RISE UP

# A NEW SICKLE CELL CLINICAL TRIAL CHALLENGING PAIN CRISES & ANEMIA

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# HELP SICKLE CELL WARRIORS RISE UP

Agios Pharmaceuticals announces a phase 2/3, double-blind, randomized, placebo-controlled, multicenter clinical trial. The RISE UP study will evaluate the efficacy and safety of treatment with mitapivat in participants with sickle cell disease.[1] See inclusion criteria inside.

Mitapivat is a pyruvate kinase activator approved by the US FDA for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency. The safety and efficacy of mitapivat in sickle cell disease is under investigation and has not been established. There is no guarantee that mitapivat will receive health authority approvals or become commercially available in any country for the uses under investigation.

RISE UP Sickle Cell Warriors, left to right: Golie, Phill, Tristian, Teonna, Dominique, DeMitrious, Blaze.

Warriors were compensated and may not have taken part in RISE UP.

Sickle Cell Warrior is a term coined and used by the sickle cell community. It refers to individuals living with sickle cell disease.

# PK ACTIVATION SUPPORTS RED BLOOD CELL HEALTH

- Mitapivat – the study drug in RISE UP – is an investigational, oral allosteric activator of the PK enzyme[1,2]
- PK enzyme activation may improve the health, energy, and lifespan of red blood cells (RBCs) for patients with hemolytic anemias[1]

# AGIOS IS A PIONEER IN PK ACTIVATION

**2014** Agios initiates clinical study of mitapivat[3]

**2020** Establishes clinical proof-of-concept for mitapivat in sickle cell disease and reports phase 1 clinical trial findings[3,4]

**2021** Reports phase 2 open-label clinical trial findings of mitapivat in patients with sickle cell disease[5]

**2022** Launches phase 2/3 RISE UP clinical trial of mitapivat in patients with sickle cell disease

BID=twice daily; PK=pyruvate kinase.

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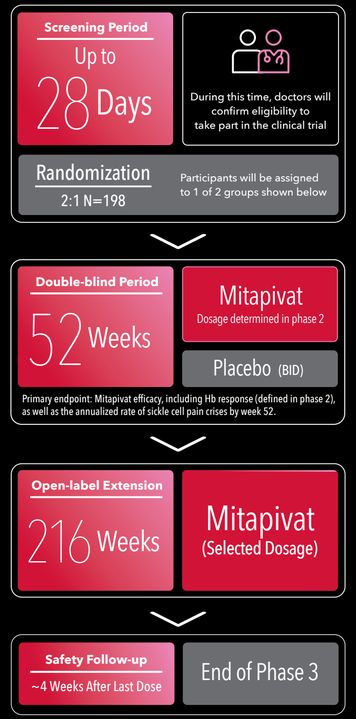
# RISE UP STUDY DESIGN

## PHASE 2

- A 3-month, placebo-controlled, dose-finding study[1]
- Evaluate the safety and efficacy of 2 dose levels of mitapivat for anemia in sickle cell disease and determine the recommended phase 3 dosage[1]


## PHASE 3

- A 52-week, placebo-controlled, efficacy and safety study[1]
- Determine the effect of mitapivat on anemia and pain crises in sickle cell disease[1]




Participants will be enrolled in either phase 2 or phase 3 of RISE UP. Once enrolled, participants cannot reenroll in a different phase.[1]

# KEY INCLUSION CRITERIA

- Patients in the US ages 16 years and older, patients in France or Germany ages 18 years and older
  - Participants ages 16 or 17 years must physically have completed puberty
- A documented diagnosis of sickle cell disease (HbSS, HbSC, HbS/β0 thalassemia, HbS/β+ thalassemia, or other sickle cell syndrome variants)[1]
- At least 2 and no more than 10 sickle cell pain crises in the 12 months prior to informed consent[1]
  - Defined as acute episodes of pain, acute chest syndrome, priapism, hepatic or splenic sequestration
- If taking hydroxyurea, the hydroxyurea dose must be stable for at least 90 days before randomization[1]

# KEY EXCLUSION CRITERIA

- Pregnant or breastfeeding[1]
- Receiving regularly scheduled transfusions[1]
- Hepatobiliary disorders, significant liver disease, gallbladder disease, or severe kidney disease[1]
- Prior exposure to gene therapy or prior bone marrow or stem cell transplantation[1]
- Currently receiving voxelotor, crizanlizumab, or L-glutamine[1]
- Currently receiving treatment with hematopoietic-stimulating agents[1]
- Taking strong CYP3A4/5 inhibitors or strong inducers of CYP3A4[1]

RISE UP

# TALK WITH YOUR PATIENTS ABOUT ENROLLMENT

For more information about RISE UP, visit and share the resources below.

## AGIOS MEDICAL AFFAIRS

For answers to specific questions about RISE UP, your patients can call **+1-833-228-8474**, Mon-Fri, 9 AM to 7 PM ET (1 PM to 11 PM GMT), or email **medinfo@agios.com**.

## CLINICAL TRIAL WEBSITE

See full enrollment details, all study objectives and endpoints, and key inclusion and exclusion criteria, at **https://clinicaltrials.gov/ct2/show/NCT05031780**.

## FOR US PATIENTS AND HEALTHCARE PROVIDERS ONLY

Healthcare Provider Website
Visit **RiseUpStudy.com/hcp**

Patient Website
Patients considering enrollment can visit **RiseUpStudy.com**.

**References: 1.** Data on file. Agios Pharmaceuticals, Inc. **2.** Howard J, Kuo KHM, Oluyadi A, et al. A phase 2/3, randomized, double-blind, placebo-controlled study of mitapivat in patients with sickle cell disease. *Blood*. 2021;138(suppl 1):3109. **3.** A timeline of innovation and patient impact. Agios Pharmaceuticals, Inc. Accessed September 21, 2022. https://www.agios.com/about-us/history/ **4.** Xu JZ, Conrey A, Frey I, et al. Phase 1 multiple ascending dose study of safety, tolerability, and pharmacokinetics/pharmacodynamics of mitapivat (AG-348) in subjects with sickle cell disease. Presented at: American Society of Hematology Annual Meeting; December 5-8, 2020. **5.** van Dijk MJ, Rab MAE, Rijneveld AW, et al. Safety and efficacy of mitapivat (AG-348), an oral activator of pyruvate kinase R, in subjects with sickle cell disease: A phase 2, open-label study (ESTIMATE). Presented at: American Society of Hematology Annual Meeting; December 11-14, 2021; Atlanta, GA.

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