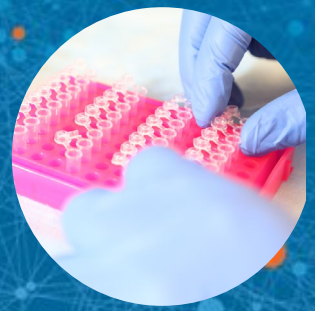
agios

Q2 2021 Financial Results

July 29, 2021



Agios Conference Call Participants

TOPIC	PARTICIPANT
Introductions	Jessi Rennekamp, Director of Corporate Communications
Business Update	Jackie Fouse, Ph.D., Chief Executive Officer
Clinical Development Update	Chris Bowden, M.D., Chief Medical Officer
Commercial Update	Darrin Miles, Chief Commercial Officer
Second 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; its chief medical officer transition plan 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 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 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.

Q2 2021 recent highlights & key updates

Recent Highlights

- Completed the submission of two regulatory filings for approval of mitapivat in adults with PK deficiency (NDA in U.S. and MAA in EU)
- Presented full analysis of data from Phase 3 ACTIVATE and ACTIVATE-T studies of mitapivat in adults with PK deficiency at EHA Virtual Congress
- Presented data from Phase 2, open-label, multicenter study of mitapivat in adults with non-transfusion dependent α- or β-thalassemia at EHA Virtual Congress
- Launched myAgios® patient support services for people living with PK deficiency
- Completed hiring and training of customer-facing and patient support team that will support the U.S. launch of mitapivat in PK deficiency upon product approval

Corporate Updates

- Outlined succession plan for Chris Bowden, M.D., who will transition from his role as chief medical officer to strategic advisor following his retirement on Sept. 1, at which time Sarah Gheuens, M.D., Ph.D., vice president of clinical development, will assume the role
- Repurchased approximately 10.5 million shares of Agios common stock, inclusive of shares acquired from BMS and its affiliates, at an average price of $50.41 per share

Clinical Development Updates

Chris Bowden, M.D., Chief Medical Officer

In mitapivat, we are building a robust pipeline with the ability to rapidly expand to three indications

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	2022	~3-8K PATIENTS IN U.S. & EU5
Transfusion Dependent Adult PK Deficiency (ACTIVATE-T)				2022	Pyruvate Kinase Deficiency
Non-transfusion Dependent Adult Thalassemia (ENERGIZE)			Initiate pivotal study in 2H 2021	2025	
Transfusion Dependent Adult Thalassemia (ENERGIZE-T)			Initiate pivotal study in 2H 2021	2025	~18-23K PATIENTS IN U.S. & EU5
Sickle Cell Disease			Initiate Phase 2/3 study by YE 2021	2026	β- and α-Thalassemia
Pediatric PK Deficiency			Initiate pivotal studies in 2022		
Pediatric Thalassemia			Planning in process		~120-135K PATIENTS IN U.S. & EU5
Pediatric Sickle Cell Disease			Planning in process		Sickle Cell Disease

Positive data from both pivotal programs in PK deficiency designed to support a broad label

ACTIVATE

- **Primary Efficacy Endpoint Achieved**: 40% of patients treated with mitapivat achieved a sustained hemoglobin increase of ≥1.5 g/dL compared to 0 placebo patients ($p<0.0001$)
- Treatment with mitapivat also demonstrated statistically significant improvements over placebo across pre-specified key secondary endpoints including: patient-reported outcomes (PRO) based on changes from baseline in pyruvate kinase deficiency diary (PKDD) score and pyruvate kinase deficiency impact assessment (PKDIA) score
- Safety profile was generally consistent with previously reported data

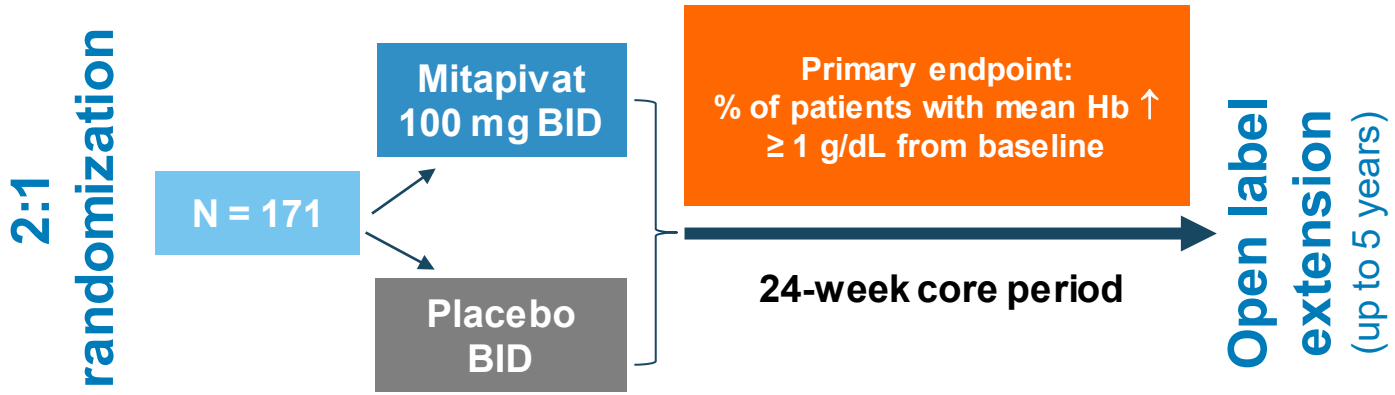
ACTIVATE-T

- **Primary Efficacy Endpoint Achieved**: 37% of patients treated with mitapivat achieved a ≥33% reduction in transfusion burden compared to individual historical transfusion burden standardized to 24 weeks (1-Sided $p=0.0002$)
- 22% of patients treated with mitapivat were transfusion-free during the 24-week fixed dose period
- Safety profile was generally consistent with previously reported data

Full data analysis from both trials, including PRO data, recently presented at EHA

Two global, Phase 3, randomized controlled trials of mitapivat in thalassemia are planned for 2021

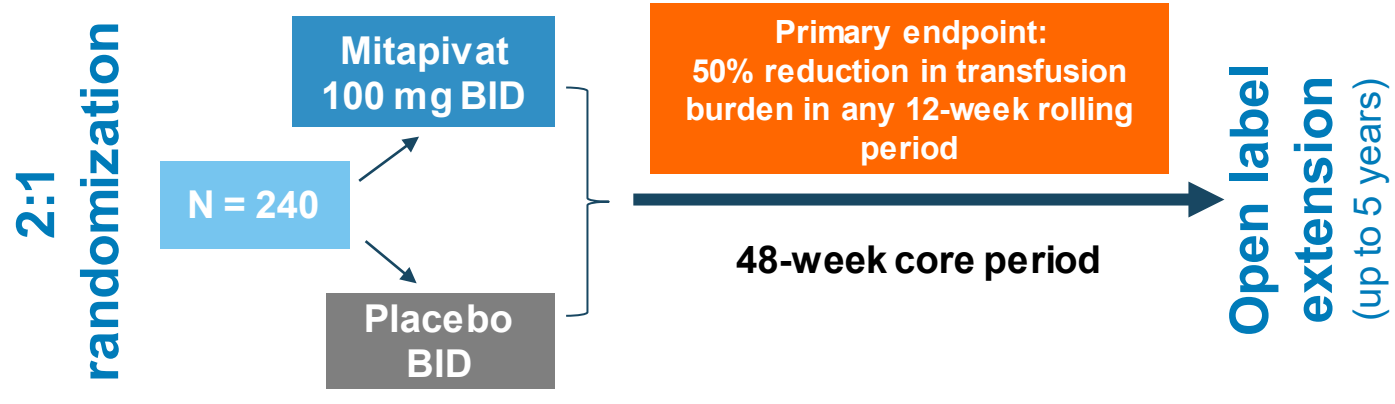
ENERGIZE



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

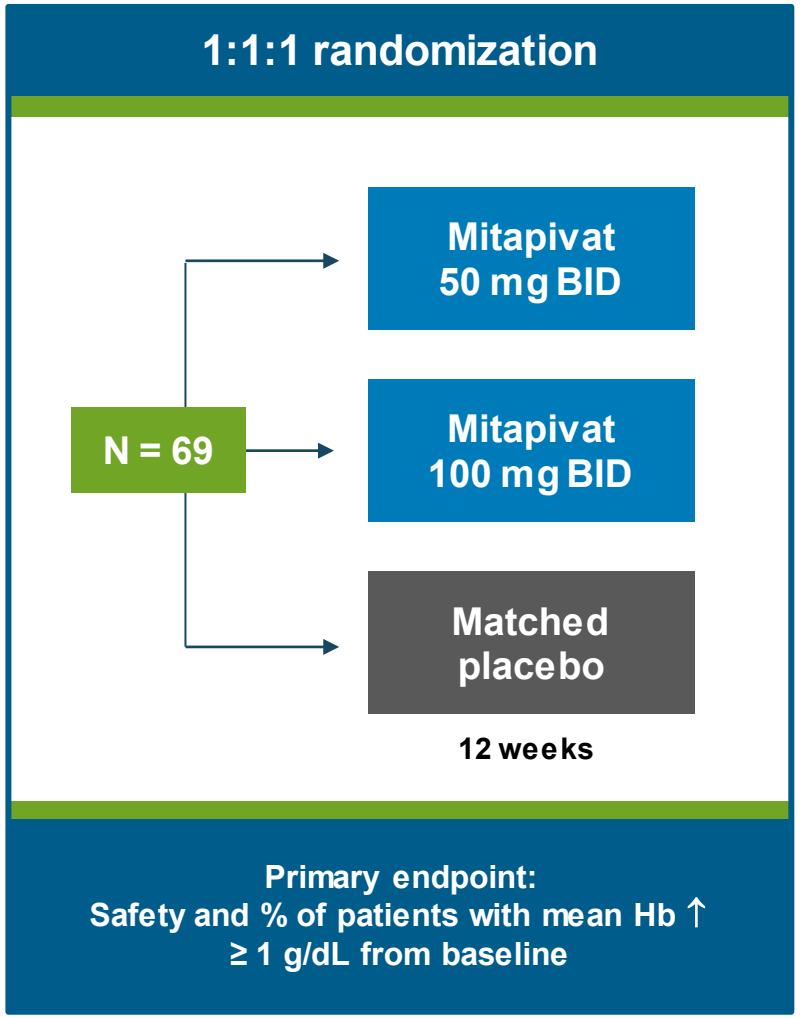
BID = twice daily; Hb = hemoglobin; HbE = hemoglobin E; HbH = hemoglobin H.

Pivotal program for mitapivat in sickle cell disease: Operationally seamless Phase 2/3 trial

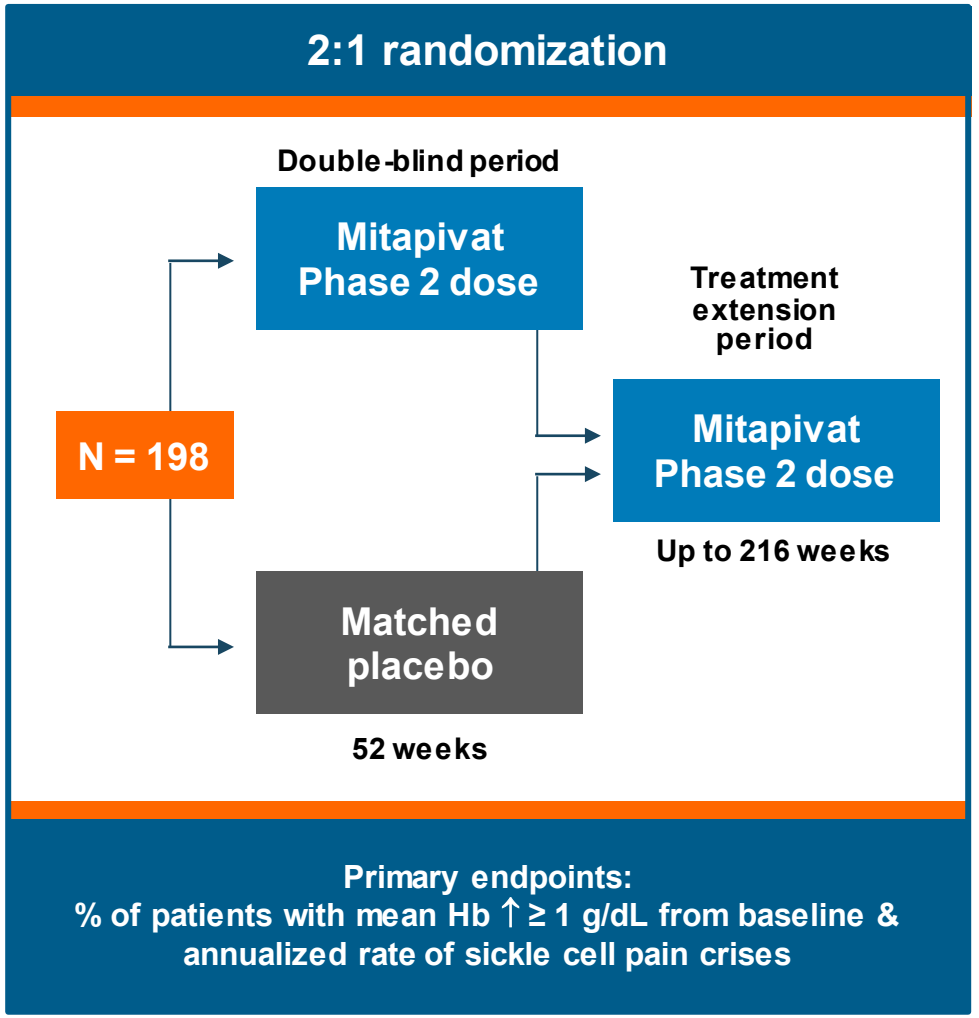
ENROLLMENT CRITERIA

- ≥ 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

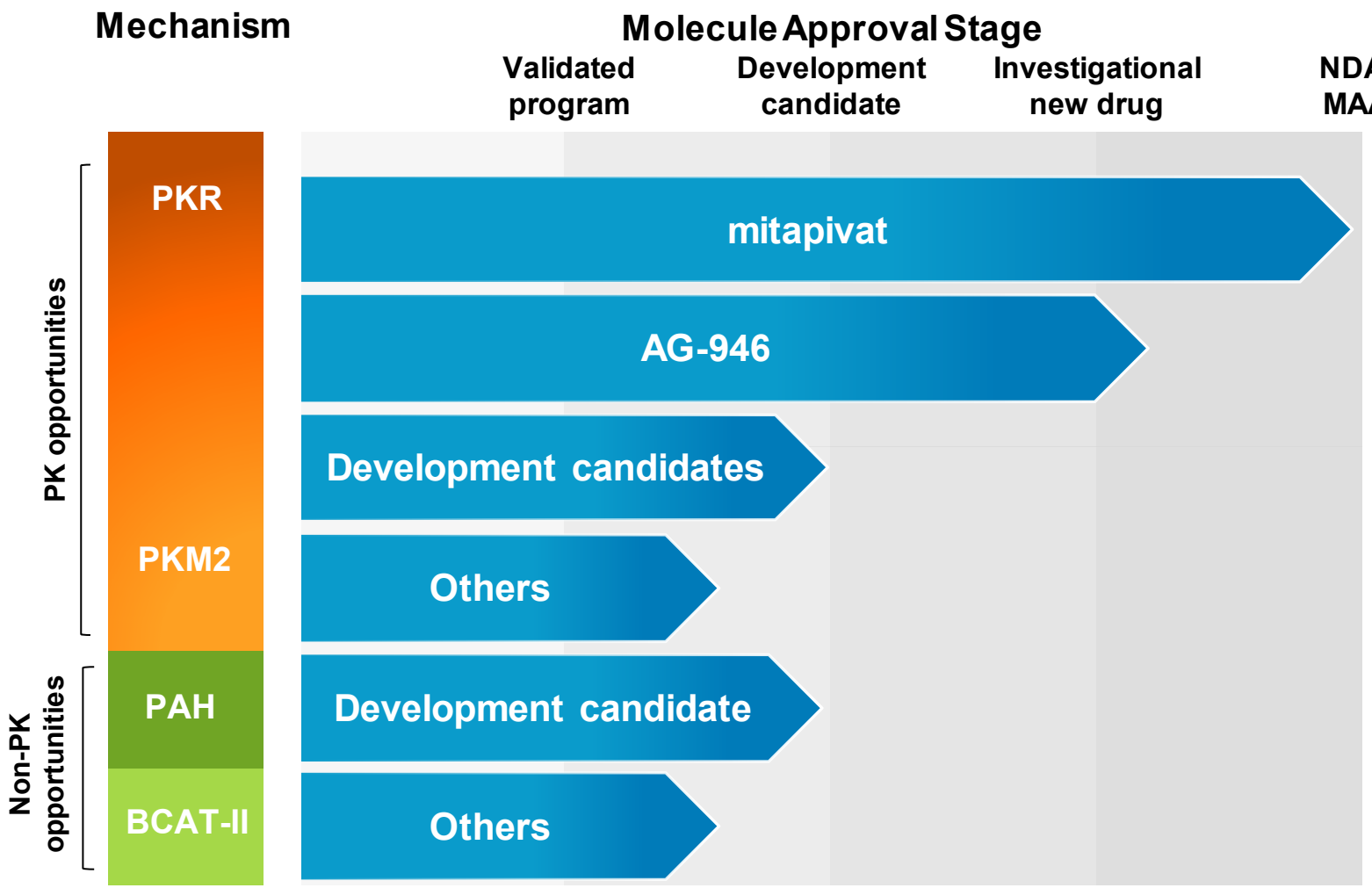


PHASE 3



BID = twice daily; Hb = hemoglobin

Significant opportunities exist beyond our initial pipeline focus



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

GDD 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
- Initiate two Phase 3 studies of mitapivat – ENERGIZE-T and ENERGIZE – in regularly transfused and not regularly transfused thalassemia by YE 2021
- Initiate Phase 2/3 study of mitapivat in sickle cell disease in 2H 2021
- Prioritize new PKR and PKM2 indications for clinical development in 2021

GDD 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
- Submit data from ongoing clinical trials of mitapivat in sickle cell disease for presentation at ASH 2021
- Submit data from the AG-946 healthy volunteer study for presentation at ASH 2021

CORPORATE

- ✓ Closed the sale of the oncology portfolio to Servier following shareholder vote
- Host investor day in fourth quarter of 2021 to highlight commercial launch planning for mitapivat in PK deficiency and research and development pipeline
- Ongoing share repurchases

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Commercial Update

Darrin Miles, Chief Commercial Officer

Mitapivat launch readiness activities & patient identification efforts

- **Launched myAgios program for PK deficiency patients and caregivers**, leveraging existing Agios infrastructure, to provide tailored 1:1 support and disease education resources

- **Completed hiring and training of customer-facing and patient support team** that will support the U.S. launch of mitapivat in PK deficiency upon product approval

- **Ongoing Anemia ID program offers free genetic testing** to help patients and physicians reach a definitive diagnosis for patients with a suspected hereditary anemia; well over 1,000 test kits requested

Second Quarter 2021 Financial Results

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

Second quarter 2021 financial results[1]

Statement of Operations	Three Months Ended 6/30/21	Three Months Ended 6/30/20
Research & Development Expense	$62.0M	$54.1M
Selling, General & Administrative Expense	$29.2M	$29.2M
Gain on Sale of Oncology Business (TIBSOVO® Royalties)	$2.0M	N/A

Balance Sheet	6/30/21	12/31/20
Cash, Cash Equivalents and Marketable Securities	$1.7B	$670.5M

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

Q&A