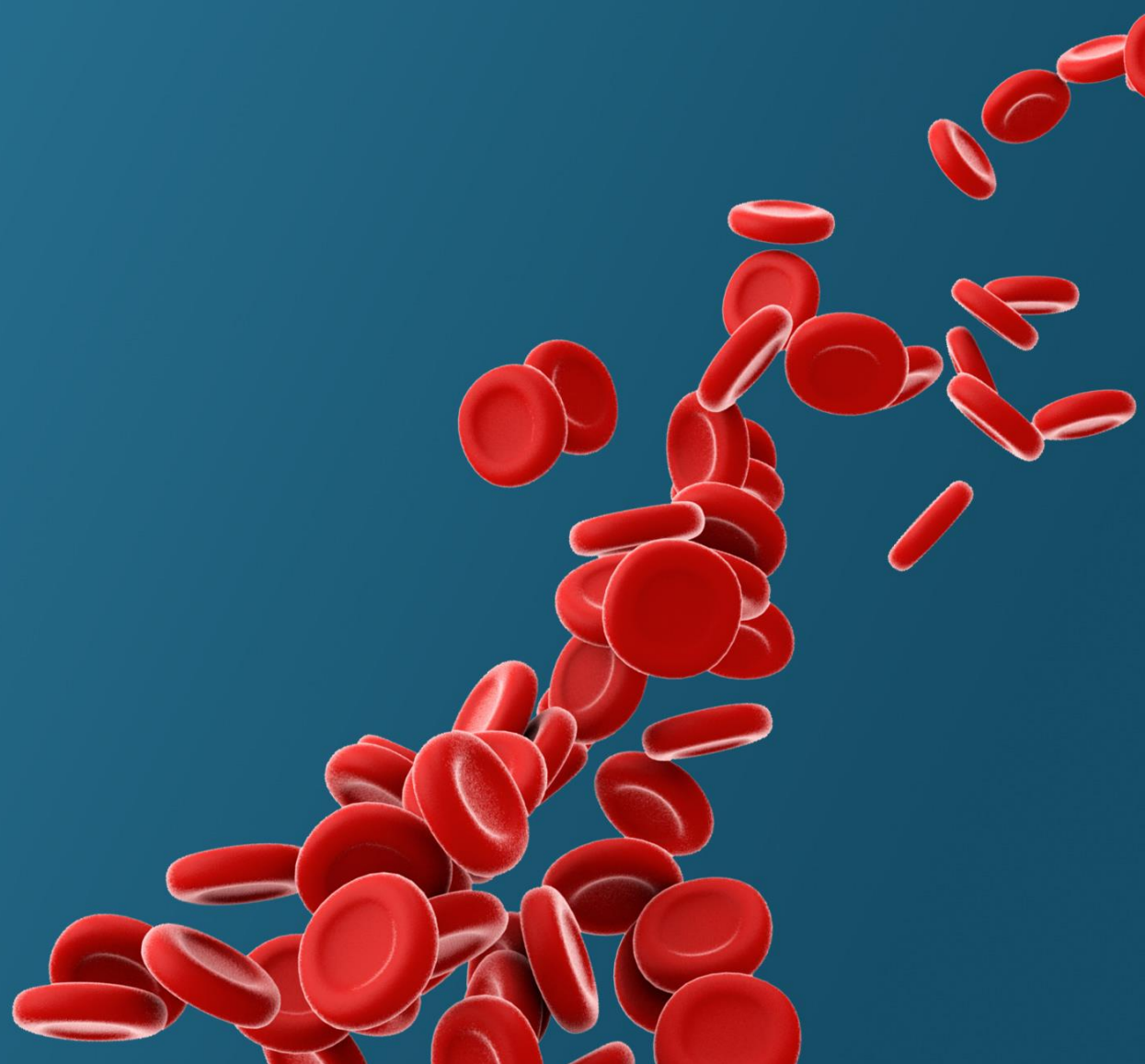
Q1 2025 Financial Results and Business Update

May 1, 2025



Agios Conference Call Participants

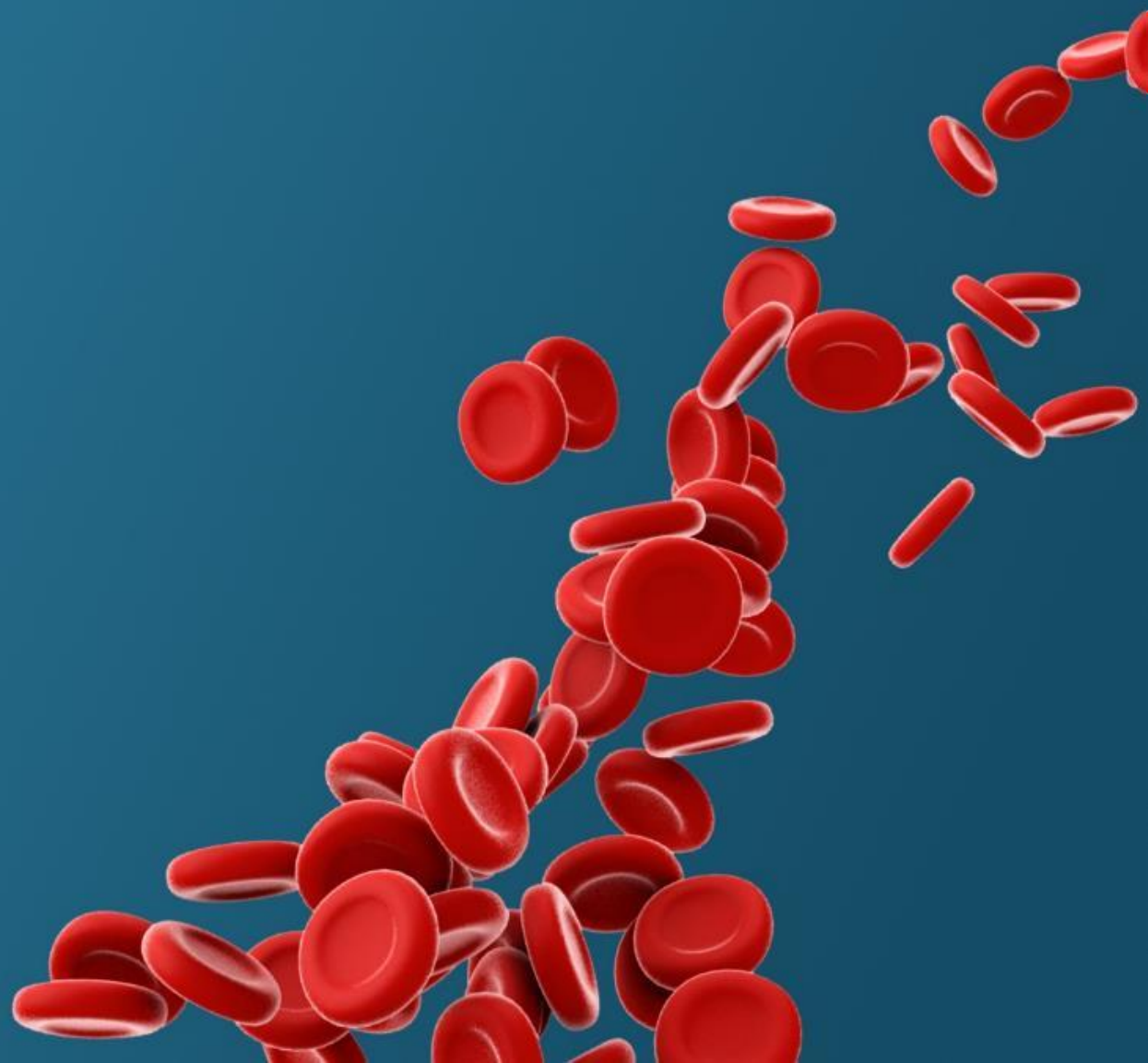
TOPIC	PARTICIPANT
Introduction	Chris Taylor, VP Investor Relations and Corporate Communications
Business Update	Brian Goff, Chief Executive Officer
R&D Update	Sarah Gheuens, M.D., Ph.D., Chief Medical Officer, Head of R&D
Commercial Update	Tsveta Milanova, Chief Commercial Officer
First Quarter 2025 Financial Results	Cecilia Jones, Chief Financial Officer
Q&A	Mr. Goff, Dr. Gheuens, Ms. Milanova, Ms. Jones

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-236 and AG-181; 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.

Business Overview

Brian Goff
Chief Executive Officer



A Rare Blueprint for Success

Multi-Billion-Dollar Market Opportunity with PYRUKYND®

Robust Pipeline, Rich with Near-Term Catalysts

Proven Executional Excellence, Powered by Highly Experienced Team

Strong Financial Position

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**

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
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)

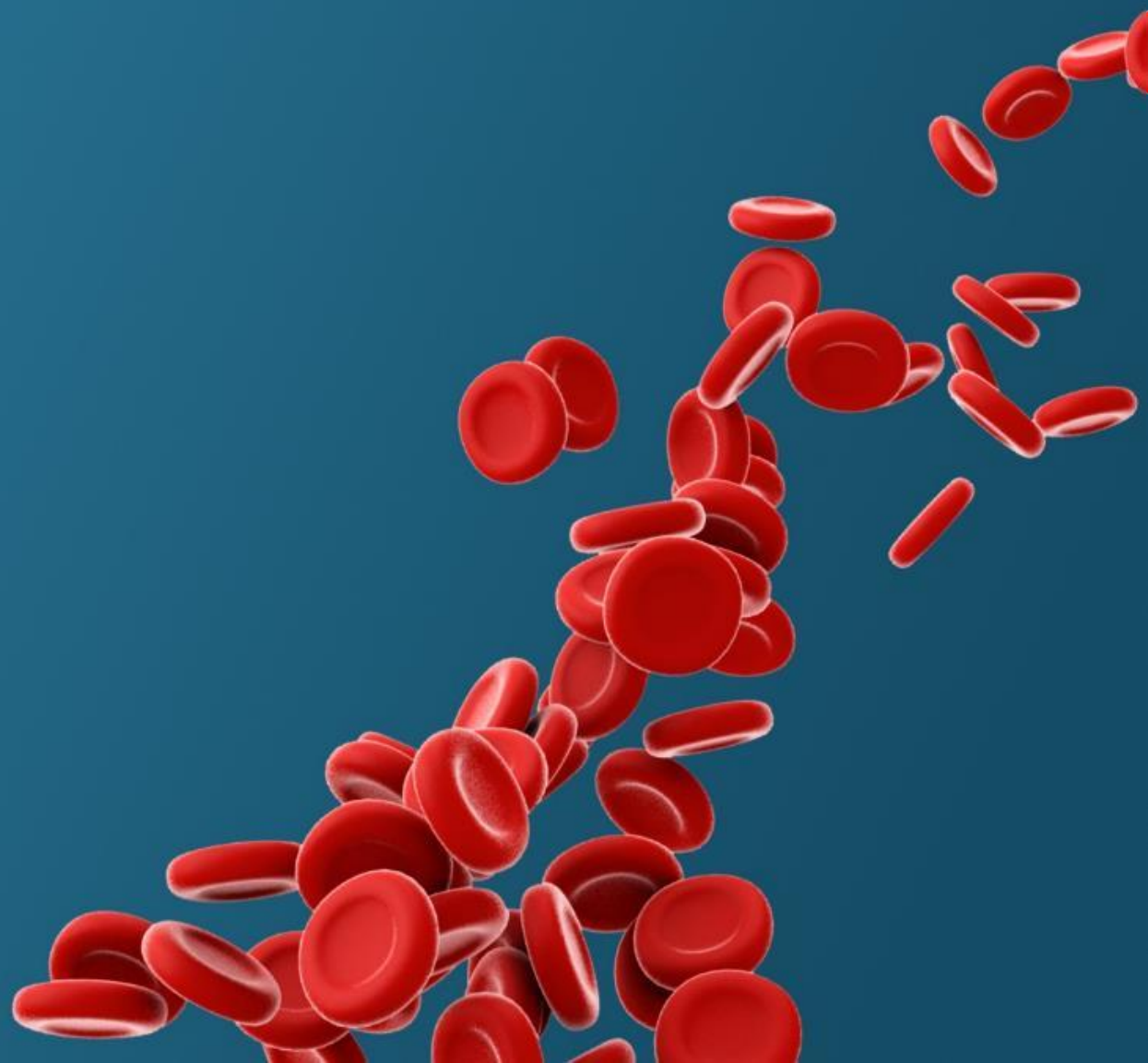
Sickle Cell Disease
PYRUKYND®
Phase 3 data readout for RISE UP study

Lower-Risk MDS
Tebapivat
Complete patient enrollment in Phase 2b study

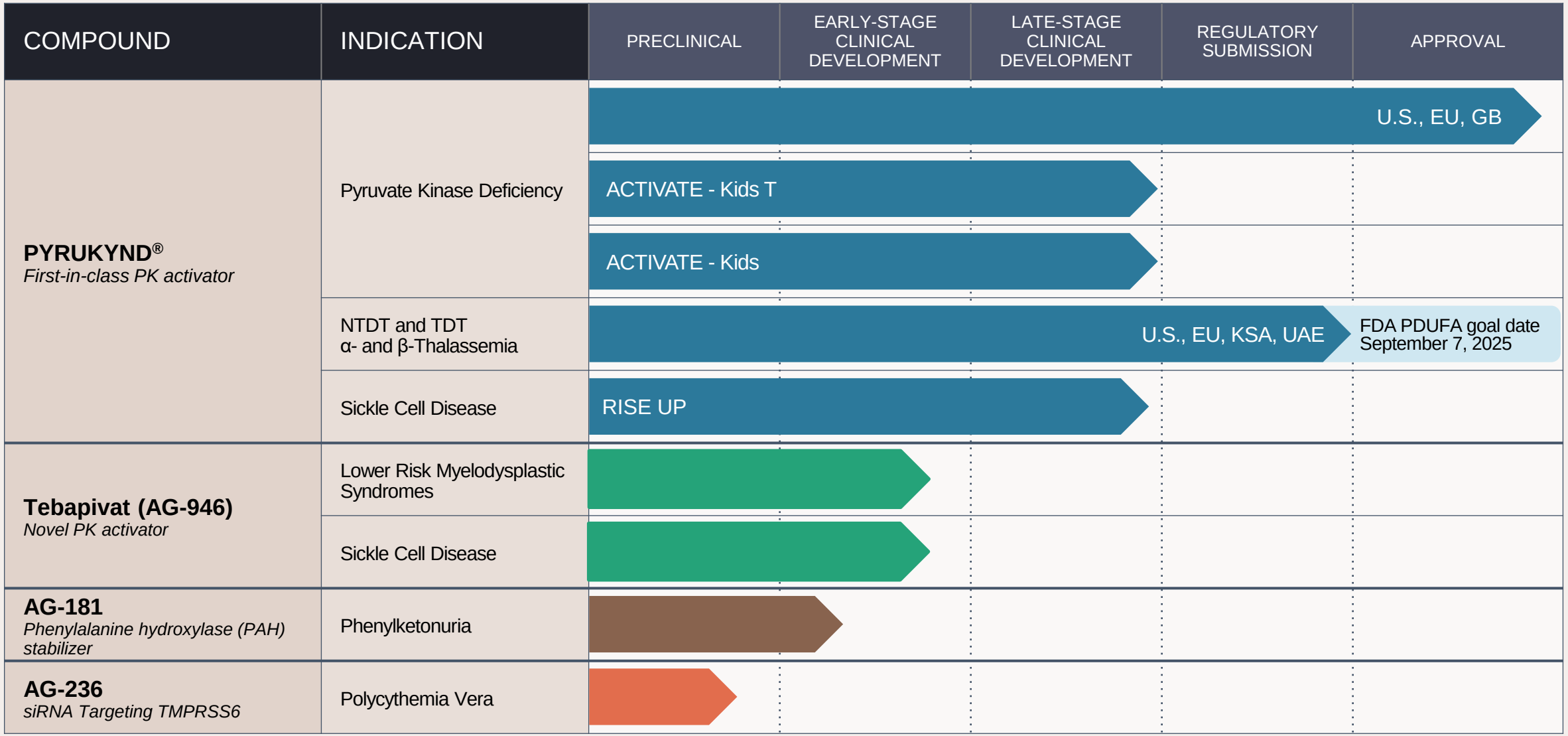
Early: January – April; Mid-Year: May – August; Late: September – December
PK deficiency: Pyruvate kinase deficiency; MDS Myelodysplastic syndromes; IND: Investigational new drug; PDUFA: Prescription Drug User Fee Act

Clinical Overview

Sarah Gheuens, M.D., Ph.D.
Chief Medical Officer, Head of R&D



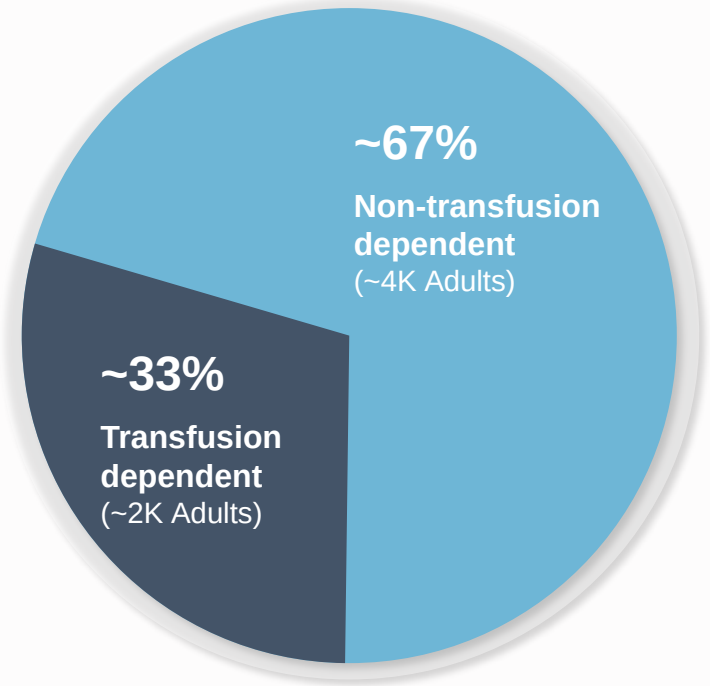
Advancing Therapies for Rare Diseases with Limited or No Treatment Options



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

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

~67% **of thalassemia patients with 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

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

Tebapivat 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

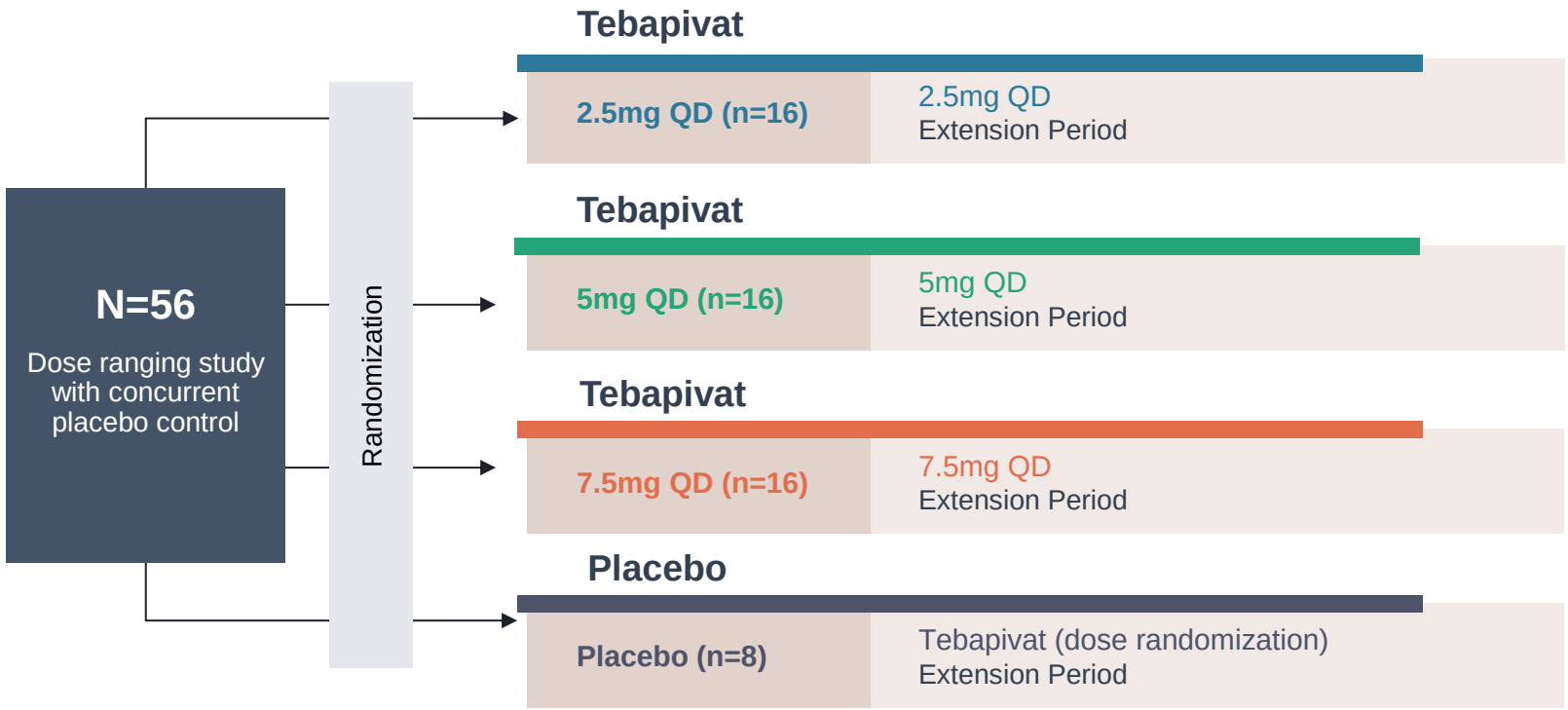
Sources: Agios internal estimates. Greenberg PL, Tuechler H, Schanz J, et al. Revised international prognostic scoring system for myelodysplastic syndromes. Blood. 2012;120(12):2454-2465.
MDS: Myelodysplastic syndromes; EU: European Union

Phase 2 Study of Tebapivat in Sickle Cell Disease

Phase 2

Primary endpoint:
Hb response, defined as ≥ 1.0 g/dL increase in hemoglobin concentration from Week 10 through Week 12 compared with baseline

Secondary endpoints: Safety, changes in hemoglobin, additional measures of hemolysis, erythropoiesis; PROs: PROMIS Fatigue, PROMIS Pain, ASCQ-Me



Core Period: **12 Weeks** | OLE: **1 Year**

Status

- Patient enrollment expected to commence mid-2025

Key inclusion criteria

- ≥ 16 years of age
- Hemoglobin 5.5-10.5 g/dL
- If taking hydroxyurea, dose stable for 90 days

Key Exclusion Criteria

- >10 SCPCs in the 12 months prior to consent
- Receiving regularly scheduled RBC transfusion therapy

Hb= hemoglobin; OLE=open label extension; PKa=pyruvate kinase activator; ASCQ-Me= Adult Sickle Cell Quality of Life Measurement Information System; PRO=patient reported outcome; SCPC=sickle cell pain crisis; RBC=red blood cells

Phase 2b Open-Label Study of Tebapivat in Lower-Risk MDS

Phase 2b

Primary endpoint:
Transfusion independence, defined as transfusion-free for ≥8 consecutive weeks during the Core Period

Secondary endpoints: safety, change in hemoglobin, TI for 12 weeks, additional measures of anemia, PK and PD biomarkers

N=60
Completion of enrollment in one cohort triggers the opening of enrollment in the next cohort

Tebapivat Treatment Period

10mg QD Core Period	10mg QD Extension Period

Tebapivat Treatment Period

15mg QD Core Period	15mg QD Extension Period

Tebapivat Treatment Period

20mg QD Core Period	20mg QD Extension Period

Core Period: **24 Weeks** | Extension Period: **156 Weeks**

Status

- Completion of enrollment expected in late-2025

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

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

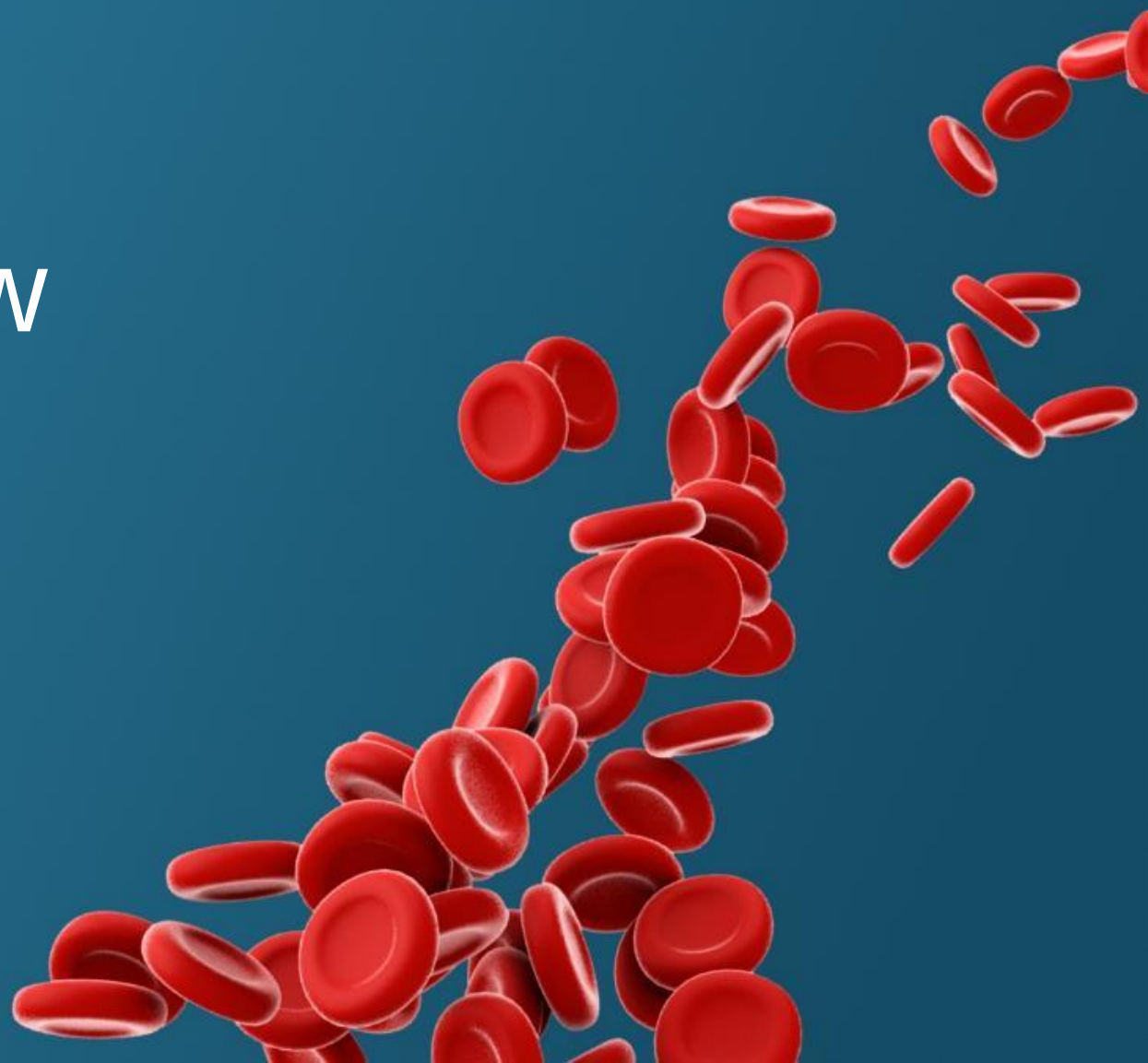
Early-Stage Pipeline Offers Opportunity for Advancement

	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 progressing to MAD in mid-2025
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; MAD=multiple ascending dose

Commercial Overview

Tsveta Milanova
Chief Commercial Officer



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

Commercial Expertise and Capabilities in Place to Deliver Strong U.S. Launch; PDUFA Goal Date September 7, 2025

Disease State Education

- ✓ Patient and HCP targeted education on unmet need via digital and personal channels
- ✓ Synergistic omni-channel approach

Commercial Presence

- ✓ Right sized customer-facing teams
- ✓ Focused targeting and HCP profiling

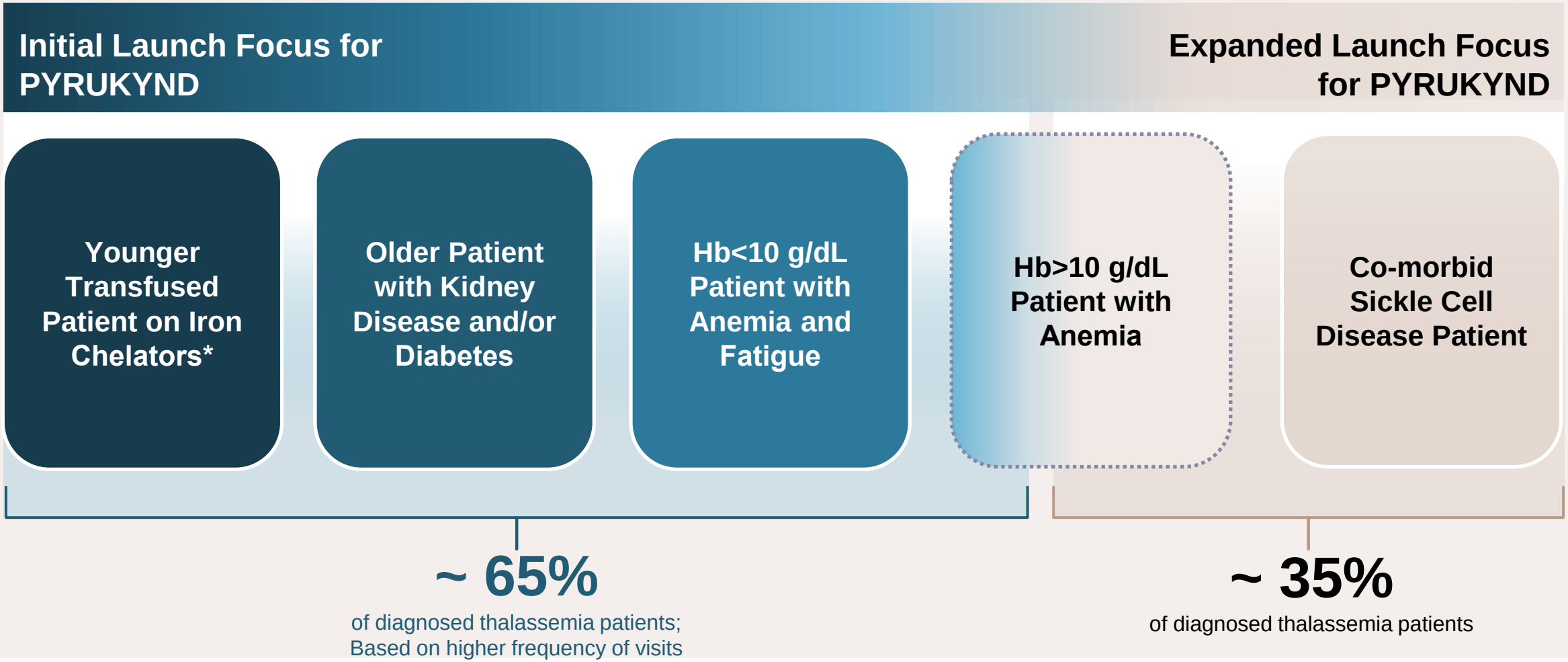
Market Access

- ✓ Payer education on Thalassemia
- ✓ Strong value proposition for payers

HCP: Healthcare Professional

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

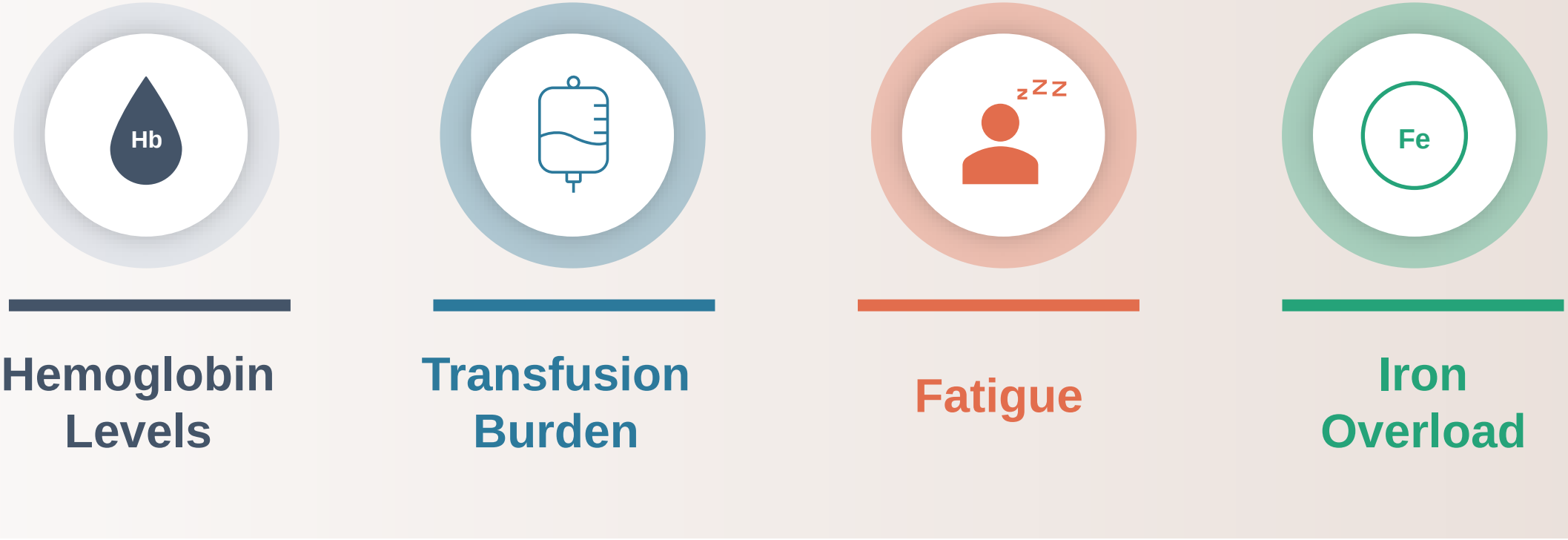
6,000 diagnosed adults with thalassemia in the U.S.



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

Agios Market Research Identified Top Clinical Characteristics Healthcare Providers Will Consider When Prescribing PYRUKYND

Top Clinical Patient Characteristics HCPs Will Consider When Prescribing PYRUKYND



Source: US THAL Demand Study (N=97 Heme/Oncs); Agios internal data, 2024

PYRUKYND® has Potential to Transform the Thalassemia Treatment Landscape

- **FIRST** Phase 3 program to include **Alpha- & Beta-thalassemia**
- **FIRST oral treatment candidate** to show potential for benefits in pivotal Phase 3
- **FIRST to demonstrate Quality-of-Life improvements** in non-transfusion dependent patients
- **FIRST to demonstrate up to 36 weeks durability** of effect on reduction of transfusion burden

PYRUKYND® Q1 2025 Performance Metrics Highlight Continued Progress

$8.7M net sales of PYRUKYND® compared with $10.7M in Q4 2024 and $8.2M in Q1 2024

136 patients on PYRUKYND®, which includes new prescriptions and those continuing treatment

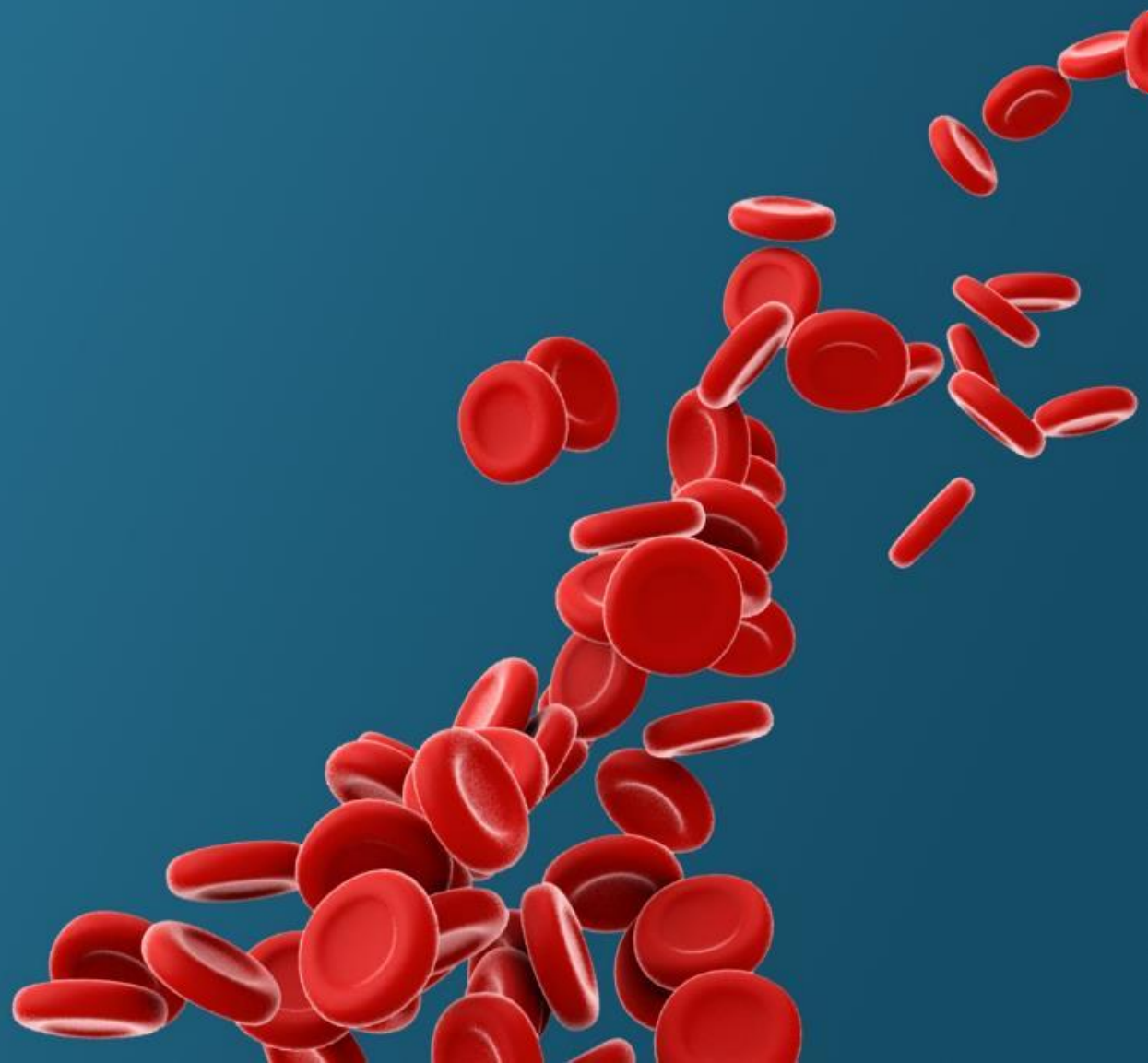
Patients on therapy represent broad demographic range; consistent with the adult PK deficiency population

234 unique patients completed PYRUKYND® prescription enrollment forms, including 11 in Q1, a 5% increase over Q4 2024

Unique prescriber base of 202 physicians, diversified across the country

Financial Overview

Cecilia Jones
Chief Financial Officer



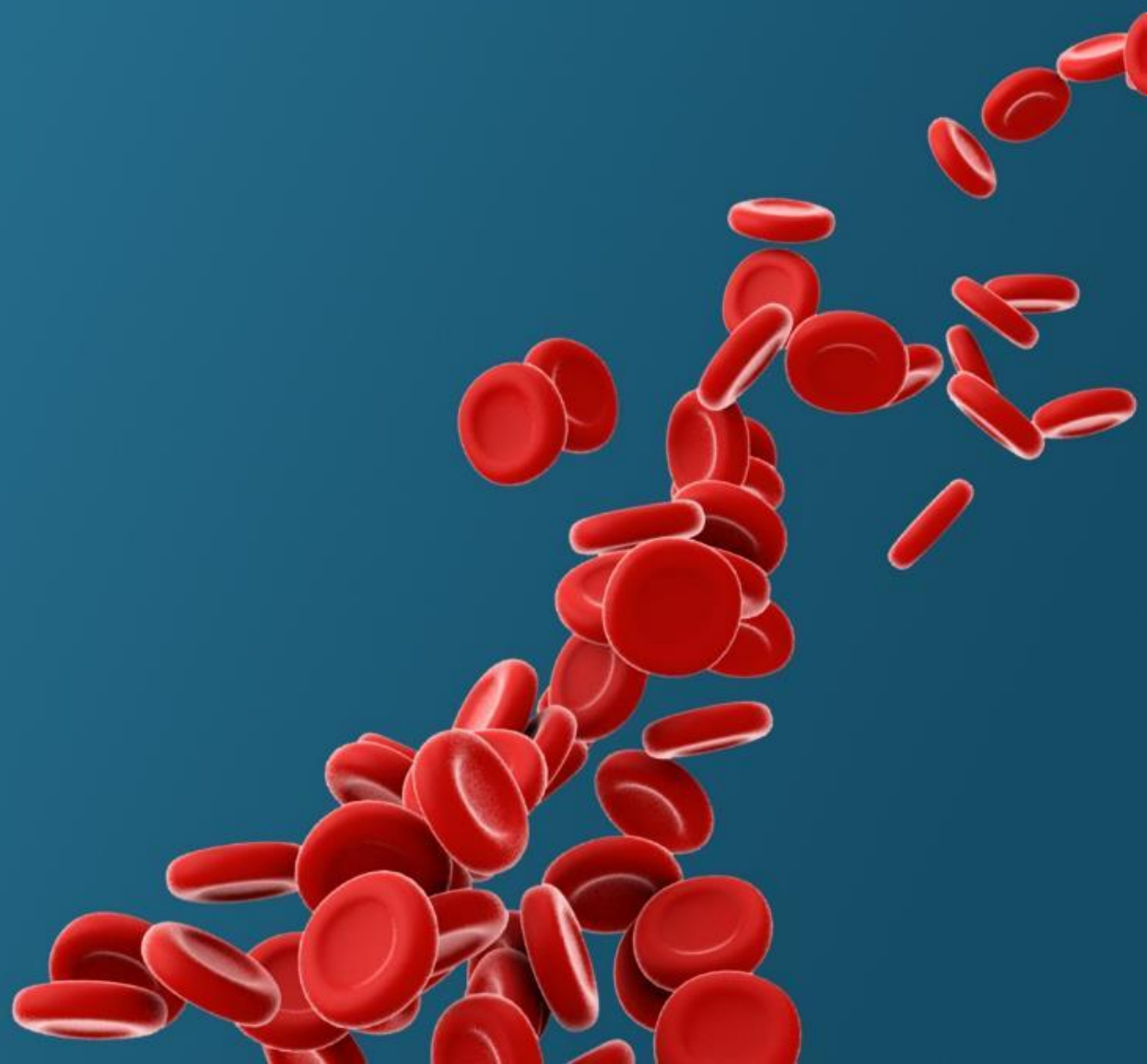
First Quarter 2025 Financial Results

Statement of Operations	Three Months Ended 3/31/25	Three Months Ended 3/31/24
PYRUKYND® Net Revenue	$8.7M	$8.2M
Cost of Sales	$1.1M	$0.6M
Research & Development Expense	$72.7M	$68.6M
Selling, General & Administrative Expense	$41.5M	$31.0M
Net Loss	($89.3M)	($81.5M)

Balance Sheet	3/31/25	12/31/24
Cash, Cash Equivalents and Marketable Securities	$1.4B	$1.5B

Closing Remarks

Brian Goff
Chief Executive Officer



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
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
Complete patient enrollment in Phase 2b study

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

Delivering Significant Value Through Strategic Capital Allocation

$1.4B Cash, Cash Equivalents and Marketable Securities*

Maximize
PYRUKYND®
Thalassemia
and Sickle Cell Disease
Potential Launches

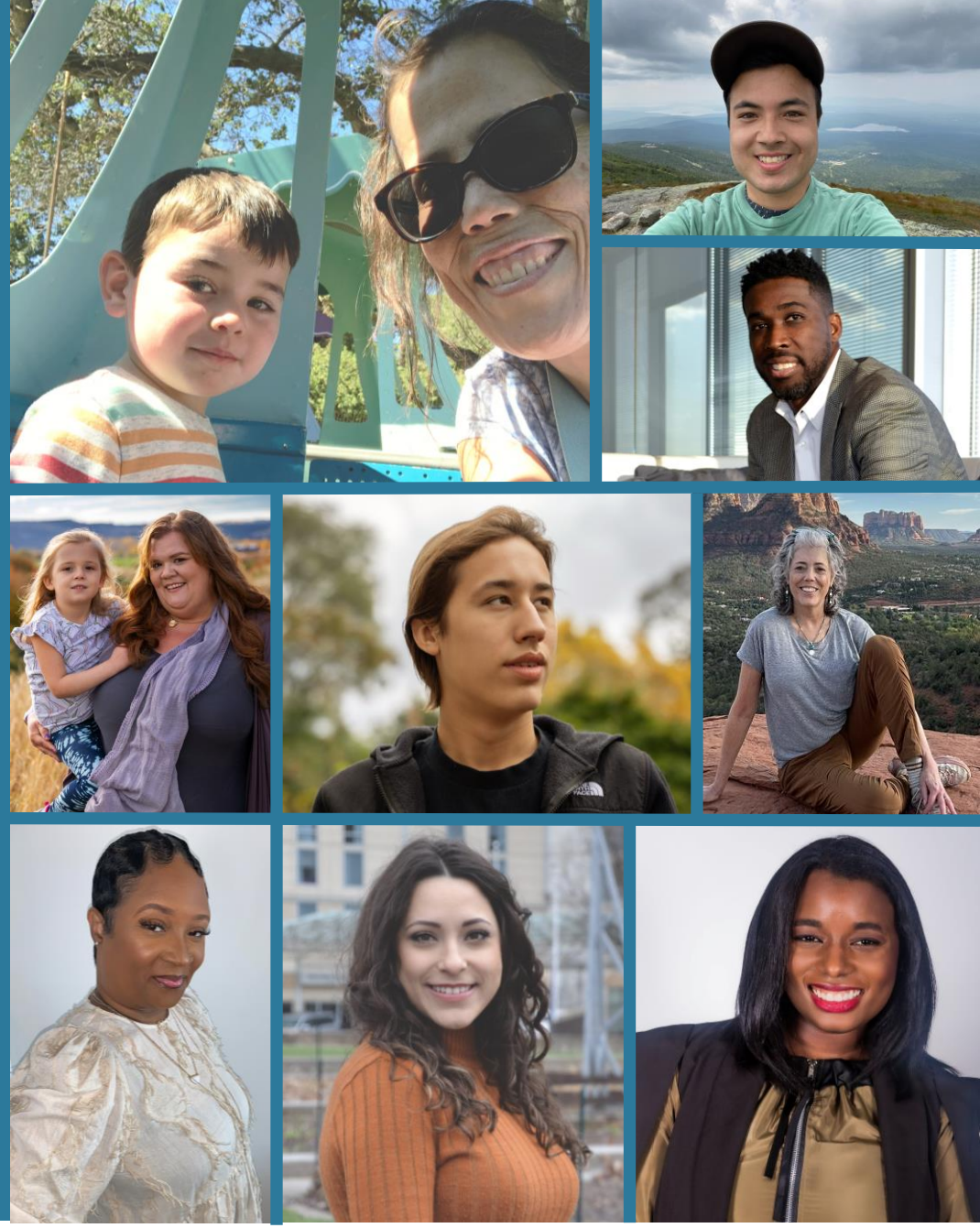
Advance
Early- and Mid-Stage
Clinical Pipeline

Expand
Pipeline with Internal
and External
Opportunities

*As of March 31, 2025

agios

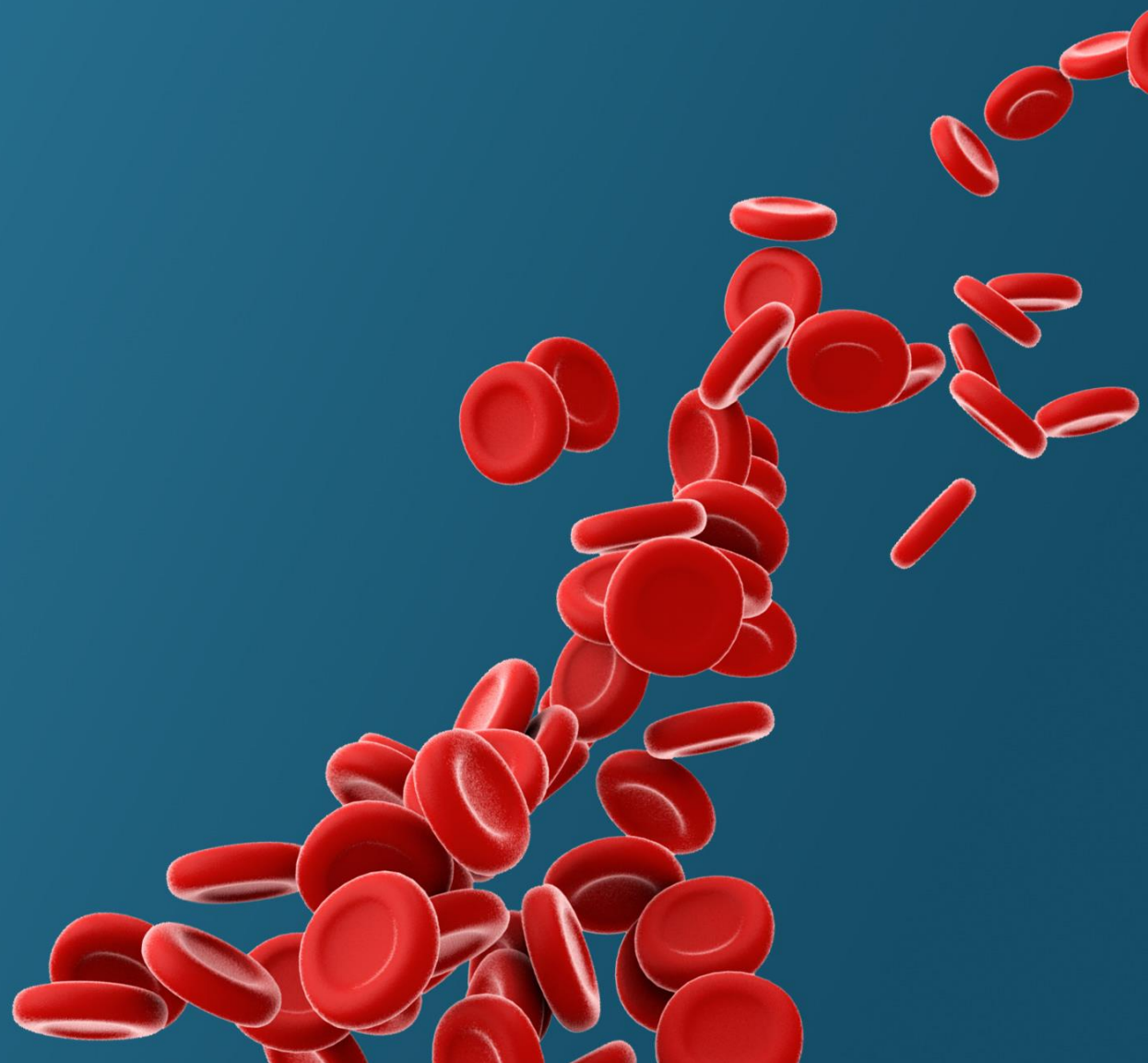
Thank You!



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

agios

Appendix



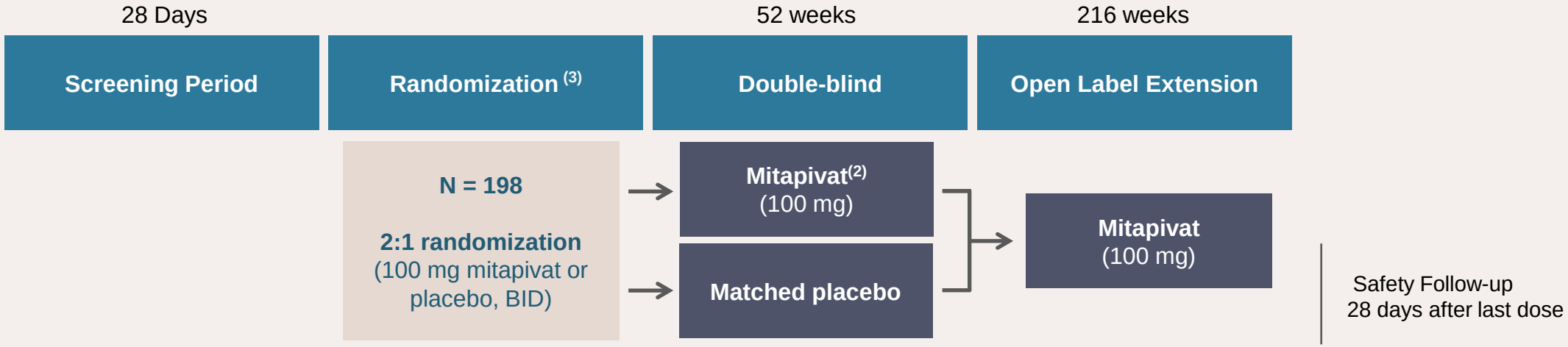
Advancing RISE UP Phase 3 Study of PYRUKYND® in Sickle Cell Disease with Expected Readout in Late 2025

RISE UP

Phase 3

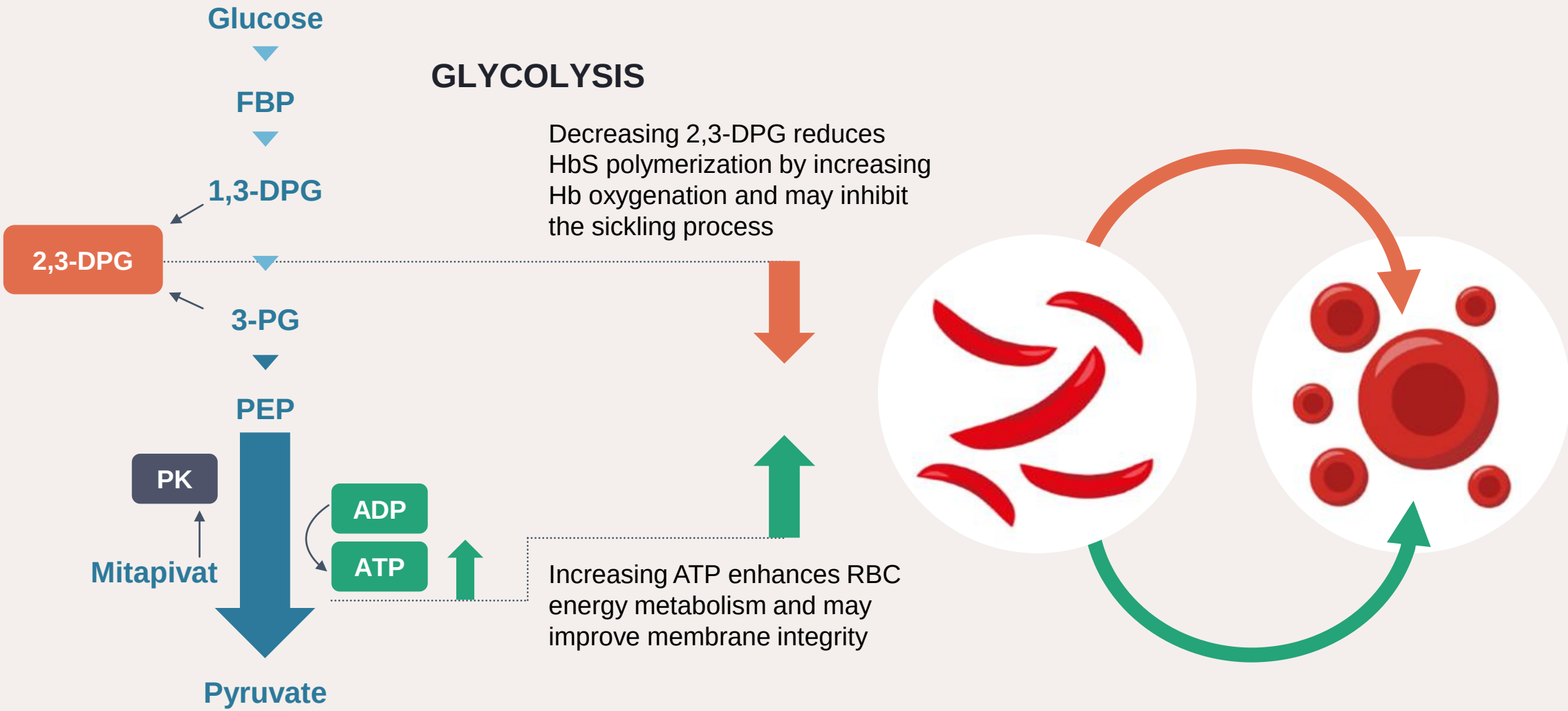
Two primary endpoints [1]:
Hb response defined as a ≥1.0 g/dL increase in average Hb concentration from Week 24 through Week 52 compared with baseline: With a planned sample size of 198 subjects there will be 91% power to detect an increase in Hb response rate from 10% in the placebo arm to 33% in the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

PK Activation in Sickle Cell Disease Modulates 2,3-DPG and ATP, which may Improve Anemia and Reduce Sickling

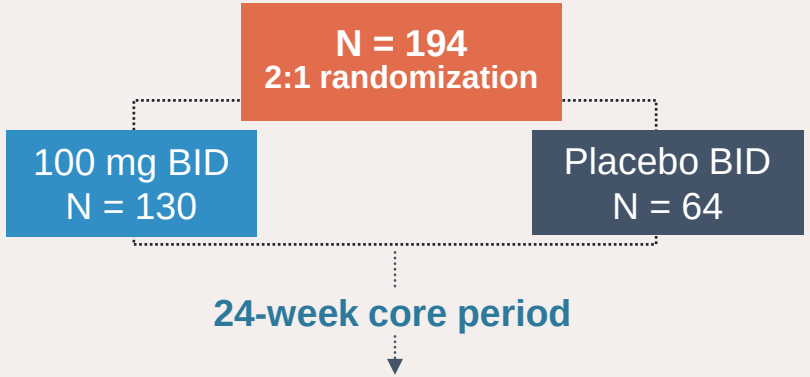


ADP = adenosine diphosphate; ATP = adenosine triphosphate; DPG = diphosphoglycerate; FBP = fructose bisphosphate; Hb = hemoglobin; HbS = sickle hemoglobin; PEP = phosphoenolpyruvate; PG = phosphoglycerate; PK = pyruvate kinase; RBC = red blood cell

1. Kung C et al. Blood 2017; 130:1347; 2. Valentini G et al. J Biol Chem 2002;277:23807; 3. Rab MAE et al. Blood 2021;137:2997-3001

Two Global, Phase 3, Randomized Controlled Trials of PYRUKYND® in Thalassemia Across Full Range of Thalassemia Patients

ENERGIZE



Primary endpoint

- Mean Hb ↑
  ≥ 1 g/dL from baseline

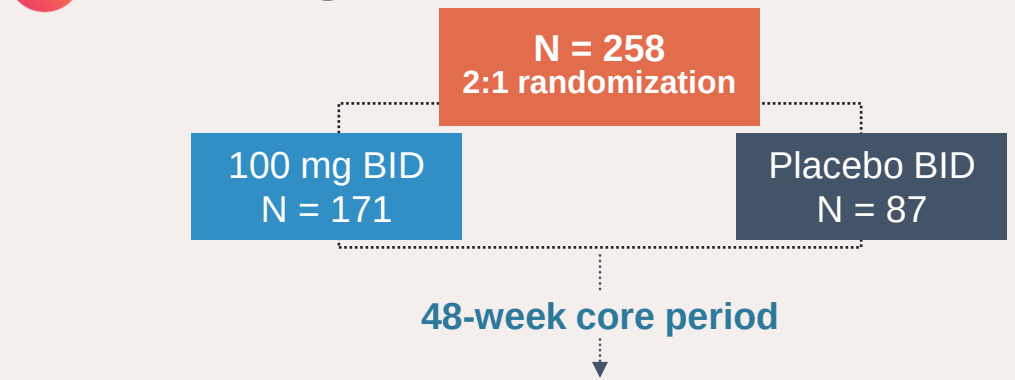
Secondary endpoints

- Fatigue, additional measures of Hb ↑, hemolysis, patient-reported outcomes, physical activity, iron metabolism, safety, PK/PD

Key inclusion criteria

- ≥ 18 years
- β-thalassemia ± α-globin mutations, HbE β-thalassemia, or α-thalassemia (HbH disease)
- Non-transfusion-dependent defined as ≤5 RBC units during the 24-week period before randomization and no RBC transfusions ≤8 weeks prior
- Hb ≤ 10.0 g/dL

ENERGIZE-T



Primary endpoint

- 50% reduction in transfusion burden in any 12-week rolling period

Secondary endpoints

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

Key inclusion criteria

- ≥ 18 years
- β-thalassemia ± α-globin mutations, HbE β-thalassemia, or α-thalassemia (HbH disease)
- Transfusion-dependent defined as 6 to 20 RBC units transfused and ≤6-week transfusion-free period during the 24-week period before randomization

Both studies completed; topline data readouts in 2024

BID = twice daily; Hb = hemoglobin; HbE = hemoglobin E; HbH = hemoglobin H; PK = pharmacokinetics; PD = pharmacodynamics.

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

U.S.

Thalassemia
~8K in US

Adult Thalassemia (18+)
~6K (~70%)

Alpha Thalassemia
~3K (~47%)

Beta Thalassemia
~3K (~53%)

Non-Transfusion Dependent Alpha Thalassemia	Transfusion Dependent Alpha Thalassemia	Non-Transfusion Dependent Beta Thalassemia	Transfusion Dependent Beta Thalassemia
~3K (~95%)	~0.1K (~5%)	~1K (~40%)	~2K (~60%)

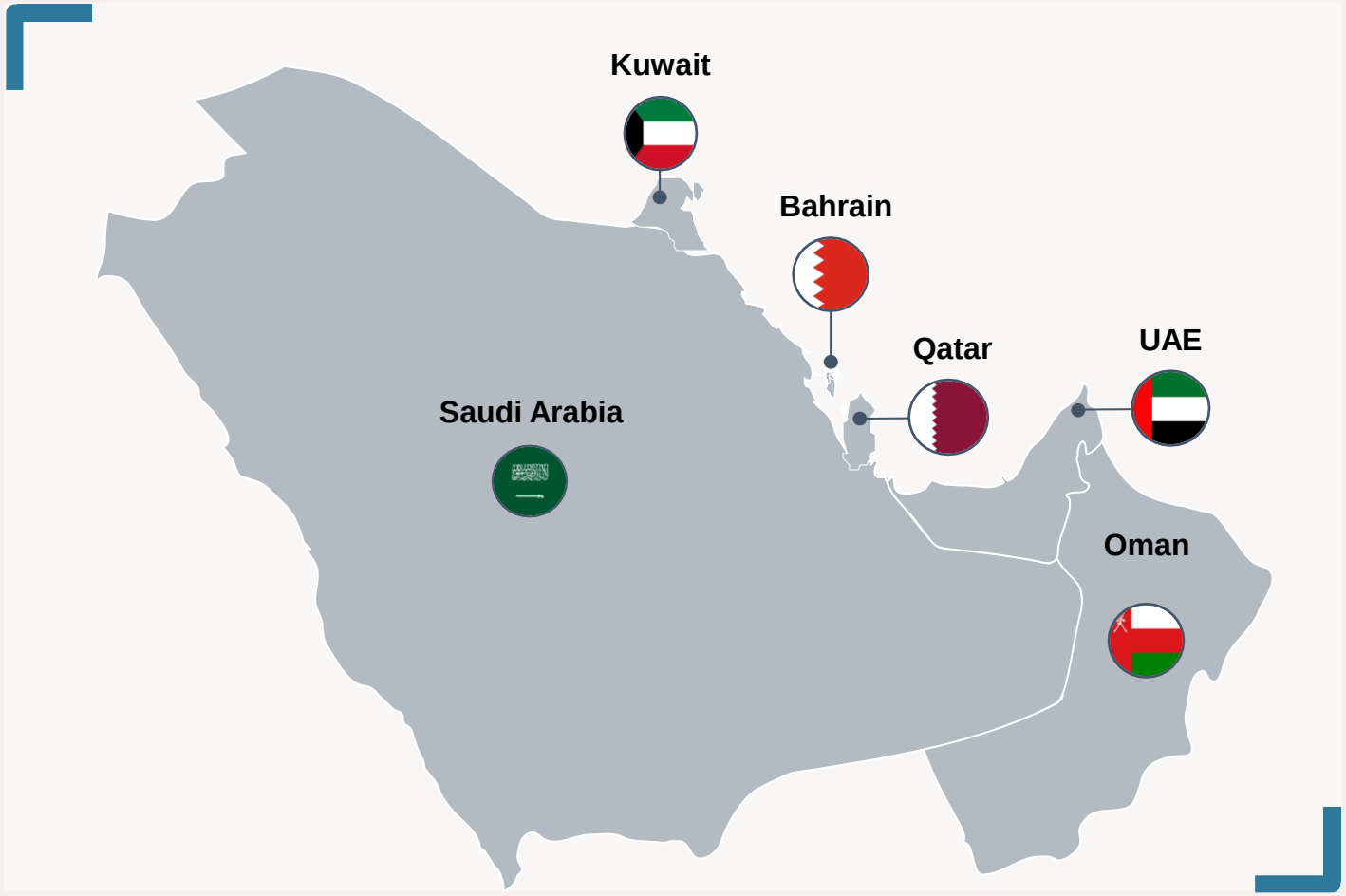
~67% OF ADULTS DO NOT HAVE AN APPROVED THERAPY IN THE US

Approved treatment in US*	✗	✗	✗	✓
PYRUKYND potential label	✓	✓	✓	✓

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

The GCC Region Represents a Significant Opportunity for PYRUKYND in Thalassemia; Regulatory Filings Under Review in Saudi Arabia and UAE

Approximately 70k Thalassemia Patients in Gulf Cooperation Council (GCC) Countries



- **High unmet need** given disproportionally high prevalence
- Entered **distribution agreement** with **NewBridge;** a **leading** specialty company with **regulatory and commercial expertise in the GCC**
- Saudi Arabia accounts for the majority of patients in GCC region
- Mitapivat received **Breakthrough Medicine Designation** by the SFDA (Saudi FDA); one of the first products to receive BMD
- The **access path** in the GCC region begins with a price set at the regulatory level, followed by access with health authorities, local institutions, and the private sector, and national tenders

GCC: Gulf Cooperation Council

LOOK CLOSER TO

SEE WHAT THALASSEMIA IS HIDING

Even if you don't receive regular transfusions, thalassemia may come with serious risks. Learn more about these risks and what you can do about them.

First Clinical Study to Demonstrate Efficacy of an Oral Therapy for Children with PK Deficiency who are Not Regularly Transfused

ACTIVATE-Kids

Topline Results

Enrollment & Completion

- A total of 30 patients aged 1 to <18 years were enrolled in the study, with 19 randomized to mitapivat twice-daily and 11 randomized to matched placebo.
- All 19 patients (100.0%) in the mitapivat arm and all 11 (100.0%) in the placebo arm completed the 20-week double-blind period of the study.

Hemoglobin Response

- Primary endpoint met. 31.6% (6/19) of patients in the mitapivat arm achieved a hemoglobin response, compared to 0.0% (0/11) of patients in the placebo arm.

Additional Observations

- Improvements in changes from baseline for markers of hemolysis (indirect bilirubin, lactate dehydrogenase and haptoglobin) were observed in the mitapivat arm compared to the placebo arm.

Safety

- In the 20-week double-blind treatment period of the study, a similar proportion of patients had adverse events (AEs) in the mitapivat and placebo arms and there were no discontinuations of study treatment due to AEs.
- Safety results in this pediatric study were consistent with the safety profile for mitapivat previously observed for adult subjects with PK deficiency who are not regularly transfused.

The analysis of the primary endpoint was based on Bayesian statistical methodology whereby the hemoglobin response data from the adult ACTIVATE study informed and contributed to the analysis of hemoglobin response in the ACTIVATE-Kids study. The analysis was performed using a range of relative borrowing from the adult ACTIVATE study, representing the prior degree of belief in the similarity of the treatment effect in the pediatric and adult populations. The prespecified statistical criterion for the primary endpoint in ACTIVATE-Kids was met for all possible borrowing weights (ranging from 0 to 1)