UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 13, 2025

Agios Pharmaceuticals, Inc.
(Exact Name of Registrant as Specified in Charter)

Delaware	**001-36014**	**26-0662915**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

88 Sidney Street, Cambridge, MA	**02139**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 649-8600

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.001 per share	AGIO	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On January 13, 2025, Agios Pharmaceuticals, Inc. (the "Company") issued a press release outlining its anticipated 2025 milestones, which will be discussed at the Company's presentation at the 43rd Annual J.P. Morgan Healthcare Conference on January 15, 2025. The full text of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference. The slides to be presented by the Company at the 43rd Annual J.P. Morgan Healthcare Conference are furnished as Exhibit 99.2 to this Current Report on Form 8-K and are incorporated herein by reference.

The information in this Item 7.01 (including Exhibit 99.1 and Exhibit 99.2) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press release issued January 13, 2025.
99.2	Presentation at the 43rd Annual J.P. Morgan Healthcare Conference
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

AGIOS PHARMACEUTICALS, INC.

Date: January 13, 2025

By: /s/ Brian Goff
Brian Goff
Chief Executive Officer

Exhibit 99.1

Agios Announces Key 2025 Milestones for Innovative Rare Disease Portfolio

– FDA Accepted Agios' Supplemental New Drug Application for PYRUKYND® (mitapivat) in Adult Patients with Non-Transfusion-Dependent and Transfusion-Dependent Alpha- or Beta-Thalassemia; PDUFA Goal Date is September 7, 2025 –

– Topline Results from Phase 3 RISE UP Study of Mitapivat in Sickle Cell Disease to be Announced in Late 2025, with Potential U.S. Commercial Launch in 2026 –

– Strong Financial Position Provides Opportunity to Maximize Potential PYRUKYND Commercial Launches, Advance Early- and Mid-Stage Clinical Programs and Expand Pipeline –

CAMBRIDGE, Mass., Jan. 13, 2025 – Agios Pharmaceuticals, Inc. (Nasdaq: AGIO), a leader in cellular metabolism and pyruvate kinase (PK) activation pioneering therapies for rare diseases, today announced its anticipated key 2025 milestones and value-driving catalysts through 2026. The company's management team will present this information at the 43rd Annual J.P. Morgan Healthcare Conference on Wednesday, January 15, 2025, at 7:30 a.m. PT / 10:30 a.m. ET.

"2024 was marked by exceptional progress at Agios. We delivered on all our key priorities, advanced our potential best- and first-in-class rare disease pipeline and further strengthened our financial position. Today, we are entering an era of growth and expansion for the company, building on a strong foundation and focus, and are well-positioned for a sustained trajectory of success," said Brian Goff, chief executive officer at Agios. "Our blueprint encompasses the potential for two additional commercial launches of PYRUKYND in thalassemia and sickle cell disease in 2025 and 2026, respectively, along with an early- and mid-stage pipeline that offers a strong foundation for innovation and growth, all supported by a highly experienced team with proven executional excellence and a strong balance sheet. Over the next 12 months, our priorities will be to maximize the potential of the PYRUKYND franchise, advance and diversify our key pipeline programs, and strategically focus our capital deployment to sustain our growth. We are excited about the future and the meaningful impact we can have in addressing the critical needs of rare disease patients."

2024 Highlights:

- *Thalassemia:* Presented positive results from the ENERGIZE and ENERGIZE-T Phase 3 trials evaluating mitapivat versus placebo in adults with non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia, respectively. The ENERGIZE randomized clinical trial results were presented at the European Hematology Association 2024 Hybrid Congress in June 2024, and the ENERGIZE-T randomized clinical trial results were presented at the 66th American Society of Hematology Annual Meeting and Exposition in December 2024. Agios filed regulatory applications for mitapivat (PYRUKYND) for the treatment of adult patients with non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia with the U.S., European Union, Kingdom of Saudi Arabia and United Arab Emirates health authorities.

- *Sickle Cell Disease:* Completed enrollment of the Phase 3 RISE UP study that is evaluating mitapivat in sickle cell disease patients who are 16 years of age or older. This Phase 3 study enrolled more than 200 patients worldwide.
- *Pediatric Pyruvate Kinase (PK) Deficiency:* Reported topline results from the Phase 3 ACTIVATE-KidsT trial of mitapivat in children with PK deficiency who are regularly transfused. Further, completed enrollment of the Phase 3 ACTIVATE-Kids study of mitapivat in children with PK deficiency who are not regularly transfused.
- *Lower-Risk Myelodysplastic Syndromes (LR-MDS):* Initiated patient enrollment in the Phase 2b study of tebapivat (AG-946) in LR-MDS. Additionally, the U.S. Food and Drug Administration (FDA) granted orphan drug designation to tebapivat for the treatment of MDS.
- *Early-Stage Pipeline*: Dosed the first healthy volunteer participants in the Phase 1 study of AG-181, a PAH stabilizer, in phenylketonuria.
- *Corporate Development*:
    - Announced a $905 million purchase agreement with Royalty Pharma for Agios' rights to its vorasidenib royalty. Under the agreement, Agios received a payment of $905 million following the approval of vorasidenib by the FDA. Royalty Pharma will receive the entirety of the 15% royalty on annual U.S. net sales of vorasidenib up to $1 billion, and a 12% royalty on annual U.S. net sales greater than $1 billion. Agios retains a 3% royalty on annual U.S. net sales greater than $1 billion. Agios also received a $200 million milestone payment from Servier following the FDA approval of vorasidenib. Altogether, Agios received a total of $1.1 billion in milestone payments as part of this purchase agreement.
    - Entered into a distribution agreement with NewBridge Pharmaceuticals to advance commercialization of PYRUKYND in the Gulf Cooperation Council (GCC) region. NewBridge, a leading specialty company headquartered in Dubai, will commercialize PYRUKYND in Bahrain, Kuwait, Oman, Qatar, Saudi Arabia and the United Arab Emirates.

Anticipated 2025 Milestones:

- *Thalassemia:* Receive FDA regulatory decision for PYRUKYND for the treatment of adult patients with non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia. The review classification for the company's supplemental New Drug Application is Standard and the Prescription Drug User Fee Act (PDUFA) goal date is September 7, 2025.
- *Sickle Cell Disease*: Announce topline results from the Phase 3 RISE UP study of mitapivat in sickle cell disease in late 2025, with a potential U.S. commercial launch in 2026. Additionally, begin patient enrollment for the Phase 2 study of tebapivat in sickle cell disease in mid-2025.

- *Pediatric Pyruvate Kinase (PK) Deficiency:* Announce topline results from the Phase 3 ACTIVATE-Kids study of mitapivat in children with PK deficiency who are not regularly transfused in early 2025.
- *Lower-Risk Myelodysplastic Syndromes (LR-MDS):* Complete patient enrollment in the Phase 2b study of tebapivat for LR-MDS in late 2025.
- *Early-Stage Pipeline:* File an Investigational New Drug Application for AG-236, a siRNA targeting TMPRSS6 intended for the treatment of polycythemia vera, in mid-2025.

Presentation at 43rd Annual J.P. Morgan Healthcare Conference

Agios' management team will present at the 43rd Annual J.P. Morgan Healthcare Conference on Wednesday, January 15, 2025, at 7:30 a.m. PT / 10:30 a.m. ET. The live webcast will be accessible on the Investors section of the company's website (www.agios.com) under the "Events & Presentations" tab. A replay of the webcast will be archived on the company's website for at least two weeks following the presentation.

About PYRUKYND® (mitapivat)

U.S. INDICATION

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

U.S. 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.

Hepatocellular Injury in Another Condition: In patients with another condition treated with PYRUKYND at a higher dose than that recommended for patients with PK deficiency, liver injury has been observed. These events were characterized by a time to onset within the first 6 months of treatment with peak elevations of alanine aminotransferase of >5× upper limit of normal (ULN) with or without jaundice. All patients discontinued treatment with PYRUKYND, and these events improved upon treatment discontinuation.

Obtain liver tests prior to the initiation of PYRUKYND and monthly thereafter for the first 6 months and as clinically indicated. Interrupt PYRUKYND if clinically significant increases in liver tests are observed or alanine aminotransferase is >5x ULN. Discontinue PYRUKYND if hepatic injury due to PYRUKYND is suspected.

Adverse Reactions: 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 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 syndrome (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), tebapivat (AG-946), AG-236 and AG-181, Agios' PAH stabilizer; Agios' plans, strategies and expectations for its preclinical, clinical and commercial advancement of its drug development, including PYRUKYND®, tebapivat, AG-181 and AG-236; the submission of PYRUKYND® to regulators for approval in alpha-and-beta thalassemia; Agios' strategic vision and goals, including its key milestones for 2025; and the potential benefits of Agios' strategic plans and focus. The words "anticipate", "expect", "goal", "hope", "milestone", "opportunity", "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 AG-236, 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.

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Exhibit 99.2

agios

J.P. Morgan Healthcare Conference

Agios Pharmaceuticals

Brian Goff, Chief Executive Officer
January 15, 2025

Forward-Looking Statements

This presentation and various remarks we make during this presentation contain 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), tebapivat (AG-946), AG-236 and AG-181, Agios' PAH stabilizer; Agios' plans, strategies and expectations for its preclinical, clinical and commercial advancement of its drug development, including PYRUKYND®, tebapivat, AG-181 and AG-236; the submission of PYRUKYND ® to regulators for approval in alpha-and-beta thalassemia; Agios' strategic vision and goals, including its key milestones for 2025; and the potential benefits of Agios' strategic plans and focus. The words "anticipate", "expect", "goal", "hope", "milestone", "opportunity", "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 presentation and various remarks we make during this presentation 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 AG-236, 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 presentation and various remarks we make during this presentation 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.

agios

Fueled by Connections to Transform Rare Diseases

All individuals featured are real patients who have been compensated for their time.

Strong Foundation to Power New Era of Growth

Built Expertise in Cellular Metabolism
2008 – 2020

Developed and launched three first-in-class oncology medicines while advancing rare disease pipeline

Solidified Foundation in Rare Disease
2021 – 2024

Strong focus on improving red blood cell health

Approval and launch of PYRUKYND® in PK deficiency

Consistent clinical execution and impactful late-stage data

Expand and Accelerate Growth
2025 – Beyond

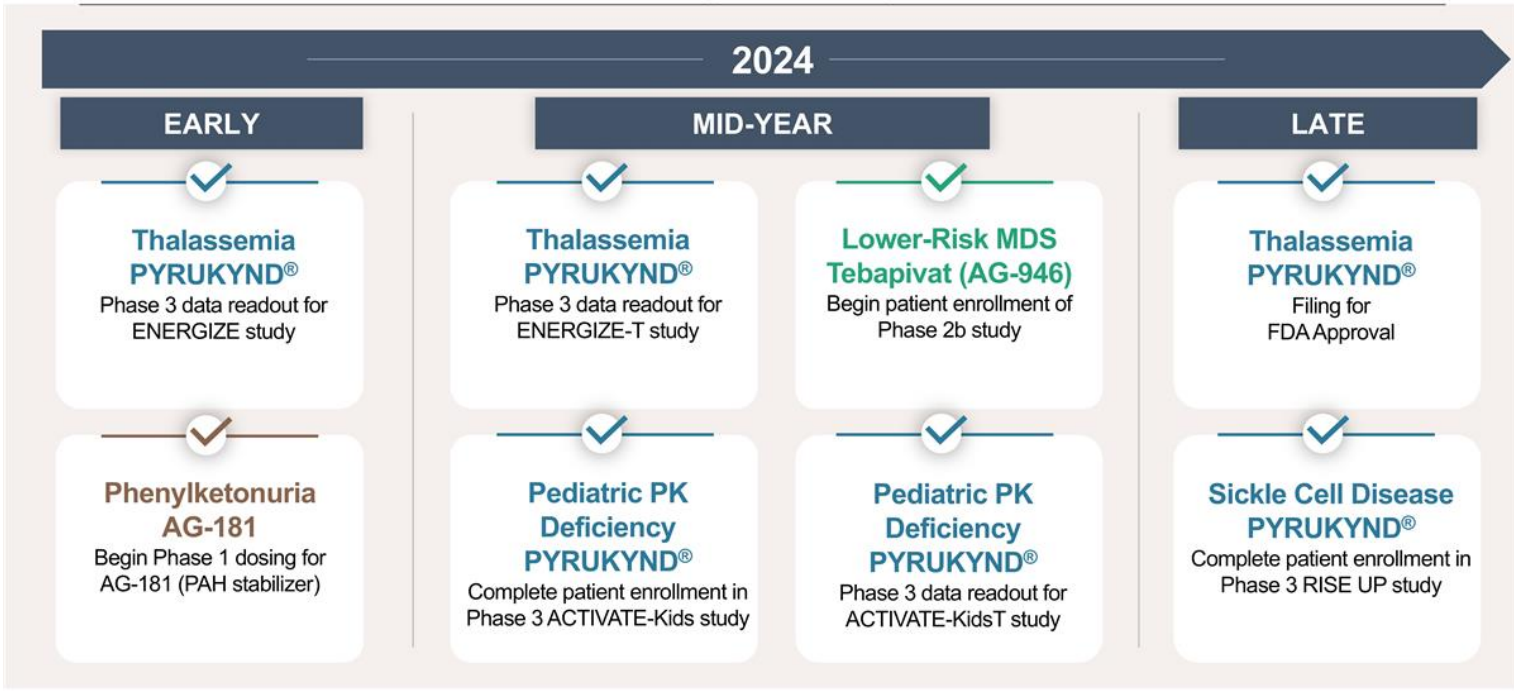
Potential for two additional PYRUKYND® indications by 2026

Strong early and mid-stage pipeline ready for clinical advancement

Financial strength supports ability to expand pipeline and execute on opportunities

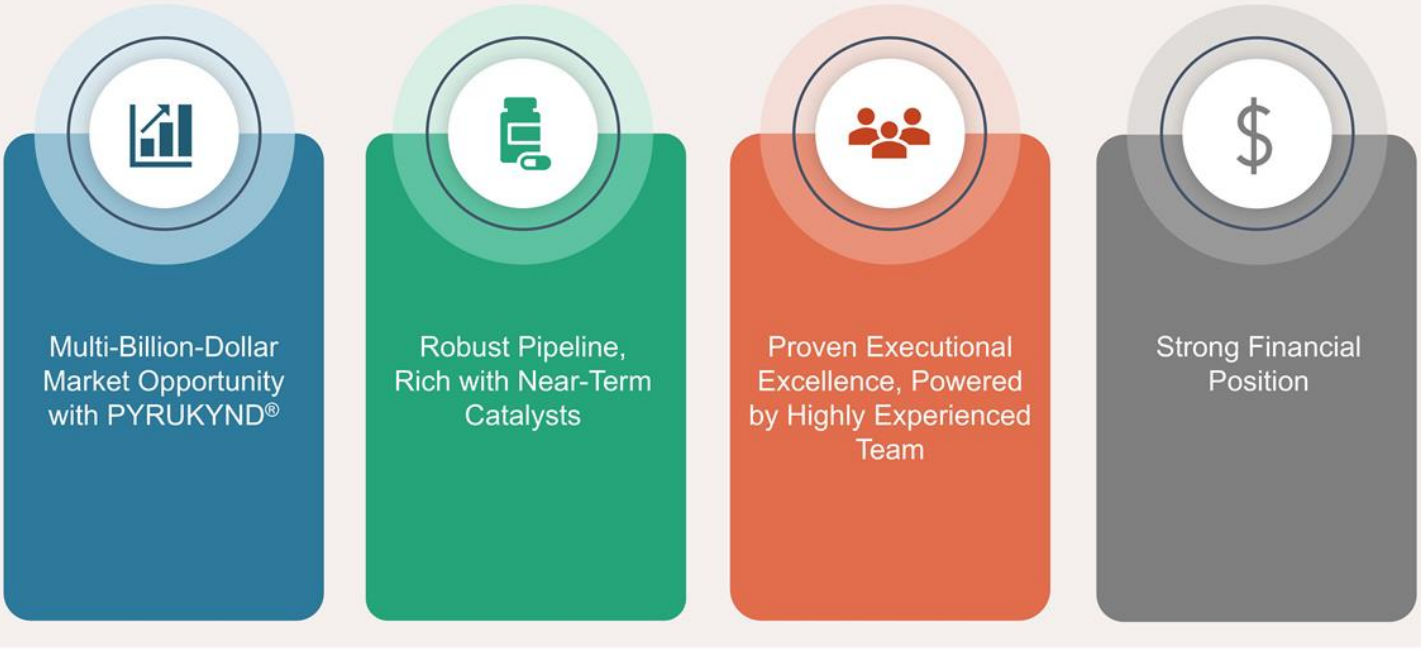
PYRUKYND® is approved in the U.S. for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency and in the Europe Union and in Great Britian for the treatment of PK deficiency in adult patients.
PK deficiency: Pyruvate kinase deficiency

2024: Transformative Year, Delivering on All Key Priorities

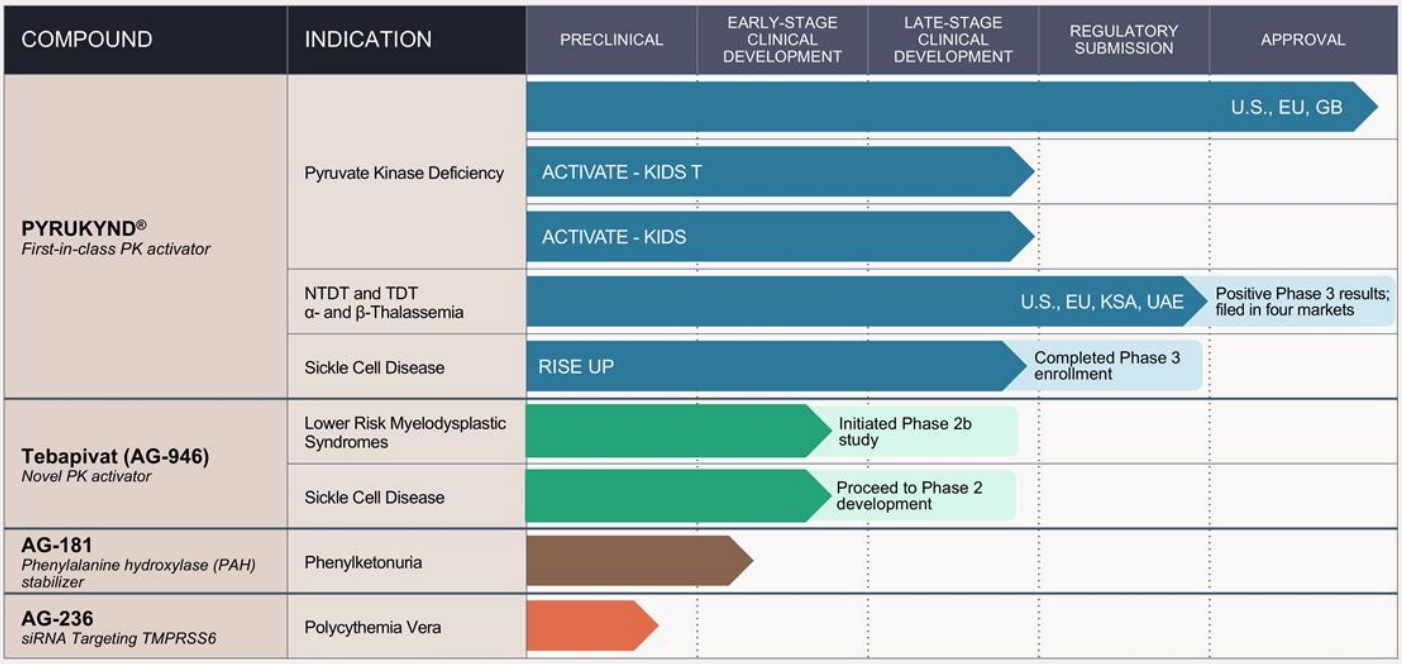


Early: January – April; Mid-Year: May – August; End: September – December
PAH: Phenylalanine hydroxylase; PK deficiency: Pyruvate kinase deficiency

A Rare Blueprint for Success



Advancing Therapies for Rare Diseases with Limited or No Treatment Options



NTDT: Non-transfusion dependent; TDT: Transfusion dependent; EU: European Union; GB: Great Britian; KSA: Kingdom of Saudi Arabia; UAE: United Arab Emirates

2025: Breakout Year

2024
Transformative Year

- **Progressed pipeline and reached critical clinical and regulatory milestones**
- **Bolstered commercialization expertise**
- **Expanded geographic commercial reach**
- **Strengthened balance sheet**

2025
Breakout Year

1. **Maximize potential of PYRUKYND® franchise**
2. **Progress and diversify key pipeline programs**
3. **Focus capital deployment priorities to sustain growth**

1

Maximize Potential of PYRUKYND® Franchise

Laurice
Living with thalassemia, and her son, Ben

PYRUKYND® Expansion into Larger Patient Populations Provides Multi-Billion-Dollar Market Opportunity

pyrukynd® (mitapivat) tablets

3-8K patients
in the U.S./EU5*

PK Deficiency
2022
Approved for adults in the U.S., EU and Great Britain

OUR GOAL
Deliver the first approved therapy for pediatric PK deficiency

18-23K patients
in the U.S./EU5*

~70K patients in GCC*

>1M patients worldwide*

Thalassemia
2025
Potential U.S. approval

OUR GOAL
Deliver the first therapy approved for all thalassemia subtypes

120-135K patients
in the U.S./EU5*

~150K patients
in GCC*

>3M patients
worldwide*

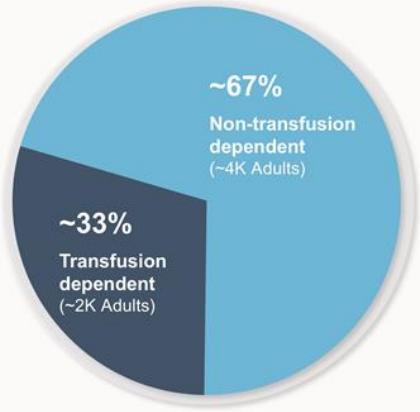
Sickle Cell Disease
2026
Potential U.S. approval

OUR GOAL
Deliver a novel oral therapy that improves anemia and reduces VOCs

PYRUKYND® is approved in the U.S. for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency and in the Europe Union and in Great Britian for the treatment of PK deficiency in adult patients. It is under investigation for pediatric PK deficiency, thalassemia, and sickle cell disease.
*Prevalence figures.
Source: Agios internal estimates
PK deficiency: Pyruvate kinase deficiency; EU: European Union; GCC: Gulf Cooperation Council; VOCs: Vaso-occlusive crisis

Thalassemia: High Patient Need with Limited or No Treatments and Significant Disease Burden

~67% No Approved Therapies in the U.S.



Increased Mortality

Lower survival for thalassemia patients, and significantly worse in patients who remain non-regularly transfused compared to regularly transfused patients

Serious Morbidities

High rates of morbidities and frequency of complications increasing as patients age

Poor Quality of Life

Adult patients with NTDT may have similar or worse Healthcare Related QoL compared with patients with TDT

Healthcare Resource Utilization and Cost

A 1g/dL decrease in average Hb levels is associated with increased inpatient, outpatient and ER visits/costs, Rx costs, and total healthcare costs in patients with NTDT

Sources: Beta-THAL prevalence: HEOR Global THAL Epidemiology SLE (XCENDA, 2021); US: Paramore, et.al; DE: Borchert, et.al; Alpha-THAL prevalence: Agios internal estimates; LEK Analysis | Beta-THAL TD/NTD split: Thuret, et.al., Haematologica 2010; Magnolia TPP MR, April 2020 | Alpha-THAL TD/NTD split; Taher, et.al., Vox Sanguinis, 2015; Magnolia TPP MR, April 2020. Musallam, K, et al.. 2022. Hemasphere 6(12) e806;Thalassemia International Federation, 2023; Musallam, K, et al., 2021. Am J Hematol 97(2) E78-E80; Association of Hemoglobin Levels with Healthcare Resource Utilization and Costs in Non-Transfusion Dependent Alpha and Beta Thalassemia: A Retrospective Observational Study Using Real-World Data (August 1, 2023); Musallam KM et al. Ann Hematol 2021. doi: 10.1007/s00277-020-04370-2; Musallam K., et al. Haematologica. 2021 Sep 1; 106(9): 2489-2492
NTDT: Non-transfusion dependent; TDT: Transfusion dependent; QoL: Quality of life; Hb: Hemoglobin; ER: Emergency Room; Rx: Prescription

PYRUKYND® Poised to Be First and Only Approved Therapy Indicated to Treat All Subtypes of Thalassemia

ENERGIZE and ENERGIZE-T Phase 3 Results Presented at EHA 2024 and ASH 2024

Population

- Enrolled a total of 452 patients reflective of the real-world thalassemia population
- Enrolled adult patients with non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia

Efficacy

- Primary and all key secondary efficacy endpoints were met
- Demonstrated significant improvements in hemoglobin and fatigue
- Demonstrated significant reductions in transfusion burden

Safety

- Overall, incidence of AEs was similar for patients on mitapivat and patients on placebo
- During the double-blind periods, there were 4.7% (n=14) of patients on mitapivat and 0.7% (n=1) of patients on placebo with TEAEs leading to treatment discontinuation
- During the double-blind periods, two patients on mitapivat experienced events of hepatocellular injury. During the open-label extension period, three patients experienced events of hepatocellular injury after switching from placebo to mitapivat. All events occurred within the first six months of exposure. Liver tests improved following discontinuation of mitapivat

Established a **favorable benefit-risk profile for mitapivat** in adult patients with non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia

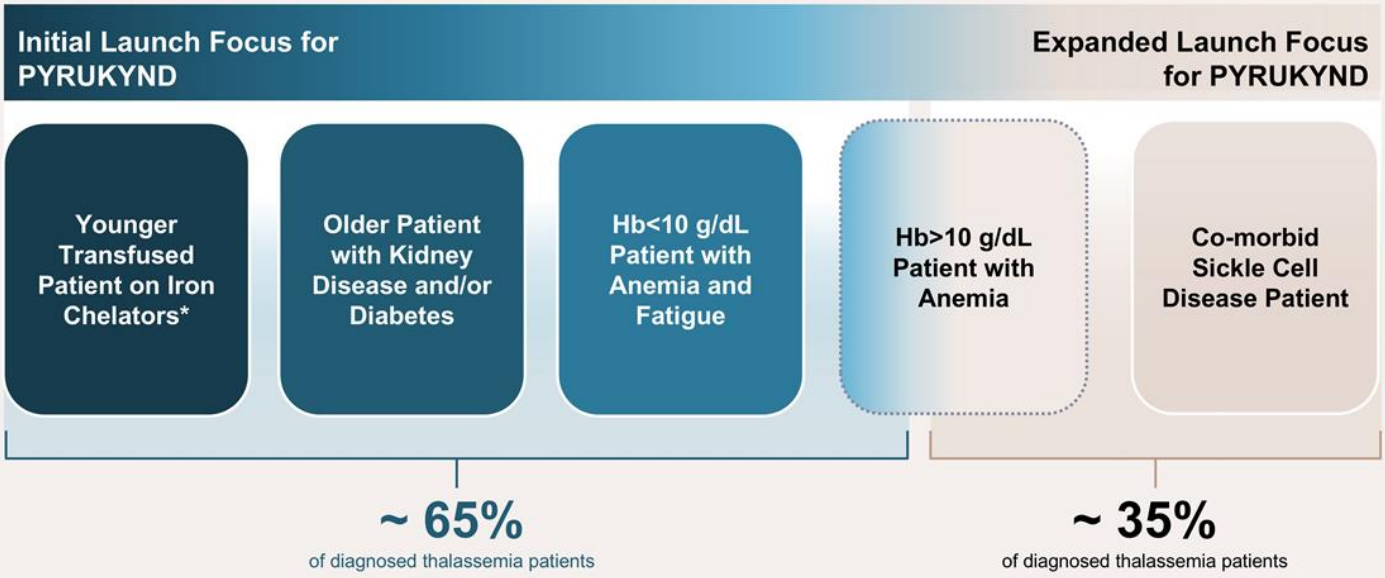
Filed for regulatory approval in the U.S., European Union, Kingdom of Saudi Arabia and United Arab Emirates

FDA accepted PYRUKYND sNDA; **PDUFA** goal date is **September 7, 2025**

PYRUKYND® is under investigation for thalassemia and is not approved anywhere for that use.
Sources: Taher AT. ENERGIZE: A global, phase 3 study of mitapivat demonstrating efficacy and safety in adults with alpha- or beta-non–transfusion-dependent thalassemia. Oral presentation presented at: European Hematology Association (EHA) Hybrid Congress; June 2024; Madrid, Spain, and Virtual. Cappellini MD. ENERGIZE-T: A global, phase 3, double-blind, randomized, placebo-controlled study of mitapivat in adults with transfusion-dependent alpha- or beta thalassemia. Oral presentation presented at: 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 2024; San Diego, CA, and online.
AEs: Adverse events; TEAEs: Treatment-emergent adverse events; sNDA: supplemental New Drug Application; PDUFA: Prescription Drug User Fee Act

Initial PYRUKYND® U.S. Launch will Focus on Addressing ~65% of Thalassemia Patient Population

6,000 diagnosed adults with thalassemia in the U.S.



*Patients aged 18 years and older
Source: U.S. EHR Data Analysis
Hb: Hemoglobin

Commercial Expertise and Capabilities in Place to Deliver Strong U.S. Launch

HCP: Healthcare Professional

Sickle Cell Disease: Urgent Need for Multiple Innovative Therapies that Demonstrate Clinically Meaningful Benefits

OUR OPPORTUNITY

120-135K patients
in the U.S./EU5*

~150K patients
in GCC*

>3M patients
Worldwide*

Increased Mortality

30-year reduction in life expectancy; 48 years median survival in patients with severe sickle cell disease

Serious Morbidities

Associated with high rates of morbidities, including anemia, increased risk of infection, acute chest syndrome, and stroke

Poor Quality of Life

Significantly disrupts various aspects of life, including fatigue, emotional and financial well-being

Healthcare Resource Utilization and Cost

Economic burden driven by frequent hospitalizations, ER visits, outpatient visits, and prolonged hospital stays

*Prevalence figures
Sources: Agios internal estimates. Faro EZ, et al. Am J Prev Med. 2016;51(suppl 1):S48-S54. National Academies of Sciences, Engineering, and Medicine. Addressing Sickle Cell Disease: A Strategic Plan and Blueprint for Action. 2020. The National Academies Press. https://doi.org/10.17226/25632. Huo J. et al. Value in Health. 2018;21(suppl 2):S108. 2. Lee S, et al. Int J Gen Med. 2020:13:361-377.
EU: European Union; GCC: Gulf Cooperation Council; ER: Emergency Room

PYRUKYND® Offers Best-in-Class Opportunity in Sickle Cell Disease with Potential to Improve Anemia, Reduce VOCs and Improve How Patients Feel and Function

Phase 3 RISE UP study topline readout in late 2025; Potential U.S. launch in 2026

STUDY POPULATION	Sickle cell disease patients 16 years of age or older 200+ patients enrolled worldwide (trial enrollment completed in October 2024)
STUDY DESIGN	52-week double blind period followed by 216-week open label extension 2:1 randomization (100 mg mitapivat or placebo, BID)
TWO PRIMARY ENDPOINTS*	Hb response defined as a ≥1.0 g/dL increase in average Hb concentration from Week 24 through Week 52 compared with baseline Annualized rate of SCPCs
SECONDARY ENDPOINTS	Additional clinical efficacy measures related to anemia, hemolysis, erythropoiesis, patient-reported fatigue and pain, annualized frequency of hospitalizations for SCPCs and 6MWT

*Powering details in appendix.
PYRUKYND® is under investigation for sickle cell disease and is not approved anywhere for that use.
Source: Andemariam B. Study design of the phase 3 portion of RISE UP: A phase 2/3, randomized, double-blind, placebo-controlled study of mitapivat in patients with sickle cell disease. Poster presentation presented at: 2024 European Hematology Association (EHA) Hybrid Congress; June 2024; Madrid, Spain, and Virtual.
VOCs: Vaso-occlusive crisis; BID: Twice daily; Hb: Hemoglobin; SCPCs: sickle cell pain crises; 6MWT: 6 minute walking test

2

Progress and Diversify Key Pipeline Programs

Teonna
Living with sickle cell disease

Tebapivat (AG-946) Provides High-Growth Potential with Best- and First-in-Class Opportunities in Areas of Critical Medical Need

	PREVALENCE	MEDICAL NEED	STATUS
Lower-Risk MDS *Potential first oral therapy for lower-risk MDS-associated anemia*	~75K-80K patients in U.S./EU5	No oral therapy addresses ineffective erythropoiesis; accounts for ~70% of all MDS cases	Phase 2b study ongoing, with patient enrollment completion expected in late 2025
Sickle Cell Disease *Expand addressable patient population*	~120-135K patients in U.S./EU5	Multiple innovative therapies that demonstrate clinically meaningful benefits	Phase 1 study complete; Phase 2 patient enrollment to be initiated in mid-2025

Sources: Agios internal estimates. Greenberg PL, Tuechler H, Schanz J, et al. Revised international prognostic scoring system for myelodysplastic syndromes. Blood. 2012;120(12):2454-2465.
MDS: Myelodysplastic syndromes; EU: European Union

Early-Stage Pipeline Offers Opportunity for Advancement

	PREVALENCE	MEDICAL NEED	STATUS
Phenylketonuria *AG-181*	~35-40k patients in U.S./EU5	Left untreated can cause range of neurocognitive issues and decrease in IQ; limited treatment options	Phase 1 study in healthy volunteers ongoing
Polycythemia Vera *AG-236*	~100k patients in U.S.	Risk of thrombosis, CV events, enlarged spleen and death; Phlebotomy is standard of care	IND application filing in mid-2025

Sources: Agios internal estimates. van Wegberg et al. Orphanet Journal of Rare Diseases (2017) 12:162. Spivak JL. Myeloproliferative Neoplasms: Challenging Dogma. J Clin Med. 2024;13(22):6957. doi:10.3390/jcm13226957.
EU: European Union; CV: Cardiovascular; IND: Investigational new drug

3

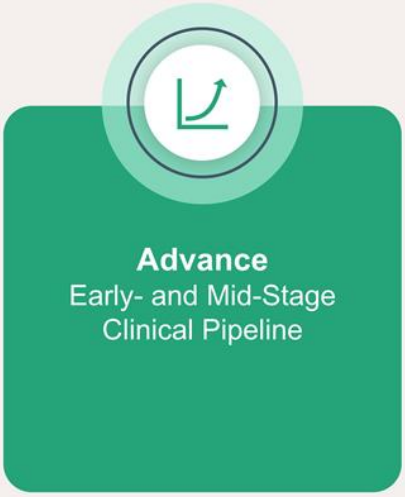
Focus Capital Deployment Priorities to Sustain Growth

Golie
Living with sickle cell disease

Delivering Significant Value Through Strategic Capital Allocation

$1.7B Cash, Cash Equivalents and Marketable Securities*

Maximize
PYRUKYND®
Thalassemia
and Sickle Cell Disease
Potential Launches



Advance
Early- and Mid-Stage
Clinical Pipeline

Expand
Pipeline with Internal
and External
Opportunities

*As of September 30, 2024

Clinical and Regulatory Near-Term Catalysts Offer Potential to Significantly Drive Shareholder Value

2025

EARLY

Pediatric PK Deficiency
PYRUKYND®
Phase 3 data readout for ACTIVATE-KIDS study

MID-YEAR

Sickle Cell Disease
Tebapivat (AG-946)
Begin patient enrollment in Phase 2 study

Polycythemia Vera
AG-236
File IND application

LATE

Thalassemia
PYRUKYND®
Potential FDA approval
(PDUFA goal date is September 7, 2025)

Sickle Cell Disease
PYRUKYND®
Phase 3 data readout for RISE UP study

Lower-Risk MDS
Tebapivat (AG-946)
Complete patient enrollment in Phase 2b study

Early: January – April; Mid-Year: May – August; End: September – December
PK deficiency: Pyruvate kinase deficiency; MDS Myelodysplastic syndromes; IND: Investigational new drug; PDUFA: Prescription Drug User Fee Act

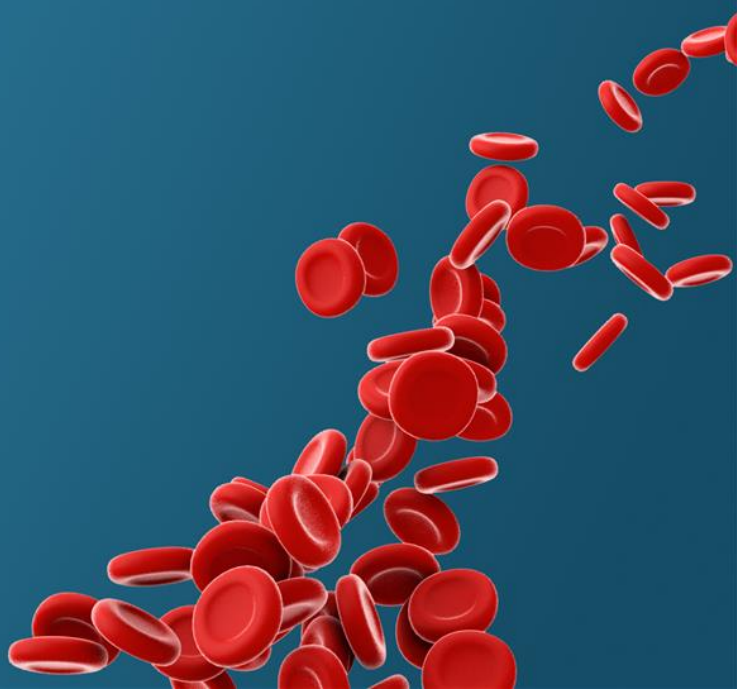
2025: Breakout Year

1. **Maximize Potential of PYRUKYND® Franchise**
2. **Progress and Diversify Key Pipeline Programs**
3. **Focus Capital Deployment Priorities to Sustain Growth**

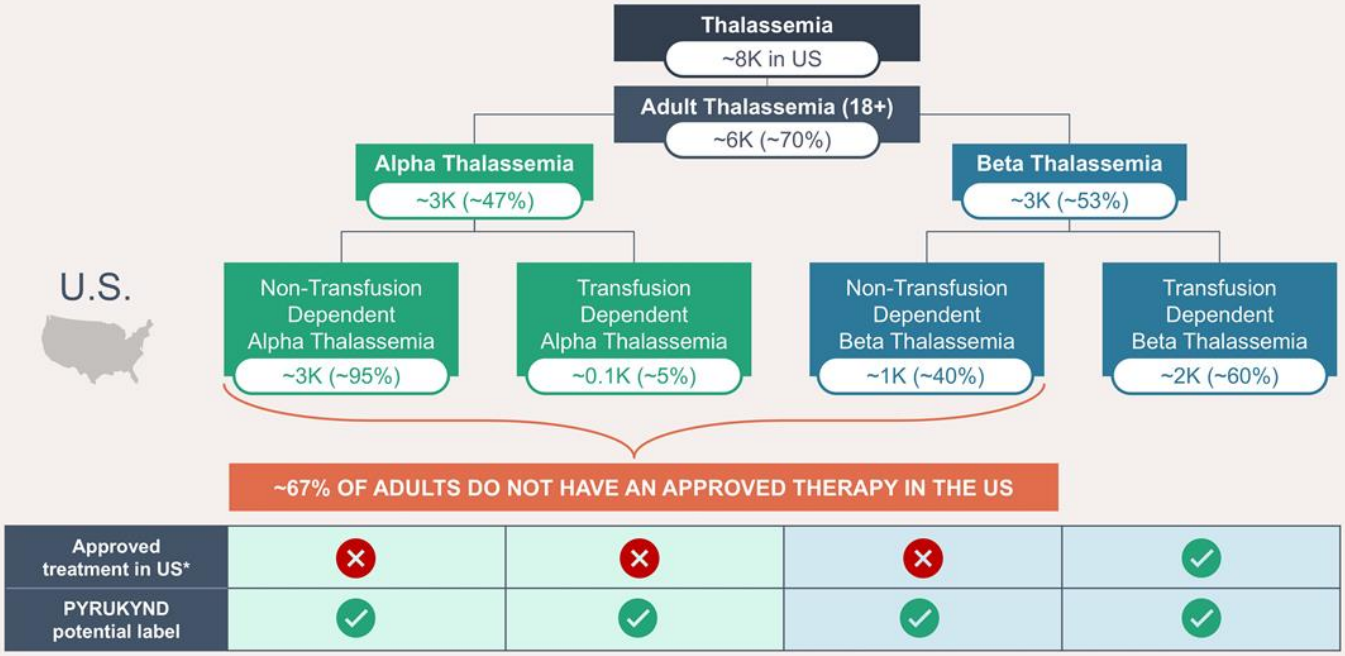
Thank you

agios

Appendix



PYRUKYND® has the Potential to Become the First and Only Therapy Approved for All Thalassemia Subtypes



Beta-THAL prevalence: HEOR Global THAL Epidemiology SLE (XCENDA, 2021); US: Paramore, et.al; Alpha-THAL prevalence: Agios internal estimates; LEK Analysis | Beta-THAL TD/NTD split (60% / 40%): Thuret, et.al., Haematologica 2010; Magnolia TPP MR, April 2020 | Alpha-THAL TD/NTD split: Taher, et.al., Vox Sanguinis, 2015; Magnolia TPP MR, April 2020.
PYRUKYND® is under investigation for thalassemia and is not approved anywhere for that use. *Note: Reblozyl also approved in non-transfusion dependent beta-thalassemia EU

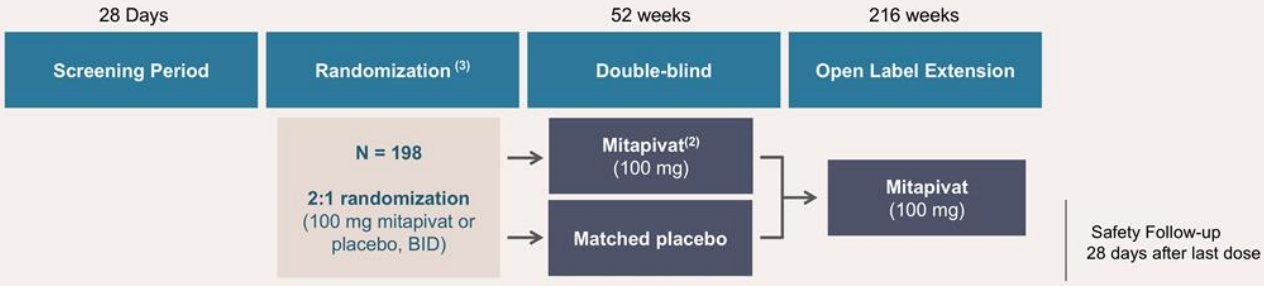
Advancing RISE UP Phase 3 Study of PYRUKYND® in Sickle Cell Disease with Expected Readout in Late 2025

RISE UP

Phase 3

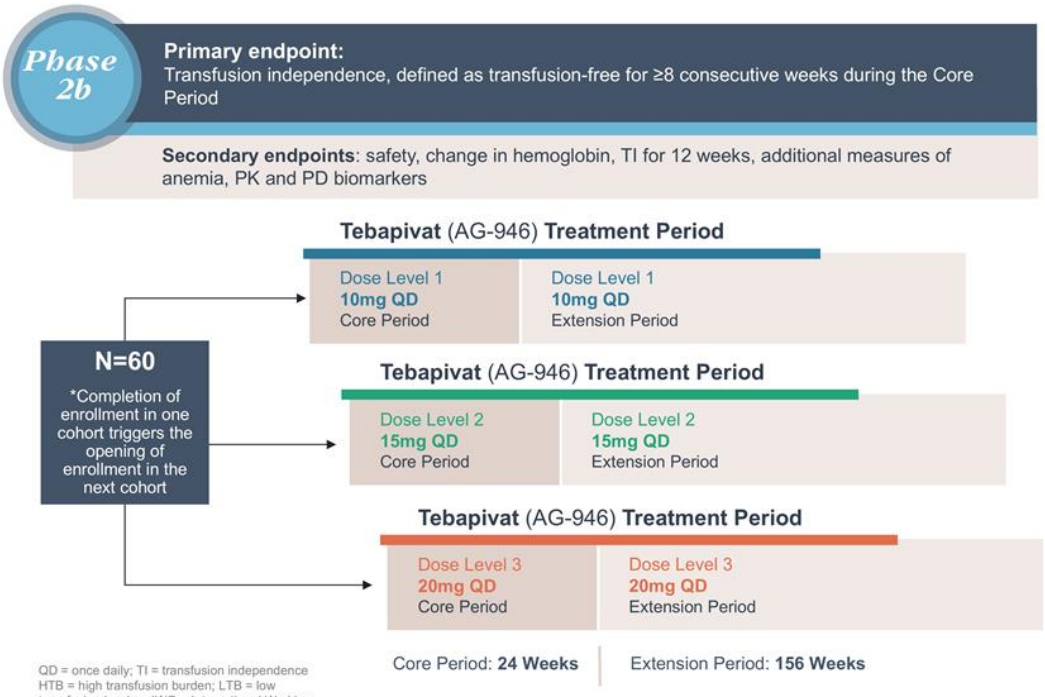
Two primary endpoints [1]:
Hb response defined as a ≥1.0 g/dL increase in average Hb concentration from Week 24 through Week 52 compared with baseline: With a planned sample size of 198 subjects there will be 91% power to detect an increase in Hb response rate from 10% in the placebo arm to 33% in the mitapivat arm based on a 2-sided significance level of 0.02

Annualized rate of SCPCs:
The sample size will also provide 90% power to detect a decrease in the annualized SCPC rate of 3 in the placebo arm to 1.95 in the mitapivat arm at a 2-sided significance level of 0.03, assuming a dropout rate of 35% with an average of 0.55-years follow up in the double-blind period, and a shape parameter of 0.2



Abbreviations: BID = twice daily; Hb = hemoglobin; SCPC = sickle cell pain crises; HU = hydroxyurea
[1] Phase 2 and phase 3 components are part of a single study/protocol; [2] Patients who receive mitapivat in the double-blind period will continue to receive the same dose of mitapivat in the open-label extension period; [3] Randomization stratification factors: Number of SCPCs in the prior year (< 5, ≥ 5), hydroxyurea use (yes, no).

Phase 2b open-label study of Tebapivat (AG-946) in lower-risk MDS (enrolling)



QD = once daily; TI = transfusion independence
HTB = high transfusion burden; LTB = low transfusion burden; IWG = International Working Group; AML = Acute myeloid leukemia

Key inclusion criteria

- ≥ 18 years of age
- Lower-risk MDS (risk score: ≤3.5) according to IPSS-R classification (WHO classification; Arber et al, 2016)
- Transfusion dependent, with LTB or HTB according to revised IWG 2018 criteria
- An Hb concentration <10.0 g/dL
- Up to 2 prior therapies, including ESAs and/or luspatercept

Key exclusion criteria

- Known history or AML or secondary MDS
- Prior exposure to a PK activator, IDH inhibitors, IST, stem cell transplant
- Currently receiving imetelstat, lenalidomide, HMAs allowed after sufficient washout period