KEROS THERAPEUTICS

Corporate Presentation

November 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 marketed products, Infuse (BMP2) for spinal fusion and Reblozyl® (modified activin receptor IIB) for treatment of anemia in β-thalassemia and myelodysplastic syndromes
- 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 address ineffective hematopoiesis 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 being developed for the treatment of anemia resulting from iron imbalance, including iron deficiency anemia (IDA) and iron-refractory iron deficiency anemia (IRIDA), as well as fibrodysplasia ossificans progressiva (FOP)
  - Expect to initiate two Phase 2 trials in 2021 – one in patients with IDA and one in patients with IRIDA
  - Potential to treat anemia associated with chronic inflammation

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

Keros is Developing Differentiated Clinical Assets in Hematological and Musculoskeletal Disorders

Program	Asset	Phase of Development				Status	Next Milestones*
		Preclinical	Phase 1	Phase 2	Phase 3		
Hematology	KER-050 (therapeutic protein)	Myelodysplastic syndromes (MDS)				Initiated Phase 2 clinical trial	Initial data: mid-2021
		Myelofibrosis (MF)				Completed Phase 1 clinical trial	Initiate Phase 2 clinical trial: 2021
Hematology	KER-047 (small molecule)	Iron deficiency anemia				Completed expanded Phase 1 clinical trial	Present topline data: end of 2020
		Anemia from high hepcidin					
Musculoskeletal		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					

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

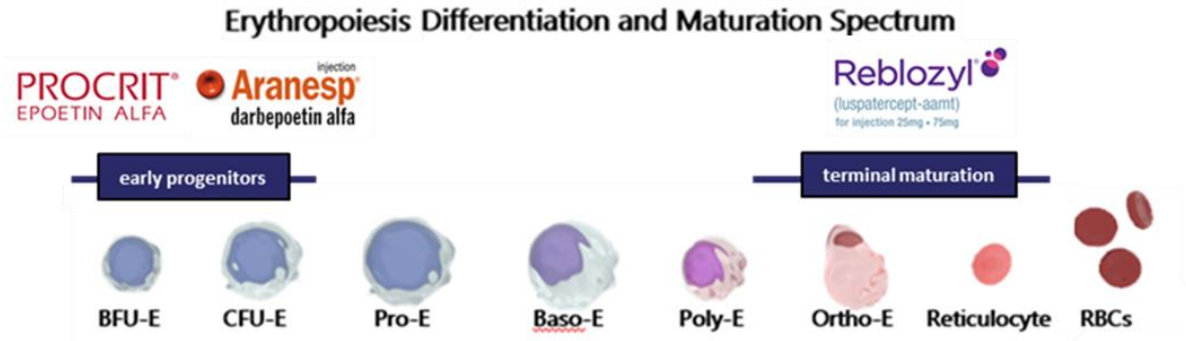
KER-050

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 MDS patients in U.S.*
  - 15,000-20,000 newly diagnosed MDS patients in U.S. each year*
- 90% of patients are anemic and 40-65% have thrombocytopenia
- Platelet transfusion for thrombocytopenia
- Anemia treatments include red blood cell (RBC) transfusions, erythropoiesis-stimulating agents (ESAs) and Reblozyl®
  - ESAs only impact early progenitors in red blood cell lineage and benefit is limited to patients with low transfusion burden and low endogenous EPO levels
  - Reblozyl® approved for treatment of anemia in RS positive patients
  - Approximately 15% of all MDS patients are RS positive and have defects in terminal maturation
    - 38% responders vs 13% placebo
    - Similar to ESAs, benefit primarily in low transfusion burden



*MDS Foundation

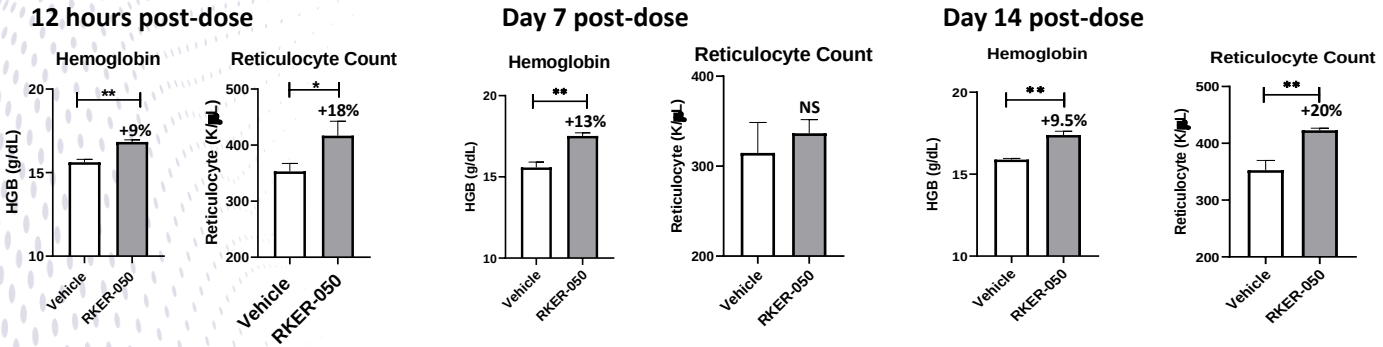
KER-050 is a Modified ActRII Fusion Protein

- Activin receptors are expressed on hematopoietic cells and modulate differentiation of precursor cells
- 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 increase RBC and platelet production by inhibiting the signaling of ligands through activin receptors
- Preclinical data demonstrate that increased RBCs by potentially increasing differentiation through multiple stages of erythropoiesis
  - Observed increases in platelets also potentially supports action throughout the thrombopoiesis pathway
- Phase 1 clinical trial of KER-050 recapitulated preclinical data with observed rapid, sustained and dose-dependent increases in RBCs and platelets

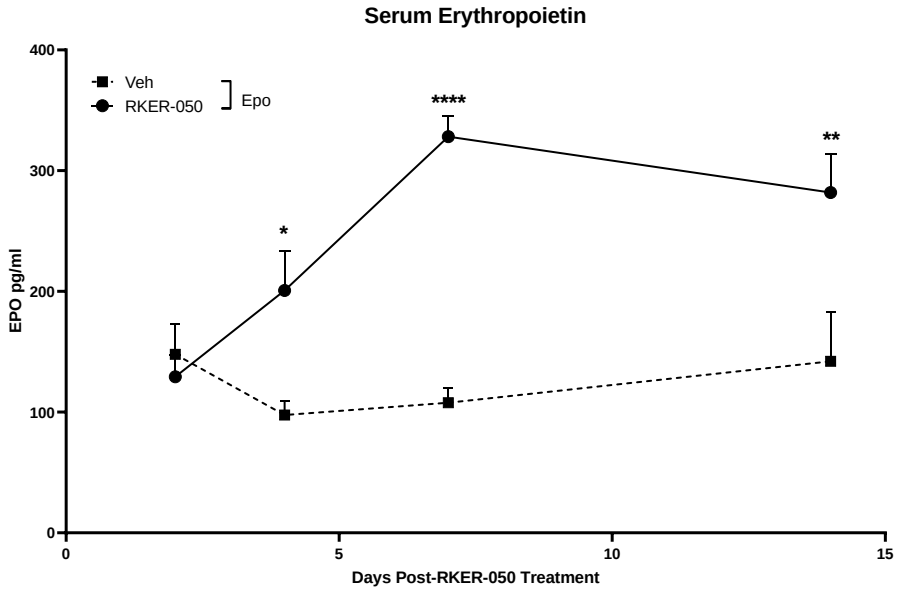
Treatment with RKER-50 Increased Erythropoiesis by Potentially Promoting Maturation at Multiple Stages and Increased Serum Erythropoietin

- In a preclinical study conducted in mice, a single, subcutaneous 10 mg/kg dose of a mouse version of KER-050 (RKER-050) resulted in:
  - Rapid increase in RBCs
  - Sustained increase continuing to at least 14 days post-dose
  - 2-3-fold increase in circulating erythropoietin
- KER-050 potentially acts on multiple stages across the RBC differentiation spectrum, including common myeloid cells

Increase in Red Blood Cells and Reticulocytes in Mice



Observed Increase in Serum Erythropoietin in Mice



* P value ≤0.05; ** P value ≤0.01; **** P value ≤0.0001

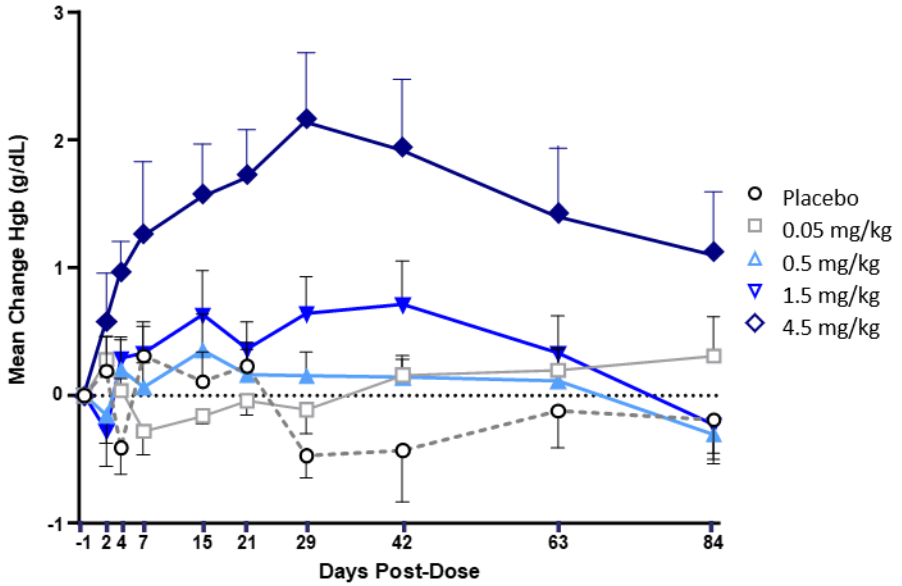
KER-050 Completed First-in-human Trial

- First-in-human trial was designed to explore the safety, tolerability and PK in healthy volunteers with a secondary objective to evaluate changes in PD (hematology and bone biomarkers)
- Observed that KER-050 drug levels were dose proportional in Part 1 of the KER-050 Phase 1 clinical trial, with a mean half-life of approximately 12 days
  - The half-life coupled with the pharmacodynamic effect observed in the hematologic parameters support the potential for administration of monthly or less frequent dosing
- Observed to be well tolerated at dose levels up to 4.5 mg/kg, the highest dose level tested
- Notable adverse event:
  - Reversible, mild hypertension events observed only in subjects with an approximately 3 g/dL increase in hemoglobin

KER-050 Phase 1 Clinical Trial Recapitulated Learnings from Preclinical Studies

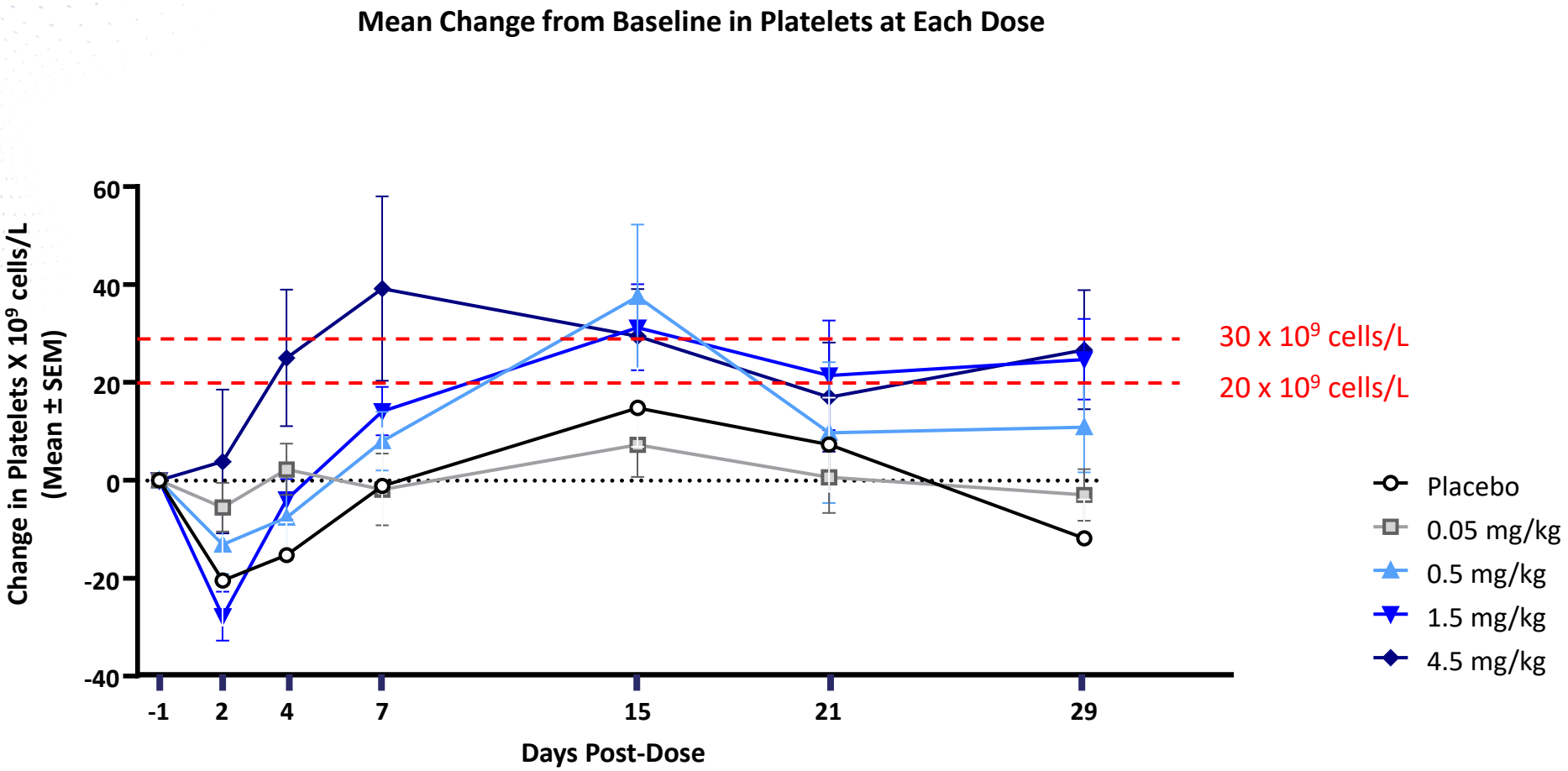
- Single, subcutaneous administration of KER-050 in healthy volunteers
- Observed rapid increase in red blood cell parameters is supportive of acceleration of maturation of late-stage precursors
  - Reticulocytes, red blood cells and hemoglobin
- Observed sustained increase from single dose supports monthly or less frequent dosing
  - Increases in RBC observed through day 29 are supportive of KER-050 acting on multiple stages of erythropoiesis
  - Maximum drug levels were observed on day 4

HEMOGLOBIN
Mean Change from Baseline



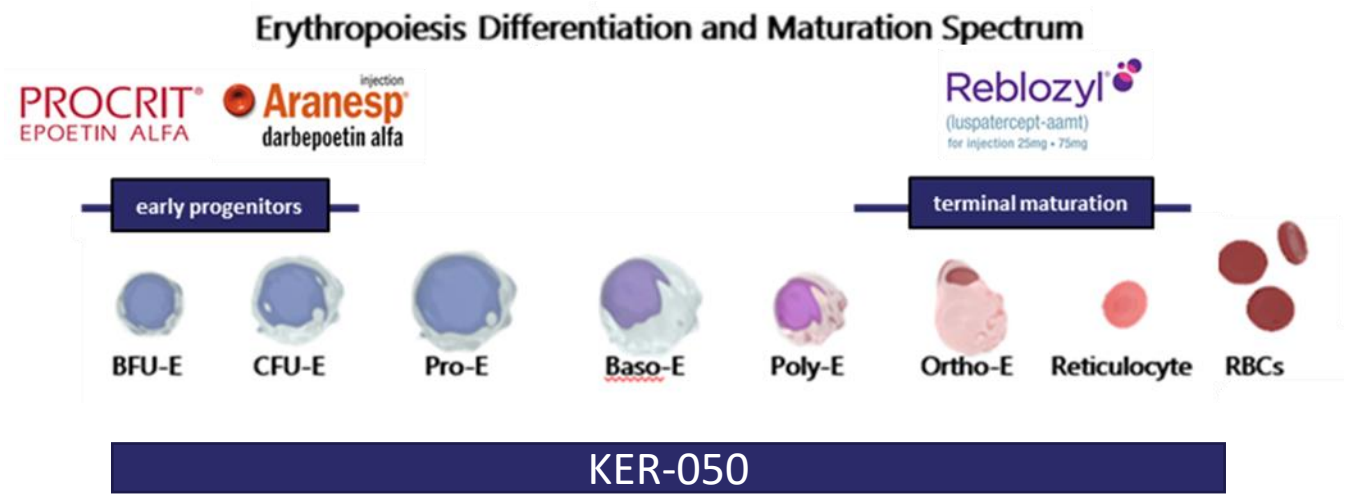
Mean change of >1.5 g/dl observed by day 15 in 4.5 mg/kg cohort

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

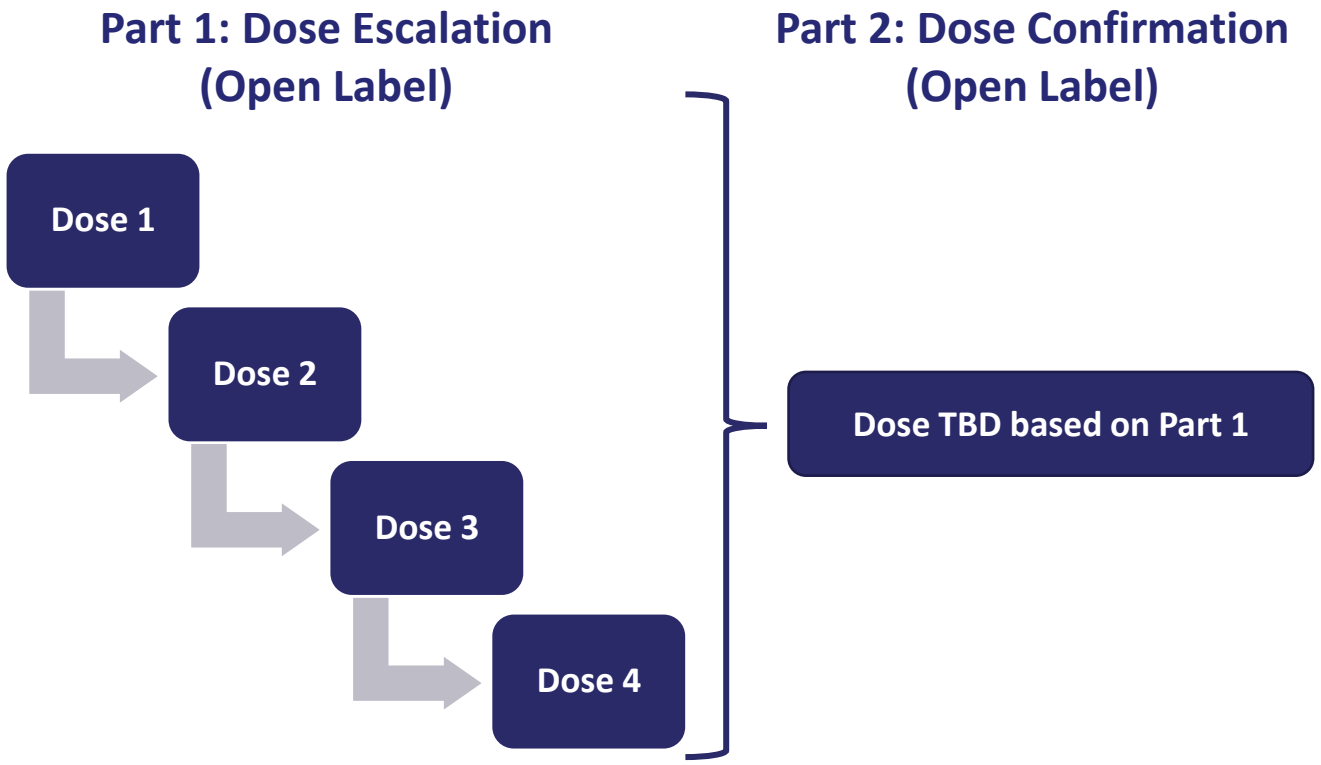
- Robust and sustained increases observed in RBCs, hemoglobin and reticulocytes support the potential for administration of monthly or less frequent dosing
- Observed sustained response potentially supports the dual mechanism of promoting early and late stages of erythropoiesis



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

Initiated a Phase 2 Trial of KER-050 in MDS

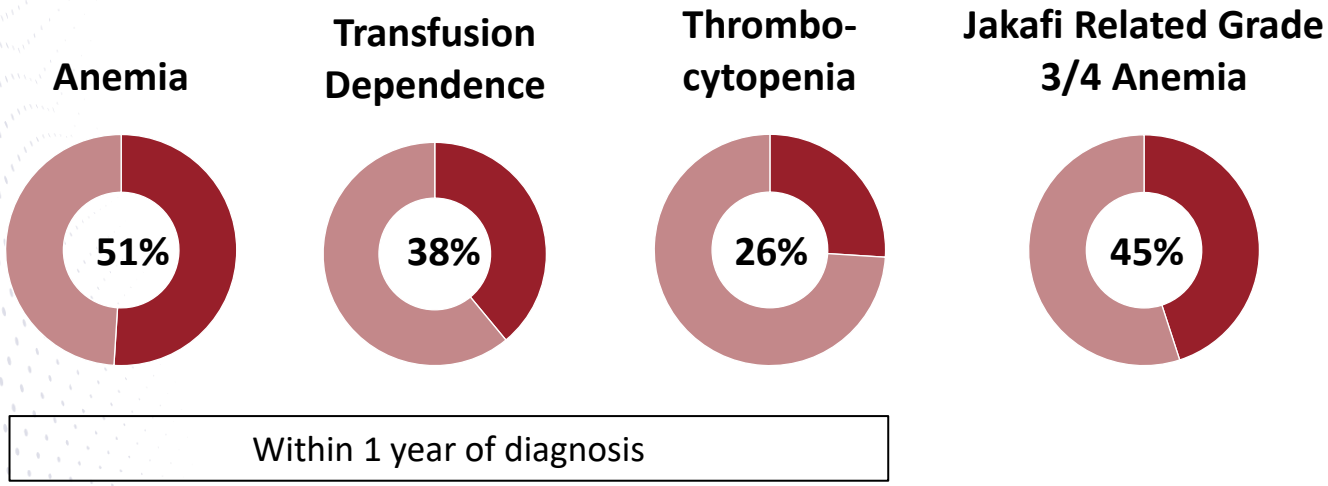
- Open label Phase 2 trial in two parts to explore changes in hematology with treatment in patients with MDS
  - Red blood cell parameters
  - Platelets
- 12-week treatment with monthly dosing and 12-week follow up
- Part 1: Dose escalation to evaluate response in RS positive and non-RS patients
- Part 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
- Plan to initiate a Phase 2 trial in MF in 2021, evaluating effect on platelets and RBCs
  - We believe that KER-050 has the potential to address ineffective hematopoiesis, which is central to MF



16,000-18,500

Prevalence of 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

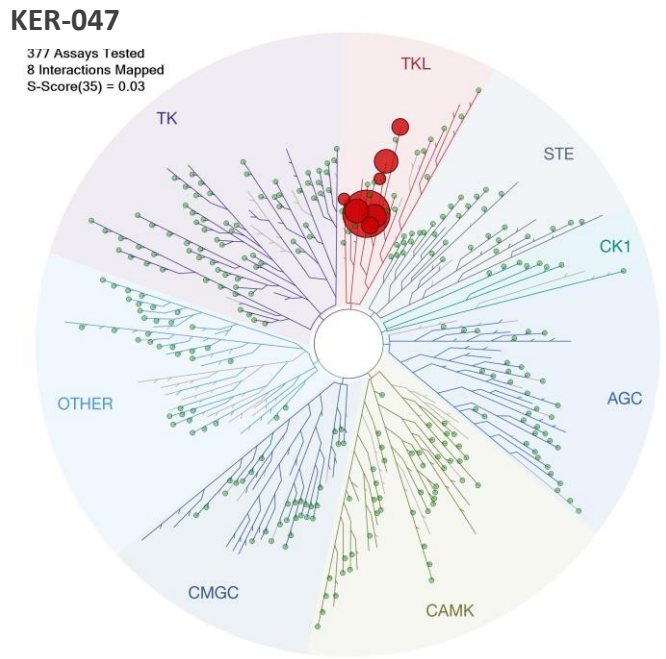
KER-047

A novel treatment designed to address:

- Anemia resulting from iron imbalance
  - Iron deficiency anemia
  - IRIDA
- Fibrodysplasia ossificans progressiva (FOP)

KER-047: A Potentially Potent and Selective ALK2 Inhibitor

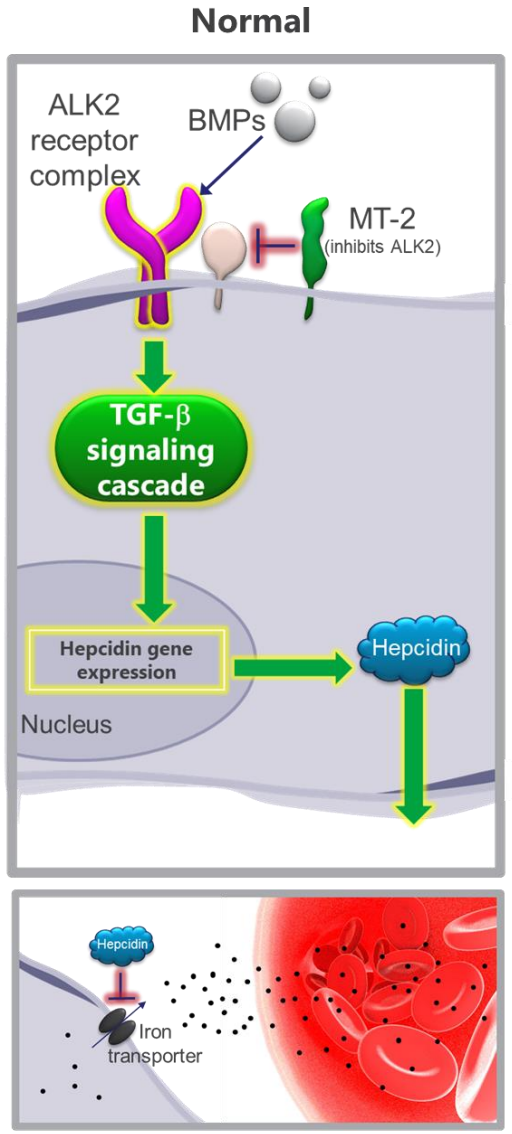
- **Small molecule inhibitor of the activin receptor-like kinase-2 (ALK2) kinase domain**
- **Potency:** Low nanomolar IC_{50}
- **Selectivity:** Highly selective over kinases outside of the TGF-β superfamily as well as other, structurally similar TGF-β receptors
  - Data from cell-based reporter assays 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 µM

ALK2 Regulates Hepcidin and Iron Homeostasis

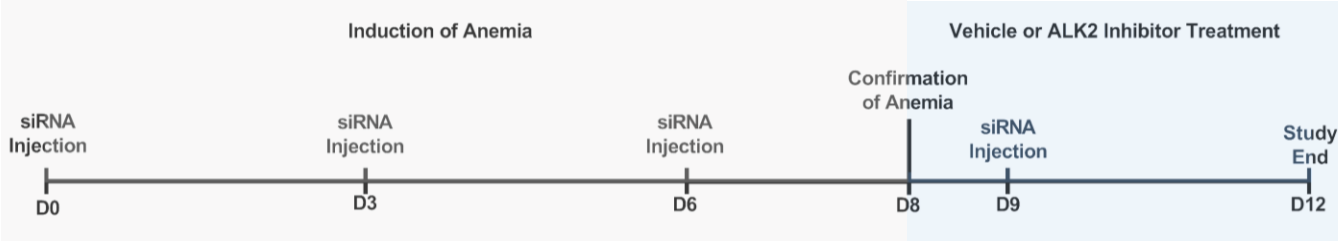
- ALK2 signaling in the liver controls hepcidin expression, a hormone that controls iron homeostasis
- Excessive ALK2 signaling results in high hepcidin and a shortage of iron availability for RBC production
- ALK2 signaling requires BMP ligand and the co-receptor hemojuvelin
- Hepcidin expression is tightly regulated and controls expression of the ALK2 suppressor protease MT-2
  - The genetic disease iron-refractory iron deficiency anemia (IRIDA) is characterized by loss of MT-2
- 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



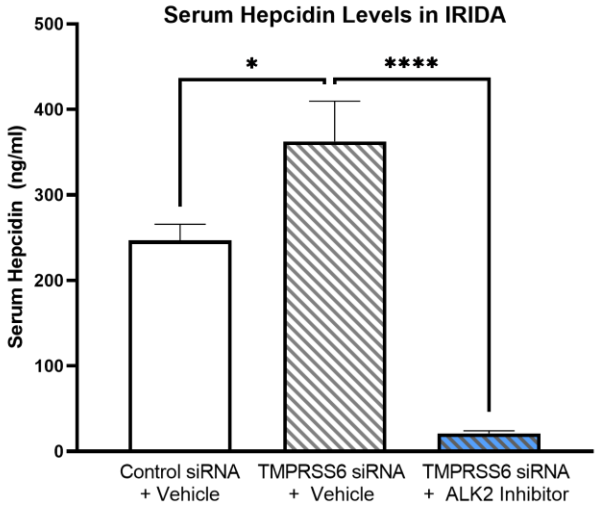
Keros ALK2 Inhibitors Shown to Resolve Anemia in the Mouse Model of IRIDA

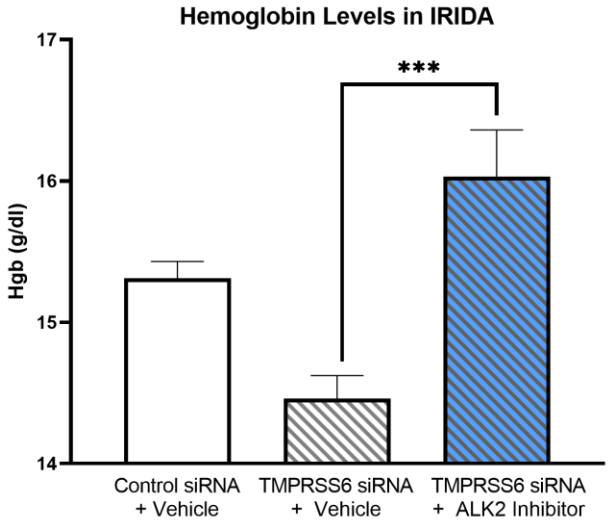
- TMPRSS6 encodes MT-2, the protease that suppresses ALK2 signaling
- MT-2/TMPRSS6 deficiency results in IRIDA
- siRNA knockdown of TMPRSS6 in mice mimics changes seen in human IRIDA patients
  - Increases hepcidin and reduces hemoglobin
- Our small molecule ALK2 inhibitor reversed high hepcidin and 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)

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

- All single ascending and multiple ascending dose cohorts evaluated (including additional cohort) (“expanded trial”)
- The objective of the Phase 1 clinical trial was 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 approximately 7 days
- Multiple pharmacodynamic biomarkers were included to assess KER-047’s inhibition of ALK2
  - Reduction in hepcidin was observed at each dose level tested in Part 2 of the expanded trial
  - Observed rapid and dose-related increases in serum iron and transferrin saturation in the expanded trial
  - We believe iron mobilization led to increased iron bioavailability for incorporation into reticulocyte hemoglobin. These erythroid precursors potentially would continue maturation into hemoglobin-rich red blood cells
- We also observed decreases in lymphocytes following peak increases in serum iron in the expanded trial
- Reductions in total cholesterol, low-density lipoproteins (LDL) and high-density lipoproteins were observed in Part 2 of the expanded trial. The reductions in total cholesterol and LDL were achieved rapidly with a mean reduction of greater than 20% at the highest dose, following seven days of dosing.
- There were no serious adverse events reported in either part of this expanded trial
- Most common adverse events observed: abdominal discomfort, chills, decreased appetite, diarrhea, dizziness, fatigue, gastroenteritis, headache, lymphopenia, myalgia, nausea, neutropenia, pyrexia, rhinorrhea, tonsilitis, upper abdominal pain and vomiting

Phase 2 Trials to Provide Proof-of-Concept for Treatment of Anemia Resulting from Iron Imbalance, Including IDA and IRIDA

Iron Deficiency Anemia

- KER-047 is designed to re-establish normal iron homeostasis by mobilizing iron out of tissues, thereby ameliorating anemia
- We expect to initiate a Phase 2 clinical trial in patients with iron deficiency anemia in 2021

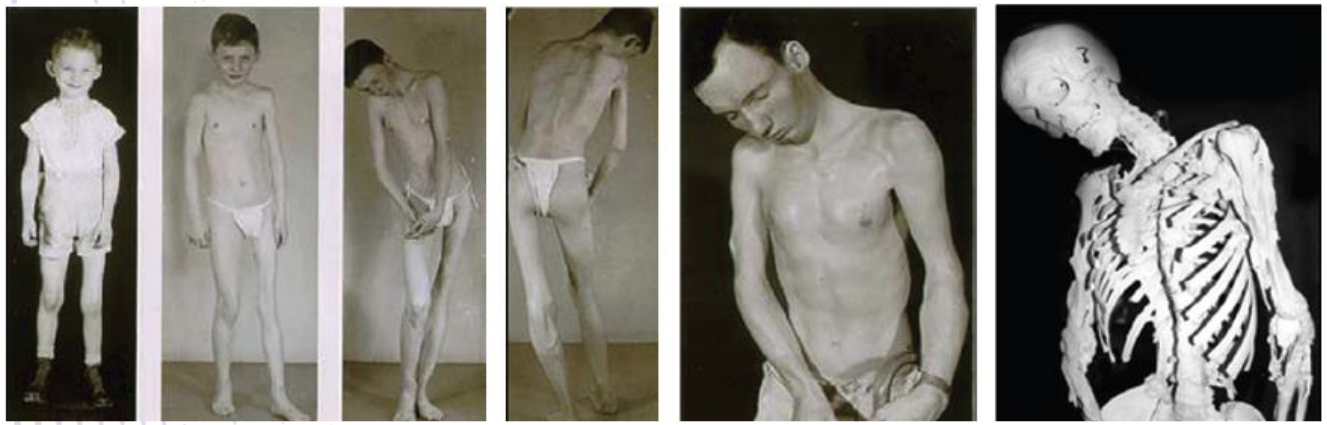
IRIDA

- 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 IRIDA in 2021

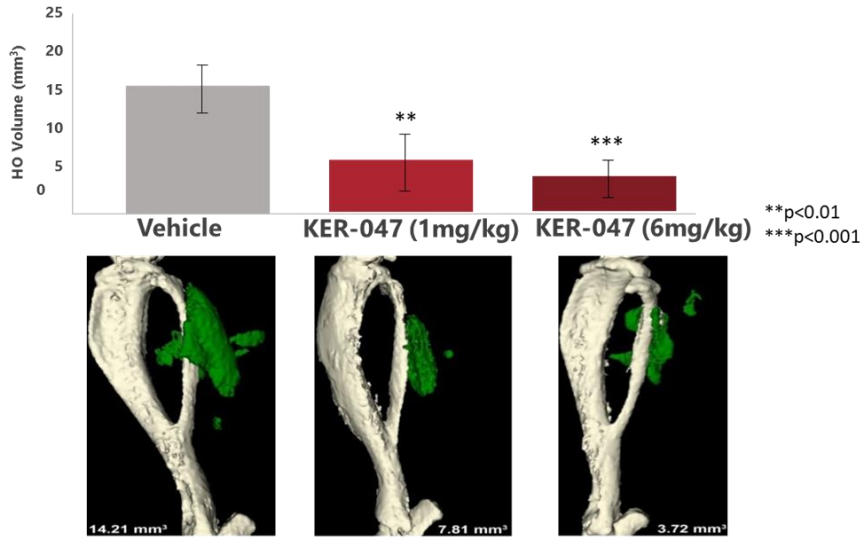
ALK2 Mutation is a Driver of FOP

- 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 lead to gain-of-function
- KER-047 is designed to target ALK2
  - Preclinical studies conducted in young animals demonstrated that ALK2 inhibition did not result in growth plate ablation or synovial joint malformations

An example of FOP progression



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



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
- In a rat model of PAH, rats receiving a rodent version of KER-012 (RKER-012) were protected from the thickening of the right ventricular wall
  - In addition, rats receiving RKER-012 were protected from PAH-associated bone loss
- 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
  - ActRII program (KER-050) is in a Phase 2 trial in patients with MDS and we expect to initiate a Phase 2 trial in patients with MF in 2021
  - Multiple Phase 2 trials for ALK2 program (KER-047) expected to commence in 2021
  - KER-012 is a selective activin receptor ligand trap expected to enter a Phase 1 trial in H2 2021
  - 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 additional preclinical data on mechanism	Q4 2020 (ASH 2020)
• Announce initial data for Phase 2 trial in MDS	Mid-2021
• Initiate Phase 2 trial in myelofibrosis	2021

KER-047

• Present Phase 1 healthy volunteer data	Q4 2020 (ASH 2020)
• Initiate Phase 2 trial in IDA	2021
• Initiate Phase 2 trial in IRIDA	2021

KER-012

• Present preclinical data on PAH at major conference	2021
• Initiate Phase 1 trial in healthy volunteers	H2 2021

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

Thank You