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Q3 2021 Financial Results

November 3, 2021

Agios Conference Call Participants

TOPIC	PARTICIPANT
Introductions	Holly Manning, Senior Director of Investor Relations
Business Update	Jackie Fouse, Ph.D., Chief Executive Officer
Clinical Development Update	Sarah Gheuens, M.D., Ph.D., Chief Medical Officer
Commercial Update	Darrin Miles, Chief Commercial Officer
Third Quarter 2021 Financial Results	Jonathan Biller, Chief Financial Officer, Head of Legal & Corporate Affairs
Q&A	Bruce Car, Ph.D., Chief Scientific Officer

Forward Looking Statements

This communication contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Agios' plans, strategies and expectations for the preclinical, clinical and commercial advancement of its drug development programs, including mitapivat and AG-946; the potential benefits of Agios' products and product candidates; Agios' key milestones and guidance for 2021; its financial guidance regarding the period in which it will have capital available to fund its operations; expectations regarding the return of capital to shareholders following the sale of Agios' oncology business; Agios' expectations for the FDA's review of its NDA for mitapivat; 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. Management's expectations and, therefore, any forward-looking statements in this communication 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 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; the impact of the COVID-19 pandemic on 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 future approved products, and launching, marketing and selling 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, including with respect to the regulatory submissions for mitapivat, 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 and 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 collaborations; 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, or SEC, including the risks and uncertainties set forth under the heading Risk Factors in our filings with the SEC. While the list of factors presented here is considered representative, this list should not be considered to be a complete statement of all potential risks and uncertainties. Any forward-looking statements contained in this communication are made only as of the date hereof, and we undertake no obligation to update forward-looking statements to reflect developments or information obtained after the date hereof and disclaim any obligation to do so other than as may be required by law.

Q3 2021 recent highlights & key updates

Recent Highlights

- Received Priority Review designation for mitapivat in PK deficiency by the FDA; Prescription Drug User Fee Act (PDUFA) action date set for February 17, 2022
- Initiated Phase 3 ENERGIZE and ENERGIZE-T trials of mitapivat in not regularly transfused and regularly transfused adults with α- or β-thalassemia
- Developed study name – RISE UP – for the Phase 2/3 study of mitapivat in sickle ell disease and unveiled it at the Sickle Cell Disease Association of America 49th Annual National Convention last month
- Repurchased approximately 5.3 million shares of Agios common stock at an average price of $47.94 per share in Q3

Key Upcoming Milestones

- Plan to host investor day on Wednesday, November 17 to share pipeline progress and commercial launch strategy/expectations for mitapivat in PK deficiency
- Submitted multiple abstracts for presentation at the ASH annual meeting, including clinical updates for mitapivat and AG-946

Clinical Development Updates

Sarah Gheuens, M.D., Ph.D., Chief Medical Officer

Mitapivat development rapidly expanding beyond adult PK deficiency; three additional pivotal trials underway by end of 2021

Mitapivat Pipeline Overview

Early Stage Clinical	Late Stage Clinical	Regulatory Submission	Near-Term Milestones	Anticipated Approval
Non-transfusion Dependent Adult PK Deficiency (ACTIVATE)			Completed NDA and MAA filing submissions; PDUFA date set for Feb. 2022	2022
Transfusion Dependent Adult PK Deficiency (ACTIVATE-T)				2022
Non-transfusion Dependent Adult Thalassemia (ENERGIZE)			Pivotal study initiated	2025
Transfusion Dependent Adult Thalassemia (ENERGIZE-T)			Pivotal study initiated	2025
Sickle Cell Disease (RISE UP)			Initiate Phase 2/3 study by YE 2021	2026
Pediatric PK Deficiency			Initiate pivotal studies in 2022	
Pediatric Thalassemia			Planning in process	
Pediatric Sickle Cell Disease			Planning in process	

~3-8K PATIENTS IN U.S. & EU5

Pyruvate Kinase Deficiency

~18-23K PATIENTS IN U.S. & EU5

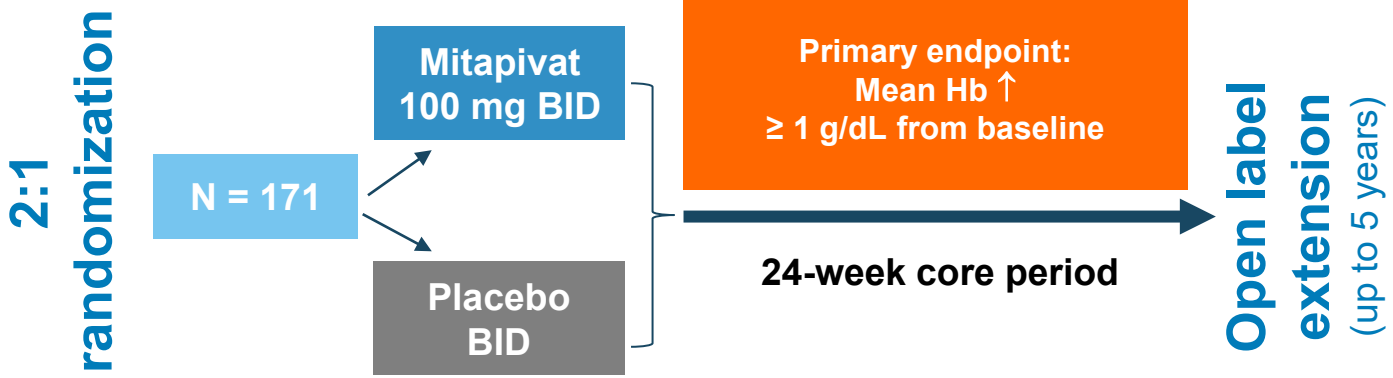
β- and α-Thalassemia

~120-135K PATIENTS IN U.S. & EU5

Sickle Cell Disease

Initiated two global, Phase 3, randomized controlled trials of mitapivat in adults with α- or β-thalassemia

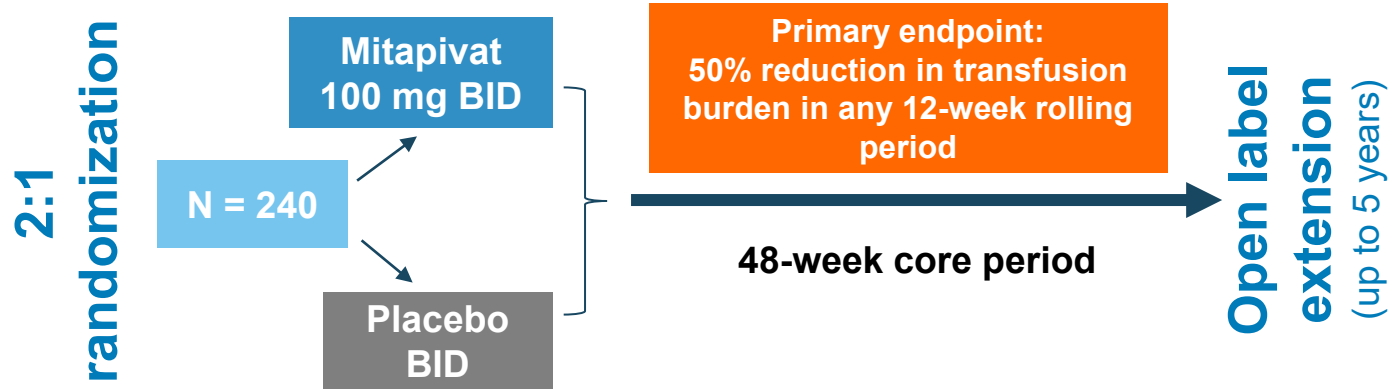
ENERGIZE



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



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

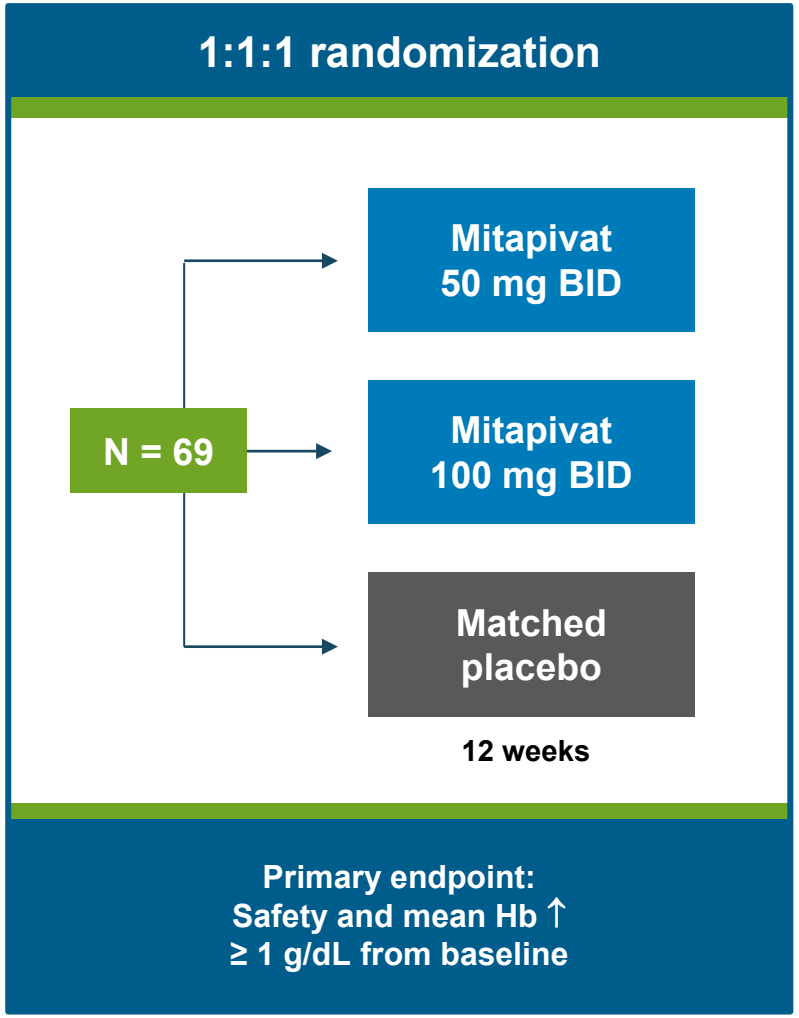
BID = twice daily; Hb = hemoglobin; HbE = hemoglobin E; HbH = hemoglobin H.

RISE UP Phase 2/3 trial in sickle cell disease to initiate by YE 2021

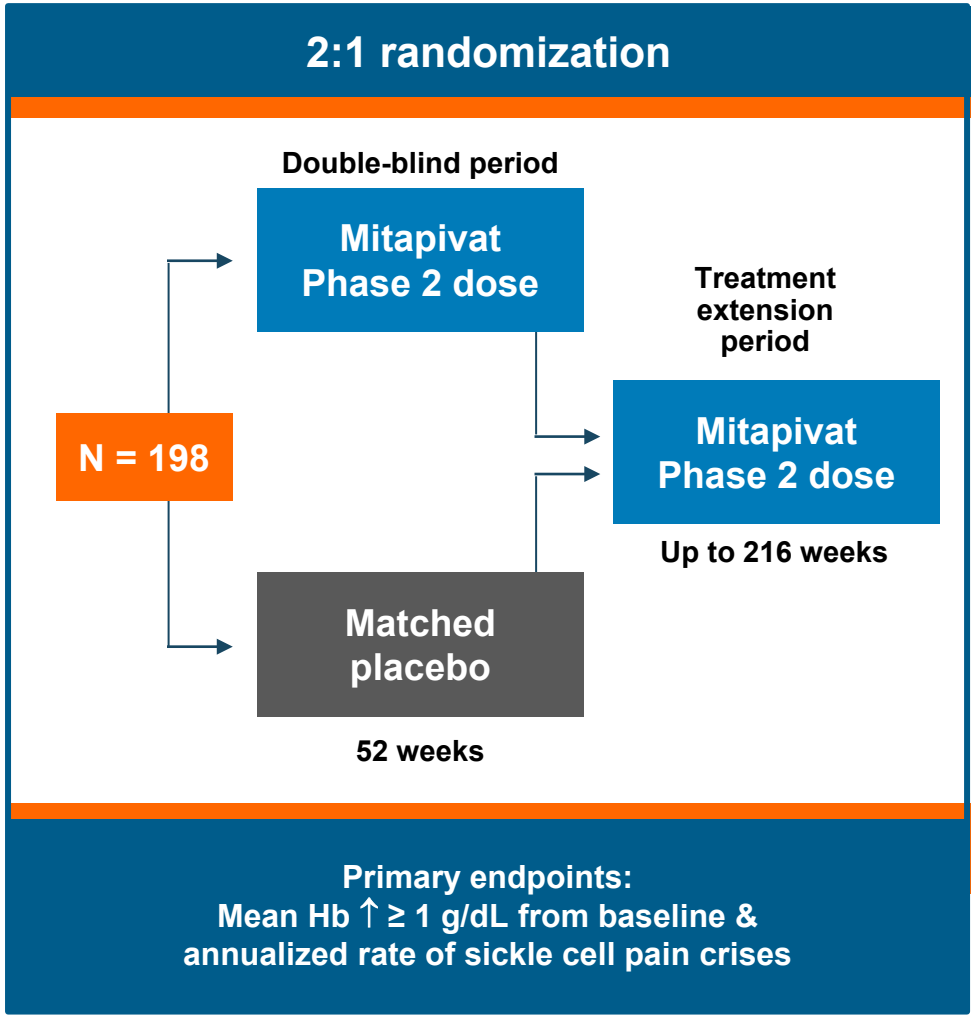
ENROLLMENT CRITERIA

- ≥ 16 years
- Had 2-10 sickle cell crises in the past 12 months
- Hb ≥ 5.5 and ≤ 10.5 g/dL
- Patients currently receiving treatment with voxelotor, crizanlizumab, or any other agent intended to increase Hb-oxygen affinity are excluded.
- Treatment with hydroxyurea is allowed.

PHASE 2

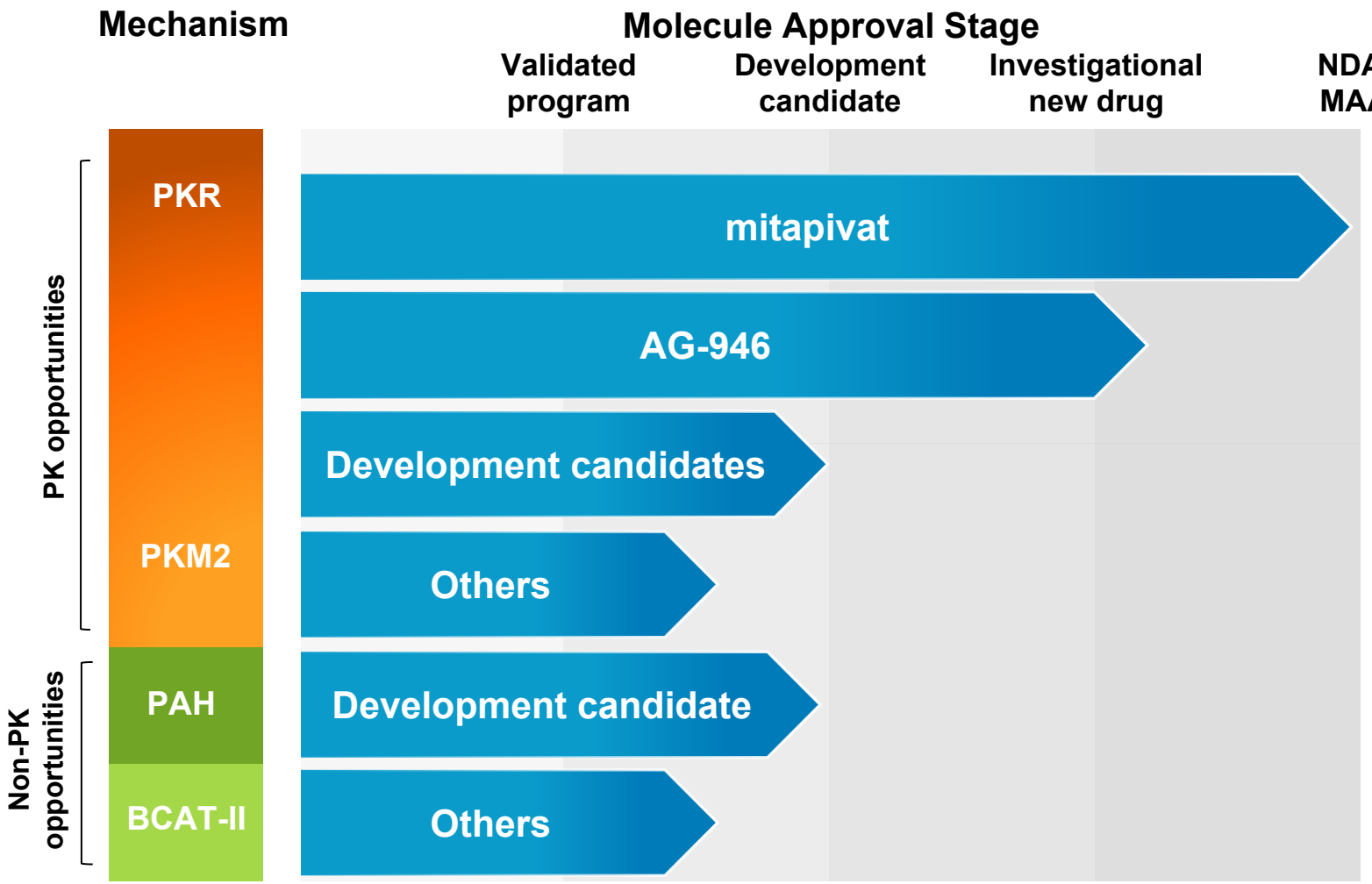


PHASE 3



BID = twice daily; Hb = hemoglobin

Significant opportunities exist beyond our initial pipeline focus; Investor day to review pipeline on November 17



Indications

***Pyruvate kinase activation*: 20+ potential indications**

- Pyruvate kinase deficiency
- Sickle cell disease
- α, β−Thalassemia

- Hereditary spherocytosis **(~64K U.S. patients)**
- Anemia of low-risk MDS **(~50K U.S. patients)**
- Multiple hereditary hemolytic anemias

- Anemia of chronic kidney disease
- Retinal indications
- Diabetic retinopathy/nephropathy
- Hereditary myopathies
- Neurologic (ALS)

***Aminoacidurias/acidemia*: 6+ potential indications**

- Phenylketonuria **(~16,500 U.S. patients)**

- Methylmalonic acidemia
- Propionic acidemia
- Multiple rare inborn errors of metabolism

Anticipated 2021 key milestones

PROGRAM MILESTONES

- ✓ Submitted NDA in the U.S. for mitapivat in adults with PK deficiency in Q2
- ✓ Submitted MAA in the EU for mitapivat in adults with PK deficiency in mid-2021
- ✓ Initiated two Phase 3 studies of mitapivat – ENERGIZE-T and ENERGIZE – in regularly transfused and not regularly transfused thalassemia
- ▪ Initiate Phase 2/3 study of mitapivat in sickle cell disease by YE 2021

DATA PRESENTATIONS

- ✓ Reported topline data from the ACTIVATE-T study of mitapivat in regularly transfused PK deficiency in Q1
- ✓ Presented full data from the mitapivat ACTIVATE and ACTIVATE-T studies at EHA
- ✓ Presented data from the mitapivat thalassemia Phase 2 study at EHA
- ▪ Data from ongoing clinical trials of mitapivat in sickle cell disease submitted for presentation at ASH
- ▪ Data from the AG-946 healthy volunteer study submitted for presentation at ASH

CORPORATE

- ✓ Closed the sale of the oncology portfolio to Servier following shareholder vote
- ✓ Complete a significant portion of share repurchases by YE
- ▪ Host investor day on Nov. 17 to highlight commercial launch planning for mitapivat in PK deficiency and research and development pipeline

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Commercial Update

Darrin Miles, Chief Commercial Officer

Mitapivat launch readiness activities & patient identification efforts

- **Continued the launch of the myAgios program for PK deficiency patients and caregivers**
- Ramped up disease education activities including live healthcare provider educational programming and patient-focused seminars

- **Completed hiring and training of customer-facing and patient support team** that will support the U.S. launch of mitapivat in PK deficiency
- **Accelerated physician and patient profiling and validation**

- **Ongoing Anemia ID program offers free genetic testing** for patients with a suspected hereditary anemia
- Observed largest Q/Q increase in requests since program established

Third Quarter 2021 Financial Results

Jonathan Biller, Chief Financial Officer, Head of Legal and Corporate Affairs

Third quarter 2021 financial results[1]

Statement of Operations	Three Months Ended 9/30/21	Three Months Ended 9/30/20
Research & Development Expense	$64.0M	$51.9M
Selling, General & Administrative Expense	$27.2M	$28.3M
Gain on Sale of Oncology Business (TIBSOVO® Royalties)	$2.0M	N/A

Balance Sheet	9/30/21	12/31/20
Cash, Cash Equivalents and Marketable Securities	$1.4B	$670.5M

[1] Includes continuing operations on a comparative basis, which excludes results from divested oncology business.

Q&A