KEROS THERAPEUTICS

Corporate Presentation

January 2025

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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

*The license agreement is subject to antitrust clearance

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 Arterial Hypertension

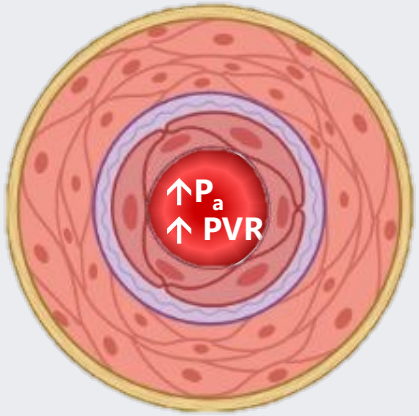
Imbalances in TGF-β Superfamily Signaling Underlies Vascular Remodeling in PAH

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 is limited to 0.7 mg/kg in the clinical trial due to increased hemoglobin observed in earlier-phase clinical trials[2,3,4]

Pulmonary Arterial Hypertension

Thickened Vasculature



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

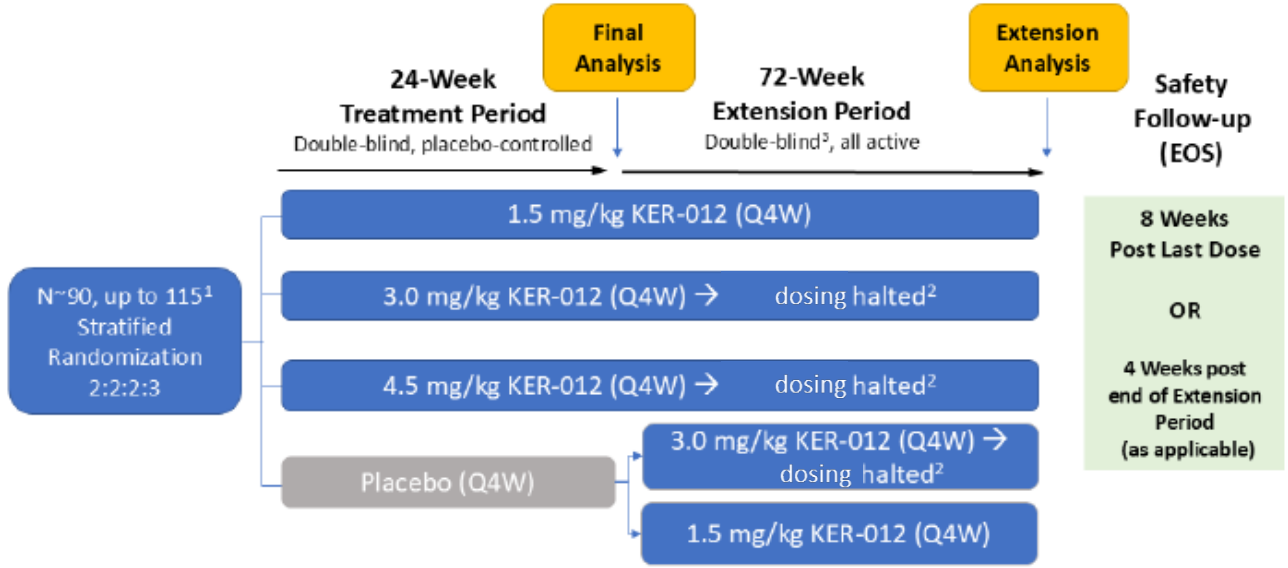
Cibotercept is an investigational modified activin receptor IIB ligand trap:

- 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; 4. Cappellini MD et al. Haematologica 2019; 104(3) 477-484; GDF = growth differentiation factor

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

- On December 12, 2024, **Keros announced that it voluntarily halted dosing in the 3.0 mg/kg and 4.5 mg/kg treatment arms in the ongoing TROPOS trial**, based on a safety review due to the unanticipated observation of pericardial effusion adverse events in the trial
- The TROPOS trial is **fully enrolled**, and **dosing in the 1.5 mg/kg treatment arm remains ongoing following completion of a risk and benefit assessment of the data from the ongoing trial that was conducted by the independent Data Monitoring Committee ("DMC") followed by a select group of unblinded individuals at Keros**
- The decision to halt the dosing in the 3.0 mg/kg and 4.5 mg/kg treatment arms and continue dosing in the 1.5 mg/kg treatment arm was made in consultation with the independent DMC for the trial
- The Company intends to continue ongoing safety and efficacy data collection for **all treatment arms in the trial and report topline data in the second quarter of 2025**



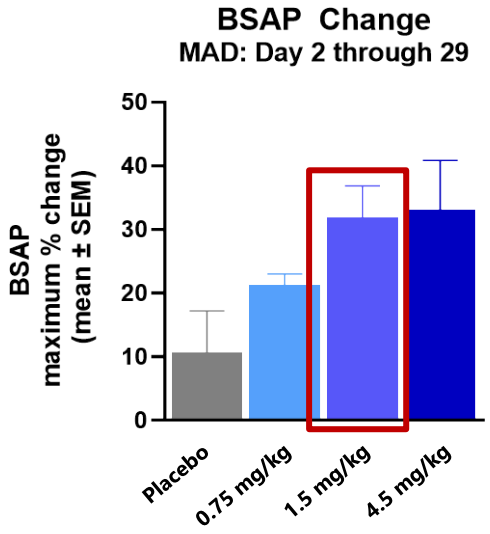
[1]Patients with a primary diagnosis of symptomatic PAH (WHO Group 1) on stable background PAH therapy. [2]In December 2024, pursuant to a trial modification, treatment of all participants originally randomized to 4.5 mg/kg cibotercept Q4W, and 3.0 mg/kg KER-012 Q4W, along with treatment of participants originally randomized to placebo who have crossed over to 3.0 mg/kg KER-012 Q4W, was halted for the duration of the trial. [3]Pursuant to a trial modification in December 2024, the 72-Week Extension Period will be open-label.
EOS = end of study; Q4W = every 4 weeks; WHO = World Health Organization

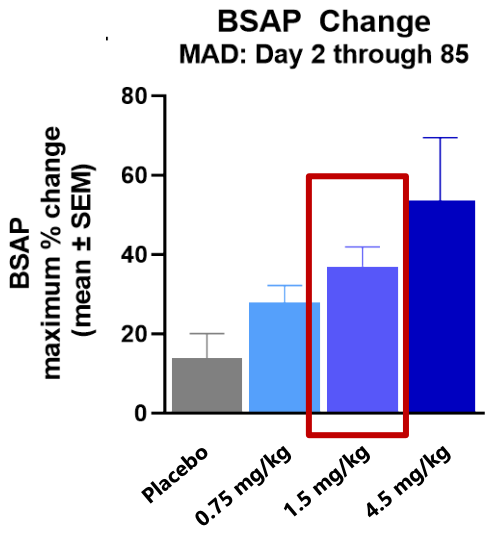
Anticipated TROPOS Readout: Opportunity for Meaningful Insights to Inform Next Steps in Development Program

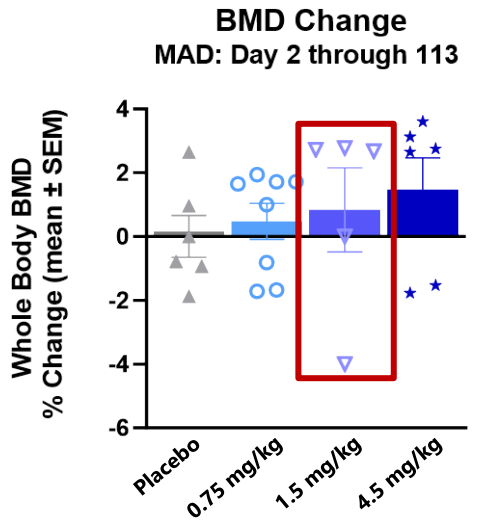
- **Robust set of endpoints, including:**
  - Pulmonary vascular resistance (PVR)
  - 6-minute walk distance (6MWD)
  - WHO Functional Class
  - Safety
  - Pharmacokinetics
  - Pharmacodynamics
- **Multiple analysis approaches, including:**
  - Pooled dose arms and individual dose arms
  - Exposure-response
  - Timepoints

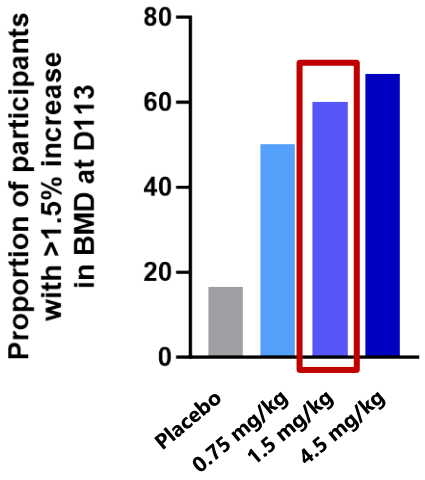
Dose Selection for Phase 2 Clinical Trial of Cibotercept in Patients with PAH based on Observed Safety, Tolerability and Pharmacodynamic Changes in Phase 1 Clinical Trial

- Preclinical safety studies established NOAEL of 50 mg/kg dosed every two weeks[1]
- Keros completed a Phase 1 randomized, double-blind, placebo-controlled, two-part 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. In this Phase 1 clinical trial[2]:
  - Monthly dosing for 3 months was generally well tolerated at doses up to 4.5 mg/kg
  - Changes in bone biomarkers and bone mineral density were observed, suggesting that biological activity was demonstrated from the 0.75 mg/kg dose









1. Sannajust S et al American College of Toxicology 2024 Annual Meeting; 2. Natarajan H, et al. American Society of Bone and Mineral Research 2023
NOAEL= no observed adverse effect level; BSAP = bone specific alkaline phosphatase; BMD = bone mineral density; MAD = multiple ascending dose

Cibotercept Designed To Have Reduced BMP Binding

***In Vitro* Ligand Binding Affinity[1]**

Strong	Semi-Strong	Semi-Weak	Weak

Activin/GDF Ligand Binding

	ActRIIA-Fc	Cibotercept (Modified ActRIIB-Fc)
Activin A	Strong	Strong
Activin B	Strong	Strong
Activin C	Weak	Weak
GDF-8	Strong	Strong
GDF-11	Strong	Strong

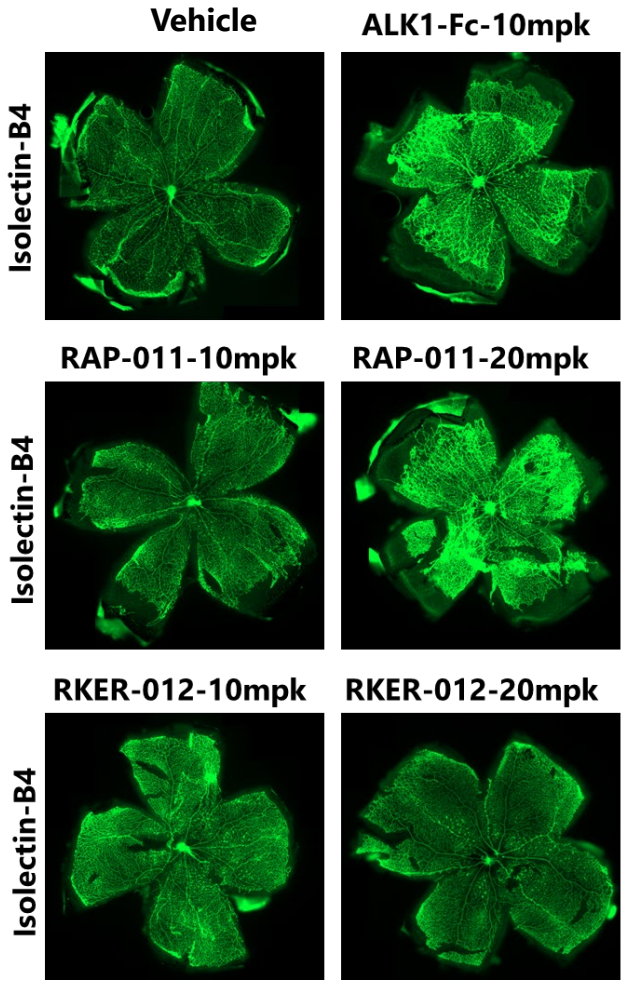
BMP Ligand Binding

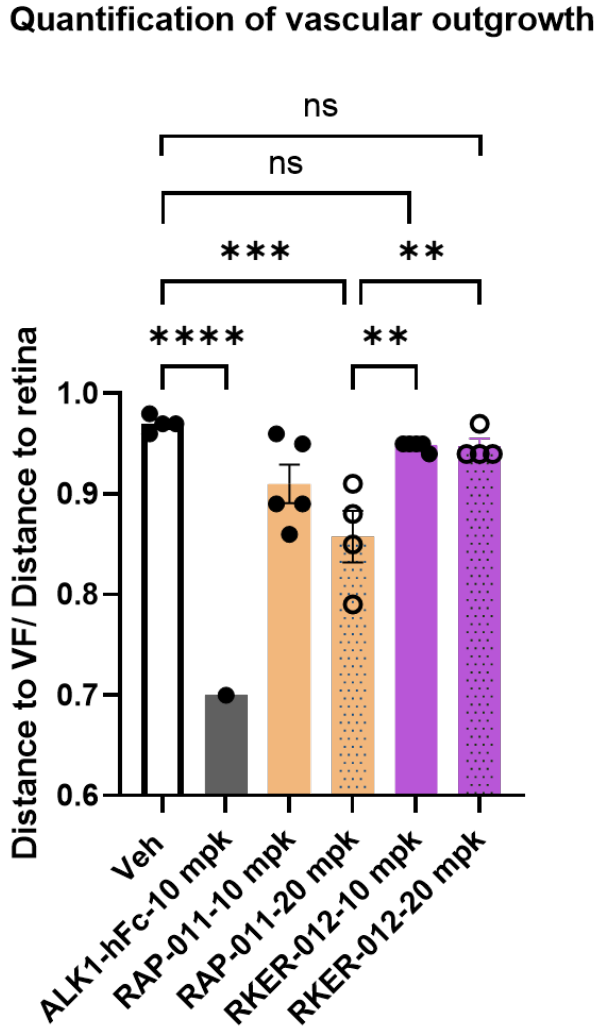
	ActRIIA-Fc	Cibotercept (Modified ActRIIB-Fc)
BMP-2	Semi-Weak	Weak
BMP-3	Weak	Weak
BMP-4	Semi-Weak	Weak
BMP-5	Strong	Semi-Strong
BMP-6	Strong	Weak
BMP-7	Strong	Semi-Strong
BMP-9	Semi-Weak	Weak
BMP-10	Strong	Strong

1. Gudelsky A et al American Thoracic Society 2023 Annual Meeting. Am J Respir Crit Care Med 2023;207:A378

Lack of Observed Perturbation of Retinal Blood Vessels of Newborn Mice Treated with RKER-012 Supports Potential for Reduced Bleeding Risk with Cibotercept

- Due to its postnatal development and easy accessibility, the mouse retinal vasculature is an established model to study vascular growth and remodeling during development and disease
  - In the mouse model of retinal vascularization, inhibition of BMP signaling leads to premature termination and increased density of blood vessels
- Treatment of newborn mice with ALK1-Fc (potent inhibitor of BMP9 and BMP10) significantly reduced retinal neovascularization
  - Increased branching and failure to vascularize to the equator of the eye
- RAP-011 (research form of sotatercept) bound BMP9 with higher affinity that RKER-012
- RAP-011 showed a dose-related inhibition of retinal vessel outgrowth
- RKER-012 (research form of cibotercept fused with Fc region of murine IgG1) did not inhibit retinal neovascularization

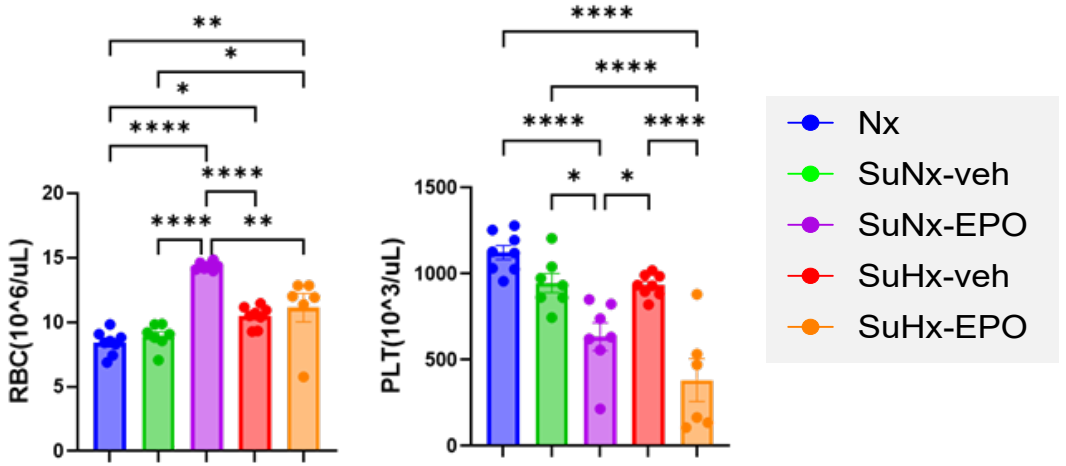


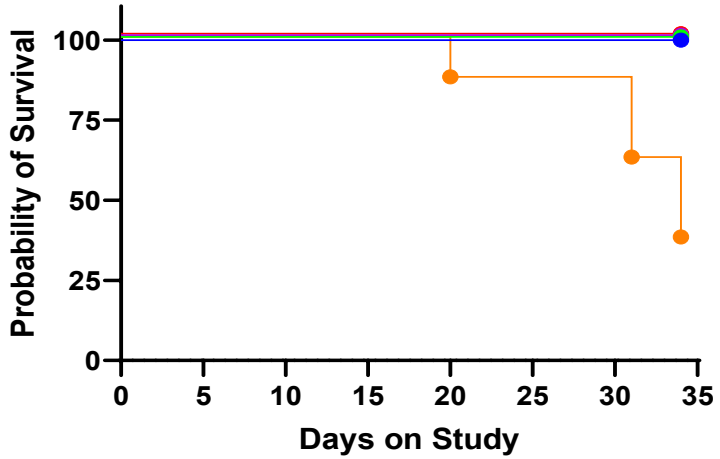


Healthy mice pups were randomly assigned to one of six groups. Treatments were administered on postnatal day 1 and 3. On day 8, retinas were dissected and stained to visualize the vasculature and measure vascular plexus. Note: There were 55% mortality for ALK1-hFc-10mpk group, and the retinas collected were extremely fragile with only one (n=1) retina able to be processed for flat mounting and staining at the end of the study period. ns = not significant; P value: *<0.05, **<0.01, *** <0.001, **** <0.0001

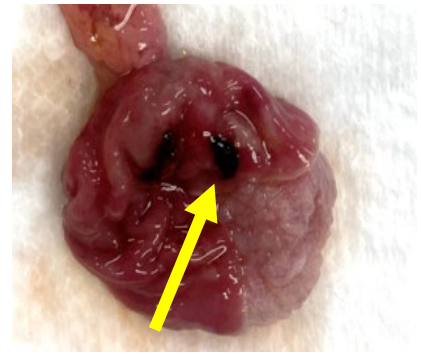
Cibotercept Designed to Lack Effect on Erythropoiesis

- **In the Phase 1 healthy volunteer clinical trial, multiple doses of cibotercept did not elicit changes in hemoglobin or red blood cells (RBCs)**
- **The lack of observed effect on erythropoiesis in humans was consistent with lack of observed effect in multiple preclinical models[1,2]**
- **We evaluated the impact of erythropoietin (EPO) and potentiation of erythrocytosis under hypoxic and normal conditions in rats and observed that erythrocytosis in hypoxic rats increased bleeding events and death**
  - Treatment with erythropoietin increased RBCs resulting in hyperviscosity syndrome
  - Treatment with erythropoietin shunted common hematopoietic precursor (MEP) to erythroid lineage
    - Depletion of MEPs resulted in thrombocytopenia
  - Treatment with EPO under normal atmospheric conditions lead to erythrocytosis without bleeding events
  - Treatment with EPO in the PAH model (Sugen/hypoxia) lead to erythrocytosis with bleeding events
    - Observed nose bleeds and gastrointestinal bleed
    - Reduced survival





Nose bleed



Gastrointestinal Bleed

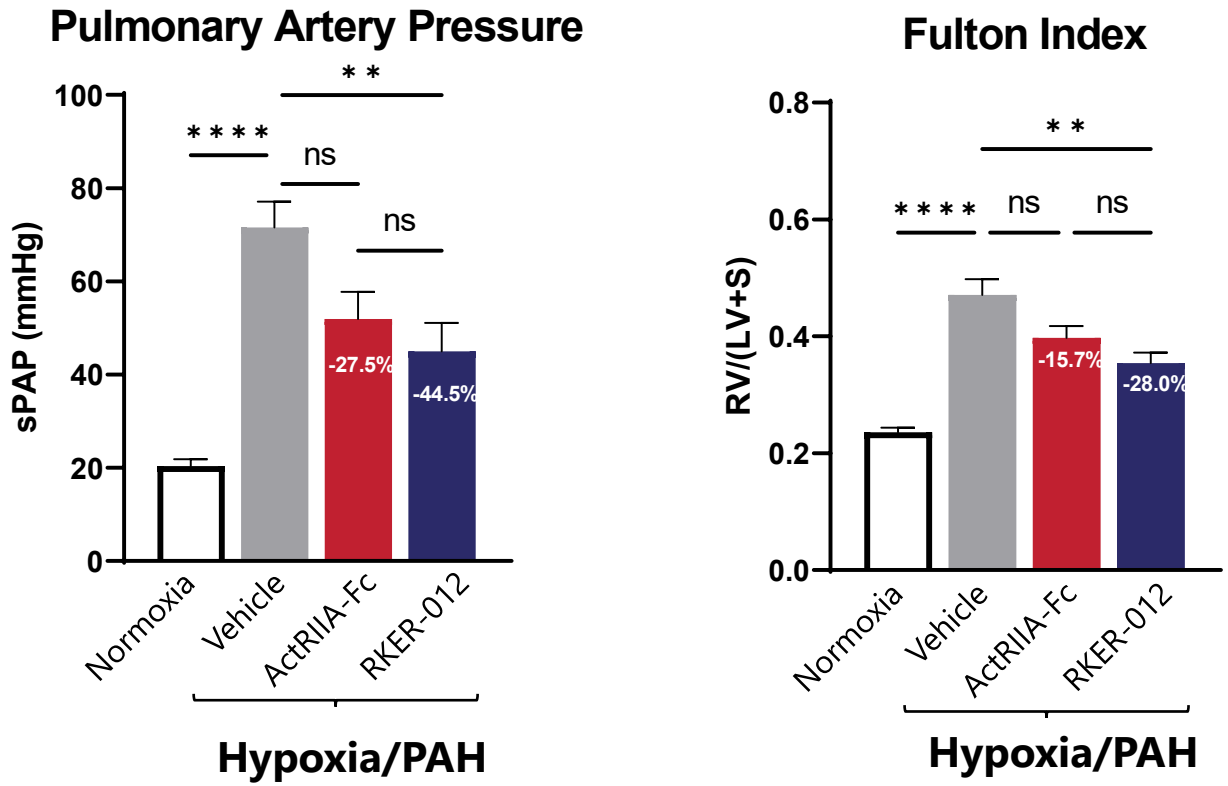
Six-week-old male Sprague Dawley rats received a single dose of Sugen5416 (Su, 20mg/Kg sc) and epoetin-alpha (EPO, 7200U/Kg thrice weekly sc) or vehicle under normoxic (SuNx-EPO and SuNx-veh) or hypoxic (SuHx-EPO & SuHx-veh, 10% O_2) conditions for 5 weeks and compared to normoxic (Nx) controls.

1. Babbs K, et al. American Thoracic Society 2021 Annual Meeting; 2. Babbs K, et al. American Thoracic Society 2022 Annual Meeting

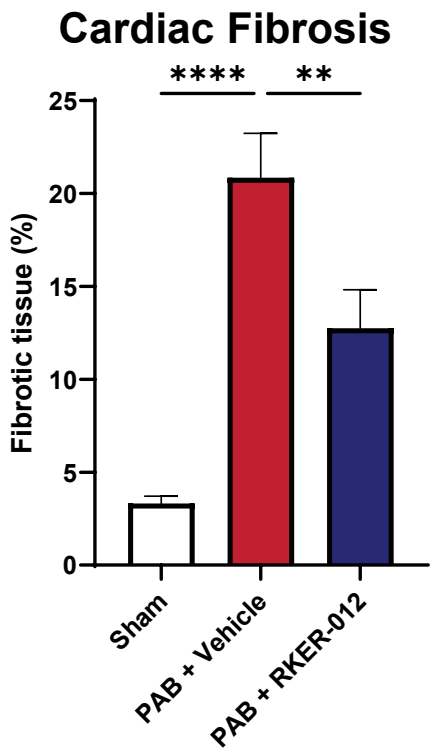
P value: *<0.05, **<0.01, *** <0.001, **** <0.0001; MEPs= megakaryocytic-erythroid progenitors Nx = Normoxia; SuNx = Sugen rat model + normoxia, SuHx = Sugen rat model + hypoxia; veh = vehicle

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, * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$.

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

KER-065:
Neuromuscular Diseases

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

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

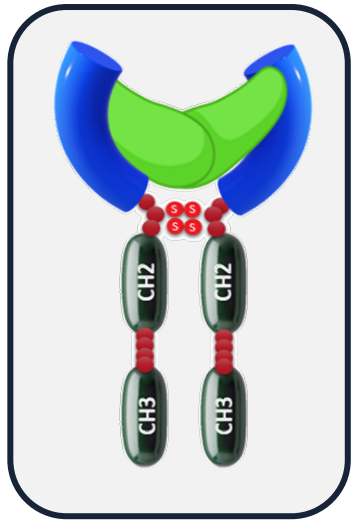
- ~50% amino acids derived from each activin receptor

KER-065 is designed to bind to the negative regulators of muscle growth, activin A and myostatin, to increase skeletal muscle and in preclinical studies, showed potent inhibition of ligands involved in the regulation of muscle and bone homeostasis

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

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

As part of its ongoing portfolio management activities, Keros has decided to deprioritize the development of KER-065 in obesity



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.

KER-065: Duchenne Muscular Dystrophy (DMD)

- **Chronic degenerative muscle diseases eventually lead to a collapse in the ability of muscle to regenerate and eventual loss of function**
- **DMD manifests as subtle motor defects postnatally leading to loss of ambulation and eventually death[1,2]**
- **In young boys with DMD, muscle undergoes continuous rounds of degeneration/regeneration, but eventually the ability of the muscle to regenerate declines due to a decline in muscle progenitor cells known as satellite cells[2-4]**
- **While glucocorticoids are catabolic and increase muscle and bone loss, paradoxically, treatment improves muscle function and delays loss of ambulation in boys with DMD**
  - The treatment of the underlying inflammation leads to short-term increase in muscle regeneration
  - While glucocorticoids help to maintain muscle function in DMD patients, long-term treatment can have significant negative side effects, including fluid retention, hyperglycemia, severe weight gain with fat deposits in the abdomen, face and neck, bone fragility, cataracts, high blood pressure and mood effects

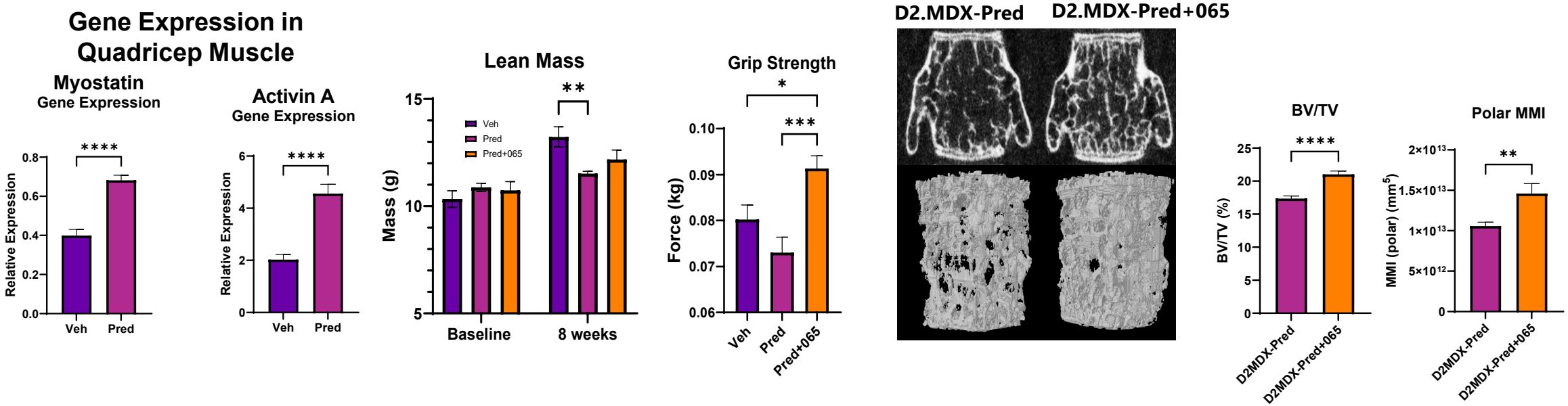
Disease Progression[6,7]

5 to 7 Years	*Motor delay, enlarged calves, toe walking, standing from supine and climbing stairs more difficult*	Early Ambulatory
8 to 11 Years	*Increasing loss of walking mobility and part time wheelchair use*	Late Ambulatory
Early Teens	*Loss of ambulation, fulltime wheelchair use and increasing loss of upper limb function*	Early Non-Ambulatory
Teens	*Increasing respiratory impairment, ventilatory support often required and unable to perform activities of daily living*	Late Non-Ambulatory
Teens to Twenties	*Increasing cardiac dysfunction, heart failure and ultimately death*	

- **Based on our preclinical data, we believe that KER-065 has the potential to treat boys with DMD, potentially by increasing muscle, preserving muscle regeneration and counteracting the negative impact of glucocorticoids on muscle and bone**
  - Increased regenerative capacity of the muscle can potentially improve the expression of utrophin and dystrophin in boys on exon skipping therapies

1. Parker, A. E., et al. (2005). QJM 98, 729–736. doi: 10.1093/qjmed/hci113; 2. Tabebordbar, M., et al. (2013). Annu. Rev. Pathol. 8, 441–475. doi: 10.1146/annurev-pathol-011811-132450; 3.Wallace, G. Q., and McNally, E. M. (2009). Annu. Rev. Physiol. 71, 37–57. doi:10.1146/annurev.physiol.010908.1632164.4; 4. Mann, C. J.,et al. (2011). Skelet. Muscle 1:21. doi: 10.1186/2044-5040-1-21 6. Bushby K, Connor E. Clin Investig (Lond) 2011; 1:1217-1235; 7. Cruz Guzman, et al. Int J Endocrinol 2012; 2012:485376

Glucocorticoids Increased Expression of Negative Regulators of Skeletal Muscle and Bone in a Preclinical Study



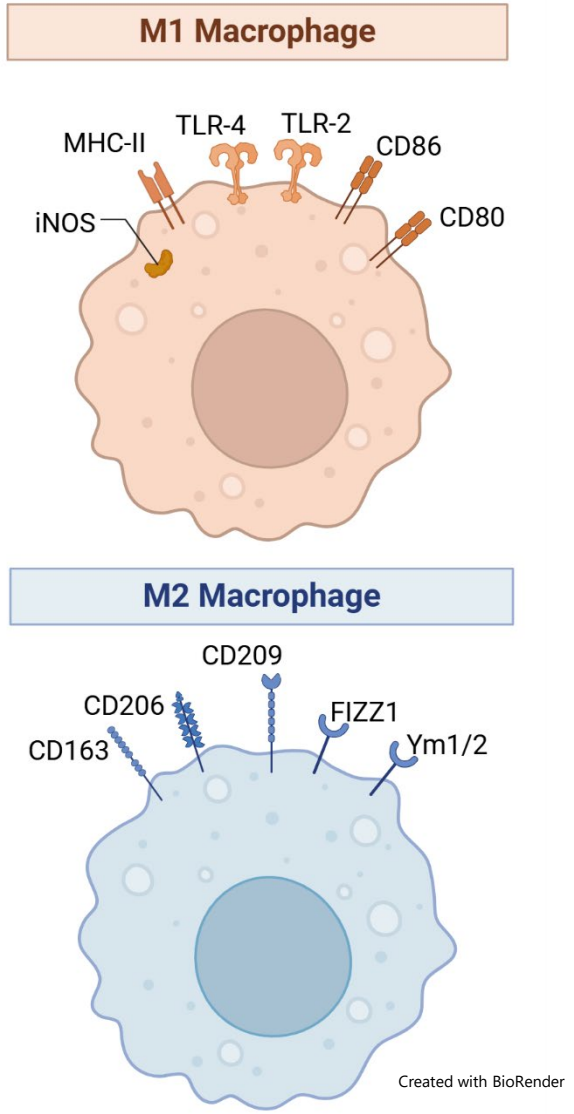
MDX mice (mouse model of DMD) were treated with vehicle (Veh) or 2-prednisolone (Pred), or cotreated with prednisolone and RKER-065 (Pred-065) (10 mg/kg, twice weekly). The changes in body weight, body composition (NMR), grip strength, skeletal muscle gene expression, and bone micro-architecture (micro-CT) were assessed.

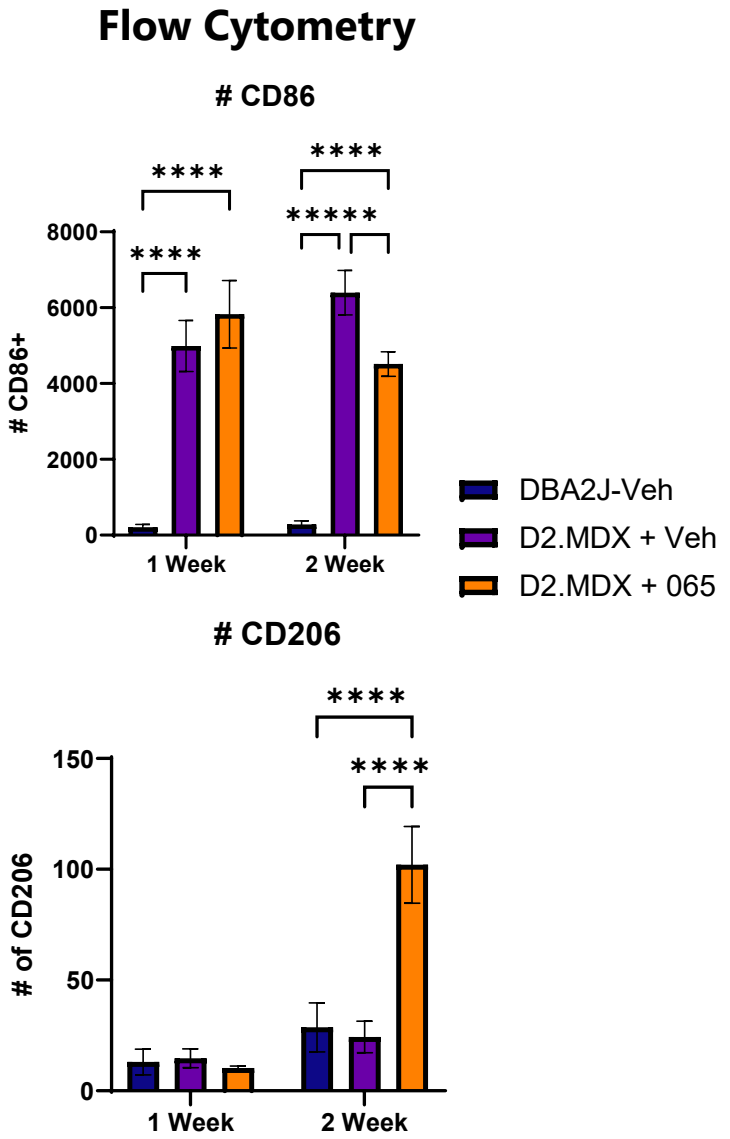
- **Prednisolone-treated MDX mice had less muscle mass and strength than vehicle-treated mice**
- **Co-treatment with prednisolone and RKER-065 increased both muscle mass and strength and trabecular bone and strength**

Data is shown as average ± SEM. * P≤0.05, ** P<0.01, *** P<0.001, and **** P< 0.0001. BV/TV = bone volume fraction; MMI = mass moment of inertia; RKER-065 = research version of KER-065

RKER-065 Reduced the Inflammatory Profile of Muscle Resident Macrophages and Shifted Towards Muscle Repairing

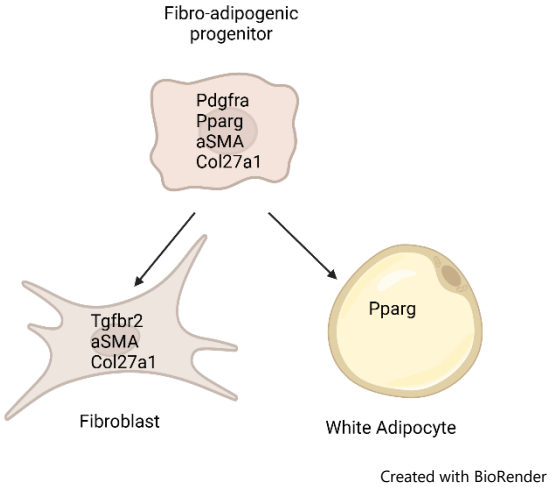
- **Under different pathophysiologic conditions, macrophages can acquire distinct functional phenotypes via undergoing different phenotypic polarization. Macrophage M1 and M2-type responses describe the opposing activities of killing or repairing**
- MDX mice were treated with a single dose of RKER-065 (10 mg/kg) or vehicle. Muscles were dissected and processed to obtain single cell suspensions on day 1, day 2, and day 4 (n=5), stained for markers of macrophage markers and analyzed by flow cytometry
- **Treatment with RKER-065 reduced the markers associated with pro-inflammatory macrophages (M1)**
- **Treatment increased markers associated with repairing macrophages (M2)**

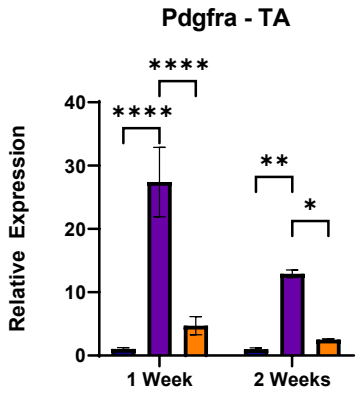


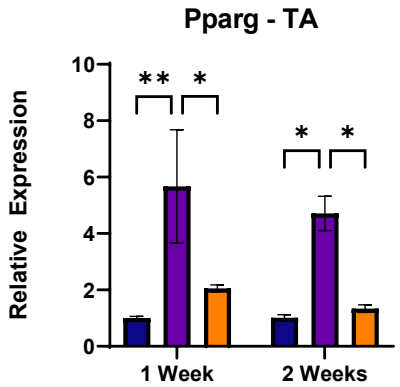


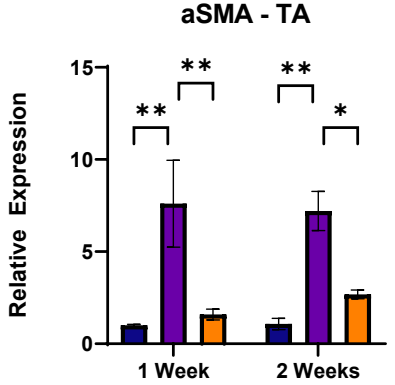
Data is shown as average ± SEM. 2-way ANOVA with repeat measures and Sidak post test. * P≤0.05, ** P<0.01, *** P<0.001, and **** P< 0.0001.

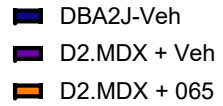
RKER-065 Reduced the Fibroblast and Fat Precursor Cells in Muscle of Dystrophic Mice



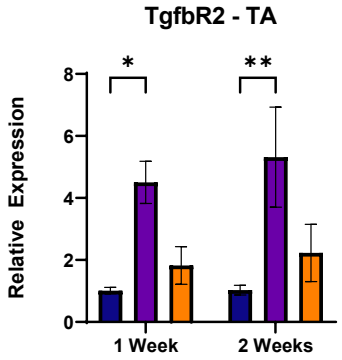


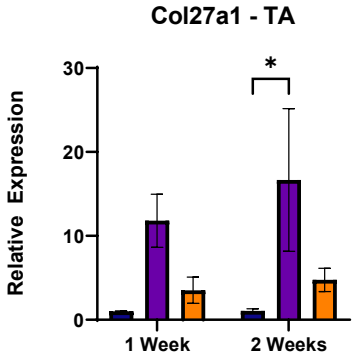






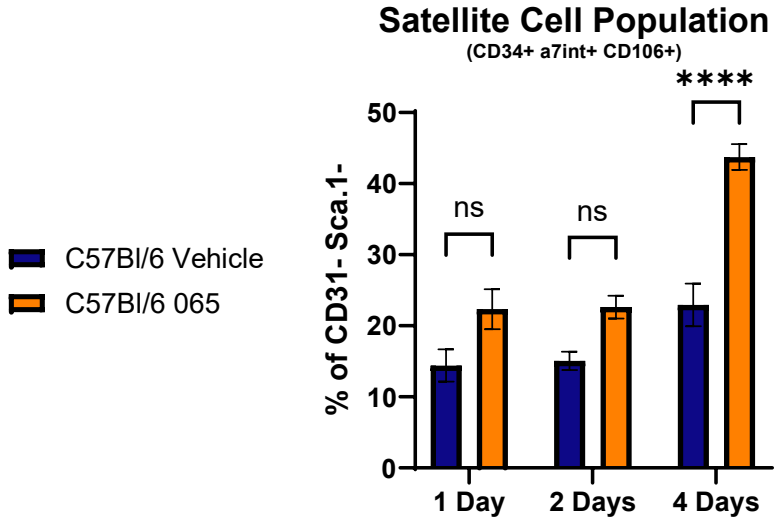
- **Failure of muscle to regenerate following injury leads to replacement of muscle fibers with fibrotic and fatty infiltrates**
- MDX mice were treated with a single dose of RKER-065 (10 mg/kg) or vehicle. Muscles were dissected and RNA isolated and analyzed by real-time QPCR
- **RKER-065 treatment reduced fibro-adipogenic progenitors, the common cell that differentiates to fibroblasts and adipocytes**



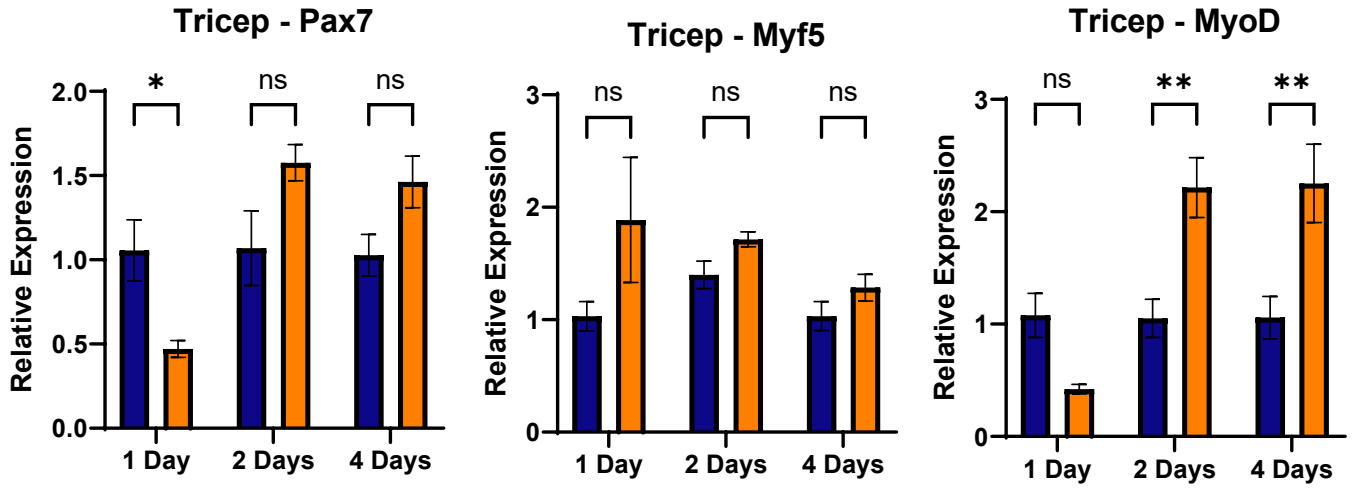


Data is shown as average ± SEM. 2-way ANOVA with repeat measures and Sidak post test. * P≤0.05, ** P<0.01, *** P<0.001, and **** P< 0.0001. TA = tibialis anterior

Treatment with RKER-065 Increased Satellite Cells in Skeletal Muscle

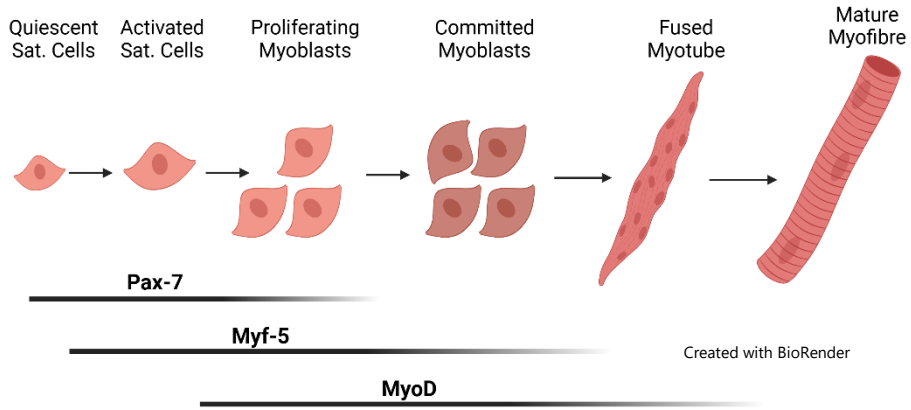


Markers of satellite cell differentiation



- Wild type mice were treated with a single dose of RKER-065 (10 mg/kg) or vehicle. Muscles were dissected and processed to obtain single cell suspensions on day 1, day 2, and day 4 (n=5, stained for markers of satellite cells (CD31, Sca.1, CD34, α7 integrin, and CD106) and analyzed by flow cytometry
- **Treatment with RKER-065 increased the pool of satellite cells in wild type mice**
- **Molecular markers demonstrated commitment/differentiation of satellite cells to muscle**

Flow Cytometry of satellite cells



* P≤0.05, ** P<0.01, *** P<0.005; Pax7 = paired box 7; Myf5 = myogenic factor 5 ; MyoD = myoblast determination protein 1

Treatment with RKER-065 Increased Utrophin Expression and Muscle Strength in Mouse Model of DMD

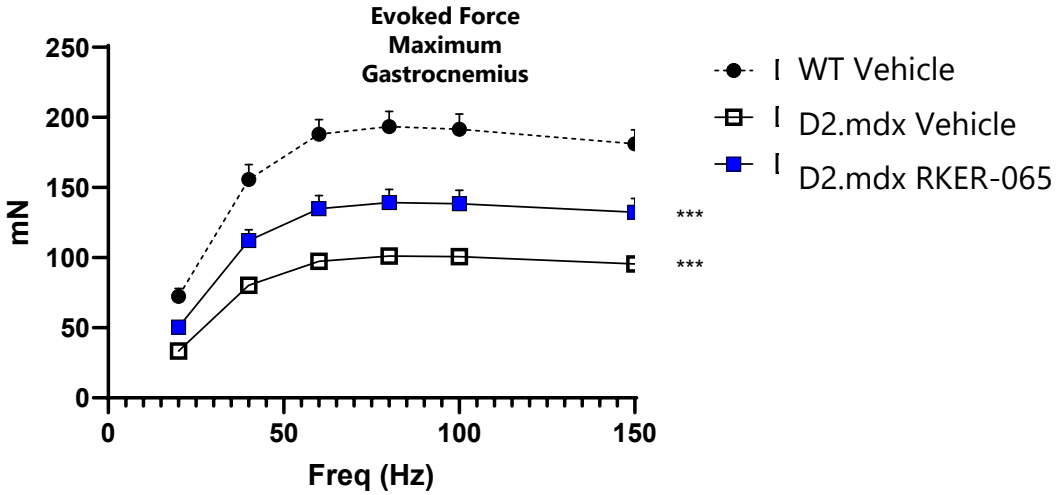
Muscle lacking dystrophin is easily damaged during the process of contraction

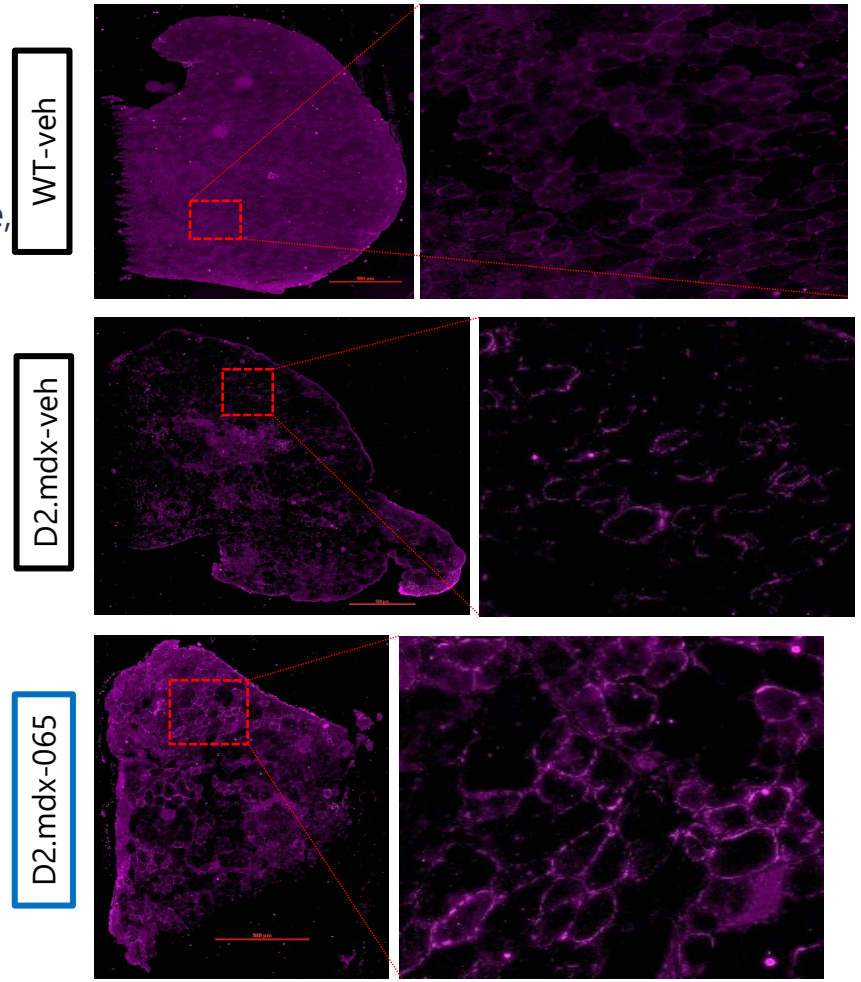
Many third-party approaches have been utilized to stabilize the muscle and provide resistance to contractile-induced damage:

- 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
- Increased expression of utrophin (a functional analog of dystrophin)

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

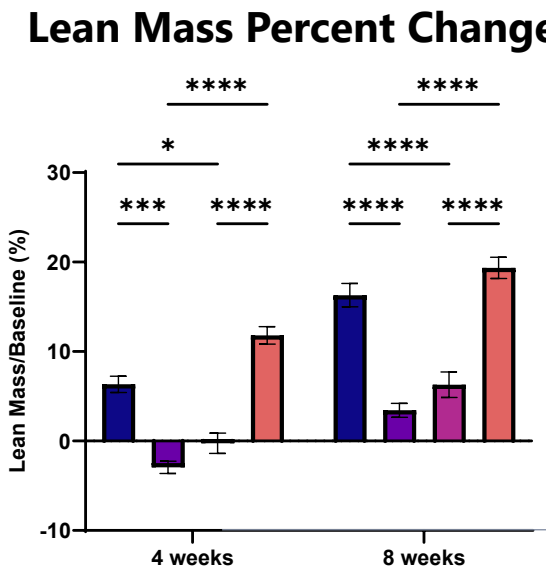
- Increased expression of utrophin in muscle fibers, potentially contributing to the observed increased strength[1]

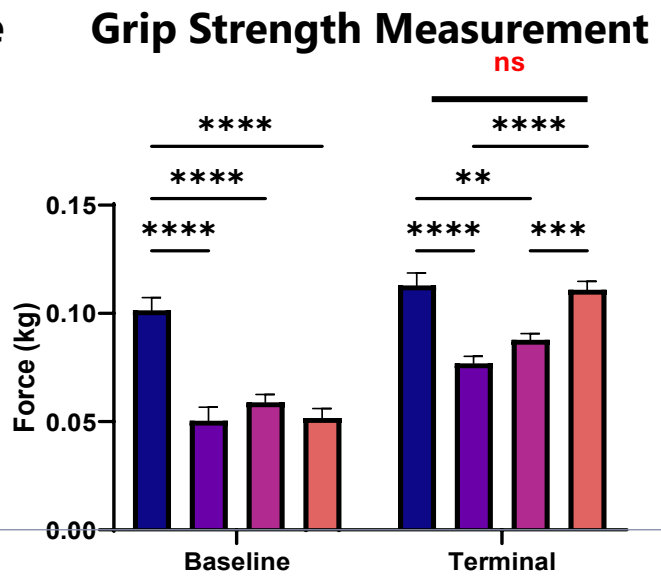


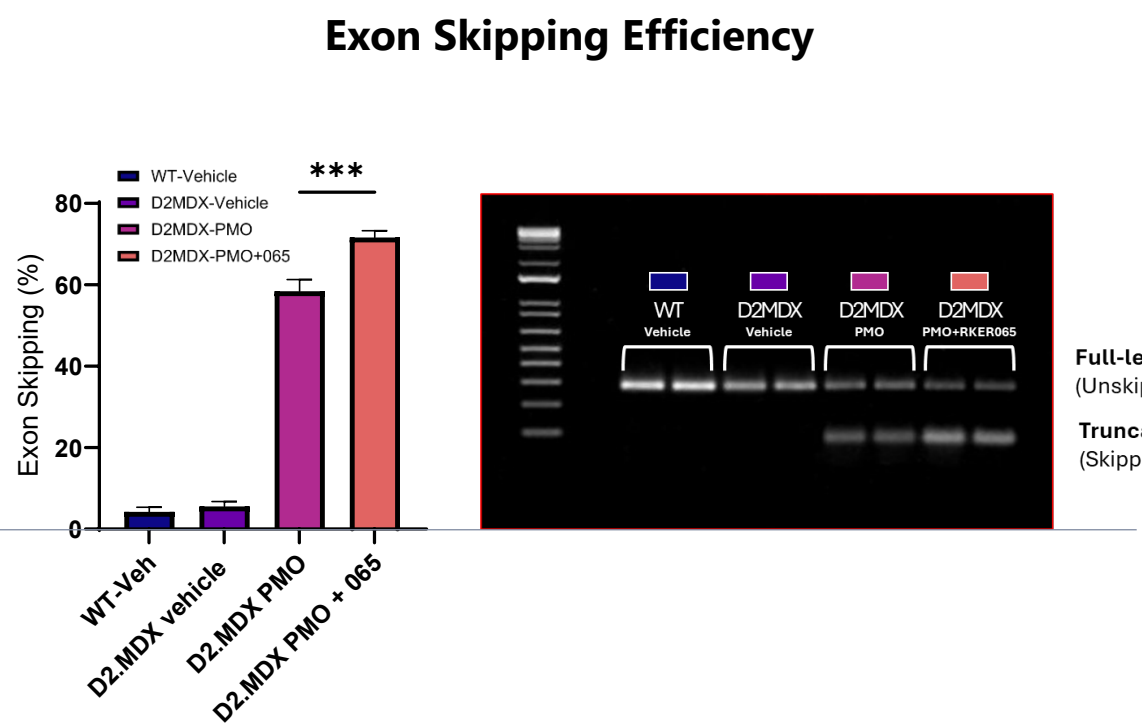


1. Nathan, R., et al. 28th International Annual Congress of the World Muscle Society; WT= wild type (control), D2.mdx = mouse model of DMD' *** P<0.001

RKER-065 Treatment Improved Efficiency of Exon Skipping







- **Treatment with PMO did not increase lean mass or muscle function**
- **Co-treatment with PMO and RKER-065 improved lean mass and grip strength**
- **RKER-065 treatment improved the efficiency of PMO driven exon skipping**

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

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 is enrolling patients with elevated body mass index (BMI) of 27-33 to evaluate the effect of KER-065 on lean mass, fat mass and bone mineral density

- Imaging by DXA and MRI

Additional exploratory biomarkers included to examine the pharmacologic effect of KER-065 on:

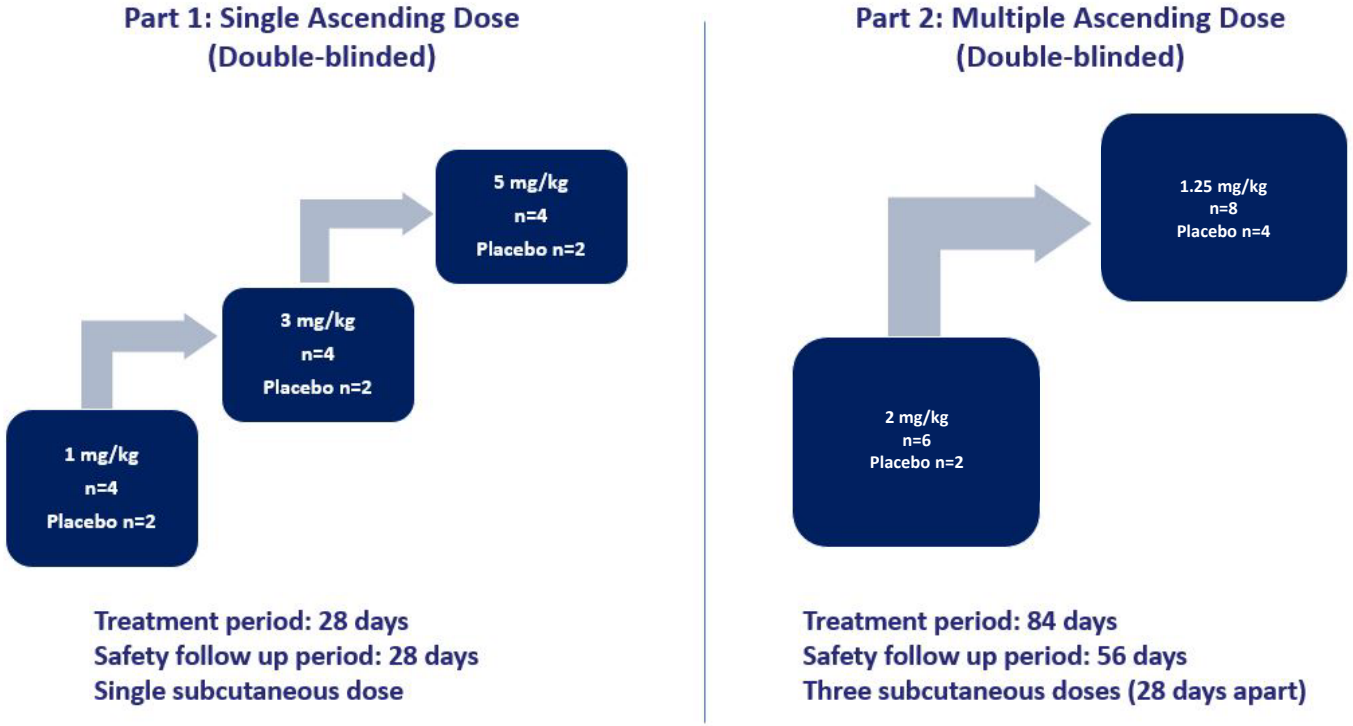
- Biomarkers of bone formation and resorption
- Adipokines
- NT-proBNP, a marker of cardiac stress
- Markers of fibrosis

We believe this trial has the potential to inform development of KER-065 in neuromuscular indications, such as 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

Elritercept (KER-050)

Investigational Treatment for Anemia and Thrombocytopenia in Patients with Myelodysplastic Syndromes and in Patients with Myelofibrosis

Global License Agreement with Takeda Pharmaceuticals*

On December 3, 2024, Keros announced it had entered into an exclusive license agreement with Takeda to develop, manufacture and commercialize elritercept globally, other than mainland China, Hong Kong, and Macau*

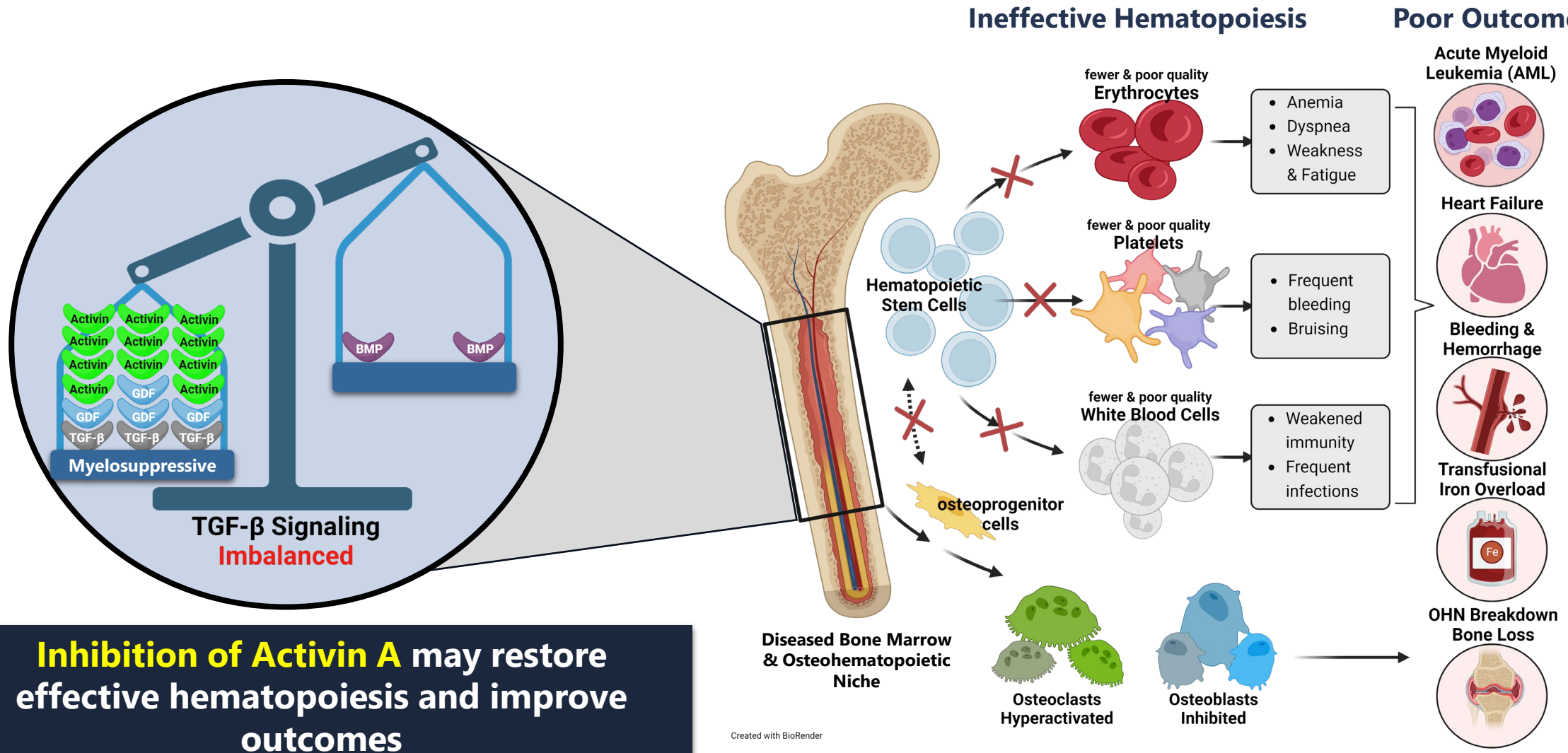
Financials:

- Keros will receive an upfront payment of $200 million
- Eligible to receive development, approval and commercial milestone payments of over $1.1 billion
- Tiered royalties on net sales in the low double-digits to high teens

Under the terms of the agreement, Takeda is responsible for all clinical development, manufacturing and commercialization as of the effective date of the definitive agreement.

***The license agreement is subject to antitrust clearance**

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

Disease Overviews

Myelodysplastic Syndrome

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.

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.

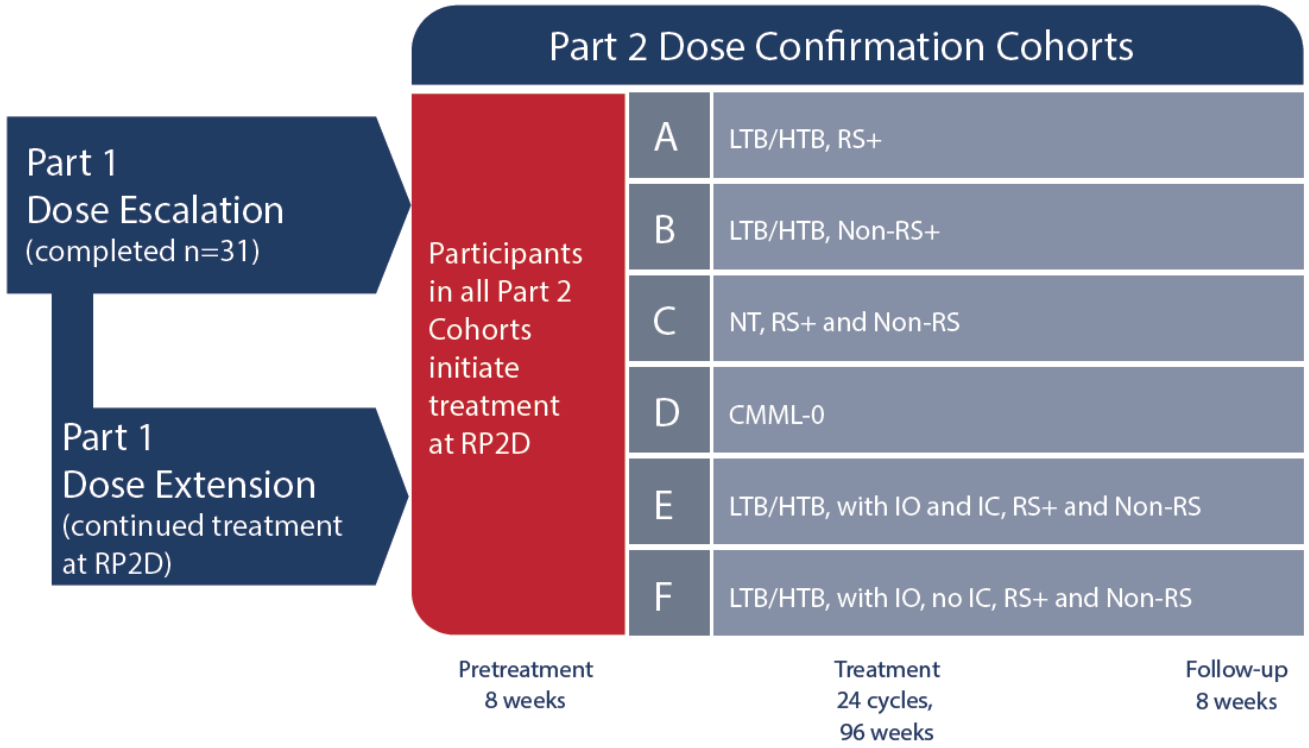
Clinical Consequences
MF is characterized by ineffective hematopoiesis, an enlarged spleen, bone marrow fibrosis and shortened survival. Both anemia and thrombocytopenia are negative prognostic indicators. Anemia is prevalent in MF (one study reported anemia in 64% of patients beyond 1 year of diagnosis[1]) 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 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 patients with at least 24 weeks of elritercept treatment or who have discontinued (n=95)

Baseline Demographics

Baseline Characteristic	RP2D, (N=95)
Median Age, years (range)	74 (53–89)
Sex, n (%) male	61 (64.2)
RS Status, n (%)	
RS+	63 (67)
Non-RS	31 (32.9)
Transfusion Burden, n (%)	
NT	15 (15.8)
LTB	23 (24.2)
HTB	57 (60)
Dysplasia Category, n (%)	
Multi-Lineage	56 (58.9)
Single-Lineage	7 (7.4)
Unknown/Missing	32
Prior erythropoietin stimulating agent, n (%)	25 (26.3)
Erythropoietin, U/L, n	86*
Median (range)	135.2 (1.1–4000)
≥500 U/L, n (%)	18 (18.9)
Platelets, median (range)	215.8 (37–442)
Thrombocytopenia (<150 x 10^9/L, n (%))	24 (25.3%)

Data are presented as of a data cut-off date of August 30, 2024.
*9 RP2D patients had missing baseline erythropoietin (EPO);
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

Elritercept was Generally Well-Tolerated

- **Majority of treatment-emergent adverse events (TEAEs) were mild (Gr 1) to moderate (Gr 2).**
- **Treatment-related TEAEs leading to discontinuation included injection site reaction (ISR), platelet count increased, and dyspnoea (worsening).**
- **4 treatment-related TESAEs: ISR (Gr 2), dyspnoea (worsening) (Gr 3), syncope (Gr 3), and adenocarcinoma gastric (Gr 3) occurred in 1 patient each.**
- **Adenocarcinoma gastric, dyspnoea (worsening), and syncope were assessed as not related to treatment by Sponsor due to underlying co-morbidities.**
- **4 Fatal TEAEs: Cardiac failure, myocardial infarction, interstitial lung disease (exacerbation) and sudden death occurred in 1 patient each; all were assessed as not related by both the Investigator and Sponsor.**
- **One patient progressed to Acute Myeloid Leukemia (AML) as of the data cutoff date.**

Category	RP2D (N=95) n (%)
Any TEAE	93 (97.9)
Any treatment-related TEAE*	43 (45.3)
Any TESAE	42 (44.2)
Any treatment-related TESAE	4 (4.2)
Any TEAE leading to death	4 (4.2)
Any TEAE leading to discontinuation	16 (16.8)
Most frequent TEAEs (in ≥ 15% of participants), all grades, all cause	
Diarrhoea	27 (28.4)
Fatigue	24 (25.3)
COVID-19	21 (22.1)
Dyspnoea	18 (18.9)
Dizziness	17 (17.9)
Anemia	17 (17.9)
Nausea	16 (16.8)
Epistaxis	15 (15.8)

Treatment-related = considered to be related to the study treatment by the treating investigator.

Data are presented as of a data cut-off date of August 30, 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 n < 500 U/L[b]	
	All (N=87)	HTB (N=51)	All (N=71)	HTB (N=39)
Overall Response[c]	48/87 (55.2)	25/51 (49)	43/71 (60.6)	22/39 (56.4)
Modified IWG 2006 HI-E[d]	42/87 (48.3)	24/51 (47.1)	37/71 (52.1)	21/39 (53.8)
RS+	33/59 (55.9)	19/35 (54.3)	29/52 (55.8)	16/30 (53.3)
non-RS	9/28 (32.1)	5/16 (31.3)	8/19 (42.1)	5/9 (55.6)
TI ≥8 weeks[e]	27/69 (39.1)	16/51 (31.4)	26/55 (47.3)	15/39 (38.5)
RS+	22/47 (46.8)	13/35 (37.1)	21/41 (51.2)	12/30 (40.0)
non-RS	5/22 (22.7)	3/16 (18.8)	5/14 (35.7)	3/9 (33.3)

- **Overall response rates in patients with HTB were similar to those observed in the overall ($mITT_{24}$) population**
- **Higher response rate was observed in the EPO <500 U/L population, particularly non-RS patients**

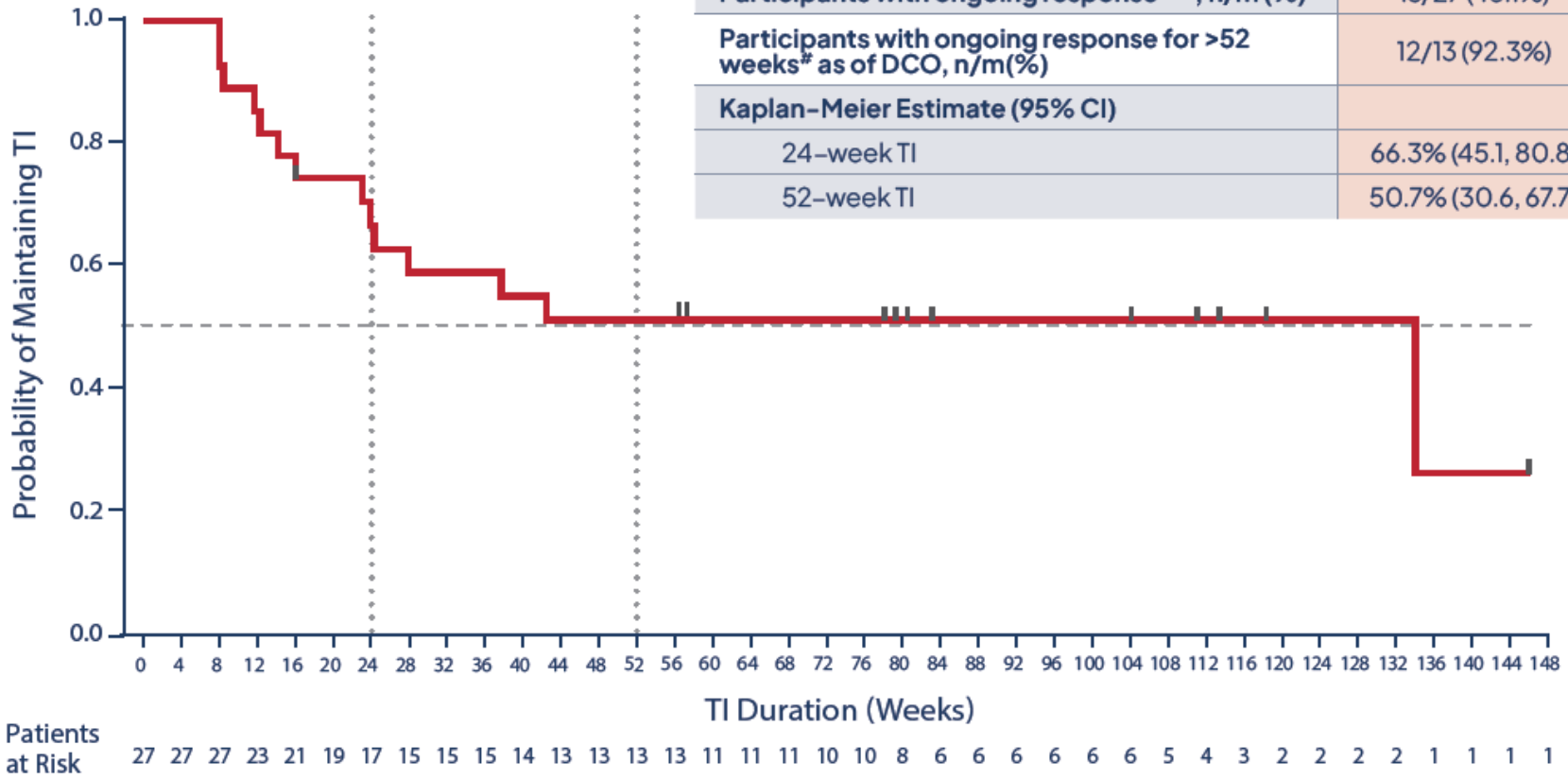
Data are presented as of a data cut-off date of August 30, 2024.

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. 9 $mITT_{24}$ patients (2LTB RS+, 1LT non-RS, 4 HTB RS+, 2 HTB non-RS) had missing baseline EPO measures and were conservatively classified as having EPO < 500 U/L; 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*

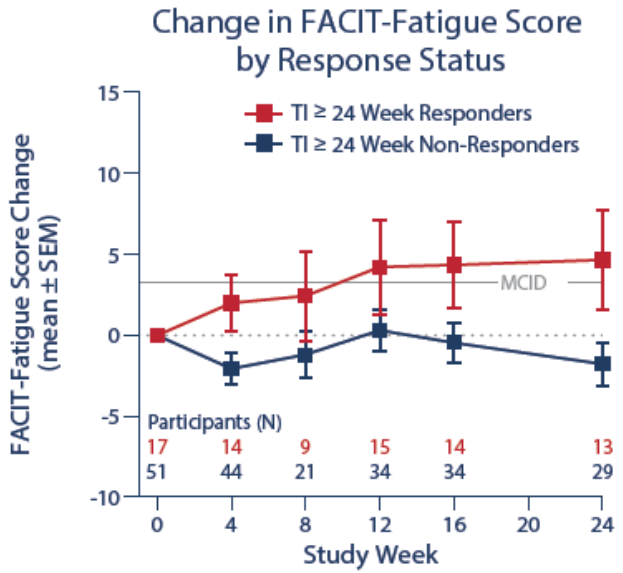
Duration of Transfusion Independence (TI)	
Median** (95% CI), weeks	134.1 (23.0, NE)
Participants with ongoing response***, n/m (%)	13/27 (48.1%)
Participants with ongoing response for >52 weeks# as of DCO, n/m(%)	12/13 (92.3%)
Kaplan-Meier Estimate (95% CI)	
24-week TI	66.3% (45.1, 80.8)
52-week TI	50.7% (30.6, 67.7)

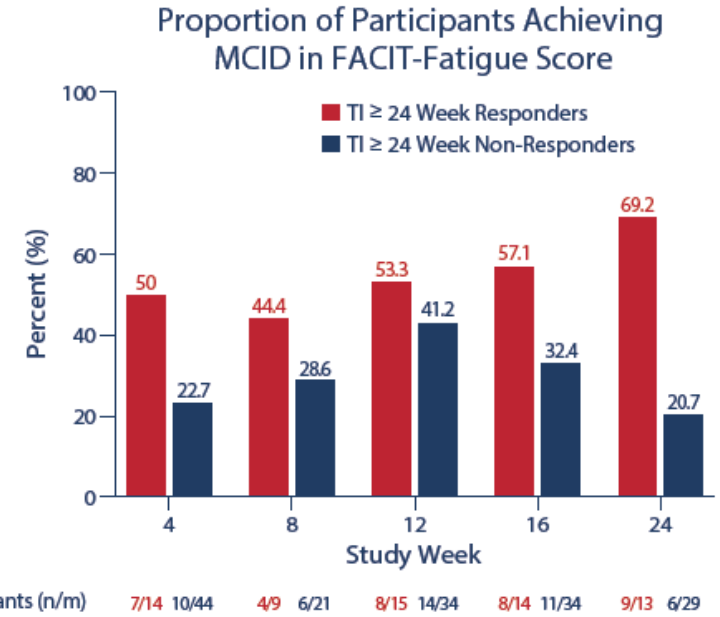


Data are presented as of a data cut-off date of August 30, 2024.
*RBC transfusions for elective surgery and intercurrent disease (i.e. bleeding events) were recorded but were not counted towards baseline requirement or efficacy assessment. ** Due to ongoing TI responses as of the data cutoff date, the median duration of TI is expected to change as data continues to accumulate. *** Patients with ongoing TI response (i.e. without transfusion event) at time of cutoff are censored and denoted by vertical lines.# 6/12 (50%) patients with ongoing TI for > 52 weeks were HTB, including patients who had received up to 11 RBC Units per 8 weeks at baseline.
NE= not evaluable; CI = confidence interval, DCO = data cutoff

Sustained and Clinically Meaningful Improvements in FACIT-Fatigue Scores Observed with Elritercept Treatment

- **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]





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	4.7 (3.1), n=13	-1.8 (1.3), n=29	6.5

Data are presented as of a data cut-off date of August 30, 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, MCID = Minimally Clinical Important Difference is defined as at least a 3-point increase in FACIT-Fatigue score

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	JAK inhibitor relapsed, refractory, intolerant or ineligible
Combination with Ruxolitinib	Prior ruxolitinib treatment ≥ 8 weeks with stable dose ≥ 4 weeks	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 August 30, 2024
- Part 1 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 (32 patients enrolled, N=8 monotherapy, N=24 combination).
- 73 patients (N=29 monotherapy, N=44 combination) enrolled in Parts 1 and 2

Post-ET = post-essential thrombocythemia; Post-PV= post polycythemia vera; JAK = Janus kinase

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

- **Most frequently reported TEAEs across both arms were thrombocytopenia and diarrhoea**
  - Grade ≥ 3 thrombocytopenia in 12 (16.4%):
    - Monotherapy: 8 (27.6%)
    - Combination: 4 (9.1%)
  - 14 of the 15 patients with a TEAE of thrombocytopenia had baseline platelets < 150 x 109/L
- **In Part 1 Dose Escalation, 1 patient (monotherapy, 1.5 mg/kg dose) experienced a dose limiting toxicity (DLT) of Hgb increase ≥ 2 g/dL, which met protocol criteria for dose reduction and was not associated with AEs**
- **There were 2 TESAEs (anemia and fall) considered related to elritercept, and 2 TESAEs (anemia and external ear neoplasm) considered related to ruxolitinib by the treating Investigator**
- **6 patients had TEAEs unrelated to drug leading to death (pneumonia, pneumonia aspiration, multiple organ dysfunction, transformation to AML, cerebrovascular accident, septic shock)**

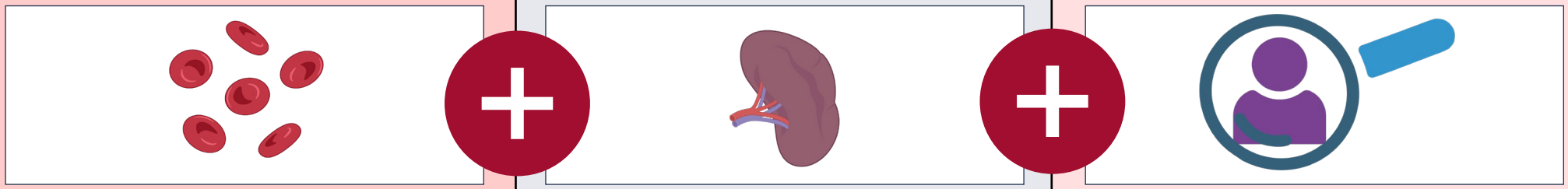
Category	Monotherapy (N=29)	Combination (N=44)	Total (N=73)
TEAEs, n (%)	29 (100)	40 (90.9)	69 (94.5)
Most Frequent TEAEs (≥ 15% of patients), n (%)			
Thrombocytopenia	10 (34.5)	5 (11.4)	15 (20.5)
Diarrhoea	5 (17.2)	9 (20.5)	14 (19.2)
TESAEs, n (%)	12 (41.4)	14 (31.8)	26 (35.6)
Treatment-Related TEAEs, n (%)			
Elritercept Related	11 (37.9)	15 (34.1)	26 (35.6)
Ruxolitinib Related	N/A	13 (29.5)	13 (17.8)
Treatment-Related TESAEs, n (%)			
Elritercept Related	1 (3.4)	1 (2.3)	2 (2.7)
Ruxolitinib Related	N/A	2 (4.5)	2 (2.7)
TEAEs Leading to Discontinuation, n (%)			
Elritercept Discontinuation	6 (20.7)	3 (6.8)	9 (12.3)
Ruxolitinib Discontinuation	N/A	3 (6.8)	3 (4.1)
TEAEs Leading to Death, n (%)	4 (13.8)	2 (4.5)	6 (8.2)

Data are presented as of a data cut-off date of August 30, 2024
N/A= not applicable

Data Support Potential for Elritercept to Address Multiple Aspects of MF

Hematopoiesis	Spleen Size	Symptoms

• 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 10/16 (62.5%) had a reduction ≥ 50% and 6/16 (37.5%) achieved TI
• Platelet counts were generally maintained or improved in patients in both arms, including those with thrombocytopenia at baseline
	• 8/20 (40%) evaluable patients showed reduction ≥ 10% in spleen size at Week 24
	  • Evaluable patients had baseline spleen size ≥ 450 cm^3 and a Week 24 spleen volume assessment
	  • 3/20 (15%) had reductions ≥ 35%
	• Among the 8 evaluable patients in the combination arm with a starting dose of 3 mg/kg or higher, 7/8 (88%) had some reduction in spleen size at week 24
	• Observed reductions in spleen volume support potential for elritercept to treat splenomegaly, particularly in combination with ruxolitinib
		• Overall, across both arms, MF-SAF-TSS symptom scores were reduced in 18/27 (67%) of 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
		• 5 patients had reductions ≥ 50% including 3 in monotherapy and 2 in combination arm



Data are presented as of a data cut-off date of August 30, 2024.

*Patients were included in the analysis if they received ≥ 3 RBC U/12 weeks at baseline with at least 12 consecutive weeks of postbaseline RBC transfusion data in the first 24 weeks. Patients without 12 consecutive weeks of transfusion data (n=10; 6 monotherapy, 4 combination) were excluded from the analysis. MF-SAF-TSS = Myelofibrosis symptom assessment for total symptom score

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 we currently have an expansive library of 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

Cibotercept

- Announce topline data from Phase 2 TROPOS trial — Q2 2025
- Regulatory interactions and development strategy — H2 2025

KER-065

- Announce initial data from Phase 1 healthy volunteer trial — Q1 2025
- Regulatory interactions and development strategy — H2 2025

Elritercept

- Commence Phase 3 RENEW trial in MDS — Q1 2025