KEROS THERAPEUTICS

Corporate Presentation

September 2020

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Harnessing the Powerful Biology of the TGF-β Superfamily

Clinical-stage biopharmaceutical company developing novel therapeutics that target the TGF-β superfamily

Approach validated by FDA-approved third-party products derived from native amino acid sequences

- Infuse (BMP2) for spinal fusion (Genetics Institute/Medtronic-Sofamor)
- Reblozyl® (modified activin receptor IIB) for β-thalassemia and myelodysplastic syndromes (MDS) (Acceleron Pharma/BMS)

Leveraging our extensive experience in TGF-β superfamily protein structure, function and protein engineering to generate a clinical pipeline of differentiated therapeutics:

KER-050: Modified activin receptor IIA (ActRIIA) ligand trap designed to be differentiated from Reblozyl®

- Addresses ineffective erythropoiesis by modulating TGF-β superfamily signaling
- Potential to correct multiple cytopenias in patients with MDS and myelofibrosis (MF)

KER-047: Activin receptor-like kinase 2 (ALK2) inhibitor designed to treat anemia caused by elevated hepcidin and fibrodysplasia ossificans progressiva (FOP)

- Initial clinical indication is iron-refractory iron deficiency anemia (IRIDA); potential to treat anemia associated with chronic inflammation and MF

KER-012: Proprietary selective activin receptor ligand trap in preclinical development for the treatment of pulmonary arterial hypertension (PAH) and bone disorders

Keros is Developing Differentiated Clinical Assets in Hematological and Musculoskeletal Disorders

Program	Asset	Phase of Development	Status	Next Milestones*
Hematology	KER-050 (therapeutic protein)	Myelodysplastic Syndrome (MDS)	Completed Phase 1 clinical trial	Initiate Phase 2 clinical trial: H2 2020
		Myelofibrosis (MF)		Initiate Phase 2 clinical trial: 2021
Hematology / Musculoskeletal	KER-047 (small molecule)	Anemia from high hepcidin	Ongoing Phase 1 clinical trial	Complete Phase 1 clinical trial: mid-2020
		Fibrodysplasia Ossificans Progressiva (FOP)		
Preclinical Pipeline	KER-012 (therapeutic protein)	Pulmonary Arterial Hypertension	Ongoing preclinical studies	Initiate Phase 1 clinical trial: H2 2021
		Bone Disorders		
Musculoskeletal	ActRII Variant	Metabolic disease — Novo Nordisk	Ongoing preclinical studies	

* Anticipated clinical milestones are subject to the impact of COVID-19 on our business.

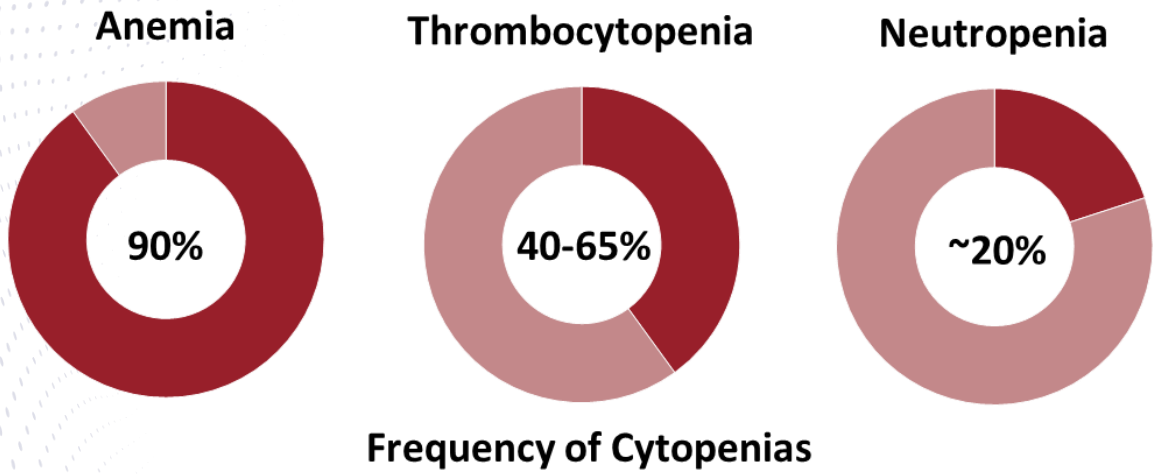
KER-050

A novel treatment designed to address diseases arising from ineffective hematopoiesis

- Myelodysplastic syndromes
- Myelofibrosis

Myelodysplastic Syndromes (MDS) Overview

Hematologic malignancy predominantly affecting the elderly, resulting in multiple cytopenias (anemia, thrombocytopenia, neutropenia) due to ineffective hematopoiesis



60,000-170,000

Prevalence of MDS patients in US*

15,000-20,000

New MDS patients diagnosed each year*

*MDS Foundation

KER-050 Designed to Fill Treatment Gap for Cytopenias in MDS

Anemia treatments

Red Blood Cell (RBC) Transfusion

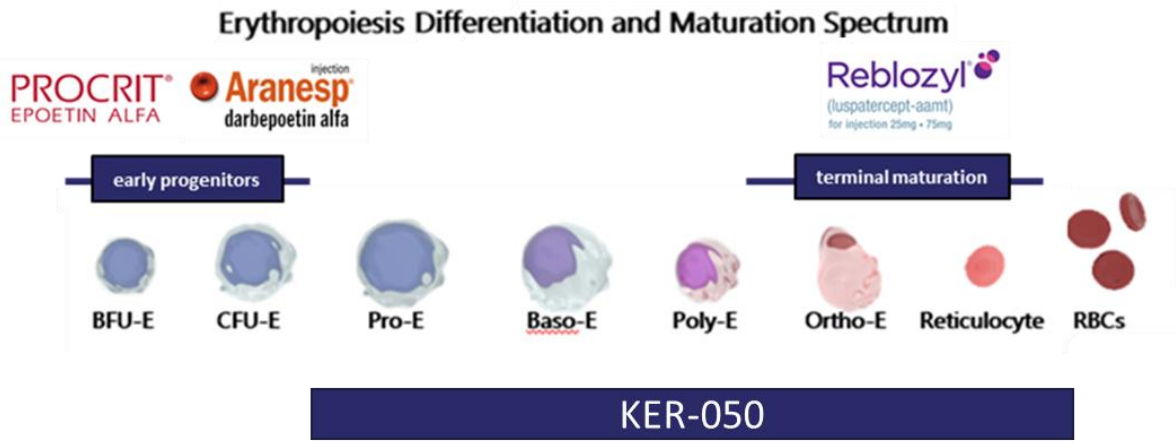
- Risk of infection and iron overload

ESAs

- Low proportion of responders in Aranesp® Phase 3 clinical trials
- Benefit limited to patients with low transfusion burden and low endogenous EPO levels
- ESAs **only impact early progenitors** in red blood cell lineage

Reblozyl®

- Phase 3 trial only evaluated RS positive patients, a subset of patients with **defects in terminal maturation**, with only 38% responders vs 13% placebo
  - RS positive patients account for an estimated 15% of MDS cases*
- **Targets terminal differentiation** of RBCs
- Similar to ESAs, benefit primarily in low transfusion burden



Thrombocytopenia treatments

Platelet Transfusion

- Risk of infection and allergic reactions

*Medscape

KER-050 is a Modified ActRII Fusion Protein

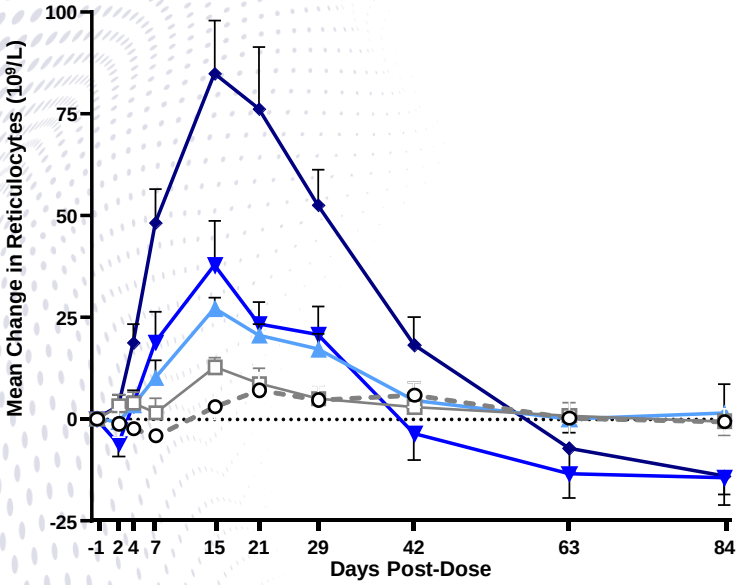
- Activin receptors are expressed on hematopoietic cells and modulate differentiation
- KER-050 is a ligand trap composed of a modified extracellular domain of activin receptor IIA (ActRIIA) fused to the Fc region of human IgG
- KER-050 is designed to bind to ligands that signal through the activin receptors and to increase RBCs and platelets

KER-050 Completed First-in-human Trial

- First-in-human trial was designed to explore the safety, tolerability and PK in healthy volunteers with a secondary objective of changes in PD (hematology and bone biomarkers)
- Observed to be well tolerated at dose levels up to 4.5 mg/kg, the highest dose level tested
- The most common adverse events observed in subjects in this trial were nausea, gastroenteritis and injection site erythema
  - Consistent with the mechanism of action of KER-050, increased hemoglobin and hypertension
  - Reversible, mild hypertension events observed only in subjects with an approximately 3 g/dL increase in hemoglobin

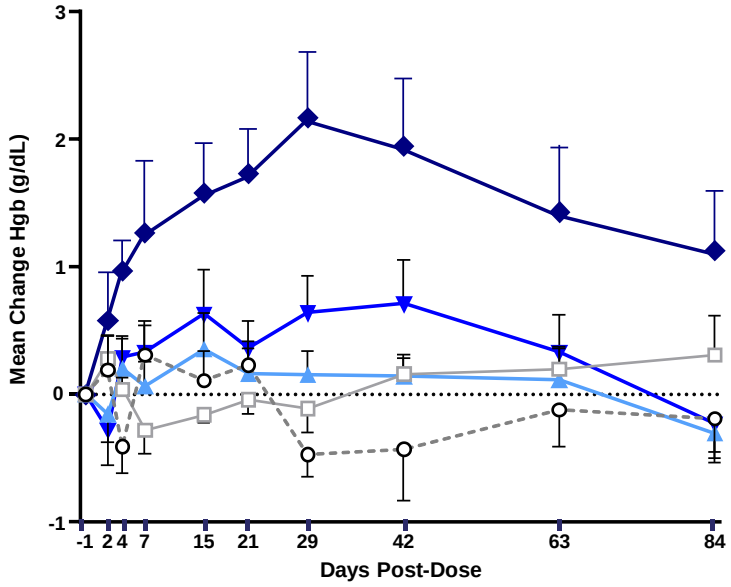
KER-050 Treatment was Observed to Lead to Robust and Sustained Increases in Reticulocytes, Hemoglobin and RBCs after a Single Dose

RETICULOCYTES
Mean Change from Baseline



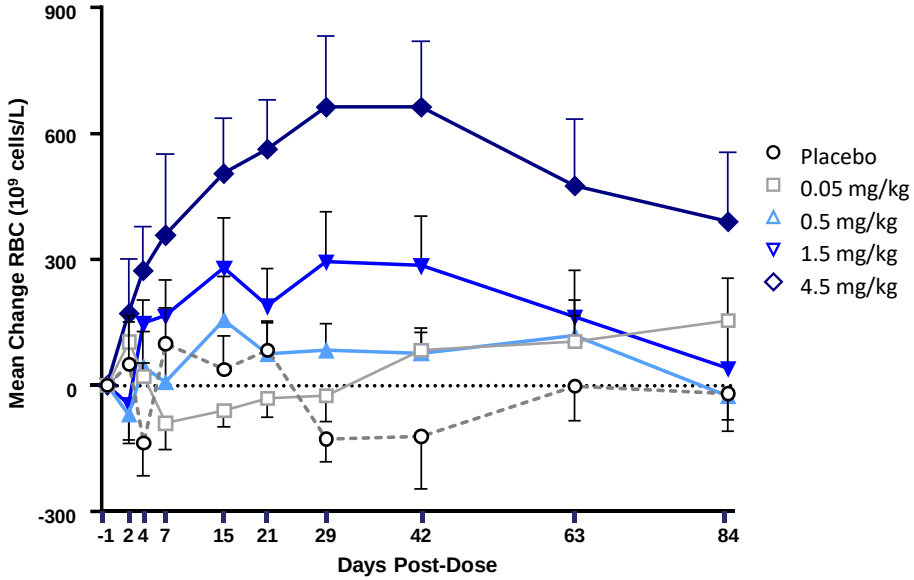
Rapid increase potentially indicative of effect on terminal differentiation

HEMOGLOBIN
Mean Change from Baseline



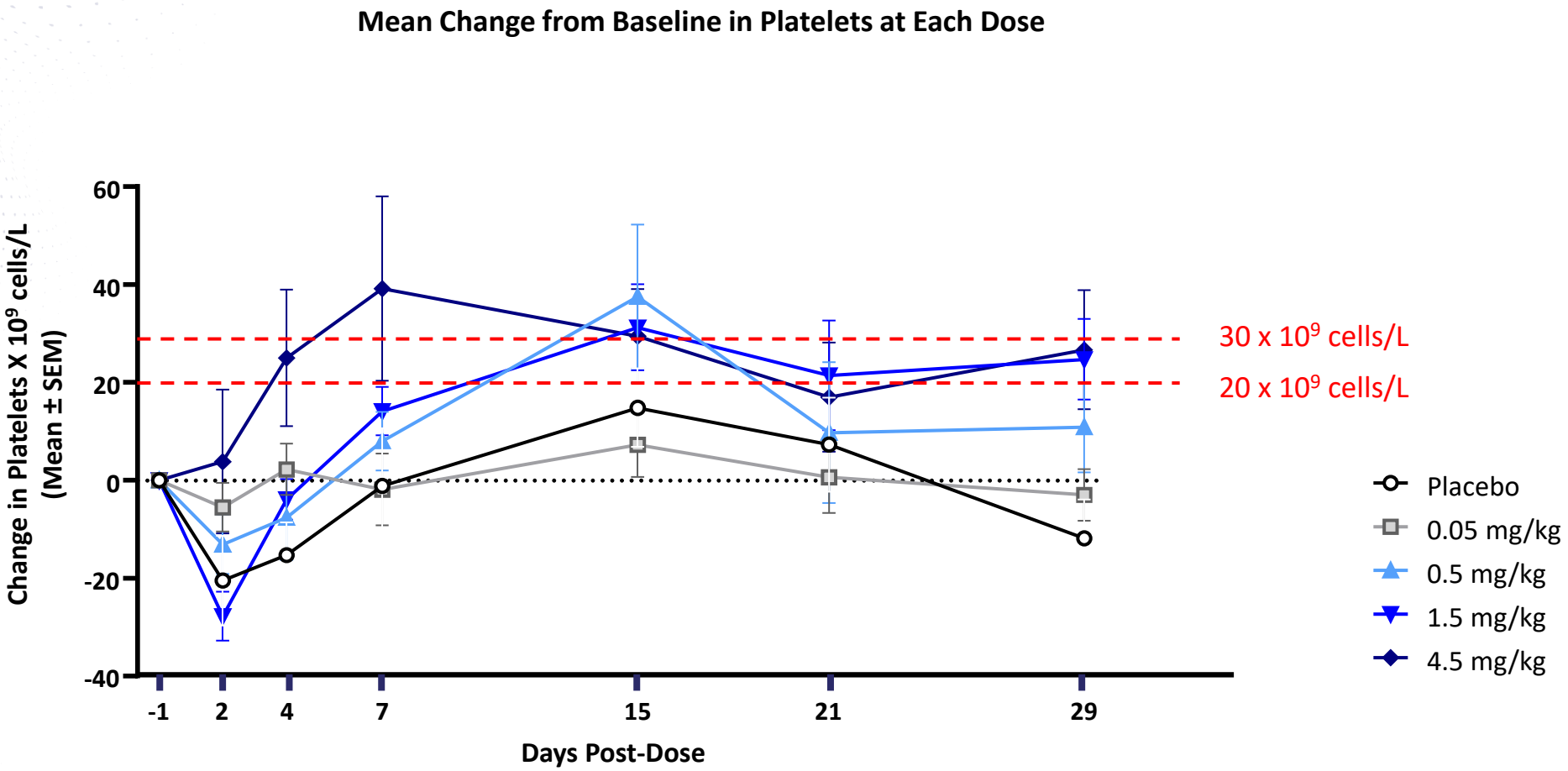
Mean change of >1.5 g/dl observed by day 15 in 4.5 mg/kg cohort

RED BLOOD CELLS
Mean Change from Baseline



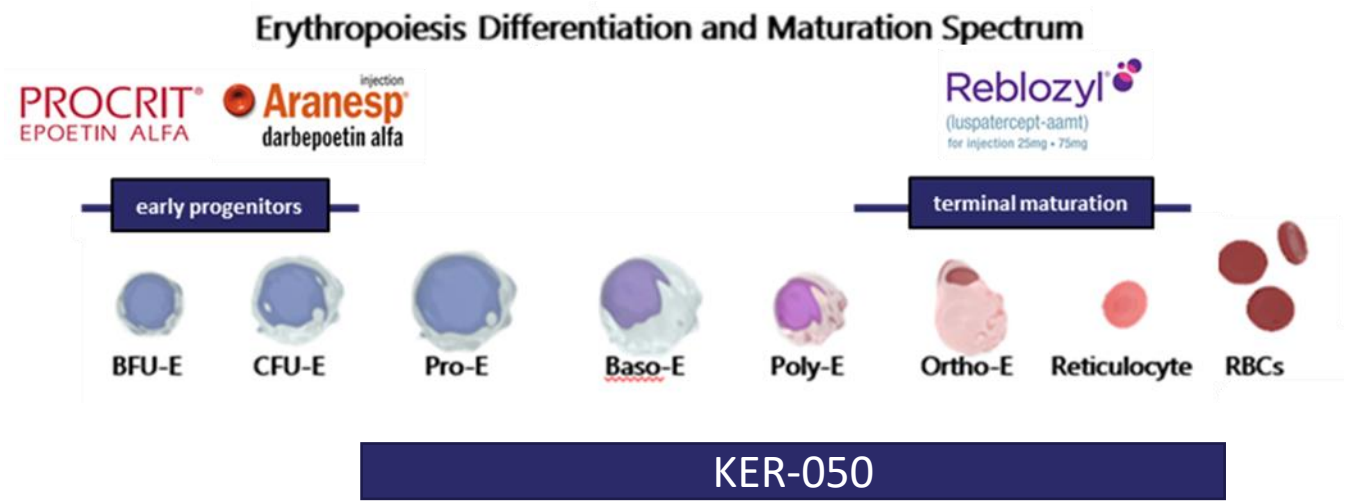
RBC durable for up to 84 days after single dose

KER-050 Treatment was Observed to Lead to Clinically Meaningful Changes in Platelets after a Single Dose



KER-050 has a Potentially Differentiated Mechanism of Action

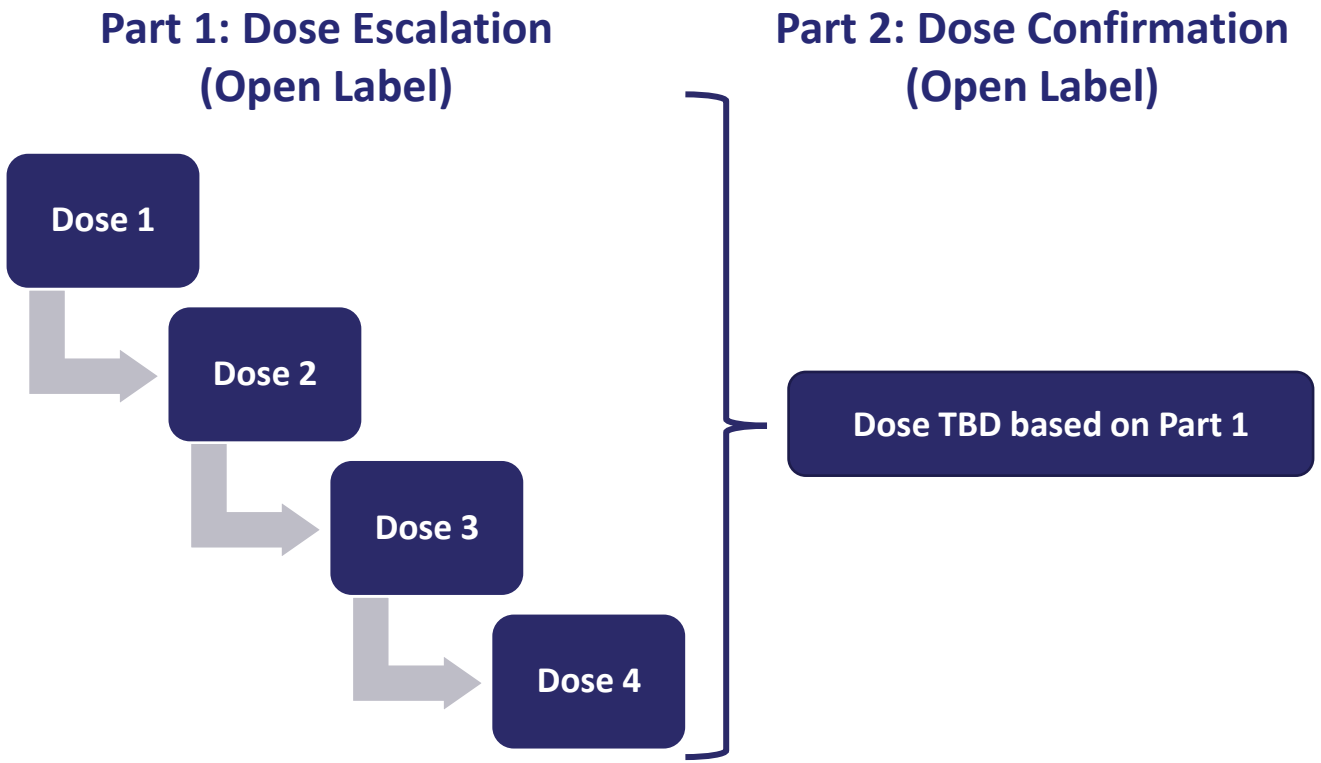
- Robust and sustained increases observed in RBCs, hemoglobin and reticulocytes support the potential for administration of monthly or less frequent dosing
- Observed sustained response potentially supports the dual mechanism of promoting early and late stages of erythropoiesis



- Clinically meaningful increase observed in platelets after a single dose, which we believe differentiates KER-050 from other agents that only affect RBCs

Expect to Commence a Phase 2 Trial of KER-050 in MDS (H2 2020)

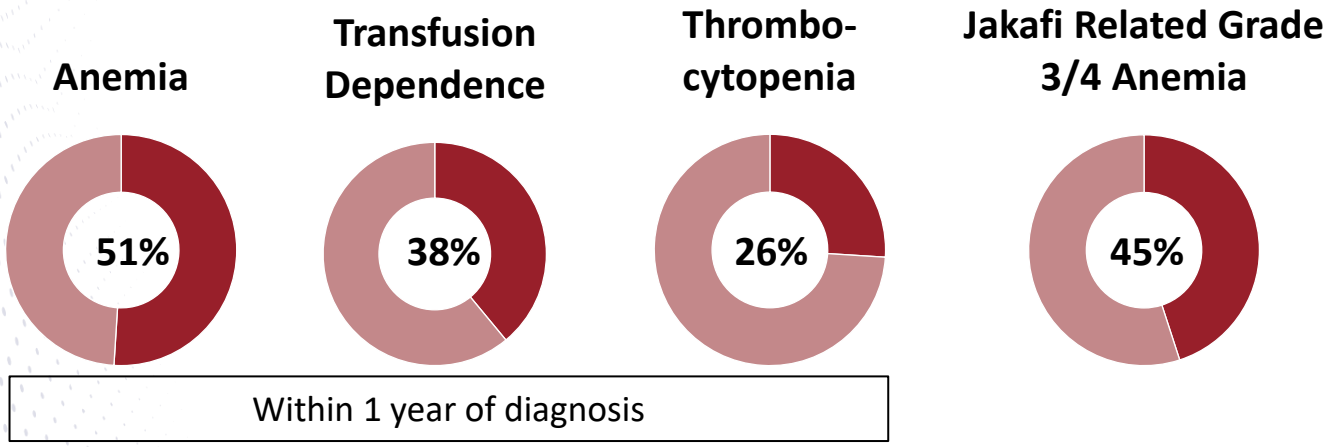
- Open label Phase 2 trial in two parts to explore changes in hematology with treatment in patients with MDS
  - Red blood cell parameters
  - Platelets
- 12-week treatment with monthly dosing and 12-week follow up
- Part 1: Dose escalation to evaluate response in RS positive and non-RS positive patients
- Part 2: Dose confirmation



Treatment in Parts 1 and 2: 12 weeks
Safety follow up: 12 weeks

Myelofibrosis (MF) is Characterized by Ineffective Hematopoiesis

- Molecular abnormalities in JAK-STAT pathway result in expansion of RBC and platelet precursors and subsequent ineffective hematopoiesis
- Megakaryocyte accumulation/breakdown is implicated in the inducement of bone marrow fibrosis
- KER-050 increased RBCs and platelets in our Phase 1 clinical trial
- We believe that KER-050 has the potential to address ineffective hematopoiesis, which is central to MF
- Plan to initiate a Phase 2 trial in MF in 2021, evaluating effect on platelets and RBCs



16,000-18,500

Prevalent MF patients in US*

>3,000

New MF patients diagnosed each year**

~100 %

Nearly all MF patients will become transfusion-dependent***

*Gangat 2011;**Srour 2016; ***Naymagon 2017

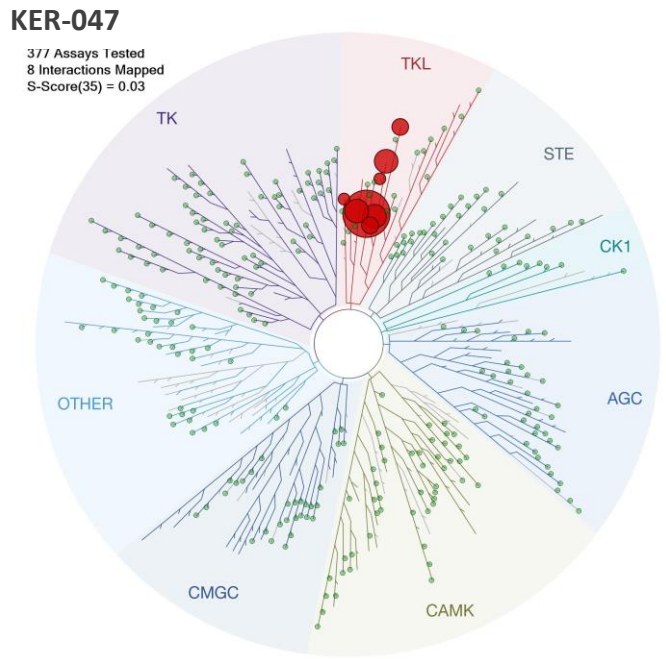
KER-047

A novel treatment designed to address

- Anemia arising from high hepcidin levels
- Fibrodysplasia ossificans progressiva (FOP)

KER-047: A Potentially Potent and Selective ALK2 Inhibitor

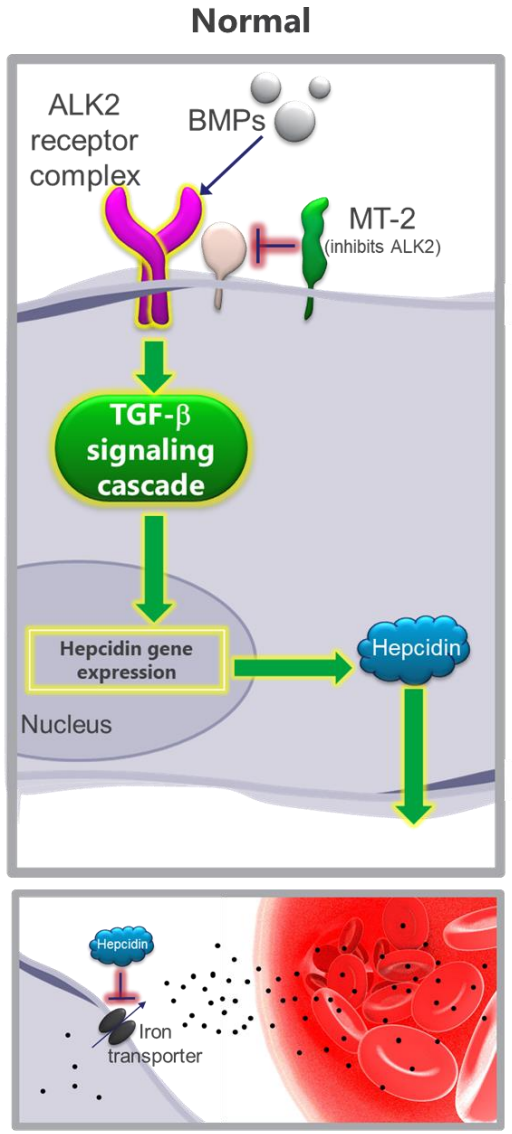
- **Small-molecule inhibitor of the activin receptor like kinase-2 (ALK2) kinase domain**
- **Potency:** Low nanomolar IC_{50}
- **Selectivity:** Highly selective over kinases outside of the TGF-β superfamily as well as other, structurally similar TGF-β receptors
  - Data from cell-based reporter assays established > 20-fold potency for ALK2 compared to ALK1 and ALK5, which have 77% and 65% homology to ALK2, respectively (Kingsley, D.M., 1994)
- **PK/ADME:** Suitable for 1x daily oral dosing



Invitrogen kinase screen at 1 mM

ALK2 Regulates Hepcidin and Iron Homeostasis

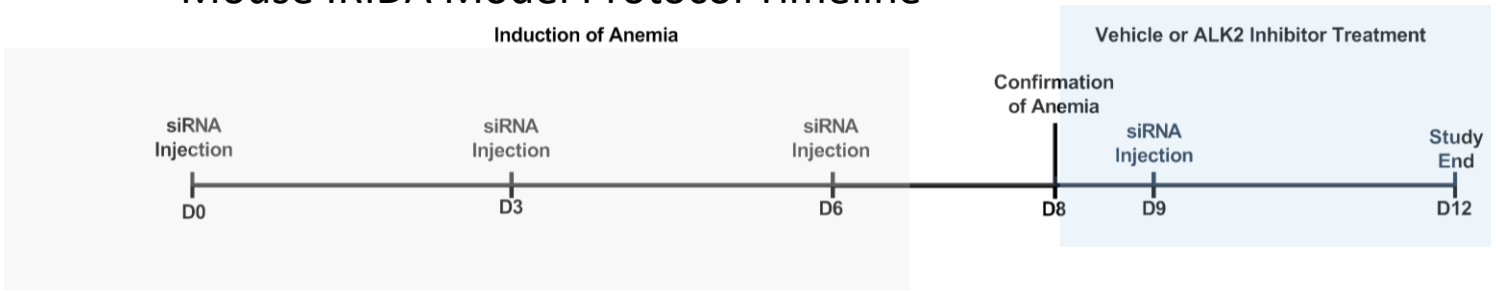
- ALK2 signaling in the liver controls hepcidin expression, a hormone that controls iron transport
- Excessive ALK2 signaling results in high hepcidin and a shortage of iron availability for RBC production
- ALK2 signaling requires BMP ligand and the co-receptor hemojuvelin
- Hepcidin expression is tightly regulated and controls expression of ALK2 suppressor protease MT-2
  - Loss of MT-2 causes the genetic disease iron-refractory iron deficiency anemia (IRIDA)
- High hepcidin has also been implicated in anemia of chronic disease
- Modulating ALK2 signaling will normalize high hepcidin levels, restore serum iron and ameliorate anemia



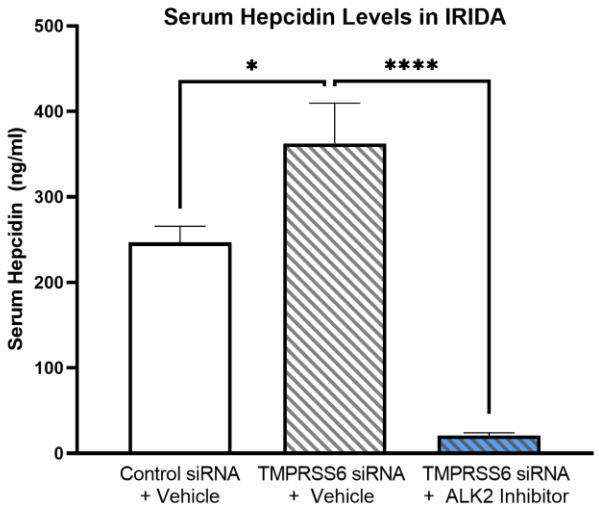
Keros ALK2 Inhibitors Observed to Resolve Anemia in TMPRSS6-Deficient Mice

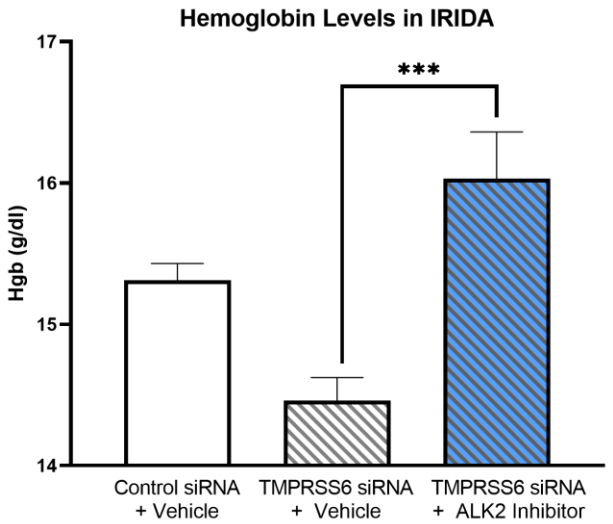
- TMPRSS6 encodes MT-2, the protease that suppresses ALK2 signaling
- MT-2/TMPRSS6 deficiency results in IRIDA
- siRNA knockdown of TMPRSS6 in mice copies human IRIDA patients
  - Increases hepcidin and reduces hemoglobin
- Our small molecule ALK2 inhibitor reversed high hepcidin and ameliorated anemia resulting from TMPRSS6 deficiency in wild-type mice

Mouse IRIDA Model Protocol Timeline



Mouse IRIDA Model Data





*P>0.05; ***P>0.001; ****P>0.0001 (Two-way ANOVA followed by Sidak post test)

ALK2 Mutation is a Driver of FOP

FOP is a rare genetic disease in which muscles and connective tissues transform into bone

No cure or effective treatments

- Most patients are confined to a wheelchair by third decade of life
- Typical life expectancy – 40 years

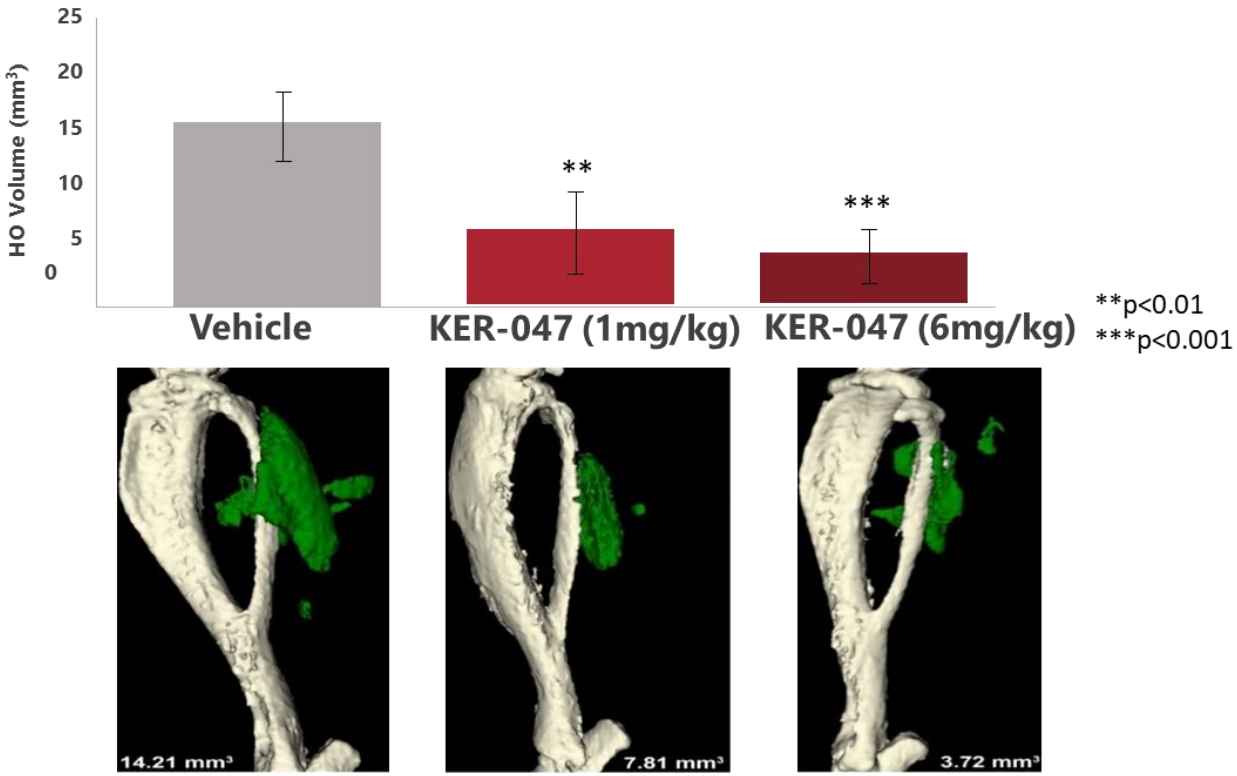
Caused by single amino acid mutations in ALK2 that leads to gain-of-function

KER-047 is designed to target ALK2

An example of FOP progression

KER-047 Exhibited Dose-dependent Efficacy in FOP Mouse Model

KER-047 dose-dependently reduced heterotopic ossification in the genetic mouse model of FOP



Preclinical studies conducted in young animals demonstrated that ALK2 inhibition did not result in growth plate ablation or synovial joint malformations

KER-047: Phase 1 Clinical Trial Recapitulated the Observations from Preclinical Studies

- Preliminary analysis of single ascending and planned multiple ascending dose cohorts completed
- The objectives of the Phase 1 clinical trial were to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamic effects of single and multiple ascending dose levels of KER-047 in healthy volunteers
  - In the multiple ascending dose cohorts, KER-047 was administered as daily doses of 50-350 mg for up to 7 days
- Single dose showed dose dependent increases in serum iron
- Multiple pharmacodynamic biomarkers were included to assess KER-047's inhibition of ALK2
  - Reduction in hepcidin was observed following 7 days of dosing in multiple ascending dose cohorts
  - Sustained increases in serum iron
  - Increases in serum iron resulted in increased hemoglobin in reticulocytes
- Increase in reticulocyte hemoglobin with administration of KER-047 is supportive of iron mobilization from tissue stores
- There were no serious adverse events reported in either part of this trial
- Most common adverse events observed: headache, nausea, vomiting, diarrhea, gastroenteritis, chills, pyrexia, myalgia, decreased appetite, lymphopenia, neutropenia, and liver enzyme increases
- Adding two cohorts to further define dosing regimens to inform the design of upcoming Phase 2 clinical trials

Two Phase 2 Trials to Provide Proof-of-Concept for Anemia Arising from High Hepcidin and FOP

Anemia Arising from High Hepcidin

- KER-047 is designed to normalize high hepcidin levels, restore serum iron and ameliorate anemia
- We expect to initiate a Phase 2 clinical trial in patients with high hepcidin, including IRIDA, in H1 2021

FOP

- KER-047 is designed to prevent the development of new, and expansion of existing, heterotopic ossification
- We expect to initiate a Phase 2 clinical trial in patients with FOP in H1 2021

KER-012

A preclinical program designed to address

- Bone loss disorders such as osteoporosis and osteogenesis imperfecta
- Pulmonary arterial hypertension (PAH)

KER-012 (Preclinical Product Candidate)

- Proprietary selective activin receptor ligand trap in preclinical development for the treatment of pulmonary arterial hypertension (PAH) and bone disorders
- In preclinical studies, KER-012:
  - Demonstrated high affinity for, and potent inhibition of, ligands involved in the regulation of bone homeostasis
  - Increased bone mineral density and trabecular bone volume in wild-type mice and mice with established osteoporosis
  - Did not increase red blood cell production in cynomolgus monkeys
- We believe KER-012 has the potential to increase the signaling of BMP pathways by inhibiting activin A and activin B signaling and, consequently, treat diseases such as PAH that are associated with reduced BMP signaling

Keros Summary

We Believe Keros is Positioned for Clinical and Commercial Success

- Keros is focused on the development of novel TGF-β therapeutics
  - Robust biology that has been validated in the clinic
- Keros is well-positioned to harness the potential of the TGF-β superfamily
  - Multiple product candidates expected to commence Phase 2 trials
  - Clinical programs have potentially differentiated mechanism of action
- Our discovery approach has the potential to identify additional molecules with differentiated profiles from existing third-party products and product candidates
  - Pipeline of preclinical assets: bone, muscle and pulmonary

Anticipated Key Milestones*

KER-050

• Present Phase 1 and preclinical data supporting hematopoietic effects	EHA25 (June 2020)
• Initiate Phase 2 trial in MDS	H2 2020
• Initiate Phase 2 trial in myelofibrosis	2021

KER-047

• Present preclinical data demonstrating potential to address anemia	EHA25 (June 2020)
• Complete Phase 1 SAD/MAD trial	mid 2020
• Present Phase 1 healthy volunteer data	H2 2020
• Initiate Phase 2 trial in anemia with high hepcidin, including IRIDA	H1 2021
• Initiate Phase 2 trial in FOP	H1 2021

KER-012

• Nominate molecule for pre-IND development	H2 2020

*Anticipated preclinical and clinical milestones are subject to the impact of COVID-19 on our business.

Thank You