agios

Q1 2021 Financial Results

April 29, 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	Chris Bowden, M.D., Chief Medical Officer
Commercial Update	Darrin Miles, Chief Commercial Officer
First 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; 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; 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; 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 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, 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.

Q1 2021 key milestones & recent highlights

Program and Advocacy Updates

- Data from our Phase 3 ACTIVATE/ACTIVATE-T studies and Phase 2 thalassemia study of mitapivat have been accepted for presentation at EHA
- Announced a collaboration with 23andMe that led to the launch of its first PK deficiency carrier status report
- Announced our sponsorship of Citizen Scientist: Unpacking the Science of Sickle Cell Disease, an initiative developed by the Sickle Cell Community Consortium to promote health literacy for sickle cell patients
- Hosted a discussion about thalassemia with Dr. Sujit Sheth of the New York Comprehensive Thalassemia Center and his patient Sam in honor of Rare Disease Day

Corporate Updates

- Closed the sale of our oncology business to Servier on March 31, 2021
- Initiated the repurchase of up to $1.2 billion of outstanding shares, as authorized by the board of directors
- Entered into a definitive agreement with BMS to repurchase 7,121,658 shares of Agios common stock held by BMS and its affiliates for an aggregate purchase price of $344.5 million, or $48.38 per share

Clinical Development Updates

Chris Bowden, M.D., Chief Medical Officer

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

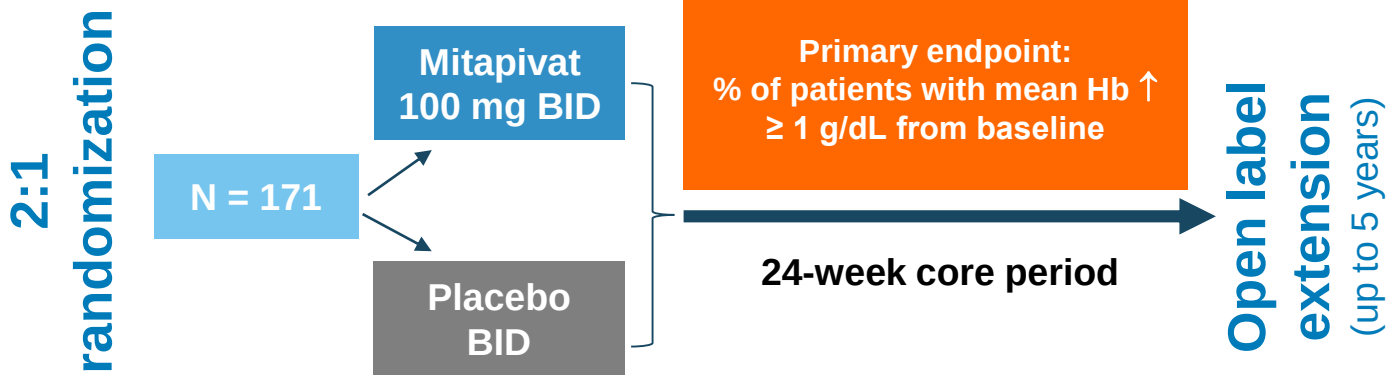
ACTIVATE-T

- **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

Data from both trials, including PRO data, have been accepted for presentation at EHA

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

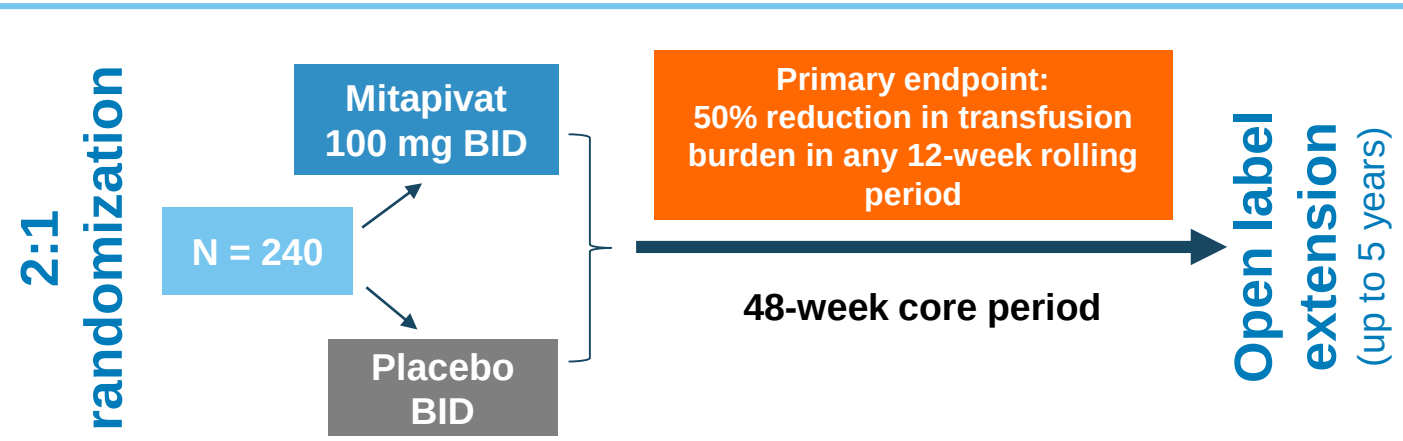
ENERGIZE



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

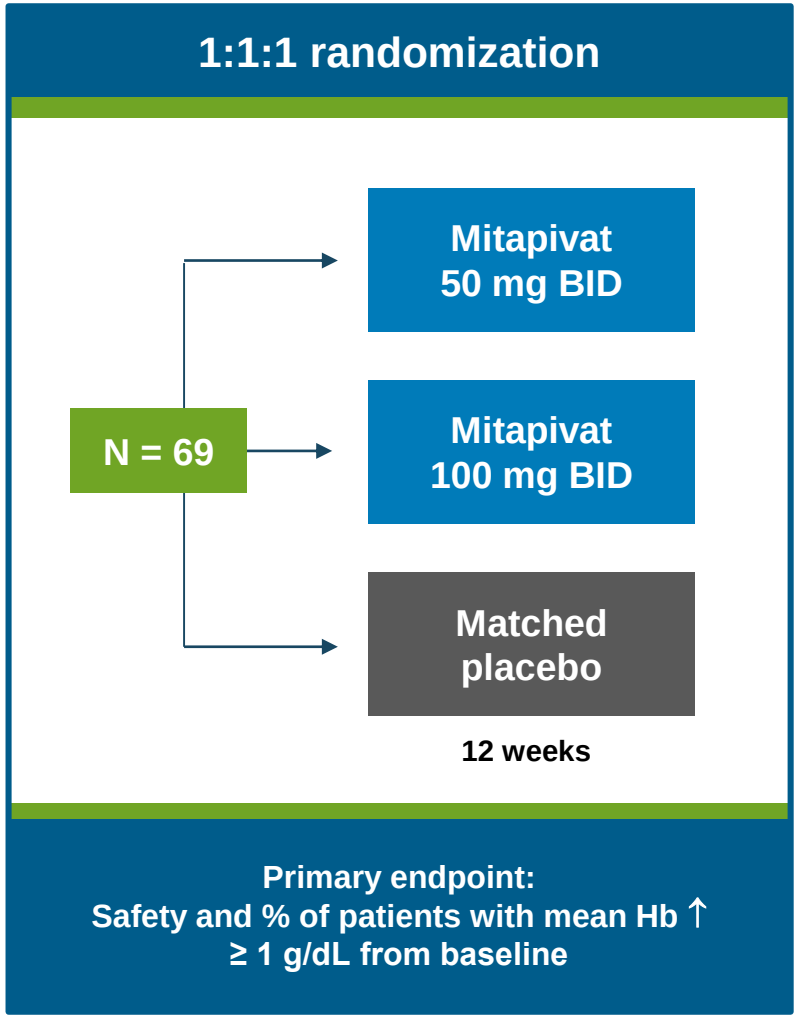
BID = twice daily; Hb = hemoglobin; HbE = hemoglobin E; HbH = hemoglobin H.

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

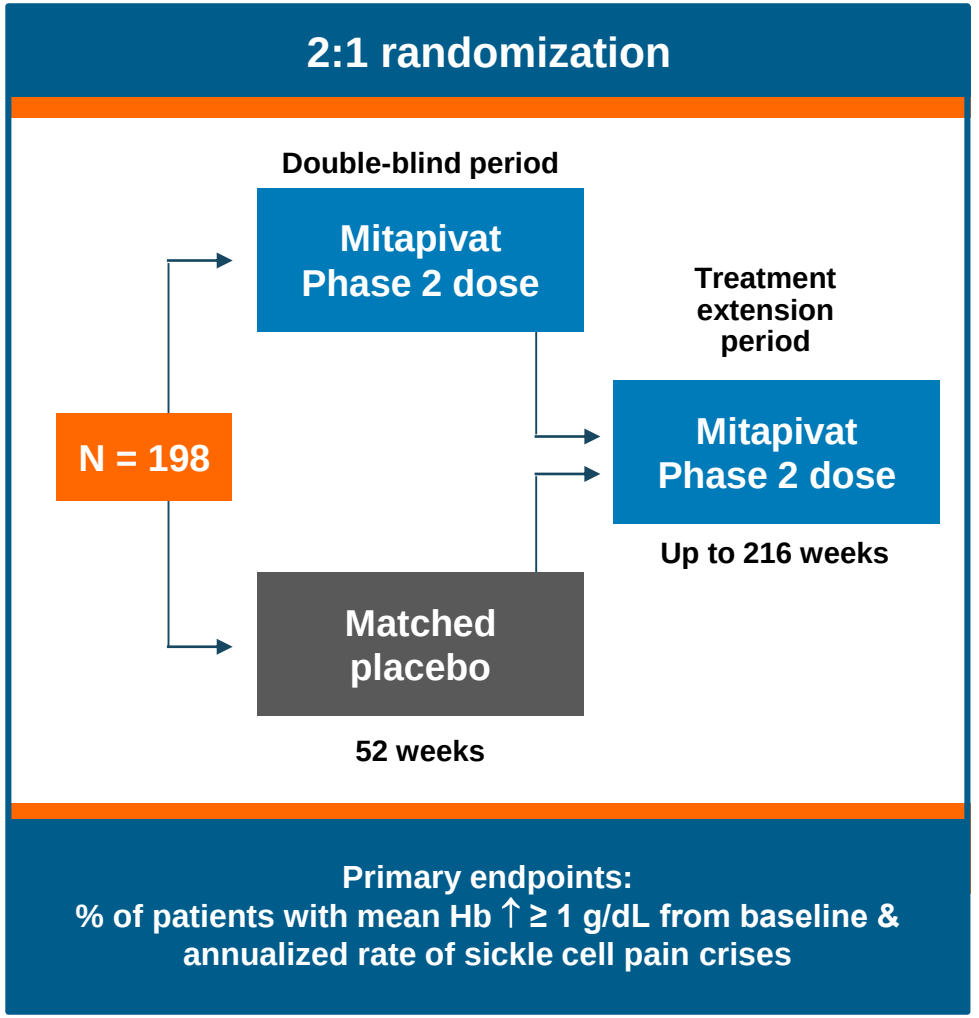
ENROLLMENT CRITERIA

- ≥ 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

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 (NTD) Adult PK Deficiency (ACTIVATE)		NDA filing in Q2; MAA filing in mid-2021	Data to be presented at EHA	2022
Transfusion Dependent Adult PK Deficiency (ACTIVATE-T)			Data to be presented at EHA	2022
Non-transfusion Dependent Adult Thalassemia (ENERGIZE)			Finalized pivotal plan in Dec. 2020; Initiate pivotal study in 2H 2021	2025
Transfusion Dependent Adult Thalassemia (ENERGIZE-T)			Finalized pivotal plan in Dec. 2020; Initiate pivotal study in 2H 2021	2025
Sickle Cell Disease			Finalized pivotal plan in Feb. 2021; Initiate pivotal study by YE 2021	2026
Pediatric PK Deficiency			Finalized pivotal plan in Nov. 2020	
Pediatric Thalassemia			Planning in process	
Pediatric Sickle Cell Disease			Planning in process	

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

Pyruvate Kinase Deficiency

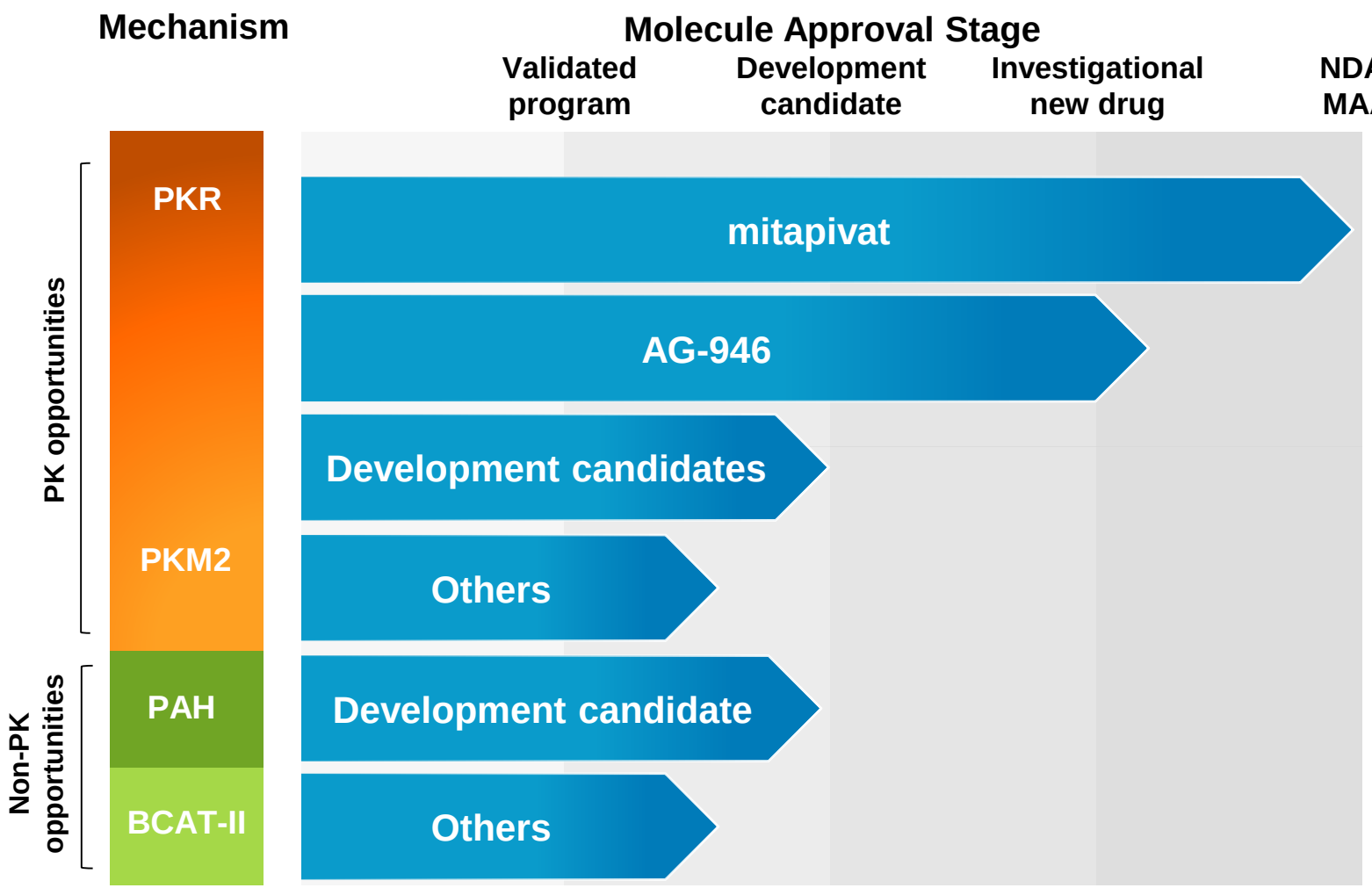
~18-23K PATIENTS IN U.S. & EU5

β- and α-Thalassemia

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

Sickle Cell Disease

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

- Submit NDA in the U.S. for mitapivat in adults with PK deficiency in Q2
- Submit 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 in 2H 2021
- Initiate Phase 2/3 study of mitapivat in sickle cell disease by YE 2021
- Prioritize new PKR and PKM2 indications for clinical development in 2021

GDD DATA PRESENTATIONS

- ✓ Report topline data from the ACTIVATE-T study of mitapivat in regularly transfused PK deficiency in Q1
- ✓ Submit data from the mitapivat ACTIVATE and ACTIVATE-T studies for presentation at EHA
- ✓ Submit data from the mitapivat thalassemia Phase 2 study for presentation at EHA
- Submit data from ongoing clinical trials of mitapivat in sickle cell disease for presentation at medical meetings throughout 2021
- Submit data from the AG-946 healthy volunteer study for presentation at a medical meeting by YE

CORPORATE

- ✓ Close the sale of the oncology portfolio to Servier following shareholder vote
- Complete share repurchases over 12-18 months post-close

agios

Commercial Update

Darrin Miles, Chief Commercial Officer

Recent mitapivat launch readiness activities & patient identification efforts

- Launched the Anemia ID program to **offer free genetic testing** to help patients and physicians reach a definitive diagnosis for patients with a suspected hereditary anemia

- Partnered with 23andMe to create a new **PK deficiency Carrier Status report** which includes a summary of signs and symptoms of PK deficiency and other relevant clinical and genetic information

- Intend to launch a robust **PK deficiency patient education program** by the end of the quarter, administered through existing Agios infrastructure, myAgios patient support

First Quarter 2021 Financial Results

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

First quarter 2021 financial results

Statement of Operations	Three Months Ended 3/31/21	Three Months Ended 3/31/20
Research & Development Expense	$57.7M	$55.4M
Selling, General & Administrative Expense	$33.6M	$31.7M
Discontinued Operations		
Total Revenue	$41.4M	$87.1M
TIBSOVO® Net Sales	$36.9M	$22.7M
Operating Expense	$50.2M	$43.3M

Balance Sheet	3/31/21	12/31/20
Cash, Cash Equivalents and Marketable Securities	$2.4B	$670.5M

Q&A