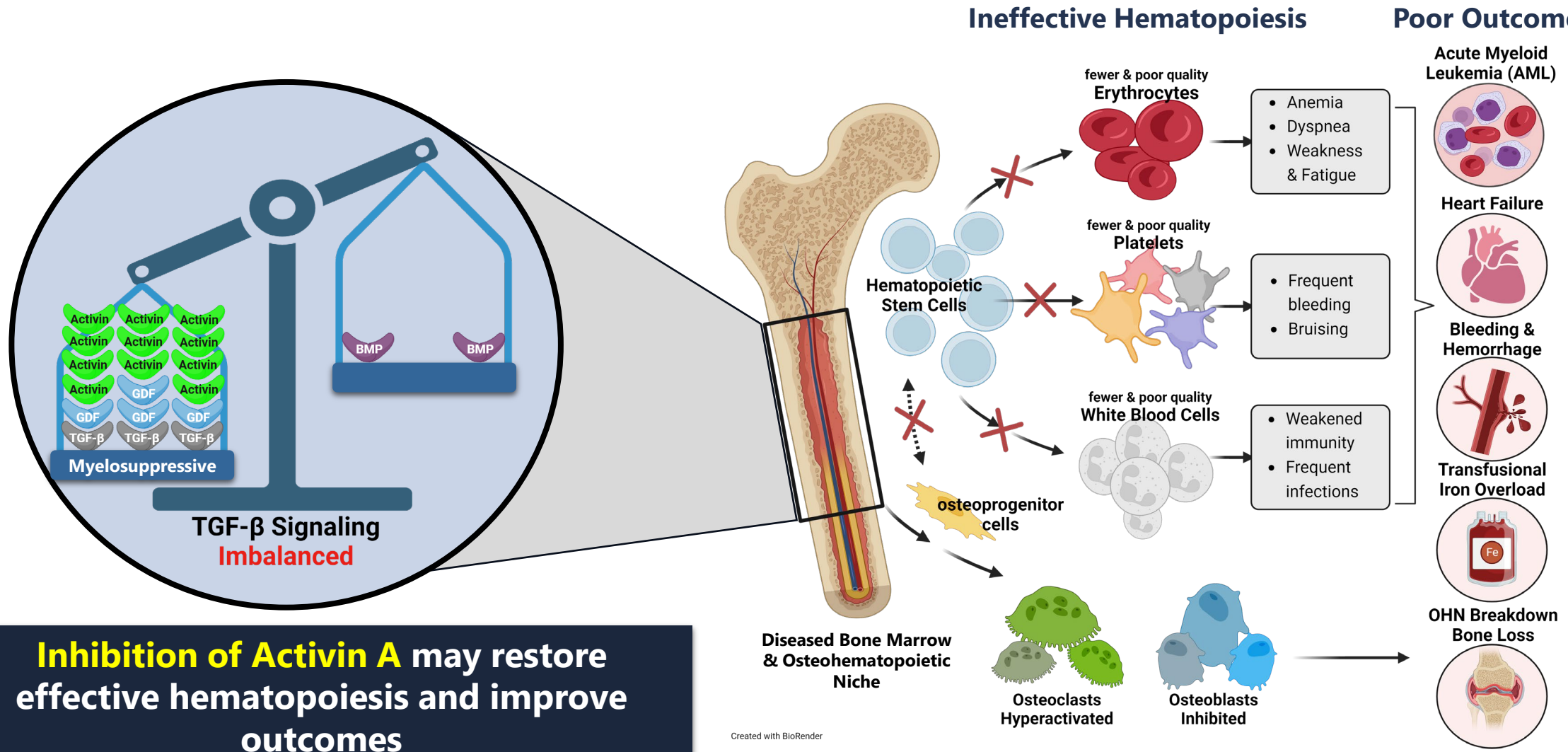


Elritercept (KER-050)

Investigational Treatment for Anemia and Thrombocytopenia in Patients with Myelodysplastic Syndromes

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

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

Myelodysplastic Syndromes (MDS)

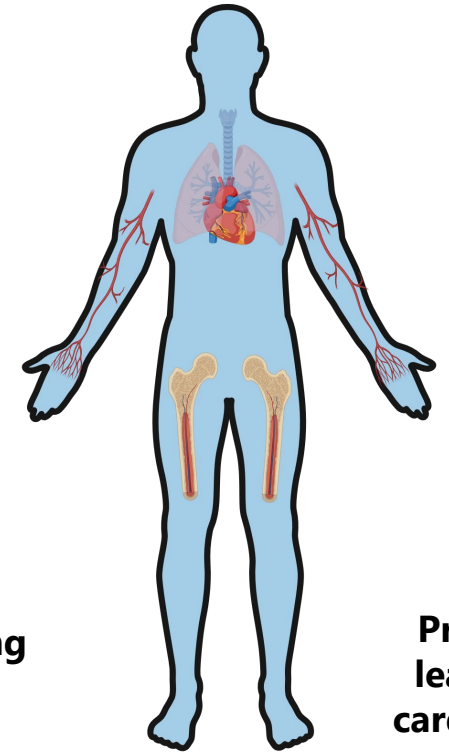
MDS
MDS is a collection of bone marrow disorders characterized by ineffective hematopoiesis and peripheral cytopenias.

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 quality of life

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 placebo[1]
- 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]

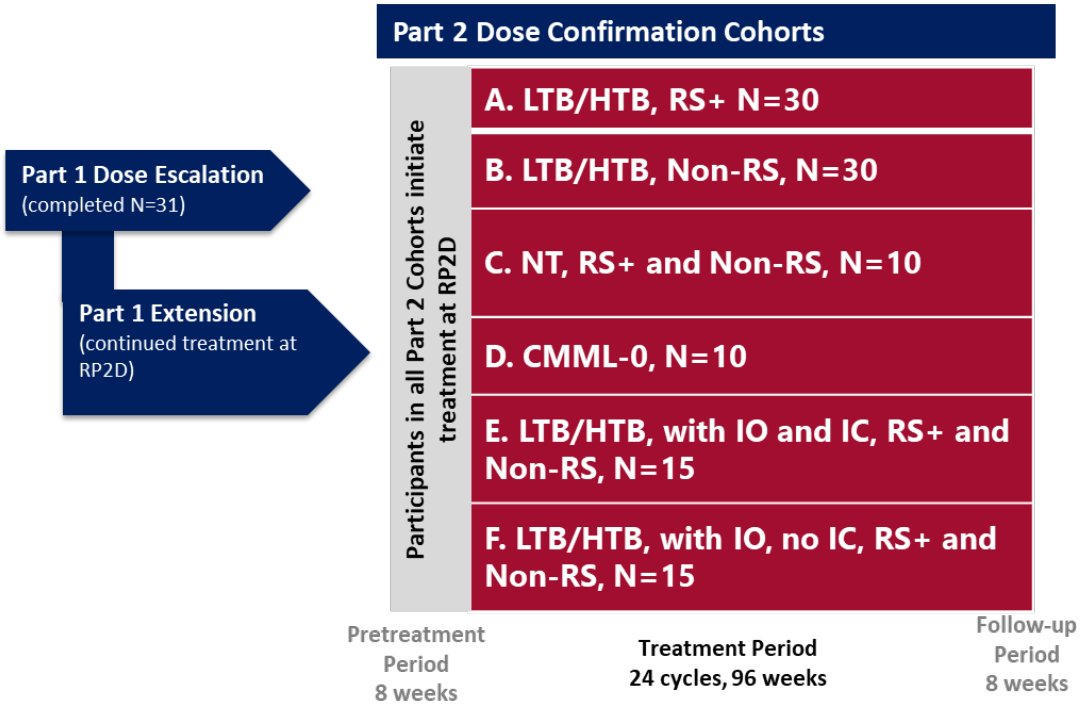
Telomerase Inhibitor

- 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.

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

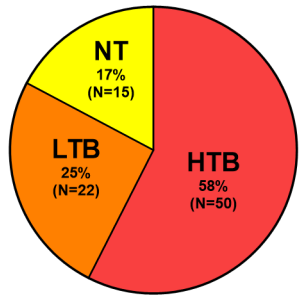


Response data are presented for the modified intent to treat 24-week population ($mITT_{24}$) that includes RP2D participants with at least 24 weeks of elritercept treatment or who have discontinued (n=81)

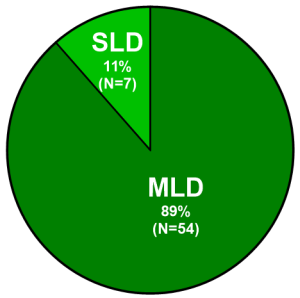
Baseline Demographics

Baseline Characteristic	RP2D (N=87)
Median Age, years (range)	74 (53-89)
Sex, n (%) male	55 (63.2)
Ring Sideroblasts Status, n (%) RS+ Non-RS	 60 (69.0) 27 (31.0)
Prior ESA, n (%)	24 (27.6)
EPO, U/L* n Mean (SD) Median (IQR)	 78 401.6 (692.1) 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 erythropoietin (EPO); **Excludes 22 RP2D participants with unknown dysplasia category

RP2D = Recommended Part 2 Dose of 3.75 mg/kg with the ability to titrate to 5 mg/kg once every four weeks; 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, SLD = Single Lineage Dysplasia, MLD = Multi Lineage Dysplasia

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 co-morbidities
- **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 TESAE	**38 (43.7)**
Any treatment-related TESAE	**4 (4.6)**
Any TEAE leading to death	**3 (3.4)**
Any TEAE leading to elritercept discontinuation*	**13 (14.9)**

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

Unrelated TEAEs leading to elritercept 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; TESAE = treatment emergent serious adverse event

Robust Responses Observed in a Broad Range of Patients Including those with High Transfusion Burden

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)**

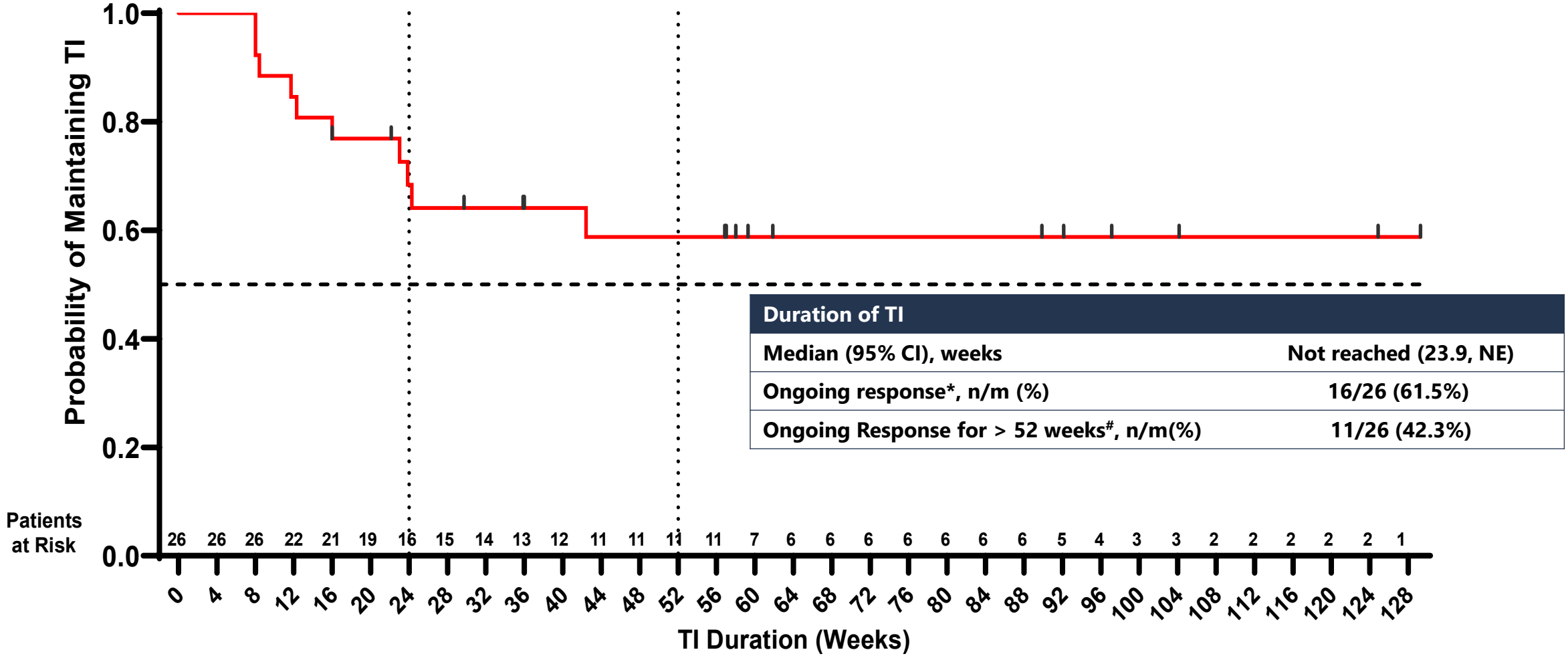
Response rates in $mITT_{24}$ patients with HTB were similar to those observed in the overall $mITT_{24}$ population, with higher rates observed in the EPO < 500 U/L population particularly in non-RS patients. These data support the potential for elritercept to treat a broad array of patients with LR-MDS

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

a. Includes data for weeks 0-24 in $mITT_{24}$ 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

Durable TI Responses Observed with Elritercept Treatment

Longest TI interval in mITT$_{24}$ participants who achieved TI ≥ 8 weeks from baseline through Week 24**



Duration of TI	
Median (95% CI), weeks	Not reached (23.9, NE)
Ongoing response*, n/m (%)	16/26 (61.5%)
Ongoing Response for > 52 weeks#, n/m(%)	11/26 (42.3%)

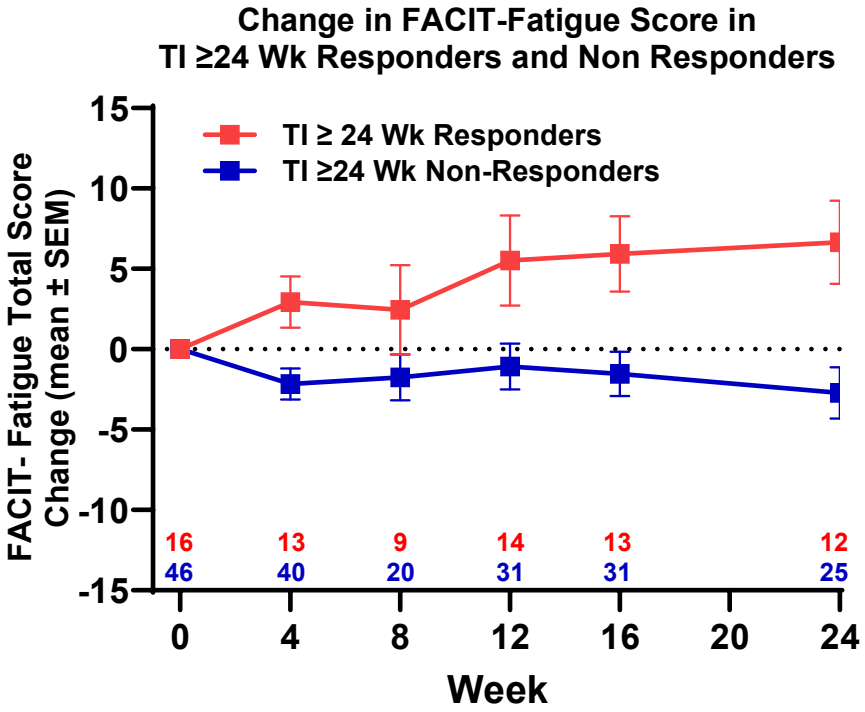
Data are presented as of a data cut-off date of April 3, 2024.

*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 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]



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 $mITT_{24}$ 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;
SEM = standard error of the mean

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

Investigational Treatment for Anemia and Thrombocytopenia in Patients with Myelofibrosis

Ongoing Phase 2 Open-Label Clinical Trial to Evaluate the Safety and Efficacy of Elritercept as Monotherapy or in Combination with Ruxolitinib in Participants 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

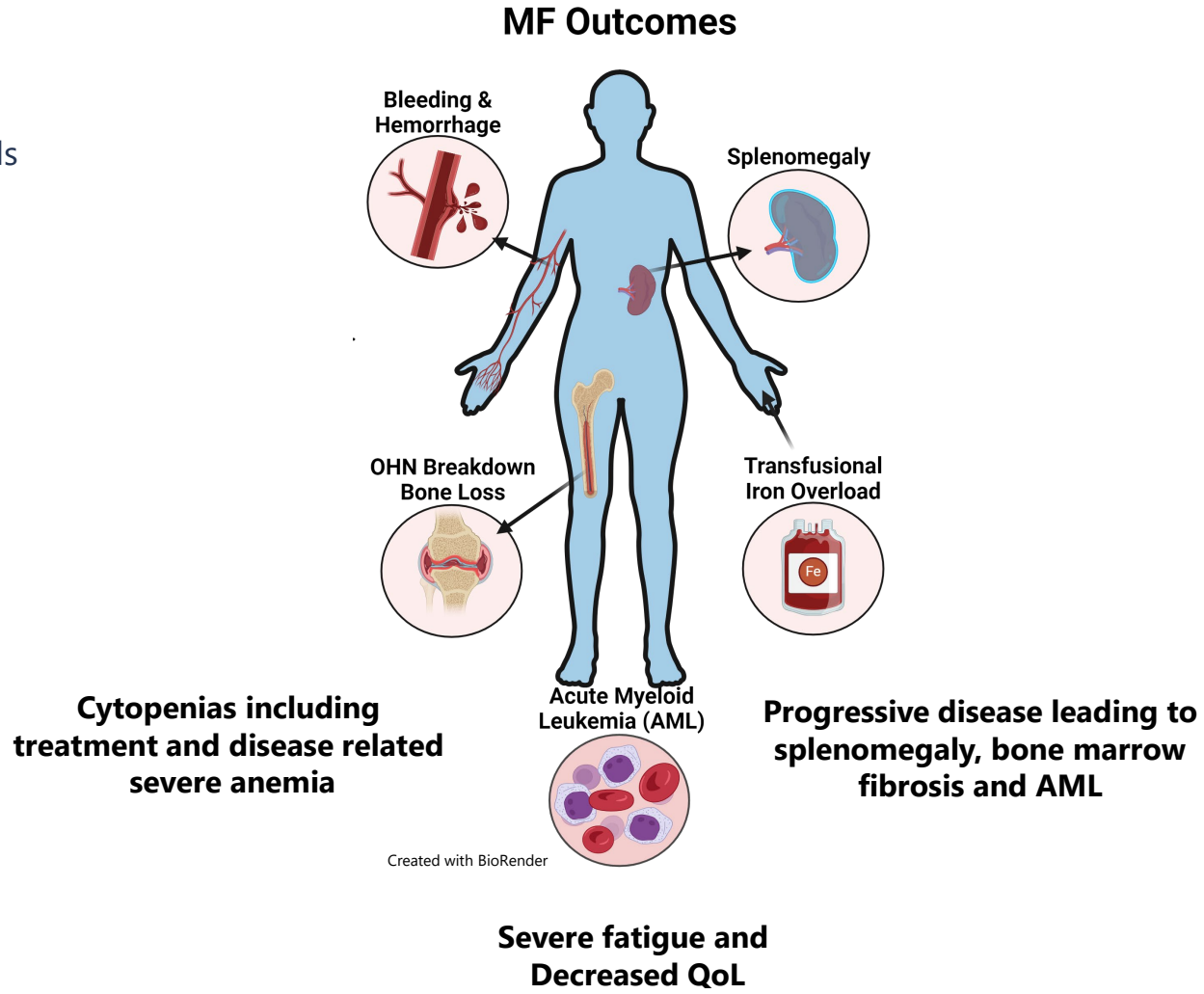
MF is characterized by ineffective hematopoiesis, an enlarged spleen, bone marrow fibrosis and shortened survival. Both anemia and thrombocytopenia are negative prognostic indicators. Anemia is prevalent in MF (one study reported anemia in 64% of patients beyond 1 year of diagnosis[1]) and is associated 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



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

RESTORE

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

Part 1: Dose Escalation 0.75 mg/kg to 4.5 mg/kg	Part 2: Dose Expansion RP2D
Monotherapy: JAK inhibitor relapsed, refractory, intolerant or ineligible	**Monotherapy:** JAK inhibitor relapsed, refractory, intolerant or ineligible
Combination with Ruxolitinib: Prior ruxolitinib treatment ≥ 8 weeks with stable dose ≥ 4 weeks	**Combination with Ruxolitinib:** Prior ruxolitinib treatment ≥ 8 weeks with stable dose ≥ 4 weeks

Key Eligibility

- 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 ≥ 25 x 10^9/L

Objectives and Endpoints

- 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:
  - Anemia, spleen volume, symptom score, exploratory biomarkers

Trial Status

- 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

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

- **Most frequent TEAEs (≥ 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%)
    - Montherapy: 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) Ongoing, n (%)	24.1 (6-120) 10 (43.5)*	23.7 (0-82) 21 (67.7)*	23.9 (0-120) 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)

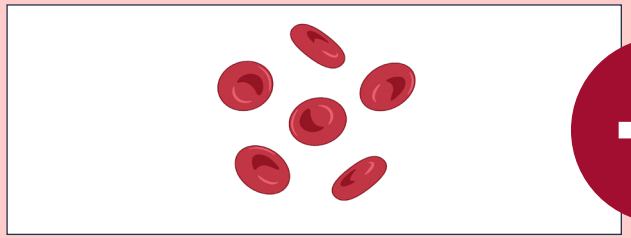
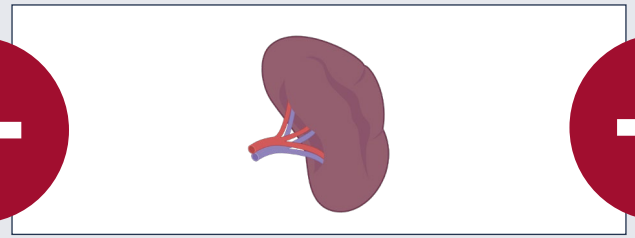
Data are presented as of a data cut-off date of April 3, 2024

*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

• 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 TI
• Improvements in platelet count were observed in patients with baseline thrombocytopenia particularly those treated with elritercept plus ruxolitinib
	• 9/17 (53%) evaluable patients (2/8 mono, 7/9 combo) showed some reduction in spleen size at Week 24
	  • Evaluable patients had baseline spleen size ≥ 450 cm^3 and a Week 24 spleen volume assessment
	  • 3/9 (33%) had reductions ≥ 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
		• 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 ≥ at baseline and a week 24 assessment
		• 3 patients had reductions ≥ 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

Cibotercept (KER-012)

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

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

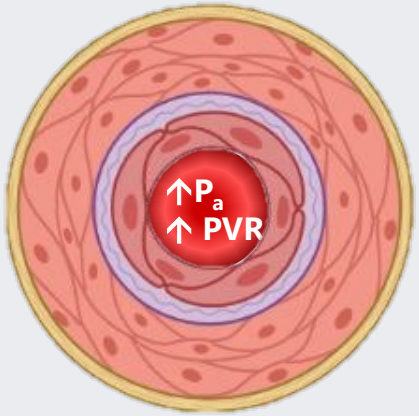
Imbalances in TGF-β Superfamily Signaling Underlies Vascular Remodeling in PAH

PAH is a debilitating disorder characterized by elevated pulmonary vascular resistance due to increased vascular smooth muscle cell proliferation and inflammation

- This results in diminished oxygenation, impaired cardiac output, and right ventricle (RV) overload
- Despite current treatment options, the 5-year survival remains only slightly above 50%
- PAH is associated with imbalanced TGF-β superfamily signaling, including insufficient bone morphogenic protein (BMP) signaling and increased signaling by activins and GDFs
  - A third-party Phase 3 clinical trial of sotatercept[1] demonstrated the importance of the TGF-β superfamily in patients with PAH
  - Maximum dose of sotatercept in PAH limited to 0.7 mg/kg in the clinical trial due to increased hemoglobin observed in earlier-phase clinical trials[2,3]

Pulmonary Arterial Hypertension

Thickened Vasculature



Imbalanced TGF-β signaling results in ↑ myogenic & fibrogenic differentiation

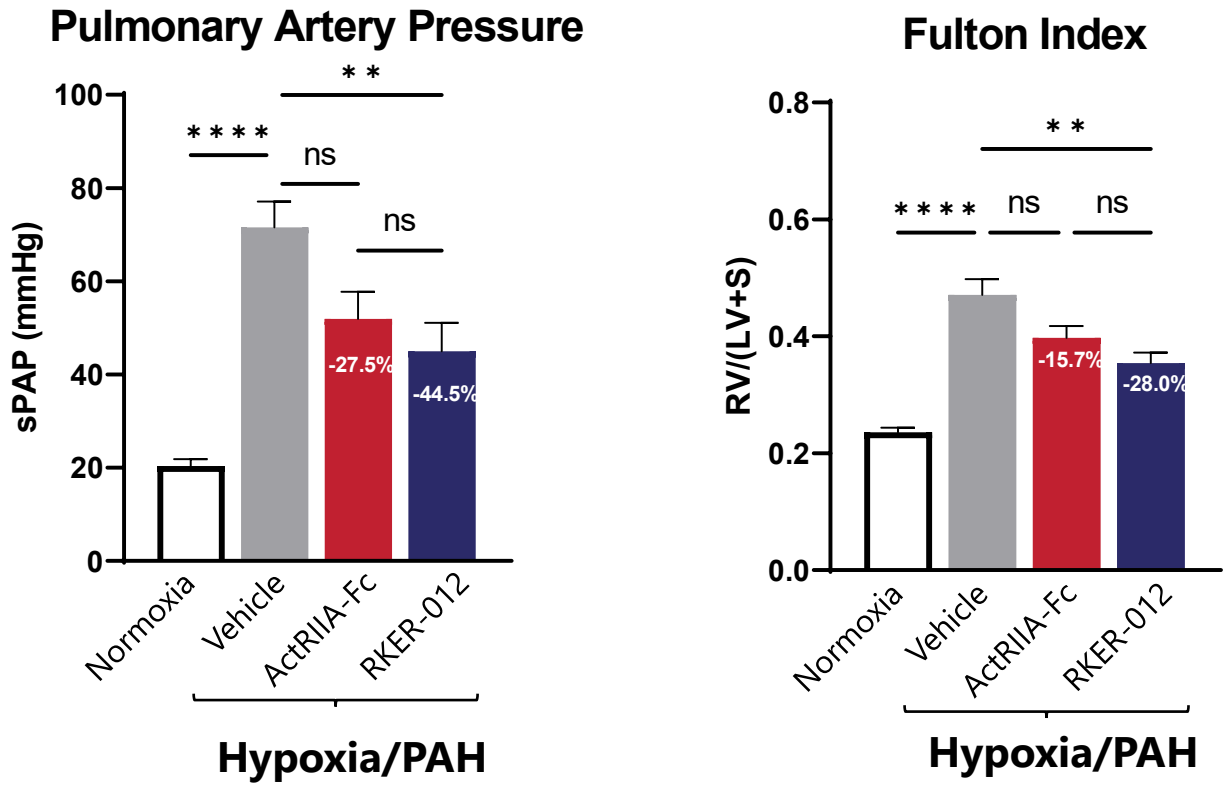
Cibotercept is a modified activin receptor IIB ligand trap:

- Designed to rebalance TGF-β superfamily signaling
- Being developed for the treatment of pulmonary and cardiovascular disorders, including PAH
- Designed to preferentially inhibit select ligands (activin A, activin B, GDF8 and GDF11) to potentially rebalance TGF-β superfamily signaling without a dose-limiting increase in RBCs

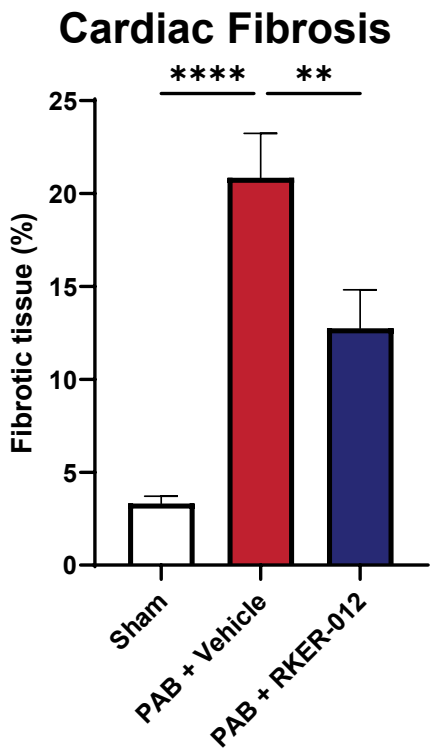
1. Hoeper M, et al. New Eng J Med 2023; 388 (16):1478-90; 2. Sherman et al 2013 J. Clin Pharmacol 53(11) 1121–1130; 3. Humbert M et al, New Engl J Med 2023; 384:1204-15; 3. Cappellini MD et al. Haematologica 2019; 104(3) 477-484

RKER-012 Reduced Pulmonary Arterial Pressure, Right Ventricle Hypertrophy and Cardiac Fibrosis in Rodent PAH Models

Sugen-Hypoxia Model of PAH[1]



Pulmonary Artery Banding[2] (Direct Cardiac Effects)



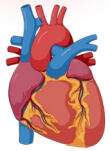
One way ANOVA followed by Sidak post-hoc test. Ns – not significant, * p ≤ 0.05, ** p ≤ 0.01, *** p ≤ 0.001, **** p ≤ 0.0001.

1. K. Babbs, et al. Am J Respir Crit Care Med 2022;205:A5776; 2. Babbs K, et al. Am Heart Association Scientific Sessions 2021; RKER-012 = Research form of cibotercept fused with Fc region of murine IgG1

Observed Cibotercept Profile Supports Therapeutic Rationale in PAH

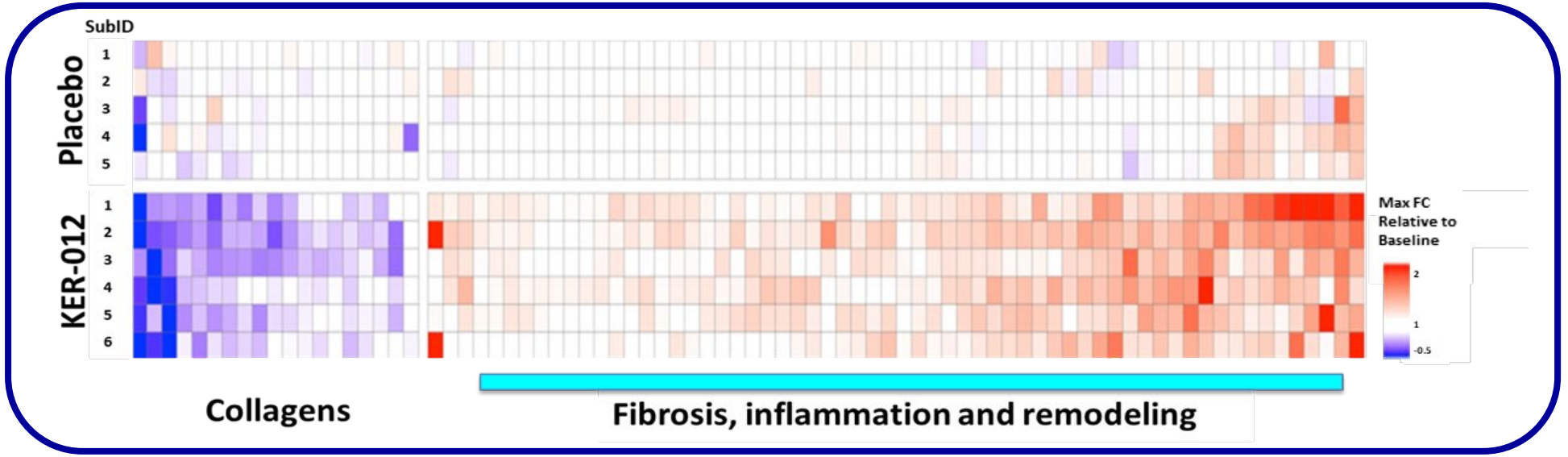
Keros completed a randomized, double-blind, placebo-controlled, two-part Phase 1 clinical trial to evaluate single and multiple ascending doses of cibotercept in healthy volunteers.

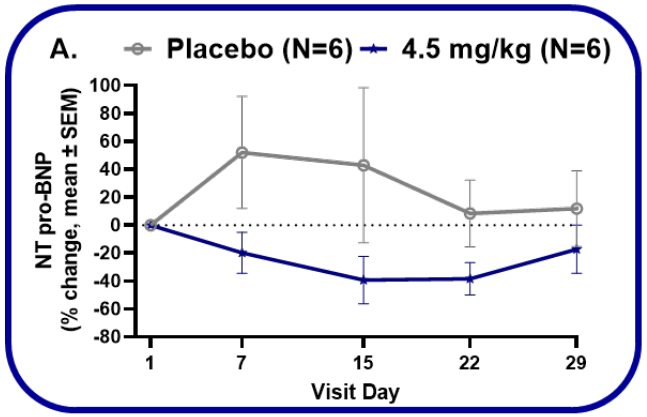
- The primary objectives of this trial were safety, tolerability and pharmacokinetics.

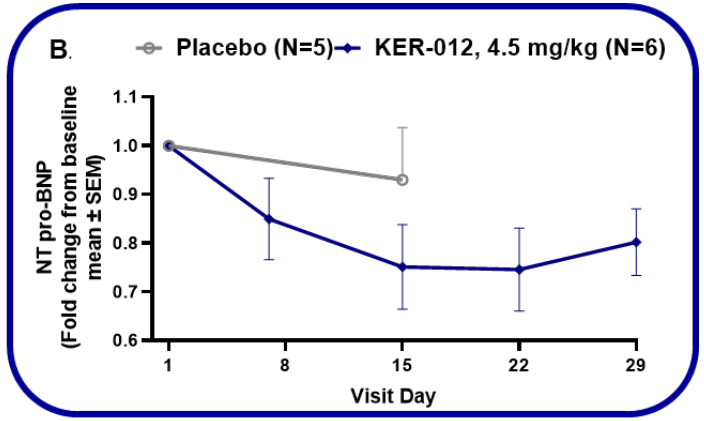
PAH Domain	Preclinical Data	Phase 1 Clinical Trial[1,2]
 MOA & Ligand Specificity:	• Strong activin/GDF binding observed • Observed to be BMP-sparing vs. ActRIIA-Fc	• We believe PD data support potential for maximal target engagement with doses in Phase 2
 Fibrosis & Inflammation:	↓ Inflammation ↓ Fibrosis	↓ Pro-inflammatory biomarkers ↑ Anti-inflammatory biomarkers ↓ Pro-fibrotic biomarkers ↑ Anti-fibrotic biomarkers
 CV & Hemodynamics:	↓ Smooth muscle hypertrophy ↓ Pulmonary arterial pressure ↓ Right & left ventricular hypertrophy ↓ Cardiac fibrosis (direct) ↓ Ventricular dysfunction biomarkers	↓ Ventricular dysfunction biomarkers ↓ Remodeling biomarkers
 Erythropoiesis (Hb/RBCs):	• No increase observed	• No clinically meaningful changes observed
 Safety & Tolerability:	N/A	• Generally well tolerated up to 4.5 mg/kg (multiple doses) in Part 2 of the trial • AEs generally mild

1. Natarajan H., et al. American Society for Bone and Mineral Research 2022 Annual Meeting; 2. Natarajan H., et al. 2023 American Thoracic Society International Conference

Cibotercept Altered Expression of Serum Proteins Associated with Inflammation and Extracellular Matrix Remodeling and Lowered NT-proBNP levels



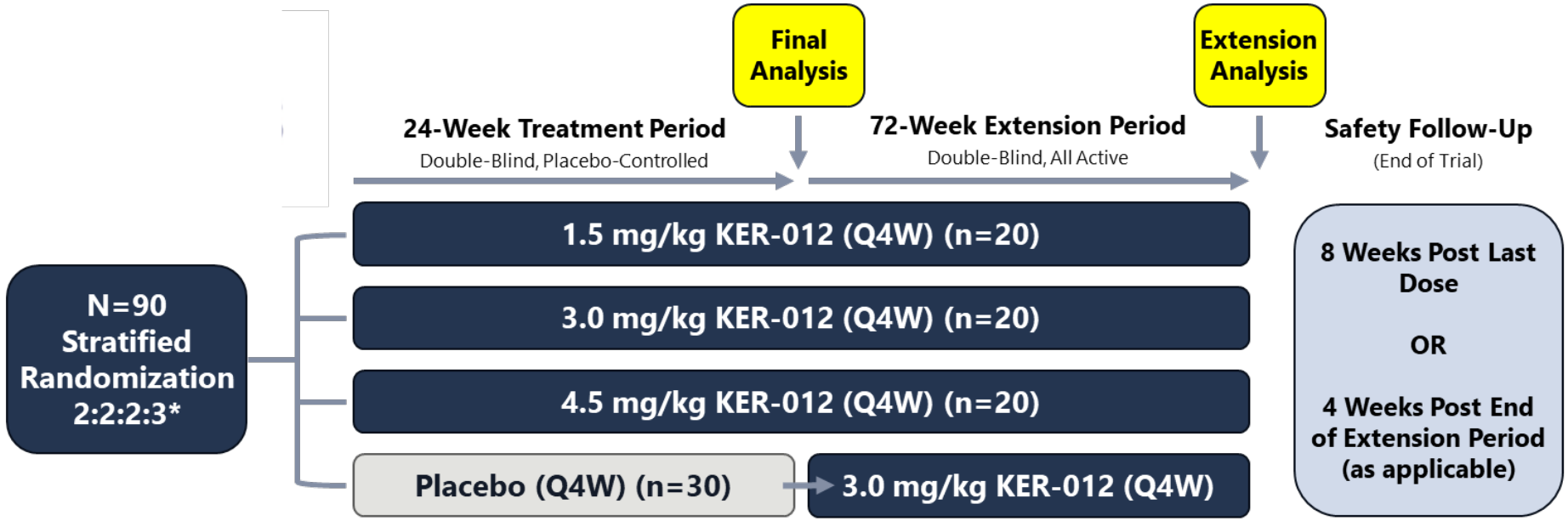




Additional exploratory biomarker data demonstrated initial target engagement at 0.75 mg/kg and maximum target engagement at 4.5 mg/kg

Natarajan H, et al Am J Respir Crit Care Med 2023;207:A1187

TROPOS Trial: Global Phase 2 Clinical Trial of Cibotercept in Patients with PAH



*Approximately 90 patients diagnosed with PAH and on stable PAH background therapy will be randomized and assigned in a 2:2:2:3 ratio to the 1.5 mg/kg, 3.0 mg/kg, and 4.5 mg/kg KER-012 doses and placebo treatment arms.

Primary Objective:

- To evaluate the effect of KER-012 on hemodynamics compared to placebo in participants on background PAH therapy

Primary Endpoint:

- Change from baseline in pulmonary vascular resistance (PVR) at Week 24

Key Secondary Objective:

- To evaluate the effect of KER-012 on exercise capacity compared to placebo in participants on background PAH therapy

Key Secondary Endpoint:

- Change from baseline in 6-minute walk distance at Week 24

KER-065:
Obesity & Neuromuscular Diseases

- **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 (monthly) subcutaneous dosing**

KER-065: Novel Activin Receptor Ligand Trap for the Treatment of Obesity and Neuromuscular Disorders

Keros' preclinical library of activin receptor ligand traps contains more than 40 distinct molecules containing sequences from ActRIIA and ActRIIB

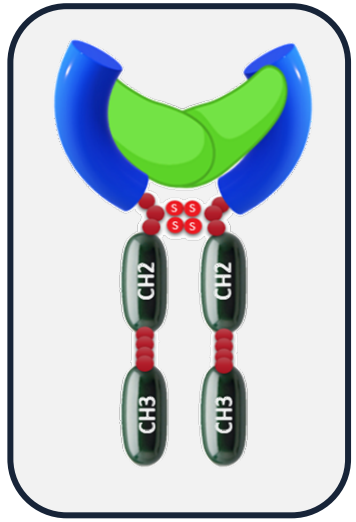
- KER-065 is the 3rd molecule selected from our preclinical library for clinical development

KER-065 is a modified activin receptor IIA (ActRIIA) and activin receptor IIB (ActRIIB) ligand trap

- ~50% amino acids derived from each activin receptor

KER-065 is designed to bind to the negative regulators of muscle growth, activin A and myostatin, to increase skeletal muscle without an increase in red blood cells

- Reduced binding to bone morphogenic proteins to avoid the vascular/bleeding observed with ActRIIb-Fc derived from the native sequence



Domain	Potential Effect[1]
Muscle	Increase in skeletal muscle Does not increase smooth muscle and cardiac muscle
Fat	Decreases fat mass
Bone	Increases bone mineral density
Fibrosis and Inflammation	Reduce fibrosis and inflammation via Activin A inhibition
Cardiac	Improve cardiac function via Activin A inhibition

1. Observed in preclinical studies.

Well-Established Rationale for Targeting Activin and Myostatin Signaling as Treatment for Obesity and Associated Cardiometabolic Disease

Muscle Tissue

- Inhibition of activin A and myostatin increase muscle hypertrophy and strength

Adipose (Fat) Tissue

- Activin A, activin B, activin E and GDF3 signal via ActRII[1] and inhibit differentiation of cells to energy-consuming "brown" fat cells
- Inhibition of these ligands increases energy expenditure by adipocytes[2]

Cardiac Disease

- Activin A and follistatin-like 3 are increased in patients with heart failure[3]

Clinical proof-of-concept established in third-party clinical trials, with multiple approaches targeting the TGF-β superfamily pathway

- Selective neutralizing antibodies to myostatin and activin A
- Neutralizing antibodies targeting ActRIIA and ActRIIB
- ActRIIB-Fc ligand trap that binds multiple ligands, including activin A and myostatin

1. Endocrinology. 2012;153:3133-46; 2. Mol. Cell. Biol. 2012;32:2871-2879; 3. Sci. Transl. Med. 2019; 11:eaau8680

Current GLP-1 RA Treatment Landscape for Obesity

GLP-1 receptor agonists (GLP-1 RAs) have recently been approved for the treatment of obesity

- Treatment with GLP-1 RAs led to 15%-21% mean weight loss[1,2], reductions in blood lipids, improvements in glycemic control and better cardiac outcomes[3]

Weight loss is due to reduction in fat mass and reduction in lean body mass as a result of treatment

- An estimated 25%-40% of total body weight loss mediated by GLP-1 RA treatment may be attributed to loss of lean muscle mass[1,2]

Majority of body weight loss is regained after stopping GLP-1 RA treatment

- In extension analyses of 327 participants, participants regained 67% of prior weight loss one year after withdrawal of once-weekly subcutaneous GLP-1 RA treatment and lifestyle intervention[4]

Need for treatment options that:

- Ameliorate the loss of lean mass due to GLP-1 RA treatment and obesity
- Provide long-term treatment option for maintenance of weight loss
- Directly impact disease processes that contribute to cardiometabolic diseases

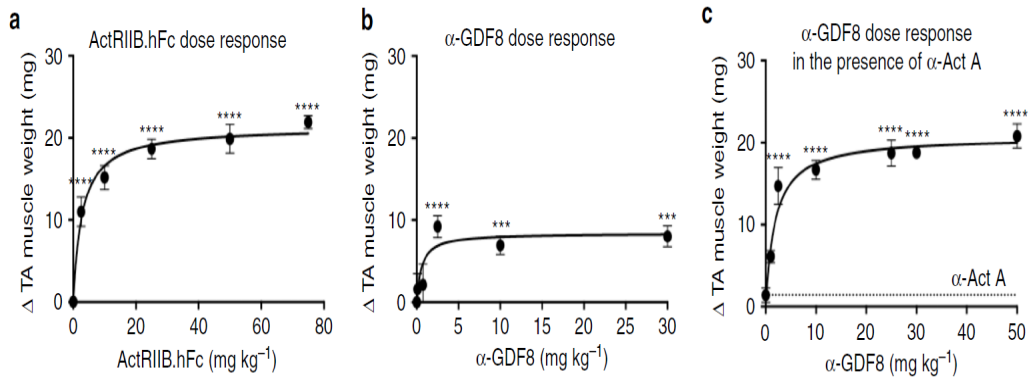
1. N Engl J Med 2021;384:989-1002; 2. N Engl J Med 2022;387:205-16; 3. N Engl J Med 2023; 389:2221-2232; 4. Diabetes Obes Metab. 2022; 8:1553–1564

Inhibition of Both Activin A and Myostatin Observed to be Required to Maximally Increase Skeletal Muscle in Mice and Monkeys

In third-party preclinical studies, selective inhibition of myostatin (GDF-8) or activin A resulted in small increases in muscle mass in rodents and non-human primates[1]

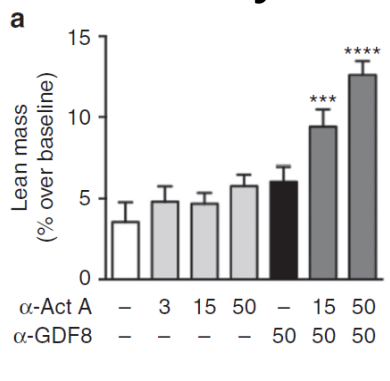
- Targeting multiple ligands in the TGF-β superfamily produced the largest increase in skeletal muscle[1]
- More than two times increase in skeletal muscle with anti-myostatin and anti-activin A combination or ActRIIB-Fc treatment compared to anti-myostatin treatment alone[1]

Mice[1]



NATURE COMMUNICATIONS | 8:15153 | DOI: 10.1038/ncomms15153

Monkey[1]



NATURE COMMUNICATIONS | 8:15153 | DOI: 10.1038/ncomms15153

ActRIIB-Fc ligand trap and neutralizing antibodies targeting ActRIIA and ActRIIB showed similar increases in muscle[2,3]

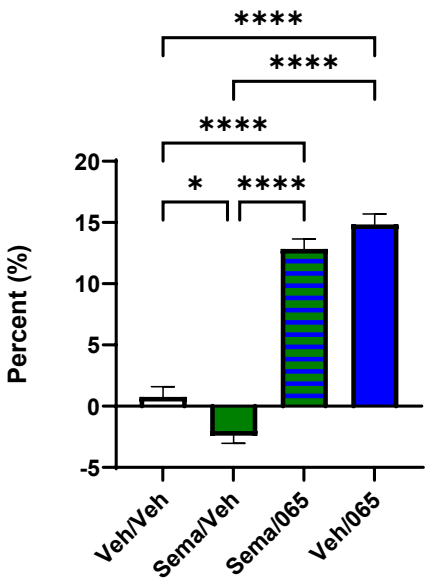
- ActRIIB-Fc subcutaneous administration
- Anti-ActRIIA/ActRIIB such as bimagrumab are intravenous administration

Keros' ActRII ligand traps are designed to inhibit myostatin and activin A to potentially produce a maximal increase in skeletal muscle

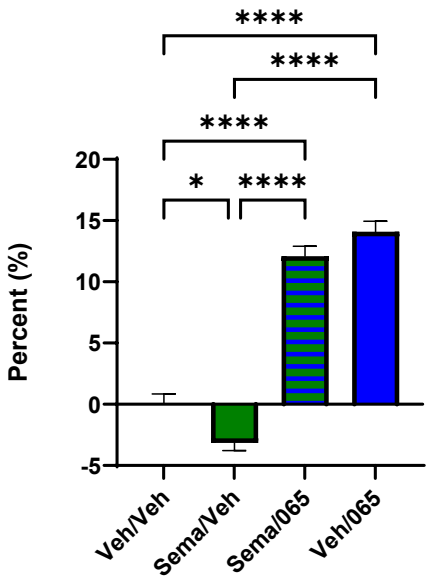
1. Latres, E., Mastaitis, J., Fury, W. *et al.* Activin A more prominently regulates muscle mass in primates than does GDF8. *Nat Commun* 8, 15153 (2017). https://doi.org/10.1038/ncomms15153
2. Mol. Cell. Bio. 2014;34:606-618
3. J. Appl Physiol 2010;109:635-642

RKER-065 Preserved Lean Mass and Enhanced Fat Loss in Obese Mice Treated with Semaglutide

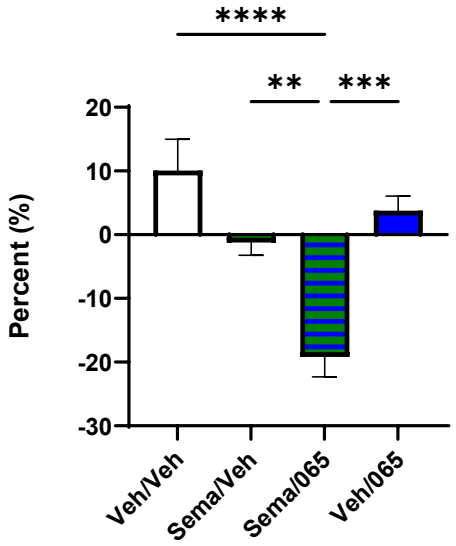
Change in Lean Mass by qNMR (from baseline)



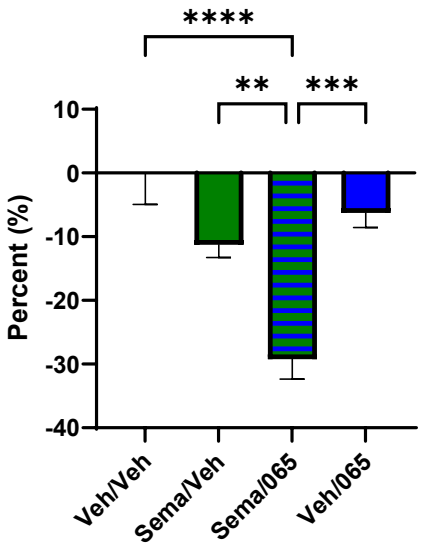
Change in Lean Mass by qNMR (% of vehicle)



Change in Fat Mass by qNMR (from baseline)



Change in Fat Mass by qNMR (% of vehicle)



- Obese mice were treated for two weeks with vehicle, sema (0.082 mg/kg twice weekly) or the research form of KER-065, RKER-065 (10 mg/kg twice weekly) in combination with sema or monotherapy
- Treatment with sema reduced fat mass and resulted in loss of lean mass compared to untreated obese mice
- Administration with RKER-065 increased lean mass and reduced fat mass compared to untreated obese mice
- Combination treatment with semaglutide and RKER-065 increased lean mass compared to untreated obese mice and had a synergistic loss in fat mass

P value: *<0.05, **<0.01, *** <0.001, **** <0.0001

KER-065 Phase 1 Clinical Trial in Healthy Volunteers

Primary objectives of this Phase 1 clinical trial are to evaluate safety, tolerability and pharmacokinetics of single and multiple ascending doses of KER-065

The multiple ascending dose portion of this trial will enroll patients with elevated body mass index (BMI) of 27-33 to evaluate KER-065's effect on lean mass, fat mass and bone mineral density

- Imaging by DXA and MRI

Additional exploratory biomarkers will be included to examine KER-065's pharmacologic effect on:

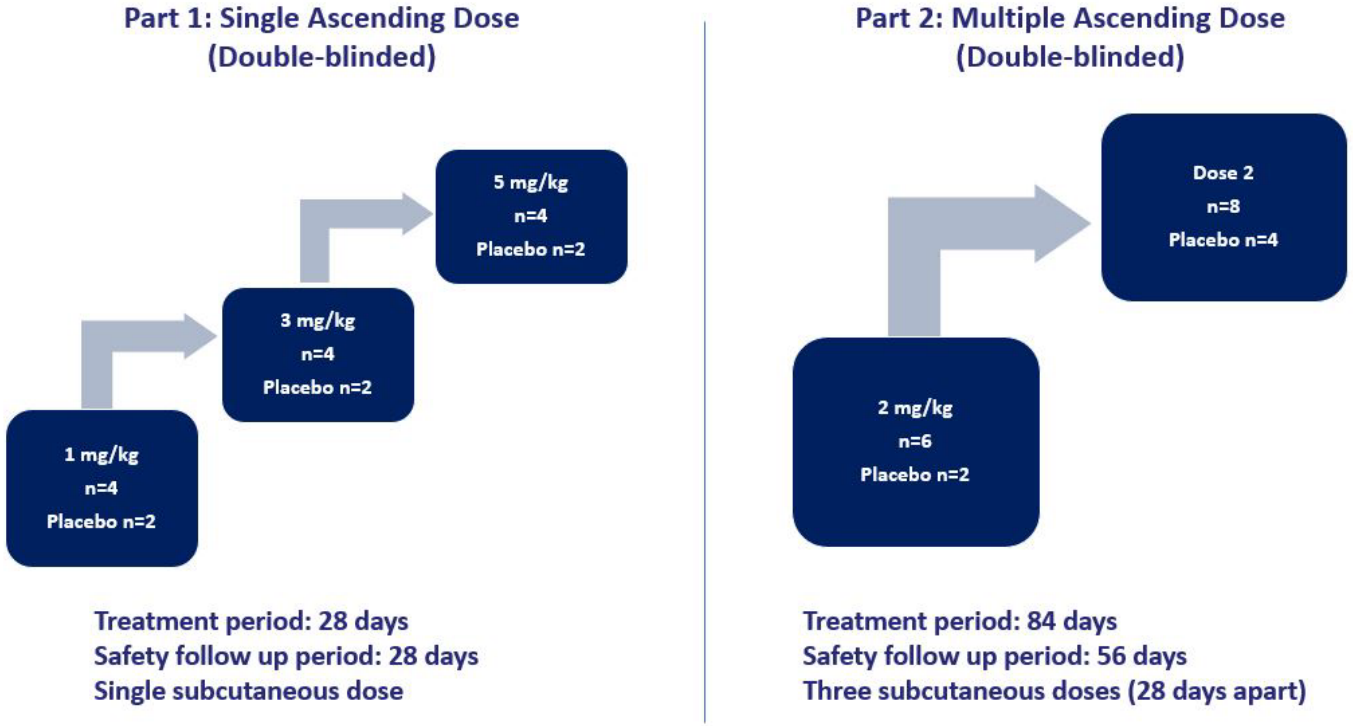
- Biomarkers of bone formation and resorption
- Adipokines
- NT-proBNP, a marker of cardiac stress
- Markers of fibrosis

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

- Informs potential development in neuromuscular indications such as Duchenne muscular dystrophy (DMD)
  - Patients on the DMD standard of care, glucocorticoids, have higher BMI, muscle loss, insulin resistance and accelerated bone loss
- We expect to announce data from this Phase 1 clinical trial in Q1 2025

KER-065 Phase 1 Trial Design

Phase 1 Clinical Trial Design



Primary Objective

- Evaluate the tolerability and safety of KER-065

Secondary Objective

- Evaluate the PK of KER-065

Exploratory Objectives

- Assess the pharmacodynamic (PD) effect on bone, adipose, muscle, cardiac tissue, and fibrosis of KER-065
- Inclusion of overweight/obese volunteers in MAD to enhance ability to detect change in PD effects

Study Subjects:

- Healthy volunteers
- Males 18-55 years of age
- Body Mass Index:
  - SAD: 18.5 – 30
  - MAD: 27 – 33

KER-065: Neuromuscular Diseases

Muscle loss can occur as a consequence of many factors, including neuromuscular disease, disuse, aging and as a side effect of some therapies

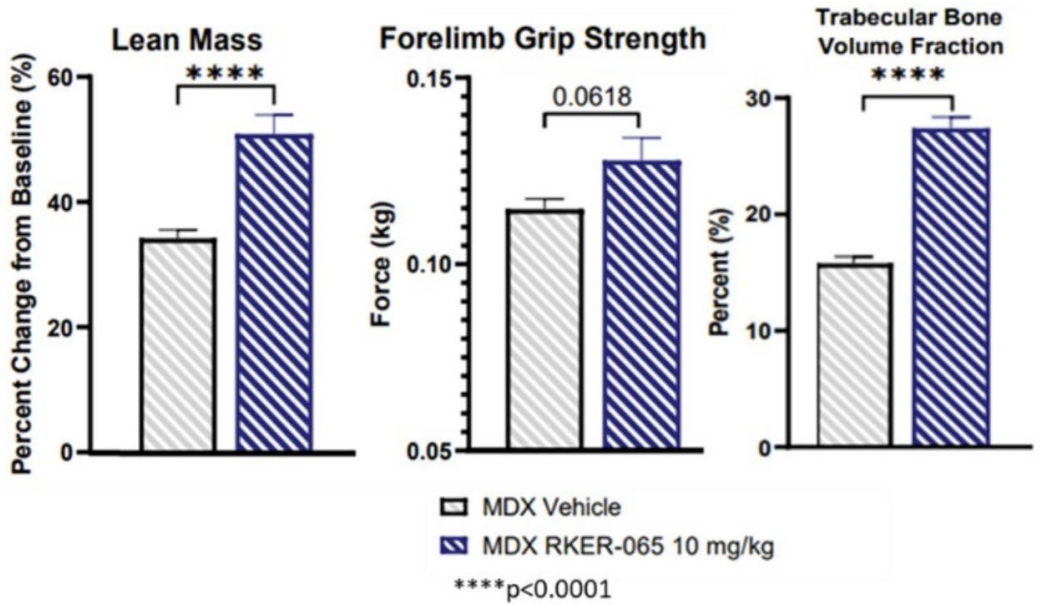
In neuromuscular diseases, muscle loss can result in muscle weakness and, with increased severity, can lead to loss of ambulation, reliance on a wheelchair, swallowing difficulties, respiratory muscle weakness and death

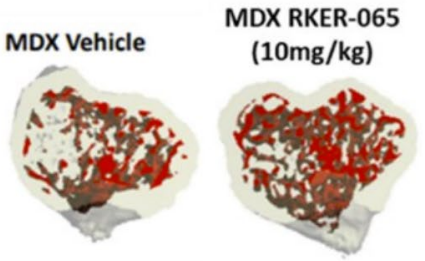
- Decline in muscle mass can also be associated with secondary osteoporosis and metabolic consequences, including obesity and insulin resistance

TGF-β pathway signaling regulates skeletal muscle, fat and bone, and activins and myostatin are powerful negative regulators of skeletal muscle

In preclinical studies, KER-065 showed high affinity for and potent inhibition of ligands involved in the regulation of muscle and bone homeostasis. Additionally, RKER-065:

- Increased muscle mass, muscle function and bone mass in wild-type mice
- Increased muscle mass, grip strength and trabecular bone in a mouse model of DMD[1]
- Increased muscle mass, improved muscle function and prevented bone loss in prednisolone-treated mice





1. Nathan, R., et al. 27th International Hybrid Annual Congress of the World Muscle Society. MDX = muscular dystrophy X-linked mouse.

Treatment with RKER-065 Led to Higher Utrophin Levels in Mouse Model of DMD

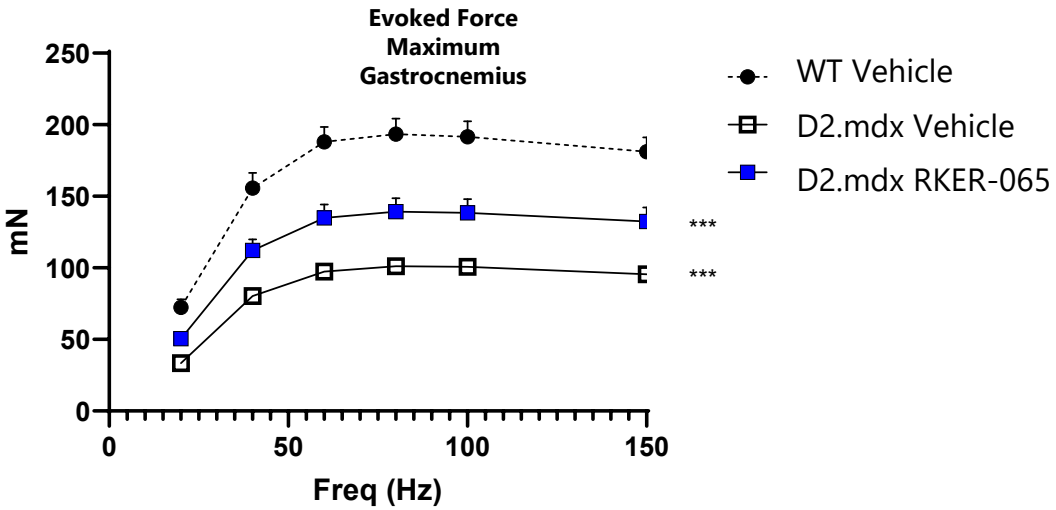
Muscle lacking dystrophin is easily damaged during the process of contraction

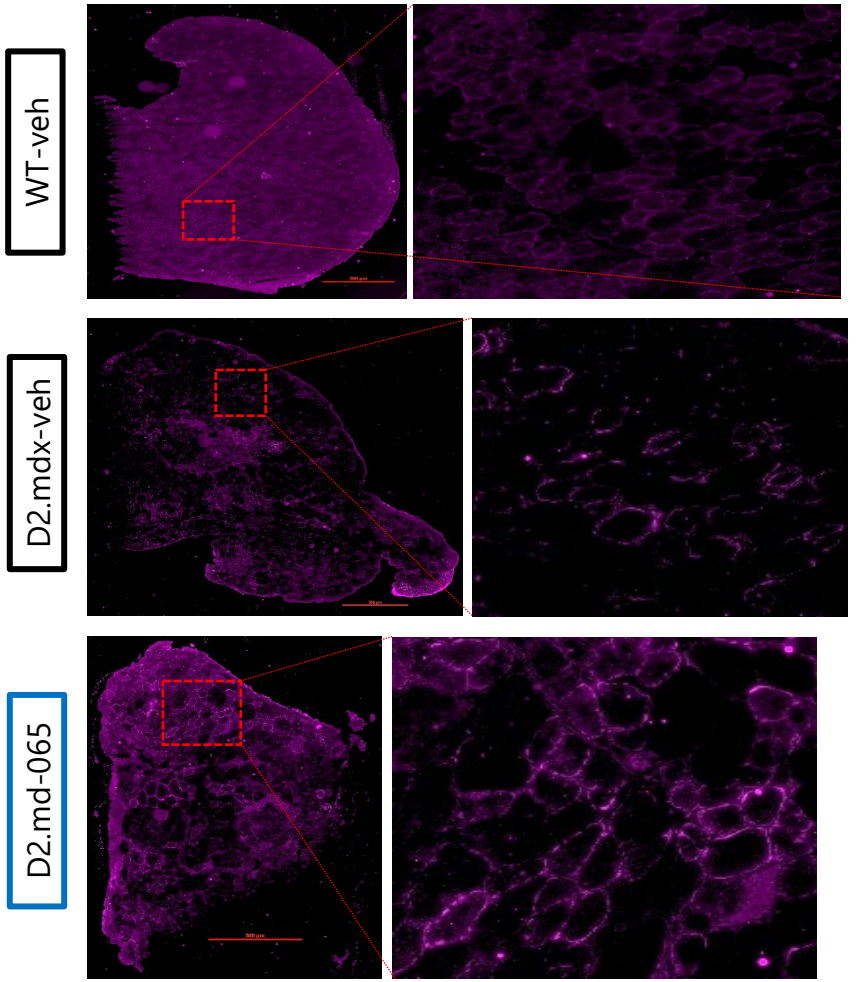
Many third-party approaches have been utilized to stabilize the muscle and provide resistance to contractile-induced damage

- Antisense oligonucleotides to trigger exon skipping, restore the mRNA reading frame, and allow production of a truncated dystrophin protein
- Gene therapy with mini and micro dystrophin
- Increase expression of utrophin (a functional analog of dystrophin)

Treatment with RKER-065 in a mouse model of DMD led to:

- Increased expression of utrophin in muscle fibers, potentially contributing to the observed increased strength[1]

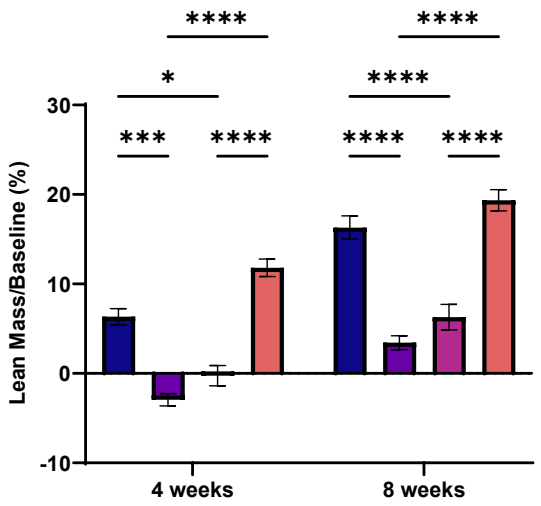




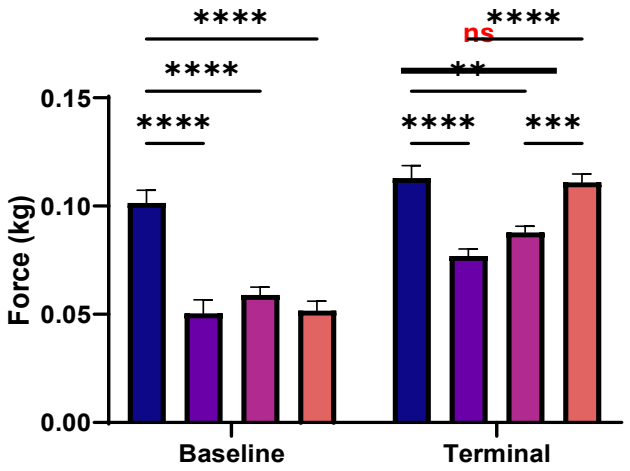
1. Nathan, R., et al. 28th International Annual Congress of the World Muscle Society; WT= wild type (control), D2.mdx = mouse model of DMD

PMO & RKER-065 Combined Treatment Demonstrated Significant Increase in Lean Mass, Muscle Function & Exon Skipping Efficiency

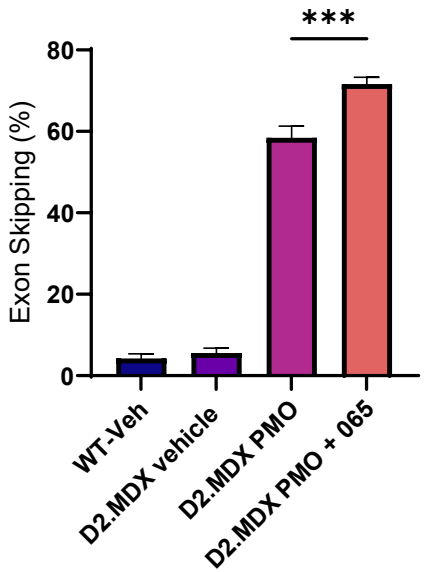
Lean Mass Percent Change

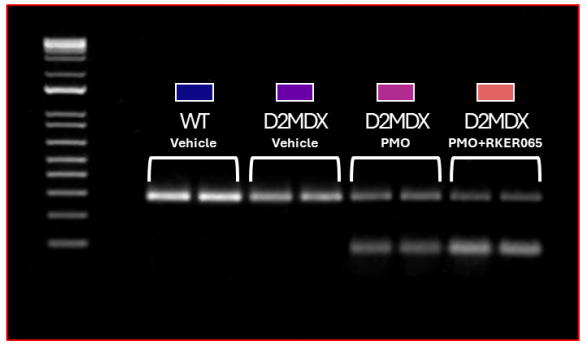


Grip Strength Measurement



Exon Skipping Efficiency





Full-length Dystrophin
(Unskipped)

Truncated Dystrophin
(Skipped)

WT-Vehicle
D2MDX-Vehicle
D2MDX-PMO
D2MDX-PMO+065

1. St. Pierre, M., et al. 2024 New Directions in Biology and Disease of Skeletal Muscle Conference; ns = not significant; P value: *<0.05, **<0.01, *** <0.001, **** <0.0001
PMO = Phosphorodiamidate morpholino oligomer.

Proprietary Discovery Approach

Proprietary Discovery Approach

We have developed a proprietary library of ActRII ligand traps by combining sequences from ActRIIA and ActRIIB

- We have engineered molecules that are designed to have the therapeutic properties of either or both parent molecules
- Our ActRII program has produced a broader pipeline of engineered ligand traps and currently contains more than 20 unique variants in preclinical development
- KER-065 was nominated out of this proprietary library of ActRII ligand traps for clinical development

This discovery approach has the potential to identify additional molecules with differentiated profiles from existing third-party products and product candidates

- Pipeline of preclinical assets: musculoskeletal; obesity; other undisclosed indications

Anticipated Key Milestones

Elritercept

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

Cibotercept

- Complete enrollment in Phase 2 TROPOS Trial — Q4 2024

KER-065

- Announce data from Phase 1 healthy volunteer trial — Q1 2025