agios

# Second Quarter 2020 Financial Results

July 30, 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 |
| Second Quarter 2020 Financial Results | Andrew Hirsch, Chief Financial Officer & Head of Corporate Development |

# 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.


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AGIOS 2025 VISION:
Focused Innovation. Ambitious Development.
Transformative Treatments for Patients Across Three Focus Areas.
4
MEDICINES
8+
INDICATIONS
6+
MOLECULES IN THE CLINIC
$
CASH FLOW POSITIVE

# Q2 2020 Highlights

## Rare Genetic Diseases

- Established clinical proof-of-concept for mitapivat in sickle cell disease
- Presented data from our Phase 2 study of mitapivat in thalassemia at EHA 2020
- Received FDA Orphan Drug Designation for mitapivat in thalassemia

## Hematologic Malignancies

- TIBSOVO® net sales of $27.6 million, an increase of 22% from Q1 2020
- Expanded total number of unique TIBSOVO® prescribers by 15% from Q1 2020

## Solid Tumors

- Published data from ClarIDHy study of TIBSOVO® in cholangio in The Lancet Oncology
- NCCN guidelines updated to recommend treatment with TIBSOVO® for advanced cholangio
- Presented data from our Phase 1 study of vorasidenib in glioma at ASCO 2020

## Corporate

- Completed a $255 million purchase agreement with Royalty Pharma for IDHIFA® (enasidenib) royalty


# Clinical Development Updates

*Chris Bowden, M.D., Chief Medical Officer*

# Anticipated Upcoming Milestones

**RARE GENETIC DISEASES**

- Mitapivat ACTIVATE and ACTIVATE-T topline data in PK deficiency between YE 2020 and mid-2021
- Finalize pivotal development plan for mitapivat in thalassemia by the end of 2020; initiate a pivotal program in 2021
- Finalize pivotal development plan for mitapivat in sickle cell disease and initiate pivotal program in 2021
- Initiate Phase 1 study of AG-946, next-generation PKR activator, in healthy volunteers in third quarter 2020

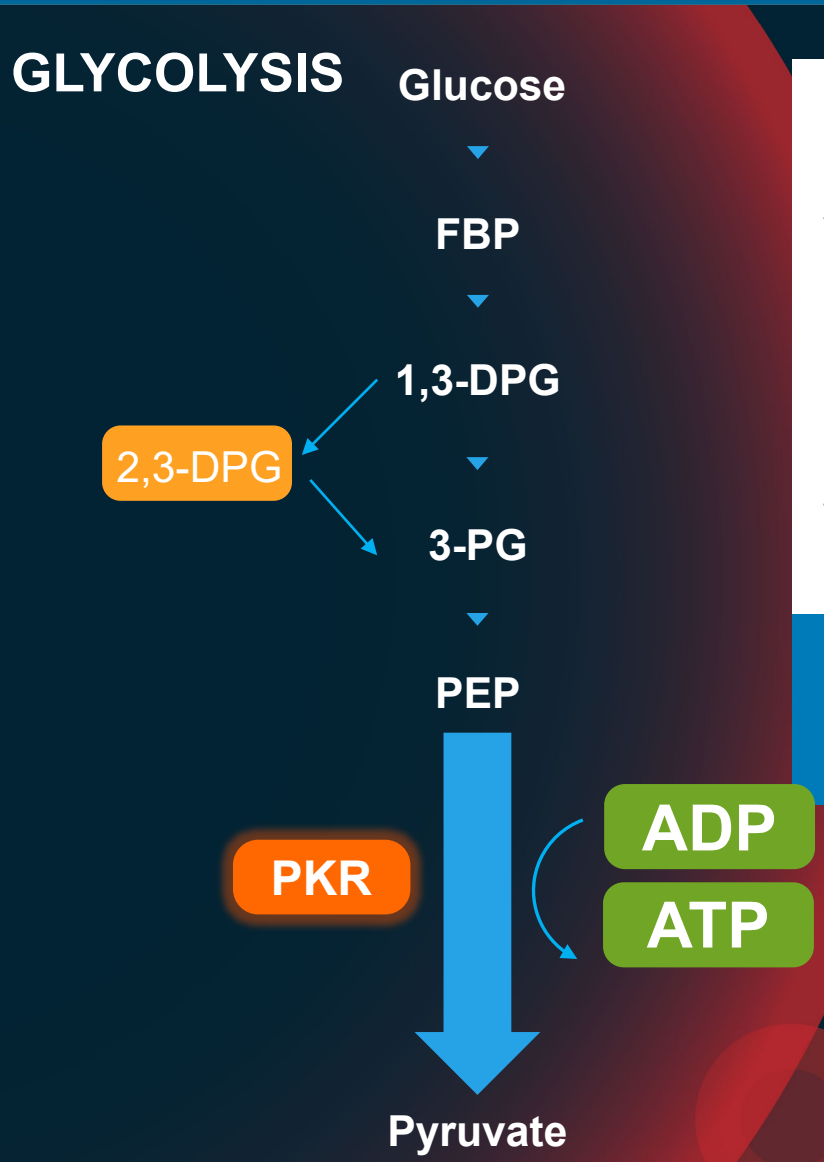
**MALIGNANT HEME**

- Achieve full-year U.S. revenue for TIBSOVO® $105-115M
- EU regulatory process for TIBSOVO® in R/R AML ongoing with a CHMP opinion expected by YE 2020

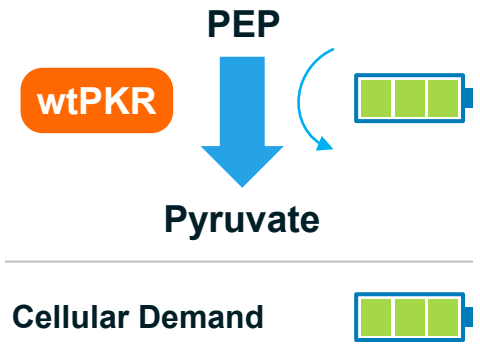
**SOLID TUMORS**

- Mature OS data from ClarIDHy study of TIBSOVO® in the third quarter 2020; cholangio sNDA filing in the first quarter 2021

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

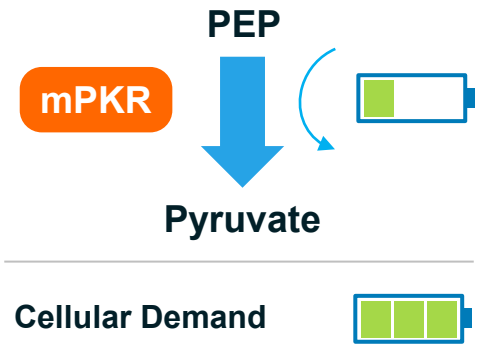



## Normal Red Cell




**ATP Production Meets Demand**

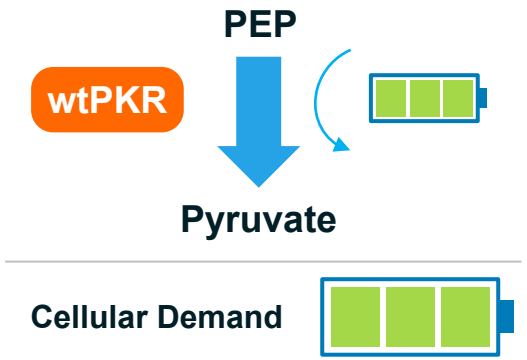
## Mutant PKR Pyruvate Kinase Deficiency




**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

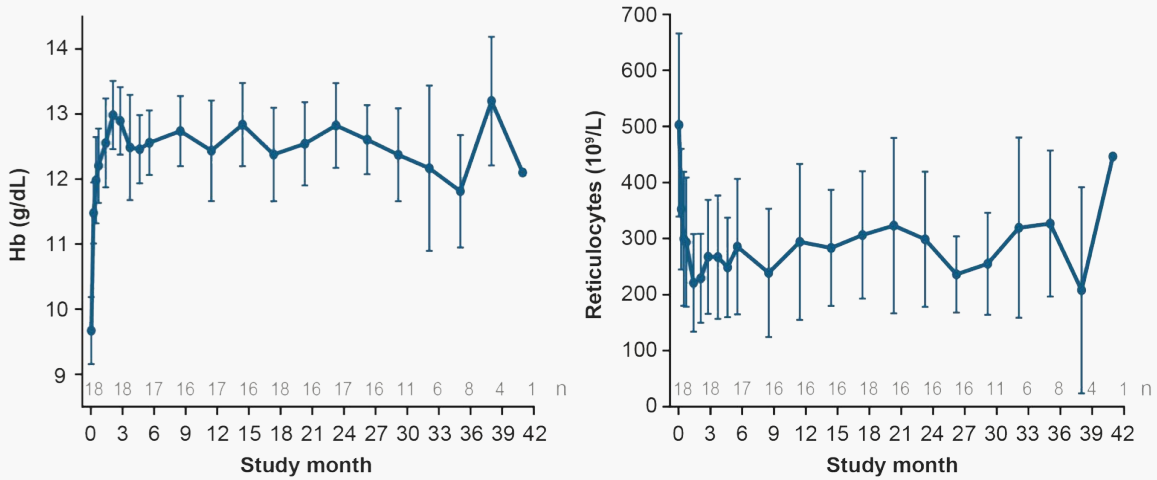



**Increased Demand of ATP**

- 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 and ACTIVATE-T expected between YE 2020 and mid-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 100% 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 year-end 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.



Pivotal plan for mitapivat in sickle cell disease to be 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 YE 2020 – mid 2021 |
| **TD Adult PKD** | Phase 3 enrollment complete; Topline data expected YE 2020 – mid 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 submitted to 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; MAA Under Review |
| **1L Monotherapy** | U.S. Approval |
| **1L HMA Combo** | Phase 3 |
| **1L 7+3 Combo** | Phase 3 |

**<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 |

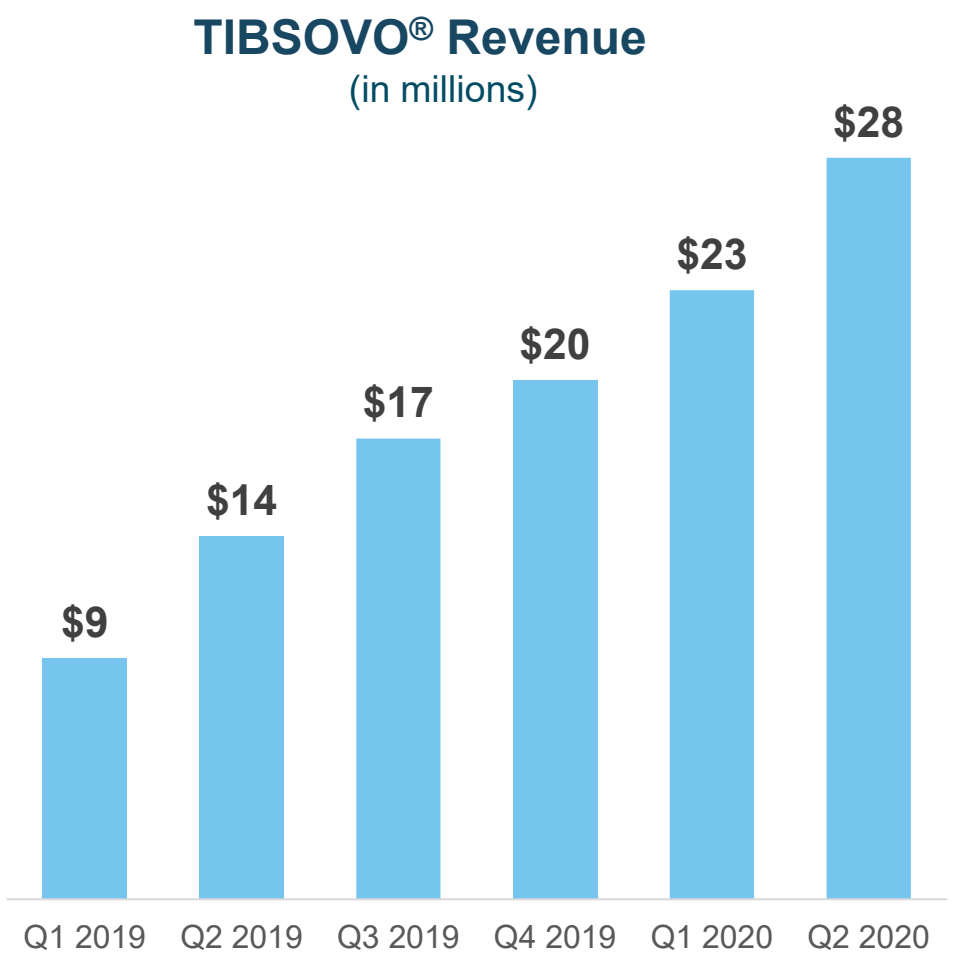


Source: Agios estimates, market research

# TIBSOVO® Performance Update

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

# Q2 Growth Driven by Increased Demand in Both R/R and Frontline AML Segments and Expanding Customer Base




**22% Growth**
In Product Revenue Quarter-over-Quarter

**$105 – 115M**
U.S. Net Sales Guidance for 2020

**15% Increase**
In Unique Prescribers Quarter-over-Quarter

**~1,600**
Patients Treated Since Launch

Source: Agios estimates


# Second Quarter 2020 Financial Results

*Andrew Hirsch, Chief Financial Officer and Head of Corporate Development*

# Second Quarter 2020 Financial Results

| Statement of Operations | Three Months Ended 6/30/20 | Three Months Ended 6/30/19 |
|---|---|---|
| Total Revenue | $37.3M | $26.2M |
| Collaboration Revenue<br>TIBSOVO® Net Sales<br>Royalty Revenue | 6.4M<br>27.6M<br>3.3M | 9.8M<br>13.7M<br>2.7M |
| Cost of Sales | 0.7M | 0.3M |
| Research & Development Expense | 90.9M | 107.4M |
| Selling, General & Administrative Expense | 36.0M | 32.4M |

| Balance Sheet | 6/30/20 | 12/31/19 |
|---|---|---|
| Cash, Cash Equivalents and Marketable Securities | $794M | $718M |



**June 30, 2020 cash balance provides runway through the end of 2022**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Q&A