Agios Announces FDA Approval of PYRUKYND® (mitapivat) as First Disease-Modifying Therapy for Hemolytic Anemia in Adults with Pyruvate Kinase Deficiency

– Approval Based on Results from ACTIVATE and ACTIVATE-T Phase 3 Studies, Supports Treatment of Adults with PK Deficiency Regardless of Transfusion Status –

– Company to Provide Robust Patient Access Programs, Including $0 Copays and Free Medication for Eligible Patients –

– Agios to Host Investor Webcast Tomorrow at 7:00 a.m. ET –

CAMBRIDGE, Mass., February 17, 2022 – Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), a leader in the field of cellular metabolism pioneering therapies for genetically defined diseases, today announced that the U.S. Food and Drug Administration (FDA) has approved PYRUKYND® (mitapivat) in the U.S. for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency, a rare, debilitating, lifelong hemolytic anemia. PYRUKYND® is a first-in-class, oral PK activator and the first approved disease-modifying therapy for this disease.

"The successful ACTIVATE and ACTIVATE-T studies demonstrate the impact of mitapivat in significantly improving hemolysis and anemia in PK deficiency," said Hanny Al-Samkari, M.D., hematologist and clinical investigator at the Mass General Cancer Center and Harvard Medical School, and an investigator in these pivotal Phase 3 studies. "The FDA approval of mitapivat, a targeted agent and first disease-modifying medication in PK deficiency, is an encouraging step forward for these patients that addresses a significant unmet need."

"PYRUKYND® is the first approved therapy for PK deficiency and marks an important milestone for these patients, who may face tremendous challenges and debilitating symptoms throughout the course of this lifelong disease," said Rachael Grace, M.D., MMSc, pediatric hematologist, director of hematology clinical research at Boston Children's Hospital and an investigator in the Phase 2 DRIVE PK and Phase 3 ACTIVATE studies. "Partnering with Agios and the PK deficiency community to improve understanding of the natural history of this rare disease and bring a new medicine to patients has been an honor, and I look forward to additional collaboration in the future."

"I am so grateful that PYRUKYND® has been approved for PK deficiency. As both patient and caregiver, I spent the majority of my life feeling alone in this disease and never thought I would see a medicine approved," said Kim Hall, who was diagnosed with PK deficiency in 1969 and is the mother of two adult daughters living with PK deficiency. All three women participated in the Phase 3 PYRUKYND® PK deficiency clinical program. "The experience of being part of the clinical trials has been impactful because of the connections we have built with other patients, healthcare providers and Agios colleagues who understand PK deficiency and are actively working to improve patients' lives."

"For more than a decade, we have been pioneering the science of PK activation in order to bring PYRUKYND® to people with PK deficiency and provide them with the first medication

approved specifically to address this rare, debilitating blood disorder," said Jackie Fouse, Ph.D., chief executive officer at Agios. "We remain committed to partnering with patients, caregivers, advocates and healthcare providers to ensure that the impact of PYRUKYND® is maximized through robust support, education and access programs. These connections have fueled today's tremendous milestone for the PK deficiency community. Each of us at Agios is dedicated to making a difference for people with PK deficiency, as well as to expanding the reach of PYRUKYND® and our clinical and research programs to many more patients with genetically defined diseases around the world."

Agios is offering a robust set of access programs aimed at reducing or eliminating patient out-of-pocket costs for PYRUKYND®, including a copay program that lowers copays to $0 for eligible commercially-insured patients and a Patient Assistance Program (PAP) that offers free prescriptions to eligible uninsured and underinsured patients. The myAgios® patient support services program provides a centralized resource to assist with support, access, education and adherence. Learn more and enroll at www.myagios.com.

PYRUKYND® is expected to be available in the U.S. approximately two weeks after approval. PYRUKYND® was reviewed by the FDA under Priority Review and was previously granted orphan drug designation. PYRUKYND® is also under review by the European Medicines Agency (EMA) as a potential treatment for adults with PK deficiency, and Agios expects a regulatory decision in the EU by the end of 2022. Learn more at www.PYRUKYND.com.

PYRUKYND® Safety and Efficacy Data

The FDA granted approval to PYRUKYND® based on results from two pivotal studies, ACTIVATE and ACTIVATE-T, conducted in not regularly transfused and regularly transfused adults with PK deficiency, respectively.

- The Phase 3 ACTIVATE trial of mitapivat achieved its primary endpoint. PYRUKYND® demonstrated a statistically significant increase in hemoglobin in patients with PK deficiency who are not regularly transfused.
    - 40 percent (n=16) of patients randomized to PYRUKYND® achieved a hemoglobin response, compared to 0 patients randomized to placebo (2-sided $p<0.0001$).
    - Statistically significant improvements compared to placebo were also demonstrated for all pre-specified secondary endpoints, including markers of hemolysis and ineffective erythropoiesis.
    - Patients treated with PYRUKYND® experienced changes in jaundice (difference in LS Mean of PYRUKYND® minus placebo: -0.4), tiredness (difference in LS Mean of PYRUKYND® minus placebo: -1.1) and shortness of breath (difference in LS Mean of PYRUKYND® minus placebo: -0.3), as assessed with the daily Pyruvate Kinase Deficiency Diary (PKDD) where lower scores represent less sign/symptom severity.
    - Serious adverse reactions occurred in 10 percent (n=4) of patients receiving PYRUKYND®, including atrial fibrillation, gastroenteritis, rib fracture and musculoskeletal pain, which each occurred in 1 patient.

- The most common adverse reactions including laboratory abnormalities (≥ 10%) in patients with PK deficiency were estrone decreased (males), increased urate, back pain, estradiol decreased (males) and arthralgia.

- The Phase 3 ACTIVATE-T trial of mitapivat achieved its primary endpoint. Mitapivat demonstrated a statistically significant and clinically meaningful reduction in transfusion burden for patients who are regularly transfused.
  - 33 percent (n=9) of patients achieved a transfusion reduction response, defined as a ≥33% reduction in transfusion burden in the 24-week fixed dose period compared with individual historical transfusion burden standardized to 24 weeks.
  - 22 percent (n=6) of patients were transfusion-free during the fixed-dose period.
  - The adverse reactions reported in the ACTIVATE-T study were consistent with those observed in ACTIVATE.

A full analysis of these data was presented at the 2021 European Hematology Association (EHA) Virtual Congress. An extension study for adults with PK deficiency previously enrolled in ACTIVATE or ACTIVATE-T is ongoing and designed to evaluate the long-term safety, tolerability and efficacy of treatment with mitapivat; initial results from the extension study were recently presented at the 2021 American Society of Hematology (ASH) Annual Meeting and Exposition.

In mid-2022, the company expects to initiate two pivotal studies – ACTIVATE-kids and ACTIVATE-kidsT – in pediatric patients with PK deficiency who are not regularly transfused and who are regularly transfused, respectively. Agios also continues to advance its Phase 3 ENERGIZE and ENERGIZE-T studies in not regularly transfused and regularly transfused adults with thalassemia, as well as its Phase 2/3 RISE UP study in sickle cell disease.

Conference Call Information
Agios will host a virtual investor event tomorrow, February 18, at 7:00 a.m. ET to discuss the FDA approval of PYRUKYND®. The event will be webcast live and can be accessed under "Events & Presentations" in the Investors and Media section of the company's website at www.agios.com. The archived webcast will be available on the company's website beginning approximately two hours after the event.

About PK Deficiency
Pyruvate kinase (PK) deficiency is a rare, inherited disease that presents as chronic hemolytic anemia, which is the accelerated destruction of red blood cells. The inherited mutation in the PKLR gene can cause a deficit in energy within the red blood cell, as evidenced by lower PK enzyme activity, a decline in adenosine triphosphate (ATP) levels and a build-up of upstream metabolites, including 2,3-DPG (2,3-diphosphoglycerate).

PK deficiency is associated with serious complications, including gallstones, pulmonary hypertension, extramedullary hematopoiesis, osteoporosis and iron overload and its sequelae, which can occur regardless of the degree of anemia or transfusion burden. PK deficiency can also cause quality of life problems, including challenges with work and school activities, social life and emotional health. Current management strategies for PK deficiency, including red blood cell transfusions and splenectomy, are associated with both short- and long-term risks. For more

information, please visit the websites of two U.S.-based independent patient advocacy groups dedicated to PK deficiency: PK Deficiency Foundation and Thrive with PK Deficiency.

myAgios® Patient Support Services
The myAgios® patient support services program is a centralized platform for people living with PK deficiency and their caregivers. After enrolling in the program, patients and caregivers are connected with a dedicated Patient Support Manager (PSM) with a clinical background to provide tailored support, educational resources, access and benefits investigation services, financial assistance programs, prescription fulfillment and opportunities to connect with other patients and caregivers in the community. To learn more or enroll, please visit www.myagios.com.

About PYRUKYND® (mitapivat)
PYRUKYND is a pyruvate kinase activator indicated for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency.

IMPORTANT SAFETY INFORMATION
Acute Hemolysis: Acute hemolysis with subsequent anemia has been observed following abrupt interruption or discontinuation of PYRUKYND in a dose-ranging study. Avoid abruptly discontinuing PYRUKYND. Gradually taper the dose of PYRUKYND to discontinue treatment if possible. When discontinuing treatment, monitor patients for signs of acute hemolysis and anemia including jaundice, scleral icterus, dark urine, dizziness, confusion, fatigue, or shortness of breath.

Adverse Reactions: Serious adverse reactions occurred in 10% of patients receiving PYRUKYND in the ACTIVATE trial, including atrial fibrillation, gastroenteritis, rib fracture, and musculoskeletal pain, each of which occurred in 1 patient. In the ACTIVATE trial, the most common adverse reactions including laboratory abnormalities (≥10%) in patients with PK deficiency were estrone decreased (males), increased urate, back pain, estradiol decreased (males), and arthralgia.

Drug Interactions:
- Strong CYP3A Inhibitors and Inducers: Avoid concomitant use.
- Moderate CYP3A Inhibitors: Do not titrate PYRUKYND beyond 20 mg twice daily.
- Moderate CYP3A Inducers: Consider alternatives that are not moderate inducers. If there are no alternatives, adjust PYRUKYND dosage.
- Sensitive CYP3A, CYP2B6, CYP2C Substrates Including Hormonal Contraceptives: Avoid concomitant use with substrates that have narrow therapeutic index.
- UGT1A1 Substrates: Avoid concomitant use with substrates that have narrow therapeutic index.
- P-gp Substrates: Avoid concomitant use with substrates that have narrow therapeutic index.

Hepatic Impairment: Avoid use of PYRUKYND in patients with moderate and severe hepatic impairment.

Please see full Prescribing Information for PYRUKYND.

About Agios
Agios is a biopharmaceutical company that is fueled by connections. The Agios team cultivates strong bonds with patient communities, healthcare professionals, partners and colleagues to discover, develop and deliver therapies for genetically defined diseases. In the U.S., Agios markets a first-in-class pyruvate kinase (PK) activator for adults with PK deficiency, the first disease-modifying therapy for this rare, lifelong, debilitating hemolytic anemia. Building on the company's leadership in the field of cellular metabolism, Agios is advancing a robust clinical pipeline of investigational medicines with active and planned programs in alpha- and beta-thalassemia, sickle cell disease, pediatric PK deficiency and MDS-associated anemia. In addition to its clinical pipeline, Agios has multiple investigational therapies in preclinical development and an industry-leading research team with unmatched expertise in cellular metabolism and genetics. For more information, please visit the company's website at www.agios.com.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding the potential benefits of Agios' products, including PYRUKYND® (mitapivat), and its strategic plans and focus. The words "anticipate," "expect," "goal," "hope," "milestone," "plan," "potential," "possible," "strategy," "will," "vision," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from Agios' current expectations and beliefs. Management's expectations and, therefore, any forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other important factors, including, without limitation risks and uncertainties related to: the failure of Agios to receive milestone or royalty payments related to the sale of its oncology business, the uncertainty of the timing of any receipt of any such payments, and the uncertainty of the results and effectiveness of the use of proceeds from the transaction; the impact of the COVID-19 pandemic to Agios' business, operations, strategy, goals and anticipated milestones, including its ongoing and planned research activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of future approved products, and launching, marketing and selling future approved products; Agios' results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. FDA, the EMA or other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; Agios' ability to obtain and maintain requisite regulatory approvals and to enroll patients in its planned clinical trials; unplanned cash requirements and expenditures and competitive factors; Agios' ability to obtain, maintain and enforce patent and other intellectual property protection for any product candidates it is developing; Agios' ability to establish and maintain collaborations; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in Agios' public filings with the Securities and Exchange Commission, or SEC, including the risks and uncertainties set forth under the heading Risk Factors in our filings with the SEC. While the list of factors presented here is considered representative, this list

should not be considered to be a complete statement of all potential risks and uncertainties. Any forward-looking statements contained in this press release are made only as of the date hereof, and we undertake no obligation to update forward-looking statements to reflect developments or information obtained after the date hereof and disclaim any obligation to do so other than as may be required by law.

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