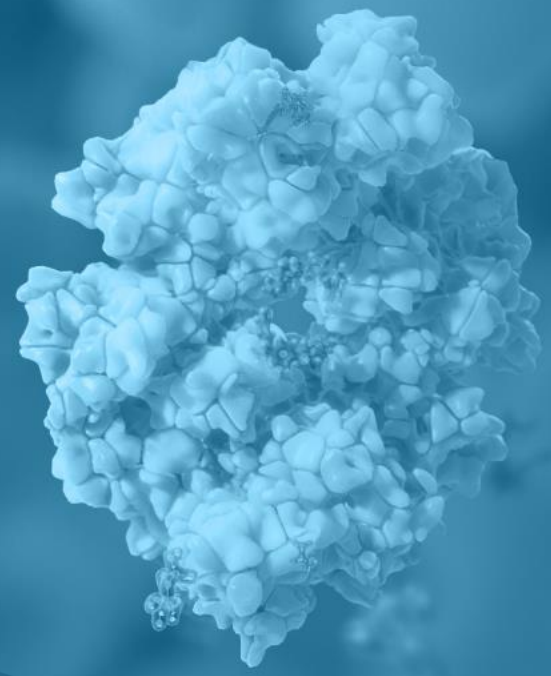
Q3 2025 Financial Results and Business Highlights

Conference call for investors and analysts

October 30, 2025



agios

Forward Looking Statements

This presentation and various remarks we make during this presentation 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-236 and AG-181; Agios' plans, strategies and expectations for its preclinical, clinical and commercial advancement of its drug development, including PYRUKYND®, tebapivat, AG-236 and AG-181; Agios' expectations for the review of marketing applications for PYRUKYND by regulatory agencies, including the FDA and European Commission; 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," "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.

Q3 2025 earnings call agenda

1	**Introduction**	Morgan Sanford, VP Investor Relations
2	**CEO Opening Remarks**	Brian Goff, Chief Executive Officer
3	**Financial Results**	Cecilia Jones, Chief Financial Officer
4	**Commercial Highlights**	Tsveta Milanova, Chief Commercial Officer
5	**R&D Highlights**	Sarah Gheuens, MD, PhD, Chief Medical Officer, Head of R&D
6	**CEO Closing Remarks and Q&A**	

CEO Opening Remarks

Brian Goff, Chief Executive Officer

Unlocking sustainable growth to deliver shareholder value

PYRUKYND® – de-risked multi-billion opportunity

- Robust Phase 2 or 3 data shown across PKD, thalassemia and SCD

Accelerating near-term high-value catalysts

- PYRUKYND PDUFA – thalassemia
- PYRUKYND Phase 3 – SCD
- tebapivat Phase 2b data – LR-MDS

Strong financial position, strategic capital allocation

- $1.3B cash on hand
- Pipeline expansion and BD to fuel long-term growth

PKD = pyruvate kinase deficiency; SCD = sickle cell disease; PDUFA = Prescription Drug User Fee Act; LR-MDS = lower-risk myelodysplastic syndrome; BD = business development.

Q3 2025 - continued portfolio and pipeline delivery[1]

Strong financial position

$12.9M net revenues
+44% vs $9.0M in Q3 2024

$1.3B cash[2] on hand
to invest behind potential U.S. launches and pipeline

Global thalassemia regulatory actions

PYRUKYND SFDA approval in Saudi for thalassemia

Positive CHMP opinion in Europe for thalassemia

Pipeline momentum

Enrollment complete in tebapivat Phase 2b trial for lower-risk MDS
top-line data anticipated in early 2026

Strong momentum into multiple high-value catalysts before year-end 2025

1. Since second quarter results announcement, 31 July 2025. 2. Cash, cash equivalents and marketable securities. SFDA = Saudi Food and Drug Authority; CHMP = Committee for Medicinal Products for Human Use; MDS = myelodysplastic syndrome

Financial Results

Cecilia Jones, Chief Financial Officer

Q3 2025 Financial Results

Statement of Operations	Q3 2025	Q3 2024
PYRUKYND Net Revenue	$12.9M	$9.0M
Cost of Sales	$1.7M	$0.8M
Research & Development Expense	$86.8M	$72.5M
Selling, General & Administrative Expense	$41.3M	$38.5M
Net (Loss) Income[1]	($103.4M)	$947.9M

Balance Sheet	Q3 2025	Q4 2024
Cash, Cash Equivalents and Marketable Securities	$1.3B	$1.5B

1. Three months ended September 30,2024 included $889.1M gain on sale of contingent payments and $200M milestone payment from gain on sale of oncology business.

Strong balance sheet, disciplined capital allocation strategy

1 **Capital efficient global commercial build out**

2 **Strategic investment to advance novel pipeline**

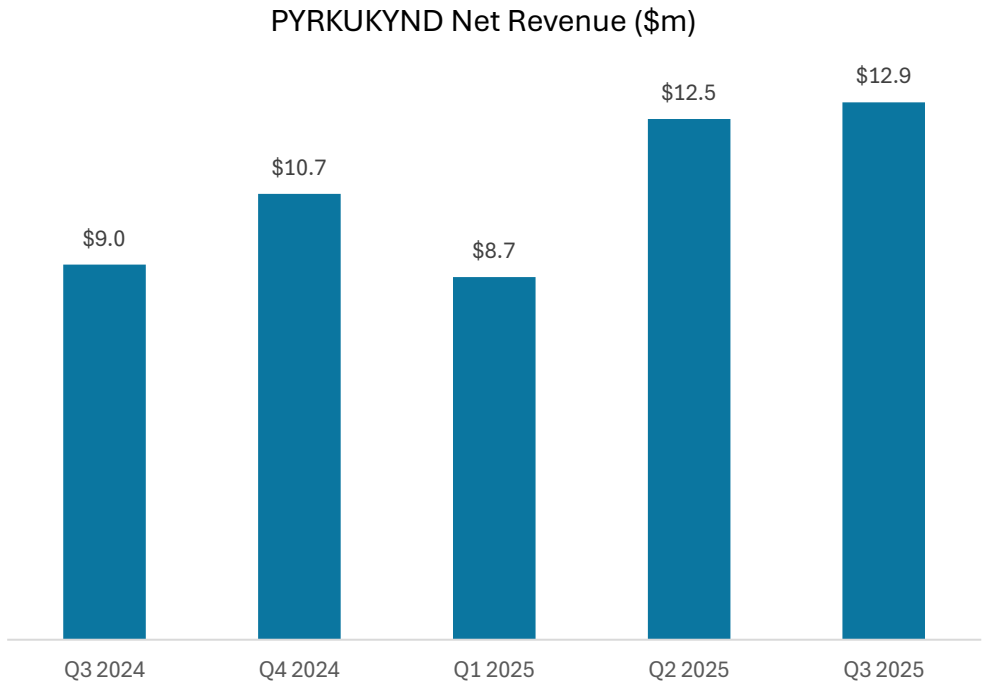
3 **Value-enhancing pipeline expansion**

Well-capitalized to execute on commercial portfolio and development pipeline

Commercial Highlights

Tsveta Milanova, Chief Commercial Officer

PYRUKYND – continued demand in Q3 2025



Quarter-on-quarter variability driven by GTN, ordering patterns and inventory dynamics related to specialty distribution

Key Performance Metrics

$12.9M net sales of PYRUKYND
compared with $12.5M in Q2 2025 and $9.0M in Q3 2024

262 unique PK deficiency patients
completed prescription enrollment forms since launch in U.S.[1]

149 net patients on treatment in U.S.
including new prescriptions and treatment continuations[2]

227 unique prescribers in U.S.

GTN = Gross to Net. 1. Cumulative since PYRUKYND launch. 2. As of end of Q3 2025.

Thalassemia – capital-efficient commercial build-out

United States

New PDUFA goal date December 7th

Launch preparation ongoing

Agios-led commercialization

GCC

SFDA approval in Saudi Arabia announced August 4th

Launch underway; patient access granted on a case-by-case basis

NewBridge partnership

Europe

Positive CHMP opinion October 16th; expected EC decision early 2026

Launch preparation ongoing

Avanzanite Bio partnership

PDUFA = Prescription Drug User Fee Act; GCC = Gulf Cooperation Council; SFDA = Saudi Food and Drug Authority; CHMP = Committee for Medicinal Products for Human Use; EC = European Commission.

Recent engagement reinforces market readiness following potential PYRUKYND approval

Robust engagement with thalassemia community reinforces launch preparedness and market understanding

Disease prevalence	Roughly 6,000 diagnosed adult thalassemia patients in the U.S.		
Treatment goals	Address anemia and hemolysis	Enhance quality of life	Reduce risk of comorbidities
Treatment sites	Patients are treated in both academic centers and the community setting		

Strong feedback and receptivity from recent community engagement

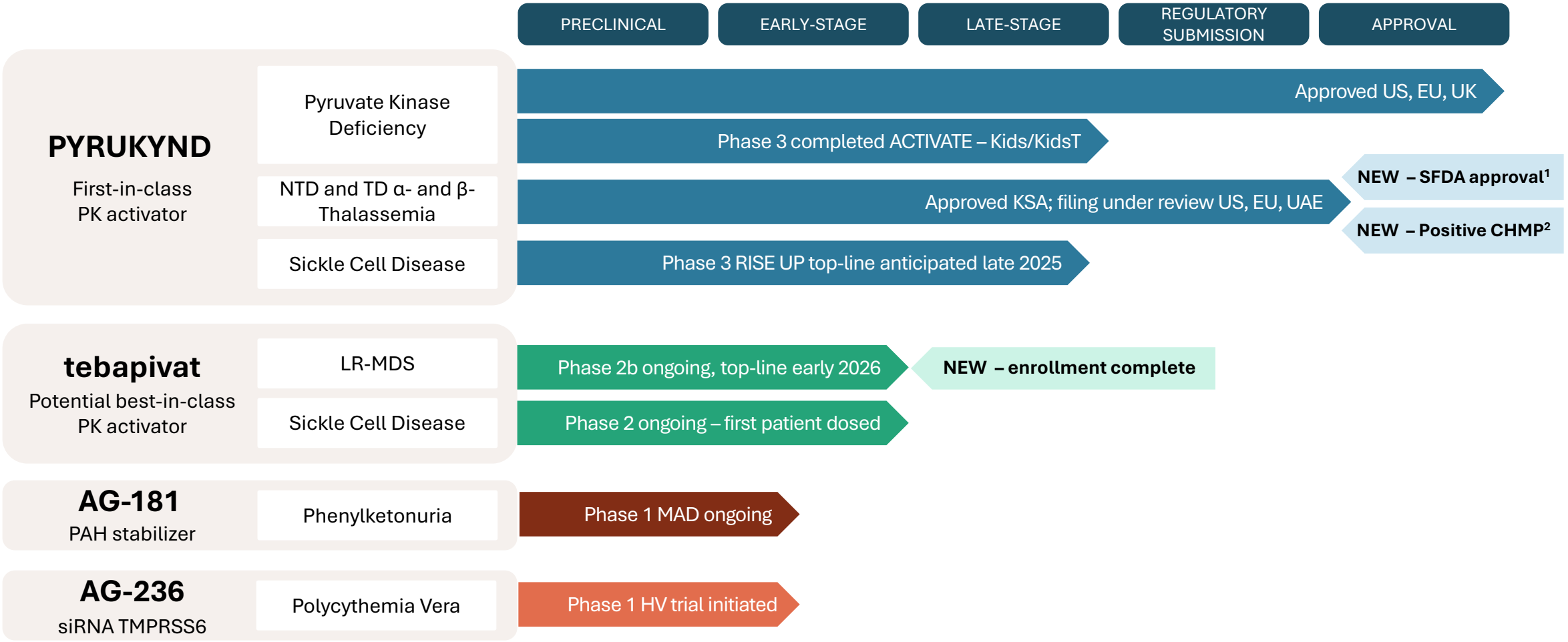
- Strong provider recognition of clear and compelling potential of PYRUKYND
- REMS familiarity across academic and community treatment settings

REMS = risk evaluation and mitigation strategy

R&D Highlights

Sarah Gheuens, MD, PhD,
Chief Medical Officer, Head of R&D

Continued pipeline momentum in Q3 2025



1. SFDA PYRUKYND approval for adult thalassemia patients announced 04 August 2025. 2. CHMP positive opinion announced 17 October 2025, recommending PYRUKYND approval in adults for the treatment of anemia associated with transfusion-dependent and non-transfusion-dependent alpha- or beta-thalassemia. 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 best-in-class oral PK activator franchise for SCD

Significant need for novel treatment options

~100,000 adult and ped patients diagnosed in the U.S.[1,2]

Lack of novel disease modifying SCD treatment that **both** address anemia and reduces SCPCs[3]

High global mortality burden – in U.S., average age of death for SCD patients is <40 years old[4]

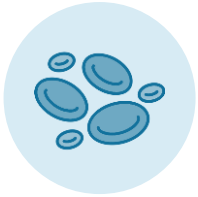
PYRUKYND and tebapivat - novel dual PK activation

- 2,3-DPG decrease reduces HbS polymerization and RBC sickling
- ATP increase improves RBC energy metabolism and membrane integrity

Mitapivat – potential first-in-class oral medicine for SCD; **tebapivat** – more potent, once-daily oral follow-on

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. 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.

PYRUKYND Phase 3 RISE UP trial designed to meet clinical needs of sickle cell disease community [1]

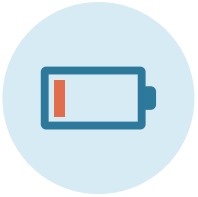


Hb increase

Directly addresses chronic anemia, reducing organ damage and increasing QoL

Annualized SCPC

SCPC linked to organ dysfunction, early mortality, and QoL



Fatigue

Baseline HRQOL comparable to diseases including cancer or cystic fibrosis[2]

Phase 3 primary and key secondary endpoints aligned with clinical needs and phenotypic features of SCD

1. Enrollment in the Phase 3 RISE UP trial for PYRUKYND in Sickle Cell Disease completed in October 2024. 2. Kato GJ, et al. *Nat Rev Dis Primers*. 2018;4:18010. Hb = hemoglobin; QoL = quality of life; SCPC = sickle cell pain crises; HRQOL= Health Related Quality of Life.

PYRUKYND Phase 3 data in SCD on track for late 2025[1]

Phase 3
RISE UP

Operationally seamless RISE UP Phase 2/3 trial

Two primary endpoints[2]:

Hb response rate[3]

- Defined as ≥1.0 g/dL increase in average Hb concentration from week 24 through week 52 vs baseline
- Planned sample size 198 with 91% power to detect increase in Hb response from 10% in PBO vs 33% in mitapivat arm
- 2-sided significance level of 0.02

Annualized rate of SCPCs

- Planned sample size 198 with 90% power to detect decrease in SCPC rate of 3 in PBO vs 1.95 in mitapivat arm
- 2-sided significance level of 0.03
- Dropout rate of 35%, average 0.55-years follow-up in double-blind period
- Shape parameter of 0.2

Key secondary endpoints, including:

Improvement in PROMIS Fatigue – fatigue is a prevalent symptom impacting daily life

RISE UP trial designed to allow multiple pathways to clinically meaningful profile

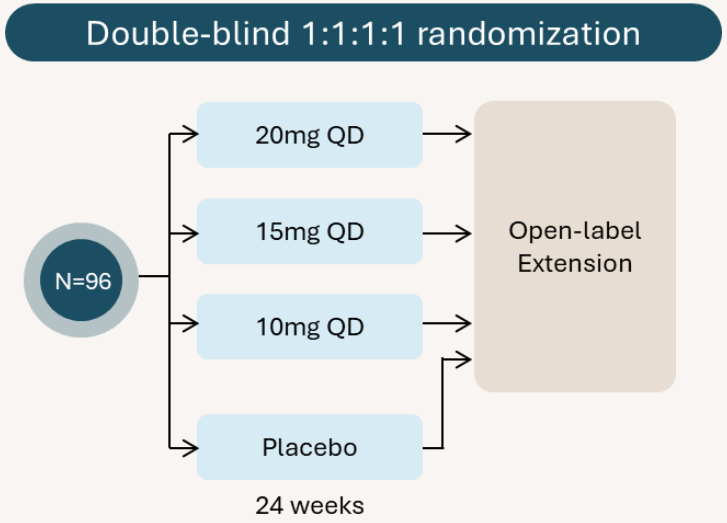
1. Enrollment in the Phase 3 RISE UP trial for PYRUKYND in Sickle Cell Disease completed in October 2024. 2. Trial success is defined by a statistically significant result in at least one of the two, dual primary endpoints.
3. Hb response defined as ≥1.0 g/dL increase in average Hb concentration from Week 24 through Week 52 compared with baseline. SCD = sickle cell disease, PBO = placebo, SCPC = sickle cell pain crises.

Tebapivat – more potent, once-daily PK activator

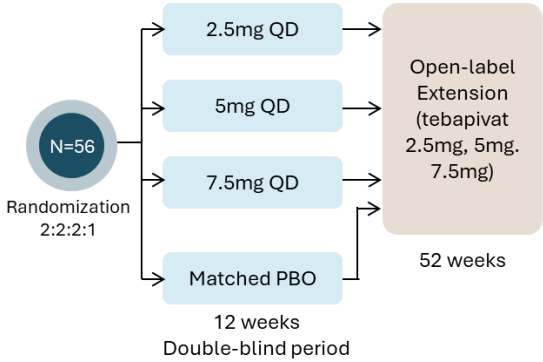
Phase 2b trial ongoing for the treatment of LR-MDS

LR-MDS >70% of MDS cases; treatment goal to improve quality of life by addressing symptomatic anemia

Tebapivat – potential first oral medicine to address ineffective erythropoiesis



Phase 2 trial ongoing for the treatment of SCD



- More potent PKa than mitapivat
- Once-daily, lower dose

Enrollment complete in Phase 2b LR-MDS trial

Potential to improve clinical profile[1]

1. Relative to clinical profile demonstrated by mitapivat across clinical program, including Phase 3 RISE UP trial with topline data anticipated by year-end 2025. PK = pyruvate kinase; LR-MDS = lower-risk myelodysplastic syndrome; QD = once-daily; SCD = sickle cell disease; PKa = pyruvate kinase activator; PBO = placebo.

Diversifying our early pipeline with AG-181 and AG-236

	AG-181 Phenylketonuria	**AG-236** Polycythemia Vera
Mechanism of Action	Small molecule PAH stabilizer – selectively binds and stabilizes PAH enzyme	siRNA targeting TMPRSS6 – selectively inhibits TMPRSS6 enzyme to improve iron metabolism
Unmet need	Safe and tolerable medicine that treats spectrum of PKU patients, especially severe	Disease-modifying treatment delivering Hct levels below 45% to reduce thrombotic events and improve quality of life
Development stage	Phase 1 HV MAD trial ongoing	Phase 1 HV SAD trial ongoing

PAH = Phenylalanine hydroxylase; PKU = phenylketonuria; MAD = multiple ascending dose; siRNA = small interfering RNA; TMPRSS6 =Transmembrane Protease, Serine 6; Hct = hematocrit; HV = healthy volunteer; SAD = single ascending dose.

CEO Closing Remarks

Brian Goff, Chief Executive Officer

Strong execution against corporate priorities for 2025

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
PYRUKYND
Potential FDA approval
(Extended PDUFA goal date December 7th)

Sickle Cell Disease
PYRUKYND
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.

Agios – foundation to deliver innovation and long-term growth

Seasoned leadership team with diverse rare disease experience

Innovative delivery fueled by connection to drive delivery of novel medicines

Focused capital allocation well-capitalized to fund U.S. launches and pipeline

Mid-to-late stage PKa franchise

PYRUKYND (mitapivat)	tebapivat
PK Deficiency	LR-MDS
Thalassemia	Sickle Cell Disease
Sickle Cell Disease	

Early-stage pipeline

AG-181 (PAH stabilizer)	AG-236 (siRNA TMPRSS6)
Phenylketonuria	Polycythemia Vera

Advancing a diversified rare disease portfolio across broad range of indications with foundation in hematology

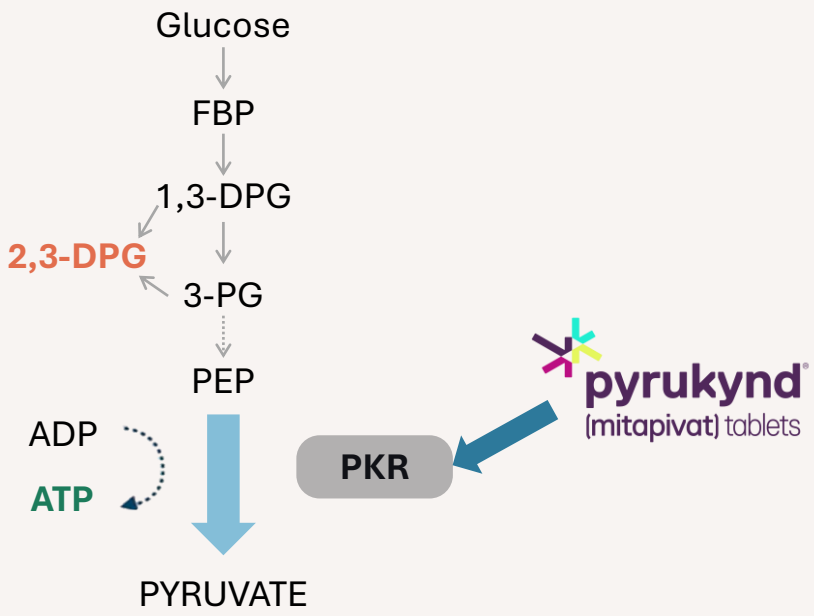
PKa = pyruvate kinase activator; LR-MDS = lower-risk myelodysplastic syndrome; PAH = phenylalanine hydroxylase; siRNA = small interfering RNA; TMPRSS6 = transmembrane protease, serine 6.

Q&A session

Appendix

Appendix – PYRUKYND MoA in sickle cell disease

Glycolytic pathway



PYRUKYND (mitapivat) novel pan-PK activation

PKR
Improves overall RBC health

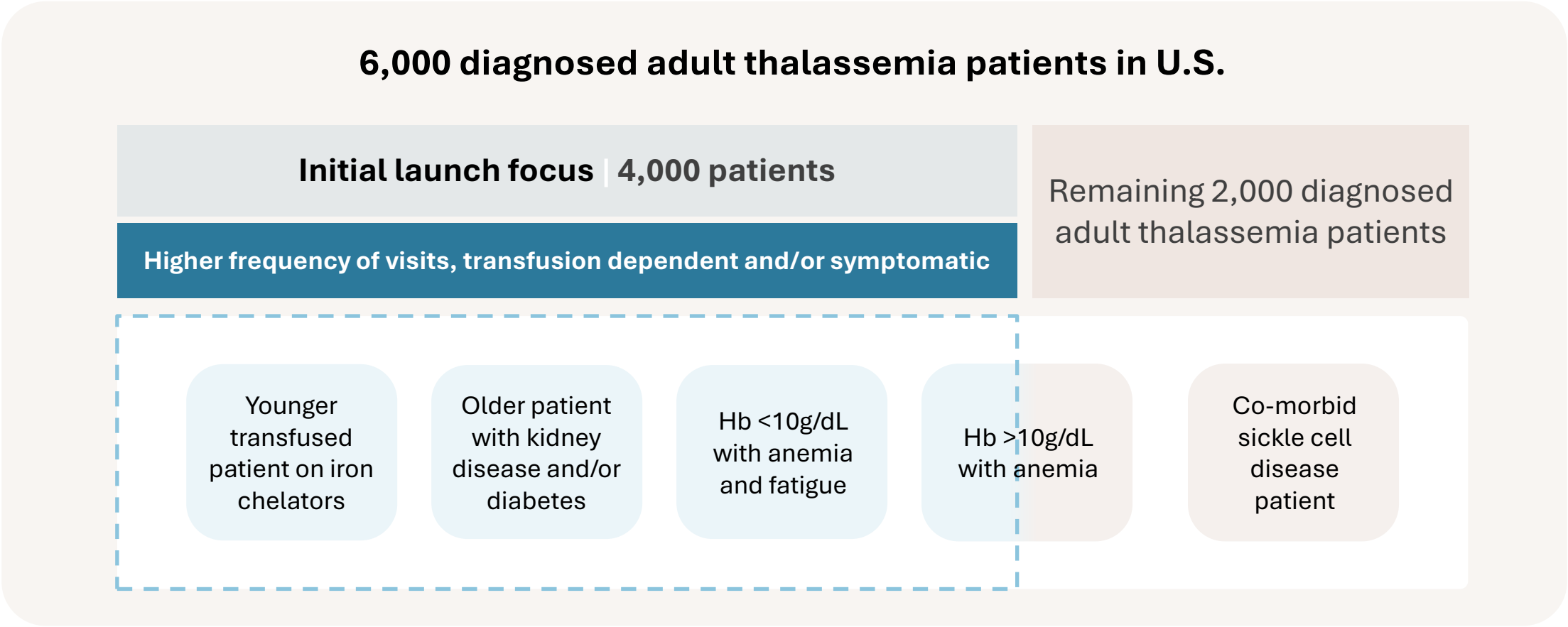
PKM2
Improves cellular energetics in tissue

PYRUKYND modulates SCD symptomology

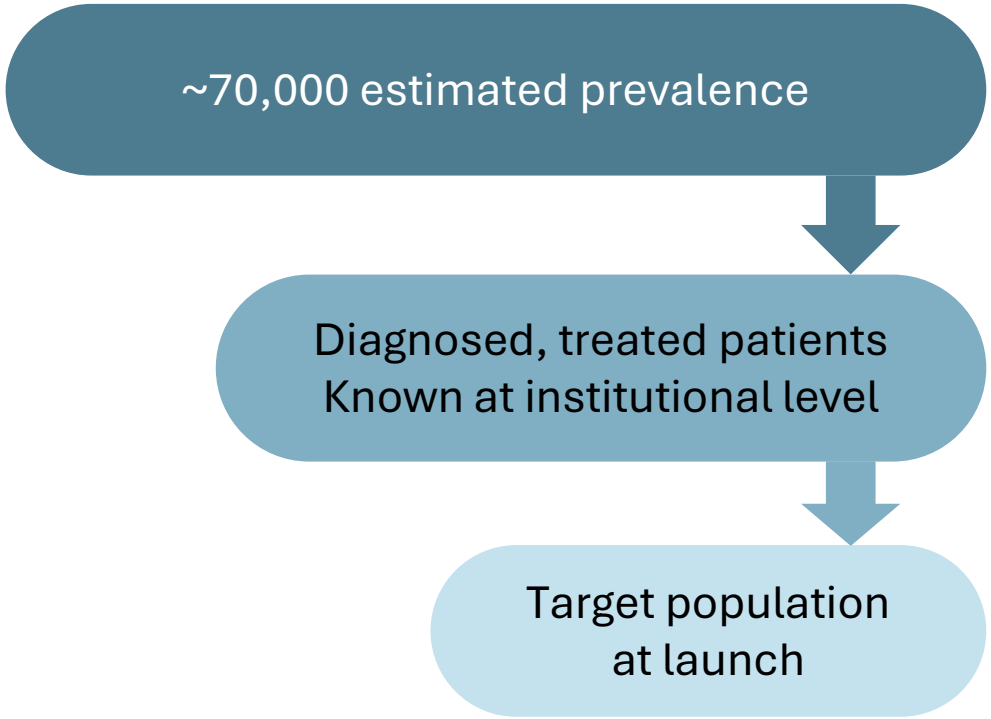
- Decreasing 2,3-DPG reduces HbS polymerization by increasing Hb oxygenation and may inhibit the sickling process
- Increasing ATP enhances RBC energy metabolism and may improve membrane integrity

MoA = mechanism of action, FBP = fructose 1,6-biphosphate, DPG = diphosphoglycerate, PEP = phosphoenolpyruvate, ADP = adenosine diphosphate, ATP = adenosine triphosphate, PK = pyruvate kinase, PKR = pyruvate kinase R isoform, PKM2 = pyruvate kinase isoform M2, RBC = red blood cells.

Appendix – U.S. thalassemia commercial opportunity



Appendix – GCC[1] thalassemia launch with NewBridge



1. **Adult and pediatric thalassemia patients, regardless of genotype or phenotype**

2. **Access and patient care spread across multiple institutions**

3. **Initial launch focus – symptomatic actively managed adult patients**
   - National procurement agreements can take ~2 years, during which access is granted patient-by-patient at list price
   - Potential expansion to institutional level following national procurement agreement at negotiated prices

1. GCC includes Bahrain, Kuwait, Oman, Qatar, Kingdom of Saudi Arabia and the United Arab Emirates; Agios has submitted regulatory filings in the Kingdom of Saudi Arabia and United Arab Emirates within the GCC.
GCC = Gulf Cooperation Council.