agios

Q3 2023 Financial Results

November 2, 2023

Agios conference call participants

TOPIC	PARTICIPANT
Introduction	Chris Taylor, VP Investor Relations and Corporate Communications
Business Update	Brian Goff, Chief Executive Officer
Research & Development Update	Sarah Gheuens, M.D., Ph.D., Chief Medical Officer, Head of Research and Development
Commercial Update	Tsveta Milanova, Chief Commercial Officer
Third Quarter 2023 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), AG-946, TMPRSS6 siRNA and Agios' 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 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 milestone or royalty payments related to the sale of its 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; 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.

agios

Opening Remarks

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

2023

Thalassemia
PYRUKYND®
Complete enrollment of Phase 3 ENERGIZE and ENERGIZE-T studies
(MID-YEAR)

Sickle Cell Disease
PYRUKYND®
Phase 2 RISE UP data readout & go/no-go to Phase 3 decision
(MID-YEAR)

Pediatric PK Deficiency
PYRUKYND®
Enroll at least half of patients in the Phase 3 ACTIVATE-kids and ACTIVATE-kidsT studies
(YEAR-END)

Pipeline
File IND for PAH stabilizer for the treatment of PKU
(YEAR-END)

Lower-Risk MDS
AG-946 (Novel PK Activator)
Complete enrollment of Phase 2a study
(YEAR-END)

Sickle Cell Disease
PYRUKYND®
Begin patient enrollment in Phase 3 RISE UP study
(YEAR-END)

Lower-Risk MDS
AG-946
Phase 2a topline data readout
(YEAR-END)

Evaluate business development opportunities to expand pipeline and build commercial capabilities to efficiently launch additional indications

★ Announced today

Q3 2023 highlights

Pipeline updates

- Dosed first patient in the Phase 3 portion of the RISE UP study of mitapivat in sickle cell disease
- Completed enrollment in the Phase 3 ACTIVATE-kidsT study of mitapivat in regularly transfused pediatric patients with PK deficiency
- Achieved goal of >50% enrollment in Phase 3 ACTIVATE-kids study
- PYRUKYND® net revenue $7.4M in Q3 2023; launch providing platform to support potential expansion in larger patient populations

Corporate updates

- On track to achieve all 2023 milestones and deliver 3 mid-to-late stage readouts by the end of 2024
- $872M in cash, cash equivalents, and marketable securities as of September 30, 2023

Potential for two additional PYRUKYND® indications by 2026

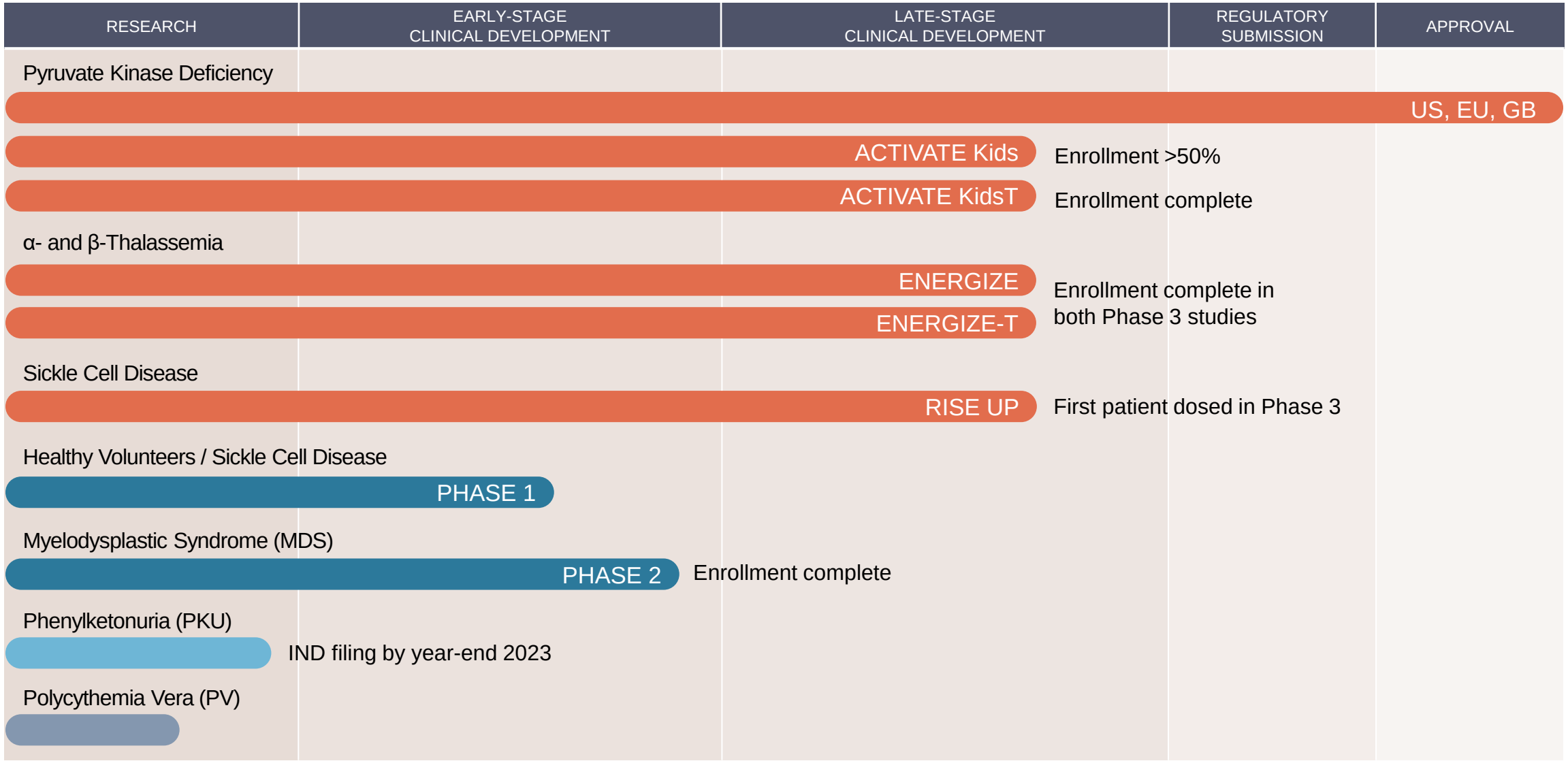
	2024	2025	2026
Thalassemia PYRUKYND®	**Phase 3 ENERGIZE (1H) and ENERGIZE-T (2H) readouts**	**Potential approval**	
Pediatric PK Deficiency PYRUKYND®		**Phase 3 ACTIVATE-kids and ACTIVATE-kidsT readouts**	**Potential approval**
Sickle Cell Disease PYRUKYND®		**Potential Phase 3 RISE UP readout**	**Potential approval**
Lower-Risk MDS AG-946 (Novel PK Activator)	**Phase 2a readout** (accelerated to YE 2023)		

1 *Clinical*

2 *Commercial*

3 *Financial*

Building a diverse pipeline leveraging our expertise in cellular metabolism



PYRUKYND®
First-in-class PK activator

AG-946
Novel PK activator

Phenylalanine hydroxylase (PAH) stabilizer

siRNA Targeting TMPRSS6

Highlighting key pipeline progress at ASH 2023

American Society of Hematology Annual Meeting

December 9-12, 2023 | San Diego

PK Deficiency

Thalassemia

Sickle Cell Disease

Patient Advocacy

Educational Session on PK Activation Organized by ASH

Abstracts go live today, November 2 at 9 a.m. ET.

RISE UP Phase 3 Study: first patient dosed

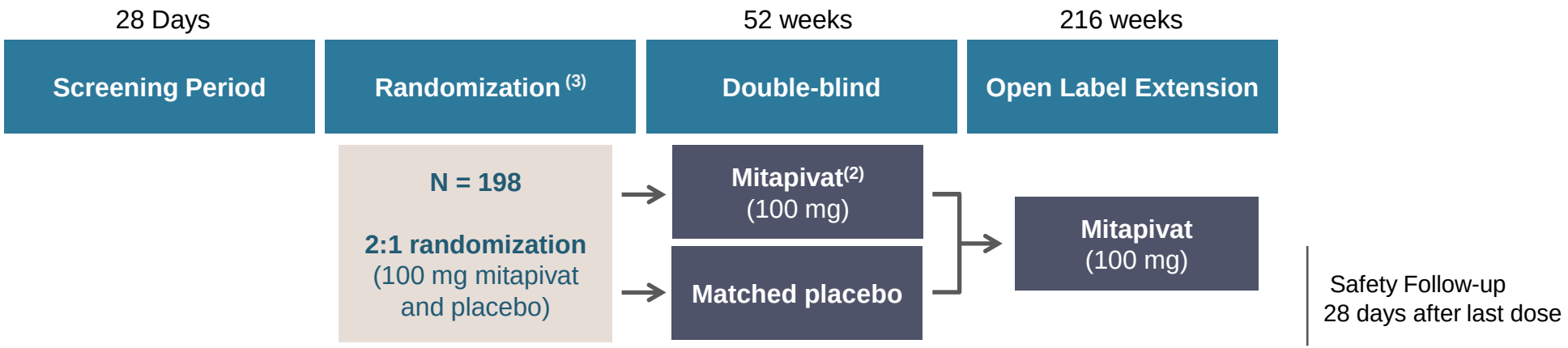
Phase 3 primary endpoints [(1)]:
Hb response, defined as a ≥ 1.0 g/dL increase in average Hb concentration over Weeks 24–52 compared with baseline, and annualized rate of SCPCs

Key inclusion criteria

- ≥ 16 years of age
- Documented SCD (HbSS, HbSC, HbSβ0/HbSβ+ thalassemia, other SCD variants)
- Recurrent VOCs (vaso-occlusive crises) – defined as the occurrence of 2–10 SCPCs (acute pain needing medical contact, acute chest syndrome, priapism, hepatic or splenic sequestration) in the prior 12 months
- Anemia – defined as a Hb level of 5.5–10.5 g/dL
- If taking HU, the dose must be stable for ≥ 90 days before starting study drug

Key exclusion criteria

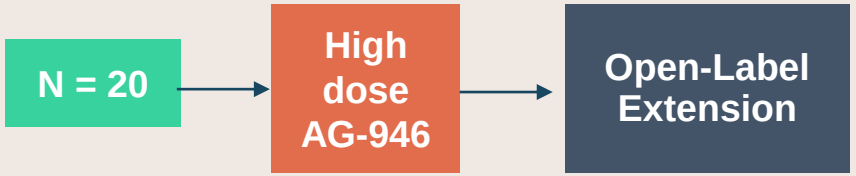
- Receiving regularly scheduled blood transfusions
- Severe kidney disease or hepatobiliary disorders
- Currently receiving treatment with SCD therapies (excluding HU)
- Prior exposure to gene therapy, or prior bone marrow or stem cell transplantation



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).

Novel PK activator AG-946: Seamless Phase 2a proof-of-concept + Phase 2b trials focused on establishing proof-of-concept and dose selection in LR-MDS

Phase 2a — Open Label

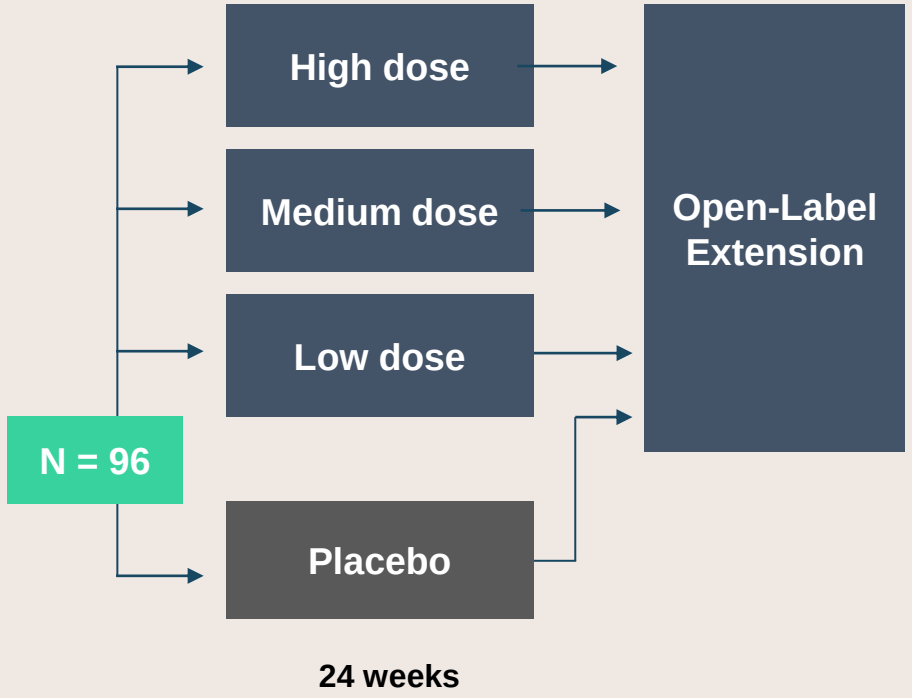


Primary endpoints:

- Hemoglobin (Hb) response, defined as a ≥1.5-g/dL increase from baseline in the average Hb concentration from Week 8 through Week 16
- Transfusion independence, defined as transfusion-free for ≥8 consecutive weeks during the Core Period (participants with low transfusion burden only)

Secondary endpoints: safety, additional measures of anemia, PK and PD biomarkers

Phase 2b — Double Blind, 1:1:1:1 Randomization

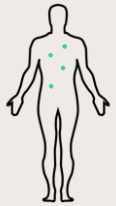


Topline data readout by year-end 2023

LR-MDS = Lower-risk Myelodysplastic Syndrome; PK = pharmacokinetics; PD = pharmacodynamics.

PAH program aimed to address the underlying cause of phenylketonuria (PKU)

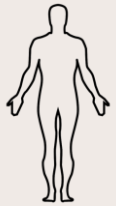
1



Normal Protein Diet

A mixed diet provides your body Phe

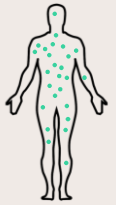
2



Defective PAH enzyme

PAH fails to process the Phe to Tyr

3



Increase in Phenylalanine

This leads to high Phe levels in the blood, which results in PKU

PHENYLKETONURIA (PKU)

- Rare, genetic disease with limited treatment options
- Prevalence: total of ~35-40K patients in the U.S. and EU5
- Driven by deficiency of phenylalanine hydroxylase (PAH) enzyme
- Lack of PAH activity leads to accumulation of phenylalanine and downstream sequelae
- PKU patients are often advised to consume a highly restricted diet, further reducing quality of life

AGIOS PROGRAM

- Oral PAH stabilizer designed to reduce phenylalanine levels

Targeting IND filing by year-end 2023

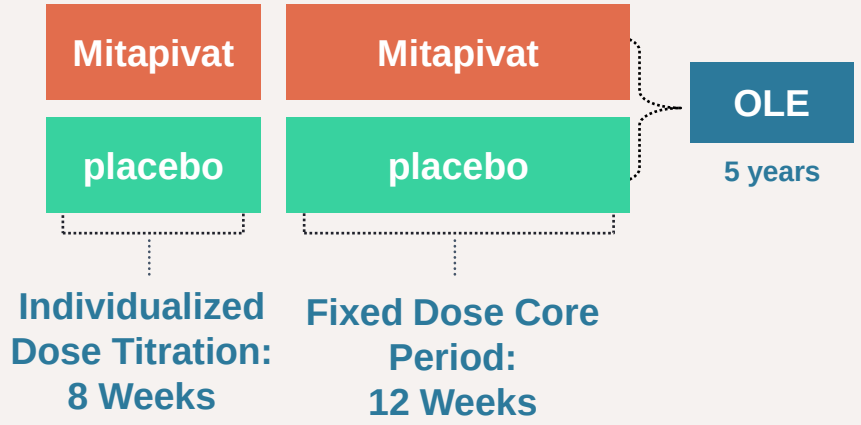
PHE = phenylalanine, TYR = tyrosine

Sources: National PKU Alliance, www.npkua.org and Weisbren et al ‘Phenylalanine blood levels and clinical outcomes in phenylketonuria’; The American Journal of Human Genetics 107, 234–250, August 6, 2020; Agios internal estimates

Enrollment complete in Phase 3 ACTIVATE-KidsT study aimed to support potential label expansion to PK deficiency patients under 18

ACTIVATE-Kids™

Not Regularly Transfused PK Deficiency N=30
Randomize 2:1



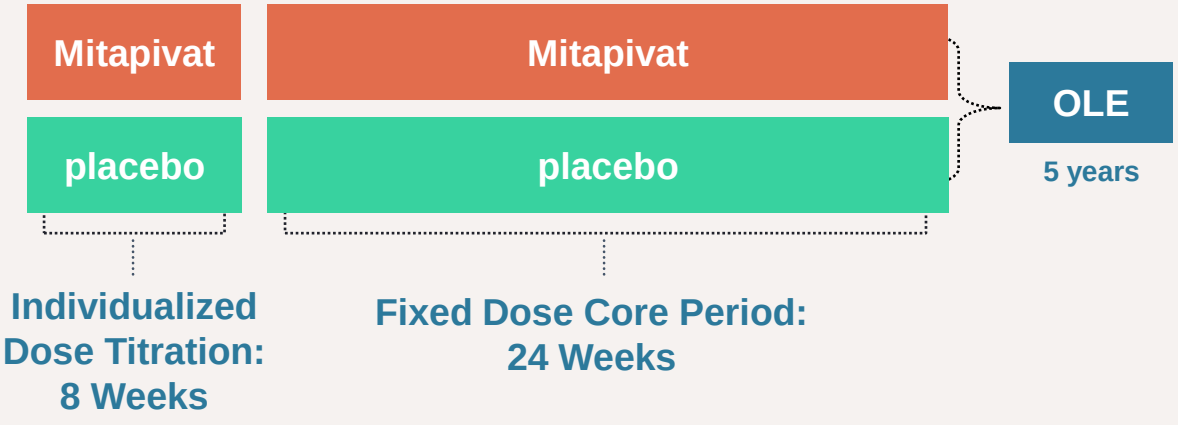
Eligibility

- 1 to <18 years of age
- Mean Hb concentration of ≤10 g/dL for patients 12 to <18 years or ≤9 g/dL for patients 1 to <12 years
- Not regularly transfused, with no more than five transfusions in the 12 months prior and no transfusions in the 12 weeks prior to the first day of study treatment

>50% enrolled

ACTIVATE-KidsT™

Regularly Transfused PK Deficiency N=45
Randomize 2:1



Eligibility

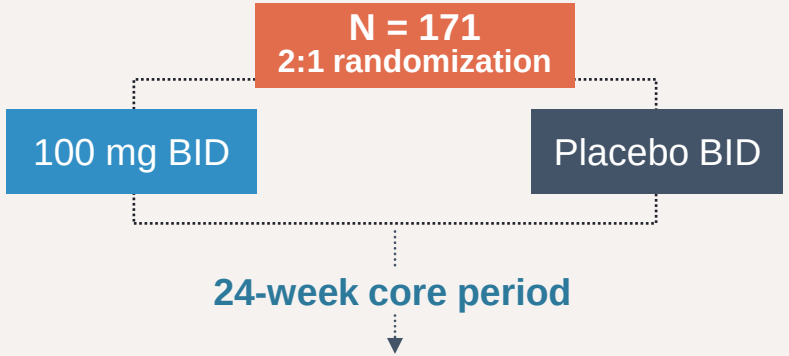
- 1 to <18 years of age
- Six to 26 transfusion episodes in the 52-week period before providing informed consent

Enrollment complete

OLE = open label extension.

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

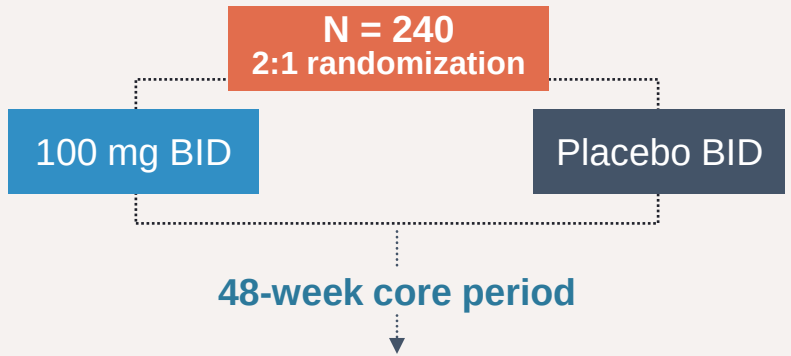
Secondary endpoints

- 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.

1 *Clinical*

2 *Commercial*

3 *Financial*

PYRUKYND® Q3 2023 performance metrics highlight continued progress

$7.4M net U.S. sales of PYRUKYND®
a 10% increase over Q2 2023

100 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

160 unique patients completed PYRUKYND® prescription enrollment forms,
a 9% increase over Q2 2023

Unique prescriber base of 142 physicians, diversified across the country, a 9% increase over Q2 2023

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., EU & GB
Potential U.S. pediatric approval in 2026

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

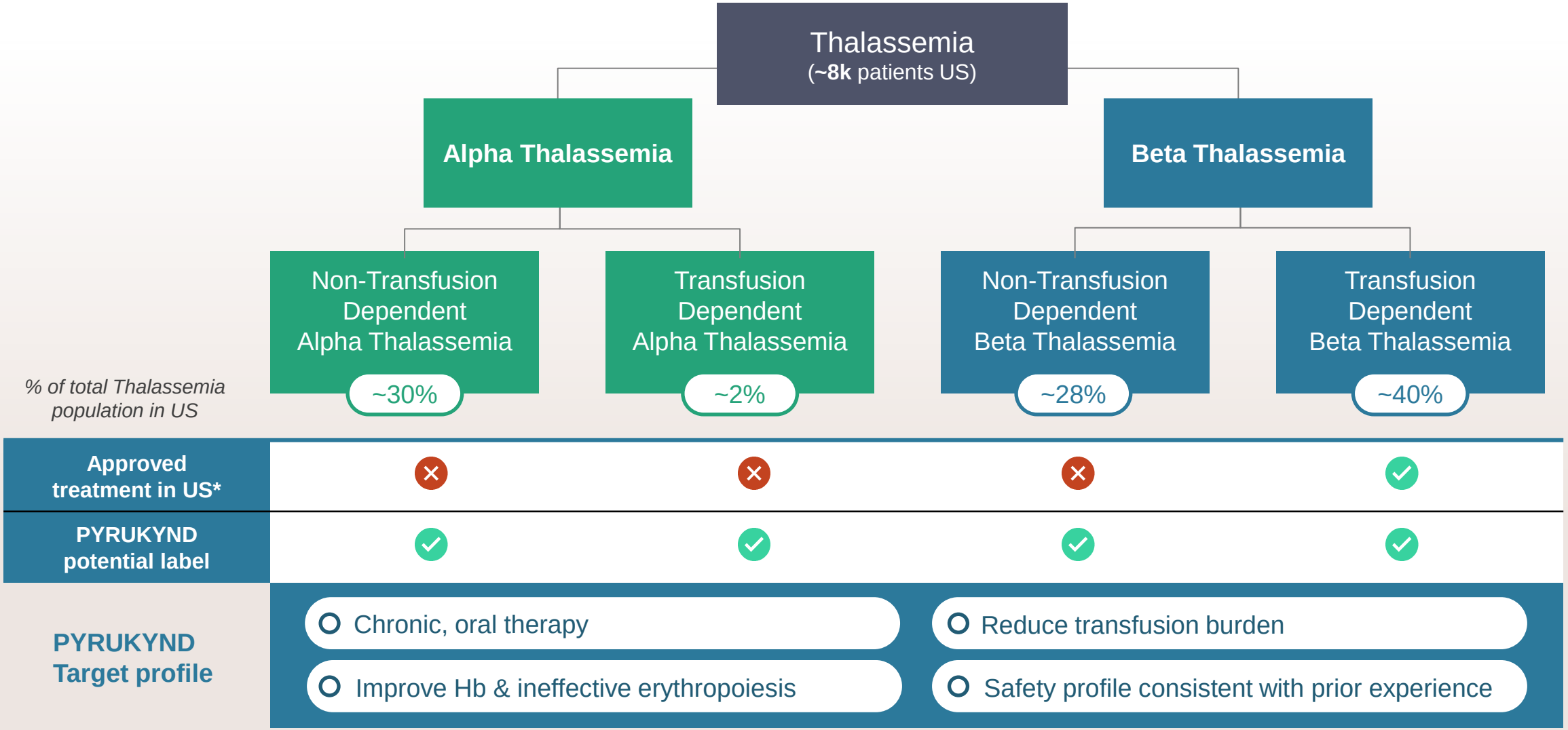
Lower-risk myelodysplastic syndrome

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

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

Source: Agios internal estimates

Agios aims to deliver the first therapy approved for all thalassemia subtypes



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.

*Note: Reblozyl also approved in non-transfusion dependent beta-thalassemia EU

US Thalassemia market has higher diagnosed prevalence and disease awareness compared to PK deficiency

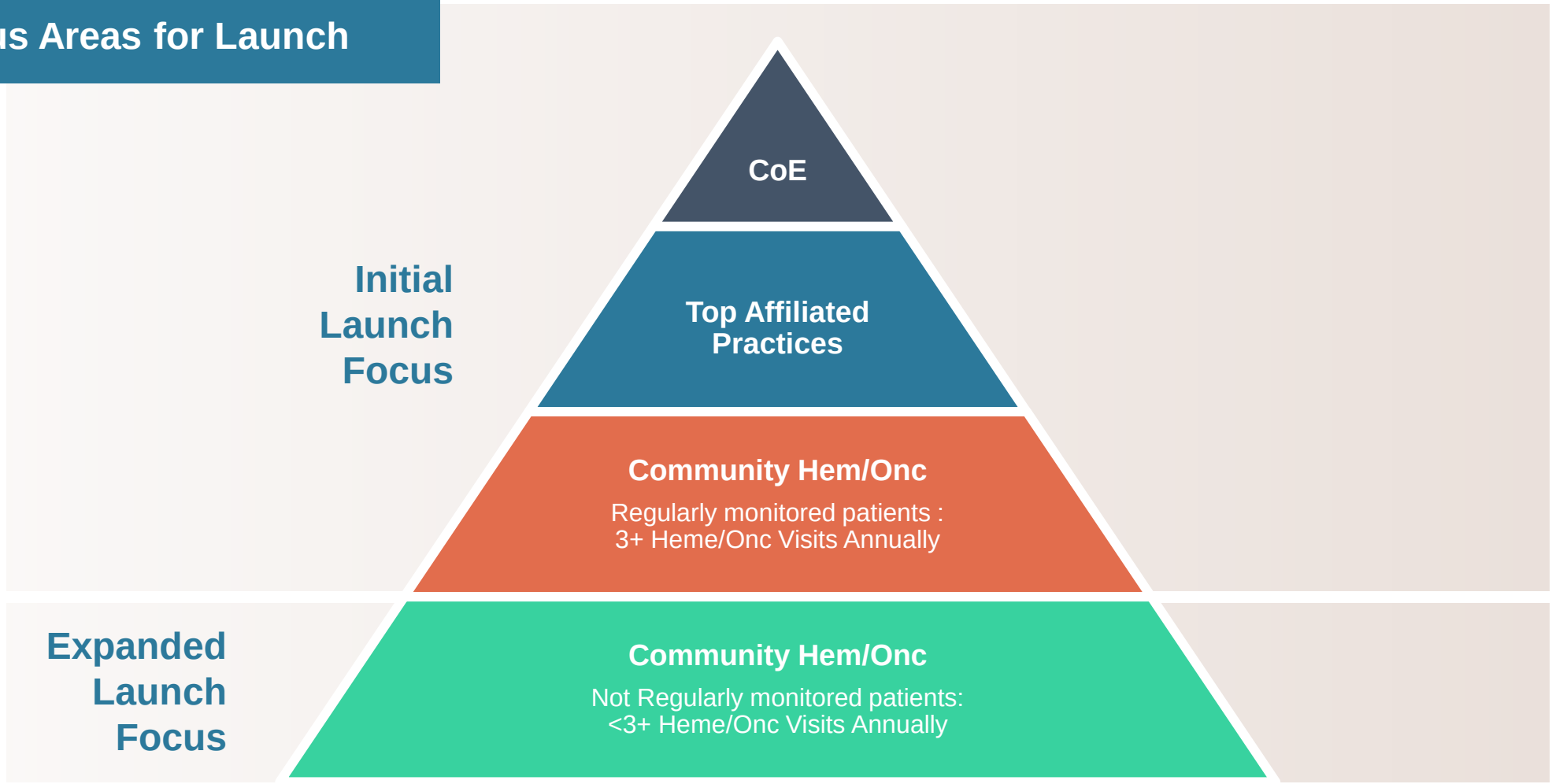
Patient Journey Continuum

	Prevalence	Diagnosis	Treatment	Treatment Setting	Patient Engagement
PK DEFICIENCY	• Ultra-rare • ~3,000 patients	• ~30% diagnosed • Estimate based on ex-US physician databases • New ICD-10 code established October 2021	• PYRUKYND only FDA approved treatment	• Highly dispersed in community setting • Undefined centers of excellence	• New advocacy groups established in 2021 (THRIVE, PKD Foundation)
THALASSEMIA	• Rare • ~8,000 patients	• ~100% diagnosed • Targeted new-born screening • Well established ICD-10 codes	• No FDA Approved Options for alpha-THAL or Non-Transfusion Dependent beta-THAL • Limited options for Transfusion Dependent beta-THAL	• ~50% of active adult patients in <150 affiliated hematology & oncology academic or community practices	• Established advocacy groups (Thalassemia International Federation, Cooley's Anemia Foundation)

PKD Prevalence: Beutler, et.al., Christensen, et.al.; PKD Diagnosis Rate: Carey, et.al., deMedicis, et.al.; 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
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

Initial launch focus represents 65-70% of adult thalassemia patients

Focus Areas for Launch



Source: Compile Claims Analysis August 2023; Note: active patients defined as those with transfusion or thalassemia ICD-10 diagnosis code in 2022; heme/oncs include PCPs and NP/PAs affiliated with heme/oncs; COEs CDC Funded Thalassemia Treatment Centers, Thalassemia Western Consortium, BMS / Agios Clinical Trial Sites; top affiliated practices include community and academic heme/onc practices in top 5 deciles; 3+ heme/onc visits within 1 year

1 *Clinical*

2 *Commercial*

3 *Financial*

Third quarter 2023 financial results

Statement of Operations	Three Months Ended 9/30/23	Three Months Ended 9/30/22
PYRUKYND® Net Revenue	$7.4M	$3.5M
Cost of Sales	$0.6M	$0.5M
Research & Development Expense	$81.8M	$65.0M
Selling, General & Administrative Expense	$25.8M	$29.1M
Gain on Sale of Oncology Business (TIBSOVO® Royalties)	--	$4.4M

Balance Sheet	9/30/23	12/31/22
Cash, Cash Equivalents and Marketable Securities	$872.4M	$1.1B

agios

Closing Remarks

Building a leading hematology franchise

Clinical Development

- Excellent execution, on track to deliver six mid-to-late-stage data readouts by the end of 2025
- Consistent and compelling data across programs sets potential for long-term value creation

Commercial

- Maximize the current launch in PK deficiency
- Strengthening our commercial capabilities to support potential future launches in meaningfully larger patient populations

Financial

- Flexibility enables continued investment towards our vision to expand portfolio fueled by disciplined business development and advance an internal pipeline aligned with our core expertise in rare disease

Q&A