Clinical Trials for PK Deficiency

Study	Identifier	Molecule	Status	Patient population
AG348-C-006 (ACTIVATE) Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of AG-348 in Not Regularly Transfused Adult Subjects with Pyruvate Kinase Deficiency	NCT03548220	AG-348	Completed	Pyruvate Kinase Deficiency (Not Regularly Transfused)
AG348-C-007 (ACTIVATE-T) Phase 3, Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of AG-348 in Regularly Transfused Adult Subjects with Pyruvate Kinase Deficiency	NCT03559699	AG-348	Completed	Pyruvate Kinase Deficiency (Regularly Transfused)
└ **AG348-C-011** Phase 3, Multicenter, Open-Label, Extension Study to Evaluate the Long-Term Safety, Tolerability, and Efficacy of AG-348 Treatment in Adult Participants with Pyruvate Kinase Deficiency Previously Enrolled in **AG348-C-006** or **AG348-C-007**	NCT03853798	AG-348	Active, Not Recruiting	Pyruvate Kinase Deficiency
AG348-C-003 Phase 2, Open-Label, Randomized, Dose-Ranging, Safety, Efficacy, Pharmacokinetic, and Pharmacodynamic Study of AG-348 in Adult Patients with Pyruvate Kinase Deficiency*	NCT02476916	AG-348	Active, Not Recruiting***	Pyruvate Kinase Deficiency
AG348-C-008 (Peak Registry) Pyruvate Kinase Deficiency, Prospective, Global, Longitudinal Registry**	NCT03481738	N/A	Recruiting	Pyruvate Kinase Deficiency
└ **AG348-C-015** Pyruvate Kinase Deficiency, Prospective, Global, Longitudinal Registry: Patient-Reported Outcomes Participants Previously Enrolled in **AG348-C-008**	NCT04964323	N/A	Recruiting	Pyruvate Kinase Deficiency
└ **AG348-C-016** Pyruvate Kinase Deficiency, Prospective, Global, Longitudinal Registry Substudy of Protocol **AG348-C-008**: Cognition in Participants with Pyruvate Kinase Deficiency	NCT04995315	N/A	Recruiting	Pyruvate Kinase Deficiency

*Eligible participants may enter an extension period to receive AG-348 for up to 8 additional years.

**This Registry will be open for enrollment for 7 years and all enrolled participants will be followed prospectively for a minimum of 2 years, and up to 9 years.

***Core study period completed, extension phase ongoing.

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Clinical Trials for Sickle Cell Disease

Study	Identifier	Molecule	Status	Patient population
19-H-0097 Early Phase 1, Interventional, Non-randomized, Pilot Clinical Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Escalating Multiple Oral Doses of AG-348 in Subjects with Stable Sickle Cell Disease*	NCT04000165	AG-348	Completed	Sickle Cell Disease
└ **000049-H** Phase 1 Evaluation of the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Long-Term Mitapivat (AG-348) Dosing in Subjects with Stable Sickle Cell Disease: An Extension of the Phase 1 Pilot Study of Mitapivat **19-H-0097***	NCT04610866	AG-348	Recruiting	Sickle Cell Disease
AG348-C-020 (RISE UP) Phase 2/3, Double-Blind, Randomized, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Mitapivat (AG-348) in Subjects with Sickle Cell Disease**	NCT05031780	AG-348	Not Yet Recruiting	Sickle Cell Disease
AG946-C-001 Phase 1 Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of AG-946 in Healthy Volunteers and in Subjects with Sickle Cell Disease	NCT04536792	AG-946	Recruiting	Healthy Volunteers & Sickle Cell Disease

*This study is run by National Institutes of Health (NIH) in collaboration with Agios.
**The long-term effect of Mitapivat (AG-348) on efficacy and safety will be explored in an open-label, 216-week extension period.

Clinical Trials for Thalassemia

Study	Identifier	Molecule	Status	Patient population
AG348-C-010 Phase 2, Open-Label, Multicenter Study to Determine the Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of AG-348 in Adult Subjects with Non-Transfusion-Dependent Thalassemia	NCT03692052	AG-348	Active, Not Recruiting*	Non-Transfusion-Dependent Alpha- and Beta-Thalassemia
AG348-C-017 (ENERGIZE) Phase 3, Double-Blind, Randomized, Placebo-Controlled, Multicenter Study Evaluating the Efficacy and Safety of Mitapivat (AG-348) in Subjects with Non-Transfusion-Dependent Alpha- or Beta-Thalassemia	NCT04770753	AG-348	Recruiting	Non-Transfusion-Dependent Alpha- and Beta-Thalassemia
AG348-C-018 (ENERGIZE-T) Phase 3, Double-Blind, Randomized, Placebo-Controlled, Multicenter Study Evaluating the Efficacy and Safety of Mitapivat (AG-348) in Subjects with Transfusion-Dependent Alpha- or Beta-Thalassemia	NCT04770779	AG-348	Recruiting	Transfusion-Dependent Alpha- and Beta-Thalassemia

*Core study period completed, extension phase ongoing.

For additional details about Agios-sponsored trials, please contact Agios Medical Information: ✉ medinfo@agios.com; ✆ 833-228-8474.

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