Agios to Present New Data on Mitapivat and Tebapivat in Rare Blood Disorders at 66th ASH Annual Meeting and Exposition

November 5, 2024

– Results from Phase 3 ENERGIZE-T Study of Mitapivat in Transfusion-dependent Thalassemia will be Presented in Oral Session –

– Tebapivat Phase 1 Data in Sickle Cell Disease and Phase 2b Trial-in-progress Update in Lower-risk Myelodysplastic Syndromes will be Presented and Published –

– Live and Webcast Investor Event with Agios Leadership and Medical Experts will be Hosted Onsite on Monday, December 9 –

CAMBRIDGE, Mass., Nov. 05, 2024 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq: AGIO), a leader in cellular metabolism and pyruvate kinase (PK) activation pioneering therapies for rare diseases, today announced that new data on mitapivat and tebapivat (AG-946), the company's PK activators, will be featured in oral and poster presentations during the 66 th American Society of Hematology (ASH) Annual Meeting and Exposition in San Diego, California from December 7-10, 2024.

"These data we are presenting at ASH reaffirm our confidence in our growing pipeline focused on improving red blood cell health," Sarah Gheuens, M.D., Ph.D., chief medical officer and head of R&D at Agios. "We will highlight the clinical progress of our two PK activators – mitapivat and tebapivat – in multiple rare blood disorders with high patient needs, including thalassemia, sickle cell disease and myelodysplastic syndromes. These advancements showcase the quality of science and potential novel solutions coming out of our research and development efforts."

Key presentations and publications at ASH 2024 will include:

- An oral presentation on results from the Phase 3 ENERGIZE-T study evaluating mitapivat in adults with transfusion-dependent alpha- or beta-thalassemia versus placebo. Alongside the positive results from the Phase 3 ENERGIZE study of mitapivat in non-transfusion-dependent alpha- or beta-thalassemia previously presented at the 2024 European Hematology Association (EHA) Congress, these data support mitapivat's potential as an oral, disease-modifying therapy across the full range of patients with thalassemia regardless of transfusion status.
- A poster presentation of a Phase 1 study assessing the safety, tolerability, pharmacokinetics and pharmacodynamics of tebapivat in patients with sickle cell disease, providing further evidence that PK activation may have beneficial effects in this patient population.
- A trial-in-progress publication that outlines the Phase 2b study evaluating the efficacy and safety of tebapivat in patients with anemia due to lower-risk myelodysplastic syndromes.

In total, 16 presentations and publications led by Agios and external collaborators will be shared at ASH 2024.

ASH 2024 Accepted Abstracts

Title	Number	Date/Time	Presenter	Acceptance
Thalassemia				
ENERGIZE-T: A Global, Phase 3, Double-Blind, Randomized, Placebo-Controlled Study of Mitapivat in Adults with Transfusion-Dependent Alpha- or Beta-Thalassemia	409	Sunday, December 8, 2024; 9:30 AM PT	Maria Domenica Cappellini, M.D., University of Milan, Italy	Oral
PKM2 binds to the regulatory regions of Gata-1 and STAT5 in β-thalassemic mouse erythroblasts	410	Sunday, December 8, 2024; 9:45 AM PT	Enrica Federti, Ph.D., University of Verona, Verona, Italy	Oral
Ex vivo treatment by mitapivat, an allosteric pyruvate kinase activator, reduced hemolysis and reactive oxygen species in red blood cells of non-regularly transfused hemolytic anemic patients with β-thalassemia/Hb E disease	2479	Sunday, December 8, 2024; 6:00 – 8:00 PM PT	Thidarat Suksangpleng, Ph.D., Siriraj Hospital, Mahidol University, Bangkok, Thailand	Poster
Thalassemia scenario in Brazil: A descriptive study	2310	Saturday, December 7, 2024; 5:30 – 7:30 PM PT	Catherine Moura, M.D., MSc, Abrasta – Brazilian Thalassemia Association, São Paulo, SP, Brazil	Poster
Understanding Health Literacy Among Patients With Thalassemia: A Global Patient Survey by the Thalassemia Advocacy Advisory Council	*Blood* Nov. 2024 supplementary issue	N/A	Sujit Sheth, M.D., Weill Cornell Medicine, New York City, New York	Publication

Molecular characterization of HbH in Spain	*Blood* Nov. 2024 supplementary issue	N/A	Ana María Villegas, M.D., University Hospital Clínico San Carlos, Complutense University of Madrid, Madrid Spain	Publication
Molecular characterization of NTDT in Spain	*Blood* Nov. 2024 supplementary issue	N/A	Ana María Villegas, M.D., University Hospital Clínico San Carlos, Complutense University of Madrid, Madrid Spain	Publication
Molecular characterization of TDT in Spain	2024 supplementary issue	N/A	Ana María Villegas, M.D., University Hospital Clínico San Carlos, Complutense University of Madrid, Madrid Spain	Publication
Sickle Cell Disease				
Results From A Phase 1 Study To Assess The Safety, Tolerability, Pharmacokinetics, And Pharmacodynamics Of Tebapivat (AG-946) In Patients With Sickle Cell Disease	2496	Sunday, December 8, 2024; 6:00 – 8:00 PM PT	Julia Xu, M.D., MScGH, Vascular Medical Institute, University of Pittsburgh, Pittsburg, PA	Poster
Dual Activation of PKR and PKM2 Reduced the Development of Fibrosis and Iron Deposition in a Sickle Cell Disease Nephropathy Mouse Model	1107	Saturday, December 7, 2024; 5:30 – 7:00 PM PT	Trang Nguyen, ScB, Agios Pharmaceuticals, Inc., Cambridge, MA	Poster
Mitapivat-Induced Improvements in RBC Deformability and Membrane Integrity in Patients with Sickle Cell Disease are Sustained During Extended Therapy	2491	Sunday, December 8, 2024; 6:00 – 8:00 PM PT	Xunde Wang, Ph.D., National Institute of Health, Bethesda, MD	Poster
Myelodysplastic Syndromes				
A Phase 2B, Open-Label Multicenter Study of Tebapivat (AG-946), a Potent Pyruvate Kinase Activator, in Patients with Anemia due to Lower-Risk Myelodysplastic Syndromes	*Blood* Nov. 2024 supplementary issue	N/A	Amer M Zeidan, Yale University School of Medicine and Yale Comprehensive Cancer Center, New Haven, CT	Publication
Pyruvate Kinase Deficiency				
Clinical Monitoring Practices Among Adult Patients with Pyruvate Kinase Deficiency Who Have Never Been Transfused	3696	Sunday, December 8, 2024; 6:00 – 8:00 PM PT	Stefan W. Eber, M.D., Ph.D., M1 Private Clinic Munich, Munich, Germany	Poster
Other				
uRADAR: European Patients Referral Frame to Improve Access to New Drugs and Therapies in Ultra-Rare Anemia Disorders and Severe Hereditary Spherocytosis	794	Monday, December 9, 2024; 10:45 AM PT	Mar Manu Pereira, Ph.D., Vall d'Hebron Barcelona Hospital, Barcelona, Spain	Oral
PIEZO1 gain-of-function variants lead to alterations in late-stage erythropoiesis by enhancing enucleation rate	3837	Monday, December 9, 2024; 6:00 – 8:00 PM PT	Barbara Eleni Rosato, Ph.D., University of Naples Federico II, Naples, Italy	Poster
A Multicenter, Single-Arm Phase 2 Trial of Mitapivat in Adult Patients with Erythrocyte Membranopathies and Congenital Dyserythropoietic Anemia Type II – Results from the 8-Week Dose-Escalation Period	3831	Monday, December 9, 2024; 6:00 – 8:00 PM PT	Thomas Doeven, M.D., Center for Benign Hematology, Thrombosis and Hemostasis – Van Creveldkliniek, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands	Poster

Please refer to the ASH 2024 online program for full session details and data presentation listings and visit the Agios booth (#105) onsite.

Investor Event at ASH 2024
Agios will host a live and webcast investor event with the company's leadership team and medical experts. The event will take place on Monday, December 9, in San Diego, starting at 7:00 a.m. PT (10:00 a.m. ET). The webcast will be accessible on the Investors section of the company's website (www.agios.com) under the "Events & Presentations" tab. The archived webcast will be available on the company's website approximately two hours after the event.

About PYRUKYND® (mitapivat)
PYRUKYND is a pyruvate kinase activator indicated for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency in the United States, and for the treatment of PK deficiency in adult patients in the European Union.

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 and Summary of Product Characteristics for PYRUKYND.

About Agios
Agios is the pioneering leader in PK activation and is dedicated to developing and delivering transformative therapies for patients living with rare 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 deep scientific expertise in classical hematology and leadership in the field of cellular metabolism and rare hematologic diseases, Agios is advancing a robust clinical pipeline of investigational medicines with programs in alpha- and beta-thalassemia, sickle cell disease, pediatric PK deficiency, myelodysplastic syndromes (MDS)-associated anemia and phenylketonuria (PKU). In addition to its clinical pipeline, Agios is advancing a preclinical TMPRSS6 siRNA as a potential treatment for polycythemia vera. 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 PYRUKYND® (mitapivat) and tebapivat; Agios' plans, strategies and expectations for its preclinical, clinical and commercial advancement of its drug development, including PYRUKYND® and tebapivat; Agios' plans regarding future data presentations; and the potential benefits of Agios' 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. For example, there can be no guarantee that any product candidate Agios is developing will successfully commence or complete necessary preclinical and clinical development phases, or that development of any of Agios' product candidates will successfully continue. There can be no guarantee that any positive developments in Agios' business will result in stock price appreciation. 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 impact of pandemics or other public health emergencies 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 current or future approved products, and launching, marketing and selling current or 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; 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 key collaborations; uncertainty regarding any royalty payments related to the sale of its oncology business or any milestone or royalty payments related to its in-licensing of TMPRSS6 siRNA, and the uncertainty of the timing of any such payments; uncertainty of the results and effectiveness of the use of Agios' cash and cash equivalents; 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. Any forward-looking statements contained in this press release speak only as of the date hereof, and Agios expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Contacts:

Investor Contact
Chris Taylor, VP, Investor Relations and Corporate Communications
Agios Pharmaceuticals
IR@agios.com

Media Contact
Eamonn Nolan, Senior Director, Corporate Communications
Agios Pharmaceuticals
Media@agios.com

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