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Fueled by Connections to Transform Rare Diseases

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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), AG-946 and its PAH stabilizer; Agios' plans, strategies and expectations for its preclinical, clinical and commercial advancement of its drug development, including PYRUKYND®, AG-946 and its PAH stabilizer; Agios' strategic vision and goals, including its key milestones for 2023 and potential catalysts through 2026; 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 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 the COVID-19 pandemic 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 maintain key collaborations; the failure of Agios to receive milestone or royalty payments related to the sale of its oncology business, the uncertainty of the timing of any receipt of any such payments, and the uncertainty of the results and effectiveness of the use of proceeds from the transaction with Servier; 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.

Unmatched expertise in cellular metabolism

The Leader in Pyruvate Kinase (PK) Activation

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Track record of success in discovering, developing and commercializing therapies

DEVELOPED APPROVED THERAPIES IN ONCOLOGY

2017 & 2018

FIRST PYRUKYND® APPROVAL ADULTS WITH PYRUVATE KINASE (PK) DEFICIENCY

2022

RARE DISEASE FOCUS: POTENTIAL APPROVALS IN THALASSEMIA AND SICKLE CELL DISEASE

By 2026

Leader in pyruvate kinase (PK) activation poised for significant growth

Compelling and consistent data across connected diseases

Robust clinical data set supports potential of PK activation to transform patient function, quality of life, and long-term outcomes

Meaningful commercial opportunities on the horizon

First rare disease launch building capabilities to maximize anticipated franchise expansion

Potential for two additional PYRUKYND® indications by 2026

Well capitalized to advance and expand

Strong cash position expected to support completion of ongoing programs and disciplined portfolio expansion

Focused on expanding from PK deficiency to other diseases with shared pathophysiology, limited treatment options, and profound unmet needs

Pediatric PK Deficiency

No approved therapy for pediatric PK deficiency patients

Our goal: Deliver the first approved therapy for pediatric PK deficiency

Thalassemia

No approved therapy for ~60% of thalassemia patients

Our goal: Deliver the first therapy approved for all thalassemia subtypes

Sickle Cell Disease

No novel oral therapy improves anemia and reduces sickle cell pain crises

Our goal: Deliver a novel oral therapy that improves anemia and reduces VOCs

Lower-Risk MDS

No oral therapy addresses ineffective erythropoiesis

Our goal: Deliver the first oral therapy that addresses ineffective erythropoiesis

PYRUKYND® is approved in the U.S., EU, and Great Britain for adult PK deficiency and is under investigation for pediatric PK deficiency, thalassemia, and sickle cell disease.
AG-946 is under investigation for LR-MDS.

PK activation franchise positioned for meaningful expansion, with near-term opportunity in thalassemia

PYRUKYND® is the first and only disease-modifying treatment approved for adults with PK deficiency

Potential for two additional PYRUKYND® indications by 2026

PK deficiency
Approved for adults in the U.S. and EU

3-8K patients
in the U.S./EU5

Thalassemia
Potential U.S. approval in 2025

18-23K patients
in the U.S./EU5

Sickle cell disease
Potential U.S. approval in 2026

120-135K patients
in the U.S./EU5

ADDITIONAL OPPORTUNITIES FOR THE FRANCHISE WITH NOVEL PK ACTIVATOR AG-946

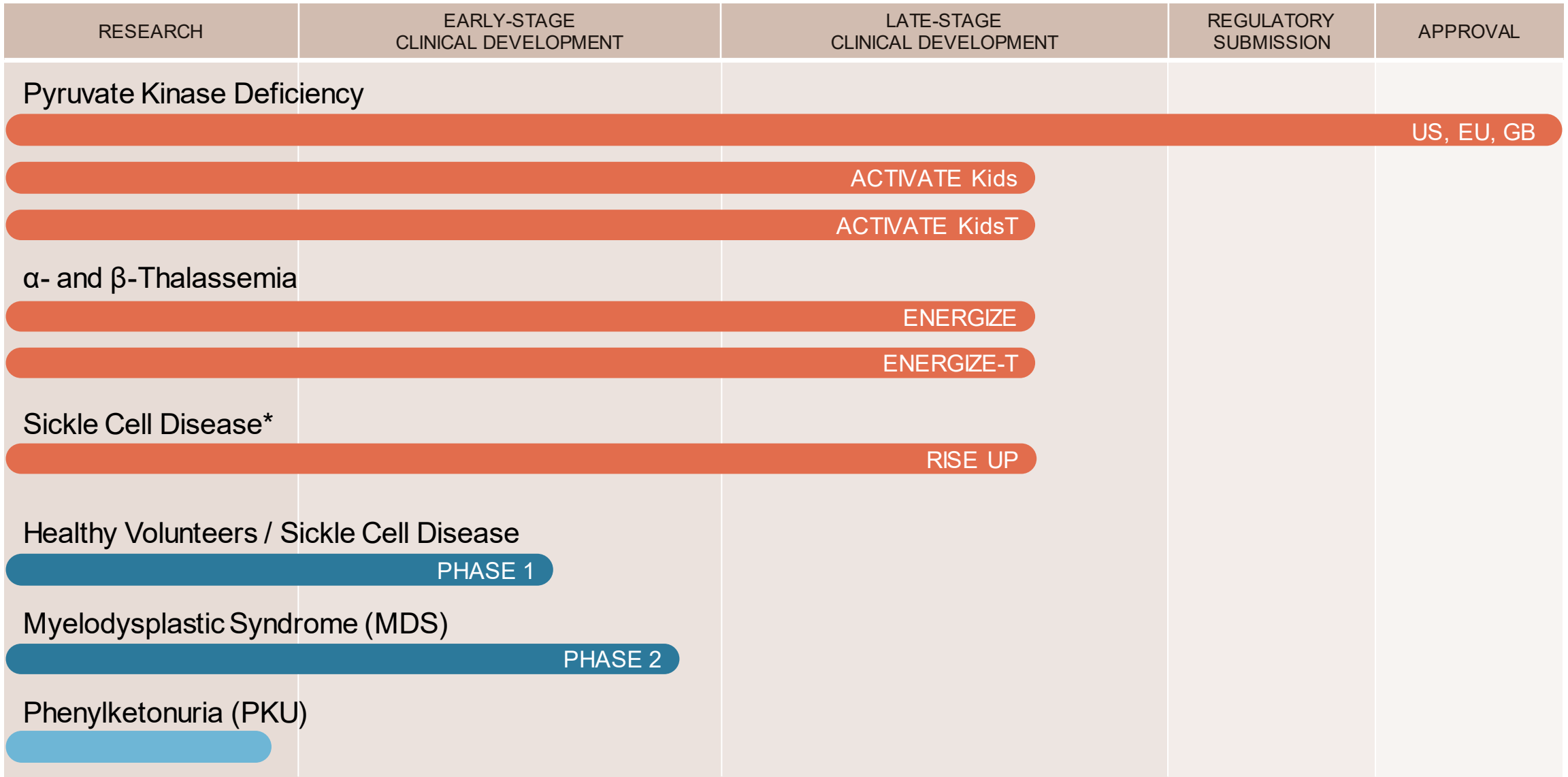
Lower-risk myelodysplastic syndrome

75-80K patients
in the U.S./EU5

- Orphan patient populations
- High unmet need
- Focused prescriber pool
- Differentiated product profile

Source: Agios internal estimates

Building a diverse pipeline leveraging our expertise in cellular metabolism



*In addition to RISE UP, two investigator-sponsored trials are ongoing with the NIH and University of Utrecht.

PYRUKYND®
First-in-class PK activator

AG-946
Novel PK activator

Phenylalanine hydroxylase (PAH) stabilizer

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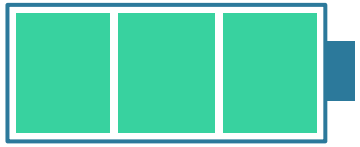
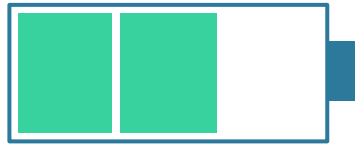
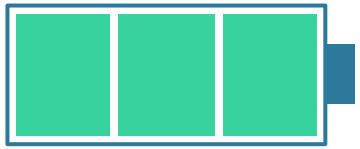
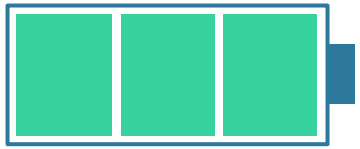
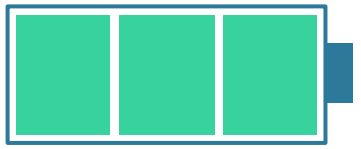
Compelling and consistent data across connected diseases

PK activation may address a range of hemolytic and acquired anemias underpinned by shared pathophysiology

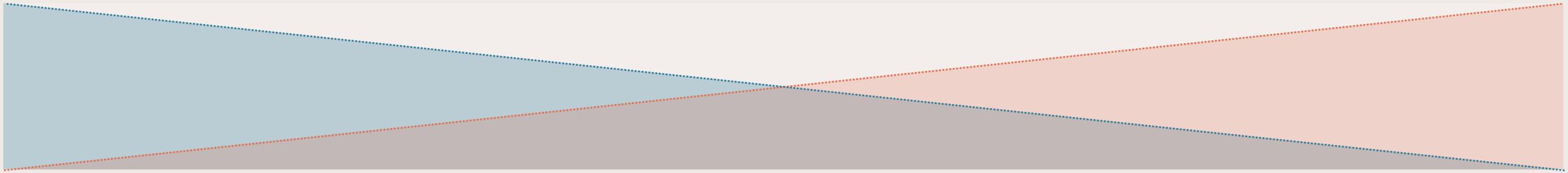
Energy imbalance in red blood cells can lead to severe hematological disease

Healthy Red Blood Cell	PK Deficiency	Other Anemias Thalassemia, Sickle Cell Disease, Lower-Risk MDS
Energy supply			
Energy demand			 
ATP production meets demand	***Insufficient ATP production*** *Leads to red blood cell metabolic stress, anemia, and reduced patient quality of life*	

Disease areas share common pathophysiology and severely impact quality of life

Red Blood Cell Metabolic Stress

PK Deficiency | Sickle Cell Disease | Thalassemia | MDS Associated Anemia



Chronic Hemolysis
Destruction of red blood cells

Ineffective Erythropoiesis
Decreased output of red blood cells

Significant near and long-term clinical consequences of chronic hemolysis and ineffective erythropoiesis…

ANEMIA	TRANSFUSION BURDEN	IRON OVERLOAD	REDUCED BONE MINERAL DENSITY	LONG-TERM ORGAN DAMAGE

..that lead to major implications for patient quality of life and how they feel and function.

CHRONIC FATIGUE, SUSCEPTIBILITY TO ILLNESS	CHALLENGES WITH BASIC SOCIAL, SCHOOL / WORK ACTIVITIES	IMPACT ON EMOTIONAL AND MENTAL HEALTH	PAIN AND FRACTURES	ECONOMIC BURDEN

Consistency of clinical data to date supports potential of PYRUKYND® to address unmet patient needs across hemolytic anemias

	Adult PK Deficiency *(Mutant PK enzyme)* *Approved in the U.S., EU and Great Britain*	**Thalassemia** *(Wild-type PK enzyme)* *Data through Phase 2*	**Sickle Cell Disease** *(Wild-type PK enzyme)* *Data through Phase 1 and ISTs*
Hemoglobin improvement	✓	✓	✓
Hemolysis improvement	✓	✓	✓
Erythropoiesis improvement	✓	✓	✓
PRO improvements	✓		
Transfusion reduction	✓		
Sickling reduction			✓
	ONGOING STUDY Phase 3 long-term extension study	ONGOING STUDIES Phase 3 ENERGIZE and ENERGIZE-T studies Phase 2 long-term extension study	ONGOING STUDIES Phase 2/3 RISE UP study Investigator-sponsored trials

1. Al-Samkari et al. N Engl J Med 2022; 386:1432-1442; 2. Glenthoj et al. The Lancet Haematology, 2022, Vol 9, e724 - e732; 3. Van Beers et al. ASH 2021: Abstract 757; 4. Al-Samakri et al. ASH 2021. Abstract 924; 5. Kuo et al. ASH 2022: Abstract 506; 6. Van Beers et al. ASH 2022: Abstract 1021; 7. Grace et al. ASH 2022: Abstract 2328; 8. Kuo KHM et al. Lancet 2022; 400:10351; 9. Kuo KHM et al. ASH 2021: Abstract 576; 10. Kuo KHM et al. ASH 2022: Abstract 1030; 11. Van Dijk MJ et al. Am J Hematol. 2022;97:E226; 12. Xu JZ et al. Blood. 2022;140:2053; 13. Van Dijk MJ et al. EHA 2022: Abstract P1501.

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Hemoglobin improvement	✓	✓	✓
Hemolysis improvement	✓	✓	✓
Erythropoiesis improvement	✓	✓	✓
PRO improvements	✓		
Transfusion reduction	✓		
Sickling reduction			✓
Emerging Long-term Data			
Bone health stabilization	✓		
Iron overload reduction	✓		
Length of exposure	OVER 7 YEARS	OVER 4.5 YEARS	OVER 2 YEARS

1. Al-Samkari et al. N Engl J Med 2022; 386:1432-1442; 2. Glenthoj et al. The Lancet Haematology, 2022, Vol 9, e724 - e732; 3. Van Beers et al. ASH 2021: Abstract 757; 4. Al-Samakri et al. ASH 2021. Abstract 924; 5. Kuo et al. ASH 2022: Abstract 506; 6. Van Beers et al. ASH 2022: Abstract 1021; 7. Grace et al. ASH 2022: Abstract 2328; 8. Kuo KHM et al. Lancet 2022; 400:10351; 9. Kuo KHM et al. ASH 2021: Abstract 576; 10. Kuo KHM et al. ASH 2022: Abstract 1030; 11. Van Dijk MJ et al. Am J Hematol. 2022;97:E226; 12. Xu JZ et al. Blood. 2022;140:2053; 13. Van Dijk MJ et al. EHA 2022: Abstract P1501.

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Meaningful commercial opportunities on the horizon

FDA approval and launch of PYRUKYND in PK deficiency builds capabilities to maximize potential product expansion

PYRUKYND® launch in PK deficiency building commercial capabilities to support potential expansion in meaningfully larger patient populations

Optimizing Patient & Provider Journey

Awareness & Education

Know **PK Deficiency**

Drive awareness and urgency to manage PK deficiency among providers and patients

Diagnostic Efficiency

Anemia ID®

Free genetic testing to help confirm diagnosis of hereditary anemias

PK deficiency patient identification via claims-based targeting

Therapy Onboarding

Activate physicians to prescribe and eligible patients to advocate for treatment

Access & Adherence

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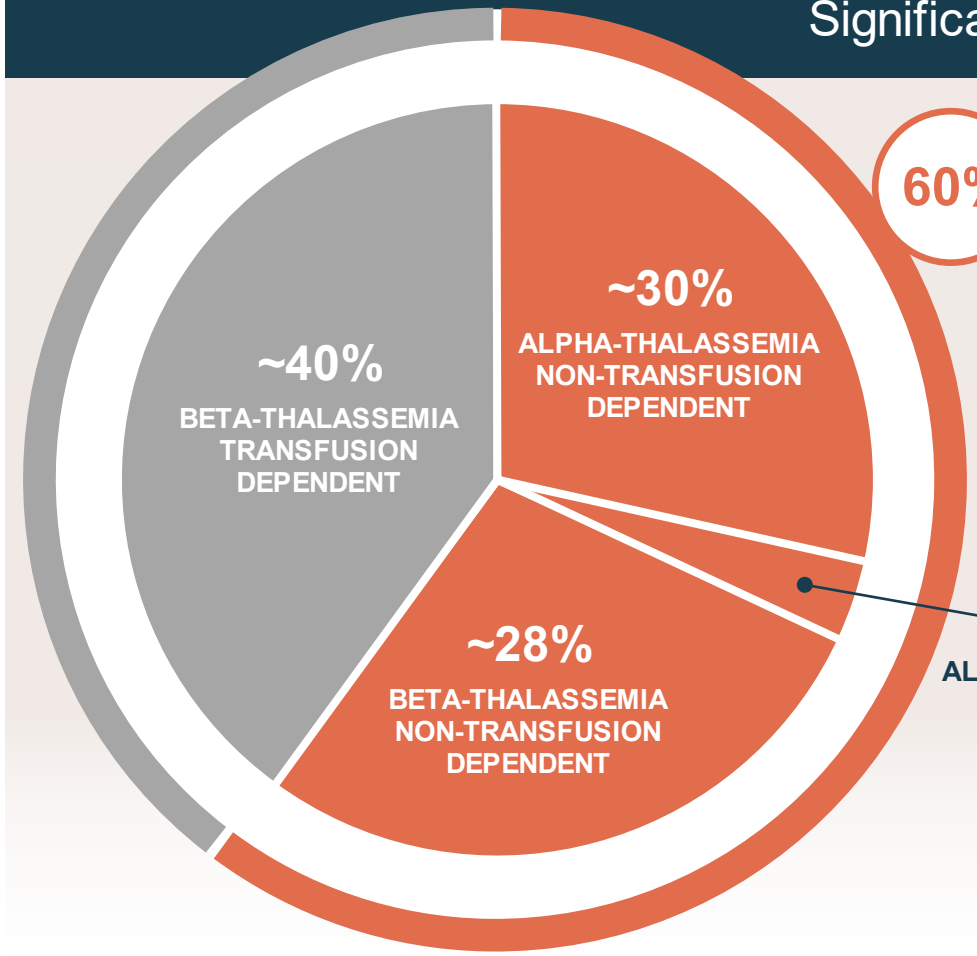
Coverage support, free product eligibility, copay program

Thalassemia: no approved therapies for ~60% of patients

High unmet need across patient segments and geographies

~18-23K Patients in U.S./EU5

Significant opportunity outside U.S./EU5



60%

NO AVAILABLE THERAPIES

TARGET PROFILE

PYRUKYND®

- Address full range of thalassemia patients
- Chronic therapy
- Oral
- Improved Hb and reduced transfusion burden
- Improved ineffective erythropoiesis
- Safety profile consistent with prior clinical experience

Beta-THAL prevalence: HEOR Global THAL Epidemiology SLE (XCENDA, 2021); US: Paramore, et.al; DE: Borchert, et.al; IT: Italian Society of Thal & Hemoglobinopathies Patient Registry, Jan 2021, Angelucci, et.al, 2017; FR: French registry for thal (Thuret, et.al.); ES: Cela, et.al.; UK Registry for Hemoglobinopathies, 2020; 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 (5% / 95%): 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.

Sickle Cell Disease: no novel oral therapy improves anemia and reduces sickle cell pain crises

- Estimated 120-135K patients across the U.S. & EU5
- Significant opportunity outside of U.S./EU

Global Reach

- Deliver a novel oral therapy that improves anemia, reduces VOCs and is supported by the largest body of clinical evidence

PYRUKYND® Opportunity

- Innovative seamless Phase 2/3 trial RISE UP developed with community input
- Global approach to clinical development
- Connections with SCD patient and physician communities

Critical Success Factors

TARGET PROFILE

PYRUKYND®

- Chronic Therapy
- Oral
- Improved hemolytic anemia
- Improvement in sickle cell pain crises (vaso-occlusive crises; VOCs)
- QoL data
- Safety profile consistent with prior clinical experience

PYRUKYND® is under investigation for sickle cell disease and is not approved anywhere for that use.

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Well capitalized to advance and expand

Long-term growth and value creation fueled by accomplished leadership team and strong balance sheet

Strong cash position expected to support portfolio advancement and expansion

Focused on rare diseases rooted in cellular metabolism

CLINICAL-STAGE PIPELINE

PYRUKYND®

- First and only disease-modifying treatment for adults with PK deficiency
- Potential for two additional indications by 2026

AG-946

- Potential to be first oral therapy to address the underlying cause of ineffective erythropoiesis in MDS

EARLIER-STAGE PIPELINE

LEAD RESEARCH PROGRAM

- PAH stabilizer for the treatment of PKU
- ~15-20K patients in the U.S.; ~20K in the EU5
- Target to file IND by year-end 2023

BUSINESS DEVELOPMENT

DISCIPLINED BD STRATEGY

- Prioritize opportunities based on:
  - Rare disease focus
  - Transformative for patients
  - Identified regulatory pathway
  - Potential to de-risk early
  - Clear path to value creation

Deliver transformative therapeutics for patient communities with profound unmet need

*PAH: phenylalanine hydroxylase; PKU: Phenylketonuria

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2023 and Beyond

Clinical development strategy driving toward broader commercial opportunities

Clinical and regulatory milestones targeted in 2023 lay the foundation for transformational data readouts

Thalassemia PYRUKYND®	Complete enrollment of Phase 3 ENERGIZE and ENERGIZE-T studies (mid-year)
Pediatric PK Deficiency PYRUKYND®	Enroll at least half of patients in the Phase 3 ACTIVATE-kids and ACTIVATE-kidsT studies (year-end)
Sickle Cell Disease PYRUKYND®	Phase 2 RISE UP data readout & go/no-go to Phase 3 decision (mid-year)
Lower-Risk MDS AG-946 (Novel PK Activator)	Complete enrollment of Phase 2a study (year-end)
Earlier-stage Pipeline	File IND for PAH stabilizer for the treatment of PKU (year-end)

Build commercial capabilities to efficiently launch additional indications and evaluate business development opportunities to expand pipeline

Potential for two additional PYRUKYND® indications by 2026

	2024	2025	2026
Thalassemia PYRUKYND®	Phase 3 ENERGIZE (1H) and ENERGIZE-T (2H) readouts	Potential approval	
Pediatric PK Deficiency PYRUKYND®		Phase 3 ACTIVATE-kids and ACTIVATE-kidsT readouts	Potential approval
Sickle Cell Disease PYRUKYND®		Potential Phase 3 RISE UP readout*	Potential approval
Lower-Risk MDS AG-946 (Novel PK Activator)	Phase 2a readout		

*Pending Go/NoGo decision in 2023

Driven to transform patient outcomes in rare diseases

2026 VISION

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Q&A