# First Quarter 2016 Financial Results

May 5, 2016

# Agios Conference Call Participants

**Prepared Remarks**

Introduction

- RENEE LECK, Sr. Manager, Investor & Public Relations

2016 Corporate Priorities and New Announcements

- DAVID SCHENKEIN, M.D., Chief Executive Officer

Clinical Development Progress

- CHRIS BOWDEN, M.D., Chief Medical Officer

First Quarter 2016 Financial Results

- GLENN GODDARD, Senior Vice President, Finance

# Cautionary Note Regarding 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, including those regarding Agios' expectations and beliefs about: the potential of IDH1/IDH2 and pyruvate kinase-R mutations as therapeutic targets; the potential benefits of Agios' product candidates targeting IDH1/IDH2 or pyruvate kinase-R mutations or other genetic mutations, including AG-221, AG-120, AG-881, AG-348 and AG-519; its plans and timelines for the clinical development of AG-221, AG-120, AG-881, AG-348 and AG-519; its plans regarding future data presentations; its financial guidance regarding the amount of cash, cash equivalents and marketable securities that the company will have as of December 31, 2016, and the potential benefit of its strategic plans and focus. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "would," "could," "potential," "possible," "hope" 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 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 or the various remarks made during this presentation could also be affected by risks and uncertainties relating to a number of other important factors, including: 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 and 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, such as its agreements with Celgene; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in Agios' Annual Report on Form 10-K for the year ended December 31, 2015, and other filings that Agios may make with the Securities and Exchange Commission in the future. Any forward-looking statements contained in this presentation or in remarks made 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.



# 2016 Corporate Priorities and New Announcements

*David Schenkein, M.D., Chief Executive Officer*

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# Our 2016 Key Priorities: Maturing into a Late-stage Company

Rapid and broad late stage clinical development for IDHm inhibitors

Demonstrate clinical activity of PKR activators in patients

Advance research and initiate preclinical development of next wave research program

# First Quarter Highlights & New Announcements

## PKR Activators

- First data from AG-348 Phase 2 DRIVE PK and AG-519 Phase 1 healthy volunteer studies accepted for presentation at EHA in June

## IDHm Inhibitors

- Completed enrollment in Phase 2 expansion cohort for AG-221 in relapsed/refractory AML
- Initiated Phase 1/2 frontline combination study of AG-221 or AG-120 with VIDAZA® (azacitidine) in newly diagnosed AML patients not eligible for intensive chemotherapy
- Received EMA Orphan Drug Designation for AG-221 for the treatment of AML

## Research

- Preclinical findings on a new research program focused on MTAP deleted cancers published in *Cell Reports*

# Clinical Development Progress

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

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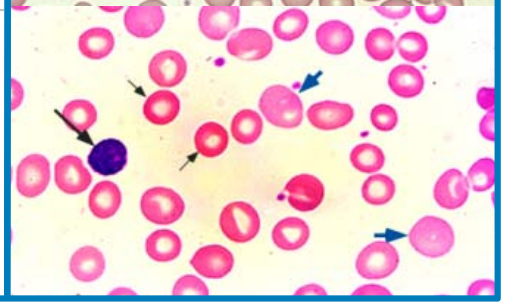
# PK Deficiency: What We Know Today

| Disease Overview | |
|---|---|
| **Description** | • Rare genetic disease often presenting at birth as neonatal jaundice<br>• ~2400 diagnosed in U.S. and EU5* |
| **Etiology** | • Caused by mutations in PK-LR gene coding for Erythrocyte Pyruvate Kinase |
| **Clinical Presentation** | • Lifelong hemolytic anemia and associated morbidities |
| **Diagnosis** | • PKR enzyme activity and genetic testing |

* Based on genetic data and diagnosis rate

**Disease Pathophysiology**

| Red Blood Cell | Blood Smear |
|---|---|
| **Normal** |  |
| **PK Deficiency** |  |

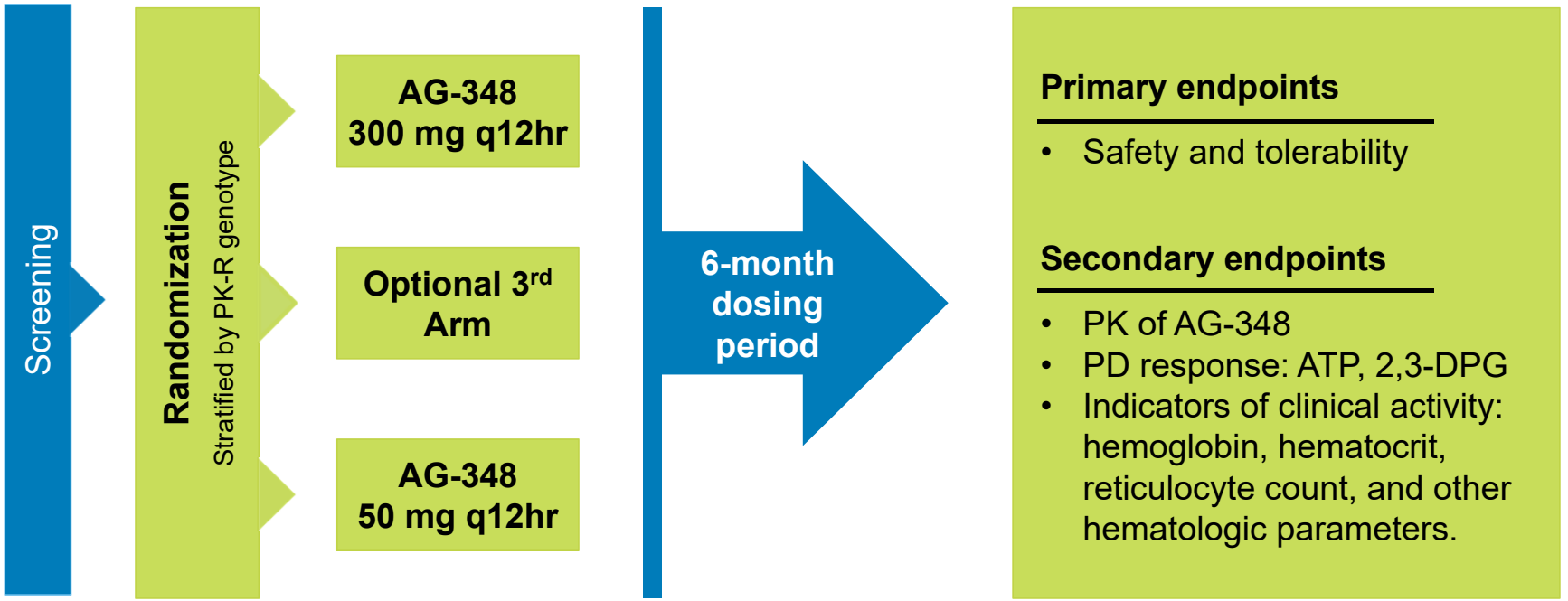


*Source: Zanella. Blood Rev. 2007; 21(4):217; Blood and Bone Marrow Pathology; Wintrobe's Clinical Hematology; Physician Interviews; Market Research.*

# AG-348 Global Phase 2 DRIVE PK Study Open and Enrolling

DRIVEPK

Transfusion-independent PK-deficient adults n=25 in each arm




**Primary endpoints**

- Safety and tolerability

**Secondary endpoints**

- PK of AG-348
- PD response: ATP, 2,3-DPG
- Indicators of clinical activity: hemoglobin, hematocrit, reticulocyte count, and other hematologic parameters.

**First AG-348 DRIVE PK Data Accepted for Presentation at EHA**

# AG-519 Healthy Volunteer Study Open and Enrolling

## AG-519

- Potent, highly selective and orally bioavailable PKR activator
- Differentiated chemical structure versus AG-348
- No preclinical activity against the aromatase enzyme
- AG-519 has similar preclinical activity in vitro, in vivo and ex vivo (patient samples) relative to AG-348

## One protocol, two steps, healthy volunteers

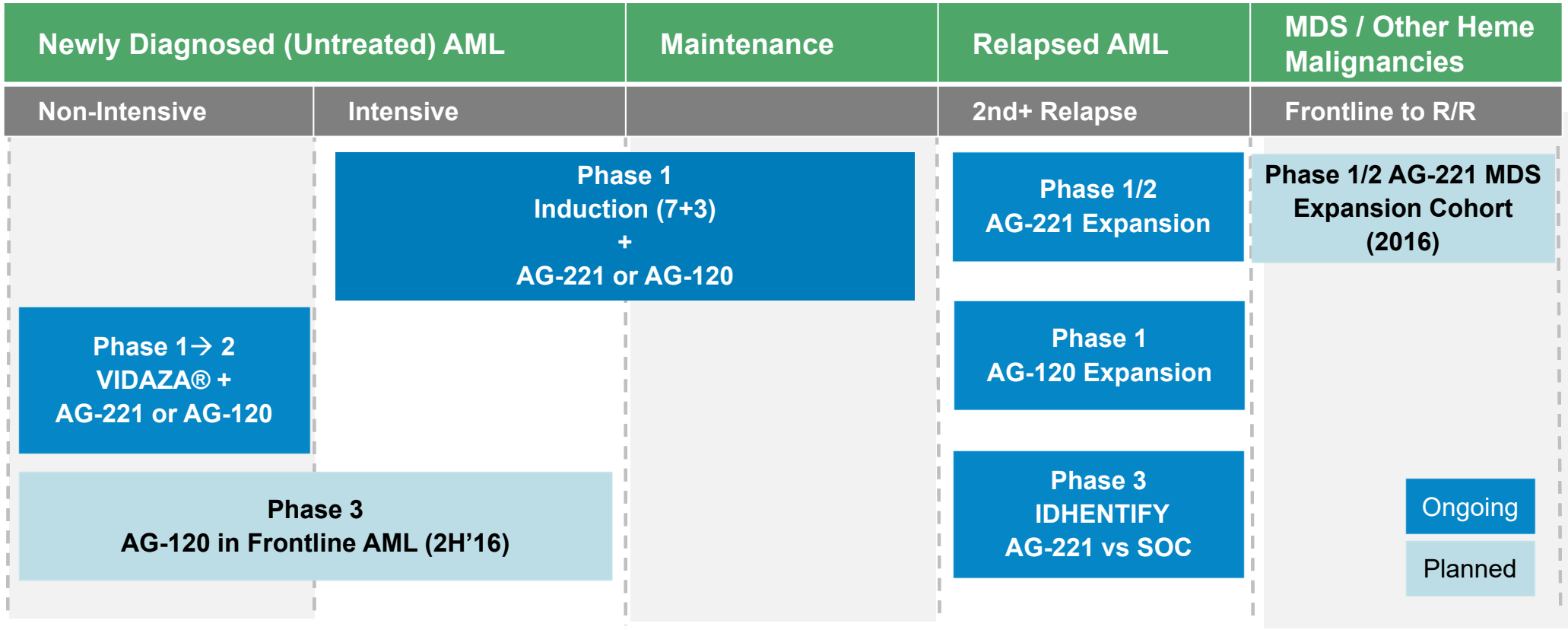
**Step 1: Integrated SAD/MAD**

- 4 dose-ascending cohorts: 8 subjects per cohort (n=32)
- Placebo controlled (6A, 2P)

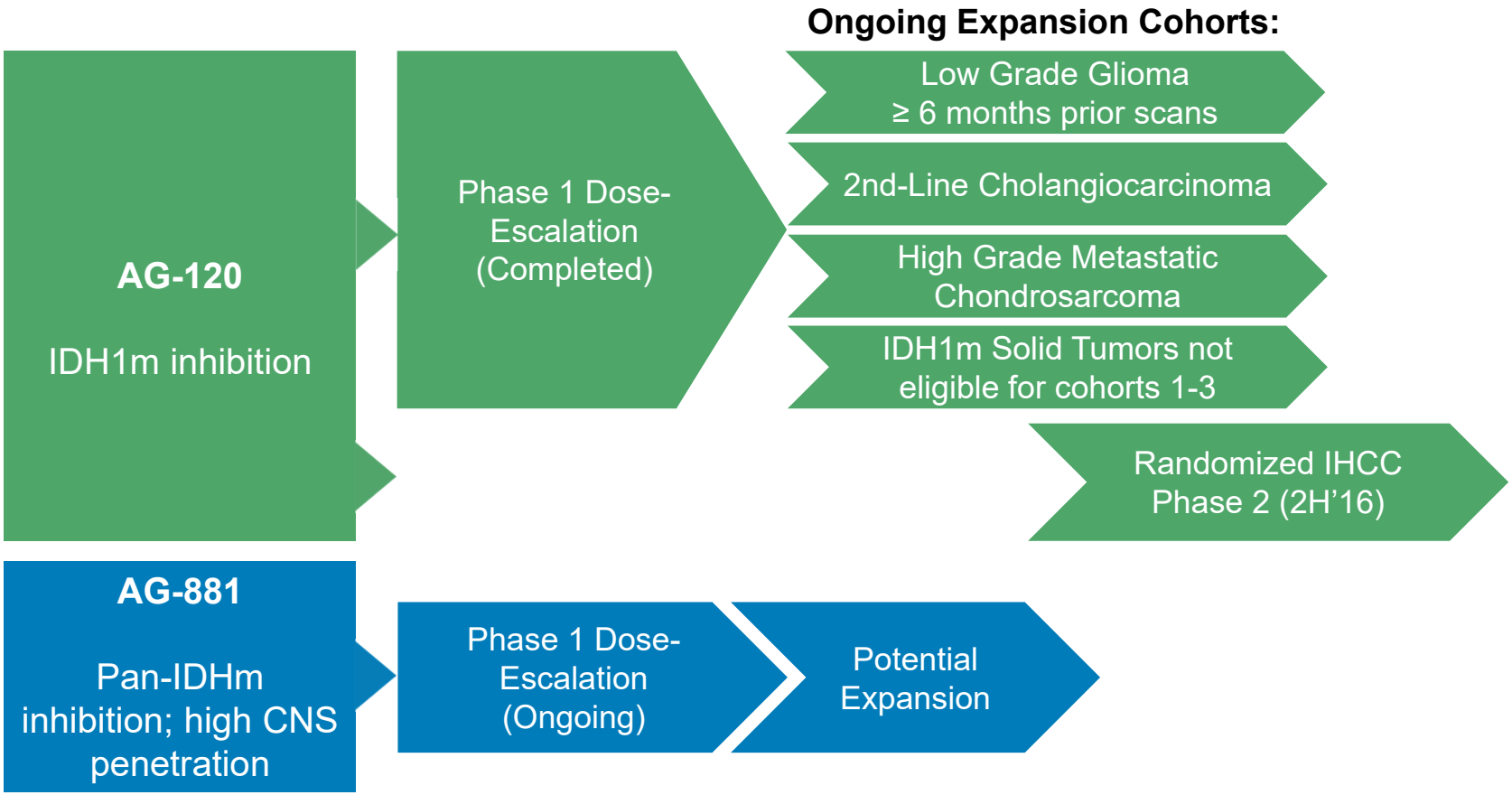
**Step 2: Bioavailability and Food Effect Study**

**First AG-519 Phase 1 Data Accepted for Presentation at EHA**

# Targeting Multiple Lines of Treatment in IDHm AML and Other Hematologic Malignancies



# Clinical Development Path in IDH1m Solid Tumors Will Be Data Driven



# First Quarter 2016 Financial Results

*Glenn Goddard, Senior Vice President, Finance*

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# First Quarter 2016 Financial Results

| Balance Sheet | March 31, 2016 | December 31, 2015 |
|---|---|---|
| Cash, cash equivalents and marketable securities | $356M | $376M |
| Total Assets | $396M | $420M |

| Statement of Operations | March 31, 2016 | March 31, 2015 |
|---|---|---|
| Collaboration Revenue | $31M | $34M |
| Research & Development Expense (1) | $44M | $32M |
| General & Administrative Expense | $11M | $7M |

*Note 1 (R&D expenses): R&D expense are presented net of amounts received from Celgene for reimbursement of certain development costs incurred on Celgene's behalf related to AG-221, AG-120 and AG-881. The R&D expense reported for the three months ended March 31, 2016 and 2015 are presented net of $8.8 million and $4.4 million, respectively, of reimbursements received.*

# 2016 Milestones

## IDHm Hematologic Malignancies

- ✓ Initiate Ph 1/2 combo study of AG-221 or AG-120 with VIDAZA®
- ✓ Complete enrollment in AG-221 Ph 2 expansion arm
- Initiate MDS expansion arm for AG-221 in 2016
- Complete enrollment in AG-120 125-patient expansion arm in 2H'16
- Initiate AG-120 Ph 3 study in frontline AML in 2H'16
- Continue to enroll patients in:
  - AG-221 Phase 3 IDHENTIFY study
  - Phase 1b frontline combo study of AG-221 or AG-120 with intensive chemo
  - AG-881 Phase 1 dose-escalation and expansion study

## IDHm Solid Tumors

- Present first data from AG-120 dose-expansion study in low grade glioma in 2H'16
- Initiate randomized Phase 2 study of AG-120 in cholangiocarcinoma in 2H'16
- Continue to enroll patients in:
  - AG-120 expansion phase of ongoing Phase 1 study
  - AG-881 Phase 1 dose-escalation and expansion study

## PKR Activators

- Present first data from AG-348 Phase 2 DRIVE PK study at EHA in June
- Present first data from AG-519 Phase 1 healthy volunteer study at EHA in June
- Outline clinical development plans for PKR activators in beta-thalassemia in 2H'16
- Present new findings from Natural History Study of PK deficiency in 2H'16

## Research

- ✓ Present preclinical findings on cancer metabolism program focused on MTAP deleted cancers at Keystone Symposia in 1Q'16
- Initiate preclinical development activities for the first molecule in the next wave of novel investigational medicines