agios

Third Quarter 2020 Financial Results

November 5, 2020

Agios Conference Call Participants

TOPIC	PARTICIPANT
Introductions	Holly Manning, Director of Investor Relations
Business Update	Jackie Fouse, Ph.D., Chief Executive Officer
Clinical Development Update	Chris Bowden, M.D., Chief Medical Officer
TIBSOVO® Performance	Darrin Miles, Senior Vice President, U.S. Commercial & Global Marketing
Third Quarter 2020 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 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 Agios' plans, strategies and expectations for its and its collaborator's preclinical, clinical and commercial advancement of its drug development programs including TIBSOVO® (ivosidenib), IDHIFA® (enasidenib), mitapivat, vorasidenib, AG-270, and AG-946; the potential benefits of Agios' product candidates; its key milestones and guidance for 2020; its strategic vision and goals for 2025; its plans regarding future data presentations; its financial guidance regarding the period in which it will have capital available to fund its operations; and the potential benefits of its 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 or its collaborators 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; 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.

Q3 2020 Business Updates

Rare Genetic Diseases

- Initiated Phase 1 healthy volunteers study of AG-946, a next-generation PKR activator
- Continued to advance mitapivat clinical development programs in PK deficiency, thalassemia and sickle cell disease

Hematologic Malignancies

- TIBSOVO® net sales of $31.7 million, a 15% increase from Q2 2020
- Expanded total number of unique TIBSOVO® prescribers from Q2 2020
- Withdrew MAA for TIBSOVO® in previously treated IDH1 R/R AML

Solid Tumors

- Reported topline mature overall survival results from ClarIDHy study of TIBSOVO® in cholangio; submitted final data for presentation at the virtual ASCO GI

Corporate

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

Anticipated Upcoming Milestones

RARE GENETIC DISEASES

- Report topline data from ACTIVATE, the global pivotal trial for mitapivat in adults with PKD who do not receive regular transfusions, by YE 2020
- Report topline data from ACTIVATE-T, the global pivotal trial for mitapivat in adults with PKD who receive regular transfusions, in Q1 2021
- Finalize pivotal development plan for mitapivat in thalassemia by YE 2020
- Finalize pivotal development plan for mitapivat in sickle cell disease by 1H 2021

MALIGNANT HEME

- Achieve full-year U.S. revenue for TIBSOVO® $113-115M

SOLID TUMORS

- Submit a sNDA TIBSOVO® in Q1 2021

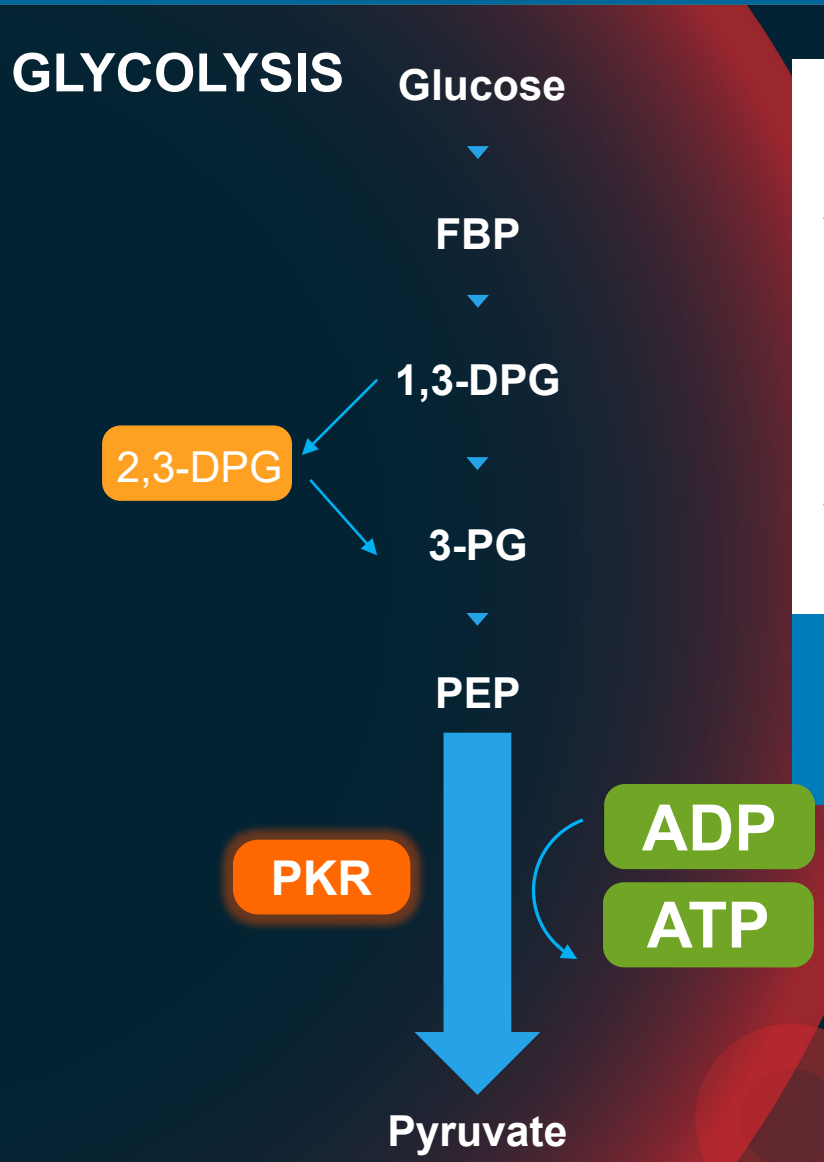
Research

- Achieve at least one new development candidate by YE 2020

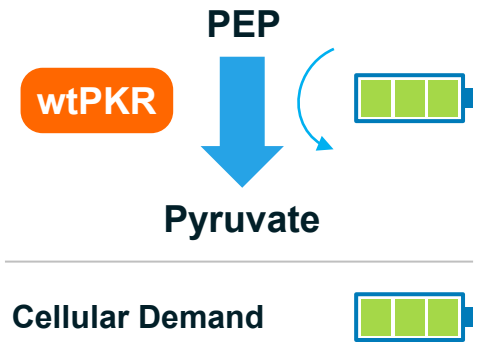
Clinical Development Updates

Chris Bowden, M.D., Chief Medical Officer

PKR Activation Represents Unique Mechanism of Action with Potential to Address Broad Range of Hemolytic Anemias

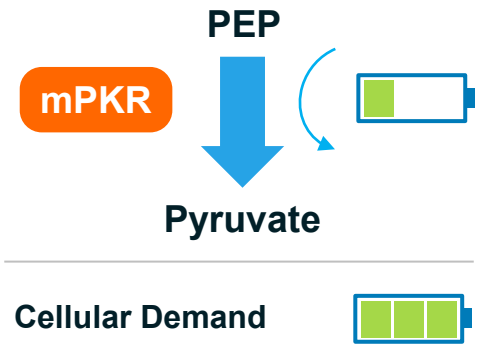


Normal Red Cell



ATP Production Meets Demand

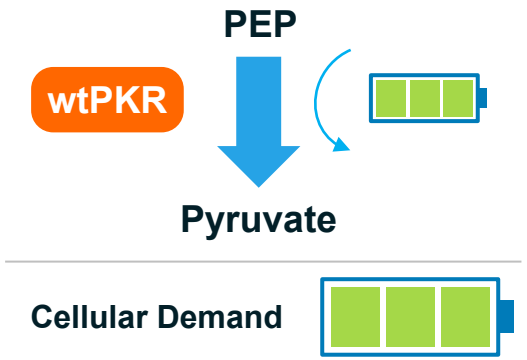
Mutant PKR Pyruvate Kinase Deficiency



Inadequate Production of ATP

- PKR mutations decrease PK stability, ATP generation and RBC membrane integrity and increase RBC destruction, leading to chronic hemolytic anemia

Wildtype PKR Other Hemolytic Anemias

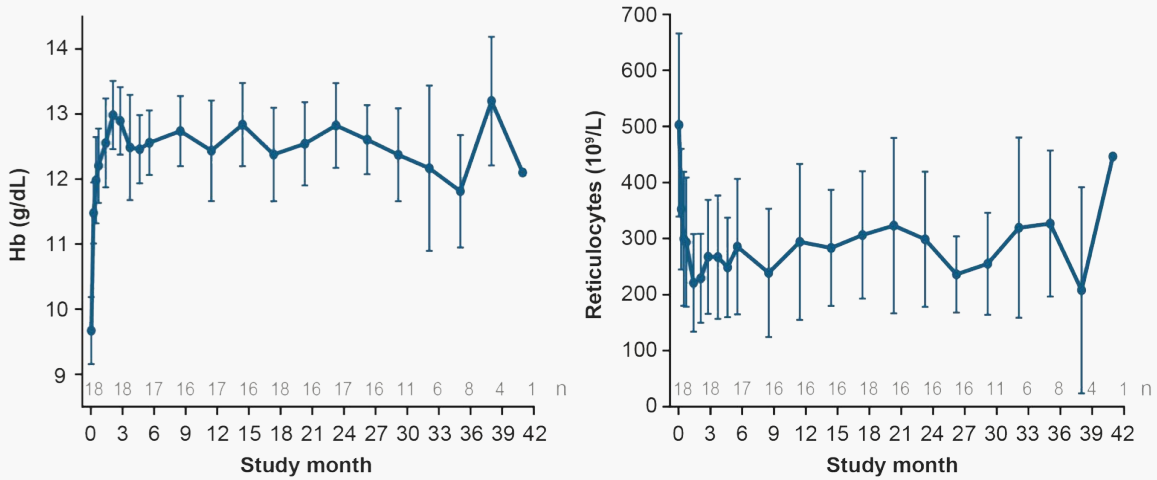


Increased Demand of ATP

- In other hemolytic anemias, there is an increase in ATP demand and impaired ATP production, leading to damage and premature death of RBCs, hemolysis and anemia

Mitapivat has Potential to be First Disease-modifying Therapy for Patients with PK Deficiency

Improvements in Hemoglobin and Other Hemolysis Markers Maintained for More Than 3 Years in Responding Patients from DRIVE PK Extension



Chronic daily dosing with mitapivat for a median of 3 years and up to 42 months was well tolerated

COMPLICATIONS & COMORBIDITIES REGARDLESS OF TRANSFUSION STATUS

HIGHER LIFETIME RATES OF PULMONARY HYPERTENSION, OSTEOPOROSIS, AND LIVER CIRRHOSIS

SUPPORTIVE CARE ONLY

0

APPROVED THERAPIES

HIGH RISK OF IRON OVERLOAD

38%

OF PATIENTS NOT RECEIVING REGULAR TRANSFUSIONS EXPERIENCE IRON OVERLOAD

Source: Data presented at ASH 2019; van Beers EJ, et al. Haematologica. 2019;104(2):e51-e53.

Topline data from ACTIVATE expected by YE 2020; ACTIVATE-T expected Q1 2021

Interim Phase 2 Results in Thalassemia: Activation of wPKR by Mitapivat Improved Hb and Associated Markers of Hemolysis and Erythropoiesis

- Treatment with mitapivat induced Hb increase of ≥1.0 g/dL in 12 of 13 evaluable patients, including 4 of 4 α-thalassemia patients; 7 of 8 evaluable patients achieved sustained Hb response
- Median (range) time to Hb increase of ≥ 1 g/dL among responders was 3.1 (1.4–7.1) weeks
- Mitapivat was generally well tolerated; the safety profile was consistent with previous studies
- Improvements in markers of hemolysis and erythropoiesis correlated with the Hb increases
- Mean ATP percent increase from baseline was similar to that previously observed with mitapivat in healthy volunteers

Pivotal plan for mitapivat in α- and β-thalassemia expected to be finalized by YE 2020 and initiated in 2021

Clinical Proof-of-concept for Mitapivat Established in Sickle Cell Disease

7 of 8 (88%) efficacy evaluable patients experienced a Hb increase, and 5 of 8 (63%) patients achieved a Hb increase of ≥1.0 g/dL from baseline (range 1.0-2.7 g/dL) at doses of 50 mg BID or lower.

Treatment with mitapivat was associated with decreases in hemolytic markers such as bilirubin, LDH and reticulocytes.

2,3-DPG decreases and increases in ATP levels were observed. Sickling curves (t50) and oxygen dissociation curves (p50) consistent with decreases in both sickling and HbS polymerization.

AEs generally consistent with previously reported data with mitapivat treatment or are to be expected in the context of SCD. One SAE, a VOC, occurred during drug taper and was possibly attributed to mitapivat.

Updated Phase 1 trial results will be presented at ASH; Pivotal plan for mitapivat in sickle cell disease to be finalized in 1H 2021 and initiated in 2021

PKR Activation Has Potential Broad Utility Across Hemolytic Anemias

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

Pyruvate Kinase Deficiency

NTD Adult PKD	Phase 3 enrollment complete; Topline data expected by YE 2020
TD Adult PKD	Phase 3 enrollment complete; Topline data expected in Q1 2021
Pediatric PKD	Pivotal plan expected by YE

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

β- and α-Thalassemia

NTD β- and α-Thalassemia	Phase 2 enrollment complete
Thalassemia	Pivotal plan expected by YE and initiation in 2021

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

Sickle Cell Disease

Adult SCD	NIH CRADA; data to be presented at ASH
Adult SCD	Pivotal study expected to initiate in 2021

Source: Agios estimates, market research

Significant Growth Potential in Malignant Hematology

~4K

PATIENTS IN U.S. & EU

IDH1 Mutant Acute Myeloid Leukemia (AML)

TIBSOVO®

R/R AML	U.S. Approval
1L Monotherapy	U.S. Approval
1L HMA Combo	Phase 3 enrolling
1L 7+3 Combo	Phase 3 enrolling

<1K

PATIENTS IN U.S.

IDH1 Mutant Myelodysplastic Syndrome (MDS)

TIBSOVO®

R/R MDS	Phase 1 Expansion

Source: Agios estimates, market research, SEER, MDS Foundation, Datamonitor

Four Distinct Solid Tumor Opportunities Across Three Clinical Molecules

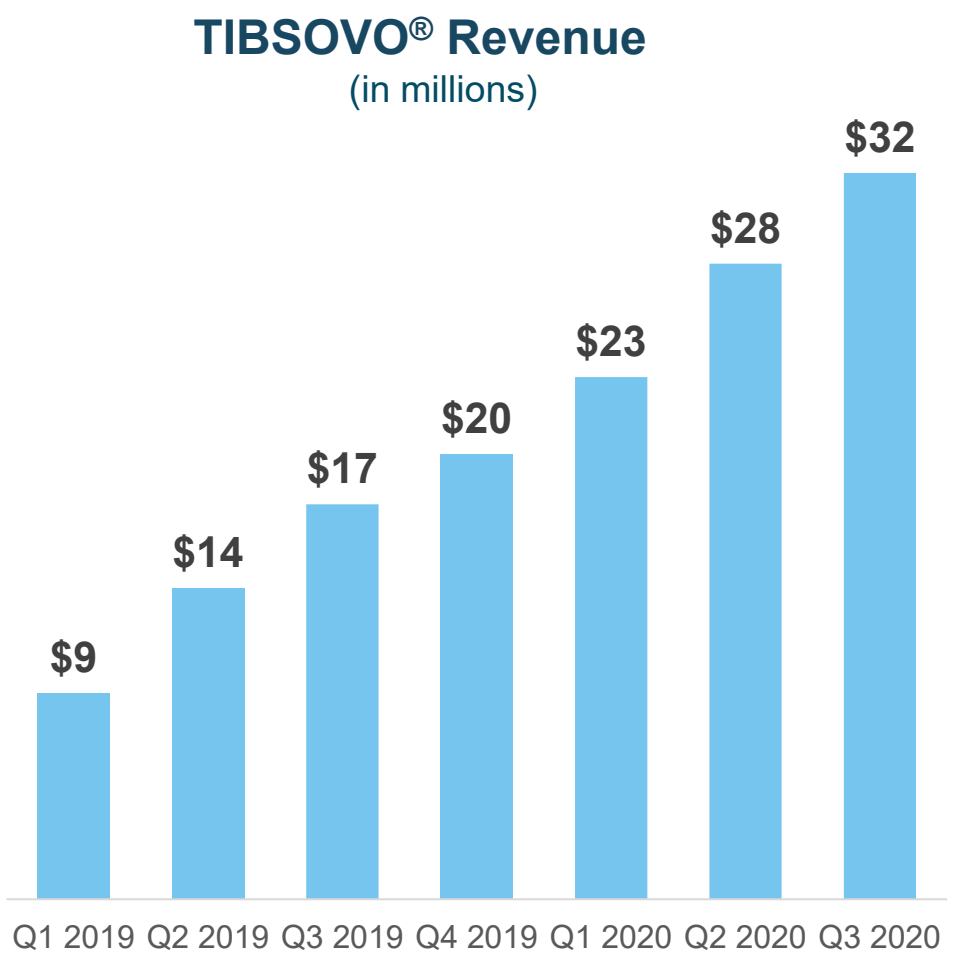
~2-3K PATIENTS IN U.S. & EU	~9K PATIENTS IN U.S. & EU	~9K PATIENTS IN U.S.	~10K PATIENTS IN U.S.
IDH1 Mutant Cholangiocarcinoma	**IDH Mutant Low Grade Glioma**	**MTAP-Deleted Non-Small Cell Lung Cancer**	**MTAP-Deleted Pancreatic Cancer**
TIBSOVO®	**Vorasidenib**	**AG-270**	**AG-270**
R/R Cholangio — sNDA expected Q1 2021	**Low-grade Glioma** — Phase 3	**2nd Line NSCLC** — Phase 1 Combo	**1st or 2nd Line Pancreatic Cancer** — Phase 1 Combo

Source: Agios estimates, market research

TIBSOVO® Performance Update

Darrin Miles, Senior Vice President, U.S. Commercial & Global Marketing

Q3 Growth Driven by Increased Demand in Both R/R and Frontline AML Segments and Expanding Customer Base



15% Growth
In Product Revenue Quarter-over-Quarter

$113 – 115M
Revised U.S. Net Sales Guidance for 2020

17% Increase
In Unique Prescribers Quarter-over-Quarter

~1,850
Patients Treated Since Launch

Source: Agios estimates

Third Quarter 2020 Financial Results

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

Third Quarter 2020 Financial Results

Statement of Operations	Three Months Ended 9/30/20	Three Months Ended 9/30/19
Total Revenue	$34.7M	$26.0M
Collaboration Revenue	2.3M	5.9M
TIBSOVO® Net Sales	31.7M	17.4M
Royalty Revenue	0.7M	2.7M
Cost of Sales	0.6M	0.4M
Research & Development Expense	89.6M	101.7M
Selling, General & Administrative Expense	34.8M	33.0M

Balance Sheet	9/30/20	12/31/19
Cash, Cash Equivalents and Marketable Securities	$722M	$718M

September 30, 2020 cash balance provides runway to the end of 2022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Q&A