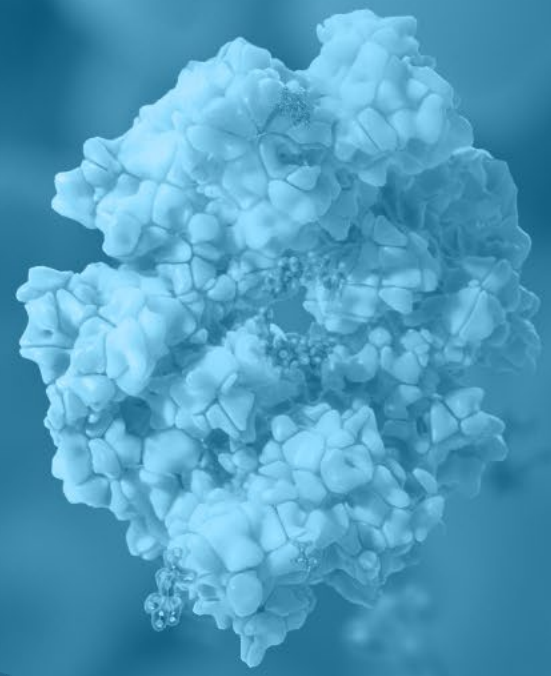
Q2 2025 Financial Results and Business Highlights

Conference call for investors and analysts

July 31, 2025



agios

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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-236 and AG-181; Agios' plans, strategies and expectations for its preclinical, clinical and commercial advancement of its drug development, including PYRUKYND®, tebapivat, AG181 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.

Q2 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 – 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; LR-MDS = lower-risk myelodysplastic syndrome; BD = business development.

Q2 2025 – continued delivery of strategic objectives

$12.5M PYRUKYND net revenues in Q2 2025

+44% vs $8.7M in Q1 2025, +45% vs $8.6M in Q2 2024

Announced commercialization and distribution partnership with Avanzanite Bioscience in Europe

Strong financial position – $1.3B cash, to invest behind launch[1] and pipeline

Strong pipeline execution in Q2 2025

tebapivat
novel potent PKa
SCD | LR-MDS

First patient dosed in Phase 2 Sickle Cell Disease trial

AG-236
siRNA TMPRSS6
Polycythemia Vera

Received IND clearance

1. Pending U.S. regulatory approval, PDUFA goal date of September 7, 2025. PKa = pyruvate kinase activator; SCD = sickle cell disease; LR-MDS = lower-risk myelodysplastic syndrome; siRNA = small interfering RNA; TMPRSS6 = transmembrane protease serine 6; IND = investigational new drug.

Financial Results

Cecilia Jones, Chief Financial Officer

Q2 2025 Financial Results

Statement of operations	Q2 2025	Q2 2024
PYRUKYND Net Revenue	$12.5M	$8.6M
Cost of Sales	$1.7M	$1.5M
Research & Development Expense	$91.9M	$77.4M
Selling, General & Administrative Expense	$45.9M	$35.5M
Net Loss	($112.0M)	($96.1M)

Balance sheet	Q2 2025	Q4 2024
Cash, Cash Equivalents and Marketable Securities	$1.3B	$1.5B

Strong balance sheet, focused capital allocation strategy

1 **Capital efficient commercial build out**

2 **Strategic investment to advance novel pipeline**

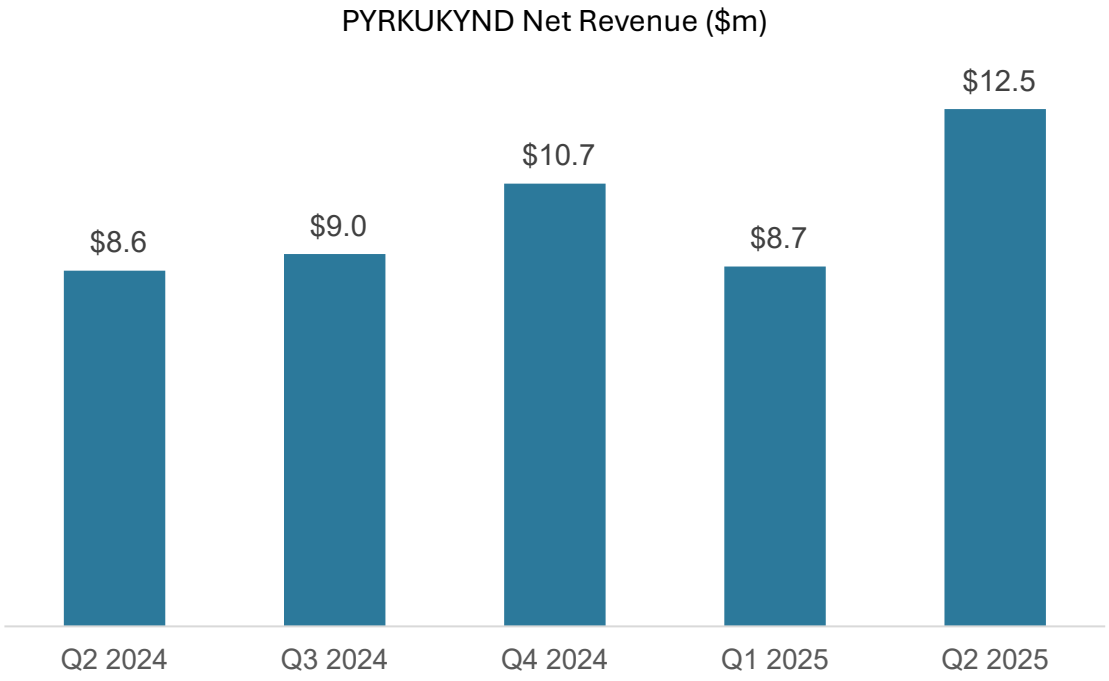
3 **Value-enhancing pipeline expansion**

Well-capitalized to execute on commercial portfolio and development pipeline

Commercial Highlights

Tsveta Milanova, Chief Commercial Officer

PYRUKYND – strong demand growth in Q2 2025



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

Key Performance Metrics

$12.5M net sales of PYRUKYND
compared with $8.7M in Q1 2025 and $8.6M in Q2 2024

248 unique PK deficiency patients completed prescription enrollment forms since launch in U.S.

142 patients on treatment in U.S.
including new prescriptions and treatment continuations

215 unique prescribers in U.S.

GTN = Gross to Net.

PYRUKYND – potential to deliver a series of “firsts” in thalassemia[1]

- First medicine to address α- and β-thalassemia
- First oral medicine
- First medicine to demonstrate quality of life improvements in non-transfusion dependent patients
- First medicine to demonstrate up to 36 weeks durability of effect on reduction of transfusion burden

PYRUKYND thalassemia U.S. FDA PDUFA goal date September 7, 2025

1. Pending FDA approval. FDA = Food and Drug Administration; PDUFA = Prescription Drug User Fee Act.

Prepared for potential PYRUKYND U.S. launch in Q3 2025[1]

Thalassemia – well-diagnosed and understood, community in need of new treatment options

1 **Patients diagnosed –** validated by ICD codes and extensive market research

2 **Clear unmet need –** lack of treatments to address broad thalassemia patient population

3 **Strong KOL and patient engagement –** high awareness and robust patient advocacy

Robust launch preparation to drive successful launch

Disease State Education

- Patient and HCP targeted education
- Focused, multi-cultural materials

Commercial Presence

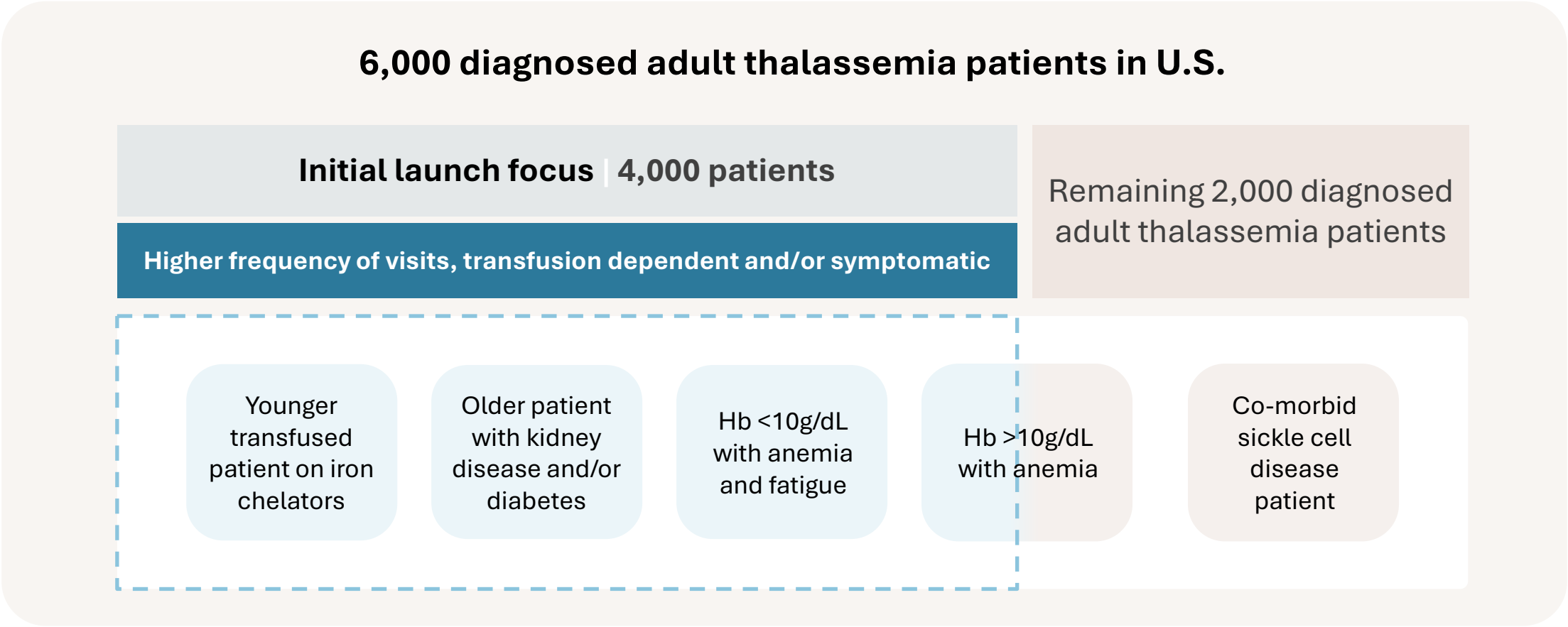
- Doubled customer facing team
- Focused targeting and HCP profiling

Market Access

- Payers receptive to new treatments
- PYRUKYND strong value proposition

1. Pending regulatory approval, US PDUFA goal date September 7, 2025. ICD = international classification of diseases; KOL = key opinion leader; HCP = healthcare professional.

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



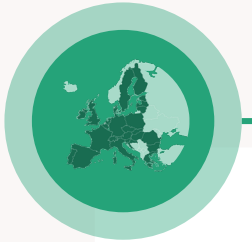
Tailored commercial build out with ex-US partnerships

GCC commercial strategy

NewBridge commercialization and distribution agreement

Anticipate first GCC regulatory approval in coming months[2]

Anticipate pace of adoption tied to KSA and UAE reimbursement dynamics



Europe commercial strategy

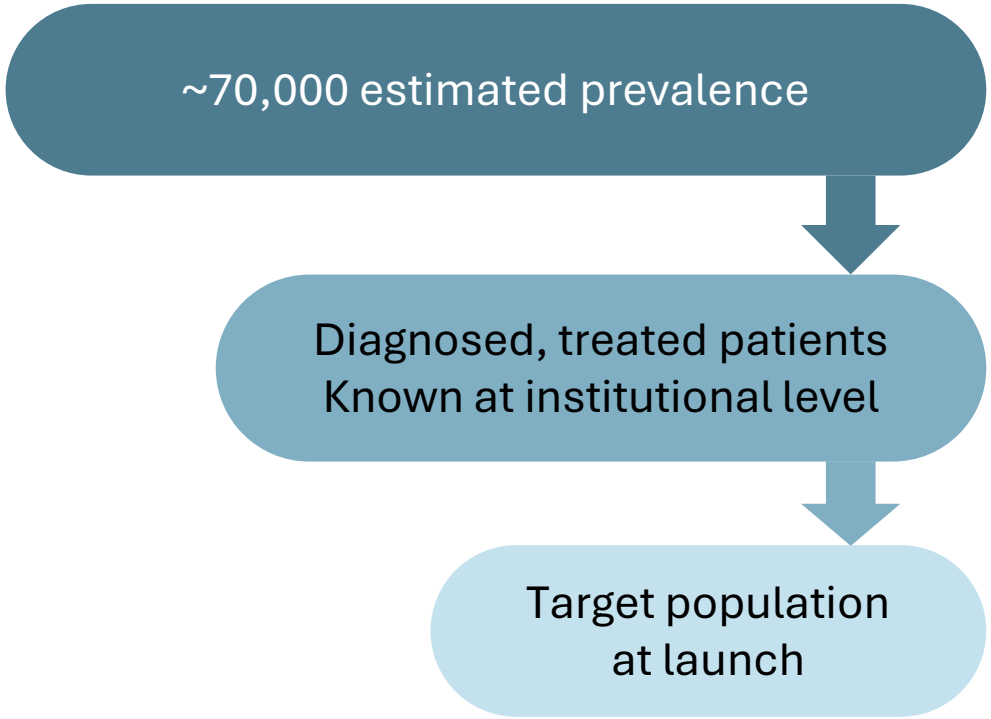
Avanzanite[1] commercialization and distribution agreement

Anticipate potential EU approval in early 2026

Focused country-by-country launch aligned with disease prevalence

1. Avanzanite Bioscience B.V. 2. Agios has submitted regulatory filings in the Kingdom of Saudi Arabia and United Arab Emirates within the GCC. GCC includes Bahrain, Kuwait, Oman, Qatar, Kingdom of Saudi Arabia and the United Arab Emirates.

Tailored commercial build out in GCC[1] 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.

R&D Highlights

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

PYRUKYND – consistent, meaningful clinical data in multiple hemolytic anemias

PK Deficiency	Thalassemia	Sickle Cell Disease
✓ Phase 2 open-label study	✓ Phase 2 open-label study	✓ Phase 2 – RISE UP
✓ Phase 3 – adults and pediatric	✓ Phase 3 – ENERGIZE/ENERGIZE-T	Phase 3 – RISE UP
✓ Long-term data in adults	✓ Ongoing long-term data in adult	✓ Phase 2 OLE ongoing
Statistically significant increase in Hb levels, decreased hemolysis and improvement in patient reported outcomes	Statistically significant increase in Hb levels and reduced transfusion burden, as well as decreased hemolysis and improvement in fatigue	Statistically significant increase in Hb levels, observed trend in reduction in sickle cell pain crises

RISE UP Phase 3 trial in sickle cell disease topline data by end of 2025

PK = pyruvate kinase; OLE = open label extension.

EHA 2025 data supports strong PKa franchise potential

ACTIVATE-KidsT
PK Deficiency

- Phase 3 data
- Clinically meaningful reduction in transfusion burden
- Higher proportion of patients achieved transfusion reduction response vs PBO
- Safety profile consistent with prior adult data

ESTIMATE
Sickle Cell Disease

- Long-term investigator-led open-label trial
- mitapivat showed sustained efficacy and tolerability over 3 years
- Improvement in anemia, hemolysis, VOC and markers of kidney damage

tebapivat
Sickle Cell Disease

- Preclinical data
- tebapivat reduced RBC sickling and adhesion in patient blood samples
- Reinforces tebapivat therapeutic potential in SCD

tebapivat
Lower-Risk MDS

- Preclinical data
- Compared to healthy controls, MDS patients had reduced PKM2 expression
- Supports potential role for tebapivat, as PKM2 and PKR activator

Data reinforce PYRUKYND and tebapivat potential indication expansion

PBO = placebo; VOC = vaso occlusive crises; RBC = red blood cell; SCD = sickle cell disease; MDS = Myelodysplastic Syndrome; PKM2 = Pyruvate Kinase M2; PKR = Pyruvate Kinase R.

PYRUKYND Phase 3 RISE UP in SCD anticipated late 2025[1]

Operationally seamless RISE UP Phase 2/3 trial, aligned with the clinical priorities of SCD community

Phase 3 RISE UP

Dual primary endpoints[2]

Hb response rate[3] (week 24-52 vs baseline)

- 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

- 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

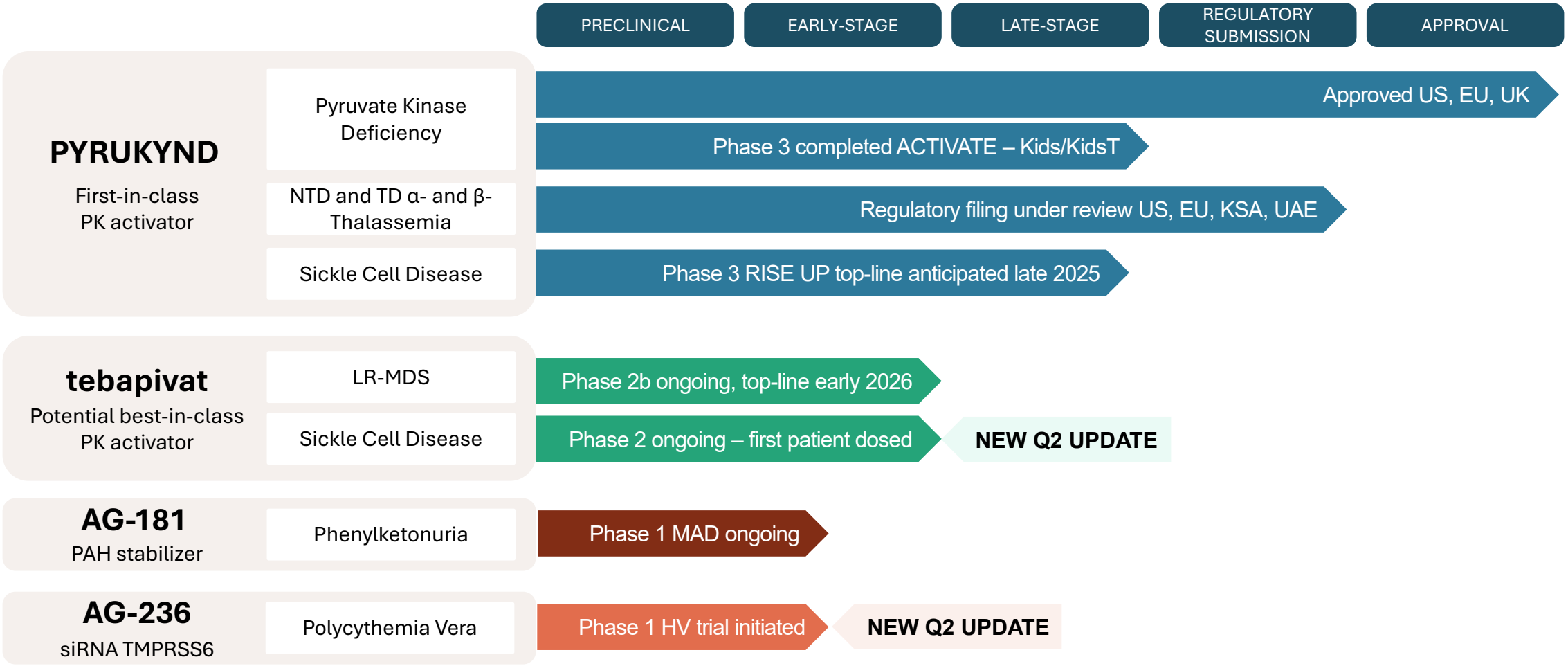
Key secondary endpoints, include:

PROMIS Fatigue assessment – 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 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.

Continued pipeline momentum in Q2 2025



PK = pyruvate kinase; NTD = non-transfusion dependent; TD = transfusion dependent; LR-MDS = lower-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.

CEO Closing Remarks

Brian Goff, Chief Executive Officer

Strong execution against R&D 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
(PDUFA goal date September 7th)

Sickle Cell Disease
PYRUKYND
Phase 3 readout RISE UP trial

Lower-Risk MDS
tebapivat
Complete enrollment in Phase2b 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

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

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

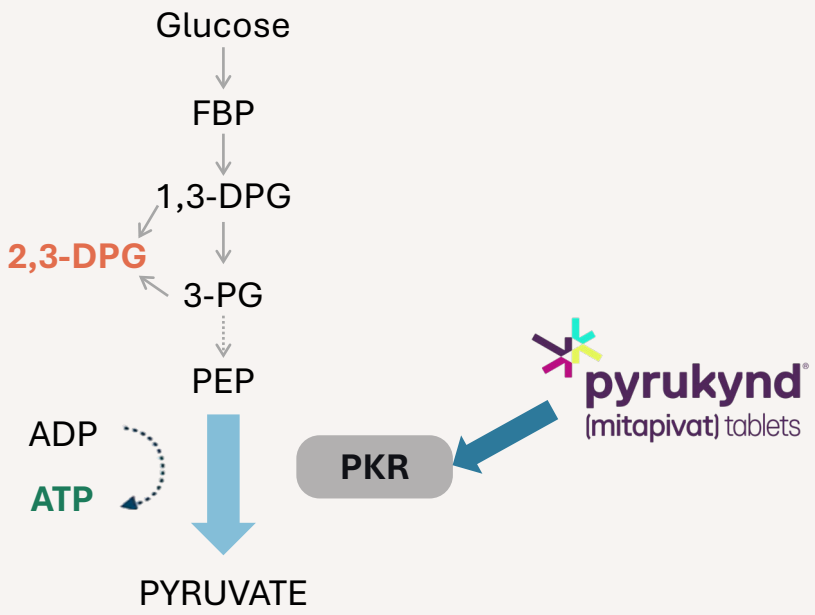
PKa = pyruvate kinase activator; LR-MDS = lower-risk myelodysplastic syndrome; PAH = phenylalanine hydroxylase; siRNA = small interfering RNA; TMPRSS6 = transmembrane protease, serine 6.

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.