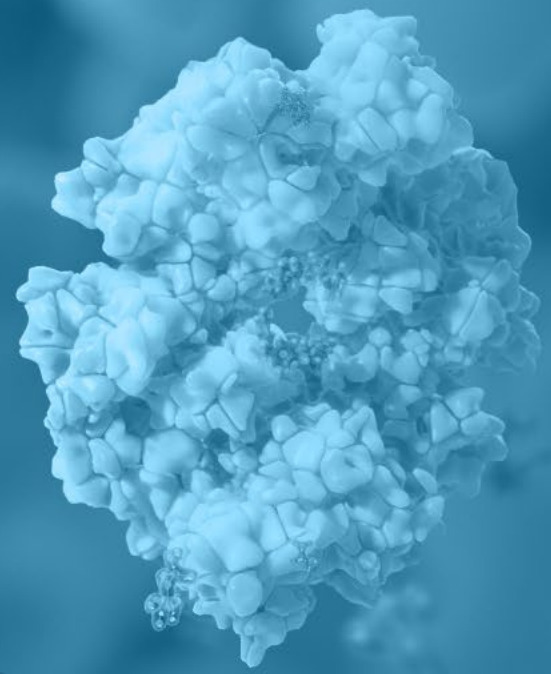
J.P. Morgan Healthcare Conference 2026



Agios Pharmaceuticals

Brian Goff, Chief Executive Officer

14 January 2026

agios

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 AQVESME™ (mitapivat) and PYRUKYND® (mitapivat); Agios' plans for future meetings with, or submissions to, regulators, including the FDA; Agios' plans for the development of mitapivat, tebapivat, AG-236 and AG-181; Agios' estimates regarding market sizes for various indications; and the potential benefits of Agios' strategic plans and focus. The words "anticipate", "estimate", "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 – positioned for a growth inflection, advancing pipeline with path to profitability

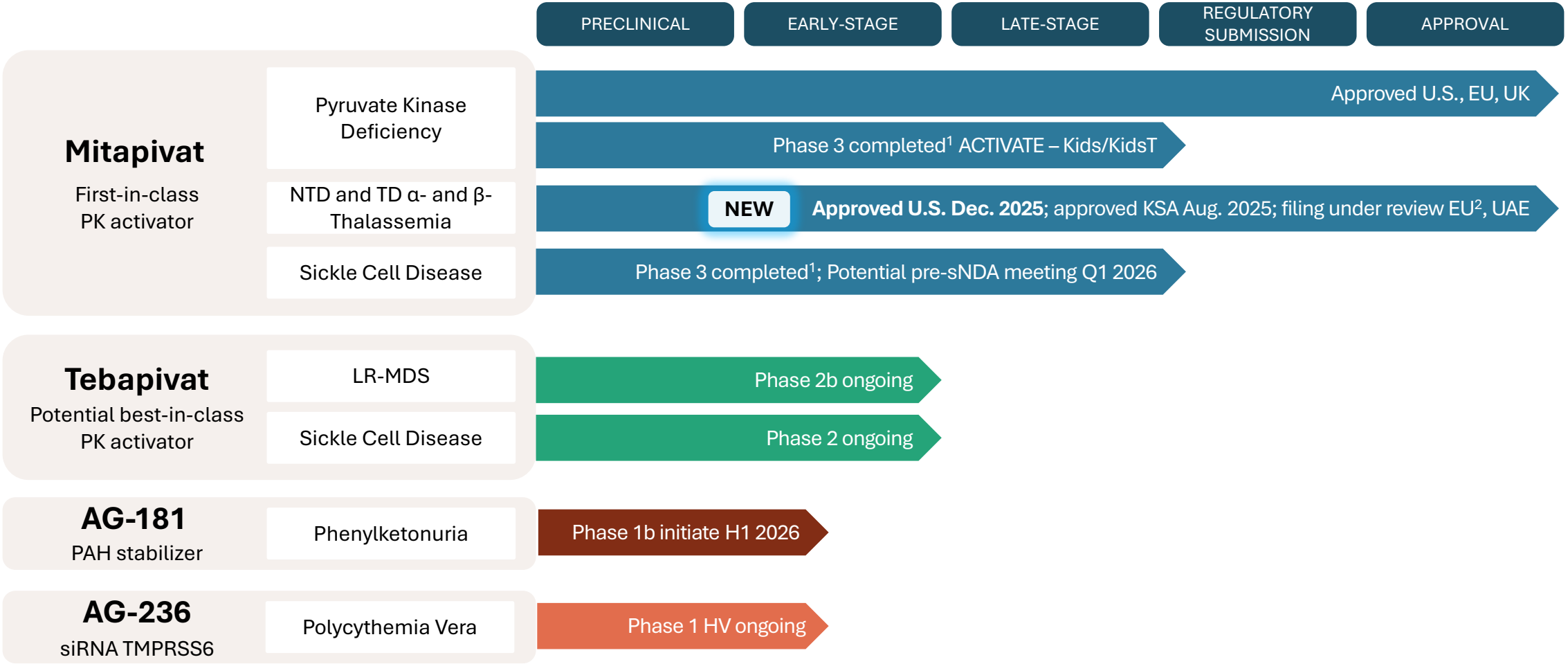
PK activator franchise as standard of care in multiple hemolytic anemias

Potential to unlock additional value with robust early and mid-stage pipeline

Clear path to **profitability** with existing commercial portfolio

Strong foundation in hematology with ambition to become sustainable rare disease company

Pipeline foundation in hematology, maturing early-stage pipeline offers potential for diversification

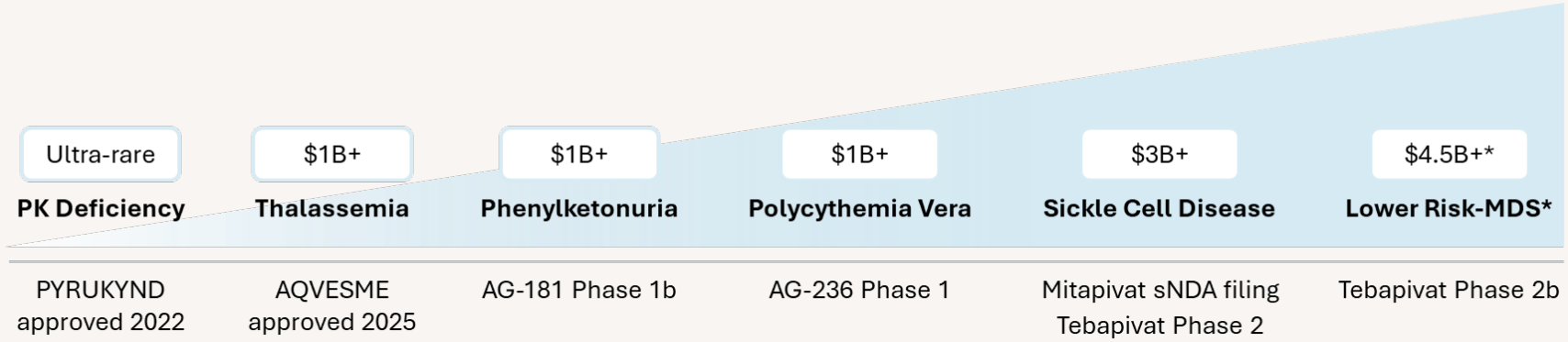


1. Defined as completion of double-blind randomized portion of the trial. 2. Positive CHMP opinion disclosed 17 October 2025. PK = pyruvate kinase; NTD = non-transfusion dependent; TD = transfusion dependent; KSA = Kingdom of Saudi Arabia; LR-MDS = lower-risk myelodysplastic syndrome; UAE = United Arab Emirates; SFDA= Saudi Food and Drug Administration; CHMP = Committee for Medicinal Products for Human Use; MAD = multiple ascending dose; PAH = Phenylalanine Hydroxylase; siRNA = small interfering RNA; TMPRSS6 = transmembrane protease serine 6; HV = healthy volunteers.

Potential to unlock significant growth with current pipeline

~$35M Net Revenues in 2025 as of Q3 in ultra-rare indication PK Deficiency

>$10B total estimated global market size for current pipeline indications by 2030*



Scalable rare disease commercial model

Dedicated field teams with deep rare disease expertise

myagios® comprehensive patient support services

Capital efficient global commercial model – EU, GCC[1]

*EvaluatePharma forecasted worldwide market value in 2030; LR-MDS represents a subset of the provided market size and prevalence is estimated ~70% of total MDS patients. 1. Agios has executed commercialization and distribution agreements with Avanzanite Bioscience in Europe and NewBridge Pharmaceuticals in GCC. PK = pyruvate kinase; sNDA = supplemental new drug application; MDS = myelodysplastic syndrome; EU = Europe; GCC = Gulf Cooperation Countries.

2026 strategic priorities – driving long-term value creation

Execute high-impact launch for AQVESME™ (mitapivat) in thalassemia

Potential to expand PK activation franchise into sickle cell disease and LR-MDS

Unlock future value in hematology and other rare disease by advancing early-stage pipeline

Ensure long-term sustainability through disciplined capital allocation and operational efficiency

PK = pyruvate kinase; LR-MDS = lower risk myelodysplastic syndrome.

Execute high impact launch for AQVESME in thalassemia

AQVESME™ (mitapivat) – now approved in U.S. with broad thalassemia label

A pyruvate kinase activator indicated for the treatment of anemia in adults with alpha- or beta-thalassemia

Only FDA approved medicine for anemia in both non-transfusion dependent and transfusion-dependent alpha- or beta-thalassemia

Aqvesme™ (mitapivat) tablets 100mg – delivering a series of “firsts” in thalassemia

- First medicine to address α- or β-thalassemia, regardless of transfusion burden
- First oral medicine
- First medicine to show quality of life improvements in NTDT patients[1]
- First medicine to show durable reduction in transfusion burden in TDT patients[2]

1. Phase 3 ENERGIZE clinical trial achieved significance on primary and key secondary endpoints; 2. Phase 3 ENERGIZE-T clinical trial achieved significance on primary and key secondary endpoints ; durable reduction in transfusion burden observed up to 36 weeks in ENERGIZE-T.

Aqvesme™ (mitapivat) tablets 100mg – ready to execute a high-impact commercial launch in the U.S.

4,000
addressable patients at launch

$425k
annual U.S. WAC for thalassemia

magios®
leading patient support services

Potential to deliver $1B global peak-year-sales across PKD and thalassemia indications

Potential to expand PK activation franchise into Sickle Cell Disease and LR-MDS

PK activation proven mechanism in hemolytic anemias

Hemolytic anemias – reduced RBC lifespan drives pathophysiology

Healthy Red Blood Cell –
120 days RBC lifespan

Hemolytic Anemias
Red Blood Cell lifespan –

- PK deficiency 20-30 days
- Thalassemia 20-30 days
- Sickle Cell Disease 10-20 days

Activating PK in glycolytic pathway improves health, energy and lifespan of RBCs

Increase ATP
to match energy needs of RBCs

Decrease 2,3-DPG
reversibly increasing oxygen affinity for Hb

Potential application in multiple hematology indications

ATP = adenosine triphosphate; DPG = diphosphoglycerate; RBC = red blood cell; PK = pyruvate kinase; Hb = hemoglobin.

Mitapivat has proven the transformative potential of PK activation in hemolytic anemias

6 positive well designed, randomized trials across 3 hemolytic anemias

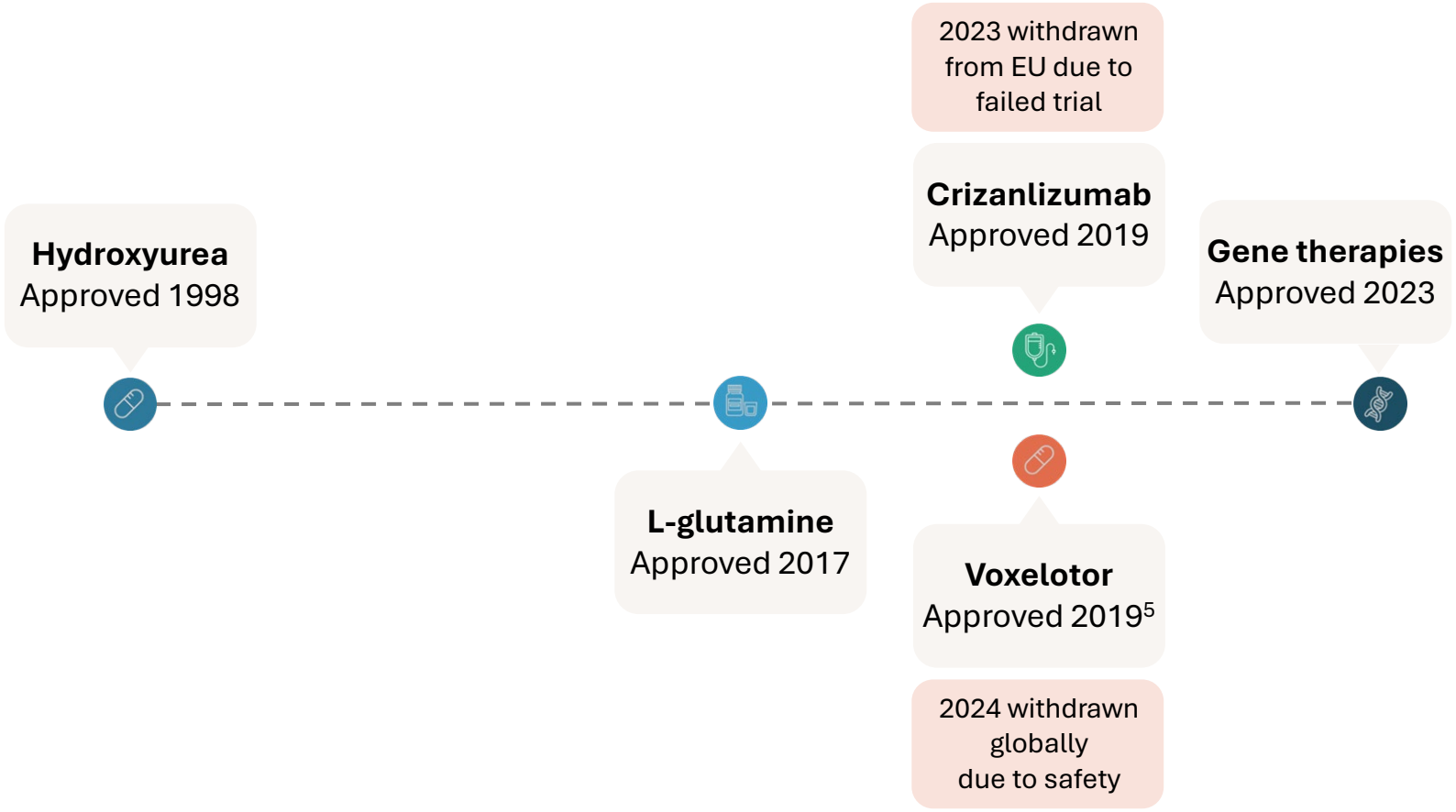
PK deficiency	Thalassemia	Sickle Cell Disease
ACTIVATE ACTIVATE-T	ENERGIZE ENERGIZE-T	Phase 2 RISE UP Phase 3 RISE UP[1]
Statistically significant increase in Hb levels, decreased hemolysis and improvements in patient reported outcomes	Statistically significant increase in Hb levels, reduction in transfusion burden – improvements in hemolysis markers and fatigue	Statistically significant increase in Hb levels, clinically meaningful benefits in Hb responders
PYRUKYND approved 2022[2]	AQVESME approved Dec 2025[2]	Phase 3 RISE UP data Q4 2025

1. Trial met primary endpoint of hemoglobin response and key secondary endpoints of change from baseline in hemoglobin concentration and indirect bilirubin; trial showed trend favoring mitapivat but did not meet statistical significance in primary endpoint of annualized rate of SCPCs (pain crises), and the key secondary endpoint of change from baseline in PROMIS Fatigue was not met. 2. Reflects date of FDA approval in U.S.

Sickle Cell Disease – significant need for novel treatments

Meaningful opportunity with lack of disease-modifying innovation

- ~100,000 diagnosed adult and pediatric patients in the U.S.[1,2]
- Lack of novel disease-modifying SCD treatment that addresses anemia and reduces SCPCs[3]
- High global mortality burden – in U.S., average age of death is <40 years old[4]



Dates presented in timeline reflect FDA regulatory approval. 1. CDC Data & statistics on sickle cell disease (Updated July 7, 2023). 2. GBD 2021 Sickle Cell Disease Collaborators. 3. Brandow AM, Llem RI. *J Hematol Oncol.* 2022; 15(20):1-13. 4. Payne AB, et al. Ann Emerg Med. 2020;76(3S):S28-S36. 5. Approved under FDA's accelerated approval program. PKa = pyruvate kinase activator; SCD = sickle cell disease; SCPC = sickle cell pain crises; PKR = pyruvate kinase R; PKM2 = pyruvate kinase M2; 2,3-DPG = 2,3- 3-diphosphoglycerate; HbS = sickle hemoglobin; ATP = Adenosine Triphosphate; RBC = Red Blood Cell.

Mitapivat – potential to expand in Sickle Cell Disease

Strong anti-hemolytic profile in total trial population with SCPC trend

- 40.6% of patients achieved Hemoglobin response (≥1 g/dL)
- Statistically significant improvement in other markers of hemolysis
  - Hemoglobin concentration
  - Indirect bilirubin

Clinically meaningful benefits in Hb-responders

- 1.6 g/dL mean increase in Hemoglobin concentration (pre-specified)
- 26% decrease in rate of SCPC
- 34% reduction in rate of SCPC hospitalizations
- Reduction in PROMIS-Fatigue T-score

Favorable safety profile

- No similar pattern of HCI as observed in thalassemia
- Low discontinuation rate in the double-blind period
- 174 out of 176 patients opted to rollover into open label extension

Anticipate pre-sNDA meeting with FDA in Q1 2026

Note: Trial met primary endpoint of hemoglobin response and key secondary endpoints of change from baseline in hemoglobin concentration and indirect bilirubin. Trial showed trend favoring mitapivat but did not meet statistical significance in primary endpoint of annualized rate of SCPCs (pain crises), and the key secondary endpoint of change from baseline in PROMIS Fatigue was not met

Tebapivat – more potent PK activator

Binds longer and stronger to PKR and PKM2 enzymes that regulate RBC energy

Reduced potential for Drug-drug interaction[1]

Improved metabolic stability – longer half-life and once-daily dosing

Potential best-in-class PKa – opportunity to deepen Hb response and expand patient reach

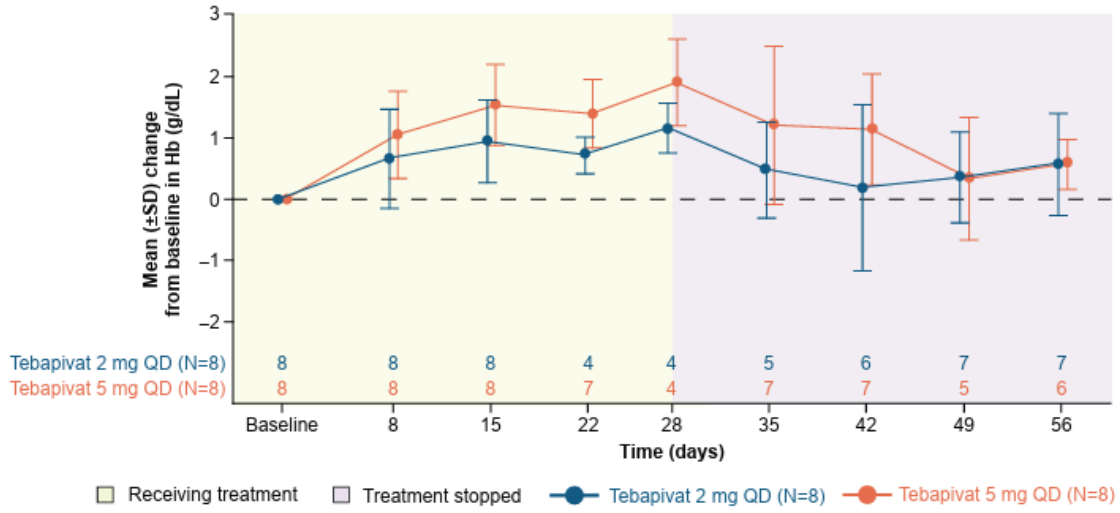
Xu JZ, Novelli EM, Ribeil J-A, et al. Results from a Phase 1 Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Tebapivat (AG-946) in Patients with Sickle Cell Disease. Blood. 2024;144(Suppl 1):2496. doi:10.1182/blood-2024-203509. 1. Based on in vitro profiling - no CYP inhibition or PXR activation. PKR = pyruvate kinase R; PKM2 = pyruvate kinase M2; RBC = red blood cell; DDI = drug-drug interaction; PKa = pyruvate kinase activator; Hb = hemoglobin.

Tebapivat – potential to show leading clinical profile in sickle cell disease

Potential to become leading PK activator in SCD

- Enhanced PK/PD profile drives increased potency
- Potential for enhanced hemoglobin response, driving clinical benefits
  - SCPC-related endpoints
  - QoL improvements
- Opportunity to reach broader patient population

Phase 1 tebapivat data demonstrates strong proof of concept in SCD



Mean change from baseline in Hb across dosing cohorts (2mg, 5mg) at Day 28:

- 1.2 g/dL increase (2mg)
- 1.9 g/dL increase (5mg)

Tebapivat Phase 2 top-line data (2.5mg, 5mg, 7.5mg) anticipated in H2 2026

Xu JZ, Novelli EM, Ribeil J-A, et al. Results from a Phase 1 Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Tebapivat (AG-946) in Patients with Sickle Cell Disease. Blood. 2024;144(Suppl 1):2496. doi:10.1182/blood-2024-203509. PK = pyruvate kinase; PK/PD = pharmacokinetics/pharmacodynamics; SCPC = sickle cell pain crises; QoL = quality of life; Hb = hemoglobin; SCD = Sickle Cell Disease.

Tebapivat – novel mechanism and oral dosing with potential for durable response

Phase 2a showed clinical PoC for tebapivat in LR-MDS

- 40% of low transfusion burden cohort achieved transfusion independence
- One patient achieved Hb response in 16-week period
- Safety consistent with Phase 1 healthy volunteer study
- Exposure lower than anticipated at 5mg; need to investigate higher doses

Ongoing open-label Phase 2b designed to test higher doses in heterogeneous patient population reflective of real world

Low or high transfusion burden

+/-

Regardless of RS status (+ or -)

2L+

≤2 prior treatments

Phase 2b (10mg, 15mg and 20mg) top-line data anticipated H1 2026

Tebapivat – high-risk, high-reward opportunity in LR-MDS

LR-MDS = lower risk myelodysplastic syndrome; PoC = proof of concept; Hb = hemoglobin; RS = ring sideroblasts.

Drive future growth with diversified rare disease pipeline

Expanding in hematology – AG-236 for Polycythemia Vera

100K diagnosed in U.S.

35% phlebotomy dependent

Currently approved treatments consist of phlebotomy, HU, cytoreductive therapies

Treatment goal – better hematocrit control and well tolerated

AG-236 – GalNAc siRNA-based TMPRSS6 inhibitor targeting iron homeostasis regulation

Q6M dosing – maintenance of effect

GalNAc siRNA has well characterized immunogenicity profile

No titration, single dose strength drives to maximum effect

Potential to show differentiated profile with applications in other iron dysregulation indications

Phase 1 HV data in H1 2026

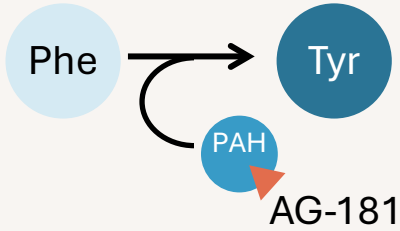
HU = hydroxyurea; GalNAc = N-acetylgalactosamine; siRNA = small interfering RNA; Q6M = every 6 months; HV = healthy volunteer.

Diversification beyond hematology – AG-181 for PKU

Significant opportunity to transform treatment of PKU

- PKU caused by dysfunctional PAH enzyme
- ~15-20k PKU patients in the U.S.
- Only ~1/6 patients are on active treatment
- Majority of patients rely on diet modification alone

AG-181 novel mechanism of action



AG-181 is a chaperone of PAH – selectively binds and stabilizes enzyme to enhance and restore function

AG-181 unique attributes

- Oral medicine targeting classical Phenylketonuria
- Potential fast onset and durable response – no titration
- Potential for improved safety and tolerability
- Novel mechanism enables potential combinability

Anticipate first patient dosed in Phase 1b proof of mechanism trial in H1 2026 with results in H2 2026

PKU = Phenylketonuria; PAH = Phenylalanine Hydroxylase; Phe = Phenylalanine; PoM = Proof of Mechanism; Tyr = Tyrosine.

Financial discipline to achieve growth and long-term sustainability

Financial discipline to deliver long-term sustainability

Anticipate Operating Expenses in 2026 to be flat compared to 2025 with potential for greater efficiencies beyond 2026[1]

- Maximize launch of AQVESME in thalassemia
- Gated investment for Sickle Cell Disease
- Operating model refinement

Clear path to profitability based on thalassemia and PK deficiency alone[2]

1. Does not include potential business development activities or one-time costs. 2. Non-GAAP. As of September 30, 2025, Agios reported approximately $1.3 billion in cash, cash equivalents and marketable securities.

Agios – Transforming for tomorrow

2025 in review – continued track record for execution

EARLY

Pediatric PK Deficiency
PYRUKYND
Phase 3 readout ACTIVATE-Kids

MID-YEAR

Sickle Cell Disease
tebapivat
Initiate enrollment in Phase 2 trial

Polycythemia Vera
AG-236
File IND application

LATE

Thalassemia
AQVESME™ (mitapivat)
FDA approval

Sickle Cell Disease
mitapivat
Phase 3 readout RISE UP trial

Lower-Risk MDS
tebapivat
Complete enrollment in Phase 2b trial

PK = pyruvate kinase; IND = investigational new drug; FDA = Food and Drug Administration; PDUFA = Prescription Drug User Fee Act.

2026 strategic priorities – driving long-term value creation

Execute high impact launch for AQVESME (mitapivat) in thalassemia

Potential to expand PK activation franchise into sickle cell disease and LR-MDS

Unlock future value in hematology and other rare disease by advancing early-stage pipeline

Ensure long-term sustainability through disciplined capital allocation and operational efficiency

PK = pyruvate kinase; LR-MDS = lower risk myelodysplastic syndrome.

2026 catalysts reinforce hemolytic anemia leadership and rare disease pipeline potential

H1 2026

Sickle Cell Disease
Mitapivat
Pre-sNDA meeting Q1

Lower-Risk MDS
tebapivat
Phase 2b topline data

Polycythemia Vera
AG-236 (TMPRSS6)
Phase 1 HV topline data

H2 2026

Sickle Cell Disease
tebapivat
Phase 2 topline data

Phenylketonuria
AG-181 (PAH stabilizer)
Phase 1b PoM data

AQVESME (mitapivat) U.S. launch underway in thalassemia

sNDA = supplemental new drug application; MDS = myelodysplastic syndrome; TMPRSS6 = transmembrane protease, serine 6; HV = healthy volunteer; PAH = phenylalanine hydroxylase; PoM = proof of mechanism.

Appendix

Appendix – AQVESME is first-and-only PK activator indicated for use in adult thalassemia patients

Indication statement	AQVESME is indicated for the treatment of anemia in adults with alpha- or beta-thalassemia
Mechanism of action	Pyruvate kinase activator that allosterically binds to the pyruvate kinase tetramer and increases pyruvate kinase activity
Dosage and administration	Tablets: 100 mg orally twice daily

For full prescribing information, visit www.aqvesme.com

Appendix – AQVESME REMS for liver monitoring

Warnings and Precautions Label Language

During the double-blind period, 2 of 301 patients (0.66%) with thalassemia treated with AQVESME experienced adverse reactions suggestive of hepatocellular injury. Three additional patients experienced adverse reactions suggestive of hepatocellular injury during the open-label extension periods after switching from placebo to AQVESME. Of these 5 patients, two had serious liver injury and were hospitalized including 1 patient who developed jaundice (peak bilirubin 32 mg/dL). Another patient developed jaundice (peak bilirubin 4 mg/dL) without being hospitalized. These reactions were characterized by a time to onset within the first 6 months of treatment with peak elevations of alanine aminotransferase of >5×ULN with or without jaundice. All patients discontinued treatment with AQVESME, and these reactions improved upon treatment discontinuation.

REMS Monitoring

- Prescriber, patient and pharmacy education and certification
- Liver testing every 4 weeks for the first 24 weeks of treatment
- After 24 weeks, liver testing as clinically indicated

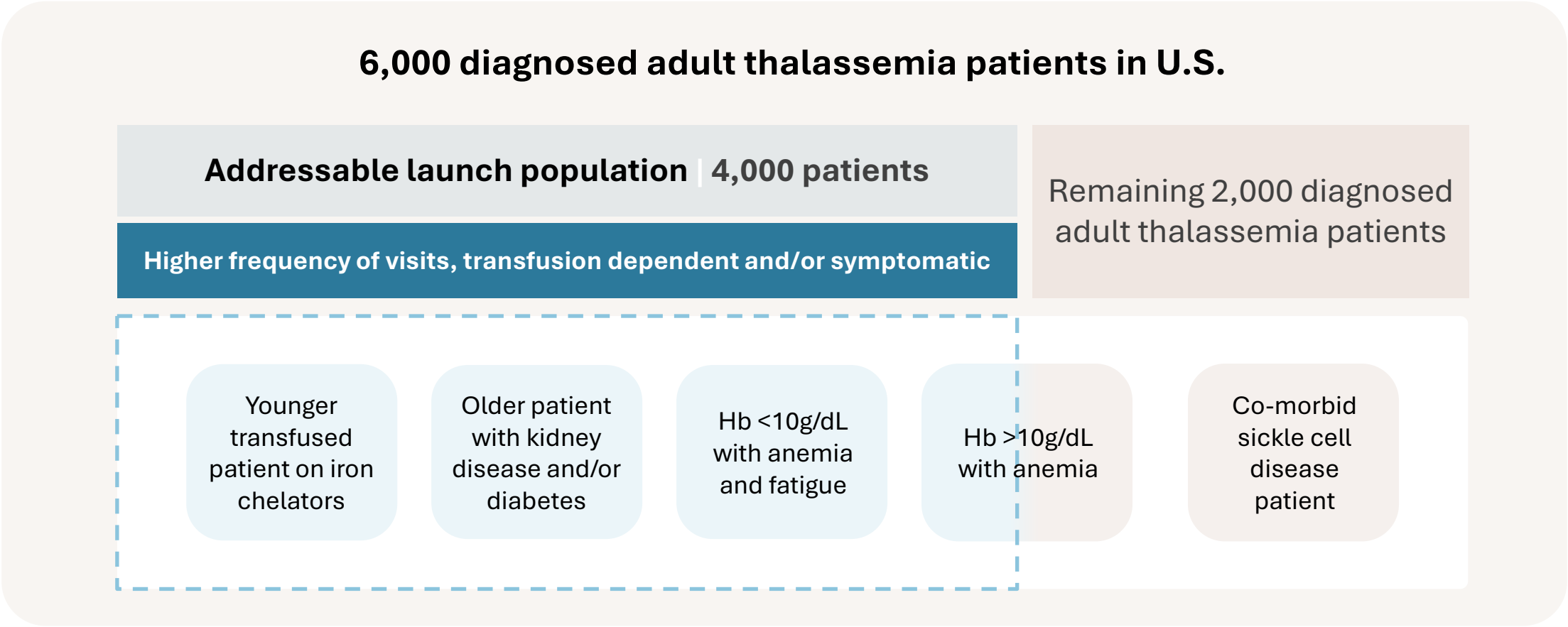
BOXED WARNING – HEPATOCELLULAR INJURY – AQVESME can cause serious hepatocellular injury. Measure liver laboratory tests (ALT, AST, alkaline phosphatase and total bilirubin with fractionation) at baseline and every 4 weeks for 24 weeks and then as clinically indicated. Avoid use of AQVESME in patients with cirrhosis. Discontinue AQVESME if hepatic injury is suspected.

For full prescribing information, visit www.aqvesme.com

1. Obtain liver tests (including ALT, AST, alkaline phosphatase, total bilirubin with fractionation) prior to the initiation of AQVESME, then every 4 weeks for the first 24 weeks, and as clinically indicated thereafter. Interrupt AQVESME if clinically significant increases in liver tests are observed or alanine aminotransferase is >5 times the upper limit of normal (ULN). Complete a comprehensive evaluation to rule out other causes of liver injury when drug-induced liver injury is suspected. Discontinue AQVESME if hepatocellular injury due to AQVESME is suspected.

REMS = risk evaluation and mitigation strategy

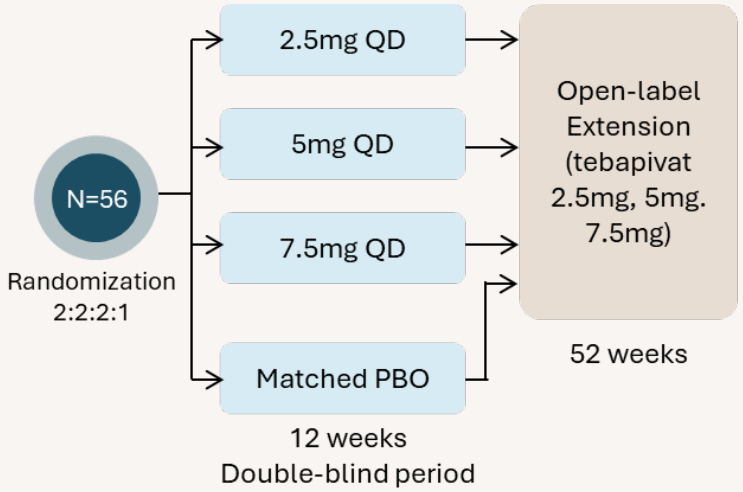
Appendix – AQVESME availability in late January



Hb = hemoglobin.

Appendix – tebapivat Phase 2 Sickle Cell Disease trial

Tebapivat Phase 2 trial for Sickle Cell Disease[1]



Phase 2 topline data expected H2 2026

Key Inclusion Criteria

- Hb ≥5.5 - ≤10.5 g/dL
- HU use permitted, if dose has been stable for at least 90 days before randomization[2]

Key Exclusion Criteria

- >10 SCPCs in the past 12 months
- Receiving treatment with voxelotor, crizanlizumab, L-glutamine, or hematopoietic stimulating agents within 90 days before randomization

Primary Endpoint

- Hb response[3] at baseline, and from Weeks 10 - 12

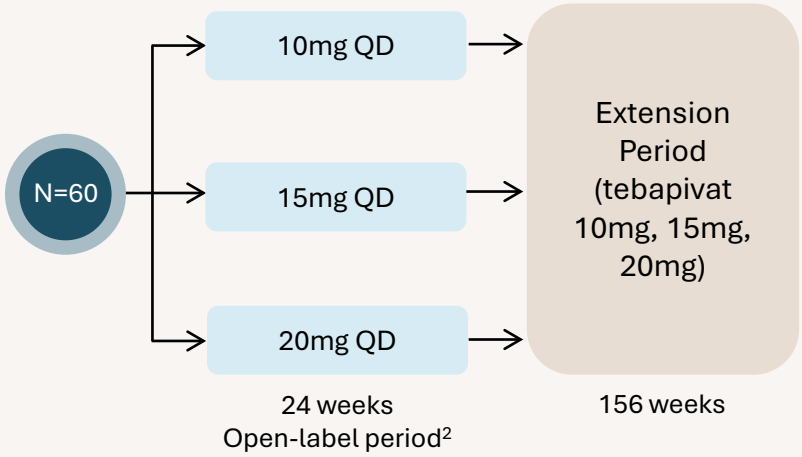
Secondary Endpoints

- Average change from baseline in Hb concentration
- Average change from baseline in markers of hemolysis and erythropoiesis
- PROs: PROMIS Fatigue, PROMIS Pain, ASCQ-Me
- Safety

1. Full study details, including participation criteria and study plan can be found at clinicaltrials.gov NCT06924970; 2. Discontinuation of hydroxyurea requires a 90-day washout before providing informed consent; 3. Hb response defined as ≥1.0g/dL increase in hb from Weeks 10-12. Hb = hemoglobin; HU = hydroxyurea.

Appendix – tebapivat Phase 2 Lower Risk-MDS trial

Tebapivat Phase 2b trial for LR-MDS[1]



Phase 2b topline data expected H1 2026

Key Inclusion Criteria

- Lower-risk MDS[3]
- Transfusion dependent[4]
- Hb <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, iMiDs, HMAs

Primary Endpoint

- Proportion of participants with transfusion independence[5] during the core period

Secondary Endpoints

- Change in hemoglobin
- Transfusion independence for 12 weeks
- Additional measures of anemia
- PK/PD biomarkers
- Safety

1. Full trial details, including participation criteria and study plan, can be found at clinicaltrials.gov NCT05490446; 2. Enrollment completion of one cohort triggers opening of enrollment in the next cohort; 3. Risk score: ≤3.5 according to IPSS-R classification (WHO classification; Arber et al, 2016); 4. LTB or HTB according to revised IWG 2018 criteria; 5. Transfusion independence defined as transfusion-free for ≥8 consecutive weeks during core period.