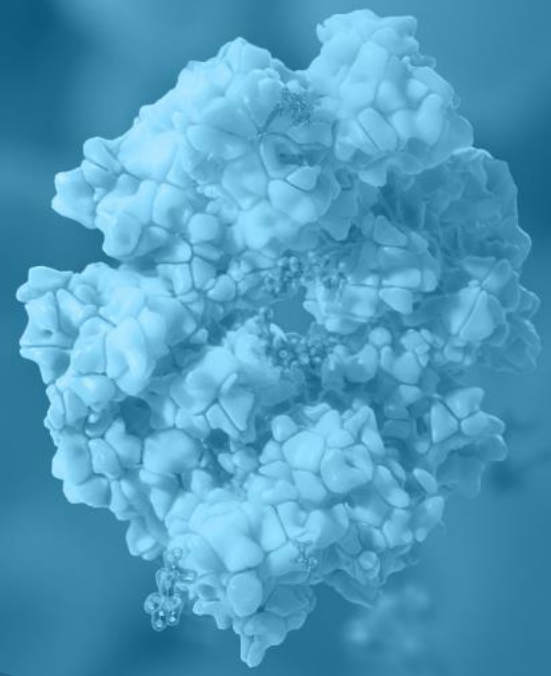
AQVESME™ (mitapivat) FDA Approval

Conference call for investors and analysts

23 December 2025



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; 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.

Agenda – AQVESME™ (mitapivat) FDA Approval

1	**Introduction**	Morgan Sanford, VP Investor Relations
2	**CEO Opening Remarks**	Brian Goff, Chief Executive Officer
3	**Thalassemia overview, clinical data and AQVESME label**	Sarah Gheuens, MD, PhD, Chief Medical Officer, Head of R&D
4	**Commercial launch**	Tsveta Milanova, Chief Commercial Officer
5	**CEO Closing Remarks and Q&A**	

CEO Opening Remarks

Brian Goff, Chief Executive Officer

AQVESME – now approved in the U.S. with broad 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

Please see Important Safety Information and full Prescribing Information at www.aqvesme.com

AQVESME – 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 show durable reduction in transfusion burden in TDT patients[2]

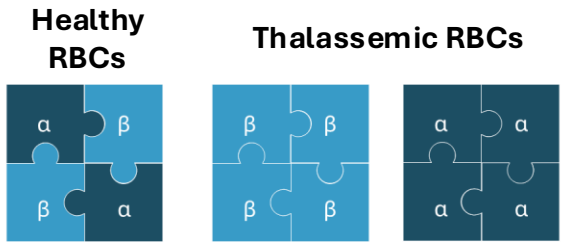
1. Phase 3 ENERGIZE clinical trial achieved significance on primary and key secondary endpoints; 2. Phase 3 ENERGIZE-T clinical trial achieved significance on primary and key secondary endpoints

Thalassemia overview, clinical data and AQVESME label

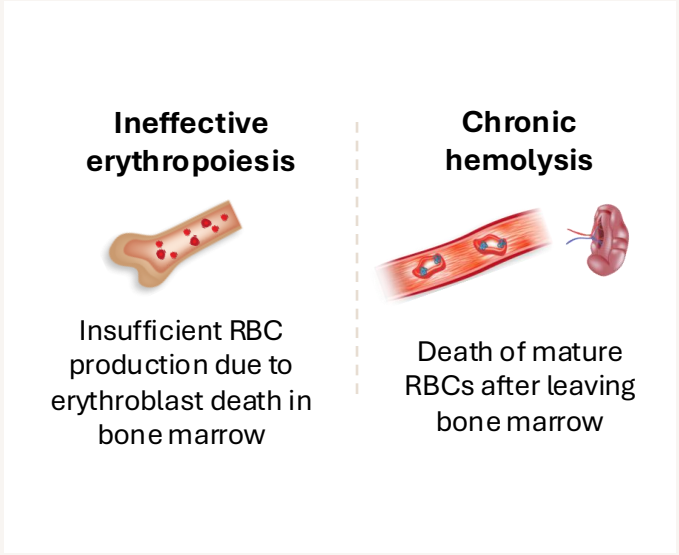
Sarah Gheuens, MD, PhD

Thalassemia is a devastating hemolytic anemia that drives increased morbidity

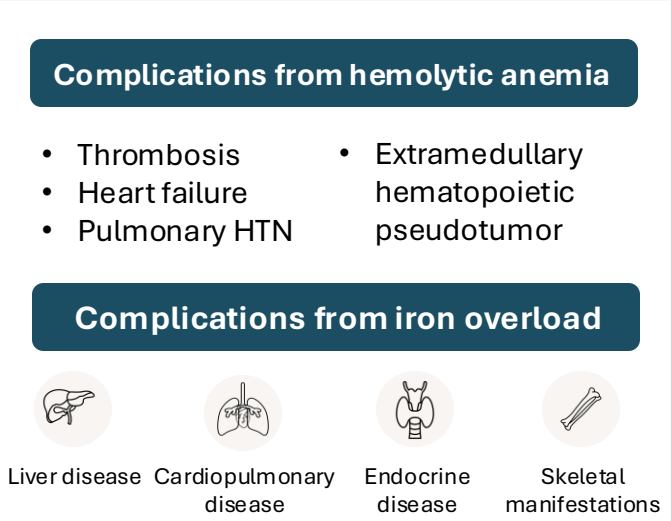
Genetic mutations cause imbalanced α- or β-globin chains



Cell damage leads to ineffective erythropoiesis (IE) and hemolysis



Hemolysis and IE cause chronic anemia and iron overload



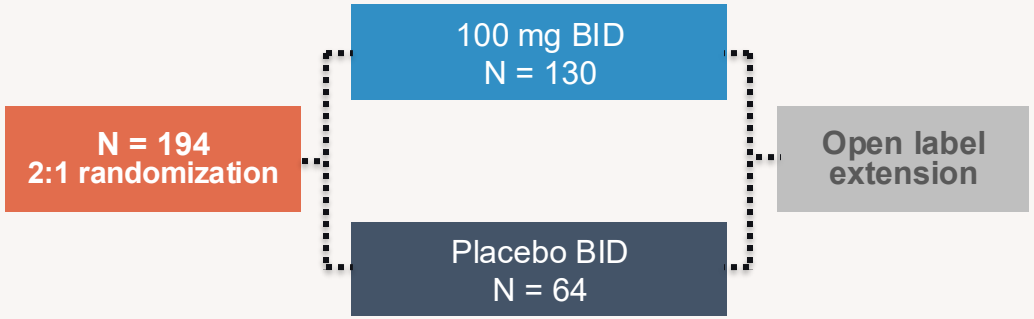
RBC = red blood cell; HTN = hypertension

Until now, no approved medicines to treat broad thalassemia population

TD β-thalassemia	 IV transfusion	 Oral chelators	 Luspatercept	 Gene therapy
	Secondary iron overload	Compliance and tolerability concern	Requires in-office administration	Requires intensive conditioning
NTD β-thalassemia	No disease-modifying treatments available in the U.S. – occasional transfusion and chelation			
NTD or TD α-thalassemia	No approved medicines for the treatment of α-thalassemia			

AQVESME approval based on results from two, global Phase 3 trials

ENERGIZE | Non-transfusion dependent



Primary endpoint

- Mean Hb increase (≥ 1g/dl)

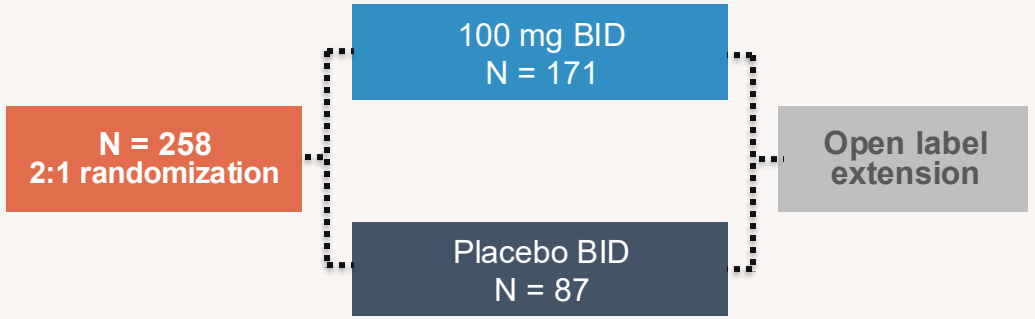
Secondary endpoint

- Fatigue, other measures of Hb increase, hemolysis, PROs, iron metabolism, safety, PK/PD

Key inclusion criteria

- ≥ 18 years
- β- or α-thalassemia
- Non-transfusion-dependent
- Hb ≤ 10.0 g/dL

ENERGIZE-T | Transfusion dependent



Primary endpoint

- 50% reduction in transfusion burden in any 12-wk period

Secondary endpoint

- Additional measures of transfusion reduction, safety, PK/PD

Key inclusion criteria

- ≥ 18 years
- β- or α-thalassemia
- Transfusion-dependent

Hb = hemoglobin; PRO = patient reported outcome

AQVESME showed statistically significant improvement in Hb and fatigue in non-transfusion dependent patients

42.3%

achieved primary endpoint of Hb response[1]

1.56 g/dL average change from baseline in Hb concentration

AQVESME showed statistically significant improvement in FACIT-Fatigue score

AQVESME showed statistically significant improvement in average Hb concentration

Other secondary endpoints – Improvement in markers of hemolysis (indirect bilirubin, LDH) also observed in mitapivat arm

1.≥1g/dL in average Hb concentration week 12 through 24 compared to baseline
FACIT = Functional Assessment of Chronic Illness Therapy; LDH = lactate dehydrogenase

AQVESME showed reduction in transfusion burden in transfusion-dependent patients

30.4%

of patients achieved primary endpoint of Transfusion Reduction Response (TRR)[1]

Statistically significant reductions in transfusion burden demonstrated on all key secondary endpoints

13.5%	achieved TRR2 vs placebo – defined as a ≥50% reduction in transfused RBC units in any consecutive 24-week period through week 48 vs baseline
14.6%	achieved TRR3 vs placebo – defined as a ≥33% reduction in transfused RBC units from week 13 through week 48 compared with baseline
7.6%	achieved TRR4 vs placebo – defined as a ≥50% reduction in transfused RBC units from week 13 through week 48 compared with baseline

Higher proportion of patients in mitapivat arm achieved transfusion independence[2] (9.9%) vs Placebo (1.1%)

1. TRR defined as a ≥50% reduction in transfused RBC units and a reduction of ≥2 units of transfused RBCs in any consecutive 12-week period through week 48 compared with baseline. 2. Transfusion independence defined as transfusion-free for ≥8 consecutive weeks through Week 48 in the double-blind period

ENERGIZE/ENERGIZE-T – adverse reactions[1] in patients with α- and β-thalassemia receiving AQVESME

	ENERGIZE		ENERGIZE-T		Total	
Most frequent (≥10%) TEAEs	**AQVESME (n=129)**	**Placebo (n=63)**	**AQVESME (n=172)**	**Placebo (n=85)**	**AQVESME (n=301)**	**Placebo (n=148)**
Headache	22.5%	9.5%	26.7%	11.8%	24.9%	10.8%
Insomnia[2]	27.1%	7.9%	22.1%	9.4%	24.3%	8.8%

1. Included adverse reactions that occurred in at least 5% of patients in the AQVESME arm and at least 5% higher than the placebo arm. 2. Term includes initial insomnia, middle insomnia and terminal insomnia.
TEAE = treatment-emergent adverse event; URTI = upper respiratory tract infection

AQVESME – 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

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
- Baseline liver test
- 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.

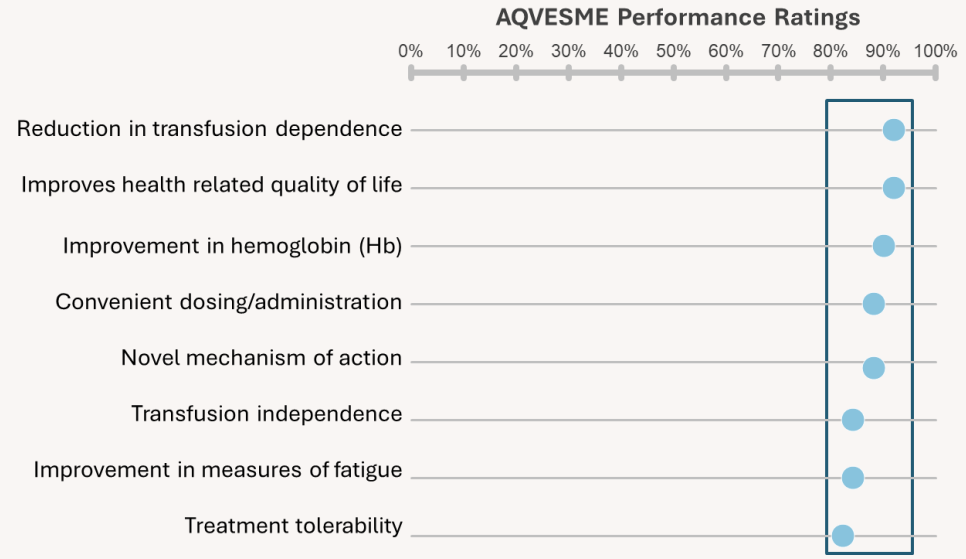
REMS = risk evaluation and mitigation strategy

AQVESME
U.S. commercial launch

Tsveta Milanova
Chief Commercial Officer

AQVESME highly anticipated by treating physicians; REMS not viewed as significant prescribing burden

Treating physicians rated AQVESME favorably on key attributes of a novel thalassemia therapy[1]



86% of surveyed HCPs plan to prescribe AQVESME within 6 months of availability based on clinical profile[2]

Anticipate more gradual rate of REMS certification for HCPs in community setting

Academic setting

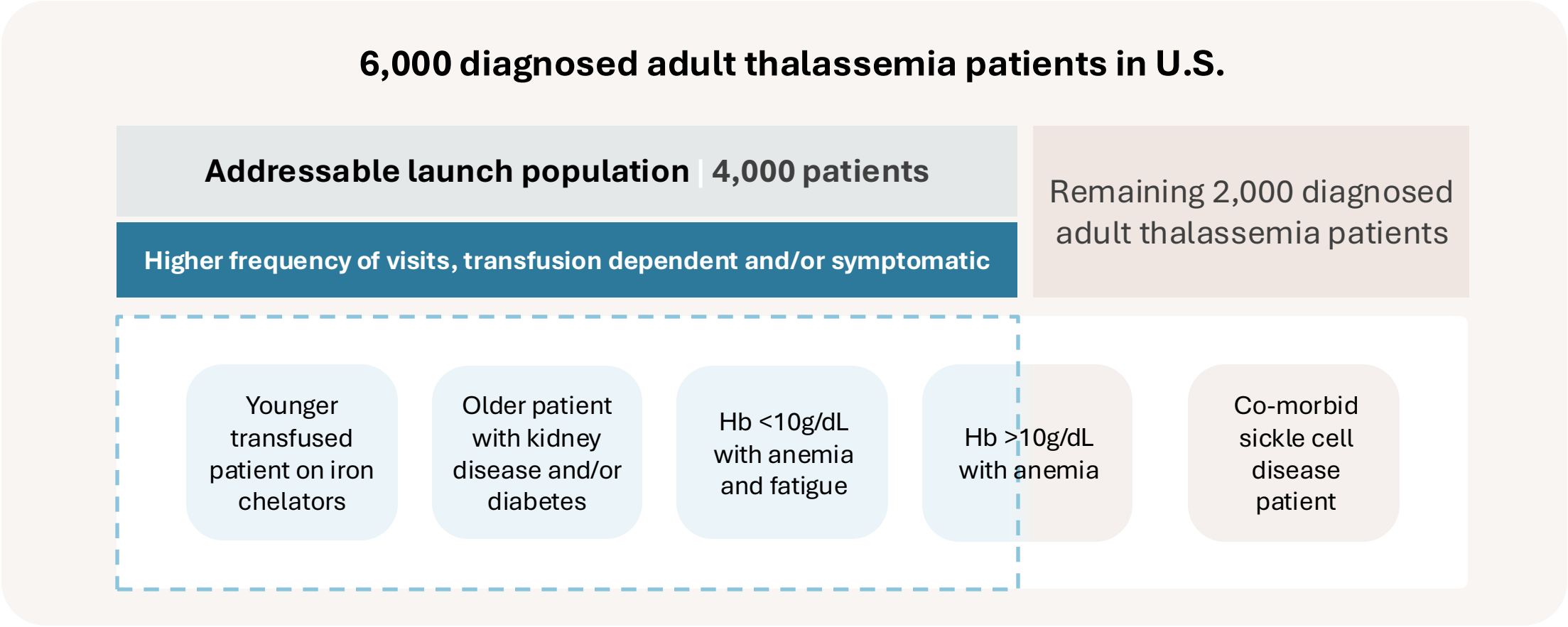
KOLs do not view REMS as barrier to prescribing behavior[3]

Community setting

- **94%** of surveyed Hem/Oncs have REMS experience[3]
- **~2/3** of surveyed HCPs indicate no to minor impact from REMS at launch[3,4]

1. Third party demand research on file (July 2024). 2. Agios market research and HAS insights, reflects engagement with top treating physician targets prior to FDA REMS request (2024 – 2025). 3. Agios market research and HAS insights, reflects engagement with top treating physician targets (2024 – 2025). 4. **No impact**: will treat as soon as approved, **Minor impact**: may slow initial patient starts. HCP = healthcare practitioner includes Hematologist-Oncologist and Hematologists; TD = transfusion dependent; NTD = non-transfusion dependent; Hem/Oncs = Hematologist Oncologist; Q4W = every 4 weeks; Q3-6M = every 3 to 6 months; HAS = Hemolytic Anemia Specialist.

U.S. represents largest commercial opportunity, driven by favorable market dynamics and defined patient population



Source: US EHR Data Analysis

Deliver successful launch of AQVESME in thalassemia

Drive **prescriber and patient awareness** based on strong value proposition

Deliver **operational excellence** with REMS program

Establish AQVESME as **standard of care** in thalassemia

Experienced sales reps, market access team, and myAgios support streamline the process from prescription to REMS enrollment and treatment initiation

Key AQVESME thalassemia launch dynamics in the U.S.

REMS Requirements

- Physician, patient and pharmacy certification
- Baseline liver test, monthly monitoring for first 6 months
- REMS fully operational in late January

Early Launch Dynamics

- Initial demand gated by HCP REMS onboarding and frequency of patient visits
- Time between start form and treatment initiation

Patient mix evolution

- Short-term mix favors transfusion-dependent
- Longer-term favors NTD patients, represent 2/3 of the total population

AQVESME – potential to become standard of care for broad thalassemia patient population

Delivering on a series of "firsts" in the treatment of 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 show durable reduction in transfusion burden in TDT patients[2]

Ready to deliver high-impact commercial launch

4,000
addressable patients at launch

$425k
annual U.S. WAC for thalassemia

myagios®
leading patient support services

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

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
QoL = quality of life; PKD = pyruvate kinase deficiency

CEO Closing Remarks

Brian Goff, Chief Executive Officer

Clear corporate priorities

Maximize mitapivat

Thalassemia FDA approval

Preparation for potential sNDA filing in Sickle Cell Disease

Advance pipeline

Tebapivat Phase 2 LR-MDS and SCD

AG-236 Phase 1 PV

AG-181 Phase 1 PKU

Financial discipline

Remain committed to maximize shareholder value

Proactive steps to reduce operating expenses to extend cash runway; update to be provided early 2026

Remain committed to becoming sustainable rare disease company

PDUFA = Prescription Drug User Fee Act ; sNDA = supplemental new drug application ; SCD = sickle cell disease; LR-MDS = lower-risk myelodysplastic syndromes; PV = polycythemia vera; PKU = phenylketonuria.

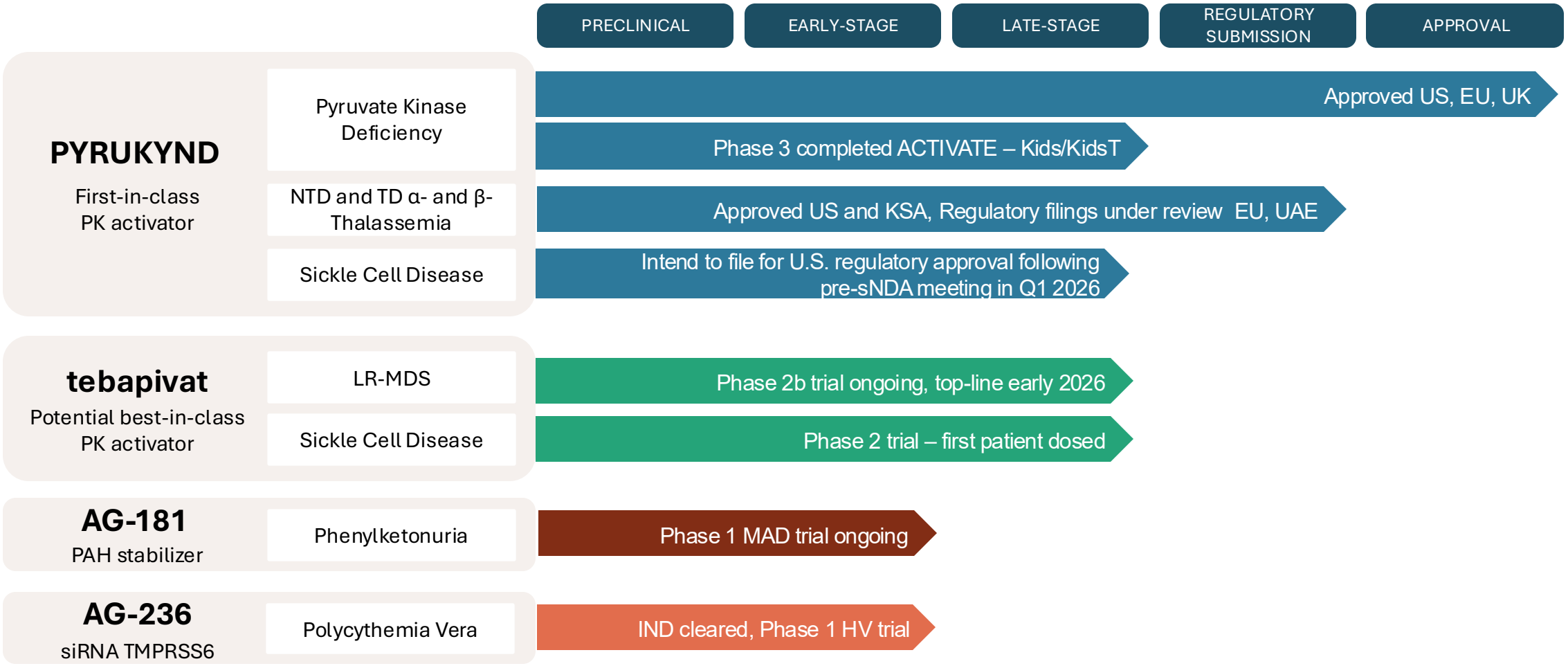
Q&A session

Appendix

APPENDIX – thalassemia capital-efficient commercial model

	United States	GCC	Europe
Regulatory status	Approved in United States	Approved in Saudi Arabia; Under review in UAE	Positive CHMP Opinion; EC decision early 2026
Addressable population	6,000 diagnosed adult patients 4,000 initial target launch	70,000 estimated prevalence Smaller % target launch	Majority of prevalence aligned with Mediterranean region
Commercial dynamics	$425,000 WAC price 10-20% estimated GTN range	Procurement agreement ~1-2 years; broad access with institutional agreements	Country-by-country launch aligned with prevalence
Commercialization strategy	Agios Commercialization	NewBridge Pharmaceuticals	Avanzanite Bioscience

APPENDIX – Agios rare disease pipeline



PK = pyruvate kinase; NTD = non-transfusion dependent; TD = transfusion dependent; LR-MDS = low-risk Myelodysplastic Syndrome; KSA = Kingdom of Saudi Arabia; UAE = United Arab Emirates; MAD = multiple ascending dose; PAH = Phenylalanine Hydroxylase; siRNA = small interfering RNA; TMPRSS6 = transmembrane protease serine 6.