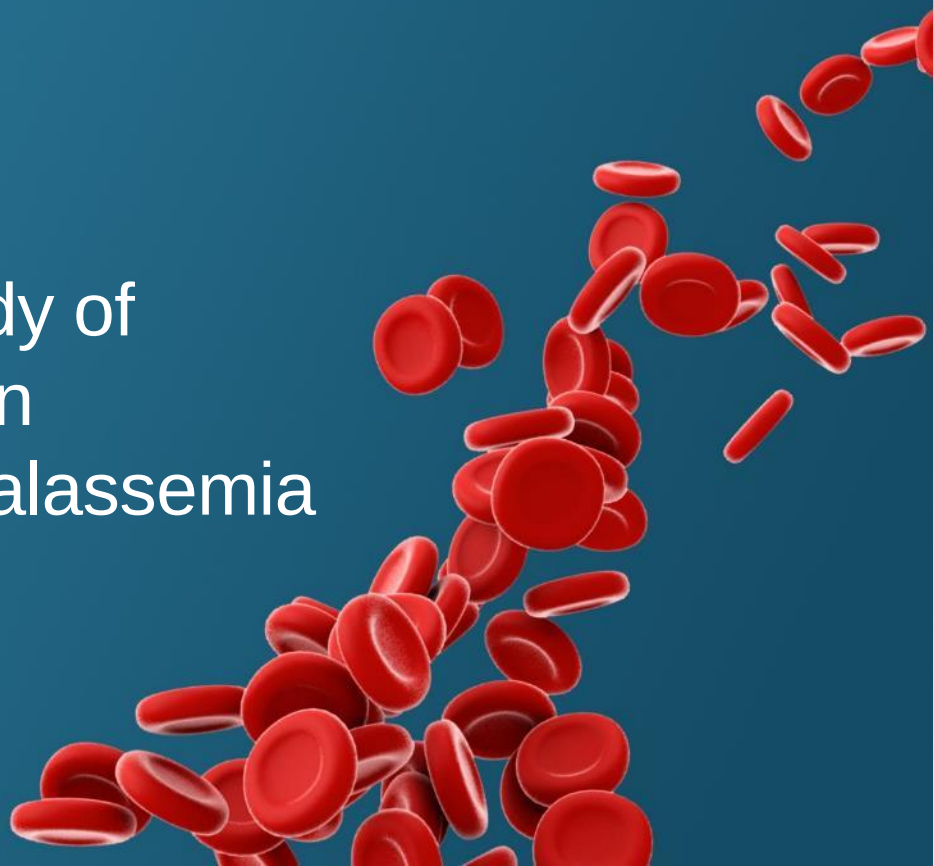
Topline Results:
Phase 3 ENERGIZE-T Study of PYRUKYND ® (Mitapivat) in Transfusion-Dependent Thalassemia

June 3, 2024



Agios conference call participants

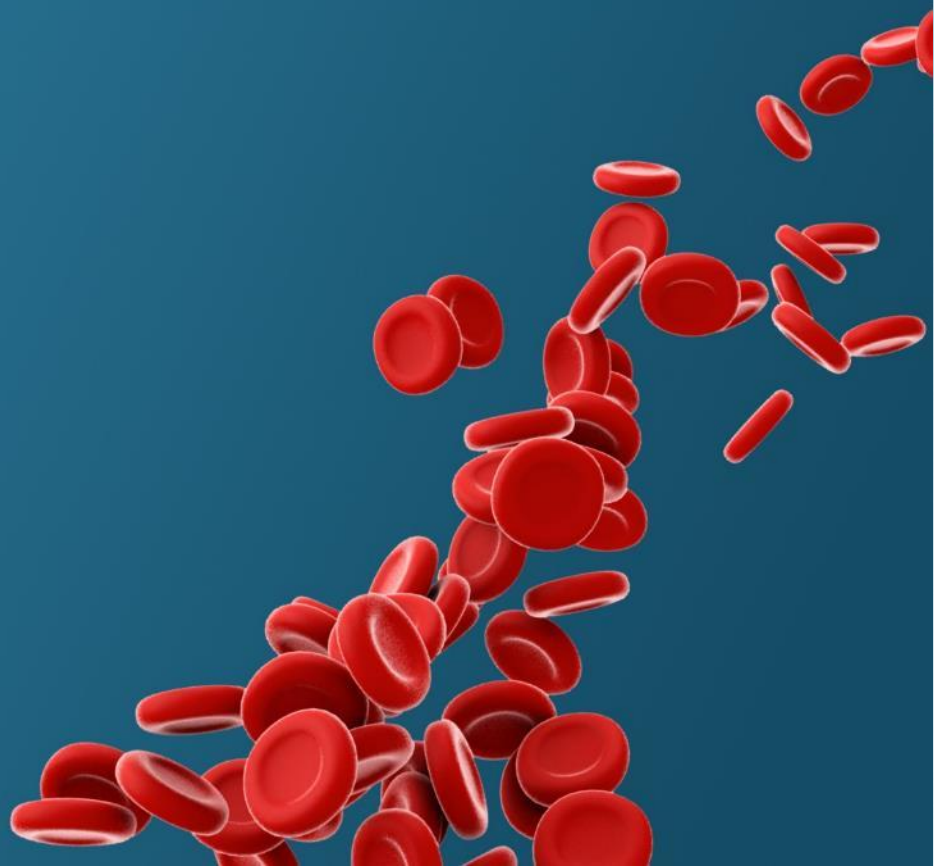
TOPIC	PARTICIPANT
Opening Remarks	Brian Goff, Chief Executive Officer
Data Highlights from Phase 3 ENERGIZE-T Study	Jeremie Estepp, M.D., Medical Director
Regulatory Strategy in Thalassemia	Sarah Gheuens, M.D., Ph.D., Chief Medical Officer, Head of Research and Development
Closing Remarks	Brian Goff, Chief Executive Officer
Q&A	Mr. Goff, Dr. Gheuens, Cecilia Jones (CFO), and Tsveta Milanova (CCO)

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 mitapivat, Agios' plans for the future clinical development of mitapivat in alpha- and beta thalassemia; Agios' plans for future regulatory submissions; and Agios' strategic plans and prospects. 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; 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 milestone or royalty payments related to the sale of Agios' oncology business or its in-licensing of TMPRSS6 siRNA, 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; competitive factors; 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.

Opening Remarks

Brian Goff
Chief Executive Officer

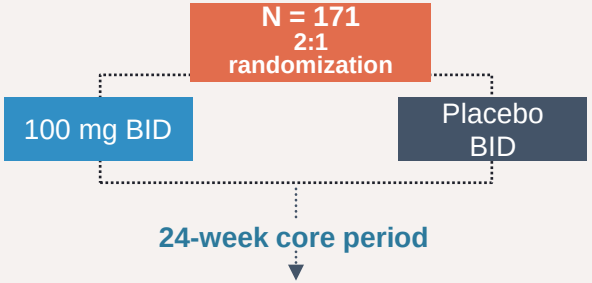


Data Highlights from Phase 3 ENERGIZE-T Study

Jeremie Estepp, M.D.
Medical Director

Two global, Phase 3, randomized controlled trials of PYRUKYND® in thalassemia encompass broad range of thalassemia patients

ENERGIZE



Primary endpoint

- Mean Hb ↑ ≥ 1 g/dL from baseline

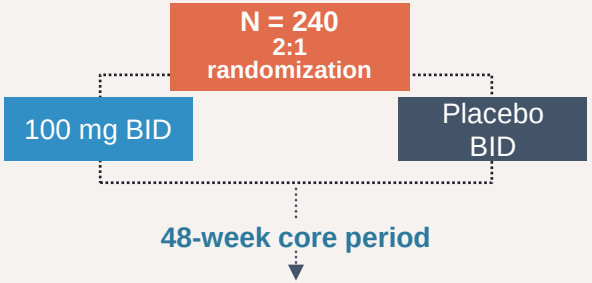
Secondary endpoints

- 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

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

Phase 3 ENERGIZE-T study: primary endpoint achieved

- Total of 258 patients were randomized 2:1 to 100 mg mitapivat (n=171) or placebo (n=87)
- 155 patients (90.6%) in the mitapivat arm and 83 patients (95.4%) in the placebo arm completed the 48-week double-blind period of the study
- Transfusion reduction response (TRR) is defined as ≥50% reduction in transfused RBC units of ≥2 units of transfused RBCs in any consecutive 12-week period compared to baseline
- **Treatment with mitapivat demonstrated a statistically significant transfusion reduction response compared to placebo**

Primary Endpoint	Placebo N=87	Mitapivat 100 mg BID N=171
TRR responders, n (%)	11 (12.6)	52 (30.4)
Adjusted difference TRR rate (Mitapivat-Placebo), %		17.6
95% CI		(8.0, 27.2)
2-sided p-value		0.0003

Abbreviations: RBC = red blood cell; TRR = transfusion reduction response. Subjects withdrawn from the study before Week 12 (Day 85) are considered non-responders.

Baseline transfusion burden standardized to 12 weeks=total number of RBC units transfused during the 24-week period (168 days) before 'reference date' x12/24, where 'reference date' is the randomization data for subjects randomized and not dosed or the start of study treatment for subjects randomized and dosed.

The 95% CI and p-value are based on the Mantel-Haenszel stratum weighted method adjusting for randomization stratification factors.

ENERGIZE-T: additional results demonstrate mitapivat's durability of effect

Efficacy

Treatment with mitapivat demonstrated statistically significant improvements on all key secondary endpoints evaluating additional measures of reduction in transfusion burden:

- ≥50% reduction in transfused RBC units in any consecutive 24-week period through week 48 compared to baseline
- ≥33% reduction in transfused RBC units from week 13 through week 48 compared to baseline
- ≥50% reduction in transfused RBC units from week 13 through week 48 compared to baseline

Transfusion independence

- A higher proportion of patients in the mitapivat arm (9.9%) compared to the placebo arm (1.1%) achieved the secondary endpoint of transfusion independence (transfusion-free for ≥8 consecutive weeks through week 48)

Safety

- Overall, during the 48-week double-blind period, incidence of adverse events (AEs) was similar across mitapivat and placebo arms
- In the mitapivat arm, 5.8% of the patients experienced an AE leading to discontinuation, compared to 1.2% of patients in the placebo arm

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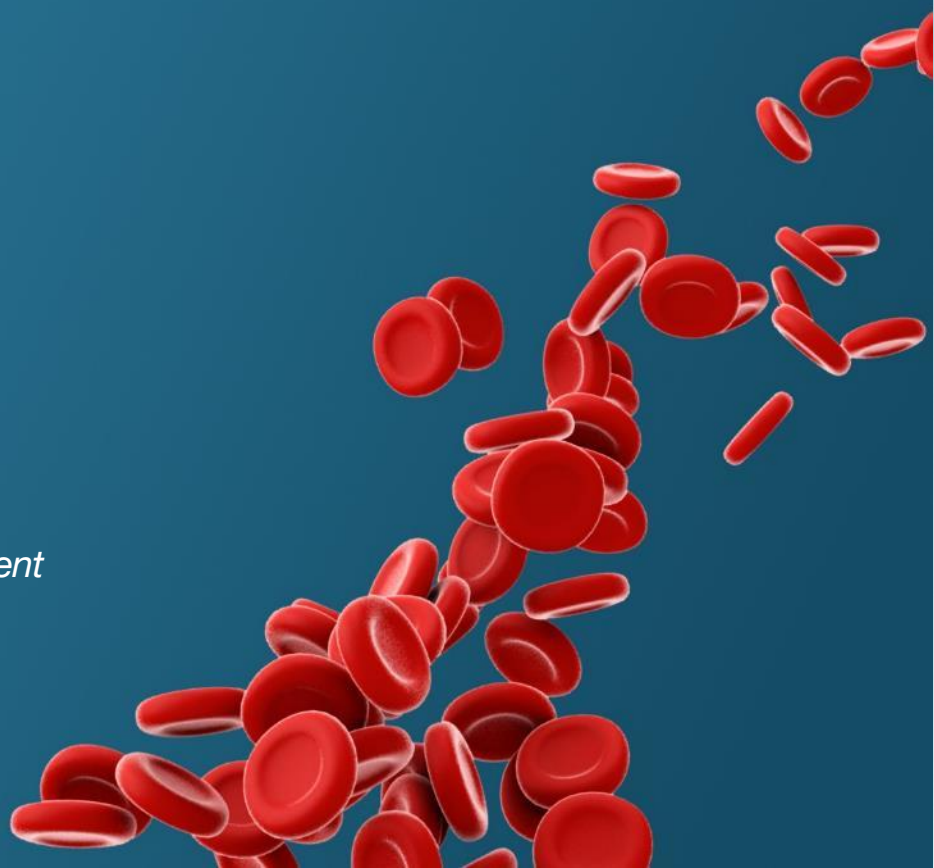
Regulatory Strategy in Thalassemia

Sarah Gheuens, M.D., Ph.D.
Chief Medical Officer, Head of Research and Development



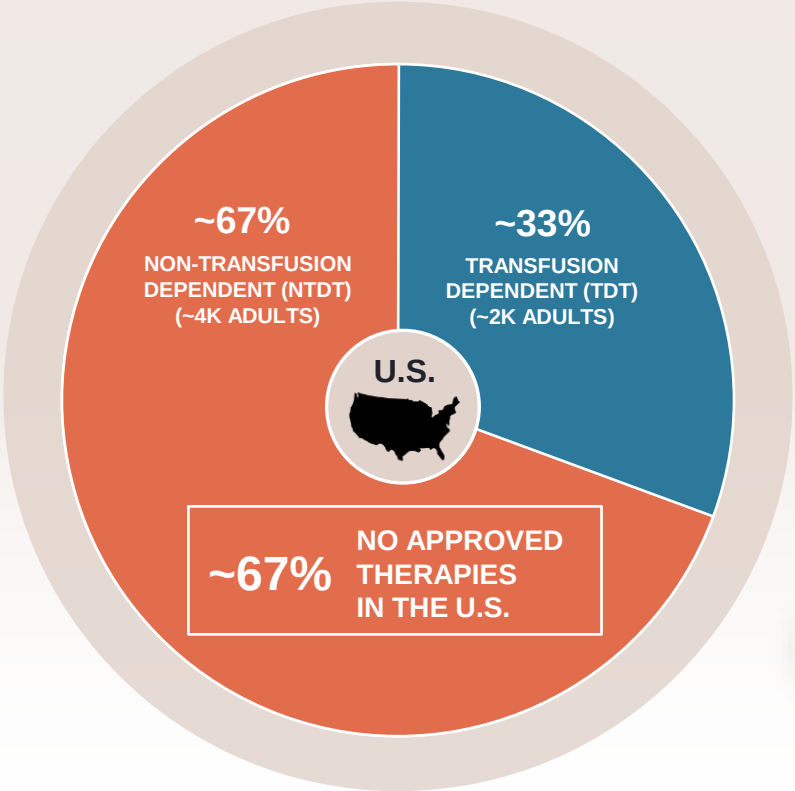
Based on strength of two pivotal Phase 3 trials, Agios has potential to deliver the first therapy for all thalassemia subtypes

Mitapivat Thalassemia Phase 3 program

ENERGIZE

- **Alpha- and Beta-thalassemia Non-transfusion dependent** patients
- Primary endpoint achieved: Hemoglobin (Hb) response

Data announced January 3, 2024



Mitapivat Thalassemia Phase 3 program

ENERGIZE-T

- **Alpha- and Beta-thalassemia Transfusion dependent** patients
- Primary endpoint achieved: Transfusion Reduction Response

Data announced June 3, 2024

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.

PYRUKYND® is under investigation for thalassemia and is not approved anywhere for that use.

ENERGIZE: achieved statistical significance across primary and key secondary endpoints with full data to be presented at EHA in June

ENERGIZE

Key findings in ENERGIZE trial

- Total of **194 patients** were randomized 2:1 to 100 mg mitapivat (n=130) or placebo (n=64)
- **Statistically significant increase in hemoglobin response rate (42.3%)** compared to patients on placebo (1.6%)
- Statistically significant improvements from baseline in both **average FACIT-Fatigue score** and **average hemoglobin concentration**
- During the 24-week double-blind period, 4 subjects in the mitapivat arm experienced adverse events (AEs) leading to discontinuation; no AEs in the placebo arm leading to discontinuation
- All pre-specified subgroup analyses favored the mitapivat treatment arm compared to placebo

Upcoming ENERGIZE data presentations at EHA 2024

Plenary Abstracts Session:

- **Title:** ENERGIZE: A Global Phase 3 Study of Mitapivat Demonstrating Efficacy and Safety in Adults with Alpha- or Beta- Non-Transfusion-Dependent Thalassemia
- **Abstract:** S104
- **Session Date and Time:** June 15, 14:45-15:15 CEST
- **Presenter:** Ali T. Taher, M.D., Ph.D.; Naef K. Basile Cancer Institute, American University of Beirut Medical Center

Poster Presentation:

- **Title:** Improvements in Fatigue and 6-minute Walk Test in Adults with Alpha- and Beta-Non-Transfusion-Dependent Thalassemia: The Phase 3 ENERGIZE Trial of Mitapivat
- **Abstract:** P1529
- **Session Date and Time:** June 14, 18-19:00 CEST
- **Lead Author:** Kevin H. M. Kuo, M.D., MSc, FRCPC; Division of Hematology, University of Toronto

Hemoglobin response is defined as ≥1.0 g/dL (10 g/L) increase in average Hb concentrations from Week 12 through Week 24 compared with baseline.

Planning single regulatory filing incorporating data from ENERGIZE and ENERGIZE-T

ENERGIZE data readout January 3, 2024 

ENERGIZE-T data readout June 3, 2024 

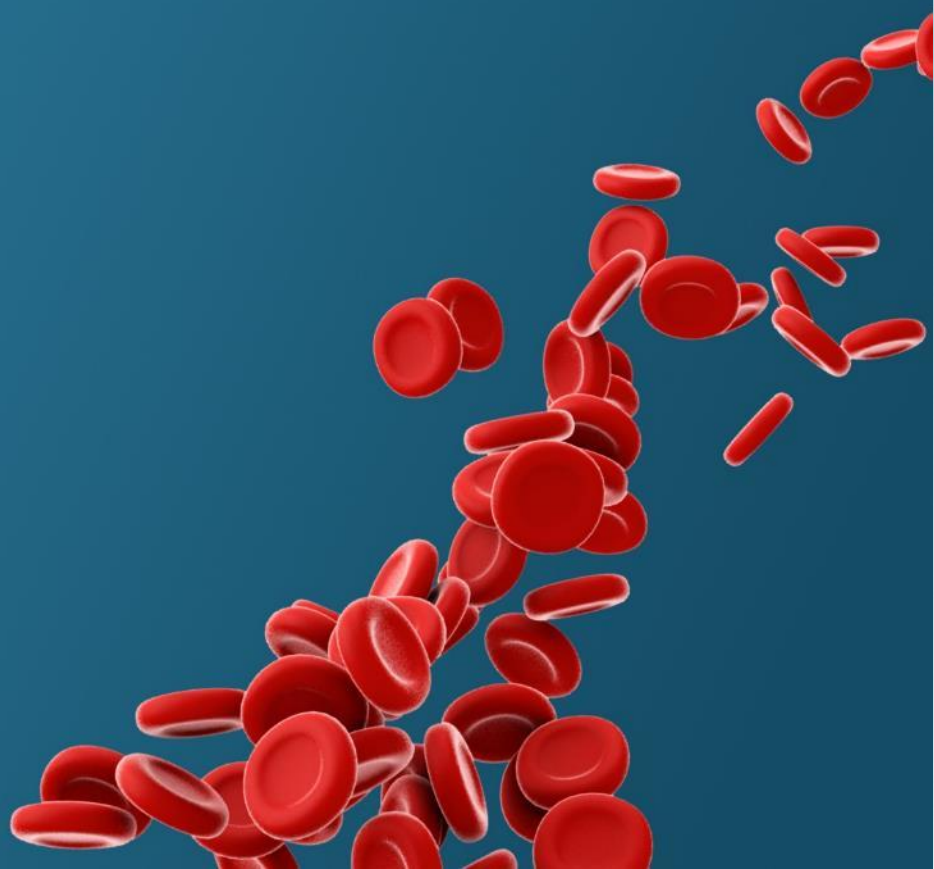
Anticipated filing encompassing data from ENERGIZE and ENERGIZE-T by year-end 2024

Seeking broad indication for all thalassemia patients

Potential FDA approval in 2025

Closing Remarks

Brian Goff
Chief Executive Officer



PYRUKYND® expansion into diseases with larger patient populations provides significant near-term growth potential for first- and best-in-class therapies

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., EU, and Great Britain for adult pyruvate kinase (PK) deficiency and is under investigation for pediatric PK deficiency, thalassemia, and sickle cell disease.
Source: Agios internal estimates

Strong beginning to 2024 with two positive Phase 3 readouts in thalassemia; three additional Phase 3 readouts expected by the end of 2025

2024

Thalassemia
PYRUKYND®
Phase 3 ENERGIZE readout

Thalassemia
PYRUKYND®
Phase 3 ENERGIZE-T readout

Pediatric PK Deficiency
PYRUKYND®
Phase 3 ACTIVATE kids-T readout

2025

Sickle Cell Disease
PYRUKYND®
Phase 3 RISE UP readout

Thalassemia
PYRUKYND®
Potential approval

Pediatric PK Deficiency
PYRUKYND®
Phase 3 ACTIVATE kids readout

2026

Sickle Cell Disease
PYRUKYND®
Potential approval

Pediatric PK Deficiency
PYRUKYND®
Potential approval

Well-positioned with multiple near-term catalysts to enter multi-billion-dollar markets and deliver significant value

PKa franchise with multi-billion-dollar potential	Differentiated mechanism of action	Increasing probability of success	Growing pipeline
Large opportunities with substantial value - potential for two additional **first and best-in-class** indications for PYRUKYND® by 2026	**Clearly differentiated** PK activation franchise targeting red blood cell health **beyond hemoglobin** increase	Proven track record supported by **compelling and consistent data** to date	Diversified pipeline addressing the underlying pathophysiology of **rare diseases with high unmet need**

- **Announced $905 million purchase agreement for vorasidenib royalty on May 28, 2024***
- **Retains rights to $200 million milestone payment from Servier upon FDA approval of vorasidenib**
- $714.3M in cash and equivalents as of March 31, 2024

PK = pyruvate kinase PKa = pyruvate kinase activation *Subject to FDA approval. Agios retains a 3% royalty on annual U.S. net sales greater than $1 billion

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Q&A